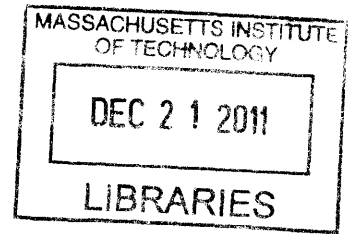


# Influenza: A Study of Contemporary Medical Politics

by

Peter N. Doshi

A.B., Brown University (2002)  
A.M., Harvard University (2006)



Submitted to the Program in Science, Technology, and Society  
in Partial Fulfillment of the Requirements for the Degree of  
Doctor of Philosophy in History, Anthropology, and Science, Technology and Society  
at the Massachusetts Institute of Technology

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Signature of Author: \_\_\_\_\_

History, Anthropology, and Science, Technology and Society  
August 9, 2011

Certified by: \_\_\_\_\_

Theodore A. Postol  
Professor of Science, Technology and National Security Policy  
Thesis Supervisor

Certified by: \_\_\_\_\_

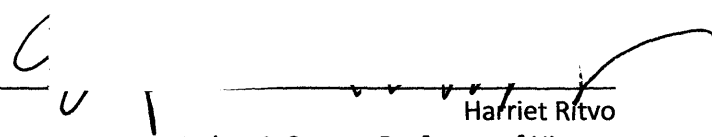
David Jones  
Professor of the Culture of Medicine  
Harvard University  
Thesis Committee Member

Certified by: \_\_\_\_\_

Sheldon Krinsky  
Professor of Urban & Environmental Policy & Planning  
Tufts University  
Thesis Committee Member



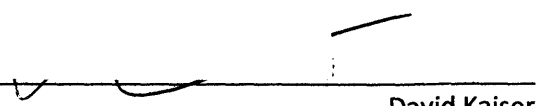
Accepted by: \_\_\_\_\_



Harriet Ritvo

Arthur J. Conner Professor of History  
Director of Graduate Studies, History, Anthropology, and STS

Accepted by: \_\_\_\_\_



David Kaiser

Professor of the History of Science, STS  
Senior Lecturer, Department of Physics  
Director, Program in Science, Technology, and Society



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## **Abstract**

Over the past decade, the prevention and control of seasonal and pandemic influenza has grown to be one of the largest and most visible public health policies. This dissertation considers contemporary influenza policy as a case study in what I call medical politics, in which a disease that for most people is rather unremarkable has become the focus of intense (and costly) public health campaigns based on a shaky scientific basis. The dissertation seeks to explain how this could happen.

The first two chapters show how influenza and its pandemics are marketed through an appeal to numerous scientific claims. Drawing on governmental marketing materials, statements by officials, and policy documents, I try to let officials speak for themselves and, as much as possible, refrain from analysis. Chapter 3 tells the story of the 2009 novel influenza H1N1 outbreak, showing how official understandings about influenza were called into question by an outbreak far milder than experts had predicted, and discusses investigations which highlighted the role of industry in shaping influenza policy. Chapter 4 analyzes official scientific claims regarding influenza, and argues that degree to which influenza is a serious public health problem is actually unclear. Furthermore, influenza vaccine effectiveness has been vastly overstated, predictive models of pandemic influenza are demonstrably flawed, and officials conflate true influenza with influenza-like illness (ILI), an often overlooked but critical distinction which allows officials to mislead the public into holding false assumptions about the potential benefits of influenza vaccine. Chapter 5 highlights the centrality of “virus-centric thinking” and the ethic of “saving lives” in public health practice as important factors that help explain how such a situation can exist and persist in light of the evidence. Chapter 6 addresses the policy implications of the dissertation’s findings.

## **Dissertation Committee**

Theodore Postol, Ph.D. (committee chair)  
Professor of Science, Technology and National Security Policy

Sheldon Krimsky, Ph.D.  
Professor of Urban & Environmental Policy & Planning  
Tufts University

David Jones, M.D., Ph.D.  
Professor of the Culture of Medicine  
Harvard University



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I am in great debt to my committee at MIT, not only for their critical reading and commenting on drafts of my dissertation, but also for their constant encouragement of me in pursuing this project. Sustaining a critique of contemporary public policy requires not just evidence but a good dose of self-confidence as well, and it is only by working with a group of people that are both critical and encouraging that one can excel. I hope this dissertation does some justice to all of their efforts and investment in me. In particular, Ted Postol's insights into public policy, experience in challenges to orthodoxies, and incredible kindness and support as advisor, mentor, and friend helped me on both an emotional and intellectual level throughout my five years at MIT. Without Ted, I surely would not be where I am today. Shelly Krinsky deserves special thanks for his generosity in taking on an MIT student and introducing me to the fascinating world of risk studies. I am also very grateful to David Jones, for mentoring me in the history of public health, for his careful reading of all my work, and constant encouragement to push my analyses deeper. Thanks also to Ken Oye, for his excellent lectures, inspiring approach to science policy, and mentoring for my general exams. I feel lucky to have found a home at MIT where I could tap such a broad array of expertise.

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There are numerous other individuals that I would like to thank individually but will not do so after a previous experience in which my acknowledgement of the help of a colleague triggered criticism towards him rather than me. In case there is any confusion, the final responsibility for the contents of this work belongs to me.

August 15, 2011

## Introduction

### Should I get the flu shot?

When people learn that I study influenza, they almost invariably ask me for my opinion on whether they should get the flu shot.<sup>1</sup> I can understand why they want advice. On the one hand, there is a clear and consistent message that we should all get vaccinated. Officials at the Centers for Disease Control and Prevention (CDC) now recommend that everyone six months and above should get a flu shot,<sup>2</sup> and many supermarkets and major chain stores like CVS, RiteAid, Walgreens, Kroger, and Target have opened flu shot clinics, making vaccination against influenza as easy as running an errand, plus around \$25. Yet despite this enthusiasm and widespread availability, many people remain hesitant, wondering if it makes sense for them. Adding to their doubts, the media often carries a story which questions the benefit of the shot. A great number of Americans also view the influenza vaccine as unsafe. Many feel they don't need it. A significant portion of healthcare workers decline the shot. Others assert that the vaccine can actually give you the flu. Some ask me for advice.

Over the years, I have come to appreciate that the most important thing about influenza vaccine may be the fact that it is voluntary. Unless one is enlisted in the military, influenza vaccine is an option, not an obligation. And I have always felt uncomfortable instructing people about what they should or should not do with their bodies. But to tell people that it is their choice and that they must make up their own mind seems irresponsible, as if I have nothing to offer despite my interest in the topic over the last six years. I therefore try to help people understand why they might be feeling some hesitancy towards a product that health officials expend significant time and resources promoting as in their best interest. I try to explain what has led me to conclude that policies promoting influenza vaccine are inappropriate, based on questionable calculations of the magnitude to which influenza is a real threat and misleading, overconfident claims regarding the degree to which vaccines can ameliorate the problem. I try to explain why it is that well-intentioned public health officials might have it wrong. This dissertation is the long form of that discussion.

This dissertation presents the study of contemporary influenza policy as a study in what I call medical politics, in which a disease that for most people is rather unremarkable has become the focus of intense (and costly) public health campaigns. These campaigns heavily market influenza and its pandemics as serious public health threats by appealing to a variety of scientific claims. But, as I argue in this dissertation, the soundness of these policies is called into question by important flaws, misrepresentations, and inconsistencies in those particular scientific claims. The degree to which

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<sup>1</sup> At the cost of obvious hypocrisy, I have intentionally chosen to make limited use the familiar terms "flu" and "flu shot" despite my objection to these phrases, because to explain why these words are objectionable at this point in the story would add confusion to what is already a morass. As the mathematician Serge Lang observed, "not the least problem which arises in dealing with a morass is how to avoid becoming part of it." Serge Lang, *Challenges* (New York: Springer, 1998), 736.

<sup>2</sup> Anthony E Fiore et al., "Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010," *Morbidity and Mortality Weekly Report* 59, no. 8 (August 6, 2010): 1-62.

influenza is a serious public health problem is actually unclear. Furthermore, influenza vaccine effectiveness has been vastly overstated, and predictive models of pandemic influenza are demonstrably flawed. Finally, officials conflate true influenza with influenza-like illness (ILI), a seeming semantic distinction which in reality carries huge ramifications, chief among these the ability for officials to mislead the public into false assumptions about the potential benefits of influenza vaccine.

Yet with highly trained, professional scientists, how is it that they have not changed their position in the face of new knowledge? I argue that these misconceptions exist and persist for multiple reasons—in part because they fit within a set of basic assumptions about the nature of infectious diseases, in part because the formation, enactment, and the evaluation of policy is carried out by people who have little incentive to be self-critical, and in part because governmental and academic science has become infused with industry. I treat the matter of influenza policy as a topic that requires understanding both its technical and social dimensions.

The view taken in this dissertation is that influenza policy is best seen as a form of advocacy. The CDC's recommendations that all Americans should get an annual influenza vaccine do not sit idly on the printed page, awaiting considered acceptance by public health groups, physicians, and the public. They are, on the contrary, actively marketed. I use the term "marketing" in part because it helps cast a critical perspective on the practice, but also in part because it is the terminology of the trade, perhaps most transparently witnessed in the CDC's National Center for Health Marketing.<sup>3</sup> As part of these marketing efforts, national awareness campaigns have arisen, such as the National Influenza Vaccination Week. Helping propel these initiatives are other marketing vehicles like the National Influenza Vaccine Summit, an annual event conceived by the CDC and American Medical Association that now draws over 300 participants from across the private and public sector, aiming to align and co-ordinate the national drive for influenza vaccination.<sup>4</sup>

Perhaps owing to the fundamental ethic of health marketing that it is to employ "science-based strategies,"<sup>5</sup> campaigns to increase public interest in influenza vaccination draw heavily on statistics which, the CDC and others assert, demonstrate that influenza is a more serious disease than people realize. My analysis in this dissertation pays particular attention to the centrality of statistics—in particular, estimates of the number of dead bodies—in the marketing of influenza and its vaccine. We must ask why is it that numbers like "36,000 deaths a year" become essential phrases in the literature of

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<sup>3</sup> U.S. Centers for Disease Control and Prevention, "What is Health Marketing?", February 2, 2011, <http://www.cdc.gov/healthcommunication/ToolsTemplates/WhatIsHM.html>, (accessed July 14, 2011); U.S. Centers for Disease Control and Prevention, "National Center for Health Marketing", 2008, <http://www.cdc.gov/maso/pdf/NCHMfs.pdf>, (accessed July 14, 2011); Earl Honeycutt and Kenneth Paul, "An Analysis of Health Marketing Quarterly 1991-2002," *Health Marketing Quarterly* 21, no. 4 (December 2004): 77-87.

<sup>4</sup> According to a recent presentation about the Summit, members include representatives from "Vaccine Manufacturers, Vaccine Distributors, Federal Agencies, Professional Medical Organizations, Specialty, State, Nursing Organizations, Public Health, Hospitals, Pharmacists, Community Immunization Providers, Occupational Health Providers, Business/Employers, Private Health Insurance and Managed Care, Long-term Care, Quality Improvement Organizations, Consumers, Advocacy Groups." (See Litjen Tan, "What is the National Influenza Vaccine Summit?", 2011.)

<sup>5</sup> U.S. Centers for Disease Control and Prevention, "What is Health Marketing?"

influenza, mentioned everywhere from CDC posters to scientific papers. Of course at this point in history it comes as little surprise that numbers drive the way those in public health understand and order the world. The very origins of public health movement were built on new ways of understanding and improving the health of populations through numbers. Edwin Chadwick's well known pioneering *Report on the Sanitary Condition of the Labouring Population of Great Britain* of 1842 may be the best example of this. Tables of vital statistics, showing the rates of birth, death, and disease, across various groups and geographical subdivisions provided insight into how living conditions were connected to the spread of infectious diseases. Campaigns to pipe clear water in and excrement out, improving the social condition of Victorian slums were not—and some argue could not be<sup>6</sup>—justified on moral or civic responsibility, but rather on the objective evidence of a new economic and technocratic rationality of disease prevention.<sup>7</sup> In this context, the tabulation of numbers helped guide organizational responses. By keeping the subjective and personal under check, quantification offers political administrators a way to achieve the semblance of objectivity and rationality.<sup>8</sup> But as the historian Ted Porter notes, it is also these qualities of quantification that make it especially useful as a tool of persuasion, in which statistics not only guide the actions of officials but simultaneously help demonstrate the rationality of those actions. Porter writes that “the appeal of numbers is especially compelling to bureaucratic officials who lack the mandate of a popular election, or divine right.”<sup>9</sup>

Understanding the how numbers figure into influenza policy and advocacy must necessarily also take into account aspects which point to a lack of objectivity—where statistics are, upon closer examination, of dubious validity, as I argue is the case in influenza policy. Here, political scientists Peter Andreas' and Kelly Greenhill's recent examination of the politics of numbers in illicit trades is especially informative. Andreas and Greenhill show how officials, non-governmental organizations, and other interested parties use and manipulate numbers, transforming guesstimates and back-of-the-envelope style, logic defying statistics into so called hard numbers in order to forward various agendas.<sup>10</sup> In their book, a United Nations Educational, Scientific and Cultural Organization (UNESCO) official who works to fight human trafficking commented, “I have been at many meetings with international organizations, activists, and NGOs where people have discussed the ‘advocacy value of numbers’ and their importance for ‘mobilization.’”<sup>11</sup> Perhaps such a fate is inevitable. After all, as Greenhill reminds us, “we live in a world

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<sup>6</sup> Christopher Hamlin, *Public Health and Social Justice in the Age of Chadwick: Britain, 1800-1854* (Cambridge, UK: Cambridge University Press, 1998).

<sup>7</sup> Andrew Lakoff, “From population to vital system: national security and the changing object of public health,” in *Biosecurity Interventions: Global Health and Security in Question*, ed. Andrew Lakoff and Stephen J. Collier, 2008, 38; Peter Washer, *Emerging Infectious Diseases and Society* (Palgrave Macmillan, 2010), 25; Hamlin, *Public Health and Social Justice in the Age of Chadwick*.

<sup>8</sup> Theodore M. Porter, *Trust in Numbers* (Princeton University Press, 1996).

<sup>9</sup> *Ibid.*, 8.

<sup>10</sup> Peter Andreas and Kelly M. Greenhill, eds., *Sex, Drugs, and Body Counts: The Politics of Numbers in Global Crime and Conflict* (Cornell Univ Pr, 2010).

<sup>11</sup> David A. Feingold, “Trafficking in Numbers: the Social Construction of Human Trafficking Data,” in *Sex, Drugs, and Body Counts: The Politics of Numbers in Global Crime and Conflict*, ed. Peter Andreas and Kelly M. Greenhill (Cornell University Press, 2010), 51.

in which things that are not measured, for all intents and purposes, do not exist.”<sup>12</sup> While there are few who doubt the existence of influenza, it is only through statistics that the disease takes on a profile as a disease deserving of public health attention. This means that even if influenza deaths are notoriously hard to tabulate with certainty, as they are, values do get attached and are marketed with an air of certainty.

Perhaps nowhere has this been more true than in the case of pandemic influenza, where conveying the threat of a pandemic was largely accomplished through the deployment of statistical projections of future mortality in the next pandemic. Some scholars have highlighted the fact that pandemic influenza became “securitized,” coming under the rubrics of national security,<sup>13</sup> and it was only after and through the enactment of wargames and other forms of “imaginative enactment” that pandemic preparedness became a national initiative.<sup>14</sup> In the anthropologist Andrew Lakoff’s analysis, pandemic preparedness is a distinct form of collective security that bears resemblance to, but differs from past articulations of nation-state and public health (population) security. Pandemic preparedness therefore does not fit into the well established categories and ways of thinking that define public health rationality, which have been focused on clearly defined, quantifiable assessments of risk. By contrast, Lakoff argues, preparing for a pandemic defies rational, objective quantification, and thus likens it to the sort of existential threats of modernity described by the notable sociologists Ulrich Beck and Anthony Giddens.<sup>15</sup> While Beck and Giddens focused on those threats created by the growth in knowledge and technology of the modern era, Lakoff and others such as sociologist Frank Furedi suggest that the contours of the response to non-technological threats like pandemic influenza or biological terrorism are much the same. Furedi emphasizes how risk management has turned from a probabilistic activity (focused on determining the frequency and impact of potential hazards) to something “possibilistic,” in which the mere possibility and absence of hard knowledge leads to overreaction and a drive to prepare for worst-case scenarios.<sup>16</sup>

While I agree with Furedi in the role that possibilistic risk assessment has played in the environmental and terrorism debates, and agree with Lakoff that imaginative enactment was an important historical element in the adoption of pandemic preparedness policy, my reading of pandemic preparedness finds more continuity between the marketing of seasonal influenza and pandemic influenza. The primary promoters of what has come to be known as “pandemic preparedness” are many of the same individuals and organizations, and, far from an “unknowable,” remote-but-still-possible disaster, pandemic influenza was cast, using statistical projections and language such as “not if, but when,” as a guaranteed disaster. Thus the great variability in statistical estimates of the next pandemic’s death

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<sup>12</sup> Kelly M. Greenhill, “Counting the Cost: the Politics of Numbers in Armed Conflict,” in *Sex, Drugs, and Body Counts: The Politics of Numbers in Global Crime and Conflict*, ed. Peter Andreas and Kelly M. Greenhill (Cornell University Press, 2010), 132.

<sup>13</sup> Washer, *Emerging Infectious Diseases and Society*; Lakoff, “From population to vital system: national security and the changing object of public health.”

<sup>14</sup> Lakoff, “From population to vital system: national security and the changing object of public health.”

<sup>15</sup> Anthony Giddens, *Modernity and Self-Identity: Self and Society in the Late Modern Age*, 1st ed. (Stanford University Press, 1991); Ulrich Beck, *Risk Society: Towards a New Modernity* (London: Sage Publications, 1992).

<sup>16</sup> Frank Furedi, “Precautionary culture and the rise of possibilistic risk assessment,” *Erasmus Law Review* 2, no. 2 (2009): 197–220.

toll—from 2 million to 1 billion—is not the point. The point is that even the lowest figures—the “best case scenarios”—were massive numbers, and indicated that a catastrophe was imminent.<sup>17</sup>

The role numbers play in defining diseases and casting them as plainly in need of intervention is hardly unique to influenza. Central to the thesis on “disease mongering,” is the view that in the effort to sell drugs, pharmaceutical companies simultaneously sell disorders by creating the impression among the public and doctors that the disorders are far more prevalent in the general population than people realize, thereby enlarging their potential market.<sup>18</sup> Conditions such as “Restless Leg Syndrome” (RLS), “Female Sexual Dysfunction” (FSD), and “Erectile Dysfunction” (ED) are a few of many recent examples of conditions that, like influenza, sophisticated marketing campaigns are helping convince the public and doctors are relatively common, serious disorders.<sup>19</sup> This is not to say that there is no physiological basis to these conditions—that they are somehow pure fictions and those who attest to suffering from them are in actuality not suffering. Rather, the disease mongering critique holds that relatively rare and little-known (yet very real) forms of suffering are made to seem like larger problems than they really are by widening the boundaries of diagnosis definitions and reaching wide audiences through public awareness campaigns.<sup>20</sup> By giving them names, generating statistics to show how common the disorder is, and showing what they can result in if left untreated, they not only gain attention, but can be brought within the purview of professional medicine as a problem in need of treatment.

Despite the similarities with the story of influenza, to my knowledge none of the critics of disease mongering have been critical of the marketing of influenza. One reason for this may be the fact that for most observers, there is a certain objectivity about influenza that is lacking for many of the conditions that have come under the disease mongering umbrella. With influenza, there is a virus that enters and infects the body, causing a disease with a well understood and predictable clinical course. As the historian of medicine Charles Rosenberg has argued, such mechanistic certainty about how a pathogen causes malfunction helps make a disease’s status as a specific entity unproblematic.<sup>21</sup> The same cannot

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<sup>17</sup> Commenting on the huge variation in expert predictions of the next pandemic, the risk communication specialists Peter Sandman and Jody Lanard wrote in 2004 that “either way it’s a big number.” See Peter M. Sandman and Jody Lanard, “Pandemic Influenza Risk Communication: The Teachable Moment”, December 4, 2004, <http://www.psandman.com/col/pandemic.htm>, (accessed July 15, 2011).

<sup>18</sup> Lynn Payer, *Disease-Mongers: How Doctors, Drug Companies, and Insurers Are Making You Feel Sick* (John Wiley & Sons Inc, 1992); David Healy, *The Antidepressant Era* (Cambridge, Mass: Harvard University Press, 1999); Ray Moynihan and Alan Cassels, *Selling Sickness: How the World’s Biggest Pharmaceutical Companies are Turning Us All into Patients*, 1st ed. (Nation Books, 2005).

<sup>19</sup> Steven Woloshin and Lisa M. Schwartz, “Giving Legs to Restless Legs: A Case Study of How the Media Helps Make People Sick,” *PLoS Medicine* 3, no. 4 (2006): e170; Joel Lexchin, “Bigger and Better: How Pfizer Redefined Erectile Dysfunction,” *PLoS Medicine* 3, no. 4 (2006): e132; Ray Moynihan and Barbara Mintzes, *Sex, Lies, and Pharmaceuticals: How Drug Companies Plan to Profit from Female Sexual Dysfunction* (Greystone Books, 2010).

<sup>20</sup> Ray Moynihan and David Henry, “The Fight against Disease Mongering: Generating Knowledge for Action,” *PLoS Medicine* 3, no. 4 (2006): e191.

<sup>21</sup> Rosenberg argues that modern conceptions of distinct disease entities are distinguished by our ability to tie them to specific material malfunction. Although this conception of disease emerged several decades prior to the rise of germ theory in the mid-nineteenth century, contagious epidemic diseases have provided powerful reassurance of the legitimacy of the mechanism-oriented way of thinking. Charles E Rosenberg, “The tyranny of diagnosis: specific entities and individual experience,” *The Milbank Quarterly* 80, no. 2 (2002): 237-260.

be said of female sexual dysfunction, erectile dysfunction, shyness, boredom, and unhappiness. For these conditions, it is precisely the lack of certainty regarding a mechanism of pathogenesis that makes placing them into distinct disease categories—and drawing lines between “normal” and “diseased”—highly debatable and contested. Looking at it through the framework articulated by the anthropologist Joe Dumit, influenza fits within a more twentieth century view of the body—of “inherent health” (with occasional attacks from outside invaders like bacteria and viruses)—not the newer, still emerging, and controversial conception of bodies as “inherently sick,” always in need of medication to regulate a state of “normalcy.”<sup>22</sup>

This is not to say that influenza is the sole “hard” disease for which great efforts are made to generate concern among a broad population. As Jeremy Greene has shown, the pharmaceutical company Merck worked in the 1950s and 1960s to redefine the threshold for declaring a person as “hypertensive,” thereby enlarging the market for their diuretic medication, Diuril. Greene’s analysis shows that even for conditions that can be measured in standardized ways, huge efforts may still be necessary to alter physicians’ clinical decision making.<sup>23</sup> But here, too, like in the disease mongering thesis, pharmaceutical companies’ desire for profit is the primary driver of the story. The case of influenza—in which government scientists generate and market the statistics—forces us to think about how and why this occurs when profit does not appear to be a fully satisfactory answer.

\* \* \*

Studying the marketing of disease provokes fundamental, more searching questions about the selection of risks. Even if influenza kills tens of thousands of Americans each year, as the CDC argues, it does not automatically follow that this merits a policy response. For which hazards (and of what magnitude) do we wish the state to intervene? What kinds of risks should individuals attempt to avoid? Which should they accept? Who is to decide?

In the 1970s, Ivan Illich radically challenged the medicalization of pain and death, arguing that “Pain has ceased to be conceived as a ‘natural’ or ‘metaphysical’ evil. ... Medical civilization teaches that suffering is unnecessary, because pain can be technically eliminated.”<sup>24</sup> Although Illich’s work was seen by many as polemical, the basic question he raises about intervention is important. When should public monies be spent on public health programs to control influenza? In many ways, the marketing of influenza is a large and concerted effort among government officials, vaccine manufacturers and others to convince the public that influenza should be taken seriously—something it seems the public would otherwise largely not be inclined to do. The marketing of influenza is then, as Mary Douglas and Aaron Wildavsky might argue, a struggle over defining what is “normal” and therefore not in need of intervention, and what crosses that line.

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<sup>22</sup> Joseph Dumit, “Drugs for Life,” *Molecular Interventions* 2, no. 3 (June 1, 2002): 124-127.

<sup>23</sup> Jeremy A. Greene, “Releasing the Flood Waters: Diuril and the Reshaping of Hypertension,” *Bulletin of the History of Medicine* 79, no. 4 (2005): 749-794.

<sup>24</sup> Ivan Illich, *Medical nemesis: the expropriation of health* (London: Calder & Boyars, 1975), 94-95.



In their discussion of the selection of risk, Douglas and Wildavsky observe that modern society may be no different than primitive societies in that we try to determine a cause for every misfortune, “as if there were no such thing as natural death, no purely physical facts, no regular accident rates, no normal incidence of disease.”<sup>25</sup> The rise of statistics and statistical knowledge theoretically could have given rise to a society in which some misfortunes would not require any deep explanation, for they were predictable and expected. Such was the defining feature of modern societies according to philosopher Lucien Lévy-Brühl—to not ask.<sup>26</sup> But as Douglas and Wildavsky explain, “the idea of normality changes with new knowledge.”<sup>27</sup> New technologies reconfigure social responsibilities, redefining what is normal and acceptable.

In relation to environmental and technological hazards, for which the most important characteristic may be that they emanate from the very technologies human societies have deployed,<sup>28</sup> discussions of “acceptable risk” are not new.<sup>29</sup> Yet there has been by comparison far less discussion over what level of illness and death is acceptable for the risks posed by infectious diseases—particularly from diseases deemed vaccine preventable.<sup>30</sup> Understanding why this is the case is of central concern to me in this dissertation.

My argument is that the act of conceiving of influenza as a “vaccine preventable disease” has radically altered the way public health officials think about, describe, and respond to influenza. Vaccines were an incredibly powerful expression of the triumph of the germ theory, which posited a clear relationship between single organisms, single diseases, and single cures. The introduction of a vaccine promised to interrupt the ability of the germ to cause disease. With a vaccine, influenza is no longer just one of the many diseases out there in the world, but qualified for the special category of “vaccine preventable diseases,” in turn leading public health officials to have little doubt that the correct way to manage influenza was through vaccination. In this way, as historian Harriet Ritvo has shown, the category helped bring order to the specialists’ world.<sup>31</sup> The existence of influenza vaccine helps to simultaneously define influenza as a problem and present its solution: vaccination. All that is left is convincing the public to do what’s right.

But, as communication theorist Geoffrey Bowker and sociologist Susan Leigh Star have shown in their study of classification, ordering the world into categories may be carried out in sincerity, but can

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<sup>25</sup> Mary Douglas and Aaron B Wildavsky, *Risk and Culture: An Essay on the Selection of Technical and Environmental Dangers* (Berkeley: University of California Press, 1982), 32.

<sup>26</sup> Lévy-Brühl, cited in *Ibid.*

<sup>27</sup> *Ibid.*, 35.

<sup>28</sup> Beck, *Risk Society*.

<sup>29</sup> Baruch Fischhoff, *Acceptable Risk* (Cambridge: Cambridge University Press, 1981).

<sup>30</sup> One interesting exception to this is a recent editorial by the bioethicist Arthur Caplan, who challenged the desirability of eradicating all infectious disease, in particular polio. Caplan argued that given the costs of eradication programs, seeking “elimination or control rather than eradication” may, all things considered, be a more ethical approach. See Arthur L Caplan, “Is disease eradication ethical?,” *Lancet* 373, no. 9682 (June 27, 2009): 2192-2193.

<sup>31</sup> Harriet Ritvo, *The Platypus and the Mermaid: And Other Fictions of the Classifying Imagination* (Harvard University Press, 1998).

nonetheless bring about unintended consequences, sometimes detrimental and damaging.<sup>32</sup> The theoretical simplicity of the virus-centric model, in which vaccination fits like a key in a lock to solve the influenza problem, is also its Achilles heel. I argue that so many of the problems in the scientific positions underpinning influenza policy—from flawed risk assessment to misleading, overly optimistic assessments of vaccine effectiveness—go uncorrected because thinking about infectious diseases has become “virus centric.”

Are these experts, then, trapped in a “paradigm,” in the Kuhnian sense, in which empirical anomalies and other problems in current theories simply cannot fit within the current framework of “normal science” and are therefore effectively invisible to current researchers?<sup>33</sup> I do not think so, for many of the problems in influenza science are known, and the contradictions are contradictions that arise within the current paradigm, not without. That influenza vaccines have failed to lower elderly mortality<sup>34</sup> is not a conclusion incompatible with the current paradigm; it is simply unfortunate information that is given little consideration in policy.

A different answer to the question of how expert systems can systematically err was offered by Lynn Eden in her study of nuclear damage.<sup>35</sup> Eden asks how the United States’ best experts on nuclear damage failed to predict the effects of nuclear fires, despite ample evidence that the impact of fire would be far more devastating than the blast itself. Eden suggests it was not that they did not or could not comprehend damage from fire. Rather, she highlights the role of path dependence, and organizational “lock-in,” in which early choices and decisions regarding where to allocate resources led to bureaucracies and organizational cultures that reinforced those choices. Predicting blast damage got early recognition and resources, while predicting fire damage did not. As time went on, the lack of organizational capacity to predict fire damage was taken as proof of the impossibility of predicting fire damage, and consequently it was ignored.<sup>36</sup>

It is worth mentioning that this dissertation does take a position about the accuracy of scientific claims. While debates have and will continue to exist over whether and to what degree academics can

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<sup>32</sup> Geoffrey C Bowker and Susan Leigh Star, *Sorting Things Out: Classification and Its Consequences*, Inside technology (Cambridge, Mass: MIT Press, 1999). Also see Ian Hacking, “Biopower and the avalanche of printed numbers,” *Humanities in Society* 5, no. 3/4 (1982): 279–295.

<sup>33</sup> Thomas S Kuhn, *The Structure of Scientific Revolutions* (Chicago: University of Chicago Press, 1962).

<sup>34</sup> See Lone Simonsen et al., “Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population,” *Arch Intern Med* 165, no. 3 (February 14, 2005): 265-272; Lisa A Jackson et al., “Evidence of bias in estimates of influenza vaccine effectiveness in seniors,” *International Journal of Epidemiology* 35, no. 2 (April 2006): 337-44; Lisa A Jackson et al., “Functional status is a confounder of the association of influenza vaccine and risk of all cause mortality in seniors,” *International Journal of Epidemiology* 35, no. 2 (April 2006): 345-352; Tom Jefferson et al., “Vaccines for preventing influenza in the elderly,” in *Cochrane Database of Systematic Reviews*, ed. The Cochrane Collaboration and Tom Jefferson (Chichester, UK: John Wiley & Sons, Ltd, 2010), <http://doi.wiley.com/10.1002/14651858.CD004876.pub3>; Dean T. Eurich et al., “Mortality Reduction with Influenza Vaccine in Patients with Pneumonia Outside ‘Flu’ Season: Pleiotropic Benefits or Residual Confounding?,” *Am. J. Respir. Crit. Care Med.* 178, no. 5 (September 1, 2008): 527-533. For a more detailed discussion of these papers, see Chapter 4.

<sup>35</sup> Lynn Eden, *Whole World on Fire: Organizations, Knowledge, and Nuclear Weapons Devastation*, Cornell studies in security affairs (Ithaca, N.Y: Cornell University Press, 2004).

<sup>36</sup> *Ibid.*, 285-6.

acceptably engage themselves as “activists” (visible in the climate change debate), it is good to see that I am not the first. The historian Allan Brandt’s detailed analysis of the ways in which knowledge of the harms of tobacco were manipulated and hidden by industry—as well as his expert testimony in tobacco litigation—is a good example of scholarship that “takes a side.”<sup>37</sup> Another is John Abraham’s study of “corporate bias” in drug development and regulation.<sup>38</sup> In the case studies he considered, Abraham showed that contested knowledge had little to do with “a clash of plural rationalities” or other contrasting value systems.<sup>39</sup> Rather, “it is often possible to demonstrate that some scientists’ claims are more consistent and truthful than others.”<sup>40</sup> I agree. What all of these works demonstrate is that expertise can be wrong, distorted by the effects of industrial influence, leading to errors both as the result of conscious decisions (e.g. in deliberate attempts to mislead the public regarding the health hazards of tobacco) and unconscious, unintentional, or more structural processes (as in the unconscious transformation of norms which affects what scientists say and do, as Sheldon Krimsky has described<sup>41</sup>).

But are conflicts of interest sufficient to understand influenza? Without any doubt, industry has had and continues to have a serious interest in influenza policy. Also without doubt are connections between those who set policy and those who stand to profit from pharmaceutical interventions. Yet in my study, industrial interests are not at center stage—in part because much of the story of conflicts of interest has already been told by investigative journalists,<sup>42</sup> but also in part because I do not think it is the full story. As important as it is to understand the influence of industry in shaping scientific research and policy agendas—the ubiquity of the term “public-private partnerships” in public health discussions today is for me the most symbolic of way in which the ethos of science has changed in the last decades<sup>43</sup>—it is equally important to develop an explanation for how inconsistent and inaccurate claims can be defended and maintained among experts who it would appear have no financial motive to endorse problematic science.

## Layout of the dissertation

The chapters in this dissertation build on one another. The first two chapters set the stage, showing how influenza (Chapter 1) and its pandemics (Chapter 2) are marketed. Drawing on governmental marketing materials, statements by officials, and policy documents, I try to let officials speak for

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<sup>37</sup> Allan Brandt, *The Cigarette Century: The Rise, Fall, and Deadly Persistence of the Product That Defined America*, 1st ed. (Basic Books, 2009).

<sup>38</sup> John Abraham, *Science, Politics And The Pharmaceutical Industry: Controversy And Bias In Drug Regulation*, 1st ed. (Routledge, 1995).

<sup>39</sup> Schwarz & Thompson, quoted in *Ibid.*, 250.

<sup>40</sup> *Ibid.* Or in Lynn Eden’s words: “Because a controversy, or even potential controversy, has not been resolved does not mean that some understandings are not better than others.” Eden, *Whole World on Fire*, 7.

<sup>41</sup> Sheldon Krimsky, *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* (Lanham: Rowman & Littlefield Publishers, 2003).

<sup>42</sup> Deborah Cohen and Philip Carter, “WHO and the pandemic flu ‘conspiracies,’” *BMJ* 340, no. jun03\_4 (June 6, 2010): c2912; Deborah Cohen and Philip Carter, “Questioning the timeline of H1N1 flu vaccination contracts,” *Nature* 466, no. 7304 (July 15, 2010): 315; Fiona Godlee, “Conflicts of interest and pandemic flu,” *BMJ* 340, no. jun03\_4 (June 6, 2010): c2947; Helen Epstein, “Flu Warning: Beware the Drug Companies!,” *The New York Review of Books*, May 12, 2011, <http://www.nybooks.com/articles/archives/2011/may/12/flu-warning-beware-drug-companies/>, (accessed June 17, 2011).

<sup>43</sup> Krimsky, *Science in the Private Interest*.

themselves and, as much as possible, refrain from analysis. Today's widespread availability of influenza vaccine, impressive size of the influenza vaccine industry, and government stockpiles of influenza vaccines and antivirals did not grow out of a response to popular demand. It is instead the culmination of a long term marketing strategy fueled largely by public health officials and pharmaceutical manufacturers aimed at increasing the number of people that get an annual influenza vaccine and efforts to put "pandemic preparedness" on the national health policy agenda. This discourse is saturated with mortality and other burden of disease statistics. Officials use these statistics—such as the number of people said to die of influenza each year—not to simply convey information, but instead to persuade, legitimate funding, and increase influenza vaccination rates.

During interviews with CDC officials in October 2010, I had the opportunity to enquire about the agency's many promotional posters and other materials which emphasize the seriousness of influenza. "Is this information or is this advocacy?" I asked, referring to a CDC poster<sup>44</sup> that states "flu is a serious contagious disease" despite the fact that the vast majority of people who contract the disease recover in a few days, even without seeking medical attention. The CDC's director of media relations responded: "This is advocacy. I mean, at the end of the day, this is advocacy, because it gets back to, we *do* want people to get a flu shot. We *do* have a point of view, as an agency. We *do* think the best you can do is to get a flu shot. That is your best protection."<sup>45</sup>

The contrast between *informing* and *advocating* is important. When officials engage in *advocacy*, what they convey is shaped not only by what they know, but by what they want to occur. An educated public that understands the risks and benefits and makes its own decision about the best way to deal with the disease is not the objective of advocacy; advocacy instead seeks to persuade people into getting the shot. Thus information about influenza is not static, but changes in response to officials' attempts to modulate popular demand for vaccine. This is what occurred in 2004, when manufacturing problems at one influenza vaccine production facility led to an unexpected shortfall of 50 million doses of vaccine. The disease officials had until then relentlessly described as "serious" was swiftly downgraded to "an annoying illness."<sup>46</sup>

Chapter 1 suggests that officials approach influenza as an orchestrated marketing campaign that has as its goal the increase of vaccination rates. I argue that this campaign in part exists because ordinary people do not find influenza important enough to take action on their own. For most people, it is a benign illness—uncomfortable and undesirable, surely, but self-limiting and transient. Our bodies recover, and we get on with our lives. And for the elderly, who suffer the bulk of influenza-related deaths, often following complications with pneumonia, even then it can be more blessing than curse. As the first Surgeon General's *Healthy People* national framework for improving America's health

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<sup>44</sup> U.S. Centers for Disease Control and Prevention, "CDC Says 'Take 3' Steps to Fight The Flu", January 12, 2010, [www.cdc.gov/flu/freeresources/2009-10/pdf/h1n1\\_take3.pdf](http://www.cdc.gov/flu/freeresources/2009-10/pdf/h1n1_take3.pdf), (accessed July 21, 2010).

<sup>45</sup> Glen Nowak, interview by Peter Doshi, October 27, 2010, pt. 42'35.

<sup>46</sup> U.S. Centers for Disease Control and Prevention, "Public Service Announcement for 2004-05 Flu Season: There are other steps you can take to fight the flu", October 22, 2004, <http://web.archive.org/web/20041025002301/http://www.cdc.gov/flu/pdf/0405psa2.pdf>, (accessed July 13, 2010).

acknowledged nearly thirty years ago, “pneumonia has been called the ‘old man’s friend’ for the painless ending of life it may provide.”<sup>47</sup> That perspective, however, has markedly changed, as campaigns frame all influenza-related deaths as unnecessary, avoidable, and tragic.

Chapter 2 explores the marketing of influenza in its pandemic form. In the early 1990s, only a small group of public health officials (most at CDC) felt pandemic preparedness was a worthwhile effort. But by 2005, almost every country around the world had a preparedness plan. This chapter explores how consensus in the scientific and non-scientific communities formed around the notion of an influenza pandemic as a disastrous, inevitable event that public health agencies could respond to with “preparedness”—prior, of course, to the outbreak of H1N1 in April, 2009.<sup>48</sup> To understand the evolution of the pandemic influenza concept and its relation to public policy, one must look not only at how public health officials understood a pandemic, but how they made the rest of us understand the meaning of pandemic.

An important first element of the scientific consensus underpinning policy was that a pandemic was a distinct event. Officials starting in the 1990s advanced the idea of a pandemic as an unusually severe form of influenza, something with consequences demanding special attention. With the backdrop of “emerging infectious diseases” rhetoric, pandemics were conceived as devastating events with unpredictable timing. Similar to seasonal influenza, a key component of defining and conveying the danger of pandemics came through risk assessment. But because pandemic preparedness was about preparing for an event that had not yet occurred, officials looked to the past for lessons. Often discussed and considered was the catastrophic 1918 pandemic. Also often discussed as relevant to pandemic preparedness was the SARS epidemic of 2003 as well as avian influenza H5N1, an epizootic occurring since 1997. By contrast, the far less deadly influenza pandemics of 1957 and 1968 received little attention. Chapter 2 discusses how this selective use of the past was linked with the policy imperative of supporting the expansive federal funding of pandemic preparedness.

Pandemic risk assessment also made heavy use of statistical models. Starting in the 1990s, morbidity and mortality, as well as economic, models gained currency both within the scientific literature and in the popular press. These predictions of future disease impact helped bolster the rationale for preparedness, and shaped the nature of response planning, as projected statistics of pandemic influenza caused death and hospitalization were incorporated as fundamental planning assumptions. In the 2000s, as pandemic preparedness moved from a personal interest among a small group of public health officials into a broad national and global concern, models proliferated. Non-profit institutions, development banks, and a host of other non-traditional public health actors published their mortality estimates, all of which pointed to the profound impact of a future pandemic. Although these mortality estimates were highly incompatible with each other, with some reports even internally inconsistent,

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<sup>47</sup> U.S. Department of Health, Education, and Welfare, *Healthy People: The Surgeon General’s Report On Health Promotion And Disease Prevention* (Washington, DC: U.S. Government Printing Office, 1979), 7-13, <http://profiles.nlm.nih.gov/ps/access/NNBBGK.pdf>, (accessed July 13, 2011).

<sup>48</sup> Debate and discussion about influenza and pandemics was radically altered by the “2009 influenza pandemic” of H1N1, so chapter 2 will examine the time period before the pandemic while chapter 3 will address the pandemic itself.

contradictions did not cause controversy—if anything, they only underlined the urgency of preparedness.

Then, on June 11, 2009, the World Health Organization declared that the first influenza pandemic in over 40 years had begun. The story of “the 2009 influenza pandemic”—or “H1N1,” as it became popularly known in the US—is recounted in Chapter 3. It is a story about how all predictions were off. The H1N1 outbreak seems to have passed, killing far fewer than even the lowest of the low-range mortality estimates had predicted. H1N1 did not leave behind a world devastated by disease, but rather a world full of confusion and accusation. In the early months of the outbreak, huge uncertainty, much visible to the public, existed over whether H1N1 even qualified as a pandemic. Six months after the WHO declared it to be one, the Council of Europe began hearings into the WHO’s handling of the pandemic, questioned WHO’s ties to industry, and the degree to which its policy decisions had been truly independent and evidence-based. Other investigations—notably, those by the British medical journal *BMJ* and the publicly funded UK television station *Channel4*—brought to light more troubling facts: that many countries had entered into multi-million dollar vaccine contracts required countries to automatically purchase vaccine upon a WHO declaration of a pandemic; that advisors to the WHO had largely unknown financial ties to the drug and vaccine industry; and that the identities of the 16-member advisory board which recommended the WHO Secretary-General declare a pandemic were secret.

Chapter 4 treats the gap between expectation and reality that the H1N1 outbreak of 2009 brought into focus as the tip of large iceberg. In this chapter, I present evidence to argue that the entire public health effort against influenza is built upon a series of fundamental misconceptions about the problem of influenza, its pandemics, and the vaccine. Influenza policy has for years been focused upon fighting upper respiratory tract infections caused by influenza virus, not “influenza-like illness,” a far more common syndrome caused only in small part by influenza viruses. As a result, influenza policy—fixated as it is on influenza vaccines—at best only addresses the minority contributor to the illness most people suffer from and call the “flu.” But even for true influenza, I show that officials’ descriptions of vaccine effectiveness are not well grounded. In addition, I show that death estimates—typically produced through statistical models—are wide ranging, inconsistent, based on spurious assumptions and lack methods of validation. Statistics about and descriptions of the disease are routinely conveyed to the public in ways that mislead.

Information about pandemics has been similarly problematic. Descriptions of pandemics as invariably catastrophic events that are distinct from seasonal influenza runs contrary to a historical record which is mixed, including a deadly pandemic in 1918 that swept the world and other pandemics with similar mortality rates compared to non-pandemic seasons.

While Chapter 4 documents that much of the scientific consensus about influenza is fundamentally misconceived, Chapter 5 refocuses the attention of the dissertation on an explanation of *how* and *why* this occurs. Scrutiny over H1N1 revealed the degree to which policy advisors are connected to the pharmaceutical industry, but the story is not as simple as commercial interests trumping sound policy decisions. Many (if not most) public health officials have no financial relationship with the

pharmaceutical industry, yet still strongly agree that the H1N1 outbreak was a pandemic, and heavily promote statistics about influenza mortality burden and vaccine effectiveness which I argue are flawed. To develop a more complete understanding of the dynamics of public health policy, it is imperative to explore the reasons why official bodies endorse and perpetuate problematic science.

During my trip to the CDC in Atlanta in October 2010, I used my invited talk to the Influenza Division as an opportunity to directly challenge officials by critiquing official policy documents. I showed two slides documenting what I believed were important contradictions in official US influenza policy—the CDC's influenza recommendations (*Prevention and Control of Influenza*) and the *HHS Pandemic Influenza Plan*. The CDC recommendations cite a publication which concludes that the popular influenza antiviral Tamiflu reduced the rate of pneumonia by 50 per cent. This conclusion made its way into the HHS's pandemic plan, indicating that a "Critical [planning] assumption" was that "Treatment with a neuraminidase inhibitor (oseltamivir [Tamiflu®] or zanamivir [Relenza®]) will be effective in decreasing risk of pneumonia, will decrease hospitalization by about half (as shown for interpandemic influenza), and will also decrease mortality."<sup>49</sup> However, the same guidance document later states that "There are no data on the effectiveness of neuraminidase inhibitors in preventing either serious morbidity (e.g., requirement for intensive care) or mortality..."<sup>50</sup> I displayed the two quotes side by side on the projector, paused, and waited for a response (Figure 0.1).

A senior medical officer from the Epidemiology and Prevention Branch told me that I had it wrong: it may be inconsistent to people with less familiarity with the data, or to those without the right credentials, he said—but to him, an epidemiologist with a background in clinical medicine, there was no contradiction. I struggled to understand how the HHS's first statement describing an assumption about decreasing mortality was consistent with the second statement about no data regarding the prevention of mortality. Nobody else in the audience spoke up to agree, disagree, or clarify the matter—and I returned home more convinced than ever that it is essential to gain a deeper understanding of the social dynamics of policy in order to understand how people who I view as intelligent and well-intentioned can passionately argue that these logical inconsistencies are unproblematic.

Chapter 5 presents my answer to this question. I argue that the simplicity of conceiving influenza as an infectious disease caused by a single pathogen (influenza virus) and preventable with a single intervention (the vaccine) dulls critical sensibility. Public health experts' labeling of influenza as a "vaccine preventable disease," or VPD as it is often abbreviated, enables them to defend the rationality basis of the entire policy—from surveillance policies and vaccination policies to pandemic preparedness, and attach more certainty about the natural world than has ever been supported by the empirical evidence. Thinking of influenza as a VPD has pushed responses in a "one disease – one cause – one drug" (or in this case vaccine) framework, which has become so commonplace and ingrained in expert thinking that it prevents most experts from addressing fundamental gaps in their effort.

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<sup>49</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan", November 2005, D-20, <http://www.hhs.gov/pandemicflu/plan/pdf/HHSPandemicInfluenzaPlan.pdf>, (accessed June 9, 2009).

<sup>50</sup> *Ibid.*, S7-12.

The final chapter of this dissertation refocuses the discussion back to matters of policy, and offers thoughts on how the status quo might change for the better. Rather than treating policy as a static set of directives and practices, I argue, following some notable theories in political science, that science policies need to “learn and adapt” over time, incorporating new information and learning from past performance. Influenza policy at present shows little sign of such learning and adaptation. It also lacks important safeguards for ensuring the integrity of scientific conclusions, such as independent evaluation.

Because this dissertation argues that many of the problems with influenza policy are fundamentally social rather than technical in nature, I suggest that public health practitioners need to carefully re-examine some of their basic assumptions about how and when to intervene. At the same time, I argue that some structural changes should be given serious consideration. At present, infectious disease policy, like influenza policy, places the responsibility for risk assessment, risk management, and risk communication about influenza (and many infectious diseases) with the same group of people: the CDC. This produces structural disincentives for rigorous review and learning, and a virtual knowledge monopoly arises that prevents independent and rigorous assessment of scientific evidence and policy. By establishing and maintaining a “clear conceptual distinction” between these activities, as the National Research Council famously advocated,<sup>51</sup> policy stands a chance of being informed by and tested against higher quality assessments of the scientific and technical knowledge base.

[ENDS]

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<sup>51</sup> Committee on the Institutional Means for Assessment of Risks to Public Health, National Research Council, *Risk Assessment in the Federal Government: Managing the Process* (Washington, D.C.: The National Academies Press, 1983).



## HHS Pandemic Influenza Plan (2005)


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- **HHS:** “Critical assumptions. Treatment with a neuraminidase inhibitor (oseltamivir [Tamiflu®] or zanamivir [Relenza®]) will be effective in decreasing risk of pneumonia, will decrease hospitalization by about half (as shown for inter pandemic influenza), and will also decrease mortality.” (p.D-20)
- **HHS:** “There are no data on the effectiveness of neuraminidase inhibitors in preventing either serious morbidity (e.g., requirement for intensive care) or mortality (see July 2005 recommendations of the AHIC [ACIP?] ....” (p.S7-12)
- **ACIP 2005:** “One study assessing oseltamivir treatment primarily among adults reported a reduction in complications, necessitating antibiotic therapy compared with placebo [Kaiser 2003].”



## ACIP Influenza Rec. (2008)

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- “In a study that combined data from 10 clinical trials, the risk for pneumonia among those participants with laboratory-confirmed influenza receiving oseltamivir was approximately 50% lower than among those persons receiving a placebo and 34% lower among patients at risk for complications ( $p < 0.05$  for both comparisons) [Kaiser, 2003].”

Figure 0.1. Slides I presented during a talk giving to CDC Influenza (October 2010).



## Chapter 1 Marketing Death to Save Lives

Since the 1960s, federal health officials have recommended that the elderly and other “high risk” populations get an annual influenza vaccination, but in 2003 the mission to vaccinate carried added urgency. In January, Centers for Disease Control and Prevention (CDC) scientists had published a new study in the *Journal of the American Medical Association* concluding that influenza was killing nearly double the number of Americans each year than had previously been estimated.<sup>1</sup>

“Using new and improved statistical models, CDC scientists estimate that an average of 36,000 people (up from 20,000 in previous estimates) die from influenza-related complications each year in the United States,” the agency wrote in a press release. CDC Director Dr. Julie Gerberding commented: “These data indicate that the magnitude of the problem is larger than we once thought. ... it is crucial that we continue to get the message out regarding the importance of high risk people getting their flu shots each and every year.”<sup>2</sup>

To raise awareness of the new study, the CDC had also called a press conference to coincide with the *JAMA* publication.<sup>3</sup> “Today, we are going to talk about an article in this week’s *Journal of American Medical Association*,” the CDC told an audience of media outlets including the *New York Times*, *Wall Street Journal*, *Reuters*, and the *Associated Press*. Dr. Keiji Fukuda, co-author of the *JAMA* article and leading influenza expert at the CDC explained that while 36,000 annual deaths was just the average, that number could go up to 50,000 to 70,000 during bad years. “Now I think that some of the bottom-line points that we hope that you take home,” Fukuda said, “is that influenza and other respiratory viruses such as RSV [respiratory syncytial virus] really have been under-appreciated health problems, and a lot of people tend to think of them as causes of things like colds, but, really, I think these figures show you that they’re really major causes of serious illnesses and death in the United States.”

The message that officials wished to convey was two-fold: first, influenza was a more important threat to the public health than people realized—the mortality figures demonstrated as much—and second, we must do something about it. “One major step is that we need to increase the use of influenza vaccine in those groups of people who are at risk of developing serious complications from influenza,” Fukuda said. Towards that end, officials had already broadened influenza vaccine recommendations to include all people 50 years and older, a recommendation Fukuda emphasized at the telebriefing. By 2004, around 188 million Americans belonged to age or risk groups recommended to get the shot (see Table 1.1. Expansion of influenza vaccination recommendations, 1960 to present).

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<sup>1</sup> William W Thompson et al., “Mortality associated with influenza and respiratory syncytial virus in the United States,” *JAMA* 289, no. 2 (January 8, 2003): 179-86.

<sup>2</sup> In this dissertation, I have used the prefix “Dr.” to denote those individuals with MD degrees, which has the effect of not identifying the degree qualifications of Ph.D. holders. This is to help put emphasis on those who can be expected, by and large, to have a more hands-on experience in clinical medicine. U.S. Centers for Disease Control and Prevention, “Press Release: CDC Finds Annual Flu Deaths Higher Than Previously Estimated”, January 7, 2003, <http://www.cdc.gov/media/pressrel/r030107.htm>, (accessed July 15, 2010).

<sup>3</sup> U.S. Centers for Disease Control and Prevention, “CDC Telebriefing Transcript: Increase in Influenza-Related Deaths in the United States”, January 7, 2003, <http://www.cdc.gov/media/transcripts/t030107.htm>, (accessed July 15, 2010).

Echoing the same messages delivered in an editorial accompanying the CDC's new analysis, David Morens, an NIH scientist and historian of influenza, emphasized the need to strengthen vaccination efforts: "Annual influenza vaccination is and must remain among the most important public health priorities."<sup>4</sup> Morens called on health care professionals—a group that has historically not been especially enthusiastic about influenza vaccine<sup>5</sup>— to endorse the vaccine. "Active and organized approaches to prevention strategies (eg, patient calls and mailings) may also help to optimize patient vaccination rates."

Promotional efforts, however, were hitting bumps. Glen Nowak, then the associate director of communications at the CDC's National Immunization Program, recalled that in November, "manufacturers were telling us that they weren't receiving a lot of orders for vaccine for use in November or even December. It really did look like we needed to do something to encourage people to get a flu shot."<sup>6</sup> Around the same time, however, news about an especially early flu season was being tracked by *The Denver Post*, news that the CDC would leverage in its efforts to encourage vaccination.<sup>7</sup> Although influenza cases had first been detected in mid-November the prior year, this year Colorado health officials were reporting significant outbreaks on the large student campus of University of Colorado. This was soon followed by Texas and Georgia, where state health departments began to report their own influenza outbreaks.<sup>8</sup> The CDC called another press conference.

"We're very concerned that the flu season has had an earlier onset than we've seen in many years, and we are seeing some parts of the country that are having very high levels of widespread flu infection ... we're here today ... to sound the alarm," Director Gerberding told reporters in the audience.

The point is that people need to get their flu shot. This is the time for Americans to really step up to the plate and get vaccinated against influenza, especially because this could be a worse-than-usual flu season ... In this country, where we have over 114,000 hospitalizations usually from influenza, we have 36,000 people die from the complications of influenza. So this is very serious.<sup>9</sup>

### **From worse-than-usual to worst-in-decades**

Active promotion of vaccine may have seemed necessary to officials that day in mid-November. But ten days later, on November 27, four children in Colorado were reported to have died of influenza, and the

<sup>4</sup> David M Morens, "Influenza-related mortality: considerations for practice and public health," *JAMA: The Journal of the American Medical Association* 289, no. 2 (January 8, 2003): 227-229.

<sup>5</sup> William D. King et al., "BRIEF REPORT: Influenza Vaccination and Health Care Workers in the United States," *Journal of General Internal Medicine* 21, no. 2 (February 2006): 181-184; Scott A Harper et al., "Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP)," *MMWR. Recommendations and Reports* 54, no. 8 (July 29, 2005): 9.

<sup>6</sup> "Analysis: Balancing science and common sense in public health" (National Public Radio, December 23, 2003).

<sup>7</sup> "Flu lands first punch of season with 32 cases in Colorado," *The Denver Post*, November 5, 2003; "Flu bug strikes early in Colorado At least 70 cases reported at CU," *The Denver Post*, November 16, 2003.

<sup>8</sup> David Wahlberg, "Flu's early appearance worries CDC director," *The Atlanta Journal-Constitution*, November 18, 2003.

<sup>9</sup> U.S. Centers for Disease Control and Prevention, "CDC News Conference Transcript: Update on Current Influenza Season", November 17, 2003, <http://www.cdc.gov/media/transcripts/t031117.htm>, (accessed June 30, 2011).

story gained immediate national attention.<sup>10</sup> Dr. Gregory Poland, director of the Mayo Clinic Vaccine Research Group in Rochester, Minnesota and a frequent influenza expert appearing in the media, told Robert Bazell of *NBC Nightly News*, “my own prediction, unfortunately, is that somewhere in the neighborhood of 50 to 70,000 people who are with us today will not be here in the succeeding months. And that will be somebody's mother, somebody's grandfather, somebody's child, because they neglected to do the one thing they should do, and that is get a flu shot this year.” The chairman of medicine at New York University and member of the Infectious Diseases Society of America, Dr. Martin Blaser, agreed:

What makes flu bad is that it infects millions of people, tens of millions of people. Some of those people are going to be compromised by age and by disease. They're going to be at higher risk of dying. But all those other millions and millions of normal people, they are also at risk of dying, a much lower risk. But when you add up the numbers, that—that's where you get these unfortunate children and—and unfortunate adults also, who—who are perfectly normal, and a few days later, they're dead.<sup>11</sup>

While the CDC had just months prior pleaded with journalists to help get out the message that influenza vaccine was the right response to a dangerous disease that Americans needed to take seriously, such prodding was no longer necessary. Demand for vaccine would soon rise sharply across the US, as if Americans had heeded the call of these experts and were now convinced of their particular vulnerability to the disease.

“The airwaves were flooded with images of the children who died in Colorado,” a NPR reporter for *All Things Considered* recalled. “People lined up for flu shots around the country. Within days, spot shortages of vaccine developed. Those, too, fed the sense of urgency about getting one of those elusive shots.”<sup>12</sup>

Efforts to encourage vaccination may have been too successful. The media, with its heavy coverage of the Colorado children who died and the subsequent spotlight on vaccine shortages, had convinced people of the seriousness of influenza. But demand had now outstripped supply, and public health officials decided to change their approach. Contrasting her call to action a month prior, encouraging the public to get vaccinated, now the CDC Director's message was one of restraint:

We don't have scientific evidence or epidemiologic evidence to suggest that this year's influenza outbreak is worse than it has been in the past or that the strain is more virulent than strains that we've dealt with before. It's just simply too early in the course of the outbreak to say for sure how this will compare overall, but obviously the early start and the early widespread activity has given us a great deal of concern, and

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<sup>10</sup> Associated Press, “Four Children Die Of Flu in Colorado,” *New York Times*, November 27, 2003.

<sup>11</sup> “Interview: Dr. Martin Blaser, Infectious Diseases Society of America, discusses flu outbreaks,” *CNBC: News With Brian Williams*, December 3, 2003.

<sup>12</sup> “Analysis: Balancing science and common sense in public health.”

obviously, it's concerned a lot of people, and that's why there's been such an interest in getting the vaccination this year. ...

We wish we had more vaccine, but there are many steps that we can take besides vaccination that will be able to have an impact on the scope and magnitude of the problem.<sup>13</sup>

Gerberding asked people to stay calm and not overwhelm the healthcare system. Influenza, she explained, was just “an annoying illness”:

... it's important to remember that for healthy people, for the vast majority of us, influenza is an annoying illness, it's certainly not fun, but it's something that we will recover from with common sense self care. It's not necessary to go to the emergency room or to visit a physician simply because you have the flu. The treatment is good old-fashioned rest, fluids and the over-the-counter medications that we typically use to treat symptoms.<sup>14</sup>

## Two footed drivers

By the end of the 2003-04 flu season, it became clear that Gregory Poland's expert prediction of the “worst flu season we've had in several decades”<sup>15</sup> was off by several decades. In a summary report, the CDC noted: “Preliminary data from national influenza surveillance systems indicate that the current season was more severe than the previous three seasons but was within the range expected for a typical A (H3N2) season,”<sup>16</sup> the last one of which was in 1999. Newspaper headline writers conveyed that message in mixed ways. Some cast it as indicative of a severe season (*Washington Post* headline: “Past Season's Flu Worst in 4 Years”), while others were more dispassionate (*Atlanta Journal-Constitution*: “CDC: U.S. flu season typical”).<sup>17</sup>

The public's response to the 2003 season—from indifference to obsession—mirrored officials' attempts to alarm first and then calm later. Numerous pre-influenza season messages had emphasized the “serious” nature of the disease, evidenced so clearly with the CDC's new mortality statistics. But by mid-season and in the face of intense demand for vaccine and a frustrated public, the CDC downgraded the threat of influenza from “serious” to “annoying,” suggesting that panic was unnecessary. Home rest would do.

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<sup>13</sup> U.S. Centers for Disease Control and Prevention, “CDC Media Relations - Telebriefing Transcript”, December 11, 2003, <http://www.cdc.gov/media/transcripts/t031211.htm>, (accessed July 13, 2010).

<sup>14</sup> Ibid.

<sup>15</sup> Associated Press, “Mayo Clinic specialist predicts worst flu season in 30 years”, November 25, 2003.

<sup>16</sup> “Update: influenza activity--United States, 2003-04 season,” *MMWR. Morbidity and Mortality Weekly Report* 53, no. 13 (April 9, 2004): 284-287. In separate testimony to the United States Senate, CDC Deputy Director Dr. Stephen Ostroff made a similar comment, saying the season ended up “on par” with other recent H3N2 virus dominant seasons. See Stephen Ostroff, “Testimony to the Special Committee on Aging, US Senate”, September 28, 2004, 16, <http://www.hhs.gov/asl/testify/t040928.html>, (accessed July 11, 2011).

<sup>17</sup> Glen Nowak, “Planning for the 2004-05 Influenza Vaccination Season: A Communication Situation Analysis [PDF Part 2]”, April 15, 2004, [http://www.ama-assn.org/ama1/pub/upload/mm/36/2004\\_flu\\_nowak02.pdf](http://www.ama-assn.org/ama1/pub/upload/mm/36/2004_flu_nowak02.pdf), (accessed August 20, 2008).

Dr. Michael Osterholm, former state epidemiologist of Minnesota and now director of the Center for Infectious Disease Research and Policy at the University of Minnesota, called public health experts “the classic two-footed drivers. We have one foot on the accelerator and one foot on the brake.”<sup>18</sup> One emphasizes threats while the other calms fears, a practice that can quickly lead to public confusion and skepticism. The year 2003 may have been turbulent, but it paled in comparison to the drama of 2004.

### **The 2004 flu crisis: 50 million vaccine doses disappear overnight**

On October 5, 2004, British drug regulators forced Chiron Corporation’s Liverpool based vaccine production facility to halt its influenza vaccine production—then in full swing to manufacture millions of vaccine doses for the upcoming 2004-2005 influenza season. But unacceptable levels of bacterial contamination had been discovered in some lots of vaccine. With immediate effect, the company was prohibited from releasing any batches of its influenza vaccine to market.<sup>19</sup> The news hit the US without warning. Even the Food and Drug Administration (FDA)—the US agency responsible for ensuring the safety and efficacy of drugs—was caught by surprise, and had no prior knowledge of the UK action until it became public.

Until October 5, Chiron had much to look forward to. Business was good for the Sunnyvale, CA based company. By 2004, it had become the world’s second largest supplier of influenza vaccine.<sup>20</sup> Influenza vaccine sales had nearly quintupled between 2001 and 2003.<sup>21</sup> And in two short years, it had doubled its supply to the US market. On October 4, the day before the shutdown, US officials were still expecting Chiron’s UK plant to produce between 46 and 48 million doses of influenza vaccine, but the British shut down action meant Americans would face a season with only half of the expected supply.

The vaccine shortage could not have come at a worse moment for President Bush. October was the height of the presidential campaign season, and as reports surfaced of anxious Americans once again overwhelming health clinics across the country, democratic challenger John Kerry took full advantage of the moment. “George Bush and the Republicans are so busy kowtowing to drug companies, so busy giving them billions, helping them price gouge, pumping up their profits, so busy selling us out, they can’t even get vaccines to keep pregnant woman safe from the flu,” Kerry said in a radio advertisement. “Four more years? They haven’t earned it.”<sup>22</sup> Kerry argued that the loss of vaccines was clear evidence of Bush’s incompetency: “If you can’t get flu vaccines to Americans, what kind of health care program are you running? It’s a serious demonstration of the failure of leadership.”

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<sup>18</sup> “Analysis: Balancing science and common sense in public health.”

<sup>19</sup> *The Nation’s Flu Shot Shortage: Where Are We Today and How Prepared are We for Tomorrow?* (U.S. Government Printing Office, 2004), 85, <http://frwebgate6.access.gpo.gov/cgi-bin/TEXTgate.cgi?WAISdocID=750558468062+0+1+0&WAIAction=retrieve>, (accessed May 24, 2010).

<sup>20</sup> Doug Pinnell, “Chiron Vaccines Presentation National Influenza Summit Meeting”, April 29, 2004.

<sup>21</sup> *SEC Form 10-K for CHIRON CORP. Annual Report.*, Form 10-K, March 3, 2004, <http://biz.yahoo.com/e/040303/chir10-k.html>, (accessed June 30, 2011).

<sup>22</sup> Bennett Roth, “Candidates trade shots over flu vaccine dilemma,” *Houston Chronicle*, October 20, 2004, <http://www.chron.com/disp/story.mpl/politics/2856397.html>, (accessed June 30, 2011).

President Bush and HHS Secretary Tommy Thompson defended themselves by focusing on what went right: "Simply put," Thompson declared, "the nation is better prepared to meet the challenges of this flu season because of the unprecedented steps taken in the last three years under President Bush."<sup>23</sup>

Partisan politics was not limited to the presidential contenders crisscrossing the country. In Washington, the House Committee on Government Reform held a hearing on November 17 to investigate the vaccine shortage. Emotions were running high. Representative Henry Waxman, democrat, of California:

Since the vaccine shortage began, senior administration officials, including Acting FDA Commissioner Lester Crawford, have been reassuring the public that the FDA made no mistakes and did everything possible to protect the vaccine supply.

Today we will evaluate those claims.

On October 13th, Chairman Davis and I asked FDA to provide copies of documents relating to its oversight of the Chiron vaccine plant in Liverpool, England. ... We have now received and reviewed over 1,000 pages of documents. ... The documents show that FDA failed to provide effective oversight. Expert scientists at FDA knew about serious problems at the Liverpool facility in June 2003, but there was not sufficient leadership at the agency to ensure that they were fixed. ...

The Chiron plant in Liverpool was not an ordinary FDA-regulated facility. It is a facility with a history of contamination problems that makes half the supply of the U.S. flu vaccine. The plant should have received the highest priority from the Food and Drug Administration. ...

What we are witnessing is the dismantling of FDA's enforcement and oversight capabilities. ... there is no better example of what is wrong at the FDA than its failures at the Chiron facility<sup>24</sup>

Waxman placed heavy emphasis on the FDA's June 2003 inspection of the Liverpool plant. "If FDA had ensured that the problems identified in June 2003 were fixed, this year's flu crisis might never have happened."<sup>25</sup>

But Republicans—and in particular the House committee chairman Tom Davis—urged for understanding and restraint. "Everyone's goal this year, MHRA [UK Medicines and Healthcare products Regulatory Agency], Chiron's, the FDA, is to get Chiron up and running so that they can produce flu vaccine next year." "There is no question that had the FDA gone in early or the MHRA gone in earlier and alerted them, we might have been able to avert this. But that was not part of their protocols at the time," Davis

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<sup>23</sup> Stephen Smith, "United States finds flu vaccine it hopes to buy abroad," *The Boston Globe*, October 29, 2004, [http://www.boston.com/news/nation/articles/2004/10/29/us\\_finds\\_flu\\_vaccine\\_it\\_hopes\\_to\\_buy\\_abroad/](http://www.boston.com/news/nation/articles/2004/10/29/us_finds_flu_vaccine_it_hopes_to_buy_abroad/).

<sup>24</sup> *The Nation's Flu Shot Shortage: Where Are We Today and How Prepared are We for Tomorrow?*, 9,128.

<sup>25</sup> *Ibid.*, 129.



said. In his questioning of the FDA commissioner Lester Crawford, Davis underscored that FDA had done nothing wrong and the flu vaccine crisis occurred *despite* everything being done according to protocol. The FDA's June 2003 finding of high levels of bacterial contamination had nothing to do with the British shut down order in October of 2004.

Chairman TOM DAVIS. FDA's routine protocol, as I understand it, is to inspect foreign manufacturers once every 2 years?

Mr. CRAWFORD. That is correct.

Chairman TOM DAVIS. The last routine inspection of Chiron's Liverpool facility, then, was June 2003. FDA informed the committee it accepted Chiron's response plan to correct the issues that were raised in June 2003 and, therefore, the file was closed on September 3, 2003, is that correct?

Mr. CRAWFORD. That is correct.

Chairman TOM DAVIS. If these steps were following standard FDA protocol, would there be a reason for FDA to go back to Chiron's Liverpool facilities prior to the 2-years time to reinspect?

Mr. CRAWFORD. No, we don't do that.

Chairman TOM DAVIS. So you were following protocol.

Mr. CRAWFORD. Yes.<sup>26</sup>

Questions considered by the committee were far ranging. How had the US's vaccine supply come to depend on a factory in a foreign country? Why were there only two companies making injectable influenza vaccine? What were CDC and FDA doing to get more vaccine this year? Could foreign vaccine be imported on an emergency or experimental use basis? And, most of all, how could this problem be avoided in the future?

While democrats and republicans may have disagreed about who was to blame, there was no disagreement over the importance of influenza vaccine. "I would submit that this is not Rogaine," Waxman declared, "this is a product that is essential to the health of millions of Americans to avert the flu and the consequences for those who are at risk."

Federal agencies assured lawmakers that they were doing everything they could to address the crisis. CDC, Director Gerberding told the Committee, was using 20 times more dollars for influenza than it did just two years before. CDC had gained the collaboration of Aventis Pasteur, the remaining major manufacturer, to access proprietary distribution information in an attempt to re-distribute vaccine to those most in need. And in addition, prior to the October announcement, CDC had already purchased millions of extra courses of antivirals and vaccines for the national stockpile. Finally, Gerberding

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<sup>26</sup> Ibid., 208-9.

stressed that vaccine is not the only way to fight influenza: "Vaccine is the most important component of prevention, but there are other steps that we have to focus on this year as well, including ... respiratory hygiene, hand hygiene, and, of course, antivirals."<sup>27</sup>

Vaccines, however, remains the focus of intense public attention as medical experts predicted a public health "catastrophe."<sup>28</sup> The CDC even created an unprecedented ethics panel to consider how to most ethically distribute the limited vaccine supply.

"My call to our fellow Americans is if you're healthy, if you're younger, don't get a flu shot this year. Help us prioritize those who need to get the flu shot, the elderly and the young," President Bush asked millions of Americans tuning into the presidential debates. Health officials across the US repeated the same message: if you're healthy and not at high risk of complications from influenza, "please step aside."<sup>29</sup>

### From shortage to surplus

By late January 2005, state officials in more than half of the country had dropped all restrictions on who could receive vaccine. What began as a shortage of 50 million "essential" doses turned into a discussion of surplus and possible wastage. In the period of three months, the public reaction to influenza vaccine had once again swung from one extreme to the other. Back in October, CDC had done what it could to reassure the public by rationing vaccine to those most in need and offering calming messages. "Take a deep breath; this is not an emergency," Director Gerberding had told the press. "We will work through this as we have with other shortages in the past."<sup>30</sup> In a public service announcement aired nationwide, the CDC once again assured Americans that influenza was not that worrisome, asking people to embrace influenza as an annoying but not serious disease: "keep in mind, most people with flu will have an annoying illness but will recover just fine."<sup>31</sup> But by February, with vaccine surpluses on the horizon, the CDC looked for ways to use up remaining vaccine. It entered into an arrangement to have Sanofi Pasteur market government-purchased vaccine to public and private providers.<sup>32</sup> Still, around 4.5 million vaccines went unused.<sup>33</sup>

Unused vaccine is not a new problem to influenza vaccination campaigns. Most years, millions of vaccines go unused, and officials bemoan the fact that so many people do not get vaccinated despite their recommendations. In 2004-05, even if Chiron's vaccine had not been condemned, the expected

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<sup>27</sup> Ibid., 139.

<sup>28</sup> Sabin Russell, "Doctors warn of flu shot 'disaster' / Organization urges Bush to call summit," *San Francisco Chronicle*, October 19, 2004.

<sup>29</sup> "TOMMY THOMPSON HOLDS A NEWS CONFERENCE REGARDING THE FLU - NEWS CONFERENCE" (Political Transcripts by Federal Document Clearing House, October 21, 2004); U.S. Centers for Disease Control and Prevention, "Public Service Announcement for 2004-05 Flu Season."

<sup>30</sup> Jeanne Whalen, Betsy McKay, and Sarah Boseley, "U.S. Flu Vaccines Face Rationing As Plant Is Shut --- British Regulators Suspend Production at Chiron Unit; Europe, Asia to Feel Effects," *Wall Street Journal*, October 6, 2004.

<sup>31</sup> U.S. Centers for Disease Control and Prevention, "Public Service Announcement for 2004-05 Flu Season."

<sup>32</sup> Julie L Gerberding, "US Influenza Supply and Preparations for the Future", February 10, 2005, 11.

<sup>33</sup> "Lessons from flu season (Editorial)," *Times-Picayune*, March 24, 2005.

100 million vaccines would have been insufficient to vaccinate the 188 million<sup>34</sup> Americans CDC recommended should be vaccinated.

Unused vaccine may not be much of a problem if vaccines could be stored and used at a later date when demand rebounds. But unlike other vaccines, influenza vaccines get reformulated and manufactured anew on an annual basis in response to constant changes in the strains of influenza virus circulating in the wild. Influenza is not a single virus, but a set of viruses which get classified according to their type (A, B, or C), subtype (e.g. H3N2, indicating the particular hemagglutinin (H) and neuraminidase (N) proteins on the virus's surface), and region and year of discovery. Influenza viruses have survived and remained able to infect human populations for centuries in part by perpetually escaping the defenses of the human immune system through slight point mutations in the genes encoding for its surface hemagglutinin and neuraminidase proteins.

Deciding which strains of influenza the annual vaccine should aim to protect against is a decision that must be taken months in advance of the winter season due to the lengthy manufacturing and licensing process. While most influenza vaccines are trivalent, containing three strains of influenza—one type A/H3N2 strain, one A/H1N1, and one influenza B strain (which are not divided into subtypes)—there is still no guarantee that these strains will match those in actual circulation. Once the decision to manufacture is made, however, the strains chosen cannot be changed mid-course, and any unused doses will expire unused. In 2000, 8 million doses were discarded. The following year, 10 million. Then 13 million. And in the 2003-04 season, four million doses went unused despite the public's initial anxiety and run on vaccines after heavy media coverage of the Colorado children deaths.

Unlike childhood vaccinations such as those for polio, measles, or whooping cough—all of which have very high rates of uptake in the United States—influenza vaccines have, historically, been considered “adult” vaccines, and were targeted towards the elderly, the group disproportionately affected by influenza's complications. That influenza vaccine is administered annually to adults, rather than once during childhood, raises an entirely different set of questions about how vaccines end up in people's bodies. Where children are often vaccinated at healthy child checkups at the doctor's office (with a well-functioning financing system to ensure even those who cannot afford vaccines receive them), and schools in addition monitor students' vaccination status, adults have been more difficult to target. Even when vaccines are available, financial barriers do not exist, and adult patients make regular doctor visits, former directors of the CDC's National Immunization Program explain: “Well child care is a major part of pediatric practice; ‘well adult care’ is not as big a part of the work of most clinicians caring for adults.”<sup>35</sup>

Furthermore, even the logic behind vaccination has been somewhat different for influenza as compared to other vaccines. Childhood vaccinations are administered in large part to gain a society-wide effect called herd immunity, preventing epidemics because a sufficient proportion of the community is

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<sup>34</sup> Testimony of CDC Director Julie Gerberding in “The Perplexing Shift from Shortage to Surplus: Managing This Season's Flu Shot Supply and Preparing for the Future, Committee on Government Reform, US House of Representatives” (U.S. Government Printing Office, February 10, 2005), 20.

<sup>35</sup> Alan R Hinman and Walter A Orenstein, “Adult immunization: what can we learn from the childhood immunization program?,” *Clinical Infectious Diseases* 44, no. 12 (June 15, 2007): 1533.

vaccinated to effectively stop the efficient spread of infectious disease. While individual protection from disease is of course part of the purpose of all vaccines, for most of influenza vaccine's history (and with few exceptions such as the now terminated program of universal vaccination of schoolchildren in Japan<sup>36</sup>), individual protection has been the *primary* goal of vaccination, which is why those with a higher than average risk of complications from influenza such as the elderly population, are targeted in vaccination campaigns. All of these factors, plus the fact that influenza vaccination is voluntary (with a few notable exceptions such as the military which has mandated influenza vaccine for all active duty personnel since 1940<sup>37</sup>), have led to a situation where despite federal guidelines suggesting that the majority of Americans "should" get the shot, in reality most do not (Table 1.2).

### **Influenza: "acceptable" threat or "serious" disease?**

Influenza experts and officials in part attribute the public's overall lukewarm response to influenza vaccines to people's "acceptance" of the disease. As the outspoken Michael Osterholm of the University of Minnesota wrote in the *New England Journal of Medicine*:

During a typical year in the United States, 30,000 to 50,000 persons die as a result of influenzavirus infection, and the global death toll is about 20 to 30 times as high as the toll in this country. We usually accept this outcome as part of the cycle of life. Only when a vaccine shortage occurs or young children die suddenly does the public demand that someone step forward to change the course of the epidemic.<sup>38</sup>

Dr. Anthony Fauci, head of the National Institute of Allergy and Infectious Diseases and one of the world's most celebrated infectious disease experts, concurs:

Seasonal influenza is a relatively predictable annual event resulting in ~36,000 deaths and 200,000 hospitalizations in the United States and a global burden of ~500,000 deaths every year. One of the challenges of seasonal influenza, like so many global diseases, such as malaria and tuberculosis, is that there is a consistent disease burden from year to year. Thus, the world has accepted this disease burden, and a general assumption exists that there is little that can be done about it.<sup>39</sup>

The general public may accept influenza as a normal part of the ups and downs of life—an unpleasant experience to be sure, but a temporary one. Most people do not actively seek vaccine to prevent influenza, nor medical attention when they come down with influenza-like symptoms. But every now and then—like in 2003 and then again in 2004—people, that is, healthy people, rush to vaccines with an

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<sup>36</sup> Thomas A. Reichert et al., "The Japanese Experience with Vaccinating Schoolchildren against Influenza," *N Engl J Med* 344, no. 12 (March 22, 2001): 889-896.

<sup>37</sup> "2009 National Influenza Vaccine Summit: June 29--July 1, 2009 Meeting Summary", 2009, 16, [http://www.preventinfluenza.org/NIVS\\_2009/summit\\_minutes.pdf](http://www.preventinfluenza.org/NIVS_2009/summit_minutes.pdf), (accessed March 31, 2010).

<sup>38</sup> Michael T Osterholm, "Preparing for the next pandemic," *The New England Journal of Medicine* 352, no. 18 (May 5, 2005): 1839.

<sup>39</sup> Anthony S. Fauci, "Seasonal and Pandemic Influenza Preparedness: Science and Countermeasures," *The Journal of Infectious Diseases* 194, no. 2 (November 1, 2006): S73-S76.

intensity that overwhelms the system. During a CDC teleconference, a *CNN* reporter asked Director Gerberding for an explanation.

MS. FALCO: Hi, Dr. Gerberding, thanks for taking our questions. I have two questions. ... why do we need to have the fear, or the idea of a shortage to get folks to get their flu shots? ...

DR. GERBERDING: The reason why people are not motivated to get a flu shot under ordinary circumstances is complex. I don't think we have a full answer. I wish we did. But certainly flu is something that for most people is such a benign illness. Many people don't appreciate that it can result in hospitalization, various complications. For about 36,000 people every year, death.

I think as a society, we drastically underestimate how important flu is to our health and the health status of our families, and we're used to it, and it just doesn't seem like such an important health issue, until you step back and really think about the big picture and look at from a population perspective.<sup>40</sup>

Officials and others who study influenza often appeal to this “population perspective.” Nationally, the agency has estimated that 200,000 hospitalizations and 36,000 deaths can be attributed to influenza each year. To put that number in perspective, 36,000 deaths is only a few thousand less than the average 40,000 that are killed in car accidents. For officials like Gerberding, “the big picture” means focusing on these statistics, not the “benign illness” most people experience. Officials argue that the statistics are *prima facie* evidence that influenza is a serious threat to the public health—and they wish more Americans would see it their way. The CDC website therefore tries to rid the public of the perception that influenza is benign despite its acknowledgement that for most people, it indeed is a benign illness:

Influenza (often called the flu) is not just a bad cold. It's a serious illness that can lead to pneumonia and even death.<sup>41</sup>

Health officials are however far from the only people who stress the statistics of influenza and portray it as a serious illness or major public health threat. The CDC's *JAMA* publication which computed estimates of deaths and hospitalizations from influenza is the second most cited article on the topic of influenza in all the scientific literature.<sup>42</sup> Many of these scientific publications which cite the CDC's statistics often do so in the opening lines of their paper. “Influenza is an annual major public health threat. In the United States, influenza epidemics usually occur during the winter months between

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<sup>40</sup> U.S. Centers for Disease Control and Prevention, “CDC Media Relations - Telebriefing Transcript - November 10, 2005,” *CDC.gov*, November 10, 2005, <http://www.cdc.gov/media/transcripts/t051110.htm>, (accessed May 20, 2009).

<sup>41</sup> U.S. Centers for Disease Control and Prevention, “Take Charge of Your Diabetes: 11. Vaccinations”, May 21, 2011, <http://www.cdc.gov/diabetes/pubs/tcyd/vaccin.htm>, (accessed June 30, 2011).

<sup>42</sup> As of June 26, 2011, the CDC's paper (Thompson et al., “Mortality associated with influenza and respiratory syncytial virus in the United States.”) was cited 1,051 times according to *ISI Web of Knowledge*.

November and April and are responsible for an average of 36,000 excess deaths per year,” declares a highly cited paper on the use of antiviral agents to contain a pandemic of influenza.<sup>43</sup> Similarly, in paper calling for the mandatory vaccination of healthcare workers, Gregory Poland and colleagues begin their paper by stressing how many people are killed by influenza each year, citing the CDC’s paper.<sup>44</sup>

By themselves, most statistics are just numbers, and numbers without context can be meaningless. But when people use disease statistics, they often do so to persuade others that the topic is important or motivate readers to behave in a certain way. Efforts to encourage donations for cancer research often stress that cancer is the second leading cause of death in the United States. Awareness campaigns for breast cancer have been driven by comparisons between the number of breast cancer deaths and the combined total of men who died in World War I, World War II, and the Korean and Vietnam wars.<sup>45</sup> Appeals for more organ donors often stress the statistics of how many people die each year because of a shortage of suitable donors.

Because statistics are numbers, they are especially useful in the art of persuasion because numbers have the tendency to be trusted as neutral and objective.<sup>46</sup> “The most useful numbers to select for raising awareness among lay audiences are those that demonstrate the large magnitude or seriousness of the problem, and that are likely to be easily understood by lay audiences,” says a textbook on the use of data in public health.<sup>47</sup> Is influenza a serious disease? The CDC attempts to convince the public it is by stressing the numbers. For the 2003-04 season, CDC created a poster to help dispel the “myths” about influenza (Figure 1.1).

**MYTH: “The flu isn’t a serious disease.”**

**FACTS: Influenza (flu) is a serious disease** of the nose, throat, and lungs, and it can lead to pneumonia. Each year about 200,000 people in the U.S. are hospitalized and about 36,000 people die because of the flu. Most who die are 65 years and older. But small children less than 2 years old are as likely as those over 65 to have to go to the hospital because of the flu.<sup>48</sup>

In the world of influenza, leveraging death statistics is a key practice in the attempt to motivate ever increasing numbers of the public to demand influenza vaccine. “We estimate that 36,000 Americans die each year from the flu, and this is just during an average flu year,” Dr. Stephen Ostroff, deputy director of the National Center for Infectious Diseases at CDC, told a congressional hearing. “Far too many of

<sup>43</sup> Ira M Longini et al., “Containing pandemic influenza with antiviral agents,” *American Journal of Epidemiology* 159, no. 7 (April 1, 2004): 623-33.

<sup>44</sup> Gregory A Poland, Pritish Tosh, and Robert M Jacobson, “Requiring influenza vaccination for health care workers: seven truths we must accept,” *Vaccine* 23, no. 17-18 (March 18, 2005): 2251-5.

<sup>45</sup> David E. Nelson, Bradford W. Hesse, and Robert T. Croyle, *Making Data Talk: Communicating Public Health Data to the Public, Policy Makers, and the Press* (Oxford University Press, 2009), 286.

<sup>46</sup> Porter, *Trust in Numbers*.

<sup>47</sup> Nelson, Hesse, and Croyle, *Making Data Talk*, 278.

<sup>48</sup> U.S. Centers for Disease Control and Prevention, “Flu Vaccine Facts & Myths”, 2007.

these hospitalizations and deaths are avoidable, even those that occur among our oldest citizens. The keys to prevention when it comes to flu are vaccination, vaccination, and vaccination.”<sup>49</sup>

The logic of the influenza vaccine campaign is therefore straightforward: with a life-saving vaccine and a disease that kills tens of thousands each year, there is an imperative to vaccinate and thereby save lives. “Influenza remains the most important cause of vaccine-preventable deaths in the United States,” according to the CDC statisticians who published the 36,000 deaths statistic.<sup>50</sup> In the elderly population, which accounts for 90% of the 36,000 estimate, vaccination is “very effective in preventing severe illness, secondary complications, and death,” a scientist from the National Institutes of Health informed a Senate special committee on aging.<sup>51</sup>

### **The evolution of influenza vaccine policy**

The emphasis that many influenza vaccine policy planners place on what remains to be achieved—the need to increase vaccination coverage and fill gaps between current and target levels—obscures an appreciation of how much has already been achieved in increasing influenza vaccine production and consumption over the 1980s and 1990s.

When influenza vaccine was first introduced on a population basis in the U.S., its target was the military, not civilians. World War I had taught military planners to expect higher levels of respiratory illness where soldiers lived and operated in close proximity of each other. The military’s response, starting in 1940, was to vaccinate.<sup>52</sup> But influenza vaccine policy did not reach the general public until the experience of the 1957 “Asian flu,” when concern over a novel influenza virus causing epidemics in East Asia prompted Congress to appropriate \$110,000 for “public information and educational purposes,” a campaign which employed press releases, press conferences, and exploited the media in order to encourage use of the vaccine “as the only preventive measure available.”<sup>53</sup> The policy decisions of 1957, however, amounted to little more than an ad-hoc response to a single epidemic. It was not until 1963-64<sup>54</sup> that a federal policy on influenza vaccination in the general population was drafted and kept up to date on an annual basis, under the leadership of the Advisory Committee on Immunization Practices (ACIP). (ACIP still drafts U.S. influenza vaccine policy today.) But through the sixties and seventies, levels of vaccination remained low despite the presence of a federal policy.

From early on, ACIP considered influenza a largely intractable disease and not amenable to significant reduction. The virus constantly mutates, thereby evading any attempt of the human body to produce

<sup>49</sup> *Combating the Flu: Keeping Seniors Alive* (U.S. Government Printing Office, 2004), 3.

<sup>50</sup> William W. Thompson et al., “Are estimates of influenza-associated deaths in the US really just PR?,” *BMJ Rapid Response* (January 18, 2006), [http://www.bmj.com/content/331/7529/1412.extract/reply#bmj\\_el\\_126308](http://www.bmj.com/content/331/7529/1412.extract/reply#bmj_el_126308), (accessed June 30, 2011).

<sup>51</sup> Pamela McInnes, “NIH’s Biomedical Research Response to Influenza”, September 28, 2004, 10.

<sup>52</sup> Herschel E. Griffin, “Influenza control in the Armed Forces,” *Public Health Reports* 73, no. 2 (February 1958): 145.

<sup>53</sup> J. Stewart Hunter, “Public information and education,” *Public Health Reports* 73, no. 2 (February 1958): 149-150.

<sup>54</sup> W W Williams et al., “Immunization policies and vaccine coverage among adults. The risk for missed opportunities,” *Annals of Internal Medicine* 108, no. 4 (April 1988): 616-625; Joel Kavet, “Vaccine utilization: trends in the implementation of public policy in the USA,” in *Influenza: Virus, Vaccines, and Strategy: Proceedings of a Working Group on Pandemic Influenza, Rougemont, 26-28 January 1976*, ed. Philip Selby (London: Published for Sandoz Institute for Health and Socio-Economic Studies by Academic Press, 1976), 297.

long-lasting immunity after infection. And vaccines, which had to be constantly reformulated in a never-ending game of catch-up, could do no better. Unlike vaccines for other well-known infectious disease such as polio or measles, influenza “vaccines are among the least satisfactory immunizing agents in general use today,” the ACIP pessimistically wrote in 1970.<sup>55</sup> Federal policymakers therefore aimed not to eliminate or eradicate influenza, but rather ameliorate its more harmful effects which tend to occur most commonly in the elderly and chronically ill.

Older and chronically ill individuals in the population are essentially the only ones who have any risk of serious complications or fatality from influenza. Therefore, annual vaccination has been recommended for them while not being recommended for the entire population.<sup>56</sup>

Public responses to influenza vaccine reflected the lack of enthusiasm at the federal-level. Among the 65-plus elderly population that officials recommended get vaccinated, only 15-20% in fact did during the late 1960s and early 1970s. A survey of 5,000 Medicare recipients conducted by the Food and Drug Administration in 1974 found 80% were unaware of the federal guidelines suggesting they get vaccinated. Forty percent of those not receiving the vaccine felt they did not need one.<sup>57</sup>

Three years later, in 1976, vaccination levels surged as the country mounted a nationwide campaign to vaccinate all Americans in anticipation of an epidemic of “swine flu.” The program was however halted prematurely amidst concern that the program was harming more than it helped: the predicted epidemic failed to materialize and news of elderly deaths and a debilitating neurological condition following vaccination were widely reported by the media. The result helped foster a general distrust among certain populations in subsequent influenza vaccination campaigns.<sup>58</sup>

Nevertheless, federal efforts continued to expand over the next years and decades. In 1979, the Surgeon General published *Healthy People: The Surgeon General’s Report On Health Promotion And Disease Prevention*, and named influenza as one of its many health priorities. “In 1977 influenza and pneumonia together constituted the fourth leading cause of death among older people,” the report declared.

It may be true that for some of the elderly who are in late stages of physical and mental deterioration, death from these acute infections may not be untimely. Pneumonia has been called the “old man’s friend” for the painless ending of life it may provide.

But many deaths occur in older people otherwise healthy and with much yet to live for. They can be prevented. ...

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<sup>55</sup> Kavet, “Vaccine utilization: trends in the implementation of public policy in the USA,” 298.

<sup>56</sup> Ibid.

<sup>57</sup> Francis A. Ennis et al., “Acceptance of vaccination by the elderly,” in *Influenza: Virus, Vaccines, and Strategy: Proceedings of a Working Group on Pandemic Influenza, Rougemont, 26-28 January 1976*, ed. Philip Selby (London: Published for Sandoz Institute for Health and Socio-Economic Studies by Academic Press, 1976), 313,315.

<sup>58</sup> Morens, “Influenza-related mortality.”



For all high-risk individuals, annual vaccination against influenza is recommended—and those over age 65 should therefore seek the advice of public health authorities and personal physicians.<sup>59</sup>

In 1984, ACIP guidelines expanded upon this recommendation. In addition to the long standing recommendation for elderly and others at high risk to get an annual influenza vaccine, the 1984 recommendations included new language advising physicians in addition to “administer vaccine to any persons in their practices who wish to reduce their chances of acquiring influenza infection.”<sup>60</sup> “The ‘highest risk’ group consisted of persons most likely to be seeing physicians regularly - i.e., persons who could be immunized during office visits,” Dr. Steve Schoenbaum, who had worked on the new recommendations under the leadership of CDC influenza head Alan Kendal, recently recalled.

We went a step further and recommended that the medical personnel caring for them, physicians, office nurses, and hospital workers, be immunized since they would be most exposed to influenza at a time that they most needed to be healthy and help others. I confess that there was not, at that time, any evidence, just “common sense”, to support the recommendation for health care workers, and such evidence only developed later.<sup>61</sup>

Federal policy, which a decade earlier had been described as “no more than a statement of policy,”<sup>62</sup> was becoming increasingly aggressive. Schoenbaum said that “the objective was to assure that people who needed it got into the habit of annual influenza immunization.” In October 1987, the ACIP warned: “Unless vigorous measures are used to control influenza in the 1987 to 1988 season, mortality due to this disease may increase because the proportion of elderly persons in the United States is rising, and age and its associated chronic diseases are risk factors for severe influenza illness.”<sup>63</sup> In 1990, a much larger and comprehensive *Healthy People 2000* was launched, pegging a national goal of reducing “epidemic-related pneumonia and influenza deaths among people aged 65 and older to no more than 7.3 per 100,000” Americans, and raising vaccination levels in the noninstitutionalized elderly population to 60%.<sup>64</sup> In 1993, Medicare began to pay for influenza vaccine, removing financial barriers to vaccination for the elderly.<sup>65</sup> Vaccine coverage in turn increased substantially. In the 1987-88 season, only 28% of seniors were vaccinated. By 1996, the proportion had more than doubled and around 60% of all American seniors were getting the vaccine (Table 1.2).

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<sup>59</sup> U.S. Department of Health, Education, and Welfare, *Healthy People: The Surgeon General's Report On Health Promotion And Disease Prevention*, 7-13.

<sup>60</sup> U.S. Centers for Disease Control, “Recommendation of the Immunization Practices Advisory Committee (ACIP) Prevention and Control of Influenza,” *MMWR* 33, no. 19 (May 18, 1984): 253-60,265-6.

<sup>61</sup> Steve Schoenbaum, “Envy of Pump Handle Removers and Eventual Gratification”, July 9, 2010, [http://scienceblogs.com/bookclub/2010/07/envy\\_of\\_pump\\_handle\\_removalers\\_a.php](http://scienceblogs.com/bookclub/2010/07/envy_of_pump_handle_removalers_a.php), (accessed October 5, 2010).

<sup>62</sup> Kavet, “Vaccine utilization: trends in the implementation of public policy in the USA,” 305.

<sup>63</sup> U.S. Centers for Disease Control, “Recommendations of the Immunization Practices Advisory Committee Prevention and Control of Influenza,” *MMWR* 36, no. 24 (June 26, 1987): 373-80,385-7.

<sup>64</sup> U.S. Department of Health and Human Services and Public Health Service, *Healthy People 2000: National Health Promotion and Disease Prevention Objectives* (U.S. Government Printing Office, 1990), 514, 521.

<sup>65</sup> Peng-Jun Lu et al., “Influenza Vaccination Trends Among Adults 65 Years or Older in the United States, 1989-2002,” *Arch Intern Med* 165, no. 16 (September 12, 2005): 1849-1856.

But subsequent years would show that vaccine consumption among many of the so-called noninstitutionalized elderly had begun to level off.<sup>66</sup> In addition, despite annual influenza vaccination levels reaching historical highs, manufacturers were leaving the business. The phenomenon was not limited to influenza vaccine, but followed trends in the overall vaccine market: from 26 companies that manufactured vaccines for the US in 1967, by 2005 there were just five. Analysts have pointed to a variety of reasons for the decline, including a smaller market compared to drugs (due to a lower price often capped by a virtual monopsony purchaser such as Medicare, and limited to far fewer doses over a lifetime), plus high fixed, sunk costs, and the ever present concern over maintaining manufacturing standards within regulations.<sup>67</sup> Even for the influenza vaccine market, excitement over the large number of individuals recommended to get the vaccine annually was dampened by the risks of production and lack of guaranteed purchase. In 1994, five manufacturers supplied influenza vaccine to the U.S. market. When a decade later British regulators temporarily suspended Chiron's license to manufacture influenza vaccine, Americans were left with just one other supplier of injectable vaccine.<sup>68</sup> As one congressman noted, "you would think normally the old adage of supply and demand would work in this environment. Obviously, the normal forces are not at work here."<sup>69</sup>

### **Persuading Americans into action**

In November 2000, the HHS released the next *Healthy People 2010* objectives. For influenza, the new target was especially ambitious: vaccinating 90% of all Americans aged 65 years and above.<sup>70</sup> But meeting these goals would require significant changes to the status quo. On the demand side, many of the financial barriers to vaccination had now been solved. A 1999 Medicare survey shows that those not getting vaccinated had other reasons including not thinking the vaccine was necessary and concerns about its safety.<sup>71</sup> Convincing these people to get vaccinated would mean changing their beliefs, not simply improving access. On the supply side, the problems were no less daunting, with many barriers in communication between the many public and private stakeholders.

The National Influenza Vaccine Summit emerged as a way to address these issues. It is a policy and advocacy forum, co-founded by the American Medical Association and CDC, and committed to the *Healthy People* goals. The Summit works to create "united influenza vaccination goals," and get all stakeholders "on the same page" by creating common understanding, clarifying various stakeholders' goals, and increasing communication.<sup>72</sup> Its first meeting was held in March 2001 following delays in

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<sup>66</sup> Ibid.

<sup>67</sup> Michelle M Mello and Troyen A. Brennan, "Legal Concerns and the Influenza Vaccine Shortage," *JAMA* 294 (October 12, 2005): 1817-1820.

<sup>68</sup> *The Nation's Flu Shot Shortage: Where Are We Today and How Prepared are We for Tomorrow?*, 226.

<sup>69</sup> Ibid.

<sup>70</sup> U.S. Department of Health and Human Services, *Healthy People 2010: Understanding and Improving Health*, 2nd ed. (Washington, DC: U.S. Government Printing Office, 2000), 14-45, <http://www.healthypeople.gov/2010/Document/pdf/uih/2010uih.pdf>.

<sup>71</sup> "Reasons reported by Medicare beneficiaries for not receiving influenza and pneumococcal vaccinations--United States, 1996," *MMWR. Morbidity and Mortality Weekly Report* 48, no. 39 (October 8, 1999): 886-890.

<sup>72</sup> Tan, "What is the National Influenza Vaccine Summit?"

influenza vaccine production and distribution in the previous season,<sup>73</sup> and brought together 30 public and private stakeholders from 15 organizations.<sup>74</sup> Its success is readily apparent. By 2010, the numbers attending had risen to nearly 300 participants from more than 120 organizations.<sup>75</sup>

For a number of years, the Summit has featured presentations by CDC specialists who have focused on shaping public messages about influenza and the vaccine. At the fourth annual summit on the morning of Wednesday, April 14, 2004, Glen Nowak, Associate Director of Health Communications at the National Immunization Program, spoke to the audience about the CDC's plans for the upcoming season. Nowak, a former University of Georgia professor of advertising with expertise in social marketing and health communications,<sup>76</sup> spoke about the relationship between media, perceptions, and the public's interest in getting vaccinated.<sup>77</sup> Following the 2003 season in which major news coverage of a few influenza-associated deaths in children in Colorado led to a rush on vaccines around the country, the CDC undertook a communications study. Nowak came to the conference to explain what he found—and what lessons could be learned.

In what he calls the “Seven-Step Recipe for Generating Interest in, and Demand for, Flu (or any other) Vaccination,” Nowak explains how messages in the media can drastically influence the public's behavior (Figure 1.2). Step 3 of the Recipe states: “Medical experts and public health authorities publicly (e.g., via media) state concern and alarm (and predict dire outcomes)— and urge influenza vaccination.” When this happens along with initial cases being associated with severe illness (like the pediatric influenza deaths in Colorado), this results in “significant media interest and attention,” Nowak notes. A graph in Nowak's presentation shows how media stories carrying the message that this “could be a bad/serious season” jumped when Dr. Poland predicted the worst season in decades. “Some component of success (i.e., higher demand for influenza vaccine) stems from media stories and information that create motivating (i.e., high) levels of concern and anxiety about influenza,” he explained.

Maintaining the media's interest in influenza can however be a challenge, according to the CDC's findings. But interest can be generated by “continued reports (e.g., from health officials and media) that influenza is causing severe illness and/or affecting lots of people helping foster the perception that many people are susceptible to a bad case of influenza” (Recipe Step 5).

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<sup>73</sup> Raymond A. Strikas, “The National Influenza Vaccine Summit: Update”, February 7, 2006, 2, [http://www.ama-assn.org/ama1/pub/upload/mm/36/nvac\\_slides.pdf](http://www.ama-assn.org/ama1/pub/upload/mm/36/nvac_slides.pdf), (accessed July 13, 2011).

<sup>74</sup> “2007 National Influenza Vaccine Summit April 19--20, 2007 Atlanta, Georgia Minutes of Meeting”, 2007, [http://www.preventinfluenza.org/summits/2007/meeting\\_minutes07.pdf](http://www.preventinfluenza.org/summits/2007/meeting_minutes07.pdf), (accessed July 21, 2010).

<sup>75</sup> Litjen Tan, “Update from the 2010 National Influenza Vaccine Summit meeting” (presented at the The National Vaccine Advisory Committee (NVAC), Washington, DC, June 2, 2010), [http://www.hhs.gov/nvpo/nvac/meetings/pastmeetings/summit\\_update\\_060210.ppt](http://www.hhs.gov/nvpo/nvac/meetings/pastmeetings/summit_update_060210.ppt), (accessed July 13, 2010).

<sup>76</sup> “Executive Leadership & Expert Bios”, June 10, 2010, <http://www.cdc.gov/media/subtopic/sme/nowak.htm>, (accessed July 13, 2010).

<sup>77</sup> Glen Nowak, “Planning for the 2004-05 Influenza Vaccination Season: A Communication Situation Analysis [PDF Part 1]”, April 15, 2004, [http://www.ama-assn.org/ama1/pub/upload/mm/36/2004\\_flu\\_nowak.pdf](http://www.ama-assn.org/ama1/pub/upload/mm/36/2004_flu_nowak.pdf), (accessed August 20, 2008); Nowak, “Planning for the 2004-05 Influenza Vaccination Season: A Communication Situation Analysis [PDF Part 2].”

Nowak envisions three broad groups in which the population can be conceptually divided: those who routinely get vaccinated against influenza, those who only sometimes do, and those who choose not to, even when recommended. Because convincing those who are already convinced would be a waste of resources, and attempting to convince those already steadfastly against vaccination may be a losing battle, Nowak puts emphasis on the middle group—those who are undecided. It is here, he asserts, that messaging may change behavior. For this population segment, “interest is often contingent on perceptions of severity of the strain, likelihood they or someone they know will contract it.” Nowak however cautions that “Inducing worry, raised anxiety, and concern in people brings forth a number of issues and presents many dilemmas for health care professionals.”

Attendance at NIVS meetings is extremely diverse, and includes individuals involved in national, state, and local public health practice and policy making, hospitals, medical organizations, pharmacists, nursing organizations, private health insurance and managed care organizations, select consumers and advocacy groups, vaccine and drug manufacturers and distributors, and the news media. What unites the group is their common desire to increasing influenza vaccine supply and demand.

Attendance is by invitation only, and while some of the more recent conferences have included reporters from various media outlets as well as public relations firms, the conference itself receives scant media attention. One notable exception came in October, 2004, when the wire service *United Press International* published an article critical of the CDC’s presentation. Titled “‘Dire’ CDC warnings hiked flu shot demand,” the UPI article highlighted Nowak’s “Seven-Step Recipe” questioning the government’s approach. Nowak defended his slides. “Nowak ... told UPI ... that he was analyzing factors that increased demand during the [previous] 2003-2004 flu season, not coaching scare tactics to increase demand for flu vaccine.”<sup>78</sup>

As the UPI is a wire service (and not a newspaper), it is up to other media outlets to put the *UPI* story in print. But none did, despite the hundreds of articles being written about influenza during the time.<sup>79</sup> As Nowak’s presentation makes clear, the media has been far more active in promoting many of what he calls “Facts we deem important,”<sup>80</sup> such as the CDC’s 36,000 estimated death statistic, than critiquing the CDC’s methods.

### **Factors that increase demand**

Knowing what messages are effective at motivating behavior is a key ingredient in any communications campaign. With so many other issues competing for the attention of the American public, convincing people that they need to get influenza vaccine is a challenge officials have struggled with for years. “It’s

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<sup>78</sup> Mark Benjamin, “‘Dire’ CDC warnings hiked flu shot demand,” *United Press International*, October 15, 2004, <http://www.upi.com/view.cfm?StoryID=20041015-112212-3043r.htm>, (accessed April 6, 2005).

<sup>79</sup> Nowak, “Planning for the 2004-05 Influenza Vaccination Season: A Communication Situation Analysis [PDF Part 1],” 16-23.

<sup>80</sup> Glen Nowak, “Communicating in Changing and Difficult Communication Environments: Some Things I’ve Learned Regarding Influenza Immunization”, May 10, 2005, 17, [http://www.ama-assn.org/resources/doc/infectious-disease/summit\\_2005\\_nowak.pdf](http://www.ama-assn.org/resources/doc/infectious-disease/summit_2005_nowak.pdf), (accessed July 22, 2010).

a lot harder to create a motivating level of concern and anxiety when a) influenza isn't yet present and b) disease severity and impact are in line with expectations," Nowak notes.

In 2002, a series of focus-group based interviews were conducted by the CDC's Office of Health Communications "to assess the understanding, appeal, and potential impact of influenza immunization messages and materials on physicians and Hispanic and African American senior citizens," populations which have historically lower influenza vaccination rates.<sup>81</sup> In order to better understand how to tailor health risk messages to specific audiences, participants in the focus groups were shown a variety of visual poster-like materials (Figure 1.3), similar to what is done in social marketing research.<sup>82</sup> One of the items tested on audiences was the "20,000 deaths" statistic. (The CDC's official estimate was revised upward to 36,000 later, in January 2003.)

The study found that among African Americans, the "Statistic of 20,000 deaths is credible and specific—lends a sense of urgency." For Hispanics, "The statement '20,000 deaths' seemed to be more eye catching and motivating than '114,000 hospitalized.'" As one participant said, "We're all trying to escape death." A more detailed report remarked: "The number 20,000 attracted people's attention. Most were shocked...." Under "Key Strengths" of the "20,000 deaths" message, the authors wrote: "20,000 deaths was compelling, frightening." They twice mentioned that the 20,000 deaths statistic "should be part of the headline."<sup>83</sup>

While the population surveyed in the focus group study was elderly senior citizens, its findings are being applied to far wider audiences. Indeed, the 36,000 mortality statistic became a central element of the CDC's strategy to market influenza vaccine. New promotional materials for the 2010-11 season, for example, claim: "Reason enough to get VACCINATED! Flu-related complications lead to about 36,000 DEATHS and 200,000 HOSPITALIZATIONS each year in the U.S." (Figure 1.4).

"Get the facts. Get vaccinated," the poster demands, as if "the facts"—or in this case, statistical estimates—speak for themselves, and inevitably will lead all readers to the conclusion that vaccination is in everyone's best interest. But on occasion, "the facts" are used for opposite effect. During the vaccine shortage of 2004, the Director of the National Institutes of Allergy and Infectious Diseases urged people to consider the facts. "Yesterday, Dr. Fauci reiterated the need for healthy residents to step aside, noting that of the 36,000 people who die of influenza each year, about 31,000 of them are elderly and the rest are infants or young children."<sup>84</sup>

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<sup>81</sup> Kari Sapsis and Alan Janssen, *Influenza and Pneumococcal Immunization: A Qualitative Assessment of the Beliefs of Physicians and Older Hispanic and African Americans* (Office of Health Communications, National Immunization Program, CDC, December 2002), <http://www.cdc.gov/vaccines/spec-grps/downloads/flubeliefs-pres.rtf>, (accessed July 3, 2010).

<sup>82</sup> Deborah C. Glik, "Risk Communication for Public Health Emergencies," *Annual Review of Public Health* 28, no. 1 (April 2007): 33-54.

<sup>83</sup> Office of Health Communications, National Immunization Program, Centers for Disease Control and Prevention, *Influenza and Pneumococcal Immunization: A Qualitative Assessment of the Beliefs of Physicians and Older Hispanic and African Americans* (Office of Health Communications, National Immunization Program, CDC, May 2003), 21, <http://www.health.gov/communication/db/FileDownload.asp?ID=171>, (accessed July 3, 2010).

<sup>84</sup> Karen A Davis, "Officials say more flu shots on way," *The Providence Journal*, October 24, 2004.

Fauci was highlighting the fact that we are not all at equal risk of death from influenza. The young adults age group featured in the many promotional CDC materials actually have an exceedingly low risk of death or hospitalization from influenza. Most of the time, however, this detail goes unmentioned—except in cases where officials are aiming to reduce demand.

### **“Grassroots” campaigns**

Motivating people to vaccinate through prominent exposure to death statistics is not the only way in which influenza vaccine is being marketed and CDC is by no means the vaccine’s sole marketer. The “Vote & Vax” project<sup>85</sup> received nearly \$750,000 from the Robert Wood Johnson Foundation<sup>86</sup> to offer influenza vaccinations to voters making their way to polling stations (Figure 1.5). In 2008, CVS/pharmacy and MinuteClinic delivered more than one million vaccines through its “Flu Shots Made Simple” marketing campaign.<sup>87</sup> A collaboration between the National Women’s Health Resource Center and The Association of Women’s Health, Obstetric, and Neonatal Nurses created the “Flu-Free and a Mom-to-Be” program, sponsored by influenza vaccine manufacturer CSL Biotherapies, which aims “create a sense of urgency surrounding influenza vaccination among pregnant women” and increase vaccination coverage rates.<sup>88</sup>

Sanofi Pasteur, a prominent influenza vaccine manufacturer, launched a major influenza vaccine marketing initiative with the American Lung Association called “Faces of Influenza” (Figure 1.6). As the name implies, the campaign aims to “put a ‘face’ on influenza illness and help Americans understand the need for annual vaccination.” Using celebrities such as former Olympian figure skater Kristi Yamaguchi, comedian and *View* talk show host Joy Behar, as well as some “not-so-famous Americans,” the campaign presents collages of faces and vignettes with which viewers might relate. Company documents describe it as a “Grassroots Regional Campaign,” including a “proven, creative, and ‘media sexy’ consumer campaign” with a “Grassroots Toolkit” including “communication templates—newsletter article, Web article, patient and consumer letter, physician letter, elected official, health official, school, office on aging.”<sup>89</sup> Sanofi Pasteur has also funded Families Fighting Flu, a campaign to raise childhood influenza vaccination rates, led by a group of parents whose children died from influenza.

### **Experts know best**

Underlying many of the promotional efforts for influenza vaccine is the assumption that the public is not rational; it is scientifically illiterate. The public holds on to “beliefs” while scientists evaluate evidence. There is the expectation that if the general public only knew what experts knew, then people would

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<sup>85</sup> Vote & Vax, “Vote & Vax”, 2011, <http://www.voteandvax.org/Home.aspx>, (accessed June 30, 2011).

<sup>86</sup> Robert Wood Johnson Foundation, “Vote & Vax 2008”, January 15, 2008, <http://www.rwjf.org/files/research/votevax2008info.pdf>, (accessed July 23, 2010).

<sup>87</sup> Donna L Haugland, “MinuteClinic & CVS Pharmacy”, June 29, 2009, [http://www.preventinfluenza.org/NIVS\\_2009/Special%20-%2020-%20Haugland.pdf](http://www.preventinfluenza.org/NIVS_2009/Special%20-%2020-%20Haugland.pdf), (accessed October 7, 2009).

<sup>88</sup> “2009 National Influenza Vaccine Summit: June 29--July 1, 2009 Meeting Summary,” 22-23.

<sup>89</sup> Sanofi Pasteur, “Influenza Vaccine Production and Immunization Update”, November 2007, <http://www.ndflu.com/Vaccine/sanofi%20pasteur%20Flu%20summit%20presentation%2011-26-07.ppt>, (accessed June 26, 2010).

behave rationally. If the public knew what experts know, it would make the same decisions regarding vaccination—that is, vaccinate.

Since the mid to late 1960s, researchers began to note a number of divergences between how experts and non-experts—usually different groups among the general/lay public—thought about various types of natural hazards and technological risks like floods, industrial chemicals, and nuclear energy. Why, for example, did people choose to live in floodplains when the likelihood of flooding was so great that it would seem to not in their best interest? Or why did people report fear and opposition to nuclear power plants in excess of driving a car, despite experts' calculation that the risk of automobile accidents far outweighed the likely harm from a nuclear reactor?

Partial answers to these questions came slowly, over a number of years, and from a variety of fields. One of the earliest answers came from the American electrical engineer Chauncey Starr, who in a 1969 paper in *Science*, suggested that the key factor to understanding risk preferences was voluntariness.<sup>90</sup> Starr suggested that the public is willing to take larger risks when the activity in question is a voluntary one. This theory offered one explanation for why smoking and automobiles, despite the high levels of risk of death associated with them, were not perceived as risky as nuclear power: the installation, operation, and management of nuclear power was involuntary, something people had little individual control over, in contrast to smoking and driving.

Many have since refined Starr's contention that voluntariness is the key factor. Slovic identified a far larger list of major factors: familiarity (versus unfamiliarity), control (or lack of control), catastrophic potential (i.e. thinking about the worst case scenario, no matter how small the likelihood), equity (i.e. are all people taking on the risk at equal levels?), and levels of knowledge (about the risk). All of these influence the magnitude of concern people had about various risks.<sup>91</sup> Slovic's so-called psychometric paradigm attempts to study individuals and quantify their perception of risk. By approaching the issue as one of risk perception, there is the assumption that hazards exist out there in the world and pose some finite risk. At times, this risk may be more or less well understood, but expert opinion can determine a best estimate and a margin of error. Nevertheless, through interviews or surveys, investigators could determine people's perception of that risk, and attempt to understand why risk perception differed from quantitative expert analyses of risk. At its best, the psychometric promised to offer a laundry list of factors which might be able to predict risk taking/aversion patterns based on the type of risk.

But while the qualities of any risk such as equity, control, and familiarity may indeed have something to do with the perception of risk, the psychometric paradigm employed a research methodology that was arguably too narrow. Psychometric research took the individual as its unit of analysis, and attempted to compare how individuals felt about risk A versus risk B. If the perceived level of risk was different, one or more of the psychometric factors could then be used to help explain why this was the case. Some have argued that this methodology misses an essential aspect of life: that we do not live in bubbles, but are instead members of society, operating under certain assumptions, with our own worldviews,

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<sup>90</sup> Chauncey Starr, "Social Benefit versus Technological Risk," *Science* 165, no. 3899 (1969): 1232 -1238.

<sup>91</sup> Paul Slovic, *The Perception of Risk*, Risk, society, and policy series (London: Earthscan Publications, 2000).

obligations, commitments, and desires. The anthropologist Mary Douglas and political scientist Aaron Wildavsky offered a new conceptualization of risk in their cultural theory of risk, and attempted to shift the central question of risk acceptability from ‘how much risk is acceptable to you?’ to ‘what kind of society do you want to live in?’<sup>92</sup> They argued, in line with Emile Durkheim, for a functionalist framework, suggesting that to understand individual behavior, perception, and preferences, we had to look beyond the individual and ask how individual action fit within the larger whole (culture, society). Understanding risk, then, required not only taking note of individual behavior, but thinking about the moral and ethical norms and factors that affected the coherence of larger society.

These cultural theories of risk argued that risks are subjective values—not numbers out there that experts calculate and about which lay people merely have more or less accurate understandings. For example, Douglas and Wildavsky argued that a death (to take a favorite unit of analysis among the quantitative theorists) could not, a priori, be assigned any particular value. It rather must be understood within a wider context: most societies, for example, distinguish and react differently to honorable deaths versus dishonorable deaths. Understanding risk, then, was not a matter of gauging the public’s rationality or irrationality, but rather understanding the ethical and moral cultural milieu within which people exist.

Some scholars even provided semi-detailed typologies to understand public reaction to potential hazards. Wildavsky and Dake, for example, argue that cultural biases in the form of “worldviews” best predict how people will react to a specific hazard. Members of each worldview—hierarchy, individualism, and egalitarianism—embody different core values, such as patriotism, law & order, or strict ethical standards.<sup>93</sup>

Most research on risk has however done little to change common beliefs about the source of divergence between expert and lay rationality, and belief that there is a true dichotomy between informed, objective, rational thinking and uninformed, irrational, and subjective thinking.<sup>94</sup> The conviction that the thoughts and beliefs of experts are ruled by this calm and objective rationality while decisions among non-experts are largely ruled by an imprecise, faulty, emotional and subjective mechanism, remains strong (Figure 1.7).

In *Making Data Talk*, a guide written by CDC employees about how to communicate scientific information to the general public, it is noted that “most scientists are strong believers in the ‘rational decision-making’ model ... people make decisions based on careful weighing of information from sources they deem as credible (i.e., scientists). ... [By contrast, lay] people use many heuristics (shortcuts), often

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<sup>92</sup> Douglas and Wildavsky, *Risk and Culture*.

<sup>93</sup> Aaron Wildavsky and Karl Dake, “Theories of Risk Perception: Who Fears What and Why?,” *Daedalus* 119, no. 4 (October 1, 1990): 41-60.

<sup>94</sup> Today this dichotomy shows up in the emerging field of neuroeconomics, where one theory holds that the brain should be conceptualized as the site of “the site of conflict between an impetuous limbic system at perpetual odds with its deliberate and provident overseer in the prefrontal cortex.” See Natasha Dow Schüll and Caitlin Zaloom, “The shortsighted brain: Neuroeconomics and the governance of choice in time,” *Social Studies of Science* 41, no. 4 (March 2011): 515-538.



relying on faulty reasoning and intuition when making decisions, rather than carefully weighing evidence.”<sup>95</sup>

At the 2005 National Influenza Vaccine Summit, one breakout group was tasked with “Increasing influenza vaccine demand” by addressing the “lack of knowledge, indifference and/or frustration in the public, priority persons and HCPs [health care providers]”:

Although there are annual media campaigns coupled with efforts of public health and medical organizations, only about a third of priority persons and about 30 million in the general public receive a vaccination each year. Clearly, the demand for vaccine by the U.S. public is lacking. The following are three obstacles to increasing public demand for influenza vaccinations. First, there are misunderstandings (myths) regarding the severity of influenza and its complications, vaccine safety; and [sic] vaccine effectiveness.<sup>96</sup>

The opinion that experts know best is also evident in the way much of the press reports on influenza. In a national poll, *Consumer Reports* asked Americans about their intention to get an influenza vaccine. Many reported that they were not seeking influenza vaccine, and the magazine ranked the most common reasons given in an article titled “12 top excuses for skipping the flu shot are exposed.”<sup>97</sup> Forty-five percent of those people said that they didn’t get sick. *Consumer Reports* called this an “excuse.”

**Excuse:** You don’t get sick (45 percent)

**Reality:** Just because you haven’t had the flu in the past doesn’t mean you won’t get it this year. And just one bout of the disease may have you running for the flu shot next year. Indeed, the Centers for Disease Control and Prevention estimates that each year the flu sends some 225,000 people to the hospital, and causes the death of 35,000.<sup>98</sup>

Apparently for *Consumer Reports*, the public is not suitably concerned. It needs a “reality check.”

## Do experts agree?

Juxtaposing “excuses” with “reality” creates the impression that experts armed with statistics and facts know what is true and what is right, and the rest of us have only lay conceptions of the world which amount to little more than uninformed “excuses” and false “myths.” But this expert-vs-lay framework is hard to reconcile with the fact that on average, no more than 40% of healthcare workers get annual influenza vaccinations. Since 1984, federal officials have advised that healthcare workers annually

<sup>95</sup> Nelson, Hesse, and Croyle, *Making Data Talk*, 15.

<sup>96</sup> “Agenda. National Influenza Vaccine Summit”, May 31, 2005, [http://webt1.ama-assn.org/resources/doc/infectious-disease/summit\\_2005\\_agenda.pdf](http://webt1.ama-assn.org/resources/doc/infectious-disease/summit_2005_agenda.pdf), (accessed November 6, 2005).

<sup>97</sup> *Consumer Reports*, “12 top excuses for skipping the flu shot are exposed”, November 2008, <http://www.consumerreports.org/health/healthy-living/health-safety/getting-the-flu-shot-this-year/12-top-excuses-exposed/getting-the-flu-shot-this-year-no-excuses-for-skipping-the-flu-shot.htm>, (accessed June 30, 2011).

<sup>98</sup> *Ibid.*

receive an influenza vaccination, but for almost thirty years, the majority do not.<sup>99</sup> Healthcare workers, who by the very nature of their job are exposed to the sick, would presumably have firsthand experience of the damage that influenza inflicts. For these people, the 200,000 hospitalizations and 36,000 deaths statistics that officials cite should be more than statistics. It is their job. It is their reality. Yet the majority of these individuals do not end up vaccinated.

Understanding why this is the case has been the subject of numerous studies, and there is no single answer. Some do not get vaccinated simply because they dislike injections. Others lack the time, find the vaccine inaccessible, do not realize vaccine was available, or simply forget. But for other healthcare workers, the calculus of risk and benefit does not weigh in the favor of vaccination: some are concerned about side effects. Others do not believe they will get influenza, and some simply feel the vaccine is unnecessary.<sup>100</sup> Several surveys have shown differences in vaccination rates by race and occupational category: e.g. whites healthcare workers tend to get the vaccine more often than minority healthcare workers;<sup>101</sup> and employees in health-diagnosing professions (doctors, nurses) and administrators tend to be more vaccinated than health aides.<sup>102</sup> Yet across almost all categories, regardless of educational attainment and geographic region, rates have stayed below 50%.<sup>103</sup>

Health officials have responded to this gap—between what they recommend and what healthcare workers actually do—by targeting healthcare workers in campaigns similar to those targeted at the public. The CDC once suggested some “friendly competition” for pizza as a way to increase vaccination rates:

Healthcare workers owe it to their patients, their families, and to themselves to be vaccinated. No excuses. ... Monitoring and reporting vaccination rates could be used to create friendly competition between various units in the facility. You could even provide an incentive to the unit with the highest vaccination rate. If workers won't be vaccinated to protect themselves and their patients, they might do it for a pizza.<sup>104</sup>

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<sup>99</sup> Poland, Tosh, and Jacobson, “Requiring influenza vaccination for health care workers.”

<sup>100</sup> Sherri L LaVela et al., “Attitudes and practices regarding influenza vaccination among healthcare workers providing services to individuals with spinal cord injuries and disorders,” *Infection Control and Hospital Epidemiology: The Official Journal of the Society of Hospital Epidemiologists of America* 25, no. 11 (November 2004): 933-940; Paula L. Sullivan, “Influenza Vaccination in Healthcare Workers: Should it be Mandatory?,” *OJIN: The Online Journal of Issues in Nursing* 15, no. 1 (November 2, 2009), <http://www.nursingworld.org/MainMenuCategories/ANAMarketplace/ANAPeriodicals/OJIN/TableofContents/Vol152010/No1Jan2010/Articles-Previous-Topic/Mandatory-Influenza-Vaccination-in-Healthcare-Workers.aspx>, (accessed August 9, 2010).

<sup>101</sup> Frances J Walker et al., “Influenza vaccination of healthcare workers in the United States, 1989-2002,” *Infection Control and Hospital Epidemiology: The Official Journal of the Society of Hospital Epidemiologists of America* 27, no. 3 (March 2006): 257-265; Mary Patricia Nowalk et al., “Self-reported influenza vaccination rates among health care workers in a large health system,” *American Journal of Infection Control* 36, no. 8 (October 2008): 574-581.

<sup>102</sup> King et al., “BRIEF REPORT.”

<sup>103</sup> Ibid.

<sup>104</sup> U.S. Centers for Disease Control and Prevention, “Final Script from ‘Immunization Update 2004’ Satellite Broadcast”, August 19, 2004.

But officials have remained unsuccessful. “Health care workers have demonstrated, over almost 25 years that they are unwilling to comply with voluntary influenza immunization programs utilizing a variety of education and incentive programs,” Gregory Poland and colleagues wrote in 2005. “We suggest that an annual influenza immunization should be required for every health care worker with direct patient contact, unless a medical contraindication or religious objection exists, or an informed declination is signed by the health care worker.”<sup>105</sup> While some back such calls for mandatory vaccination,<sup>106</sup> other doctors caution that making influenza vaccination mandatory could alienate staff, damage morale, violate individual freedom to work and earn a living—in other words, be hugely counter-productive.<sup>107</sup> After the British medical journal *BMJ* hosted a debate on the matter, one doctor responded that mandatory vaccination did not amount to a violation of individual rights—indeed, he argued, allowing healthcare workers to go unvaccinated amounted to a violation of the *patient’s* right to a safe environment. Invoking the British philosopher and proponent of the “greatest-happiness” conception of utilitarianism, he wrote, “John Stuart Mills [sic] would support, not oppose, a mandatory programme.”<sup>108</sup>

Over the past few years, some private health systems and some states have experimented with mandating influenza vaccination as a way to increase vaccine uptake.<sup>109</sup> Since 2010, the American Academy of Pediatrics (AAP),<sup>110</sup> the Society for Healthcare Epidemiology of America (SHEA),<sup>111</sup> the Infectious Diseases Society of America (IDSA),<sup>112</sup> and Association for Professionals in Infection Control and Epidemiology (APIC)<sup>113</sup> have all called for the adoption of mandatory influenza vaccination policies for healthcare workers. It remains to see whether such recommendations will be enacted, as mandatory systems have so far been unpopular among the people the mandate targets. Where they

<sup>105</sup> Poland, Tosh, and Jacobson, “Requiring influenza vaccination for health care workers,” 2251.

<sup>106</sup> Charles M Helms and Philip M Polgreen, “Should influenza immunisation be mandatory for healthcare workers? Yes,” *BMJ* 337, no. oct28\_3 (October 28, 2008): a2142.

<sup>107</sup> David Isaacs and Julie Leask, “Should influenza immunisation be mandatory for healthcare workers? No,” *BMJ* 337, no. oct28\_3 (October 28, 2008): a2140-a2140.

<sup>108</sup> S. B Lambert, “Patient care drives mandatory vaccination,” *BMJ* 337, no. nov19\_1 (November 2008): a2588-a2588.

<sup>109</sup> Sullivan, “Influenza Vaccination in Healthcare Workers: Should it be Mandatory?”.

<sup>110</sup> H. H. Bernstein, J. R. Starke, and Committee on Infectious Diseases, “Recommendation for Mandatory Influenza Immunization of All Health Care Personnel,” *Pediatrics* 126, no. 4 (September 2010): 809-815.

<sup>111</sup> Thomas R. Talbot et al., “Revised SHEA Position Paper: Influenza Vaccination of Healthcare Personnel,” *Infection Control and Hospital Epidemiology* 31, no. 10 (October 2010): 987-995.

<sup>112</sup> Infectious Diseases Society of America, “Nation’s Leading Infectious Diseases Experts Call for Mandatory Flu Vaccine for All Healthcare Personnel: Vaccination Should Be Requirement for Continued Employment for Healthcare Personnel, Epidemiologists and Infectious Disease Physicians Say”, August 31, 2010, <http://www.idsociety.org/Content.aspx?id=16980>, (accessed April 18, 2011).

<sup>113</sup> Association for Professionals in Infection Control and Epidemiology, “APIC Position Paper: Influenza Vaccination Should Be a Condition of Employment for Healthcare Personnel, Unless Medically Contraindicated”, January 27, 2011, [http://www.apic.org/Content/NavigationMenu/GovernmentAdvocacy/PublicPolicyLibrary/APIC\\_Influenza\\_Immuni\\_zation\\_of\\_HCP\\_12711.PDF](http://www.apic.org/Content/NavigationMenu/GovernmentAdvocacy/PublicPolicyLibrary/APIC_Influenza_Immuni_zation_of_HCP_12711.PDF), (accessed April 18, 2011).

have been introduced, nurse and other healthcare workers associations have publicly opposed the policy.<sup>114</sup>

\* \* \*

Through a combination of successful marketing, a cooperative media, financial incentives, laws, regulations, pricing negotiations, liability reform, and the overall alignment and cooperation between governmental and private sector interests through collaborative vehicles such as the National Influenza Vaccine Summit, more Americans are receiving an annual influenza vaccination than ever before in the vaccine's seventy year history. But, as those involved in policymaking know, this is less the result of supply meeting demand, but instead the result of years of effort creating demand. One CDC official from the National Immunization Program explained the vision in congressional testimony in 2004:

I believe the best way to increase the production of vaccine is to increase the demand of vaccine, but it has to be done in a way that is orchestrated such that we do not outstrip the production by expanding our recommendations and thereby, pushing too much demand at one time ... ultimately we would like to weave influenza vaccination much more closely into the fabric of society.<sup>115</sup>

Unlike other diseases such as AIDS or cancer, for most of the American public, influenza remains an unremarkable disease; flus are like colds, a short lived and relatively inconsequential "fact of life." To be sure, there are occasional moments of panic when vaccine demand outstrips supply, but the disease soon fades into the background of everyday life. We do not talk about influenza "survivors" the way we celebrate those who have beat cancer. There are no "influenza walks" the way people march to raise funds for AIDS. The disease is not a major concern. It is something few would do anything about on their own volition. But for a few months each year, increasingly sophisticated and elaborate campaigns aim to combat these "myths" and convince the public otherwise. Influenza is a serious disease, we are told, and death statistics are repeated to reinforce the point. Vaccines promise to save lives. Who in their right mind would object?

**[ENDS]**

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<sup>114</sup> PRNewswire, "Nurses Outraged by Virginia Mason Medical Center's Mandatory Flu Vaccination Policy", September 21, 2004, <http://www.prnewswire.com/news-releases/nurses-outraged-by-virginia-mason-medical-centers-mandatory-flu-vaccination-policy-73858217.html>, (accessed June 30, 2011); Delithia Ricks, "LI nurses to rally against mandatory swine flu vaccines", September 21, 2009, <http://www.newsday.com/long-island/nassau/li-nurses-to-rally-against-mandatory-swine-flu-vaccines-1.1465858>, (accessed June 30, 2011).

<sup>115</sup> *Combating the Flu: Keeping Seniors Alive*, 34.

Table 1.1. Expansion of influenza vaccination recommendations, 1960 to present

Population	1960	1984	1987	2000	2004	2006	2008	2009	2010
<b>Recommendations by age</b>									
Adults ≥ 65 years	X	X	X	X	X	X	X	X	X
Adults ≥ 50 years				X	X	X	X	X	X
Children 6 to 23 months					X	X	X	X	X
Children 6 to 59 months						X	X	X	X
Children 6 months to 18 years, if feasible							X	X	X
Children 6 months to 18 years								X	X
Everyone ≥ 6 months									X
<b>Recommendations by condition/occupation</b>									
Pregnant women (2nd and 3rd trimester)				X	X	X	X	X	X
Pregnant women (all trimesters)					X	X	X	X	X
Healthcare workers		X	X	X	X	X	X	X	X
Household contacts of high risk groups			X	X	X	X	X	X	X
Household contacts and out of home caregivers of children 0-23 months					X	X	X	X	X
Household contacts and out of home caregivers of children 0-59 months						X	X	X	X

Sources: ACIP,<sup>116</sup> Osterholm,<sup>117</sup> and Layton et al.<sup>118</sup>

<sup>116</sup> U.S. Centers for Disease Control, "Recommendation of the Immunization Practices Advisory Committee (ACIP) Prevention and Control of Influenza"; Scott A Harper et al., "Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP)," *MMWR. Recommendations and Reports* 53, no. 6 (May 28, 2004): 1-40; Harper et al., "Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP)"; Nicole M Smith et al., "Prevention and Control of Influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP)," *MMWR. Recommendations and Reports* 55, no. 10 (July 28, 2006): 1-42; Anthony E Fiore et al., "Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2007," *MMWR. Recommendations and Reports* 56, no. 6 (July 13, 2007): 1-54; Anthony E Fiore et al., "Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008," *MMWR. Recommendations and Reports* 57, no. 7 (August 8, 2008): 1-60.

<sup>117</sup> Michael T Osterholm, "Influenza Vaccine Efficacy and Effectiveness: A Comprehensive Review", May 10, 2011, 5, [http://www.preventinfluenza.org/NIVS\\_2011/2-osterholm\\_vaccine\\_efficacy.pdf](http://www.preventinfluenza.org/NIVS_2011/2-osterholm_vaccine_efficacy.pdf), (accessed May 18, 2011).

<sup>118</sup> Christine Layton, Tara Robinson, and Amanda Honeycutt, "Influenza Vaccine Demand: The Chicken And The Egg", October 2005, <http://aspe.hhs.gov/pic/fullreports/06/8476-4.doc>, (accessed June 20, 2011).

Table 1.2. Influenza vaccination rates among selected populations, USA 1972-2011

Year	Doses produced (millions)	Number of Americans recommended to get influenza vaccine (millions)	Proportion of elderly $\geq 65$ years old vaccinated (%)	Proportion of adults 50-64 years old vaccinated (%)	Proportion of adults 18-49 years old vaccinated (%)
1972-1973			16		
1973-1974			17		
1974-1975			22		
1975-1976			21		
1976-1977			38		
1977-1978			23		
1978-1979			22		
1979-1980			19		
1980-1981	15.7		20		
1981-1982			21		
1982-1983			21		
1983-1984			22		
1984-1985			23		
1985-1986	23.1		24		
1986-1987			25		
1987-1988			28		
1988-1989			31		
1989-1990			37		
1990-1991	32.3		42		
1991-1992			48		
1992-1993			52		
1993-1994			55		
1994-1995			58		
1995-1996	71.5		62		
1996-1997			63		
1997-1998			63	31.9	14.3
1998-1999			63	33.1	15.5
1999-2000	77.2		65	34.1	16.4
2000-2001	77.9		65	34.6	17.1
2001-2002	87.7		63.1	32.2	15.0
2002-2003	95		65.7	34	16.3
2003-2004	86.9		65.5	36.8	16.9
2004-2005	61	188	64.6	35.9	17.9
2005-2006	88.5		59.7	23	10.7
2006-2007	120.9	218	64.3	33.2	15.5
2007-2008	140.6		66.7	36.2	17.8
2008-2009	135.9	~270	66.9	39.4	19.9
2009-2010	114 million seasonal vaccines; 117 million		66.7	40.7	22.9

	H1N1 vaccines				
<b>2010-2011</b>	171 (est)	~300	63.6	41.2	24.5

Note: Blank spaces in this table are due to the inability to locate statistics for many years. Because vaccine production and distribution figures are proprietary, definitive numbers are difficult to obtain. A variety of sources, primarily referenced to CDC material, were referenced to compile this table.<sup>119</sup> Sources of error in this table include: error in the representativeness of survey data used to generate estimates of the proportion of target populations who received influenza vaccine; error in categorization of vaccination rates to the correct season because of variation in timing of CDC National Health Interview Survey in response to question about receipt of vaccine "during the past 12 months;"<sup>120</sup> error in estimating numbers of Americans recommended for vaccination due to difficulty in obtaining population estimates of some target populations (e.g. healthcare workers); use of data from multiple survey sources (e.g. Behavioral Risk Factor Surveillance System, National Health Interview Survey, and potentially the Medicare Current Beneficiary Survey).

<sup>119</sup> Personal correspondence with Litjen Tam, June 27, 2011, and Simonsen et al., "Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population," 267; Osterholm, "Influenza Vaccine Efficacy and Effectiveness: A Comprehensive Review," 25; Tan, "Update from the 2010 National Influenza Vaccine Summit meeting," 8; Fauci, "Seasonal and Pandemic Influenza Preparedness," S74; U.S. Centers for Disease Control and Prevention, "2009 H1N1 Influenza Vaccine Doses Allocated, Ordered, and Shipped By Project Area", March 4, 2010, <http://www.cdc.gov/h1n1flu/vaccination/vaccinesupply.htm>, (accessed June 30, 2011); U.S. Centers for Disease Control and Prevention, "Vaccination coverage estimates from the National Health Interview Survey: United States, 2008", July 2009, [http://www.cdc.gov/nchs/data/hestat/vaccine\\_coverage/vaccine\\_coverage.pdf](http://www.cdc.gov/nchs/data/hestat/vaccine_coverage/vaccine_coverage.pdf), (accessed June 30, 2011); U.S. Centers for Disease Control and Prevention, "Early Release of Selected Estimates Based on Data From the 2010 National Health Interview Survey", June 22, 2011, fig. 4.1a, <http://www.cdc.gov/nchs/data/nhis/earlyrelease/earlyrelease201106.pdf>, (accessed June 26, 2011); Gerberding, "US Influenza Supply and Preparations for the Future," 20; Smith et al., "Prevention and Control of Influenza"; U.S. Centers for Disease Control and Prevention, "Prevention and control of influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP).," *MMWR. Recommendations and Reports* 45, no. 5 (May 3, 1996): 1-24.

<sup>120</sup> U.S. Centers for Disease Control and Prevention, "Early Release of Selected Estimates Based on Data From the 2010 National Health Interview Survey."

**Flu Vaccine**  
**Facts & Myths**

**MYTH** "The flu isn't a serious disease."  
**FACTS** Influenza (flu) is a serious disease of the nose, throat, and lungs, and it can lead to pneumonia. Each year about 200,000 people in the U.S. are hospitalized and about 36,000 people die because of the flu. Most who die are 65 years and older. But small children less than 2 years old are as likely as those over 65 to have to go to the hospital because of the flu.

**MYTH** "The flu shot can cause the flu."  
**FACTS** The flu shot cannot cause the flu. Some people get a little soreness or redness where they get the shot. It goes away in a day or two. Serious problems from the flu shot are very rare.

**MYTH** "The flu shot does not work."  
**FACTS** Most of the time the flu shot will prevent the flu. In scientific studies, the effectiveness of the flu shot has ranged from 70% to 90% when there is a good match between circulating viruses and those in the vaccine. **Getting the vaccine is your best protection against this disease.**

**MYTH** "The side effects are worse than the flu."  
**FACTS** The worst side effect you're likely to get from a shot is a sore arm. The nasal mist flu vaccine might cause nasal congestion, runny nose, sore throat and cough. The risk of a severe allergic reaction is less than 1 in 4 million.

**MYTH** "Only older people need a flu vaccine."  
**FACTS** Adults and children with conditions like asthma, diabetes, heart disease, and kidney disease **need to get a flu shot**. Doctors also recommend children 6 months and older get a flu shot every year until their 5th birthday.

**MYTH** "You must get the flu vaccine before December."  
**FACTS** Flu vaccine can be given before or during the flu season. The best time to get vaccinated is October or November. **But you can get vaccinated in December or later.**

For more information, ask your healthcare provider or call  
**800-CDC-INFO (800-232-4636)** Website [www.cdc.gov/flu](http://www.cdc.gov/flu)

Department of Health and Human Services  
Centers for Disease Control and Prevention

Figure 1.1. CDC Poster - Flu Vaccine: Facts & Myths (2006)<sup>121</sup>

<sup>121</sup> U.S. Centers for Disease Control and Prevention, "Flu Vaccine: Facts & Myths", September 2006, [http://www.cdc.gov/flu/professionals/flugallery/2007-08/pdf/f\\_factmyth\\_8x11.pdf](http://www.cdc.gov/flu/professionals/flugallery/2007-08/pdf/f_factmyth_8x11.pdf), (accessed May 17, 2009).



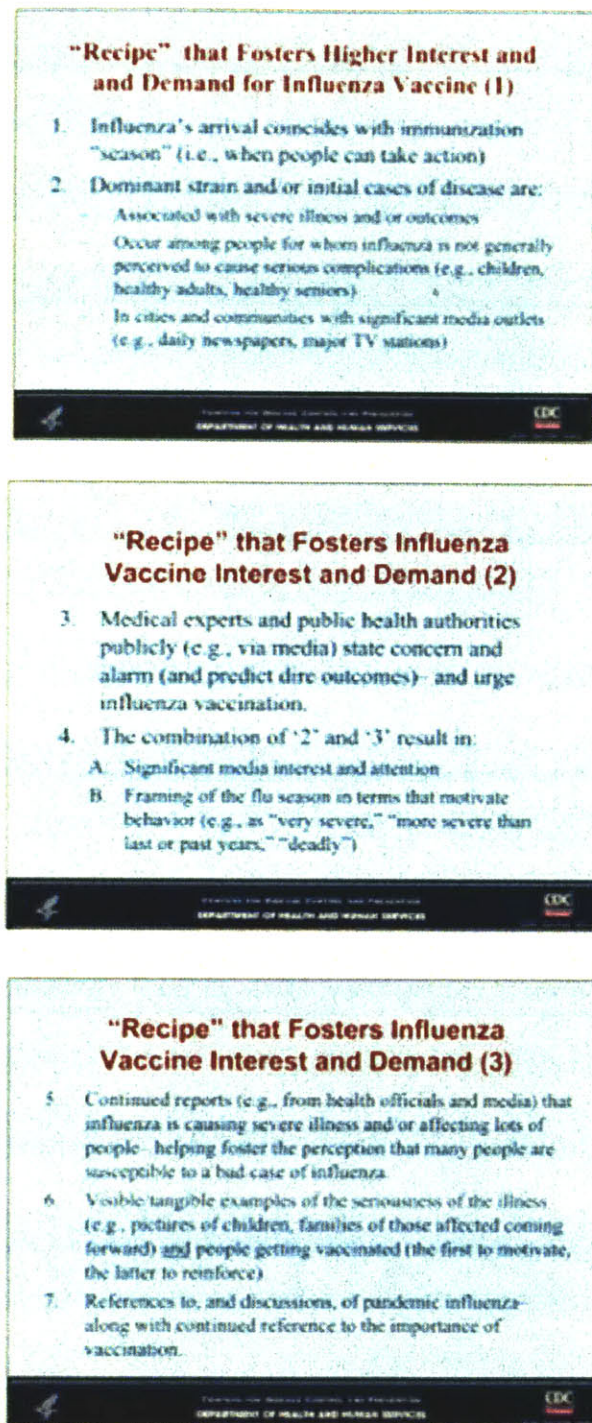
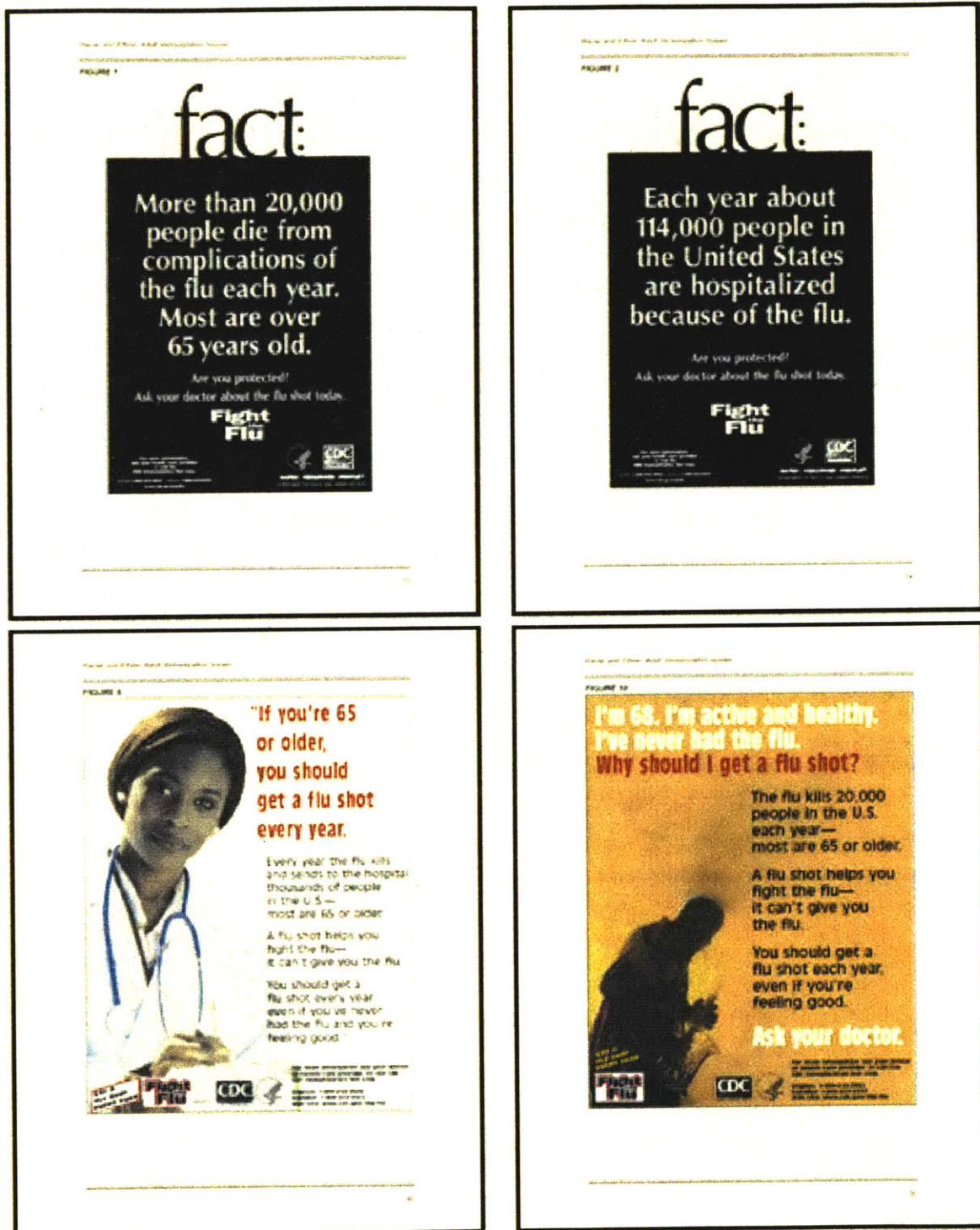


Figure 1.2. CDC's "Seven-Step Recipe" (2004)<sup>122</sup>

<sup>122</sup> Nowak, "Planning for the 2004-05 Influenza Vaccination Season: A Communication Situation Analysis [PDF Part 1]"; Nowak, "Planning for the 2004-05 Influenza Vaccination Season: A Communication Situation Analysis [PDF Part 2]."

Figure 1.3. Test messages shown to CDC focus group participants (2003)<sup>123</sup>



<sup>123</sup> Office of Health Communications, National Immunization Program, Centers for Disease Control and Prevention, *Influenza and Pneumococcal Immunization*, 73,74,80,82.

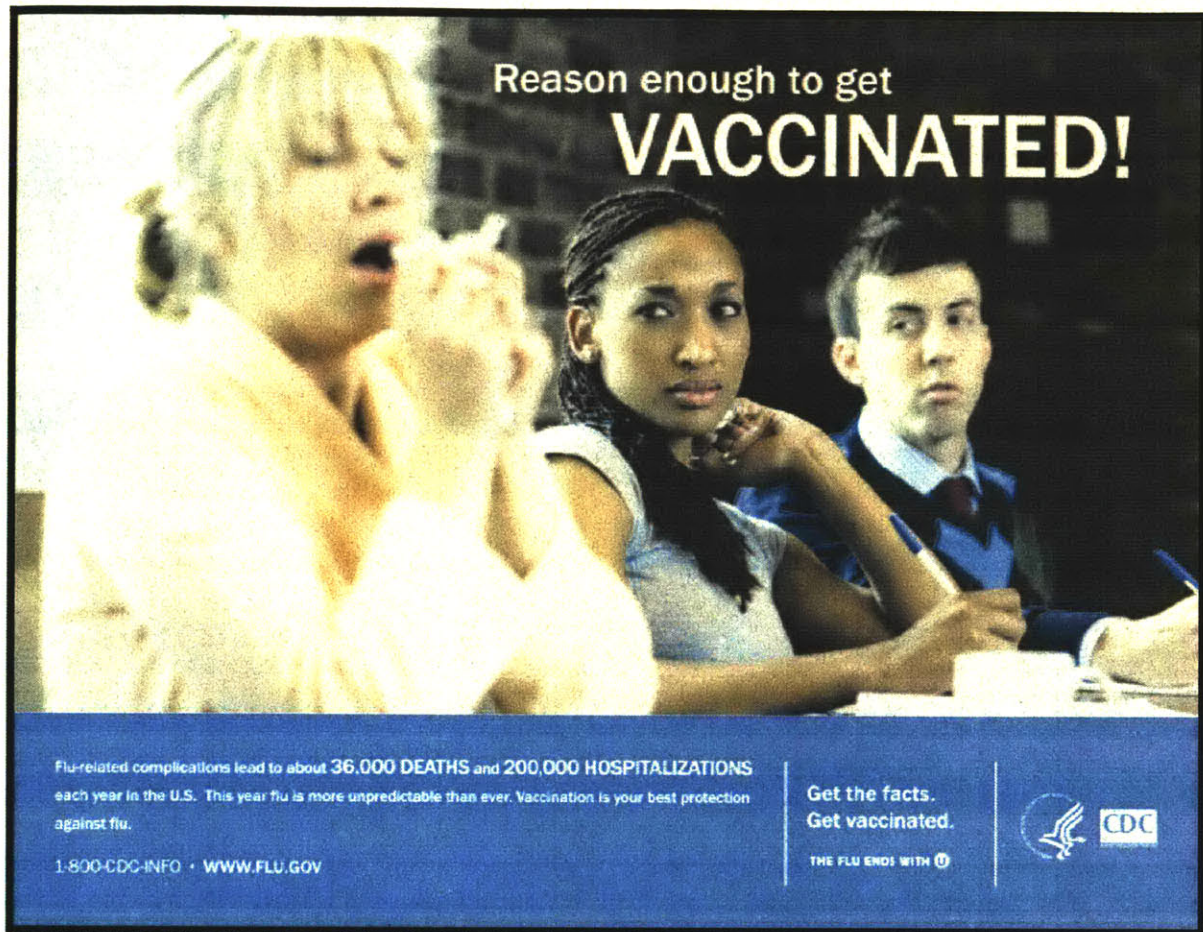
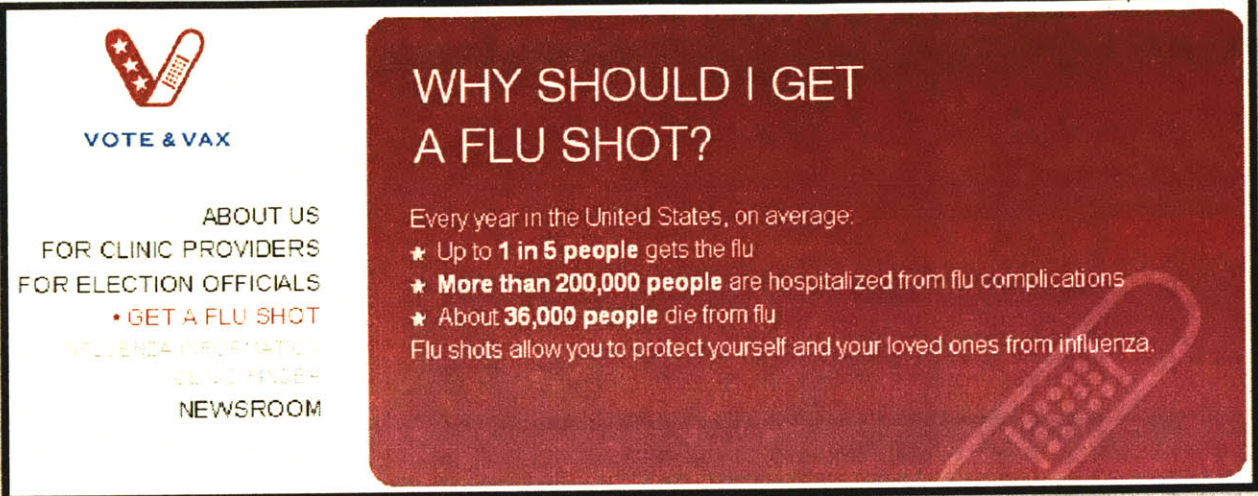



Figure 1.4. CDC Promotional material for the 2010-11 influenza season. The poster states: “Reason enough to get VACCINATED! Flu-related complications lead to about 36,000 DEATHS and 200,000 HOSPITALIZATIONS each year in the U.S.” Source: CDC<sup>124</sup>

<sup>124</sup> U.S. Centers for Disease Control and Prevention, “Reason enough to get VACCINATED!”, July 21, 2010, [http://www.cdc.gov/flu/freeresources/2009-10/pdf/flu\\_ad\\_24-64\\_sneezing.pdf](http://www.cdc.gov/flu/freeresources/2009-10/pdf/flu_ad_24-64_sneezing.pdf), (accessed September 25, 2010).



  
VOTE & VAX

ABOUT US  
FOR CLINIC PROVIDERS  
FOR ELECTION OFFICIALS  
• GET A FLU SHOT  
INFLUENZA INFORMATION  
CLINIC FINDER  
NEWSROOM

## WHY SHOULD I GET A FLU SHOT?

Every year in the United States, on average:

- ★ Up to **1 in 5 people** gets the flu
- ★ **More than 200,000 people** are hospitalized from flu complications
- ★ About **36,000 people** die from flu

Flu shots allow you to protect yourself and your loved ones from influenza.

Figure 1.5. "Why should I get a flu shot?" from the website of the Vote & Vax Project<sup>125</sup>

<sup>125</sup> Vote & Vax, "Why You Need a Flu shot and Where to Get One", 2008, <http://www.voteandvax.org/GetAFluShot.aspx>, (accessed July 16, 2011).

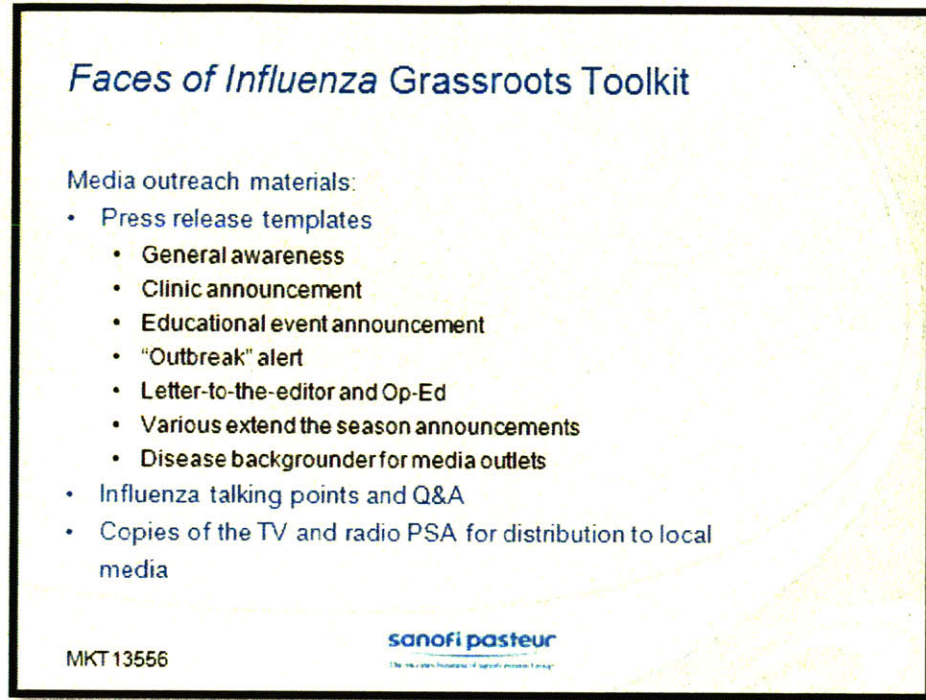
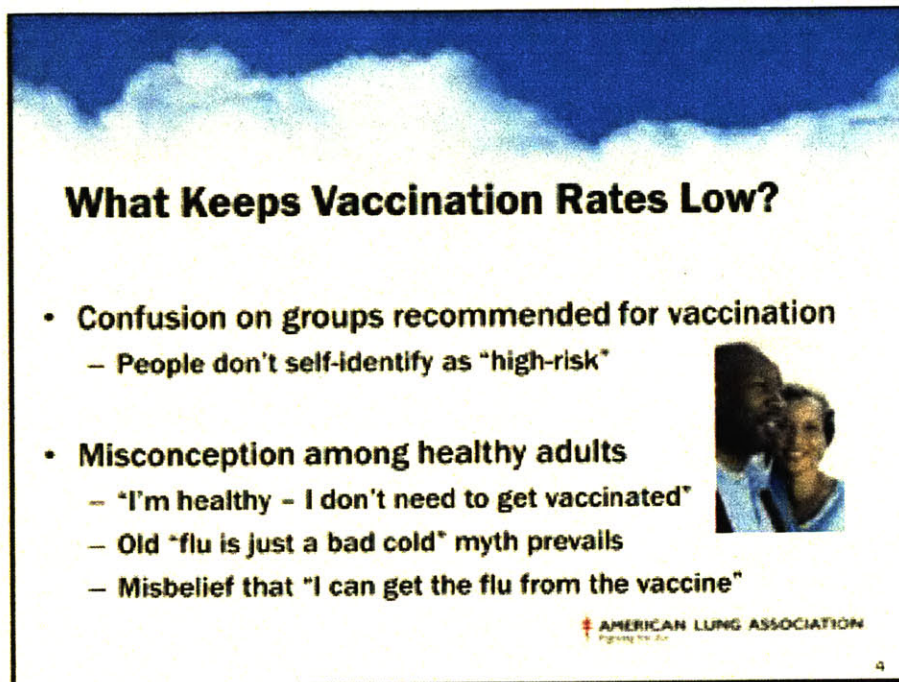



Figure 1.6. Sanofi Pasteur's "Faces of Influenza Grassroots Toolkit" (2007)<sup>126</sup>


<sup>126</sup> Sanofi Pasteur, "Influenza Vaccine Production and Immunization Update," 23.



**What Keeps Vaccination Rates Low?**

- **Confusion on groups recommended for vaccination**
  - People don't self-identify as "high-risk"
- **Misconception among healthy adults**
  - "I'm healthy - I don't need to get vaccinated"
  - Old "flu is just a bad cold" myth prevails
  - Misbelief that "I can get the flu from the vaccine"



 **AMERICAN LUNG ASSOCIATION**  
Fighting the Lung Disease Epidemic

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Figure 1.7. American Lung Association presentation from the 2010 National Influenza Vaccine Summit<sup>127</sup>

<sup>127</sup> Stacey Mortenson, "Healthy Adults: Engaging a 'Hard to Reach' Population on Influenza & Annual Vaccination", May 19, 2010, 2, [http://www.preventinfluenza.org/NIVS\\_2010/4\\_Mortenson.pdf](http://www.preventinfluenza.org/NIVS_2010/4_Mortenson.pdf), (accessed September 25, 2010).

## Chapter 2 Pandemic Influenza: Marketing Catastrophe

### A World Unprepared

Writing in the magazine *Science* in late 2004, experts from the World Health Organization (WHO) asked readers to ponder a horrifying scenario.

Twenty per cent of the world's population falls ill. One in every hundred of those ill is hospitalized (if enough beds are available). Seven million deaths occur in a few months and 28 million are hospitalized. This is how the next influenza pandemic might look, according to optimistic estimates. Estimates from other models are far more frightening, but even this best-case scenario is cause for considerable concern.<sup>1</sup>

Centered at the top of the page was a simple bar chart of projected deaths among highly industrialized nations—topping the list was the United States, with a projected 1.8 million deaths. The article was a plea for swift and sweeping action towards the production of pandemic influenza vaccines. Calling vaccines “the best line of defense against the high morbidity and mortality invariably associated with influenza pandemics,” WHO scientists Klaus Stöhr and Marja Esveld said that the hurdles to development are no longer technical, but “political and economic in nature.” Public health had not risen to the challenge of past pandemics, they warned, as no significant level of vaccines was available in any past influenza pandemic. But with proper preparation, public health might be able to do something about the next influenza pandemic.

If the traditional enemy was complacency and a lack of political will, by 2005, the tide was turning. Discussion about the threat of pandemic influenza—and the need for “preparedness”—was not confined to specialist circles, but moving into the larger society. From the front page of major American newspapers to congressional briefings in Washington, D.C. and daytime talk shows like *Oprah*, by the end of 2005, there were few who had not heard about the coming influenza pandemic. Media coverage was nearly constant, filled with updates about one particular avian influenza virus—subtype H5N1—that was devastating poultry flocks, and most importantly, at times infecting humans. By mid 2005, over 108 human infections with H5N1 had been recorded by the World Health Organization, mostly in the Far East. Half of the time, those infected with H5N1 died.<sup>2</sup>

\* \* \*

“Death rates approaching this order or magnitude are unprecedented for any epidemic disease,” Dr. Tara O’Toole, CEO of the University of Pittsburgh’s Center for Biosecurity, told congressional staffers at a Washington, D.C. briefing on pandemic influenza. Dr. Gregory Poland, the influenza specialist from the

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<sup>1</sup> Klaus Stöhr and Marja Esveld, “Public health. Will vaccines be available for the next influenza pandemic?,” *Science* (New York, N.Y.) 306, no. 5705 (December 24, 2004): 2195-2196.

<sup>2</sup> World Health Organization, “Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO”, June 28, 2005, [http://www.who.int/csr/disease/avian\\_influenza/country/cases\\_table\\_2005\\_06\\_28/en/index.html](http://www.who.int/csr/disease/avian_influenza/country/cases_table_2005_06_28/en/index.html), (accessed July 10, 2011).

Mayo Clinic who had a year earlier (incorrectly) predicted the worst flu season in several decades, also attended the meeting as an expert: "I want to emphasize the certainty that a pandemic will occur... When this happens, time will be described, for those left living, as before and after the pandemic. The key to our survival, in my opinion, and to the continuity of government," is vaccination. "And we do not have a licensed or approved vaccine,"<sup>3</sup> Poland added. A *Washington Post* reporter in attendance at the meeting described the tense atmosphere of the meeting, noting that the experts' "dire warnings proved gripping enough to silence the usual back-of-the-room chatter."<sup>4</sup>

The congressional briefing followed months of increased reporting of the deadly avian influenza virus. In May, the international science journal *Nature* ran a special issue on avian influenza. Senior staff reporter Declan Butler wrote that, "The past week has seen the release of worrying data on the risk of a human pandemic, alongside almost daily news of further cases of avian flu."<sup>5</sup> The article mentioned that the virus was mutating, that cases were increasing, and antiviral resistance had even been detected. The virus had also been found in migratory birds—not just poultry flocks—raising the possibility of additional and rapid spread across the world. A separate *Nature* news report explained:

Trouble is brewing in the East. A highly pathogenic strain of avian influenza is endemic in southeast Asia. Many millions of chickens have been culled, but there is a persistent reservoir in domesticated ducks and wild birds. The H5N1 virus isn't going to go away. And each time it emerges, people can be infected. ... The stage is set for the emergence of a fresh human influenza pandemic.

\* \* \*

The story of highly pathogenic avian influenza H5N1—or H5N1 as it is usually abbreviated—does not begin in 2005 but nearly a decade earlier. On May 9, 1997, a previously healthy 3 year old boy from Hong Kong came down with fever, sore throat and cough—all typical symptoms of influenza. He was treated with salicylates<sup>6</sup> (likely a form of aspirin), but the symptoms persisted, and on May 21, the boy died. Analysis of a specimen taken from his trachea days earlier revealed infection with an influenza "A" virus, but of a subtype of influenza A virus that the original lab could not determine. In 1997, influenza A subtypes H3N2 and H1N1 were expected to circulate,<sup>7</sup> but the boy was not infected with either of these. The specimen was forwarded to more sophisticated labs, and by August, three international laboratories—at the Centers for Disease Control and Prevention (CDC) in the United States, the National Influenza Center in Rotterdam, Netherlands, and the National Institute for Medical Research in London—had all independently come to the same conclusion: the virus was an avian influenza virus,

<sup>3</sup> Dana Milbank, "Capitol Hill Flu Briefing Was No Trick, and No Treat," *The Washington Post*, October 13, 2005.

<sup>4</sup> *Ibid.*

<sup>5</sup> Declan Butler, "Flu bulletins," *Nature* 435 (May 26, 2005): 391.

<sup>6</sup> R Snacken et al., "The next influenza pandemic: lessons from Hong Kong, 1997," *Emerging Infectious Diseases* 5, no. 2 (April 1999): 195-203.

<sup>7</sup> World Health Organization, "1997 - Influenza vaccine for 1997-1998 season", February 20, 1997, [http://www.who.int/csr/don/1997\\_02\\_20/en/index.html](http://www.who.int/csr/don/1997_02_20/en/index.html), (accessed July 10, 2011).



type A subtype H5N1.<sup>8</sup> Researchers reported their results in the CDC's weekly publication, *Morbidity and Mortality Weekly Report* (MMWR).

"A strain of influenza virus that previously was known to infect only birds has been associated with infection and illness in humans in Hong Kong," they wrote. The event was noteworthy because the boy's infection challenged the prevailing wisdom that avian influenza viruses were just that—avian—and therefore of concern to bird populations, but unable to infect humans. Just a few months earlier, an article on pandemic influenza in the British medical journal *Lancet* had said as much: "human cells do not have receptors for avian influenza viruses, so it seems there would have to be an intermediate host that would allow coinfecting avian and human influenza viruses to swap or reassert their genes."<sup>9</sup> But if the May 1997 event by itself was just suggestive evidence that the prevailing wisdom was wrong, by the year's end, researchers would identify an additional six cases of confirmed avian influenza H5N1 infection in humans, beginning to set off alarms among the infectious diseases community.<sup>10</sup>

"Infection with this influenza strain that is new to humans prompts consideration about whether this virus has the potential to spread globally and cause a pandemic," the *MMWR* report noted.<sup>11</sup> Conscious of this potential of the virus to spread, nearly 1.5 million chickens<sup>12</sup> were culled under the direction of Margaret Chan, then director of health in Hong Kong. (When Chan was appointed Director-General of the World Health Organization years later, the WHO recalled her handling of avian influenza as among her greatest accomplishments.<sup>13</sup>) In the end, 18 cases and 6 deaths were recorded as caused by the new virus, all in Hong Kong. But the virus resurfaced in late 2002, and by 2003, was seen to be spreading—first China, then Thailand and Vietnam,<sup>14</sup> until by late 2004, 44 human cases and 32 deaths had been reported, worldwide.<sup>15</sup> Public health experts at the international, national, and local level warned of the danger, and aimed to mobilize political will to address it.

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<sup>8</sup> U.S. Centers for Disease Control and Prevention, "Isolation of avian influenza A(H5N1) viruses from humans--Hong Kong, May-December 1997," *MMWR. Morbidity and Mortality Weekly Report* 46, no. 50 (December 19, 1997): 1204-1207.

<sup>9</sup> D Bonn, "Spared an influenza pandemic for another year?," *Lancet* 349, no. 9044 (January 4, 1997): 36.

<sup>10</sup> U.S. Centers for Disease Control and Prevention, "Isolation of avian influenza A(H5N1) viruses from humans--Hong Kong, May-December 1997."

<sup>11</sup> *Ibid.*

<sup>12</sup> Ministry of Foreign Affairs of the People's Republic of China, "Complete curriculum vitae of Dr Margaret Chan", 2006, <http://margarechan.fmprc.gov.cn/eng/jl/default.htm>, (accessed May 4, 2009).

<sup>13</sup> World Health Organization, "Dr Margaret Chan to be WHO's next Director-General", November 9, 2006, <http://www.who.int/mediacentre/news/releases/2006/pr66/en/index.html>, (accessed July 10, 2011).

<sup>14</sup> U.S. Centers for Disease Control and Prevention, "Avian Influenza A Virus Infections of Humans", May 23, 2008, <http://www.cdc.gov/flu/avian/gen-info/avian-flu-humans.htm>, (accessed July 10, 2011).

<sup>15</sup> World Health Organization, "Cumulative Number of Confirmed Human Cases of Avian Influenza A(H5N1) since 28 January 2004", October 25, 2004, [http://www.who.int/csr/disease/avian\\_influenza/country/cases\\_table\\_2004\\_10\\_25/en/index.html](http://www.who.int/csr/disease/avian_influenza/country/cases_table_2004_10_25/en/index.html), (accessed July 10, 2011).

### “A time for advocacy and action”

Advocacy for what came to be known as “pandemic preparedness” was marked by an insistence on the enormity of the threat and a warning that the world was far from being ready to respond. *Nature’s* special issue on avian influenza in May 2005, the journal criticized governments for their lack of will:

Each human case [of H5N1] that occurs in Asia is potentially a global threat. ... National governments’ performance is half-hearted, incomplete and far too slow. International organizations are working with their hands tied behind their backs, for bureaucratic and diplomatic reasons. In short, the level of current efforts is not commensurate with the threat we face.<sup>16</sup>

Appealing to international organizations that might be able to do something about stopping avian influenza H5N1 from ever becoming a human pandemic disease by controlling its spread among animals, the *Nature* editors declared that politics was blocking prudent public health, echoing the WHO Influenza scientists’ view from five months earlier. The international effort that had emerged to deal with the threat of pandemic influenza “is shaky and far from united or sure in its purpose. Its efforts are grossly underfunded, and undermined at every turn by conflicts between global public health, sovereignty and the stakes of trade and economics. ... Above all, greater top-level political oversight of the campaign is needed. The time for diplomacy and denial is over. It is time for advocacy and action,” *Nature* concluded.

Following its own advice, the UK-based journal had joined forces with the influential American policy magazine *Foreign Affairs*, which was also publishing its own a special issue on pandemic influenza the following month. The two journals were also joined by the Royal Institution World Science Assembly, a private institution in the United Kingdom chaired by the former president of the US National Science Foundation, Rita Colwell. RiSci, as it was called, wanted to help bring together top scientists, politicians, and industry representatives in a common cause to tackle the threat of pandemic influenza. It aimed to convince countries of the need for self-preparedness, and to do so in a unified way.<sup>17</sup>

James Hoge, the editor of *Foreign Affairs*, described the motivation behind their joint effort: “It was our feeling at *Foreign Affairs*, at *Nature* magazine, and at the Royal Institution World Science Assembly [RiSci] that a catalytic push was needed in addition to coverage that might help inform the public to a problem out there that needs to be addressed.”<sup>18</sup> To that effect, *Foreign Affairs* had placed an illustration of the Grim Reaper on the special issue’s table of contents, hooded and holding a chicken in his hand with the caption: “Scientists have long forecast the appearance of an influenza virus capable of killing unimaginable numbers of people—and avian flu has shown signs of becoming that disease.”

The *Foreign Affairs* issue, like that of *Nature*, was meant “as a call to action,” and included articles by Laurie Garrett, senior fellow for global health at the Council on Foreign Relations (the publisher of

<sup>16</sup> “On a wing and a prayer,” *Nature* 435, no. 7041 (May 26, 2005): 385.

<sup>17</sup> Council of Foreign Relations, “The Threat of Global Pandemics”, June 16, 2005, <http://www.cfr.org/technology-and-foreign-policy/threat-global-pandemics/p8198>, (accessed September 1, 2010).

<sup>18</sup> *Ibid.*

*Foreign Affairs*), but better known to those in infectious disease circles as the author of *The Coming Plague*, one of a handful of books that helped popularize the concept of emerging infectious diseases, as well as Michael Osterholm, the former state epidemiologist of Minnesota who had become associate director of the Department of Homeland Security's National Center for Food Protection and Defense. Garrett put the spotlight on a world out of balance: "In a world where most of the wealth is concentrated in less than a dozen nations representing a distinct minority of the total population, the capacity to respond to global threats is, to put it politely, severely imbalanced." Garrett argued that this imbalance would, in the aftermath of a pandemic, lead to political and diplomatic crisis: "The international community would look to the United States, Canada, Japan, and Europe for answers, vaccines, cures, cash, and hope. How these wealthy governments responded, and how radically the death rates differed along worldwide fault lines of poverty, would resonate for years thereafter."<sup>19</sup>

If it was the world's disjointed mixture of rich and poor nations that would ultimately divide us in the aftermath of a pandemic, Michael Osterholm suggested that the world's interconnectedness might even bring even the richest nations to a grinding halt. "What would happen if the pandemic begins tonight?" Osterholm asked rhetorically, painting a grim portrait of a chaotic, desperate world struggling to survive:

... the decision would likely be made to close most international and even some state or provincial borders—without any predetermined criteria for how or when those borders might be reopened. Border security would be made a priority, especially to protect supplies of pandemic-specific vaccines from nearby desperate countries. Military leaders would have to develop strategies to defend the country and also protect against domestic insurgency with armed forces that would likely be compromised by the disease. Even in unaffected countries, fear, panic, and chaos would spread as international media reported the daily advance of the disease around the world.

In short order, the global economy would shut down. ... The private and public sectors would have to develop emergency plans to sustain critical domestic supply chains and manufacturing and agricultural production and distribution. The labor force would be severely affected when it was most needed. Over the course of the year, up to 50 percent of affected populations could become ill; as many as five percent could die. The disease would hit senior management as hard as the rest of the work force. There would be major shortages in all countries of a wide range of commodities including food, soap, paper, light bulbs, gasoline, parts for repairing military equipment and municipal water pumps, and medicines, including vaccines unrelated to the pandemic. Many industries not critical to survival—electronics, automobile, and clothing, for example—would suffer or even close. Activities that require close human contact—school, seeing movies in theaters, or eating at restaurants—would be avoided, maybe even banned.<sup>20</sup>

While Osterholm argued that a pandemic was inevitable, he urged leaders to act with "decisiveness and purpose," to mitigate its effects by preparing. "The cost of failing to invest: a global economy that

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<sup>19</sup> Ibid.

<sup>20</sup> Ibid.

remains in a shambles for several years.”<sup>21</sup> And if that was not enough to motivate leaders to act, Osterholm warned, “Someday, after the next pandemic has come and gone, a commission much like the 9/11 Commission will be charged with determining how well government, business, and public health leaders prepared the world for the catastrophe when they had clear warning. What will be the verdict?”

### Vaccines—too little, too late

Criticism of the government for not doing enough to prepare for pandemic influenza was broad based. Beyond the specialist medical and public policy circles, mainstream US newspapers repeated the same core argument: we are unprepared for a threat of unprecedented proportions. “World Not Set to Deal With Flu: Strategy for Pandemic Needed, Experts Say,” reported the *Washington Post*.<sup>22</sup> (One of the experts quoted was the outspoken Michael Osterholm.)

A particular problem routinely focused on was the lack of an effective vaccine. “Here we go again. With flu season approaching—and an even bigger bird-flu threat brewing—this country’s creaking vaccine system is falling apart,” the *San Francisco Chronicle* editorialized in June 2005 after influenza vaccine manufacturer Chiron again announced that it would not meet production targets by around 30 million doses.<sup>23</sup> “Last year was a good time to make repairs. ... But nothing changed.” And now, they wrote, “there is another unknown in the picture,” referring to H5N1, “meaning a powerful new disease may come our way. ... The old methods and lax public-health planning argue no. It’s time to fix an ailing system before the flu bug arrives.”

Complaints of a “creaky,” antiquated and fragile vaccine production process based on technology now decades old was central to the argument that government must do something to protect the public. “Today we’re using a human vaccine with one slight change to it, and an important change, but it’s basically the same basic vaccine we used in the 1950s, 1960s, a vaccine that was common when we used a slide rule as the state of the art for mathematical calculations, and today we use the computer,”<sup>24</sup> Osterholm explained at the 2005 Council on Foreign Relations discussion panel. At its fastest, the production cycle takes six months from the initial isolation of a wild influenza virus to initial vials of vaccine.<sup>25</sup> Even under the best circumstances, most assumed that a vaccine would never arrive in time to prevent worldwide spread of a novel virus.

And even if the production timeline could be shortened, other problems remained. One in particular, was the lack of capacity to produce enough vaccines for the presumed global demand. In 2005, the worldwide market for influenza vaccines had grown to around 300 million doses per year, the largest it had ever been, but still far short of the roughly 6 billion inhabitants of the world which the World Health

<sup>21</sup> Ibid.

<sup>22</sup> David Brown, “World Not Set To Deal With Flu: Strategy for Pandemic Needed, Experts Say,” *The Washington Post*, July 31, 2005, <http://www.washingtonpost.com/wp-dyn/content/article/2005/07/30/AR2005073001429.html>, (accessed July 10, 2011).

<sup>23</sup> “Flu vaccines need a shot,” *San Francisco Chronicle*, June 17, 2005, [http://articles.sfgate.com/2005-06-17/opinion/17379408\\_1\\_vaccine-doses-vaccine-supply-flu](http://articles.sfgate.com/2005-06-17/opinion/17379408_1_vaccine-doses-vaccine-supply-flu), (accessed July 10, 2011).

<sup>24</sup> Council of Foreign Relations, “The Threat of Global Pandemics.”

<sup>25</sup> John Treanor, “Weathering the Influenza Vaccine Crisis,” *N Engl J Med* 351, no. 20 (November 11, 2004): 2037-2040; W. Wayt Gibbs and Christine Soares, “Preparing for a Pandemic,” *Scientific American*, November 2005, 58.

Organization assumed would all want to obtain vaccine. Furthermore, “unlike seasonal influenza epidemics caused by viruses that mutate in small but important ways from year to year ... pandemic influenza is caused by a virus that is dramatically different from those that have circulated previously...”<sup>26</sup> This—and studies on candidate H5N1 vaccines—led many researchers to assume that not one, but two doses, of vaccine would be needed in order to elicit a sufficient immune response. The challenge of meeting such a hypothetical demand was enormous.

### From inaction to action

Throughout 2005, medical journals, leaders in public health, and the mainstream press repeatedly chastised political leaders for the inadequacy of their response to the threat of pandemic influenza and attempted to raise concern among the broader American public. By mid-to-late 2005, those efforts were bearing fruit, as pandemic influenza came to occupy a firm spot on the political agenda. Politicians now were part of the community advocating the need for immediate action.

On October 4, thirty-two Democratic senators co-authored a letter to President Bush explaining their “grave concern that the national is dangerously unprepared for the serious threat of avian influenza.”<sup>27</sup> But concern about pandemic influenza was not limited to one political party. On the same day, Bush himself held a press conference where he emphasized the avian influenza threat, discussed the difficult decisions that would have to be made during a pandemic, and raised the issue of whether the military might be helpful in responding to a pandemic virus. According to Bush, the military was “able to plan and move. So that's why I put it on the table. I think it's an important debate for Congress to have.”<sup>28</sup> Months earlier, he had signed Executive Order 13375 which amended the Public Health Service Act and added “influenza caused by novel or reemergent influenza viruses that are causing, or have the potential to cause, a pandemic” to the list of quarantinable diseases.<sup>29</sup>

It is not surprising that isolation and quarantine were put on the pandemic influenza agenda. They were some of the many techniques employed to address the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003. Indeed, as part of the classic repertoire of public health interventions, many credit the quick end of SARS to the successful use of isolation, quarantine, and reporting.<sup>30</sup> Others, however, challenge the role quarantine played in stopping SARS, and question its ethical basis.<sup>31</sup> Many think

<sup>26</sup> Anthony S Fauci, “Pandemic influenza threat and preparedness,” *Emerging Infectious Diseases* 12, no. 1 (January 2006): 73.

<sup>27</sup> Gardiner Harris, “Fear of Flu Outbreak Rattles Washington,” *The New York Times*, October 5, 2005.

<sup>28</sup> George Bush, “Transcript of President Bush’s Press Conference”, October 4, 2005, [http://www.washingtonpost.com/wp-dyn/content/article/2005/10/04/AR2005100400584\\_pf.html](http://www.washingtonpost.com/wp-dyn/content/article/2005/10/04/AR2005100400584_pf.html), (accessed August 27, 2010).

<sup>29</sup> George Bush, “Executive Order 13375 of April 1, 2005: Amendment to Executive Order 13295 Relating to Certain Influenza Viruses and Quarantinable Communicable Diseases,” *Federal Register* 70, no. 64 (April 5, 2005): 17299.

<sup>30</sup> Washer, *Emerging Infectious Diseases and Society*, 106; Matthew K Wynia, “Ethics and public health emergencies: restrictions on liberty,” *American Journal of Bioethics* 7, no. 2 (February 2007): 2.

<sup>31</sup> Richard Schabas, “Severe acute respiratory syndrome: Did quarantine help?” 15, no. 4 (2004): 204-204; George J. Annas, “Terrorism, Torture and other Post 9/11 Epidemics: Must We Sacrifice Human Rights in the Name of Security?” (presented at the First Biennial Seminar on Human Rights and Bioethics, Fundação Lusco-Americana, Lisboa, June 2, 2005), <http://www.ensp.unl.pt/dispositivos-de-apoio/cdi/cdi/sector-de->

Americans would be unlikely to even comply with quarantine, arguing that it is fundamentally incompatible with the American ethic of “rugged individualism.”<sup>32</sup> Regardless of its potential efficacy, however, influenza is a disease known to spread rapidly and quarantine has historically never stopped an epidemic of influenza. Consequently, the best that experts in public health could hope for was for quarantine to help slow spread of the disease, thereby mitigating its overall impact.<sup>33</sup>

Bush discussed other ways in which he was addressing the threat:

... during my meetings at the United Nations, not only did I speak about it publicly, I spoke about it privately to as many leaders as I could find, about the need for there to be awareness, one, of the issue and two, reporting -- rapid reporting to WHO, so that we can deal with a potential pandemic. The reporting needs to be not only on the birds that have fallen ill, but also on tracing the capacity of the virus to go from bird to person to person. That's when it gets dangerous: when it goes bird, person, person.

“Thirdly, the development of a vaccine. I've spent time with Tony Fauci on the subject,” Bush said, referring to the director of the National Institutes of Allergy and Infectious Diseases and one of the world’s most respected public health officials. “So one of the issues is how do we encourage the manufacturing capacity of the country, and maybe the world .... I take this issue very seriously ... The people of the country ought to rest assured that we're doing everything we can.”<sup>34</sup>

Bush was also enlisting the support of nations abroad. In early October, the State Department hosted more than 80 countries and eight international organizations for the inaugural conference of the International Partnership on Avian and Pandemic Influenza (IPAPI), aimed not only to rally political leadership to address the pandemic threat, but to also establish a framework for the “increased coordination and harmonization of preparedness, prevention, response, and containment activities among nations” including achieving the rapid sharing of virus samples and epidemiological information.<sup>35</sup>

At home and abroad, Michael Leavitt, Bush’s new secretary of Health and Human Services (HHS), was also speaking out about the threat, trying to reassure the public that the White House was taking it seriously. “Mr. Leavitt acknowledged in an interview that the United States was not prepared for a pandemic flu outbreak,” the *New York Times* noted prior to Leavitt’s in-person visit to those southeast Asian countries suffering the most cases of H5N1,<sup>36</sup> but the U.S. had already purchased “millions of courses” of antiviral treatment and was funding vaccine research that would ideally speed the creation

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publicacoes/precario/publicacoes\_em\_coedicao/conteudos-livros-pl/livro-1/02%20Annas.pdf, (accessed July 26, 2011); Wynia, “Ethics and public health emergencies.”

<sup>32</sup> Mark A. Rothstein, “Are traditional public health strategies consistent with contemporary American values,” *Temple Law Review* 77 (2004): 190.

<sup>33</sup> Howard Markel et al., “Nonpharmaceutical Interventions Implemented by US Cities During the 1918-1919 Influenza Pandemic,” *Journal of the American Medical Association* 298, no. 6 (2007): 644 -654; U.S. Department of Health and Human Services, “HHS Pandemic Influenza Plan.”

<sup>34</sup> Bush, “Transcript of President Bush’s Press Conference.”

<sup>35</sup> U.S. Homeland Security Council, “National Strategy for Pandemic Influenza”, November 2005, 12.

<sup>36</sup> Harris, “Fear of Flu Outbreak Rattles Washington.”

of new vaccines against the disease.<sup>37</sup> Leavitt indicated the Bush administration would soon release a comprehensive plan to combat pandemic influenza, including a request to Congress for funding in the range of \$6 billion to \$10 billion.

That promise was fulfilled on November 1, when President Bush unveiled the “National Strategy for Pandemic Influenza” along with a request to congress for \$7.1 billion. The *National Strategy*, authored by the National Security Council, outlined three pillars of Preparedness and Communication, Surveillance and Detection, and Response and Containment, and was meant to provide broad “strategic advice” to federal agencies and departments. In a letter introducing the 17-page document, President Bush wrote that, “While your government will do much to prepare for a pandemic, individual action and individual responsibility are necessary for the success of any measures.”<sup>38</sup> To help manage the enormity of the task, a “one stop” website was launched, [www.PandemicFlu.gov](http://www.PandemicFlu.gov).

The next day, the Department of Health and Human Services released its own *Pandemic Influenza Plan*—a detailed, nearly 400-page document including ten appendices and 11 supplements covering everything from planning assumptions, legal authorities, antiviral and vaccine distribution to surveillance and laboratory diagnostic procedures.<sup>39</sup>

At the international level, the United Nations accelerated its efforts to improve the global response to pandemic influenza with the creation of a new position. In late September, 2005, the UN announced Dr. David Nabarro to be its first Senior UN System Influenza Coordinator—better known as the “flu czar” in the press.<sup>40</sup> Operating with an initial budget of \$2 million, Nabarro’s office would help coordinate efforts among UN agencies such as WHO and the Food and Agricultural Organization (FAO), but also include non-UN organizations such as the World Bank, the World Organization for Animal Health, development banks, and NGOs like the International Federation of Red Cross and Red Crescent Societies.<sup>41</sup> In his inaugural speech, Nabarro stressed the urgency of the work: “I am certain that there will be another influenza pandemic sometime.” The UN press release announcing Nabarro’s appointment continued:

Health experts agreed that the long period of time since the last serious flu epidemic, which had killed tens of millions of people in 1918-1919, meant the world was overdue for another epidemic.

He [Nabarro] said the likelihood of the bird flu virus jumping into the human population was generally thought by health officials to be high. “I’m not sure whether ‘almost certain’ is the impression I’d like to have conveyed to you, but it does seem very likely

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<sup>37</sup> Ibid.

<sup>38</sup> U.S. Homeland Security Council, “National Strategy for Pandemic Influenza.”

<sup>39</sup> U.S. Department of Health and Human Services, “HHS Pandemic Influenza Plan.”

<sup>40</sup> “U.N. Flu Czar Warns of Coming Flu Pandemic,” *ABC News Online*, September 29, 2005, <http://abcnews.go.com/print?id=1170432>, (accessed September 9, 2010).

<sup>41</sup> United Nations, “Press conference by UN System Senior Coordinator for avian, human influenza”, September 29, 2005, [http://www.un.org/News/briefings/docs/2005/050929\\_Nabarro.doc.htm](http://www.un.org/News/briefings/docs/2005/050929_Nabarro.doc.htm), (accessed September 2, 2010).

and it would be extremely wrong for me as a public health person to be ignoring this threat.” ...

He [Nabarro] said that the number of deaths that would result from any pandemic would depend on where the outbreak occurred, the speed with which health and Government officials discovered the outbreak, the response initiatives and the quality of these initiatives. Countries with limited health-care systems that could not care for many ill people and that did not openly transfer information from the local to the national levels would affect the final number of deaths. “I’m not, at the moment, at liberty to give you a prediction on numbers, but I just want to stress, that, let’s say, the range of deaths could be anything from 5 to 150 million.”<sup>42</sup>

Nabarro said that the world’s efforts to prepare would determine whether the final death tally was closer to the “5” or the “150” in that range. His predictions of mass casualties was reported worldwide. The following week, fears of an impending catastrophic influenza pandemic would surge with front page stories in the *New York Times*,<sup>43</sup> *Boston Globe*,<sup>44</sup> *San Francisco Chronicle*,<sup>45</sup> and *Atlanta Journal-Constitution*,<sup>46</sup> describing new research—simultaneously being published in *Nature*<sup>47</sup> and *Science*<sup>48</sup>—into the great 1918 “Spanish flu” pandemic influenza virus, and linking it to avian influenza. The *New York Times* story began, “The 1918 influenza virus, the cause of one of history’s most deadly epidemics, has been reconstructed and found to be a bird flu that jumped directly to humans, two teams of federal and university scientists announced yesterday.”

“This is huge, huge, huge,” Professor John Oxford, an influenza virologist, commented about the research. “It’s a huge breakthrough.”<sup>49</sup> The research—carried out by groups from the Armed Forces Institute of Pathology, Mount Sinai School of Medicine, and the CDC—involved recovering influenza virus from a frozen corpse found in Alaska. It was the culmination of more than a decade of research. Previously, only parts of the virus’s genome were known, painstakingly recovered from pieces of deceased American soldiers’ lung tissue that had been preserved in an Army pathology warehouse. But the October 6, 2005 publication reported the contents of the final three segments of the 1918 influenza virus genome. Immediately, some claimed that “the researchers may have inadvertently handed terrorists a potential weapon.”<sup>50</sup> But it was the researcher’s conclusion that the 1918 virus was bird-like

<sup>42</sup> Ibid.

<sup>43</sup> Gina Kolata, “Experts unlock clues to spread of 1918 flu virus,” *New York Times*, October 6, 2005, Late Edition - Final edition.

<sup>44</sup> Scott Allen, “Scientists re-create 1918 flu pandemic virus,” *The Boston Globe*, October 6, 2005, 3rd edition, sec. National/Foreign.

<sup>45</sup> Sabin Russell, “Deadliest flu bug given new life in U.S. laboratory / Some applaud scientific feat, but others decry move as reckless,” *San Francisco Chronicle*, October 6, 2005.

<sup>46</sup> M.A.J McKenna, “Deadly 1918 flu reborn for study,” *The Atlanta Journal-Constitution*, October 6, 2005.

<sup>47</sup> Jeffery K. Taubenberger et al., “Characterization of the 1918 influenza virus polymerase genes,” *Nature* 437, no. 7060 (October 6, 2005): 889-893.

<sup>48</sup> Terrence M Tumpey et al., “Characterization of the reconstructed 1918 Spanish influenza pandemic virus,” *Science* 310, no. 5745 (October 7, 2005): 77-80.

<sup>49</sup> Kolata, “Experts unlock clues to spread of 1918 flu virus.”

<sup>50</sup> Allen, “Scientists re-create 1918 flu pandemic virus.”



that sent long-lasting reverberations through the press, which had been covering outbreaks of the highly lethal avian influenza H5N1. The same day's *Washington Post*:

The strain of avian influenza virus that has led to the deaths of 140 million birds and 60 people in Asia in the past two years appears to be slowly acquiring genetic changes typical of the "Spanish flu" virus that killed 50 million people nearly a century ago, researchers said yesterday.

How far "bird flu" virus has traveled down the evolutionary path to becoming a pandemic virus is unknown. Nor is it certain that the much-feared strain, designated as influenza A/H5N1, will ever acquire all the genetic features necessary for rapid, worldwide spread.

Nevertheless, the similarities between the Spanish flu virus of 1918 and the H5N1 strain slowly spreading through Asia provide unusually concrete evidence of how dangerous the newer virus is. At least four of its eight genes now contain mutations seen in the deadly strain that circled the globe during and after World War I.

"These H5N1 viruses might be acquiring the ability to adapt to humans, increasing their pandemic risk . . . there is a suggestion there may be some parallel evolution going on," said Jeffery K. Taubenberger, a molecular pathologist at the Armed Forces Institute of Pathology in Rockville.<sup>51</sup>

The British medical journal *Lancet* carried a similar message in an editorial:

Some of the ten aminoacid [sic] changes in the polymerase proteins that differentiate the 1918 virus sequence from avian virus sequences have been found in the H5N1 strain that has caused the deaths of 60 human beings so far. So, the fear that the H5N1 virus might adapt further to facilitate human infection and human-to-human transmission, that it might be the precursor of a new influenza pandemic, is no longer far-fetched speculation.<sup>52</sup>

"Without these measures," the *Lancet* concluded, referring to its call for strong national and regional leadership, transparency, and research, "what is already looking like an inevitable influenza pandemic may be as deadly as that which struck in 1918." (Half a year later, *Nature* published on its website two letters<sup>53</sup> critical of the conclusion that the reconstructed 1918 virus was avian in origin: "We do not believe that this conclusion, which has been widely disseminated in the popular press and in scientific

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<sup>51</sup> David Brown, "Changes Cited in Bird Flu Virus," *The Washington Post*, October 6, 2005, [http://www.washingtonpost.com/wp-dyn/content/article/2005/10/05/AR2005100501098\\_pf.html](http://www.washingtonpost.com/wp-dyn/content/article/2005/10/05/AR2005100501098_pf.html), (accessed September 10, 2010).

<sup>52</sup> The *Lancet*, "A threatening influenza pandemic," *The Lancet* 366, no. 9494 (October 15, 2005): 1331.

<sup>53</sup> Janis Antonovics, Michael E Hood, and Christi Howell Baker, "Molecular virology: was the 1918 flu avian in origin?," *Nature* 440, no. 7088 (April 27, 2006): E9; discussion E9-10; Mark J Gibbs and Adrian J Gibbs, "Molecular virology: was the 1918 pandemic caused by a bird flu?," *Nature* 440, no. 7088 (April 27, 2006): E8; discussion E9-10.

journals, is supported by their phylogenetic evidence,” Janis Antonovics and colleagues from the University of Virginia wrote in one of the letters. Their criticism, highlighting the lack of certainty over the virus’s true origins, however did not get similar press attention.)

The intense media coverage of avian and pandemic influenza in late 2005 seems to have had an effect on the larger society as well. “As the potential for an influenza pandemic has galvanized the medical community and the public into action, physicians and patients alike have been heartened by the availability of effective antiviral drugs,”<sup>54</sup> a doctor wrote in the *New England Journal of Medicine*. In the public discussion of pandemic influenza, Tamiflu was always the drug of choice. Two classes of antiviral drugs existed to treat influenza infections—neuraminidase inhibitors (which included Tamiflu) and adamantanes. Adamantanes, however, were generally thought to be ineffective against avian influenza H5N1 because of viral resistance, and additionally had well known central nervous system toxicities associated with their use.<sup>55</sup> Attention fell to neuraminidase inhibitors, and among these, Tamiflu ruled the market, likely because of its ease of administration and storage.<sup>56</sup> (Tamiflu can be taken orally while its competitor, Relenza, must be inhaled through a special device.) In 2003, oseltamivir was added to the United States’ Strategic National Stockpile.<sup>57</sup> But while the government was stockpiling Tamiflu for use during a pandemic, citizens were taking action into their own hands. According to another report in *New England Journal of Medicine*, “So much oseltamivir (Tamiflu) has been prescribed — presumably for personal stockpiling in case of an avian influenza pandemic, given that the human influenza season has not yet begun — that at the end of October, the drug’s manufacturer stopped shipping it to the United States.”<sup>58</sup> In fact, in an analysis published a few years later, it turned out that Tamiflu prescriptions peaked in October/November 2005, before the influenza virus was circulating that year, but coinciding exactly with intense media coverage of pandemic and avian influenza.<sup>59</sup> Experts feared the public, acting on its own, would improperly use the drug, possibly leading to viruses resistant to the medication.<sup>60</sup> Such fears strengthened the perceived importance of the drug as well as the sense of vulnerability to the threat of pandemic influenza.

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<sup>54</sup> Anne Moscona, “Oseltamivir Resistance — Disabling Our Influenza Defenses,” *The New England Journal of Medicine* 353, no. 25 (December 22, 2005): 2633-2636.

<sup>55</sup> U.S. Department of Health and Human Services, “DRAFT Pandemic Influenza Preparedness and Response Plan”, August 2004, Annex 1, page 15, <http://web.archive.org/web/20041016003906/http://www.dhhs.gov/nvpo/pandemicplan/finalpandemiccore.pdf>, (accessed July 5, 2010).

<sup>56</sup> Tom Jefferson et al., “Possible harms of oseltamivir—a call for urgent action,” *Lancet* 374, no. 9698 (October 17, 2009): 1312-1313.

<sup>57</sup> U.S. Department of Health and Human Services, “DRAFT Pandemic Influenza Preparedness and Response Plan,” 4.

<sup>58</sup> Allan S. Brett and Abigail Zuger, “The Run on Tamiflu — Should Physicians Prescribe on Demand?,” *New England Journal of Medicine* 353, no. 25 (December 22, 2005): 2636-2637.

<sup>59</sup> Justin R Ortiz et al., “Oseltamivir prescribing in pharmacy-benefits database, United States, 2004-2005,” *Emerging Infectious Diseases* 14, no. 8 (August 2008): 1280-1283.

<sup>60</sup> Marc Lipsitch et al., “Antiviral Resistance and the Control of Pandemic Influenza,” *PLoS Med* 4, no. 1 (January 23, 2007): e15.

## Agreement all around

A remarkable feature of the intense interest in H5N1 and pandemic influenza that had gathered by late 2005 was the degree of agreement and interest among a broad range of sectors. Political leaders, doctors, emergency responders, historians, virologists, business leaders, journalists, think tanks, consulting companies, and concerned citizens on the internet were all fundamentally in agreement that pandemic influenza posed a major, global threat. Some saw it as a threat to the public's health. Others characterized it as a threat to national security. Still others saw the grave implications for diplomacy and international relations. *That* pandemic influenza was a major threat was not debated; the only question was how best to prepare.

The momentum that existed in late 2005 was all the more remarkable because the broad and highly publicized interest was unprecedented. For years, members of the public health community had been arguing for the need to prepare. "Historical records suggest that another pandemic of influenza is overdue," the renowned avian influenza virologist Robert Webster wrote in 1994.<sup>61</sup> But only until human cases of avian influenza H5N1 became widely known and publicized did political will develop to put substantial public funding behind the effort. For those in the influenza community, H5N1 was evidence of a conclusion that had been reached long before this particular virus surfaced and began to infect humans: that the next influenza pandemic was, to quote the FDA and CDC in a joint paper delivered in 1995, "an event considered by most experts to be inevitable."<sup>62</sup> Indeed, the National Institutes of Health held an international conference, "Pandemic Influenza: Confronting a Re-emergent Threat" in December 1995 in Bethesda, Maryland, to gather experts in an attempt come up with ideas for how reduce morbidity, mortality, and social disruption in the event of a pandemic. At the meeting, members of the U.S. Federal Working Group on Influenza Pandemic Preparedness and Emergency Response circulated a draft pandemic preparedness plan, a joint effort between the CDC, FDA, as well as the U.S. military. Meetings in conjunction with the plan were held with a vast range of actors at the international, national, state, and local level—medical, volunteer, and trade organizations; national advisory committees, consumer groups, the World Health Organization, and foreign ministries or departments of health. "Extensive input from the pharmaceutical industry has also been actively solicited to address and overcome a series of problems that emerged during the 1976 swine influenza vaccination program."<sup>63</sup> In a theme familiar to the discussion of avian influenza in 2005, University of Michigan professor of epidemiology Dr. Arnold Monto and colleagues from the NIH wrote in 1997 that, "The scope of action requires international cooperation among government agencies, international organizations, and the vaccine and pharmaceutical companies."

While this group of influenza experts that convened in Bethesda, Maryland in late 1995 was convinced of the threat of pandemic influenza, the broader public health community took time to win over. A nationwide survey conducted by the Council of State and Territorial Epidemiologists in 1995, for

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<sup>61</sup> R G Webster, "While awaiting the next pandemic of influenza," *BMJ* 309, no. 6963 (November 5, 1994): 1179-1180.

<sup>62</sup> P A Patriarca and N J Cox, "Influenza pandemic preparedness plan for the United States," *The Journal of Infectious Diseases* 176 Suppl 1 (August 1997): S4.

<sup>63</sup> *Ibid.*

instance, found that most state and local public health agencies had no plan for managing an influenza pandemic, and only 59% of states even perceived a need to develop one.<sup>64</sup> To forward the goal of comprehensive pandemic preparedness, formal funding mechanisms were developed within CDC. Meetings between CDC and state and local health departments were held, and creation of a draft document, "Pandemic Influenza, a Planning Guide for States and Local Officials." It was hoped that by sharing the planning guide with state and local health departments, these officials would come to understand the need for preparedness, and begin to take concrete steps in that direction, including "marketing the plan to appropriate partners to obtain the necessary support for implementing the plan..."<sup>65</sup> With some seed money, six sites around the country pilot tested the draft guidelines. Using the lessons learned from that experience, in 1999, four states were initially selected to receive funding to produce their own state level pandemic influenza plans. In 2000, a second wave of states was chosen to do the same.

In Europe, planning for pandemics was progressing apace. In 1997, less than two years after the US began first circulating its draft pandemic plan, Britain's health department published its own.<sup>66</sup> At the World Health Organization in Geneva, an international meeting was convened in February 1999 to commemorate the fiftieth anniversary of influenza surveillance at WHO. Here, the WHO released a draft copy of its first "Influenza Pandemic Preparedness Plan" to participants of the meeting.<sup>67</sup> The WHO plan had been drafted in collaboration with the European Scientific Group on Influenza (ESWI),<sup>68</sup> a "multidisciplinary group of key opinion leaders"<sup>69</sup> founded in 1992, to promote the study of influenza. ESWI is a group supported by industry, "but has strict scientific independence," an ESWI influenza bulletin explained in 1999, listing sponsorship from Chiron Vaccines, F. Hoffmann-La Roche Ltd, Glaxo Wellcome, Medeva Pharma Ltd, Pasteur Mérieux MSD, SmithKline Beecham Biologicals and Solvay Pharmaceuticals.<sup>70</sup>

The themes of ESWI were similar to those in American influenza circles, a perhaps unsurprising fact given the many professional connections between the American and European influenza communities. In a 1999 paper, ESWI members René Snacken (Belgium), Lars Haaheim (Norway), John Wood (UK) and American ESWI advisor Alan Kendal (formerly of the Influenza Branch at CDC) asked, "One year after concerns were raised in Hong Kong about another influenza pandemic, are we really much further along in establishing the most effective early warning systems and developing the ability to deal with a true

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<sup>64</sup> Kathleen Gensheimer, "Influenza pandemic planning: review of a collaborative state and national process," *International Congress Series* 1219 (October 2001): 734.

<sup>65</sup> *Ibid.*

<sup>66</sup> R T White, "When the next influenza pandemic comes," *BMJ* 315, no. 7102 (July 26, 1997): 204.

<sup>67</sup> Daniel Lavanchy, "World Health Organization, 50 years of influenza surveillance: a challenge for the 21st century Meeting 17–19 February 1999, WHO, Geneva," *Vaccine* 20 Suppl 2 (May 15, 2002): S1.

<sup>68</sup> R Snacken, "Pandemic planning," *Vaccine* 20 Suppl 2 (May 15, 2002): S88.

<sup>69</sup> European Scientific Working group on Influenza, "About ESWI", 2010, <http://www.eswi.org/who-are-we/about-eswi>, (accessed May 10, 2010).

<sup>70</sup> European Scientific Working group on Influenza, "Influenza: information and news on influenza", November 1999, 8, <http://www.eswi.org/modulefiles/publications/pdfs/no-11-april-1999.pdf>, (accessed October 5, 2010).

pandemic?” The authors were pessimistic. “Without increased urgency about this matter, the next pandemic will find most of the world unprepared.”<sup>71</sup>

## The lessons of 1976

Despite the pleas of those in the influenza community in both the US and Europe, there was a significant but still an unbalanced approach to pandemic preparedness during the 1990s. While many in the public health sector were becoming convinced of the threat, there remained a serious lack of interest from the political sector which, it could be expected, would ultimately have to appropriate money for any major changes to take place. But since the events of 1976, politicians were wary of predictions from their scientific advisors, especially those about epidemics of influenza. In 1976, at the behest of the CDC, the US had embarked on its most ambitious vaccination program ever, aiming to vaccinate the entire population against swine flu over a period of just a few months in response to a disease that was predicted might appear sometime that winter, but was acknowledged may not appear.

The story of 1976 begins with a death. A young Army recruit, in training during a cold January winter, refused hospitalization after a bout of respiratory illness and went on an overnight hike. He died. Many others had been sick on the Fort Dix, New Jersey Army training center, with a large number of soldiers reporting respiratory illness, but a laboratory investigation revealed that Fort Dix was not simply suffering from the Victoria strain of influenza virus (a well-known virus that had been circulating for some years). With support from the CDC, it was determined that other cases of influenza were being caused by a new, significantly different swine-origin virus—and most worryingly, the new virus was isolated from a culture taken from the dead man.<sup>72</sup>

The CDC response was swift. More detailed investigations were undertaken leading to the conclusion that the new virus had achieved limited human to human spread within the Fort Dix site, but not elsewhere. The reason for the virus’s disappearance, as sudden as its arrival, was unknown, but suggested the possibility that the virus might re-emerge in the following winter. As the CDC debated the best way to react, it could not dismiss the possibility—however small—that unless precautions were taken, the nation would experience a brutal epidemic of influenza later that year. The virus that killed the young man at Fort Dix was not just a new strain of familiar virus, but an antigenically shifted influenza virus, differing in both of its (hemagglutinin and neuraminidase) surface proteins, and a similar virus had not circulated for decades, leading to the assessment that “the entire U.S. population under the age of 50 is probably susceptible to this new virus.”<sup>73</sup> Furthermore, as Neustadt and Fineberg noted in their detailed study of the vaccination campaign, “in 1976, it was assumed by leading experts that pandemics follow antigenic shifts as night from day.”<sup>74</sup> Most alarmingly, perhaps, was the swine-like nature of the virus. In 1976, it was widely believed that the great 1918 pandemic was caused by a swine virus, and while most thought it less than probable, the possibility of a repeat 1918 experience was not taken lightly.

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<sup>71</sup> Snacken et al., “The next influenza pandemic,” 201.

<sup>72</sup> Richard E Neustadt and Harvey V Fineberg, *The epidemic that never was: policy-making and the swine flu scare*, 1st ed. (New York: Vintage Books, 1983), 17-22.

<sup>73</sup> Memorandum dated March 18, 1976, from Assistant Secretary for Health to Secretary of Health, in *Ibid.*, 198.

<sup>74</sup> *Ibid.*, 18.

The CDC held a series of meetings to discuss possible responses. If swift action were taken, the CDC reasoned, vaccine production and administration in the general population might just be accomplishable before the virus returned. On the other hand, if the virus did not return, the CDC would be accused of crying wolf. “There was nothing in this for CDC except trouble,” one CDC officer recalled.<sup>75</sup>

A 1977 report of the General Accounting Office summarized:

Faced with the possibility of an epidemic that could cost many lives and billions of dollars and offered a chance to prevent it, the Department Of Health, Education, and Welfare planned, and the Congress approved, the \$135 million swine flu program. The decision to proceed with the program was based primarily on scientific evidence that an epidemic could scourge the Nation and that the health care system could carryout the mass immunizations.<sup>76</sup>

The anticipated epidemic, however, never materialized. In fact, not a single additional case of the swine flu virus was found during the following influenza season. Nonetheless, around 45 million Americans were vaccinated before the program was prematurely terminated after highly publicized cases of death and a debilitating neurological condition called Guillain-Barre syndrome occurred following vaccination.

The episode—referred to by critics as the “Swine Flu Fiasco” (the title of a December 1976 article in the *New York Times*<sup>77</sup>)—has been the subject of numerous histories. 1976 was an election year, and in the early days of the new Carter presidency, the incoming secretary of Health and Human Services Joseph Califano commissioned two Harvard professors, Richard Neustadt, a political scientist, and Harvey Fineberg, a doctor and expert in public health policy, to study the experience for lessons to be learned. In their report, the authors highlighted an important sociological dimension to the response. Public health authorities’ robust response to the 1976 H1N1 virus was in part driven by a professional desire to show the world the importance of public health and power of preventative medicine. Health officials had not delivered vaccines in time for the 1957 “Asian flu” pandemic, but early detection of the 1976 virus offered public health a valuable chance to redeem itself.<sup>78</sup> Neustadt and Fineberg’s report faulted specialists, however, for their “overconfidence ... in theories spun from meager evidence,” and “insufficient questioning of scientific logic.”<sup>79</sup>

Nonetheless, the accused have defended their decisions. Reflecting on the swine flu vaccination program which cost him his job as director of the CDC, Dr. David Sencer said he had made the right choices, and regretted how the media came to portray the effort as one of politics, “rather than a public health response to a possible catastrophe.”

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<sup>75</sup> Ibid., 24.

<sup>76</sup> U.S. General Accounting Office, *The Swine Flu Program: An Unprecedented Venture In Preventive Medicine*, Report to the Congress by the Comptroller General of the United States, June 27, 1977, i.

<sup>77</sup> Harry Schwartz, “Swine Flu Fiasco,” *New York Times*, December 21, 1976.

<sup>78</sup> Neustadt and Fineberg, *The epidemic that never was*, 20.

<sup>79</sup> Ibid., 12.

When lives are at stake, it is better to err on the side of overreaction than underreaction. Because of the unpredictability of influenza, responsible public health leaders must be willing to take risks on behalf of the public. This requires personal courage and a reasonable level of understanding by the politicians to whom these public health leaders are accountable. All policy decisions entail risks and benefits: risks or benefits to the decision maker; risks or benefits to those affected by the decision. In 1976, the federal government wisely opted to put protection of the public first.<sup>80</sup>

The dramatic end to the United States' most highly publicized and largest vaccination program cast a chilling effect on the relationship between health officials, politicians, and the public. Those in government felt misled. The public became skeptical and suspicious. Consequently, public health lost credibility amongst its two more important constituencies. No matter what health officials might have felt about the science of pandemics and the inevitability of a pandemic in the years following 1976, it would take years for the scars from the swine flu program to heal.

But a number of events in the early 1990s set the stage for a renewed interest in influenza.

### **The new world of “emerging infectious diseases”**

The swine flu affair of 1976 was, in a sense, anachronistic. It occurred near the end of an era of continuous triumphs in medicine leading to the impression the end of infectious diseases was in sight. Historical plagues like cholera, typhus, malaria, and yellow fever, were becoming less and less of a problem. Health, itself, was being reconceptualized. In 1978, the Declaration of Alma Ata emphasized primary health care and “health for all.” Alma Ata changed the goal of international health from one of simply preventing the transmission of disease between states to a redefined role in which eliminating the inequalities in health status of people around the world became “common concern to all countries.”<sup>81</sup> The old emphasis which international health regulations placed on stopping inter-state transmission of infectious disease was losing relevancy as infectious disease itself appeared on its way out. In perhaps the most symbolic moment, the WHO-led global campaign to eradicate smallpox ended in a declared victory in 1980.<sup>82</sup> For the first time in history, modern medicine could claim the complete conquest of a disease. (Samples of the virus were, however, purposely kept for research purposes by the US and Russian governments. Following the dissolution of the Soviet Union, the location and distribution of those samples remains a topic of considerable concern.<sup>83</sup>)

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<sup>80</sup> David J Sencer and J Donald Millar, “Reflections on the 1976 swine flu vaccination program,” *Emerging Infectious Diseases* 12, no. 1 (January 2006): 29-33.

<sup>81</sup> International Conference on Primary Health Care, “Declaration of Alma-Ata”, September 12, 1978, [http://www.who.int/hpr/NPH/docs/declaration\\_almaata.pdf](http://www.who.int/hpr/NPH/docs/declaration_almaata.pdf), (accessed October 7, 2010).

<sup>82</sup> The second time came just months ago, with the declared worldwide eradication of rinderpest in cattle. See Anders Kelto, “The Eradication of Rinderpest”, June 28, 2011, <http://www.theworld.org/2011/06/eradication-rinderpest/>, (accessed July 17, 2011).

<sup>83</sup> Jonathan B. Tucker, “Breaking the Deadlock Over Destruction of the Smallpox Virus Stocks,” *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* (January 2011): 110110114218037.

By the late 1980s, however, the euphoria that once celebrated the “end of infectious diseases” had dissipated. New problems arose, one after another, as diseases began to appear in unexpected ways.<sup>84</sup> AIDS was seen as incontrovertible proof of the devastation of novel infectious diseases—an uncontrollable epidemic that threatened the entire world. Cholera, long out of the public’s consciousness, reappeared in 1991 in South America. Then, in 1994, an outbreak of plague—a disease many associated with the fourteenth century Black Death in Europe—occurred in Surat, India.<sup>85</sup> Just one year later, an outbreak of Ebola hemorrhagic fever in the Democratic Republic of Congo occurred—but unlike previous outbreaks of Ebola, the 1995 outbreak was highly publicized.

The massive attention paid to these outbreaks helped heighten concerns over the developed world’s vulnerability to infectious disease from other (usually poor) countries.<sup>86</sup> Concurrent with these events, a new concept called “emerging infectious diseases” was gaining momentum following the publication of a 1992 report by the United States’ Institute of Medicine (IOM), entitled *Emerging infections: microbial threats to health in the United States*. If the message of Alma Ata was one of interlinked responsibility, the message of the outbreaks of the 1980s and 1990s and the IOM report was of interlinked risk: what happened thousands of miles away was only a plane ride away from becoming a domestic terror.<sup>87</sup>

Those urging more attention to the problem of pandemic influenza understood the importance of the IOM report. “The current change in approach has much to do with the recognition of the global danger of emerging and reemerging microbial pathogens. In the report of the Institute of Medicine, influenza, especially in its pandemic manifestation, was prominently used as a case requiring much more attention than it has received in the past,”<sup>88</sup> the influenza epidemiologist Arnold Monto wrote in 1997. The IOM report “defines influenza virus as the prototype emerging infection,”<sup>89</sup> another influenza researcher explained.

Politicians were also responding to the changing sensitivities towards emerging threats. The release of toxic sarin gas in the Tokyo subway system in 1995—wounding many and killing five—helped establish “bioterrorism” on national security agendas across the world. If it happened there, it was argued, it could happen anywhere.<sup>90</sup> While influenza had been singled out as a prototype infection, a fear that

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<sup>84</sup> Bruce Jay Plotkin, “Mission possible: the future of the international health regulations,” *Temple International and Comparative Law Journal* 10 (1996): 503; David P. Fidler, “Germs, governance, and global public health in the wake of SARS,” *The Journal of Clinical Investigation* 113, no. 6 (March 2004): 800.

<sup>85</sup> Philippe Calain, “Exploring the international arena of global public health surveillance,” *Health Policy and Planning* 22, no. 1 (December 2006): 4.

<sup>86</sup> Plotkin, “Mission possible,” 503-4; N Tomes, “The making of a germ panic, then and now,” *American Journal of Public Health* 90, no. 2 (February 2000): 191-198.

<sup>87</sup> Nicholas B King, “The scale politics of emerging diseases,” *Osiris* 19 (2004): 62-76.

<sup>88</sup> Arnold S. Monto, Dominick A. Iacuzio, and John R. La Montagne, “Pandemic Influenza—Confronting a Reemergent Threat,” *The Journal of Infectious Diseases* 176, no. 1 (August 1997): S1.

<sup>89</sup> W. Paul Glezen, “Emerging infections: pandemic influenza,” *Epidemiologic Reviews* 18, no. 1 (1996): 64.

<sup>90</sup> Sarin is a toxic chemical, not biological agent. There is significant evidence that the group responsible for the sarin attacks, Aum Shinrikyo, had also attempted and failed to weaponize anthrax, leading many to challenge the degree to which terrorists can effectively deploy bioweapons. See U.S. General Accounting Office, “Combating Terrorism: Observations on the Threat of Chemical and Biological Terrorism”, October 20, 1999, 2, <http://www.gao.gov/new.items/ns00050t.pdf>, (accessed July 10, 2011).



modern societies were especially vulnerable to new (emerging) and old (reemerging) infectious diseases, whether naturally occurring or deployed by terrorists, fueled a growing, more broad-based effort to achieve “preparedness.”

“Most of us believe our public health system has adequate resources to provide the network needed to protect us from the dangers of epidemics and terrorism,” Senator Lauch Faircloth of North Carolina declared, opening a special Senate hearing on “Preparedness for Epidemics and Bioterrorism,” on June 2, 1998. “This is simply not true. ... For those who feel we should just ignore the public health folks and let law enforcement or the military take charge, I suggest you think again. The first sign of a deadly new epidemic of serious terrorist attack is not going to be announced on the evening news. We’re not going to see a battleship pull up to our shores and offload a microbe army. It will simply start with a large number of people falling ill and going to the doctor or emergency rooms in the area.”<sup>91</sup> Michael Osterholm, who testified on behalf of the American Society for Microbiology as an expert witness arguing for sweeping reform, concurred: “... several expert committees, including one convened by the Institute of Medicine, have concluded that the ability of the U.S. public health system and allied health professionals to deal with emerging disease is in serious jeopardy.”<sup>92</sup>

## Disease Diplomacy

If the US public health system was in serious jeopardy, the global situation was no more reassuring. Historically, an international governance mechanism maintained by the WHO and known as the International Health Regulations (IHR) coordinated states’ behavior, aiming to limit the spread of disease while inflicting the least damage to trade and commerce. But by the mid 1990s, the IHR were under fire. International law scholar David Fidler wrote at the time that “most experts agree ... that the IHR have failed badly because states routinely ignore the duties of notification and of limited response to disease outbreaks in other states.”<sup>93</sup> Indeed, when plague surfaced in Surat, India in 1994, the Indian government first attempted (unsuccessfully) to hide the epidemic, in contravention to their obligations under the IHR.<sup>94</sup> As the epidemic grew in proportions, so, too, did fear. Dozens died and hundreds of thousands fled the city, despite regular pronouncements that plague is readily treatable with antibiotics.<sup>95</sup>

Even when the threat was plague, an old disease and against which the IHR were originally created, the IHR were doing little to reduce the impact of epidemics. Of non-compliance, health law scholar Lawrence Gostin wrote, “it is in a country’s self-interest to overlook WHO recommendations and

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<sup>91</sup> *Preparedness for Epidemics and Bioterrorism* (U.S. Government Printing Office, 1998), 2.

<sup>92</sup> *Ibid.*, 36.

<sup>93</sup> David P. Fidler, “Mission Impossible? International Law and Infectious Diseases,” *Temple International and Comparative Law Journal* 10 (1996): 495.

<sup>94</sup> Simon Carvalho and Mark Zacher, “The International Health Regulations in Historical Perspective”, July 28, 1999, 13.

<sup>95</sup> John F. Burns, “Thousands Flee Indian City in Deadly Plague Outbreak,” *The New York Times*, September 24, 1994; Manas Dasgupta, “Fear of ‘plague’ Haunts Surat,” *The Hindu*, August 25, 2006; D T Dennis, “Plague in India,” *BMJ (Clinical Research Ed.)* 309, no. 6959 (October 8, 1994): 893-894.

regulations. Rule compliance may risk national prestige, travel, trade, and tourism.”<sup>96</sup> But the impact of non-compliance was changing in nature. While disease notification remained, according to the IHR, the onus of states, new technologies such as the Internet were by the mid 1990s, making it ever more difficult to hide epidemics. A WHO report in 1995 noted that, “in this age of wide media coverage, nothing can be hidden.”<sup>97</sup> Aware of this explosion in information, the WHO in 1997 began to data mine the news and Internet looking for signs of outbreaks of disease.<sup>98</sup> It designed the Global Public Health Intelligence Network (GPHIN), a tool to search websites, news wires, bulletin boards, and other electronic media for real-time coverage of events and potential early warning signs of disease outbreaks and other public health threats. Such a capability meant that the WHO’s reliance on governments to voluntarily notify them of outbreaks was lessened.

Technical advantage, however, had its limits. The WHO remained frustrated by the lack of any formal mechanism for incorporating such information into their advisory process. The IHR required States to report disease outbreaks happening on their territories to the WHO; no formal mechanisms permitted the WHO to act on intelligence gathering done on its own. As such, the value of non-States sources was diminished.

The IHR was also proving inadequate in another fundamental way: it failed to limit states from imposing excessive measure on world traffic and trade. If states did not abide by the Regulations and imposed trade or travel restricting measures in excess of what was perceived to be warranted, the IHR was failing in fulfilling its core mission to limit the spread of disease while imparting the least possible disruption to world traffic.

For all these reasons, WHO in 1995 called for a radical revision of the IHR.<sup>99</sup> Simultaneously noting the necessity of international health regulations and the failure of the then current IHR (passed in 1981),<sup>100</sup> WHO argued that the successful control of infectious disease was no longer possible by simply reacting to diseases that had already broken out. Effective control of infectious diseases required a more forward-looking approach capable of preempting outbreaks, finding and containing diseases before they erupted into cross-border epidemics. And WHO saw itself as central to this effort: “Public health emergencies require a measured and evidence-based response from a credible third party,” the

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<sup>96</sup> Lawrence O. Gostin, Ronald Bayer, and Amy L. Fairchild, “Ethical and Legal Challenges Posed by Severe Acute Respiratory Syndrome: Implications for the Control of Severe Infectious Disease Threats,” *Journal of the American Medical Association* 290, no. 24 (December 2003): 3236; L. O. Gostin, “International Infectious Disease Law: Revision of the World Health Organization’s International Health Regulations,” *Journal of the American Medical Association* 291, no. 21 (June 2004): 2626.

<sup>97</sup> Quoted in David P. Fidler, “From International Sanitary Conventions to Global Health Security: The New International Health Regulations,” *Chinese Journal of International Law* 4, no. 2 (September 2005): 346.

<sup>98</sup> David P. Fidler, *SARS: Governance and the Globalization of Disease* (New York: Palgrave Macmillan, 2004), 67.

<sup>99</sup> World Health Assembly, “Revision and Updating of the International Health Regulations”, May 12, 1995.

<sup>100</sup> Obijiofor Aginam, “Globalization of Infectious Diseases, International Law and the World Health Organization: Opportunities for Synergy in Global Governance of Epidemics,” *New England Journal of International and Comparative Law* 11, no. 1 (2004): 67.

Organization wrote, “and under its United Nations constitution WHO is well placed to perform this function.”<sup>101</sup> But without revision of the IHR, the WHO was limited in its ability to take a proactive role.

In 2003, however, acting without legal justification, WHO displayed its ability to act as conductor in the global response to an novel emerging infection—SARS. On March 12, 2003, the WHO issued “a global alert about cases of atypical pneumonia,”<sup>102</sup> its first such alert in 10 years. The report, based on information gained from unofficial channels, described the WHO’s effort to confirm a suspected outbreak of severe pneumonia in several areas in Southeast Asia. Later, it was revealed that much of this information came from private doctors in China and media reports—sources of information that the WHO had no legal basis for using.<sup>103</sup> Furthermore, it is unclear on what legal basis the WHO was initially involving itself in a disorder not subject to the three notifiable diseases of the IHR (cholera, plague, and yellow fever).<sup>104</sup> While the WHO had involved itself in initiatives on diseases not on the IHR list (e.g. polio), the role WHO assumed during SARS was one of facilitating multilateral coordination—a cornerstone of IHR’s purpose. Perhaps most surprising was the WHO’s decision to declare travel advisories for Toronto, Beijing, and Shanxi Province (China). Nothing in the then-current IHR nor the WHO constitution granted WHO such a mandate,<sup>105</sup> and “such geographically specific travel advisories were historically unprecedented.”<sup>106</sup>

Confrontation ensued, and governments protested. Toronto officials were especially vocal and opposed to the WHO decision.<sup>107</sup> And while other governments such as the United States showed support of the Canadian opposition in WHO meetings the next year,<sup>108</sup> dissent was limited and ultimately ineffective, as WHO remained largely in charge of the SARS response. Focus instead remained on fighting SARS and bringing an end to the epidemic. As timing would have it, the US Institute of Medicine had just completed another study<sup>109</sup> on the threat of infectious disease outbreaks, a successor to its 1992 landmark report *Emerging Infections: Microbial Threats to Health in the United States*, which had predicted outbreaks like SARS. The SARS outbreak seemed to be proof of the IOM panel’s effort, and experts seized the moment. “National borders offer little impediment to such threats,” declared IOM

<sup>101</sup> World Health Organization, “Global Crises – Global Solutions: Managing public health emergencies of international concern through the revised International Health Regulations”, 2002, 3, [http://whqlibdoc.who.int/hq/2002/WHO\\_CDS\\_CSR\\_GAR\\_2002.4.pdf](http://whqlibdoc.who.int/hq/2002/WHO_CDS_CSR_GAR_2002.4.pdf), (accessed July 10, 2011).

<sup>102</sup> World Health Organization, “WHO issues a global alert about cases of atypical pneumonia”, March 12, 2003, [http://www.who.int/csr/sarsarchive/2003\\_03\\_12/en/](http://www.who.int/csr/sarsarchive/2003_03_12/en/), (accessed July 10, 2011).

<sup>103</sup> Fidler, “Germs, governance, and global public health in the wake of SARS,” 801.

<sup>104</sup> Later, the World Health Assembly adopted a resolution that urged Member States to report SARS cases to WHO. See World Health Assembly, “Revision of the International Health Regulations (Provisional agenda item 14.16)”, May 17, 2003, <http://www.who.int/csr/sars/WHA56-48.pdf>, (accessed July 10, 2011).

<sup>105</sup> Fidler, “Germs, governance, and global public health in the wake of SARS,” 801.

<sup>106</sup> Gostin, Bayer, and Fairchild, “Ethical and Legal Challenges Posed by Severe Acute Respiratory Syndrome,” 3231.

<sup>107</sup> National Advisory Committee on SARS and Public Health, “Learning from SARS: Renewal of Public Health in Canada”, October 2003, 35, <http://www.phac-aspc.gc.ca/publicat/sars-sras/pdf/sars-e.pdf>, (accessed July 10, 2011); Allison Dunfield, “WHO Warning Sparks Outrage,” *The Globe and Mail*, April 23, 2003; Allison Dunfield and Oliver Moore, “WHO Travel Warning Draws Fiery Response,” *The Globe and Mail*, April 23, 2003.

<sup>108</sup> Stephanie Nebehay, “U.S. Urges WHO to Go Softly on Travel Alerts,” *Reuters Health E-Line*, January 22, 2004.

<sup>109</sup> Mark S. Smolinski, Margaret A. Hamburg, and Joshua Lederberg, eds., *Microbial threats to health: emergence, detection, and response* (Washington, DC: National Academies Press, 2003), xiii.

panel co-chair Margaret Hamburg (now director of the Food and Drug Administration). "One nation's problem soon can become every nation's problem."<sup>110</sup> CDC Director Julie Gerberding emphasized the same points, appealing to what historian Nicholas King has called a "scalar narrative," describing the way in which single and limited disease outbreak events in remote areas of the world were made into pressing concerns demanding international attention and intervention.<sup>111</sup> "We must recognize these are global problems that require global solutions,"<sup>112</sup> Gerberding told a Senate committee hearing. "The emergence of SARS, a previously unrecognized microbial threat, has provided a strong reminder of the threat posed by emerging infectious diseases."<sup>113</sup>

The WHO's leadership and the rapid control of SARS have led many academics to describe the WHO's handling of the disease as a major success, a "tipping point", and proof of a fundamental shift past national sovereignty and into a "post-Westphalian" system of public health.<sup>114</sup> When the epidemic was declared over, little less than six months had passed before a new revamped draft of the prospective IHR was released. Though the revision process had started nine years earlier, by 2004, the necessity of revising the IHR was being increasingly justified on modern threats, seen as the proof of the very reason the IHR was in need of overhaul. As WHO Director-General Dr. LEE Jong-wook stated in an address to the international working group on the revised IHR, "Experience in recent years, especially with SARS and avian influenza, has taught Member States and WHO a great deal about how to work together to prevent and contain outbreaks. The revisions in the Regulations reflect that experience."<sup>115</sup> The next May, a radically new IHR was passed by the fifty-eight World Health Assembly in Geneva.

### A growing concern

The SARS epidemic also revealed to policymakers the degree to which the effect of epidemics needed to be thought of not simply in terms of the number of people sick or killed, but events gauged by their social, political, and economic cost as well. The SARS outbreak is only known to have infected 8,096 people globally, but the response to it "temporarily transfixed the world and did extraordinary economic damage in Canada, China, Hong Kong, and other countries,"<sup>116</sup> the NIH's Anthony Fauci noted (with over \$18 billion in losses, according to the Asian Development Bank<sup>117</sup>). Nonetheless, SARS was hailed as the triumph of a new public health concept. Fauci, continued:

<sup>110</sup> Alicia Ault, "US unready for bioterror, disease outbreak - report," *Reuters Health E-Line*, March 18, 2003.

<sup>111</sup> King, "The scale politics of emerging diseases."

<sup>112</sup> USA Today. 19 March 2003. PAGE D5. "Global problems require global solutions"

<sup>113</sup> Julie L. Gerberding, "Testimony: Statement by Julie L. Gerberding, M.D., M.P.H. Director Centers for Disease Control and Prevention, HHS on CDC Response to Severe Acute Respiratory Syndrome (SARS) before the The Committee on Health, Education, Labor and Pensions United States Senate", April 7, 2003, <http://www.hhs.gov/asl/testify/t030407.html>, (accessed July 10, 2011).

<sup>114</sup> Fidler, "From International Sanitary Conventions to Global Health Security," 343, 354; Fidler, *SARS*, 106.

<sup>115</sup> Jong-Wook Lee, "Intergovernmental Working Group on Revision of the International Health Regulations", November 1, 2004, [http://www.who.int/dg/lee/speeches/2004/ihrworking\\_group/en/index.html](http://www.who.int/dg/lee/speeches/2004/ihrworking_group/en/index.html), (accessed July 10, 2011).

<sup>116</sup> Anthony S Fauci, "Emerging and reemerging infectious diseases: the perpetual challenge," *Academic Medicine* 80, no. 12 (December 2005): 1079-1085.

<sup>117</sup> Asian Development Bank, "Assessing the Impact and Cost of SARS in Developing Asia," in *Asian Development Outlook 2003 Update*, 2003, 75, <http://www.adb.org/Documents/Books/ADO/2003/update/sars.pdf>.

SARS taught us an important lesson. Academic scientists, public health officials, and pharmaceutical companies acted together in a way that was unprecedented, leading to the development of promising vaccine candidates in record time. The new microbe was identified in March 2003 and was rapidly sequenced; a vaccine was developed by the following March. In December 2004, a clinical trial of the SARS vaccine began. This likely was the fastest time frame in the history of biomedical research from the identification of a previously unknown microbe to the beginning of a clinical trial. Such rapid progress could not have occurred 30 to 40 years ago.<sup>118</sup>

Though no influenza pandemic had occurred in the decade since the IOM's 1992 *Emerging Infectious* report highlighting the danger of emerging infectious diseases, events over the decade—concerns over bioterrorism, followed by the experience of SARS, and the discovery of a new and extremely deadly avian influenza virus H5N1—resulted in a substantial and growing diversity of stakeholders interested in responding to a future pandemic of influenza.

Then, in late August, 2005, Hurricane Katrina struck the Gulf of Mexico coast. In New Orleans, a majority of the city was submerged by water after the levee system failed. Tens of thousands of people were displaced, thousands went “missing,” and over a thousand lost their life. Many more, and overwhelmingly poor and black, were left in the city, unable to leave. Federal agencies such as the Federal Emergency Management Agency were the subject of investigations after coming under severe criticism for failure to anticipate and respond to the crisis. Furthermore, top Bush administration officials, including the President and Vice President, had been on vacation during the early days of the crisis, despite—it was later learned—being briefed that the New Orleans' levee system might fail.<sup>119</sup>

Katrina carried many messages, but one of them was that natural disasters were real, that they can affect the United States, and that they can be extremely costly—in human lives, in economic dollars, and (as the Bush administration was forced to learn) politically. No more than a couple of months had passed before links would be made connecting Katrina to influenza: “Health officials have warned for years that a virulent bird flu could kill millions of people, but few in Washington have seemed alarmed. After a closed-door briefing last week, however, fear of an outbreak swept official Washington, which was still reeling from the poor response to Hurricane Katrina,” the *New York Times* wrote.<sup>120</sup> By proactively responding to the next impending threat—avian influenza—the Bush administration hoped to turn around its image.<sup>121</sup> “Pandemic preparedness” soon became a household term as media coverage grew nearly 10-fold.<sup>122</sup>

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<sup>118</sup> Fauci, “Emerging and reemerging infectious diseases.”

<sup>119</sup> “New Orleans in Peril,” *The New York Times*, August 31, 2005, sec. Opinion, <https://www.nytimes.com/2005/08/31/opinion/31wed1.html>, (accessed July 27, 2011); Roger Simon, “A heck of a job,” *U.S. News & World Report*, September 12, 2005, <http://www.usnews.com/usnews/opinion/articles/050912/12simon.htm>, (accessed July 26, 2011).

<sup>120</sup> Harris, “Fear of Flu Outbreak Rattles Washington.”

<sup>121</sup> Bernard Wysocki Jr., “U.S. Sees Need to Better Prepare Against Avian Flu,” *Wall Street Journal*, October 6, 2005.

<sup>122</sup> Trust for America's Health, “Covering the Pandemic Flu Threat: tracking articles and some key events: 1997 to 2005”, May 2006, <http://healthyamericans.org/reports/flumedia/CoveringReport.pdf>, (accessed October 7, 2010).

## Preparing for the Inevitable Disaster

The ubiquity of the word “pandemic” today obscures the way in which its meaning crystallized in the mid 2000s amidst concern over H5N1, and rapidly became a shorthand to represent a rare but inevitable catastrophic outbreak of influenza. In 1976, when US health officials feared what today we would call a “pandemic” of influenza, a term often used to describe the threat was simply a possible “epidemic.” In a leaflet distributed by the US Public Health Service in 1976, it wrote:

With the vast majority of Americans being susceptible to swine flu, it is possible that there could be an epidemic this winter. No one can say for sure. However, if an epidemic were to break out, millions of people could get sick.<sup>123</sup>

In 2006, by contrast, officials had come to describe “epidemics” of influenza as important but to be expected, part of the year in and year out impact of the virus. “Pandemics” on the other hand, the CDC explained in a document *Pandemic Flu: Key Facts*, are exceptional:

An influenza pandemic is a global outbreak of disease that occurs when a new influenza A virus appears or “emerges” in the human population, causes serious illness, and then spreads easily from person to person worldwide. Pandemics are different from seasonal outbreaks or “epidemics” of influenza. Seasonal outbreaks are caused by subtypes of influenza viruses that already circulate among people, whereas pandemic outbreaks are caused by new subtypes, by subtypes that have never circulated among people, or by subtypes that have not circulated among people for a long time. Past influenza pandemics have led to high levels of illness, death, social disruption, and economic loss.<sup>124</sup>

In a planning document, the CDC noted that “without mitigating interventions, even a less severe pandemic would likely result in dramatic increases in the number of hospitalizations and deaths.”<sup>125</sup> Pandemic preparedness therefore was fundamentally predicated upon the assertion that an influenza pandemic presented a rare but qualitatively different threat than influenza in its seasonal form.

Some scholars have characterized the policy challenge of responding to such threats as the conundrum of preparing for “low probability—high consequence” events—events, Dr. Harvey Fineberg (today president of the Institute of Medicine) explains,

that are relatively unlikely, but that would have catastrophic consequences should they occur. When you have such an event in prospect, the naysayer who argues that you are over-reacting is more likely to be right than wrong. It is just like the person who says,

<sup>123</sup> U.S. General Accounting Office, *The Swine Flu Program: An Unprecedented Venture In Preventive Medicine*, 89.

<sup>124</sup> U.S. Centers for Disease Control and Prevention, “Pandemic Flu Questions and Answers”, January 17, 2006, 1, <http://www.cdc.gov/flu/pandemic/pdf/pandemicfluQandA.pdf>, (accessed November 27, 2010).

<sup>125</sup> U.S. Centers for Disease Control and Prevention, “Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States - Early Targeted Layered use of Non-Pharmaceutical Interventions”, February 2007, 7, [http://www.pandemicflu.gov/plan/community/community\\_mitigation.pdf](http://www.pandemicflu.gov/plan/community/community_mitigation.pdf).

“Don’t buy insurance for your house this year; it’s not going to burn down.” At the end of the year, for most of us in most years, that would have been an economical decision, but its wisdom can be judged only in retrospect. In prospect, it’s foolhardy not to have the insurance. This is a fundamental challenge for policy-makers in the face of many threats of this type, including natural pandemic threats.<sup>126</sup>

It is not clear, however, whether the insurance analogy is valid. Not all houses burn down, and the value of insurance will only be realized “if” a fire occurs. Fire may be a threat, but its occurrence is not a foregone conclusion. It may or may not occur. Pandemics were not described as “low probability—high consequence” events, but “high probability—high consequence” events, inevitable disasters for which preparedness was essential (Table 2.1). As the HHS wrote in its “fact sheet,” *Pandemic Flu Basics*, “The threat of a flu pandemic is real. The Centers for Disease Control and Prevention (CDC) and other leading public health experts agree that it is not a question of IF a pandemic will occur, but WHEN it will occur”<sup>127</sup> (italics in the original). Certainty about a catastrophic pandemic is also evident in a speech by WHO Director-General Dr. Lee Jong-wook speech in 2005:

There is no outbreak of human pandemic influenza anywhere in the world today. However, the signs are clear that it is coming. The 1918 pandemic resulted from a changed avian flu virus. Since its appearance in Hong Kong in 1997, highly pathogenic H5N1 avian flu has spread to 15 countries in Asia, and Europe.

It is only a matter of time before an avian flu virus - most likely H5N1 - acquires the ability to be transmitted from human to human, sparking the outbreak of human pandemic influenza.

We don't know when this will happen. But we do know that it will happen.

This is the time to build global consensus. This is the time for every country to prepare their national action plan - and act on it.<sup>128</sup>

At an international meeting held at the WHO headquarters in Geneva and jointly conveyed by the WHO, the Food and Agriculture Organization (FAO), the World Organization for Animal Health (OIE), and the World Bank, Dr. LEE Jong-wook described the grave and certain danger of pandemics: “If we are unprepared, the next pandemic will cause incalculable human misery. Both directly from the loss of human life, and indirectly through its widespread impact on security. No society would be exempt. No economy would be left unscathed.”<sup>129</sup> A report produced by this meeting concluded, “Much was at stake, from the documented enormous consequences for agriculture and the livelihoods of millions of

<sup>126</sup> Harvey V Fineberg, “Swine flu of 1976: lessons from the past,” *Bulletin of the World Health Organization* 87, no. 6 (June 2009): 414-415.

<sup>127</sup> U.S. Department of Health and Human Services, “IV. Fact Sheet: Pandemic Flu Basics”, November 29, 2007, [http://www.pandemicflu.gov/takethelead/fact\\_sheet\\_basics.pdf](http://www.pandemicflu.gov/takethelead/fact_sheet_basics.pdf), (accessed October 12, 2010).

<sup>128</sup> Jong-Wook Lee, “Meeting on avian influenza and pandemic human influenza”, November 7, 2005, <http://www.who.int/dg/lee/speeches/2005/flupandemicgeneva/en/>, (accessed July 10, 2011).

<sup>129</sup> Ibid.

small farmers to the most pressing concern of all: mounting evidence that another influenza pandemic may be imminent. That prospect was described by participants variously as inevitable, in the cards, on the doorstep or, simply, expected by nearly everyone.”<sup>130</sup>

### Assessing the risk of a pandemic

The rhetoric over avian influenza reflected a simultaneous certainty and uncertainty. Certainty that a massively destructive and costly infectious disease outbreak was imminent, but uncertainty of the exact details. While “not if, but when” remained the dominant mantra, when, really, would the predicted pandemic actually occur? And how many, exactly, would die? How many would get sick and require hospitalization? Would H5N1 ultimately be the virus to cause the next pandemic—or would it be something else? How fast would the virus sweep the world, and where would it emerge? Unlike seasonal influenza, where statistics such as 36,000 deaths per year were employed to convey the notion of a substantial *and* predictable threat, many important aspects of pandemic influenza were unpredictable.

Decision making around preparing for pandemic influenza thus necessarily had to occur in an environment of substantial uncertainty. Extrapolating the threat of a future pandemic by looking at past pandemics was frequently done, but nonetheless fraught with difficulties given the rarity of past pandemics—just three in the past century. Influenza virus was discovered in 1933, and there had only been two pandemics since then—in 1957 and 1968—and only one more pandemic—in 1918—for which substantial detailed records existed. Pandemics before 1918 remained largely in the realm of speculation. These three data points—the pandemics of “Spanish flu” in 1918, “Asian Flu” in 1957, and “Hong Kong flu” in 1968—were mostly all experts could learn from.

The extreme variability in mortality impact of the three pandemics made any straightforward forecasting of future pandemic mortality nearly impossible. What the three pandemics could unambiguously demonstrate was that pandemics are periodic, recurring events. It would only be a matter of time before another was to come. What the three pandemics taken together could not demonstrate was a consistent severity impact. Learning from the past nonetheless often took the form of conveying estimates of how many people had lost their lives in pandemics of the past. Despite three pandemics, the latter two of which occurred during the era of modern virology, learning from the past in practice meant giving major consideration to what happened during the severe 1918 “Spanish flu,” with far less attention given to the less severe pandemics of 1957 and 1968. As the early 1999 WHO pandemic plan explained:

Influenza viruses are unique in their ability to cause sudden, pervasive illness in all age groups on a global scale. Three such “pandemics” have occurred in this century, one of which -- the infamous ‘Spanish flu’ of 1918 -- was responsible for more than 20 million deaths worldwide, primarily in young adults. Although mortality rates associated with the more recent pandemics of 1957 (A/Asia [H2N2]) and 1968 (A/Hong Kong [H3N2])

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<sup>130</sup> World Health Organization, “Avian influenza and human pandemic influenza: Summary report”, 2005, 2, [http://www.who.int/mediacentre/events/2005/avian\\_influenza/summary\\_report\\_Nov\\_2005\\_meeting.pdf](http://www.who.int/mediacentre/events/2005/avian_influenza/summary_report_Nov_2005_meeting.pdf), (accessed October 12, 2010).



were reduced in part by antibiotic therapy for secondary bacterial infections and more aggressive supportive care, both were associated with high rates of morbidity and social disruption.<sup>131</sup>

This tendency—to emphasize the mortality of 1918 over details about the most recent and far less deadly pandemics in 1957 and 1968—became more pronounced by the mid-2000s. The 2005 pandemic plan, for example, states:

In the century past, we have experienced influenza pandemics three times: as recently as 1968 and 1957 and what has been called the Great Influenza in 1918, a pandemic that killed 40-50 million people worldwide. At some point in our nation's future another virus will emerge with the potential to create a global disease outbreak.<sup>132</sup>

[...]

An influenza pandemic has the potential to cause more death and illness than any other public health threat. If a pandemic influenza virus with similar virulence to the 1918 strain emerged today, in the absence of intervention, it is estimated that 1.9 million Americans could die and almost 10 million could be hospitalized over the course of the pandemic, which may evolve over a year or more. Although the timing, nature and severity of the next pandemic cannot be predicted with any certainty, preparedness planning is imperative to lessen the impact of a pandemic.<sup>133</sup>

As in the concern over swine flu in 1976, in 2005 all attention was directed to the specter of a 1918-like outbreak.<sup>134</sup> "I have thought through the scenarios of what an avian flu outbreak could mean," President Bush remarked at an October 4, 2005 press conference. "I tried to get a better handle on what the decision-making process would be by reading Mr. Barry's book on the influenza outbreak in 1918. I would recommend it." This small endorsement of John Barry's *The Great Influenza* did not just help put a detailed, 500-page history of the horrors that was 1918 on the *New York Times* bestseller list. It helped sow confusion about the differences between avian influenza (a disease of birds) and pandemic influenza (a disease of humans).<sup>135</sup> The top of the CDC Pandemic Influenza homepage asked, "How are Pandemic, Avian and Seasonal Flu different?" attempting to educate readers unsure of the difference.<sup>136</sup> But "1918" had already become synonymous with "pandemic" and images of "1918

<sup>131</sup> National Vaccine Program Office, "Pandemic Influenza: A Planning Guide for State and Local Officials (Draft 2.1)", 1999, <http://web.archive.org/web/20030624173906/http://www.cdc.gov/od/nvpo/pubs/pandemicflu.htm>, (accessed September 1, 2010).

<sup>132</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan," 1.

<sup>133</sup> *Ibid.*, 4.

<sup>134</sup> Sander L Gilman, "Moral panic and pandemics," *The Lancet* 375, no. 9729 (June 2010): 1866-1867.

<sup>135</sup> Luc Bonneux and Wim Van Damme, "An iatrogenic pandemic of panic," *BMJ (Clinical Research Ed.)* 332, no. 7544 (April 1, 2006): 786-788.

<sup>136</sup> U.S. Centers for Disease Control and Prevention, "Pandemic Influenza: Worldwide Preparedness", December 7, 2005, <http://www.cdc.gov/flu/pandemic/>, (accessed December 17, 2005).

Influenza: the Mother of All Pandemics,<sup>137</sup> as one article put it, flooded popular culture. One series of images, in particular, taken at a crowded emergency hospital at Camp Funston, Fort Riley, Kansas, and filled with influenza victims, was extremely commonplace. A recent historical article noted that the 1918 pandemic was “the first to be widely photographed.”<sup>138</sup> The 1918 influenza was, most probably, also the most widely photographed pandemic of the twentieth century. One historian of the 1918 pandemic noted in reference to the far less severe 1968 pandemic that “few people who lived through it even knew it occurred.”<sup>139</sup>

Further preferential treatment towards the 1918 pandemic over other pandemics is visible in the CDC’s online storybook on pandemic influenza. On the 90<sup>th</sup> anniversary of the 1918 pandemic, the CDC launched a *Pandemic Influenza Storybook*, an online storybook with personal vignettes of experience of past pandemics meant to be used as a training tool, “‘translating’ the staggering morbidity and mortality rates from these pandemics into individual events that impacted families for decades”<sup>140</sup> (Figure 2.1). But of “these pandemics,” it was 1918 that received almost all the attention. The CDC’s effort began in 2006 and gathered 45 personal stories of the distant 1918 pandemic, but only five from the more recent 1957 pandemic. “CDC is actively seeking 1968 stories,” the CDC wrote in 2008. (As of July 2011, there are still no stories from 1968.)

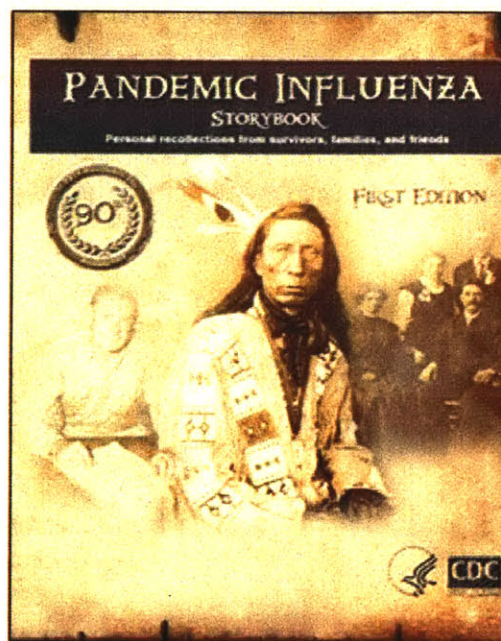


Figure 2.1. CDC's *Pandemic Influenza Storybook*, launched in 2008, available on the HHS website <http://www.pandemicflu.gov/storybook/> (Photo credit: CDC)

### The statistical side of the argument

Although by 2005, highly pathogenic avian influenza H5N1, the Great Influenza of 1918, and SARS had become firmly established as the major reference points in promotional materials on pandemic preparedness, policy planners and other decision makers required a more concrete set of assumptions with which to work. “Central to preparedness planning is an estimate of how deadly the next pandemic is likely to be,” the WHO declared in December 2004.<sup>141</sup> The need for such quantitative estimates was realized early on at CDC, where CDC influenza scientists Dr. Keiji Fukuda (who would go on to become the WHO’s top influenza chief) and Nancy Cox (who would become

<sup>137</sup> Jeffery K Taubenberger and David M Morens, “1918 Influenza: the mother of all pandemics,” *Emerging Infectious Diseases* 12, no. 1 (January 2006): 15-22.

<sup>138</sup> Julian A. Navarro, “Influenza in 1918: An Epidemic in Images” 125, no. 3 (2010): 9.

<sup>139</sup> John M. Barry, “Lessons from the 1918 Flu,” *Time*, October 9, 2005.

<sup>140</sup> U.S. Centers for Disease Control and Prevention, “During 90th Anniversary Year, Pandemic Influenza Storybook Stirs Memories and Learning”, August 22, 2008, [http://www.cdc.gov/news/2008/08/panflu\\_storybook.html](http://www.cdc.gov/news/2008/08/panflu_storybook.html), (accessed October 15, 2010).

<sup>141</sup> World Health Organization, “Estimating the impact of the next influenza pandemic: enhancing preparedness”, December 8, 2004, [http://www.who.int/csr/disease/influenza/preparedness2004\\_12\\_08/en/](http://www.who.int/csr/disease/influenza/preparedness2004_12_08/en/), (accessed June 30, 2009).

director of the CDC's Influenza Division) approached one of the CDC's few health economists in the late 1990s, Martin Meltzer, to help produce a model with estimates of the impact of a future pandemic. Meltzer recounted that experience during an interview in Atlanta.

"Keiji and Nancy Cox, who is still the division director, basically came to me and said we work on this idea of pandemic influenza. And I said 'OK, what's that?' and so they explained it to me."<sup>142</sup> A national pandemic plan existed at the time, but the three felt it to be severely lacking—a short 40 page document "with a lot of blank space," Meltzer said, and too little detail to motivate bureaucracies and other relevant constituencies to get ready.

At first when they talked to me they said, look—we need to get people's attention and saying you know having 40 pages with a lot of blank space in it isn't adequate for any response. We will be caught with our pants down. ... they were really concerned that we were not adequately prepared. So the first thing you need is a set of education materials, and one of the ways that they wanted, and what they wanted from me, and I provided, was just an estimate saying *What if it were to occur? What might we expect in cases, hospitalizations, and deaths?*

As Meltzer came up to speed with the evidence on influenza, he hesitated in producing a model based on a 1918 like scenario. "1918 is so exceptional," he told me. "So what is a more moderate, but clearly identifiable risk? For example, with 68. With 68 there's a lot more data." Meltzer, Fukuda, and Cox thus settled on estimates based on a 1968-like scenario.

They were quite happy because literally they said 'it sounds good. Quite frankly, if you can produce anything that looks reasonable, it will be a step forward from what we don't have.' Again, if you've seen that 40 page plan, there was very, very little in there that talked about, that you could take to a policymaker and say '*this is why we're worried.*' It was very, very abstract.

The result was published in late 1999 in the CDC journal *Emerging Infectious Diseases*, a complex statistical model that provided health planners with a range of estimates for deaths, hospitalizations, outpatient visits, and numbers of people simply "ill" (but not seeking care).<sup>143</sup> Using various assumptions—percentage of the population infected, number of "high risk" patients, hospital capacity, etc.—the authors compared computed pandemic impact estimates against estimates of the economic cost (of sickness and of a vaccine of varying degrees of effectiveness). They hoped to give decision makers a tool to help simplify the weighing of a highly complex list of pros and cons associated with various response measures. Meltzer, Cox, and Fukuda concluded: "we estimated 89,000 to 207,000 deaths; 314,000 to 734,000 hospitalizations; 18 to 42 million outpatient visits; and 20 to 47 million additional illnesses" could possibly occur. To "assist state and local level planners in preparing for the

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<sup>142</sup> Interview of Martin Meltzer (CDC), October 27, 2010.

<sup>143</sup> Martin I. Meltzer, Nancy J. Cox, and Keiji Fukuda, "Modeling the economic impact of pandemic influenza in the United States: Implications for setting priorities for intervention (Background paper)", April 30, 1999, [http://www.cdc.gov/ncidod/eid/vol5no5/melt\\_back.htm](http://www.cdc.gov/ncidod/eid/vol5no5/melt_back.htm), (accessed June 13, 2010).

next influenza pandemic by providing estimates of potential impact specific to their locality,” the CDC packaged the new model into software, FluAid, available for free download on its website.<sup>144</sup>

Adoption was not instantaneous, but after avian influenza and SARS, interest was rising. At a WHO conference in March 2004, Meltzer presented the results of his model projected onto a global population: 2 to 7.4 million in a 1968-like outbreak.<sup>145</sup> The WHO soon updated its pandemic preparedness homepage. Under the subheading “Consequences of an influenza pandemic,” the WHO had since at least 2003 stated:

Epidemiological models project that in industrialized countries alone, the next pandemic is likely to result in 57-132 million outpatient visits and 1.0-2.3 million hospitalizations, and 280 000-650 000 deaths over less than 2 years.<sup>146</sup>

The updated June 2004 text stated:

Although health care has improved in the last decades, epidemiological models from the Centers for Disease Control and Prevention, Atlanta, USA project that today a pandemic is likely to result in 2 to 7.4 million deaths globally. In high income countries alone, accounting for 15% of the worlds [sic] population, models project a demand for 134–233 million outpatient visits and 1.5–5.2 million hospital admissions.<sup>147</sup>

The global figures—which stayed on the WHO’s website until 2009—were computed to be based on a 1968-like scenario, following the Meltzer model. Other constituencies, however, apparently felt the numbers weren’t big enough. The US Department of Health and Human Services (HHS) had cited Meltzer’s *Emerging Infectious Diseases* paper in its 2004 *Draft Pandemic Influenza Preparedness and Response Plan*.<sup>148</sup> But by the time HHS published the plan in 2005, it included estimates of deaths, hospitalizations and illness for not only a “Moderate (1958/68-like)” but also a “Severe (1918-like)” scenario.<sup>149</sup> For deaths, the projected range was between 209,000 and 1,903,000 Americans. The 2005 HHS Pandemic Plan stated:

Pandemic planning is based on the following assumptions about pandemic disease: ...  
The number of hospitalizations and deaths will depend on the virulence of the pandemic virus. Estimates differ about 10-fold between more and less severe scenarios. Because

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<sup>144</sup> U.S. Centers for Disease Control and Prevention, “FluAid 2.0”, July 25, 2000, <http://www.cdc.gov/flu/tools/fluaid/index.htm>, (accessed July 17, 2011).

<sup>145</sup> Sandman and Lanard, “Pandemic Influenza Risk Communication: The Teachable Moment.”

<sup>146</sup> World Health Organization, “Pandemic preparedness”, June 14, 2004, <http://web.archive.org/web/20040614041903/http://www.who.int/csr/disease/influenza/pandemic/en/>, (accessed July 17, 2011).

<sup>147</sup> World Health Organization, “Pandemic preparedness”, June 26, 2004, <http://web.archive.org/web/20040626092138/http://www.who.int/csr/disease/influenza/pandemic/en/>, (accessed July 17, 2011).

<sup>148</sup> U.S. Department of Health and Human Services, “DRAFT Pandemic Influenza Preparedness and Response Plan,”

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<sup>149</sup> U.S. Department of Health and Human Services, “HHS Pandemic Influenza Plan,” 18.

the virulence of the influenza virus that causes the next pandemic cannot be predicted, two scenarios are presented based on extrapolation of past pandemic experience.<sup>150</sup>

Meltzer recalled for me what happened:

The 1918 was actually—and I'll tell you this, and I could even lose my job over it, and I know you've got the recorders on and all that—1918 scenario was never my idea. It was prompted to me by some colleagues who came from HHS and said, you know, 'we need to get the politicians more moving on this idea of planning and preparing, and we need to give them, you know, an upper estimate, you know, a worst-case scenario', and I said, you know, I'm not... I never thought that my colleagues here on the whole really supported the idea of worst-case scenarios and scaring them, but I got pushed and prodded, and in fact, they had sat down with that, because even in the original version, everything can be changed. So they just went in and they said 'OK, we're gonna do this,' and I thought, 'oh no...' so I had to get involved, and I said, if you're gonna put in 1918, because you cannot tell me the probability of 1918 reoccurring versus 68—and they are vastly different—I said, you at least have to have two scenarios side by side. You at least have to give them a range.<sup>151</sup>

In 2006, Meltzer produced a guide that showed how to use the FluAid modeling software to compute both 1968-like and 1918-like estimates.<sup>152</sup> However Meltzer's hesitation about the 1918-like scenario seems to come across in the guide's disclaimer, featured prominently on the cover page:

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<sup>150</sup> Ibid.

<sup>151</sup> Interview of Martin Meltzer (CDC), October 27, 2010. Meltzer's statement that he could lose his job by telling me the history of how official estimates were increased to include 1918-like pandemic projections is troubling. In 2008, the Union of Concerned Scientists conducted a survey to gauge the degree to which scientists working in the federal government felt able to speak freely with the media and public about their research. They rated the CDC's written policies as "excellent" but suggested that interviews with CDC employees revealed a different reality. Their report stated, "The CDC's official information and communications policies are excellent, with provisions that allow scientists to state their personal views and review press releases describing their research. Yet in many cases practice diverges from policy. Survey respondents generally did not agree that they are allowed to speak freely to the media, and most doubted that they could state their personal views without fear of retaliation." See Union of Concerned Scientists, "Freedom to Speak? A Report Card on Federal Agency Media Policies", 2008, 2, [http://www.ucsusa.org/assets/documents/scientific\\_integrity/Freedom-to-Speak.pdf](http://www.ucsusa.org/assets/documents/scientific_integrity/Freedom-to-Speak.pdf), (accessed August 2, 2011).

<sup>152</sup> Martin I. Meltzer, "Using FluAid and FluSurge to estimate the potential impact of the next influenza pandemic upon Locale Y: Basic Instructions and Template of Draft Report", March 22, 2006, <http://www.cdc.gov/flu/pandemic/pdf/pandemic-impact-estimate-instructions.pdf>, (accessed July 17, 2011). In at least one case, another national authority—Japan—based its national pandemic planning based on 1957-like and 1918-like hospitalization and mortality estimates (530,000 to 2 million hospitalized; 170,000 to 640,000 deaths) developed using CDC's *FluAid 2.0* software. Conference of relevant ministries and agencies on pandemic influenza and avian influenza (Japan), "Shingata Infuruenza Koudou Keikaku [Pandemic Influenza Preparedness Action Plan]", February 2009, 3, <http://www.cas.go.jp/jp/seisaku/ful/kettei/090217keikaku.pdf>, (accessed July 27, 2011). In Canada, the national pandemic influenza plan suggested that local governments may want to use Meltzer's model to project the impact of the next influenza pandemic. Public Health Agency of Canada, *The Canadian pandemic influenza plan for the health sector* (Ottawa: Public Health Agency of Canada, 2006), H-5, <http://www.phac-aspc.gc.ca/cpip-pclcpi/pdf-e/cpip-eng.pdf>, (accessed July 27, 2011).

The numbers contained in this report should be treated as illustrations of what *could* happen (with unknown probability of actual occurrence). The numbers in this report, therefore, are intended solely as a guide to help public health officials and policymakers plan and prepare for the next influenza pandemic.<sup>153</sup>

## Projections, everywhere

As concerns over H5N1 mounted, statistics forecasting the possible impact of the next influenza pandemic proliferated—and usually with plenty of attention in the press. Writing in *Foreign Affairs*, Michael Osterholm estimated 180-360 million deaths worldwide if H5N1 were to turn pandemic, citing “recent clinical, epidemiological, and laboratory evidence.”<sup>154</sup> *National Geographic*, in its article “The Next Killer Flu,” took Osterholm’s projection and declared in text placed inside a large red circle that nearly filled the physical page: “Today 180-360 million could die.”<sup>155</sup>

Estimates served multiple purposes. Taken literally, projections of future mortality helped the public imagine what the future might hold, underscoring the urgency and magnitude of the threat. But mortality projections also served a more practical purpose, providing decision makers with “a useful and plausible planning target,”<sup>156</sup> according to WHO. How many ventilators would be needed? How many hospital beds? What proportion of hospital staff could be relied upon to be healthy enough to serve these patients? “Even in the best case scenarios of the next pandemic, 2 to 7 million people would die and tens of millions would require medical attention. If the next pandemic virus is a very virulent strain, deaths could be dramatically higher,” the WHO wrote in late 2004, urging all Member States to ramp up their preparedness.<sup>157</sup>

In an article published in *The Lancet*, researchers from Harvard University estimated that if a 1918-like pandemic were to re-emerge, it would kill 62 million people globally.<sup>158</sup> This estimate, derived by considering the relationship between per-capita income and the likelihood of dying, projected that the vast majority (96%) of these deaths would occur in developing nations. The US, with 4.5% of the world’s population, would only account for less than 1% of total deaths, or 383,881. The *Washington Post* wrote that such an outbreak could double global mortality if it were to occur in a single year.<sup>159</sup> London’s *Sunday Times* noted that “A new pandemic might not mimic precisely the course of the 1918

<sup>153</sup> Italics in the original. Meltzer, “Using FluAid and FluSurge to estimate the potential impact of the next influenza pandemic upon Locale Y: Basic Instructions and Template of Draft Report.”

<sup>154</sup> Michael T Osterholm, “Preparing for the Next Pandemic,” *Foreign Affairs*, August 2005, 26.

<sup>155</sup> Tim Appenzeller, “Tracking the Next Killer Flu,” *National Geographic*, October 2005, 25.

<sup>156</sup> World Health Organization, “Ten things you need to know about pandemic influenza”, October 14, 2005, <http://www.who.int/csr/disease/influenza/pandemic10things/en/>, (accessed June 9, 2009).

<sup>157</sup> World Health Organization, “Estimating the impact of the next influenza pandemic.”

<sup>158</sup> Christopher JL Murray et al., “Estimation of potential global pandemic influenza mortality on the basis of vital registry data from the 1918–20 pandemic: a quantitative analysis,” *The Lancet* 368, no. 9554 (December 2006): 2211-2218.

<sup>159</sup> David Brown, “World Death Toll Of a Flu Pandemic Would Be 62 Million,” *The Washington Post*, December 22, 2006, [http://www.washingtonpost.com/wp-dyn/content/article/2006/12/21/AR2006122101466\\_pf.html](http://www.washingtonpost.com/wp-dyn/content/article/2006/12/21/AR2006122101466_pf.html), (accessed July 10, 2011).

flu, but it is the best model there is.”<sup>160</sup> In a separate projection of 1918-like pandemic mortality, a researcher from the U.S. Army Center for Health Promotion and Preventive Medicine in Washington, D.C., derived estimates over three times as severe—over 71 million Americans sick and 1,278,089 dead.<sup>161</sup>

Estimating future mortality was not limited to specialist circles. Trust for America’s Health (TFAH), the Washington based non-profit, produced its own projections of influenza morbidity and mortality, published in its report, *A Killer Flu?* which carried the headline “Scientific Experts Estimate that ‘Inevitable’ Major Epidemic of New Influenza Virus Strain Could Result in Millions of Deaths if Preventive Actions Are Not Taken.”<sup>162</sup> Using the CDC’s FluAid software, TFAH calculated state-by-state estimates of pandemic mortality for all 50 states. Across the nation, 180,478 deaths could occur in a “mild” 1968-like pandemic, the report noted; 541,433 deaths in a “mid-level” pandemic, and 1,082,866 deaths in a “more severe,” 1918-like pandemic. The report, which also contained a state-by-state breakdown of the gap in capacity to treat the projected sick with the anti-influenza drug Tamiflu, was produced prior to the release of the 2005 HHS pandemic plan, and was submitted during testimony to the U.S. House of Representatives Committee on Government Reform investigating *The Next Flu Pandemic: Evaluating U.S. Readiness*.<sup>163</sup> TFAH’s projections were reported widely; *USA Today* even reproduced its state-by-state table listing numbers dead, hospitalized, and sickened.<sup>164</sup>

Estimates of future pandemic mortality varied widely, even when they sought to assess events of similar severity. While the US official planning estimate posited 1.9 million US deaths in a “1918-like” scenario, the *Lancet* paper estimated such a pandemic would kill less than 400,000—closer to officials’ low-end “1958/68-like” estimate of 209,000. But variability was neither secret<sup>165</sup> nor problematic. It simply reinforced the bottom line: pandemics may be unknowable in detail, but could be counted on to be catastrophic, far more deadly and destructive than an ordinary influenza season. “... [W]e can assume, however, that they [the next pandemic] will be of greater magnitude than even the most severe epidemic of ‘ordinary’ flu,” a UK Department of Health guide to “Explaining pandemic flu” declared in 2005.<sup>166</sup> Pandemics simply are, in the words of the editors of *Scientific American*, “the ‘big ones.’”<sup>167</sup> As

<sup>160</sup> Nigel Hawkes, “New flu pandemic ‘would kill 62 million’: Poor would suffer most in outbreak Figures based on study of 1918 deaths,” *The Times*, December 22, 2006, <http://www.timesonline.co.uk/tol/news/article1263917.ece>, (accessed July 10, 2011).

<sup>161</sup> John F Brundage, “Cases and deaths during influenza pandemics in the United States,” *American Journal of Preventive Medicine* 31, no. 3 (September 2006): 254.

<sup>162</sup> Trust for America’s Health, “A Killer Flu?”, June 2005, <http://healthyamericans.org/reports/flu/Flu2005.pdf>, (accessed October 14, 2005).

<sup>163</sup> Shelley Hearne, “Written Testimony of Shelley Hearne, DrPH, Executive Director Trust for America’s Health, Submitted to U.S. House of Representatives Committee on Government Reform, The Next Flu Pandemic: Evaluating U.S. Readiness”, June 30, 2005, <http://healthyamericans.org/policy/testimony/Hearne063005.pdf>, (accessed October 16, 2010).

<sup>164</sup> Steve Sternberg, “Officials race to head off a bird flu pandemic,” *USA Today*, October 10, 2005, [http://www.usatoday.com/news/health/2005-10-10-avian-flu-cover\\_x.htm](http://www.usatoday.com/news/health/2005-10-10-avian-flu-cover_x.htm), (accessed July 10, 2011).

<sup>165</sup> Michael James, “How Many People Could Bird Flu Kill?”, September 30, 2005, <http://abcnews.go.com/print?id=1173856>, (accessed September 2, 2010).

<sup>166</sup> UK Department of Health, “Explaining pandemic flu: A guide from the Chief Medical Officer (October 2005 edition)”, October 19, 2005, 12,

the HHS bluntly put it, “Uncertainty about the magnitude of the next pandemic mandates planning for a severe pandemic such as occurred in 1918.”<sup>168</sup> Or as the CDC’s health economist Martin Meltzer himself is quoted as saying: “The point isn’t the exact number. The point is: Imagine a lot of people ill in a very short space of time. More than you’ve ever seen.”<sup>169</sup>

Statistical projections thus served a dual function. On the one hand, governments employed them as concrete planning assumptions to guide their planning in anticipation for a pandemic. On the other, projections of the future dead were leveraged in the effort to convince politicians and other policymakers, state health departments, hospital administrators, and many more to commit greater resources towards pandemic preparedness. Whether the next pandemic would kill between 2 and 7.4 million, the range of the WHO’s self-described “relatively conservative estimate,”<sup>170</sup> or 180 million to 360 million, as Michael Osterholm warned, the numbers symbolized the imperative to prepare for a disaster.

### The Promise and the Problem

First, there was evidence of a new strain with man-to-man transmission. Second, always before when a new strain was found there was a subsequent pandemic. And third, for the first time, there was both the knowledge and the time to provide for mass immunization. So he [an advisor] said, “If we believe in preventive medicine we have no choice.” I asked the committee to sleep on it and let us phone them the next day to make sure they still felt the same way, which we did—and they did.

David Sencer, CDC Director (1966-77), recalling the events of 1976.<sup>171</sup>

We are the first generation ever to have an opportunity to prepare in advance of a pandemic. Government alone can’t prepare the nation for a pandemic. This is a shared responsibility and the challenge requires leadership from those most trusted and respected in their communities.

HHS Secretary Leavitt, 2007<sup>172</sup>

The promise of pandemic preparedness was that when knowledge that a pandemic would happen was responded to with concrete investments and planning, the impact of the next pandemic could be

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[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4121751?IdcService=GET\\_FILE&dID=15246&Rendition=Web](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4121751?IdcService=GET_FILE&dID=15246&Rendition=Web), (accessed June 28, 2009).

<sup>167</sup> Gibbs and Soares, “Preparing for a Pandemic.”

<sup>168</sup> U.S. Department of Health and Human Services, “HHS Pandemic Influenza Plan,” 5.

<sup>169</sup> Martin Meltzer, quoted in Helen Branswell, “Avian Flu Presentation”, September 19, 2005, [http://www.wilsoncenter.org/events/docs/Avian%20Flu%20Presentation%20Branswell%20\(amended%20for%20posting\).ppt](http://www.wilsoncenter.org/events/docs/Avian%20Flu%20Presentation%20Branswell%20(amended%20for%20posting).ppt), (accessed July 4, 2009).

<sup>170</sup> World Health Organization, “Ten things you need to know about pandemic influenza.”

<sup>171</sup> Neustadt and Fineberg, *The epidemic that never was*, 28-29.

<sup>172</sup> U.S. Department of Health and Human Services, “HHS Convenes America’s Leaders to Help Americans Prepare for Pandemic Flu”, May 24, 2007, <http://www.hhs.gov/news/press/2007pres/05/20070524a.html>, (accessed July 10, 2011).



reduced. The rationale was simple, but the task large, complex, and costly. Whether the next pandemic virus were to be the feared H5N1 or something else, improvements in surveillance promised to decrease the time to detection of a novel strain with high transmissibility among humans. The WHO even posited that finding a pandemic virus early in its evolution might allow for an extra-ordinary response—strict quarantine of the infected area and massive use of antiviral medications—to extinguish a nascent pandemic threat before it had time to spread worldwide.<sup>173</sup> But even if it did spread, the movement of the virus might be stopped through so-called “non-pharmaceutical interventions” like social distancing. By closing schools or suspending the right of public assembly, planners hoped to slow the spread of the disease while buying valuable time to move forward with vaccine production.<sup>174</sup> Those infected could be treated with influenza antivirals, and weeks-long prophylactic use of antivirals was hoped to reduce or at least delay new infections of the pandemic virus. Nations around the world bought huge quantities of antivirals, particularly the drug Tamiflu, and stored them in national stockpiles.

Vaccines were perhaps highest on the pandemic preparedness agenda. Anticipating near global demand for vaccines once a pandemic began, nations around the world entered into contracts with vaccine manufacturers to guarantee priority delivery of the first pandemic influenza vaccines. Commentators worried that in the event of a pandemic, nations that under ordinary circumstances were friendly allies, might nationalize their vaccine supply, blocking export. The US responded by investing in manufacturers’ capacity to produce vaccines on US soil. The possibility that H5N1 may turn into the next pandemic virus similarly led the National Institutes of Health to subsidize research into H5N1 influenza vaccine candidates. At least 13 million doses (out of a target of 20 million doses) of so-called “pre-pandemic” vaccines were put into the US Strategic National Stockpile for use among high-priority groups in the earliest days of a possible H5N1 pandemic.<sup>175</sup>

The degree of progress that had been made in the weeks and months following President Bush’s announcement of the National Strategy for Pandemic Influenza was unprecedented. Never before had so much money been spent in support of measures to promote ‘preparedness’ for a future pandemic. Across party lines and across national governments, and propelled by fears of avian influenza H5N1, by late 2005, political will had aligned squarely behind the types of preparedness activities that health experts had been advocating for years.

But no sooner did support coalesce to deal with the threat of H5N1 and pandemic influenza than did health authorities begin to worry about a new threat: fatigue.<sup>176</sup> In late 2007, one newspaper noted “a

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<sup>173</sup> World Health Organization, “WHO Interim Protocol: Rapid operations to contain the initial emergence of pandemic influenza”, October 2007, [http://www.who.int/entity/csr/disease/avian\\_influenza/guidelines/RapidContProtOct15.pdf](http://www.who.int/entity/csr/disease/avian_influenza/guidelines/RapidContProtOct15.pdf), (accessed May 17, 2011).

<sup>174</sup> U.S. Centers for Disease Control and Prevention, “Interim Pre-pandemic Planning Guidance.”

<sup>175</sup> U.S. Department of Health and Human Services, “Implementation Plan Two Year Summary”, 2008, <http://www.flu.gov/professional/federal/summaryprogress2008.html>, (accessed July 18, 2011).

<sup>176</sup> Crawford Kilian, “Combat fatigue already?”, April 26, 2006, [http://crofsblogs.typepad.com/h5n1/2006/04/combat\\_fatigue\\_.html](http://crofsblogs.typepad.com/h5n1/2006/04/combat_fatigue_.html), (accessed July 10, 2011); Simeon Bennett and Jason Gale, “‘Flu Fatigue’ Poses Public Health Threat, WHO Says (Update1),” *Bloomberg*, September 15, 2008, <http://www.bloomberg.com/apps/news?pid=21070001&sid=at0oOdQTLVE0>, (accessed July 10, 2011).

growing cynicism about a virus that has been in the headlines for almost four years without starting a pandemic.”<sup>177</sup> Human infections of H5N1 had risen to 115 cases in 2006, up from 98 the year before. But in 2007, there were only 88 infections, and the next year saw even further declines, to 44.<sup>178</sup> Dr. Takeshi Kasai, an influenza advisor in the WHO regional office in Manila, said “I have observed ‘avian influenza fatigue’ or apathy among the people ... They think they have already done enough, and that is our worry in the WHO.”<sup>179</sup> The political mood had also shifted. The financial crisis that began in late 2008 led officials to scrutinize every aspect of their budgets. Did pandemic preparedness really deserve the funding it had so far achieved? Most public health experts believed it did. Kasai said that the risk that H5N1 would turn pandemic remained unchanged. Keiji Fukuda, no longer at CDC, but now head of the WHO’s global influenza program, agreed: “If we begin to withdraw our attention and move our attention to something else which is completely different, then we really stand to lose a lot of the work which has been built up over the past four years. To do this over and over again is truly ... it’s like being Sisyphus.”<sup>180</sup>

Not all critics were willing to heed the caution of influenza specialists. Questioning the right—or wrong—headedness of pandemic preparedness also came from the inside the medical community. In an “Editor’s Choice” article, one editor of the British medical journal *BMJ* opined:

Somewhere, I imagine, there’s a small group of people proud to be counted among the Friends of Avian Flu, or FAF for short. I suspect they have a catchy mission statement, such as “Keeping the nightmare alive,” and lapel badges of vaguely bird-like shape. Their challenge is to keep bird flu forever in the public eye. This should be getting harder, as influenza H5N1 is proving particularly resistant to undergoing the killer mutation that would allow efficient human to human transmission of the virus. Ten years after the strain first appeared in humans, it has killed just 191 people. This is despite the most propitious of circumstances: millions of people and poultry living in very close proximity in South East Asia. Although these deaths are a tragedy for the victims and their families, it’s as well to remember that a similar number of people die on the roads world wide every 84 minutes.<sup>181</sup>

The article triggered an immediate flurry of angry responses to the *BMJ* website. Peter Sandman, risk communication specialist and deputy editor of Michael Osterholm’s *CIDRAP Business Source* journal, and

<sup>177</sup> Mark Henderson, “Dealing with flu fatigue,” *The Times*, November 24, 2007, [http://women.timesonline.co.uk/tol/life\\_and\\_style/women/body\\_and\\_soul/article2929775.ece](http://women.timesonline.co.uk/tol/life_and_style/women/body_and_soul/article2929775.ece), (accessed July 10, 2011).

<sup>178</sup> World Health Organization, “Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO”, August 31, 2010, [http://www.who.int/csr/disease/avian\\_influenza/country/cases\\_table\\_2010\\_08\\_31/en/index.html](http://www.who.int/csr/disease/avian_influenza/country/cases_table_2010_08_31/en/index.html), (accessed July 10, 2011).

<sup>179</sup> Stella Gonzales, “WHO Warns Against ‘Bird Flu Fatigue’”, October 8, 2008, <http://ipsnews.net/news.asp?idnews=44170>, (accessed July 10, 2011).

<sup>180</sup> Helen Branswell, “‘Flu fatigue’ sets in among scientists after global spread of virus slows,” *The Globe and Mail*, January 1, 2009, <http://www.theglobeandmail.com/news/national/article963723.ece>, (accessed July 10, 2011).

<sup>181</sup> Tony Delamothe, “FAFing about,” *BMJ* 334, no. 7608 (June 2007), <http://www.bmj.com/cgi/doi/10.1136/bmj.39259.443646.47>, (accessed July 10, 2011).

a strong proponent of pandemic preparedness, was so angered by the article that he penned an editorial. “Whenever my commitment to pandemic preparedness starts to flag, I read something wrongheaded by an opponent of preparedness,”<sup>182</sup> Sandman wrote at the top of his article. David Fedson, a prominent influenza vaccine researcher, was equally dismissive of the *BMJ*’s “reckless and deeply uninformed” article, accusing the editor of being representative of a “cultural inability to ‘envision the worst’.”<sup>183</sup>

Although the central arguments of proponents of pandemic preparedness remained unchanged—the world was unprepared, the risk was high, a pandemic was overdue—cynicism and skepticism was setting in. One WHO advisor declared, “The biggest threat that we have now is ‘flu fatigue’.”<sup>184</sup>

[ENDS]

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<sup>182</sup> Peter M. Sandman, “Read ‘FAffing About’ if you need some motivation,” *CIDRAP Business Source*, July 17, 2007, <http://www.psandman.com/CIDRAP/CIDRAP16.htm>, (accessed July 10, 2011).

<sup>183</sup> David S. Fedson, “Envisioning the worst,” *BMJ Rapid Response* (July 3, 2007), [http://www.bmj.com/content/334/7608/0.1.extract/reply#bmj\\_el\\_170927](http://www.bmj.com/content/334/7608/0.1.extract/reply#bmj_el_170927), (accessed July 10, 2011).

<sup>184</sup> Dr. Julie Hall, deputy regional adviser on communicable disease surveillance and response, WHO Western Pacific Region, quoted in Bennett and Gale, “‘Flu Fatigue’ Poses Public Health Threat, WHO Says (Update1).”

Table 2.1. Explaining pandemic influenza. Pandemic influenza was described as a threat of high consequence and high probability.

Year	Quotation	Citation
2009	"What we say about pandemic flu is not if, but when."	John C. Martin, chief executive, Gilead Sciences (inventor of influenza antiviral Tamiflu) <sup>185</sup>
2008	"When it comes to flu pandemics, scientists say the question is not if, but when."	<i>Hamilton Spectator</i> (Canada) <sup>186</sup>
2008	"Influenza scientists repeat like a mantra that when it comes to flu pandemics, the question is not if, but when."	<i>Canadian Press</i> (Canada) <sup>187</sup>
2007	"The director of Britain's new centre for avian flu research said yesterday that it was a question of 'not if but when' the disease would cause a pandemic."	<i>The Times</i> (UK) <sup>188</sup>
2007	"A growing number of scientists are using the term 'not if, but when' in referring to the likelihood of another influenza pandemic that could kill thousands (maybe millions) worldwide."	<i>Topeka Capital-Journal</i> <sup>189</sup>
2006	"At the very start of 'Pandemic', tonight's feature-length helping of Horizon (BBC2 9.00pm), the commentary states baldly, arrestingly, that what we are about to witness is 'the true story of the next pandemic'. As this statement segues directly into terrifying suggestions as to the scale of the disaster facing humanity at any moment, you may feel - and hope - that it is going too far to present such a gloomy hypothesis as the truth. By the end, after listening to expert after expert stating that this is a 'not if but when' scenario, you will probably be working out how to order six months' household supplies and get hold of enough anti-viral drugs to protect your loved ones."	<i>Financial Times</i> (UK) <sup>190</sup>
2006	"According to Capt. Bernita Bush, public information officer with the Clay County Department of Public Safety the flu kills around 36,000 people nationwide every year. The victims, she said, are usually the sick, frail and elderly. In the case of a pandemic, she said thousands of people not usually affected by the flu could die. Bush, like Chilson, agrees that it is not if, but when a flu outbreak of this kind will arrive in the United States"	<i>Florida Times-Union</i> <sup>191</sup>
2006	"States have a spotty record in preparing for bird flu and it is matter	<i>Associated Press</i> <sup>192</sup>

<sup>185</sup> Amy Zipkin, "On the discovery trail," *The New York Times*, October 11, 2009.

<sup>186</sup> "Could influenza epidemic happen again?," *The Hamilton Spectator*, September 17, 2008.

<sup>187</sup> Helen Branswell, "Medical reporter," *The Canadian Press*, September 15, 2008.

<sup>188</sup> Melanie Reid, "Bird flu pandemic is inevitable, expert says after new outbreak," *The Times*, May 25, 2007.

<sup>189</sup> "It's coming," *Topeka Capital-Journal*, March 31, 2007.

<sup>190</sup> Karl French, "Pandemic," *Financial Times*, November 7, 2006.

<sup>191</sup> Patti Levine-Brown, "Flu preparedness is key, officials say Clay officials had a summit to discuss readiness in case of a pandemic," *The Florida Times-Union*, July 19, 2006.

<sup>192</sup> Lara Jakes Jordan, "Many states are unprepared for bird flu, federal doctor says," *Deseret Morning News*, May 19, 2006.

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	of 'not if, but when' the deadly virus reaches the United States, the Homeland Security Department's top doctor said Thursday."	
2006	"Hurricane season is a month away. The arrival of a pandemic flu that may kill hundreds of thousands across the nation is talked about in terms of 'not if, but when.' The threat of terrorism, including radiologic bombs, isn't only the stuff of nightmares."	<i>Providence Journal</i> <sup>193</sup>
2006	"The fear is that the deadly strain could trigger a pandemic to rival the 1918 Spanish flu, which killed tens of millions of people worldwide. A substantial number of scientists and health experts say the question is not if but when."	<i>Washington Post</i> <sup>194</sup>
2006	"It is important not to panic. While experts believe that the only question about a global pandemic is not if but when, avian flu has killed fewer than 100 people worldwide as of Friday, none from human-to-human transmission. Researchers are furiously working on a preventive vaccine. But at the same time, states across the country - Maryland included - have been warned: It's time to get very busy preparing to protect ourselves."	<i>Baltimore Sun</i> <sup>195</sup>
2005	"Well, we've been ringing that bell for quite awhile. It's kind of like with Hurricane Katrina. That you saw it on the radar screen. And people for years and years before that, had been warning about these levees. And the same thing is happening here with health officials. ... We've been watching or concerned about a pandemic. We know it's a question, really, only of not if but when. And so the key issue is, just like those levees, if you don't strengthen them, we're going to have a terrible disaster, and we could be doing better."	Dr. Shelley Hearne, executive director, Trust For America's Health <sup>196</sup>
2005	"Well, you know, I was reading <i>Time</i> magazine from this week [Oct 9, 2005 <sup>197</sup> ] and it said, 'The World Health Organization declared in September once again that as far as influenza pandemic is concerned, the question is not if, but when. Not whether millions would die, but how many millions.'"	Katie Couric ( <i>NBC News</i> ) <sup>198</sup>
2005	"Margaret Chan, chief of influenza pandemic preparedness at the World Health Organization, no longer talks about if it is going to happen: 'The only question is: When? I don't think anybody has the answer to it. We have to be on the lookout for it any time, any day.'"	<i>Toronto Star</i> (Canada) <sup>199</sup>

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<sup>193</sup> Amanda Milkovits, "Local officials are frontline disaster defense," *The Providence Journal*, April 27, 2006.

<sup>194</sup> Susan Levine, "D.C. Plans Summit on Pandemic Response; Meeting April 28 Is Part of Effort to Coordinate Business, School, Religious Groups," *The Washington Post*, March 21, 2006.

<sup>195</sup> "EDITORIAL: On our own," *The Baltimore Sun*, March 5, 2006.

<sup>196</sup> Stated during a TV appearance on "The Situation With Tucker Carlson for October 12, 2005" (MSNBC, October 11, 2005).

<sup>197</sup> Christine Gorman, "Avian Flu: How Scared Should We Be?," *Time*, October 9, 2005, <http://www.time.com/time/magazine/article/0,9171,1115685,00.html>, (accessed July 10, 2011).

<sup>198</sup> "Interview: Dr. Sue Bailey, former assistant secretary of defense for health affairs, discusses possibility of Avian flu pandemic," *Today* (NBC, October 10, 2005).

<sup>199</sup> Lynda Hurst, "Deadly flu: 'The only question is when'; 'Canada prepared to respond' Avian's arrival called inevitable Experts fear global pandemic Not if, but when for outbreak of disease: Experts Avian flu virus is possible candidate for global infection," *The Toronto Star*, August 27, 2005.

2002	“Most experts believe that it is not a question of whether there will be another severe influenza pandemic but when.”	Professor Sir Liam Donaldson, Chief Medical Officer for England (UK) <sup>200</sup>
2005	“Pandemic influenza is an uncommon type of influenza A that causes greater morbidity and mortality than seasonal influenza. An influenza pandemic occurs when a new influenza A virus (a ‘pandemic influenza virus’) emerges in the human population, causes serious illness, and then spreads easily from person to person worldwide.”	US Department of Health and Human Services <sup>201</sup>
	“When a pandemic virus strain emerges, 25% to 35% of the population could develop clinical disease, and a substantial fraction of these individuals could die.”	
2004	“Although the impact of influenza on morbidity and mortality in a normal epidemic year is substantial, much more serious influenza pandemics also can occur.”	NIAID Director Anthony Fauci, in congressional testimony <sup>202</sup>
2005	“Influenza pandemics are associated with high morbidity, excess mortality, and social and economic disruption.”	WHO Director-General LEE Jong-Wook <sup>203</sup>
2007	“Mortality due to pandemic influenza is expected to be much higher than in inter-pandemic years, when an average of 12,000 influenza-related deaths are estimated to occur in England and Wales each year.”	<i>Pandemic Flu: A national framework for responding to an influenza pandemic</i> (UK) <sup>204</sup>

<sup>200</sup> Quote appears on the cover of UK Department of Health, “Explaining pandemic flu.”

<sup>201</sup> U.S. Department of Health and Human Services, “HHS Pandemic Influenza Plan,” 16, 1-12.

<sup>202</sup> Anthony S. Fauci, “Testimony: Statement by Anthony S. Fauci, M.D., Director National Institute of Allergy and Infectious Diseases National Institutes of Health, U.S. Department of Health and Human Services on The NIH Biomedical Research Response to Influenza before the The Committee on Energy and Commerce United States House of Representatives”, November 18, 2004, <http://www.hhs.gov/asl/testify/t041118.html>, (accessed July 10, 2011).

<sup>203</sup> World Health Organization, *Avian influenza: assessing the pandemic threat*, January 2005, 3, <http://www.who.int/csr/disease/influenza/H5N1-9reduit.pdf>.

<sup>204</sup> UK Department of Health, “Pandemic flu: a national framework for responding to an influenza pandemic”, November 22, 2007, 26, [http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/@dh/@en/documents/digitalasset/dh\\_080745.pdf](http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_080745.pdf), (accessed June 16, 2011).

### Chapter 3 2009 H1N1 Influenza: scare, skepticism, and accusation

Influenza is said to be so unpredictable that there is a saying common among those that have spent their career studying the disease: if you've seen one season, you've seen one season. And so perhaps in retrospect, there should be little surprise that "the first influenza pandemic in four decades,"<sup>1</sup> as the World Health Organization (WHO) calls it, was not detected in southern China, but southern California; caused not by the dreaded avian H5N1 virus, but a swine influenza virus; and its first victims were not left dead, ravaged by a killer virus, but alive and well.

#### Scare

"On April 17, 2009, CDC determined that two cases of febrile respiratory illness occurring in children who resided in adjacent counties in southern California were caused by infection with a swine influenza A (H1N1) virus," the CDC wrote in its first public notice of the new virus.

Although this is not a new subtype of influenza A in humans, concern exists that this new strain of swine influenza A (H1N1) is substantially different from human influenza A (H1N1) viruses, that a large proportion of the population might be susceptible to infection, and that the seasonal influenza vaccine H1N1 strain might not provide protection. The lack of known exposure to pigs in the two cases increases the possibility that human-to-human transmission of this new influenza virus has occurred.<sup>2</sup>

By the time of the report—published online early in the *MMWR*—the two children had already recovered. The first, a 10-year old boy living in San Diego County, had developed a fever, cough and vomiting on March 30. By the time CDC came to hear about the case, he was well again. The second, a 9 year old girl, had also recovered from her cough and fever. But without a known exposure to pigs, investigators could not rule out the possibility that the children might have been infected with a virus capable of human to human transmission—and that they had transmitted the infection on to others. In addition, the boy had recently traveled to Texas, and so the CDC, working with state and local health departments in California and Texas, called on clinicians to enhance surveillance.

Responding to the April 21 dispatch, the European CDC (ECDC, the European Centre for Disease Prevention and Control) informed its readers that while the event was "of concern," the risk of pandemic was small. While the virus could trigger a pandemic, "it is noticeable that both the children's illnesses were mild and essentially self-limiting, neither required specific therapy or hospitalisation. Indeed the viruses only came to light because the children were taken to clinics taking part in a clinical study and a surveillance exercise." The fact that the infections were caused by a swine influenza virus was itself not all that alarming. Swine influenza infections were seen every year in the US. Indeed, one review paper from 2007 cataloged 50 apparent human infections with swine influenza virus, of which

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<sup>1</sup> Margaret Chan, "Experts begin their assessment of the response to the H1N1 influenza pandemic", April 12, 2010, [http://www.who.int/dg/speeches/2010/ihr\\_20100412/en/index.html](http://www.who.int/dg/speeches/2010/ihr_20100412/en/index.html), (accessed April 12, 2010).

<sup>2</sup> U.S. Centers for Disease Control and Prevention, "Swine Influenza A (H1N1) Infection in Two Children --- Southern California, March--April 2009," *MMWR. Morbidity and Mortality Weekly Report* 58, no. Dispatch (April 21, 2009): 1-3.

several had no known exposure to pigs.<sup>3</sup> The ECDC concluded that “these mild US cases ... are not reflecting the emergence of a pandemic strain...” and cautioned that while the enhanced surveillance might turn up additional cases, “if this happens it should not be misinterpreted as a change in that conclusion.”<sup>4</sup>

The ECDC’s April 23 prediction was partially correct: hours later, the CDC called a press briefing and announced that enhanced surveillance had turned up five additional cases. “The good news is that all seven of these patients have recovered. One of them required hospitalization but has been discharged. And so far this is not looking like very, very severe influenza. Seven patients all recovered,” explained Anne Schuchat, director of CDC’s National Center for Influenza and Respiratory Diseases.<sup>5</sup> The CDC emphasized that it was moving quickly and aggressively to gain a better understanding of the situation, including preparation of a vaccine seed strain should the need for a vaccine arise, and working with a variety of partners at the local, state, and international level. It stressed that because surveillance activities were being enhanced, “we’re likely to find more cases. So that’s not going to be surprising.” The CDC promised to post situational updates to its website at 3pm each day, but cautioned journalists dialed into the teleconference, “We don’t think this is time for major concern around the country...”

But the CDC’s thinking was about to undergo a major shift. “On the 23rd, we held a press briefing about additional cases in the United States, again not really knowing whether this was a big deal or a small deal but just wanting people to be on the alert and to look for unusual influenza viruses,” recalled Rear Admiral Anne Schuchat, director of the National Center for Immunization and Respiratory Diseases.<sup>6</sup> “It was at that point, on the 23rd, when Mexico, Canada and CDC were able to connect the idea that the virus in Canada from Mexico was the same as the virus that we were testing in the US.”

Reports of increased respiratory disease in Mexico had been publicly discussed in infectious disease circles, but until April 23 when the results of detailed laboratory testing results performed in Canada were known, no firm connection between these outbreaks and the new “swine flu” virus that had sickened a handful of individuals in California and Texas had been made. Signaling the increase in concern, the April 24 press briefing was led by the acting director of the CDC. “Today, Mexico’s Minister of Health confirmed that they have cases of swine influenza in people and that they believe some of the

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<sup>3</sup> Kendall P. Myers, Christopher W. Olsen, and Gregory C. Gray, “Cases of Swine Influenza in Humans: A Review of the Literature,” *Clinical Infectious Diseases* 44, no. 8 (April 15, 2007): 1084-1088.

<sup>4</sup> European Centre for Disease Prevention and Control, “Swine Influenza A(H1N1) Infection in Two Children in Southern California, March-April 2009”, April 23, 2009, [http://www.ecdc.europa.eu/en/activities/sciadvice/Lists/ECDC%20Reviews/ECDC\\_DisForm.aspx?List=512ff74f-77d4-4ad8-b6d6-bf0f23083f30&ID=556&RootFolder=%2Fen%2Factivities%2Fsciadvice%2FLists%2FECDC%20Reviews](http://www.ecdc.europa.eu/en/activities/sciadvice/Lists/ECDC%20Reviews/ECDC_DisForm.aspx?List=512ff74f-77d4-4ad8-b6d6-bf0f23083f30&ID=556&RootFolder=%2Fen%2Factivities%2Fsciadvice%2FLists%2FECDC%20Reviews), (accessed July 11, 2011).

<sup>5</sup> U.S. Centers for Disease Control and Prevention, “CDC Briefing on Public Health Investigation of Human Cases of Swine Influenza”, April 23, 2009, <http://www.cdc.gov/media/transcripts/2009/t090423.htm>, (accessed July 11, 2011).

<sup>6</sup> Testimony of Anne Schuchat to Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, April 28, 2009, *Hearing on Public Health Response to Swine Flu* (Washington, DC, 2009), <http://www.senate.gov/fplayers/CommPlayer/commFlashPlayer.cfm?fn=appropsA042809&st=1000>, (accessed April 30, 2009).



people who were infected died from swine influenza,” Richard Besser said. “We hear from the public and from others about their concern, and we are worried, as well.”<sup>7</sup> CDC indicated plans to send teams to Mexico to assist authorities there. “It’s really critically important we learn more about what’s going on in Mexico because reports from Mexico are raising concerns about much more severe disease,” Besser said.

From Geneva, the World Health Organization issued its first public notice regarding the emerging outbreak on April 24: seven confirmed and nine suspected cases of swine influenza H1N1 in the United States—but more alarmingly, influenza-like illness activity in Mexico’s capital, with more than 800 cases of pneumonia and around 60 deaths.<sup>8</sup> The next day, WHO’s director-general Margaret Chan, declared: “the Director-General has determined that the current events constitute a public health emergency of international concern, under the Regulations,”<sup>9</sup> a decision arrived at under consultation with an Emergency Committee rapidly assembled under provisions of the International Health Regulations

News about the problem in Mexico was racing around the world: unusually severe cases of pneumonia in previously healthy young adults, a seemingly prolonged influenza season, and outbreaks of unidentified etiology.<sup>10</sup> Mexico’s epidemic also seemed larger than anybody had at first realized. In its second global update, on April 26, WHO reported “suspect clinical cases” of influenza in 19 of Mexico’s 32 states.<sup>11</sup> The Mexican government declared a suspension of all schools nationwide. Images of Mexicans wearing bright blue surgical face masks saturated the international media. In the capital of Mexico City, where President Calderón had just published an order conferring “emergency powers” to the government, two *New York Times* reporters wrote of “flooded government health hot lines” and “jittery residents,” one telling the *Times*, “I know all of us will die one day, but I want to last out the week.” The army had been called in to distribute four million masks.<sup>12</sup>

Across the border, America’s outbreak was also growing—from California and Texas to Kansas, then Ohio. In New York City, officials reported on April 25 that 100 students missed school because of a “flu-like symptoms”<sup>13</sup>—and attention was growing. On April 26, John Brennan, assistant to the president for

<sup>7</sup> U.S. Centers for Disease Control and Prevention, “CDC Press Briefing Transcripts April 24, 2009”, April 24, 2009, <http://www.cdc.gov/media/transcripts/2009/t090424.htm>, (accessed July 15, 2011).

<sup>8</sup> World Health Organization, “Influenza-like illness in the United States and Mexico”, April 24, 2009, [http://www.who.int/csr/don/2009\\_04\\_24/en/index.html](http://www.who.int/csr/don/2009_04_24/en/index.html), (accessed July 12, 2011).

<sup>9</sup> Margaret Chan, “Swine influenza”, April 25, 2009, [http://www.who.int/mediacentre/news/statements/2009/h1n1\\_20090425/en/index.html](http://www.who.int/mediacentre/news/statements/2009/h1n1_20090425/en/index.html), (accessed May 28, 2009).

<sup>10</sup> Jon Cohen, “Exclusive: Interview With Head of Mexico’s Top Swine Flu Lab,” *ScienceInsider*, May 1, 2009, <http://news.sciencemag.org/scienceinsider/2009/05/exclusive-inter.html>, (accessed July 12, 2011).

<sup>11</sup> World Health Organization, “Swine flu illness in the United States and Mexico - update 2”, April 26, 2009, [http://www.who.int/csr/don/2009\\_04\\_26/en/index.html](http://www.who.int/csr/don/2009_04_26/en/index.html), (accessed August 12, 2009).

<sup>12</sup> Marc Lacey and Elisabeth Malkin, “Mexico Takes Powers to Isolate Cases of Swine Flu,” *The New York Times*, April 26, 2009, sec. International / Americas, <http://www.nytimes.com/2009/04/26/world/americas/26mexico.html>, (accessed July 12, 2011).

<sup>13</sup> New York City Department of Health and Mental Hygiene, “Health Department Testing Finds Probable Cases of Swine Influenza in Students at a Non-Public School in Queens”, April 25, 2009, <http://www.nyc.gov/html/doh/html/pr2009/pr015-09.shtml>, (accessed July 12, 2011).

homeland security and counterterrorism, joined CDC director Besser and the secretary of homeland security Janet Napolitano in a press briefing held at the White House: “President Obama is very concerned about the recent cases of swine flu that have been identified in the United States, as well as the outbreak in Mexico,” Brennan said. “The President’s thoughts are with those who have been affected by this illness....”<sup>14</sup> By the end of the day, swine flu was formally declared a “public health emergency” by the Department of Health and Human Services.<sup>15</sup>

As the outbreak spread across the US, the mystery only deepened as to why Mexico’s epidemic seemed severe in contrast to the infections in the US where all cases had recovered, and only one required hospitalization. “I expect as we continue to look for cases, we are going to see a broader spectrum of disease,” Besser remarked at the national press briefing. “What we know about this virus is it looks to be the same virus as is causing the situation in Mexico. And given the reports out of Mexico, I would expect that over time we’re going to see more severe disease in this country.” At the CDC’s daily press briefing in Atlanta, held just a few hours later, Schuchat repeated the message: “I think we really need to prepare for the idea that we will have additional cases, additional affected states and I do fear that we will have deaths here.”<sup>16</sup>

As testing ability increased, confirmed cases of the new “swine flu”—which officials would soon encourage be called “H1N1” in recognition of its viral subtype and out of fear of causing needless harm to the pork industry—began to appear in other countries. On April 27, WHO had received reports of six cases in Canada (and no deaths), with one case in Spain (no deaths).<sup>17</sup> WHO raised its official pandemic phase alert from Phase 3 to Phase 4. “The change to a higher phase of pandemic alert indicates that the likelihood of a pandemic has increased, but not that a pandemic is inevitable,” Dr Chan said.<sup>18</sup> By the next day, New Zealand, the United Kingdom, and Israel were added to WHO’s growing list of countries with confirmed infection. The following morning, the United States reported its first death—a Mexican toddler visiting relatives in Texas.<sup>19</sup> And on the same day, WHO added Germany and Austria to the list

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<sup>14</sup> Office of the Press Secretary, “Press Briefing On Swine Influenza, 4/26/09”, April 26, 2009, [http://www.whitehouse.gov/the\\_press\\_office/Press-Briefing-On-Swine-Influenza-4/26/09/](http://www.whitehouse.gov/the_press_office/Press-Briefing-On-Swine-Influenza-4/26/09/), (accessed July 12, 2011).

<sup>15</sup> U.S. Department of Health and Human Services, “HHS Declares Public Health Emergency for Swine Flu”, April 26, 2009, <http://www.hhs.gov/news/press/2009pres/04/20090426a.html/nation>, (accessed July 12, 2011); Donald G. McNeil Jr, “U.S. Declares Public Health Emergency Over Swine Flu,” *The New York Times*, April 27, 2009, sec. World, <http://www.nytimes.com/2009/04/27/world/27flu.html>, (accessed May 1, 2009).

<sup>16</sup> U.S. Centers for Disease Control and Prevention, “CDC Press Briefing Transcripts April 26, 2009”, April 26, 2009, <http://www.cdc.gov/media/transcripts/2009/t090426.htm>, (accessed July 12, 2011).

<sup>17</sup> World Health Organization, “Swine influenza - update 3”, April 27, 2009, [http://www.who.int/csr/don/2009\\_04\\_27/en/index.html](http://www.who.int/csr/don/2009_04_27/en/index.html), (accessed July 12, 2011).

<sup>18</sup> Margaret Chan, “Swine influenza”, April 27, 2009, [http://www.who.int/mediacentre/news/statements/2009/h1n1\\_20090427/en/index.html](http://www.who.int/mediacentre/news/statements/2009/h1n1_20090427/en/index.html), (accessed July 12, 2011).

<sup>19</sup> The City of Houston, “HDHHS ADVISORY ON SWINE FLU DEATH”, April 29, 2009, <http://www.houstontx.gov/health/NewsReleases/swineflunewsbrief.html>, (accessed July 12, 2011).

of affected countries, and announced the outbreak had reached Phase 5,<sup>20</sup> signaling that a pandemic was “imminent.”<sup>21</sup>

In a televised press conference, Margaret Chan emphasized the unknowns—that “new diseases are, by definition, poorly understood. Influenza viruses are notorious for their rapid mutation and unpredictable behavior,” but promised to get answers in due course.

The biggest question, right now, is this: how severe will the pandemic be, especially now at the start? It is possible that the full clinical spectrum of this disease goes from mild illness to severe disease. ... From past experience, we also know that influenza may cause mild disease in affluent countries, but more severe disease, with higher mortality, in developing countries.<sup>22</sup>

Chan declared that “Above all, this is an opportunity for global solidarity as we look for responses and solutions that benefit all countries, all of humanity. After all, it really is all of humanity that is under threat during a pandemic.” She urged countries to “ramp up preparedness and response”; the Phase 5 alert was “a signal to governments, to ministries of health and other ministries, to the pharmaceutical industry and the business community that certain actions should now be undertaken with increased urgency, and at an accelerated pace.”

In the US, the response to the new virus had already taken on increased urgency. In his third prime time address to the nation, President Obama announced a request to Congress for \$1.5 billion in emergency funding “to support our ability to monitor and track this virus and to build our supply of antiviral drugs and other equipment.” Schools with confirmed or suspected cases of the new influenza were suggested to “strongly consider temporarily closing.”<sup>23</sup> The Obama administration’s proactive stance against the new virus was to be somewhat expected: as the Democratic US senator from Illinois, Obama together with Senator Lugar had in an editorial in the *New York Times* in 2005 called on the international community “to take decisive action to prevent a pandemic.”<sup>24</sup>

As authorities proceeded to take the steps necessary to prepare new influenza vaccines against the novel H1N1 strain,<sup>25</sup> public forums both on- and off-line were bursting with commentary on swine flu.

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<sup>20</sup> Margaret Chan, “Influenza A(H1N1)”, April 29, 2009, [http://www.who.int/mediacentre/news/statements/2009/h1n1\\_20090429/en/index.html](http://www.who.int/mediacentre/news/statements/2009/h1n1_20090429/en/index.html), (accessed July 12, 2011).

<sup>21</sup> World Health Organization, *Pandemic influenza preparedness and response: a WHO guidance document*, April 2009, 25, <http://www.who.int/entity/csr/disease/influenza/PIPGuidance09.pdf>, (accessed July 3, 2009).

<sup>22</sup> Chan, “Influenza A(H1N1).”

<sup>23</sup> Office of the Press Secretary, “News Conference by the President, 4/29/2009”, April 29, 2009, [http://www.whitehouse.gov/the\\_press\\_office/News-Conference-by-the-President-4/29/2009/](http://www.whitehouse.gov/the_press_office/News-Conference-by-the-President-4/29/2009/), (accessed July 12, 2011).

<sup>24</sup> Barack Obama and Richard Lugar, “Grounding a Pandemic,” *The New York Times*, June 6, 2005, sec. Opinion, [http://www.nytimes.com/2005/06/06/opinion/06obama.html?\\_r=1&pagewanted=print](http://www.nytimes.com/2005/06/06/opinion/06obama.html?_r=1&pagewanted=print), (accessed October 20, 2010).

<sup>25</sup> Declan Butler, “The virus grower,” *Nature* (May 14, 2009), <http://www.nature.com/doi/10.1038/news.2009.482>.

John Barry, author of the bestselling book in the 1918 pandemic, argued for the urgency of manufacturing a vaccine. "Even if this virus were to peter out soon," Barry wrote in an April 27 op-ed in the *New York Times*, "there is a strong possibility it would only go underground, quietly continuing to infect some people while becoming better adapted to humans, and then explode around the world."<sup>26</sup> Barry explained that "all four of the well-known pandemics seem to have come in waves," and by implication, the new swine flu could follow in that pattern. A vaccine was thus essential, and discussions of vaccine rationing began to appear in the press.<sup>27</sup> As Barry explained:

In all four instances, the gap between the time the virus was first recognized and a second, more dangerous wave swelled was about six months. It will take a minimum of four months to produce vaccine in any volume, possibly longer, and much longer than that to produce enough vaccine to protect most Americans. The race has begun.<sup>28</sup>

Comparisons with the 1918 pandemic were all but inevitable given that by the time of the 2009 H1N1 outbreak, the deadly "Spanish flu" pandemic had become the preeminent historical anchor for "pandemic preparedness." On an early morning CNN broadcast, Dr. Martin Blaser was interviewed to comment on Barry's recent warning. Blaser, chairman of New York University's Department of Medicine, past president of the Infectious Diseases Society of America, and former CDC Epidemic Intelligence Officer, added his voice to those emphasizing the extraordinary risk posed by the new virus.

CNN HOST: When Dr. Margaret Chan of WHO says 'all humanity is under threat', put this in perspective for us. What really, Dr. Blaser, is the risk here, in this country?

BLASER: She's right. This is a pandemic. It's all over the world. Right now, it's early and it's mild, so everybody's at risk. But right now the risk is low.

CNN: But her warning that this could be serious, serious trouble. Is that any more to the developing world or to the developed world, or is it really into everybody?

BLASER: It's really everybody, because in this one, we're all combined. It's traveling from person to person. All people are at risk.

CNN: People are trying to game out what this virus is going to do. And John Barry, who wrote a fabulous book on the 1918 flu pandemic called 'The Great Influenza', thinks this is just the opening act of a very long play. That this virus is probably going to go away for a little while, go to ground, hide in the background. And then maybe next winter or early next year come back with a vengeance. What do you think?

BLASER: I think that's the most likely scenario because of, because influenza is very influenced by the season and in 1918 it came. There was a little bump in the early

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<sup>26</sup> John M. Barry, "Where Will the Swine Flu Go Next?," *The New York Times*, April 28, 2009, sec. Opinion, [http://www.nytimes.com/2009/04/28/opinion/28barry.html?\\_r=1](http://www.nytimes.com/2009/04/28/opinion/28barry.html?_r=1), (accessed July 12, 2011).

<sup>27</sup> National Public Radio, "WHO Boosts Flu Alert Level To Phase 5", April 29, 2009, <http://www.npr.org/templates/story/story.php?storyId=103593687>, (accessed July 12, 2011).

<sup>28</sup> Barry, "Where Will the Swine Flu Go Next?".

summer. It went underground and then it did come back with a vengeance. And that would be predictable here. And I think we have to think of this more, as one of our secretaries said, as a marathon, and not as a sprint.<sup>29</sup>

In numerical terms, the “cause for deep concern” that Obama had spoken of had, by April 29, been confirmed to have infected 91 individuals across ten US states with one death. In its daily update, the CDC warned that “as it continues to spread, more cases, more hospitalizations and more deaths are expected in the coming days and weeks.”<sup>30</sup> And while the move garnered praise from circles long interested in pandemic preparedness (“That is excellent risk communication,” the risk communications specialist Peter Sandman commented in *Nature*<sup>31</sup>), an alternative yet tenuous narrative surfaced in the sea of opinion, one that suggested “swine flu” may not be a disaster.

“Based on history and what we know about the flu virus, the threat is not as bad as it may seem,” the well-respected influenza virologist Peter Palese explained in an op-ed “Why Swine Flu Isn’t So Scary.”<sup>32</sup> Palese pointed out that the virus lacked an important protein that was present in both the 1918 virus and highly lethal avian influenza H5N1, and therefore “doesn’t have what it takes to become a major killer.” Joining Palese, noted influenza virologist Richard Webby was quoted as saying, “This virus doesn’t have anywhere near the capacity to kill like the 1918 virus.”<sup>33</sup> Nancy Cox, the CDC’s top influenza virologist, seemed to agree, echoing the message in a May 1 press briefing: “we do not see the markers for virulence that we’re seeing in the 1918 virus.”<sup>34</sup>

There was also an alternate and perhaps reassuring explanation for the seemingly bleak situation in Mexico where the proportion of infected people who died appeared alarmingly high. (Of more than 150 confirmed cases, nine deaths were recorded by May 1,<sup>35</sup> with many more cases and deaths suspected but still awaiting laboratory confirmation.) According to CDC’s director of global migration and quarantine, Dr. Martin Cetron, “We may just be looking at the tip of the iceberg, which would give you a skewed initial estimate of the case fatality rate.” If Cetron was right, huge numbers of Mexicans with mild H1N1 infections were going undetected, which would suggest that although the outbreak was

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<sup>29</sup> “W.H.O. Warns of Imminent Pandemic; NYC Building Collapsed; GOP Response to Obama 100 Days News Conference Remarks; The China Factor: How Much Do We Owe?; Obama Lays Out Challenges Ahead,” *American Morning* (CNN, April 30, 2009).

<sup>30</sup> U.S. Centers for Disease Control and Prevention, “H1N1 Flu Daily Update: April 29, 2009”, April 29, 2009, <http://www.cdc.gov/h1n1flu/updates/042909.htm>, (accessed July 12, 2011).

<sup>31</sup> Peter M. Sandman, “Pandemics: good hygiene is not enough,” *Nature* 459, no. 7245 (May 21, 2009): 323.

<sup>32</sup> Peter Palese, “Why Swine Flu Isn’t So Scary,” *wsj.com*, May 2, 2009, <http://online.wsj.com/article/SB124122223484879119.html>, (accessed May 12, 2009).

<sup>33</sup> Karen Kaplan and Alan Zarembo, “Scientists see this flu strain as relatively mild,” *The Los Angeles Times*, April 30, 2009, sec. Map: Swine flu’s spread, <http://www.latimes.com/features/health/la-sci-swine-reality30-2009apr30,0,119808,full.story>, (accessed May 1, 2009).

<sup>34</sup> U.S. Centers for Disease Control and Prevention, “CDC Press Briefing Transcripts May 1, 2009”, May 1, 2009, <http://www.cdc.gov/media/transcripts/2009/t090501.htm>, (accessed July 12, 2011).

<sup>35</sup> World Health Organization, “Influenza A(H1N1) - update 8.1”, May 1, 2009, [http://www.who.int/csr/don/2009\\_05\\_01a/en/index.html](http://www.who.int/csr/don/2009_05_01a/en/index.html), (accessed July 12, 2011).

large, the virus was far less deadly than feared.<sup>36</sup> Cetron's hypothesis could explain the disparity between the frightening picture in Mexico and more reassuring one in the US—the result of “ascertainment bias.” But only time and more detailed investigations would tell whether Cetron was right.

And while virologists were in agreement that the new H1N1 virus did not represent a repeat of the 1918 scenario, they all urged caution. “We know that there's a great deal that we do not yet understand about the virulence of the 1918 virus or other influenza viruses that have a more severe clinical picture in humans. So we're continuing to learn,” said Cox.<sup>37</sup> Even Peter Palese, who had penned the reassuring editorial, seemed willing to rethink his position if events changed. “If this virus keep [sic] going through our summer,” Palese said, “I would be very concerned.”<sup>38</sup>

### Continued spread, and blame

Time and time again, epidemics of infectious diseases have had the ability to cause not only physical suffering but also evoke a variety of moral and social judgments. H1N1 proved to be no exception. The virus did keep going, continuing to spread through the summer. By the end of the first week of May, the only two continents which had not reported confirmed cases were Antarctica and Africa, and nations around the world were taking tough actions.

In China, authorities were placing thousands of passengers arriving from ‘affected areas’ under quarantine. One of these passengers was Dr. Jonathan Metzl, a psychiatrist by training and director of the Program in Culture, Health, and Medicine at the University of Michigan. Metzl criticized the response in a story he recounted for the *Los Angeles Times*. After touching down in Shanghai, he had had no fever and no recent history of contact with pigs, cleared the passenger screening and was let enter China. The next evening, while still symptom-free, Chinese authorities informed him that a passenger “three rows in front and five seats across” from him had tested positive for H1N1; given 30 minutes to pack his belongings, he was transported in the middle of the night to a hotel-based quarantine where he and other passengers would stay for seven days under medical observation. “We couldn't leave our rooms, so we passed much of the time standing in our doorways, talking across the empty corridors about the mice, the heat, the food, the missed opportunities, and especially the isolation.”<sup>39</sup>

Japan had also activated its pandemic response plan immediately following early declarations by the US and WHO. From late April, in accordance with its pandemic planning, flights into Japan were restricted to certain airports, and all passengers arriving from affected areas (such as the US) underwent screening before being allowed entry to Japan. Those with confirmed novel influenza virus infection would be mandatorily quarantined. But unlike China, few people were quarantined, and the initial cases in the

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<sup>36</sup> Donald G. McNeil Jr, “Flu Outbreak Raises a Set of Questions,” *The New York Times*, April 27, 2009, sec. Health, <http://www.nytimes.com/2009/04/27/health/27questions.html>, (accessed April 29, 2009).

<sup>37</sup> U.S. Centers for Disease Control and Prevention, “CDC Press Briefing Transcripts May 1, 2009.”

<sup>38</sup> Kaplan and Zarembo, “Scientists see this flu strain as relatively mild.”

<sup>39</sup> Jonathan M. Metzl, “China's ill-considered response to the H1N1 virus,” *Los Angeles Times*, July 12, 2009, <http://articles.latimes.com/print/2009/jul/12/opinion/oe-metzl12>, (accessed July 12, 2011).

community largely occurred among Japanese students in the western Osaka and Hyogo prefectures. There, more than 4,000 schools were shut down in mid-May—one of the so-called “non-pharmaceutical interventions” designed to slow the spread of infection and thousands of children were put on prophylactic antivirals like Tamiflu. Despite the fact that only a handful of H1N1 cases had been reported (with no deaths) and the infection was, on the whole, mild in Japan as it was in much of the rest of the world, the *Japan Times* reported that those infected and their families were subjected to “an onslaught of hostility.” “Many schools have been under attack, receiving anonymous phone calls and e-mail criticizing them and their students for ‘bringing the new flu virus into the community.’”<sup>40</sup> In Toyooka city, the board of education received threatening emails. “Don't take the students on school trips. If we find someone catching the virus in Disneyland, we will blame you,” one email stated.

By contrast to the West where those first infected were often happy to tell reporters of their experience with the illness—such as Iain and Dawn Askham, the UK's first two confirmed cases, whose story appeared in *The Guardian* along with their wedding photo prior to their honeymoon in Mexico<sup>41</sup>—in Japan, the real names of those infected was kept private in order to help protect their safety. During SARS, although no Japanese contracted the illness, many Japanese felt vulnerable as it spread in neighboring Asian countries.<sup>42</sup> Japanese travelers returning from trips to Beijing “were met with slurs,” recalled a Japanese psychiatrist who worked for the Japanese Embassy in Beijing at the time. He told of cases where children were teased, called names like “Mr. SARS,” and had rocks thrown at them.<sup>43</sup>

In Egypt, authorities leveraged the concept of the H1N1 influenza virus as a “swine flu” in which pigs were said to put the Egyptian human population at risk to justify and carry out mass culling of Egyptian pigs, largely kept by the Zabaleen, a small Christian group of garbage collectors. Although the WHO refuted the idea that one could get the H1N1 swine flu through contact with pigs or pork products, it did not stop Egypt from culling the pigs. It only changed the justification to one of “public hygiene.” The decision to rid the country of pigs (a stigmatized animal considered unclean by the majority Muslim population) is therefore suspected to be more about religious politics than public health. The political scientist Mariz Tadros has shown how scientific arguments were used “to legitimize a response largely grounded in a religious abhorrence of pigs and a deep-seated sectarian antipathy towards the Christian minority who breed them and eat their meat.”<sup>44</sup>

Whether one looks to the situation in Japan, where those infected had to “apologize” to the majority uninfected population for bringing the disease into their country, or to the situation in Egypt, where the differences between the threat of swine flu, pigs, or to the Christian minority garbage collecting

<sup>40</sup> Setsuko Kamiya and Natsuko Fukue, “Did media go too far on swine flu?,” *The Japan Times*, June 5, 2009, <http://search.japantimes.co.jp/cgi-bin/nn20090605f1.html>, (accessed June 15, 2009).

<sup>41</sup> Severin Carrell, “First swine flu victims in UK say they caught virus on plane home | World news | guardian.co.uk”, May 1, 2009, <http://www.guardian.co.uk/world/2009/may/01/swine-flu-askhams-plane>, (accessed July 12, 2011).

<sup>42</sup> Teppei Imai et al., “SARS risk perceptions in healthcare workers, Japan,” *Emerging Infectious Diseases* 11, no. 3 (March 2005): 404-410.

<sup>43</sup> Kamiya and Fukue, “Did media go too far on swine flu?”.

<sup>44</sup> Mariz Tadros, “Scapepigging: H1N1 Influenza in Egypt,” in *Epidemics: Science, Governance and Social Justice*, ed. Sarah Dry and Melissa Leach (EarthScan, 2010), 214.

population were being conflated in an effort to cull pigs, responses to the H1N1 epidemic were tinged with fear and blame. Sociologists and historians of medicine have for this reason often argued that the responses that societies mount in response to calamities or other hazards often reveals important aspects of the complex social and moral universe of those societies.<sup>45</sup> It seems plausible, as Tadros suggests, that Egyptian authorities in particular emphasized the threat of “swine flu” (even before a single case had appeared in the country) because it offered a seemingly objective, rational way to justify discriminatory actions against the Christian ethnic minority. Such scapegoating—also usually aimed at the disadvantaged, immigrant, foreign, or otherwise already marginalized population—has defined the human response to epidemic disease for centuries.<sup>46</sup> Following release from the rundown hotel where he was kept in quarantine for seven days, Metztl felt an element of xenophobia underlined the Chinese response: “Chinese passengers were allowed to stay in their homes during the quarantine period instead of being confined to the high-security quarters the rest of us shared. The set-up promoted the narrative that H1N1 was being spread by ‘foreigners.’”<sup>47</sup> In the US, some dubbed the outbreak “Mexican flu” and demanded to know why the government was not closing the border.<sup>48</sup>

In other ways, however, the H1N1 outbreak was breaking with some historical patterns. The US and Mexico, the first two countries with known H1N1 infections, were freely reporting their cases to WHO. To international health planners who have long feared the hiding of epidemics, such cooperation was a major relief, and WHO repeatedly praised countries for their “transparent reporting” new cases.<sup>49</sup> Border control measures, believed by many to represent a fear of foreigners more than a credible shield against influenza, were not widespread but instead limited to just a few countries, and where they had been instituted, they were being discontinued. In Japan, for instance, where at one point the government had advised people to postpone travel to Mexico, warnings were relaxed by late May, as were airplane screenings.<sup>50</sup>

## Skepticism

Government responses grew alongside a tally of cases and deaths which steadily increased in number. On May 22, the CDC shipped candidate virus strains to vaccine manufacturers,<sup>51</sup> and HHS Secretary

<sup>45</sup> Charles E Rosenberg, “What is an epidemic? AIDS in historical perspective,” *Daedalus* 118, no. 2 (1989): 1-17; Douglas and Wildavsky, *Risk and Culture*.

<sup>46</sup> Howard Markel, *Quarantine!: East European Jewish Immigrants and the New York City Epidemics of 1892* (Baltimore, Md: Johns Hopkins University Press, 1997).

<sup>47</sup> Metztl, “China’s ill-considered response to the H1N1 virus.”

<sup>48</sup> Cindy Carcamo, “Swine flu cases prompt calls for closing Mexican border”, April 29, 2009, <http://www.oregister.com/news/immigration-128828-mexico-coe.html>, (accessed July 12, 2011). The powerful use of language to shape perceptions of the nature of disease and cast blame was especially evidence in the case of AIDS, where the GRID, “gay plague” and other names proliferated. (See Paula A. Treichler, “AIDS, Homophobia, and Biomedical Discourse: An Epidemic of Signification,” *October* 43 (December 1, 1987): 31-70; Susan Sontag, *Aids and its metaphors* (Penguin Books, 1990).)

<sup>49</sup> Margaret Chan, “Influenza A(H1N1): lessons learned and preparedness”, July 2, 2009, [http://www.who.int/dg/speeches/2009/influenza\\_h1n1\\_lessons\\_20090702/en/index.html](http://www.who.int/dg/speeches/2009/influenza_h1n1_lessons_20090702/en/index.html), (accessed July 3, 2009).

<sup>50</sup> Isabel Reynolds, “Japan relaxes flu guidelines as cases near 300,” *Reuters* (Tokyo, May 22, 2009), <http://www.reuters.com/article/2009/05/22/us-flu-japan-idUSTRE54J1JJ20090522>, (accessed July 12, 2011).

<sup>51</sup> Butler, “The virus grower.”



Kathleen Sebelius announced \$1 billion towards development of a novel H1N1 vaccine.<sup>52</sup> But as the US effort expanded, so too did skepticism over the true danger of the disease, revealing major concerns about a media overreaction and a distinct hesitation to labeling the H1N1 outbreak a “pandemic.” The WHO’s well-publicized “Phase 5” declaration of April 29 suggested that, by definition, a pandemic was “imminent,” but weeks later, the world remained in Phase 5—the so-called imminent pandemic had yet to materialize, and doubts were growing about a disease that remained unremarkable and mild in the vast majority of people.

“There are two groups of questions that are coming to WHO fairly often, and I think they reflect some ongoing uncertainty and questions about the Phases and about severity,” the WHO’s top influenza expert Keiji Fukuda said during a May 11 press conference.<sup>53</sup> WHO tried to explain what to non-experts in influenza seemed almost contradictory: the possibility of a pandemic of mild disease.

If we do go up to Phase 6 – this question has come a couple of times – what does it mean? And I think here is where we begin to get into some of the confusion about does this mean that the pandemic or the spread of disease has become more severe? What it really indicates again, is that the spread of this virus has continued, has progressed and that it has become established in other parts of the world. ... Severity is a different characteristic, it is a different feature.<sup>54</sup>

Unlike other numerical scales, such as the five “category” Saffir-Simpson Hurricane Wind Scale, the WHO explained that its six-point pandemic phase determinations were unrelated to clinical severity but instead reflected the likelihood of occurrence of global spread.<sup>55</sup> Phase 5 reflected “sustained community transmission, from person-to-person, occurring in two countries in one region, which is North America –which is one of the WHO Regions,” Fukuda said. A declaration of Phase 6 would indicate that the spread of H1N1 had become “established in another region outside of North America and is really going on at the community level.”<sup>56</sup>

To many outside WHO, the idea that the world could be on the verge of a “pandemic” of overwhelmingly mild disease seemed counterintuitive. “In the past few weeks, we have been repeatedly asked: ‘Is this a mild event?’,” Fukuda went on, “And I think that the response we have given back is that we are not sure right now.”

We have said that we know that most people who get infected develop mild illness, but in fact some people develop serious illness, some of the people die. We know that

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<sup>52</sup> U.S. Department of Health and Human Services, “HHS Takes Additional Steps Toward Development of Vaccine for the Novel Influenza A (H1N1)”, May 22, 2009, <http://www.hhs.gov/news/press/2009pres/05/20090522b.html>, (accessed May 27, 2009).

<sup>53</sup> World Health Organization, “Transcript of virtual press conference with Gregory Hartl, WHO Spokesperson for Epidemic and Pandemic Diseases, and Dr Keiji Fukuda, Assistant Director-General ad Interim for Health Security and Environment, World Health Organization”, May 11, 2009, [http://www.who.int/mediacentre/influenzaAH1N1\\_prbriefing\\_20090511.pdf](http://www.who.int/mediacentre/influenzaAH1N1_prbriefing_20090511.pdf), (accessed July 11, 2011).

<sup>54</sup> Ibid.

<sup>55</sup> Fineberg, “Swine flu of 1976: lessons from the past.”

<sup>56</sup> World Health Organization, “WHO May 11, 2009 virtual press conference.”

among those people who develop serious illness and who die, we know that many of them are young and healthy adults, people who don't normally die from an influenza infection. This picture is changing, and so this is why we have stressed about the evolving nature of the situation, this is why we have really refrained from jumping to quickly to say: "this is mild", "this is something", because we know that we are seeing things change on an almost daily basis.<sup>57</sup>

The WHO stressed that accurately characterizing severity was a far more elusive goal. "Severity is one of those terms and concepts that mean different things to different people," Fukuda said in response to a *USA Today* reporter attending the Geneva press briefing. "What is severe to politicians, is different than from what is severe to epidemiologists or what is severe to clinicians."

But the desire for WHO to provide some concrete statements on severity was clear. "I just want to understand if there is any plan to sort of change the alert system so that it reflects the actual degree of concern that should be as well as the geographical spread of it. Even though I understand that severity is something that is hard to pin down," a German reporter asked. Another, from Canada, commented, "I wanted to get back to the issue of severity if I could. I understand the notion that this is not what the Phases are about. But I think it is very confusing to the public that we could be in this Phase with a disease that appears at the moment to be mild..."<sup>58</sup>

The WHO at first remained reluctant to clear up the confusion, because to do so to the satisfaction of others seemed to require coupling its Pandemic Phase alert system with an evaluation of outbreak severity, and for a variety of reasons the Organization argued that this was too complicated to do. Nonetheless, WHO did address the severity issue, focusing on the impact the disease was having on people—the symptoms, the frequency of severe cases and deaths. In a report it produced the same day as the conference, "Assessing the severity of an influenza pandemic," WHO described the illness as "overwhelmingly mild outside Mexico," tending to cause "very mild illness in otherwise healthy people."<sup>59</sup> Reassuring as that might have been, WHO warned against drawing any firm conclusions about the pandemic's overall severity, and offered many reasons to remain concerned and wary of first impressions. First, the virus "appears to be more contagious than seasonal influenza." Second, the population had an "almost universal vulnerability to infection" and a higher prevalence of chronic diseases in today's population (of particular concern because of "the tendency of the H1N1 virus to cause more severe and lethal infections" in such populations). In addition, pandemics were said to come in waves. "The emergence of an inherently more virulent virus during the course of a pandemic can never be ruled out," WHO warned. Finally there was concern about poor nations. "The same virus that causes only mild symptoms in countries with strong health systems can be devastating in other countries where health systems are weak...."

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<sup>57</sup> Ibid.

<sup>58</sup> Ibid.

<sup>59</sup> World Health Organization, "Assessing the severity of an influenza pandemic", May 11, 2009, [http://www.who.int/csr/disease/swineflu/assess/disease\\_swineflu\\_assess\\_20090511/en/index.html](http://www.who.int/csr/disease/swineflu/assess/disease_swineflu_assess_20090511/en/index.html), (accessed May 12, 2009).

It was a mixed message, and responses among the public were equally polarized. Emergency rooms reported being overwhelmed with walk-in visits from healthy people, symptom free, who just wanted to be checked to make sure they did not have swine flu.<sup>60</sup> Others were skeptical, “even mocking,” the *New York Times* wrote, at the idea that people would alter their daily life in response to a mild disease that had still affected so few people.<sup>61</sup>

Publicly, governments were loathe to appear as if they were not taking the threat seriously. In Singapore, which lost 33 of its citizens to SARS in 2003, the government announced that it was ready to fight a “new war” against H1N1.<sup>62</sup> In Japan, cases of the new disease were being reported daily in press briefings held at the Ministry of Health, Labour and Welfare—and newspapers gave the matter front page coverage for weeks. The pattern repeated around the world, as more and more countries discovered H1N1 cases within their borders. But privately, a number of nations were becoming increasingly alarmed about the WHO’s pandemic alert system. They worried about the proportionality between the response and the severity of the disease. The chairman of the WHO’s special Emergency Committee later recalled that “several countries made quite an impassioned plea” that WHO did not prematurely declare Phase 6.<sup>63</sup>

At an emergency meeting of nations in Bangkok on May 8, Asian ASEAN+3 nations convened to consider the proper response. They were joined by the WHO’s Fukuda and senior officials from CDC, linked by video conference.<sup>64</sup> Here, CDC’s Schuchat delivered some good news: further investigations of the Mexico situation had revealed that “severity is not as grave as what was originally reported from colleagues in Mexico.” Schuchat nevertheless argued that responding to the outbreak must remain “our highest priority.”<sup>65</sup> The WHO addressed the pandemic declaration issue, repeating that a Phase 6 declaration “does not mean that the disease is becoming more severe.” Although transcripts of this meeting are not publicly available, it would seem that at least some members of the ASEAN+3 group were uncomfortable with the WHO’s approach to declaring pandemics. Keiji Fukuda later told media that at this meeting, WHO was encouraged to take “into consideration everything which ought to be considered”—not just the virus’s spread.

The WHO was taking notes. By mid-May, a Phase 6 declaration seemed eminent. “The number of swine flu cases in Japan soared over the weekend, raising the likelihood that the World Health Organization will soon have to raise its pandemic alert level to 6,” the *New York Times* reported on May 18. New

<sup>60</sup> Madison Park, “‘Walking well’ flood hospitals with -- or without -- flu symptoms”, May 2, 2009, <http://www.cnn.com/2009/HEALTH/05/02/worried.well.hospitals/index.html>, (accessed July 3, 2009).

<sup>61</sup> Monica Davey, “Thousands Face a Balancing Act Over Flu Fears,” *The New York Times*, May 1, 2009, sec. Health, [http://www.nytimes.com/2009/05/01/health/01fear.html?\\_r=1](http://www.nytimes.com/2009/05/01/health/01fear.html?_r=1), (accessed July 12, 2011); Park, “‘Walking well’ flood hospitals with -- or without -- flu symptoms.”

<sup>62</sup> Bertha Henson, “S’pore geared up to fight swine flu,” *Straits Times*, April 30, 2009.

<sup>63</sup> John Mackenzie, quoted in Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, “Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009”, May 5, 2011, 78, [http://apps.who.int/gb/ebwha/pdf\\_files/WHA64/A64\\_10-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf), (accessed May 5, 2011).

<sup>64</sup> Tokyo Development Learning Center, “ASEAN +3 on A/H1N1 Crisis”, May 8, 2009, [http://www.jointokyo.org/en/featured\\_stories/story/asean\\_3\\_on\\_a\\_h1n1\\_crisis/](http://www.jointokyo.org/en/featured_stories/story/asean_3_on_a_h1n1_crisis/), (accessed March 30, 2011).

<sup>65</sup> *Ibid.*

H1N1 infections were turning up in increasing numbers in Japan and the United Kingdom, both nations outside of the WHO region initially hit. If the outbreaks in those countries were deemed “community-level” outbreaks, the H1N1 virus had met the Phase 6 definition. All that remained was the WHO announcement to make it official.

That very day, however, criticism towards WHO was intensifying over the appropriateness of the Pandemic Phase Alert system. At the World Health Assembly meeting in Geneva—the WHO’s most important annual meeting—representatives from the UK, Japan, China—even Mexico—urged the WHO to reconsider its pandemic scale.<sup>66</sup> “We need to give you and your team more flexibility as to whether we move to phase 6,” UK health secretary Alan Johnson diplomatically informed the WHO’s Director-General.<sup>67</sup>

In response, the WHO suggested it would rewrite its Phase 6 definition. Following the World Health Assembly (WHA), Keiji Fukuda told reporters that the pandemic planning process had been “driven by concerns about avian influenza,” and the pandemic phases were a product of that thinking about what that disease might look like if it became a pandemic. He continued:

At the WHA, what the countries raised was a concern and they said that currently the criteria from going to 5 to 6 are based on geographical spread, and this is true. ... These were the criteria which were developed by the scientists advising and working with WHO over the past couple of years and in a sense they were developed to provide very clear criteria about the evolution of a potential pandemic.

But what the countries have said is that we are in a situation that is different than the spread of H5N1. In fact most of the cases that we are seeing right now are clinically mild and we are not having the kind of high death rates that we might expect if we were to see an H5N1 pandemic. Moreover, what the countries said is that we are in this mixed situation and we are concerned that if we go to Phase 6 the message to our populations will be: “You should be very afraid”, whereas in fact we think that it indicates that the virus is spreading out but the level of fear should not go up and there should not be an increase in anxiety. So, in taking these comments in from countries, what we did, what we thought about and what we discussed, is that right now, when we step back and say what is most important, the most important things are that, countries are as prepared as possible. This is a single most important action and this is a single biggest help that WHO can provide to countries. ...

The large lesson that we have learnt here is that the response to these kinds of situations really have to be flexible, they cannot be rigid according to pre-made plans and I think that the comments from the countries reflect their same assessment of the

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<sup>66</sup> Frank Jordans, “WHO bows to pressure not to declare pandemic”, May 19, 2009, [http://articles.sfgate.com/2009-05-19/news/17202546\\_1\\_pandemic-announcement-swine-flu-new-influenza](http://articles.sfgate.com/2009-05-19/news/17202546_1_pandemic-announcement-swine-flu-new-influenza), (accessed October 20, 2010).

<sup>67</sup> A. O’Dowd, “UK urges more flexibility in criteria for flu pandemic alerts,” *BMJ* 338, no. may21 3 (May 2009): b2067-b2067.

situation. We have to have some level of flexibility here. Taking all of this into consideration at the here and now I cannot tell you what the new criteria for Phase 6 are, but I can tell you that what we are looking for and what we will be looking for is something which are events which signify a really substantial increase in risk of harm to people.

This is the sense of what Phase 6 is meant to convey and this is what we will be focusing on. This has been a very interesting request from countries, it has led to very intense discussions about what is the appropriate response to pandemic influenza at this stage and given this evolution. This really reflects where we are, right now, at this time.<sup>68</sup>

Indications that the WHO would listen to Member States' concern triggered a mixed set of reactions. The *New York Times* read the WHO's response as suggestive that "the swine flu circling the globe will probably never be declared a full-fledged pandemic."<sup>69</sup> The well-known risk communication consultants Peter Sandman and Jody Sandman (whose clients have included the WHO) posted a "tongue-in-cheek 'modest proposal'."<sup>70</sup>

If WHO decides not to call a widespread "mild" swine-origin Influenza A/H1N1 pandemic a pandemic, then we believe they are obliged to announce that the H2N2 event of 1957 and the H3N2 event of 1968 were also not pandemics.

They should then announce that the last influenza pandemic occurred in 1918, and there have been no flu pandemics since that time.

WHO should also review the list of pre-1918 "pandemics" and decide which of those events were also not really pandemics, so we can re-calculate how many times per century, on average, a pandemic can be expected.

That way, we can be doubly relieved: Not only that swine flu H1N1 isn't a pandemic, but also that pandemics are very much rarer than previously thought.<sup>71</sup>

These critiques suggested that the WHO's interest in listening to Member States and rewriting the rules for a Phase 6 declaration amounted to putting politics ahead of science. "I think it is unnecessary and even foolish for WHO to change its definition of 'pandemic' in order to avoid frightening people with the

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<sup>68</sup> World Health Organization, "Transcript of virtual press conference with Gregory Hartl, WHO Spokesperson for Epidemic and Pandemic Diseases, and Dr Keiji Fukuda, Assistant Director-General ad Interim for Health Security and Environment, World Health Organization", May 22, 2009,

[http://www.who.int/mediacentre/influenzaAH1N1\\_presstranscript\\_20090522.pdf](http://www.who.int/mediacentre/influenzaAH1N1_presstranscript_20090522.pdf), (accessed July 11, 2011).

<sup>69</sup> Donald G. McNeil Jr, "W.H.O. to Rewrite Its Pandemic Rules," *The New York Times*, May 23, 2009, sec. Health / Health Care Policy, <http://www.nytimes.com/2009/05/23/health/policy/23who.html>, (accessed October 9, 2010).

<sup>70</sup> Personal correspondence with Peter Sandman, November 17, 2010.

<sup>71</sup> Peter Sandman and Jody Lanard, quoted in "Revere" (pseudonym), "When is a pandemic not a pandemic?," *Effect Measure*, May 19, 2009, [http://scienceblogs.com/effectmeasure/2009/05/when\\_is\\_a\\_pandemic\\_not\\_a\\_pande.php](http://scienceblogs.com/effectmeasure/2009/05/when_is_a_pandemic_not_a_pande.php), (accessed May 21, 2009).

word,” Peter Sandman commented.<sup>72</sup> Elsewhere, virologist Vincent Racaniello wrote in an agitated online post: “According to the virology textbooks (one of which I wrote), the word pandemic means ‘global epidemic’. ... WHO redefining pandemic is absurd. Pandemic is an epidemiological definition that has nothing to do with virulence. ... WHO should leave textbook writing to others. ... a pandemic is a pandemic.”<sup>73</sup> *Nature* magazine’s influenza beat reporter Declan Butler editorialized that redefining Phase 6 would amount to ‘moving the goalposts’. “Adding a requirement of severity may sound like common sense. But it is not, because the severity of a pandemic is unpredictable,” he wrote. Using many of the arguments WHO had previously laid out, Butler argued that:

... what might be deemed a mild disease in a rich country with many doctors, drugs and intensive-care units might be more severe and cause considerable mortality in a poor country with little health infrastructure, and where underlying diseases may worsen outcomes of a flu infection.

So what's the big hang-up with calling a pandemic a pandemic? Those fretting over the term include news pundits in denial about the scale of the threat, along with politicians and scientists who fear that using the word may induce public panic.<sup>74</sup>

“The importance of the phase 6 designation is overrated,” Butler declared. “It is time to call a pandemic a pandemic.”

Some notable authorities, however, showed more sympathy for the delicacy of the situation. “The formalization of an influenza pandemic does have cascading consequences,” former champion of pandemic preparedness, HHS secretary Michael Leavitt told *Bloomberg* news. Likewise, Alan Kendal, the former head of the CDC’s influenza laboratory, said that “Much of our preparation for a pandemic was done in anticipation of a more lethal virus ... this is taking us by surprise in that it doesn’t appear so lethal.”<sup>75</sup>

*New York Times* veteran health reporter Lawrence K. Altman commented in a column: “After decades of warnings about the inevitability of another pandemic of influenza, it is astonishing that health officials have failed to make clear to the public, even to many colleagues, what they mean by the word pandemic.”<sup>76</sup> Altman’s article was titled, “Is This a Pandemic? Define ‘Pandemic,’” and was just one of a number of articles questioning the meaning of a pandemic. Two days later, the *Times* carried an op-ed “When is a Pandemic Not a Pandemic?” in which science journalist Laurie Garrett argued that the WHO needed to include a severity-like measure into its pandemic categorization schema similar to what is

<sup>72</sup> Helen Branswell, “WHO under pressure from member states to rewrite pandemic requirement”, May 23, 2009, <http://cnews.canoe.ca/CNEWS/Politics/2009/05/22/pf-9539386.html>, (accessed August 14, 2009).

<sup>73</sup> Vincent Racaniello, “WHO will redefine pandemic”, May 23, 2009, <http://www.virology.ws/2009/05/23/who-will-redefine-pandemic/>, (accessed July 11, 2011).

<sup>74</sup> Declan Butler, “When is a pandemic not a pandemic?,” *Nature* (May 2009), <http://www.nature.com/doifinder/10.1038/news.2009.501>.

<sup>75</sup> Jason Gale, “Flu Is No Typical Pandemic; WHO Tries to Reassure (Update1),” *Bloomberg.com*, June 2, 2009, <http://www.bloomberg.com/apps/news?pid=20601124&sid=aHGvmKBE0alg>, (accessed June 2, 2009).

<sup>76</sup> Lawrence K. Altman, “Is This a Pandemic? Define ‘Pandemic,’” *The New York Times*, June 9, 2009, sec. Health, <http://www.nytimes.com/2009/06/09/health/09docs.html>, (accessed June 9, 2009).

done for hurricanes: “in the case of the H1N1 swine flu, WHO should declare that the world is now facing a Phase 6 pandemic influenza spread, caused by a Category 1 organism of low severity.”<sup>77</sup>

### All guesses off

The absence of extreme morbidity and mortality was not the only expectation that the H1N1 outbreak was defying. Not only did the virus usually only cause mild illness, but it had seemed to have emerged from Mexico. For decades, scientists had considered Southeast Asia to be the epicenter of novel emerging influenza viruses. As new influenza viruses were believed to be the result of mutation that takes place in animal hosts, the close proximity between humans, pigs, and birds in Southeast Asia was believed to increase the likelihood that a pandemic virus would be conceived in this area of the world. Southern China’s wet poultry markets were in particular singled out by both the expert and lay press as a dangerous “breeding ground” for pandemic viruses. Most cases of H5N1 had also appeared in that part of the world, giving experts faith in the theory. Some had even suggested a large stockpile of anti-influenza vaccines, drugs, masks and gloves be established in Hong Kong—“the middle of the ecological zone that has spawned the bulk of all influenza strains known to have emerged over the last three decades.”<sup>78</sup>

Nor was the new H1N1 of avian origin. So common was the conception that the next pandemic would be caused by an avian influenza virus that by mid 2009 “bird flu” had become virtually interchangeable with “pandemic flu.”<sup>79</sup> The ubiquity of government pandemic preparedness promotional materials discussing the difference between pandemic, avian, and seasonal forms of influenza suggests most people were unaware of the difference.<sup>80</sup> While human infections with swine influenza viruses were well known to occur—a few cases each year had been consistently discovered for decades<sup>81</sup>—the possibility of a human pandemic with a swine influenza origin virus had been little discussed since the 1976 “fiasco.” The attention of most experts was rather on tracking the evolution of avian influenza viruses—and worldwide surveillance of birds had increased to unprecedented levels in response to pandemic preparedness funding.

Another well established concept toppled by the H1N1 outbreak was the expectation that two doses of a pandemic influenza vaccine would be necessary to prevent infection. Unlike seasonal influenza vaccines, which are only administered once except in some cases such as small children, the working assumption had been that a pandemic influenza vaccine would need to be administered to all individuals twice before the desired level of antibody response could be achieved. This assumption in fact lasted well into June, when US officials announced that they were planning for a vaccination program of 600 million doses—twice the US population—by far, the largest and most costly vaccination

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<sup>77</sup> Laurie Garrett, “When Is a Pandemic Not a Pandemic?,” *The New York Times*, June 11, 2009, sec. Opinion, <http://www.nytimes.com/2009/06/11/opinion/11iht-edgarrett.html?ref=global>, (accessed June 10, 2009).

<sup>78</sup> Laurie Garrett and David P. Fidler, “Sharing H5N1 Viruses to Stop a Global Influenza Pandemic,” *PLoS Med* 4, no. 11 (November 20, 2007): e330.

<sup>79</sup> Bonneux and Van Damme, “An iatrogenic pandemic of panic.”

<sup>80</sup> U.S. Centers for Disease Control and Prevention, “Pandemic Flu Questions and Answers.”

<sup>81</sup> Myers, Olsen, and Gray, “Cases of Swine Influenza in Humans.”

program ever.<sup>82</sup> But by September, the story had dramatically changed. Two early studies of the novel H1N1 vaccine indicated that a single dose of the new vaccine was sufficient to produce the desired antibody response.<sup>83</sup>

What was more, other data indicated that not everyone even needed the vaccine. At the same time the WHO was defending its aggressive response to H1N1, repeating the consensus view that there an “almost universal vulnerability of the world’s population to infection,”<sup>84</sup> (Table 3.1), evidence from early studies of blood serum was suggesting a substantial level of pre-existing immunity to the new virus among the elderly population.<sup>85</sup> Days later, on May 29, in a more technical report published in the WHO’s *Weekly Epidemiological Record*, the WHO reversed its position, and spoke of “pre-existing immunity” to a novel pandemic virus. “The vulnerability of a population to a pandemic virus is related in part to the level of pre-existing immunity to the virus,” the report stated. “Depending on the pandemic virus, certain segments of the population (for example, the elderly) might already be partially immune because of previous infection.”<sup>86</sup> Indeed, data published four days after Chan’s speech to the World Health Assembly indicated that one-third of Americans aged 60 years and above were immune to the virus. A report published later suggested that even before the emergence of the 2009 H1N1 virus, nearly one in five Americans (19%) had pre-existing antibody concentrations considered protective to prevent infection.<sup>87</sup> Data collected in clinical trials in other countries such as Australia confirmed the presence of high levels of pre-existing antibodies, particularly in the elderly adult population.<sup>88</sup>

Another accepted wisdom prior to the emergence of H1N1 was that influenza pandemics are caused by new subtypes of influenza viruses. Prior to 2009, officials suggested that only new subtypes of influenza were capable of causing a pandemic of influenza (Table 3.2). As the CDC wrote in 2006:

Seasonal outbreaks are caused by subtypes of influenza viruses that already circulate among people (for example, influenza A (H3N2) and A (H1N1) viruses have circulated

<sup>82</sup> Mike Stobbe, “Swine flu shot campaign could involve 600M doses,” *The Associated Press*, June 27, 2009, <http://www.google.com/hostednews/ap/article/ALeqM5hjdCHRp82YTFser5vD6CzTK1az6wD992K3L01>, (accessed June 29, 2009).

<sup>83</sup> Michael E. Greenberg et al., “Response to a Monovalent 2009 Influenza A (H1N1) Vaccine,” *New England Journal of Medicine* 361, no. 25 (December 2009): 2405-2413; Tristan W. Clark et al., “Trial of 2009 Influenza A (H1N1) Monovalent MF59-Adjuvanted Vaccine,” *New England Journal of Medicine* 361, no. 25 (December 2009): 2424-2435.

<sup>84</sup> Margaret Chan, “Concern over flu pandemic justified”, May 18, 2009, [http://www.who.int/dg/speeches/2009/62nd\\_assembly\\_address\\_20090518/en/index.html](http://www.who.int/dg/speeches/2009/62nd_assembly_address_20090518/en/index.html), (accessed June 9, 2009).

<sup>85</sup> U.S. Centers for Disease Control and Prevention, “Serum cross-reactive antibody response to a novel influenza A (H1N1) virus after vaccination with seasonal influenza vaccine,” *MMWR. Morbidity and Mortality Weekly Report* 58, no. 19 (May 22, 2009): 521-524.

<sup>86</sup> World Health Organization, “Considerations for assessing the severity of an influenza pandemic,” *Relevé Épidémiologique Hebdomadaire / Section D’hygiène Du Secrétariat De La Société Des Nations = Weekly Epidemiological Record / Health Section of the Secretariat of the League of Nations* 84, no. 22 (May 29, 2009): 197-202.

<sup>87</sup> D. M. Morens, J. K. Taubenberger, and A. S. Fauci, “The 2009 H1N1 Pandemic Influenza Virus: What Next?,” *mBio* 1, no. 4 (September 2010): e00211-10-e00211-15.

<sup>88</sup> Greenberg et al., “Response to a Monovalent 2009 Influenza A (H1N1) Vaccine.”



among people since 1977). In contrast, pandemic outbreaks are caused by new subtypes, by subtypes that have never circulated among people, or by subtypes that have not circulated among people for a long time.<sup>89</sup>

When several human infections of the new influenza virus subtype H1N2 were reported in early 2002, CDC posted a message addressing questions about the likelihood of a pandemic:

**Is this the start of a pandemic?**

No. A pandemic virus has to have a new hemagglutinin or a new hemagglutinin and neuraminidase protein on an influenza A virus that has not circulated among humans and to which most or all of the population has no protective antibodies. Because the H1N2 virus has the hemagglutinin of the currently circulating H1N1 virus and the neuraminidase of the currently circulating H3N2 virus, most people will have been exposed to and have antibodies against these viruses.<sup>90</sup>

But since the early days of the 2009 H1N1 outbreak, officials were no longer sticking to this conventional view. In a press conference, the CDC addressed the issue head on, arguing that while the H1N1 virus found in 2009 was not a new subtype—indeed another H1N1 virus had been continuously circulating among the human population since 1977—the virus was different enough to render the subtype issue moot.

... based on the distance, if you want to call it that, of this new H1N1 from the previously circulating seasonal H1N1, there's a very good distance. It's a long way away. And so while it may not be a different subtype, it is distant enough for us to be very concerned about its potential impact. And so, in that sense, the drift versus shift is an ongoing discussion, but I think the distance between it and its nearest cousins is far enough that we're going to treat it in a way that we want to make sure that the most people are protected.<sup>91</sup>

**The severity issue**

Most of the inconsistencies aroused little concern. Influenza was unpredictable, after all. Perhaps in this light the emergence of a swine and not avian influenza virus is understandable. So, too, is its emergence in Mexico, not Southeast Asia. The need for only one dose of the vaccine instead of two—and pre-existing immunity in a good proportion of the elderly population—were also unexpected, but welcome news. These inconsistencies did not challenge expert credibility. Nor were many concerned by the fact that the H1N1 outbreak was not simultaneous in all parts of the world as WHO had predicted.

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<sup>89</sup> U.S. Centers for Disease Control and Prevention, "Pandemic Flu Questions and Answers."

<sup>90</sup> U.S. Centers for Disease Control and Prevention, "Questions and Answers About Influenza A(H1N2) Viruses", n.d., <http://www.cdc.gov/flu/about/h1n2qa.htm>, (accessed June 25, 2009).

<sup>91</sup> U.S. Centers for Disease Control and Prevention, "CDC Press Briefing Transcripts May 20, 2009", May 20, 2009, <http://www.cdc.gov/media/transcripts/2009/t090520.htm>, (accessed May 21, 2009).

What did cause concern was the mildness of it all. To be sure, a mild pandemic was better than a severe pandemic. But years of pandemic preparedness had built the expectation among the public as well as officials, that pandemics were necessarily catastrophic events. By late May the virus had spread to over fifty countries around the world with over 15,000 cases reported to the WHO,<sup>92</sup> yet nowhere was the outbreak causing the economic or social disruption that officials had long predicted.<sup>93</sup>

“There are some pandemics that look very much like a bad flu season,” the CDC’s acting director matter-of-factly explained in an official ‘webcast’,<sup>94</sup> countering popular assumptions reinforced by years of official statements about pandemic influenza such as: “rates of illness and death from influenza-related complications can increase dramatically” (CDC<sup>95</sup>), “particularly virulent strains of flu that spread rapidly from person to person,” (HHS<sup>96</sup>) “large numbers of deaths will occur,” (WHO<sup>97</sup>) and “greater magnitude than even the most severe epidemic of ‘ordinary’ flu” (UK<sup>98</sup>).

### Pandemic of “moderate” severity declared

H1N1 was not shaping up to be the outbreak experts had predicted, but in the end, the WHO did not rewrite its pandemic phase definitions, and on June 11, 2009, Margaret Chan declared “the start of the 2009 influenza pandemic.”<sup>99</sup>

“Worldwide, the number of deaths is small,” Chan said, “and we have to brace ourselves to see more.” “On present evidence, the overwhelming majority of patients experience mild symptoms and make a rapid and full recovery, often in the absence of any form of medical treatment.” Despite this, Chan described the pandemic as one of “moderate severity,” a phrase that would get repeated for months in the world press representing the WHO’s official determination of the pandemic severity level.

The “moderate severity” phrase had surfaced at least a week earlier when Keiji-Fukuda used it at a press conference in Geneva. “In terms of an overall assessment of the severity of what we are seeing, it is probably fair to call the situation something like ‘moderate’ right now,” Fukuda said. “We do have some hesitation in calling the situation mild for a couple of reasons.” First, Fukuda explained, WHO did not feel it had “a full handle on the number of people with serious illnesses.” Second, “this infection can be fatal in a number of individuals and this includes both people who have some underlying medical

<sup>92</sup> World Health Organization, “Influenza A(H1N1) - update 41”, May 29, 2009, [http://www.who.int/csr/don/2009\\_05\\_29/en/index.html](http://www.who.int/csr/don/2009_05_29/en/index.html), (accessed July 12, 2011).

<sup>93</sup> World Health Organization, “Ten things you need to know about pandemic influenza.”

<sup>94</sup> U.S. Department of Health and Human Services, “H1N1 Flu Update with HHS Sec. Kathleen Sebelius”, April 30, 2009, <http://www.pandemicflu.gov/secretarywebcast.html>, (accessed May 25, 2009).

<sup>95</sup> Carolyn B. Bridges et al., “Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 49, no. 3 (April 14, 2000): 1-38; quiz CE1-7.

<sup>96</sup> National Institute of Allergy and Infectious Diseases, National Institutes of Health, “Flu (Influenza) Definitions and Overview”, October 14, 2008, <http://www3.niaid.nih.gov/topics/Flu/understandingFlu/DefinitionsOverview.htm>, (accessed July 17, 2009).

<sup>97</sup> World Health Organization, “Ten things you need to know about pandemic influenza.”

<sup>98</sup> UK Department of Health, “Explaining pandemic flu.”

<sup>99</sup> Margaret Chan, “Transcript of statement by Margaret Chan, Director-General of the World Health Organization”, June 11, 2009, [http://www.who.int/mediacentre/influenzaAH1N1\\_presstranscript\\_20090611.pdf](http://www.who.int/mediacentre/influenzaAH1N1_presstranscript_20090611.pdf).

conditions – it includes women who are pregnant – but it also includes people who are perfectly healthy, and so we do have some hesitation calling such an infection mild.”<sup>100</sup> Fukuda suggested the “moderate” determination was made on a three-point scale of mild-moderate-severe.

Chan’s pandemic declaration emphasized the unusual epidemiology of the new disease:

We know that the novel H1N1 virus preferentially infects younger people. In nearly all areas with large and sustained outbreaks, the majority of cases have occurred in people under the age of 25 years.

In some of these countries, around 2% of cases have developed severe illness, often with very rapid progression to life-threatening pneumonia.

Most cases of severe and fatal infections have been in adults between the ages of 30 and 50 years.

This pattern is significantly different from that seen during epidemics of seasonal influenza, when most deaths occur in frail elderly people.

Many, though not all, severe cases have occurred in people with underlying chronic conditions. Based on limited, preliminary data, conditions most frequently seen include respiratory diseases, notably asthma, cardiovascular disease, diabetes, autoimmune disorders, and obesity.

At the same time, it is important to note that around one third to half of the severe and fatal infections are occurring in previously healthy young and middle-aged people.

The WHO offered advice to countries at different stages in the pandemic:

Although the pandemic appears to have moderate severity in comparatively well-off countries, it is prudent to anticipate a bleaker picture as the virus spreads to areas with limited resources, poor health care, and a high prevalence of underlying medical problems. ...

Countries should prepare to see cases, or the further spread of cases, in the near future. Countries where outbreaks appear to have peaked should prepare for a second wave of infection. ... Countries with no or only a few cases should remain vigilant.

Countries with widespread transmission should focus on the appropriate management of patients. The testing and investigation of patients should be limited, as such measures are resource intensive and can very quickly strain capacities.<sup>101</sup>

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<sup>100</sup> World Health Organization, “Transcript of virtual press conference with Gregory Hartl, WHO Spokesperson for Epidemic and Pandemic Diseases, and Dr Keiji Fukuda, Assistant Director-General ad Interim for Health Security and Environment, World Health Organization”, June 2, 2009, [http://www.who.int/mediacentre/influenzaAH1N1\\_presstranscript\\_20090602.pdf](http://www.who.int/mediacentre/influenzaAH1N1_presstranscript_20090602.pdf).

In the US, where a press conference was similarly convened to respond to the WHO declaration, the CDC's newly sworn in director Dr. Thomas Frieden explained that "really for all intents and purposes, the U.S. government has been in phase 6 of the pandemic for some time now." But the WHO's declaration of Phase 6 "is important because it does send the strong message that virus is here, it's in all likelihood here to stay, and it's important that we continue our aggressive efforts to prepare and respond."<sup>102</sup>

"Here in the United States we've been reacting as though we were in a pandemic already in terms of our intensive efforts to prepare individuals and respond as a nation," echoed Dr. Anne Schuchat, who advised communities which had not yet responded that it was time to "dust off those pandemic plans."

On the severity question, Schuchat said, "Right now the World Health Organization is characterizing this as a moderately severe pandemic. They're not saying it is the same thing as that 1918 devastating pandemic, but it's something we have to take seriously and we need the countries to be paying attention to." Contrasting the disease against seasonal influenza, Schuchat explained that the CDC was seeing a disproportionate amount of illness in younger people as compared with the elderly, and "a disproportionate amount of pregnant women among those who have had infection."

The language of the press conference was dramatic. "This is a shared responsibility -- government, health care providers, the private sector and the public," Director Frieden announced. "All of us are in this together to respond to what can be a challenging situation." Frieden noted that "Up until now we have been fortunate that we have not seen a level of severity that's greater than seasonal flu." Frieden nonetheless emphasized the uncertainty surrounding the situation. "We wish we could foresee the future. We wish we could know what course it will take. But what we're doing now is getting information as effectively as we can so that we can take the steps that are most sensible now to reduce the number of people severely ill or tragically, who may die from H1N1 influenza."

The rhetoric of H1N1 came to be dominated by a language of extremes—that on one side stressed the moral gravity of the situation (the "shared responsibility," the need to "dust off" pandemic plans, news of "tragic" deaths and a disproportionate burden of illness on the youngest members of society) and on the other, increased public skepticism (messages that H1N1 was no worse than seasonal influenza). As cases increased in September and October and outbreaks at schools and colleges received wide media attention, concern rose along with demands for a vaccine that had not yet been produced in large quantities.

Yet anxieties existed alongside a broad-based questioning of officials' recommendations. "Fewer than half of Americans say that they are planning to receive the new H1N1 swine flu vaccine, according to recent polls," *NPR* reported in October, as the vaccination program in the US was just beginning to deliver its first doses. "The public's skepticism over the vaccine has persisted despite health experts'

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<sup>101</sup> Chan, "Transcript of statement by Margaret Chan, Director-General of the World Health Organization."

<sup>102</sup> U.S. Centers for Disease Control and Prevention, "CDC Press Briefing Transcripts June 11, 2009", June 11, 2009, <http://www.cdc.gov/media/transcripts/2009/t090611.htm>, (accessed June 13, 2009).

warning that the unpredictable H1N1 virus, which can cause very severe complications even in healthy young adults and children, has reached pandemic proportions.”<sup>103</sup>

Many blamed celebrity media personalities such as Rush Limbaugh, Glenn Beck, and Bill Maher for causing undue public skepticism over the vaccine.<sup>104</sup> But polls in the UK, Hong Kong, and Israel indicated that from one quarter to two-thirds of the public and health care workers were planning to refuse the novel H1N1 vaccine as well.<sup>105</sup> In 2006, the WHO had assumed that a production capacity sufficient to vaccinate all of the world’s inhabitants would be required in a pandemic.<sup>106</sup> But in 2009, the new surveys put such assumptions in doubt. In Hong Kong, more than half of 8500 healthcare workers surveyed indicated they would not be vaccinated because of concerns about the vaccine’s safety.<sup>107</sup> In Israel, the ministry of health reported 25% of its population was not willing to be vaccinated.<sup>108</sup>

In Canada, the former chief medical officer of health in Ontario declared: “It’s really not causing — and is not going to cause and nowhere has caused — significant levels of illness or death.” Dr. Richard Schabas told the Canadian *CBC News* that H1N1 had “ultimately turned out to be, from a pandemic perspective, a dud.”<sup>109</sup>

Disease statistics were also fast becoming the source of considerable scrutiny. As science studies scholar Steven Epstein has shown in the case of AIDS, statistics are not always the sole domain of officials or scientists, but can at times be appropriated by lay and activist groups to strengthen claims in battles over legitimacy, public opinion, and policy.<sup>110</sup> At the beginning of the H1N1 outbreak, each case, hospitalization and death had garnered immense attention and caused substantial fear, documenting the spread and impact of the disease. But as the largest mass vaccination program in history kicked off in countries around the world, the threat itself began to look a lot less threatening. Whereas in past year, officials had employed statistics like “36,000 deaths” per year to convince the public to get vaccinated, in 2009, the tables had turned, and public commentators were making use of official statistics to challenge the need for vaccination. Compared to seasonal influenza, H1N1 deaths seemed paltry. In September, an article on the *NewAmerican* website commented:

The current death toll varies depending on the source. A recent WHO report pegged the number of deaths worldwide at 2,138 since April, although some U.S. government

<sup>103</sup> Kevin Whitelaw, “Flu, Me? Public Remains Wary Of H1N1 Vaccine,” *NPR.org*, October 17, 2009, <http://www.npr.org/templates/story/story.php?storyId=113873021>, (accessed July 12, 2011).

<sup>104</sup> *Ibid.*

<sup>105</sup> Zosia Kmietowicz, “Opposition to swine flu vaccine seems to be growing worldwide,” *BMJ* 339, no. aug26\_1 (August 26, 2009): b3461.

<sup>106</sup> Marie Paule Kieny et al., “A global pandemic influenza vaccine action plan,” *Vaccine* 24, no. 40-41 (September 29, 2006): 6367-6370.

<sup>107</sup> J. S Y Chor et al., “Willingness of Hong Kong healthcare workers to accept pre-pandemic influenza vaccination at different WHO alert levels: two questionnaire surveys,” *BMJ* 339, no. aug25 2 (August 2009): b3391-b3391.

<sup>108</sup> Kmietowicz, “Opposition to swine flu vaccine seems to be growing worldwide.”

<sup>109</sup> *CBC News*, “H1N1 a ‘dud’ pandemic, Ont. health official says,” *CBC News*, November 12, 2009, <http://www.cbc.ca/health/story/2009/11/12/h1n1-vaccine-costs.html>, (accessed November 17, 2009).

<sup>110</sup> Steven Epstein, *Impure science: AIDS, activism, and the politics of knowledge* (Berkeley: University of California Press, 1996).

reports place the number around 3,000. While these deaths are tragic, the U.S. Centers for Disease Control claims that seasonal flu kills 36,000 Americans every year ... one can see that, taking the high number of 3,000 deaths worldwide in five months, the death toll of H1N1 pales compared to their [CDC and WHO's] estimate of the death toll of the seasonal flu.<sup>111</sup>

CDC's initial estimates of the US mortality impact of H1N1 were released in November: 3,900. Over time, this estimate was revised, and eventually incorporated an entire year—from April 2009 to April 2010. But the CDC's full year estimate, 12,470 deaths, still fell far short of the familiar 36,000 figure from "ordinary" influenza.

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By late November 2009, epidemiological data was indicating a steep decline in cases. The "second wave" seemed to be nearing its end, and public demand for vaccines was low.<sup>112</sup> But officials maintained their aggressive approach, realizing that acting too strongly might cost them valuable credibility. "Privately, federal health officials say they fear that if they concede the flu has peaked, Americans will become complacent and lose interest in being vaccinated, increasing the chances of another wave," *New York Times* health reporter Donald McNeil, Jr. wrote.<sup>113</sup> But a period of broad-based reflection and assessment was nonetheless beginning to take hold as cases of H1N1 retreated with no sign of a "third wave."<sup>114</sup>

Nowhere was this more true than in Europe. There, questions were being asked—what worked and what did not? Had the responses been appropriate? And had advice been taken on a firm scientific basis? Many countries health authorities had launched large, and costly responses to combat H1N1. In the UK, where the total response cost around US \$1.8 billion,<sup>115</sup> a National Pandemic Flu Service was set into action. Antiviral medications were dispensed over the internet, bypassing clinical consultation, with prescriptions delivered through the web or telephone based on an individual's self-reported symptoms. Other public health and clinical activity came to "a virtual standstill during the first wave," one doctor in the UK reported.<sup>116</sup> "Most routine work was put to one side," a Joint Director of Public Health in Britain's National Health Service recalled. "Sometimes our speed was, in hindsight, perhaps too quick. For instance, we wrote to all our residents to inform them of their NHS number to use on the National

<sup>111</sup> John Burns, "Chicken Little and the Swine Flu Scare," *NewAmerican*, September 16, 2009, <http://www.thenewamerican.com/usnews/health-care/1899-chicken-little-and-the-swine-flu-scare>, (accessed July 17, 2011).

<sup>112</sup> Council of Europe, "The handling of the H1N1 pandemic: more transparency needed", June 7, 2010, 15, <http://assembly.coe.int/Documents/WorkingDocs/Doc10/EDOC12283.pdf>, (accessed June 10, 2010).

<sup>113</sup> Donald G. McNeil, Jr, "Signs Swine Flu Wave May Have Peaked in U.S.," *The New York Times*, November 20, 2009, sec. Health, [http://www.nytimes.com/2009/11/21/health/21flu.html?\\_r=1](http://www.nytimes.com/2009/11/21/health/21flu.html?_r=1), (accessed November 27, 2009).

<sup>114</sup> Heath A Kelly, "A Pandemic Response To a Disease of Predominantly Seasonal Intensity," *The Medical Journal of Australia* 192, no. 2 (January 18, 2010): 81-83.

<sup>115</sup> Jacqui Wise, "UK response to H1N1 pandemic was highly satisfactory, independent review says," *BMJ* 341, no. jul05 1 (July 2010): c3569-c3569.

<sup>116</sup> Dyfed Wyn Huws, "Flu pandemonium," *Public Health Today*, March 2010.

Flu Line. This cost us £80k, and wasn't necessary in the end...."<sup>117</sup> A report from 2010, compiled via a Freedom of Information Act request, revealed that to respond to the pandemic, one in six primary care trusts had been forced to cut other services.<sup>118</sup>

As part of their pandemic preparedness activities prior to the 2009 outbreak, various countries had also established contracts with vaccine manufacturers assuring them a supply of pandemic influenza vaccines in the event of a pandemic. Some of these contracts, such as GlaxoSmithKline's contracts with Britain, Belgium, France,<sup>119</sup> Switzerland, Denmark, and Iceland<sup>120</sup> would be set in motion once WHO declared a pandemic. These "sleeping contracts," to use the terminology of the UK government, were "to be triggered by WHO declaring a pandemic."<sup>121</sup> Reports in the media that the committees advising the WHO on its response to the pandemic were working with the pharmaceutical industry raised questions about the scientific objectivity of those decisions.<sup>122</sup> In one case, a Finnish vaccine advisor to WHO, the deputy director general of the Finnish National Institute for Health and Welfare, had received £5.6 million from GlaxoSmithKline (a vaccine manufacturer) for research on vaccines in 2009. But he did not disclose this information to WHO before its meeting of the Strategic Advisory Group of Experts on Immunization (SAGE) to discuss H1N1 influenza vaccine in October 2009, a fact which only came to attention following a freedom of information request by a Danish newspaper. WHO, subsequently contacted about the matter, said it was satisfied there were no conflicts of interest in this case.<sup>123</sup>

"WHO is aware of some concerns, expressed in the media, that ties with the pharmaceutical industry among experts on the Organization's advisory bodies may influence policy decisions, especially those relating to the influenza pandemic," the WHO wrote on its website.<sup>124</sup> "Conflicts of interest: safeguards in place," "Criticisms: understandable but unfounded" the WHO declared in a briefing note, arguing that the Organization had robust measures in place to guard against the improper influence of industry on its decision making.

<sup>117</sup> Caron Grainger, "Twitter and blogs helped put Coventry ahead on flu," *Public Health Today*, March 2010.

<sup>118</sup> A. O'Dowd, "Trusts forced to cut services because of costs of swine flu," *BMJ* 340, no. may07 1 (May 2010): c2485-c2485.

<sup>119</sup> Maria Cheng and Frank Jordans, "WHO gears to declare swine flu pandemic", June 10, 2009, [http://www.usatoday.com/news/world/2009-06-10-WHO-flu\\_N.htm](http://www.usatoday.com/news/world/2009-06-10-WHO-flu_N.htm), (accessed June 10, 2010).

<sup>120</sup> "GlaxoSmithKline Signs Contract For Its Pandemic Flu Vaccine With UK Government," *Medical News Today*, August 20, 2007, <http://www.medicalnewstoday.com/releases/80067.php>, (accessed July 12, 2011).

<sup>121</sup> Deirdre Hine, "The 2009 Influenza Pandemic: An independent review of the UK response to the 2009 influenza pandemic", July 2010, 21, <http://www.cabinetoffice.gov.uk/sites/default/files/resources/the2009influenzapandemic-review.pdf>, (accessed July 11, 2011).

<sup>122</sup> Jason Gale, "WHO Defends Flu Response Amid Exaggeration Claims (Update2)", December 4, 2009, <http://www.bloomberg.com/apps/news?pid=20601086&sid=anDw8Gp5w4eA>, (accessed December 9, 2009); "Experts work with industry [Experter samarbetar med industrin]," *SvD*, November 30, 2009, [http://www.svd.se/nyheter/inrikes/expertes-samarbetar-med-industrin\\_3866171.svd](http://www.svd.se/nyheter/inrikes/expertes-samarbetar-med-industrin_3866171.svd), (accessed July 12, 2011).

<sup>123</sup> Jo Carlowe, "WHO vaccine expert had conflict of interest, Danish newspaper claims," *BMJ* 340, no. jan12\_2 (January 12, 2010): c201.

<sup>124</sup> World Health Organization, "WHO use of advisory bodies in responding to the influenza pandemic", December 3, 2009, [http://www.who.int/csr/disease/swineflu/notes/briefing\\_20091203/en/index.html](http://www.who.int/csr/disease/swineflu/notes/briefing_20091203/en/index.html), (accessed April 29, 2010).

However, WHO's reassurances did not put the matter to rest. Earlier reporting in the European press had indicated that the so-called "Emergency Committee" that WHO Director-General Margaret Chan had assembled to provide advice on Pandemic Phase declarations—the very group that advised Chan to declare H1N1 a pandemic—was itself secret. Its membership, even size, was undisclosed. About this group, the WHO statement only said: "All members of the Emergency Committee sign a confidentiality agreement, provide a declaration of interests, and agree to give their consultative time freely, without compensation."<sup>125</sup>

### **Accusation: decision making under scrutiny**

On December 18, a motion was introduced in the Parliamentary Assembly of the Council of Europe proposing an investigation into the WHO's handling of the pandemic. Titled "Faked Pandemics - a threat for health," its fourteen co-signers declared:

In order to promote their patented drugs and vaccines against flu, pharmaceutical companies have influenced scientists and official agencies, responsible for public health standards, to alarm governments worldwide. They have made them squander tight health care resources for inefficient vaccine strategies and needlessly exposed millions of healthy people to the risk of unknown side-effects of insufficiently tested vaccines.<sup>126</sup>

The Council of Europe—a sixty year old body with 47 member nations which works to promote human rights, democracy, and the rule of law throughout Europe—adopted the motion. At the first of its two public hearings, held in January, Dr. Wolfgang Wodarg, former German member of parliament and chairman of the Subcommittee for Health in the Council of Europe, who had introduced the motion, told the audience:

We were told this was a 'flu which would threaten humanity, and millions would fall ill. This is why millions of dollars of medications were bought. The WHO basically held the trigger for the pandemic preparedness plans, they had a key role to play in deciding on the pandemic. Around 18 billion dollars was spent on this pandemic worldwide.<sup>127</sup>

Wodarg discussed the role of pandemic vaccine contracts that many countries had entered into with pharmaceutical companies, the details of which were still largely secret (except in some instances where

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<sup>125</sup> Six months later, WHO Director-General Margaret Chan explained its reasoning: "Our decision not to make these names public was motivated by a desire to protect the experts from commercial or other influences. The members themselves welcomed this decision as a protective measure, and not as an attempt to veil their deliberations and decisions in secrecy." Margaret Chan, "WHO Director-General's letter to BMJ editors", June 8, 2010, [http://www.who.int/mediacentre/news/statements/2010/letter\\_bmj\\_20100608/en/index.html](http://www.who.int/mediacentre/news/statements/2010/letter_bmj_20100608/en/index.html), (accessed June 15, 2010).

<sup>126</sup> Wolfgang Wodarg, "Faked Pandemics - a threat for health", December 18, 2009, <http://assembly.coe.int/Documents/WorkingDocs/Doc09/eDOC12110.pdf>, (accessed July 11, 2011).

<sup>127</sup> Council of Europe, "Extracts of statements made by the leading participants at the public hearing on 'The handling of the H1N1 pandemic: more transparency needed?', organised by the Committee on Social, Health and Family Affairs of the Parliamentary Assembly of the Council of Europe (PACE) in Strasbourg on Tuesday 26 January 2010", January 26, 2010, <http://assembly.coe.int/ASP/APFeaturesManager/defaultArtSiteView.asp?ID=900>, (accessed July 12, 2011).



the contracts had been leaked by whistleblowers). Not only did contracts exist which would guarantee countries a priority supply of vaccine upon a WHO declaration of a pandemic, but several of the contracts shielded companies from any legal liability should side-effects occur following vaccination, as they did in the 1976 “swine flu” in the United States.

Such was the case in the UK, which had not made details of its contracts public, but was reported to have granted H1N1 vaccine makers legal immunity from compensation claims.<sup>128</sup> In the US, legal immunity from lawsuits related to “2009 H1N1 Vaccines and any associated adjuvants” was likewise granted to both vaccine manufacturers and federal officials by declaration under the Public Readiness and Emergency Preparedness (PREP) Act.<sup>129</sup> The decision was made the previous June, well in advance of a supply of actual vaccine, and was “intended to encourage manufactures to produce vaccine, and other entities to participate in distribution, dispensing, administration, and use of the vaccine,” the HHS explained on its website.<sup>130</sup>

“WHO basically held the trigger for the implementation of the pandemic preparedness plans and with this for high revenues for the involved producers of pandemic vaccines and some antiviral drugs,” Wodarg told the Council of Europe.<sup>131</sup> “The pharmaceutical companies must have been waiting for this announcement, which was made even though the flu was relatively mild.”<sup>132</sup>

Dr. Ulrich Keil, a German epidemiologist and director of the WHO Collaborating Centre for epidemiology and prevention of cardiovascular and other chronic diseases, criticized the “hysterical announcements and reactions of ministries, scientific bodies and not least the media” despite the evidence of a mild disease. Keil argued that instead of spending money on the real killers of man—hypertension, smoking, high cholesterol—money was being squandered on “pandemic scenarios whose evidence base is weak.”<sup>133</sup>

The WHO, which was invited to participate at the hearing, defended itself against claims that it exaggerated the pandemic threat. “Let me state clearly and for the record. The influenza pandemic policies and responses recommended and taken by WHO were not improperly influenced by the

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<sup>128</sup> Nina Lakhani, “Swine flu in Britain: The guessing game”, July 19, 2009, <http://www.independent.co.uk/life-style/health-and-families/health-news/swine-flu-in-britain-the-guessing-game-1752302.html>, (accessed August 11, 2009).

<sup>129</sup> Kathleen Sebelius, “Pandemic Influenza Vaccines--Amendment”, June 25, 2009, <http://edocket.access.gpo.gov/2009/pdf/E9-14948.pdf>; Mike Stobbe, “Legal immunity set for swine flu vaccine makers,” *Associated Press*, July 17, 2009, <http://www.google.com/hostednews/ap/article/ALeqM5hjdChrP82YTFser5vD6CzTK1az6wD99GH8580>, (accessed July 26, 2009).

<sup>130</sup> U.S. Department of Health and Human Services, “Vaccines, Vaccine Allocation and Vaccine Research”, n.d., <http://www.pandemicflu.gov/vaccine/vacresearch.html>, (accessed July 30, 2009).

<sup>131</sup> Wolfgang Wodarg, *The handling of the H1N1 pandemic: more transparency needed?* (Strasbourg, France, 2010), 3, [http://www.assembly.coe.int/CommitteeDocs/2010/20100126\\_Statement%20Wodarg.pdf](http://www.assembly.coe.int/CommitteeDocs/2010/20100126_Statement%20Wodarg.pdf), (accessed October 14, 2010).

<sup>132</sup> *Ibid.*

<sup>133</sup> Ulrich Keil, *The handling of the H1N1 pandemic: more transparency needed?* (Strasbourg, France, 2010), [http://www.assembly.coe.int/CommitteeDocs/2010/20100126\\_ContributionKeil.pdf](http://www.assembly.coe.int/CommitteeDocs/2010/20100126_ContributionKeil.pdf), (accessed July 16, 2011).

pharmaceutical industry,” influenza chief Keiji Fukuda said in a prepared statement. Cooperation with the private sector, he argued, “is essential for optimally addressing the public health challenges of today and tomorrow.” In closing, Fukuda struck back at Wodarg’s charge: “The labeling of the pandemic as ‘fake’ is to ignore recent history and science and to trivialize the deaths of over 14,000 people and the many additional serious illnesses experienced by others.”<sup>134</sup>

Representing the European vaccine manufacturers, the executive director of influenza vaccine manufacturer Sanofi Pasteur MSD also defended industry’s role in the pandemic. Industry was not making the decisions, he said—that was the role of scientists, international institutions and governments. Industry just “did what it was asked to do,” Dr. Luc Hessel said, which was to produce safe and effective vaccines.<sup>135</sup>

At its second public hearing, the Council of Europe heard from the health minister of Poland. In dramatic contrast to most nations in Europe and around the world, the Polish government had decided to not seek H1N1 vaccines in response to the H1N1 threat—and by the time of the hearing, the decision had become the source of considerable pride. Minister Kopacz presented her side of the story: during the early months of May and June, Poland had paid close attention to the situation in the Southern Hemisphere which was heading into its winter season. From these data, she said, “we were becoming very aware of the moderate nature this pandemic.” Considering the population at high risk of complications of influenza, the government nonetheless brought the vaccine manufacturers into negotiations to discuss a potential acquisition of H1N1 vaccine.

... but the conditions of purchase for vaccines proposed by producers were dubious for us, vaccines were to be purchased only by governments and not available directly to individuals, and to units of health care system, the producers of the vaccine expected that Polish government would take full responsibility for any undesirable side effects offering sale at the risk and on the responsibility of the purchaser.

In addition, manufacturers set the price at two to three times the seasonal influenza vaccine price.

It is really not acceptable that producers of a medical vaccine thanks to the media campaign and taken [sic] advantage of fear that they should force government to take certain decisions; it is not acceptable for producers not to take responsibility for product for safety of patients and for undesirable side effects. It is not acceptable that governments should become hostages to interest groups and should take decision in an atmosphere of panic resulting from alarmist announcements in the media or the

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<sup>134</sup> Keiji Fukuda, “Statement by Dr Keiji Fukuda on behalf of WHO at the Council of Europe hearing on pandemic (H1N1) 2009”, January 26, 2010, [http://www.who.int/csr/disease/swineflu/coe\\_hearing/en/index.html](http://www.who.int/csr/disease/swineflu/coe_hearing/en/index.html), (accessed March 24, 2010).

<sup>135</sup> European Vaccine Manufacturers, “EVM statement to the Council of Europe hearing ‘The handling of pandemic preparedness: more transparency needed?’ On the motion ‘Faked pandemics – a threat for health’”, January 26, 2010, [http://assembly.coe.int/CommitteeDocs/2010/20100126\\_EVM\\_E.pdf](http://assembly.coe.int/CommitteeDocs/2010/20100126_EVM_E.pdf), (accessed January 26, 2010).

opinion of experts who have an interest in the situation themselves and who have not based their analysis on scientific terms, that is not acceptable at all.<sup>136</sup>

Poland decided to decline the vaccine manufacturers' offer.

A similar criticism of WHO's response, and designation of the H1N1 outbreak as a "Phase 6" event came from Dr. Klaus Stöhr, who until 2007 was the WHO's top influenza expert and responsible for its pandemic preparedness. (This was the job that Keiji Fukuda took over.) Stöhr had penned the well read *Science* article in 2004 which projected that even the most mild pandemic would kill 2 million.<sup>137</sup> Now working for the vaccine manufacturer Novartis, Stöhr criticized the WHO for its lack of ability to properly assess and respond to the threat of H1N1, saying early data from the summer of 2009 had already indicated the mildness of the virus: "In July and August [the winter season in the southern hemisphere] the Australia and New Zealand national influenza centres were indicating the southern hemisphere outbreak was mild," he told the *BBC*. "Virologists, myself included, thought well, it's not so likely that this virus will become more severe." But "at the end of August the WHO website was still calling the virus severe. I personally would have thought there could have been more assessments, and more advice to governments." Stöhr suggested the WHO's decision to declare Phase 6 was wrongheaded:

The pandemic planning I was involved with was always based on a severe public health event ... Moving to Phase 6 meant that we wanted governments... to kick in their plans whether they thought it was urgent or not. ... I personally think that moving to Phase 6 that early was, in hindsight, not needed.<sup>138</sup>

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While most media coverage of the Council of Europe meetings focused on its criticisms of the WHO, its task was never conceived so narrowly. Rather, rapporteur of the Council inquiry, British Member of Parliament Paul Flynn was charged with evaluating the response to the pandemic—by not only the WHO, but the pharmaceutical industry, European Union and European Parliament, and Council of Europe member states. In his interim report, Flynn said that France's experience illustrates "very well the extent to which the H1N1 pandemic might have been overstated and the consequences for public health budgets."<sup>139</sup> Only a couple hundred people had died from H1N1 (compared to a seasonal average of between 4,000 to 6,000), Flynn wrote, and France had successfully managed to cancel orders for 50 million of the 94 million vaccine doses it ordered. By March 2010, only 5.7 million people had been vaccinated—at a cost of 365 million Euros—and the French National Assembly and French Senate

<sup>136</sup> Ewa Kopacz, *The handling of the H1N1 pandemic: more transparency needed?* (Strasbourg, France, 2010), [http://assembly.coe.int/CommitteeDocs/2010/20100329\\_MinisterKopaczAddress.pdf](http://assembly.coe.int/CommitteeDocs/2010/20100329_MinisterKopaczAddress.pdf), (accessed July 16, 2011).

<sup>137</sup> Stöhr and Esveld, "Public health. Will vaccines be available for the next influenza pandemic?"

<sup>138</sup> Imogen Foulkes, "WHO faces questions over swine flu policy," *BBC*, May 20, 2010, sec. Europe, <http://news.bbc.co.uk/2/hi/world/europe/10128604.stm>, (accessed May 21, 2010).

<sup>139</sup> Paul Flynn, "The handling of the H1N1 pandemic: more transparency needed", March 23, 2010, [http://assembly.coe.int/CommitteeDocs/2010/20100329\\_MemorandumPandemie\\_E.pdf](http://assembly.coe.int/CommitteeDocs/2010/20100329_MemorandumPandemie_E.pdf), (accessed March 29, 2010).

had launched public hearings to review their handling of H1N1. (The Senate investigation in particular aims to investigate the role of pharmaceutical companies in the official handling of H1N1.)<sup>140</sup>

Flynn worried that the gap between the relatively mild disease and the responses of public health at the national and international level had “gambled away” not only money but also the confidence of the European public in WHO and other “highly reputed organizations,” a problem which he said was further compounded by a lack of transparency in decision making. Titled *The handling of the H1N1 pandemic: more transparency needed*, Flynn’s interim report criticized WHO’s continued refusal to release the names of the Emergency Committee that advised the Director-General on the pandemic. Should the privacy of experts “prevail over the right of 800 million citizens to be openly and fully informed about major decisions that might have an impact on their individual health and well-being?” Flynn asked.<sup>141</sup>

A subsequent fact-finding mission to the World Health Organization did little to rest the Council of Europe’s concerns. To understand how decisions were made, transparency was needed, the Council argued, but the WHO divulged little more than it had publicly stated, citing a need to protect the experts’ privacy (in Margaret Chan’s words, WHO was “motivated by a desire to protect the experts from commercial or other influences”<sup>142</sup>). But “in a situation where uncertainty is coupled with risks for human health and lives,” Flynn argued in his final report, “there is also a danger that public opinion can be manipulated in favour of particular commercial interests.” Policy makers might tend towards choices that shield them from accusations rather than the choices “dictated by the search for the optimal solution.” In such a context, Flynn said that transparency was of utmost importance.<sup>143</sup>

“[T]he Assembly serious regrets that they [WHO and European health institutions] have not been willing to share some essential information, in particular to publish the names and declarations of interest of the members of the Emergency Committee of WHO and relevant European advisory bodies directly involved in recommendations concerning the handling of the pandemic,” the Parliamentary Committee wrote in its final report adopted June 4, 2010.

The Parliamentary Assembly is alarmed about the way in which the H1N1 influenza pandemic has been handled, not only by the World Health Organization (WHO) but also by the competent health authorities at the level of the European Union and at national level. It is particularly troubled by some of the consequences of decisions taken and advice given leading to distortion of priorities of public health services across Europe, waste of large sums of public money and also unjustified scares and fears about health risks faced by the European public at large.<sup>144</sup>

<sup>140</sup> Council of Europe, “The handling of the H1N1 pandemic: more transparency needed,” 16.

<sup>141</sup> Flynn, “The handling of the H1N1 pandemic: more transparency needed.”

<sup>142</sup> Chan, “WHO Director-General’s letter to BMJ editors.”

<sup>143</sup> Council of Europe, “The handling of the H1N1 pandemic: more transparency needed,” 10.

<sup>144</sup> *Ibid.*, 2.

## Conflicts of Interest

Paul Flynn's final report was necessarily tentative, full of speculation, but lacking definitive proof:

"Amongst the factors leading to the suspicion of undue influence were the early measures taken on contractual arrangements for vaccine delivery between member states and pharmaceutical companies, as well as the enormous profits that companies were able to make as a result of the pandemic," he explained. "The main suspicion, however, arises with regard to the issue of whether members of WHO advisory bodies have professional links to pharmaceutical groups, bringing into question the neutrality of their advice. Unfortunately, due to WHO's refusal to release the names and declarations of interest of persons concerned, any current research on the matter depends entirely on the results of investigative journalism."<sup>145</sup>

Flynn, who was joined in the final Parliamentary session in a public forum with editor-in-chief of the British medical journal *BMJ* Fiona Godlee, was likely aware that such investigative journalism was on its way as he finished drafting his report. The same day the Council of Europe received Flynn's final report, the *BMJ* and London-based Bureau of Investigative Journalism reported that "Key scientists advising the World Health Organization on planning for an influenza pandemic had done paid work for pharmaceutical firms that stood to gain from the guidance they were preparing. These conflicts of interest have never been publicly disclosed by WHO, and WHO has dismissed inquiries into its handling of the A/H1N1 pandemic as 'conspiracy theories.'"<sup>146</sup>

The *BMJ/The Bureau* investigation suggested that financial conflicts of interest riddled not only WHO's handling of H1N1, but a decade of WHO's pandemic preparedness efforts. Among the report's findings: the WHO had failed to disclose that its first pandemic plan, drafted in 1999, was written in collaboration with the European Scientific Working Group on Influenza (ESWI), a group that was "funded entirely by Roche and other influenza drug manufacturers." Furthermore, two members of ESWI (Professor Karl Nicholson of Leicester University in the UK and Professor Ab Osterhaus of Erasmus University in the Netherlands) were co-authors of a manufacturer-funded clinical trial of the drug Tamiflu, published in *Lancet*<sup>147</sup> that was subsequently revealed<sup>148</sup> to have been ghostwritten.

The report also showed that WHO did not disclose any financial conflicts of interest information related to the authors of its 2004 guidance document, *WHO Guidelines on the Use of Vaccines and Antivirals During Influenza Pandemics*. Arnold Monto, listed as a professor of epidemiology at the University of Michigan, was the author of an annex on the use of vaccines in a pandemic. The *BMJ/The Bureau* reported that, "Between 2000 and 2004—and at the time of writing the annexe—Dr Monto has consistently and openly declared honorariums, consultancy fees, and research support from Roche, consultancy fees and research support from GlaxoSmithKline; and also research funding from ViroPharma." Frederick Hayden, author of an annex on antivirals during a pandemic, was at the time

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<sup>145</sup> Ibid., 11.

<sup>146</sup> Cohen and Carter, "WHO and the pandemic flu 'conspiracies'."

<sup>147</sup> K G Nicholson et al., "Efficacy and safety of oseltamivir in treatment of acute influenza: a randomised controlled trial. Neuraminidase Inhibitor Flu Treatment Investigator Group," *Lancet* 355, no. 9218 (May 27, 2000): 1845-1850.

<sup>148</sup> Deborah Cohen, "Complications: tracking down the data on oseltamivir," *BMJ* 339, no. dec08\_3 (December 8, 2009): b5387.

being paid by Roche for lectures and consultancy work, and had received payments from GlaxoSmithKline until 2002—but in the WHO guidance document, is only listed as a professor at the University of Virginia. Finally, a third scientist—Karl Nicholson—who also authored an annex to the WHO guidance document, had received travel sponsorship, honorariums, and consultancy and speaking fees from GlaxoSmithKline and Roche, manufacturers of the influenza antivirals Relenza and Tamiflu. Like the others, Nicholson is only mentioned by his academic affiliation as “Professor of Infectious Diseases” in Leicester, UK.

All authors, however, told the *BMJ/The Bureau* that they submitted declaration of interest forms to WHO, suggesting that WHO was ultimately the party responsible for the non-disclosure. In its defense, the WHO posted an explanation on its website: “In line with WHO policy, all experts who participated in this meeting were required to submit a declaration of interest form and all such forms were duly reviewed by WHO. However, a summary of relevant interests was not issued together with the publication. WHO regrets this oversight.”<sup>149</sup>

It is unclear, however, to what degree it was a matter of simple oversight. The *BMJ/The Bureau* article reports that while being assured by a spokesperson of the Organization that Director-General Margaret Chan “is very committed personally to transparency,” Chan personally denied the *BMJ/The Bureau’s* request for conflict of interest declarations related to the 2004 guidance document. Consequently, declarations of interest remain unpublished.

Finally, the investigative report documented that two scientists which feature in Roche marketing material also presented to the European Medicines Agency (EMA), the European equivalent to the FDA, regarding the licensure of Tamiflu, a drug on which governments would spend billions of dollars stockpiling. One (Rene Snacken, also a member of ESWI and key author of the WHO’s original 1999 pandemic influenza plan<sup>150</sup>) gave his presentation to the EMA as a representative of the Belgian Ministry of Public Health, urging the use of Tamiflu during a pandemic. The second (Annike Linde) appeared as a representative of the Swedish Institute for Infectious Disease. It is unclear what information about these scientists’ relationship with pharmaceutical companies was disclosed to EMA; under the Freedom of Information Act, the *BMJ/The Bureau* requested declaration of interest statements submitted to EMA, but reported the EMA “was unable to provide statements for those particular people at that time.”

The authors of the report commented: “The investigation by the *BMJ/The Bureau* reveals a system struggling to manage the inherent conflict between the pharmaceutical industry, WHO, and the global public health system, which all draw on the same pool of scientific experts.”

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<sup>149</sup> World Health Organization, “The international response to the influenza pandemic: WHO responds to the critics”, June 10, 2010, [http://www.who.int/csr/disease/swineflu/notes/briefing\\_20100610/en/index.html](http://www.who.int/csr/disease/swineflu/notes/briefing_20100610/en/index.html), (accessed June 10, 2010).

<sup>150</sup> World Health Organization, *Influenza Pandemic Plan. The Role of WHO and Guidelines for National and Regional Planning*, April 1999, 33, <http://www.who.int/entity/csr/resources/publications/influenza/whocdscsredc991.pdf>, (accessed April 12, 2010).

## Pandemic over

In August, 2010, the announcement many in Europe were waiting for finally arrived. Declaring that “the world is no longer in phase 6 of influenza pandemic alert,” Margaret Chan said H1N1 was now in a “post-pandemic period.”<sup>151</sup> With this announcement, WHO also published the membership of the secretive Emergency Committee, revealed to be composed of sixteen influenza experts with primary affiliations mostly in government and academia, of which six had declared interests, five of which were with pharmaceutical companies. The WHO noted that these “interests ... do not give rise to a conflict of interest such that the experts concerned should be partially or totally excluded from participation in the Emergency Committee.”

Of the six committee members reporting disclosures of interest, some of the specifics had been elsewhere already documented, such as in the *BMJ/The Bureau* investigative report or in scientific publications. But others appeared to have been disclosed for the first time ever, such as the director of the CDC’s Influenza division, Nancy Cox, who reported receiving financial support from the International Federation of Pharmaceutical Manufacturers & Associations, “for activities of CDC as a WHO Collaborating Centre in the field of influenza vaccine research and virus isolation work.”<sup>152</sup>

The Emergency Committee declarations were reported on in the press, but amidst the rapidly declining media interest in H1N1 following the WHO’s announcement of the end of the pandemic, they did not themselves cause much of a stir. Defending the WHO and the general prevalence of academic and government relationships with industry, the *Nature* website posted a comment: “In case it needs spelling out: no member declared anything that might be considered even slightly out of the ordinary for an expert on influenza.”<sup>153</sup> Paraphrasing Emergency Committee member Arnold Monto, *Nature* warned that “extreme rhetoric about the WHO’s connections with the pharmaceutical industry ... may reduce the willingness of scientists to offer advice when asked.” Yet Monto told *Nature*: “full disclosure is the appropriate way to go.” (WHO reported that Monto disclosed “current and past consultancies in the field of pandemic and/or seasonal influenza for GSK, Novartis, Roche, Baxter and Sanofi. The remuneration for each of these consultancies is below US\$10 000. In addition, his research unit at the University of Michigan has received a grant from Sanofi Pasteur for a clinical trial conducted in 2007-2008 on the comparative efficacy of inactivated and live attenuated influenza vaccines.”<sup>154</sup>)

The WHO has openly acknowledged how problematic its decision was to keep the names of its Emergency Committee secret for so long, and has stated that it is reviewing its procedures for revealing names of members of future Emergency Committees formed in response to public health emergencies

<sup>151</sup> Margaret Chan, “H1N1 in post-pandemic period”, August 10, 2010, [http://www.who.int/mediacentre/news/statements/2010/h1n1\\_vpc\\_20100810/en/index.html](http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html), (accessed July 17, 2011).

<sup>152</sup> World Health Organization, “List of Members of, and Advisor to, the International Health Regulations (2005) Emergency Committee concerning Influenza Pandemic (H1N1) 2009”, August 10, 2010, [http://www.who.int/ihr/emerg\\_comm\\_members\\_2009/en/index.html](http://www.who.int/ihr/emerg_comm_members_2009/en/index.html), (accessed August 11, 2010).

<sup>153</sup> Daniel Cressey, “H1N1 ‘emergency committee’ members named - August 11, 2010,” *Nature News Blog*, August 11, 2010, [http://blogs.nature.com/news/2010/08/h1n1\\_emergency\\_committee\\_membe.html](http://blogs.nature.com/news/2010/08/h1n1_emergency_committee_membe.html).

<sup>154</sup> World Health Organization, “List of Members of, and Advisor to, the International Health Regulations (2005) Emergency Committee concerning Influenza Pandemic (H1N1) 2009.”

of international concern. The agency, however, seems confident in its handling of potential conflicts of interests among the experts it taps for advice: "Procedures are in place for identifying, investigating and assessing potential conflicts of interest, disclosing them, and taking appropriate action such as excluding an expert from participating in a meeting," WHO declared in a briefing last year.<sup>155</sup>

But while the WHO may be collecting and assessing disclosures of interest, a series of discrepancies and inconsistent explanations point to systematic problems in WHO's handling and disclosure of potential conflicts of interest.

### **Conflicts of Interest and the IHR Review Committee**

Conflicts of interest have a special history at WHO. In the late 1970s, the Organization entered into de-facto battle with multinational corporations by drafting international codes on breast milk substitutes. Then, in 1977, WHO again challenged industrial interests by designing a system of rational drug selection through its adoption of a short, "essential medicines list," and encouragement of Member States to develop a domestic drug production capacity. Though the move was strongly opposed by the pharmaceutical industry, WHO held its ground.<sup>156</sup> Twenty-two years later, in the summer of 1999, then WHO Director-General Gro Harlem Brundtland received an internal report suggesting that tobacco companies had made widespread efforts to undermine tobacco control policies within United Nations agencies. Brundtland responded swiftly, assembling an expert committee to investigate the matter. In July 2000, the committee reported back with its findings. They wrote that

In the course of this inquiry, the committee of experts has identified many reasons for concern about the integrity of the process for international decision-making about tobacco. The evidence shows that tobacco companies have operated for many years with the deliberate purpose of subverting the efforts of the World Health Organization (WHO) to address tobacco issues. The attempted subversion has been elaborate, well financed, sophisticated and usually invisible.<sup>157</sup>

The WHO's response was to radically strengthen its commitment to avoiding conflicts of interest. It is in this context that Margaret Chan's assurances ten years later that all of her decisions in response to H1N1 had been made on the hard evidence only and that "At no time, not for one second, did commercial interests enter my decision-making" struck some as knee-jerk and perhaps premature.<sup>158</sup>

Nevertheless, following all the criticisms of its decision-making, in January 2010, WHO announced the formation of an expert committee to review WHO's handling of the pandemic. In her opening remarks to the International Health Regulations (IHR) Review Committee's first meeting, Margaret Chan told the

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<sup>155</sup> World Health Organization, "WHO use of advisory bodies in responding to the influenza pandemic."

<sup>156</sup> Fiona Godlee, "WHO in retreat: is it losing its influence?," *BMJ* 309, no. 6967 (December 3, 1994): 1491-1495.

<sup>157</sup> Report of the Committee of Experts on Tobacco Industry Documents, "Tobacco Company Strategies to Undermine Tobacco Control Activities at the World Health Organization", July 2000, 228, [http://www.who.int/entity/tobacco/en/who\\_inquiry.pdf](http://www.who.int/entity/tobacco/en/who_inquiry.pdf), (accessed June 12, 2011).

<sup>158</sup> Godlee, "Conflicts of interest and pandemic flu."



group, “WHO is not defining or restricting the scope of specific issues that may arise ... we want a frank, critical, transparent, credible and independent review of our performance.”<sup>159</sup>

The IHR Review Committee began its work in April 2010 and was chaired by US Institute of Medicine president Harvey Fineberg. Its final report was delivered to the World Health Assembly in Geneva in May 2011. Fineberg, who is known for his probing analysis of the 1976 experience with Harvard political scientist Richard Neustadt, *The Swine Flu Affair: Decision-Making on a Slippery Disease*,<sup>160</sup> said that his committee’s report would be “critical” and transparent.<sup>161</sup>

However the degree to which the inquiry could independently analyze information is debatable. Following the IHR Review Committee’s third meeting, I had the chance to sit in on a press conference chaired by Fineberg at WHO headquarters in Geneva. Given the panel’s high profile status—in addition to Fineberg, many of the Committee members are prominent people in their respective fields and presumably quite busy—I asked Fineberg what kind of time was being spent on the review, and what kind of support staff he had at the Institute of Medicine. Fineberg explained that the committee’s support staff was not from the Institute of Medicine, but WHO itself—an answer that did not sit well with some members of the press in the audience.

[Harvey Fineberg:] ... on your last question, which I do remember, because it was reminding me how much time we’re spending on this; the committee is putting a great deal of time into this and indeed I would say for many, if not all members of the committee it’s taking up more time than they might have understood at the very outset of accepting the obligation. We have a support staff based here in Geneva, who are dedicated to our work on the committee and have been very helpful to us. And in answer to your specific question, that’s the staff on which I rely for this project. So it’s not an Institute of Medicine activity. I’m here as an individual and working on this in the capacity as an individual.

Peter Doshi: So that staff that’s supporting you is staff at WHO staff [sic]?

HF: They are based at WHO, but dedicated to us.

MF [the press—lit., Member of the Floor]: But they are WHO staff?

HF: They are employed by WHO, yes.

MF: Don’t you think you need to have an arm’s length relationship with them?

HF: With that staff? Well they’re not staff who were involved in the...

<sup>159</sup> Chan, “Experts begin their assessment of the response to the H1N1 influenza pandemic.”

<sup>160</sup> Richard E Neustadt and Harvey V Fineberg, *The Swine Flu Affair: Decision-Making on a Slippery Disease* (Washington, D.C.: The National Academies Press, 1978).

<sup>161</sup> J. Zarocostas, “Head of inquiry into WHO’s handling of the H1N1 pandemic says he will present a ‘critical’ report,” *BMJ* 342, no. jan20 3 (January 20, 2011): d385-d385.

MF: But they still work for WHO.

HF: They still work for WHO, that is true. I think that, you know, we're very aware of that, but this is going to be the committee's report, that I can assure you. As I think every member of this committee, working on every element of this, would assure you. Well, if there are no further questions, thank you all very much for being here....<sup>162</sup>

## The Final Report

In its final report following a year of deliberations, subsequently adopted by the World Health Assembly,<sup>163</sup> the Review Committee criticized WHO for a "lack of a sufficiently robust, systematic and open set of procedures for disclosing, recognizing and managing conflicts of interest among expert advisers."<sup>164</sup> In particular, it found several shortcomings in the way WHO handled the disclosure and management of conflicts of interest among the Emergency Committee which advised the WHO Director-General during the H1N1 outbreak.

Although confidentiality represented an understandable effort to protect the members from external pressures, this paradoxically fed suspicions that the Organization had something to hide. While the decision was consistent with WHO practices for other expert committees, whose identities are normally divulged only at the end of what is often a one-day consultation, this practice was not well suited to a Committee whose service would extend over many months.<sup>165</sup> ...

The Review Committee appreciates the desire to protect members of the EC [Emergency Committee] from external influence by keeping their identities confidential for the duration of their appointment. The Review Committee also appreciates the need for expert consultations to be held in confidence so that the Director-General will have the benefit of candid discussion and advice. At the same time, the lack of disclosure fosters suspicion about the interests and motivations of members of the EC. On balance, the Review Committee concluded that, in the interest of transparency, it would have been better for WHO to have disclosed from the outset the names of EC members.<sup>166</sup>

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<sup>162</sup> World Health Organization, "Transcript of press briefing with Dr Harvey Fineberg, Chair, International Health Regulations Review Committee", September 29, 2010, [http://www.who.int/entity/mediacentre/multimedia/pc\\_transcript\\_30\\_september\\_10\\_fineberg.pdf](http://www.who.int/entity/mediacentre/multimedia/pc_transcript_30_september_10_fineberg.pdf), (accessed March 27, 2011). (I have made minor edits to the WHO-provided transcription for accuracy, using the WHO's audio recording at 1hr, 7min, 8 secs. See [http://terrance.who.int/mediacentre/audio/IHR/IHR\\_PRESS\\_29SEP2010.mp3](http://terrance.who.int/mediacentre/audio/IHR/IHR_PRESS_29SEP2010.mp3).)

<sup>163</sup> World Health Assembly, "Implementation of the International Health Regulations (2005)", May 20, 2011.

<sup>164</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, "Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009," 16.

<sup>165</sup> *Ibid.*

<sup>166</sup> *Ibid.*, 79.

The Review Committee also criticized WHO for a “Failure to acknowledge legitimate reasons for some criticism, in particular, inconsistent descriptions of a pandemic.”<sup>167</sup>

Nevertheless, the Review Committee’s report is overall optimistic, mentioning “that WHO is taking steps to improve its management of conflicts of interest, even as this review has proceeded.” Finding “no evidence of malfeasance,” the Review Committee uses the term “misunderstanding” to describe concerns that conflicts of interest may have affected decision making, and urged WHO to respond “professionally and vigorously to unwarranted criticisms” in the future.

The IHR Review Committee’s findings were received enthusiastically by WHO. Margaret Chan remarked:

For me, personally, as head of this agency, the assessment of the pandemic response needed to address two absolutely critical questions and to give everyone a firm answer.

First, did WHO make the right call? Was this a real pandemic or not?

Second, were WHO decisions, advice, and actions shaped in any way by ties with the pharmaceutical industry?

In other words, did WHO declare a fake pandemic in order to line the pockets of industry?

The document exonerates WHO on both counts.<sup>168</sup>

The Review Committee’s report also met the approval of the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), which wrote that “the R&D pharmaceutical industry fully welcomes the IHR report’s recommendation for countries to immunize their high-risk populations yearly against seasonal influenza.”<sup>169</sup> The IHR Review Committee’s report urged “countries to immunize their high-risk populations yearly against seasonal influenza,”<sup>170</sup> echoing longstanding advice of the World Health Assembly “to establish and implement strategies to increase vaccination coverage of all people at high risk.”<sup>171</sup> The IHR Review Committee also called for advancing the production of influenza vaccines

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<sup>167</sup> Ibid., 16.

<sup>168</sup> Margaret Chan, “Director-General responds to assessment of WHO’s handling of the influenza pandemic”, March 28, 2011, [http://www.who.int/dg/speeches/2011/ihr\\_review\\_20110328/en/index.html](http://www.who.int/dg/speeches/2011/ihr_review_20110328/en/index.html), (accessed July 17, 2011).

<sup>169</sup> International Federation of Pharmaceutical Manufacturers & Associations, “R&D Pharmaceutical industry welcomes main conclusions of 2009 flu pandemic response”, May 19, 2011, [http://www.ifpma.org/fileadmin/content/News/2011/all/IFPMA\\_News\\_Release\\_IHR\\_19May2011.pdf](http://www.ifpma.org/fileadmin/content/News/2011/all/IFPMA_News_Release_IHR_19May2011.pdf), (accessed May 21, 2011).

<sup>170</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, “Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009,” 21.

<sup>171</sup> World Health Assembly, “Prevention and control of influenza pandemics and annual epidemics (WHA56.19)”, May 28, 2003, [http://whqlibdoc.who.int/waha/2003/WHA56\\_19.pdf](http://whqlibdoc.who.int/waha/2003/WHA56_19.pdf), (accessed September 25, 2010); World Health Assembly, “Strengthening pandemic-influenza preparedness and response (WHA 58.5)”, May 23, 2005.

worldwide,<sup>172</sup> initiatives that WHO had already been spearheading through programs such as the Global Action Plan to Increase Supply of Pandemic Influenza Vaccines (GAP). GAP was born out of a WHO-led consultation in May 2006 to address the “anticipated gap between potential vaccine demand and supply during an influenza pandemic,”<sup>173</sup> and held as its first goal to “increase seasonal vaccine demand to stimulate market forces and augment supply.”<sup>174</sup>

## Inconsistencies

Surprisingly, the IHR Review Committee does not discuss conflicts of interest in relation to the arguably most central WHO pandemic influenza policy document: *Pandemic Influenza Preparedness and Response*. This document, published in April 2009, took over a year to draft, and was the culmination of multiple international consultations involving over 139 experts.<sup>175</sup> The document’s foreword stated that “All external experts and contributors for all meetings and consultations, including those in the public review, have signed a declaration of interest statement in accordance with WHO policy. A small number of participants indicated a conflict of interest.” Under a section titled “Declaration of Interest” it explained that “three working group members” and “two other participants” reported “some conflicts of interest.”<sup>176</sup> But the document did not contain any details, instead stating that “the declarations of interest are available upon request.”<sup>177</sup>

I requested the declarations from WHO in June 2010, following the *BMJ/The Bureau* investigation into conflicts of interest amongst WHO expert advisors<sup>178</sup> as well as comments from several journalists that WHO was not furnishing the promised declarations. WHO responded to me that “we do not release individual declaration of interests.”<sup>179</sup> I was instead sent “summary” declarations of interest—a list compiled by WHO—stating that “of the 139 experts who participated in the substantive elaboration of this guidance document, eight declared interests.” Details for the eight individuals were given. But problems with the list were readily apparent—some minor (two of the eight individuals’ names were misspelt) and some serious (one individual’s inclusion was entirely erroneous). During an interview with WHO communications staff in Geneva in late September, I requested WHO to check the original

<sup>172</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, “Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009,” 22.

<sup>173</sup> World Health Organization, “The Global Action Plan (GAP) to Increase Supply of Pandemic Influenza Vaccines: First Meeting of the Advisory Group (AG)”, October 19, 2007, 3, [http://whqlibdoc.who.int/HQ/2008/WHO\\_IVB\\_08.10\\_eng.pdf](http://whqlibdoc.who.int/HQ/2008/WHO_IVB_08.10_eng.pdf), (accessed December 12, 2009).

<sup>174</sup> Kieny et al., “A global pandemic influenza vaccine action plan,” 6368.

<sup>175</sup> World Health Organization, *Pandemic influenza preparedness and response: a WHO guidance document* (Geneva: World Health Organization, 2009), 4-5, <http://www.who.int/entity/csr/disease/influenza/PIPGuidance09.pdf>.

<sup>176</sup> *Ibid.*, 58.

<sup>177</sup> *Ibid.*, 3. The WHO’s practice stands in contrast to many medical journals like *BMJ* and *Journal of the American Medical Association* which print a synopsis of disclosures of potential conflicts of interest accompanying any published article. (*New England Journal of Medicine* has recently even begun offering direct access on its website to the disclosure forms provided by authors.)

<sup>178</sup> Cohen and Carter, “WHO and the pandemic flu ‘conspiracies’.”

<sup>179</sup> Email correspondence with Aphaluck Bhatisevi, Media Officer, Global Alert and Response Department, World Health Organization, July 2, 2010.

disclosure forms and confirm the accuracy of what I was sent.<sup>180</sup> WHO later confirmed all of these errors, and explained the more serious error as “due to a cut-and-paste error and has since been corrected.” WHO did not respond to my question asking for an explanation of why the original report mentioned that five individuals reported interests, but the list I was sent included eight names.

Then, around January 2011, the WHO released a “reprinted” version of its 2009 guidance document. Two sections of the new document (the Foreword and the “Declaration of interest”) have changed; the rest of the document is nearly identical to the original, except for occasional typographical changes such as the capitalization of words.

The reprinted Foreword states that “In accordance with WHO policy, participating experts were requested to submit a duly completed and signed Declaration of Interest for WHO Experts form. Representatives of industry ... participated as observers and, in accordance with WHO rules, were not therefore required to submit a Declaration of Interest.”<sup>181</sup> (Incidentally, WHO staff participating in compiling the document also did not have to submit forms.) In the new “declaration of interest” section, a summary of interests is provided. The declarations are nearly identical to those I previously received from WHO, but for three of the seven individuals listed, there are some troubling discrepancies. In two cases (Monto and Phin), additional declarations are shown in the reprinted guidance document that were not included in the summary I received in July 2010; for another individual (Van-Tam), some declarations that were on the original list have disappeared and new ones have appeared (Table 3.3).

To clarify, I asked WHO to confirm the source of the summary declaration of interests. WHO spokesman Gregory Härtl, Team Leader for Communications for Global Alert and Response, said that

WHO uses the standard WHO Declaration of Interest forms to assess whether there is a conflict of interest. External experts fill in these forms and the secretariat evaluates them. We do not go to other sources to either seek additional information or to confirm the declared interests (or lack thereof).<sup>182</sup>

Despite such assurances, this does not appear to always be true. In the case of the novel H1N1 influenza Emergency Committee, the declarations of interest (DOI) related to those members were initially released on August 10, 2010, and then revised on October 1, 2010, based on information that did not come from previously signed WHO Declaration of Interest forms, but rather from post-publication information. Explaining the change, WHO stated, “This document has been updated to reflect revisions in the summary of interests and affiliation information of Professor Neil M. Ferguson

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<sup>180</sup> Interview with Kristen Kelleher and Gregory Härtl, communications officers, World Health Organization, September 30, 2010, Geneva, Switzerland.

<sup>181</sup> World Health Organization, *Pandemic influenza preparedness and response: a WHO guidance document*, 2010, 3, [http://whqlibdoc.who.int/publications/2009/9789241547680\\_eng.pdf](http://whqlibdoc.who.int/publications/2009/9789241547680_eng.pdf), (accessed January 31, 2011).

<sup>182</sup> Email correspondence with Gregory Härtl, Team Leader, Communications for Global Alert and Response (GAR), World Health Organization, February 22, 2011.

based upon additional information received from him after initial confirmation and publication of this List.”<sup>183</sup> Mr. Härtl further explained:

As preparations for the second reprint, the secretariat went back to the DOI forms received from the experts and prepared a more detailed summary to address the queries raised from the international community on this issue during the pandemic 2009.<sup>184</sup>

While WHO’s concern for transparency and the handling of potential conflicts of interest was heightened in response to widespread public concern, it does not appear true that discrepancies in the summary differences can be attributed to a “more detailed summary” based on the original DOI forms because what is presented in the reprinted guidance document are not simply additional details beyond what was included in the list I received the previous July, but true revisions, including not only the addition but also the deletion of information. For example, in July 2010, Jonathan Nguyen Van-Tam was reported to have had received “honoraria to speak at meetings sponsored by GSK, Novartis, Solvay and Roche.” But the reprinted guidance, states that he received “honoraria to speak at meetings sponsored by GSK, Sanofi, Baxter and Roche.” The first list includes Novartis and Solvay, but the new list does not. The second list instead includes Sanofi and Baxter, which were not in the first list.

Further attempts for clarification were unsuccessful. On March 16, 2011 despite an on-and-off correspondence of over nine months, WHO ended its correspondence with me, noting that “we cannot devote a substantial amount of our working time in replying to questions for a doctoral dissertation.”<sup>185</sup> In its last email, WHO unfortunately did not answer my specific questions about the source of the summary declarations of interest, or why discrepancies existed between different versions.

When WHO publicly releases summaries of expert disclosures, there is an expectation that this is a complete and accurate representation of what those experts disclosed to WHO at the time of their expert advice (in this case, between November 2007 and January 2009, when experts were consulted in preparing WHO’s revised pandemic plan). If this were the case, however, it is hard to understand why WHO’s summary of those declarations would have changed between July 2010 and January 2011, long after the pandemic plan was finalized. Without publication of the original forms, signed and submitted by those giving advice to WHO, there is little way to independently verify the accuracy of WHO’s published summaries. If we do not know what was disclosed to WHO at the time, how can observers trust WHO’s determination that the experts’ declarations “were not sufficient in conflict with the recommendations, to exclude them from the guidance development process”?<sup>186</sup>

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<sup>183</sup> World Health Organization, “List of Members of, and Advisor to, the International Health Regulations (2005) Emergency Committee concerning Influenza Pandemic (H1N1) 2009”, October 1, 2010, [http://www.who.int/ihr/emerg\\_comm\\_members\\_2009/en/index.html](http://www.who.int/ihr/emerg_comm_members_2009/en/index.html), (accessed December 3, 2010).

<sup>184</sup> Email correspondence with Gregory Härtl, Team Leader, Communications for Global Alert and Response (GAR), World Health Organization, February 22, 2011.

<sup>185</sup> Email correspondence with Gregory Härtl, Team Leader, Communications for Global Alert and Response (GAR), World Health Organization, March 16, 2011.

<sup>186</sup> World Health Organization, *Pandemic influenza preparedness and response: a WHO guidance document*, 9.

## Changing webpages

Casting further doubts on the IHR Review Committee's ability to conduct a thorough and critical assessment of the WHO's response to H1N1 is its treatment of criticisms towards the WHO. The Committee's final report notes:

### External criticisms

273. Criticisms about WHO's response to the pandemic began to appear in the media in July 2009. One of the charges against WHO was that it changed the definition of a pandemic without notice. In the regular content review of web pages related to influenza pandemics as part of established emergency procedures, WHO's web manager identified two pages that required modification. The first, related to pandemic preparedness (63), was changed on 4 May 2009 after the review showed that the terms "pandemic" and "H5N1 pandemic" were being used interchangeably. These terms created the impression that a pandemic would be caused only by H5N1.

274. The wording "enormous numbers of deaths and illness" referred to a lethal H5N1 pandemic scenario. The text was edited to be more reflective of the current H1N1 outbreak. The second page was a posting concerning H5N1, with a title that implied that it described an influenza pandemic in general terms. For clarity, "avian influenza" was added to the title. WHO followed standard industry practice by not deleting web pages. However, modifications to page content and versioning were not evident to readers. These changes, which were made without special notice or explanation, invited suspicion of a surreptitious shift in definition rather than an effort to make the descriptions of a pandemic more precise and consistent. From May 2009, all web-page changes were tracked and each revision was dated.

There appear, however, to be at least four important discrepancies in these paragraphs. First, it appears to be the media outlet *CNN* that brought this issue to the attention of WHO, not "WHO's web manager."<sup>187</sup> Second, the terms "pandemic" and "H5N1 pandemic" could not have been being used interchangeably, because on an archived version of the referenced webpage, the term "H5N1" does not appear.<sup>188</sup> Third, it is difficult to understand how the phrase "enormous numbers of deaths and illness" could have referred to H5N1. The webpage does not mention H5N1 and the phrase "enormous

<sup>187</sup> Elizabeth Cohen, "When a pandemic isn't a pandemic," *CNN.com*, May 4, 2009, <http://edition.cnn.com/2009/HEALTH/05/04/swine.flu.pandemic/index.html>, (accessed May 5, 2009). This recounting of events is consistent with WHO's statement: "Some of the confusion may stem from the fact that there was a document on WHO's website for some months that said a pandemic would include 'enormous amounts of cases and deaths'. This was removed when it was brought to our attention." See World Health Organization, "WHO Key Messages - Conflict of Interest Issues", January 11, 2010, [http://www.wpro.who.int/vietnam/media\\_centre/press\\_releases/h1n1\\_8jan2010.htm](http://www.wpro.who.int/vietnam/media_centre/press_releases/h1n1_8jan2010.htm), (accessed April 9, 2010).

<sup>188</sup> World Health Organization, "Pandemic preparedness", April 22, 2009, <http://web.archive.org/web/20090422172703/http://www.who.int/csr/disease/influenza/pandemic/en/>, (accessed July 19, 2011).

numbers of deaths and illness” dates back to at least February 2003, when only 18 human cases of H5N1 were known, worldwide, dating from 1997.<sup>189</sup>

Fourth, it is not true that from May 2009 all webpage changes were tracked and dated. For example, the title of the WHO webpage “Ten things you need to know about pandemic influenza” was changed to “Ten concerns if avian influenza becomes a pandemic” sometime between November 11, 2009 and November 20, 2009, yet the date of the webpage in July 2011—even after I first documented this problem in April 2010—still shows “14 October 2005.”<sup>190</sup> By altering the title, WHO changed self-described must-know information about “pandemic influenza” into “concerns” that were only relevant to “avian influenza.” Of the “ten things” WHO insisted one needs to know were “Widespread illness will occur,” “Medical supplies will be inadequate,” “Large numbers of deaths will occur,” and “Economic and social disruption will be great.” But while WHO and the IHR Review Committee might argue otherwise, the webpage was not “a posting concerning H5N1” in particular, but pandemic influenza in general, with mention of avian influenza H5N1. For example, it gave estimates of future pandemic mortality based on a “mild” 1957 pandemic scenario:

Large numbers of deaths will occur. ... WHO has used a relatively conservative estimate – from 2 million to 7.4 million deaths – because it provides a useful and plausible planning target. This estimate is based on the comparatively mild 1957 pandemic.<sup>191</sup>

### Where to from here?

In discussions of how to protect against financial conflicts of interest in medicine, disclosure and disclosure have become the mantra—a fundamental (but not sufficient) first step.<sup>192</sup> Unfortunately, more than a decade after the World Health Organization (WHO) took major steps to limit undue industry influence, problems apparently remain.

<sup>189</sup> Peter Doshi, “The elusive definition of pandemic influenza,” *Bulletin of the World Health Organization* 89, no. 7 (July 1, 2011): 532-538.

<sup>190</sup> For my documentation of the problem in a letter to *BMJ*, please see Peter Doshi, “More changing webpages at WHO,” *BMJ Rapid Response*, April 12, 2010, [http://www.bmj.com/cgi/eletters/340/apr06\\_2/c1904#234351](http://www.bmj.com/cgi/eletters/340/apr06_2/c1904#234351), (accessed April 12, 2010). The “Archive.org” project archives webpages on the Internet, allowing for the tracking of the web over time. For historical copies of the WHO webpage in question, captured on November 11, 2009 and November 20, 2009, showing the change in title between these dates, see World Health Organization, “Ten things you need to know about pandemic influenza”, October 14, 2005, <http://web.archive.org/web/20091111222554/http://www.who.int/csr/disease/influenza/pandemic10things/en/index.html>, (accessed July 19, 2011); World Health Organization, “Ten concerns if avian influenza becomes a pandemic”, October 14, 2005, <http://web.archive.org/web/20091120072551/http://www.who.int/csr/disease/influenza/pandemic10things/en/index.html>, (accessed July 19, 2011).

<sup>191</sup> World Health Organization, “Ten things you need to know about pandemic influenza.” Note that this is also likely in error, as the 2 to 7.4 million deaths estimate appears to be based on a calculation by Martin Meltzer (CDC), who projected the impact of a modern 1968-like (not 1957-like) pandemic. See Sandman and Lanard, “Pandemic Influenza Risk Communication: The Teachable Moment.”

<sup>192</sup> Bernard Lo and Marilyn J. Field, eds., *Conflict of interest in medical research, education, and practice* (Washington D.C.: National Academies Press, 2009); Krimsky, *Science in the Private Interest*.



If WHO seeks a deeper reflection on its activities and performance, it will need to answer tougher questions—in particular, about its role in fostering a pandemic that led to heavy criticism over the proportionality of response. From the earliest days of the H1N1 outbreak, when it was already clear that the outbreak was far from the outbreak many expected, WHO deflected responsibility for this gap. In May 2011, the Director-General Margaret Chan declared that highly pathogenic avian influenza virus “H5N1 has conditioned the public to equate an influenza pandemic with very severe disease and high mortality. Such a disease pattern is by no means inevitable during a pandemic. On the contrary, it is exceptional.” However, it is not viruses, but rather public health organizations, that have shaped the public's understanding of pandemic influenza for the last decade. It is their narrative and their guidance about how to think about those viruses that led to gap between expectation and reality.

[ENDS]

Source	Statement regarding immunity to pandemic virus
Australia 2006	"An influenza pandemic occurs when a new influenza virus subtype to which there is little or no immunity emerges, is easily spread between humans and is capable of causing severe disease in humans." <sup>193</sup>
Canada 2006	"Influenza viruses spread easily and from time to time, new strains emerge. Humans may have <b>little or no immunity</b> to these new viruses." <sup>194</sup>
Japan 1997	"In the event that a new influenza virus emerges, it will be difficult to quickly determine whether it is capable of causing a pandemic. However, if it happens to be a completely new virus for the human population, it is expected that <b>most people will be susceptible to it (i.e. lack immunity)</b> ..." <sup>195</sup>
Japan 2007	"In particular, pandemic (new) influenza viruses may cause a serious pandemic, due to their potential ability to transmit from humans to humans highly efficiently, because <b>most humans lack immunity</b> against such viruses that have never existed before." <sup>196</sup>
UK 2009	"Pandemic flu occurs when a new influenza virus emerges for which <b>people have little or no immunity</b> , and for which there is no vaccine. The disease spreads easily from person to person, causes serious illness and can sweep across the country in which it originates and around the world in a very short time." <sup>197</sup>
US 1997	"When antigenic shift occurs, <b>the population does not have antibody protection</b> against the virus." <sup>198</sup>
US 2005	"A pandemic occurs when a novel influenza virus emerges that can infect and be efficiently transmitted among individuals because of a <b>lack of pre-existing immunity</b> in the population. ... Pandemic planning is based on the following assumptions about pandemic disease: <b>Susceptibility to the pandemic influenza subtype will be universal.</b> " <sup>199</sup>
US 2005	"Since, by definition, a novel virus is a virus that has never previously infected humans, or hasn't infected humans for a long time, it's likely that almost no one will have immunity, or antibody to protect them against the novel virus." <sup>200</sup>

<sup>193</sup> Council of Australian Governments and Working Group on Australian Influenza Pandemic Prevention and Preparedness, *National Action Plan for Human Influenza Pandemic* (Commonwealth Government—Department of the Prime Minister and Cabinet, 2006), 4.

<sup>194</sup> Public Health Agency of Canada., *Highlights from the Canadian pandemic influenza plan for the health sector: preparing for an influenza pandemic, the Canadian health perspective*. (Ottawa: Public Health Agency of Canada, 2006), 2, [http://www.phac-aspc.gc.ca/cpip-pclcpi/hl-ps/pdf/CPIP-highlights-2006\\_e.pdf](http://www.phac-aspc.gc.ca/cpip-pclcpi/hl-ps/pdf/CPIP-highlights-2006_e.pdf).

<sup>195</sup> Working Group on Pandemic Influenza Plan, "Report on New Influenza Strain Preparedness Measures", October 24, 1997, 6.

<sup>196</sup> Japan Ministry of Health, Labour and Welfare, "Guidelines for the Prevention and Control of Pandemic Influenza (Phase 4 Onwards)", March 26, 2007, 241.

<sup>197</sup> UK Department of Health, "About pandemic flu," Article, May 1, 2009, [http://www.dh.gov.uk/en/PublicHealth/Flu/PandemicFlu/DH\\_065150](http://www.dh.gov.uk/en/PublicHealth/Flu/PandemicFlu/DH_065150), (accessed July 26, 2009).

<sup>198</sup> U.S. Centers for Disease Control and Prevention, "Emerging Infections: Influenza Pandemic Facts, Released 12/31/97 by the CDC Office of Communications, Division of Media Relations", December 31, 1997, <http://www.cdc.gov/od/oc/media/pressrel/panfacts.htm>, (accessed May 29, 2009).

<sup>199</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan," 4,18.

<sup>200</sup> U.S. Department of Health and Human Services, "Influenza Pandemics: How They Start, How They Spread, and Their Potential Impact", October 18, 2005, <http://www.dhhs.gov/nvpo/pandemics/flu2.htm>, (accessed June 16, 2009).

<b>WHO 2003</b>	“When a major change in either 1 or both of their surface proteins occurs spontaneously, <b>no one will have partial or full immunity against infection</b> because it is a completely new virus. If this new virus also has the capacity to spread from person-to-person, then a pandemic is most likely to occur.” <sup>201</sup>
<b>WHO 2009</b>	“A defining characteristic of a pandemic is the <b>almost universal vulnerability of the world’s population</b> to infection. Not all people become infected, but nearly all people are at risk.” <sup>202</sup>
<b>New York City 2006</b>	“Compared to seasonal outbreaks, which happen every winter, pandemics can cause more severe illness because <b>most people have never been exposed</b> to the new strains of flu and therefore have no immunity.” <sup>203</sup>



Table 3.1. Statements regarding the expected immunity to a pandemic influenza virus (emphasis added)

<sup>201</sup> World Health Organization, “Pandemic preparedness”, February 2, 2003, <http://web.archive.org/web/20030202145905/http://www.who.int/csr/disease/influenza/pandemic/en/>.

<sup>202</sup> Chan, “Concern over flu pandemic justified.”

<sup>203</sup> New York City Department of Health and Mental Hygiene, “Pandemic Influenza Preparedness and Response Plan”, July 2006, <http://www.nyc.gov/html/doh/downloads/pdf/cd/cd-panflu-plan.pdf>, (accessed July 3, 2010).

Table 3.2. Statements concerning the expected type of virus that would be necessary to start a pandemic.

Source	Statement regarding the necessity of a novel influenza virus to cause a pandemic
UK DoH 2009	<p>"A pandemic can only start when three conditions have been met:</p> <ul style="list-style-type: none"> <li>• a new influenza virus subtype emerges</li> <li>• it infects humans, causing serious illness</li> <li>• it spreads easily and sustainably among humans."<sup>204</sup></li> </ul>
US HHS 2005	<p>"An influenza pandemic occurs when a new influenza A virus (a 'pandemic influenza virus') emerges in the human population, causes serious illness, and then spreads easily from person to person worldwide."<sup>205</sup></p>
US HHS 2005	<p>"A pandemic is possible when an influenza A virus makes a dramatic change (i.e., "shift") and acquires a new H or H+N"<sup>206</sup></p>
CDC <sup>207</sup> 2009 and WHO <sup>208</sup> 2009	<div style="display: flex; align-items: flex-start;"> <div style="background-color: #002060; color: white; padding: 10px; width: 50%;"> <p style="text-align: center; color: yellow;"><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 style="text-align: center;">AND</li> <li>• Causes serious illness</li> <li style="text-align: center;">AND</li> <li>• Spreads easily from human-to-human</li> </ul> </div> <div style="width: 50%; padding-left: 10px;">  <p style="text-align: center; color: #002060;"><b>Requirements for a Pandemic</b></p> <p style="text-align: center; color: #002060;">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 style="font-size: small; color: white; background-color: #002060; padding: 2px;">Pandemic Influenza – Rapid Containment</p>  </div> </div>

<sup>204</sup> UK Department of Health, "About pandemic flu."

<sup>205</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan," I-12.

<sup>206</sup> U.S. Department of Health and Human Services, "Influenza Pandemics: How They Start, How They Spread, and Their Potential Impact."

<sup>207</sup> U.S. Centers for Disease Control and Prevention and U.S. Department of Health and Human Services, "ABCs of Influenza and Pandemics", 2008, <http://influenzatraining.org/collect/whoinfluenza/files/s15473e/s15473e.ppt>, (accessed April 25, 2010).

<sup>208</sup> World Health Organization, "Seasonal, Animal and Pandemic Influenza: An Overview", May 18, 2009, <http://influenzatraining.org/collect/whoinfluenza/files/s15546e/s15546e.ppt>, (accessed April 25, 2010).

Table 3.3. Discrepancies in summary declaration of interests statements among WHO Experts, provided by WHO, in July 2010 and those in the reprinted 2009 guidelines (reprinted in December 2010). Underlined companies indicate differences between the two lists.

Individual	Summary declarations of interest received from WHO, July 2010 <sup>209</sup>	Reprinted 2009 guidelines <sup>210</sup>
<b>Professor Arnold Monto</b>	"Professor Monto has been an ad-hoc consultant for Roche, GSK, Novartis and Aventis Pasteur."	"Professor Monto has been an ad-hoc consultant for Roche, GSK, Novartis, <u>Solvay</u> and Aventis Pasteur."
<b>Professor Jonathan Nguyen Van-Tam</b>	"Professor van Tam is a former employee of GSK, Roche and Sanofi Pasteur."	"Professor van Tam is a former employee of GSK, Roche, <u>MSD</u> and Sanofi Pasteur."
<b>Dr Nick Phin</b>	"... and honoraria to speak at meetings sponsored by GSK, <u>Novartis</u> , <u>Solvay</u> and Roche." "Dr Phin has participated in scientific discussion panels sponsored by pharmaceutical companies, including for example Sanofi Pasteur in relation to public acceptance of influenza vaccines."	"and honoraria to speak at meetings sponsored by GSK, <u>Sanofi</u> , <u>Baxter</u> and Roche." "Dr Phin has participated in scientific discussion panels sponsored by pharmaceutical companies, including for example <u>MSD</u> and Sanofi Pasteur in relation to public acceptance of influenza vaccines."

<sup>209</sup> Email correspondence with Ashaluck Bhatiasevi, Media Officer, Global Alert and Response Department, World Health Organization, July 2, 2010.

<sup>210</sup> World Health Organization, *Pandemic influenza preparedness and response (reprinted)*.



## Chapter 4 False Assumptions: a Shaky Foundation for Consensus

“An appraisal of experience for the past three and a half years indicates little progress in control of influenza. The basic assumptions of the control program must be reassessed. There is little evidence that recent vaccines have significantly prevented clinical illness, as well as equally little evidence to evaluate effects on mortality. How long such a program should be continued without better scientific evidence is problematic. Sounder bases are needed for an influenza control program.”<sup>1</sup>

Alexander D. Langmuir, Donald A. Henderson, and Robert E. Serfling  
Communicable Disease Center,<sup>2</sup> 1964

Colds are different than flu. Influenza is a serious disease. 36,000 Americans die each year from influenza. Flu shots are your best protection. The vaccine saves lives. Pandemics are catastrophes. As the first two chapters showed, these claims dominate the official discourse on influenza. They are influenza policy’s reason for being. But the H1N1 outbreak of 2009 prompted a serious rethinking of the accepted wisdom—reason to think the policy may not have been grounded and guided by the most solid science, and was possibly influenced by commercial interests.

In this chapter, I take the critique further, and argue that the entire public health effort against influenza is built upon a series of fundamental misconceptions about the problem of influenza, its pandemics, and the vaccine. In some areas, the science is thin. In other areas, there is sufficient evidence to demonstrate serious inconsistencies and errors in official claims. The purpose of presenting this material is to demonstrate that there are numerous fundamental scientific problems in officials’ assessment of the risk posed by influenza and its pandemics, which is important because officials justify their policies through claims about the risk posed by seasonal and pandemic influenza. If serious problems exist regarding the validity of risk assessment, as I argue they do, it calls into question the rationality of the policy.

### “A virus or something”

Before Thomas L. Morris, Jr. died on October 22, 2001, he dialed 911 for an ambulance. “My breathing is labored; my chest feels constricted,” Morris said. “I am getting air, but I -- to get up and walk and what

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<sup>1</sup> Alexander D. Langmuir, Donald A. Henderson, and Robert E. Serfling, “The Epidemiological Basis for the Control of Influenza,” *Am J Public Health Nations Health* 54, no. 4 (April 1, 1964): 563-571.

<sup>2</sup> What is today known as the Centers for Disease Control and Prevention (CDC) was, between 1946 and 1967, known as the Communicable Disease Center. There have been multiple name changes throughout the agency’s history.

have you -- it just feels like I'm going to pass out if I stay up too long."<sup>3</sup> Morris was a postal worker, and suspected anthrax. He was employed at the Brentwood mail processing facility which had handled the letter addressed to Senator Tom Daschle, determined days earlier by federal investigators to have been laced with anthrax. Morris, however, had not been informed whether his postal facility itself was contaminated, but reported having worked near a woman who found a letter with powder in it two days before the infamous Daschle letter.

Morris might have lived if his anthrax had been diagnosed earlier. The first symptoms—aches and headaches—began on October 16, presumably three days after being exposed to powder in the mail room. Two days later, Morris saw a doctor, informing the doctor that he thought he had been exposed to anthrax. Cautious, the doctor took a throat culture<sup>4</sup> and called the state health department.<sup>5</sup> The department of health, however, said that mail facility employees were not at risk and that antibiotics should not be prescribed.

Morris didn't live long enough to hear the results of the throat culture. On the 911 phone call, Morris told the operator, "I guess there was some hang-up over the weekend. I'm not sure ... The doctor thought that it was just a virus or something." He was prescribed Tylenol for the aches and pains, and was sent home. The ambulance arrived, but by then it was too late to save Morris' life.

Sadly, Morris was not the only victim of a late diagnosis. The *Wall Street Journal* reported:

On Oct. 21 -- one day after the mayor of Washington, D.C., announced that a worker at the Brentwood postal center possibly had anthrax -- two other Brentwood workers showed up at hospitals 26 miles apart. Both complained of run-of-the-mill flu symptoms. Both were actually suffering from inhalation anthrax.

By the end of the day, one of the men was diagnosed with the flu and sent home, where he died the next day. The other man was put on the antibiotic Cipro -- hours before tests would confirm that he had anthrax. He's now resting at his home.<sup>6</sup>

\* \* \*

Almost every federal agency came under harsh criticism for their response to the anthrax investigations, but the CDC, in particular, was accused of not providing the highest quality scientific advice. Postal workers wanted to know why CDC officials had in the early days of the investigation, assured them there was nothing to worry about, and why health officials had not taken precautionary measures and more

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<sup>3</sup> "Postal worker who died suspected anthrax, according to 911 call," *CNN Health*, November 7, 2001, [http://articles.cnn.com/2001-11-07/health/911.anthrax\\_1\\_joseph-curseen-brentwood-facility-anthrax-laced-letter?\\_s=PM:HEALTH](http://articles.cnn.com/2001-11-07/health/911.anthrax_1_joseph-curseen-brentwood-facility-anthrax-laced-letter?_s=PM:HEALTH), (accessed July 18, 2011).

<sup>4</sup> Ibid.

<sup>5</sup> Barbara Martinez, "Anthrax Victims' Fate Varied by What Hospital, Which Doctor They Saw," *Wall Street Journal*, November 27, 2001.

<sup>6</sup> Ibid.



liberally advocated for early treatment with antibiotics, as had been done for staffers on Capitol Hill.<sup>7</sup> In its defense, CDC director Jeffrey Koplan explained that it was learning:

The letters we had seen or had described to us ... were described to us as well-taped, meaning that the seams along that letter were taped in a way that would have minimized, if not eliminated, the ability of a powder to seep out through openings around the letter. You would have to open the letter. And, indeed, we were told that the letter that was sent to Senator Daschle had to be opened by a scissors because of how well it was sealed.

So through this period of time we were still operating on the assumption that in order for a letter to convey this—the anthrax, it had to be either opened by someone who was opening mail, or in some way torn or disrupted in the sorting process, because the concept of a powder in a sealed letter was one that suggested that it would stay in that letter. And that was our epidemiologic experience with the cases we had seen so far. That construct obviously changed markedly with the report of inhalation anthrax in mail workers in the Brentwood facility...<sup>8</sup>

A reporter on the CDC telebriefing asked Koplan a pointed question: “How frustrating is it that the two postal workers who died in the D.C. area, it seemed were—at least their diagnosis was missed and were sent home, either from a physician's office or an emergency room? And what can be done to prevent that in the future?”

Dr. Koplan said that clinicians' job was not easy, “the trouble with the early stages of anthrax, as you're all well aware, is that it mimics lots of illnesses. You know, I can't be critical of whoever saw those patients 'cause I've been in emergency rooms and seen hundreds of patients with similar illnesses, and they do fine when treated as those people were treated.” The difficulty of identifying true anthrax was that in the early stages of illness—the very time when patients see their doctor—the symptoms are remarkably common: fever, fatigue, aches and pains. Director Koplan therefore called on physicians to more thoroughly evaluate their patients and rule out the possibility of an early anthrax infection by assessing possible sources of anthrax exposure:

Even somebody comes in with a recent cough and a light headache, and thoughts may be overwhelming that it's a viral infection, still, people need to say, Where do you work? What tasks do you do? Do you handle mail in a facility? Do you open the letters?, et cetera. It's now part of what needs to be part of a medical history.<sup>9</sup>

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<sup>7</sup> “CDC, USPS, Criticized Over Anthrax Spread,” *ABC News*, October 23, 2001, <http://abcnews.go.com/US/story?id=92289&page=1&singlePage=true>, (accessed July 18, 2011).

<sup>8</sup> U.S. Centers for Disease Control and Prevention, “Anthrax update: October 25, 2001, telebriefing transcript”, October 25, 2001, <http://www.cdc.gov/media/transcripts/t011025.htm>, (accessed July 18, 2011).

<sup>9</sup> *Ibid.*

In the following days, the CDC would provide more specific guidance to clinicians on how to distinguish anthrax from other influenza-like illness, or ILI.<sup>10</sup>

### The ILI Conundrum

Every year, tens of millions of patients walk into a doctor's offices complaining of fever, aches and pains. During the winter, these influenza-like illnesses (or ILI as it is often abbreviated) can become so common that they will, at their peak, account for up to six to eight percent of all outpatient visits.<sup>11</sup> An even greater number of people may suffer ILI but not seek professional care. The CDC writes that "yearly, adults and children can average one to three and three to six ILI, respectively."<sup>12</sup> But for the patients that do seek care, it is the healthcare provider's responsibility to reach a diagnosis and treat the patient.

In many cases—as Thomas Morris' case tragically made clear—doctors treat patients without determining the exact cause of the patient's ILI. Many doctors see laboratory tests as impractical and irrelevant: physicians need to make treatment decisions immediately, and lab tests can take days or even a week or longer to process, by which time most ILI patients have already made a full recovery.<sup>13</sup> Physicians therefore examine patients' signs and symptoms, attempting to find the right diagnosis out of a handful of possibilities often encountered in the course of general practice: Is it allergies? A cold? The flu? Acute bronchitis? Strep throat? Gastroenteritis? Sinusitis?<sup>14</sup>

Because many patients do not even seek medical care for ILI, a number of health websites have aimed to help the public make its own determination. "Follow this chart for information about how to treat the symptoms of a cold or the flu and how to know when to see a doctor. Other illnesses may also cause flu- or cold-like symptoms. Self-care is often all that is needed to treat common viral illnesses," says familydoctor.org.<sup>15</sup> A similar article on the Mayo Clinic website coaches readers on how to determine the difference between a cold and allergies.<sup>16</sup>

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<sup>10</sup> U.S. Centers for Disease Control and Prevention, "Considerations for distinguishing influenza-like illness from inhalational anthrax," *MMWR. Morbidity and Mortality Weekly Report* 50, no. 44 (November 9, 2001): 984-986.

<sup>11</sup> See "Outpatient Illness Surveillance" figure in U.S. Centers for Disease Control and Prevention, "FluView: 2010-2011 Influenza Season Week 25 ending June 25, 2011", July 1, 2011, <http://www.cdc.gov/flu/weekly/weeklyarchives2010-2011/weekly25.htm>, (accessed July 18, 2011).

<sup>12</sup> U.S. Centers for Disease Control and Prevention, "Considerations for distinguishing influenza-like illness from inhalational anthrax."

<sup>13</sup> This trend is changing to some degree due to the growing availability of so-called rapid "bed-side" tests which can provide results in the range of half an hour or less—but the accuracy of these tests remains variable, and accurate interpretation of results depends on the quality of the test and knowledge about the current prevalence of influenza in the community, something many doctors would have only a limited sense about. See U.S. Centers for Disease Control and Prevention, "Rapid Diagnostic Testing for Influenza", July 6, 2011, <http://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm>, (accessed July 18, 2011).

<sup>14</sup> These conditions are listed on American Academy of Family Physicians' website, familydoctor.org. American Academy of Family Physicians, "Cold and Flu," *FamilyDoctor.org*, 2011, <http://familydoctor.org/online/famdocen/home/tools/symptom/517.html>, (accessed July 18, 2011).

<sup>15</sup> *Ibid.*

<sup>16</sup> James M. Steckelberg, "Cold or allergy: Which is it?", n.d., <http://www.mayoclinic.com/health/common-cold/AN01229>, (accessed July 18, 2011).

Picking out anthrax among the many causes of ILI became important in the wake of the anthrax attacks. After all, the cost of missing a diagnosis of anthrax was the life of a patient. Anthrax, however, remained an extremely rare disease: only 22 people developed the infection, of which five died. Because the disease is so uncommon and affects so few, but the symptoms of ILI—fever, fatigue, cough, etc—are by contrast so common, the chances that any given patient walking into a doctor’s office in the United States with an ILI was actually infected with anthrax was, and remains, extraordinarily low.

The vast majority of ILIs, however, fit in the realm of what get colloquially called “cold” and “flu.” These ILI are self-limiting illnesses:<sup>17</sup> people make full recoveries, even in the absence of medical care. And it is for this reason that most patients with ILI are told, just as Thomas Morris was told, that they probably have “a virus or something,” offered some pain killers or other medicine to help alleviate symptoms, and sent home.

### **Cold versus flu: what is the difference?**

The shelves of any drug store makes clear that selling cold medicine is big business. A search for “cold medicine” in Google now even offers the following promotional links at the top of the results page: “Related searches for cold medicine: Brands: Zicam Sudafed NyQuil Tylenol Mucinex.”<sup>18</sup> One study found that Americans spend nearly three billion dollars each year on over-the-counter drugs like these in treating their symptoms. An additional \$400 million is spent on prescription drugs. When considering the toll on the U.S. economy—including \$17 billion in healthcare usage as well as an additional \$22.5 billion in “indirect costs” such as the productivity loss due to employees being out sick—the figure rises to \$40 billion per year.<sup>19</sup> Despite this, public health officials today do not concentrate much on fighting colds; their target is influenza.

“Because these two types of illnesses have similar flu-like symptoms, it can be difficult to tell the difference between them based on symptoms alone,” the CDC explains on its “Cold Versus Flu” webpage.<sup>20</sup> “Colds are usually milder than the flu. ... Colds generally do not result in serious health problems, such as pneumonia, bacterial infections, or hospitalizations.” By contrast to the cold, CDC promotional material frequently stresses the severity of influenza: “Influenza is a serious disease that can lead to hospitalization and sometimes even death,” one webpage says, and the impact in deaths and hospitalizations is frequently cited.<sup>21</sup>

It is this measure of seriousness—hospitalizations and deaths—that seems to justify the attention on influenza. Research on colds, by contrast, is not driven by statistics that convey the sense of an enormous threat. “Common cold is the most common disease,” the Cardiff University based Common

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<sup>17</sup> Joanne Stockton et al., “Human metapneumovirus as a cause of community-acquired respiratory illness,” *Emerging Infectious Diseases* 8, no. 9 (September 2002): 897-901.

<sup>18</sup> <http://www.google.com/search?q=cold+medicine> (search run on December 9, 2010)

<sup>19</sup> A Mark Fendrick et al., “The economic burden of non-influenza-related viral respiratory tract infection in the United States,” *Archives of Internal Medicine* 163, no. 4 (February 24, 2003): 487-494.

<sup>20</sup> U.S. Centers for Disease Control and Prevention, “Q & A: Cold Versus Flu”, February 8, 2011, <http://www.cdc.gov/flu/about/qa/coldflu.htm>, (accessed July 18, 2011).

<sup>21</sup> U.S. Centers for Disease Control and Prevention, “Q & A: Seasonal Flu Vaccine”, July 1, 2011, <http://www.cdc.gov/flu/about/qa/flu vaccine.htm>, (accessed July 18, 2011).

Cold Centre declares, one of the few research centers that studies colds. But can a cold *kill*? The Common Cold Centre website answers: “Yes! Babies and the very elderly can develop chest infections such as bronchiolitis caused by the RSV virus that can be fatal.” But no statistics are posted allowing for the comparison of that threat to the impact of influenza.

Colds may affect us all, and millions of dollars may be made selling remedies to ameliorate symptoms, but if public health policy accurately represents a disease’s true importance, the bottom line is that colds do not deserve our attention. Influenza does.

However, there are several reasons to seriously question the official dichotomy of “colds versus flu.” First, “colds” are not all mild. The CDC itself writes, “non-flu viruses include rhinovirus (one cause of the ‘common cold’) and respiratory syncytial virus (RSV), which is the most common cause of severe respiratory illness in young children as well as a leading cause of death from respiratory illness in those aged 65 years and older.”<sup>22</sup> Second, influenza is not all serious. In an influential 1982 text, Dr. Gary Noble, of the CDC’s Viral Disease Division, wrote that “... it is important to remember that the spectrum of symptoms which occurs during influenza virus infections is quite variable, ranging from the classical febrile respiratory disease with systemic manifestations to a minor respiratory illness.”<sup>23</sup> As the CDC states, most cases of influenza “are mild”<sup>24</sup>—a self-limiting illness that may not be pleasant, but nonetheless resolves in the absence of medical attention. (But since not all cases are mild, CDC urges vaccination of the entire population.<sup>25</sup>)

Third, many cases of influenza are so benign that the person infected does not even notice it. Known as “asymptomatic illness,” the proportion of people infected with influenza who do not develop any symptoms is sizeable: in past epidemiological studies carried out over several influenza seasons, more than half of people found to be infected with influenza virus showed no signs of infection.<sup>26</sup> Finally, there is not simply *some* overlap in these two disease categories, there is so much overlap that based on symptoms alone, the two cannot be distinguished apart, even by doctors.<sup>27</sup>

The conceptual division of ILI into two major subcategories—“colds” and “flu”—in which one is described as usually mild and the other is said to be “serious”—and further statements that “the flu is a contagious respiratory illness caused by influenza viruses,”<sup>28</sup> is not only inaccurate, but highly

<sup>22</sup> U.S. Centers for Disease Control and Prevention, “Q & A: Seasonal Influenza (Flu): The Disease”, July 6, 2011, <http://www.cdc.gov/flu/about/qa/disease.htm>, (accessed July 18, 2011).

<sup>23</sup> Gary R. Noble, “Epidemiological and clinical aspects of influenza,” in *Basic and Applied Influenza Research*, ed. A. S. Beare (Boca Raton, Florida: CRC Press, Inc., 1982), 25.

<sup>24</sup> U.S. Centers for Disease Control and Prevention, “Questions & Answers: Novel H1N1 Influenza Vaccine”, 2010, [http://www.cdc.gov/h1n1flu/vaccination/public/vaccination\\_qa\\_pub.htm](http://www.cdc.gov/h1n1flu/vaccination/public/vaccination_qa_pub.htm), (accessed July 18, 2011).

<sup>25</sup> *Ibid.*

<sup>26</sup> A S Monto, J S Koopman, and I M Longini Jr, “Tecumseh study of illness. XIII. Influenza infection and disease, 1976-1981,” *American Journal of Epidemiology* 121, no. 6 (June 1985): 811-822.

<sup>27</sup> Stephanie A Call et al., “Does this patient have influenza?,” *Journal of the American Medical Association* 293, no. 8 (February 23, 2005): 987-97.

<sup>28</sup> U.S. Centers for Disease Control and Prevention, “Key facts about influenza and influenza vaccine”, August 26, 2008, <http://www.cdc.gov/flu/pdf/keyfacts.pdf>, (accessed May 17, 2009).

misleading. It is misleading because of a gap between what the public calls “flu” and what influenza experts call “flu.”

“To virologists and influenza experts, ‘influenza’ means the influenza virus and only the disease produced by that virus. To members of the public, ‘flu’ is the disease regardless of viral cause,”<sup>29</sup> Richard Neustadt and Harvey Fineberg wrote in their study of the 1976 “swine flu.” This means that the illness that presents to doctors, and what the public has learned to call “the flu” is not influenza, but most accurately termed ILI, because it describes a non-specific syndrome with unknown etiology. This “flu”—that is, ILI—has not one cause, but hundreds of causes, of which influenza virus is just one. Other causes include rhinoviruses, respiratory syncytial virus (RSV), adenoviruses, and parainfluenza viruses.<sup>30</sup> Some bacteria can even cause ILI.<sup>31</sup>

Public health policy, however, is focused on controlling influenza, not ILI. Influenza vaccines and influenza antivirals are the backbone of such policies, but they are ineffective against ILI not caused by influenza.<sup>32</sup> Evaluating the degree to which this public policy addresses the threat of what the public calls “the flu,” then, requires us to know what proportion of ILI is caused by influenza viruses.

### Ask the experts

Driven by an interest in the possible use of influenza antivirals in patients, a team of researchers published a paper in the *Journal of the American Medical Association* in 2005 that tried to determine just how easy or difficult it was to make an accurate influenza diagnosis. Antivirals such as Tamiflu have been licensed for use against influenza, but the Food and Drug Administration advises that administration of this class of drugs must commence within 48 hours of symptom onset.<sup>33</sup> Even for patients that seek medical attention early in their illness, many doctors still “struggle with the decision of whether to test or to empirically treat,” the authors explain: rapid tests are not always accurate, and more accurate lab work can take days to complete.<sup>34</sup>

The researchers did a systematic review of the literature hoping to discover whether certain clinical signs—perhaps single signs like fever, or in combination such as fever and cough—might reliably confirm influenza among other causes of ILI. However, their search concluded that while ILI could be

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<sup>29</sup> Neustadt and Fineberg, *The epidemic that never was*, 139.

<sup>30</sup> U.S. Centers for Disease Control and Prevention, “Considerations for distinguishing influenza-like illness from inhalational anthrax.”

<sup>31</sup> Tom Jefferson, “How to deal with influenza?: Real time surveillance providing information on circulating agents is the key,” *BMJ* 329, no. 7467 (September 18, 2004): 633–634; Call et al., “Does this patient have influenza?”.

<sup>32</sup> U.S. Centers for Disease Control and Prevention, “Key facts about influenza and influenza vaccine”; James Smith, Regina Dutkowski, and Penelope Ward, “Antivirals for influenza in healthy adults,” *Lancet* 367, no. 9522 (May 13, 2006): 1571; author reply 1573.

<sup>33</sup> Hoffman-La Roche, Ltd., “Product label. Tamiflu (oseltamivir phosphate) capsules and for oral suspension”, February 22, 2010, [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2010/021087s048s049,021246s034s0351bl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021087s048s049,021246s034s0351bl.pdf), (accessed September 13, 2010); GlaxoSmithKline, “Product label. RELENZA (zanamivir) Inhalation powder, for oral inhalation”, December 9, 2010, [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2010/021036s0251bl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021036s0251bl.pdf), (accessed July 18, 2011).

<sup>34</sup> Call et al., “Does this patient have influenza?”.

determined (an unsurprising finding given that ILI is a clinical diagnosis), clinical findings “are not particularly useful for confirming or excluding the diagnosis of influenza.” In other words, without employing some kind of laboratory test, influenza cannot be distinguished from ILI.

\* \* \*

Another possible way to assess the question of how much ILI is influenza may be by analyzing viral surveillance data. During the influenza season, CDC receives voluntary weekly reports from more than 150 laboratories across the country. These labs indicate how many respiratory specimens were tested at that laboratory and of those tested, how many were positive for influenza virus. The CDC collects these reports and publishes the collective national statistics in its weekly report, FluView. These data, published on the web, show that influenza was on average found in 15% of specimens tested each season (1997-98 to 2010-11, range 10% to 22%; see Table 4.1).

Yet it is difficult to know how to properly apply these results to the question of influenza’s contribution to ILI. While the system has grown considerably over the past decade, it is still capturing only an extremely small proportion of all the cases of ILI that occur each year in the United States.<sup>35</sup> Furthermore, there is no guarantee that all people tested even had ILI as no standardized case definition is used when accepting specimens. In an email, the CDC informed me that specimens received “are subjected to testing practices and test methods in use in the local area and are not standardized.”<sup>36</sup> This means that while the proportion that tests positive may hover between ten and twenty percent, it is unclear precisely what this proportion represents.

The lack of standardization in testing practices may partially explain why results vary by lab and location. In Michigan, for example, the state health department collects reports of influenza testing that record the source of the report. In data I was sent, the proportion of influenza-positive specimens was 49%, 83%, or 100%, depending on the type of lab doing the testing (Sentinel Provider, “Other,” or Sentinel Lab, respectively). This suggests a strong connection between the way a specimen is procured and processed and its likelihood that it will test positive for influenza. The influenza positive percentage therefore may indicate little about the actual prevalence of influenza in the community. In data I received from the New York State Department of Health (NYSDOH), similarly large discrepancies in the influenza positivity rate could be seen in labs across the state, even between labs that were less than 20 miles apart (Table 4.2). The influenza specialist at NYSDOH suggested that variations in human behavior—differences in the reasons why certain people get chosen for influenza tests and others do not—might best explain the range of positivity rates. NYSDOH has noticed large variations in the tendencies of different doctors to send in tests. For reasons not fully understood, some doctors do far more testing than others.<sup>37</sup>

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<sup>35</sup> If ILI is as common as CDC stated in its anthrax advisory, it is only capturing around 250,000 of the hundreds of millions of ILI episodes each year in the United States.

<sup>36</sup> Correspondence with CDC, June 24, 2008.

<sup>37</sup> Correspondence with NYSDOH, July 20, 2011.

To understand just how to interpret all these numbers, and to better understand how surveillance of influenza works in the United States, beginning in the summer of 2008 I systematically began to contact all state health departments across the nation. I asked them to tell me how influenza surveillance worked in their state, and what proportion of ILI could be attributed to influenza. None gave me exact numbers, and most said they simply don't know. "We don't know ... and that's the honest answer," one epidemiologist from Maryland Department of Health and Mental Hygiene told me.<sup>38</sup> Another told me that "the amount of ILI that truly is influenza is a black box."<sup>39</sup> The CDC itself told me "We too have been interested in knowing how much of the ILI is truly influenza and to do that we are piloting a new system this fall [2008] to try and get at that information."<sup>40</sup> CDC informed me, however, that the pilot project "was not successful," but a new project—the Influenza Incidence Surveillance Project—was launched in 2009, and attempts to answer similar questions.<sup>41</sup> But as of June 2011, the CDC has not yet made any of the data public, though it intends to in the future. As it stands, then, the US influenza surveillance system, despite being the most sophisticated in the world, at present is unable to answer the key question of what proportion of ILI is caused by influenza.

### **The majority of ILI is not influenza**

Nevertheless, there does seem to be a sense that, as the surveillance data indicate, influenza is a minority cause of ILI. The Maryland DHMH epidemiologist explained that while there may not be solid data, "we do look at trends. In the winter, the trend is that between 5% and 30% of people with ILI who see a healthcare provider and are tested are positive for influenza by rapid antigen test, PCR, culture, or other means."<sup>42</sup> In 2001, as part of educating clinicians about the similarities between the early stages of anthrax infection and ILI, the CDC told clinicians that

The majority of ILI cases is not caused by influenza but by other viruses (e.g., rhinoviruses and respiratory syncytial virus [RSV]), adenoviruses, and parainfluenza viruses). Less common causes of ILI include bacteria such as *Legionella* spp., *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and *Streptococcus pneumoniae*.<sup>43</sup>

Others have conducted studies which numerically quantify the proportion of ILI that is influenza.

In a study taking place over four winter seasons in the United Kingdom, researchers analyzed the respiratory specimens of 408 children suffering "more than a cold" (Figure 4.1). Influenza was found in one-third of all specimens. RSV and parainfluenza virus together accounted for another third.<sup>44</sup>

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<sup>38</sup> Interview with Rene Najera (MDHMH), July 2, 2008.

<sup>39</sup> Interview with Stephanie Schauer, Immunization Program, Massachusetts Department of Public Health, June 18, 2008.

<sup>40</sup> Email correspondence with Lynnette Brammer (CDC), July 9, 2008.

<sup>41</sup> Email correspondence with Ashley Fowlkes (CDC), June 30, 2011.

<sup>42</sup> Interview with Rene Najera (MDHMH), June 20, 2011.

<sup>43</sup> U.S. Centers for Disease Control and Prevention, "Considerations for distinguishing influenza-like illness from inhalational anthrax."

<sup>44</sup> Anthony Harnden et al., "Respiratory infections for which general practitioners consider prescribing an antibiotic: a prospective study," *Archives of Disease in Childhood* 92, no. 7 (July 2007): 594-597.

In a similarly designed study, a different set of researchers considered the cause of upper respiratory tract infections in the elderly. This time, many of the same agents were found, but in different proportions. Rhinoviruses has caused a quarter of infections. Coronaviruses were the second most common agent found, yet only accounted for 12% of the 291 elderly tested. Influenza had caused just 5% of the total. By far, most illnesses were of unknown etiology: no agent could be discovered (Figure 4.2).<sup>45</sup>

A third study, published in 1998, on the etiology of the common cold in Finland found 44% were caused by rhinovirus; 7% by coronavirus; and 5% by influenza viruses. 26% were of unknown etiology.<sup>46</sup>

Finally, a more recent study of ILI in nearly 7000 people of all ages seeking medical care in 13 Peruvian cities over two years found 55% to be of unknown origin. Influenza was found in 37%. Other viruses were found, but only rarely.<sup>47</sup> (Figure 4.3)

The inconsistencies between each study's results demonstrates the inadequacy of such single studies to definitively answer the question of what proportion of ILI is caused by influenza. It varies depending on the season, the population being tested, and location. But the studies, taken together, do tell one story consistently: that a mixed bag of agents are causing people to develop illnesses with similar symptoms.

If no single study can provide answers, is there any way to measure the proportion of the ILI pie caused by influenza? The influenza researcher Tom Jefferson from the Cochrane Collaboration has proposed combining vaccine and epidemiological studies to determine a better estimate of the incidence and etiology of ILI. (In the interest of full disclosure, I should note that Jefferson is a close colleague, and I have worked with Jefferson and his colleagues on some of this research.) Influenza vaccine trials in which one group is vaccinated with influenza vaccine and another group either receives a placebo or "do nothing" (they are left alone) offer a good chance to figure out just how many people naturally become ill with influenza. While the group vaccinated with influenza vaccine may not be representative because of some level of protection from the vaccine, the group which does not receive influenza vaccine can be expected to develop influenza at the rate that exists in nature. And because subjects enrolled in clinical trials are expected to be monitored closely during the course of the trial, such vaccine studies may represent the best evidence currently available to determine the proportion of the population that develops ILI.

The cause of those ILI, however, may not be distinguished by all vaccine studies. Some studies may record that the patient developed an ILI, but not do sufficient laboratory testing to determine its etiology. Jefferson therefore combined these studies with 28 epidemiological studies which

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<sup>45</sup> K G Nicholson et al., "Acute viral infections of upper respiratory tract in elderly people living in the community: comparative, prospective, population based study of disease burden," *BMJ* 315, no. 7115 (October 25, 1997): 1060-1064.

<sup>46</sup> M J Mäkelä et al., "Viruses and bacteria in the etiology of the common cold," *Journal of Clinical Microbiology* 36, no. 2 (February 1998): 539-542.

<sup>47</sup> V. Alberto Laguna-Torres et al., "Influenza-Like Illness Sentinel Surveillance in Peru," *PLoS ONE* 4, no. 7 (July 1, 2009): e6118.



investigated the cause of ILI. He published the results in the journal *BMJ Clinical Evidence* in 2009.<sup>48</sup> The epidemiological studies indicated that influenza virus was a minority cause of ILI: in only around 1 in 10 ILIs was influenza detected. But the vaccine studies indicated that ILI itself—of any etiology—was not especially common, in contrast to CDC statements. In the 274 vaccine studies analyzed, ILI affected an average seven in one hundred people each “flu season.” Taken together, Jefferson found that influenza virus caused symptoms in about 1 person per 100 people per year (Figure 4.4).

Jefferson’s results question what is reported on the CDC website and prominently repeated by the media—that 5 to 20% of the population “gets the flu” each year.<sup>49</sup> (Note that the CDC’s claim, despite the imprecise choice of words, refers to influenza virus, not “flu” in the colloquial sense of an influenza-like illness.<sup>50</sup>)

The 5-20% statistic is five to twenty times higher than what Jefferson’s review found. It also diverges with what the CDC itself said during the 2009 H1N1 outbreak. Comparing the H1N1 outbreak to a “typical” season, Anne Schuchat declared that “In a typical influenza season, about 7% to 10% of the people in a community may become infected with an influenza virus.” The disparity between the 5-20% and 7-10% statistics is even more pronounced when one considers that the 7-10% “infected” presumably includes both symptomatic and asymptomatic illness while the 5-20% that “gets the flu” presumably includes only those developing symptoms.

While on first glance it seems impossible to reconcile the differences in statistics, it might be possible by considering the underlying methods used to generate the numbers. Unfortunately, the 5-20% statistic is well publicized but lacks citation. In the most comprehensive US policy document on influenza with over 500 references, statistics on mortality and hospitalization are given, but annual incidence is not.<sup>51</sup>

The ambiguity in statistics and lack of documentation is not uncommon, nor is it limited to the United States. In the most recent 2005 WHO position paper on influenza vaccines, it is stated that “Influenza occurs all over the world, with an annual global attack rate estimated at 5–10% in adults and 20–30% in children.”<sup>52</sup> The guidance document however lacks a bibliography or references to support statements made in the text.

## Is influenza a serious disease?

While accurate numbers regarding how many people develop symptomatic influenza each year remain elusive, it seems reasonable to expect that for an illness affecting humans for centuries, officials’ claim that influenza is a serious disease would be trustworthy. But there is no clear consensus on this basic point. Officials in the United States would like us to believe that the matter is clear cut. “MYTH ‘The flu isn’t a serious disease’” the CDC printed at the top of a promotional poster in 2007. “FACT: Influenza

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<sup>48</sup> Tom Jefferson, “Mistaken identity: seasonal influenza versus influenza-like illness,” *BMJ Clinical Evidence* (October 5, 2009), <http://clinicalevidence.bmj.com/downloads/05-10-09.pdf>.

<sup>49</sup> U.S. Centers for Disease Control and Prevention, “CDC - Seasonal Influenza (Flu) - Q & A.”

<sup>50</sup> Correspondence with CDC-INFO Contact Center, November 21, 2006.

<sup>51</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.”

<sup>52</sup> “Influenza vaccines,” *Weekly Epidemiological Record* 80, no. 33 (August 19, 2005): 279-287.

(flu) is a serious disease of the nose, throat, and lungs, and it can lead to pneumonia,” the poster insisted.<sup>53</sup> A newer CDC poster likewise states: “Flu is a **serious contagious** disease that can lead to **hospitalization** and even **death**” (emphasis in the original).<sup>54</sup>

But in the United Kingdom, the public has been targeted with a very different message: “For most people, flu is nasty but not serious: a short period of chills, aches and pains and then a return to normal health”<sup>55</sup> (Figure 4.5).

During a recent visit to Atlanta, I shared the contrasting promotional materials with the CDC’s Director of Media relations, and asked him to explain how influenza could be serious in the United States but not serious in the United Kingdom. Glen Nowak told me that:

The reality is that it *can* be a serious disease, and one of the challenges with messaging, when you are giving messages, is that you have to be mindful that it’s hard to do one-size-fit-all messages, but people want one-size-fit-all messages. And so what we’re trying to do at CDC is recognize that it *is* a serious disease, *can* be a serious disease, and if it wasn’t a serious disease, we wouldn’t be taking it as seriously as we do. ...

Now in terms of course of illness, for most people, it’s gonna just be, you know, maybe 5 to 7 days of feeling really awful. And we said that last year during H1N1, that for many people, for most people, that’s what it’s gonna look like.

Now the problem with putting too much emphasis on that message, though, is that you also don’t want people to fall into a false sense of security because the reality is that we can’t predict which people—you know, which individuals—are going to experience a serious course of illness. We have seen healthy people—younger healthy people—with H1N1 experience very severe outcomes and some of them die. And so if you want people to take the recommendation to heart, which we do at CDC—get vaccinated—you have to recognize that we’re doing it because this is serious, this is an important matter. ...

That’s different, than I guess what you’re saying this one says [Nowak is referring to the UK NHS promotional material I have brought along to the interview—the right pane of Figure 4.5], is that if you get influenza, the typical course of influenza is not gonna be somebody who’s going to be hospitalized, suffer pneumonia, or some kind of severe consequence. Yeah—the typical course of influenza, is gonna be that you’re gonna feel

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<sup>53</sup> U.S. Centers for Disease Control and Prevention, “Flu Vaccine Facts & Myths.”

<sup>54</sup> U.S. Centers for Disease Control and Prevention, “Take 3’ Actions”, 2010, [http://www.cdc.gov/flu/pdf/freeresources/general/take3\\_print\\_reverse.pdf](http://www.cdc.gov/flu/pdf/freeresources/general/take3_print_reverse.pdf), (accessed July 19, 2011).

<sup>55</sup> UK National Health Service, “If you knew about flu you’d get the jab”, 2008, [http://www.immunisation.nhs.uk/publications/289667\\_FluLeaflet\\_A4.pdf](http://www.immunisation.nhs.uk/publications/289667_FluLeaflet_A4.pdf), (accessed August 15, 2009).

awful, really bad for 5 to 7 days, but even there, that warrants your attention and it seems like getting a flu vaccination is a simple and effective way to avoid that.<sup>56</sup>

Nowak's reference to healthy children dying of H1N1 is a theme that was repeatedly raised throughout the 2009 H1N1 outbreak. According to a *USA Today* editorial, Dr. Anthony Fauci, one of the nation's top infectious disease officials, said: "I've never seen, in seasonal flu, a normal, robust healthy person die from influenza."<sup>57</sup> Such deaths were, Fauci said, "almost unheard of" in non-pandemic, seasonal influenza. But with H1N1, the *USA Today* explained, "almost a third of those who die may be otherwise healthy and robust."

To be sure, influenza deaths in children are uncommon. However the factual basis for Fauci's statement is unclear. It is true that for years, little precise information existed regarding influenza-related pediatric mortality. No formal, mandatory, or other systematic mechanism existed to track such deaths. But that changed in 2003-04, when the CDC began to collect such data from state health departments.<sup>58</sup> Today, the reporting of influenza-associated pediatric mortality is mandatory.<sup>59</sup> What closer inspection of such deaths has revealed is that a striking number occur among previously healthy children—contrary to Fauci's statement.

In a prominent article in the *New England Journal of Medicine* in 2005, CDC researchers reported on the deaths of 153 children during the 2003-04 influenza season. Of them, nearly half (47%) had been previously healthy.<sup>60</sup> A subsequent study in 2008, also published by the CDC, confirmed the finding: "the majority of deaths occurred in previously healthy children without an underlying medical condition."<sup>61</sup>

What changed in the H1N1 outbreak was the sheer number of pediatric deaths being reported. In the twelve months since H1N1 was first detected in April 2009, over 300 influenza-associated pediatric deaths were reported to CDC—more than double than the previous highest season (2003-04).<sup>62</sup> (The CDC argues that their reported numbers, while high, are still a serious undercounting because many children may die of H1N1 but never be counted, and has estimated the true number to be far higher—or between 910 and 1,880 deaths in those under the age of 18.<sup>63</sup> Others have challenged the likelihood

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<sup>56</sup> Interview with Glen Nowak (CDC), October 27, 2010.

<sup>57</sup> "Benefits of swine flu vaccine greatly exceed the risks," *USA Today*, October 9, 2009.

<sup>58</sup> Niranjana Bhat et al., "Influenza-associated deaths among children in the United States, 2003-2004," *The New England Journal of Medicine* 353, no. 24 (December 15, 2005): 2559-67.

<sup>59</sup> Lyn Finelli et al., "Influenza-Associated Pediatric Mortality in the United States: Increase of *Staphylococcus aureus* Coinfection," *Pediatrics* 122, no. 4 (October 1, 2008): 805-811.

<sup>60</sup> Bhat et al., "Influenza-associated deaths among children in the United States, 2003-2004."

<sup>61</sup> Finelli et al., "Influenza-Associated Pediatric Mortality in the United States."

<sup>62</sup> U.S. Centers for Disease Control and Prevention, "FluView: 2009-2010 Influenza Season Week 16 ending April 24, 2010", April 30, 2010, <http://www.cdc.gov/flu/weekly/weeklyarchives2009-2010/weekly16.htm>, (accessed July 18, 2011).

<sup>63</sup> U.S. Centers for Disease Control and Prevention, "CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations and Deaths in the United States, April 2009 – January 16, 2010", March 29, 2010, [http://www.cdc.gov/h1n1flu/estimates\\_2009\\_h1n1.htm](http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm), (accessed April 11, 2010).

that the cause of a pediatric death due to H1N1 would be so easily missed:<sup>64</sup> when children die, people want to know why.) But where studies have been done, there was no surprising increase in the proportion of these children which were previously healthy. There may have actually been a decrease: in the UK, for example, fifteen of the 70 children who are reported to have died of H1N1, or 21%, were previously healthy.<sup>65</sup>

Nowak told me that despite influenza being an unpleasant yet short lived disease for the vast majority of people, the “serious disease” label was appropriate because, in his words, “we can’t predict which people—you know, which individuals—are going to experience a serious course of illness.” Nowak is of course correct, but by this criterion, almost any disease could be labeled “serious.” But despite the lack of complete predictability, it does not therefore follow that influenza’s impact is completely random. Indeed, the justification for targeting the elderly in vaccination campaigns has always been that they, as a segment of the population, are more likely than others to suffer serious complications, or even die, from a bout of influenza. So while CDC may not be able to predict precisely which individual persons will experience a serious course of illness, the agency can and does predict that particular “high-risk” groups (such as the elderly and those with chronic medical conditions) are more likely to suffer serious complications of influenza than others.<sup>66</sup>

By describing influenza as a “serious” disease in its promotional materials, CDC generalizes what happens in a minority of mostly predictable populations (namely, the very elderly), and implies that everybody is at equal risk of infection and death.

### **Does influenza kill an average 36,000 per year?**

That statistics are used to convey the threat of influenza is not surprising. The severity of most diseases is expressed in the language of statistics. (“In 2006, 631,636 people died of heart disease,” the CDC’s website for diabetes declares.<sup>67</sup> Stroke “killed 137,119 people in 2006,” says the American Heart Association. For motor vehicle traffic deaths, CDC reports that 42,031 died in 2007.<sup>68</sup>) But with influenza, no such specificity exists. Rather, since 2003, it is the rounded 36,000 figure that gets used.

The difference in specificity is due to the vastly different ways in which officials arrive at these numbers. For every one of the 631,636, 137,119, and 42,031 people that were reported to have died of heart disease, stroke, or motor vehicle traffic deaths, respectively, there exists a death certificate on which the cause of death fits within these categories. For the approximately 2.4 million Americans that die each

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<sup>64</sup> Meryl Nass, “Suddenly there are many more deaths from swine flu, per CDC,” *Anthrax Vaccine*, November 13, 2009, <http://anthraxvaccine.blogspot.com/2009/11/suddenly-there-are-many-more-deaths.html>, (accessed July 18, 2011).

<sup>65</sup> Nabihah Sachedina and Liam J Donaldson, “Paediatric mortality related to pandemic influenza A H1N1 infection in England: an observational population-based study,” *The Lancet* 376, no. 9755 (November 2010): 1846-1852.

<sup>66</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.”

<sup>67</sup> U.S. Centers for Disease Control and Prevention, “Heart Disease Facts”, December 21, 2010, <http://www.cdc.gov/heartdisease/facts.htm>, (accessed July 18, 2011).

<sup>68</sup> U.S. Centers for Disease Control and Prevention, “Accidents or Unintentional Injuries”, May 12, 2011, <http://www.cdc.gov/nchs/fastats/acc-inj.htm>, (accessed July 18, 2011).

year, the CDC's National Center for Health Statistics (NCHS) receives a copy of the death certificate. Ranking them by the underlying cause of death arrived at after applying a uniform algorithm, the CDC tabulates just how many people were recorded to have died from the thousands of possible causes of death. CDC publishes this info in an annual *National Vital Statistics Report (NVS)*—and it is from this report where many mortality statistics originate.

According to the *NVS*, “Influenza and pneumonia” killed 56,326 in 2006, making it the eighth leading cause of death (Table 4.3). This point has not been lost on groups advocating for vaccination. “Last year, Lili Estefan became one of nearly 17 million Hispanics who contracted the flu. She didn't know it was the seventh leading cause of death among Latinos 65+,” claims the AARP, an organization with over 40 million members focused on improving the quality of life for the elderly.<sup>69</sup> The American Lung Association similarly states: “Influenza and Pneumonia are a leading cause of death in the U.S. The sad part of these diseases is that they can easily be prevented by a vaccination, yet continue to cause disease and death for thousands each year.”<sup>70</sup>

The reason influenza mortality has been expressed as an average of 36,000—rather than specific numbers—is in large part because the 36,000 number does not come from a count of death certificates. When the “Influenza and pneumonia” category is split into its components, the CDC report indicates that pneumonia claimed 55,477 of the total 56,326; influenza was the cause of death in the remaining 849.

The year 2006 was not an anomaly. In the recorded mortality between 1979 and 2007 (the most recent year for which finalized mortality data is available), influenza deaths never exceeded even 10% of the 36,000 estimate (Table 4.4).

While CDC seems comfortable to cite the death certificate data to explain how many people died of heart disease or motor vehicle traffic accidents, with influenza, CDC argues that the numbers appearing in its underlying causes of death tables represent a significant under-counting of the true impact of influenza. “Only counting deaths where influenza was included on a death certificate would be a gross underestimation of seasonal influenza's true impact,” the agency says.<sup>71</sup> Therefore, CDC employs statistical modeling techniques to estimate what it feels is a more likely representation of influenza's real impact. The CDC's statistical model—published in the *Journal of the American Medical Association (JAMA)* in 2003—calculated an annual average of 36,155 deaths during the 1990s. It was here that the “36,000 deaths” statistic was born.

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<sup>69</sup> AARP VIVA, “Flu: Latinos at Higher Risk”, 2010, [http://www.aarp.org/health/conditions-treatments/info-12-2010/flu\\_latinos\\_at\\_higher\\_risk.html](http://www.aarp.org/health/conditions-treatments/info-12-2010/flu_latinos_at_higher_risk.html), (accessed July 18, 2011).

<sup>70</sup> American Lung Association, “Influenza and Pneumonia,” in *State of Lung Disease in Diverse Communities 2010*, 2010, 45-53, <http://www.lungusa.org/assets/documents/publications/solddc-chapters/i-p.pdf>, (accessed December 14, 2010).

<sup>71</sup> U.S. Centers for Disease Control and Prevention, “Questions and Answers: Estimating Deaths from Influenza in the United States”, June 24, 2011, [http://www.cdc.gov/flu/about/disease/us\\_flu-related\\_deaths.htm](http://www.cdc.gov/flu/about/disease/us_flu-related_deaths.htm), (accessed July 18, 2011).

William Thompson of the CDC, who led the *JAMA* study, explained why death certificates—used to tally statistics on heart disease, cancer, diabetes, and many other causes of death—is not appropriate for influenza:

For several reasons, the number of influenza-related deaths cannot be determined solely by reports of influenza-coded deaths. First, most adult patients with symptoms consistent with influenza infection are not tested for influenza. Those who are generally receive rapid tests of only modest sensitivity. In addition, many influenza-associated deaths occur one or two weeks after the initial infection (when viral shedding has ended), either because of secondary bacterial infections or because the influenza has exacerbated chronic illnesses (e.g., congestive heart failure or chronic obstructive pulmonary disease). Even when influenza infection is confirmed by laboratory testing, those results are rarely reported on death certificates. ... The inability of death certificates to reliably and consistently attribute death to influenza has been understood for many decades, and this understanding led to the development of statistical models to better estimate influenza-associated deaths.<sup>72</sup>

Deaths calculated through modeling—termed “influenza-related” or “influenza-associated” deaths—are “deaths that occur in people for whom seasonal influenza infection was likely a contributor to the cause of death, but not necessarily the primary cause of death.”<sup>73</sup> “Based on modelling,” Thompson told me, “we think it's associated. I don't know that we would say that it's the underlying cause of death.”<sup>74</sup>

Martin Meltzer, a CDC health economist and co-author with Thompson on the *JAMA* paper, explained it this way: “Somebody can have flu and go to a hospital and die of a heart attack, but he might not have had the heart attack if he hadn't had the flu ... The death certificates don't read ‘influenza.’ ... They read ‘heart attack,’ ‘diabetes’ and all the fancy things people write down because they don't know what they died of.”<sup>75</sup>

The use of statistical models to more accurately gauge influenza's impact is not new. The understanding that more people tend to die in winters with epidemics of influenza gave rise to the concept of “excess mortality,” a phrase coined by the statistician William Farr in the mid nineteenth century.<sup>76</sup> The practice was refined over time, and modern statistical methods have been strongly influenced by a 1963 paper by Robert E. Serfling, then chief of statistics in the CDC's epidemiology branch.<sup>77</sup> Even in the absence of influenza, more people die during the colder months of the year than the warmer months, so Serfling

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<sup>72</sup> William W. Thompson et al., “Estimating Influenza-Associated Deaths in the United States,” *Am J Public Health* 99, no. 2 (October 1, 2009): S225-230.

<sup>73</sup> U.S. Centers for Disease Control and Prevention, “Questions and Answers: Estimating Deaths from Influenza in the United States.”

<sup>74</sup> Peter Doshi, “Are US flu death figures more PR than science?,” *BMJ* 331, no. 7529 (December 2005): 1412.

<sup>75</sup> Anita Manning, “Study: Annual flu death toll could be overstated,” *USA Today*, December 12, 2005.

<sup>76</sup> Alfred S. Evans and Richard A. Kaslow, eds., *Viral infections of humans: epidemiology and control* (Springer, 1997), 474.

<sup>77</sup> Robert E. Serfling, “Methods for current statistical analysis of excess pneumonia-influenza deaths,” *Public Health Reports* 78, no. 6 (June 1963): 494-506.

developed a method for computing this “normal” seasonal variation in mortality data and estimating an “epidemic threshold” above which the mortality impact of influenza epidemics could be computed. This basic model was developed further over time, and some modelers still use it, but the CDC’s 2003 *JAMA* paper modeled influenza-associated deaths in a totally new way, by incorporating virological surveillance data (the weekly proportion of specimens testing positive for influenza). When the press reported on the CDC’s new model in 2003, most presented a story that was sympathetic to and accepting of<sup>78</sup> the CDC’s attempts at developing “more precise estimates.”<sup>79</sup> However, experts in the field—some of whom had developed their own models—were less impressed. When *JAMA* published three letters in response to the Thompson paper, all were critical.

“We are concerned that their model was inappropriate,” wrote Nigel Gay and colleagues from the Communicable Disease Surveillance Centre in London in the first letter.<sup>80</sup> They raised the question of whether the CDC’s new model was overstating influenza deaths. “Thompson et al used a Poisson model in which the number of deaths increased exponentially with the number of laboratory reports and the effects of each virus (and the seasonal background) on the number of deaths were multiplicative rather than additive. We do not believe there is plausible justification for fitting such a model to these data.”

The second criticism came from authors at the National Institutes of Health who were not excited about the sudden change in methods. “The authors propose that this model replace Serfling-type models, which have been used for 40 years ... Although Thompson et al offer their model as superior, they do not provide graphical or statistical evidence of acceptable fit or model validation. Nor do they compare their influenza mortality estimates with those based on Serfling models.”<sup>81</sup> Lone Simonsen and co-author Thomas Reichert argued against immediate adoption of the Thompson model. “We propose that rigorous demonstrations of validity and benefit precede adoption of this new modeling approach.”

But with no media coverage of the letters, published months after the CDC’s original paper, little pressure existed to compel the CDC to re-think its strategy. Moreover, the CDC argued it was on the right track. “Mr Gay and colleagues suggest that we used an incorrect statistical model to analyze our data,” the CDC wrote in its response letter. “We compared the effects of using a Poisson regression model with a log-link vs with a linear-link as suggested by Gay et al and found that the results were highly correlated ( $R^2 > 0.95$ ). Furthermore, our models had lower mean square errors.”<sup>82</sup> To Simonsen and Reichert’s concern about abandoning the former Serfling method of estimation, they replied: “We

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<sup>78</sup> Associated Press, “Flu-Related Deaths Are Up Fourfold Since ’70s,” *The Washington Post*, January 8, 2003; “CDC reports jump in flu-related deaths,” *CNN Health*, January 7, 2003, [http://articles.cnn.com/2003-01-07/health/flu.deaths\\_1\\_flu-related-deaths-flu-season-keiji-fukuda?\\_s=PM:HEALTH](http://articles.cnn.com/2003-01-07/health/flu.deaths_1_flu-related-deaths-flu-season-keiji-fukuda?_s=PM:HEALTH), (accessed July 18, 2011).

<sup>79</sup> U.S. Centers for Disease Control and Prevention, “CDC Telebriefing Transcript: Increase in Influenza-Related Deaths in the United States.”

<sup>80</sup> Nigel J Gay et al., “Estimating deaths due to influenza and respiratory syncytial virus,” *Journal of the American Medical Association* 289, no. 19 (May 21, 2003): 2499; author reply 2500-2.

<sup>81</sup> Lone Simonsen et al., “Estimating deaths due to influenza and respiratory syncytial virus,” *JAMA: The Journal of the American Medical Association* 289, no. 19 (May 21, 2003): 2499-500; author reply 2500-2.

<sup>82</sup> William W. Thompson et al., “Estimating Deaths Due to Influenza and Respiratory Syncytial Virus—Reply,” *Journal of the American Medical Association* 289, no. 19 (May 2003): 2500-2502.

compared their model and ours ... we suggest that these results highlight the similarities not the differences, between different model estimates.”

### **Too big, too small, just right**

There is also a large degree of arbitrariness in the interpretation of the model. The CDC’s *JAMA* paper did not present a single estimate of influenza-associated death; it presented ninety-six: the result of computing estimates of influenza-associated death for each season between 1976 and 1999 across three different disease categories using two related statistical models. In summary, the estimates were:

- Influenza Model
  1. 5,977 influenza-associated underlying pneumonia and influenza deaths (average of estimates for 23 seasons, 1976-77 to 1998-99)
  2. 25,420 influenza-associated underlying respiratory and circulatory deaths (average of estimates for 23 seasons, 1976-77 to 1998-99)
  3. 34,470 influenza-associated underlying all-cause deaths (average of estimates for 23 seasons, 1976-77 to 1998-99)
- Influenza and RSV Model
  4. 8,097 influenza-associated underlying pneumonia and influenza deaths (average of estimates for 9 seasons, 1990-91 to 1998-99)
  5. 36,155 influenza-associated underlying respiratory and circulatory deaths (average of estimates for 9 seasons, 1990-91 to 1998-99)
  6. 51,203 influenza-associated underlying all-cause deaths (average of estimates for 9 seasons, 1990-91 to 1998-99)

Differences between the “Influenza Model” and “Influenza and RSV Model” are small and partially reflect differences in the date range. But why the CDC settled on the middle 36,155 and not 8,097 or 51,203 is explained in the paper:

Influenza-associated all-cause death estimates have been previously used to represent the full spectrum of deaths associated with influenza infections. However, these estimates include deaths such as those caused by fires and motor vehicle crashes, which are not directly associated with respiratory viral infections. Therefore, we also modeled a third category of deaths, underlying respiratory and circulatory deaths (which includes pneumonia and influenza deaths), to provide an estimate of deaths that was more directly associated with viral respiratory infections.

Deciding that the “underlying respiratory and circulatory deaths” category—or people whose deaths had been recorded as due to a respiratory or circulatory cause but was somehow “associated” with influenza—was the a better category on which to model influenza-associated mortality is not straightforward; indeed the CDC broke from convention by going with the new category. W. Paul Glezen and Robert B. Couch protested in a letter that “we see no reason to abandon total excess



mortality and substitute ‘respiratory and circulatory deaths.’”<sup>83</sup> Glezen and Couch, two prominent academic influenza researchers who have consulted for influenza vaccine manufacturers, argued “Even cases listing burns or trauma as the underlying cause of death may be influenza-related if the virus infection occurred coincident with the trauma or was nosocomial.” It seems that had Glezen and Couch authored the new model, they would have opted for the even higher 51,203 deaths estimate.

### Validating the CDC’s mortality model

I first raised doubts about the 36,000 figure in 2005. “Before 2003 CDC said that 20,000 influenza-associated deaths occurred each year. The new figure of 36,000 reported in the January 2003 *JAMA* paper is an estimate of influenza-associated mortality over the 1990s,” I wrote in an essay for the *BMJ*.

Keiji Fukuda, a flu researcher and a co-author of the paper, has been quoted as offering two possible causes for this 80% increase: “One is that the number of people older than 65 is growing larger...The second possible reason is the type of virus that predominated in the 1990s [was more virulent].”

However, the 65-plus population grew just 12% between 1990 and 2000. And if flu virus was truly more virulent over the 1990s, one would expect more deaths. But flu deaths recorded by the NCHS were on average 30% lower in the 1990s than the 1980s.<sup>84</sup>

Figure 4.6 provides a graphical representation of the contrast between the increase in estimates of annual influenza-associated mortality and the corresponding decrease in recorded influenza deaths.

In response to my article, authors from the NIH dismissed my concerns over the reliability of the CDC’s statistical estimates. They assured readers that statistical methods for estimating influenza-related mortality were “extensively vetted in the scientific literature, and are quite robust.”<sup>85</sup> Such a position, however, is apparently contradicted by what one of the authors had elsewhere written:

Measuring the health burden imposed by influenza is an important, and still controversial, question. Some authors argue that influenza is directly or indirectly responsible for the majority of seasonal excess deaths in temperate countries, while others argue that they trigger only a small minority.<sup>86</sup>

Indeed, according to others, it is the effects of cold weather alone that triggers epidemic-like peaks in wintertime mortality, “mainly from thrombotic and respiratory disease,” even in the absence of influenza.<sup>87</sup> One such researcher has argued that traditional methods to assess influenza deaths have

<sup>83</sup> W. Paul Glezen and Robert B. Couch, “Estimating deaths due to influenza and respiratory syncytial virus,” *JAMA: The Journal of the American Medical Association* 289, no. 19 (May 21, 2003): 2500.

<sup>84</sup> Doshi, “Are US flu death figures more PR than science?”

<sup>85</sup> Lone Simonsen et al., “US Flu Mortality Estimates Are Based on Solid Science” (January 11, 2006), [http://www.bmj.com/content/331/7529/1412.extract/reply#bmj\\_el\\_125778](http://www.bmj.com/content/331/7529/1412.extract/reply#bmj_el_125778), (accessed July 18, 2011).

<sup>86</sup> Jonathan Dushoff, “Assessing influenza-related mortality: Comment on Zucs et al.,” *Emerging Themes in Epidemiology* 2, no. 1 (2005): 7.

<sup>87</sup> G C Donaldson and W R Keatinge, “Excess winter mortality: influenza or cold stress? Observational study,” *BMJ* 324, no. 7329 (January 12, 2002): 89-90.

produced an “exaggerated picture,” as they fail to capture the effect of especially cold weather. “If allowance is made for the cold weather by multiple regression analysis, influenza epidemics account for less than 5% of the excess winter mortality in Britain over the last ten years.”<sup>88</sup>

Nevertheless, the NIH authors further stated that, despite differences in methods between the classical Serfling “excess mortality” based models and the CDC’s new virological data based model, “All these approaches yield similar estimates of the average seasonal US influenza mortality burden” when applied to the same years.<sup>89</sup> The CDC has made the same argument. Referencing a journal article it published in 2009 in which the results of multiple statistical models were compared, CDC authors concluded that all models “produced a similar picture” of influenza-associated mortality.<sup>90</sup> However, despite assurances that annual estimates were “at least moderately correlated ( $r > 0.53$ ),” model estimates can at times differ greatly. For example, the “Linear regression model” calculated 14,116 deaths in the 2001-02 season, while the “Summer-season 15% rate-difference model” calculated 74,808 deaths in the same season (Figure 4.7).

Nonetheless, the CDC claimed that the old 36,000 figure “was corroborated in 2009,” citing their 2009 publication as evidence. “Results from this study showed that during this time period, 36,171 flu-related deaths occurred per year, on average.”<sup>91</sup> However, the similarity here between 36,000 and 36,171 is somewhat coincidental, as the CDC is no longer comparing the same time period. 36,171 refers to the 1993-94 through the 2002-03 seasons, whereas the 36,000 figure refers to the 1990-91 and 1998-99 period. Had the same time periods been compared, the new paper found the old estimate around 10% too high. (The 2009 paper shows an average of 32,928 deaths per year between 1990-91 and 1998-99.)

Discrepancies in results became even more pronounced after CDC published a further update of its influenza mortality statistics, in August 2010. At a press briefing called for the occasion, disease modeler Dr. David Shay explained in his opening statement that the idea behind the latest publication was to “really just update previous estimates last made in 2009 using the same methodology, incorporating an additional four years of data.”

The update, however, did more than provide an addition four years of influenza-associated death estimates. The *MMWR* publication calculated new estimates for all 31 seasons between 1976-77 and 2006-07. For the 1990-91 and 1998-99 period during which the CDC previously estimated an average of 36,000 deaths per year, the CDC’s latest model found just 24,973 (Figure 4.8).

In opening remarks, the CDC however did not place the new statistics in the context of the well-known 36,000 figure. After a season in which much attention had been paid to the fact that the reported and

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<sup>88</sup> W R Keatinge, “Winter mortality and its causes,” *International Journal of Circumpolar Health* 61, no. 4 (November 2002): 292-299.

<sup>89</sup> Simonsen et al., “US Flu Mortality Estimates Are Based on Solid Science.”

<sup>90</sup> William W. Thompson et al., “Estimates of US influenza-associated deaths made using four different methods,” *Influenza and Other Respiratory Viruses* 3, no. 1 (2009): 37-49.

<sup>91</sup> U.S. Centers for Disease Control and Prevention, “CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations and Deaths in the United States”, January 15, 2010, [http://www.cdc.gov/h1n1flu/estimates/April\\_December\\_12.htm](http://www.cdc.gov/h1n1flu/estimates/April_December_12.htm), (accessed April 11, 2010).

estimated deaths from “pandemic” influenza H1N1 were dwarfed by the 36,000 deaths estimated to be caused by “run-of-the-mill” influenza, the CDC abandoned reporting a single number and instead told reporters it was “relatively meaningless” to report a point average because “when you look at sort of our data, there are very few of those 31 seasons where you would have an average outcome.” CDC said it was instead “trying to move towards away from a single number, and rather, give a range over a particular period of time to give a better time text to what flu really means in terms of what it does to the community.” “[A] simple average, I think, fails to give the impact of flu in an understandable fashion,” Shay said.<sup>92</sup> Instead of a single mean average, like 36,000, the press was encouraged to report on influenza as an unpredictable threat with a mortality impact ranging between 3,000 to 49,000 deaths per year.

Members of media on the telebriefing, however, who had for years printed the 36,000 figure following CDC’s lead, were understandably concerned about the dramatic shift in the CDC’s message and struggled to put the new paper in the context of the old “36,000.” Betsy McKay from the *Wall Street Journal* pointed out that the text of the CDC’s latest paper actually did present an average—23,607—representing the average over the 31 seasons, 1976-2007. She asked Shay, “is that an average number we can use and does that compare to the 36,000?”

Shay explained that years which had averaged 36,000 deaths had many “more severe” seasons, and that over the whole time period of the 2003 paper, the average was “about 25,000.” Therefore, “this average that we’re coming up with now, 23,600, is consistent with what we’ve published in the past” (Figure 4.9).

Don Sapatkin of the *Philadelphia Inquirer* was next to probe the 36,000 issue. “I know you don’t want us to use a range ... I mean an average. But what does the 36,000 actually equate to in the new study—even though you don’t want us to use it? I’m trying to understand it.”<sup>93</sup>

Shay repeated that 36,000 “was for 1990 through 1999,” but did not explain that mortality over this time period had been re-estimated in the new paper. Shay did not explain that the CDC’s latest estimate was no longer 36,155 but rather now 24,973 (Figure 4.8). Instead, Shay focused on the theme that the new study simply confirms the old study, and directed attention away from the 1990s and towards the full study range: “That 2003 paper actually looked at a broader range of seasons, from ’76 through 1999. So, from that whole time period, the average was approximately 23,000-25,000 deaths, excuse me. And for this time period, this broader 31-season time period that we’re looking at, the average is approximately 23,600. So, they’re very similar” (Figure 4.9).

Despite multiple reporters’ questions about the 36,000 figure, the CDC did not disclose during the press briefing that, according to what it knew now, the widely cited and well known 36,000 statistic had been inaccurate and was 46% too high; that its new estimate of yearly death during the 1990s is 24,973, not 36,155. (Figure 4.8) Instead, it continued to discuss that period as an “outlier of a decade.” The CDC

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<sup>92</sup> U.S. Centers for Disease Control and Prevention, “CDC Press Briefing Transcript: August 26, 2010”, August 26, 2010, <http://www.cdc.gov/media/transcripts/2010/t100826.htm>, (accessed August 26, 2010).

<sup>93</sup> *Press Briefing*, 2010, <http://www.cdc.gov/media/transcripts/2010/audio/0826.mp3>, (accessed August 26, 2010).

also did not explain why its estimates of annual influenza-associated mortality differ across various publications, despite assertions that it is using “the same methodology” (Figure 4.10). In the 2004-05 season, for example, there were 14,377 influenza-associated underlying respiratory and circulatory deaths according to the CDC’s 2009 publication—but in the 2010 publication, the re-calculated estimate showed 47,117 deaths. Instead, the CDC stressed the dangers of influenza and assured the audience that “this is an update that confirms really what we have seen previously in terms of flu.”<sup>94</sup>

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Although the CDC argues that its models and estimates have been “corroborated,” important discrepancies remain. But even if statistical models all did produce similar estimates, there remains a fundamental need to validate models. Multiple models could be built upon similar but inaccurate assumptions. Models may also fail to distinguish between true influenza deaths and those triggered by other influenza-like illnesses. Similarity in model estimates would not resolve these questions. Unfortunately, estimation of influenza-associated deaths remains a controversial area because there is no established or widely accepted way to determine their accuracy. That is, to quote the CDC, “there is no gold standard currently available for assessing the performance of the different models...”<sup>95</sup> Until such a gold standard comes to be,<sup>96</sup> evaluations of the magnitude of the threat of influenza will remain nothing more than problematic, self-contradictory, controversial guesswork.

### **The CDC’s Pandemic Severity Index**

If quantifying the severity of seasonal influenza is fraught with problems, measuring the magnitude in deaths and illness of a future pandemic that has not yet occurred poses challenges of a new kind. But the problem is no less important if the goal is to keep responses to infectious disease in proportion to the severity of the threat. The CDC therefore developed a method for assigning pandemics a Pandemic Severity Index.

The background for developing the Pandemic Severity Index was the assumption that at the start of an influenza pandemic, pandemic influenza vaccine may not be available. In addition, fearing insufficient supplies of antiviral medications (that may not even work against the novel pandemic virus), pandemic planners around the world gave serious thought to other means by which they might mitigate the impact of a pandemic.<sup>97</sup> Much enthusiasm gathered around what came to be called “non-pharmaceutical interventions,” or NPIs, that could be initiated at the beginning of an outbreak. These included social distancing measures such as isolation of the ill, voluntary home quarantine of those exposed to the ill, school closures, the cancelation of public gatherings, and alteration of workplace environments to decrease the density of people.<sup>98</sup>

<sup>94</sup> U.S. Centers for Disease Control and Prevention, “CDC Press Briefing Transcript: August 26, 2010.”

<sup>95</sup> Thompson et al., “Estimates of US influenza-associated deaths made using four different methods.”

<sup>96</sup> Thompson et al., “Estimating Deaths Due to Influenza and Respiratory Syncytial Virus--Reply.”

<sup>97</sup> U.S. Centers for Disease Control and Prevention, “Interim Pre-pandemic Planning Guidance,” 17-18.

<sup>98</sup> U.S. Centers for Disease Control and Prevention, “Interim Pre-pandemic Planning Guidance”; Markel et al., “Nonpharmaceutical Interventions Implemented by US Cities During the 1918-1919 Influenza Pandemic.”

Some researchers, after reviewing the 1918 experience, suggested that such interventions could have a significant effect in reducing the morbidity and mortality of a pandemic.<sup>99</sup> Other researchers challenged this finding, suggesting that the case was not proven that NPIs impacted the course of the 1918 influenza.<sup>100</sup> The CDC acknowledged the uncertainty: the “hypothesis remains unproven,” it wrote in its hefty, 97-page national guidance document *Community Strategy for Pandemic Influenza Mitigation in the United States*. Nevertheless, “if the experience of the 1918 pandemic is relevant,” the document stated, NPIs “would, in all likelihood, be implemented in most communities at some point during a pandemic.” The question was less about *whether* to implement NPIs, but *how best* to implement them.

A primary concern with NPIs was their potential to adversely affect society itself. Having millions of people simultaneously isolating themselves in their homes in order to avoid infection carried the potential to disrupt modern life and the economy as much as the disease itself. As witnessed during the 2009 H1N1 outbreak, school closures forced many parents to skip work in order to tend to their children, something that may have been more difficult for the poor.<sup>101</sup> “The U.S. Government recognizes the significant challenges and social costs that would be imposed” by NPIs, the CDC’s 2007 guidance stated. CDC therefore planned on advocating for NPIs “matched to the severity” of a pandemic. An NPI would only be recommended if the severity of the outbreak suggested the benefits of the NPI outweighed its costs.

This was to be achieved in two steps. First, the pandemic would be assigned a Pandemic Severity Index along a 5-point scale of increasing severity (Category 1 to Category 5), driven by the disease’s case-fatality ratio (“the proportion of deaths among clinically ill persons”) (Figure 4.11). Then, based on the pandemic’s severity, particular interventions either would—or would not—be recommended (Figure 4.12). “The most controversial elements (e.g., prolonged dismissal of students from schools and closure of childcare programs) are not likely to be needed in less severe pandemics, but these steps may save lives during severe pandemics.”<sup>102</sup> School closings would only be “considered” in a Category 2 or 3 pandemic, but “generally not recommended” in a Category 1 pandemic.

While the Pandemic Severity Index appeared to be a reasonable response to the difficulties in balancing the costs and benefits of NPIs, its scientific merit was questionable from the beginning.

Although graphs and tables in the guidance document (Figure 4.13, Figure 4.14) indicated that pandemic severity increased along a continuum beginning with “Severe Seasonal Influenza” (Category 1), followed by the 1968 pandemic (Category 2), 1957 pandemic (Category 2), and finally the 1918 pandemic (Category 5), such a depiction is inconsistent with historical mortality estimates (see Table 4.5, Table 4.6, Table 4.7). The 1968 pandemic was in fact inaccurately categorized. With a case fatality ratio of 0.04%,

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<sup>99</sup> Markel et al., “Nonpharmaceutical Interventions Implemented by US Cities During the 1918-1919 Influenza Pandemic.”

<sup>100</sup> John M. Barry, “Comments on the nonpharmaceutical interventions in New York City and Chicago during the 1918 flu pandemic,” *Journal of Translational Medicine* 5 (December 11, 2007): 65-65.

<sup>101</sup> Thomas L. Gift, “Household Effects of School Closure during Pandemic (H1N1) 2009, Pennsylvania, USA,” *Emerging Infectious Diseases* 16, no. 8 (August 2010), <http://wwwdev.cdc.gov/eid/content/16/8/1315.htm>, (accessed July 18, 2011).

<sup>102</sup> U.S. Centers for Disease Control and Prevention, “Interim Pre-pandemic Planning Guidance,” 19.

its severity is half that of a “severe seasonal influenza,” and should have been categorized as a Category 1 pandemic. In addition, the “moderate (1958/68-like)” pandemic influenza scenario described in the 2005 *HHS Pandemic Influenza Plan* has a CFR of 0.23%, which does not lie somewhere between the 1968 pandemic (0.04%) and 1957 pandemic (0.17%), but is greater than both. Finally, based on CDC estimates of actual mortality in the United States, the case fatality ratio of “the first influenza pandemic of the 21st century”<sup>103</sup> in 2009 was 0.02%, rendering it a Category 1 pandemic with a CFR milder than the mildest influenza season since 1976.

The reason why these inconsistencies went undetected is unclear, but it may be due to the fact that CFRs for the three pandemics were not published alongside similar estimates for seasonal influenza. Yet because the CFR is a measure of the proportion of those infected who die, it can be calculated by the simple formula:

$$CFR = \frac{\# \text{ deaths}}{\# \text{ infected}}$$

The exact numbers of people infected in any given year are unknown, however, because many if not most people with influenza do not seek medical attention. But smaller studies have attempted to estimate an Illness Rate by surveying a certain town or other population (as depicted in the X-axis of Figure 4.14, which appears in the guidance document); multiplying the overall Illness Rate by the total United States population will yield an estimate of the number infected. Therefore:

$$CFR = \frac{\# \text{ deaths}}{\# \text{ infected}} = \frac{\# \text{ deaths}}{\text{illness rate (\%)} * \text{total population}}$$

Another reason the inconsistencies and miscategorization may have occurred is that the Pandemic Severity Index was never used in the actual 2009 outbreak. While the 2007 CDC document stated, “Upon declaration by WHO of having entered the Pandemic Period (Phase 6) and further determination of U.S. Government Stage 3, 4, or 5, the CDC’s Director shall designate the category of the emerging pandemic based on the Pandemic Severity Index ...,” and despite various determinations of CFR that were made,<sup>104</sup> the U.S. government never assigned the H1N1 outbreak a Pandemic Severity Index.

The reason why declared pandemics like 1968 and 2009 are paradoxically less severe than seasonal influenza is because severity, according to the Pandemic Severity Index, is defined by the CFR, and the number of deaths in 1968 and 2009 is not substantially larger than seasonal influenza in relation to the numbers said to have been infected by the new virus. The 1968 H3N2 and 2009 H1N1 viruses are believed to have spread and infected far more widely and efficiently than seasonal influenza (perhaps because more people lacked pre-existing immunity), but for most, the clinical course was milder than seasonal strains of influenza.

<sup>103</sup> Margaret Chan, “Address to the Regional Committee for the Americas (61st session)”, September 28, 2009, [http://www.who.int/dg/speeches/2009/paho\\_committee\\_20090928/en/index.html](http://www.who.int/dg/speeches/2009/paho_committee_20090928/en/index.html), (accessed July 18, 2011).

<sup>104</sup> Christophe Fraser et al., “Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings,” *Science* 324, no. 5934 (June 19, 2009): 1557-1561; Anne M. Presanis et al., “The Severity of Pandemic H1N1 Influenza in the United States, from April to July 2009: A Bayesian Analysis,” *PLoS Med* 6, no. 12 (December 8, 2009): e1000207.

## Pandemic versus Non-pandemic influenza

While the distinction of pandemic influenza as a different and far deadlier form of influenza was emphasized in repeated statements of governments—“Pandemics are different from seasonal outbreaks or ‘epidemics’ of influenza,” the CDC wrote—numerical estimates and projections of future pandemic influenza mortality crystallized the assumption that next pandemic would inevitably be far deadlier than seasonal influenza (Table 4.8). In the United States, for example, officials predicted that even the mildest future pandemic would kill 209,000, or around four times more than they assert died in even the worst of the past 31 non-pandemic seasons.

Here, too, the historical record does not support any clear cut distinctions between those seasons that officials have labeled a pandemic and those said to be non-pandemic.<sup>105</sup> Comparing the number of deaths classified as due to influenza over the twentieth century shows that only one pandemic—the great influenza of 1918—stands out (Figure 4.15). Peak monthly (Figure 4.16) and overall seasonal death rates (Figure 4.17) in the 1957 and 1968 pandemics are not higher than—and in some cases are exceeded by—the death rate in non-pandemic seasons.

The similarity in mortality impact between past pandemics and non-pandemics has seldom been given serious attention, particularly in the lay press, but it has been acknowledged by Thompson, Simonsen, and other disease modelers at the CDC and NIH. Thompson and colleagues from the CDC, for example, wrote that “it cannot be assumed a priori that pandemics will cause more mortality than interpandemic seasons.”<sup>106</sup> Likewise, Simonsen and others from the NIH have written that “mortality caused by the 1968 pandemic virus was unimpressive relative to surrounding severe epidemics”<sup>107</sup> and “the mild 1968 pandemic was actually exceeded by a few more recent severe A(H3N2) seasons.”<sup>108</sup> (For additional statements by notable authorities, see Table 4.9)

Furthermore, while since around 2005, pandemic influenza has been described as inherently deadly, in older documents, officials did not mention mortality as a key characteristic of influenza pandemics: in 1998, Nancy Cox and Keiji Fukuda (then colleagues at the CDC) wrote of the 1918, 1957 and 1968 pandemics that “Each pandemic was associated with high rates of morbidity, considerable social disruption, and substantial economic losses.” It was only with regard to the 1918 pandemic that the authors mentioned “a relatively high case-fatality rate in young and previously healthy adults.”<sup>109</sup> By contrast, a CDC document, *Key Facts About Pandemic Influenza*, from 2006, carried a similar sentence, but added death to the list: “Past influenza pandemics have led to high levels of illness, *death*, social

<sup>105</sup> Peter Doshi, “Trends in recorded influenza mortality: United States, 1900-2004,” *American Journal of Public Health* 98, no. 5 (May 2008): 939-45.

<sup>106</sup> Thompson et al., “Are estimates of influenza-associated deaths in the US really just PR?”

<sup>107</sup> L. Simonsen et al., “Pandemic Influenza and Mortality: Past Evidence and Projections for the Future, S. Knobler, A. Mack, A. Mahmoud, The Threat of Pandemic Influenza: Are We Ready” (Washington, DC: National Academies Press, 2005), 89-114.

<sup>108</sup> Simonsen et al., “US Flu Mortality Estimates Are Based on Solid Science.”

<sup>109</sup> Nancy J. Cox and Keiji Fukuda, “Influenza,” *Infectious Disease Clinics of North America* 12, no. 1 (March 1998): 27-38.

disruption, and economic loss” (emphasis added).<sup>110</sup> (The CDC subsequently took this webpage down as most pandemic related information was shifted to the HHS-managed [www.pandemicflu.gov](http://www.pandemicflu.gov), which itself was later renamed [www.flu.gov](http://www.flu.gov).)

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While pandemics do not appear to be deadlier than influenza in its nonpandemic forms, either in terms of the total number killed or the chances of dying if one is infected (the CFR), some have pointed to a different aspect of mortality as the feature that sets pandemics apart. Simonsen and colleagues have emphasized that pandemic influenza’s mortality signature is an age shift: whereas seasonal influenza deaths overwhelmingly occur amongst the elderly, in pandemics there is an “age shift” downwards such that many more deaths occur among the under 65 population.<sup>111</sup> The change in age distribution has even structured part of the WHO’s defense of its response to H1N1. Highlighting how H1N1 “differed in striking ways” in its patterns of illness, the WHO has declared that “H1N1 virus affected a younger age group in all categories: those most frequently infected, those requiring hospitalization, those requiring intensive care, and those dying from their infection.”<sup>112</sup> In the US, the CDC believes 90% of hospitalizations and 87% of deaths occurred in those under 65.<sup>113</sup>

## Influenza vaccines

The marketing of influenza vaccine in the United States is saturated with the concept that the simple act of getting vaccinated holds the key to saving lives. “Prevents influenza-related death,” a CDC-produced influenza vaccine promotional poster from 2006 declares as the top reason to get vaccinated (Figure 4.18).<sup>114</sup> In a more technical paper, authored by CDC, the message remains explicit: “Vaccination is the most effective way to prevent influenza-associated morbidity and mortality.”<sup>115</sup> Similarly, in the introduction to the national influenza vaccination recommendations, the CDC states that “Annual influenza vaccination is the most effective method for preventing influenza virus infection and its complications.”<sup>116</sup> It is important to consider the evidence base upon which such claims are made.

To substantiate this claim, the national recommendations point to a 1999 paper written by Nancy Cox, today the CDC’s top influenza scientist. Cox’s paper, published in the *Lancet*, is a review paper which discusses virological, epidemiological, and clinical aspects of influenza, as well as strategies for control

<sup>110</sup> Emphasis added. U.S. Centers for Disease Control and Prevention, “Pandemic Flu: Key Facts”, January 17, 2006, <http://www.cdc.gov/flu/pandemic/pdf/pandemicflufacts.pdf>, (accessed October 12, 2010).

<sup>111</sup> Simonsen et al., “Pandemic Influenza and Mortality”; *Ibid*.

<sup>112</sup> World Health Organization, “The international response to the influenza pandemic: WHO responds to the critics.”

<sup>113</sup> U.S. Centers for Disease Control and Prevention, “CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations and Deaths in the United States, April 2009 – January 16, 2010.”

<sup>114</sup> U.S. Centers for Disease Control and Prevention, “Top 3 reasons to get your flu vaccine”, 2006, <http://www.cdph.ca.gov/programs/immunize/Documents/3reasons.pdf>, (accessed July 12, 2010).

<sup>115</sup> U.S. Centers for Disease Control and Prevention, “Influenza vaccination coverage among children aged 6-59 months—eight immunization information system sentinel sites, United States, 2007-08 influenza season,” *MMWR. Morbidity and Mortality Weekly Report* 57, no. 38 (September 26, 2008): 1043-1046.

<sup>116</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010,” 2.



and prevention. Concerning the matter of how well influenza vaccines work in the elderly population—importantly, the population in which most influenza-related complications and deaths occurs—Cox writes, “immunisation was cost effective and associated with reductions in rates of hospital admission and deaths from influenza-related complications.”<sup>117</sup> This statement is supported by a further reference to a single study published in 1994 in the *New England Journal of Medicine*. Authors of this study had done a retrospective study of over 25,000 persons above the age of 65, comparing the rates of influenza and its complications (including death) between those that had received influenza vaccine versus those that had not. They concluded that influenza vaccination “produces direct dollar savings,” and was associated with reductions in complications, hospitalizations—even deaths. “Vaccination was also associated with reductions of 39 to 54 percent in mortality from all causes during the three influenza seasons ( $P < 0.001$ ).”<sup>118</sup>

This study, which strongly supports the conclusions that influenza vaccines are especially effective at saving lives, is far from the only study to draw that conclusion. In 2002, researchers published the results of a meta-analysis, reconfirming the mortality benefits of influenza vaccination. The authors trawled the medical literature looking for trials that has been conducted which investigated questions such as the effect of influenza vaccines on outpatient visits for pneumonia, hospitalization, and overall mortality. They found 15 eligible studies, and concluded that

Influenza vaccine was effective in reducing influenza-like illness by 35% (95% confidence interval (CI) 19–47%), hospitalization for pneumonia and influenza by 33% (CI 27–38%), mortality following hospitalization for pneumonia and influenza by 47% (CI 25–62%); and mortality from all causes by 50% (CI 45–56%).<sup>119</sup>

As a meta-analysis that attempts to synthesize the results of all research, its methodology is considered by many to lead to higher quality results and conclusions than any single study can offer. The study, led by Trang Vu of The Royal Melbourne Hospital in Australia, has been cited by the New York City Health Department in its promotional flyer *Flu Shots Save Lives*, and is extensively cited in the medical literature.<sup>120</sup>

### **But do influenza vaccines really save lives?**

In 2005, Lone Simonsen and colleagues from the National Institutes of Health published an analysis in *Archives of Internal Medicine* that took much of the medical community by surprise, by questioning the reliability of past studies. Simonsen’s study considered over three decades of influenza mortality and

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<sup>117</sup> Nancy J. Cox and Kanta Subbarao, “Influenza,” *Lancet* 354, no. 9186 (October 9, 1999): 1277-1282.

<sup>118</sup> Kristin L. Nichol et al., “The Efficacy and Cost Effectiveness of Vaccination against Influenza among Elderly Persons Living in the Community,” *New England Journal of Medicine* 331, no. 12 (1994): 778-784.

<sup>119</sup> Trang Vu et al., “A meta-analysis of effectiveness of influenza vaccine in persons aged 65 years and over living in the community,” *Vaccine* 20, no. 13-14 (March 15, 2002): 1831-1836.

<sup>120</sup> P Noyes et al., “Flu Shots Save Lives: Why Aren’t More Central Brooklyn Residents Getting Vaccinated?” (New York City Department of Health and Mental Hygiene, 2006), <http://www.nyc.gov/html/doh/downloads/pdf/dpho/dpho-brooklyn-report-flu-2006.pdf>, (accessed August 1, 2011). The Vu et al. meta-analysis has been cited 144 times since its publication in 2002, according to “Web of Science” (August 1, 2011).

vaccination data. Despite a steep rise in the number of Americans getting vaccinated between 1968 and 2001—from 15% to 65%—they could detect no impact on mortality. “We could not correlate increasing vaccination coverage after 1980 with declining mortality rates in any age group.”<sup>121</sup>

The Simonsen paper did more than provide a dissenting opinion—it pointed out that previous results were simply implausible. The authors wrote that

there are not enough influenza-related deaths to support the conclusion that vaccination can reduce total winter mortality among the US elderly population by as much as half.

Previously, studies such as the Vu meta-analysis had concluded influenza vaccines could cut the number of elderly deaths in half. But these conclusions are irreconcilable with Simonsen’s calculation that at most influenza is responsible for just 10% of winter-time deaths. This implied that some kind of serious methodological flaw was present in previous studies like the Vu meta-analysis.

Simonsen’s paper caused considerable controversy. “This is a very important, troubling study,” Walter Orenstein, the former head of the National Immunization Program stated. “It is a paradigm shift.” Some at the CDC were more dismissive. “I think it’s extremely weak and overstates the results,” CDC disease modeler William Thompson told *Science* magazine.<sup>122</sup> But the study was hard to ignore, achieving considerable attention in the national press. The *Washington Post* told its readers that “the study challenges government dogma and is bound to confuse the public.”<sup>123</sup>

The CDC and NIH moved quickly to assure the public that, despite the new study’s finding that influenza vaccination was thus far unable to reduce deaths, there was no need for alarm or a change in policy. In a joint press release, the CDC and NIH wrote that contrary to the Simonsen study, “Numerous studies have shown that influenza vaccination works- including to help protect the elderly from serious illness and hospitalizations- but the degree to which it works varies from year to year and can be difficult to measure.” To address the “confusion” Simonsen’s study had supposedly caused over the value of the vaccine, the CDC and NIH said that “Vaccination remains the best protection from influenza available for people 65 and older and their loved ones. ... In the current study by Simonsen et al, the authors in no way imply that the elderly should not receive influenza vaccine.” Far from challenging the value of the vaccine, the press release said that the Simonsen study highlighted the “room for improvement in prevention efforts,” and described the possibility of expanding vaccination recommendations.

... recently published studies raise the possibility that it may be beneficial to vaccinate larger numbers of healthy persons, including children, to prevent transmission of influenza viruses to high-risk persons such as the elderly. Expansion of groups for whom

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<sup>121</sup> Simonsen et al., “Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population.”

<sup>122</sup> Jon Cohen, “INFLUENZA: Study Questions the Benefits of Vaccinating the Elderly,” *Science* 307, no. 5712 (February 2005): 1026-1026.

<sup>123</sup> “FINDINGS,” *The Washington Post*, February 15, 2005.

influenza vaccination is recommended is under discussion by the ACIP and CDC, and is partly contingent on adequate vaccine supply in the future.<sup>124</sup>

Meanwhile, Thompson, Cox, Fukuda and others from the CDC wrote a letter to the editor of *Archives* challenging Simonsen's paper. They took issue with Simonsen's claim that the 50% mortality reduction was implausible: "Simonsen et al also suggest that influenza vaccine cannot be 50% effective because only 10% of all winter excess deaths are influenza related. A 50% reduction in the relative rates of influenza-associated deaths could occur, however, without a corresponding 50% decline in absolute death rates."<sup>125</sup>

In response, Simonsen pointed out that the CDC authors "misinterpret the claims of the cohort studies." Studies such as Vu's do not claim that influenza vaccines reduce by 50% just those deaths triggered by influenza, but half of all wintertime deaths, regardless of cause. To emphasize the point, they offered a sample calculation:

If we apply the 50% vaccine effectiveness figure from cohort studies to the observation that about 670 000 elderly die during winter months in the United States in recent years, we estimate that at 65% vaccination coverage about 323 000 deaths in the elderly are prevented each winter. It should have been easy to spot such a huge mortality decline as vaccine coverage increased from 15% to 65%—but it was not there.

Since 2005, additional studies have been published which, like Simonsen's, challenge the previously assumed benefits of influenza vaccination in the elderly population. A central concern that has emerged is the possibility of a "healthy user bias" which posits that the elderly who are most healthy—and thus least likely to die from influenza or any other disease—are more likely to get vaccinated than their less healthy counterparts. In other words, the vaccinated group and unvaccinated group may not be comparable, meaning that the cause of differences in outcomes (e.g. less deaths in the vaccinated group) may not have anything to do with the vaccine. The people might simply be healthier to begin with.

Lisa Jackson and colleagues from the University of Washington, for example, studied the records of over 70,000 elderly over an eight year period, and found the vaccine reduced hospitalizations from pneumonia by 18% and deaths from any cause by 44%. In this way, the study results were similar to many past studies. However, in the period before the influenza season began, the authors found an even larger benefit: a 61% reduction in the risk of death from any cause. The authors thus argued that the apparent mortality benefits associated with influenza vaccine were counterintuitive, and cast doubt on their validity:

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<sup>124</sup> U.S. Centers for Disease Control and Prevention and U.S. National Institutes of Health, "'Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population' by Simonsen et al. (2005): A Statement by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH)", February 18, 2005, <http://www.cdc.gov/flu/pdf/statementeldmortality.pdf>, (accessed October 23, 2010).

<sup>125</sup> William W. Thompson et al., "Influenza Vaccination Among the Elderly in the United States," *Arch Intern Med* 165, no. 17 (September 26, 2005): 2038-a-2039.

We found the greatest reductions in the risk of death and of pneumonia hospitalization in the period before influenza season, when there should be no true vaccine effect. ... The reductions in risk before influenza season suggest the presence of bias due to preferential receipt of vaccine by relatively healthy seniors on the estimates of influenza vaccine effectiveness observed during influenza season.<sup>126</sup>

To further test the hypothesis, they undertook a more detailed analysis of 252 elderly who died during an influenza season, and compared them to 576 age-matched controls. Reviewing the individuals' medical records, they investigated the effect of "functional status limitations" such as the ability to independently walk or bathe without help. The researchers found that the functional limitations were simultaneously associated with an increased risk of death and decreased likelihood of influenza vaccination. They therefore concluded that "Functional status limitations may confound the association of influenza vaccination and risk of all cause mortality in seniors, but these factors are not captured in the administrative data sources used in many of the published evaluations of influenza vaccine effectiveness."<sup>127</sup>

A group of researchers in Canada conducted a similar analysis in Canada, and published their results in 2008. (In the interest of full disclosure, I should note that I was one of the peer-reviewers for this paper.) They hypothesized that if influenza vaccine was not the true cause of the seemingly fantastic mortality benefits that past studies had attributed to influenza vaccine, then the vaccine should look like it's saving lives even when influenza virus is not in circulation. Their hypothesis was confirmed: even during the months when influenza was not circulating, the data indicated that "influenza vaccination was associated with a 51% mortality reduction." The team of researchers, led by Dean Eurich of the University of Alberta, posited that the so-called "healthy user" effect was likely at play, for after adjusting for functional and socioeconomic status, the benefits seemed to disappear. They concluded that "The results of this study suggest that many previous observational studies have overestimated the mortality benefits of influenza vaccination due to difficult-to-correct confounding attributable to the 'healthy-user' effect."<sup>128</sup>

In a commentary appearing in the *Journal of Clinical Epidemiology*, authors Tom Jefferson and colleagues from the Cochrane Collaboration who have been reviewing the evidence behind influenza vaccines for over a decade, complain about the lack of good quality evidence:

Cochrane and other systematic reviews have shown overall poor quality methods of relevant studies, a lack of randomized controlled trials of sufficient duration, and power to detect and effect on serious outcomes (such as hospitalization and death) and over-reliance on nonrandomized studies.<sup>129</sup>

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<sup>126</sup> Jackson et al., "Evidence of bias in estimates of influenza vaccine effectiveness in seniors."

<sup>127</sup> Jackson et al., "Functional status is a confounder of the association of influenza vaccine and risk of all cause mortality in seniors."

<sup>128</sup> Eurich et al., "Mortality Reduction with Influenza Vaccine in Patients with Pneumonia Outside 'Flu' Season."

<sup>129</sup> Tom Jefferson et al., "Inactivated influenza vaccines: Methods, policies, and politics," *Journal of Clinical Epidemiology* 62, no. 7 (July 2009): 677-686.

While popular accounts of vaccine effectiveness speak of vaccines as either interventions that “work” or “don’t work,” the details reveal a more complex story, where vaccine protect against some outcomes in some populations, but not against other outcomes in other populations. The Cochrane team’s systematic reviews of the literature have found that for small children under 2 years of age, the vaccine’s effects are no different than a placebo—“possibly a reflection of the rarity of the disease and its complications.”<sup>130</sup> But for older children, adolescents, and healthy adults, “better quality randomized studies show an effect against cases of influenza (but not its complications or its transmission).” This means that if the past is any prediction of the future, healthy adults who receive influenza vaccine can expect to have a decreased chance of developing the symptoms of influenza. However, while the risk of coming down with influenza may be reduced, influenza vaccines do not confer a reduced chance of developing severe complications associated with influenza, like pneumonia, or of dying. While all of this amounts to a clearly a suboptimal situation, it is reassuring to note that complications and death from influenza amongst children, adolescents, and healthy adults is rare.

It is in the elderly population where the vast majority of complications, hospitalizations, and deaths from influenza occur, about which the Cochrane reviewers write that “an implausible sequence of effects” occurs, whereby influenza vaccine is “apparently effective for the prevention of nonspecific outcomes, such as death from all causes, but not for the prevention of influenza or death caused by pneumonia and influenza.” The Cochrane group—like Simonsen, Jackson, and others<sup>131</sup>—argues that confounding biases like the healthy user effect are probably to blame. “This is especially likely because in the general elderly population, the bulk of evidence (hundreds of thousand observations) comes from poor quality, large, retrospective, data-linked cohorts in which data had been collected for other purposes.”

Unfortunately, so much discussion and debate over these so-called “non-randomized” studies exists because they are pretty much the only kind of evidence that is available. Far higher quality evidence could be achieved by studying the results of randomized controlled trials (RCT), but such trials are extremely rare. In the last four decades, only one RCT “assessed currently available vaccines and reached satisfactory completion,” the Cochrane reviewers wrote.<sup>132</sup> The trial—by Govaert and colleagues in the Netherlands—was conducted on elderly aged 60 and above *not* belonging to any known high risk groups, and suggested that influenza vaccination could halve the incidence of influenza.<sup>133</sup> Unfortunately, the trial was too small to answer the question of whether influenza vaccines also have any effect on reducing deaths. The vast majority of elderly participants in the trial were between 60 and 74 years of age, with only ten percent 75 years of age or greater, and the trial lasted just one winter in 1991-92. Also of note was that for most endpoints studied, the observed benefits dropped substantially with advancing age.

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<sup>130</sup> Ibid.

<sup>131</sup> Jennifer Clark Nelson et al., “New strategies are needed to improve the accuracy of influenza vaccine effectiveness estimates among seniors,” *Journal of Clinical Epidemiology* 62, no. 7 (July 2009): 687-694.

<sup>132</sup> Jefferson et al., “Vaccines for preventing influenza in the elderly.”

<sup>133</sup> Th. M. E. Govaert et al., “The Efficacy of Influenza Vaccination in Elderly Individuals,” *JAMA: The Journal of the American Medical Association* 272, no. 21 (December 7, 1994): 1661-1665.

In a separate analysis, the Cochrane reviewers analyzed 274 influenza vaccine studies, considering “study concordance” (whether data presented supported the authors’ conclusions), study quality, study take home message, study funding, and journal impact factors. They found serious problems with study concordance—but overwhelmingly in the direction of attributing undue benefits towards influenza vaccines not supported by study data. They also found that studies funded by industry had a higher likelihood of being published in prestigious journals and to be cited more often—a finding that could be not be explained by study quality or size.<sup>134</sup>

The Cochrane review of influenza vaccines in the elderly concluded that “As our elderly dataset formed a major part of our overview of influenza vaccines studies, it is likely that that data presented in this review are so biased as to be virtually uninterpretable.” Jefferson and his colleagues have called for the carrying out of publicly funded, large placebo-controlled clinical trials over multiple influenza seasons in order to generate higher quality evidence and answer the question of what benefit, exactly, influenza vaccines have in the elderly population,<sup>135</sup> a proposition Simonsen, Jackson and others would seem to agree with.<sup>136</sup> But health officials have thus far been opposed to such a trial, arguing such a trial would be unethical, on the grounds that it would mean that some elderly would receive a placebo contrary to national recommendations that say they should be vaccinated.<sup>137</sup>

### “False and misleading” claims

If no convincing evidence exists to suggest that influenza vaccines are saving lives, it calls into question officials’ practice of using influenza mortality statistics as a way to encourage vaccination. Here, historical precedent exists with a related therapeutic: influenza antivirals.

Within a year of approving Relenza, a novel antiviral for the treatment of influenza, the Food and Drug Administration (FDA) sent the drug’s manufacturer Glaxo Wellcome a warning letter. The company had distributed promotional materials which the FDA’s Division of Drug Marketing, Advertising, and Communications had determined were illegal, in violation of the Federal Food, Drug, and Cosmetic Act. In its March 2000 letter, the FDA declared that the Glaxo Wellcome material “lacks fair balance, contains misleading safety and efficacy claims, unsubstantiated comparative claims, misleading drug resistance claims, and misleading productivity and pharmacoeconomic claims.”<sup>138</sup> One of the problematic

<sup>134</sup> Tom Jefferson et al., “Relation of study quality, concordance, take home message, funding, and impact in studies of influenza vaccines: systematic review,” *BMJ* 338 (2009): b354.

<sup>135</sup> Tom Jefferson and Carlo Di Pietrantonj, “Inactivated influenza vaccines in the elderly—-are you sure?,” *Lancet* 370, no. 9594 (October 6, 2007): 1199-1200.

<sup>136</sup> Lone Simonsen et al., “Influenza vaccination and mortality benefits: New insights, new opportunities,” *Vaccine* 27, no. 45 (October 2009): 6300-6304.

<sup>137</sup> Lone Simonsen et al., “Mortality benefits of influenza vaccination in elderly people: an ongoing controversy,” *The Lancet Infectious Diseases* 7, no. 10 (October 2007): 658-66; Shannon Brownlee and Jeanne Lenzer, “Does the Vaccine Matter?,” *The Atlantic*, November 2009, <http://www.theatlantic.com/magazine/archive/2009/11/does-the-vaccine-matter/7723/>, (accessed October 15, 2009).

<sup>138</sup> U.S. Food and Drug Administration to Glaxo Wellcome Inc., “NDA 21-036 Relenza (zanamivir for inhalation) MACMIS ID#8708”, March 13, 2000, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM165384.pdf>, (accessed July 18, 2011).

statements was a statement about the impact of influenza. (Figure 4.19) The FDA did not challenge the accuracy of the claim—which in this case was based on statistics drawn from the published scientific literature—the FDA instead challenged Glaxo Wellcome’s use of the statistics.

... the presentation of the statement in promotional materials for Relenza, ***“Influenza afflicts 25 to 55 million people annually in the United States, resulting in 20,000 deaths and 50,000 to 300,000 hospitalizations,”*** would be misleading because this presentation suggests that Relenza has been shown to impact hospitalizations and deaths from influenza when such has not been demonstrated by substantial evidence.<sup>139</sup>

The company was ordered to “immediately cease publication or dissemination” of such claims. It was further ordered to describe to FDA its plans to comply. Nearly a decade later, Glaxo Wellcome (now GlaxoSmithKline) refrains from marketing the benefit of its drug in the context of statistics describing the deadliness of influenza. On the official website, Relenza.com, a page “About the Flu” describes influenza, but unlike similar webpages such as those maintained by CDC, it does not offer statistics regarding influenza mortality or hospitalization impact.<sup>140</sup>

Tamiflu.com, the official homepage for Roche’s blockbuster drug Tamiflu, a competitor influenza antiviral medication, contains a similar webpage. “What You Need to Know About the Flu” states that influenza is a “contagious virus” and “can be a serious illness,” but here, too, death and other serious complications like pneumonia are not mentioned. The month after the FDA cited Glaxo Wellcome, it wrote to Roche, alleging that claims Roche had made in promotional material such as “Tamiflu reduces incidence of secondary complications (i.e. bacterial infections) by 45%” were “misleading because they suggest greater efficacy for Tamiflu than has been demonstrated by substantial evidence.”<sup>141</sup> Roche, too, was instructed to immediately cease dissemination of such these and other “false and misleading” claims, which FDA judged to be in violation of US law. Since then, the Tamiflu product package insert has contained the following text: “Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. TAMIFLU has not been shown to prevent such complications.”<sup>142</sup>

Without a proven ability—that is, proven to the satisfaction of the FDA—to reduce endpoints like pneumonia, hospitalization and death, FDA regulations forbid companies like GlaxoSmithKline and Roche to even discuss the threat of influenza in ways that might imply their medications can reduce those effects. But the FDA’s jurisdiction does not extend to other governmental bodies such as CDC,

<sup>139</sup> Emphasis in the original.

<sup>140</sup> GlaxoSmithKline, “About the Flu”, 2011, <http://www.relenza.com/about-the-flu/about-the-flu.html>, (accessed July 18, 2011).

<sup>141</sup> U.S. Food and Drug Administration to Roche Laboratories Inc., “NDA 21-087 TAMIFLU (oseltamivir phosphate) MACMIS ID#8675”, April 14, 2000, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM166329.pdf>, (accessed July 18, 2011).

<sup>142</sup> Hoffman-La Roche, Ltd., “Product label. Tamiflu.”

leaving CDC free to deploy its own standards of evidence in support of statements about therapeutic effectiveness.

### **Official policy**

In a 2010 poster carrying the headline “Reason enough to get VACCINATED!” the CDC writes, “Flu-related complications lead to about 36,000 DEATHS and 200,000 HOSPITALIZATIONS each year in the U.S.”<sup>143</sup> (Figure 1.4, page 59). The unstated implication of the poster is similar to those in the Relenza promotional materials—namely, that the promoted intervention (here, influenza vaccines) can reduce the cited heavy morbidity and mortality burden of influenza.

But here, the CDC is actually aware of that much of the published studies regarding influenza vaccines may be flawed to the extent that it is meaningless. Citing the work of Simonsen, Jackson, Jefferson, and others, the national ACIP recommendations state that

... studies demonstrating large reductions in hospitalizations and deaths among the vaccinated elderly have been conducted using medical record databases and have not measured reductions in laboratory-confirmed influenza illness. These studies have been challenged because of concerns that they have not controlled adequately for differences in the propensity for healthier persons to be more likely than less healthy persons to receive vaccination.<sup>144</sup>

The CDC however does not rebut or in any other way respond to these criticisms. It simply acknowledges them, and in this as well as promotional material, continues to claim that the shots save lives.<sup>145</sup>

[ENDS]

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<sup>143</sup> U.S. Centers for Disease Control and Prevention, “Reason enough to get VACCINATED!”.

<sup>144</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.”

<sup>145</sup> Ibid.



Table 4.1. Proportion of specimens testing positive for influenza at World Health Organization (WHO) Collaborating Laboratories and 60 National Respiratory and Enteric Virus Surveillance System (NREVSS) laboratories through the United States. Data are compiled and published by CDC. (Source: CDC<sup>146</sup>)

Season	Specimens Tested	Influenza negative	Influenza positive	Percent positive for influenza
1997-1998	99072	86143	12929	13%
1998-1999	98582	84340	14242	14%
1999-2000	92403	78630	13773	15%
2000-2001	99497	88991	10506	11%
2001-2002	109139	92737	16402	15%
2002-2003	96871	87030	9841	10%
2003-2004	152262	127158	25104	16%
2004-2005	186590	162020	24570	13%
2005-2006	179772	158362	21410	12%
2006-2007	179268	155515	23753	13%

<sup>146</sup> U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 1997 - 1998 Season", n.d., <http://www.cdc.gov/flu/weekly/regions1997-1998/datafinal/wholaballregion97-98.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 1998 - 1999 Season", n.d., <http://www.cdc.gov/flu/weekly/regions1998-1999/datafinal/wholaballregion98-99.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "1999-2000 Influenza Season Summary", October 19, 2002, <http://www.cdc.gov/ncidod/diseases/flu/WeeklyArchives1999-2000/99-00summary2.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "2000-2001 Laboratory Data Summary for All Regions", n.d., <http://www.cdc.gov/ncidod/diseases/flu/regions2000-2001/wholaballregion00-01.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2001 - 2002 Season", n.d., <http://www.cdc.gov/flu/weekly/regions2001-2002/datafinal/wholaballregion01-02.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2002 - 2003 Season", n.d., <http://www.cdc.gov/flu/weekly/regions2002-2003/datafinal/wholaballregion02-03.htm>, (accessed March 10, 2009); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2003 - 2004 Season", n.d., <http://www.cdc.gov/flu/weekly/regions2003-2004/datafinal/wholaballregion03-04.htm>, (accessed March 10, 2009); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2004-2005 Season", n.d., <http://www.cdc.gov/flu/weekly/regions2004-2005/datafinal/wholaballregion04-05.htm>, (accessed March 10, 2009); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2005 - 2006 Season", n.d., <http://www.cdc.gov/flu/weekly/regions2005-2006/datafinal/wholaballregion05-06.htm>, (accessed March 10, 2009); U.S. Centers for Disease Control and Prevention, "2006-07 U.S. INFLUENZA SEASON SUMMARY", n.d., <http://www.cdc.gov/flu/weekly/weeklyarchives2006-2007/06-07summary.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "2007-08 U.S. INFLUENZA SEASON SUMMARY", October 6, 2008, <http://www.cdc.gov/flu/weekly/weeklyarchives2007-2008/07-08summary.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2008 - 2009 Season", n.d., <http://www.cdc.gov/flu/weekly/weeklyarchives2008-2009/data/whoAllregt39.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2009 - 2010 Season", n.d., <http://www.cdc.gov/flu/weekly/weeklyarchives2009-2010/data/whoAllregt20.htm>, (accessed July 18, 2011); U.S. Centers for Disease Control and Prevention, "Influenza viruses isolated by WHO/NREVSS Collaborating Laboratories 2010 - 2011 Season", n.d., <http://www.cdc.gov/flu/weekly/weeklyarchives2010-2011/data/whoAllregt20.htm>, (accessed July 18, 2011).

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2007-2008	225329	185502	39827	18%
2008-2009	519543	412765	106778	21%
2009-2010	456302	366067	90235	20%
2010-2011	246128	191902	54226	22%
<b>Average</b>				<b>15%</b>

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Table 4.2. Proportion of specimens tested that are positive for influenza in New York laboratories, by laboratory and season. Data provided by New York State Department of Health.

Laboratory	1997-1998	1998-1999	1999-2000	2000-2001	2001-2002	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008
<b>Albany</b>	20%	29%	26%	19%	39%	32%	54%	47%	38%	36%	49%
<b>Westchester</b>		31%	28%	12%	8%	11%	13%	14%	7%	5%	14%
<b>Bronx</b>	19%	17%	19%	18%	22%	7%	14%	8%	3%	5%	10%
<b>Brooklyn A</b>	7%	17%	10%	10%	11%	9%	10%	8%	8%	4%	4%
<b>Brooklyn B</b>							8%	7%	4%	5%	5%
<b>Buffalo A</b>			9%	4%	7%	3%	9%	12%	6%	4%	7%
<b>Buffalo B</b>	20%	22%		3%	17%	1%	13%	16%	7%	2%	11%
<b>Long Island A</b>	20%	15%	11%	2%	2%	1%	5%	10%	2%	2%	4%
<b>Long Island B</b>							10%	10%	10%	11%	14%
<b>Manhattan A</b>	9%	7%	1%	6%	5%	3%	9%	7%	4%	3%	5%
<b>Manhattan B</b>							11%	10%	7%	5%	11%
<b>Rochester A</b>	15%	18%	10%	11%	17%	6%	16%	23%	10%	8%	23%
<b>Rochester B</b>			6%	11%	8%	4%	11%	12%	7%	7%	19%

Table 4.3. Top ten leading causes of death, 2006, United States. Data obtained from CDC's *National Vital Statistics Report*<sup>147</sup>

Cause of death (based on the <i>International Classification of Diseases, Tenth Revision, Second Edition, 2004</i> )	Rank	Number of deaths
All causes	--	2,426,264
Diseases of heart	1	631,636
Malignant neoplasms	2	559,888
Cerebrovascular diseases	3	137,119
Chronic lower respiratory diseases	4	124,583
Accidents (unintentional injuries)	5	121,599
Diabetes mellitus	6	72,449
Alzheimer's disease	7	72,432
Influenza and pneumonia	8	56,326
Nephritis, nephrotic syndrome and nephrosis	9	45,344
Septicemia	10	34,234

<sup>147</sup> Melonie Heron, *Deaths: Leading Causes for 2006*, vol. 58, National vital statistics reports 14 (Hyattsville, MD: National Center for Health Statistics, 2010), 6, [http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58\\_14.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58_14.pdf), (accessed July 25, 2011).

Table 4.4. Recorded influenza deaths, 1979-2007. Source: vital statistics obtained from CDC Wonder<sup>148</sup>

Year	Deaths
1979	604
1980	2702
1981	3006
1982	727
1983	1431
1984	1096
1985	2054
1986	1838
1987	632
1988	1943
1989	1593
1990	2098
1991	1137
1992	1006
1993	1044
1994	1229
1995	606
1996	745
1997	720
1999	1665
2000	1765
2001	257
2002	727
2003	1792
2004	1100
2005	1812
2006	849
2007	411

<sup>148</sup> U.S. Centers for Disease Control and Prevention, "CDC Wonder Query for ICD-9 code 487 (influenza)", 2010, <http://wonder.cdc.gov/controller/datarequest/D16;jsessionId=1E21114D9D6889ABAB2C2AE6B1D80FCF>, (accessed December 14, 2010); U.S. Centers for Disease Control and Prevention, "CDC Wonder Query for ICD-10 codes J10 and J11 (influenza)", 2010, <http://wonder.cdc.gov/controller/datarequest/D53;jsessionId=EF150DD0676D05AB8880798B5DB304A8>, (accessed December 14, 2010).

Table 4.5. Case fatality ratio (CFR) calculations for historical "low," mean, and "high" CFR non-pandemic influenza seasons

	low (1986/87-like)	mean (1976-2007)	high (2003/04-like)
US population	240,132,887	254,897,975	290,326,418
Illness rate	0.05	0.13	0.20
Number of deaths	3,349	23,607	48,614
Number infected	12,006,644	31,862,247	58,065,284
Case fatality ratio	0.03%	0.07%	0.08%

Table 4.6. Case fatality ratio calculations for historical pandemic influenza seasons

Pandemic year	1918	1957	1968	2009
US population	103,208,000	171,984,130	200,706,052	307,006,550
Illness rate	0.29	0.24	0.39	0.20
Number of deaths	675,000	69,800	33,800	12,470
Number infected	29,930,320	41,276,191	78,275,360	61,000,000
Case fatality ratio	2.26%	0.17%	0.04%	0.02%

Table 4.7. HHS projections of future pandemic influenza scenarios

Season	Moderate (1958/68-like)	Severe (1918-like)
US population	300,000,000	300,000,000
Illness rate	0.30	0.30
Number of deaths	209,000	1,903,000
Number infected	90,000,000	90,000,000
Case fatality ratio	0.23%	2.11%

Sources for Table 4.5, Table 4.6, Table 4.7: US Census Bureau (seasonal and pandemic population estimates)<sup>149</sup>; HHS (population, illness rate, and number of deaths in future "moderate" and "severe" scenarios)<sup>150</sup>; HHS (number of deaths in 1918, 1957, 1968)<sup>151</sup>; CDC (number of infections and deaths in H1N1 2009)<sup>152</sup>; CDC (number of deaths in 'low', 'mean', and 'high' seasonal influenza). The illness rates in "low," "mean," and "high" seasonal influenza (Table 4.5) are assumptions based on the CDC assertion

<sup>149</sup> U.S. Census Bureau, "Historical National Population Estimates: July 1, 1900 to July 1, 1999", June 28, 2000, <http://www.census.gov/popest/archives/1990s/popclockest.txt>, (accessed December 14, 2010); U.S. Census Bureau, "Annual Estimates of the Resident Population for the United States, Regions, States, and Puerto Rico: April 1, 2000 to July 1, 2009 (NST-EST2009-01)", December 2009, <http://www.census.gov/popest/states/tables/NST-EST2009-01.xls>, (accessed December 14, 2010).

<sup>150</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan."

<sup>151</sup> U.S. Health and Human Services, "Pandemics and Pandemic Threats since 1900", n.d., <http://www.pandemicflu.gov/general/historicaloverview.html>, (accessed July 26, 2009).

<sup>152</sup> U.S. Centers for Disease Control and Prevention, "CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations and Deaths in the United States, April 2009 – January 16, 2010."

that between 5% and 20% of the US population “gets the flu” each year.<sup>153</sup> Deaths in Table 4.5 are based on CDC’s annual estimates of influenza-associated mortality, published in 2010.<sup>154</sup>

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<sup>153</sup> U.S. Centers for Disease Control and Prevention, “CDC - Seasonal Influenza (Flu) - Q & A.”

<sup>154</sup> U.S. Centers for Disease Control and Prevention, “Estimates of deaths associated with seasonal influenza --- United States, 1976-2007,” *MMWR. Morbidity and Mortality Weekly Report* 59, no. 33 (August 27, 2010): 1057-1062.

Table 4.8. Pre-2009 estimates of mortality in a future pandemic compared with official estimates of seasonal influenza mortality.

Area	Estimates of seasonal influenza mortality	Pre-2009 estimates of future pandemic mortality
Canada	2,000—8,000 <sup>155</sup>	11,000—58,000 <sup>156</sup>
United Kingdom	600—13,000 <sup>157</sup>	50,000—750,000 <sup>158</sup>
United States	3,349—48,614 <sup>159</sup>	209,000—1,903,000 <sup>160</sup>
World	250,000—500,000 <sup>161</sup>	2—7.4 million <sup>162</sup>

<sup>155</sup> Public Health Agency of Canada, "Influenza", March 3, 2011, <http://www.phac-aspc.gc.ca/influenza/index-eng.php>, (accessed July 18, 2011).

<sup>156</sup> Public Health Agency of Canada., *Highlights from the Canadian pandemic influenza plan for the health sector: preparing for an influenza pandemic, the Canadian health perspective.*, 9.

<sup>157</sup> UK NHS Choices, "Seasonal Flu", February 15, 2011, <http://www.nhs.uk/Conditions/Flu/Pages/Introduction.aspx>, (accessed July 18, 2011).

<sup>158</sup> UK Department of Health, "Pandemic flu - frequently asked questions," FAQ, n.d., [http://www.dh.gov.uk/en/Publichealth/Flu/PandemicFlu/FAQonly/DH\\_065088](http://www.dh.gov.uk/en/Publichealth/Flu/PandemicFlu/FAQonly/DH_065088), (accessed September 14, 2009).

<sup>159</sup> U.S. Centers for Disease Control and Prevention, "Estimates of deaths associated with seasonal influenza --- United States, 1976-2007."

<sup>160</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan," 18.

<sup>161</sup> World Health Organization, "Influenza (Seasonal)", April 2009, <http://www.who.int/mediacentre/factsheets/fs211/en/>, (accessed June 9, 2009).

<sup>162</sup> World Health Organization, "Ten things you need to know about pandemic influenza."



Table 4.9. Additional statements on the similarity of pandemic and non-pandemic influenza

<p>CDC Director Julie Gerberding on the comparability of the 1957 pandemic with seasonal influenza</p>	<p>Senator SPECTER. Dr. Gerberding, let me interrupt you there where you say it is inevitable. That is pretty stark. That means it's going to happen.</p> <p>Dr. GERBERDING. It will happen, I believe. I don't know when, and I don't know what virus will be the culprit. H5 is one possibility, but there are many other possibilities.</p> <p>Senator SPECTER. All right. When you talk about inevitability, that's a good warning. That's not a shot across the bow; that's a shot into the ship. How serious will it be? Will it be like 1918? What's your professional judgment on that?</p>
<p>NIAID Director Anthony Fauci on the comparability of the 1968 pandemic with seasonal influenza</p>	<p>Dr. GERBERDING. My professional judgment is that I can't tell you, and I don't know, and I don't think anyone does. We've had a 1918 pandemic. That's probably not as bad as it could get. But we've also had very mild pandemics. For example, in 1957 it was not much different than a regular seasonal flu year, which is bad enough. Thirty-six thousand people die every year from regular flu.<sup>163</sup></p> <p>"If you look historically, pandemic flu isn't necessarily all gloom and doom. There is an enormous spectrum of severity of pandemic flu. Pandemic means it's widespread, and it's a brand new virus to which you have had no contact. In 1918, which is the worst-case scenario, more than 50 million people died. On the other end of the spectrum was 1968, which was a pandemic because it was the first time we had seen H3N2 (virus). The 1968 pandemic was not substantially more severe than the normal, run-of-the-mill seasonal flu."<sup>164</sup></p>
<p>John Barry, best-selling author of <i>The Great Influenza</i>, on the 1968 pandemic</p>	<p>"The last time a new influenza virus reached pandemic levels was in 1968, but the episode was not significantly deadlier than a typical bad flu season. Few people who lived through it even knew it occurred."<sup>165</sup></p>

<sup>163</sup> *Pandemic Influenza: Progress Made and Challenges Ahead* (Washington, DC: U.S. Government Printing Office, 2007), 40.

<sup>164</sup> Anthony S. Fauci, "Bird flu: Things to know, not fear," *USA Today*, April 12, 2006, [http://www.usatoday.com/news/opinion/editorials/2006-04-11-bird-flu\\_x.htm](http://www.usatoday.com/news/opinion/editorials/2006-04-11-bird-flu_x.htm), (accessed February 12, 2011).

<sup>165</sup> Barry, "Lessons from the 1918 Flu."

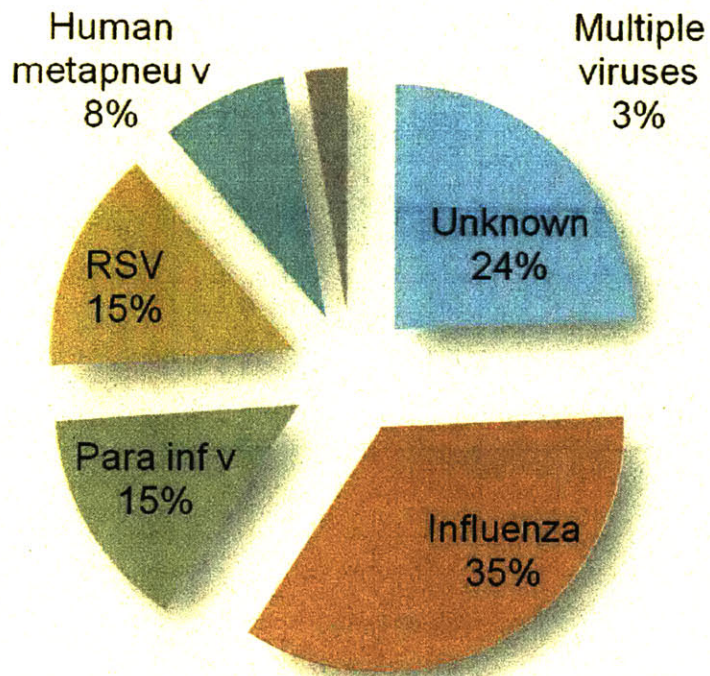


Figure 4.1. Cause of “more than a cold” in 408 children aged 6 months to 12 years, United Kingdom, over 4 winters. Source: Harnden (2007)<sup>166</sup>

<sup>166</sup> Harnden et al., “Respiratory infections for which general practitioners consider prescribing an antibiotic.”

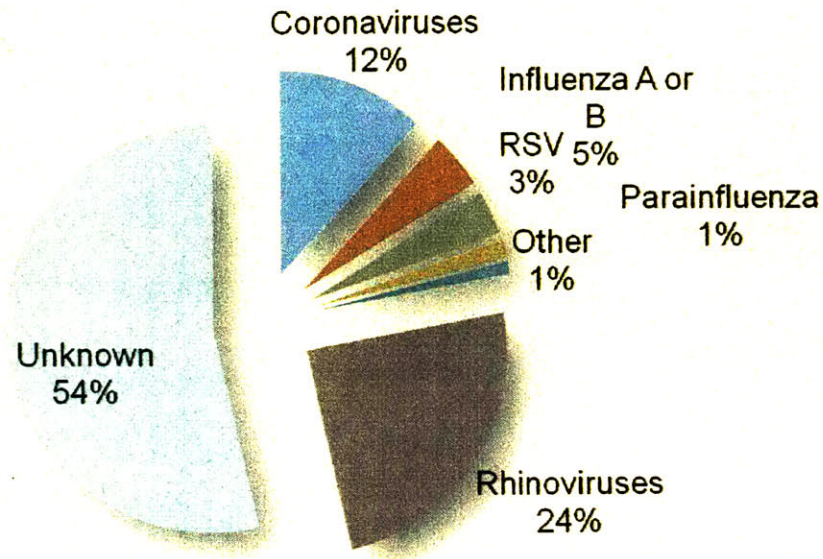


Figure 4.2. Causes of acute upper respiratory tract infections in 291 elderly, United Kingdom. Source Nicholson (1997)<sup>167</sup>

<sup>167</sup> Nicholson et al., "Acute viral infections of upper respiratory tract in elderly people living in the community."

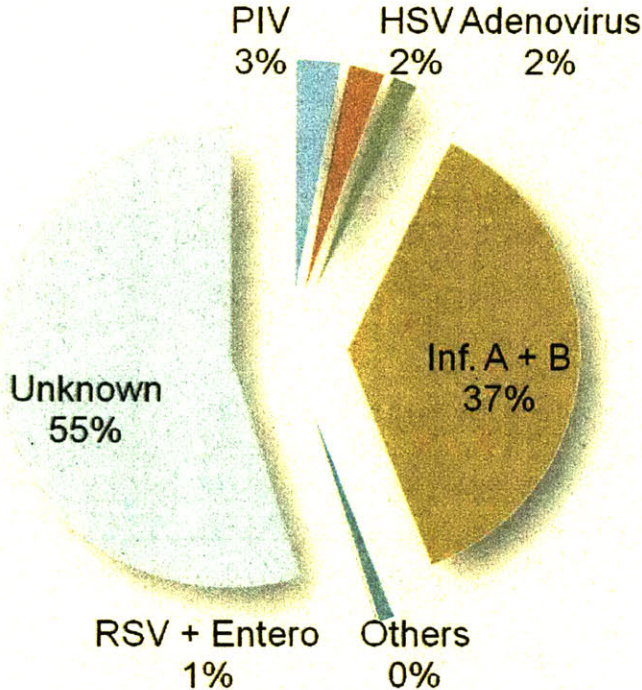


Figure 4.3. Influenza-like illness in 6835 people, of all ages, seeking medical care in 13 Peru cities, over 2 years. Source: Laguna-Torres (2009)<sup>168</sup>

<sup>168</sup> Laguna-Torres et al., "Influenza-Like Illness Sentinel Surveillance in Peru."

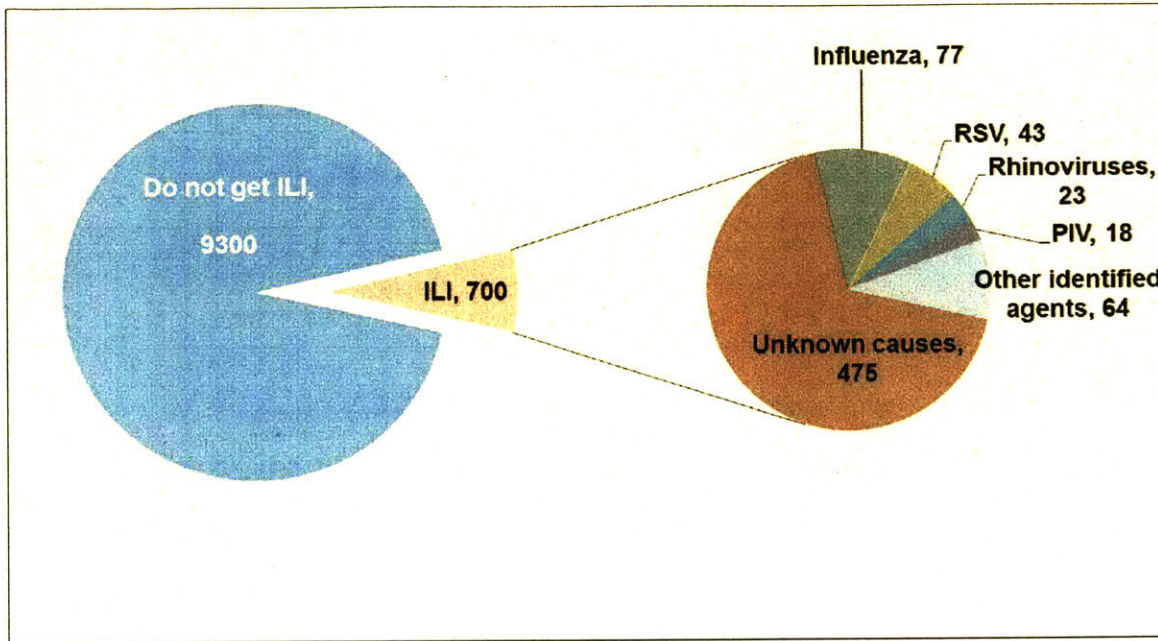


Figure 4.4. Incidence of influenza-like illnesses (ILI) per 10,000 people (calculated from prospective studies), with breakdown by agent, based on information in pie studies. Source: Jefferson (2009)<sup>169</sup>

<sup>169</sup> Jefferson, "Mistaken identity: seasonal influenza versus influenza-like illness."

### **Flu is a serious contagious disease.**

Each year in the United States, on average, more than 200,000 people are hospitalized and 36,000 people die from seasonal flu complications.

### **This flu season could be worse.**

There is a new and very different influenza virus causing illness called 2009 H1N1. CDC expects both 2009 H1N1 flu and seasonal flu to cause illness, hospital stays and deaths this season and is preparing for an early and possibly severe flu season.

### **Flu – what harm can it do?**

For most people, flu is nasty but not serious: a short period of chills, aches and pains and then a return to normal health.

But some people are at greater risk from the effects of flu. For them, flu can increase the risk of more serious illnesses such as bronchitis and pneumonia or can make existing conditions worse. In the worst cases, flu can result in a stay in hospital – or even death.

This leaflet explains who is more likely to be affected, and how a simple and free flu jab can reduce the risk.

If you are at greater risk, don't wait for winter or for a flu epidemic to ask for the jab. Arrange to see your GP or practice nurse in the autumn to get the best possible protection.

Figure 4.5. Contradictory positions on influenza's seriousness between the US CDC (left) and UK NHS (right).<sup>170</sup> In contrast to the United States, where officials recommend annual influenza vaccination to the majority of the US population, UK officials only recommend the vaccine to much smaller high risk groups, in particular individuals 65 years and greater.<sup>171</sup>

<sup>170</sup> U.S. Centers for Disease Control and Prevention, "Take 3' Actions"; UK National Health Service, "If you knew about flu you'd get the jab."

<sup>171</sup> UK National Health Service, "Seasonal Flu Vaccination: Who Should Have It and Why", 2010, 6-7, [http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/@dh/@en/@ps/documents/digitalasset/dh\\_119314.pdf](http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_119314.pdf), (accessed July 18, 2011).

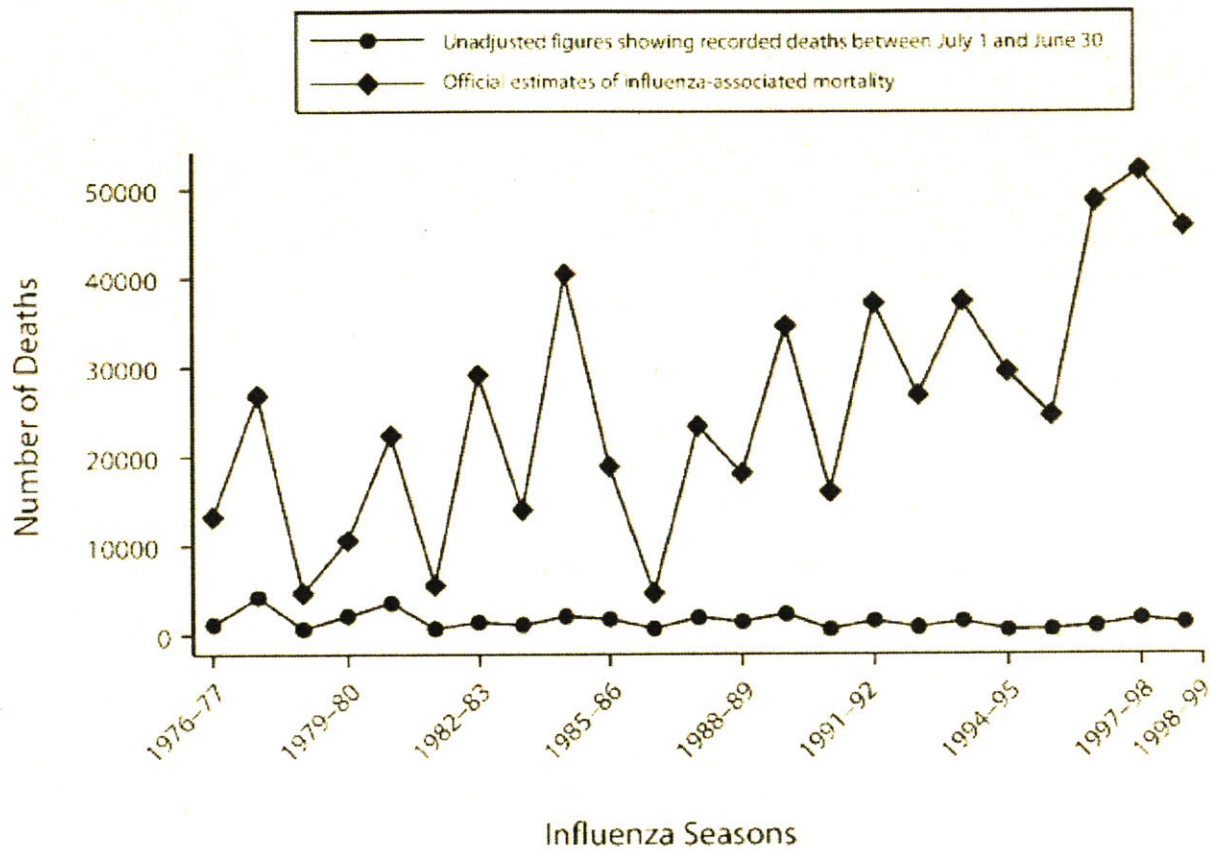


Figure 4.6. Comparison of total recorded influenza deaths and CDC estimates (2003) of influenza-associated mortality for the seasons 1976-1977 to 1998-1999, in the United States. (Reproduced with permission from Peter Doshi, "Trends in recorded influenza mortality: United States, 1900-2004," *American Journal of Public Health* 98, no. 5 (May 2008): 939-45. Copyright held by American Public Health Association.) Sources: CDC influenza-associated mortality estimates are from Table 2 in Thompson et al.;<sup>172</sup> recorded deaths are from CDC Wonder.<sup>173</sup>

<sup>172</sup> Thompson et al., "Mortality associated with influenza and respiratory syncytial virus in the United States."

<sup>173</sup> U.S. Centers for Disease Control and Prevention, "CDC Wonder Query for ICD-9 code 487 (influenza)."

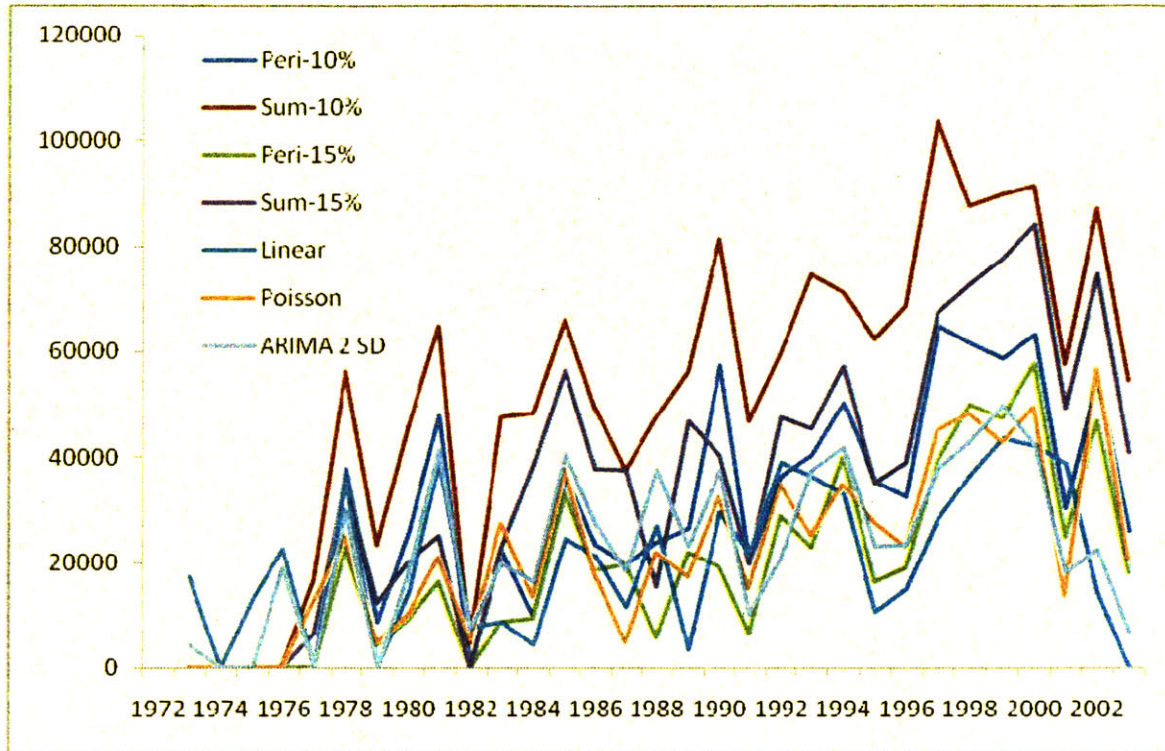


Figure 4.7. Comparison of CDC estimates of influenza-associated mortality using multiple statistical models for the seasons 1972-1973 to 2002-2003. Graph has been reconstructed from data presented in Table 6 in a 2009 paper by CDC.<sup>174</sup>

<sup>174</sup> Thompson et al., "Estimates of US influenza-associated deaths made using four different methods."



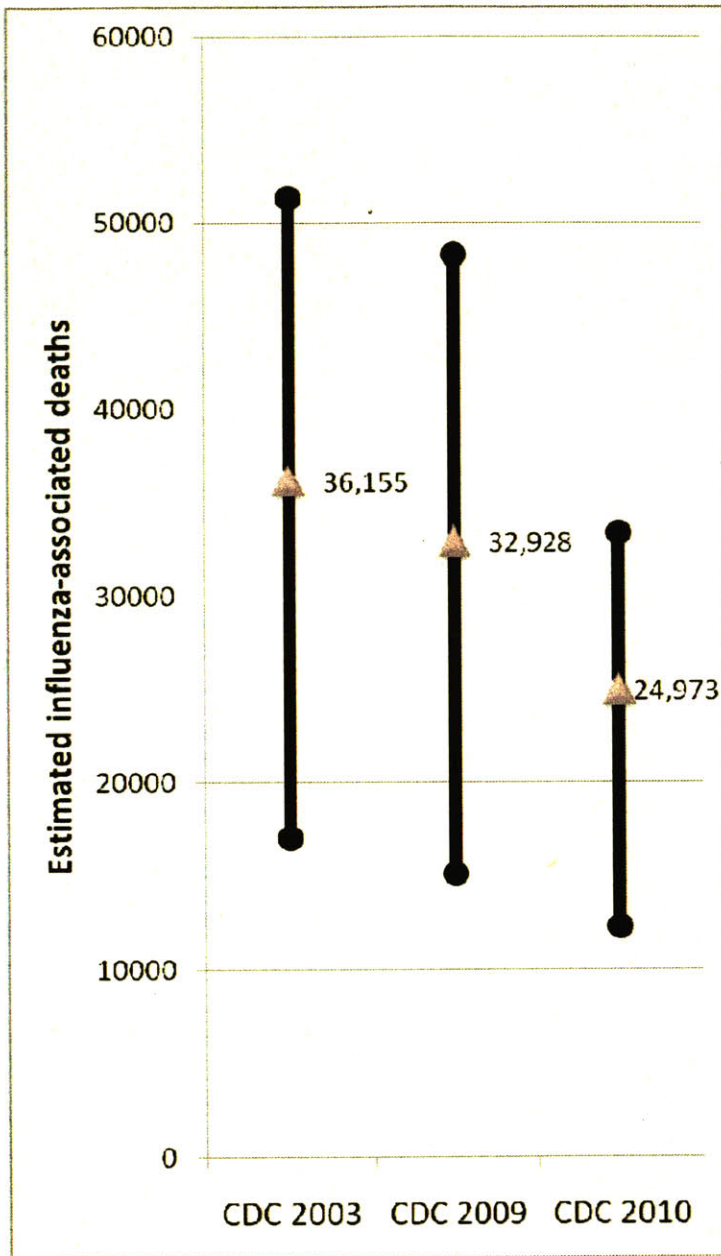


Figure 4.8. Estimates of influenza-associated underlying respiratory and circulatory deaths for 1990-91 to 1998-99, according to data presented in three CDC publications<sup>175</sup>

<sup>175</sup> Thompson et al., "Mortality associated with influenza and respiratory syncytial virus in the United States"; Thompson et al., "Estimates of US influenza-associated deaths made using four different methods"; U.S. Centers for Disease Control and Prevention, "Estimates of deaths associated with seasonal influenza --- United States, 1976-2007."

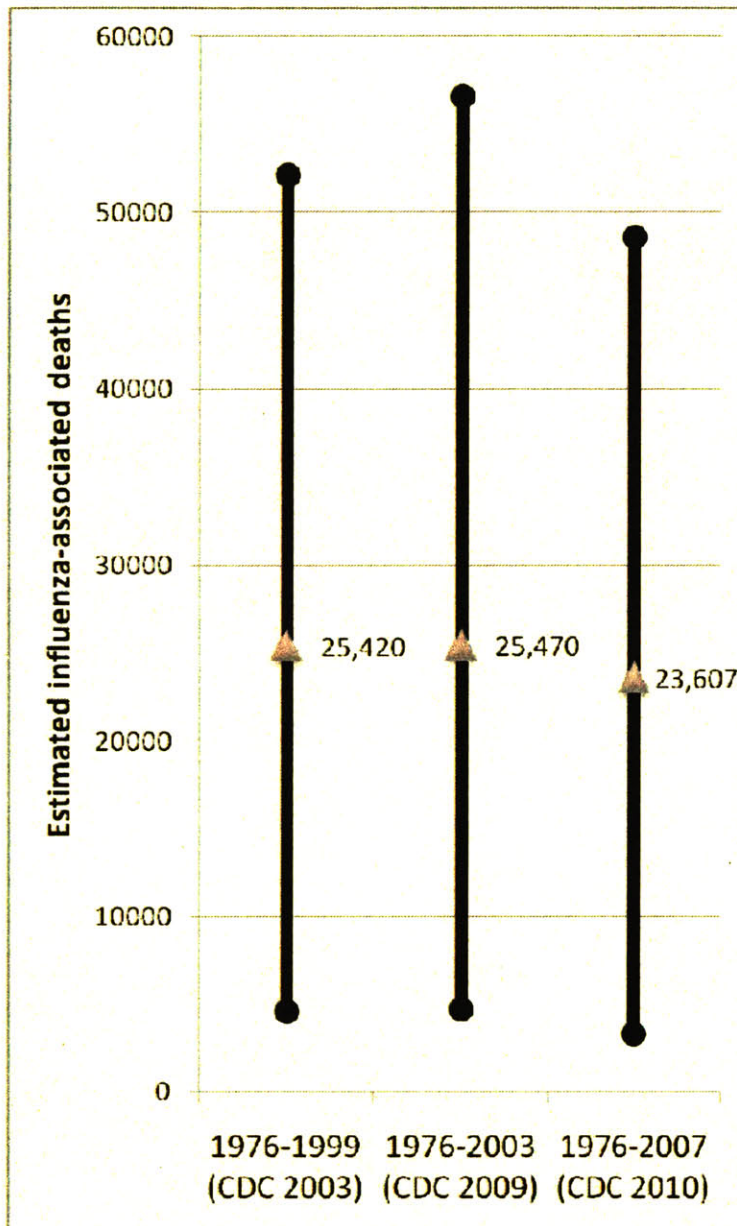


Figure 4.9. Minimum, maximum, and mean values of influenza-associated death over the entire study period, as calculated by the CDC's 2003 model<sup>176</sup> with updates in 2009<sup>177</sup> and 2010<sup>178</sup>

<sup>176</sup> Thompson et al., "Mortality associated with influenza and respiratory syncytial virus in the United States."

<sup>177</sup> Thompson et al., "Estimates of US influenza-associated deaths made using four different methods."

<sup>178</sup> U.S. Centers for Disease Control and Prevention, "Estimates of deaths associated with seasonal influenza --- United States, 1976-2007."

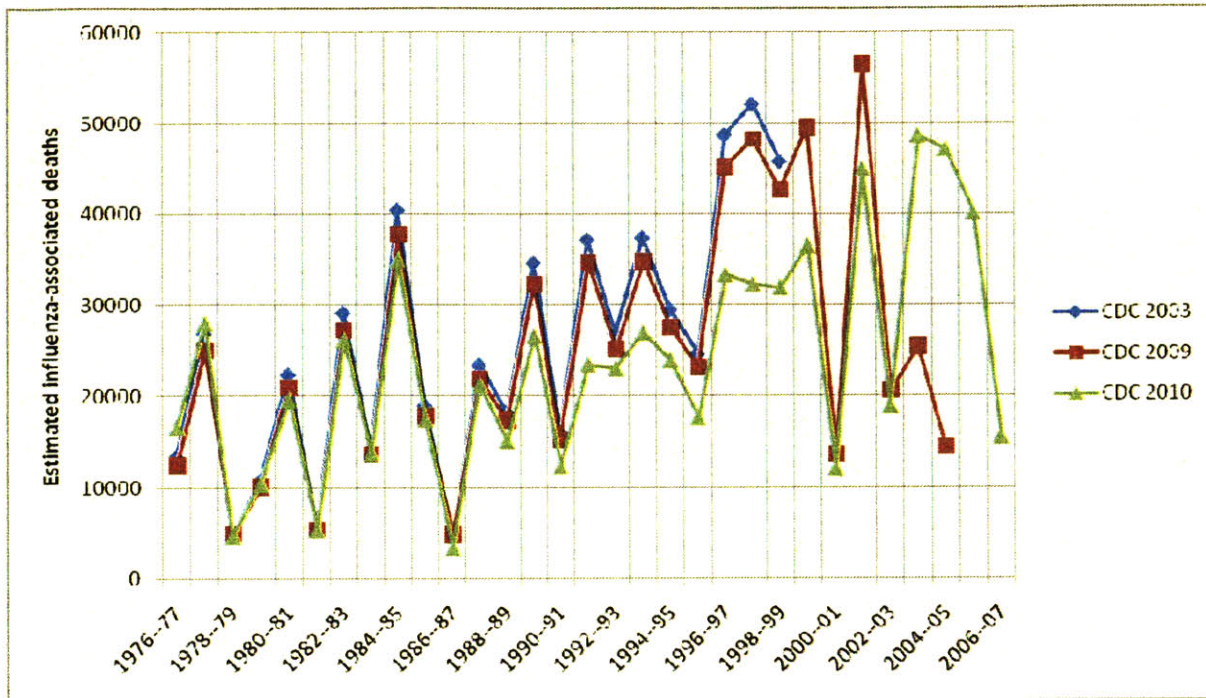


Figure 4.10. Reportedly using the same methods, CDC estimates of annual influenza-associated mortality differ across various publications. Reconstructed graph based on CDC data.<sup>179</sup>

<sup>179</sup> Thompson et al., "Mortality associated with influenza and respiratory syncytial virus in the United States"; Thompson et al., "Estimating Influenza-Associated Deaths in the United States"; U.S. Centers for Disease Control and Prevention, "Estimates of deaths associated with seasonal influenza --- United States, 1976-2007."

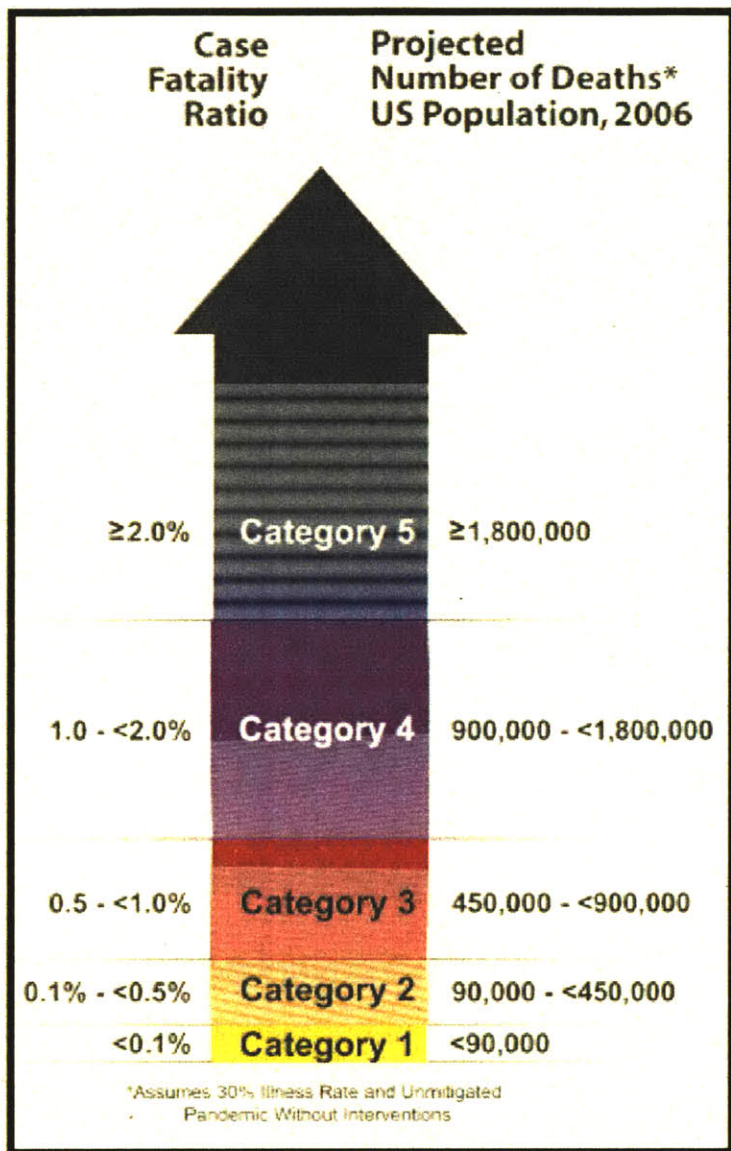


Figure 4.11. CDC's Pandemic Severity Index. Source: CDC<sup>180</sup>

<sup>180</sup> U.S. Centers for Disease Control and Prevention, "Interim Pre-pandemic Planning Guidance," 34.

Pandemic Severity Index			
Interventions* by Setting	1	2 and 3	4 and 5
<b>Home</b> <b>Voluntary isolation</b> of ill at home (adults and children); combine with use of antiviral treatment as available and indicated	<b>Recommend†§</b>	<b>Recommend†§</b>	<b>Recommend†§</b>
<b>Voluntary quarantine</b> of household members in homes with ill persons† (adults and children); consider combining with antiviral prophylaxis if effective, feasible, and quantities sufficient	<b>Generally not recommended</b>	<b>Consider**</b>	<b>Recommend**</b>
<b>School</b> <b>Child social distancing</b> -dismissal of students from schools and school based activities, and closure of child care programs -reduce out-of-school social contacts and community mixing	<b>Generally not recommended</b>  <b>Generally not recommended</b>	<b>Consider:</b> ≤4 weeks††  <b>Consider:</b> ≤4 weeks††	<b>Recommend:</b> ≤12 weeks§§  <b>Recommend:</b> ≤12 weeks§§
<b>Workplace / Community</b> <b>Adult social distancing</b> -decrease number of social contacts (e.g., encourage teleconferences, alternatives to face-to-face meetings) -increase distance between persons (e.g., reduce density in public transit, workplace) -modify postpone, or cancel selected public gatherings to promote social distance (e.g., postpone indoor stadium events, theatre performances) -modify work place schedules and practices (e.g., telework, staggered shifts)	<b>Generally not recommended</b>  <b>Generally not recommended</b>  <b>Generally not recommended</b>  <b>Generally not recommended</b>	<b>Consider</b>  <b>Consider</b>  <b>Consider</b>  <b>Consider</b>	<b>Recommend</b>  <b>Recommend</b>  <b>Recommend</b>  <b>Recommend</b>

Figure 4.12. Community mitigation strategy by pandemic severity. Source: CDC<sup>181</sup>

<sup>181</sup> Ibid., 36.

Characteristics	Pandemic Severity Index				
	Category 1	Category 2	Category 3	Category 4	Category 5
Case Fatality Ratio (percentage)	<0.1	0.1-<0.5	0.5-<1.0	1.0-<2.0	≥2.0
Excess Death Rate (per 100,000)	<30	30-<150	150-<300	300-<600	≥600
Illness Rate (percentage of the population)	20-40	20-40	20-40	20-40	20-40
Potential Number of Deaths (based on 2006 U.S. population)	<90,000	90,000-<450,000	450,000-<900,000	900,000-<1.8 million	≥1.8 million
20 <sup>th</sup> Century U.S. Experience	Seasonal Influenza (illness rate 5-20%)	1957,1968 Pandemic	None	None	1918 Pandemic

Figure 4.13. Seasonal influenza was said to be of Pandemic Severity Category 1. By contrast, the 1968 and 1957 pandemics were Category 2. Source: CDC.<sup>182</sup>

<sup>182</sup> Ibid., 32.

Figure 3A. Projected Mortality\* of a Modern Influenza Pandemic Compared with that of 20th Century Pandemics (1918, 1957, 1968)

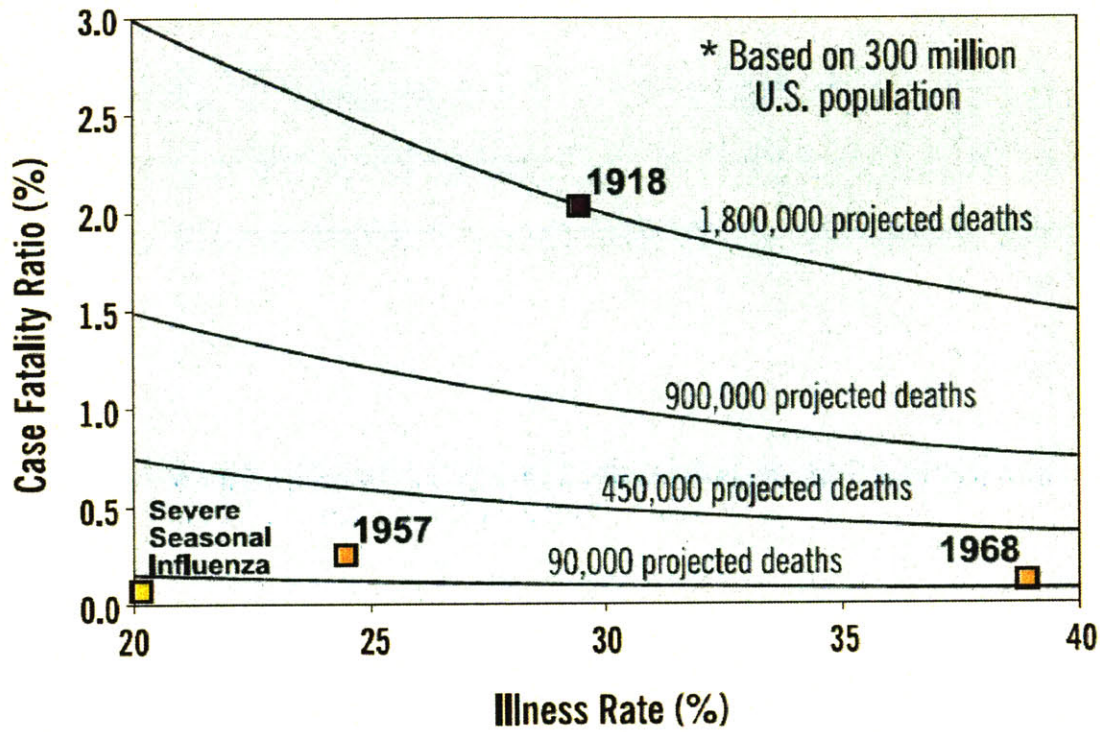


Figure 4.14. CDC graph indicating the projected impact of a pandemic with past pandemics (1918, 1957, 1968) and "Severe Seasonal Influenza" Source: CDC.<sup>183</sup>

<sup>183</sup> Ibid., 33.

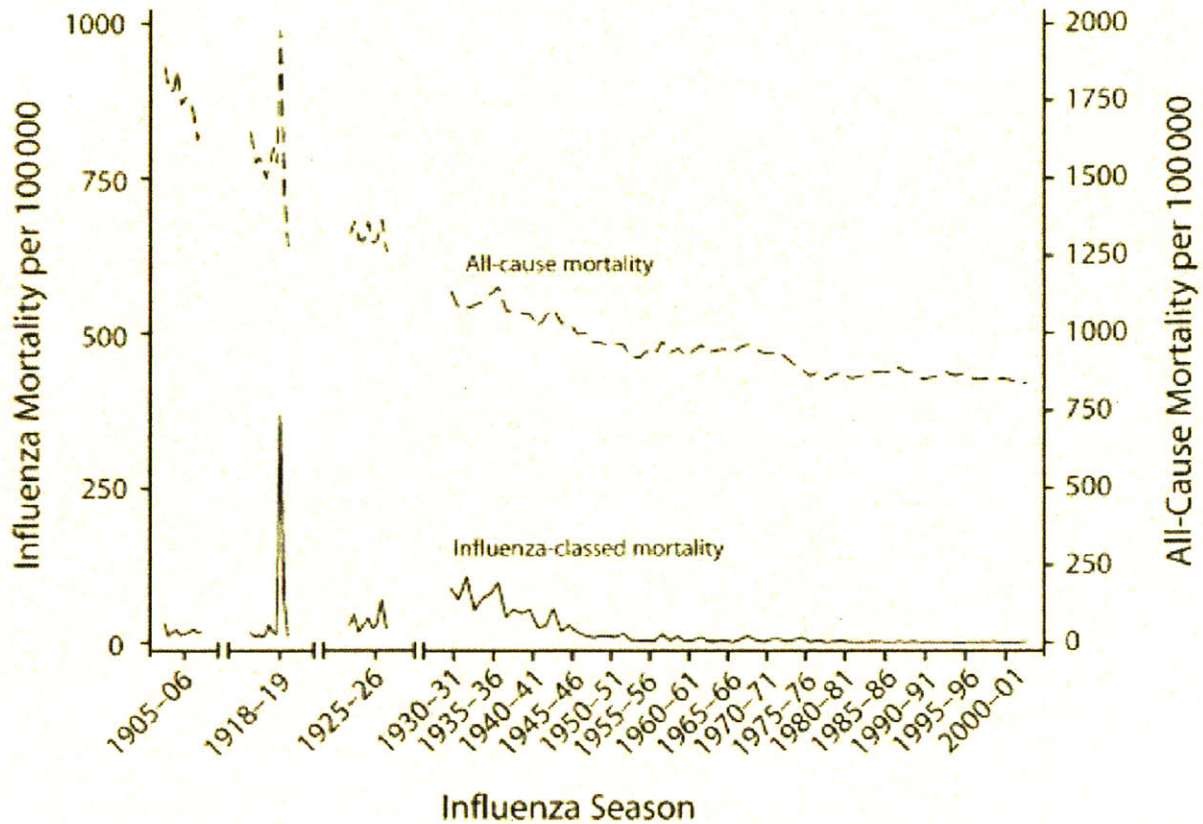


Figure 4.15. Crude mortality per 100 000 population, by influenza season (July to June of the following year), for seasons 1900–1901 to 2003–2004, United States. *Note.* International Classification of Diseases (ICD) revision 1 was used from 1900 to 1909, revision 2 from 1910 to 1920, revision 3 from 1921 to 1929. Comparability ratios are unavailable for revisions 1 to 3. Beginning in 1930, influenza mortality rates have been adjusted for changes in ICD revisions to reflect conditions in the current ICD revision 10. (Reproduced with permission from Peter Doshi, “Trends in recorded influenza mortality: United States, 1900–2004,” *American Journal of Public Health* 98, no. 5 (May 2008): 939–45. Copyright held by American Public Health Association.)



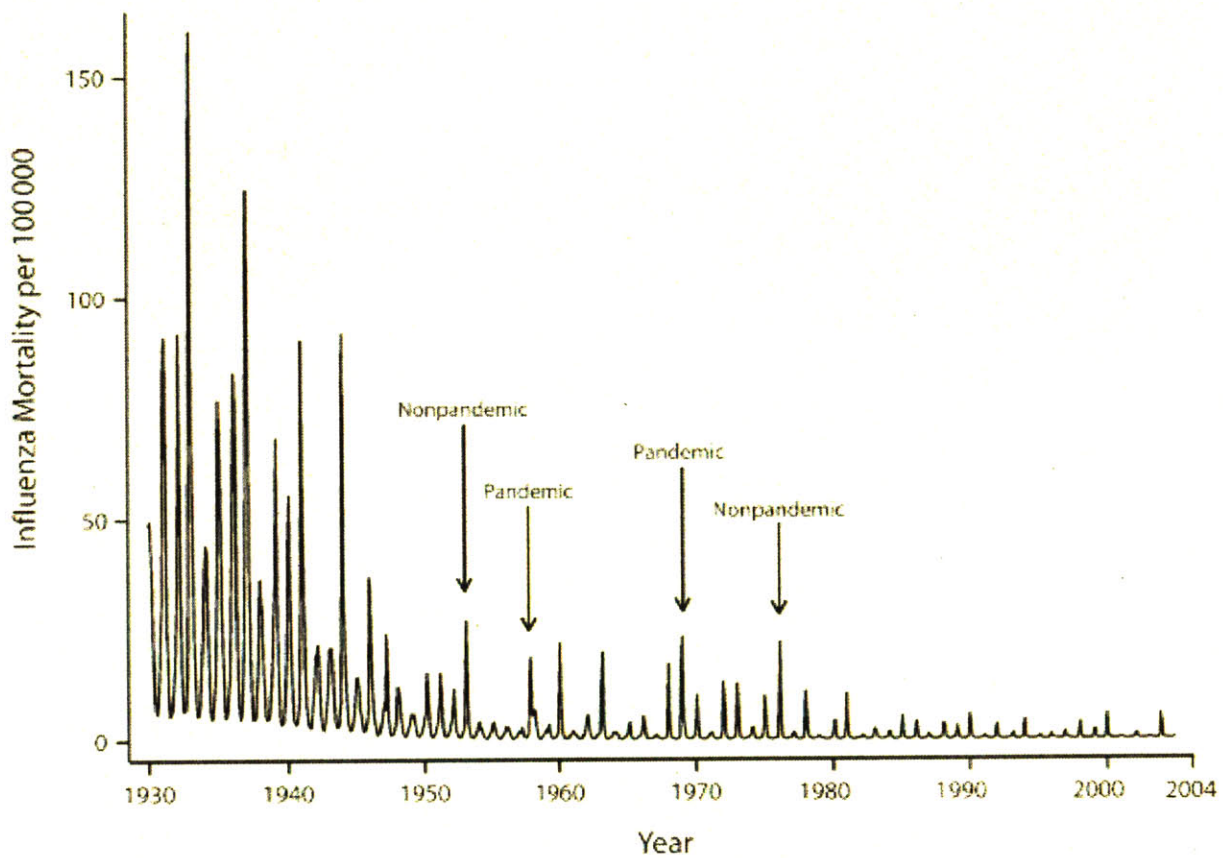


Figure 4.16. Crude influenza-classed mortality per 100 000 population, by month for 1930–2004, United States. (Reproduced with permission from Peter Doshi, “Trends in recorded influenza mortality: United States, 1900–2004,” *American Journal of Public Health* 98, no. 5 (May 2008): 939–45. Copyright held by American Public Health Association.)

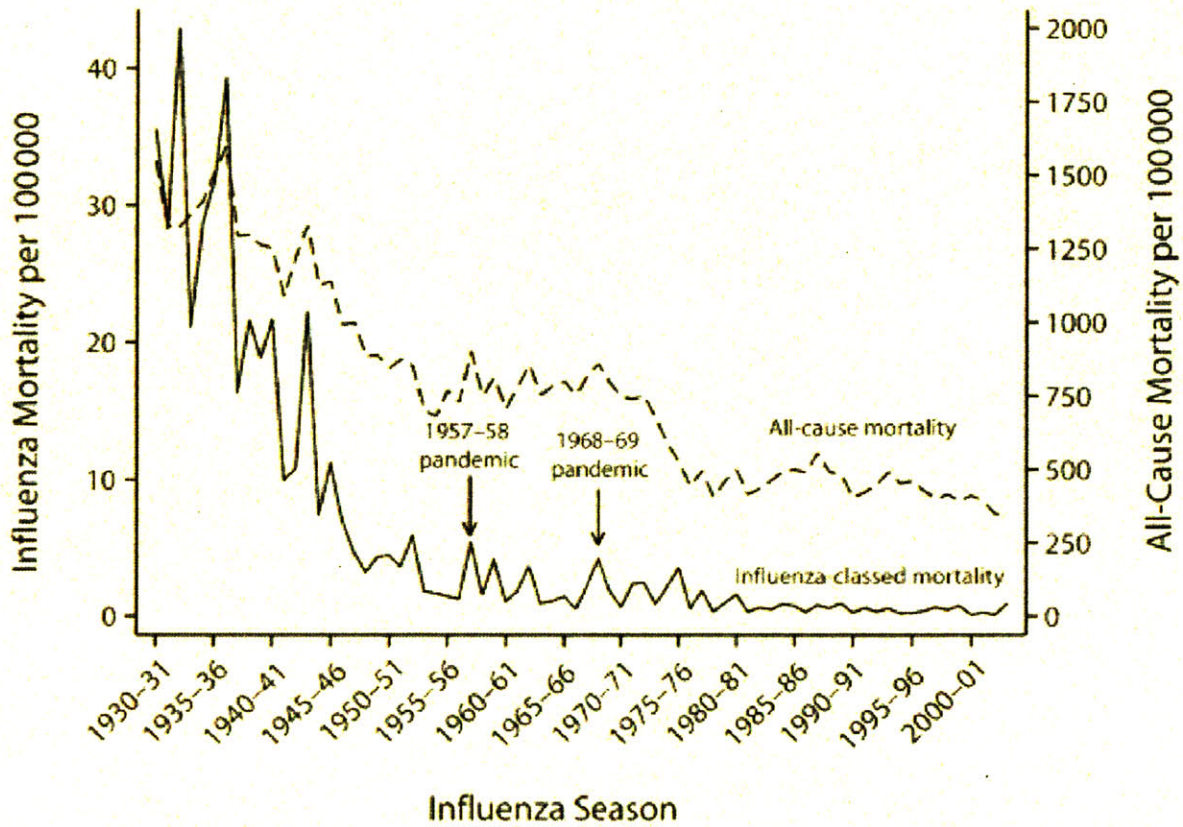


Figure 4.17. Crude mortality per 100 000 population, by influenza season (July to June of the following year), for seasons 1930–1931 to 2003–2004, United States. Note. Influenza mortality rates have been adjusted for changes in ICD revisions to reflect conditions in the current ICD revision 10. (Reproduced with permission from Peter Doshi, “Trends in recorded influenza mortality: United States, 1900–2004,” *American Journal of Public Health* 98, no. 5 (May 2008): 939–45. Copyright held by American Public Health Association.)

**TOP**  
**3** reasons to get your **flu vaccine**

- 1 Prevents influenza-related death.**  
Each year over 36,000 people in the U.S. die because of the flu—most are 65 or older. More people die from flu than from any other vaccine-preventable disease.
- 2 Prevents severe illness.**  
In the U.S. influenza puts about 200,000 people in the hospital each year. Children younger than 2 years old are as likely to be hospitalized as adults who are 65 or older.
- 3 Protects other people.**  
You should get vaccinated if you live with or care for others who are at high risk of complications from the flu. Getting a flu vaccination yourself can help protect your family members, including seniors and young children.

**CDC**  
Centers for Disease Control and Prevention  
Department of Health and Human Services

**Protect yourself. Protect your loved ones.**  
Get your flu vaccine.

For more information, ask your healthcare provider or call 800-CDC-INFO (800-232-4636) Website [www.cdc.gov/flu](http://www.cdc.gov/flu)

Figure 4.18. CDC promotional materials have often emphasized the morbidity and mortality burden of influenza the disease.<sup>184</sup>

<sup>184</sup> U.S. Centers for Disease Control and Prevention, "Top 3 reasons to get your flu vaccine."

**Slide 2**

**Influenza:  
A significant public health issue**

- Approximately 314,000 hospitalizations annually due to influenza and its complications<sup>1</sup>
- 20,000 to 40,000 influenza-related deaths each year<sup>1</sup>
- Annual direct and indirect costs totaling over \$12 billion<sup>2</sup>
- 75 million lost workdays per year<sup>3</sup>

<sup>1</sup> Sullivan P.M. Pharmacoeconomics 1996  
<sup>2</sup> Nishi K. N. Eng. J. Med. 1994  
<sup>3</sup> Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/ncidod/diseases/flu.htm>  
Accessed 1999

**The burden of influenza:  
significant morbidity and  
mortality**

Influenza is a serious disease affecting 108 million Americans in a given year— with 20,000 to 40,000 influenza-related deaths.<sup>1,2</sup>

Figure 4.19. Clipping from one of several Glaxo Wellcome promotional materials for Relenza (October 1999) that was cited by the FDA as in violation of the law.<sup>185</sup>

<sup>185</sup> Glaxo Wellcome Inc., "Want to get over the flu sooner?", October 1999, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM165381.pdf>, (accessed July 25, 2011).

## Chapter 5 Viral Essentialism and the Logic of VPDs

*Save a patient's life  
(Get your flu vaccine)*

Poster displayed at University of Virginia<sup>1</sup>

For over a decade, Tom Jefferson has led efforts at the Cochrane Collaboration, conducting systematic reviews of the safety and effectiveness of influenza vaccines and antivirals. Since 2007, he began doing the same for interventions such as hand washing, face masks, gowns, and other “physical interventions.”<sup>2</sup> At the Council of Europe hearings in 2010, Jefferson cited his research, declaring that “public health interventions such as hygiene measures and barriers have a much better evidence base than vaccines. They are also cheaper and socially acceptable, as well as being life savers in poor countries, yet they are almost ignored.”<sup>3</sup> Jefferson argued that World Health Organization (WHO) had its priorities wrong, and had become an agency preoccupied with vaccines and antivirals. He pointed out that in the WHO’s 62-page guidance document on pandemic influenza, “handwashing and masks were mentioned only twice ... but vaccines and antivirals appeared 24 and 18 times, respectively.” Emphasizing that the problem is the syndrome influenza-like illness, not any particular virus over another, Jefferson cited evidence from the SARS experience to impress upon people the power of non-pharmacological interventions like hand washing. “To give some idea of how they compare with influenza vaccines as a public health measure,” he said, citing a systematic review<sup>4</sup> he had recently updated, “six studies carried out in the Far East during the 2003 SARS epidemic shows that just 3-4 people have to wash hands, and wear masks to prevent one case of SARS.”<sup>5</sup>

In the United States, I had previously criticized the Centers for Disease Control and Prevention (CDC) for a similar lack of attention to the effectiveness of hand washing, citing Jefferson’s findings. In a letter to the British medical journal *BMJ* in 2008, I commented that while the United States’ policy recommendations for the prevention and control of influenza are over 25,000 words long, “only one sentence of that document mentions non-pharmaceutical interventions, only to brush them off as having ‘not been studied adequately.’”<sup>6</sup> Since this letter, successive editions of national recommendations have given more attention to hand washing, but US officials’ mood remains overwhelmingly pessimistic (Table 5.1). The most recent recommendations state that “the impact of hygiene interventions such as handwashing on influenza virus transmission is not well understood, and

<sup>1</sup> Cassandra D Salgado et al., “Influenza in the acute hospital setting,” *The Lancet Infectious Diseases* 2, no. 3 (March 2002): 145-155.

<sup>2</sup> Tom Jefferson et al., “Physical interventions to interrupt or reduce the spread of respiratory viruses,” *Cochrane Database of Systematic Reviews (Online)*, no. 1 (2010): CD006207.

<sup>3</sup> Tom Jefferson, *The handling of the H1N1 pandemic: more transparency needed?* (Strasbourg, France, 2010), 12, [http://assembly.coe.int/CommitteeDocs/2010/Jefferson\\_statement.pdf](http://assembly.coe.int/CommitteeDocs/2010/Jefferson_statement.pdf), (accessed March 30, 2010).

<sup>4</sup> Jefferson et al., “Physical interventions to interrupt or reduce the spread of respiratory viruses.”

<sup>5</sup> Jefferson, *The handling of the H1N1 pandemic: more transparency needed?*, 12.

<sup>6</sup> Peter Doshi, “Preventing flu-like illness: Reason for optimism,” *BMJ* 336, no. 7637 (January 26, 2008): 172.

hygiene measures should not be advocated as a replacement or alternative to specific prevention measures such as vaccination.”<sup>7</sup>

However in 2009, in the first few months of the H1N1 outbreak, the US government made an enormous investment promoting good hand hygiene<sup>8</sup>—Secretary of Health and Human Services Kathleen Sebelius co-starred in public service commercials with Sesame Street characters, urging people to regularly and thoroughly wash their hands and cough into their elbows,<sup>9</sup> a message repeated all the way up to the president.<sup>10</sup> But even here, officials apparently did not do so out of any firm conviction in the strength of the evidence. “We don’t have solid data on the effect that hand washing has on the transmission of H1N1,” a spokesman for the CDC explained. But, the spokesman added, “There are studies that show hand washing was effective in reducing transmission of other respiratory diseases.”<sup>11</sup>

### **Based on sound science**

The CDC’s statement—in defense of its promotion of hand washing while simultaneously acknowledging the lack of data to support its efficacy—is emblematic of the agency’s interest in being known as a fundamentally scientific agency. Part of the “CDC Pledge” states that the agency shall “base all public health decisions on the highest quality scientific data, openly and objectively derived.”<sup>12</sup> Yet as the previous chapter detailed, there are a series of fundamental problems with contemporary influenza policy.

First, the emphasis on influenza vaccines and antivirals is myopic, as these interventions only fight one virus (influenza) and not the broader syndrome the public knows as the “flu” (but is better termed influenza-like illness), a fact the public is unaware of because it is continually misled into believing “flu” is influenza. Second, the efficacy of pharmacological interventions—even against true influenza—is overstated. Finally, there are major problems with risk assessment: no ongoing surveillance systems exist today that are capable of accurately estimating the degree to which influenza is responsible for the morbidity and mortality attributable to influenza-like illness, and official model-derived estimates for influenza-associated deaths are inconsistent.

All of these problems are well known within the specialist community of experts that study influenza. Nevertheless, the problems have done little to slow the enthusiasm around influenza and vaccines.

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<sup>7</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010,” 9-10.

<sup>8</sup> Anne Schuchat, Beth P Bell, and Stephen C Redd, “The science behind preparing and responding to pandemic influenza: the lessons and limits of science,” *Clinical Infectious Diseases* 52 Suppl 1 (January 1, 2011): S10.

<sup>9</sup> U.S. Department of Health and Human Services, “HHS Secretary Kathleen Sebelius, Sesame Workshop, and the Ad Council Launch National Campaign to Protect Families from H1N1 Virus and Stay Healthy”, May 22, 2009, <http://www.hhs.gov/news/press/2009pres/05/20090522a.html>, (accessed April 27, 2011).

<sup>10</sup> Barack Obama, “Remarks by the President on 2009-H1N1 National Preparedness and Response”, September 1, 2009, [http://www.whitehouse.gov/the\\_press\\_office/Remarks-by-the-President-on-2009-H1N1-National-Preparedness-and-Response/](http://www.whitehouse.gov/the_press_office/Remarks-by-the-President-on-2009-H1N1-National-Preparedness-and-Response/), (accessed April 27, 2011).

<sup>11</sup> Elizabeth Cohen, “Some doubt hand washing stops H1N1,” *CNN Health*, September 24, 2009, <http://www.cnn.com/2009/HEALTH/09/24/hand.washing.helpful/index.html>, (accessed April 20, 2011).

<sup>12</sup> U.S. Centers for Disease Control and Prevention, “Vision, Mission, Core Values, and Pledge”, January 11, 2010, <http://www.cdc.gov/about/organization/mission.htm>, (accessed June 17, 2011).

Initiatives like the annual National Influenza Vaccine Summit, led by the CDC and the American Medical Association (AMA), have helped align and increase coordination amongst a growing list of organizations from the public and private sector dedicated to increasing the number of people who get influenza vaccine each year. Following the CDC's expansion of its annual influenza vaccination recommendation in 2010 to all Americans, the American Academy of Pediatrics (AAP),<sup>13</sup> the Society for Healthcare Epidemiology of America (SHEA),<sup>14</sup> the Infectious Diseases Society of America (IDSA),<sup>15</sup> and Association for Professionals in Infection Control and Epidemiology (APIC)<sup>16</sup> all called for the mandatory vaccination of healthcare practitioners, suggesting that receipt of influenza vaccine should be a condition of employment. More recently, in April 2011, the US Joint Commission—the accreditation body of over 18,000 US healthcare organizations—released “proposed requirements addressing influenza vaccination of staff and licensed independent practitioners” which, if enacted, will tie institutional accreditation with a responsibility to intensify efforts to increase influenza vaccine uptake.<sup>17</sup> The situation is much the same at the international level. The WHO-appointed International Health Regulations committee to review WHO's response to H1N1 recommended that “in so far as it is consistent with national priorities, risk assessments and resources, the Review Committee urges countries to immunize their high-risk populations yearly against seasonal influenza.”<sup>18</sup> All of these policymakers emphasize the burden of the disease influenza—its complications and impact on society—and all advocate influenza vaccine, reinforcing the notion that vaccines will substantially reduce that disease burden.

For those who see the gap between evidence and policy as the result of industrial interests trumping sound science, there is a considerable amount of evidence to argue the case. The perhaps most well publicized case is that of former Defense secretary Donald Rumsfeld, who was once chairman of Gilead Sciences, the company that invented Tamiflu.<sup>19</sup> When governments began stockpiling the drug in anticipation of a pandemic—the United States is reported to have stockpiled somewhere around \$12.5 billion worth<sup>20</sup>—Rumsfeld's stock holdings were reported to have turned profits in the millions.<sup>21</sup>

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<sup>13</sup> Bernstein, Starke, and Committee on Infectious Diseases, “Recommendation for Mandatory Influenza Immunization of All Health Care Personnel.”

<sup>14</sup> Talbot et al., “Revised SHEA Position Paper.”

<sup>15</sup> Infectious Diseases Society of America, “IDSA call for mandatory influenza vaccination of HCW.”

<sup>16</sup> Association for Professionals in Infection Control and Epidemiology, “APIC Position Paper: Influenza Vaccination Should Be a Condition of Employment for Healthcare Personnel, Unless Medically Contraindicated.”

<sup>17</sup> The Joint Commission, “Influenza Vaccination of Staff and Licensed Independent Practitioners”, 2011, [http://www.jointcommission.org/standards\\_information/field\\_reviews.aspx?StandardsFieldReviewId=KUB%2fsbNgRkNRMRqj62GdO2RnacCewOVZR6%2bkN1Vlply%3d](http://www.jointcommission.org/standards_information/field_reviews.aspx?StandardsFieldReviewId=KUB%2fsbNgRkNRMRqj62GdO2RnacCewOVZR6%2bkN1Vlply%3d), (accessed April 18, 2011).

<sup>18</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, “Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009,” 21.

<sup>19</sup> Gilead Sciences, “Donald H. Rumsfeld Named Chairman of Gilead Sciences”, January 3, 1997, [http://www.gilead.com/wt/sec/pr\\_933190157/](http://www.gilead.com/wt/sec/pr_933190157/), (accessed June 4, 2011).

<sup>20</sup> New York Times, “Tamiflu (Drug)”, April 28, 2009, <http://topics.nytimes.com/topics/news/health/diseasesconditionsandhealthtopics/tamiflu-drug/index.html>, (accessed August 1, 2011).

But numerous other cases exist at the domestic and international policy levels. Dr. Gregory Poland, for example, was a voting member of the federal Advisory Committee on Immunization Practices (and remains on the ACIP Influenza Work Group), which sets influenza policy in the United States. Poland, who is editor-in-chief of the journal *Vaccine* and a professor of medicine at the Mayo Clinic College of Medicine, has long urged ACIP to make a universal influenza vaccination recommendation.<sup>22</sup> He is also well connected to pharmaceutical companies, and has reported chairing a Merck Data Monitoring and Safety Board, serving on the DVC scientific advisory board and conducting clinical trials for Chiron, Merck, and Vaxgen.<sup>23</sup> More recently, he has reported offering “consultative advice on novel influenza vaccine development to Merck & Co., Inc., Avianax, Theraclone Sciences (formally Spaltudaq Corporation), MedImmune LLC, Liquidia Technologies, Inc., Novavax, EMD Serono, Inc., Novartis Vaccines and Therapeutics and PAXVAX, Inc.”<sup>24</sup> Similarly, Dr. John Treanor, professor of medicine at the University of Rochester Medical Center, and also a member of ACIP in 2006 when the committee made its first clear statement of intent to move to a universal vaccination policy,<sup>25</sup> reported “conducting influenza vaccine clinical trials for Merck, GlaxoSmithKline (ID Biomedical); Protein Sciences Corporation, and conducting laboratory studies for AlphaVax.”<sup>26</sup>

The many key architects of European and global influenza policy over the last decade who recent investigations have shown were likewise simultaneously working for companies that manufactured influenza vaccines and antivirals has brought attention to the way in which industrial interests have shaped influenza policy.<sup>27</sup> Most recently, five individuals on the formerly secret 16-member committee that advised the WHO Director-General to declare a pandemic disclosed financial relationships with the pharmaceutical industry, including the director of CDC’s Influenza Division.<sup>28</sup>

### More than money

Yet as important as industrial relationships are to understanding the formation of global and domestic influenza policy, it seems unlikely to fully explain the gap between evidence and practice. Considerable conflicts of interest certainly exist among those that advise government and set policy, but what about the other many individuals who have not received money from industry yet still largely agree with and carry out current policy? When ACIP discussed the possibility of an evolving strategy towards universal influenza vaccination in February 2006, Drs. Poland and Treanor may have voted in favor of the

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<sup>21</sup> Geoffrey Lean and Jonathan Owen, “Donald Rumsfeld makes \$5m killing on bird flu drug,” *The Independent*, March 12, 2006, <http://www.independent.co.uk/news/world/americas/donald-rumsfeld-makes-5m-killing-on-bird-flu-drug-469599.html>, (accessed July 18, 2011).

<sup>22</sup> Gregory A. Poland, “The Long Road to a Universal Influenza Immunization Recommendation: What Took So Long?”, May 19, 2010, [http://www.preventinfluenza.org/NIVS\\_2010/4\\_Poland.pdf](http://www.preventinfluenza.org/NIVS_2010/4_Poland.pdf), (accessed May 21, 2010).

<sup>23</sup> “Record of the meeting of the Advisory Committee on Immunization Practices”, February 21, 2006, 42, <http://www.cdc.gov/vaccines/recs/acip/downloads/min-archive/min-feb06.pdf>, (accessed June 16, 2011).

<sup>24</sup> Gregory A. Poland, “Mandating influenza vaccination for health care workers: Putting patients and professional ethics over personal preference,” *Vaccine* 28, no. 36 (August 2010): 5759.

<sup>25</sup> Smith et al., “Prevention and Control of Influenza,” 42.

<sup>26</sup> “Record of the meeting of the Advisory Committee on Immunization Practices,” 6.

<sup>27</sup> Cohen, “Complications”; Cohen and Carter, “WHO and the pandemic flu ‘conspiracies’.”

<sup>28</sup> World Health Organization, “List of Members of, and Advisor to, the International Health Regulations (2005) Emergency Committee concerning Influenza Pandemic (H1N1) 2009.”



initiative—which would clearly carry huge benefits to vaccine manufacturers—but so too did five others on the committee, none of whom declared conflicts of interest. A fuller understanding of influenza policy making therefore must seek to explain why these individuals appear convinced of the threat of influenza and the promise of influenza vaccines despite the fragility of the scientific evidence base. In Geneva, the WHO’s response to H1N1 in 2009 was heavily guided by its 2009 pandemic plan, a document that had been shaped and reviewed by over 100 outside experts. But only seven of these individuals declared potential conflicts of interest—the great majority had nothing to declare, yet were presumably comfortable with the Organization’s advice.<sup>29</sup> Similarly, while it is true that many of WHO’s decisions during the 2009 H1N1 outbreak were of great benefit to industry, the majority of those advising the Director-General had no potential conflicts of interest to declare. Yet they, too, felt confident that the H1N1 outbreak qualified as a pandemic—and all seem to stand by their decisions.

Understanding the reason why so many official bodies—and the individuals who comprise them—endorse and perpetuate problematic science despite having no financial ties to industry is the aim of this chapter. I want to propose an explanation for why officials simultaneously embraced and advocated measures like hand washing in 2009, yet distanced themselves from that same advice when asked to speak in their scientific role. I will seek to explain the enthusiasm behind influenza vaccines, despite the well-known limitations in the strength of evidence in their favor—and the zeal to which pandemic preparedness has been pursued as a strategy to mitigate against a future worst-case, 1918-like catastrophic event with little attention to other pandemics, which were no more deadly than ordinary influenza.

In a nutshell, my argument is that the simplicity of conceiving influenza as an infectious disease caused by a single pathogen (influenza virus) has conferred a definitiveness and stability that has the appearance of being value neutral and objective, enabling certain mindsets and approaches to influenza, while disabling others. I will focus on how, in particular, by using the label of influenza as a “vaccine preventable disease,” or VPD as it is often abbreviated, public health experts defend the sensibility of the entire policy—from surveillance policies and vaccination policies to pandemic preparedness, thereby attaching more certainty about the natural world than has ever been supported by the empirical evidence. Thinking of influenza as a VPD has pushed responses in a “one disease – one cause – one drug” (or in this case vaccine) framework that is emblematic of what I call *virus-centric thinking*. This kind of essentialist thinking has become so commonplace and ingrained in the logics of public health that it prevents most practitioners from even seeing and addressing fundamental gaps in their effort.

\* \* \*

### **Fixated on technology**

In the summer of 2010, Dr. Kathleen Gensheimer agreed to sit down with me and discuss influenza control policy. Gensheimer is a friend and equally passionate about influenza, but more often than not, we disagree about the right headedness of official policies, many of which she was responsible for

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<sup>29</sup> World Health Organization, *Pandemic influenza preparedness and response (reprinted)*.

during her 28-year career as the state epidemiologist of Maine. I asked Gensheimer to describe the reason why most experts seem relatively unenthusiastic about measures like handwashing.

Gensheimer lumped hand washing with other nonpharmaceutical interventions like isolation (staying home when sick) and getting lots of rest, one of many “humdrum recommendations” out there.<sup>30</sup> She explained that of course experts could implore people to “Wash your hands like your mother always told you to.” But she doubted the public would take it seriously. Most people would reason that “because your mother told you to do it, it must not be worth that much.” Moreover, she reasoned, it’s not technical.

Kathleen Gensheimer: You know people are looking for these technological fixes.

Peter Doshi: Who are the people you’re talking about?

Gensheimer: I think the public even... I think the public wants a prescription to go to the doctor. They don’t want to be told to wash their hands. They want something fancier than that, something that’s going to make them feel more assured. And washing your hands and telling you to stay home when you’re sick and covering your cough... I mean, we’ve done a lot done a lot to promote that and it’s being done more and more...

But they are not technological fixes whereas vaccines are—and a spectacular one at that. There is rarely a list of public health achievements that does not include vaccination. At the turn of the millennium, CDC director Jeffrey Koplan called on the agency<sup>31</sup> to publish a celebratory list of the “Ten Great Public Health Achievements” over the twentieth century.<sup>32</sup> The CDC’s list included the “recognition of tobacco use as a health hazard,” “safer workplaces,” the “control of infectious diseases” (from clean water and improved sanitation), and “healthier mothers and babies.” The list, however, also included—and began with—vaccination. “Vaccines are one of the greatest achievements of biomedical science and public health,” the CDC declared, recalling the history of smallpox eradication and announcing the United States’ plans to eradicate polio worldwide through vaccination by the end of the year 2000.<sup>33</sup>

“The impact of vaccination on the health of the world’s people is hard to exaggerate. With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction and population growth,” wrote Susan Plotkin and Stanley Plotkin in their introduction to the second edition of the definitive textbook *Vaccines*.<sup>34</sup> In a separate publication, two historians of medicine from the University of Michigan fully agreed:

<sup>30</sup> Interview with Kathleen Gensheimer, August 16, 2010.

<sup>31</sup> J. P. Koplan, “I’ve got a little list,” *BMJ* 334, no. 1 (January 2007): s20-s20.

<sup>32</sup> “Ten great public health achievements--United States, 1900-1999,” *MMWR. Morbidity and Mortality Weekly Report* 48, no. 12 (April 2, 1999): 241-243.

<sup>33</sup> “Impact of vaccines universally recommended for children--United States, 1990-1998,” *MMWR. Morbidity and Mortality Weekly Report* 48, no. 12 (April 2, 1999): 243-248.

<sup>34</sup> Susan L. Plotkin and Stanley A. Plotkin, “A short history of vaccination,” in *Vaccines*, ed. Stanley A. Plotkin and Edward A. Mortimer, 2nd ed. (W B Saunders Co, 1994), 1.

[I]f you asked a public health professional to draw up a top-ten list of the achievements of the past century, he or she would be hard pressed not to rank immunization first. Millions of lives have been saved and microbes stopped in their tracks before they could have a chance to wreak havoc. In short, the vaccine represents the single greatest promise of biomedicine: disease prevention.<sup>35</sup>

In an online poll conducted by the medical journal *BMJ* in 2007, doctors, academic researchers, medical students and other readers of the *BMJ* voted among 15 choices for “the most important medical advance since 1840.”<sup>36</sup> While the list included basic scientific discoveries (such as the structure of DNA), theories (germ theory), technologies (computers), and specific interventions (oral contraceptive pill, chlorpromazine), vaccines came in fourth—trailing sanitation, antibiotics, and anesthesia.<sup>37</sup>

### Vaccines as “miracles”

Microsoft co-founder turned philanthropist billionaire Bill Gates has been particularly struck by the power of vaccines. “Vaccines are a miracle,” he declared in his *Annual Letter from Bill Gates*, arguing that rich countries have a moral imperative to secure the welfare of the poor. The business mogul focused his argument on the necessity of ending polio, writing that vaccines are “the most effective and cost-effective health tool ever invented. I like to say vaccines are a miracle.”<sup>38</sup> “They’re miracles because giving children a couple of drops or a shot in the arm can prevent some of the worst childhood diseases for a lifetime. And that, to me, is a miracle.”<sup>39</sup>

Gates is far from the only one to speak of vaccines as a form of “magic,” a “modern miracle” so transformative and effective as to wipe diseases from the face of the planet.<sup>40</sup> Enthusiasm about vaccines is not hard to understand: today, the success story of vaccines is often told through the story of smallpox. In 1966, when the World Health Assembly resolved to intensify its efforts in a global campaign to eradicate the disease, smallpox virus was estimated to be causing 10 to 15 million cases annually, with two million deaths. A decade later, following a massive, worldwide vaccination campaign, those numbers dropped to zero.<sup>41</sup>

While the global eradication of smallpox is today the most commonly portrayed example of vaccines as miracles, it is not the first. A particularly American drama unfolded during the 1950s in the race to develop a vaccine as the cure for polio. At its height in the 1940s and 1950s, polio epidemics terrorized

<sup>35</sup> Alexandra Minna Stern and Howard Markel, “The History Of Vaccines And Immunization: Familiar Patterns, New Challenges,” *Health Affairs* 24, no. 3 (May 1, 2005): 611 -621.

<sup>36</sup> “Medical Milestones,” *BMJ*, 2007, [http://www.bmj.com/content/334/suppl\\_1/rel-suppl/e2c7f6624909d7b0/suppl/DC3](http://www.bmj.com/content/334/suppl_1/rel-suppl/e2c7f6624909d7b0/suppl/DC3), (accessed July 18, 2011).

<sup>37</sup> Koplan, “I’ve got a little list”; “Medical Milestones.”

<sup>38</sup> Bill Gates, “2011 Annual Letter from Bill Gates”, 2011, 9, <http://www.gatesfoundation.org/annual-letter/2011/Documents/2011-annual-letter.pdf>, (accessed May 4, 2011).

<sup>39</sup> *Bill Gates: Vaccines Save Lives*, 2011, <http://www.youtube.com/watch?v=JZvpF6gaGH4>, (accessed July 18, 2011).

<sup>40</sup> UK NHS Choices, “The power of vaccines”, November 12, 2010, <http://www.nhs.uk/Planners/vaccinations/Pages/miracles.aspx>, (accessed May 4, 2011); D A Henderson, “The miracle of vaccination,” *Notes and Records of the Royal Society of London* 51, no. 2 (July 1997): 244; Michael Gerson, “A shot at hope,” *The Washington Post*, January 18, 2011.

<sup>41</sup> Henderson, “The miracle of vaccination,” 238.

families across the country. The disease most commonly struck society's most vulnerable—children—and did so in seemingly random patterns, and without warning. If contracted, polio could kill. For others, infection would lead to deformations of the body, particularly the limbs, leading many to a life of wheelchairs, leg braces, or crutches. Some even needed help breathing. Although polio was, even at its height, an uncommon disease, organized efforts to fund raise, advertise and promote the disease and its potential cure in vaccination, helped ensure that polio become one of America's most feared diseases, and that the vaccine, once developed, would be welcomed by a public desperate for a long-awaited cure.<sup>42</sup>

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Many histories identify the year 1796 as the birth of the vaccine miracle. Edward Anthony Jenner is the hero of this story, credited with the discovery of smallpox vaccine after demonstrating the ability to induce protective immunity against smallpox following inoculation of material from cowpox blisters. While other methods of inducing protective immunity against smallpox preceded Jenner's smallpox vaccine by perhaps a thousand or more years—notably variolation (the deliberate inoculation of infectious material to produce an attenuated form of the disease and thereafter confer immunity, practiced in North Africa, India, China, and other parts of the world<sup>43</sup>) and in addition Jenner appears to have had been aware of cowpox vaccinations prior to his own vaccination—Jenner's "vaccination" generated a huge amount of interest among the general public, intellectual circles, and royalty, likely because he was the first person to confer scientific status to the method.<sup>44</sup> In the United Kingdom, Jenner's home, Jenner received numerous honors, and was appointed Physician Extraordinary to King George IV. Another measure of the degree to which Jenner's vaccine was considered a major advance: the Vaccination Act of 1840 made variolation illegal and enabled anyone to be vaccinated at public expense.<sup>45</sup> Then, in 1853, the United Kingdom made smallpox vaccination compulsory for all infants three months and younger.

For decades, different investigators experimented in the production and application of vaccines, but for 87 years, the scope of vaccines did not expand beyond vaccines for smallpox. It is for this reason that some consider Jenner's smallpox vaccine to be a "one-off" success, a technique that did not translate to other contagious diseases and therefore cannot be considered the real birth of the modern vaccine miracle.<sup>46</sup> Fundamental principles on which modern vaccination are based, such as attenuation of the infectious agent, did not really develop until Louis Pasteur administered the first rabies vaccines to a young boy in 1885, a practice he had been earlier performed on animals. When first introduced, Pasteur's activities were controversial—while Pasteur claimed success, some of Pasteur's closest colleagues objected. The ancient technique of variolation had been made illegal on the grounds that it

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<sup>42</sup> David M. Oshinsky, *Polio: An American Story*, 1st ed. (Oxford University Press, USA, 2005), 5.

<sup>43</sup> William H. McNeill, *Plagues and Peoples*, Updated. (Anchor, 1998), 259.

<sup>44</sup> Robert M Wolfe and Lisa K Sharp, "Anti-vaccinationists past and present," *BMJ (Clinical Research Ed.)* 325, no. 7361 (August 24, 2002): 430-432.

<sup>45</sup> Colin R. Howard, "The impact on public health of the 19th century anti-vaccination movement," *Microbiology Today*, February 2003, 23.

<sup>46</sup> M. Worboys, "Vaccines: conquering untreatable diseases," *BMJ* 334, no. 1 (January 2007): s19-s19.

used the actual disease to induce immunity, and Pasteur's methods were, in that respect, no different.<sup>47</sup> Nevertheless, Pasteur's discoveries were occurring simultaneous to the ascendance of the germ theory and nascent field of bacteriology, and within the year, vaccines for two more diseases were developed: typhoid and cholera. In the new age of germs, "the most glamorous of these vistas of progress was the potential for discovering new vaccines and drugs," the historian Nancy Tomes observed in her book *The Gospel of Germs*.<sup>48</sup> "Inspired by the known value of the smallpox vaccination, converts to the germ theory dreamed of devising concoctions of tamed germs that would confer similar protection against other deadly diseases."

In 1938, when President Franklin Delano Roosevelt launched the National Foundation for Infantile Paralysis hoping to end polio—likely the most public and successful campaigns to find the cure for an infectious disease—vaccines had already been developed for tuberculosis, pertussis, diphtheria, influenza, tetanus, and yellow fever. Seventeen years later, the world's appetite for Jonas Salk's polio vaccine was enormous. By this point in the mid twentieth century, the public had certainly become well accustomed to a host of personal hygiene measures to keep germs at bay—boiling water, avoiding fecal contamination, and practicing isolation when taking care of sick family members—but the hope for combating intractable diseases like polio came through a miracle of medicine, the vaccine. Unlike drugs and therapies, vaccines promised to prevent a disease from occurring. The belief that a vaccine was synonymous with a preventative cure had become firmly entrenched.

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The astounding success that vaccination programs against infectious disease such as smallpox, polio, rubella, and measles have had in reducing the number of cases of these diseases was a triumph with far reaching effects. For parents and doctors wishing to protect children, it offered a straightforward means to protect a child from unpleasant, potentially debilitating, and even deadly diseases. For those charged with improving and protecting the public's health, vaccines offered a straightforward approach to population based disease control strategy. But on a more subtle level, the efficacy of vaccination programs helped solidify the victory of the germ theory of disease.

Germ theory, a theory which has no unambiguous and specific date or place of birth but rather came into the fore over a period of decades in the nineteenth century, posited that human illness resulted from a process that begins with a microorganism. For each microbe, a different disease would result. But before the spate of laboratory discoveries of the late 1800s, various theories competed to explain the cause of diseases. Wherever boards of health instituted campaigns to rid cities of "filth," improvements in health were noted and gave credence and support to a belief in miasmatism—a centuries old concept that decaying matter caused ill health through the spread of foul odors. Miasmatists and others who opposed the competing "contagionist" theory pointed out that while some contagious diseases clearly did exist, such as smallpox or syphilis, it was difficult to see how other epidemic diseases like yellow fever, plague, and cholera could be seen as contagious. For example, how

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<sup>47</sup> Plotkin and Plotkin, "A short history of vaccination," 3.

<sup>48</sup> Nancy Tomes, *The Gospel of Germs: Men, Women, and the Microbe in American Life* (Cambridge, Mass: Harvard University Press, 1998), 45.

could it be explained that people who came in close contact with the sick did not always get sick, despite the fact that these diseases had the ability to attack a single person multiple times? Furthermore, quarantines—a key measure advocated by contagionists—were often unable to stop diseases from spreading. If these diseases were contagious, quarantines ought to work. Observations such as these made non-contagious explanations for the etiology of epidemic diseases attractive.<sup>49</sup>

To a significant extent, the mid nineteenth century debate between so-called contagionists and anticontagionists was sustained because the evidence available at the time was inconclusive. Empirical observations could be used to support both theories, but gave neither a decisive victory. It was in this space, lacking conclusive evidence, that the late historian of medicine Erwin Ackerknecht argues that non-scientific reasons—namely political and social leanings—proved to be the factor that led scientists to favor one theory over another. In particular, Ackerknecht argues that anti-contagionists rallied against quarantines as antiquated and ugly “engines of despotism,” considering the restrictions on liberty that they entailed.

But around 1855, various understandings derived from the rapid new worlds of bacteriology and microscopy—the notion of the asymptomatic (healthy) carrier, and animal vectors—began to tip the evidential balance in favor of contagion. Over the next decade, some of anti-contagionism’s most famous champions, such as Rudolf Virchow who had stressed the need to understand the social conditions of people in order to understand and respond to disease, changed their minds.<sup>50</sup> Contagionism had triumphed over anticontagionism. Aided by the laboratory, bacteriologists could do what the anti-contagionists could not: produce visible evidence of the previously hidden world of microbes.<sup>51</sup> Germs were not just a theory, but a hard reality the microscope could reveal. Here, the new vaccines in the bacteriological era provided an even stronger argument in favor of germ theory because, modeled off an understanding of the germ-host interaction, they were effective in preventing illness. The success of some early vaccines helped transform a simple concept into a truism: that there exists a clean causal chain from a specific microbe to a specific disease, and that this causal chain can be interrupted with a specific vaccine, or terminated with a specific medicine.

Whether it takes form as a vaccine or a drug, germ theory provides what contemporary epidemiologist Philip Alcabes calls a “simple certainty” that the response to epidemic diseases is straightforward: Kill or block the bug, and you have the cure. While discovery of any particular magic bullet remains a formidable task, once a vaccine or drug is developed, society will have its technological fix, and the disease will soon be a thing of the past.<sup>52</sup>

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<sup>49</sup> Erwin H Ackerknecht, “Anticontagionism between 1821 and 1867,” *Bulletin of the History of Medicine* 22 (September 1948): 562-593.

<sup>50</sup> *Ibid.*

<sup>51</sup> Philip Alcabes, *Dread: How Fear and Fantasy have Fueled Epidemics from the Black Death to the Avian Flu*, 1st ed. (PublicAffairs, 2009), 90.

<sup>52</sup> *Ibid.*, 138.

## The optimism of vaccination

Germ theory's tight conceptual linkage between cause, effect, and cure helps shape the way in which many infectious diseases, including influenza, are conceptualized. Until the early 1930s, influenza was a term applied to any seasonal outbreaks of epidemic disease with certain characteristics—fever, malaise, and the many symptoms we still today label “flu-like symptoms.” The discovery of influenza virus in 1933, however, began to cast influenza in a new, technology-dependent light: influenza could be *suspected* based on its symptoms, but only *confirmed* by testing for the presence of the newly discovered influenza virus. The further development of the first influenza vaccine, in 1936, helped fulfill the promise of germ theory: a method for eliminating the problem.

Optimism ran high in the first years following development of an influenza vaccine. With a long-standing realization that the conditions of war, especially crowding, helped exacerbate the impact of influenza, the Army was the earliest adopter—and for many years, the only major adopter—of influenza vaccination for the reduction of influenza-related morbidity. Dr. Thomas Francis, who would later become central to the success story of polio vaccine, led the Influenza Commission of the Army Epidemiological Board to field test influenza vaccine. The results showed influenza vaccine to be a success, reducing the incidence of influenza from 7.1 per cent to 2.2 per cent. But in 1947, there was a substantial outbreak against which the vaccine provide no protection. Investigations revealed that the causative agent was a previously unknown influenza virus, underscoring a growing awareness of the virus's mutability. Some researchers feared that a protective vaccine against influenza was an impossibility given the virus's propensity for constant and unpredictable viral change. Others were more optimistic, particularly the American researchers Thomas Francis and his protégé Jonas Salk, who felt that with proper laboratory surveillance, the threat of influenza could be better understood, and a universal vaccine could be created.<sup>53</sup>

## The rhetoric of unnecessary suffering

That optimism has never left. The very fact that influenza vaccines exist and are available drives major transformations in the way in which the disease is conceived and attitudes about technology's ability to respond to the threat. With a vaccine available, influenza is no longer one of many infectious diseases, but at once a *vaccine preventable disease*, joining diseases like smallpox, typhoid, and rabies. The CDC often appears to be at pains to convince people that their understanding of influenza is flawed: at the top of the agency's poster, *Flu Vaccine Facts & Myths*, they write that it is a “myth” to think that influenza isn't a serious disease (see Figure 1.1, page 56).<sup>54</sup> It is “not just a bad cold,” but “a serious illness,” the CDC's webpage for diabetics likewise states.<sup>55</sup> So strong is this conviction, it appears, that in a paper co-authored by CDC, Pan American Health Organization, academic physicians, and others on the topic of improving influenza surveillance systems worldwide, the authors seem to express disappointment over a “primary limitation of most existing influenza sentinel-site networks” that “are

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<sup>53</sup> John M. Eyler, “Influenza and the Remaking of Epidemiology, 1918-1960,” in *Influenza and Public Health: Learning from Past Pandemics*, ed. Tamara Giles-Vernick, Susan Craddock, and Jennifer Gunn (EarthScan, 2010), 174-175.

<sup>54</sup> U.S. Centers for Disease Control and Prevention, “Flu Vaccine Facts & Myths.”

<sup>55</sup> U.S. Centers for Disease Control and Prevention, “Take Charge of Your Diabetes: 11. Vaccinations.”

focused on mild disease, which supports the notion that influenza is a benign disease.”<sup>56</sup> They propose the target of surveillance shift and “collect clinical data and laboratory specimens from persons with a prevalent and severe infectious disease.”

Part of this framing and focus on influenza as a serious disease may be attributable to what I discussed in Chapter 1: public health’s focus on mortality as a way of understanding the true impact of disease. But attitudes about how best to describe influenza are simultaneously being shaped by public health experts’ attitudes toward the availability of vaccine.

With a vaccine available, any suffering—no matter how mild—becomes “needless,” “unnecessary,” and “tragic.” In an announcement, the Sanofi Pasteur funded American Lung Association’s *Faces of Influenza* campaign stated that “Any death is a tragedy, especially one that could have been prevented. Annual vaccination is the simplest and best protection against seasonal influenza.”<sup>57</sup> Because a vaccine exists, the implicit argument is that a life lost to influenza is a death that could have been prevented.

“Tragically, influenza and flu related complications take American lives each year,” President Barack Obama declared in an official Proclamation. “During National Influenza Vaccination Week, we remind all Americans that the flu vaccine is safe and effective in preventing the spread of flu viruses.”<sup>58</sup>

The rhetoric of “unnecessary suffering” and “tragedy” is by no means specific to influenza; it is applied to all diseases against which a vaccine exists. A decade ago, the National Vaccine Advisory Committee commented that “Vaccines are among the nation’s most important public health tools: they save lives and money, protect people (particularly infants and young children) from unnecessary suffering caused by vaccine-preventable diseases, and improve the quality of life for infants, children, adolescents, and adults.”<sup>59</sup> It is in the mission statement of The Sabin Vaccine Institute—“to reduce needless human suffering from vaccine preventable and neglected tropical diseases through innovative vaccine research and development”<sup>60</sup>—a non-profit advocacy organization primarily funded by The Bill & Melinda Gates Foundation, but also the US government, numerous pharmaceutical companies, and other philanthropic organizations.<sup>61</sup>

In a CDC issued press release announcing National Infant Immunization Week in 2008, Dr. Anne Schuchat, director of the National Center for Immunization and Respiratory Diseases and a primary

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<sup>56</sup> Justin R Ortiz et al., “Strategy to enhance influenza surveillance worldwide,” *Emerging Infectious Diseases* 15, no. 8 (August 2009): 1272.

<sup>57</sup> American Lung Association, “American Lung Association Urges ‘Faces’ of Influenza to Help Prevent Seasonal Flu by Getting Vaccinated”, November 4, 2009, <http://www.lungusa.org/about-us/our-impact/top-stories/faces-of-influenza-vaccination.html>, (accessed May 19, 2011).

<sup>58</sup> Barack Obama, “Proclamation 8615 of December 7, 2010: National Influenza Vaccination Week, 2010,” *Federal Register* 75, no. 237 (December 10, 2010): 77519-77520.

<sup>59</sup> National Vaccine Advisory Committee, “Development of Community- and State-Based Immunization Registries”, January 12, 1999, <http://www.cdc.gov/vaccines/programs/iis/pubs/nvac.htm>, (accessed July 25, 2011).

<sup>60</sup> Sabin Vaccine Institute, “Mission”, 2011, <http://www.sabin.org/about-us/mission-vision>, (accessed July 25, 2011).

<sup>61</sup> U.S. Department of Health and Human Services, “IV. Fact Sheet: Pandemic Flu Basics”, 2007, [www.pandemicflu.gov/takethelead/fact\\_sheet\\_basics.pdf](http://www.pandemicflu.gov/takethelead/fact_sheet_basics.pdf), (accessed October 12, 2010).



public official in charge of the 2009 H1N1 response, declared: “The suffering or death of even one child from a vaccine-preventable disease is an unnecessary human tragedy. Let us renew our efforts to ensure that no child, adolescent, or adult will have to needlessly suffer from a vaccine-preventable disease.”<sup>62</sup>

Despite achieving historical highs in vaccination coverage, the logic of vaccine preventable diseases (or “VPDs”), is such that anything less than near-universal coverage is inadequate. “A substantial number of children in the United States still aren’t adequately protected from vaccine-preventable diseases,” Schuchat stated. A former CDC director commented: “A quarter century ago, the objective of 90% school-age immunization coverage with common childhood vaccines was regarded by many as too ambitious. That objective proved achievable but still insufficient...”<sup>63</sup>

### **Intervention defines disease**

A powerful outgrowth of the rhetoric of “unnecessary suffering” from “vaccine preventable diseases” is the concrete manifestation of the overly-simplistic “pathogen—disease—vaccine” model. Seeing influenza through this model obscures questions over the vaccine’s actual efficacy. Are all cases and deaths from influenza truly vaccine preventable? The question does not logically arise when the phrase “vaccine preventable disease” confidently assures us they are. Are influenza epidemics and pandemics even caused by influenza—as opposed to a host of respiratory agents including, but not limited to, influenza? This question seldom arises, too, as some hospitals in the Philadelphia area found out in October 2009. Authorities there had, like the rest of the country, been preparing for waves of H1N1 swine influenza—but later realized that many of those cases were being triggered by a different virus. “When this began happening, we all believed what we were seeing was influenza,” one doctor remarked, whose 16 year old son got sick the previous month. “I went around telling my friends, ‘I’m positive she had flu.’ And now, looking back, I think she probably had rhinovirus.”<sup>64</sup> Locations with fewer laboratory resources, however, may not do the testing, and incorrectly assume that all that looks like influenza is indeed influenza. In 2009, laboratories with the ability to do the testing were overwhelmed, and testing for H1N1 detracted from their ability to carry out tests for other diseases, with little clinical benefit derived from such testing. This was in part the reason that CDC issued guidance to states to stop testing suspected cases of H1N1.<sup>65</sup> The lack of testing, however, contributes to the incorrect assumption that all influenza-like illness is influenza, and therefore should be prevented through vaccination.

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<sup>62</sup> U.S. Centers for Disease Control and Prevention, “Press Release: More Than Twenty Percent of Children Not Fully Protected Against Vaccine-Preventable Disease”, April 14, 2008, <http://www.cdc.gov/media/pressrel/2008/r080424.htm>, (accessed May 19, 2011).

<sup>63</sup> William H. Foege, “CDC’s 60th anniversary. Director’s perspective--William H. Foege, M.D., M.P.H., 1977-1983,” *MMWR. Morbidity and Mortality Weekly Report* 55, no. 39 (October 6, 2006): 1071-1074.

<sup>64</sup> Don Sapatkin, “Ill this fall? Maybe it wasn’t swine flu after all,” *Philadelphia Inquirer*, November 12, 2009, [http://www.philly.com/inquirer/health\\_science/daily/20091112\\_Tests\\_show\\_fall\\_outbreak\\_is\\_rhinovirus\\_\\_not\\_swine\\_flu.html?viewAll=y](http://www.philly.com/inquirer/health_science/daily/20091112_Tests_show_fall_outbreak_is_rhinovirus__not_swine_flu.html?viewAll=y), (accessed November 19, 2009).

<sup>65</sup> Sharyl Attkisson, “Swine Flu Cases Overestimated?,” October 21, 2009, [http://www.cbsnews.com/stories/2009/10/21/cbsnews\\_investigates/main5404829.shtml](http://www.cbsnews.com/stories/2009/10/21/cbsnews_investigates/main5404829.shtml), (accessed October 22, 2009).

The pathogen—disease—vaccine model may also partially explain why influenza pandemics were assumed to be catastrophic in their basic nature. Believing that pandemics result from evolutionarily changed influenza viruses, many assumed that humans would lack any immunity to the new virus. Lacking immunity, it seemed reasonable to assume that people would suffer a more severe bout of disease than seasonal counterparts. (The 2005 HHS pandemic plan stated: “when a pandemic virus strain emerges, 25% to 35% of the population could develop clinical disease, and a substantial fraction of these individuals could die.”<sup>66</sup>) Conceptual simplicity however does not equate with empirical validity, as the pandemic-labeled 1957, 1968, and 2009 influenza seasons have shown, with morbidity and mortality impact registering within the range of non-pandemic labeled influenza seasons, despite the overall unavailability of specific therapeutics. Nevertheless, seeing influenza pandemics as fundamentally about the circulation of novel influenza viruses, influenza vaccination is unsurprisingly heralded as the key prophylactic countermeasure.

### Transforming risk assessment

With vaccines available, fighting influenza becomes not about *whether* to use vaccines, but *how* to use vaccines. Perhaps the most symbolic representation of this disposition is the fact that for decades, the federal US policy document on the “Prevention and Control of Influenza” has been written by the Advisory Committee on *Immunization Practices* (italics mine). With ACIP appointed a leadership role in guiding the nation on the control of influenza, that its advice would take the form of vaccine recommendations seems, from the start, to be structurally guaranteed. As ACIP’s homepage on the CDC website states: “the role of the ACIP is to provide advice that will lead to ... an increase in the safe use of vaccines and related biological products.”<sup>67</sup> (The title of ACIP’s recommendations was changed and incidentally made more accurate in 2009 with the new name *Prevention and Control of Seasonal Influenza with Vaccines*, but the name change was only done to reflect the separation of recommendations for vaccines and antivirals into two publications.<sup>68</sup>)

There are further implications of conceiving influenza as, at a fundamental level, a “vaccine preventable disease” (VPD). At an influenza conference celebrating the life and career of influenza epidemiologist Arnold Monto of the University of Michigan last November, Canadian hospital epidemiologist Alison McGeer spoke about the obviousness of the problem of influenza, on the one hand, and the difficulties she experiences in trying to convince doctors to take the disease seriously.

“Influenza Is the #1 Cause of Death Due to Vaccine-Preventable Diseases,” a bold headline on her PowerPoint presentation declared, citing data from three CDC studies, with statistics showing greater than 500,000 deaths from influenza in the US between 1989 and 1998, more than four times the second leading VPD, pneumococcal pneumonia.

<sup>66</sup> U.S. Department of Health and Human Services, “HHS Pandemic Influenza Plan,” 16.

<sup>67</sup> U.S. Centers for Disease Control and Prevention, “Advisory Committee on Immunization Practices (ACIP)”, July 25, 2011, <http://www.cdc.gov/vaccines/recs/acip/>, (accessed July 25, 2011).

<sup>68</sup> Correspondence with Joseph Bresee, CDC Influenza Division, March 9, 2011.

McGeer said, “I want you to think about why it is that it is so hard to get healthcare workers vaccinated. And it’s particularly difficult to understand when you look at data like these, which are summary data looking at the impact and burden of influenza.” She continued:

It is very clear that influenza carries by far the largest burden of mortality and morbidity of any infectious disease in the developed world. Wide margin. It should be obvious that we should be paying attention to it, right? But the truth of the matter is, that the problem out there is, that clinicians don’t think so. OK?

The difficulty we’ve got with clinicians is that they think influenza makes you sick for a couple of days, and then you get better—that’s a quote from a cardiologist friend of mine, ok? And the reason for that is that the data that we have on influenza mortality and morbidity are complicated. They come from public health studies. They’re ecologic studies. They’re based on excess mortality during winter seasons and influenza season, and if you’ve done any study of influenza at all, they’re perfectly reasonable and logical and they must be true.

What McGeer claims “must be true” refers to the CDC modeling study of influenza-associated mortality, published in 2003,<sup>69</sup> which argued an annual average of 36,000 deaths each year. However by the time of McGeer’s talk, CDC had released revised figures suggesting its prior 36,000 deaths estimate was overstated by around 45%.<sup>70</sup> Nevertheless, McGeer continued to explain why clinicians’ understanding of influenza is flawed.

But if you haven’t done any study of influenza—and that of course includes most people, including most people in medicine and nursing—then these just look like ecologic data, and in clinical medicine we don’t much believe in ecologic data, OK? And if they don’t match our clinical opinion, we just kind of assume they’re fundamentally flawed. And I would put it to you that this is our big issue with getting all sorts of people to deal with influenza, OK? The federal government in Canada to fund influenza vaccine development for new influenza vaccines ... our willingness to get vaccinated as healthcare professionals. Many things that happen in influenza [sic] are much harder to do because we haven’t yet persuaded clinicians that influenza is a problem.<sup>71</sup>

McGeer is convinced that influenza is a vaccine preventable problem. As #1 VPD killer, McGeer and her colleagues set out to conduct studies aimed at generating data that would convince others that influenza was the major threat McGeer claimed it was.

So we started surveillance for influenza associated with hospitalization in south central Ontario in the 2004-5 influenza season, and the underlying goal of this surveillance,

<sup>69</sup> Thompson et al., “Mortality associated with influenza and respiratory syncytial virus in the United States.”

<sup>70</sup> U.S. Centers for Disease Control and Prevention, “Estimates of deaths associated with seasonal influenza --- United States, 1976-2007.”

<sup>71</sup> Allison McGeer, “Clinical Influenza -- three challenges”, November 12, 2010, <http://inst-tech.engin.umich.edu/leccap/view/c10sphinf-anygwonn42/10434>, (accessed July 18, 2011).

truthfully, is to demonstrate to people that influenza really does kill you. OK? That's its sole purpose in life.<sup>72</sup>

McGeer's approach reveals the stakes in the risk assessment of influenza. What gets performed and publicized are studies that demonstrate the number of deaths and hospitalizations from the alleged vaccine preventable disease. What gets much less attention are the results of studies that test the pathogens in circulation during so-called "influenza" seasons, studies that have shown influenza viruses as comprising just a proportion of the influenza-like illnesses (ILI) labeled "flu." Vaccines for non-influenza ILI are almost non-existent: the military employed adenovirus vaccine for 25 years, but its one manufacturer ceased production which stopped administration of the vaccine in 1996.<sup>73</sup> (Adenovirus vaccination however is expected to resume in military recruits following FDA approval, in March 2011, of a new live, oral adenovirus vaccine.<sup>74</sup>) Rhinovirus, coronavirus, and respiratory syncytial virus vaccines are in various stages of research and development, but are still commercially unavailable.<sup>75</sup> Attention thus falls on the only ILI considered vaccine preventable. Risk assessment focused on the burden of influenza may not tell us the magnitude of suffering attributable to what people think of as the "flu," but it does provide statistics that can and are leveraged in marketing campaigns about this "#1 VPD," identifying the margin of potential opportunity to reduce morbidity and mortality.

In this setting, there are few incentives to reduce scientific errors in risk assessment. Errors in the assessment of morbidity and mortality become forgivable because correcting the record does little to change what is relevant at the level of policy: whether influenza kills 25,000 per year or 36,000 per year, deaths attributed to this disease will be framed as "unnecessary suffering" due to a vaccine preventable disease.

Policy gets focused on what is "under the lamppost"—that is, what is targetable with available interventions—namely, influenza vaccine. I asked Professor Ronald Eccles, director of the UK Common Cold Centre, whose life work is focused on non-influenza respiratory viruses, why he thought policy was focused so much on influenza, not influenza-like illnesses.

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<sup>72</sup> Ibid.

<sup>73</sup> Kevin L. Russell et al., "Vaccine-preventable adenoviral respiratory illness in US military recruits, 1999-2004," *Vaccine* 24, no. 15 (April 5, 2006): 2835-2842; Institute of Medicine, *Urgent Attention Needed to Restore Lapsed Adenovirus Vaccine Availability: A Letter Report* (Institute of Medicine, 2000), [http://www.nap.edu/openbook.php?record\\_id=9993&page=R1](http://www.nap.edu/openbook.php?record_id=9993&page=R1), (accessed July 19, 2011).

<sup>74</sup> U.S. Food and Drug Administration to Teva Women's Health, Inc., "March 16, 2011 Approval Letter - Adenovirus Type 4 and Type 7 Vaccine, Live, Oral," WebContent, March 16, 2011, <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm247511.htm>, (accessed July 19, 2011); Military Vaccine (MILVAX) Agency, "Adenovirus Questions & Answers", 2011, <http://www.vaccines.mil/default.aspx?cnt=resource/qaAll&dID=50&cID=397>, (accessed July 19, 2011).

<sup>75</sup> National Network for Immunization Information, "Respiratory Syncytial Virus", December 21, 2006, <http://www.immunizationinfo.org/issues/vaccines-development/respiratory-syncytial-virus>, (accessed July 19, 2011); J. Craig Venter Institute, "Complete Genomes of All Known Human Rhinoviruses Are Published", February 12, 2009, [http://www.jcvi.org/cms/nc/press/press-releases/full-text/article/complete-genomes-of-all-known-human-rhinoviruses-are-published/?tx\\_ttnews\[backPid\]=67](http://www.jcvi.org/cms/nc/press/press-releases/full-text/article/complete-genomes-of-all-known-human-rhinoviruses-are-published/?tx_ttnews[backPid]=67), (accessed July 19, 2011).

You are right in that the greatest morbidity and economic burden comes from other viruses than influenza. I think that the focus on influenza prevention and research by government is related to two factors: firstly there are effective vaccines so something can be done to prevent influenza in the community and the burden of seasonal illness: secondly influenza grabs the headlines because of the pandemics that occur when a new virus circulates around the world and a large percentage of the population is ill at the same time. The other respiratory viruses do not exhibit the same pandemic behaviour as they do not exhibit the genetic shift that generates new influenza viruses, hence the other viruses such as RSV and parainfluenza etc. are present every year and cause a lot of morbidity over a prolonged period which in sum is greater than that caused by influenza but the influenza viruses have the potential to cause peaks of morbidity that grab the headlines and create public anxiety and responses from government to do something to allay this anxiety.<sup>76</sup>

### **Disease mongering and bioevangelism<sup>77</sup>**

Influenza is far from the only disease for which enormous efforts are made in the attempt to change the public's opinion from general apathy to concern and alarm. "Erectile Dysfunction" (ED) and "Female Sexual Dysfunction," (FSD) for example, are two examples of conditions that, like influenza, the majority of people were generally unconcerned about but for which concern has risen alongside media based awareness campaigns.<sup>78</sup> In the case of ED and FSD, however, these efforts have been spearheaded and paid for by pharmaceutical companies, which not coincidentally sell their therapeutics to treat the advertised condition, a practice that many academics have labeled "disease mongering."<sup>79</sup>

In contrast to these other conditions, in the case of influenza, it is public health agencies that play a major role in getting the message out. Drug companies of course still play a role, but governments are central to the story of influenza, active in their marketing of the disease and the vaccine, and it is perhaps for this reason that influenza vaccines have thus far avoided being brought into the disease mongering debate. The disease mongering storyline claims that Big Pharma creates markets for its therapeutics by enlarging the definition of illness, and convincing the public that relatively rare and little-known conditions are larger problems than they really are. For other conditions, disease mongering entails medicalizing the ordinary vagaries of life, such as sadness, doubt, or shyness, tagging them with sophisticated and medical sounding terms like Social Anxiety Disorder (SAD), and selling pills claimed to treat these diseases.

Although awareness of disease mongering only surfaced in the last decade or so, the connections between marketing diseases and marketing therapeutics has a longer history. Historian of medicine Jeremy Greene has described how the pharmaceutical company Merck played a major role in the 1950s and 1960s, in redefining the threshold for hypertension, thus enlarging the potential market for its

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<sup>76</sup> Correspondence with Ronald Eccles, December 10, 2010.

<sup>77</sup> I thank John Richardson for bringing this term to my attention, which I believe he coined.

<sup>78</sup> Lexchin, "Bigger and Better"; Moynihan and Mintzes, *Sex, Lies, and Pharmaceuticals*.

<sup>79</sup> Payer, *Disease-Mongers*; Healy, *The Antidepressant Era*; Moynihan and Cassels, *Selling Sickness*.

diuretic medication, Diuril.<sup>80</sup> The same has occurred with cholesterol guidelines. In 2001, the official National Cholesterol Education Program released updated guidelines that tripled the number of patients who, based on the new risk profile, would be expected to qualify for drug treatment.<sup>81</sup> Financial disclosures from 2004 showed that many members of the guideline drafting panel had ties to companies which stood to gain from the increased market of patients.<sup>82</sup> Examples like this show that the selling of sickness is not limited to psychiatric diseases, but a host of chronic conditions, and industry has a major interest in defining illness.

While financial ties between industry and those individuals who set influenza policy do exist, the marketing of influenza vaccine may have avoided the degree of skepticism associated with disease mongering because many of these marketers do not stand to gain financially from vaccination campaigns. The theory of disease mongering urges us to frame our understanding in terms of simple markets, but doing so misses what occurs in the story of influenza: the way in which virologists find satisfaction in being “germ hunters” (*Virus Hunting*, *Virus Hunter*, and *Germ Hunter* being the title of at least six books<sup>83</sup>), and the way public health experts find satisfaction in the prospect of saving lives by urging vaccination. Far from a desire to financially profit, saving lives is basic to the ethos of public health. At Johns Hopkins University, the nation’s oldest school of public health has given itself the motto “Protecting Health, Saving Lives - *Millions at a Time*” (italics in the original).<sup>84</sup> The CDC’s motto, visible on every page of its website, is “CDC 24/7: Saving lives, protecting people, reducing health costs.”<sup>85</sup> Vaccines, touted as one of medicine’s greatest inventions, offer experts a clear way to feel they are reducing unnecessary suffering, and saving lives.

## Vaccination politics

Dr. Peter Collignon is an infectious diseases physician, the director of the Infectious Diseases Unit and Microbiology at the Canberra Hospital in Australia, and a professor at the Medical School of the Australian National University. He has served on numerous WHO expert advisory panels.<sup>86</sup> He was one of the earliest voices during the 2009 H1N1 outbreak, urging people to consider that the outbreak may

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<sup>80</sup> Greene, “Releasing the Flood Waters.”

<sup>81</sup> G Russell Warnick et al., “Impact of the third cholesterol report from the adult treatment panel of the national cholesterol education program on the clinical laboratory,” *Clinical Chemistry* 48, no. 1 (January 2002): 11-17.

<sup>82</sup> Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), “ATP III Update 2004--Financial Disclosure, NHLBI, NCEP”, 2004, [http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3upd04\\_disclose.htm](http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3upd04_disclose.htm), (accessed July 25, 2011).

<sup>83</sup> Robert C. Gallo, *Virus Hunting: Aids, Cancer, And The Human Retrovirus: A Story Of Scientific Discovery* (Basic Books, 1993); C. J. Peters and Mark Olshaker, *Virus Hunter: Thirty Years of Battling Hot Viruses Around the World*, 1st ed. (Anchor, 1998); Rick Emmer, *Virus Hunter* (Ferguson Pub, 2005); Joseph B. McCormick and Susan Fisher-Hoch, *The Virus Hunters: Dispatches from the Frontline* (Bloomsbury Publishing PLC, 1997); Greer Williams, *Virus Hunters. The Lives and Triumphs of Great Modern Medical Pioneers*. (Hutchinson 1960., 1960); Elaine Marie Alphin, *Germ Hunter: A Story about Louis Pasteur* (Carolrhoda Books, 2003).

<sup>84</sup> Johns Hopkins Bloomberg School of Public Health, “School of Public Health at Johns Hopkins - Home”, 2011, <http://www.jhsph.edu/>, (accessed July 25, 2011).

<sup>85</sup> U.S. Centers for Disease Control and Prevention, “Centers for Disease Control and Prevention”, July 25, 2011, <http://www.cdc.gov/>, (accessed July 25, 2011).

<sup>86</sup> World Health Organization, “Prof. Peter Collignon”, n.d., [http://www.who.int/foodborne\\_disease/resistance/Collignon/en/index.html](http://www.who.int/foodborne_disease/resistance/Collignon/en/index.html), (accessed July 25, 2011).

not be as bad as they had feared. Collignon contacted me in August 2009 after finding my 2008 article in the *American Journal of Public Health*,<sup>87</sup> which challenged the assumption that pandemics were extraordinarily deadly events. Collignon, too, had been expressing the opinion that the 2009 H1N1 virus was far from extraordinary. His early commentary predicted that “this fear is out of proportion to the risk this virus represents, not only now but what is likely in the future.”<sup>88</sup>

Peter Collignon, we now know in retrospect, was right. But his continued outspokenness about the risks of influenza vaccine, and concern that policies of universal influenza vaccination may do more harm than good has not won him friends. In June 2010, Collignon, Tom Jefferson and I penned a letter to the *BMJ* expressing concern about influenza vaccination policy following Australia’s tragic experience.<sup>89</sup> Data released by the Australian government showed that 1 in every 110 young children vaccinated with the vaccine manufacturer CSL’s seasonal influenza vaccination suffered a febrile seizure.<sup>90</sup> Our letter pointed out that in trials conducted by the same manufacturer during the previous year, between 30% and 60% of young children under 3 years of age had developed a fever following vaccination—a result made all the more alarming by the fact that these data were placed in online-only appendices of the trial, not the body of the paper. Despite knowledge that fever is the most important risk factor for febrile seizures, these vaccines were allowed to go to market, and were recommended for all children.

In response to our letter, three doctors from Children’s Hospital at Westmead wrote that our criticism was unfounded and dangerous: “When doctors are prepared to be cavalier with data, the anti-immunisation lobby needs look no further for ammunition.” Even after the vaccine was suspended by the Australian government for children under five following realization of the large number of febrile convulsions, these authors claimed that their “analysis of benefits and risks continues to strongly favour influenza immunisation for children aged under 5 years.”<sup>91</sup>

As Collignon has pressed on with his critique of policy, expressing dismay over Australia’s lack of active surveillance mechanisms to rapidly detect potential harms associated with vaccination, so, too, have his detractors. Pediatric and Child Health specialist Professor Robert Booy of the University of Sydney<sup>92</sup>

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<sup>87</sup> Doshi, “Trends in recorded influenza mortality.”

<sup>88</sup> Peter Collignon, “Take a deep breath--Swine flu is not that bad,” *Australasian Emergency Nursing Journal* 12, no. 3 (August 2009): 71.

<sup>89</sup> Peter Collignon, Peter Doshi, and Tom Jefferson, “Ramifications of adverse events in children in Australia,” *BMJ* 340, no. jun09\_3 (June 9, 2010): c2994.

<sup>90</sup> Jim Bishop, “Seasonal Flu Vaccine Remains Suspended for young children without risk factors - Advice from the Chief Medical Officer” (Australian Government Department of Health and Ageing, June 1, 2010), <http://www.health.gov.au/internet/main/publishing.nsf/Content/mr-yr10-dept-dept010610.htm>, (accessed July 19, 2011).

<sup>91</sup> David Isaacs, Kristine Macartney, and Peter McIntyre, “Benefits and risks of childhood influenza vaccination,” *BMJ Rapid Response* (June 28, 2010), [http://www.bmj.com/content/340/bmj.c2994.full/reply#bmj\\_el\\_237918](http://www.bmj.com/content/340/bmj.c2994.full/reply#bmj_el_237918), (accessed July 25, 2011).

<sup>92</sup> Robert Booy reports having “received funding from CSL, Roche, Sanofi, GlaxoSmithKline (GSK) and Wyeth to attend and present at scientific meetings,” according to a recent article. See Robert Booy et al., “Cross-reacting antibodies against the pandemic (H1N1) 2009 influenza virus in older Australians,” *The Medical Journal of Australia* 194, no. 1 (January 3, 2011): 19-23.

claims that “if parents are told by a reputable, responsible professor not to immunise,” referring to Collignon, “they might be very disappointed to find their children very ill, in intensive care or dying.”<sup>93</sup>

Professor Jim Bishop, who was Australia’s chief medical officer during the 2009 H1N1 outbreak and responsible for the decision to suspend the seasonal influenza vaccine in children under five years, is also upset with Collignon. He fears that when Collignon voices concerns about influenza vaccine, he will turn the public off vaccines altogether. Bishop even telephoned Collignon to “discuss the fact it’s up to all of us to realise the huge gains that have occurred through vaccination.” “When I was a child ... my classmates were dropping off with polio. Vaccination has made a huge impact on our ability to look after diseases. Things that damage people’s trust in vaccines are problematic.”<sup>94</sup>

Collignon feels caught in a bind. “There’s been a lot of pressure on me. Like a lot of medical people, I believe vaccines are terrific – but it has come to the situation where it’s almost like motherhood, that you cannot question it, especially in the public arena, for fear you’ll undermine the vaccination program.”<sup>95</sup>

If the particular medical intervention Collignon had concerns about came in the form of a pill, it is unlikely Collignon would be so disparaged by his colleagues. Criticism of the drug industry has gone mainstream, with books such as *On the Take* and *The Truth About the Drug Companies*, penned by some of the most powerful names in academic medicine.<sup>96</sup> Numerous video documentaries have detailed the power of the pharmaceutical industry to game the patent system, sell useless drugs, influence policymakers, and forcefully market pills to doctors and consumers—altogether painting a portrait of an industry little different than Big Tobacco.<sup>97</sup>

Collignon’s criticism did not find a natural home in the larger critique of the pharmaceutical industry for the simple reason that vaccines figure little into the debate on Big Pharma. Vaccines have their own debate, a debate with roots that go back to the time of Jenner’s coxpox derived smallpox vaccine. Today, like then, much of this debate hinges on questions of free choice and autonomy, on the one hand, versus compulsion, duty, and obligation on the other.<sup>98</sup> While a more critical discourse on drugs

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<sup>93</sup> Natasha Bitá, “Free flu vaccine eyed for children,” *The Australian*, March 21, 2011, <http://www.theaustralian.com.au/news/health-science/free-flu-vaccine-eyed-for-children/story-e6frg8y6-1226025034551>, (accessed July 19, 2011).

<sup>94</sup> Ibid.

<sup>95</sup> Ibid.

<sup>96</sup> Jerome P. Kassirer, *On the Take: How Medicine’s Complicity with Big Business Can Endanger Your Health* (Oxford University Press, USA, 2005); Marcia Angell, *The Truth About the Drug Companies: How They Deceive Us and What to Do About It*, 1st ed. (Random House, 2004).

<sup>97</sup> Catherine Scott, *Selling Sickness* (Icarus Films, 2004); Andrew Liebman, “Dangerous Prescription,” *Frontline*, 2003, <http://www.pbs.org/wgbh/pages/frontline/shows/prescription/>, (accessed July 25, 2011); *Big Bucks, Big Pharma: Marketing Disease & Pushing Drugs* (Media Education Foundation, 2006); Jon Palfreman and Barbara Moran, “The Other Drug War,” *Frontline*, 2003, <http://www.pbs.org/wgbh/pages/frontline/shows/other/>, (accessed July 25, 2011).

<sup>98</sup> Daniel A Salmon et al., “Compulsory vaccination and conscientious or philosophical exemptions: past, present, and future,” *The Lancet* 367, no. 9508 (February 2006): 436; Wolfe and Sharp, “Anti-vaccinationists past and present.”



has reached a substantial level of general scientific and professional acceptability, as witnessed by the number of academics who publicly critique the pharmaceutical industry, criticism of vaccine-related policies largely emanates from members of the lay public.<sup>99</sup> There are some academics and other medical researchers who are openly critical of vaccine policy, but their numbers are small, and lay and scientific media portrayals of the vaccination debate frame the issue as one of two neatly divided groups: a scientific consensus surrounding the importance and overall safety of vaccination versus a small but vocal group of parents, usually of sick, injured, or deceased children, with ill-founded fears of vaccines.<sup>100</sup>

*PBS Frontline's* 2010 documentary, *Vaccine Wars*, captured much of the heated controversy with in-depth interviews with many of the battle's protagonists. Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, enthusiastically defended vaccine policy and spoke of the benefit of vaccines.

I don't think there's any question that vaccines are among the very short list of beneficial health interventions literally in history, if you look at everything from the number of lives that have been saved over decades and decades since we began actively vaccinating people for diseases that sometime ago were devastating and frightening, particularly for children, that are now essentially either completely suppressed, to the point where there are only rare cases, or in many cases actually eliminated. So when you look at the cost-benefit -- cost both in economic cost as well as cost in suffering and death, and the benefit of the vaccine -- it's an absolutely striking and stunning, in a positive way, beneficial intervention. ...

In some respects, vaccines are the victims of their own success, because first of all, they're still, as they were in the beginning, highly effective and very safe, when you look at risk-benefit ratio of a disease versus the very, very, very small risk of any adverse event that you would have with a vaccine. However, the motivation to get vaccinated is crystal clear and sharp when you look around you and you see people getting serious disease.<sup>101</sup>

By talking about the "cost in suffering and death," Fauci suggests that all of the diseases vaccines aim to prevent are severe. The same messages were on display at the October 2010 ACIP meeting in Atlanta, Georgia. It was here, on a table outside the meeting hall, that I found two bumper stickers and a

<sup>99</sup> Howard, "The impact on public health of the 19th century anti-vaccination movement," 22.

<sup>100</sup> Jason Fagone, "Will this Doctor Hurt Your Baby?," *Philadelphia Magazine*, June 4, 2009, [http://www.phillymag.com/scripts/print/article.php?asset\\_idx=252013](http://www.phillymag.com/scripts/print/article.php?asset_idx=252013), (accessed June 4, 2009); Gardiner Harris, "British Journal Retracts Paper Linking Autism and Vaccines," *The New York Times*, February 2, 2010, sec. Health / Research, <https://www.nytimes.com/2010/02/03/health/research/03lancet.html>, (accessed July 25, 2011); Amesh A. Adalja, "Deadly Choices: How the Anti-Vaccine Movement Threatens Us All," *Journal of the American Medical Association* 305, no. 23 (June 2011): 2469-2469.

<sup>101</sup> Anthony S. Fauci, "Interview: Anthony S. Fauci, M.D.," interview by *Frontline*, March 22, 2010, <http://www.pbs.org/wgbh/pages/frontline/vaccines/interviews/fauci.html>, (accessed July 25, 2011).

postcard, one of which contained just three words, plus a period: “VACCINES SAVE LIVES.”<sup>102</sup> Another carried the picture of four infants in diapers with the headline, “Get the Facts. Vaccines Save Lives,” plus a link to the organization’s website ([www.VaccinateYourBaby.org](http://www.VaccinateYourBaby.org)). The postcard—from the Immunization Action Coalition, a group funded by CDC, philanthropic institutions, and industry—featured a number of website links and the slogan “Save Lives. Immunize!”

What these materials and Fauci’s statements have in common is an argument that is not about any particular vaccine, but all vaccines. When Fauci speaks of “the benefit of the vaccine,” and vaccines being “highly effective and very safe,” he uses language that suggests that all vaccines can be discussed in the same breath. The “Vaccines Save Lives.” bumper sticker does not claim what any particular vaccine might do (e.g. the benefits of polio vaccine)—it makes a claim about what *all* vaccines do. Perhaps because vaccines have been heralded as one of public health’s greatest achievements, it seems unsurprising to speak of vaccines as *all* highly effective, *all* very safe, and *all* lifesaving.

But the sweeping language in discussions of vaccines seems paradoxical when considered in contrast to pharmaceutical drugs. The development and application of many drugs, such as antibiotics, have saved countless lives, yet few make broad claims about all drugs like “DRUGS SAVE LIVES.” After all, despite the centrality of pharmaceutical drugs in biomedicine, everyone knows that drugs can help and hurt. It depends on the drug, the patient, and the setting. Many drugs end up being ineffective for patients and do not cure. Most drugs treat non-life threatening conditions. And almost all carry the risk of causing side-effects. While it’s hard to predict ahead of time, some well-known estimates suggest that upwards of 100,000 deaths per year in the United States are caused by “nonerror, adverse effects of medication.”<sup>103</sup> Few doubt that drugs can save lives, but we know that the story is far more complicated.

Physicians like Peter Collignon and Tom Jefferson, who have challenged the effectiveness and safety of *some* vaccines but not *all* vaccines, have found out that most of their colleagues in the medical profession have little tolerance for public discussions about weighing the benefits and harms of any particular vaccine. Lisa Jackson has also witnessed the personal cost of challenging orthodox views. After finishing her epidemiological study which found that the widely assumed ability of influenza vaccine to reduce elderly deaths was actually an artifact of messy data and therefore not real, her results were not welcomed. “People told me, ‘No good can come of [asking] this,’” she recalled. “‘Potentially a lot of bad could happen’ for me professionally by raising any criticism that might dissuade people from getting vaccinated, because of course, ‘We know that vaccine works.’ This was the prevailing wisdom.”<sup>104</sup>

Unlike drugs, vaccines are not about individual medicine but population-based public health—and the public health strategy is straightforward. The assumption of all VPDs is the same: the disease is caused

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<sup>102</sup> “Bumper stickers,” *AAP News* 31, no. 3 (March 1, 2010): 24-d.

<sup>103</sup> Barbara Starfield, “Is US health really the best in the world?,” *Journal of the American Medical Association* 284, no. 4 (July 26, 2000): 483-485.

<sup>104</sup> Recounted in Brownlee and Lenzer, “Does the Vaccine Matter?”.

by a certain microbe, approved vaccines are necessarily safe and effective, suffering is therefore unnecessary and tragic, and vaccines promise to save lives.

These are not empirically validated claims. First, vaccines may be believed to be safe and effective, but they are biological products grown in non-sterile environments, and risks of contamination run much higher than in pharmaceutical manufacturing. Reducing unwanted bacterial growth, for example, is part of the manufacturing process in most vaccines, as the US Congress learned when investigating the Chiron influenza vaccine debacle of 2004. Second, for unknown reasons, vaccines sometimes cause unexpected side-effects. In the past two years, influenza vaccines have been associated with febrile seizures in Australia<sup>105</sup> and narcolepsy in Finland, Sweden, and other countries, leading to suspensions of influenza vaccination programs.<sup>106</sup>

With the theoretical certainty of the “vaccine preventable disease” concept applied to any infectious disease for which a vaccine exists, such as influenza, failure in policy will be explained in ways that do not cause a rethinking of basic assumptions. The NIH study in 2005, which concluded that influenza vaccines could not be shown to have reduced death in any age group,<sup>107</sup> was not interpreted as a repudiation of the vaccine, but rather as a sign that not enough people were being vaccinated. The study’s lead author Lone Simonsen herself remarked: “In a way, this study is good news: It says there’s room for improvement.”<sup>108</sup> She argued that the “investigation of other options for influenza control, including ... vaccination of children, becomes much more urgent.”<sup>109</sup>

A similarly optimistic outlook is evident in officials’ response to safety concerns. In July 2011, the European Medicines Agency’s investigation into the association between Pandemrix H1N1 influenza vaccine<sup>110</sup> and narcolepsy in children in Finland and Sweden reported:

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<sup>105</sup> Bishop, “Seasonal Flu Vaccine Remains Suspended for young children without risk factors - Advice from the Chief Medical Officer.”

<sup>106</sup> In Finland, a government appointed panel investigated the association between receipt of influenza vaccination and narcolepsy following reports of dozens of children falling ill with narcolepsy following receipt of influenza vaccine in 2009-2010. In an interim report, the panel reported finding the incidence of narcolepsy in vaccinated children to be a statistically significant 9.2-fold higher than those not vaccinated. See National Institute for Health and Welfare (THL), *National Narcolepsy Task Force Interim Report*, January 31, 2011, 14, <http://www.thl.fi/thl-client/pdfs/dce182fb-651e-48a1-b018-3f774d6d1875>, (accessed July 29, 2011). Similar reports were investigated in Sweden, where the problem could also not be attributed to faculty vaccine lots alone. See European Medicines Agency, “Questions and answers on the review of Pandemrix Influenza vaccine (H1N1) (split virion, inactivated, adjuvanted) A/California/7/2009 (H1N1)v like strain (X-179A)”, July 27, 2011, 2, [http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/public\\_health\\_alerts/2011/07/human pha\\_detail\\_000034.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d126#](http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/public_health_alerts/2011/07/human pha_detail_000034.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d126#), (accessed July 29, 2011); World Health Organization, “Statement on narcolepsy and vaccination”, April 21, 2011, [http://www.who.int/vaccine\\_safety/topics/influenza/pandemic/h1n1\\_safety\\_assessing/narcolepsy\\_statement/en/index.html](http://www.who.int/vaccine_safety/topics/influenza/pandemic/h1n1_safety_assessing/narcolepsy_statement/en/index.html), (accessed July 29, 2011).

<sup>107</sup> Simonsen et al., “Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population.”

<sup>108</sup> Cohen, “INFLUENZA: Study Questions the Benefits of Vaccinating the Elderly.”

<sup>109</sup> Lone Simonsen, Cecile Viboud, and Robert Taylor, “Influenza vaccination in elderly people,” *Lancet* 366, no. 9503 (December 17, 2005): 2086.

<sup>110</sup> Pandemrix is an adjuvanted influenza A (H1N1) 2009 monovalent vaccine manufactured by GlaxoSmithKline.

... that the epidemiological studies relating to Pandemrix in Finland and Sweden were well designed and show an association between Pandemrix vaccination and narcolepsy in children and adolescents in those countries. The results indicate a six to 13-fold increased risk of narcolepsy in vaccinated as compared with unvaccinated children and adolescents, corresponding to about three to seven additional cases in every 100,000 vaccinated subjects.<sup>111</sup>

Despite this, EMA investigators stopped short of blaming the manufacturer or the vaccine, and “noted that the vaccine is likely to have interacted with genetic or environmental factors which might raise the risk of narcolepsy, and that other factors may have contributed to the results.”<sup>112</sup>

Nonetheless, the safety issues stand in contrast to US agencies’ assurances that the many decades of successful use of influenza vaccine in the general population ensures that the process is safe. In a video “How Safe are Flu Vaccines?” posted to the HHS’s *flu.gov* website, Director of the National Institute of Allergy and Infectious Diseases Anthony Fauci states: “the track record for serious adverse events is very good. It’s very, very, very rare that you ever see anything that’s associated with the vaccine that’s a serious event.”<sup>113</sup> In the words of Australian epidemiologist Heath Kelly, who calculated that the now suspended seasonal influenza vaccine there might have caused 2-3 hospital admissions for every hospital admission prevented, “a good past benefit-risk profile for a vaccine may not guarantee a favourable profile in future years.”<sup>114</sup>

### Why do major errors go uncorrected?

For more than two decades, national US guidelines have consistently stated that influenza vaccines are the “most effective” means for reducing the impact of influenza.<sup>115</sup> For agencies like CDC which clearly advocate the need to base policy on good scientific evidence—current guidelines contain a bibliography with over 500 entries—how do officials reach such certainty about matters they deem major public health problems?

In its visit to Geneva, the Council of Europe posed a question to WHO (which likewise claims influenza vaccine as the “best protection”<sup>116</sup>) that offers some insight: “Has WHO done any head-to-head studies

<sup>111</sup> European Medicines Agency, “Questions and answers on the review of Pandemrix Influenza vaccine (H1N1) (split virion, inactivated, adjuvanted) A/California/7/2009 (H1N1)v like strain (X-179A).”

<sup>112</sup> The WHO has also speculated about the role of “still unknown, genetic and/or environmental factors.” See World Health Organization, “Statement on narcolepsy and vaccination.”

<sup>113</sup> *How Safe is the Flu Vaccine?*, 2009, <http://www.youtube.com/watch?v=TE4cNqcBCEQ>, (accessed May 8, 2010).

<sup>114</sup> Heath Kelly et al., “Quantifying benefits and risks of vaccinating Australian children aged six months to four years with trivalent inactivated seasonal influenza vaccine in 2010,” *Euro Surveillance* 15, no. 37 (September 16, 2010), <http://www.ncbi.nlm.nih.gov/pubmed/20929647>, (accessed July 29, 2011).

<sup>115</sup> U.S. Centers for Disease Control and Prevention, “Prevention and control of influenza: Part I, Vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 42, no. 6 (May 14, 1993): 2; Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010,” 9-10.

<sup>116</sup> World Health Organization, “What is post-pandemic?”, August 10, 2010, [http://www.who.int/csr/disease/swineflu/frequently\\_asked\\_questions/post\\_pandemic/en/index.html](http://www.who.int/csr/disease/swineflu/frequently_asked_questions/post_pandemic/en/index.html), (accessed July 25, 2011).

to compare behavioural interventions such as hand washing versus vaccines?”<sup>117</sup> Such studies would provide evidence regarding the relative effectiveness of hand washing versus influenza vaccines, and in a world of limited resources, ideally help guide public health decision makers prioritize their efforts. However, in a written response, WHO explained that it had not carried out any such studies. The agency downplayed the idea that there was even a need for such research, arguing that behavioral interventions and vaccines “are complementary rather than competitive options.”<sup>118</sup>

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In this chapter, I have tried to explore the question of why public health officials can endorse and perpetuate problematic science—why the bad news tends to get emphasized when it comes to the threat of influenza and its pandemics, and the good news tends to get emphasized when it comes to the potential of vaccines. And why questions such as “is all ‘flu’ influenza?” “How well does the vaccine really work?” and “Is public money best spent on vaccines—or something else?” do not get sufficient attention. Admittedly, “why” questions are inherently difficult to answer. They are often inseparable from questions of motivation, for which answers typically suffer from lack of empirical validation. Given these limitations, my argument of viral essentialism and the logic of VPDs is an unavoidably speculative answer to these questions, but one that I believe reveals important elements of the social, political, and linguistic factors which foster false assumptions. Characterizing influenza as a VPD helps render invisible many key analytical questions that could potentially identify red flags in current science and policy.

To be sure, the role of industry remains important. Conflicts of interest are a powerful explanatory mechanism for understanding mismatches between evidence and policy, policies not in the public’s best interest, and policies that show evidence of corporate bias. In the field of influenza, investigations over the last year have shown that numerous experts have ties to industry.<sup>119</sup> But conflict of interest appears insufficient to understand the dynamics of influenza policy in light of the substantial degree of agreement between experts with and without financial relationships with industry. Even if the government took over vaccine manufacturing and private industry had no stakes in influenza policy, approaches to managing influenza would likely remain focused on vaccines and pharmacological measures because they support most public health practitioners’ preconceived notions of vaccination as the best response to epidemic disease. This, I argue, is the power of virus-centric thinking, the logic of “vaccine preventable diseases.” Unlike disease mongering, in which Big Pharma spends enormous amounts of resources convincing the public, doctors, and decision makers about the value of a new medication, VPDs have a logic of their own that is well established in biomedicine and requires little

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<sup>117</sup> Council of Europe, “The handling of the H1N1 pandemic: more transparency needed,” 24.

<sup>118</sup> *Ibid.*

<sup>119</sup> Cohen and Carter, “WHO and the pandemic flu ‘conspiracies’”; Epstein, “Flu Warning”; Fiona Macrae and Sophie Borland, “Swine flu taskforce’s links to vaccine giant: More than half the experts fighting the ‘pandemic’ have ties to drug firms | Mail Online”, January 14, 2010, <http://www.dailymail.co.uk/news/article-1243034/Swine-flu-taskforces-links-vaccine-giant-More-half-experts-fighting-pandemic-ties-drug-firms.html>, (accessed March 28, 2010); CBC News, “CBC Tamiflu probe sparks drug policy review”, May 24, 2011, <http://www.cbc.ca/news/canada/story/2011/05/22/tamiflu-documentary-conflict.html>, (accessed July 29, 2011); “The ghost of the pandemic [Il fantasma della pandemia],” *Falo*, February 7, 2010, [http://la1.rsi.ch/\\_dossiers/player.cfm?uuid=18d78f7c-c2a8-4422-acd0-17f9d56c1f0a](http://la1.rsi.ch/_dossiers/player.cfm?uuid=18d78f7c-c2a8-4422-acd0-17f9d56c1f0a).

persuasion. So long as biomedical thinking approaches epidemic diseases in a simplistic “one disease – one cause – one drug” manner, the problem will be framed as a “vaccine preventable disease,” in which a vaccine will be understood as the obvious answer.

[ENDS]

Table 5.1. CDC ACIP statements concerning physical interventions to interrupt influenza, 2005 to 2010

Year	Guidance document word count	Number of references	ACIP statement on non-pharmaceutical interventions
2005-2006	20,428; 20,191	349; 375	<i>Hand hygiene, masks, school closures not mentioned in guidelines.</i>
2007	26,172	473	Nonpharmacologic interventions (e.g., advising frequent handwashing and improved respiratory hygiene) are reasonable and inexpensive; these strategies have been demonstrated to reduce respiratory diseases (86) but have not been studied adequately to determine if they reduce transmission of influenza virus. Similarly, few data are available to assess the effects of community-level respiratory disease mitigation strategies (e.g., closing schools, avoiding mass gatherings, or using masks) on reducing influenza virus transmission during typical seasonal influenza epidemics (87,88). <sup>120</sup>
2008-2009	30,285; 26,912	502; 455	Nonpharmacologic interventions (e.g., advising frequent handwashing and improved respiratory hygiene) are reasonable and inexpensive; these strategies have been demonstrated to reduce respiratory diseases; reductions in detectable influenza A viruses on hands after handwashing also have been demonstrated (76–78). Few data are available to assess the effects of community-level respiratory disease mitigation strategies (e.g., closing schools, avoiding mass gatherings, or using respiratory protection) on reducing influenza virus transmission during typical seasonal influenza epidemics (79,80). <sup>121</sup>
2010	33,360	552	Reductions in detectable influenza A viruses on hands after handwashing have been demonstrated, and handwashing has been demonstrated to reduce the overall incidence of respiratory diseases (122–124). Nonpharmacologic interventions (e.g., frequent handwashing and improved respiratory hygiene) are reasonable and inexpensive. However, the impact of hygiene interventions such as handwashing on influenza virus transmission is not well understood, and hygiene measures should not be advocated as a replacement or alternative to specific prevention measures such as vaccination. Few data are available to assess the effects of community-level respiratory disease mitigation strategies (e.g., closing schools, avoiding mass gatherings, or using respiratory protection) on reducing influenza virus transmission during typical seasonal influenza

<sup>120</sup> Fiore et al., "Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2007," 8.

<sup>121</sup> Anthony E Fiore et al., "Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009," *MMWR. Recommendations and Reports* 58, no. 8 (July 31, 2009): 7; Fiore et al., "Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008," 8.

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epidemics (125–127). An interventional trial among university students indicated that students living in dormitories who were asked to use surgical face masks, given an alcohol-based hand sanitizer, and provided with education about mask use and hand hygiene during influenza season had substantially lower rates of ILI compared with students in dormitories for whom no intervention was recommended. However, neither face mask nor hand sanitizer use alone was associated with statistically significant reduction in ILI (128). During the 2009 pandemic, one study indicated that having members of households in which an influenza case was identified discuss ways to avoid transmission was associated with a significant reduction in the frequency of additional cases after one household member became ill, suggesting that education measures might be an effective way to reduce secondary transmission (129). Limited data suggest that transmission of seasonal influenza or ILI among household members can be reduced if household contacts use a surgical face mask or implement hand washing early in the course of an ill index case patient's illness (130,131). However, these interventions might supplement use of vaccine as a means to reduce influenza transmission or provide some protection when vaccine is not available (130–132).

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Table 5.2. Historical development of vaccines<sup>122</sup>

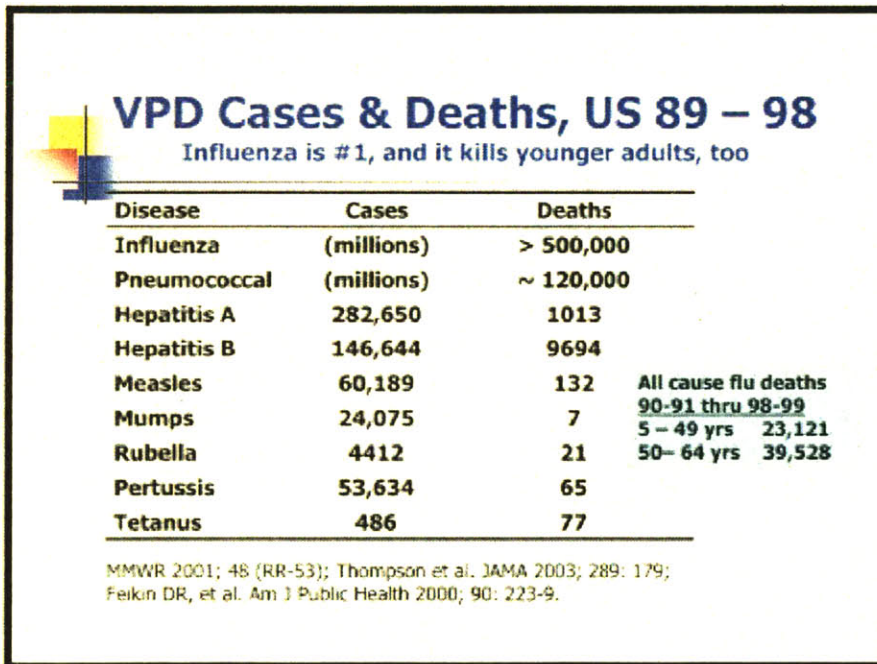
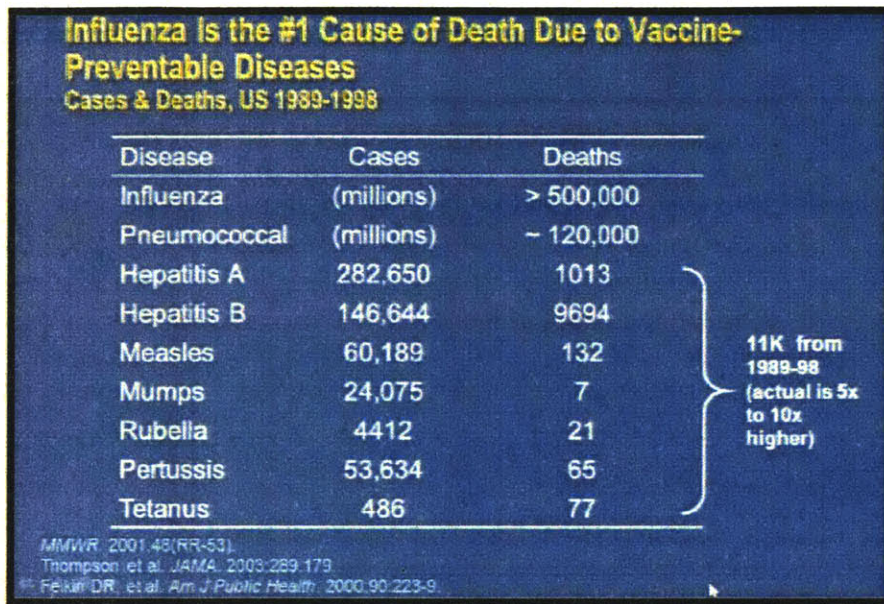
Disease	Year etiology determined	Year vaccine developed
Cholera	1883	1896
Diphtheria	1884	1923
Influenza	1933	1936
Measles	1954	1961
Mumps	1934	1948
Pertussis	1906	1926
Plague	1894	1897
Polio	1908	1952
Rabies		1885
Rubella	1938	1965
Smallpox		1796
Tetanus	1884	1927
Tuberculosis	1882	1927
Typhoid	1884	1896
Yellow fever	1927	1935

Note: sources of error in the table include the imprecision associated with many discoveries and inventions which usually do not occur at a single point in time, but as a process over time.<sup>123</sup> The dates should therefore be treated as approximate.

<sup>122</sup> Sources referenced include: Plotkin and Plotkin, "A short history of vaccination," 3; Kenrad E. Nelson and Carolyn F. Masters Williams, "Early history of infectious disease: epidemiology and control of infectious diseases," in *Infectious disease epidemiology: theory and practice* (Jones & Bartlett Learning, 2007), 11; Washer, *Emerging Infectious Diseases and Society*, 35; C Kemper and J P Atkinson, "Measles virus and CD46," *Current Topics in Microbiology and Immunology* 329 (2009): 31-57; Military Vaccine (MILVAX) Agency, "Mumps", 2011, <http://www.vaccines.mil/default.aspx?cnt=disease/minidv&dID=37>, (accessed July 29, 2011); U.S. Centers for Disease Control and Prevention, *Epidemiology and Prevention of Vaccine-Preventable Diseases*, ed. William Atkinson, Charles Wolfe, and Jennifer Hamborsky, 12th ed. (Public Health Foundation, 2011). Pink book page 205;

<sup>123</sup> For a critique of the process of "discovery," see Theodore Arabatzis, *Representing Electrons: A Biographical Approach to Theoretical Entities* (University Of Chicago Press, 2005).

Figure 5.1. Presentation slides indicating that influenza is the leading "vaccine preventable disease" (VPD). The slide above was presented by Alison McGeer in 2010.<sup>124</sup> The nearly identical slide below was presented by Kristin Nichol to the National Influenza Vaccine Summit in 2004.<sup>125</sup>



<sup>124</sup> Allison McGeer, "Clinical Influenza - Three Challenges" (presented at the Influenza as a Global Concern: Where Do We Go From Here? A symposium in honor of Professor Arnold Monto, University of Michigan, November 12, 2010), 3, <http://inst-tech.engin.umich.edu/leccap/view/c10sphinf-anygwnn42/10434>, (accessed June 21, 2011).

<sup>125</sup> Kristin L. Nichol, "Universal Influenza Vaccination: Issues for Consideration", April 2004, 12, [http://www.ama-assn.org/ama1/pub/upload/mm/36/2004\\_flu\\_nichol.pdf](http://www.ama-assn.org/ama1/pub/upload/mm/36/2004_flu_nichol.pdf), (accessed June 21, 2011).

## Chapter 6 Implications for Policy

By the middle of the year 2011, influenza policy has come to be discussed in two considerably divergent frames. One framing, promoted by officials and by far the dominant perspective, suggests that nearly eighty years after the discovery of influenza virus, influenza remains a major threat, in large part due to the virus's propensity to keep mutating. Influenza is a serious disease, and illness and deaths from it are especially tragic because it is not just any disease, but a vaccine-preventable disease. Luckily, a science driven policy based on influenza vaccines—the best way to prevent influenza—has however shown great signs of progress in controlling the disease: more people are recommended to get vaccinated than ever, and more do. While notable gaps in coverage still exist, such as the low proportion of healthcare workers receiving the vaccine, stronger recommendations—and in an increasing number of cases, mandates—promise to fill these gaps in the near future. Pandemic policy and planning has also succeeded. The long predicted influenza pandemic arrived in 2009, and with some caveats about room for improvement, health authorities have declared their response an overall model of success,<sup>1</sup> saving over a thousand lives in the United States<sup>2</sup> alone. This optimistic assessment suggests that the billions spent on influenza control are worth the cost.

The second framing, which I have forwarded in this dissertation, does not present a parallel or alternative way of seeing influenza so much as it is a sustained critique of policy, in which the validity of most scientific aspects of the official policy are questioned. These critiques first came to major public attention in 2009 with the emergence of novel H1N1 influenza virus, when health authorities mounted massive campaigns to fight a virus of ordinary and non-spectacular severity. Almost all the predictions about what was to occur in the next influenza pandemic were wrong, as H1N1 began and remained far milder than even the most optimistic, “best case” scenarios had envisioned. Compounding these discrepancies between expectation and reality were the voices of many in public health which vigorously defended its decisions. Suspicions only ran deeper after investigations, particularly in Europe, revealed that numerous pandemic influenza policy advisors were also being paid by pharmaceutical companies.

I have argued that the problems in influenza policy run far deeper than a poor ability to predict the future. The entire public health effort has been based on flawed and internally inconsistent risk assessment, coupled with improbable, overly-optimistic expectations about the benefit of the vaccine—problems that were all documented well before the emergence of H1N1 in 2009. Rather than understanding influenza as a serious disease (which it is in the minority of cases), influenza should be seen for what it is in the vast majority of cases: an unpleasant, but self-limiting disease from which people recover on their own without intervention. Even when it does kill, the degree to which it is a killer is unclear because credible risk assessment does not exist. Moreover, current influenza policies

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<sup>1</sup> D. J. Sencer, “Perspective: Swine-Origin Influenza: 1976 and 2009,” *Clinical Infectious Diseases* 52, no. 1 (December 2010): S4-S7; Schuchat, Bell, and Redd, “The science behind preparing and responding to pandemic influenza.”

<sup>2</sup> U.S. Centers for Disease Control and Prevention, “Ten great public health achievements --- United States, 2001--2010,” *MMWR. Morbidity and Mortality Weekly Report* 60, no. 19 (May 20, 2011): 619-623.

are narrowly focused on the wrong problem—infections caused by influenza A and B viruses—rather than influenza-like illness (ILI), the set of symptoms that officials, doctors, and the public alike label “flu,” caused by a variety of agents such as coronaviruses, rhinoviruses, adenoviruses, and respiratory syncytial virus. And if influenza is indeed only a minority cause of ILI—perhaps around 10% of ILI as one large analysis showed<sup>3</sup>—the public is being misled when it is told that the influenza vaccine prevents flu “most of the time.” Even for true influenza, evidence suggests that the potential benefits have been overstated. Pandemic planning efforts have likewise been misdirected, based almost entirely on worst case scenarios, with massive investments into drugs and vaccines of questionable effectiveness.<sup>4</sup>

Although financial conflicts of interest are an important element of understanding how all this came to happen, I argue that it cannot be the whole story because the public health effort is enormous, involving a great many practitioners who do not have financial relationships with industry. Understanding how these individuals do not detect serious problems in the policy they deploy, I believe, requires understanding something about the ethos of public health and the persuasiveness of viral essentialism. My argument is that for the simple reason that influenza vaccine exists, influenza becomes seen as a “vaccine preventable disease,” and policies targeting the disease become, in their essential features, uncontroversial and simple: vaccinate. It is only as a “vaccine preventable disease” that influenza cases and deaths become “tragic” and “needless” because it is assumed that all suffering is unnecessary and avoidable through vaccination. But, as Chapter 4 showed, these assumptions are inaccurate. The relationship between disease, virus, and vaccine is not as tight as many expect. Not all flu is influenza, and the vaccine does not always prevent the disease. Perhaps the most problematic of all is that the goal of reducing the number of elderly who die from influenza—long the implicit (and sometimes explicit) goal of influenza vaccination policy<sup>5</sup>—has been a complete failure, with no evidence the vaccine

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<sup>3</sup> Jefferson, “Mistaken identity: seasonal influenza versus influenza-like illness.”

<sup>4</sup> Peter Doshi, “Neuraminidase inhibitors—the story behind the Cochrane review,” *BMJ* 339, no. dec07\_2 (December 8, 2009): b5164; Luc Bonneux and Wim Van Damme, “Health is more than influenza,” *Bulletin of the World Health Organization* 89, no. 7 (July 1, 2011): 539-540.

<sup>5</sup> There are few instances of unambiguous statements of objectives of influenza vaccination policy. However, since annual influenza vaccination policies were instituted in 1960, the disproportionate burden influenza places on the elderly has always been stressed as a key rationale for the policy. In 1964, CDC influenza branch Chief Alexander Langmuir and colleagues wrote that the original 1960 recommendation for annual vaccination “was based on three broad assumptions: 1. That excess mortality was the most important consequence of epidemic influenza. 2. That polyvalent virus vaccines had been at least partially effective in preventing clinical illness during most epidemics and therefore presumably would reduce the risk of death among the aged and chronically ill. 3. That epidemics cannot be predicted with sufficient accuracy to permit confident planning of control measures on a year to year basis.” (Langmuir, Henderson, and Serfling, “The Epidemiological Basis for the Control of Influenza.”) Twenty years later, ACIP recommendations stated: “Because of the increasing proportion of elderly persons in the United States and because age and its associated chronic diseases are risk factors for severe influenza illness, the future toll from influenza may increase, unless control measures are used more vigorously than in the past. ... For about 20 years, efforts to reduce the impact of influenza in the United States have been aimed primarily at immunoprophylaxis [vaccination] of persons at greatest risk of serious illness or death.” (U.S. Centers for Disease Control, “Recommendation of the Immunization Practices Advisory Committee (ACIP) Prevention and Control of Influenza.”) Today, the recommendation—aimed at the entire population-state: “Annual influenza vaccination is the most effective method for preventing influenza virus infection and its complications.” (Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.”)

has saved lives.<sup>6</sup> But none of this has caused any rethinking of policy because for many, the problems are difficult to reconcile with the assumptions of a “vaccine preventable disease.”

This final chapter attempts to move from diagnosis to prescription, offering thoughts on what kind of changes might help improve influenza policy making, strengthen the scientific evidence base that informs it, and ultimately result in better health outcomes for the public that pays for it all.

## Planned Adaptation

It might be best to begin by taking a step back. The notion that policies are not in line with the latest, most comprehensive reviews of the scientific evidence base are by no means limited to the case of influenza. Rather than the exception, in situations where policy decisions are made on uncertain or changing evidence, it is common. When regulators create rules governing environmental risks—air or water safety standards, for example—data may be incomplete, uncertain, and subject to change. Some risks, in particular, may interact with each other, such that the degree to which each is a hazard depends on another, and may vary in ways that are unpredictable at the time regulation is passed. Decision making under uncertainty in these situations is less a shortcoming of science policy than it is a predictable inevitability. Sound policy, some analysts have argued, does not result from getting it right up front, so much as it is about a commitment to reviewing and revising existing policies over time as new or improved scientific information is generated, priorities, sensitivities, and situations change, and new technology emerges.<sup>7</sup>

In 1994, legal scholar Daniel Farber put forward, with reference to environmental regulation, a vision of a new kind of policy:

Rather than viewing policy making as a one-shot exercise, in which the goal is to adopt the optimum solution, we might do better to think of a continuous process of learning and experimentation. “What is the optimum decision today?” may be less important

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<sup>6</sup> See Simonsen et al., “Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population”; Jackson et al., “Evidence of bias in estimates of influenza vaccine effectiveness in seniors”; Jackson et al., “Functional status is a confounder of the association of influenza vaccine and risk of all cause mortality in seniors”; Jefferson et al., “Vaccines for preventing influenza in the elderly”; Eurich et al., “Mortality Reduction with Influenza Vaccine in Patients with Pneumonia Outside ‘Flu’ Season.” For a more detailed discussion of these papers, see Chapter 4.

<sup>7</sup> Daniel A Farber, “Environmental Protection as a Learning Experience,” *Loyola of Los Angeles Law Review* 27 (1994 1993): 791; Lawrence E. McCray, Kenneth A. Oye, and Arthur C. Petersen, “Planned adaptation in risk regulation: An initial survey of US environmental, health, and safety regulation,” *Technological Forecasting and Social Change* 77, no. 6 (July 2010): 951-959; Arthur Petersen et al., “Anticipation and Adaptation in Particulate Matter Policy: The European Union, the Netherlands, and United States” (presented at the Trans-Atlantic Uncertainty Colloquium, Washington, D.C., 2006), [http://www.modeling.uga.edu/tauc/background\\_material/Anticipation%20and%20Adaptation\\_PM%20Policies\\_EU&US.pdf](http://www.modeling.uga.edu/tauc/background_material/Anticipation%20and%20Adaptation_PM%20Policies_EU&US.pdf), (accessed June 16, 2011); James Lloyd Foster, “The Dead Hand of Environmental Regulation”, September 1999, <http://dspace.mit.edu/handle/1721.1/1679>, (accessed June 21, 2011); W Walker, “Adaptive policies, policy analysis, and policy-making,” *European Journal of Operational Research* 128, no. 2 (January 2001): 282-289.

than “What is the best strategy for developing and responding to new information about the problem?”<sup>8</sup>

More recently, Lawrence McCray and Kenneth Oye asked “whether practical means can be devised to keep policy yoked to an evolving knowledge base, once decisions are put on the books.”<sup>9</sup> In their judgment, implementing these “practical means” is the essential feature of what they call “Planned Adaptation.” The drawbacks to not employing Planned Adaptation can be enormous. Dutch and American analysts of science policy have similarly argued for the need for adaptive policies, and warned when “adaptation does not occur, policies remain designed around initial, unavoidably incorrect, anticipation of outcomes. This can carry high social costs, either in the form of excessive cost burdens ... or in the form of forgone health benefits....”<sup>10</sup>

For a variety of reasons, infectious disease control policies would seem to have much to gain from Planned Adaptation. Today’s measures to reduce burden of disease may over time become unnecessary if they are so successful as to eradicate the disease, as in the case of smallpox, and policy would need to change. Even in cases where complete eradication of an infectious disease is not possible, measures that begin aggressive in order to address a disease epidemic throughout society may need to be scaled back once the disease has been reduced to endemic levels. Conversely, vaccination efforts may need to be intensified against a disease for which a new technology has enabled the manufacture of a far cheaper and safer vaccine, changing the cost-effectiveness of a vaccination program.

McCray and Oye suggest that there are two essential elements required to operationalize genuine Planned Adaptation in policy: first, a prior commitment to periodic “*de novo* re-evaluation”; second, a systematic effort to incorporate new factual information into those re-evaluations. Both seasonal influenza policy and pandemic influenza policy have many of the markings of policies with a firm commitment to Planned Adaptation.

### **Seasonal influenza policy**

Following a decade which saw the development of new vaccines, the Advisory Committee on Immunization Practices (ACIP) was established by order of the Surgeon General in 1964 to advise the federal government on the control of diseases for which a vaccine is licensed for use in the civilian population. The birth of ACIP marked the beginning of a formal national vaccine policy in the United States,<sup>11</sup> and in 1972, it became a Federal Advisory Committee under the Federal Advisory Committee Act (FACA).<sup>12</sup> Although ACIP formally only makes “recommendations,” which do not carry legal mandate, these recommendations carry enormous weight as “they are generally regarded as national

<sup>8</sup> Farber, “Environmental Protection as a Learning Experience,” 791.

<sup>9</sup> McCray, Oye, and Petersen, “Planned adaptation in risk regulation,” 952.

<sup>10</sup> Petersen et al., “Anticipation and Adaptation in Particulate Matter Policy,” 6-7.

<sup>11</sup> Jean Clare Smith, “The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP),” *Vaccine* 28 (April 2010): A68-A75.

<sup>12</sup> Hajime Kamiya and Nobuhiko Okabe, “Leadership in Immunization: The relevance to Japan of the U.S.A. experience of the Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP),” *Vaccine* 27, no. 11 (March 10, 2009): 1724-8.

policy and are respected and adopted by most private insurers.”<sup>13</sup> ACIP recommendations furthermore trigger large government and private programs aimed to raise vaccination rates of targeted populations, such as the Vaccines for Children Program.<sup>14</sup> Although the Director of CDC, who is delegated to adopt vaccine policy on behalf of HHS, may revise or reject ACIP recommendations, “in practice, due to the lengthy process of data presentation and review that typically goes on overall several months and years before an ACIP vote is ever taken, virtually all ACIP recommendations are adopted by CDC/HHS.” There has only been one exception in ACIP’s history where its recommendations were overridden (on smallpox vaccine).<sup>15</sup>

Subjecting existing policy to constant review and update, ACIP holds regular meetings three times a year, and additional meetings as circumstances dictate. In accordance with FACA, meetings of the ACIP must be announced at least 15 days in advance, and the public may register and attend almost all meetings,<sup>16</sup> where some time is allotted for public comment. Meeting minutes and presentations are made available within 90 days of the meeting on the CDC’s website.<sup>17</sup> The Committee’s commitment to Planned Adaptation seems enshrined in its Charter, which states: “The committee may alter or withdraw their recommendation(s) regarding a particular vaccine as new information becomes available or the risk of disease changes.”<sup>18</sup> Recently, the ACIP Secretariat has even launched an initiative to ensure that every ACIP recommendation is reviewed every 3-5 years, and “revised, renewed, or retired as needed.”<sup>19</sup> Such corrections have already occurred, as in the case of rotavirus vaccine policy. Originally licensed and recommended for use in 1998, concerns soon arose that the vaccine was triggering intussusception of the intestine, and in 1999 ACIP withdrew its recommendation.<sup>20</sup> (Following the development of a new vaccine, recommendations for rotavirus vaccine were reinstated in 2006.) Examples like these provide evidence that US vaccine policy is built around a model that allows for self-correction.

In addition, ACIP recommendations are aimed to be based on the highest quality scientific evidence. As the CDC explains:

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<sup>13</sup> Smith, “The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP),” A71.

<sup>14</sup> Alexandra Stewart, “Childhood vaccine and school entry laws: the case of HPV vaccine,” *Public Health Reports* 123, no. 6 (December 2008): 801-803.

<sup>15</sup> Smith, “The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP),” A73.

<sup>16</sup> Larry K Pickering and Walter A Orenstein, “Development of pediatric vaccine recommendations and policies,” *Seminars in Pediatric Infectious Diseases* 13, no. 3 (July 2002): 148-154.

<sup>17</sup> Smith, “The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP),” A70.

<sup>18</sup> U.S. Centers for Disease Control and Prevention, “ACIP Charter”, April 2010, 2, <http://www.cdc.gov/vaccines/recs/acip/downloads/charter.pdf>.

<sup>19</sup> Smith, “The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP),” A71.

<sup>20</sup> U.S. Centers for Disease Control and Prevention, “Withdrawal of rotavirus vaccine recommendation,” *MMWR. Morbidity and Mortality Weekly Report* 48, no. 43 (November 5, 1999): 1007.

To formulate policy recommendations, the ACIP reviews data on morbidity and mortality associated with the disease in the general US population and in specific risk groups along with available scientific literature (both published and unpublished) on the safety, efficacy, effectiveness, cost-effectiveness, and acceptability of the immunizing agent, with consideration of the relevant quality and quantity of data.<sup>21</sup>

The ACIP Influenza Work Group, one of ACIP's four permanent working groups, holds meetings every 2-4 weeks throughout the year, and considers a range of issues including disease risk data, vaccine safety and effectiveness, current vaccine coverage levels, cost-effectiveness, and vaccine supply levels. In its annual influenza vaccine recommendations, the Influenza Work Group explains its methodology:

Published, peer-reviewed studies are the primary source of data used by ACIP in making recommendations for the prevention and control of influenza, but unpublished data that are relevant to issues under discussion also are considered. Among studies discussed or cited, those of greatest scientific quality and those that measure influenza-specific outcomes are the most influential.<sup>22</sup>

Another way ACIP tries to ensure its recommendations are consistent with evidence is to keep vested interests out of decision making, something especially important given the financial implications that recommendations can have on the private and public sectors. Individuals nominated for membership in ACIP undergo screening for potential conflicts of interest before names are submitted for final consideration.<sup>23</sup> "If potential members have certain conflicts, they have a choice: they can either relinquish those conflicts, or they can be nominated to serve on ACIP," Dr. Larry Pickering, executive secretary of ACIP, explained to me in 2010, but acknowledged that there are certain financial relationships in which members may be involved for which they can receive a waiver. Pickering however assured me that ACIP was composed of "very high quality people who are critical thinkers" in scrutinizing the scientific evidence they review.<sup>24</sup>

While ACIP appears to be an exemplary model of Planned Adaptation, I have argued in this dissertation that policy is misconceived, lacking a proper assessment of risk and evaluation of therapeutics like vaccines. While aspects of Planned Adaptation are evident in official statements and positions of ACIP, McCray and Oye suggest that a rulemaking agency's efforts to advance the production of new knowledge are as important as an agency's commitment to analyze new information. On this count, ACIP's efforts have been minimal. The influenza guidelines do not treat CDC's estimates of mortality and hospitalization attributable to influenza as one estimate among competing estimates, nor even as an estimate, but as a fact. ("Influenza epidemics were associated with estimated annual averages of

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<sup>21</sup> Smith, "The structure, role, and procedures of the U.S. Advisory Committee on Immunization Practices (ACIP)," A72.

<sup>22</sup> Fiore et al., "Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010," 3.

<sup>23</sup> Jean C Smith, Dixie E Snider, and Larry K Pickering, "Immunization policy development in the United States: the role of the Advisory Committee on Immunization Practices," *Annals of Internal Medicine* 150, no. 1 (January 6, 2009): 46.

<sup>24</sup> Larry Pickering, interview by Peter Doshi, July 28, 2010.



approximately 36,000 deaths during 1990–1999 and approximately 226,000 hospitalizations during 1979–2001.”<sup>25</sup>) Furthermore, despite ACIP’s awareness that randomized controlled trial evidence is lacking regarding the vaccine’s ability reduce deaths among the elderly, ACIP states that the creation of such “best evidence” would be unethical. “[R]andomized controlled trials cannot be performed ethically in populations for which vaccination already is recommended,”<sup>26</sup> ACIP wrote, suggesting that it will instead rely on observational cohort studies<sup>27</sup> which support its current recommendations but have been shown to suffer from overwhelming bias.<sup>28</sup>

There are other reasons why influenza control policies are problematic. First, even the best policies in which Planned Adaptation is well implemented do not guarantee that policies will be error-free, even after many years and revisions. Although pharmaceuticals are approved as “safe and effective” by the Food and Drug Administration, there is widespread recognition by professionals and the public alike that most medications carry a host of potential side effects. Although few may realize the magnitude of the harms from drugs,<sup>29</sup> the point is that expert systems such as clinical trials and drug regulation do not guarantee the absence of error.

Second, peer-review is far from perfect. Despite the fact that influenza control recommendations refer to hundreds of peer-reviewed scientific articles, the inference that guidelines referring to peer-reviewed articles must be robust and evidence based is questionable. While the practice of peer review far predates the entrance of industry into science, modern conceptions of peer review have maintained it as a robust mechanism for scientists to self-regulate and produce the highest quality knowledge.<sup>30</sup> It was the “professional standards of science,” some argued, which generated and coordinated an environment in which scientists could exercise their authority over each other in a form of self-rule.<sup>31</sup> But beginning principally in the 1980s, serious skepticism emerged over the ability of peer-review and other mechanisms of self-regulation to remedy error in science. The notion of fraud in science gained widespread awareness with high profile cases such as that of Margaret O’Toole, Thereza Imanishi-Kari, and Nobel laureate David Baltimore, which involved Secret Service investigations and congressional hearings, helping reframe science as an enterprise gone corrupt, with its actors driven by greed, vanity,

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<sup>25</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010,” 2.

<sup>26</sup> Ibid., 3.

<sup>27</sup> J Nordin et al., “Influenza vaccine effectiveness in preventing hospitalizations and deaths in persons 65 years or older in Minnesota, New York, and Oregon: data from 3 health plans,” *The Journal of Infectious Diseases* 184, no. 6 (September 15, 2001): 665-670; Kristin L. Nichol et al., “Effectiveness of influenza vaccine in the community-dwelling elderly,” *The New England Journal of Medicine* 357, no. 14 (October 4, 2007): 1373-1381; J P Mullooly et al., “Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintenance organization,” *Annals of Internal Medicine* 121, no. 12 (December 15, 1994): 947-952.

<sup>28</sup> Simonsen et al., “Influenza vaccination and mortality benefits”; Jackson et al., “Evidence of bias in estimates of influenza vaccine effectiveness in seniors”; Jefferson et al., “Vaccines for preventing influenza in the elderly”; Lone Simonsen, Cecile Viboud, and Robert J Taylor, “Effectiveness of influenza vaccination,” *The New England Journal of Medicine* 357, no. 26 (December 27, 2007): 2729-2730; author reply 2730-2731.

<sup>29</sup> Starfield, “Is US health really the best in the world?”

<sup>30</sup> Sheila Jasanoff, “Technologies of humility: citizen participation in governing science,” *Minerva* 41, no. 3 (2003): 223–244.

<sup>31</sup> Michael Polanyi, “The republic of science: its political and economic theory,” *Minerva* 1 (1962): 54-73.

jealousy, and careerism.<sup>32</sup> However, as other ways of valuing knowledge claims in science are still largely lacking, skepticism over the objectivity of science at large has done relatively little to change the hierarchy of knowledge within medical science, and results published in peer-reviewed journals remain to be seen as the most credible and trustworthy source of information.

Nevertheless, an additional reason to question the validity of peer-review has come through analysis of the ways in which peer-review can and has been used as a mechanism for suppressing dissent. Brian Martin and Gordon Moran have both documented the difficulties that scholars and other scientists with unpopular theories have had in getting their articles published in refereed journals.<sup>33</sup> In the field of influenza, Lisa Jackson had originally tried to publish her findings—overturning the long-assumed benefits of influenza vaccine to reduce the risk of death in the elderly—in the prestigious *Journal of the American Medical Association*. One peer-reviewer for *JAMA* however wrote that “to accept these [Jackson’s] results would be to say that the earth is flat!”<sup>34</sup> *JAMA* rejected the paper, and Jackson ultimately published her paper in the less prestigious and more specialized but peer-reviewed journal *International Journal of Epidemiology*.<sup>35</sup>

Conversely, just as the system of peer-review can function in such a way as to keep important research from gaining prominence, it can give problematic, faulty, or even fraudulent research a veneer of certitude and respectability. Such was the case in two blockbuster COX-2 inhibitor anti-arthritis drugs, Vioxx (manufactured by Merck) and Celebrex (manufactured by Pfizer). The two key clinical trials of these drugs were the “VIGOR” and “CLASS” studies, respectively, both carried out by the drugs’ manufacturers. In these studies, neither Vioxx nor Celebrex provided any better relief of arthritis symptoms or pain than over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs) which cost one seventh to one twentieth of the price of the new drugs.<sup>36</sup> The new drugs also showed little to no safety advantage over cheaper and older medications. Those taking Vioxx, in fact, had significantly more serious complications. All of these data were shared with the Food and Drug Administration. Despite this, the drugs were not only approved, but went on to become blockbusters, with around \$20 billion in sales. How this happened, John Abramson and Barbara Starfield argue, “lies in the process by which raw data becomes medical ‘knowledge’—through publication in respected medical journals and incorporation into clinical practice guidelines.” They explain:

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<sup>32</sup> Lang, *Challenges*; Daniel Kevles, *The Baltimore case: a trial of politics, science, and character* (New York; London: W. W. Norton, 2000); Jasanoff, “Technologies of humility”; Robert Bell, *Impure Science: Fraud, Compromise and Political Influence in Scientific Research* (Wiley, 1992); William J. Broad and Nicholas Wade, *Betrayers of the truth* (New York: Simon and Schuster, 1982).

<sup>33</sup> Brian Martin, *Suppression Stories* (Wollongong: Fund for Intellectual Dissent, 1997); Gordon Moran, *Silencing Scientists and Scholars in Other Fields: Power, Paradigm Controls, Peer Review, and Scholarly Communication*, Contemporary studies in information management, policy, and services (Greenwich, Ct: Ablex Publishing, 1998).

<sup>34</sup> Brownlee and Lenzer, “Does the Vaccine Matter?”

<sup>35</sup> Jackson et al., “Evidence of bias in estimates of influenza vaccine effectiveness in seniors.”

<sup>36</sup> John Abramson and Barbara Starfield, “The effect of conflict of interest on biomedical research and clinical practice guidelines: can we trust the evidence in evidence-based medicine?,” *The Journal of the American Board of Family Practice* 18, no. 5 (October 2005): 415.

The *JAMA* published the results of the CLASS study in September of 2000. The article concluded that Celebrex “when used for 6 months . . . is associated with a lower incidence” of GI complications. But CLASS was a 12-month study, and all 12 months had been completed at the time the manuscript reporting the results of only the first half of the study was submitted to *JAMA*. In the unreported second 6 months of the study, all but one of the 7 serious GI complications occurred in people taking Celebrex, not older NSAIDs. All 16 of the authors of this article had financial ties to or were employed by the manufacturer of Celebrex.

When the editor of *JAMA* learned that data from only the first half of the study had been included in the article, she told the *Washington Post*, “I am disheartened to hear that they had those data at the time that they submitted [the manuscript] to us. . . We are functioning on a level of trust that was, perhaps, broken.” Reprints of this article distributed by drug reps for marketing purposes were stamped with a disclaimer stating that it contains “Comparative results that are not supported by substantial clinical evidence” (presumably based on the FDA’s rejection of the manufacturer’s analysis of the data from only the first half of the study). Nonetheless, the article was never retracted by the journal.

The *NEJM* published the results of the VIGOR study in November of 2000. This article concluded that Vioxx causes fewer serious GI complications than naproxen [a generic NSAID] and left even diligent readers with the impression that for most patients, Vioxx is safer than naproxen. Although the *NEJM* article reported that patients taking Vioxx who had a previous history of cardiovascular disease were at greater risk of suffering a myocardial infarction, it failed to report that patients who took Vioxx developed significantly more serious thrombotic cardiovascular complications in toto (the prespecified cardiovascular outcome, not myocardial infarction alone) whether or not they had a previous history of cardiovascular problems. The article also failed to report that patients who took Vioxx developed overall significantly more serious illnesses than those who took naproxen. All 13 of the authors of this article had financial ties to or were employed by Merck. (The *NEJM* article did report that those who took Vioxx were more likely to suffer myocardial infarction but that this risk was not statistically significant in those without a previous history of cardiovascular disease.)<sup>37</sup>

Far from providing the highest quality of scientific information, in the case of Vioxx and Celebrex, the publication of research in peer-reviewed medical journals<sup>38</sup> helped buttress inaccurate understandings

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<sup>37</sup> Ibid.

<sup>38</sup> Claire Bombardier et al., “Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis,” *New England Journal of Medicine* 343, no. 21 (2000): 1520-1528; F E Silverstein et al., “Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: A randomized controlled trial. Celecoxib Long-term Arthritis Safety Study,” *Journal of the American Medical Association* 284, no. 10 (September 13, 2000): 1247-1255.

of the benefits and harms of certain drugs, and swayed clinical practice in ways that were largely to the detriment of patient care.

The Vioxx and Celebrex cases also highlight another element of modern medical research: the role of industry. In the last quarter of the twentieth century, biomedical research has become increasingly funded by the pharmaceutical industry, and influenza science is no exception. Sheldon Krimsky argues that it is not only public confidence in science which has eroded as a result. The ethical norm of disinterestedness (one of the four key institutional imperatives identified by sociologist Robert Merton as necessary for science to operate in its most enlightened forms<sup>39</sup>) is altered by the influx of corporate money into academic science, and introduces bias. While scientific knowledge may eventually converge on the truth, a “science driven by private interests” will take longer to get there, Krimsky notes. Furthermore, industrial sponsorship redirects scientists away from their proper public orientation such that academic scientists end up “pursuing knowledge in certain fields for selected problems where there are commercial interests,” such that science of “little commercial but of great public interest” gets comparatively less attention.<sup>40</sup>

Other observers are equally pessimistic about the effects of science driven by private interests. Sociologist John Abraham argues that “corporate bias” alters the conduct of science to such a degree that Mertonian norms of science are of limited relevance in industrial science.<sup>41</sup> After detailed study of five non-steroidal anti-inflammatory drugs (NSAIDs), Abraham concludes that scientists working for industry “have put forward self-contradictory arguments or made claims that were logically inconsistent with the established scientific standards of drug testing and medication at the time.”<sup>42</sup>

While government funding has propelled a considerable amount of influenza research—a recent systematic review of 274 studies comparing influenza vaccines against placebo or no intervention found 48% were government financed<sup>43</sup>—industry still finances much research in the field, including crucial clinical trials of vaccines and antivirals which form the basis of regulatory approval. In the last decade, research on the effects of industry funding of medical science has shown that funding, publication, and peer review interact in consistent patterns: industry sponsorship is significantly correlated with pro-industry conclusions,<sup>44</sup> meta-analyses with financial ties to drug companies are more likely to report favorable conclusions (but not favorable results),<sup>45</sup> and “systematic bias favours products which are made by the company funding the research.”<sup>46</sup> In the field of influenza vaccine studies, Jefferson and

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<sup>39</sup> Robert King Merton, *Social theory and social structure* (New York: The Free Press, 1968).

<sup>40</sup> Krimsky, *Science in the Private Interest*, 73-81.

<sup>41</sup> Abraham, *Science, Politics And The Pharmaceutical Industry*, 241.

<sup>42</sup> *Ibid.*, 242.

<sup>43</sup> Jefferson et al., “Relation of study quality, concordance, take home message, funding, and impact in studies of influenza vaccines.”

<sup>44</sup> Justin E. Bekelman, Yan Li, and Cary P. Gross, “Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review,” *Journal of the American Medical Association* 289, no. 4 (January 2003): 454-465.

<sup>45</sup> Veronica Yank, Drummond Rennie, and Lisa A. Bero, “Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study,” *BMJ* 335, no. 7631 (November 2007): 1202-1205.

<sup>46</sup> Joel Lexchin et al., “Pharmaceutical industry sponsorship and research outcome and quality: systematic review,” *BMJ* 326, no. 7400 (May 2003): 1167-1170.

colleagues found that “publication in prestigious journals is associated with partial or total industry funding, and this association is not explained by study quality or size.”<sup>47</sup> What these issues point to is the difficulty in assessing clinical trials and other information that appears in the peer-reviewed literature, even in prestigious journals which are still considered the best source of objective information. A clear first step would be the setting of pre-defined, transparent, reproducible methods for analyzing and synthesizing all information, as advocated by groups such as the Cochrane Collaboration. While ACIP does not currently present details regarding its strategy for selecting and synthesizing data it incorporates into its recommendations, there are initiatives underway to incorporate evidence-based medicine in a more deliberate and obvious way.<sup>48</sup>

A final reason for why Planned Adaptation is only superficially being applied to ACIP policy recommendations may be that there has never been a true commitment to an adaptive policy, but rather a policy of continual expansion of influenza vaccine recommendations. Since at least 2006, ACIP’s interest in moving towards a policy of universal influenza vaccination has been readily apparent in its guidance documents, despite knowledge that the scientific data was lacking. In minutes from the meeting when the first formal commitment to the possibility of universal vaccination was made, it is noted that “ultimately, the meeting participants reached consensus to move toward a universal recommendation, but recommended that implementation occur in stages over time to avoid unintended consequences and to have time to fill the information gaps.”<sup>49</sup> But even before this, Alan Hinman, the former director of what is now the National Immunization Program, recalled that one of the lessons of the 1976 swine flu debacle was “a realization that expansion to pandemic level vaccination of the entire population would be much easier if there was an effective, stable, ongoing [influenza] vaccination program.”<sup>50</sup>

### **Pandemic influenza policy**

As major public health policies, pandemic influenza plans are another area that could stand to benefit greatly from Planned Adaptation. As planning for a pandemic is fundamentally about preparing for a future and therefore unknown event, there is a high level of uncertainty inherent to the process. Efforts to get the policy right will therefore need to review and revise planning policies in light of new evidence and greater knowledge of pandemics. This might happen both before a pandemic (by making sure that policies are consistent with up to date understandings of pandemics), during a pandemic (by reviewing and adjusting policies as the outbreak situation evolves), and after a pandemic (by revising overarching planning guidelines in light of the “lessons learned” during the pandemic).

As with seasonal influenza policy, pandemic planners seem to have been tuned into the virtues of Planned Adaptation, mostly saliently acknowledged in the emphasis planning documents placed on the

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<sup>47</sup> Jefferson et al., “Relation of study quality, concordance, take home message, funding, and impact in studies of influenza vaccines.”

<sup>48</sup> Pickering, interview; “Record of the meeting of the Advisory Committee on Immunization Practices”, February 10, 2005, <http://www.cdc.gov/vaccines/recs/acip/downloads/min-archive/min-feb05.rtf>, (accessed June 16, 2011).

<sup>49</sup> “Record of the meeting of the Advisory Committee on Immunization Practices,” 64/111.

<sup>50</sup> *Update: Preparing for the Next Influenza Pandemic*, 2000, [http://video.cdc.gov/ramgen/phppo/PublicAccess/NIP/influenza/influenza\\_pandemic.rm](http://video.cdc.gov/ramgen/phppo/PublicAccess/NIP/influenza/influenza_pandemic.rm).

need for flexibility and adaptation during an evolving outbreak response. For example, HHS's pandemic influenza plan stated:

An effective local response will depend on pre-established partnerships and collaborative planning by public health officials, hospital administrators, and community leaders, who have considered a range of best-case and worst-case scenarios. It will require flexibility and real-time decision-making, guided by epidemiologic information on the pandemic virus.<sup>51</sup> ...

Given some uncertainty about the characteristics of a new pandemic strain, all aspects of preparedness planning for pandemic influenza must allow for flexibility and real-time decision-making that take new information into account as the situation unfolds.<sup>52</sup>

Likewise, guidelines for vaccine allocation took into account not only a variable supply of vaccines in the event of a pandemic, but the need to allocate vaccine in different ways depending on the severity of the outbreak. The guidance document, co-published by HHS and Department of Homeland Security, stated:

... it is important that plans are flexible as the guidance may be modified based on the status of vaccine technology, the characteristics of pandemic illness, and risk groups for severe disease – factors that will remain unknown until a pandemic actually occurs.<sup>53</sup>

In the United States, the CDC-led community mitigation guidance document, which introduced the "Pandemic Severity Index" tool for measuring pandemics in real-time, divided pandemics into five "categories" primarily based on the case fatality ratio which could be measured fairly easily and early in an evolving pandemic outbreak. It is perhaps the most lucid example of a policy firmly written with a built-in notion of Planned Adaptation. Nonpharmaceutical interventions such as voluntary isolation, school closures, and the cancellation of public gatherings were to be recommended in accordance with the severity of the pandemic such that they remained calibrated to the threat. The Introduction to the planning document stated:

Response guidance will need to remain flexible and likely will require modification during a pandemic as information becomes available and it can be determined if ongoing pandemic mitigation measures are useful for mitigating the impact of the pandemic. Pandemic planners need to develop requirements for community-level data collection during a pandemic and develop and test a tool or process for accurate real-time and post-wave evaluation of pandemic mitigation measures, with guidelines for modifications.<sup>54</sup>

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<sup>51</sup> U.S. Department of Health and Human Services, "HHS Pandemic Influenza Plan," 1-2.

<sup>52</sup> *Ibid.*, 1-7.

<sup>53</sup> U.S. Health and Human Services, "Guidance on Allocating and Targeting Pandemic Influenza Vaccine", July 23, 2008, 1, <http://www.pandemicflu.gov/vaccine/allocationguidance.pdf>.

<sup>54</sup> U.S. Centers for Disease Control and Prevention, "Interim Pre-pandemic Planning Guidance," 20.

Elsewhere, pandemic plans placed similar attention on the need for flexibility as an adaptive strategy for handling uncertainty:

The plan is also intended to be flexible so that our response can be adapted as a pandemic evolves and knowledge about the new virus, its impact and the effectiveness of available countermeasures emerges.<sup>55</sup>

“Introduction,” *UK Influenza Pandemic Contingency Plan* (2005)

Response arrangements must be flexible enough to deal with a range of possibilities and be capable of adjustment as they are implemented.<sup>56</sup>

“Key planning assumptions,” UK Department of Health, *Pandemic Flu: a national framework for responding to an influenza pandemic* (2007)

The proposed measures are based upon current knowledge of outbreaks of seasonal influenza and past pandemics. Recommendations may be adjusted based on new evidence and experience.<sup>57</sup>

“Overarching goals, objectives and actions for each phase,” *WHO global influenza preparedness plan* (2005)

Even when flexibility and adaptation are not explicitly mentioned, the very fact that pandemic planning documents were continually updated—the WHO’s original plan was published in 1999 and updated in 2005 and 2009, for example—is evidence that public health experts were aware of the need to constantly adapt to new information. The SARS and avian influenza H5N1 experiences had a major effect in probing governments to rethink and revise their plans should an influenza pandemic emerge. In the United States, it was a disaster from a source completely unrelated to disease—Hurricane Katrina—that prompted the Bush administration to significantly overhaul its pandemic influenza response plan.

But for all the signs of Planned Adaptation, the 2009 H1N1 outbreak has shown that the commitment to adjusting plans based on new information and changing circumstances was limited. As information emerged over the summer of 2009 suggesting that H1N1’s impact may be far less than even the best-case scenarios envisioned in any national plan,<sup>58</sup> response efforts largely stayed within the range identified by pandemic plans. During the outbreak, public health officials continually stressed a

<sup>55</sup> UK Department of Health, “UK Influenza Pandemic Contingency Plan”, October 20, 2005, 11, [http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/@dh/@en/documents/digitalasset/dh\\_4121744.pdf](http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4121744.pdf), (accessed June 16, 2011).

<sup>56</sup> UK Department of Health, “Pandemic flu: a national framework for responding to an influenza pandemic,” 23.

<sup>57</sup> World Health Organization, “WHO global influenza preparedness plan”, 2005, 10, [http://www.who.int/csr/resources/publications/influenza/WHO\\_CDS\\_CSR\\_GIP\\_2005\\_5.pdf](http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5.pdf).

<sup>58</sup> Peter Doshi, “Pandemic Influenza: Severity Must Be Taken into Account,” *The Journal of Infectious Diseases* 201, no. 9 (May 2010): 1444-1445.

precautionary approach of preparing for the worst, and spoke of a general uncertainty about the disease, with frequent reference to the seemingly severe situation in Mexico and the always unknown future.<sup>59</sup> Data from the southern hemisphere, indicating an outbreak of intensity in many ways comparable or even less severe than seasonal influenza, was not as readily acted upon.<sup>60</sup>

Some responses certainly were scaled back in line with an evolving evidence base which early in the H1N1 outbreak suggested that the problem may be less severe than expected—Japan, for instance, terminated its strict border control screening measures and other countries did not repeat Mexico's decision to virtually shut down its capital city—but overarching assumptions, such as the necessity of a universal vaccination program and the prudence of using pandemic plans (which were based on the assumption of an outbreak of extraordinary severity) to respond to a disease of seasonal intensity, were not seriously questioned by public health leaders themselves, only by outside critics.

In the United Kingdom, one of the earliest countries to be affected by H1N1—and where there was much criticism of officials for “overreacting”<sup>61</sup> to H1N1—an independent review was commissioned. Its first recommendation is for a more flexible response: “Ministers should determine early in a pandemic how they will ensure that the response is proportionate to the perceived level of risk and how this will guide decision-making.”<sup>62</sup> This theme—for flexibility and proportionality—is a fundamental conclusion of the Council of Europe investigation<sup>63</sup> as well as the independent review panel set up by WHO, which declared that there is a need for plans that “emphasize a risk-based approach to enable a more flexible response to different scenarios.”<sup>64</sup>

The CDC, which had the most sophisticated and detailed guidelines for a flexible, risk-based response in place before H1N1 2009 emerged, in the end did not employ its Pandemic Severity Index; and H1N1 was never classified as a Category 1, 2, 3, 4, or 5 pandemic. Emergency measures such as the more liberal use of influenza antivirals—to children under one year of age, and using these drugs past their expiration dates—were kept in place for over a year on the basis that H1N1 constituted a public health emergency.<sup>65</sup> The United States has not commissioned an external review of its handling of the H1N1 outbreak, nor has it announced plans to do so.

## Revisiting conflicts of interest

The critique that influenza policy is unduly shaped by industrial interests is a compelling framework that has been offered to explain the problems identified during the H1N1 outbreak of 2009, particularly

<sup>59</sup> Council of Europe, “The handling of the H1N1 pandemic: more transparency needed.”

<sup>60</sup> Foulkes, “WHO faces questions over swine flu policy.”

<sup>61</sup> Eleanor Bradford, “Did the authorities overreact to swine flu?,” *BBC*, April 27, 2010, sec. Scotland, [http://news.bbc.co.uk/2/hi/uk\\_news/scotland/8646754.stm](http://news.bbc.co.uk/2/hi/uk_news/scotland/8646754.stm), (accessed June 17, 2011).

<sup>62</sup> Hine, “The 2009 Influenza Pandemic,” 5.

<sup>63</sup> Council of Europe, “The handling of the H1N1 pandemic: more transparency needed,” 10.

<sup>64</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, “Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009,” 19.

<sup>65</sup> Margaret A. Hamburg to Thomas R. Frieden, “Termination of Declarations of Emergency Justifying Emergency Use Authorization (EUA) of Certain Antiviral Drugs--Zanamivir, Oseltamivir Phosphate, Peramivir”, June 21, 2010, <http://www.cdc.gov/H1N1flu/EUA/pdf/Antivirals.pdf>, (accessed June 17, 2011).



concerning claims that public health institutions overreacted to H1N1, not only misusing public money, but also injuring the public trust in public health guidance.<sup>66</sup> Perhaps the divergences between what should have happened and what did happen were the effects of money. Many details have emerged that point in the direction of the conclusion that a profit-driven industry has indeed been able to use the state for its own (private) purposes: documented examples of influenza policy makers who also have financial relationships with the pharmaceutical industry, governments' outlay of enormous sums of money stockpiling antiviral medications and purchasing influenza vaccines of questionable effectiveness, and the general trend within academia and government to work with industry as a "partner." If true, it would hardly be the first instance. Forty years ago, the political scientist George Stigler, in fact, said such a relationship was fundamental to the nature of regulation. Stigler wrote that no matter whether industry seeks out regulation or is bound to it by law, "as a rule, regulation is acquired by the industry and is designed and operated primarily for its benefit."<sup>67</sup> While admitting that some regulations would indeed put onerous demands on industry, Stigler nonetheless argued that in the main, regulation was in industry's benefit.

Stigler's "theory of economic regulation" was not focused on examples such as vaccine policy—which strictly speaking are not matters of regulation but of official advice—but rather in the effects of governmental regulation on controlling market entry in certain industries, or setting prices. Nevertheless, ACIP recommendations on vaccines carry enormous implications, privileging certain modes of medical care over others. In the case of influenza, ACIP's focus on vaccines as a way to prevent and control the disease helps ensure that alternative or competing approaches, such as hand washing, remain peripheral. The influenza vaccine industry, quite unsurprisingly, advocates for ACIP to continue and expand its support of its product—efforts that get amplified at annual meetings such as the National Influenza Vaccine Summit.

Following the *BMJ/The Bureau* investigation by Cohen and Carter which revealed that a World Health Organization pandemic planning guidance document had not disclosed that some of its authors had been paid for work by the pharmaceutical industry, a number of scientists and some public health agencies objected to the suggestion that decision making at WHO might have been compromised by industry. Two major arguments were voiced: first, drawing on the best influenza experts inevitably means tapping people who have at some point worked with industry, because all bodies, including industry, want to use the best experts; second, the insinuation that experts who had not had relationships with pharmaceutical companies would have provided different advice is false.<sup>68</sup> Considering how policy making might improve in the future requires a thorough examination of both of these claims.

In an interview, WHO spokesperson Gregory Härtl explained the Organization's position regarding the scarcity of high quality expertise:

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<sup>66</sup> Epstein, "Flu Warning."

<sup>67</sup> George J. Stigler, "The economic theory of regulation," *Bell Journal of Economics* 2, no. 1 (1971): 3.

<sup>68</sup> Declan Butler, "Flu experts rebut conflict claims," *Nature* 465, no. 7299 (June 10, 2010): 672-673; Elizabeth Sukkar, "WHO reveals H1N1 committee's links with big pharma", August 11, 2010, <http://www.ghwatch.org/who-watch/h1n1>, (accessed June 16, 2011).

If you are the best footballer, everyone wants that footballer ... The influenza community is quite small and we can understand the experience [these experts] have accumulated before working with us. Also, [the experts] have more to lose without declaring their interests. The quality of [members in] the emergency committee was very high. You want those types of people advising on monumental decisions [such as H1N1 pandemic].<sup>69</sup>

There is an unstated assumption in Härtl's comment that the best quality advice on decision making necessarily comes from the influenza experts. There are several reasons to question the soundness of this judgment. First, as epidemiologists Luc Bonneux and Wim Van Damme have argued, there may be adverse effects when policy is largely driven by disease experts whose professional identity is tied to a single disease. They argue that such experts are not necessarily competent to judge a disease's relative importance against competing health priorities, and given the reality that in public health, as other areas of public spending, budgets are limited, they argue that "final evidence-based policy advice should be drafted by independent scientists trained in evaluation and priority setting."<sup>70</sup> Harvey Fineberg and Richard Neustadt came to similar conclusions in their study of the abortive 1976 "swine flu" epidemic in the United States:

The best of expert panels should be supplemented by separate scientific advice. In a swine flu case when evidence is thin—with unobserved phenomena vastly outweighing observations from the three pandemic years of 1918, 1957, 1968—it is not only the assumptions but appraisal of their scientific quality that top decision-makers need. Panels tend toward "group think" and over-selling, tendencies nurtured by long-standing inter-changes 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. In medicine, as in law, there are rules of evidence by which argument can be tested. A [Secretary of Health, Education and Welfare] Califano needs an assured source of such review to do for him what a good science adviser does for the President. The Secretary may not need one designated "adviser." In medical fields his Department has plenty of scientists. The problem is to make them scrutinize and check each other's logic for his benefit.<sup>71</sup>

In the "highly competitive market of health governance," Bonneux and Wim Van Damme write, "the struggle for attention, budgets and grants is fierce."<sup>72</sup> Disease experts therefore have a vested interest to keep the spotlight on their particular area of expertise.

Härtl's claim about the limited availability of influenza experts who are free of financial conflicts of interest is hard to verify empirically, as surveys have not been carried out and will inevitably struggle with defining who is and is not an "expert," but nonetheless raises a more fundamental question about

<sup>69</sup> Sukkar, "WHO reveals H1N1 committee's links with big pharma."

<sup>70</sup> Luc Bonneux and Wim Van Damme, "Preventing iatrogenic pandemics of panic. Do it in a NICE way," *BMJ* 340, no. jun09\_3 (June 9, 2010): c3065.

<sup>71</sup> Neustadt and Fineberg, *The Swine Flu Affair*, 89-90.

<sup>72</sup> Bonneux and Van Damme, "Health is more than influenza," 539-540.

whether industry involvement in the conduct of public interest science is inherently corrupting. Does it change the ethos of science such that industry relationships are now seen as “inevitable” rather than “unacceptable,” a fact of life to be “managed” rather than “avoided”? Given the documented biasing effects of commercial interests in medicine, public health agencies would seem to have an imperative to create the circumstances and incentives for truly commercial-free advice.

The second rebuttal to those concerned over conflicts of interest has been the argument that advice from scientists free of industry funding was no different than the advice of those with industry funding, and therefore conflicts of interest are not as problematic as some critics have suggested.<sup>73</sup> To a great extent, it is true that public health practitioners have been in agreement over fundamental aspects of influenza—its epidemiology and proper methods of control. But this general agreement does not dismiss the power of money to bias scientific research and policy. At the same time, it points to the need to locate additional factors which may account for the general consensus about influenza, and conviction that while imperfect, the decisions that were made in response to H1N1 in 2009, were the fully justified.

In its report, the IHR Review Committee stressed the role of the “ethos of public health”:

The core values of public health shaped the response of public-health leaders around the world to the pandemic. The main ethos of public health is one of prevention: to prevent disease and avert avoidable deaths. The response of WHO and many countries to the pandemic was a reflection of this mindset. This was affirmed in the sentiments expressed by many Member States to the Review Committee: in the face of uncertainty and potentially serious harm, it is better to err on the side of safety. Public-health officials believe and act on this conviction. It is incumbent upon political leaders and policy-makers to understand this core value of public health and how it pervades thinking in the field.<sup>74</sup>

In 1976, President Ford made a similar argument. Knowing that the mass vaccination program could end up a massive waste of public money if the anticipated virus did not appear, it was nonetheless declared better to “gamble with dollars, not lives.”<sup>75</sup> Four decades later, the IHR Review Committee suggested that this same ethos—not financial interests—accounted for WHO’s behavior during the 2009 H1N1 outbreak:

Some commentators accused WHO of rushing to announce Phase 6 and suggested the reason was to enrich vaccine manufacturers, some of whose advance-purchase agreements would be triggered by the declaration of Phase 6. Far from accelerating the

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<sup>73</sup> Butler, “Flu experts rebut conflict claims.”

<sup>74</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, “Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009,” 10.

<sup>75</sup> Walter Dowdle, “Lessons from 1976” (presented at the Committee on Implementation of Antiviral Medication Strategies for an Influenza Pandemic, Washington, DC, January 7, 2008), 3, <http://www.iom.edu/~media/Files/Activity%20Files/Disease/FluAntiviralStrat/Dowdle.ashx>, (accessed June 17, 2011).

declaration of Phase 6, WHO delayed declaration until evidence of sustained community spread in multiple regions of the world was undeniably occurring. As far as the Review Committee can determine, no critic of WHO has produced any direct evidence of commercial influence on decision-making. In its interviews with staff and advisory committee members, including the Strategic Advisory Group of Experts and the Emergency Committee, and with representatives of industry, and through its review of internal and external documents, the Review Committee found no evidence of attempted or actual influence by commercial interests on advice given to or decisions made by WHO. In the Committee's view, the inference by some critics that invisible commercial influences must account for WHO's actions ignores the power of the core public-health ethos to prevent disease and save lives.<sup>76</sup>

This explanation suggests that two basic intertwined positions ruled the response to H1N1: that putting something into action is always preferable to inaction, and that vaccines and antivirals were better interventions than no intervention. The implication is that even if vaccines arrived after the peak of the epidemic (as they did in the case of H1N1), using them would be better than nothing. This position is similar to that voiced by the epidemiologist Lone Simonsen, in response to more research showing influenza vaccines had lower efficacy than advertised: "The vaccine is still important. Thirty percent protection is better than zero percent."<sup>77</sup>

The "public health ethos" is an admittedly strong and powerful explanatory mechanism for understanding public health decision making, particularly under situations of high uncertainty and high risk, but it leaves unanswered questions such as:

- Why did public health officials assume that H1N1 vaccination programs would do more good than harm?
- Why were contradictory conclusions between FDA and CDC on the effects of the stockpiled antiviral Tamiflu not treated as problematic?

It also leaves unexplained a host of observations relevant to the handling of seasonal influenza:

- The continual expansion of who is "at risk" from influenza, and therefore in need of annual vaccination
- The lack of interest in educating the public about the difference between influenza versus "flu" (ILI, influenza-like illness) despite emphasis in educating people about the dangers of influenza
- The response to data showing influenza vaccines have not reduced deaths was a call for expanding the groups of people said to need annual influenza vaccination

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<sup>76</sup> Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009, "Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009," 17.

<sup>77</sup> Brenda Goodman, "Doubts Grow Over Flu Vaccine in Elderly," *The New York Times*, September 2, 2008, sec. Health, <https://www.nytimes.com/2008/09/02/health/02flu.html>, (accessed June 17, 2011).

- The lack of interest in randomized controlled trials of influenza vaccine despite acknowledgement that current policy is not based on high quality data and uncertainty over ability of influenza vaccine to reduce the risk of death
- The lack of interest (until recently) to determine what proportion of influenza-like illness (ILI) is caused by influenza and other agents
- The lack of interest in sponsoring head-to-head trials of influenza vaccine versus other non-pharmaceutical interventions but simultaneous conviction that influenza vaccine is the “best” protection against “flu”
- Belief that a severe, 1918-like pandemic has the same probability of repeating as an relatively uneventful, 1968-like pandemic
- The advocacy of policy which sets as its goal the vaccination of certain percentages of the population without any guarantee that this will result in less morbidity or mortality

While any one of these questions may be answered by pointing to the possible effects of industry, it must be recalled that these observations apply to not only influenza experts, but many other public health practitioners at the federal, state, and local level, most of whom do not have relationships with industry. Implementing influenza control activities such as vaccination programs involves a large number of public health practitioners, and it is only an extreme minority of those individuals who are influenza experts and aware of problems in the evidence base.

My argument is that virus-centric thinking dominates the logic of public health, and by influenza’s mere status as a “vaccine preventable disease,” the vast majority of officials will find vaccines and other virus-specific interventions to be the obvious answer to influenza even without having done any research of their own, or perhaps even feeling the need to do independent research. It is a policy that is easy to get behind and defend. Consider the case of the state health departments of California, Arizona, Texas, and New York—the four largest states of the Pacific, Mountain, Central, and Eastern regions, respectively. There is almost no variation among statements the four state health departments make about who should get influenza vaccine, and how safe and effective the vaccine is (Table 6.1; Table 6.2). The reason for this uniformity is that the information all points back to CDC. State health departments, despite their independence from CDC, evidently trust CDC’s conclusions about the science and policy of influenza. These chains of trust, embedded in a shared logic of virus-centric thinking, perpetuate error, impeding the adaptation and improvement of influenza policy.

### **Doing reliable knowledge assessment**

Making public policy consistent with the best syntheses of evidence requires adopting methods to ensure that high quality assessments of knowledge get incorporated into policy. A first step may be to ensure that credible knowledge assessment can even occur.

In the case of influenza policy, current institutional arrangements would seem to provide disincentives for “getting the science right” because of built-in conflicts of interest. In the same way that pharmaceutical money can bias academic researchers by imparting a dual responsibility—both to the integrity of science and to advancing industry’s interest in profit—bias may also occur without the

presence of money, and may be equally powerful. Whenever an individual or group of people have multiple responsibilities in which successfully accomplishing one responsibility may impede the ability to successfully accomplish another responsibility, a non-financial conflict of interest (i.e., conflict of commitment) exists.

In the United States, the same group of people who calculate the risk from influenza also make recommendations on what to do about it. These same individuals likewise have official capacity to report on the effectiveness of those recommendations and conduct public awareness campaigns to raise vaccination levels.<sup>78</sup> This quadruple responsibility—to risk assessment, risk management, effectiveness assessment, and risk communication—creates disincentives to correct error. Providing unbiased knowledge assessments is compromised by these multiple responsibilities.

Political scientist Katherine Martin has written that “in most cases, there are incentives for policymakers to exaggerate certainty in support of their attempts to anticipate the impacts of policies. If they then acknowledge that original policies were wrong, they will be undercutting their own credibility.”<sup>79</sup> While officials always describe influenza as a mutating and inherent unpredictable virus, they project certainty regarding the threat that influenza poses and the importance of pharmacological approaches. Public health, like many governmental institutions, renders itself accountable by being able to justify its actions on quantifiable measures of morbidity, mortality, and therapeutic efficacy. The CDC’s now superseded estimate of an average of 36,000 annual deaths from influenza that was published in the *Journal of the American Medical Association*<sup>80</sup> was one such way the agency could demonstrate that it was fulfilling its mission of basing decisions on “the highest quality scientific data.”<sup>81</sup> In what some anthropologists have termed our “audit cultures,”<sup>82</sup> the mere existence of these figures—published and citable—can be seen as more important than their accuracy. To acknowledge basic problems in the assessment of influenza’s impact or the effectiveness of vaccines would potentially cast doubt on the scientific competence of those experts, risk the public trust, and possibly lead to the reprioritization of governmental funding away from influenza.

Likewise, for policymakers responsible for both recommending interventions and evaluating how well those interventions work, there are incentives to ensure the evidence for vaccine effectiveness is consistent with recommendations, projecting an image that prior policy decisions are validated by the latest evidence. The fact that a single agency—CDC—is responsible for so many aspects of policy formation and review may be considered a kind of knowledge monopoly. Doing reliable knowledge

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<sup>78</sup> My critique about conflicts in responsibilities builds on a critique that has been voiced numerous times by those who oppose the CDC’s responsibility for both recommending vaccines and conducting vaccine safety research, not limited to the case of influenza. See, for example, Arthur Allen, *Vaccine: The Controversial Story of Medicine’s Greatest Lifesaver* (W. W. Norton & Company, 2008), 403; SafeMinds, “Federal Vaccine Court Rules Against Autism Families”, March 12, 2010, [http://www.safeminds.org/news/pressroom/press\\_releases/SafeMinds%20VICA%20Thimerosal%20rulings%20FINAL3-12-09.pdf](http://www.safeminds.org/news/pressroom/press_releases/SafeMinds%20VICA%20Thimerosal%20rulings%20FINAL3-12-09.pdf), (accessed June 14, 2011).

<sup>79</sup> Petersen et al., “Anticipation and Adaptation in Particulate Matter Policy,” 58.

<sup>80</sup> Thompson et al., “Mortality associated with influenza and respiratory syncytial virus in the United States.”

<sup>81</sup> U.S. Centers for Disease Control and Prevention, “Vision, Mission, Core Values, and Pledge.”

<sup>82</sup> Marilyn Strathern, *Audit Cultures: Anthropological Studies in Accountability, Ethics and the Academy*, 1st ed. (Routledge, 2000).

assessments may require that this knowledge monopoly be broken. The way in which the National Transportation Safety Board (NTSB) helps ensure aviation safety may provide a useful example of institutional arrangements which improve the quality of knowledge assessment.

### **Lessons from aviation safety**

According to its mission statement, the Federal Aviation Administration (FAA), housed within the Department of Transportation, strives to make America the safest and most efficient system aerospace system in the world. "Safety is our passion," their website reads.<sup>83</sup> To that end, the FAA has been vested with the powers to regulate all aspects of civil and commercial aviation in this country. FAA promotes safety in part by setting rules for licensure—from the pilots who fly the planes to the aircraft itself, all must meet FAA standards to legally fly. But accidents happen, and it is here where the National Transportation Safety Board helps the FAA (and ultimately the public) strengthen the commitment to safety by conducting thorough independent investigations of transportation accidents.

The work of the NTSB has a high degree of public visibility, which helps ensure that its investigations and safety recommendations are implemented by other government agencies, in particular the FAA. What however perhaps gives the Board the most leverage is its congressional mandate to be independent of the other federal agencies. In 1974, Congress established the NTSB as an independent agency, noting that

Proper conduct of the responsibilities assigned to this Board requires vigorous investigation of accidents involving transportation modes regulated by other agencies of Government: demands continual review; appraisal, and assessment of the operating practices and regulations of all such agencies; and calls for the making of conclusions and recommendations that may be critical of or adverse to any such agency or its officials. No Federal agency can properly perform such functions unless it is totally separate and independent from any other department, bureau, commission, or agency of the United States.<sup>84</sup>

Until 1974, the NTSB had been housed in the same Department of Transportation (DOT) with FAA. It was only after several aircraft accidents that pressure mounted to give the NTSB greater authority by making it independent of DOT. A design defect in cargo doors on some aircraft had resulted in the crash of a DC-10 aircraft. Subsequent investigations revealed a design flaw that NTSB had already made recommendations to fix—recommendations that the airlines, FAA, and the White House had not implemented.<sup>85</sup> The establishment of NTSB as an agency operating independently of the agencies which it must necessarily critique helps ensure the proper oversight of transportation security.

Improving decision making in public health may not require introducing any institutional separation as in the case of transportation safety, but it does highlight the benefit of clearly identifying who has responsibility for the various aspects of public health priority setting and response. In the case of

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<sup>83</sup> Federal Aviation Administration, "Mission", 2011, <http://www.faa.gov/about/mission/>, (accessed June 17, 2011).

<sup>84</sup> *Independent Safety Board Act of 1974*, 1975.

<sup>85</sup> McCray, Oye, and Petersen, "Planned adaptation in risk regulation," 955.

influenza, the same general group of people pose and answer virtually all critical questions regarding problem identification and risk assessment (*Is influenza a problem? What is the nature of the problem? How big of a problem is it? To whom? Why?*), priority setting and risk management (*Should anything be done about it? What are the options for prevention and treatment? What are the costs? Is it worth it?*), program execution (awareness campaigns to increase vaccination rates), and program evaluation (*Are risk management strategies working?*)

It seems structurally incongruous to expect the Advisory Committee on Immunization Practices, whose stated mission is to help increase vaccination rates, can dispassionately and fairly consider alternative approaches to controlling influenza other than vaccination. There are no formalized outside checks, either on the science of risk assessment, or on the far more subjective questions of proper risk management. Policy is thus little affected by the concerns of others who may have competing judgments about the soundness and appropriateness of public health guidance.

It is not clear that public health needs a FAA/NTSB like arrangement. In the early 1980s, the National Research Council (NRC) deliberated on the question of whether it is beneficial to separate “the analytic functions of developing risk assessments from the regulatory functions of making policy decisions.”<sup>86</sup> Bitter controversies, particularly over the regulation of chemicals in the environment, had grown between members of the public and regulatory agencies such as the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and the Occupational Safety and Health Administration (OSHA). These federal agencies became increasingly accused of risking the public’s health through overly lax regulation of potentially risky chemicals and industries. Identifying the inherent conflict of interest when the same agency conducted both risk assessment and risk management, some called for a clear separation of those functions. The NRC was asked to deliberate on what might be done to improve policy making.

While the NRC admitted that “organizational separation may help to ensure that risk management considerations do not influence the conduct of risk assessment,”<sup>87</sup> it cautioned that organizational separation also carried several disadvantages, chiefly that it would reduce “the responsiveness of the risk assessment process to the needs of the regulatory agencies for timely reports.”<sup>88</sup> The NRC argued that “other approaches are more likely to maintain the distinction between science and policy in risk assessment,”<sup>89</sup> a distinction it felt important because in the NRC’s view, risk assessment was a fundamentally scientific synthesis of factual knowledge while risk management was inherently a question of social and political calculus. The NRC therefore did not advocate for clear institutional separation—as is witnessed in the FAA/NTSB relationship—but did conclude that a “conceptual distinction” must be maintained:

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<sup>86</sup> Committee on the Institutional Means for Assessment of Risks to Public Health, National Research Council, *Risk Assessment in the Federal Government*, 2.

<sup>87</sup> *Ibid.*, 141.

<sup>88</sup> *Ibid.*, 6.

<sup>89</sup> *Ibid.*, 143.



Regulatory agencies should take steps to establish and maintain a clear conceptual distinction between assessment of risks and the consideration of risk management alternatives; that is, the scientific findings and policy judgments embodied in risk assessments should be explicitly distinguished from the political, economic, and technical considerations that influence the design and choice of regulatory strategies.<sup>90</sup>

### **A refocus on patients**

In an ideal world, the knowledge monopolies in influenza policy would be broken, industry influence would be eliminated, and public health officials would become more self-critical about the many false assumptions of virus-centric thinking. But until that day comes, there may be some actions that can help reveal the many problems in influenza policy and eventually bring officials closer to achieving their fundamental goal of ensuring the health of the public.<sup>91</sup>

First, we must achieve transparency about the goals, and performance, of the policy. At present, the goals of influenza policy are vague and implied: is it to save elderly lives? reduce cases of influenza-like illness? workplace absenteeism? school absenteeism? hospital infections? All of the above? Some of the above? None of the above? Explicit and unambiguous goals—goals identified as goals with quantifiable targets—would allow a benchmark against which the policy can be judged. While a reduction in elderly mortality may be the assumed or implicit goal, the lack of clear specification may be the reason why no formal mechanisms exist to evaluate whether and how well the policy is achieving its goals.

One exception to this is the HHS publication *Healthy Americans 2020*, which sets national objectives and a framework for improving the health of Americans. Like its predecessors, *Healthy Americans 2020* emphasized the continued threat of infectious diseases—including from influenza—and stresses the importance of vaccination. But the benchmark by which the document measures success is the achievement of certain levels of vaccination coverage (e.g. 80% of all healthy adults receiving annual influenza vaccination by 2020), not a measured reduction in morbidity or mortality.<sup>92</sup> This might be the biggest reason that the failure in influenza vaccines to reduce the estimated mortality burden of influenza has caused little controversy or broad questioning over the soundness of policy: the goals of the policy are set such that those implementing the policy can declare success despite a failure to save lives—or even reduce cases of “flu” (ILI), the disease ordinary people are led to believe they can avoid with a “flu shot.”

Incorporating general, primary care physicians and other non-disease experts in policy making may be one way to tie policy goals to endpoints relevant to patients (not disease experts). To not do so risks the protraction of a policy that misses the point. In 2006, the family practice journal *American Family*

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<sup>90</sup> *Ibid.*, 151.

<sup>91</sup> James F Childress et al., “Public health ethics: mapping the terrain,” *The Journal of Law, Medicine & Ethics: A Journal of the American Society of Law, Medicine & Ethics* 30, no. 2 (2002): 170-178.

<sup>92</sup> U.S. Department of Health and Human Services, “Immunization and Infectious Diseases”, December 2, 2010, <http://healthypeople.gov/2020/topicsobjectives2020/pdfs/Immunization.pdf>, (accessed June 17, 2011).

*Physician* posed the following question in its “Cochrane for Clinicians: Putting Evidence into Practice” section:

A healthy one-year-old girl presents in the fall for well-child care and an immunization update. The girl’s mother asks you whether her child should have an influenza vaccination. ... Would an influenza vaccination prevent illness in this patient, and would it be safe?<sup>93</sup>

The journal’s answer was not clear cut: while keeping in mind ACIP’s recommendation to vaccinate, *American Family Physician* noted that the most recent Cochrane systematic review on the subject had found the evidence base left much to be desired. While vaccines appeared to reduce absenteeism in schools, “Effectiveness (i.e., prevention of influenza-like illness, perhaps a clinically more important measure) is poor for all influenza vaccines in healthy children” and safety data were lacking. For children less than two, the vaccine was “no better than placebo and there are no good-quality safety data.” The journal recommended that physicians explain to parents that CDC recommended the vaccine, that the evidence base was lacking, and then leave it to the parent to decide.

The article provoked a letter from Carol Baker and William Schaffner, of the National Foundation of Infectious Diseases, and Richard Zimmerman.<sup>94</sup> The authors rebuffed the journal’s focus on influenza-like illness as a meaningful outcome:

<sup>93</sup> Steven E Roskos, “Vaccines for preventing influenza in healthy children,” *American Family Physician* 74, no. 7 (October 1, 2006): 1123-1125.

<sup>94</sup> In a statement of disclosures accompanying their letter, neither Baker nor Schaffner mentioned that they were both Liaison Representatives to the ACIP at the time. Schaffner was a member of ACIP in 1993 and 1994, liaison representative from 1995-2010, and has been on the ACIP Influenza Working Group since 1999. Zimmerman was a Liaison Representative from 1994-2002, Member of ACIP from 2002-2004, on the ACIP Influenza Working Group from 1999-2004, and its chair in 2004. What the authors did mention was: “Dr. Baker has served as a consultant to Novartis Pharmaceuticals and Inhibitex, as a member of a Safety Evaluation Committee for Merck & Co., and as a speaker for Sanofi-Pasteur. Dr. Schaffner has served as an ad hoc consultant for MedImmune and GlaxoSmithKline, and as a member of a Safety Evaluation Committee for Merck & Co. Dr. Zimmerman has received research and educational grants via nonprofit foundations with original funding from Merck & Co.” For references, see U.S. Centers for Disease Control and Prevention, “Prevention and control of influenza”; “Prevention and control of influenza: Part I, Vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 43, no. 9 (May 27, 1994): 1-13; “Prevention and control of influenza recommendations of the Advisory Committee on Immunization Practices (ACIP). Centers for Disease Control and Prevention,” *MMWR. Recommendations and Reports* 44, no. 3 (April 21, 1995): 1-22; U.S. Centers for Disease Control and Prevention, “Prevention and control of influenza”; “Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 46, no. 9 (April 25, 1997): 1-25; “Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). Centers for Disease Control and Prevention,” *MMWR. Recommendations and Reports* 47, no. 6 (May 1, 1998): 1-26; “Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 48, no. 4 (April 30, 1999): 1-28; Bridges et al., “Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP)”; Carolyn B. Bridges, Keiji Fukuda, Nancy J. Cox, et al., “Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 50, no. 4 (April 20, 2001): 1-44; Carolyn B Bridges, Keiji Fukuda, Timothy M Uyeki, et al., “Prevention and control of influenza. Recommendations of the Advisory Committee on

The article characterizes “prevention of influenza-like illness” as a clinically more important measure of vaccination effectiveness than prevention of influenza. But influenza-like illness is a surrogate marker of effectiveness, measured only to reduce expense and time associated with measuring the more specific laboratory-confirmed infection. Influenza vaccine protects against the influenza virus, not the many other viruses that co-circulate during winter months and cause “influenza-like” illnesses. It is unreasonable to expect any vaccine to protect against infections other than those for which it was designed.<sup>95</sup>

Steven Roskos, author of the original *American Family Physician* article,<sup>96</sup> responded:

Actually, influenza-like illness is a more patient-oriented outcome, whereas influenza infection is a disease-oriented outcome. In other words, patients and their parents are concerned about avoiding illness, missing school or work, and being hospitalized. They are much less concerned about which virus caused their illness.

The debate once again highlights the divergence between the views of disease experts and general physicians, and how policy suffers when it stays in the hands of disease experts. (In 2009, Baker became the chair of ACIP, and national influenza control recommendations continue to privilege influenza-specific outcomes over influenza-like illness.<sup>97</sup>) While disease experts are essential for certain technical advice, decision making would be better placed in the hands of general scientists and clinicians,<sup>98</sup> who may usefully refocus the spotlight on patient-centered outcomes (such as influenza-like illness), not disease-centered outcomes (only those influenza-like illnesses caused by influenza virus).

By refocusing the policy on patients and setting transparent goals to clinically meaningful endpoints (not surrogate markers like vaccination coverage levels), failure to achieve policy goals may help reveal the problems with influenza science to broader public scrutiny, and compel change.

[ENDS]

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Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 51, no. 3 (April 12, 2002): 1-31; Carolyn B. Bridges, Scott A. Harper, et al., “Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP),” *MMWR. Recommendations and Reports* 52, no. 8 (April 25, 2003): 1-34; quiz CE1-4; Harper et al., “Prevention and control of influenza”; Harper et al., “Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP)”; Smith et al., “Prevention and Control of Influenza”; Fiore et al., “Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2007”; Fiore et al., “Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008”; Fiore et al., “Prevention and control of seasonal influenza with vaccines”; Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.”

<sup>95</sup> Carol J Baker, William Schaffner, and Richard K Zimmerman, “Importance of influenza vaccination for children,” *American Family Physician* 76, no. 3 (August 1, 2007): 343-344; author reply 344, 347.

<sup>96</sup> Regarding potential conflicts of interest, Roskos declared: “Nothing to disclose.”

<sup>97</sup> Fiore et al., “Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.”

<sup>98</sup> Bonneux and Van Damme, “Health is more than influenza.”

Table 6.1. Who should get vaccinated, according to state health departments

Agency	Who should get vaccinated?	Rationale/evidence cited (if any)
Pacific state (CA)	<i>Not explicitly stated.</i> <sup>99</sup>	N/A
Mountain state (AZ)	"... everyone six months or older is encouraged to get a vaccine at this time." <sup>100</sup>	Link to CDC website <sup>101</sup>
Central state (TX)	"Everyone 6 months and older should get vaccinated now." <sup>102</sup>	<i>None given.</i>
Eastern state (NY)	"Everyone 6 months and older should get a flu vaccine." <sup>103</sup>	<i>None given.</i>

<sup>99</sup> California Department of Public Health, "Influenza (Flu)", 2010, <http://www.cdph.ca.gov/HealthInfo/discond/Pages/Influenza%28Flu%29.aspx>, (accessed June 17, 2011).

<sup>100</sup> Arizona Department of Health Services, "Influenza (Flu) in Arizona", April 4, 2011, <http://www.azdhs.gov/flu/>, (accessed June 17, 2011).

<sup>101</sup> U.S. Centers for Disease Control and Prevention, "CDC Says 'Take 3' Actions To Fight The Flu", March 7, 2011, <http://www.cdc.gov/flu/protect/preventing.htm>, (accessed June 17, 2011).

<sup>102</sup> Texas Department of State Health Services, *TexasFlu.org*, 2011, <http://www.texasflu.org/>, (accessed June 17, 2011).

<sup>103</sup> New York State Department of Health, "Seasonal Influenza (Flu)", November 2010, <http://www.health.ny.gov/diseases/communicable/influenza/seasonal/>, (accessed June 17, 2011).

Table 6.2. How safe and effective is influenza vaccine, according to state health departments

Agency	How safe and effective is influenza vaccine?	Rationale/evidence cited (if any)
Pacific state (CA)	"The best way to prevent influenza is by getting a flu vaccination each year." <sup>104</sup>	None. However the influenza homepage states, "For more flu information, visit <a href="http://www.flu.gov">www.flu.gov</a> ." <sup>105</sup>
Mountain state (AZ)	"The best way to prevent the flu is to get a flu vaccination." <sup>106</sup>	None. However wording is similar to the CDC claim, "The best way to prevent the flu is by getting a flu <b>vaccination</b> each year." <sup>107</sup>
Central state (TX)	"About the Vaccine" webpage does not make claims about safety and effectiveness. It however, links to numerous CDC influenza webpages.	N/A
Eastern state (NY)	"The flu vaccine takes about two weeks after vaccination for the antibodies to provide protection against influenza virus infection. Until then, you are still at risk for getting the flu." <sup>108</sup>	Specific safety claims are not made on the main pages of the influenza website, however numerous links to CDC's influenza website are provided.

<sup>104</sup> California Department of Public Health, "Influenza (Flu)."

<sup>105</sup> Ibid.

<sup>106</sup> Arizona Department of Health Services, "Influenza (Flu) in Arizona."

<sup>107</sup> U.S. Centers for Disease Control and Prevention, "Key facts about influenza and influenza vaccine."

<sup>108</sup> New York State Department of Health, "What Everyone Should Know About Seasonal Flu and the Seasonal Flu Vaccine", March 2011, [http://www.health.ny.gov/diseases/communicable/influenza/seasonal/what\\_everyone\\_should\\_know.htm](http://www.health.ny.gov/diseases/communicable/influenza/seasonal/what_everyone_should_know.htm), (accessed June 17, 2011).



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