Will Routine Annual Influenza Prevention and Control Systems Serve the United States Well in a Pandemic?

Jeanne S. Ringel, PhD, Melinda Moore, MD, MPH, John Zambrano, MS, and Nicole Lurie, MD, MSPH

ABSTRACT

Objective: To assess the extent to which the systems in place for prevention and control of routine annual influenza could provide the information and experience needed to manage a pandemic.

Methods: The authors conducted a qualitative assessment based on key informant interviews and the review of relevant documents.

Results: Although there are a number of systems in place that would likely serve the United States well in a pandemic, much of the information and experience needed to manage a pandemic optimally is not available.

Conclusions: Systems in place for routine annual influenza prevention and control are necessary but not sufficient for managing a pandemic, nor are they used to their full potential for pandemic preparedness. Pandemic preparedness can be strengthened by building more explicitly upon routine influenza activities and the public health system's response to the unique challenges that arise each influenza season (eg, vaccine supply issues, higher than normal rates of influenza-related deaths). (*Disaster Med Public Health Preparedness.* 2009;3(Suppl 2):S160–S165)

The US public health system is preparing for an eventual influenza pandemic. As part of this preparation, it is important to understand how relevant day-to-day public health systems and activities can be used in a pandemic, a point emphasized recently by an expert panel that was convened to define public health preparedness.[1] Pandemic preparedness can be strengthened by building upon routine elements of the public health system in general, and in particular by building upon routine influenza prevention and control activities and the public health system's response to the unique challenges that arise each influenza season. For example, a number of jurisdictions used the influenza vaccine shortage in 2005 to identify lessons learned and strategies for improvement—lessons that improve preparedness for both future seasonal influenza outbreaks and a future pandemic.[2–7]

Building upon systems used for annual influenza provides an opportunity to leverage resources to improve pandemic preparedness. However, systematic approaches are needed to evaluate the current systems and capabilities. In this article, we present results from an examination of the performance and timeliness of several federal-level systems that are important both for annual influenza season and pandemic preparedness. In discussing these systems, we recognize that the information and experiences that each system generates need to be integrated and tied together with information from other systems and agencies to provide the situational awareness necessary to guide decision making in a pandemic. Moreover, we understand that this may be challenging in the absence of a well-developed model for sharing and accountability across these systems and operational agencies. This study provides a snapshot of the systems in place during the 2005–2006 influenza season and assesses the extent to which these systems could provide the information needed to effectively manage a pandemic.

METHODS

The goal of this study was to assess how well existing systems (eg, surveillance systems, systems to select strains for flu vaccines) could support a pandemic response. Therefore, we sought to identify system elements and related activities that would be needed in a pandemic, have an analog in the annual influenza season, and lend themselves to examination of system performance. The initial selection was informed by a review of annual influenza activities and discussions with experts. The list was then discussed with officials at the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response (DHHS ASPR).

https://doi.org/10.1097/DMP.0b013e3181a61633 Published online by Cambridge University Press

We conducted a review of relevant Web sites and documents as well as informal discussions with experts to identify for each selected activity the systems in place that support those activities and the people within DHHS who are the most knowledgeable about them. Beginning in October 2005, we conducted interviews with the initial set of key informants. We then used a "snowball" approach to identify additional informants and systems. Interviewees were asked to describe the relevant systems and the data they generate and to demonstrate how quickly the data could be obtained. In cases in which the present systems were unable to produce the needed data, we solicited ideas for improving those systems. Between October 2005 and January 2006 we interviewed 24 people across DHHS. (We interviewed representatives from offices within DHHS [ASPR, National Vaccine Program Office, Assistant Secretary for Planning and Evaluation] and within its operating divisions [Centers for Disease Control and Prevention {CDC}, Food and Drug Administration {FDA}, Health Resources and Services Administration, Indian Health Service, Centers for Medicare and, Medicaid Services].) Relying on interviewees who are part of the system to assess its strengths and weaknesses may lead to an overly optimistic assessment of strengths and underestimate of potential weaknesses. Because the present analysis is based on data from both the document review and key informant interviews, this problem is mitigated to some extent.

RESULTS

We identified a total of 14 annual influenza activities that are critical components of the management of a pandemic (Table 1). These activities were spread across 3 preparedness areas: surveillance, vaccines and antiviral drugs, and communications. Although we address issues related to vaccines and antiviral drugs, we do not specifically address systems for the distribution of these potential countermeasures nor do we address systems for implementing nonpharmaceutical interventions because these would need to occur largely at the state and local levels and are not typically part of routine annual influenza activities.

Surveillance

We identified 6 relevant routine influenza surveillance activities: strain selection, tracking disease spread and severity, identification of initial cases, monitoring antiviral resistance,

TABLE 1

Annual Influenza Activities Relevant to Pandemic Preparedness, Systems Involved, and Agency Owners

Surveillance	Systems	Agencies
Activity		
Selecting strain for vaccine	NREVSS	CDC
	GISP	WHO
	VRBPAC	FDA
Tracking disease spread	SSN, BioSense	CDC
Identifying initial cases	NREVSS, EIP, NVSN, NNDSS	CDC
Monitoring antiviral resistance	NREVSS	CDC
Monitoring antibiotic resistance	NNDSS, ABCs	CDC
Monitoring vaccine effectiveness	Marshfield clinic	CDC funded
Monitoring vaccine safety	VAERS	CDC and FDA
	VSD	CDC
Vaccines and antivirals		
Activity		
Making priority group recommendations	ACIP	DHHS
	NVAC-PIWG	NVPO
Testing, licensing, and releasing vaccines	Annual renewal process	FDA
Tracking vaccine ordering	Manufacturer's report	CDC and FDA
Tracking vaccine supply and distribution	Manufacturer's report	CDC and FDA
	SDN	CDC
Monitoring vaccine uptake and unmet need	NIS, BRFSS, Gallup	CDC
Communications		
Activity		
Developing and disseminating prepandemic messages	Online materials	CDC
Developing and testing pandemic messages	Influenza vaccine summit	CDC and AMA
Coordinating communications across DHHS	Interagency coordination processes	Office of the DHHS secretary

ABCs = Active Bacterial Core surveillance program; ACIP = Advisory Committee on Immunization Practices; AMA = American Medical Association; BRFSS = Behavioral Risk Factor Surveillance System; CDC = Centers for Disease Control and Prevention; EIP = Emerging Infections Program; FDA = Food and Drug Administration; GISP = Global Influenza Surveillance Program; NIS = National Immunization Survey; NNDSS = National Notifiable Diseases Surveillance System; NREVSS = National Respiratory and Enteric Virus Surveillance System; NVAC-PIWG = National Vaccine Advisory Committee-Pandemic Influenza Working Group; NVPO = National Vaccine Program Office; NVSN = New Vaccine Surveillance Network; SDN = Secure Data Network; SSN = Sentinel Surveillance Network; VAERS = Vaccine Adverse Events Reporting System; VRBPAC = Vaccines and Biological Products Advisory Committee; VSD = Vaccine Safety Datalink; WHO = World Health Organization.

monitoring antibiotic resistance, and monitoring vaccine effectiveness.

Strain Selection

The National Respiratory and Enteric Virus Surveillance System (NREVSS) and the World Health Organization's Global Influenza Surveillance Program collect, characterize, and report on viral isolates from various parts of the United States and around the world. Surveillance data are used to select strains for annual vaccine. The basic system is robust and is expected to function well in a pandemic as long as viral isolates are immediately shared throughout the international community. Sharing has been a problematic issue; however, the World Health Organization is working to resolve it.[8]

Tracking Disease Spread and Severity

The Sentinel Surveillance Network measures the incidence and geographic distribution of influenza-like illness (ILI) from a number of "sentinel providers" during annual influenza season. The Influenza Division at the CDC uses an electronic network to disseminate comprehensive weekly reports, including ILI surveillance summary data.

The robustness of the present sentinel system may need improvement both for routine operations and to serve during a pandemic. CDC data for the 2005–2006 influenza season indicate that only slightly more than one third of network providers submitted reports during 6 of the previous 9 reporting periods. CDC may need to increase the number and geographic dispersion of sentinel providers and to encourage more consistent reporting from designated providers.

BioSense is a syndromic surveillance system that collects and analyzes outpatient diagnosis data from the Department of Defense, the Department of Veterans Affairs (VA), and other public and private health care organizations. The percentage of visits with any *International Classification of Disease-9* code for an acute respiratory infection is calculated by age group and compared to baselines. The CDC reports that at least 1 BioSense hospital in each of the 10 DHHS regions is sending real-time data. Interviewees reported that running the data through signal detection algorithms can be done quickly, but the accuracy, validity, and interpretation of the data remain a challenge. The outpatient data from VA and the Department of Defense captures mostly military families and VA patients, thus limiting their representativeness.

Identification of Initial Cases

Laboratory-confirmed diagnoses are needed to identify the initial cases of a pandemic. A number of CDC-sponsored programs that provide such data, including the NREVSS, the Emerging Infections Program, the New Vaccine Safety Network, and the National Notifiable Disease Surveillance System (NNDSS). The NREVSS, described above, receives isolates from around the United States and conducts laboratory testing. However, interviewees felt that this system could not provide data quickly enough to be useful in identifying early cases. The other 3 systems are limited in scope and magnitude, focusing only on pediatric hospitalizations or deaths in certain geographic areas.

Thus, no existing influenza surveillance system is designed to detect novel influenza cases wherever they may arise and to ensure laboratory diagnosis and timely reporting. Therefore, it is clear that these systems will need to be redesigned, or a new system developed, to be more sensitive and timely if a goal of surveillance is to detect the earliest cases as a pandemic emerges in the United States.

Monitoring Antiviral Resistance

The NREVSS conducts antiviral resistance monitoring on a convenience sample of viral isolates every 1 to 2 months. Although testing could likely be expanded during a pandemic, processes would be needed to ensure that the system could be scaled up quickly.

Monitoring Antibiotic Resistance

At the time of our assessment there were no systems to track pathogens associated with seasonal or pandemic influenza, that is, bacterial pathogens responsible for secondary infections in influenza patients. However, there are now 2 systems that have the potential to provide information on antibiotic resistance patterns during a pandemic: the NNDSS and the Active Bacterial Core surveillance program. Within the NNDSS, drug-resistant invasive *Streptococcus pneumoniae* is a nationally notifiable condition for adults and invasive *S. pneumoniae* is nationally notifiable for children younger than age 5 years. The collection of data on the incidence of this infection could be used to monitor resistance. The Active Bacterial Core surveillance program is a population-based laboratory surveillance program that monitors disease rates over time and antibiotic resistance levels for up to 6 pathogens, 3 of which can occur as secondary flu infections (*S. pneumoniae*, *H. influenzae* and methicillin-resistant *Staphylococcus aureus*). At this time only 10 states are included and only some report on all 6 pathogens.

Monitoring Vaccine Effectiveness

There is no robust system to assess vaccine effectiveness at a national or regional level. Data to test effectiveness are available only from the Marshfield Clinic in Wisconsin. Reliance on data from a single site is inadequate to support decision making in a pandemic. As evidence, during the 2003–2004 season, researchers using Marshfield data concluded that the season's influenza vaccine was ineffective when, in fact, the strain circulating in Wisconsin differed not only from the strains in the vaccine but also from strains circulating in the rest of the country. (The CDC has issued a request for proposal to create 3 to 5 additional Marshfield-like [ie, able to rapidly assess vaccine effectiveness] sites in the United States, ideally resulting in 1 site for rapid vaccine effectiveness assessment in each census region of the United States, to be in place by the next flu season.)

Monitoring Vaccine Safety

The Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD) are the 2 systems that are used to monitor vaccine safety. VAERS is a passive nationwide reporting system that is run cooperatively by the CDC and the FDA. The VSD monitors vaccine safety through a linked database of 8 large managed care organizations. Often the VSD system is used to investigate concerns raised by VAERS.

Interviewees noted that the VSD does not cover a large enough population base to allow for rapid assessments of influenza vaccine safety, even though it includes data on more than 5.5 million people annually. Interviewees reported that a recent safety signal had come through VAERS as a cluster of illnesses in a population of patients who had received influenza vaccine. It took 3 months to investigate and determine that the problems reported were not related to the vaccine because it was difficult to reliably determine whether the rate of reported events differed from the background event rate. Were a potential safety signal to be detected with the use of pandemic vaccine, several months would be far too long to provide the needed information to health officials or to reassure the public.

Vaccines and Antiviral Drugs

We identified 5 influenza activities related to vaccines and antiviral drugs: making priority group recommendations; testing, licensing, and releasing vaccines; tracking vaccine ordering; tracking vaccine and antiviral supply and distribution; and tracking vaccine coverage and unmet need.

Making Priority Group Recommendations

The Advisory Committee on Immunization Practices makes annual evidence-based recommendations on which groups should receive priority for vaccine. This process would likely work well in a pandemic. The efforts of the National Vaccine Advisory Committee Pandemic Influenza Working Group to develop pandemic influenza priority group recommendations before an outbreak supplement the advisory committee's annual process and serve as a starting point in the event of a pandemic.

Testing, Licensing, and Releasing Vaccines

The Center for Biologics Evaluation and Research at FDA works with manufacturers to facilitate the annual renewal of vaccine licenses. FDA has indicated that a pandemic vaccine can be licensed as a strain change as long as the vaccine is made with existing processes (ie, does not use new cell culture–based manufacturing processes and/or include an adjuvant). It is unclear, however, whether the present systems would function efficiently under different circumstances. Because the time needed for the egg-based production process is a limiting factor, there is much ongoing research on new production technologies. Processes will have to be developed to address the testing, licensing, and release of vaccines made using new methods.

Tracking Vaccine Ordering

An informal system exists to monitor orders from manufacturers, but it is insufficient to facilitate redistribution in a pandemic. Manufacturers report annually to CDC on the number of vaccine orders, but not on the distribution of orders by geographic area or sector (eg, physician offices, "big box" stores). CDC staff report that, due to past spot shortages and delays, some providers now double- and triple-book vaccine, making it difficult to know how much is truly needed. Data are available regarding how much annual influenza vaccine is ordered by the federal government, but this is useful only if the federal government is a major purchaser of vaccine.

Tracking Vaccine and Antiviral Supply and Distribution

The National Center for Immunization and Respiratory Disease (NCIRD) at CDC coordinates meetings with vaccine manufacturers to assess the supply and market availability of influenza vaccine. This information is of limited usefulness for vaccine redistribution because it is proprietary and can be used only to indicate aggregate totals of vaccine availability. Moreover, staff noted that manufacturers sometimes present overly optimistic production targets. FDA also monitors the manufacturing process. These data may be more realistic because FDA does not report the information publicly even in aggregate, but their wider use is limited as similar proprietary constraints apply.

The NCIRD works with manufacturers and distributors to provide vaccine distribution information to state public health departments via the Secure Data Network. This system is limited in its usefulness because it can track vaccine only to the distributor level, and not to the individual clinic or provider site to which the vaccine is shipped.

The NCIRD is supporting the development of the Vaccine Management Business Improvement Project (VMBIP), which tracks distribution of vaccine purchased by the Vaccines for Children program to the provider level and ultimately to the level of the recipient. Although this system is expected to track only federally purchased vaccine, the structure of the VMBIP could serve as a model for a more comprehensive system to track vaccines beyond the relatively small share purchased through the Vaccines for Children program.

There is no system to monitor the supply or distribution of antiviral drugs nationwide. FDA's Center for Drug Evaluation and Research has a Drug Shortage Program through which purchasers may report difficulty obtaining a product, but the system is voluntary and not suitable for tracking overall market supply or distribution of antivirals.

Tracking Vaccine Coverage and Unmet Need

No existing system is able to rapidly assess annual progress toward vaccine coverage goals for the full population. However, the Indian Health Service system sets and monitors progress toward an annual target for the population it serves.

CDC uses the National Immunization Survey to provide nationally representative estimates of vaccine coverage. However, these are generally not available for at least 1 year after collection, and are thus insufficient to provide timely information to inform the next season's vaccine strategy or to monitor real-time trends in vaccine uptake and alter strategies midseason. At times, CDC has used the Behavioral Risk Factor Surveillance System (BRFSS) to monitor vaccine uptake. The BRFSS tracking module used during the 2004–2005 influenza season was able to produce data much faster than the National Immunization Survey, and thus, with some advance planning, has the potential to be useful in a pandemic. However, surveys may not be able to provide reliable information about coverage in small geographic areas (eg, cities).

Vaccine registries are another source of information on vaccine coverage during a pandemic. Although registries would provide a census of people who have received vaccination, they do not provide any information on those who have not. Survey data are better suited to measuring vaccine coverage at the population level. Therefore, some combination of survey and vaccine registry data may be needed.

The CDC does not use its existing survey mechanisms to identify unmet demand for vaccine; however, during the 2005–2006 season, the CDC contracted with the Gallup organization to conduct polls to ascertain this information. Thus, there are potential mechanisms for obtaining this information quickly both during annual influenza season and in the event of a pandemic.

Communications

We identified 3 relevant communication activities: developing and disseminating pre-pandemic messages, developing and testing pandemic messages, and coordinating communications across DHHS operating divisions.

Developing and Disseminating Prepandemic Messages

Each year, the CDC creates communications materials to support vaccine uptake campaigns and makes them available to providers, public health educators, and the public via the Internet. Although relatively flat vaccine uptake rates at the time suggest that these communication activities had not been effective, it is difficult to disentangle the effectiveness of communications in this area from problems related to ineffective vaccines or limited or delayed supplies.

The systems in place for communicating with the public about how to limit transmission of disease are generally passive. More active communication approaches (eg, media campaigns, targeted mailings to vulnerable populations) should be developed.

Developing and Testing Pandemic Messages

The National Influenza Vaccine Summit reports annually on the development of seasonal influenza communications material. Consultation with NCIRD staff and focus groups and the tracking of downloaded materials posted on the CDC's Web site reportedly help inform which materials work best. The BRFSS or collaborations with Gallup and other survey groups provide the CDC with the potential to measure and improve the effectiveness of their communications. These systems function well for annual influenza season, but it is unclear whether they could provide information quickly enough to identify problems and suggest message revisions during a pandemic.

Coordinating Communications Across DHHS Operating Divisions

Although the CDC has the capability to communicate with diverse audiences, there are few mechanisms that allow messages to be coordinated across DHHS and disseminated in an expedited fashion. Staff reported that the main barriers to coordinating and putting out timely messages are a lack of DHHS-wide assumptions, a slow and limiting clearance process, and differences in communications infrastructure between agencies.

DISCUSSION

Our review of systems in place for annual influenza identified a number of robust systems that would likely serve the United States well in a pandemic. We also found that much of the information needed to effectively manage a pandemic is unavailable. In some cases, systems do not yet exist, whereas in other cases, systems exist but cannot produce all of the needed information or cannot produce the information quickly enough to be useful in a pandemic. Moreover, as noted earlier, in the event of a pandemic, none of these systems would be sufficient if they functioned in isolation; rather, the information from each of these systems, and information from different agencies, would need to be integrated. This may be challenging in the absence of a model for sharing and accountability across these systems and operational agencies that functions on a day-to-day basis. Although it is hoped that the US National Incident Management System and the National Response Framework would facilitate such sharing and accountability, an assessment of these systems was beyond the scope of our study. In addition, we note the inherent challenges in monitoring both the disease and the response to it in a system that is dependent on a largely private health care system, including hospitals, physicians, and pharmaceutical companies, each of which have their own challenges in obtaining, integrating, and sharing relevant information.

Nonetheless, identifying what the present systems can and cannot provide may help in developing a plan for allocating resources to take better advantage of the opportunities provided by seasonal influenza outbreaks to improve systems and improve pandemic preparedness. In some cases, incremental improvements are needed to increase the breadth, depth, or timeliness of existing systems. Such improvements could be

relatively straightforward and relatively inexpensive. In other cases, it will be necessary to build new systems, thus necessitating a greater investment of time and resources. In these cases, it will also be important to identify short-term solutions that can address at least some information gaps in the event that a pandemic occurs before the new system is developed and implemented.

Our review identified several areas where it would be relatively straightforward to strengthen the present system and significantly enhance the nation's ability to respond to and mange a pandemic. It is important to note that our examination represents a snapshot of the 2005–2006 influenza season and that certainly some improvements have been made since that time. Opportunities to strengthen the system include the following:

- *ILI surveillance:* Although the Sentinel Surveillance Network has expanded, regular reporting by providers is suboptimal. Careful attention to the timeliness and completeness of reporting can make this existing system much more robust for tracking the spread and severity of a pandemic. Improving the performance of the system is challenging because it is so dependent on the participation of physicians, who are outside of its direct control. One option would be to use a quality improvement approach in which reporting performance is tracked and reported to providers. This could be coupled with a program that provides incentives for providers to report on a consistent basis.
- *System for monitoring the effectiveness of influenza vaccine:* It appears possible and feasible to build on the present systems, in particular the VSD. Discussions with staff at VSD suggest that it would be relatively inexpensive to set up vaccine effectiveness testing at each of their sites. In addition, in 2008, the CDC released a request for applications for sites to undertake effectiveness testing.
- *Monitoring vaccine safety:* The combination of VAERS and VSD appears to be insufficient to appropriately monitor and investigate vaccine safety concerns during a pandemic; however, the VSD is a well-functioning system, which, if expanded, could meet this need. Options for expansion include incorporating data from additional national health plans, the Department of Defense, and VA.
- *Vaccine ordering and tracking:* Although the VMBIP system, currently under development, addresses only federally purchased vaccine, it holds the promise of being able to monitor and track inventories of pandemic vaccine more broadly. It is not clear, however, that manufacturers would agree to enter nonfederally purchased vaccine in such a system. Plans should be developed to address both scenarios in which the federal government purchases all of the pandemic vaccine (even to resell) and multiple public and private purchasers.
- *Stimulating annual vaccine uptake:* Performance in this area would likely benefit from annual vaccination targets, regular performance assessments, and escalating vaccine production. Targets for the general population and potentially additional population subgroups should not be difficult to establish.

Pandemic preparedness can be strengthened by building upon routine influenza prevention and control activities; however, it is important to note that improving these systems is only part of the preparation needed to effectively respond to a pandemic. As noted earlier, other activities, such as countermeasure distribution and the implementation of nonpharmaceutical public health interventions, will be needed in a pandemic. A discussion of these was beyond the scope of our review, which focused primarily on systems that are relevant both to annual influenza season and a pandemic. To assess and strengthen these systems, public health and emergency preparedness experts recommend ongoing exercising and updating of these systems, and learning from real but fortunately less catastrophic events.

About the Authors

All of the authors are with the RAND Corporation.

Address correspondence and reprint requests to Jeanne S. Ringel, PhD, RAND Corporation, 1776 Main St, Santa Monica, CA 90407 (e-mail: ringel@rand.org).

Received for publication December 10, 2007; accepted December 29, 2008.

Authors' Disclosures

The authors report no conflicts of interest.

ISSN: 1935-7893 © 2009 by the American Medical Association and Lippincott Williams & Wilkins.

DOI: 10.1097/DMP.0b013e3181ad1833

REFERENCES

1. Nelson C, Lurie N, Wasserman J, Zakowski S. Conceptualizing and defining public health emergency preparedness. *Am J Public Health*. 2007;97:S9–S11.
2. Bennett NM, Casey M, Cleveland T, et al. 2004–2005 influenza vaccine shortage: vaccine-redistribution model. *J Public Health Manag Pract*. 2006; 12:335–339.
3. Gaglia MA Jr, Davis MM. States' emergency orders regarding the 2004–05 influenza vaccine shortage. *Human Vaccines*. 2006;2:34–37, Epub January 22.
4. Ransom J. Another year of influenza vaccine supply and distribution problems: why does this keep happening and what can be done about it? *J Public Health Manag Pract*. 2006;12:210–212.
5. Roddy MF, Tracy D, Ehresman K. A local and state partnership for influenza preparedness: the Minnesota Influenza Vaccine Inventory Log. *J Public Health Manag Pract*. 2006;12:330–334.
6. Shimabukuro TT, Wortley PM, Bardenheier B, et al. Survey of state practices during the 2004–2005 influenza vaccine shortage. *Public Health Rep*. 2007;122:311–318.
7. Tate T. Four years of lessons learned: the 2001–2004 Maryland influenza prevention seasons. *J Public Health Manag Pract*. 2006;12:308–316.
8. Zamiska N. Groups consider funding bird-flu stockpile. *Wall Street Journal*; March 27, 2007, p. D2.