

UPDATED PREPARATION FRAMEWORK AND RESPONSE TO A PANDEMIC FLU

Prof. univ. Asoc. Dr. Nicolae STEINER

Doctor of Medical Sciences
Member of the U.E. Health Security Committee
Member of the World Society of Disaster and Emergency Medicine (WADEM)

Member of the European Academy of Crisis Management
Member of the International Society for Disaster Medicine

Honorary member of the National Disaster Medical System of the U.S.A.

Process manager for emergencies, crises and pandemics within the "Stamina" group at the Institute of Virology "Stefan S. Nicolau" Bucharest

Dr. Corneliu Nicolae ZAHARIA, Doctor of

Physical sciences, Senior researcher
Group Manager "Stamina" at Romanian Academy Virology Institute Bucharest

SUBSTANTIATION

The framework describing the evolution of influenza pandemics has evolved over time. The WHO Global Pandemic Plan of 2005 introduced the concept of pandemic phases [8]. Six phases were used to describe the evolving risk of efficient human-to-human transmission as a basis for defining a pandemic.

In November 2005, the President of the United States launched a national strategy for pandemic influenza [9], and the related implementation plan was launched in May 2006 [10]. These documents introduced the concept of using the steps to determine the response to pandemic influenza, including stage 0 (new outbreak in domestic animals in a country at risk), steps 1–3 (suspected, confirmed and widespread human outbreaks) and stages 4–6 (the first case in a North American man, widespread in the United States, recovery and preparation for subsequent waves). The US government stages provided greater specificity for US preparedness and response efforts than the WHO stages and facilitated initial planning efforts by identifying objectives, actions, policy decisions, and message considerations for each stage. The stages provided an overview of the approach to a pandemic response; however, detailed pandemic response planning requires a higher level of specificity to determine federal, state, and local response actions during a pandemic. In addition, the stage framework involved geographical spread from outside the United States to the United States. In 2007, the CDC developed the CDC Intervals, a common framework from which the CDC and other federal, state, and local governments and agencies could plan and coordinate their pandemic response actions. The 2007 CDC intervals refined the stage framework in the following ways:

- Providing more details to reflect the evolution of a pandemic, including when decisions and actions could take place;
- Provided improved definitions to identify transition points between intervals to reduce variability in interpretation;
- Considering that pandemic influenza could occur inside or outside the States Unite;

Planning and reacting to a number of possible consequences following the emergence of a new influenza A virus is complex. These viruses can spread rapidly and explosively throughout the world, as in the influenza pandemics of 1918, 1957, 1968 and 2009 [1,2]; causes limited outbreaks, such as influenza A (H3N2) (H3N2v) in the United States associated with agricultural fairs in the summer months of 2011, 2012 and 2013 [3]; or continues to cause limited human-to-human transmission of the virus, such as influenza A (H5N1) and influenza A (H7N9) virus in Asia [4,5]. Moreover, new influenza A viruses, even when transmitted in a closed environment, do not always lead to a pandemic, such as the 1976 influenza A (H1N1) outbreak in Fort Dix, New Jersey and the 2011 H3N2v outbreak. 2013 in the United States [3,6]. Identifying and responding to this wide range of situations requires systematic frameworks that describe the evolution of events; weigh the risk of the new virus and the potential impact on public health; assesses the potential for transmissibility, antiviral resistance and disease severity; and can be used to develop sensible timely decisions about interventions (e.g., community mitigation measures, medical countermeasures, and vaccines). Training and response frameworks provide a common basis for planning in different jurisdictions and ensure the transparency of decisions and actions taken.

Significant progress has been made in developing pandemic plans, as well as preparedness and response frameworks over the past decade. The efforts of the World Health Organization (WHO), the CDC, other US government agencies, and state and local jurisdictions have addressed pandemic preparedness planning. Lessons learned from gaps in US influence decision-making frameworks became apparent with each event and exercise [7]. The recent emergence of human disease caused by H3N2v in the United States [3] and H7N9 in China [5] has demonstrated the need to align existing documents and frameworks into a useful tool that can be used to guide planning and response efforts.

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- Probably accommodated in the synchronization of pandemic stages and progress in different jurisdictions to allow local, state, regional and national actions appropriate to the specific conditions of the jurisdiction;
- Provided a structure that allowed planning for multiple waves.

The resulting document (Proposal for the Use of Intervals, Triggers, and Actions in CDC Pandemic Influenza Planning, 2008) was revised, published as an appendix to the Department of Health and Human Services of the Pandemic Influenza Operational Plan [11], and used during the H1N1 pandemic. since 2009 to describe the evolution of the pandemic and to help guide the response.

Pandemic influenza virus interval

New influenza A pandemic intervals are based on what is known about past flu transmission and experience from recent events (eg, 2009 H1N1 pandemic, H3N2v in the United States, H7N9 in China, and ongoing sporadic human cases of H5N1), epidemic curves are used to monitor an outbreak as it happens, to describe the outbreak retroactively and to document the timing of interventions regarding the acceleration and deceleration of the outbreak. Patterned epidemic curves or pandemic curves can also be used to describe potential events over time. The use of these models for forecasting purposes can be particularly valuable for anticipating conditions and identifying actions that may otherwise flatten or mitigate the epidemic or pandemic curve.

In order to respond to new influenza viruses and potential pandemics, the six intervals (investigation, →

recognition, initiation, acceleration, deceleration, and preparedness) represent events that occur along a hypothetical pandemic curve. Pandemic curves differ in duration and intensity depending on many factors, including the geographical area in which they occur, the season of their occurrence and the dynamics of the related population. The WHO phases of pandemic influenza, which can be used to describe and communicate the evolution of the disease worldwide, provide an overview of the emerging epidemiological situation, essentially by aggregating epidemic curves around the world. CDC intervals serve as additional reference points to provide a common orientation and a clearer epidemiological picture of what is happening and when it needs to intervene. The intervals are flexible enough to accept the likelihood of asynchrony of pandemic progression in different areas to allow local, state, and federal actions appropriate to jurisdiction-specific conditions (e.g., a case-by-case jurisdiction but a case-by-case jurisdiction that is close to a case area). State and local health authorities may even choose to implement interventions asynchronously in their jurisdictions, focusing early efforts on communities that are affected for the first time. State / local initiation, acceleration, deceleration and readiness indicators can be asynchronous with federal indicators.

For local and state planning, the intervals describe the evolution of the pandemic within communities and provide a detailed framework for defining when to respond with various actions and interventions at any time during a pandemic. These actions should be proportionate to the transmissibility and severity of the emerging virus.

The intervals are further stratified into eight areas, so that the trajectory of planning and response activities for any area can be more easily followed. The eight areas are incident management, surveillance and epidemiology, laboratory, community mitigation, health care and countermeasures, vaccine, risk communications and state / local coordination. Intervals can also be valuable as a common reference point, as they can be used to link the state of a pandemic with specific interventions.

The experiences of the U.S. during recent flu events have been useful for testing concepts in the proposed intervals and the decisions and actions that have been implemented in these intervals. The impact on public health of influenza virus strains can differ substantially, both in terms of geographical spread and in terms of mortality. For example, the 2009 H1N1 outbreak was caused by a high-transmission influenza virus, which occurred in North America and led to a pandemic [2], while the H3N2v virus, which also occurred in North America, caused approximately 300 cases in humans and limited outbreaks involving human-to-human transmission [3]. The outbreak of H7N9 was caused by a new flu virus that spread outside the United States and had a high mortality rate, but has not yet spread to other countries [5]. These experiences provided opportunities to test the validity and usefulness of the intervals and the recommendations for public health actions triggered by each interval to ensure that they are applicable in a wide range of scenarios.

Pandemic range definitions

To define the intervals, the relationship between the time between the general phases of the WHO and the more detailed planning intervals was examined. In addition to

the relationship with WHO phases, intervals are characterized by specific indicators on transmission (table) and the types of response activities that should take place in each interval (appendix).

Interval progression is not exclusively linear.

For example, the identification of a new influenza A virus does not require progression to the next interval (recognition interval) if the virus does not demonstrate the potential for ongoing transmission. Similarly, after the training interval, subsequent outbreaks will cause federal, state and local public health officials to reintroduce the acceleration, deceleration and training intervals. The duration of each pandemic interval can vary from weeks to months, depending on the characteristics of the virus and the public health response.

1. Investigation interval: Investigation of new influenza cases

The investigation interval is initiated by identifying and investigating a new influenza A infection in humans or animals from around the world, which are estimated by experts in the field to have potential implications for human health. Public health actions focus on targeted surveillance and epidemiological investigations to identify human infections and to assess the potential of the virus to cause serious human disease, including person-to-person transmission, co-investigations of animal outbreaks with animal health representatives, and consideration of case-based control measures (ie, antiviral treatment and post-exposure antiviral prophylaxis for infected people and isolation of infected people and animals). Following the recognition of a new human influenza infection in humans, as with the H7N9 and H3N2v viruses, animal investigations subsequently identified the circulation of influenza viruses in birds and pigs, respectively, and identified the reservoir of these previously unrecognized new influenza viruses.

The CDC performs an IRAT assessment in the investigation interval to characterize the potential for occurrence, and if the virus occurs, the severity of human infection [12]. In general, the identification of human cases of new influenza A infection is reported by WHO in accordance with international health regulations [15].

2. Recognition interval: recognition of the increased potential for continuous transmission

The recognition interval is initiated when an increasing number of human cases or groups of influenza A infections are identified anywhere in the world, and the characteristics of the virus indicate an increased potential for continuous human-to-human transmission. Public health actions focus on outbreak control, with a focus on the potential use of case-based control measures, including the treatment and isolation of sick people and the voluntary quarantine of contacts.

3. Initiation interval: initiation of the Pandemic wave

The initiation interval begins when human cases of a pandemic influenza virus infection are confirmed anywhere in the world, with efficient and sustained human-to-human transmission. The definition of efficient and sustained transmission is established during an



event based on the epidemiological characteristics of the emerging virus. For example, effective transmission could be defined as a household or an institutional attack rate $\geq 20\%$ in more than two communities, and support could be defined as the transmission of the virus for three or more generations in several groups. Continued implementation of case-based control measures and routine personal protective measures (eg hand hygiene) is essential, as is improved surveillance for the detection of additional cases of new virus to determine when measures will be implemented. community mitigation. If possible, PSAF results [13] should be used to ensure that actions are proportionate to the severity of the disease caused by the virus.

4. Acceleration interval: acceleration of the Pandemic wave

The acceleration interval is indicated by a steady increase in pandemic influenza cases identified in the United States, indicating established transmission. Considering the immediate initiation of appropriate community mitigation measures, such as school closures and childcare facilities and social distancing [16], in addition to the effective management of public health resources (including medical measures and vaccines, if available), are of primary importance in this range [17] and are guided by the results of the PSAF. Isolation and treatment of sick people and voluntary quarantine of contacts continue as key mitigation measures. Historical analysis and mathematical modeling indicate this early institution.

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6. Preparation interval: Preparing for a subsequent pandemic wave

The preparation interval is characterized by low pandemic influenza activity, although outbreaks may continue to occur

in some jurisdictions. Primary actions focus on discontinuing community mitigation measures; facilitating the recovery of public health, healthcare and the community

7. Risk assessment to improve decision making

In addition to describing the progression of a pandemic, certain assessments, interpretations and findings (ie indicators) are used to define transition points between intervals (table). At each interval, certain actions can be determined for state, local and federal governments. Each indicator also initiates a set of important decisions that affect actions in the current and beyond. These decisions can range from formal generation and analysis of options to more informal but equally important discussions between experts in the field, pandemic response leaders and various stakeholders.

Decisions on appropriate actions require information on the actual or potential impact of the new virus on public health. At all times, decisions about the actions to be considered should take into account many factors, such as virus transmission parameters, the severity of the disease between different age groups and risks, the availability and effectiveness of control measures and treatment options. treatment (eg community interventions, antivirals and vaccines) and the impact on healthcare, schools, businesses and the community.

Although the data needed to make decisions may be limited in the early stages, delay may weaken the effectiveness of the response. Therefore, estimating the likelihood of risks, especially the risks of transmissibility, severity and antiviral resistance, is critical [12, 13, 22]. In addition, certain actions, such as the decision to produce a pandemic vaccine, require extensive preparation or implementation time, mandating that decision-making be initiated and completed as early as possible before the intervals during which such actions are to take place. and adequate data is usually available well in advance to support the need for action with certainty.

The CDC has developed two risk assessment tools for the decision-making framework, IRAT [12] and PSAF [13]. Both are designed to be used in the initial intervals when data is limited, to allow iterative updates, as new information becomes available, and to adapt to different potential scenarios. Once completed, the results of both instruments are communicated to federal, state, and local decision makers to guide public health actions.

8. Influenza risk assessment tool

When an influenza A virus is identified in humans but does not circulate widely in the human population, it is important to assess 1) the risk of the virus developing an efficient and sustained human-to-human transmission and 2) the risk that the virus will affect substantially public health. IRAT was developed to facilitate such an assessment [12]. Therefore, the indicator for the investigation interval, which is a newly identified influenza A virus in animals or the identification of a new influenza A virus recovered from humans, can serve as an initial trigger for performing the IRAT score.

IRAT is used by the United States Government and the WHO Global Influenza Surveillance and Response System as a risk assessment process that involves data collection, discussion, and consensus building among experts to assign a risk score. Ten predefined risk elements → **7**

are given a risk score. These 10 elements fall into three categories:

1) attributes that refer to the biological properties of the virus (four elements), 2) population attributes (three elements) and 3) attributes of virus ecology and epidemiology (three elements) [12]. A team of experts assigned to each specific element provides a virus risk score for that element. A weighting is then applied to the item scores for each of the two risk questions (ie occurrence and impact). The results of this process can be used to decide whether and how to act and communicate concerns about both the occurrence and potential impact on public health. As new information becomes available, the notation may be repeated. This process was used to assess recent emerging viruses, such as H3N2v and H7N9, for vaccine development, manufacturing and stocking decisions. Once a new virus has achieved efficient and sustained transmission, PSAF can then be used to characterize the potential impact of a pandemic relative to previous influenza epidemic and pandemic experiences.

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10. Pandemic Severity Assessment Framework

Once a new influenza virus has appeared and is circulating in human populations, the risk of a pandemic can be assessed.

In 2007, as part of the interim guidelines for communi-

ty mitigation strategies, the pandemic severity index was introduced as a tool to define the severity of a future influenza pandemic. To facilitate communication with risks, the index had five similar categories with the hurricane severity scale, which varies in severity from category 1 (moderate severity) to category 5 (most severe) and is based on a hypothetical 30% attack rate and fatality intervals. reports associated with a particular influenza virus [16]. Experiences from the 2009 H1N1 pandemic identified that early data on less severe but highly transmissible virus characteristics of the community were limited. Consequently, the pandemic severity index, which is based on severity exclusively on mortality, tended to overestimate the severity, as more severe cases may be reported at the onset of a pandemic. Based on these lessons, PSAF was developed to characterize the potential impact of a pandemic relative to previous influenza epidemic experience and pandemic experiences [13]. PSAF can be used early in a pandemic and assessments can be repeated as information changes. Although IRAT focuses on the risk of occurrence and potential impact if it occurs, PSAF focuses on the epidemiological parameters of transmissibility and severity after a virus has emerged with efficient and sustained transmission and requires a sufficient number of human cases and clusters to allow the evaluation to be completed. Depending on the number of cases, the size of the groups and the geographical location of the outbreaks, the trigger for PSAF use could be as early in the pandemic as the recognition interval, but is more likely to be triggered during the initiation interval and regularly updated as the pandemic is progressing. PSAF is based on transmissibility and clinical severity parameters and uses different scales for initial assessments in an emerging pandemic and for subsequent, more refined assessments.

The initial assessment, performed at the beginning of the outbreak, when epidemiological data are limited, uses a dichotomous scale of low-moderate versus moderate-high severity.

Subsequent evaluation, performed when more reliable data are available, is more refined, using a 5-point scale for transmissibility and a 7-point scale for clinical severity. After the available data are evaluated on these scales, the overall results are represented by measures of transmissibility along a y-axis and measures of severity along an x-axis and by comparison with benchmarks such as previous pandemics or seasons particularly severe influenza [13]. In the very early stages of an emerging pandemic, public health officials reiterate the importance of early treatment of sick people, as well as community mitigation measures to slow the spread of the flu, including voluntary isolation (ie, sick people staying home when they are sick), respiratory labeling, hand hygiene and antiviral treatment guidelines. The results of the PSAF assessments help national, state and local decision-makers determine whether to implement additional community mitigation measures, including those that can be very disruptive and could have a more severe economic and social impact on people, and individual communities (e.g. school, layoffs or quarantine of contacts).

11. Use of intervals, influenza risk assessment tool and pandemic severity assessment framework



potential impact provides information that can guide decision-making and actions in different jurisdictions and levels of government and helps inform appropriate risk communication strategies. A list of some of the key decisions and action options that are triggered by progression through each interval is described (Appendix). Recent pandemic influenza A virus planning and response efforts have been organized into eight areas to ensure that expertise is properly applied to all aspects of the event. Decisions and actions are further layered in these areas, so that the path of planning and response activities for any area can be more easily tracked. The eight areas are incident management, surveillance and epidemiology, laboratory, community mitigation, health care and countermeasures, vaccine, risk communications and state / local coordination. The tables are not intended to be prescriptive or comprehensive, but rather to identify many priority issues that need to be addressed at each interval. The circumstances of each situation dictate the timing of decisions and actions.

12. DISCUSSIONS -CONCLUSIONS

The updated influenza pandemic framework provides six intervals and indicators for public health decision-making and actions during the progression of a new influenza A virus since the outbreak of the pandemic. Intervals are based on events that occur along an epidemic curve. Although the actual shape of a future epidemic curve cannot be accurately predicted and can be modified by interventions, the use of an idealized curve allows the definition of generally applicable intervals.

The concept of describing the intervals of a pandemic can be applied to a single outbreak in an individual state or community, or information from multiple outbreaks can be aggregated to describe the situation at the national level.

Because resources and demographics vary widely across regions and states in the United States, it is impossible to define detailed indicators that address each potential situation. Some indicators may not be scalable at all levels of government, and others do not have appropriate action by each group of participants. However, the proposed intervals, decision-makers and actions are meant to be flexible enough to allow the implementation of local, state and federal actions appropriate to jurisdiction-specific conditions.

This framework is designed to help decision-making, but does not diminish or replace the role of scientific expertise, especially when a new flu outbreak develops. An effective pandemic response is based on numerous assumptions and actions that must be continually reassessed with the data accumulated as the pandemic progresses. The content of this framework is intended to support and organize planning, response, and response efforts at the federal, state, and local levels. The use of common concepts is essential for tracking the course of the pandemic, for communication and for implementing coordinated response efforts in a timely manner.

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