Proposal of an ethics-based framework for prioritization of scarce resources during an influenza pandemic

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Table of Contents **Page**

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Summary

The goal of pandemic influenza planning is to minimize health and economic losses in the event of a future pandemic. One of the numerous challenges associated with this goal is the need to ration limited medical supplies such as vaccines and antivirals. This thesis seeks to formulate an ethical framework for priority access to these resources. Prioritization strategies must be consistent with the goal of pandemic planning and should reflect societal norms for equitable distribution. According to an ethics framework based on the principles of utility and equity, three groups were granted highest priority for influenza vaccine, namely health care workers, emergency service workers, and high-risk individuals predisposed to severe outcomes following influenza infection. In the case of antivirals, the expectation is that there will be competition between treatment and prophylaxis uses of these drugs. The resulting dilemma—providing primary access to the critically ill in respect of the medical profession's duty of care or prioritizing prophylaxis of health care workers in respect of their right to protection—is the major question which the framework presented in this thesis seeks to resolve.

Sommaire

Le but d'un plan de lutte contre la pandémie d'influenza est de restreindre les taux de morbidité et de mortalité ainsi que la perturbation sociale suite à une pandémie. Parmi les nombreux défis organisationnels liés à la mise en œuvre d'un tel plan, figure l'établissement des priorités dans un contexte où les ressources médicales, tels les vaccins et les antiviraux, sont limitées. Ce mémoire vise à définir un cadre éthique servant à la création d'une échelle de priorités pour l'accès à ces ressources. Toute stratégie de ce genre devrait respecter les objectifs du plan et refléter les normes sociales de distribution équitable. Suivant une stratégie de distribution guidée par une éthique utilitaire ainsi qu'égalitaire, les trois groupes saillants pour la distribution d'un vaccin pandémique sont les professionnels de la santé, le personnel des services d'urgence et les individus à haut risque de conséquences graves suivant une telle infection. En ce qui concerne les antiviraux, deux intérêts s'affrontent dans l'établissement des priorités : leur nécessité pour le traitement des malades et leur utilisation prophylactique chez les travailleurs de la santé. Le dilemme qui en résulte est la principale question que cette thèse tente de résoudre.

1. Introduction

The recent avian influenza outbreak has reinforced public understanding that future influenza pandemics are inevitable and that preparedness will be key to reducing morbidity and mortality as well as the disruption of social order seen in past pandemics. In the absence of contingency planning to mitigate the impact of such an event, the toll in terms of human life and economic losses could be devastating. In this vein, Dr Lee Jong-wook, director general of the World Health Organization (WHO), stated, "If we are unprepared, the next pandemic will cause incalculable human misery both directly from the loss of human life, and indirectly through its widespread impact on security. No society would be exempt. No economy would be left unscathed"[1]. In terms of economic losses, World Bank economist, Milan Brahmbhatt, calculated that an avian flu pandemic could cost the world economy as much as $950 billion (cdn) in lost growth over one year based on figures extrapolated from the recent SARS pandemic[2]. Many nations have taken heed of such dire predictions by developing a plan for readiness in the event of an influenza pandemic.

There are numerous ethical considerations involved in the drafting of a contingency plan for pandemic preparedness. The objective of this thesis is to concentrate on one of these elements, namely the development of an ethics framework for distribution of limited resources. The WHO pandemic planning guidelines urge nations to develop priority lists for vaccine and antiviral distribution

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[1] Opening speech delivered at the WHO Meeting on Avian Influenza and Pandemic Human Influenza, Geneva, November 7-9, 2005. www.who.int/mediacentre/events/2005/avian-influenza/avian-influenza-meeting-presentations/htlm (accessed November 24, 2005).

[2] World Bank perspective delivered at the WHO Meeting on Avian Influenza and Pandemic Human Influenza, Geneva, November 7-9, 2005. www.who.int/mediacentre/events/2005/avian-influenza/avian-influenza-meeting-presentations/htlm (accessed November 24, 2005).

(WHO 2004a,b). The Canadian Pandemic Influenza Plan (CPIP or the Plan) (Health Canada 2004) was the first to list priority groups for vaccine and antiviral rationing. The Plan provides a rationale for the priority lists based largely on perception of medical need. The recently published USA plan (US Department of Health and Human Services 2005) essentially follows the Canadian lead on this issue. On the other hand, the plan prepared by the UK Health Department (2005), while admitting to the importance of a prioritization scheme for allocation of pandemic vaccine and antivirals, does not provide a numbered listing. Rather, it lists in bullet form the provisional aims for vaccine distribution, emphasizing the importance of protecting health care workers and key essential service workers. The UK antiviral distribution strategy is vague, stating "the drugs will need to be given in the most effective way on operational, clinical and cost-effective grounds taking into account the stocks available" (UK Health Department 2005). There was no information in any of these plans to indicate that a proper ethical analysis had been performed to guide the prioritization exercise.

The work presented in this thesis was therefore undertaken in recognition that an ethics-based framework was needed to justify the ranking of priority groups and to guide decision-making on prioritization issues. Following a background section to contextualize the pandemic planning effort, the ethical analysis begins in Part 3 with a discussion of ethical theory in the context of the public health mission guiding pandemic planning, followed by a description of applicable principles and distribution models for the rationing of health care resources. The criteria system is proposed as a valid instrument for distribution of scarce resources. Part 4 provides a discourse on competing values to illustrate the dilemma inherent in prioritization exercises. This chapter illustrates, at a pragmatic level, two types of triage situations

describing scenarios which might be operative in a mild versus severe pandemic. Parts 5 and 6 discuss attempts to maximize resources, namely recourse to private stockpiling of antivirals and the need for a global antiviral stockpile. The importance of transparency and public consultation is also emphasized. Finally, the proposed framework is used to re-assess the ranking of the priority groups in Part 7, followed by the conclusions of the study in Part 8.

The formulation of an ethics-based framework for the fair distribution of limited resources in a pandemic setting is unique to this thesis in that, to the best of my knowledge, no publication exists on this subject matter. This would therefore constitute the first such report.

2. Background—the Pandemic Context

2.1 - Contingency planning

Contingency planning is essential for mitigating the impact of any mass catastrophe on human life and societal function. The requirement for formulating and operationalizing any such plan is that the disaster be anticipated or foreseeable. In fact, many observers commenting on the tsunami that hit the South Pacific in December 2004 expressed the view that much of the devastation in terms of losses in human lives could have been avoided if a surveillance system had been in place to allow for timely evacuation of the affected areas. We live in an era where advanced knowledge and technologies permit prediction of certain natural disasters, hence the call on governments to produce contingency plans in preparation for such events.

Influenza pandemics fall into the category of predictable disasters because they are known to occur at a rate of approximately three per century (Hampson

2002). While expected, neither the magnitude nor the exact timing of the next pandemic can be known with certainty. Still, consideration of the impact on human life, societal function and economic repercussions caused by influenza pandemics is reason enough to call for a contingency plan which can be operationalized immediately upon observation of sustained human-to-human transmission of a novel pandemic flu strain.

Recent developments surrounding the H5N1 avian flu outbreaks in Asia have given rise to fears that the next influenza pandemic might be brewing at this very moment (Guan et al 2004; Li et al 2004; Osterholm 2005; Specter 2005). The World Health Organization (WHO) has recently released its updated Global Influenza Preparedness Plan on the role of the WHO and its recommendations for national measures before and during a pandemic (WHO 2005). This document urges member states to formulate a comprehensive plan for preparedness and response strategies in the event of a pandemic. Among the plans available for public consultations are those of Canada (Health Canada 2004), the United States (US Department of Health and Human Services 2005) and the United Kingdom (UK Health Department 2005). It is not the aim of this thesis to delve into the particulars of each of these plans. Rather they are used simply as reference documents for the purpose of discussing the ethical issues surrounding prioritization of scarce resources such as vaccines and antivirals essential to the pandemic relief effort. My analysis will focus almost exclusively on the CPIP[3].

[3] As volunteer 'health ethicist' of the Canadian Pandemic Influenza Committee since September 2002, I have participated in numerous discussions during meetings and teleconferences. These discussions focused on the medical, scientific and logistic issues of pandemic preparedness. A working draft of the Plan was already written when I joined the Committee. My role was to contribute by way of ethical reflection on such problematic matters as private stockpiling, off-label use of antiviral drugs and prioritization lists. My work for the Committee inspired me to a further and more comprehensive analysis of the prioritization dilemma which became the subject of this thesis.

The Plan was first released publicly on February 12, 2004 (Health Canada 2004). This document described how the federal minister of health, in concert with his provincial and territorial counterpart, will mobilize public health resources in an effort to mitigate the impact of an influenza pandemic on Canadians. The CPIP is designed as a guideline for federal, provincial and territorial departments of health, emergency service workers, public health officials and health care workers. It presents a framework to guide the actions of the various intervening bodies in the event of an influenza pandemic. Its 448 pages include guidelines and checklists that government and health officials can use in emergency response planning. No other pandemic in history has seen such intensive preparedness activity. So why is the Canadian government willing to invest such effort now? Certainly, influenza pandemics have been known to exert an enormous toll on human life and to precipitate exorbitant economic losses. People still shudder at the recollection of the Spanish flu of 1918-1919 which killed twenty to forty million individuals worldwide (Hampson 2002). The pandemics of 1957 and 1968, while less devastating, nonetheless resulted in death rates that were ten-fold higher than normal. The global tragedy inflicted by influenza pandemics incited the WHO to establish an alert system for influenza (WHO Bulletin). This global surveillance system saw its beginnings in 1948 and now consists of over 110 state-of-the-art national monitoring laboratories and four WHO collaborating centres serving as sentinels for rapid isolation and identification of novel viral strains in animals and in humans. The WHO also formulated its influenza pandemic preparedness plan (WHO 1999) and urged member countries to develop comprehensive strategies for pandemic preparedness, a challenge that Canada has dutifully met. Other events that have made pandemic planning possible are improved vaccine production processes (Gerdil 2003) and the

development of well tolerated and effective antivirals (Leneva et al 2000; Moscona 2005) allowing prophylaxis and treatment options not available during previous influenza pandemics.

The process of outlining a strategic plan for confronting the next influenza pandemic is not a trivial undertaking. The proposal to draft a Canadian plan was first conceived in 1983, with two preliminary versions filed before releasing the 'final' document in February 2004. The latter was completed after establishment of the Pandemic Influenza Committee (PIC) under a working agreement between the government of Canada and the provincial and territorial ministers of health, signed on March 26, 2001 (Government of Canada 2001). According to this agreement, the mandate of the PIC included the provision of technical advice, expertise and recommendations, liaison and other activities associated with interpandemic and pandemic periods to support the health and safety mandates of all orders of government. PIC was also instructed to provide advice, assistance and expertise concerning the development, maintenance, testing and evaluation of the CPIP and, when requested to do so, any provincial/territorial contingency plan. The Plan is purposefully multifaceted, and thus is concerned with various planning aspects, from selection of vaccine manufacturers, stockpiling of essential resources, optimizing laboratory protocols for surveillance, conversion of schools and other public buildings into health facilities to accommodate the multitude of patients with pandemic flu, to funeral and morgue arrangements for handling the overwhelming number of casualties. Ethical and legal issues abound. However, I shall be concerned here with the Plan only as it relates to scarce resource allocation, specifically with regard to vaccine and antiviral rationing, as both of these will be in short supply particularly during the first wave of the pandemic.

It is recognized that, conceptually, pandemics fall within the 'disaster' category. Thus prioritization strategies that are being formulated for pandemic influenza may be applicable to other catastrophes, most particularly those which involve a biological threat to humans, whether the agent arises through a natural process or deliberate release. This thesis will strive to provide a framework and rationale for priority allocation that can be used in situations involving biological threats against the mass public, regardless of the causative agent. It is understood, however, that the primary motive for developing any pandemic plan is the absolute conviction that future influenza pandemics are inevitable, a statement that is far more debatable, for example, in the case of bioterrorist threats.

Preparedness planning of this nature demands substantial resources and dedicated political will in order for the program to be initiated and supported over an indefinite time span. The fact that the Canadian government has responded to the cautionary call of public health experts is to be applauded on grounds that such precautionary thinking is not standard practice for governments whose modus operandi seems to be more reactionary given the tight budgets and the necessity to select among the innumerable causes for urgent support.

In reality, the Canadian Plan can only prove its worth once the pandemic actually strikes. Carefully planned mock exercises are useful tests of the Plan's capacity to meet its goals[4]. Such exercises will test whether mock vaccine can be prepared and tested within a given time frame by the manufacturers. Further, if any benefit can be said to derive from the 2003 SARS experience in Canada, it is the

[4] For example, the Centre for Emergency Preparedness and Response organized Fast Relief 1, an umbrella exercise to test various facets of the Plan and its ability to interface with other related federal, provincial and territorial plans. A presentation of Fast Relief 1, prepared in March 2004 by Gordon Laing of the Centre for Emergency Preparedness and Response, was provided to PIC for informational purposes.

fact that this unfortunate incident provided a preview, although on a smaller scale, of how an influenza epidemic might devastate hospitals, communities and the economy. Further, SARS was seen to be especially brutal to frontline health care workers. So it would behoove us to take this experience into account when developing prioritization strategies for scarce resource allocation. The experience with SARS was also a reminder of the enormous economic toll that can befall a nation as a result of a respiratory-borne contagion bearing a high mortality index. With pandemic influenza the effects can only be worse, by many orders of magnitude. Nonetheless, the SARS experience has created procedural precedents for infection control in hospitals (WHO 2003a) hence preparing the terrain for other such calamities that might befall us in the future.

2.2 - Genesis of an influenza pandemic

In his article in The New Yorker, reporter Michael Specter likens pandemics to a perfect storm (Specter 2005). This metaphor appropriately alludes to the multifactorial trigger of both of these events. A pandemic, like the perfect storm, is triggered by the chance collision of a series of mishaps leading to a catastrophic outcome. For the perfect storm, there must be development of a nor'eastern with gale-force winds entering an area of extremely low barometric pressure and heavy moisture content. This type of tempest is most likely to occur over a wide uninterrupted expanse, such as tropical ocean waters, which allows for high wind speeds and the formation of large pockets of moisture. But these two events must cross courses before conditions are ripe for the perfect storm. Similarly, for a pandemic, the chain of biological events begins with a new influenza virus variant emerging from the animal reservoir, usually brought in by wild aquatic birds which

transmit the virus onto local fowl such as chickens (Hampson 1997). Any unusual pattern of behaviour and heightened death rate in these bird species can signal a potential infection with a new influenza virus strain. Suspicious birds would be sent to a local laboratory or a WHO sentinel centre for viral detection. The virus is flagged if tests indicate the presence of antigenically diverse proteins on its outer surface compared to those found on strains circulating in the human population in recent decades[5]. But, by and large, most avian strains cannot infect humans. Hence, a necessary second requirement for a pandemic is that the viral strain must acquire the capacity to infect and cause disease in the human host. This process of adaptation is thought to occur by passage through an intermediate animal species, such as the pig, which can replicate both human and avian influenza viruses (Kitler 2002). However, direct avian-to-human transmission can also occur as demonstrated recently with the H5N1 and H9N2 strains (Guo et al 2000; Horimoto et al 2001; Lee et al 1999; Saito et al 2001). The H5N1 virus has been responsible for wide-spread deaths in Asia including probable human-to-human transmission in a family cluster in Thailand (Peiris et al 2004; Ungchusak et al 2005). Mechanistically, such variants are produced if, by chance, the intermediate host or a human is co-infected by the new avian strain and by a circulating human influenza virus (Kitler et al 2002). The simultaneous replication of both viruses in the same host cell allows for reassortment of the viral genes creating hybrid strains with various combinations of human and avian genes. Through this combinatorial process a rare hybrid might

[5] The type of reassortment of viral genes required to give rise to a new pandemic strain is referred to as 'antigenic shift' because the process causes radical changes in one or both of the viral proteins, namely hemagglutinin (H) and neuraminidase (N), located on the outer surface of the virus. In contrast, seasonal influenza epidemics occur because of small variations, called 'antigenic drift', in these two proteins.

emerge with the capacity to efficiently infect, replicate and cause disease in human respiratory tissue.

Third, the unsanitary and crowded living conditions prevalent in many Southeast Asian countries increase the likelihood of viral transmission between humans and animals, hence creating the ideal milieu for the release of a potential pandemic strain into the human population (Osterholm 2005). Lastly, severe outbreaks will only occur if the virus is highly aggressive in its ability to replicate in the host's tissues and cause rapidly progressing disease. If such virus were to be released among an immunologically naïve population, there would be no effective immune response to temper its prowess, allowing the virus to run rampant. Today's fast efficient means of transportation would rapidly spread it to all parts of the world—hence the genesis of a global pandemic (Grais 2003).

The historical logbook indicates that influenza pandemics invade the human population approximately every ten to forty years (Hampson 2002). Ten pandemics have been recorded during the last 300 years and three have made the registry for the 20th century, with the last of these occurring in 1968 (Gust 2001). The world is due, therefore, for another important outbreak. In fact, many experts tracking the course of the H5N1 avian flu strain which is circulating presently are of the belief that the perfect storm is brewing at this very moment (Osterholm 2005; Specter 2005). This virus is highly virulent, having infected and killed many wild and domestic bird species, and caused the recent culling of millions of chickens in an effort to prevent transmission to humans (Li 2004). Nonetheless, the human death toll is rising steadily from incidences of avian transmission to humans (WHO Global Influenza Program Surveillance Network 2005) and with this comes the fear of potential human-to-human spread (Ungchusak 2005). The WHO is particularly apprehensive

about the situation and has recently amassed its own antiviral stockpile, consisting of three million treatment doses of oseltamivir[6], to be used in a strategic effort to contain initial localized clusters of human cases (Butler 2005; WHO Media Centre 2005). The identification of a cluster signals that the virus has attained the necessary level of adaptation to be transmitted within the species. The WHO strategy is to use its surveillance network to rapidly identify and suppress the initial spark in an effort to avert a full-blown pandemic.

2.3 - Phases of an influenza pandemic

A pandemic is not an event per se but a process which may be divided into sequential phases. The phase categorization provides a contextual element which will assist in efforts to communicate at a global level, provided that all countries agree to harmonize their classification scheme. In May 2005, the WHO expanded its original three phases into six phases. The new definition takes into account the very real possibility that a pandemic flu strain would first be identified in a non-human host. This stems from recent observations with three distinct avian viruses all of which managed to cross the species barrier to infect humans, namely the H5N1 strain which first emerged in 1997 in Hong Kong (Chan 2002), the H7N7 in the Netherlands (Fouchier 2004), and the H7N3 in British Columbia, Canada (Hirst et al 2004; Tweed et al 2004).

For purposes of public health planning, the WHO proposes six phases divided into three periods (WHO 2005). Not all phases need necessarily occur in any

[6] Brand name Tamiflu®, manufactured by Roche Pharma.

given pandemic. The following, then, are the six putative phases in an influenza pandemic, as described in the WHO classification scheme.

Interpandemic period

Phase 1: No new influenza virus subtypes have been detected in humans. However, an influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low.

Phase 2: No new influenza virus subtypes have been detected in humans. However, an animal influenza virus subtype that poses substantial risk to humans is circulating in animals.

N.B. The distinction between phase 1 and phase 2 is based on scientific knowledge regarding the risk of human disease or infection from strains circulating in animals.

Pandemic alert period

Phase 3: Human infections with a new subtype are occurring, but no human-to-human spread or, at most, rare instances of spread to a close contact. Example: sporadic human cases of H5N1 occurring in Asia and Europe in connection to an avian outbreak. This phase reflects the present situation with H5N1.

Phase 4: Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.

Phase 5: Larger cluster(s) but human-to-human spread is still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).

N.B. The distinction between phases 3, 4 and 5 is based on the size of the cluster, the overall setting and the potential to contain the pandemic.

Pandemic period

Phase 6: Increased and sustained transmission in the general population has been observed.

Public health measures will vary depending on the phase of the pandemic. Phase 3 warrants treatment of patients and prophylaxis of caretakers. The presence of progressively larger clusters in phases 4 and 5 argues for more intensive containment strategies with prophylaxis of all close contacts in an effort to contain the spread of the virus in humans. Quarantine may also be helpful during phases 4 and 5. Large-scale prophylaxis of Canadians, as per the priority groups defined in the Plan, would not be justified before there is evidence that the virus has acquired the capacity to spread readily between humans and that the pandemic flu strain has been identified in patient clusters in Canada.

2.4 - Stakeholders in pandemic planning

History has shown that influenza pandemics can be detrimental to human health and to societal structure. With a predicted attack rate of over 25% of the population, there is little that can match the devastating toll that such pandemics exert on humans and societies globally. The belief that the morbidity, mortality and societal disruption associated with pandemics can be mitigated by strategic advanced planning was the impetus that led to conception of preparedness planning (WHO 1999). The development of concrete action plans to allow the realization of

the goals of pandemic planning requires many years of strategic effort on the part of all levels of government. Further, achievement of the goals requires cooperation and participation from all stakeholders, which in turn demands awareness of the pandemic mission. This invites reflection as to who can be considered a stakeholder in pandemic influenza planning. Generally, for disaster preparedness, stakeholders should include individuals who can function as mitigation experts such as law enforcement and civil defense experts, firemen, as well as medical and paramedical personnel (Government of Canada 2002). Also considered to be stakeholders are government agencies and legislative bodies at federal, provincial, territorial and local levels, including tribal leaders (WisdomSource News 2005). Businesses should also be included, especially utilities and communications companies. Good Samaritan organizations such as the Red Cross are also stakeholders. Because pandemic influenza affects all Canadians, one can broadly refer to the mass population composed of every man, woman and child residing in Canada as a stakeholder. Identification of stakeholders is important from an ethical standpoint in order to bring to the forefront any special needs which would warrant prioritization of a given group.

As the term implies, stakeholders have a keen interest in terms of the capacity of the Plan to meet their needs. The government, for example, has a primary interest in pandemic planning because of its role to "promote, protect and provide the public good"[7]. Our elected officials should fulfill this moral obligation to their electorate. However, government bodies can govern effectively only on the condition that their own health is maintained. First responders can tend to an emergency provided that the structure of their unit is sufficiently intact which, in turn,

[7] Quoted from James Orbinski's talk presented at the University of Montreal within a public forum on Fundamental Rights and Access to Essential Medicines, September 30, 2005.

depends on a core number of individuals reporting to work. Health care providers can aid the sick on condition that hospitals, clinics and other designated sites keep their infrastructure at a functional level of operation. At the core of all such emergency planning and response operations is the need for an effective communication system in order to keep the flow of information moving among key international health organizations such as the WHO, national decision makers, the public health system, first responders, hospital frontlines and the general public. Other essential commodities in any catastrophic situation are food, water and sources of energy, as well as the manpower to maintain their outsourcing to the public. All of this service infrastructure must remain relatively intact if we are to meet the goals of pandemic planning.

The key to maintaining the level of societal order required to adequately meet the Plan's mission is to limit spread of the infection and curtail length of illness so that absenteeism is minimized and societal functions are maintained. This logic attests to the cohesion of the two goals proposed by the Plan, with each relying on the other for accomplishment of the Plan's mission. From this perspective, therefore, the stakeholder's claim cannot be self-directed, as all individuals must act in the interest of the aggregate. No one can predict when the next influenza pandemic will strike or how severe it will be. One certainty, however, is that vaccine availability will be very limited during the first wave of a pandemic. Hence favorable outcomes will depend on the availability of antiviral drugs (Monto 2003) which are now being amassed in order to confront the pandemic when it first arrives at our borders. But these too are expected to be in short supply; thus it is critical to undertake the task of developing a prioritization scheme which will best allow fulfillment of the Plan's goals. Further, this scheme must satisfy the Canadian ideal for equitable access to

health care as inferred by the Canadian legislature (Canada Health Act 1984) and stipulated in more recent documents (National Forum on Health 1997; Romanow 2002).

2.5 - Priority groups as defined in the Canadian Pandemic Influenza Plan

The scarcity of certain essential goods during a pandemic demands that a portion of the preparedness effort be dedicated to the identification of population groups which can justifiably be given priority access to these resources. There must be proper justification in terms of how the prioritization of a group allows the goals of pandemic planning to be fulfilled. The Plan rationalizes the prioritization of certain groups based on need for protection due to the increased risk imparted either by a pre-existing medical condition or enhanced exposure[8]. This would meet the requirements for goal one in that protecting those at increased risk would curtail the incidence of morbidity and mortality consequent to a pandemic. The essential nature of one's occupation in disaster response also constitutes reason for prioritization, as this would be considered especially important in order to meet the goals of pandemic planning.

The Plan recommends different prioritization strategies for scarce resource allocation of the vaccine versus antivirals[9]. Vaccination is exclusively a preventive measure and, as such, might be used to target the various priority groups in an order which would differ from that appropriate for antivirals, seeing that the latter may be used either therapeutically or prophylactically. In a general sense the Plan has identified three priority groups, namely health care workers, essential service

[8] See Health Canada 2004, annexes D and E, on vaccine and antiviral recommendations, respectively.
[9] Idem

workers and patients at high-risk of severe outcomes following influenza infection. Health care workers are perceived to be at increased risk of contagion due to contact with infected patients. Further, absenteeism in this group could negatively impact the health care system, which would constitute a compelling reason for prioritized access of health care workers to vaccine and antivirals. Essential service workers are critical to keeping societal order. The high-risk group encompasses individuals with a weakened immune system, or with other underlying health conditions (e.g. cardiac problems, diabetes) predisposing them to a poor outcome upon infection with pandemic influenza.

Identification of priority groups during the pandemic planning stage is important in a pragmatic sense because the catastrophic conditions imposed by a pandemic will not provide an environment conducive to rational decision-making. Further, this exercise cannot be regarded as optional because Canada's national health care system is founded on the principle of equity, meaning that all persons have equal access to health care resources, except where differential treatment is required to remove or minimize health-based differences between individuals (Kluge 2000)[10]. Hence there is a duty to identify and prioritize these groups based on true need. This general logic provided the rationale for the priority groups recommended in the February 2004 version of the Plan. Reflections on such considerations gave rise to the following prioritization scheme for vaccine distribution (see Annex D in Health Canada 2004):

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[10] The concepts of 'equity' and 'equality' are often used interchangeably. I favour the position that equality means equal treatment for all, while equity is equality with the added twist that preferential treatment is justified if it can raise a person's ability to benefit from opportunities offered by society to a level equal to the norm.

1. Health care workers, paramedics/ambulance attendants and public health workers
2. Essential service workers
3. Persons at high risk of severe or fatal outcomes following influenza infection
4. Healthy adults
5. Children older than 6 months of age

For antivirals, the order is as follows (see Annex E in Health Canada 2004):

1. Treatment of persons hospitalized for influenza
2. Treatment of ill health care and emergency service workers
3. Treatment of ill high-risk persons in the community
4. Prophylaxis of health care workers
5. Control of outbreaks in high-risk residents of institutions (nursing homes and other chronic care facilities)
6. Prophylaxis of essential service workers
7. Prophylaxis of high-risk persons hospitalized for illnesses other than influenza
8. Prophylaxis of high-risk persons in the community

A glance at the vaccine list confirms that the ranking scheme was established in accordance with the public health mission of pandemic planning, which, as explained in the Plan (Health Canada 2004), is to minimize overall morbidity and mortality, and to limit societal disruption. Justifiably, health care workers are given uppermost prioritization for vaccine distribution because they are essential to the running of the health care system. Also, this group constitutes the most vulnerable population in terms of exposure risk. Unless protected, they are likely to bear an

unfair proportion of unfavorable outcomes[11]. However, during the early months of a flu pandemic, vaccine will not be available because of the lengthy lead time required for its manufacture. Thus, antiviral drugs will constitute the only option to control the infection. Judging from the above ranking for influenza antivirals such as the neuraminidase inhibitor, oseltamivir, it is evident that these will be provided primarily for treatment and, as such, to those who are critically ill—namely, hospitalized patients with influenza. It must be recognized, however, that oseltamivir is also prescribed for use in prophylaxis (Cinti et al 2005; Hoffmann LaRoche 2004; Moscona 2005). This latter indication would fulfill the need for protection of health care workers before the availability of a vaccine. In fact, the WHO has recommended this indication (WHO 2005), but makes no statement as to whether the prophylactic option should rank above or below treatment indications. Both the Canadian and US pandemic plans (Health Canada 2004; US Department of Health and Human Services 2005) have ranked the prophylaxis indication for health care workers second to that of treatment for the severely ill (i.e. hospitalized) patient. This is a point of potential contention which requires deliberation. The arguments will be presented later on in the context of section 3.7 'Precedence as a factor in risk assessment: Lessons learned from SARS'.

Interpandemic stocks of oseltamivir and other influenza antivirals are minimal and will not be able to meet pandemic needs. Therefore, as argued by the WHO, it will be essential to stockpile substantial quantities of these drugs in order to maintain an adequate reserve for pandemic response needs (WHO 2005). The size of the stockpile will reflect the dollar amount that the government has agreed to invest for

[11] The burden on health care workers is discussed further in section 3.7 'Precedence as a factor in risk assessment: Lessons learned from SARS'.

this purpose, which in turn depends on the priority attributed to the pandemic cause. In order to predict coverage capacity for the approved stockpile with respect to the antiviral priority list, it will be important to obtain fair estimates of the number of individuals in each priority group. Only then can one reasonably calculate how far down the list the cutoff line can be drawn.

Further, if the lead time for vaccine availability is approximately six months—based on estimates using presently available technology—and antiviral prophylaxis with oseltamivir is recommended for only six weeks (Hoffmann-LaRoche 2004), there may be a window during which an individual can no longer receive antiviral and does not have the benefit of a vaccine. Thus studies to determine safety of oseltamivir extension beyond the recommended six-week prophylactic course will be required. These should be performed prior to the pandemic, i.e. during interpandemic years. To extend the period of oseltamivir use without supporting experimental evidence ensuring safety under such circumstances would constitute off-label use of the drug. Should it not be feasible to perform these safety studies by the time the pandemic strikes then one might consider rotation of health care workers through six weeks of service time. This scenario may not be very practical because influenza pandemics inevitably drain the health care system, hence requiring support from as many workers as possible on the frontlines. Yet another option is to switch to a different antiviral, such as amantadine, following a six-week treatment course with oseltamivir. One must consider, however, that amantadine is less well tolerated (McGeer et al 2004) and may not be acceptable to health care workers for long-term use.

When the scarce resources in question are also public goods (Woodward and Smith 2003)—as is the case for pandemic vaccines and antivirals—the distribution

process must adhere to norms of fairness and transparency. An objective process will require that criteria for fairness be established within the confines of an accepted value system which, for example, might rely on one or more principles for initial guidance. The distribution of organs for transplantation in the voluntary donation context is the prototype scenario whereby the principles of beneficence and justice are key to the establishment of an allocation process which provides organs according to the criteria of need and best match. Another example of limited resource allocation—to be discussed later in this thesis—is with regard to priority setting in the health care context[12]. I resolved to approach the prioritization exercise by turning to established principles of bioethics for initial guidance.

3. Ethical Theory and Scarce Resource Allocation

3.1 - Pandemic planning as a utilitarian endeavour

Two basic categories of theory have been postulated to guide Western moral philosophy. These are deontology and utilitarianism. Deontologists believe that morality depends on adherence to a set of principles, while utilitarians promote the view that it rests on the consequences of actions, which ultimately involves calculation of costs and benefits (Seedhouse 1998). The utilitarian ideology is guided by the principle of utility, which holds the 'greater good' as its ultimate goal. Since public health strategies have been described as being 'teleological' or 'tail-oriented', a proper ethics analysis might begin with an evaluation of whether the outcome justifies the intervention (Childress et al 2002). For example, a vaccine program would have to show that the benefit to the population as a whole is greater than the risk to any given individual. Hence, numbers and scales constitute essential tools

[12] See section 3.4 'Resource allocation: Criteria for priority determination'.

because best consequences are expressed as figures which should equate with better health for the majority of the population.

Prima facie, it would seem that the prioritization exercise for scarce resource allocation in the context of pandemic planning should also involve an evaluation of consequences. Maximization of best outcomes for the population as a whole would therefore constitute an acceptable strategy for allocating scarce resources. In such situations the criteria for priority determination must respect the principle of utility, which dictates that "we ought always to produce the maximum balance of positive value (i.e. health) over negative value (i.e. disease)" (Beauchamp and Childress 1994).

By contrast, the deontological theory regards all human beings as ends in themselves and never as the means to an end. This 'Kantian' approach regards each life as having unique and intrinsic value not measurable against any standard (Rachels 1999). From this perspective, aggregate concerns are secondary to individual welfare. The Kantian logic as applied to the prioritization issue might begin with the premise that the limited amount of vaccine/antivirals will allow only a few individuals to benefit. If every life is equally important, then it follows that each individual must be given equal opportunity to access the drug.

A deontologist might shun prioritization lists because the demarcation of priority groups essentially promotes the view that some individuals should be favoured over others. Deontologists might distribute vaccine and antivirals based on a random lottery-type selection method. For example, a computer might be used to randomly draw identifiers such as birth dates, social insurance numbers or the like. Because the deontological approach focuses on the individual, it cannot be compatible with the public health cause. By definition, population health initiatives

must favour aggregate welfare or at least balance what is best for the population with protection for the individual (Nieburg et al 2003; Nixon et al 2005), in which case best outcome depends on whichever intervention strategy produces the most impact in increasing the overall well-being of the population in terms of health indices. It would seem, therefore, that the utilitarian theory, with its emphasis on consequences of actions, should provide a better fit for ethical analysis of public health dilemma. This point is illustrated a priori in the phrasing of the goals of most public health interventions. This is certainly true for the Plan, which seeks to minimize overall morbidity, mortality and societal disruption. By extension, strategies that promise to promote or improve the health of the population in a pandemic, as assessed by available scientific evidence or mathematical modeling studies, would be expected to give rise to favourable outcomes, namely decreased duration and severity of disease, increased survival curves and associated benefits, such as decreased hospital stay and decreased absenteeism from work.

3.2 - Pandemic planning within the public health context

The Plan's mission is to develop strategies, infrastructures and guidelines to mitigate the physical and social harm imposed by future influenza pandemics on the people of Canada (Health Canada 2004). In terms of specific goals, the Plan seeks to:

1. minimize overall morbidity and mortality, and
2. minimize societal disruption

As such, the goals are consistent with the public health scope of seeking to improve the health of the population through government initiated prevention programs, ministerial oversight and public accountability. The innumerable facets of pandemic

planning associated with these goals involve strategies that call into question notions of individual rights and freedoms as well as concerns for fair distribution of public goods, hence urging an ethics analysis of the Plan (Kotalik 2005). The latter is critical in order for the Plan to meet the required moral standards necessary for its endorsement by the Canadian public.

The formulation of an ethics framework for pandemic planning is not a simple endeavour largely because the support literature on public health ethics is limited, hence making it difficult to draw on precedence[13]. Medical ethics emerged as a discipline during the past half century, fostering replacement of paternalism in the doctor-patient relationship with the more liberal ethos of individual autonomy and personal rights (Jonsen 1998). Medical research was similarly infused with this new doctrine which taught that the research subject was sovereign and, as such, could not be subjected to experimentation without his free and informed consent (Belmont Report 1979; Nuremberg Code 1981; World Health Association 2004). This quiet revolution gradually gave rise to a new medicine guided by principles that went far beyond the Hippocratic Oath to include freedoms such as the patient's right to self-determination. In contrast, public health, as the term implies, is concerned with the health of populations for which it must often subordinate individual rights and freedoms, as exemplified by imposed measures such as quarantine, obligatory vaccination programs and outbreak investigation (Nieburg et al 2003). Nonetheless, various authors have identified the need for an ethics framework in public health (Bayer and Fairchild 2004; Childress et al 2002; Kass 2001; Maddox 1998). The

[13] While there is a profusion of literature on the legal implications of public health interventions, the ethics literature per se is scant, as also recognized by other authors who have attempted the search (see Kotalik 2005, Childress et al 2002, Bayer and Fairchild 2004, Kass 2001, Nixon et al 2005).

relevant literature proposes the institution of general principles in public health decision-making (Maddox 1998), as well as a call for criteria to facilitate handling of contentious situations in distribution of health care resources (Armstrong and Whitlock 1998).

3.3 - The principles of bioethics as applied to priority determination

The overriding concern in resource allocation is centered on the issue of *justice*, which mandates fairness in the distribution process. This would ensure that the allocation of vital resources which are in such limited supply as to be inaccessible to the population at large cannot be simply relegated to an exercise of chance, as for example, giving priority to first comers. Nor can social status and ability to pay be allowed to facilitate access to scarce public goods. Thus, while it would stand to reason that prioritization exercises be guided by a fair allocation process, the latter must be defined in the context of the Plan's goals which, as already established in this thesis, are subservient to a public health cause, hence primarily utilitarian in scope. Also, because certain standards of justice are based on socially determined mores, consideration must be given to the value which Canadian society places on equal rights, freedoms and opportunity for all persons. These concerns are fundamental to the structure of the Canadian health care system (Flood et al 2002; National Forum on Health 1997; Romanow 2002) and will necessarily impact the Plan's priority lists. Further, a just and equitable distribution system cannot be formulated without call to the other fundamental principles of bioethics, namely autonomy, beneficence and non-maleficence (Beauchamp and Childress 1994). The following provides a brief rationalization for applicability of these principles to pandemic planning:

1. Autonomy: this principle is relevant to the extent that the individuals prioritized would have the choice to accept or refuse the vaccine or antiviral in question. Their decision should be based on the perceived risk of the vaccine/antiviral in the context of a real or impending disease outbreak. Expected benefits should outweigh the risks of treatment (Meltzer 2003). For example, in the case of the smallpox vaccine, there is a non-negligible risk of severe adverse events (Centers for Disease Control and Prevention 2003; Chen and Lane 2003; Wollenberg and Engler 2004) which can be justified only if the chances of a bioterrorist attack involving deliberate release of smallpox virus are believed to be substantial; hence the benefit to the vaccinee (i.e. military) might be worth the risk incurred. In wartime, individual needs of soldiers and other government defense personnel are necessarily subservient to aggregate welfare (Gross 2004), but one can argue that in the absence of war a defense strategy which confers substantial risk to the person and which is mandated by a perceived rather than an actual threat should not be imposed. In a pandemic scenario the distribution of vaccine and antiviral would only occur once the pandemic is declared, therefore there is obvious benefit in the protection conferred by the vaccine/antiviral. Still, the members of the priority groups are not soldiers, thus rules which apply in the military might be considered unethical in other contexts. The individual's free and informed consent is dependent on his perception of the risk following provision of expert medical and scientific information. Questions then arise in terms of whether health care workers who refuse vaccine or prophylactic antiviral would be obliged to report to work during a pandemic. A related issue is whether health care workers would be forced to accept the vaccine (or antiviral) in the event

of conscription. Most disconcerting would be the eventuality that priority in ranking should translate to loss of autonomy.

2. Beneficence: the primary aim of any medical intervention, such as vaccination, is to benefit the patient. Public health interventions have a more encompassing goal which is to benefit society at large. Childhood vaccination programs were instituted to protect children and society by curbing the burden of morbidity and mortality associated with infectious diseases. Such programs persist in spite of the fact that rare recipients of the vaccines suffer severe consequences[14], suggesting that beneficence to the community is achieved through involuntary maleficence to the unfortunate few (Nieburg et al 2003). Someone influenced by Kantian thinking might argue that no individual should be made to undertake undue risk to benefit a public health cause. The utilitarian would resolve to examine the benefit-to-risk ratio to ensure that it weigh heavily in favour of the person undertaking the risk. In the case of vaccines, the benefit to the individual is protection from highly morbid and often lethal pathogens. By immunizing a frontline health care worker against a pandemic influenza strain, the health care worker is provided the essential protection without which she would be at high risk of contracting a serious illness. But there is also communal benefit in that, if the health care worker remains in good health during the pandemic, she will be able to continue caring for the ill. Further, she arrests the chain of infection by not passing the virus on to others. There are, however, concerns with regard to the pandemic vaccine. This vaccine will be developed as soon as the causal flu strain is identified. In order to release the vaccine as rapidly

[14] Hence the necessity for government legislation such as Québec's *Public Health Act* R.S.Q. c. S-2.2 articles 70-78, stipulating rules for compensating vaccination victims regardless of responsibility.

as possible, regulatory and licensing processes might be fast-tracked (Wood and Levandowski 2003). Vaccine manufacturers might also feel compelled to produce larger than normal batches of vaccine in order to respect their time limitations as stipulated in their contractual agreement. These procedural changes may result in a poorer product which may give rise to increased adverse reactions (Kotalik 2005). Using reverse genetics protocols developed following the 1997 H5N1 avian outbreak in Hong Kong, some countries, including Canada, are developing a prototype vaccine against genetically modified H and N antigens from the presently circulating H5N1 avian influenza strain (Li et al 2002; WHO 2004a). It is yet unknown what level of protection, if any, this vaccine would provide if a pandemic against a circulating human H5N1 strain were to occur. Nonetheless, at the very least, such experimentation will test current capacity for producing pandemic vaccine and allow manufacturers to resolve some of the problematic issues that would otherwise be unsuspected (Fedson 2003). Such endeavours are clearly intended to be beneficent, hence inspiring trust in the pandemic flu vaccination effort.

3. Non-maleficence: if beneficence cannot be guaranteed, then a public health intervention should at least respect the principle of doing no harm. This, like beneficence, will entail a realistic assessment of risk and benefit to the healthy individual taking the vaccine or drug for prophylactic or treatment purposes. A real or impending danger scores higher than an assumed threat; thus an influenza pandemic (at phase 4 or 5) must be given more regard than a pandemic scare at phase 3. More concretely, it would clearly be a breach of the non-maleficence principle to quarantine individuals returning to Canada from Asia which is now experiencing a WHO phase 3 avian flu pandemic, but it might be considered wise to

quarantine individuals coming into Canada from a country experiencing a WHO phase 4 pandemic[15]. This argues for enacting quarantine measures only when it is determined that these will clearly benefit the population. Unnecessary quarantine is a maleficent act because it severely restricts individual freedom. Hence people are forced to abstain from essential activities such as work, with potentially harmful repercussions (e.g. loss of income).

4. Justice: the selection and ranking of priority groups for allocation of vaccine, antivirals and other scarce resources during a pandemic requires a system of distributive justice to guide efforts in the equitable distribution of the resources along with all associated benefits and risks. Cookson and Dolan propose three substantive principles of justice for rationing health care resources, namely *need*, *maximization* and *egalitarian* principles (Cookson and Dolan 2000). The *need* principle guides rationing decisions according to immediate clinical need and capacity to benefit from an intervention. This principle targets the individual patient and, therefore, is less public health oriented, as compared to *maximization* principles which promote a 'best consequences' approach. *Egalitarian* principles derive from the concept of equity, thus favouring an allocation system based on the equalization of health-based differences between individuals[16]. These principles give rise to at least three models of distributive justice which can apply in various degrees to the scarce resource allocation of public goods.

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[15] See section 2.3 'Phases of an influenza pandemic' for an explanation of the pandemic phases.
[16] While, strictly speaking, equity and equality are not synonymous (see Braveman and Gruskin 2003), many authors use the two terms interchangeably. See footnote 10.

- *The utilitarian model*: This distribution model, as expounded by the norms of utilitarian logic, promotes maximization of the commodity so as to allow the greatest number of individuals to benefit without regard to the needs of any one member of the community. Based on Jeremy Bentham's principle of utility, this approach promotes a distribution scheme to satisfy the maxim 'the greatest good for the greatest number' or, in consequentialist terms, 'the end justifies the means'. Simply phrased, the utilitarian principle requires that whenever we have the choice between two alternatives, we must always choose the one that brings about the best overall consequences. Bentham's disciples, James Mill and his son, John Stuart Mill, were staunch promoters of this Benthamite movement, using utilitarianism as a tool for active social reform (see Rachels 1999, pages 97-98). They believed that the ultimate goal of any society was to bring about the greatest state of happiness to all people. This, obviously, is but a theoretical ideal. In more pragmatic terms, application of this model to allocation of limited supplies of vaccine and antivirals would generate a distribution scheme whereby all or most members of society could directly or indirectly benefit. For example, the priority allocation of antivirals for the prophylaxis of health care workers is consistent with the utilitarian concept of 'the end justifies the means' in that protection of these workers prevents absenteeism and, in so doing, keeps them available to care for the ill.

- *The egalitarian model*: The egalitarian ethic can be seen in John Rawls' theory of justice as fair opportunity (Rawls 1999) and was extended by Norman Daniels to allocation issues in health care (Daniels 1985). It seeks to equalize health disparities between individuals so that all can pursue their fair share of opportunities. Hence the distribution process will pay attention to inherent differences in need among individuals. In the case of pandemic vaccine distribution, the stake of the various

members in the population differs since some individuals are at higher risk than others of infection or of serious consequences. Given that in a free and just society everyone holds equal rights to avail themselves of opportunities for a good life, then equality of access to these societal goods would dictate that any disparities in health between individuals must, where possible, be equalized. In the words of Eike-Henner Kluge, "equity requires that persons be treated the same except where differential treatment is mandated to allow them to retain or restore their ability to take equal advantage of the opportunities that are available in society" (Kluge 2000). For example, patients with underlying medical conditions such as chronic diseases (immunosuppression, diabetes, cardiac and pulmonary problems) are at higher risk of serious outcomes (Hak et al 2005), and thus would legitimately deserve priority on vaccine lists.

- *The communitarian model*: The community imposes a value system on its citizens as a standard of behaviour. The sense of belonging induces commitment and solidarity of citizens toward their community. A distribution system that does not respect the values of the community it serves would be shunned. Canadian societal norms, for example, dictate respect for our elders. The many benefits extended to senior citizens exemplify society's sense of obligation to them. In fact, the Plan's vaccine and antiviral priority lists reflect our concern for their welfare (Health Canada 2004, see annexes D and E). Evidently, any community-endorsed prioritization of a given group would have to be based a priori on the existence of scientific evidence that the intervention would result in health benefits. Seniors, in fact, have been shown to benefit from influenza vaccination as shown by lowered rates of hospitalization and mortality (Gross et al 1995; Hak et al 2002).

- *The libertarian model*: The fourth approach is independent of the need, maximization and egalitarian principles. Rather, it is founded on the principle of liberty and its associated doctrine of free choice (Beauchamp and Childress 1994, see pages 336-337) and sense of entitlement. This model thus expounds libertarian ideals, whereby health care is regarded as a commodity that can be bought. This suggests that those who can afford the price (or the insurance premium) will be able to access health care services more readily compared to those who cannot.

Western democratic traditions advocate a combination of these four models in their strategies for allocation of scarce resources. Each of these models has its advantages and limitations. As depicted in the examples above, the prioritization schemes in the Plan reflect a combination of utilitarian, egalitarian and communitarian approaches. Any private acquisition of vaccine or antiviral stockpiles would portray a more libertarian perspective. Lastly, the need principle also seems to have influenced prioritization in the case of the antiviral priority list, as shown by the fact that patients who are clinically in most crucial need of therapy are given foremost priority.

3.4 - Resource allocation: Criteria for priority determination

As a means of gathering information on prioritization of scarce resources in a communal setting, I turned to the resource allocation literature applicable to priority setting within publicly funded health care systems in Canada. Publications were found which discuss priority setting within hospital care units such as surgery (Martin et al 2003a) as well as for advisory committee assessments of technologies, teaching and drug formulary use (Martin et al 2001; Martin et al 2003b; Singer et al 2000). A useful concept brought forth in these publications was the use of criteria for

resource allocation and priority setting. Notably, no mention was made of ethics in the priority setting process. However, by expanding the search based on the keywords *criteria* and *ethics*, one article was identified from the US literature on resource allocation (Armstrong and Whitlock 1998) proposing an appeal to pre-determined ethics criteria as a fair and unbiased means of allocating limited resources in the health care system. Four of these criteria, namely *need*, *equity*, *contribution* and *scientific merit* seem applicable to the Canadian public health cause in general. These might also be adaptable to the specific case of scarce resource allocation in the context of pandemic planning. Any given policy on distribution of limited resources would require that policy makers weigh each of these in balance in order to convince stakeholders that justice is being served. The issue of vaccine and antiviral distribution in a pandemic is no exception. Hence all groups approved for priority status would have to be subjected a priori to analysis based on the above criteria. Each of these criteria will be defined briefly below:

- *Need*: in the context of influenza pandemics, *need* may be perceived as a function of risk of serious consequences. For example, it would seem reasonable to assume that individuals who are ill from influenza would be in more immediate need of antiviral therapy than individuals who are prescribed antivirals for prophylaxis.

- *Equity*: this criterion rests on the premise that health disparities must be equalized to whatever degree is reasonable in order to protect individuals who would otherwise be severely disadvantaged in their ability to profit from opportunities extended by society[17]. The *equity* criterion derives from egalitarian norms of justice which apply the fair opportunity standard to scarce resource allocation. In the pandemic context

[17] The *equity* and *need* criteria are distinct in that the former is applied to situations where there is evidence of inherent differences in health between individuals, whereas the latter is not.

individuals with pre-existing medical conditions which would predispose them to a serious outcome are clearly disadvantaged. In respect of the *equity* criterion this group would be able to claim priority status for pandemic vaccine and antivirals. In fact, there is precedence in prioritizing this group for influenza vaccines during interpandemic years. Thus, it would stand to reason that these individuals be given priority for vaccine distribution during a pandemic.

- *Contribution*: a pandemic will make more demands on certain individuals due to the nature of their professions. Health care and emergency service workers will be called upon to serve the public cause in order to fulfill the goals of the Plan. Hence an allocation strategy that is in tune with the Plan's mission should consider the *contribution* criterion when defining priority groups.

- *Scientific merit*: this criterion refers to the reliance on scientific evidence for justifying a priority group. For example, there are studies supporting the use of antivirals in sick patients who present within 48 hours of initial symptoms (Aoki et al 2003; Leneva et al 2000), beyond which antiviral therapy becomes futile. Therefore, patients who present beyond 48 hours of onset of symptoms should not be referred for treatment in respect of the *scientific merit* criterion. It is unsettling, however, that medical decisions often are not based on the optimal scientific evidence. For example, science has yet to provide data as to whether influenza antivirals are best used in a treatment or prophylactic context. It will be difficult to rationalize priority of one indication versus the other without the scientific facts to give weight to the decision.

Notably, the criteria system is key to establishing waiting lists for organ allocation. Prioritization on transplant waiting lists is based on well-accepted criteria, namely age, blood type, medical urgency, waiting time, geographic distance

between donor and recipient and type of organ (UNOS; Wilmot and Ratcliffe 2002). It would seem, therefore, that the criteria system constitutes a fair and well-accepted means of rationing resources in the context of scarcity, provided of course that the criteria selected are in themselves unbiased.

3.5 - Utility and equity: Two competing principles

The preceding pages have attempted to lay out the ethical framework for a strategy that would allow fairness in scarce resource allocation within the confines of the public health terrain. It seems reasonable to expect that a just distribution scheme should primarily reflect the utilitarian mission of all public health initiatives, which in the case of influenza preparedness is to "minimize overall morbidity and mortality" and "minimize societal disruption". But pure utilitarianism is indifferent to the needs of specific individuals. It is more concerned with the greater good or best outcome for the majority of individuals affected. Societal mores in Canada have favoured a health care system founded on the principle of equity. Thus any viable prioritization scheme must also integrate egalitarian ideals. A quick glance at the Plan's priority groups (Health Canada 2004, see Annexes D and E) suggests that both principles—utility and equity—have had a bearing on its genesis. The latter is reflected in the prioritization of high-risk individuals in whom influenza infection is highly morbid. This conglomerate of special needs individuals would encompass, for the most part, individuals with chronic illnesses such as diabetes, cardiac and pulmonary insufficiency, the immunosuppressed population, people over 65 years old and children under the age of two. Health care and emergency service workers are also prioritized. The latter are justified as meeting utilitarian standards because health care providers and emergency service workers must be protected a priori in

order to keep the health care system as intact as possible and to keep other essential elements of society (e.g. fire and police departments, high ranking government offices, health ministries) functional.

The vaccine distribution scheme lists normal adults and children in the last two groups, i.e. groups 4 and 5, respectively. The prioritization of adults over children can be viewed as respecting utilitarian standards because adults are needed to keep society functional and to care for their minor children. In contrast, children generally do not fulfill a societal function in terms of usable labour. Hence, in a utilitarian sense, they are not immediately essential to the running of our community. However, one should consider that vaccinating children a priori might serve a utilitarian role seeing that this population group is an efficient transmitter of influenza. Vaccination of children before adults might therefore reduce the attack rate by protecting those in contact with children. This might constitute a compelling reason to move children higher on the vaccine priority list.

Utility and equity can be perceived as two competing forces in the determination of a priority list. A mild pandemic might favour the equity component, whereas a severe pandemic would be more catastrophic and therefore might have to rely more heavily on the salvage concept prevalent in wartime, which in turn is utility based (Gross 2004). For example, in a worst case scenario similar to the 1918-19 pandemic which hit young healthy adults most severely (Hampson 2002), it would seem reasonable to shift adults to the highest priority group. Because this group incorporates such a large fraction of the population, there will be a need to subdivide it into smaller subgroups. The subgroups would then require a ranking system which, in the dire circumstances of a 1918-type pandemic, would have to be almost exclusively geared towards ensuring best outcomes for the population as a whole.

Therefore, as written, the Plan's priority lists seem to reflect expectation of a relatively mild pandemic, such as the Hong Kong flu of 1968.

An extreme form of utilitarianism is reflected in the QALY (quality adjusted life years), a tool used mostly by health economists to rate a health program before it is instituted (Roberts and Reich 2002; Seedhouse 1998). QALYs can be beneficial, for example, if they are used to determine which of two rival therapies should be given to a patient. Problems arise when QALYs are used to decide which group of patients to treat, because they inevitably stratify patients according to age, type of condition, socioeconomic status and other such biased criteria. The elderly and those with conditions that are costly to treat will be disadvantaged in such a system. A pandemic prioritization list based on the QALY system is expected to be problematic because it would discriminate against these same groups of people. Western communitarian values and moral traditions would simply not support such discrimination.

3.6 - Dilemma: Treatment versus prophylaxis

Unlike the influenza vaccine which is used uniquely for prophylaxis, influenza antivirals serve both prophylactic and treatment purposes (Nicholson et al 2003; WHO 2004b). This fact complicates the prioritization issue as we must now first analyze the antiviral ranking strategy with regard to the importance of treatment versus prophylaxis. The primary dilemma is whether to prioritize treatment of the severely ill versus prophylaxis of the health care professionals who care for them.

Prima facie, it would seem that treatment should be a first option, if only because the severely ill patient is perceived to be in more immediate need compared to the individual who is well, regardless of the risk of contagion. A look at the priority

groups for antivirals shows that the Plan does indeed take the position of urgency coming first[18]. Top priority is therefore given to the severely ill group consisting of individuals sick enough to be hospitalized for influenza related illness. Second in priority are health care workers and essential service providers who would be given early treatment at the first sign of illness (fever, cough, malaise), before they become sick enough to be hospitalized. Third priority would go to early treatment of ill high risk individuals in the community. The prophylactic indications follow, with health care providers as group 4, treatment and prophylaxis (i.e. outbreak control) of residents of chronic care facilities as group 5, and essential service workers as group 6, followed by high-risk persons hospitalized for illnesses other than influenza as group 7. Lastly, prophylaxis of high-risk persons in the community is featured as group 8.

In the previous section of this thesis a set of four criteria were proposed to assist in resolving dilemma in scarce resource allocation. The criteria proposed were clinical need, equity, contribution and scientific merit. The exercise will require that each option be scored in terms of the number of criteria that are met. For simplicity and sake of argument each criterion that applies will be given an arbitrary value of 1. In practice, however, these categories would likely not be given equal weighting. It will be mandatory to have a fully transparent process operative when assigning weight to such criteria. The extent of importance given to each would ideally be decided through discussion with specific stakeholders and the general public by convening special focus groups or forums.

[18] The UK plan takes the same position, which is also the case for the US plan (UK Health Department 2005; US Department of Health and Human Services 2005).

If we now consider the criteria fulfilled by group 1 (treatment of persons hospitalized with influenza), it is evident that the gravely ill meet the criterion of clinical need, while health care professionals fulfill the criterion of contribution. There is scientific evidence to support the use of antivirals for both treatment and prophylaxis (Aoki 2003; Monto 2003; Moscona 2005), but no convincing data as to which produces the best outcome. Thus the criteria strategy yields a tie for treatment indications versus prophylaxis of health care and emergency service workers. Hence, based on the proposed four-criteria system, the dilemma between the treatment and prophylaxis of critically ill patients versus health care workers is proving difficult to solve. The Plan proposes early treatment of health care and essential service workers, meaning that they will be offered antiviral at the earliest sign of infection. While this strategy promises to reduce the length of their illness, the workers would still be removed from their stations until they are deemed to be no longer infectious. This option, while well-intended, will clearly be counterproductive to the goals of the Plan because it results in absenteeism. To meet the Plan's goals health care and emergency service workers must be protected from illness in order to prevent collapse of the health care system and to keep societal order, respectively. The following section looks to precedence in order to justify the need for preferential prioritization of these groups.

3.7 - Precedence as a factor in risk assessment: Lessons learned from SARS

Given the heavy toll that the recent SARS epidemic has taken on health care workers (Hsin et al 2004; Reilley et al 2003; WHO 2003b), it would be difficult to argue against the proposition to provide enhanced protection for this group in the event of a pandemic. In fact, one of the lessons learned from the experience with

SARS is that the risk to health care workers of contracting an emerging pathogen from infectious disease outbreaks is very high (WHO 2003b). The health care professions impose a duty on their members to care for the ill in spite of the associated risks, but it is unclear as to what level of risk is considered tolerable (Huber and Wynia 2004). Both the American Medical Association and the Canadian Medical Association fail to specify a physician's responsibilities to treat when risk of infection is high. For example, Article 18 of the Canadian Medical Association code of ethics urges physicians to "...Provide whatever appropriate assistance to any person with an urgent need for medical care" (CMA 2004). Interpretation of 'appropriate' is contentious with regard to supererogatory acts (Downie 2002; McKay 2002; Thomasma et al 1995). The advent of the AIDS pandemic brought about much reflection on the clinician's duty to treat in situations of extreme risk (Annas 1988; Arras 1988; Daniels 1988; Dunne 1989; Emanuel 1988; Fox 1988; Freedman 1988; O'Flaherty 1991; Pellegrino 1987). Precedence with diseases such as occupationally acquired tuberculosis, measles, diphtheria and scarlet fever suggests that, when risk is an issue, health care workers can legitimately argue for the right to protection following best standards (Bolyard et al 1998; Mahoney et al 1997; Sepkowitz and Eisenberg 2005; Traynar 2005). Protection may involve use of suitable garb such as proper clothing, gloves, masks and face shields, as well as providing access to vaccines, antibiotics and antivirals, when available.

It is an accepted fact, however, that certain protective measures such as vaccination incur risks of their own. The principle of beneficence requires that the chance of exposure to a dangerous infectious agent be balanced against the risk of experiencing a non negligible adverse event following vaccine administration. For example, efforts to combat perceived bioterrorist threats led to a campaign to

vaccinate members of the United States military against smallpox. The program was later stopped because cardiac problems were reported in a significant number of vaccine recipients (CDC 2003; Chen and Lane 2003; Wollenberg and Engler 2004). In such cases one must evaluate whether the perceived risk of exposure to a deliberately released biological agent warrants placing healthy people at risk by inoculating them with a less than safe vaccine. In the case of pandemic influenza, risk evaluation based on experience with seasonal influenza split vaccine preparations indicates that such vaccines are relatively safe for use in healthy humans over the age of six months. These vaccines do not contain 'live' virus and therefore cannot transmit the infection following inoculation. Apart from soreness at the site of injection, fatigue, allergic reactions to components used in preparing the vaccine such as ovalbumin and, in rare cases, ocular respiratory syndrome (De Serres et al 2005; Scheifele et al 2003), there is very little risk to this vaccine. Thus, by inference from experience with regular influenza seasons, one can argue that the risks of an adverse reaction to the pandemic flu vaccine are expected to be minor[19] compared to the anticipated benefit, namely protection from a highly morbid or even fatal infection.

The recent experience with SARS adds to the list of occupationally acquired infections that provide compelling support for protecting frontline health care workers (Sepkowitz and Eisenberg 2005). The vulnerability of this population fulfills the *need* criterion, which in this case can be redefined to include *occupational* need, to distinguish it from *clinical* need. This, in addition to *contribution* and *merit*, brings the score to a total of three for health care workers. The group of patients hospitalized

[19] This logic assumes that the manufacturing and testing processes for pandemic flu vaccine are identical to the processes used for interpandemic vaccine preparations.

with influenza would obtain a priority score of two based on the *need* and *merit* criteria. Thus, assuming equal weighting of the four criteria, and in the absence of discussions with stakeholders and the general public, the criteria system would argue for prioritizing prophylaxis of frontline health care workers over treatment of hospitalized patients. Essentially, the argument presented above supports the prioritization of frontline health care workers insofar as this respects the Plan's overall mission. Again, we must keep in mind that the goals of influenza preparedness are 1) to minimize morbidity and mortality in the population, and 2) to minimize societal disruption. Both of these require that negative outcomes be kept to a minimum, thereby allowing the positive outcomes to prevail. This would mean that as few people as possible would fall ill, and that society would experience the lowest possible level of inefficiency during an influenza pandemic. Otherwise stated, the goals of pandemic preparedness are realized if as large a fraction of the population as possible suffers the fewest possible ill effects. These ill effects may refer either to deterioration of the stakeholders' health or to stresses incurred by disruption in their daily routine.

The point which is being defended here is how granting health care workers highest priority in accessing vaccines and antivirals respects the Plan's overall mission. Consideration of alternative scenarios might assist in the rationalization process. For example, if the opposite situation, whereby health care workers—especially those on the frontline—were not to be given priority relative to the other groups, then these workers would consequently not receive vaccine as soon as it becomes available and would not be among the first to receive antivirals for prophylaxis when pandemic influenza arrives at our borders. As health care workers, these individuals are bound by duty to care for the sick, and those among them who

serve at the frontline are especially at risk of exposure. Once infected and incapacitated, they would be removed from the pool of personnel available to treat the massive influx of patients who will purportedly be admitted for influenza related illness. In addition, they pose a high risk of contagion to their contacts, including other patients (Potter 1997), staff and family members. As a result the health care system would very rapidly become overwhelmed.

Now let us consider the opposite scenario whereby health care workers are prioritized with respect to antiviral prophylaxis. This would mean that, because these individuals are in large measure protected from contracting the disease, they can remain on service to maintain the health care system at a time when it will be severely overwhelmed from the deluge of patients ill with influenza, this in addition to the routine workload. Health care workers will be made to labour long hours under stressful conditions and for prolonged periods. Without these workers at their job the sick would not receive adequate care, precipitating even higher rates of morbidity and mortality. Hence it follows that in protecting health care workers first and foremost, we would be increasing the likelihood of keeping the health care system in functioning order, which in turn should reduce severe illness and death, thereby promoting the goals of the Plan.

Our scenario suggests, therefore, that protecting health care workers in the context of pandemic influenza planning is largely a question of utility. If one draws an analogy between health care workers during an influenza outbreak and soldiers in battle, several points of comparison can be observed. During armed conflict the individual claims of soldiers are subordinate to the collective welfare (Gross 2004). This mirrors the public health mission in general. During armed conflict soldiers are provided arms because they are expected to be in contact with enemy fire while

working for the security of their homeland. Similarly, if one assumes that risk of contagion increases proportionately with frequency of close contact with infectious cases, then frontline workers would incur a disproportionately high risk of infection relative to the general population (Sepkowitz and Eisenberg 2005)[20]. Without adequate prophylaxis some of these individuals might opt not to report to work. To do otherwise would represent a danger that they may not wish to assume. Thus, in order to counter the perils that health care workers confront while tending to the ill, a moral society should opt to prioritize prophylaxis of this group first and foremost, with top priority given to the frontline. If these frontline health care workers were not to be prioritized for prophylaxis against a pandemic flu strain, could they be held to their duty of care? More specifically, could doctors and nurses be legally bound by their employers to report to service even if they stand a high likelihood of severe illness or death through the act of caring for the ill? Or would they be breaking their codes of ethics by not fulfilling their duty to society?

Without adequate protection the soldier risks serious injury or death while carrying out the mission of defending his country. No nation could hope to win a war with an armed enemy unless its soldiers are adequately protected. Without the proper gear the likelihood of defeat is so great that it would be morally wrong to expect soldiers to risk their lives in vain. Hence, ethically, it should not be considered an abdication of his duty if a soldier chooses not to go to the battlefield on grounds that his armament fails to meet the best standard that his country has to offer. By analogy, frontline health care workers not given prophylaxis are akin to the unarmed

[20] Some will dispute this point arguing that the use of masks and meticulous hand hygiene will diminish exposure risk to a level no higher than that encountered through daily activities outside the health care context. This remains to be proven. Nonetheless, when faced with the risk of contracting a severely debilitating disease from patients, one cannot ethically use such speculation-based logic to persuade health care workers to stay at their job.

soldier. Influenza virus is so infectious that doctors and nurses caring for patients on the frontline would be subjected to almost certain exposure. Their constant contact with patients would place them at higher risk of exposure than the general population (Sepkowitz and Eisenberg 2005). Given the availability of prophylactic medication, it would be unethical to expect our health care workers to fulfill their duty of care without reciprocal social obligations. It would be difficult to rationalize a requirement that these frontline workers report to work unless they opt to do so of their own accord, in which case the deed might be in the realm of the supererogatory. Such acts are considered above and beyond one's call of duty because they place significant risk on the perpetrator of the act without direct benefit to her. In such cases health care workers would be good Samaritans acting on the virtue of courage. Simply stated, the call of duty for a health care professional is to do all one can to save a life, but not to risk one's own life in the process (Huber and Wynia 2004).

3.8 - Prioritization of health care workers versus the critically ill: the options

The analogy with the soldier in battle makes the point that just as the soldier on the frontline is provided gear for protection against enemy fire, so too must the frontline health care provider be given the defenses necessary to confront a viral attack. Because present-day technology demands at least six months to produce and test initial stocks of flu vaccine, antivirals remain the only option for protection until the vaccine becomes available. The Plan recommends—and the Canadian government has approved—funds to purchase and stockpile an initial 16 million

doses of antiviral[21]. Even in a mild pandemic this amount of drug will fall short of covering the eight priority groups. In fact, projected figures for a pandemic with a less than 20% attack rate (mild category) indicate that the public stockpile would cover only a fraction of health care workers (group 4) for prophylaxis. Obviously, in the event of a severe pandemic with an attack rate of over 35%, the available quantity of drug would be grossly limited, with the possibility that health care workers might be covered for treatment (group 2) but not for prophylaxis (group 4). The point has already been made earlier in this section that the health care system would rapidly crumble consequent to a high rate of absenteeism in health care workers. This would translate into a lack of trained personnel to treat priority groups 1 to 3. Otherwise stated, if the priority ranking scheme is to allow the fragile health care system to remain functional during a pandemic, then health care providers must have absolute priority over other groups in accessing antivirals. Thus they must rank first for treatment because they risk their lives in rendering service to the public, and because they are needed back on the workforce as quickly as possible. They must also rank first for prophylaxis because precedence dictates that persons whose societal duty obliges them to work under high-risk conditions must be protected.

Logistically, it might be problematic to prioritize prophylaxis at the expense of treatment because a very sick individual is seen to be in more immediate need than one who *risks* illness following exposure to infected patients. One can imagine that during a pandemic urgent treatment needs would occur while drug would be dispensed for prophylactic use. Health care professionals will have access to the antiviral stockpile while their patients would be dying of pandemic influenza. It will be

[21] In fact, 9.6 million doses, equivalent to 60% of the total, are purchased with federal funds and the remaining 40% is supplied through provincial and territorial input.

difficult to explain to the patient why she/he cannot have the medication, and that all available stocks of the drug are being reserved for prophylactic purposes. This moral distress—defined as the inability to provide what is believed to be the appropriate level of care (Oberle 2001; Austin et al 2003)[22]—might result in honest cheating, whereby some of the antiviral stockpile reserved for prophylaxis would be quietly diverted by benevolent health care personnel to the treatment of their patients[23].

In the case of prioritizing health care workers versus the critically ill, there are valid arguments in defense of each group over the other. Hence, a viable resolution may not be attained by discourse alone. Short of lobbying government for more funds in order to increase the size of the stockpile, one might consider communicating the problem to the Canadian public so as to educate the people with regard to the concerns of this situation prior to the occurrence of a pandemic, and to allow public input in the decision-making process. As part of the process one might present the public with the following options: 1) keep the antiviral priority list as is, with health care providers below the treatment groups as priority group 4; 2) identify health care providers who operate at the frontline[24] (emergency rooms, walk-in clinics, infectious disease wards, etc), and bump this group up to priority group 3, thereby ensuring that they all receive antiviral prophylaxis, while still retaining treatment groups 1 and 2 at absolute priority; 3) give first priority to frontline health care workers followed by the two treatment groups—renumbered as groups 2 and 3, with priority group 4 consisting of the remaining health care workers who are not

[22] As distinguished from moral dilemma which is defined as not knowing what is the right thing to do.
[23] Another issue relevant to this discussion is whether family members of health care workers would also require antiviral prophylaxis. This follows from the argument that illness in a family member might force the health care worker to take a leave of absence from work in order to care for the sick relative. Also, it has been suggested that health care workers might be tempted to siphon off antiviral drugs for their families (see commentary by Ian Brown entitled 'Salvations Army' in the *Globe and Mail*, November 19, 2005).

frontline; and 4) give absolute priority to prophylaxis of all health care workers by bumping all members up to priority group 1, thereby ensuring coverage for the group as a whole, followed by the other groups in the order listed. This latter option would essentially reflect the strategy proposed for vaccine distribution, with the difference that vaccine is employed solely as a prophylactic measure, hence sidestepping the dilemma of prioritizing prophylaxis versus treatment. Each of the prioritization choices presented above is problematic and requires debate with stakeholder groups. An informed audience will be more likely to understand the difficulties of making such choices and will tend to be more cooperative once the event actually occurs.

3.9 - Prioritization of the essential service provider

To be effective in promoting the well-being of the population, societal structure relies on a network of properly functioning systems each delivering a service or product to one or more arms of the network. Certain services are deemed 'essential' in that they constitute the minimal requirements for a community to maintain its organizational structure. If we are to fulfill goal 2 of pandemic planning then it becomes mandatory to identify essential service providers and ensure that they will be at their task during the course of the pandemic. Failure to do this will place a great toll on society as it struggles not only to control the ravages of the pandemic, but also to keep its own fabric intact when all of its systems begin to falter.

[24] The Pandemic Influenza Committee has defined the frontline health care worker as one whose job description entails working within 1 meter of patients.

Who then are our essential service providers? This group includes police officers and fire fighters along with their managers, as well as individuals working in correctional services including probation and parole officers, the RCMP, members of our national defense, high-ranking politicians, morgue and funeral operators, communications personnel and the like[25]. There is unlikely to be any dispute as to the essential nature of the services that this group provides to the community. Society maintains its functional integrity through its network of essential service providers, who must be protected from the contagion in order to provide essential service continuity. This appears to be the logic behind their ranking as group 2 for vaccine distribution. However, the vaccine will not become available for several months after the start of the pandemic, by which time the disease is likely to have already reached Canada. During this critical initial wave, antiviral use for both treatment and prophylaxis will be essential in order to achieve the goals of the Plan. In fact, this is the very *raison d'être* for the national antiviral stockpile. In this regard it is noteworthy that essential service providers are listed as priority group 6 for prophylaxis. Even in a mild pandemic the 16 million doses approved for the public stockpile should only cover priority groups 1-3 and approximately one-third of priority group 4. Thus the recommendation to rank essential service workers as priority group 6 for prophylaxis would not give them access to the national stockpile. Their lack of protection is clearly not consistent with goal 2 of the Plan which aims to "minimize societal disruption". The resulting chaos would affect every element of society with grave emotional and economic consequences. One has only to recall the all too recent SARS outbreak to imagine the toll that society would have to bear

[25] These groups have been identified as mitigation stakeholders (see reference Government of Canada 2002).

with a pandemic of much larger proportions (Skowronski 2005). Pandemics, like all disasters of great magnitude, present inarguable justification for rethinking the ranking of essential service workers.

3.10 - Prioritization of the high-risk individual

Certain individuals—roughly 20% of the population—are labeled high-risk because they are afflicted with chronic diseases which either weaken their immune system or otherwise impair their health such as to make them more susceptible to suffer negative consequences following infection with pandemic influenza. People who fall in this category are the immunosuppressed (HIV-infected, transplant patients and others on immunosuppressive therapy), patients with chronic diseases (diabetes, heart disease), the elderly and the very young.

The Plan recognizes that these individuals are more fragile, thus requiring priority status for treatment and prophylactic medications. The ethical framework presented earlier in this thesis justifies their prioritization based on clinical need and equity considerations. A practical rationale for prioritizing these high-risk individuals is that altogether they comprise approximately 20% of the population, or roughly six million people in Canada. Even a relatively mild pandemic flu outbreak at a 20% attack rate would affect 1.2 million people. This alone would quickly overwhelm the health care system because many in the high-risk group would require hospitalization. Even with the conversion of non-traditional sites into acute care centres, there simply would not be enough space to house this number of patients along with all others who would require hospitalization. For this reason the effort to protect high-risk individuals is well in line with the utility goal of pandemic planning.

Perusal of the Plan's vaccine priority list indicates third ranking for the high-risk group, after health care and essential service providers who, according to our argument above, should be given uppermost priority based on occupational need, contribution and merit criteria versus high-risk individuals who are prioritized based on equity and merit considerations. High-risk individuals are considered as part of priority group 1 for antiviral treatment if they are hospitalized for influenza related illness, as priority group 3 for antiviral treatment if they are ill but not hospitalized, as priority group 5 for antiviral treatment + prophylaxis if they are institutional dwellers, as priority group 7 for antiviral prophylaxis if they are hospitalized for reasons other than influenza, and as priority group 8 for antiviral prophylaxis if they are included in the general community.

Even in a mild case scenario the 16 million doses of oseltamivir contained in the national stockpile would not be sufficient to cover the high-risk population within priority groups 5, 7 and 8. Hence high-risk individuals would effectively only be covered for treatment. This situation is worrisome from a utility perspective because infection of these patients by pandemic flu will place great demands on the health care system. As discussed in the preceding paragraph, hospitals would be quickly overwhelmed by an influx of high-risk individuals becoming ill with the flu. It is safe to assume that most of these individuals would come down with severe illness and require hospitalization as part of group 1, with some in group 3. This population would also require more intensive care beds, thereby consuming other scarce resources, such as ventilators. Therefore, in the interest of society and the Plan's goals, it might be more strategic to place these patients on antiviral prophylaxis in preference to providing treatment post-infection. The problem is that the oseltamivir stockpile is not large enough to offer prophylaxis to 20% of the population during a

prolonged time period because this would be done at the expense of other groups, namely health care and essential service providers. This, therefore, becomes a circular argument—if health care and essential service workers cannot be offered prophylaxis, there would be no one to care for the sick and deal with the hazards of everyday life in society.

3.11 - Nursing homes and chronic care facilities

This group is given third priority for vaccination and fifth priority for antiviral treatment + prophylaxis as an outbreak control strategy. The Plan recognizes that chronic care institutions are particularly susceptible to influenza outbreaks. Even during interpandemic seasons when vaccination offers at least partial protection, there exists a high rate of morbidity and mortality among the frail elderly residents. The introduction of a pandemic flu strain in such an environment without the benefit of prior vaccination would impose a very high casualty rate in these institutions. Therefore, in respect of the first goal of pandemic planning—to decrease overall morbidity and mortality—the Plan sees fit to prioritize residents of these chronic care facilities. It is noteworthy that outbreak control is prioritized in fifth rank for antiviral distribution. Outbreak control involves a treatment and prophylaxis strategy such that the first case(s) identified in a given institution would sound the alarm to administer antiviral prophylaxis to all other residents in an effort to control the outbreak which would otherwise claim the health and lives of many among this very fragile population. The requirement, in terms of overall doses of oseltamivir for outbreak control in the case of a relatively low impact pandemic (20% attack rate) is estimated at 2.4 million doses, representing approximately one sixth of the federal stockpile. This strategy represents the sole means of dealing with outbreaks during the initial

months of a pandemic before vaccine becomes available. The present size of the national stockpile, however, would not allow it to cover group 5. Hence there would be no effective protection for the high-risk institutional dwellers during the first wave of the pandemic. Use of the criteria based system gives this population a score of at least two out of four (for need and merit). Further, it would be difficult to argue against prioritization of this group in view of the recommendation that they be given influenza vaccine each fall for protection against yearly outbreaks.

One might ask whether residents of chronic care institutions could be protected in other ways. After all, during a pandemic one might suggest that these institutions be closed off to all but the care takers who in theory would have received antiviral prophylaxis as part of group 4. However, this would constitute involuntary confinement, which, like quarantine, is a restrictive measure—a morally (and legally) problematic issue, even more so because isolation measures are not expected to be effective under the circumstances of a full-blown influenza pandemic (WHO 2005).

3.12 - Healthy adults

The Plan places the adult population fourth on its priority list for vaccines. Given the lead time required to grow the seed strain, manufacture enough vaccine to perform toxicity and efficacy studies and gear up production for wide-scale distribution, it is expected that no less than six months would elapse before Canada receives its first batch of vaccine. It is anyone's guess as to how long it would take a pandemic flu strain to reach our borders. The timeframe may be less than that observed for seasonal strains given that there is no natural immunity in the population to slow down the spread (WHO 2005). Even the SARS coronavirus, now known to be inefficiently transmitted between humans, reached eight countries within

four months after its initial detection in Hong Kong (Skowronsky et al 2005). Thanks to the globalization phenomenon spurred by rapid transportation and world market economies, humans and the viruses they harbour are rapidly swept between countries and continents, a fact which might make the next pandemic the quickest to circle the globe (Grais 2003). Let us recall that the Spanish flu of 1918 was spread worldwide by soldiers returning home following the end of World War I (Johnson and Mueller 2002). Influenza vaccine production is a lengthy process requiring strict regulatory control. Hence experts feel that, despite the best of efforts, vaccine would not be available by the time the first wave of the pandemic reaches Canada (Fedson 2005). This means that healthy adults would have absolutely no recourse for prophylaxis during the first pandemic wave because they are not featured in the priority list for antivirals. However, should they become ill enough to require hospital care, they would be given antivirals for treatment purposes.

In light of the above one might recall that the Spanish flu of 1918 disproportionately afflicted able-bodied adults in the 20-40 year old group. The latter two pandemics of 1957 and 1968 showed a more traditional pattern in the groups they targeted, essentially the elderly and the very young (Nguyen-Van-Tam and Hampson 2003). This would suggest that the Plan's priority groups be revised based on the epidemiological data observed in countries first experiencing the pandemic. The Plan's Appendix D and Appendix E do, in fact, contain a clause stipulating that epidemiological observations will influence the priority lists such that, should an inordinate number of deaths be found within an age group, the priority lists will be shifted in favour of the disadvantaged (Health Canada 2004). However, if the newly identified priority group were to encompass a large proportion of the population, it

would be unlikely that the present antiviral stockpile could cover all individuals in the group.

Others might argue that, whatever the epidemiological data should suggest, the healthy adult is the workhorse of society and deserves prophylaxis in order to ensure that the second goal of pandemic planning is attained. One might well agree with the logic as to why treatment precedes prophylaxis and why health care and essential service providers are given first priority, but it might still appear incomprehensible as to why healthy working age adults are not at all featured for antiviral prophylaxis. Even with health care and essential services in working order, society would be severely disrupted if 20% or more of its adult population were to become ill with pandemic flu during the first attack wave. Such massive incapacitation provides strong support for an increase in the size of the stockpile, or for more research into augmenting vaccine production and antigenicity so as to be able to vaccinate more people with smaller quantities of vaccine. This reasoning may also compel individuals or organizations to inquire about purchasing a private stockpile[26].

3.13 - Children

The Plan gives this group last priority with respect to vaccine allocation but fails to consider children altogether for antiviral prioritization, unless their health status following pandemic flu infection is sufficiently deteriorated to warrant hospitalization and treatment within group 1. Children would also be considered for prophylaxis if they fit the high-risk profile due either to a pre-existing condition (e.g.

[26] See section 5.1 'Private stockpiles'.

immunosuppression) or their very young age (less than two years old) in which case they are granted priority along with the other high-risk individuals discussed above. This, of course, is not indicative of the value which our society places on its children. Rather, the evidence from past pandemics suggests that children over four years of age do not seem to be the most afflicted (Nguyen-Van-Tam and Hampson 2003). Therefore, one cannot justify their preferential prioritization in order to satisfy goal 1. Also, because children as minors do not play a vital role in societal functions, they cannot justify contribution towards goal 2 either. Thus, children as a group respect none of the four criteria for prioritization, which as we recall are need, equity, contribution and scientific merit. Nonetheless, a child at high-risk would be able to access both vaccine and antivirals as per group 3 requirements, thus satisfying the needs and equity criteria, as well as society's duty to protect children at heightened risk of harm.

There is, however, a utility-based reason for reconsidering prioritization of the pediatric group for vaccination[27]. Children are known to be efficient transmitters of influenza (Brownstein et al 2005). Hence prioritizing vaccination of this group beyond the recommended 6-23 month olds who are considered high-risk might decrease the rate of spread of influenza (Hurwitz et al 2002). This reasoning, however, is based purely on extrapolation from seasonal outbreaks and requires scientific justification for applicability in the pandemic context.

Some might argue that children should be given higher status for priority with regard to vaccination and antiviral prophylaxis seeing that they have more to gain in terms of life years compared to nursing home residents or chronic care patients.

[27] See section 3.5 'Utility and equity: Two competing principles', for a utility-based argument for prioritizing children over adults.

However, justification for this line of reasoning would require an endorsement of QALYs as a means of rationing health care resources. The ethical dilemma inherent in QALYs has been addressed earlier in this thesis[28] .

4. Concepts of Triage

4.1 - Triage based on science: The 48-hour rule

Influenza pandemics can be likened to global warfare with respect to their capacity to generate great harm and fatalities in humans, along with general unrest and chaos in society. In fact, the worst pandemic in recorded history, the Spanish flu of 1918, is reported to have killed from 20 to 40 million people worldwide—more than the two world wars combined (Johnson and Mueller 2002). In formulating a planning and response strategy for pandemic influenza, the goal of the Canadian government is to mitigate the staggering casualties that would inevitably ensue from a battle with pandemic influenza within Canada's borders. A necessary part of any such plan is to prioritize resources based on the stated goals and the ethical norms of the communities which the plan intends to serve.

The predicted scarcity of resources during a pandemic can be partially mitigated by planning ahead and storing stockpiles of medicines and other needed supplies. However, limited financial resources necessarily place a cap on the size of the stockpile. Hence a crucial exercise for any planning strategy involves the generation of priority lists for allocation of scarce resources. Thus far, the exercise of prioritization has been a theoretical one based largely on the opinion of public health experts. Its value will be tested during a real life pandemic.

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[28] See discussion of QALYs in section 3.5 'Utility and equity: Two competing principles'.

The prioritization scheme for vaccine distribution can probably be followed exactly as indicated in the Plan. The logic seems simple enough. Essentially, one would be dealing with a population of uninfected people and stratifying them based on their own needs for protection (goal 1) as well as society's needs for their services (goal 2). In contrast, let us imagine the scenario within a designated care centre where patients with influenza are expecting treatment. We recall that the limited stockpile of antivirals means that only certain individuals would have access to the drug. Thus a process of triage must be in place in order for the drug to be put to the best use. The Plan's priority list for antivirals gives first priority to the treatment of individuals hospitalized for influenza. But do all individuals who are hospitalized have access to the antiviral stockpile? Medical and scientific evidence indicates that therapy is generally not useful unless begun within 48 hours of the start of symptoms (Aoki et al 2003; Leneva et al 2000). So triage rule number 1 would stipulate that only patients hospitalized for influenza within 48 hours of presentation of symptoms (fever, cough, fatigue) would have access to antivirals. This will require accurate recollection of the onset of symptoms by the patient and the timely dispensing of drug. Some patients may not recall precisely when their symptoms began or may have influenza-like illness due to other causes. This uncertainty would inevitably give rise to unnecessary treatment in a percentage of cases. Other patients may not have easy access to antiviral medication and will forgo treatment until it is too late.

Scientific justification for the 48-hour cutoff is based on recent data suggesting that the virulence of pandemic influenza strains, such as the H1N1 responsible for the 1918 pandemic, stems from their ability to hyperstimulate the production of immune cell-derived factors called cytokines, such as the tumour necrosis factor alpha (TNFα) (Kobasa 2004). These chemicals set in motion a

cascade of events intended to destroy infected cells, except that, when the cytokine burst is too intense, uninfected tissue is also attacked. This is supported by in vivo findings indicating an overabundance of expression in the lungs of a child who died following infection with the avian flu strain H5N1 (Uiprasertkul et al 2005). In vitro data showing that H5N1 isolated from human disease can cause hyperinduction of TNFα in cultured human macrophages (Guan et al 2004) further substantiates the postulate. Overall, these results suggest that delaying antiviral treatment for influenza should not be recommended because the toxic effects of the virus beyond the initial replication period are due to mechanisms that cannot be arrested by antiviral therapy. There is, however, room for skepticism as to whether doctors would respect this triage rule when confronted with seriously ill patients whose survival hinges on the possibility that oseltamivir *might* be effective beyond the 48 hour limit.

Triage dilemma will inevitably occur with other issues as well. It is a given fact that numerous resources will be in short supply, the most obvious of which is the presence of beds equipped with ventilators in intensive care units. While the Plan does mention the possible shortage of ventilators, it forgoes the details, essentially leaving the particulars to the health care providers. The severe scarcity of resources imposed by the disaster setting has precedence during wartime. It may, therefore, be appropriate here to contemplate the ethics of *battlefield* triage.

4.2 - Utility and the concept of *battlefield* triage

The concept of triage saw its beginning during the battles of World War I in France where a process of medical decision-making was needed to establish order of treatment (Auf der Heide 2002). The rules of *battlefield* triage gave priority treatment to the "walking wounded" as these soldiers were expected to benefit most

from immediate intervention. Those determined to have fatal injuries were provided only comfort since they were not expected to survive. *Battlefield* triage is therefore consistent with utilitarian thinking in that its intention is to save as many lives as possible, thus maximizing the good outcomes. Therefore, in a context of severe scarcity of resources, as might occur during a pandemic, a system of dispensing medical care based on prioritizing those who are most likely to recover might have merit.

This system is in contrast to the more familiar emergency room triage method. Essentially, the triage system in the Canadian hospital emergency room is designed to allow the sickest individuals to receive immediate medical care. Priority allocation of resources is ranked downward, from most serious to least serious ailment. No other considerations are taken into account. Ability to pay is not a factor in the Canadian system so long as the nature of the patient's injury does not require skill and equipment beyond that which Canadian hospitals can offer.

By ethical standards, *battlefield* triage would be in line with utilitarian ethical theory (Baker and Strosberg 1992), while emergency room triage is consistent with an equity based ethics approach. With proper planning, a mild pandemic should not generate a situation necessitating *battlefield*-style prioritization. On the other hand, a severe pandemic may not be able to avert recourse to this form of triage. Should *battlefield* triage be condoned as an acceptable process for management of patients with pandemic influenza, the Plan would have to describe in detail how it would apply it. For example, because of the highly infectious nature of their malady, symptomatic patients would be routed to another emergency area or to another site intentionally set up for patients with pandemic flu. The Plan makes mention of erecting such non-traditional sites as a necessary part of preparedness activities

(Health Canada 2004, see Annex J). There is no specific indication in terms of which buildings or institutions would be designated as nontraditional sites. Their existence, however, is paramount because of the need to separate flu victims from other patients. One does not expect other diseases to disappear during the pandemic flu outbreak. Therefore, it will be important to keep hospitals running with the usual standards. Only the makeshift care centres would be subject to changed standards, such as new triage rules. This separation would help to keep confusion to a minimum in terms of caregivers' responsibilities, as well as to curb infection rate in the traditional hospital setting.

Since it is expected that a significant portion of the population will suffer moderate to severe illness during a pandemic, it is difficult to imagine how it will be possible for the health care system to cope if any number of these individuals seek medical attention. Even with the institution of non-traditional sites, the system will be overwhelmed quickly unless the triage process is efficient and medical equipment is in adequate supply. This means that triage on location will have to be limited to worst cases only. It may be worthwhile to consider telephone triage as an option. This system would allow nurses or other medical personnel with experience in recognizing and treating pandemic flu to advise and screen callers for specificity and severity of symptoms. This would curtail the toll on the health care system by keeping patients who are less severely affected away from hospitals and medical centres, including nontraditional sites.

Nonetheless, given that the health care system is accustomed to functioning without any real surge capacity, it is doubtful whether our strategic disaster planning efforts to mitigate the effects of impending pandemics will produce the type of resource building required to completely avert shortages in times of high demand.

Consequently, we can expect shortages of such essential goods as ventilators, antivirals, and antibiotics. It would seem that *battlefield* triage should work well in very severe disaster settings where massive casualties must be managed in the context of very limited medical resources. The problem with using this system for pandemic flu patients is that it may be difficult to predict who will recover and who will not. Therefore, *battlefield* triage may not be reliable under such situations. The guesswork does not serve the patients well, thereby severely undermining the overarching goal of medicine which is to cure the sick or, at the very least, to do no harm. Ethically, one cannot condone haphazard medicine; therefore only scientifically valid restrictions to access medical supplies (example: the 48-hour rule) are valid. The fact that the situation is labeled a disaster does not mean that standards should be lowered. Quite the contrary, since advanced planning is possible, our aim should be to prepare strategically in order to ensure maximization of resources to benefit the greatest number of people.

The second option is classical emergency room triage, whereby order of treatment is dictated by the seriousness of the ailment. Thus, the sickest patients are the first to receive care because they can least afford to wait. The process and methods used to gauge degree of illness may be imperfect, but the difference with *battlefield* triage is that one is not asking "who can be saved?", but rather "how can the situation be managed so that the greatest number of patients can recover?". Use of emergency room triage requires that a planning process be established to mitigate the severity of the pandemic.

The third option for resolving issues of scarcity that might occur during a pandemic would be to simply follow the order provided in the antivirals prioritization scheme. The antiviral priority list proposed in the Plan gives top priority to the sick

individual for treatment. Therefore the triage rules for group 1 would follow those in effect in the emergency room. For example, ventilator triage would be carried out according to urgent need. However, this latter option would not allow us to resolve the hypothetical but plausible situation whereby there is one remaining ventilator and two very ill patients arriving at the same time—a nurse and a single mother of four young children. The ethical dilemma here is wrenching. The nurse might have acquired the infection while on the call of duty. Should she not deserve to be saved? The single mother has four young children in tow depending on her. There is no ethical norm to back the decision-maker in such situations, because the one life is as precious as the other and no less worthy than any other person who could just as well have been in the situation of 'bidding' for the last ventilator. Nonetheless, a decision must be made quickly. The bottom line is that only one life can be saved. So, short of tossing a coin or using other lottery-type strategies, we may resolve to decide in favour of the person who would best further the Plan's goals of reducing morbidity and mortality, and minimizing societal disruption. The criteria presented in previous sections of this thesis and reflected in the antiviral priority list would argue for prioritization of the nurse. This corroborates the utilitarian mission of public health which argues quite convincingly that in a situation where resources are extremely scarce, decisions must be goal-oriented and more in tune with aggregate welfare (Tauber 2003).

5. Strategies to Maximize Resources

5.1 - Private stockpiles

The national antiviral stockpile constitutes an essential component of pandemic preparedness (Public Health Agency of Canada 2005, see Annex E), with

federal and provincial contributions totaling 60% and 40%, respectively. This action follows recommendations of the WHO whose pandemic planning guidelines urge antiviral stockpiling by all member states (WHO 2004b). Several modeling exercises have been cited in favour of such strategic planning (Balicer et al 2005; Longini et al 2005). Another report postulates that a return of the Hong Kong influenza strain would result in substantially more cases than in 1968-69, and more rapid spread of the pandemic (Grais 2003). Also, a Dutch scenario analysis suggests that pandemic preparedness is essential if the morbidity and mortality consequent to a pandemic are to be curtailed (van Genugten et al 2003).

The need to maximize resources in order to cover all priority groups identified in the Plan might involve the creation of private stockpiles. From an ethics perspective, the best argument in favour of allowing individuals, institutions and corporations to acquire private stockpiles is that this initiative would further the Plan's mission of mitigating serious illness and minimizing societal disruption. Private purchase by those who can afford the cost would also free up part of the national stockpile, thus allowing more individuals in the publicly funded priority list to be covered. For example, if hospitals and health care centres could acquire their own antiviral stocks then all health care workers could theoretically have access to antiviral prophylaxis, which in turn would prevent absenteeism of medical staff, thus ensuring care for the ill. Also, businesses as a group are expected to favour private stockpiling as this would allow them to continue operations during a pandemic. Business continuity is deemed to be essential if societal disruption (i.e. goal 2 of pandemic planning) is to be minimized.

Negative considerations to private stockpiling invoke the issue of money as a barrier to access. This would interfere with distributive justice principles because, in

essence, a higher morbidity/mortality toll during a pandemic might be borne by the financially disadvantaged sector of society. On the other hand, one can counter-argue that any process which promotes continuity of societal functions benefits everyone, rich as well as poor.

Transparency is a key element when making pronouncements on such sensitive issues. In Canada, public consultation on the antiviral prioritization strategy has yet to be undertaken. In spite of the contentious legal and ethical issues on private stockpiling of influenza antivirals, it is difficult to argue for strong government oversight of this practice, unless such private acquisition limits the quantity of the national stockpile[29]. In fact, the Canada Health Act (1984) allows Canadians the freedom to purchase any essential drug as long as a doctor's prescription is obtained. In other words, ability to pay—whether out of pocket or through insurance—has been the rule on drug purchase in Canada. Hence private stockpiling may constitute a feasible option for Canadians. However, given that the issue is ethically charged, there must be public forums and debates on this subject with input from government, manufacturers, physician organizations, ethicists and societal representatives in order to discuss any reservation against such practice.

5.2 – Global reserves: Quenching the *spark*

Pandemics essentially begin as a *spark*[30] of viral activity. Theoretically, this initial *spark* can occur anywhere, but evidence indicates that certain factors might promote the genesis of new pandemic strains. The recipe calls for transmission of

[29] In any case it is incumbent on the manufacturer to honour its contractual agreement with governments and to prioritize on a needs basis. This has been seen recently when Roche froze shipments of Tamiflu for pandemic stockpiling purposes in order to ensure that the more immediate seasonal demands were met (Washington Post 2005).

[30] The 'spark' refers to a very small cluster of people whose infection can be traced to an infected individual.

virus among three species, namely humans, pigs and birds. Wild aquatic birds are primary hosts to new influenza virus mutants and pass these onto domestic chickens which then transmit the new virus to pigs and humans (Hampson 1997). Pigs can serve as mixing vessels for porcine and avian flu strains, which can recombine their genes as they replicate (Kitler et al 2002). Once adapted to replicate in porcine tissue, the new viral strains can more readily infect humans since viral receptors on porcine and human cells are highly homologous. Direct avian-to-human spread is also possible as shown with the recent H5N1 and H9N2 outbreaks (Saito et al 2001; Guo et al 2000; Horimoto and Kawaoka 2001; Lee et al 1999). However, as explained earlier in this thesis, demonstration of efficient human-to-human transmission is the final step of the adaptive process in humans. The *spark* is the first evidence of human-to-human infection by a new lethal strain of influenza. Use of mathematical modeling argues for the potential validity of treating initial sparks with antivirals in an attempt to quench further transmission among humans (Longini et al 2005). The hope in using this strategy would be to avert a pandemic or at least to delay it sufficiently in order to gain more lead time to manufacture vaccine and set in motion other elements in the preparedness plan (organize non-traditional sites, distribute antivirals, prepare testing laboratories, etc). Some have questioned whether this containment effort is feasible given the poor surveillance capacity in many rural parts of Southeast Asia where influenza pandemics are most likely to originate (Butler 2005).

Alternatively, a suggestion might be to close borders between countries in the hope of preventing entry or exacerbation of the pandemic. However, to think of influenza as an entity that can be demarcated and contained within political borders is unrealistic. Setting boundaries cannot be envisaged as the principal means of

control simply because the globalization of world economies, fed by the transportation industry, would not allow it (Grais et al 2003). Further, control at the global level, as seen in the WHO initiative to acquire an antiviral reserve specifically intended to suppress initial sparks of activity, is more likely to decrease the impact of the pandemic in all countries. This perspective is reflected in a statement by Vora who wrote, "the plagues know no boundaries, and in our efforts to prevent them, neither should we" (Vora 2004).

5.3 - Emergency response vaccines

These vaccines are included as a category within the larger classification of 'essential' vaccines. According to Milstien and Lambert (2002), emergency response vaccines comprise at least three categories, namely those designated for epidemics such as yellow fever and meningitis, for pandemics including influenza, and for global threats with intentionally released agents whereby vaccine has been discontinued leaving an essentially non-immune population. The concept of such vaccines derives from an ethic of concern for global welfare and the definition of a global public good. The term 'global public good' refers to benefits intended for consumption by the global population without regard to ability to pay (Woodward and Smith 2003). Hence, these benefits are said to be non excludable and non rivalrous (Kaul et al 1999). Pandemic influenza, by exerting an enormous human and economic toll on the entire population, will affect all people; thus vaccines for such infections should be included in the category of global public goods. It follows therefore that monopolization of a candidate pandemic flu vaccine by any one country would infringe on the capacity of the less privileged nations to attain this global public good (Milstien and Lambert 2002). Unfortunately, privatization of many

global public goods interferes with the capacity of all people to access such goods, as is presently the case for HIV drugs. Hence, as argued by Labonte and Schrecker (2004), it is incumbent on G8 governments to increase support for global public goods.

Canada's contract with ID Biomedical obliges the latter to produce a minimum of eight million monovalent doses per month to meet Canada's objective of vaccinating its entire population within four months of isolating the seed strain[31]. Because vaccine manufacturing capacity is dependent on the availability of certain key ingredients such as eggs, vials and preservative, there is a limit as to the rate of production. In order to honour its commitment to Canada and other developed countries, ID Biomedical may not be able to furnish demands for poorer countries. By prioritizing its own population Canada may have forsaken its duty to use initial vaccine supplies (together with a global supply of antivirals) to dampen activity in the country of origin so as to delay pandemic spread and, in the process, allow more time to manufacture vaccine for the Canadian population. The more altruistic approach would therefore involve less hoarding by the richer countries by gifting initial vaccine stocks to countries reporting manageable clusters, hence providing benefit to all nations by delaying pandemic spread.

The above argument points to the necessity of a global response to a pandemic in terms of prioritizing essential materials to quench the initial spark or cluster of activity in order to totally avert or delay the pandemic. Such actions are less altruistic than they are sensible. They are borne out of the realization that human beings everywhere must unite in efforts to confront the tribulations of living

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[31] The source for this information is Dr Arlene King, co-chair of the Pandemic Influenza Committee.

on a planet shared by all. Prioritization lists are surely needed, but some may argue that too much emphasis on such lists provides only a very a near-sighted solution to pandemic preparedness.

6. Communications and Public Input

Transparency is a key component of the decision-making process on issues of concern to public health (Nieburg et al 2003). Transparency entails that decisions be made in an atmosphere of openness and that the language be one that the general public can comprehend. Once the public has grasped the medical and scientific issues in question, their input should be more informed. Public communication of a sensitive matter through forums such as surveys, debates or seminars is useful as a means of providing information to a mass audience. The public's opinion may or may not be accepted in the final decision; however this does not take away from the importance of communicating the problem to those whose health is at stake based on pronouncements being made on their behalf.

Clearly, planning exercises for future pandemic influenza outbreaks are intended to benefit society as a whole. Every citizen is therefore a stakeholder whose welfare will be impacted by the decisions made. However, in the context of limited resources, all needs cannot be served. It is not unethical in such circumstances to think in favour of the common good. However, this principle of utility cannot be introduced after the fact. Basically, if one waits until the pandemic occurs to brief the population on the prioritization scheme, the groups which are excluded will be outraged. If efforts at communicating the scheme were to be made a priori, the public would hopefully understand the reasoning behind the priority determinations. There will always be those who might judge the lists as being partial,

but the ensuing debates would allow venting of the issues well before the actual pandemic strikes.

As with all issues involving resource allocation from government coffers, any sum given to an initiative deducts money from another cause. Pandemic influenza planning is important not least because it represents a proactive initiative. Government decisions are usually reactive and therefore based on urgency of need. Planning for a pandemic is a precautionary act based on the conviction that a future pandemic will inevitably occur. Canada's Pandemic Plan, first released in February 2004, is a public document. Nonetheless, much of the population is still unaware of its existence. There has yet to be an effort on the part of government to consult the public on any element of the Plan. Clearly, there is the necessity to do so because the ease with which the Plan is carried out in the event of a pandemic will depend in large part on public cooperation.

Programs for resource allocation in health care are often initiated or strengthened by patient advocacy groups. The louder the voice the more money is injected into the program. The main advocate for pandemic preparedness planning has been the WHO (WHO 1999). Public health specialists have taken heed and prompted governments to take action. Their conviction derives from knowledge of influenzavirus mutational capacity, genesis of new strains in animal reservoirs and historical epidemiology (WHO Global Influenza Program Surveillance Network 2005). These are complex scientific issues and therefore difficult to transmit to the general public. Nonetheless, the educational element is important if the public is to understand the reasons behind the ranking scheme for scarce resource allocation. For example, without educational resources, it will be difficult for the lay person to accept that children are featured last on the vaccine list (Geddes 2005).

It has been suggested (Jiwani 2001) that one might educate the public on this sensitive prioritization issue by taking recourse to John Rawls' 'behind the veil of ignorance' concept, whereby an individual is asked to imagine himself as belonging to no given group with regard to socioeconomic class, religion, sex, or health status (Daniels 1985; Rawls 1999). The individual is then requested to partition resources among the population in a fair manner. This can only be accomplished if he is blinded in terms of which group he belongs to and therefore has no interest in choosing any particular group over the others. In the case of influenza, the resources to be partitioned are vaccines and antivirals, as well as antibiotics and such emergency equipment as ventilators. The individual may turn out to be healthy, or he may have a chronic illness such as diabetes, AIDS, heart disease, etc. He may be a frontline physician, a police officer, an elderly patient in a retirement home or a child. Beneath the veil of ignorance he must establish priority lists for the allocation of resources that would be considered scarce during a potential pandemic. At the end of the exercise he blindly selects an identity card, whereupon the 'veil of ignorance' is lifted.

John Rawls' premise is that one's lot in life is a matter of chance, not choice, and therefore is not based on social merit. Thus it follows that, in the interest of justice, one must make up for the inequities between individuals. This 'difference principle' is acceptable only if it means that the worst off will end up in a better position than they would if the resources were repartitioned differently. Hence this principle can be used to explain the priority given to high-risk individuals and to health care and emergency service providers.

In the end, public education with regard to pandemic planning will be time well invested because instilling awareness builds trust and counters fear. Knowledge

empowers people, allowing them the confidence to voice what they find less appealing. Thus, once the pandemic does strike, the public will be better prepared psychologically to handle the stress that such an event will generate. This will inevitably aid the planners to accomplish their goals.

7. Revisiting the Priority Lists

If we accept that the goals of pandemic planning are utilitarian in scope, then it would be logical and consistent to apply an ethical theory that reflects this public health mission as our framework for the just prioritization of scarce resources. The utilitarian position promotes the overall good, thereby favouring allocation schemes that protect the interests of the community as an aggregate rather than focusing on the individual (Nieburg et al 2000). A purely utilitarian system such as one based on QALYs would therefore be expected to ignore individuals with special needs. Clearly, the priority lists incorporated in the February 2004 version of the Plan are not wholly utilitarian. In fact, they abide by the principle of equity in seeking to equalize health disparities between the healthy and those with underlying health conditions. This gives an egalitarian edge to the allocation schemes within the Plan. An egalitarian distribution strategy within an essentially utilitarian framework would be in conformity with the goals of pandemic planning because the special needs groups identified, namely health care workers and high-risk persons would experience higher rates of infection and/or disease compared to others in the community. This needs-based distribution scheme is in perfect unison with the goal of minimizing overall morbidity and mortality and, as discussed earlier, the prioritization of health care and essential service workers also enables fulfillment of goal 2 of the plan, namely to reduce societal disruption.

Scarce resource distribution in a pandemic is problematic because there are unknowns in the equation. For example, it is unforeseeable as to what the attack rate will be or which age group will be the hardest hit (Cox et al 2003). Therefore, one might argue that deliberating priority lists based on pure speculation is a futile exercise. One can forego the exercise and hope for a relatively mild pandemic, in which case the attack rate will be low enough so as not to overly tax our health care resources. However, the experts are telling us otherwise. They are warning that the increased death rate in birds due to avian flu is a sign that the conditions are ripe for the generation of recombinants that will prove highly morbid for other species as well, including humans (Li et al 2004; Osterholm 2005; Webby and Webster 2003). Given such a dire forecast it may well be worth our while to prepare strategically. Canadians can boast a comprehensive Plan, as well as an antiviral stockpile containing 16 million capsules of antiviral reserve (Health Canada 2004; Public Health Agency of Canada 2005). Still, this barely covers 5% of the Canadian population (approx. 30 million people) for treatment[32]. Therefore, it is expected that there will be severe shortages.

The scarcity issue is the reason for which prioritization lists are required. We may thus infer that if the shortage problem were to be obliterated then we would no longer have to deal with the painstaking ranking exercise for distribution of limited resources. Where vaccine is concerned, the impediment for Canada is not the inability or unwillingness to buy the product, but rather the commitment of the manufacturer—subject to restrictions imposed by egg-based technology, regulatory requirements and licensure (Gerdil 2003; Wood and Levandowski 2003)—to provide only eight million doses of the vaccine per month. Thus, unless there is a

[32] One treatment dose = 10 capsules at 75 mg per capsule.

breakthrough in the manufacturing process, we cannot expect to have enough vaccine in stock by the time the pandemic reaches our borders. Fortunately, there is potential for mass stockpiling of antivirals. While the Canadian and provincial/territorial governments have pledged 16 million doses, this is not nearly enough to completely cover the first four priority groups, let alone the population at large. We should ask, first and foremost, whether the government can be enticed to dedicate more funding to meet the goals of the pandemic mission. Since this thesis is not intended as an advocacy to alter political will, it will be assumed that all has been done to convince our political leaders that the mission is important and that our politicians have dedicated maximum effort to the cause, given all other calls that they must tend to. Therefore, at this point in time, the expectation of scarcity justifies the exercise of prioritization.

The prioritization lists featured in the February 2004 version of the Plan have been the subject of this analysis. In this thesis I presented arguments suggesting that the ranking scheme might benefit from a revisitation. Health care workers pose a difficult ethical dilemma because of the risk of exposure while performing their duty of tending to the sick. The need to protect this group is recognized in the vaccine prioritization list where they occupy first rank. The vaccine priority list is judged to be acceptable in its present form in that by protecting health care workers they will be encouraged to continue working, hence keeping the hospitals staffed and, therefore, less apt to collapse. The remaining prioritization order for vaccines generally reflects the situation present during interpandemic years and therefore seems unproblematic. With respect to children, it has been suggested earlier in this thesis

that there may be advantage to moving them above adults in the vaccine priority list in order to reduce overall infection rates[33].

The antiviral priority list is more complex because treatment and prophylaxis must compete with each other for priority ranking. The list prioritizes treatment indications ahead of prophylaxis, but I have argued earlier in this thesis that some prophylaxis indications may require prioritization over treatment. The Canadian experience with SARS suggests that health care workers will be facing a risk of contagion every time they treat a patient with pandemic flu (Skowronski et al 2005). Without adequate protection these workers may experience an attack rate over and above that seen in the general population. Vaccine will not be available during the first wave, making antivirals the only recourse for protecting personnel at such high risk. Unless antivirals are provided for prophylaxis, many may choose not to report for work, resulting in increased absenteeism and the possibility that the health care system may not be able to meet staffing demand. The Good Samaritans will see their numbers diminish because many will fall ill from influenza. Therefore, in the interest of efficiency, the health care system should provide antivirals for prophylaxis of medical personnel. To do otherwise might be construed as being irresponsible.

One may dispute whether this large group should be subdivided into subgroups (e.g. frontline and non-frontline) to reflect the potential risk of contact with infectious patients, and whether there should be a six-week rotation schedule of the frontline. This strategy would entail dividing the frontline into two groups which would alternate their activity on the frontline based on the six-week maximum period for oseltamivir prophylaxis (Hoffmann-LaRoche 2004). This strategy may be all but practical during a pandemic as there will surely be a high demand for health care

[33] See sections 3.5 and 3.13.

workers on call at the frontline to triage and treat the ill. Given the high safety profile of oseltamivir it may be possible to consider its use off-label for longer periods. If the latter is not recommended then one may have to resort to other influenza antivirals for continued prophylaxis or to early treatment strategies.

In theory, the non-frontline workers are exposed to less risk, thereby justifying a strategy of post-exposure prophylaxis or early treatment. The important issue is that there be enough antiviral in reserve for health care workers to enable them to stay functional until vaccine becomes available. The relative order of other priority groups should not change if we apply our egalitarian principles as discussed earlier. Hence the new priority list for antivirals would be as follows:

1. Prophylaxis of frontline health care workers
2. Treatment of persons hospitalized for influenza
3. Early treatment of health care workers and essential service workers
4. Treatment of high-risk groups in the community
5. Treatment and prophylaxis to control outbreaks in high-risk institutionalized patients
6. Prophylaxis of non-frontline health care workers
7. Prophylaxis of essential service workers
8. Prophylaxis of high-risk hospital patients with other illnesses
9. Prophylaxis of high-risk persons in the community

In spring of 2005 the Federal Ministry of Health announced a budget for the purchase of 16 million doses of oseltamivir for pre-emptive stockpiling in case of a pandemic (Public Health Agency of Canada 2005). The immediate concern was to determine how far down the priority list this amount of drug would go. The projected

demand per priority group could only be calculated once census data on the number of individuals per group was obtained. Table A (see page 83) uses census figures provided by the Public Health Agency of Canada (Sciberras J, personal communication). Based on the amount of drug required per priority group as per the assumptions listed in the footnote to Table A, it was determined that the 16 million available doses would cover the first four priority groups, but only if the pandemic proves to be relatively mild at an attack rate of under 20%. Further, the stockpile is expected to be completely depleted during the first pandemic wave, leaving none left over for the second and subsequent waves. It is noteworthy that the historical record indicates a greater toll for the second wave (Fedson 2005). Therefore, if vaccine is still unavailable by the arrival of the second wave, there will be no option with which to help those in need. Hence, according to this scenario, even a mild pandemic would be devastating in terms of health and economic losses.

A recent study (Balicer 2005) examined the cost-benefit of stockpiling oseltamivir for pandemic use. This study assumed use of oseltamivir for treatment and post-exposure prophylaxis of contacts. Estimates of the health-related impact of pandemic influenza were based on the Meltzer model (Meltzer 1999) using rates derived from previous pandemics. The Balicer study predicts that for every dollar invested in the purchase of oseltamivir there is an economic return of >$3.68 in terms of reduction in lost workdays, in addition to saving many lives. Hence, stockpiling would allow furthering of the Plan's goals by reducing morbidity and mortality, alleviating the drain on the health care system and promoting business continuity. The benefit/cost ratio clearly supports the decision to stockpile antivirals.

These data suggest that while Canada has taken the important initiative to acquire an antiviral reserve, government may need to consider the benefits of expanding it[34].

8. Conclusions and Perspectives

The concept of utility is central to the founding norms of the public health system which, as its name implies, is designed to serve the population on issues that affect the community at large. One such issue is communicable disease, which spreads from an infected source and propagates within the community placing all immunologically naïve individuals at risk of infection. Protection strategies demand a consequentialist approach such that the highest possible number of individuals can benefit. Any strategy that raises the number of positive events merits consideration within the public health scope.

Pandemic influenza is a highly contagious respiratory disease responsible for killing millions of people worldwide as witnessed during past pandemics (Hampson 2002). Due to mass incapacitation and high death tolls, both the health care system and the economies of even the most advanced western nations will be severely drained. Hence the WHO has urged pre-emptive action in order to mitigate the devastation.

The Canadian government, through its public health agency, has heeded the advice of the WHO and taken the lead in establishing preparedness and response guidelines for the next influenza pandemic. The Canadian Pandemic Influenza Plan was first released publicly in February 2004 (Health Canada 2004). Its mission is distinctly utilitarian, namely to reduce morbidity and mortality as well as societal

[34] In fact, new information obtained through the Pandemic Influenza Committee at its meeting on October 3-4, 2005 suggests that Canada is preparing to significantly increase its national antiviral stockpile.

disruption within the Canadian population in the event of an influenza pandemic. The Plan outlines how to accomplish this mission in four chapters and twelve annexes. While organization is the key to proper planning, it is clear after reading the Plan that the saving of Canadian lives will be in part dependent on the availability of certain key products, specifically vaccines, antivirals, antibiotics and ventilators, during the pandemic. Therefore, an important part of the planning effort should centre on the acquisition of these products through contractual dealings with the manufacturers and their strategic distribution to the Canadian people.

Canada's contractual agreement with ID Biomedical stipulates that a minimum of eight million doses of influenza vaccine per month shall be provided upon declaration of a pandemic and isolation of the seed strain. Vaccine manufacture entails a lag time before a first batch can be made available; therefore the initial eight million doses likely would only be available beyond the first wave of the pandemic. Hence the only means of protection during the initial months of the pandemic will be provided through antivirals. Still, the availability of antiviral drugs will be dependent on the size of the stockpile. Canada and the provinces/territories have contracted Roche Pharma to furnish 16 million doses of the antiviral oseltamivir. This amount of antiviral would only be sufficient to treat 1.6 million people. The ethical dilemma is to decide who should receive the putatively life-saving medicine. The WHO instructs that prioritization lists should be an integral part of the planning process. The analysis contained within this thesis examined whether the lists reflect the goals of the Plan. Treatment prioritization favours the critically ill and those most at risk of serious consequences and is therefore in tune with the Plan's first goal. Prophylactic prioritization favours health care and emergency service workers because the former are most at risk of infection and are needed to

keep the health care system from collapsing, while the latter must keep social order, all of which are in synchrony with the Plan's second goal. It is unclear at this time whether treatment indications should precede prophylaxis or vice versa. Mathematical modeling studies should be performed based on the Canadian scenario. In fact, these are required before any antiviral prioritization strategy can be properly discussed. However, models are only as good as the strength of the assumptions on which they are based. All we know with certainty is that future influenza pandemics will strike, but the attack rate and epidemiology are unpredictable in advance of the event. Hence modeling studies must be interpreted with caution.

The Plan's guidelines are not meant to be static; rather the document is in constant evolution. Discussions are presently in progress at the public health and government level which will almost certainly alter the allocation strategy[35]. Moreover, the priority lists are subject to change based on the epidemiology of the pandemic and other unknowns. Based on the Canadian experience with SARS, I believe more justice would be served to health care workers by giving them top priority in the antiviral list. To do otherwise is to request that they care for the ill without adequate protection for themselves when the means for protection is available. The lack of prophylaxis for health care workers would only favour absenteeism which in turn would rapidly bring down the health care system if enough health care professionals decide to take this course. From a utilitarian perspective, if the health care worker is kept healthy, the goals of the Plan are advanced more so than if early treatment becomes the recommended strategy. This is because the latter option allows health

[35] Changes will be incorporated in the revised version of the Plan due for release in 2006.

care workers to become ill before they can be treated. Thus, early treatment, while seemingly more cost-effective (because treatment depletes less of the stockpile compared to prophylaxis), constitutes a second choice at best, due to its allowance for incapacitation and losses in work time. Hence, in a situation where human lives and the well-being of society depend on a functional health care system, there may be a better return if a little more money were invested now.

The existence of a public stockpile does not preclude establishment of a parallel privately funded reserve. Any company wishing to maintain business continuity might be able to acquire a private stockpile provided that the manufacturer is capable of furnishing demand and that private acquisition does not infringe on the size of the public stockpile. Licensing agreements would bring more players into the field, thus helping to ensure that demands are met. Physicians might purchase a stockpile of antivirals for prescribing to their patients. Individuals with special needs who are not on the priority list might also decide to purchase their own supply of antiviral. The controversy in this regard is that some people may not be in a favorable position to access the private stockpile, either because their employer cannot afford the cost or because their own finances do not allow the investment. Hence the economically disadvantaged may be the ones to bear the heavier burden of the pandemic. The counterargument is that the existence of a private stockpile will allow the public stockpile to stretch further.

Lastly, it is incumbent on government to involve the public in the pandemic planning effort since all members of the population are stakeholders. Canadians, for example, should be knowledgeable of the preparedness strategy for influenza pandemics not only because these efforts are funded through tax dollars but also because citizens should be able to provide input on matters that may dramatically

affect their health. The process of public consultation well ahead of time will serve to inform and instruct as to the steps which will have to be followed upon declaration of a pandemic. In fact, these processes are likely to be very similar whatever the causative agent, be it a natural event or the deliberate release of a biological weapon. A properly educated public will be better able to handle the stressful conditions resulting from such catastrophes, as opposed to a naive public which would inevitably cave in the chaos. It is the duty of government in concert with public funding agencies to make grants available for public consultation studies. For example, one unresolved area of research identified in this thesis is the definition of criteria for priority allocation of antivirals and vaccines. I would propose that focus groups and public forums be convened to establish and rank a criteria list to resolve this issue.

In summary, pandemic preparedness is a process that begins with conviction that future influenza pandemics are inevitable, the only uncertainties being timing and intensity. It is the mission of the Canadian Pandemic Influenza Plan to "serve the government, its public health institutions and the people of Canada in dealing with the next pandemic to ensure that loss of life and incapacitation are minimized and that societal function is kept as intact as possible". No such undertaking can be complete without an ethics framework to guide certain key strategic planning issues such as scarce resource allocation which may well have an ultimate impact on who survives 'the big one'.

Table A. Antivirals – Projected Demand by Priority Groups

Priority group	Estimated number of persons*	Anticipated uptake/coverage**	Number of doses required
1. Prophylaxis of frontline HCW and key health decision-makers	235 819	90%	8 913 945
2. Treatment of persons hospitalized for influenza	82 937	50%	414 685
3. Early treatment of HCW and ESW	276 866	75%	2 076 647
4. Treatment of high-risk groups in the community	584 315	75%	4 382 360
5. Treatment and prophylaxis to control outbreaks in high-risk institutions	393 204	50%	2 398 544
6. Prophylaxis of non-frontline HCW	335 863	90%	12 695 619
7. Prophylaxis of ESW	535 863	90%	20 255 629
8. Prophylaxis of high-risk hospitalized patients with other illnesses	40 000	75%	1 260 000
9. Prophylaxis of high-risk persons in the community	5 525 579	75%	174 118 737

Abbreviations: HCW, health care worker; ESW, essential service worker.
*Numbers are based on an attack rate of 20%, with 33% of health care workers on the frontline.
**Refers to percentage of group expected to comply with the regimen.

BIBLIOGRAPHY

Annas G. 1988. Legal risks and responsibilities of physicians in the AIDS epidemic. Hastings Cent Report, April/May: 26-32.

Aoki FY, Macleod MD, Paggiaro P, et al. 2003. Early administration of oral oseltamivir increases the benefits of influenza treatment. J Antimicrob Chemother 51: 123-129.

Armstrong CR, Whitlock R. 1998. Resource allocation. The cost of care: two troublesome cases in health care ethics. Physician Exec 24: 32-35.

Arras J. 1988. The fragile web of responsibility: AIDS and the duty to treat. Hastings Center Report, April/May: 10-20.

Auf der Heide E. 2002. Principles of hospital disaster planning. In: Hogan D, Burstein JL, editors. Disaster medicine. Philadelphia: Lippincott, Williams & Wilkins; p. 57–89.

Austin W, Bergum V, Goldberg L. 2003. Unable to answer the call of our patients: mental health nurses' experience of moral distress. Nursing Inquiry 10: 177-183.

Baker R, Strosberg M. 1992. An historical reassessment of utilitarian analyses of triage. Kennedy Institute of Ethics J 2: 103-123.

Balicer RD, Huerta M, Davidovitch N, Grotto I. 2005. Cost-benefit of stockpiling drugs for influenza pandemic. Emerg Infect Dis 11: 1280-1282.

Bayer R, Fairchild AL. 2004. The genesis of public health ethics. Bioethics 18: 473-492.

Beauchamp TL, Childress JF. 1994. Principles of Biomedical Ethics, 4th edition, Oxford University Press, New York.

Belmont Report. 1979. Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Washington (DC), Government Printing Office.

Bolyard EA, Tablan OC, Williams WW, et al. 1998. Guideline for infection control in healthcare personnel. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 18: 407-463.

Braveman P, Gruskin S. 2003. Defining equity in health. J Epidemiol Comm Health 57: 254-258.

Brownstein JS, Kleinman KP, Mandl KD. 2005. Identifying pediatric age groups for influenza vaccination using a real-time regional surveillance system. Am J Epidemiol 162: 686-693.

Butler D. 2005. Drugs could head off a flu pandemic – but only if we respond fast enough. Nature 436: 614-615.

Canada Health Act. 1984. Section C-6.

Centers for Disease Control and Prevention. 2003. Update: Cardiac and other adverse events following civilian smallpox vaccination. United States. MMWR 52: 639-642.

Chan PK. 2002. Outbreak of avian influenza A (H5N1) virus infection in Hong Kong in 1997. Clin Infect Dis 34: S58-64.

Chen RT, Lane JM. 2003. Myocarditis: the unexpected return of smallpox vaccine adverse events. Lancet 362: 1378-1380.

Childress JF, Faden RR, Gaare RD, et al. 2002. Public health ethics: mapping the terrain. J Law Med Ethics 30: 170-178.

Cinti S, Chenoweth C, Monto AS. 2005. Preparing for pandemic influenza: should hospitals stockpile oseltamivir? Infect Control Hosp Epidemiol 26: 852-854.

CMA. 2004. Code of Ethics. http://policybase.cma.ca/PolicyPDF/PD-04-06.pdf.

Cookson R, Dolan P. 2000. Principles of justice in health care rationing. J Med Ethics 26: 323-329.

Cox NJ, Tamblyn SE, Tam T. 2003. Influenza pandemic planning. Vaccine 21: 1801-1803.

Daniels N. 1988. Duty to treat or right to refuse? Hastings Cent Report, April/May: 36-46.

Daniels N. 1985. Just Health Care. Cambridge University Press, New York.

De Serres G, Toth E, Menard S, et al. 2005. Oculo-respiratory syndrome after influenza vaccination: trends over four influenza seasons. Vaccine 23: 3726-3732.

Downie RS. 2002. Supererogation and altruism: a comment. J Med Ethics 28: 75-76.

Dunne R. 1989. AIDS: The duty to treat. The Mount Sinai Journal of Medicine 56: 252-253.

Emanuel E. 1988. Do physicians have an obligation to treat patients with AIDS? N Engl J Med 318: 1686-1690.

Fedson DS. 2003. Pandemic Influenza and the Global Vaccine Supply. Clinical Infectious Diseases 36: 1552-1561.

Fedson DS. 2005. Preparing for pandemic vaccination: an international policy agency for vaccine development. J Pub Health Policy 26: 4-29.

Flood CM, Stabile M, Tuohy CH. 2002 (summer). The borders of solidarity: How countries determine the public/private mix in spending and the impact on health care. Health Matrix Clevel 12: 297-356.

Fouchier RA, Schneeberger PM, Rozendaal FW, et al. 2004. Avian influenza A virus (H7N7) associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. Proc Natl Acad Sci USA 101: 1356-1361.

Fox D. 1988. The politics of physicians' responsibility in epidemics: a note on history. Hastings Cent Report, April/May: 5-9.

Freedman B. 1988. Health professionals, codes, and the right to refuse to treat HIV-infectious patients. Hastings Center Report, April/May: 20-25.

Geddes J. 2005. Wait your turn. Canada's pandemic plan has kids last in line. MacLean's Magazine, April 4, 2005: 46.

Gerdil C. 2003. The annual production cycle for influenza vaccine. Vaccine 21: 1776-1779.

Glasser RJ. 2004. We are not immune: influenza, SARS and the collapse of public health. Harper's Magazine, July 2004. Web posting on October 4, 2004 at http://www.harpers.org/WeAreNotImmune.html.

Government of Canada and the provincial and territorial governments. 2001. Memorandum of understanding on pandemic influenza. Signed March 26, 2001.

Government of Canada. 2002. Office of critical infrastructure protection and emergency preparedness. Discussion paper: Towards a national disaster mitigation strategy, pp. 1-16.

Grais RF, Ellis JH, Glass GE. 2003. Assessing the impact of airline travel on the geographic spread of pandemic influenza. Eur J Epidemiol 18: 1065-1072.

Gross ML. 2004. Bioethics and armed conflict. Mapping the moral dimensions of medicine and war. Hastings Center Report 34: 22-30.

Gross PA, Hermogenes AW, Sacks HS, et al. 1995. The efficacy of influenza vaccine in elderly persons. A meta-analysis and review of the literature. Ann Intern Med 123: 518-527.

Guan Y, Poon LL, Cheung CY, et al. 2004. H5N1 influenza: a protean pandemic threat. Proc Natl Acad Sci USA 101: 8156-8161.

Guo Y, Krauss S, Senne D, et al. 2000. Characterization of the pathogenicity of members of the newly established H9N2 influenza virus lineages in Asia. Virology 267: 279-288.

Gust ID, Hampson AW, Lavanchy D. 2001. Planning for the next pandemic of influenza. Rev Med Virol 11: 59-70.

Hak E, Buskens E, van Essen GA, et al. 2005. Clinical effectiveness of influenza vaccination in persons younger than 65 years with high-risk medical conditions: the PRISMA study. Arch Intern Med 165: 274-280.

Hak E, Nordin J, Wei F, et al. 2002. Influence of high-risk medical conditions on the effectiveness of influenza vaccination among elderly members of 3 large managed-care organizations. Clin Infect Dis 35: 370-377.

Hampson AW. 1997. Surveillance for pandemic influenza. J Infect Dis 176(suppl. 1): S8-S13.

Hampson AW. 2002. Pandemic influenza: history, extent of the problem and approaches to control. In: Brown F, Gust I (eds), Orphan Vaccines—Bridging the Gap. Dev Biol 110: 115-123. Basel, Karger.

Health Canada. 2004. Canadian Pandemic Influenza Plan. Ottawa, Health Canada. http://www.phac-aspc.gc.ca/cpip-pclcpi/index

Hirst M, Astell CR, Griffith M, et al. 2004. Novel avian influenza H7N3 strain outbreak, British Columbia. Emerg Infect Dis 10: 2192-2195.

Hoffmann-LaRoche. 2004. Oseltamivir (Tamiflu) Canadian Product Monogram. Mississauga (ON).

Horimoto T, Kawaoka Y. 2001. Pandemic threat posed by avian influenza A viruses. Clin Microbiol Rev 14: 125-149.

Hsin DH, et al. 2004. Heroes of SARS. J Infect Dis 49: 210-215.

Huber SJ, Wynia MK. 2004. When pestilence prevails...Physician responsibilities in epidemics. Am J Bioethics 4: W5-11.

Hurwitz ES, Haber M, Chang A, et al. 2002. Effectiveness of influenza vaccination of day care children in reducing influenza-related morbidity among household contacts. JAMA 284: 1677-1682.

Jiwani B. 2001. "Pandemics and ethics". http://www.phen.ab.ca/pcons/docs/ethics_&pandemics.pdf#searchJiwani%20and%20pandemic%20influenza.

Johnson NPAS, Mueller J. 2002. Updating the accounts : global mortality of the 1918-1920 « Spanish » influenza pandemic. Bull Hist Med 76: 105-115.

Jonsen JR. The Birth of Bioethics. Oxford University Press, 1998.

Kass NE. 2001. An ethics framework for public health. Am J Public Health 91: 1776-1782.

Kaul I, Grunberg I, Stern M. 1999. Defining global public goods. In: Kaul I, Grunberg I, Stern M (eds), Global Public Goods: International Cooperation in the 21st Century. New York: UNDP/Oxford University Press.

Kenny NP. 1997. Values, health, and health care. Ann R Coll Physicians Surg Can. April 30 (3): 144-146.

Kitler ME, Gavinio P, Lavanchy D. 2002. Influenza and the work of the World Health Organization. Vaccine 20: S4-S14.

Kluge E-HW. 2000. Social values, socioeconomic resources, and effectiveness coefficients: An ethical model for statistically based resource allocation. In: R Cohen-Almagor (ed), Medical Ethics at the Dawn of the 21st Century. Ann NY Acad Sci 913: 23-31.

Kobasa D, Takada A, Shinya K, et al. 2004. Enhanced virulence of influenza A viruses with the haemagglutinin of the 1918 pandemic virus. Nature 431: 703-707.

Kotalik J. 2005. Preparing for an influenza pandemic: ethical issues. Bioethics 19: 422-431.

Labonte R, Schrecker T. Fatal Indifference: The G8, Africa and Global Health. The University of Cape Town Press, 2004: pp 47-49.

Lee SY, Mak SH, Saw TA. 1999. The Avian Flu (H5N1): one year on. Public Health Epidemiol Bull 8(1): 1-6.

Leneva IA, Roberts N, Govorkova EA, et al. 2000. The neuraminidase inhibitor GS4104 (oseltamivir phosphate) is efficacious against A/Hong Kong/156/97 (H5N1) and A/Hong Kong/1074/99 (H9N2) influenza viruses. Antiviral Res 48: 101-115.

Li KS, Guan Y, Wang J, et al. 2004. Genesis of a highly pathogenic and potentially pandemic H5N1 influenza virus in eastern Asia. Nature 430: 209-213.

Li S, Perdue ML, Patzer E. 2002. Seed viruses containing novel avian HA and NA antigens for prevention against potential influenza pandemic. In: Brown F, Gust I (eds). Orphan vaccines—bridging the gap. Develop Biol 110: 135-141.

Longini IM, Nizam A, Xu S, et al. 2005. Containing pandemic influenza at the source. Science 309: 1083-1087.

Maddox PJ. 1998. Administrative ethics and the allocation of scarce resources. Online Journal of Issues in Nursing (Dec 31, 1998).

Mahoney FJ, Stewart K, Hu H, et al. 1997. Progress toward the elimination of hepatitis B virus transmission among health care workers in the United States. Arch Intern Med 157: 2601-2605.

Martin D, Shulman K, Santiago-Sorrell P, Singer P. 2003a. Priority-setting and hospital strategic planning: a qualitative case study. J Health Serv Res Policy 8: 197-201.

Martin DK, Hollenberg D, MacRae S, et al. 2003b. Priority setting in a hospital drug formulary: a qualitative case study and evaluation. Health Policy 66: 295-303.

Martin DK, Pater JL, Singer PA. 2001. Priority-setting decisions for new cancer drugs: a qualitative case study. Lancet 358: 1676-1681.

McGeer AJ, Lee W, Loeb M, et al. 2004. Adverse effects of amantadine and oseltamivir used during respiratory outbreaks in a center for developmentally disabled adults. Infect Control Hosp Epidemiol 25: 955-961.

McKay AC. 2002. Supererogation and the profession of Medicine. J Med Ethics 28: 70-73.

Meltzer MI, Cox NJ, Fukuda K. 1999. The economic impact of pandemic influenza in the United States: priorities for intervention. Emerg Infect Dis 5: 659-671.

Meltzer MI. 2003. Risk and benefits of preexposure and postexposure smallpox vaccination. Emerg Infect Dis 9: 1363-1370.

Milstien J, Lambert S. 2002. Emergency response vaccines -- a challenge to the public sector and the vaccine industry. Vaccine 21: 146-154.

Monto AS. 2003. The role of antivirals in the control of influenza. Vaccine 21: 1796-1800.

Moscona A. 2005. Drug therapy: Neuraminidase inhibitors for influenza. N Engl J Med 353: 1363-1373.

National Forum on Health. 1997. Canada Health Action: Building the legacy. Ottawa.

Nguyen-Van-Tam JS, Hampson AW. 2003. The epidemiology and clinical impact of pandemic influenza. Vaccine 21: 1762-1768.

Nicholson KG, Wood JM, Zambon M. 2003. Influenza. Lancet 362: 1733-1745.

Nieburg P, Bernheim RG, Bonnie RJ. 2003. Ethics and the practice of public health. In: Goodman RA, Rothstein MA, Hoffman RE, et al (eds), Law in Public Health Practice, Oxford University Press.

Nixon S, Upshur R, Robertson A, et al. 2005. Public Health Ethics. In: Bailey TM, Caulfield T, Ries NM (eds), Public Health Law and Policy in Canada. LexisNexis Butterworths.

Nuremberg Code. Reprinted in Dictionary of Medical Ethics, 2nd Edition. In: Duncan AS, Dunstan GR, Welbourn RB (eds). Darton, Longman and Todd, London (1981), pp 130-132.

Oberle K, Hughes D. 2001. Doctors' and nurses' perceptions of ethical problems in end-of-life decisions. J Adv Nursing 33: 707-715.

O'Flaherty J. 1991. The AIDS patient: a historical perspective on the physician's obligation to treat. Pharos Alpha Omega Alpha Honor Med Soc 54(3): 13-16.

Osterholm MT. 2005. Preparing for the next pandemic (perspective). N Engl J Med 352: 1839-1842.

Peiris JS, Yu WC, Leung CW, et al. 2004. Re-emergence of fatal human influenza A subtype H5N1 disease. Lancet 363: 617-619.

Pellegrino E. 1987. Altruism, self-interest, and medical ethics. JAMA 258: 1939-1940.

Potter J, Stott D, Roberts M, et al. 1997. Influenza vaccination of health care workers in long-term care hospitals reduces the mortality of elderly patients. J Infect Dis 175: 1-6.

Public Health Agency of Canada. 2005. New Release: Minister Dosanjh announces federal contribution towards creation of a national antiviral stockpile. February 4, 2005. Available at: http://www.phac-aspc.gc.ca/media/nr-rp/2005/2005_3_e.html

Rachels J. 1999. The Elements of Moral Philosophy. McGraw-Hill, pp 122-142.

Rawls J. 1999. A Theory of Justice. Harvard University Press, Cambridge, MA.

Reilley B, Van Herp M, Sermand D, Dentico N. 2003. SARS and Carlo Urbani. N Engl J Med 348: 1951-1952.

Roberts MJ, Reich MR. 2002. Ethical analysis in public health. Lancet 359: 1055-1059.

Romanow RJ. 2002. Building on Values: The Future of Health Care in Canada (Final Report). Commission on the Future of Health Care in Canada. www.healthcarecommission.ca.

Saito T, Lim W, Suzuki T, et al. 2001. Characterization of a human H9N2 infuenza virus isolated in Hong Kong. Vaccine 20: 125-133.

Scheifele DW, Duval B, Russell ML, et al. 2003. Ocular and respiratory symptoms attributable to inactivated split influenza vaccine: evidence from a controlled trial involving adults. Clin Infect Dis 36: 850-857.

Seedhouse D. Ethics: the Heart of Healthcare. Chapter 7: Theories of ethics. Wiley 1998.

Sepkowitz KA, Eisenberg L. 2005. Occupational deaths among healthcare workers. Emerg Infect Dis 11: 1003-1008.

Singer PA, Martin DK, Giacomii M, Purdy L. 2000. Priority setting for new technologies in medicine: qualitative case study. BMJ 321: 1316-1318.

Skowronski DM, Astell C, Brunham RC, et al. 2005. Severe acute respiratory syndrome (SARS): a year in review. Annu Rev Med 56: 357-381.

Specter M. 2005. Nature's bioterrorist (Is there any way to prevent a deadly avian-flu pandemic?). The New Yorker, February 28.

Tauber AI. 2003. A philosophical approach to rationing. Med J Aust 178: 454-456.

Thomasma DC et al. 1995. A dialogue on compassion and supererogation in medicine. Cambridge Quarterly for Healthcare Ethics 4: 415-425.

Traynor K. 2005. HIV occupational exposure guidelines revised. Am J Health Syst Pharm 62: 2332-2334.

Tweed SA, Skowronski DM, David ST, et al. 2004. Human illness from avian influenza H7N3, British Columbia. Emerg Infect Dis 10: 2196-2199.

Uiprasertkul M, Puthavathana P, Sangsiriwut K, et al. 2005. Influenza A H5N1 replication sites in humans. Emerg Infect Dis 11: 1036-1041.

UK Health Department. 2005. Influenza Pandemic Contingency Plan. http://www.dh.gov.uk/assetRoot/04/12/17/44/041211744.pdf. (accessed Nov 7, 2005).

Ungchusak K, Auewarakul P, Dowell SF, et al. 2005. Probable person-to-person transmission of avian influenza A (H5N1). N Engl J Med 352: 333-340.

UNOS (United Network for Organ Sharing). Http://www.transplantliving.org/beforethetransplant/allocation/waiting ForOrgan.aspx. (accessed August 4, 2005).

US Department of Health and Human Services. HHS Pandemic Influenza Plan. http://www.hhs.gov/pandemicflu/plan. (accessed Nov 7, 2005).

van Genugten MLL, Heijnen M-LA, Jager JC. 2003. Pandemic influenza and healthcare demand in the Netherlands: scenario analysis. Emerg Infect Dis 9: 531-538.

Vora SK. 2004. Living with the plagues. Emerg Infect Dis 10: 956-957.

Washington Post. 2005. Shipments of flu drug suspended (October 28, 2005).

Webby RJ, Webster RG. 2003. Are We Ready for Pandemic Influenza? Science 302: 1519-1523.

Wilmot S, Ratcliffe J. 2002. Principles of distributive justice used by members of the general public in the allocation of donor liver grafts for transplantation: a qualitative study. Health Expect 5: 199-209.

WisdomSource News. 2005. Effective disaster planning and true preparedness. Posted November 21, 2005. http://www.wisdomsource.com/tf/wisdomsource.asp?a=432. (accessed November 21, 2005).

Wollenberg A, Engler R. 2004. Smallpox, vaccination and adverse reactions to smallpox vaccine. Curr Open Allergy Clin Immunol 4: 271-275.

Wood JM, Levandowski RA. 2003. The influenza vaccine licensing process. Vaccine 21: 1786-1788.

Woodward D, Smith RD. 2003. Global public goods and health: Concepts and issues. In: Smith RD, Beaglehole R, Woodward D, Drager N (eds). Global public goods for health: Health economic and public health perspectives. Oxford University Press, UK.

World Health Association. 2004. Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects.

World Health Organisation. 1999. Influenza Pandemic Preparedness Plan. The role of WHO and guidelines for national and regional planning. Geneva, Switzerland.

World Health Organisation. 2003a. Hospital Infection Control Guidance for Severe Acute Respiratory Syndrome (SARS). http://www.who.int/crs/sars/infectioncontrol/en/. (accessed October 31, 2005).

World Health Organisation. 2003b. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Sept 26 [cited 2005 April 28]. Available from http://www.who.int/csr/sars/country/table2003_09_23/en/

World Health Organisation. 2004a. Vaccines for pandemic influenza. Informal meeting of WHO, influenza vaccine manufacturers, national licensing agencies, and government representatives on influenza pandemic vaccines (Summary report). November 11-12, 2004. Geneva, Switzerland.

World Health Organisation. 2004b. Guidelines on the use of vaccines and antivirals during influenza pandemics. WHO. Geneva. http://www.who.int/csr/resources/publications/influenza/11_29_01_A.pdf

World Health Organisation. 2005. WHO global influenza preparedness plan. The role of WHO and recommendations for national measures before and during pandemics. Geneva, Switzerland. http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5.pdf.

World Health Organisation Bulletin. http://www.who.int/emc/diseases/flu/index.htlm.

World Health Organisation Global Influenza Program Surveillance Network. 2005. Evolution of H5N1 avian influenza viruses in Asia. Emerg Infect Dis 11: 1515-1521.

World Health Organisation Media Centre. 2005. Donation of three million treatments of oseltamivir to WHO will help early response to an emerging influenza pandemic. Posted 24 August, 2005. http://www.who.int/mediacentre/news/releases/2005/pr36/en/index.htlm. (accessed August 30, 2005).