



Antiviral Targeting and Distribution Strategies during the 2009 Influenza A (H1N1) Pandemic

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Key Points

- Antivirals (e.g. oseltamivir and zanamivir) were the only medical intervention available during the initial phases of the 2009 influenza A (H1N1) pandemic before vaccines could be developed.
- Stockpiling of antivirals for prophylactic and therapeutic use was an integral component of the pandemic preparedness plan in many countries.
- While pre-exposure prophylaxis was generally not recommended, prophylactic use of antivirals for individuals who were pregnant or had serious underlying conditions, and who had been in close contact with an infectious case may have been warranted and required clinical judgement.
- Optimal use of the antiviral stockpiles requires clear objectives, eligibility and triggers, protocols, and an administration and delivery system. The possibility of the emergence of resistant influenza strains should also be considered.
- A number of countries found innovative solutions to dispensing antivirals during the 2009 pandemic. For example, the National Pandemic Flu Service in the U.K. implemented a telephone-based self-assessment and antiviral prescription system which was linked to antiviral collection points in pharmacies and other establishments in local communities.

Introduction

Antivirals were an important element in combating the 2009 influenza A (H1N1) pandemic. Antivirals are usually the only medical intervention available during the initial phases of a pandemic, as it takes time to develop a vaccine (1, 2). In the case of the 2009 pandemic, it took more than six months from the initial outbreak of the disease in Mexico, in March 2009, to the distribution of the first shipment of the vaccine (3). Thus, antivirals are an important tool for filling potential gaps in the vaccine supply (2), and they were used for both treatment and prevention during the 2009 pandemic.

This Evidence Review summarizes strategies used in Canada and internationally to distribute antivirals to vulnerable groups in a timely manner, both as a prophylactic measure and as treatment. Evidence exists for the efficacy of antivirals to reduce complications of and mortality from influenza (1). Clinical trials in healthy adults have suggested that antivirals can prevent the onset of influenza in 70%-90% of cases,



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knowledge that's contagious!

Des saviors qui se transmettent!

when taken as prescribed (2). Prior to 2009, however, practitioners in North America had relatively little experience using antivirals in the primary care setting. Antivirals had been used primarily to control seasonal influenza outbreaks in health-care and long-term care institutions (1).

This review also identifies challenges to using antivirals, and how some of these challenges could be overcome. Finally, it summarizes lessons learned through nation- or region-wide evaluations of the response to the 2009 pandemic.

Antiviral Stockpiles as Part of National/Regional Pandemic Preparedness Plans

National Goals

The goals of pandemic preparedness planning were fairly consistent across countries: to minimize serious illness and overall deaths, minimize societal disruption, and optimize the use of health resources to contain or delay the spread of disease (1, 4, 5, 6). Reducing the economic impact of the disease, and maintaining the confidence of the public were also cited in planning documents.

The overall goal in using antivirals was to minimize the spread of pandemic influenza A (H1N1) (pH1N1). However, the European Centre for Disease Prevention and Control (ECDC) noted that specific objectives varied between countries, depending on national public health goals, availability of antivirals, and operational considerations. Countries, and provinces or regions within countries, often developed individual pandemic preparedness plans, which helped ensure that approaches were responsive to the needs of different populations and varying operational concerns (7).

As antiviral drugs are generally in

short supply at various points during pandemics, European guidance suggested a hierarchical approach to setting priorities for their use (8). During the 2009 pandemic, the strategy prioritized those who were very ill, followed by people at most risk of severe disease, then those who were at the onset of an illness (2). Prophylactic use was recommended for target groups in countries with larger stockpiles of antivirals (2). Prophylaxis priorities varied between countries, but included family and close contacts of cases, people capable of transmitting infection to high risk persons (such as caregivers and health professionals), and essential workers involved in critical infrastructure (1, 2, 6, 9). Canada and the U.S., among other countries, now have detailed processes for determining priorities.

Although most countries recommended using antivirals early in the treatment of people with pH1N1 (within 48 hours of symptom onset), European guidelines advised that those with severe illness should also be treated with antivirals (2).

Practice Guidance

During the 2009 pandemic, antivirals were recommended for use primarily in treatment, and to a lesser extent, prevention and containment of disease clusters (1, 2, 6).

Treatment

As of February 2010, there were no systematic reviews or randomized controlled trials assessing the efficacy and safety of antivirals for pH1N1 infection (10). However, interim guidance early in the onset of the pandemic (June 2009) noted that evidence supported the use of certain antiviral drugs (particularly the neuraminidase inhibitors oseltamivir and zanamivir) to reduce the duration of illness, complications from the disease and the need for antibi-

otics (2). Treatment with antivirals was also projected to be the best use of limited resources (11). Most studies had been done with healthy adults during seasonal influenza outbreaks, although vulnerable groups such as elderly and children were also studied. Guidance directed that to be effective, antiviral drugs need to be administered within 48 hours of the onset of symptoms, although some evidence from observational studies suggested that antivirals could reduce morbidity and even mortality in severely ill patients even if the drugs were given after the 48 hour window (2).

Modelling studies conducted in Italy, the U.S. and the U.K. on pandemic influenza (although not specific to pH1N1) suggested that the most effective single intervention strategy was the treatment of index cases and prophylactic treatment of exposed household contacts with antivirals (12). Modelling in Australia consistently demonstrated that, for a country with a sufficiently large stockpile of antiviral drugs, treatment with targeted post-exposure prophylaxis was more efficient than treatment alone, and that extensive use of drugs for preventive purposes did not compromise the treatment of infected patients (13). In the U.K., treatment and prophylaxis occurred together, making it impossible to determine the most effective approach; however, the authors of an independent review believed that most of the effect had been due to prophylaxis (14).

Because few people had prior immunity to the pH1N1 virus, the pandemic affected a wide range of people of various ages, nonetheless most commonly and seriously, children and young adults (15). Guidance issued later in the pandemic recommended that this group should seek medical care early (16). The Pan American Health Organization

(PAHO) also suggested that clinical teams be trained on assessment and identification of complications in this group.

Prevention

Most countries did not recommend deploying antivirals for pre-exposure prophylaxis, for a number of reasons (1, 2, 17). Aside from logistical issues and the limited available quantity of antivirals, insufficient clinical and population-based trial data existed at the time of the outbreak to recommend widespread use of drugs which is known to cause side effects to healthy people. There were also concerns about emergence of resistant pH1N1 virus strains (1).

Modelling done in Australia suggested that continuous pre-exposure prophylaxis should be provided to healthcare workers in order to maintain a functional health workforce, while not putting a measurable burden on drug stockpiles (13). Some researchers speculated that school and workplace prophylaxis could have dramatically reduced rates of disease (12). They cautioned that for future pandemics, having sufficient antiviral stockpiles is critical, covering between 35% and 53% of the population. The range in coverage depends on the reproduction number (R_0) of the pandemic influenza strain, on how quickly a vaccine is developed, and whether social distancing measures are put in place.

Recommendations from most countries mirrored the advice from the U.K.: “In most cases prompt and early treatment of symptomatic illness is the preferred course” (18). It was suggested that clinical judgement be used regarding the prophylactic use of antivirals for individuals who were pregnant or had serious underlying conditions, and who had been in close contact with an infectious case.

There is some evidence suggesting that prophylactic use of antivirals can reduce transmission of the influenza virus, particularly among those who are at high risk of becoming infected, thus significantly reducing the number of hospitalizations and deaths (1, 2). The Health Protection Agency (U.K.) recommended testing early cases in care homes to inform treatment options (18). In Canada, guidelines for seasonal outbreak control recommend antiviral prophylaxis for all susceptible residents in nursing homes, healthcare and correctional facilities, regardless of vaccination status (1).

The World Health Organization suggested that governments stockpile sufficient influenza antiviral drugs to treat approximately 25% of their populations as part of preparations for the next influenza pandemic.

Home stockpiles were not recommended, although some health authorities anticipated that individuals would seek them out from their physicians, or through direct internet sales from unregulated sources (2). Some organizations were also thought to have stockpiled antivirals as part of their pandemic or business continuity plans (1). It

was recommended that countries establish a position on the practice of individuals and companies securing quantities of antiviral as part of their pandemic plans (2).

Antiviral Stockpiling Strategies

Governments around the world stockpiled antivirals as part of their strategy to mitigate the effect of a pandemic. Stockpiles assured them of a certain quantity of medication to address the disease, given concerns over the lack of vaccine supplies (2). The World Health Organization (WHO) suggested that governments stockpile sufficient influenza antiviral drugs to treat approximately 25% of their populations as part of preparations for the next influenza pandemic (12). In countries where stockpiles were well below the coverage of 25% of the population, it was suggested that priority be decided based on age-specific case fatality rates (12). In addition, strategic reserves should be used to ensure that areas first affected did not exhaust national supplies (2).

Reported stockpiles among European countries varied widely, from coverage for a small percentage, to more than 50% of the population (2). The U.K. set a goal of having enough antiviral medication to treat up to 50% of their population (7). Canada procured enough antiviral to treat 20-25% of the population (1). This was based on estimates of the benefits of early oseltamivir therapy, including:

- 25%-30% reduction in symptom duration plus a reduction in illness severity
- 59% reduction in hospitalizations (range: 30% to 70%)
- 63% reduction in antimicrobial drug use (range: 40% to 80%)
- 1-day reduction in work days lost under treatment (range: 0.5 to 1.5 days) (1).

A key recommendation by the ECDC was that a strategic plan be developed to optimize use of the stockpiles, including agreed objectives, protocols, administration and delivery systems (2). Plans were to take into account “the total volume and availability of antivirals, underlying epidemiology, anticipated size and duration of transmission and the size of the population groups being given antivirals” (2).

Issues regarding use of stockpiles were identified part-way through the pandemic in Canada (June 19, 2009) (19), and in a post-pandemic review in the U.S. (20) Both pointed to the need for clarification of eligibility and triggers and/or strategies for use of national stockpiles – an issue which made management of medication difficult for local health departments. Issues in Canada included monitoring the quantity of antivirals stockpiled, determining an equitable allocation strategy for antiviral distribution, using antivirals that were close to expiry, and having the correct formulation of the drug (capsule or liquid suspension). In the U.S., issues included dispensing fees and costs of recovering and disposing of expired medication.

Another consideration raised in planning for stockpiles was the possibility of resistance of the circulating strain to antiviral drugs. Future planning should account for the fact that influenza tends to come in waves, so there is a distinct possibility that future stockpiles would have to be adjusted to ensure that antivirals would be effective against the circulating virus (12).

Finally, the U.S. raised the alarm that guidance on the use and dosing of oseltamivir for children was lacking, making it impossible to set stockpile goals for antivirals suitable for children (20). Canada stockpiled



Photo Credit: U.S. Centers for Disease Control and Prevention.

2 million doses of pediatric oseltamivir and 5 million doses of zanamivir (1).

Improved Access to Antivirals in Remote Communities

The WHO made special mention of resource-poor settings, noting that decentralized stocks of antiviral medications were important to reach at-risk groups and disadvantaged populations (15). In Canada, the Yukon Territory and seven provinces chose to pre-position antiviral stocks in remote and isolated communities to facilitate rapid access (19).

Targeting Antivirals

Some jurisdictions explored mathematical models to optimize distribution of national antiviral stockpiles. One algorithm projected the epidemiological impacts of various antiviral distribution schedules and priorities on a model of pH1N1 transmission within and among U.S. cities. A near-optimal policy involved the periodic distribution of small quantities of antivirals that are proportional to population densi-

ties. The authors cautioned, however, that this antiviral distribution scheme depended upon a scenario where a higher proportion of cases were identified and promptly treated with antivirals than was happening during the 2009 pandemic (21).

Refinement of the estimates of the required antiviral stockpile could be achieved through modelling of interventions on specific populations, such as patients who are already ill, those in close contact with patients, including health care workers and emergency medical service providers, high risk patients and others (12). However, the WHO cautioned other ethical considerations should be taken into account when developing a public health response to pandemic influenza (22).

Implementation of Antiviral Strategies

High Risk Populations

The WHO noted that populations at higher-risk for severe disease from pH1N1 were similar to those identi-

fied for complications from seasonal influenza (10). They included infants and young children (particularly those <2 years), pregnant women, people over the age of 65, and people with underlying respiratory or other chronic conditions, including asthma, diabetes and immunosuppression (23). They also found a higher risk of severe complications in obese people, and among disadvantaged and indigenous populations. In addition, healthcare workers are usually included among high-risk populations due to their regular contact with infected patients (1, 2, 6, 9).

Mathematical modelling of the use of antivirals under various scenarios shows that for individuals at high risk of severe outcome, including those who are immunosuppressed (particularly children) and possibly those with neurological disorders, pre-dispensing is always beneficial, even with modest assumptions on the relative benefit of early treatment. Pre-dispensing remained beneficial after including a larger number of people, such as pregnant women and morbidly obese adults (24).

Aboriginal Populations

Canada's experience reflected WHO's suggestion that indigenous populations were at higher risk of infection from pH1N1 (25). As of September 2009, the Public Health Agency of Canada (PHAC) had identified 885 cases among First Nations, Métis and Inuit peoples, comprising 12% of the total cases of pH1N1 in Canada (26). However, some provincial estimates put the number of cases at three times that amount. Critics say that difficulties in estimating cases stem from an inadequate surveillance system and that the numbers reported by PHAC were based on laboratory-confirmed pH1N1 cases rather than physicians' reporting of influenza-like illness (25). They note

that collection of accurate data is extremely important for developing effective pandemic responses (25).

Saskatchewan First Nations had the highest per capita number of antiviral prescriptions filled in Canada, with uptake closely following the waves of pH1N1. Use of antivirals was highest among adults, while immunization rates in children and seniors were greatest (27).

In Canada, the Yukon Territory and seven provinces chose to pre-position antiviral stocks in remote and isolated communities to facilitate rapid access.

British Columbia (B.C.) had far fewer hospitalizations than other provinces, including hospitalizations for Aboriginal peoples (26). The B.C. government credits a comprehensive First Nations pH1N1 Action Plan developed early in the outbreak, in consultation with the First Nations Health Council and other First Nations stakeholders (28). As part of the plan, antivirals and diagnostic kits were pre-positioned in 21 remote First Nations communities to expedite diagnosis and care.

Children

Children under the age of five years or with certain chronic medical conditions, especially neurodevelopmental diseases, were found to be at increased risk for complications and death from pH1N1. Data from

the U.S. showed that the number of deaths among children with high-risk medical conditions (67%) was higher during the 2009 pandemic than in previous influenza seasons (29). Early diagnosis and initiation of antiviral therapy were deemed very important for this group.

Recommendations by the Canadian Paediatric Society include prophylactic use of antivirals in institutional settings whenever an outbreak is diagnosed. In a home setting, they recommend considering treatment for unaffected family members (30).

One concern is the continuing void of published randomized controlled trials assessing the efficacy and safety of oseltamivir in children aged <1 year (10).

Pregnant Women

Pregnant women experienced a disproportionately high risk of death as a result of pH1N1 infection. In Canada and the U.S., they accounted for 4% and 5% of total deaths during the 2009 pandemic, respectively, while representing only about 1% of the population (26, 31). Early antiviral treatment appeared to be associated with fewer admissions to an intensive care unit (ICU) and fewer deaths. If treatment was initiated more than four days after symptoms appeared, the patients were six times more likely to be admitted to an ICU than those treated within two days after symptom onset. Early treatment was also associated with a shorter duration of illness, less severe symptoms and fewer complications, hospitalizations and need for antibiotics (31).

In Canada, most pregnant women accessed antivirals through their physicians (32). Guidance for treatment of pregnant women was confusing, with varied messages coming from different levels of government. This led to scepticism among physicians and the



public and an overload of messages. Going forward, there remains a need for clinical guidance for the care and treatment of pregnant women (33).

Remote Communities

To make treatment more readily available in remote and underserved areas, the argument has been made that community health workers, paramedics or other officials be allowed to dispense antivirals to residents during an outbreak, if no doctor or registered nurse is available (34). While it may put some people at risk of getting antivirals when they have not been properly diagnosed, evidence suggests that any delay in treatment for those affected by pH1N1 puts that person at greater risk of severe illness and complications (2).

Benefits of Broader Targeting

About one-third of severely ill patients admitted to an ICU were previously healthy and did not belong to any known risk group (10). In November 2009, the WHO revised its guidelines to note that, in places where pH1N1 was circulating, symptomatic people without risk factors should be treated without laboratory confirmation (35). In the U.S., 40%

of children and 20% of adults who were hospitalized with complications of pH1N1 had no risk factors. It was suggested that in the future, clinical judgement be applied on the use of antivirals, on a case-by-case basis (36).

The results of broader targeting can be seen by comparing the death rates in Chile *versus* Argentina. Chile began broad distribution of antivirals from the beginning of the pandemic, while in Argentina, treatment was reserved for hospitalized patients until after its peak, when pregnant women and members of high risk groups were also treated. Only near the end of the pandemic was treatment of all cases recommended. Over the course of the pandemic, Argentina had 1.44 deaths per 100,000 population, while in Chile 0.8 deaths per 100,000 population were recorded (37).

Prevention versus Treatment Containment versus Mitigation Strategies

Early on in the pandemic, Europe and North America followed very different strategies. An assessment of the European approach of containment (trying to stop influenza

spread beyond initial outbreaks) *versus* the strategy used in North America, which began mitigation strategies from the beginning, provides important lessons for future pandemics (38). In Europe, some countries, including the U.K., carried out active case-finding, contact tracing and treatment with antivirals to delay transmission of the virus. North American strategies followed WHO advice to manage cases (Phase 4 and beyond) – treating only those at higher risk of experiencing severe disease with antivirals.

Generally, containment strategies require substantial public health efforts and resources to track and treat cases quickly, and pose additional communication challenges, as the strategy moves from containment to mitigation. It proved unsustainable in Europe in 2009, and the U.K. and other countries moved to mitigation fairly quickly to make best use of resources (39).

A review by PAHO concluded that “effective containment of the 2009 pandemic was not possible because of the rapid spread of the virus” (5). Containment can be a viable option when influenza begins towards the end of the normal season, when transmission is expected to slow. Aggressive containment can then delay acceleration of the pandemic, allowing for better preparations and the development of vaccines. In addition, identifying and documenting the first cases helps to gather clinical information needed to amend strategies that respond to the particular viral strain at hand. Assessment of first cases can provide information on the proportion of people affected in a family, the ages of those most affected, length of the infectious period, and the effectiveness of antivirals in ending virus shedding and assisting in the development of immunity.

Containment can be considered effective at the individual level, as those found and treated early will likely suffer for shorter periods with less severe illness. At the population level, however, the success of delaying tactics is harder to measure (40).

Modelling data suggest that treatment of cases and prophylaxis of their close contacts reduced spread of the disease in the U.K. by about 16% (95% CI 12%-20%). The population-level effect is assumed to have been smaller than this, as most affected individuals did not seek care (40). It is speculated that more rigorous containment measures, such as earlier and longer school closures, might have had a greater impact on preventing the spread of disease; however at a greater cost and increased social disruption (14).

In any case, only countries with well-resourced national public health workforces are likely to be able to implement containment at the population level. Australia and New Zealand are unusual in having formal containment phases in their pandemic plans. However, both moved through and beyond containment rapidly into mitigation (41, 42).

Social Distancing Measures

Containment approaches sometimes include measures such as school closures. The U.K. pursued this approach early in the pandemic, but realizing that most people infected with pH1N1 had only mild symptoms, the widespread prophylactic use of antivirals in schools was no longer deemed appropriate and the practice was applied only to the closest contacts of suspected or confirmed cases, then discontinued entirely (7).

School closures have widespread ramifications for students, parents, and employers (20). Generally, poli-

cies for limiting mass gatherings are problematic, but in Europe and the U.S., the recommendation stands that possibly infected people not gather in close proximity (2, 20).

Distribution and Logistics

A number of countries found innovative local solutions to the challenges of assessing those who are most at risk of developing severe disease, prioritizing eligibility and dispensing antivirals (2). Several are described here.

National Pandemic Flu Service (U.K.)

In the U.K., the National Pandemic Flu Service (NPFS) was introduced as a novel way to speed the delivery of treatment to members of the public (43). The system allowed people to be assessed over the telephone or through an online self assessment, to determine if they had influenza. If so, they were issued a unique reference number and were able to collect antiviral medication from their local community pharmacy, or in the absence of a pharmacy, through antiviral collection points (ACP) established and staffed by NHS community health staff. The system was mobilized as needed, with capacity adjusted in response to demand.

The objectives of the system were to provide antiviral treatment to those who needed it, while reducing demand on frontline health services (44). The system provided advice on symptom relief as well. According to a report by National Health Service (NHS) Somerset, the NPFS allowed staff to refocus activity on day-to-day work, and was “generally welcomed by staff” (44). A mid-stream survey (July 2009) noted that uptake of NPFS was positive and that users were satisfied with both the online service (88%) and the telephone service (85%) (4).

The ACP pharmacy model was deemed instrumental in the success in NHS Somerset’s antiviral distribution strategy (44). Cooperation with pharmacies who handled delivery, storage and distribution of antivirals was extremely successful, and is a practice that has since been included in national pandemic planning. Another ‘best practice’ identified by the Department of Health was the use of ‘flu friends’, who collected the antivirals for the symptomatic patient, thereby protecting others from exposure.

The NHS Somerset report points to some issues, including the fact that information on the ACPs provided to the public was frequently inaccurate and slow to be corrected or changed (44). Generally, communication and clear roles for various players were stressed as important to smooth operations. Maintaining the appropriate number of staff required for various tasks proved problematic, due to the high workload and staff illness. A business continuity plan was suggested to prepare for future pandemics. Maintaining up-to-date information on antiviral stock levels was also a problem, despite an electronic tracking system that was introduced part-way through the process.

The official review of the U.K. response to the 2009 influenza pandemic notes that an independent evaluation of the NPFS is required, addressing “value for money, risk analysis and any potential for wider application” (7). It also recommends that triggers for the activation and stand-down of the NPFS be developed prior to any future pandemics.

The U.S. 2009/2010 influenza preparedness plan includes rapid access to telephone consultation and clinical evaluation for patients at risk of

complications and those who report severe illness (45).

Distribution via Pharmacies

Ontario, B.C. and possibly other Canadian provinces followed a process of dispensing antivirals primarily through pharmacies. The Ontario Ministry of Health and Long-Term Care (MOHLTC) partnered with the Ontario Pharmacists' Association to ensure that antiviral medications were readily available to those who needed them (46). Pre-determined quantities of antivirals were distributed from the provincial stockpile to pharmacies, which were responsible for secure storage, separate from the commercial supply. In B.C., antivirals were provided at no charge to anyone who had a prescription (28). Post-exposure prophylaxis was used only for specific circumstances (e.g. outbreak control in long-term care homes).

In B.C., the highest rate of prescriptions was filled for children and youth between the ages of 1 and 17. A report on B.C.'s response estimates that free distribution of the antivirals may have cut the number of severe outcomes by almost half (28).

Members of the Registered Nurses' Association of Ontario agreed that having access to the provincial antiviral stockpile was "extremely beneficial". The process allowed them to purchase antivirals without corporate approval, which empowered staff to act responsibly and without interference (47).

In response to the rapid spread of the pH1N1 virus in Norway, oseltamivir and zanamivir were dispensed without a prescription, after consultation with a qualified pharmacist (48). The Norwegian health minister said that, "We are offering the

drugs without prescription to make it easier for those who are sick to get the medicine, and to ease the work load for the doctors" (48).

Use of Volunteers

The U.S. Medical Reserve Corps is a national network of community-based volunteer units that support local public health, particularly in the case of a public health emergency (20). They were valuable in addressing the pH1N1 outbreak in a number of ways, including staffing

In B.C., antivirals were provided at no charge to anyone who had a prescription.

triage phone lines, receiving, taking inventory and sorting of Strategic National Stockpile pharmaceuticals, delivering supplies, and teaching proper hand washing at local schools.

Improving Antiviral Distribution and Targeting - Lessons Learned

While few comprehensive, independent reviews of various nations' responses to the 2009 pandemic have been published, common themes have emerged from those available. They are summarized here.

Planning

Experience has shown that effective responses are based on plans informed by scientific evidence, along with the detail, infrastructure and formalized agreements required to be operational (7, 20). Reviews of the 2009 pandemic response emphasize the challenges inherent in coordinating efforts among various levels of governments and the private sector

(7, 20). They note that plans must be practiced and tested (32). To assist planners, policy-makers and health-care professionals, an ethical framework, drawn up by an independent body, was proposed to ease decisions such as prioritizing populations to receive antivirals (7).

Responses also need to be flexible so that they can be adapted as information about the specific and changing circumstances of particular pandemics are learned (32, 49). As noted in a review of the U.S. response: "Even if preparations are based on past experiences, each disease outbreak is unique and unpredictable, and requires constant reassessment of priorities and guidance for the public and medical community" (20). Issues on whether to adopt a containment or mitigation approach, whether or not to close schools, and how best to communicate with the public must match changing circumstances, differing resources and situations across locations. While the U.K. review concluded that different antiviral strategies in each country were "entirely comprehensible" (7), one reviewer felt that national pandemic plans should be revised only with guidance from WHO to ensure that plans do not significantly diverge from each other (50).

Guidance

A number of reviews noted that guidance to health professionals changed frequently and was sometimes conflicting (20, 51). In Canada, the U.S., as well as parts of Europe, there were concerns that differing guidelines made implementation of plans challenging for healthcare staff and confusing to the public. The Canadian Medical Association called for "advanced pan-Canadian commitment to a harmonized and singular national response to clinical practice guide-



lines (including use of antivirals)... during times of potential public health crisis” (51).

Part of the difficulty may be in adapting plans to reflect rapidly changing conditions. Real-world factors influence the effectiveness of proposed approaches that must take into account both individual and population benefits (13). Mathematical modelling has been suggested to systematically investigate various factors and approaches (13).

Communication and Education

The importance of communication, both to and among healthcare practitioners and to the public was a recurring theme. Educating the public to encourage appropriate behaviours (e.g., coughing in sleeve, hand washing, staying home) is critical (32). During the 2009 pandemic, guidance evolved and information from national health leadership was sometimes difficult to obtain, mak-

ing communication to the public difficult and hindering timely access to antivirals by local health departments (20, 44).

Several reviews of the pandemic response emphasize the importance of effective communication between public health and primary care, and to the general public (8, 20, 51). The Canadian Medical Association called for a national communication strategy that builds upon communication processes to physicians already in place. They suggested that, “Embedding primary care expertise into public health planning at all levels would help us avoid problems and improve our response” (51).

A review of the U.S. response noted the particular issues of communicating with high risk populations. Racial and ethnic minorities tend to be disproportionately impacted by outbreaks, and at the same time, often have the lowest level of trust for government recommendations and

messages (20). They recommended special efforts to develop relationships with racial and ethnic minority groups prior to emergency situations, and to communicate transparent, straightforward messages tailored to resonate with these groups during a pandemic.

Organization

A number of countries experienced difficulty in determining when to trigger various actions to address the pandemic. Clear definitions and an evidence-based approach to triggering actions during a pandemic were called for (7, 13, 20). In addition, it was pointed out that clear case definitions to guide treatment are needed to avoid needless delays in treatment (13).

Similarly, clear plans need to be in place to make sure stockpiles are used to their best advantage. Agreed upon objectives, protocols, administration and delivery systems are required (2).

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