Project on Addressing Ethical Issues in Pandemic Influenza Planning

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Hippocrates explaining the importance of contagion in the plague epidemic

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Equitable access to therapeutic and prophylactic measures

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Conclusions and recommendations

General

In preparation to a pandemic, governments and public health institutions should develop criteria and policies for allocation of medical resources. These should take into account:

(1) Efficiency: To maximize health benefits with given resources, preferably (though not necessarily) in terms of saving most lives.

(2) Equity: to avoid unjustified discrimination. Equity also supports giving priority to groups who are at highest risk for influenza-related death, and to prioritize children and young adults.

> Equity and efficiency will often conflict. Moreover, cut-off points in group definitions (e.g. where to draw the line if young adults are given priority) will inevitably be arbitrary. Policies for priority setting will therefore be controversial, which further underlines the need for

(3) fair and reasonable procedures for justification, public consultation, and enforcement of compliance (Accountability).

> Priority access to protection or therapeutic treatment can be justified for some groups.

(1) Professionals like health care workers who are involved in saving the lives of many others, should be given priority access to protection against infection (protective equipment, chemoprohylaxis in early stages, vaccination). This helps to sustain health care functions and prevent nocosomial infections. The group of 'life-savers' further may consist of vaccine developers and other professionals who are necessary in response to the pandemic. Moreover, professionals who are involved in saving many persons from non-influenza related death might be included as well. This argument to prioritize life-savers can inflate rapidly and may also be easily abused at the cost of vulnerable groups. Governments should be very reluctant to apply and broaden such criteria.

(2) Persons who are at high-risk to get severe complications and die from influenza have a stronger claim to vaccination and to antiviral treatment (if they get ill) compared to persons who are at lower risk and for whom these interventions are less urgent.

(3) The fair innings argument supports giving priority to saving the lives of the young rather than the old. This applies to prevention (vaccination) as well as to treatment. The fair innings argument does not specify 'where to draw a line' between persons who are eligible to priority access, and those who are not. Such a 'line' will always be rather arbitrary, and depend on availability of resources. Such arbitrariness is however no reason to reject age-criteria altogether.

Antiviral drugs

It is essential that there will be international (WHO) stockpiles for geographical antiviral prophylaxis, as part of rapid response to a first outbreak of pandemic influenza, aiming to contain the outbreak at the source or delay further spread. On a national level, countries should use antiviral stockpiles primarily for treatment of patients, and they should avoid massive pre-emptive prophylactic use of antiviral drugs. In their decisions about the magnitude of antiviral stockpiles and their application, governments should also support low income countries for which antiviral drugs may be unaffordable.

Within a country, a number of priorities for antiviral drugs can be justified:

1. Post-exposure prophylaxis for health care workers, at least in the beginning of the pandemic. This may both reduce the risk of nocosomial infection and prevent that the health care system will be break down during the first stage of the pandemic.

2. Antiviral treatment of all symptomatic patients

If it is not possible to treat all symptomatic patients there are strong reasons to prioritize:

a) *Professionals who are essential for saving lives and who get ill themselves because this increases the chance that they will recover and continue their work.*
b) *Symptomatic patients in pandemic high-risk groups who are at increased risk for severe disease and death, because for them treatment is more urgent.*
c) *Symptomatic younger adults and children on the basis of the fair innings argument.*

In times of drug scarcity it is tempting to treat more patients with a decreased dose or shortened course of antiviral drugs. This will facilitate the development of drug resistant virus strains, which is harmful to treated patients as well as to public health at large. Distributing reduced doses among a larger group therefore should not be considered as a fair and just response to scarcity.

Medical care for patients

Most influenza patients will require (at least) basic medical and nursing care and relief of symptoms. Developing and maintaining health care infrastructures for primary care is a major priority for pandemic preparedness in those contexts, especially because such investments will be beneficial at all times, and not only during a pandemic.

In intensive care facilities, priority setting during a pandemic should focus on saving the most lives possible, which means giving priority to those patients who are expected to recover relatively fast. This can be done by developing several tiers of successively more strict medical criteria for inclusion and exclusion of patients. Yet even when the most restrictive criteria are applied, there will be situations where there are two or more patients eligible for one ICU. In such a case, it is fair either to give priority to the patient who is significantly younger, or to give all eligible patients an equal chance to treatment (i.e. a lottery).

Exclusion criteria should apply to all diseases and not just to influenza-related illness. Moreover, they may apply to withholding as well as withdrawing life-support.

It is difficult to specify clear guidelines for allocating non-ICU hospital bed on the basis of the general principles of efficiency and equity. Considerations of equity support prioritization according to medical need. Some practical recommendations are to avoid nosocomial infections by creating special departments for influenza patients and to give persons without support of family or neighbours priority access to basic care facilities.

Vaccination

There are several justified, though sometimes competing directions for priorities in vaccination:

1. Prioritizing health care workers and other ‘life-savers’ helps to sustain the health care system and produces indirect (health) benefits.
2. Vaccinating children may be most effective in reducing transmission and hence in reducing the attack rate of pandemic influenza. This approach may not save most lives, but it does offer all persons (who are not yet immune) within a population a prospect of benefit.
3. For persons in pandemic high-risk groups, vaccination is more urgent than for others, but it is unfair to vaccinate only them if not all can be vaccinated. If the increasing supplies of vaccine will be sufficient to vaccinate all eligible persons in a population within a limited time, then it is reasonable to vaccinate high-risk groups first. If not, fairness may require different priorities.
4. Children and young adults have a strong claim to vaccination on the basis of the fair innings argument. (1) and (3) together give strong support to prioritizing children.

1. Aim and context

It is generally expected that sooner or later a genetic shift or reassortment of an (avian) influenza virus will result in a new highly pathogenic virus that can transmit from human to human. Humans will then have no or little immunity against this virus, which will spread as easily as common seasonal influenza, infect many people worldwide and may potentially result in very high mortality and morbidity rates. Some scenarios assume attack rates of up to 40 percent and lethal disease in 1-2 percent of all persons who develop symptoms, yet such assumptions may be a gross overestimation or underestimation of the crisis (e.g. currently the mortality of H5N1 is above 50 percent). An effective vaccine will not be available, for six months or more, and, in the mean time the possibilities for preventive and curative treatment are limited. Depending on supplies, antiviral drugs could play an important therapeutic and prophylactic role. The global demand for antiviral drugs and medical care will however exceed global (and affordable) supplies. Many patients may develop respiratory problems and require mechanical ventilation. The need for such intensive care might go far beyond available resources. Moreover, health care professionals and related personnel will be hit by the disease as well: working in the frontline they will probably run greater risks of infection than other citizens. This only reinforces pressure on the health care system, where much more must be done with less staff. Triage decisions for allocating scarce possibilities for treatment will be inevitable. These decisions need to be made about supportive medical care (e.g. ventilators), antibiotics, antiviral drugs, and vaccines.

One essential way to avoid chaos and promote adequate response to a pandemic is to develop action plans for pandemic preparedness. Allocation of scarce antiviral drugs, medical care and development of vaccination strategies are important issues in such these plans. In 2006 many countries have published action plans for an influenza pandemic (Cf. Mounier-Jack & Coker, 2006). Triage and priority setting clearly raise ethical questions: can it be morally justified to give certain persons access to life-saving treatment and to refuse others – and if so, which choices should be made and who should make them? Few action plans provide discussion of such ethical issues, and even less offer systematic ethical justification for priority setting.

This report formulates ethical principles and arguments for setting priorities in the distribution of scarce medical resources during a pandemic. The focus is on antiviral drugs, medical care, and vaccination. Priority setting in a pandemic will be a deeply controversial issue. This is not only because there will be extreme shortages in supply of potentially life-saving treatment, but also because common health care practices and procedures may not be applicable or appropriate where drastic interventions are required to mitigate the effects of the pandemic. Ethical theories however do provide clarification and reasonable justification of principles that should guide decision making. The report argues for specific priorities on the basis of *maximizing health benefits* *(notably saving most lives)* and *equity* but also acknowledges that the basic moral principles of maximizing health benefits and equity leave room for certain other priorities. Conclusions and recommendation may be provisional and incomplete given the lack of important data and inevitable conflicts between and within the basic moral principles. Moreover, some situations involve emergencies and tragedies of such magnitude that ethical theory has little practical guidance to offer.

2. Ethics and scarcity in a pandemic—General considerations and principles

2.1 Circumstances

Throughout the last decades it has been very difficult to establish consensus-based or well-justified principles for priority setting in health care (Daniels & Sabin 2002). In times of an influenza pandemic, the same controversies arise, but now in extraordinary circumstances. The demand and need for health care will be much higher than in normal times and simultaneously the health care system (like many other societal institutions) will be weakened as a result of ill staff. If only few persons get the care they need, this may raise distrust in professionals, institutions and governments. Moreover, fear for the disease might paralyse societal life or lead to panic and further distrust in governments and institutions. In such circumstances, the objective of developing principles for priority setting seems even more controversial than in 'normal' health care settings. Finally, important factual issues that are more or less known in normal circumstances (how effective are the various medical options; which groups are most at risk; which patients most urgently need treatment; and how many are they) are not known in advance.

However, these extraordinary features do not necessarily render any attempt to priority setting impossible, and to some extent they might even facilitate the development of some principles for priority setting. First, a pandemic is to be considered as a world-wide emergency situation where complete populations are threatened, and then obviously policies should focus on protection of all members of the population at large. This is an objective that few will reject. Second, the uncertainties about *who* will be most at risk for severe illness and death in a pandemic might necessitate (hence promote) a focus on general principles and arguments, instead of a focus on specific groups or persons who should be given priority. If all are uncertain about who would benefit from certain proposals and who not, this might help generate some agreement on principles.

Two further complexities need to be mentioned at this stage. The discussion focuses on priority setting of three types of health care delivery (antiviral drugs; patient care; vaccination) that strongly differ in many relevant respects. Vaccination is purely meant for preventive purposes aimed at those who have not been infected yet; (hospital) medical care involves therapy aimed at the (very) ill, and antiviral treatment can be used as early treatment of patients, or post-exposure and pre-exposure prophylaxis for the healthy. Moreover, the conditions of scarcity will be different: supplies of antivirals may be available in the beginning of the pandemic but decrease very soon; intensive medical care and hospital beds will probably be very scarce throughout the epidemic; while vaccination will be unavailable at least during the first months of a pandemic, and then gradually becoming available in increasing quantities. This clearly requires three separate discussions.

An additional complexity to be mentioned is that the differences between high-income countries and middle- and low-income countries will be immense. High-income countries like the Netherlands expect to have sufficient stockpiles of antiviral drugs for treating all persons who develop symptoms of influenza. Low-income countries will probably have no stockpiles at all.

Something similar applies to vaccination. Many high-income countries are signing contracts with pharmaceutical companies, in order to reserve production capacity and get vaccines as soon as these are produced. Low income countries will not have such contracts, and hence might have nothing to distribute. These facts obviously raise questions concerning international aid and justice, which will be discussed more extensively in a different report (Archer 2006).

Many options and dilemmas that will be discussed in this paper may not be available to low-income countries. On the other hand, it will be clear that low-income countries must weigh their efforts in pandemic preparedness to regular health care needs, given that such needs often remain unmet even in 'normal circumstances'. Any adequate response to a pandemic requires infrastructures for primary care and prevention. Hence for many low-income countries the first priority for pandemic preparedness may involve strengthening such facilities and infrastructure.

2.2 General principles for priority setting: efficiency, equity, and procedural fairness

When a major disaster is overwhelming a population, and many lives are at stake, there are strong moral reasons to protect the population and save as many as possible with available resources. On the other hand, distribution of scarce medical resources should also be equitable and fair. These principles are very general and require further explanation and specification.

The first principle—to save the greater number of lives—can be considered as a principle of efficiency or utility, to maximize the aggregate benefit of public health interventions with available means. This involves, among other things, a focus on interventions (and patient groups) that have a high chance of success. The importance of efficient action is obvious, but it is not obvious that success should be measured in terms of *saving most lives.* An alternative approach would be to aim at broader health benefits, in terms of life-years or quality-adjusted life-years (QALYs) gained. Or even broader, public health interventions could aim at maximizing expected utility, which also includes non-health benefits such as the protection of essential economic functions. This is a discussion on the level of ethical theory, but the implications are very practical. In section 2.3 it is argued that there are strong reasons to maximize saving lives and not QALYs or general utility.

The second principle—equity—is not concerned with the best aggregate outcome of policies, but with how benefits and burdens are distributed within the population. Fairness implies that equal weight is given to equal claims of persons. Policies in which access to health care depends on nationality, ethnic group, social security registration, or gender are clearly unjust. But also policies that succeed in saving as many lives as possible can be unfair, for example if priority is given to vaccination of people in urban cities (where vaccination might be most efficient and prevent most infections) and persons in rural areas have little or no prospect to get vaccination. Equity may also support giving priority to saving young persons above elderly. Various implications of fairness are discussed in section 2.4.

Obviously then, the two basic principles can and do conflict if priorities are to be set. Where decisions are based upon weighing competing values, it is important that there are fair procedures for accountability in place (see section 2.5 below).

Before discussing the principles and their conflicting interpretations in more detail, it must be emphasized that many general practical policy objectives, as outlined by the WHO (2005) can be supported from any of those interpretations. In case of a first outbreak, rapid response is essential, aiming at containment at the source. Subsequently, interventions should aim at prevention, as long as possible, of the introduction of the virus into non-affected populations. If an outbreak cannot be contained, policies will aim at reducing possibilities of transmission within the population (social distancing, face masks, post-exposure prophylaxis, etc.) and gain time for further actions and responses, including vaccine development. Ultimately it will be important to mitigate the effects of the pandemic, which involves protecting and sustaining public health care systems. Such steps are essential in any account of equitable and efficient response to pandemic influenza.

2.3 Efficiency: maximize protection with available means

This section discusses in more detail the principle to maximize protection of the population with available means (efficiency). The key message is that *saving most lives* is the preferable outcome measure. There are strong reasons to avoid focusing on non-health benefits (e.g. general utility) but it is reasonable to include *indirect health benefits*, which implies that in some cases it is justified to give persons who save lives priority access to prevention and treatment.

Departing from principles that are considered most relevant and decisive in normal health care priority setting

A common assumption in health care is that patients who are most ill and urgently require treatment, should be treated first. In an influenza pandemic a different approach might be justified and necessary. Pandemic influenza will spread rapidly, potentially affecting or killing many people, and it will put the health care system under very heavy pressure. All persons run the risk of acquiring infection, many are at risk of fatal illness, and clearly not all can be saved from that. Moreover, vaccination and antiviral prophylaxis are not only beneficial for the persons who get the vaccine or drug; they also help to prevent further spread of the virus and hence offer benefits to others as well. In these circumstances it makes sense to depart from the principle to prioritize the most needy and urgent, and allocate health care resources in such a way that as many persons as possible are protected – within certain constraints of fairness.

Consequentialist and non-consequentialist arguments for saving the greater number of lives

The idea that scarce resources should be allocated in such a way that maximum beneficial effect can be expected, is clearly consequentialist. Consequentialism is the ethical theory which requires us to compare the options we have and then to choose the option with the best expected aggregate outcome. If we consider human life to be of central value, this theory supports allocation of resources that saves as many lives as possible. The restriction to 'saving lives' however can be criticized. Many consequentialist approaches, for example utilitarianism, will endorse a broader account of value, e.g. welfare, or utility, in which goods are combined as diverse as life, health, happiness, economic flourishing, etc. As a result, utilitarianism can sometimes prioritize protecting the economy above protecting lives. Other consequentialist approaches would favour maximizing health benefits in terms of life years gained (or QALYs, DALYs, etc.) However, *saving most lives* may be preferable from a moral point of view.

First of all, this principle can also be justified by appeal to non-consequentialist theories. For example, Thomas Scanlon's contractualist theory (1998) rejects interpersonal aggregation of harms and benefits because this would allow policies that sacrifice someone's life or basic health in order to secure small benefits for the greater number. Such a trade-off however can be avoided if the ultimate focus is only on saving lives and not on smaller health benefits. [1] Moreover, the

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[1] Hirose (2001) shows that in a contractualist framework it is even possible to accept the principle to save the greater number without relying on aggregation. Assuming that all persons whose life is in danger have an equal claim to be saved, the Pareto principle and the requirement of universalization are sufficient to argue for saving most lives.

principle to save the greater number of lives can be consistent with a rights-based theory that assumes that all persons have an equal right to life and hence have an equal claim to protection of their lives. Such non-consequentialist theories can accept that, if not all lives can be protected, it is justified to protect as many lives as possible.

Secondly, there are also consequentialist reasons for preferring policies that save most lives over policies that maximize general utility. Arguably, the latter policies would aim to protect societal and economic functions, which in turn supports giving governments and other leaders priority access to prevention and treatment. Now, if governments and persons in power receive a level of protection that is inaccessible to large parts of the public, this will easily raise suspicion and distrust among the public. In contrast, a principle to *save as many lives as possible* is very simple and clear, and cannot be easily tailored to secure just the interests of groups who are in power. This further helps to avoid unfairness and to promote public acceptance.

Separate spheres and indirect benefits

These considerations support to adopt an approach that distributes health care during the pandemic on the basis of maximizing *health* benefits. The scope of concerns is restricted to concerns about health, and non-health benefits should not determine rationing policies. Of course, protecting the economy and other sources of welfare are important considerations for pandemic preparedness, but these should play a role in determining the (extra) budget available for pandemic response. For example, building a stockpile will require large amounts of extra funds and deliberation about how much resources should be made available will depend on weighing the importance of non-health goods, such as welfare or education (Cf. Brock 2003).

A further restriction to focus on *saving most lives* as measure for efficiency makes sense because this can be supported by consequentialist and non-consequentialist theories. The reasons for this restriction however are not compelling and therefore a principle that maximizes broader health benefits (e.g. in terms of life years saved, or DALYs or QALYs gained) can be reasonable as well. For that matter, there is no reason to separate care for pandemic influenza patients from care for patients with other diseases: if health care resources are allocated to maximize health benefits, all patient groups must be taken into account.

If the focus is on health benefits, and saving lives in particular, a second issue is whether *indirect* benefits can be taken into account (Brock 2003). For example, treating a health care worker is not only beneficial because it might save her life, but if she recovers, she will contribute to saving the lives of further persons. Therefore, it makes sense to give health care workers priority access to treatment. In normal health care circumstances, such considerations are often considered as inappropriate and unfair. In a pandemic however, many persons will die from influenza, and the number will strongly increase if essential health services cannot be sustained. A policy that gives some priority to protecting and treating persons who save lives, will reduce overall mortality and hence significantly increase each person's chance to survive. For that reason, the policy can be justified to anyone.

In conclusion, in response to a pandemic it is essential for governments to protect the population at large. Even though a pandemic will be a threat for all values in societal life, there are strong consequentialist and non-consequentialist reasons for focusing on policies that maximize health benefits. The principle to save as many lives as possible is a reasonable specification of that, though other specifications can also be acceptable. Even though a focus on 'saving lives' will be less unfair than a focus on broader health benefits, conflicts with equity are still inevitable.

2.4 Equity

The second principle, equity, or fairness, involves giving equal weight to equal claims. This general idea already played a role in shaping the principle of saving lives. There are however further implications of equity (notably egalitarian concerns) which need to be clarified. In short, equity supports (1) a rejection of various forms of discrimination, (2) attempts to minimize unfairness, and (3) giving priority to groups who have a relatively strong claim to life-saving treatment, such as persons at high risk of severe disease and death, but also persons who are relatively young.

Discrimination and group favouritism
Some practices are inconsistent with any account of fairness. In the face of a pandemic there is a danger that authorities who have the power to set priorities and allocate resources will favour their own friends and families or ethnic group, or otherwise discriminate according to religion, gender, etc. For example, authorities might decide to use limited stockpiles of antivirals to prophylactically protect themselves and their groups, and leave others in a situation where no antivirals will be available for treating persons who become ill. Such discrimination is grossly unfair and violates basic human rights. If decisions about whom to save from a lethal disease and who not, are just based upon personal characteristics of members in the population (kinship, friends, ethnicity, nationality, gender, etc), than obviously such decisions violate the equal worth of persons. Priority setting should be based upon criteria that are relevant and justifiable to all – not just to one's own group. If priorities are set on the basis of personal preferences of those in power, this will normally lead to a situation where groups who are suppressed or otherwise worse off will be neglected. Moreover such policies will probably not protect the health of the public in any efficient way.

Minimizing unfairness
Issues of fairness do not just arise in cases of explicit discrimination. A policy that aims to save the greater number of lives (or to maximize health benefits more generally) can be unfair as well. For example, focusing vaccination on urban areas might save more lives more efficiently than giving equal attention to rural areas, just because in urban areas there will be more people with more interaction, hence more transmission of the virus, compared to rural areas. Suppose only 8 million vaccine doses are available for a population of 20 million, half of them living in a city, and the other half living in a very large rural area. Arguably, vaccinating 80 percent of all persons living in the densely populated areas would save much more lives than vaccinating 40 percent of the whole population. Yet this would leave the rural areas completely unprotected, and that would at least seem unfair. If the sole principle is to save most lives with given resources, such forms of unfairness may be inevitable. However, priorities should be devised in such a way that unfairness is minimized where possible. In the example above this would support a more proportionate distribution of vaccines over urban and rural areas. This does not necessarily imply that vaccine is given to 40 percent of both populations. Modelling studies suggest that vaccinating 80 percent of all children with influenza vaccines might be as effective in preventing infection as vaccinating 80 percent of the whole population (Longini 2004). Results of modelling studies should be used with caution, but if these results can be accepted, they provide strong evidence for giving priority to vaccinating children in both groups, because this would give everyone (children and adults) a reasonable prospect of protection. Such policy would then strike a reasonable balance between *saving most lives* and *equity*.

Priority to worst-off: risks and fair innings
These considerations however do not exhaust the implications of equity. Equity also supports giving priority to persons who are worst off (Arneson 2002). This idea is one of the basic principles in John Rawls's egalitarian theory of justice (Rawls 1971).

As mentioned earlier, normal health care practices are often based upon egalitarian considerations, where priority is given to treating patients who are sickest. This principle is less obvious in the emergency context of a pandemic where the population at large needs to be protected. At the same time, it would be problematic to focus all resources on preventing illness, and leave untreated all persons who become ill. Yet which persons could rightly claim they are 'worst off' and should therefore be given priority in rationing policies?

If priorities are set with the aim of saving lives (and not more broadly, maximizing welfare) then it makes sense to restrict evaluation of the situation of people to issues that are relevant for the value that is at stake, that is, their life. Persons who are worst-off from an economic point of view do not have a stronger claim to be saved than any other. On the other hand, someone who is very ill, has a stronger claim to care than someone who now is and might remain healthy. This supports prioritizing therapeutic treatment over prophylaxis in many cases, which is especially relevant in decision-making about antiviral treatment. For the same reasons, one might argue that persons in high-risk groups (e.g. elderly, immune-compromised patients) can have a stronger claim to protection – they run a greater risk to die – than other persons. For that matter, which groups will be highest-risk will depend on the specific features of the influenza virus, and they may differ from the well-known risk groups for seasonal influenza.

There is also a different way in which certain persons have a stronger claim than others to have their lives protected. This has to do with age and the opportunities one has already had in life. In this sense, a child or young adult has a stronger claim to protection than an elderly person who has been able to live up to a full life-span (Daniels 1985; Williams 1997). In this respect, death at 80 is not as bad as death at 40, and death at 5 is worse than at 40. This leads to a specific account of fairness, known as the *fair innings argument*. The basic egalitarian principle is that institutions should promote equality of opportunity. Older persons will have had much more opportunities in their life then persons who die at young age. Therefore, when we can save some but not all, it is fair to save younger persons, who would be worse off if they died at their age, then elderly.[2] There are also completely different (non-egalitarian) arguments for prioritizing children and especially young adults. If society at large is at risk, then, from a utilitarian point of view it makes sense to protect those groups that will be most important for the sustainment and rebuilding of societal functions, now and in the future (Emanuel & Wertheimer 2006).

It is clear that egalitarian approaches can point to completely different directions: some will give priority to saving elderly, assuming they run a higher risk to severe disease and death than others, others will prioritize children, given that they have not had the many opportunities of life which elderly had.

Reciprocity towards persons who accept risk for the common good of saving lives
Special consideration should be given to the circumstances of health care workers and others who play an essential role in fighting the pandemic and may do so in a situation in which they themselves run a great risk of being infected (University of Toronto 2005). If health care workers

[2] While the fair innings argument as such supports giving priority to saving the lives of the young above saving the elderly, it does not specify age-groups or cut-off points for prioritization. Decisions about where to draw the line will also be based on availability of resources.

who treat influenza patients, but also persons who clean contaminated spaces run significant risks in their work, they may have a very strong claim to be protected against disease or be treated as good as possible when they get ill. Society needs them to accept risks and therefore it would be fair if society offers them protection which might compensate for the increased risk. This argument raises questions about scope: which groups should be given special treatment for reasons of fairness, but also, what level of protection can they reasonably claim? Is the provision of personal protective equipment (PPE) sufficient? Or should they also have priority access to vaccination or even priority treatment if they get ill?

This argument of reciprocity however depends on whether health care workers and other pandemic responders indeed do run a significantly greater risk of severe illness then other citizens. This is not obvious, given that influenza, unlike SARS, spreads very easily through the community, infecting pandemic responders, children, elderly, and others alike. *If* there is an increased risk, then reciprocity supports giving priority access to protection and treatment in such a way that their risk will be similar to that of other citizens.

However, there are also independent (consequentialist) arguments for prioritizing health care workers and other pandemic responders as a group to be protected. Protecting them will contribute to sustaining the health care system, preventing nocosomial infections, and otherwise save the lives of people. It does support priority access to PPE, post-exposure prophylaxis, and vaccination of health care workers. It may also support anti-viral treatment if they get ill as this would increase the chance that they will recover and be able to continue their (life-saving) work.[3] These arguments however are not a matter of fairness or equity.

2.5 Accountability: fair procedures, public consultation, and trust

Even though there is reasonable justification for using these general principles for priority setting, this will not take away moral conflict. Concerns of efficiency and equity will clash in a number of cases, and moreover, the principles themselves can be understood in diverging ways. Given these controversies and given that decisions will have grave impact on the lives of all, it is important that decisions about priorities are legitimate and trustworthy. Daniels and Sabin (2002) emphasize that setting limits to health care can only be legitimate if rationing decisions are made on the basis of fair and reasonable procedures. During a pandemic, panic and anger might undermine trust in government and health care, which would lead to further societal problems. Clear and fair procedures that also promote public justification of policies may help to sustain trust and prevent public resistance to some extent, even though the possibilities for accountability *during* the pandemic might be limited. These procedures should at least concern:

1. *Publicity* Decisions and rationales for rationing of antiviral drugs, vaccination and medical care should be public. If decisions and justification are not public, people have no reason to believe that priority setting is done in a legitimate way. In most countries, pandemic preparedness plans are in the public domain, yet much more needs to be done to inform the public about policies and procedures.

2. *Reasonableness* The rationales should be reasonable, that is, appeal to reasons and principles that are accepted as relevant by people who are disposed to find terms of cooperation that are mutually justifiable. Obviously such reasons should be as clear as possible. Public consultations might help to develop arguments and hence to strengthen justification and support for the policy.

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[3] Note that the reciprocity argument only applies to pandemic responders who are at increased risk. The consequentialist argument may apply to a much broader group of persons who are important for saving the lives of others (including vaccine producers and firefighters).

3. *Revision procedures* Decisions about priority should be revisable in the light of new evidence or new arguments and the public must be aware of this possibility. There should be clear procedures for such revisions: who is to decide about that, on what sort of evidence?

A distinction should be made between revisions on the basis of new clinical and epidemiological evidence and other factual issues (e.g. exhaustion of resources) and revisions on the basis of moral or political reasons. Normative principles for priority setting (i.e. applications the general objectives and principles mentioned in the previous section) should preferably be settled in pre-pandemic times: notwithstanding the manifold empirical uncertainties, it is possible to outline general moral arguments for priority-setting in pandemic preparedness plans; and more importantly, the emergency situation of a pandemic does not offer a fruitful context for moral discussion and public consultation. On the other hand, in pre-pandemic times many relevant clinical and epidemiological data will not be available, and therefore, new evidence will have implications for policies. E.g. if the primary strategy for using antiviral drugs is to contain a local outbreak, new evidence about the virus might clarify *whether* such objective can be attained, and how to do it.

4. *Compliance regulations.* From a point of view of fairness it is not only important that there fair policies, criteria and procedures are developed, but also that these are complied to. Hence, there should be clear regulations and authorities to promote, to control and to enforce compliance.

One procedural strategy to avoid inequity and to sustain trust in professional ethics of health care workers, is to separate clinical and allocation roles: allocation is done by politicians and managers, and physicians can focus on treating their patients. Robert Veatch argues that, though this makes sense in normal medical care, it does not in a mass disaster where it is inevitable for health care workers to do triage and select patients onsite (Veatch 2005, 238). Whether such distinction is possible with respect to resource allocation in a pandemic is not completely clear. Determining who should get priority access to antiviral treatment or prophylaxis, or for vaccination should be done on a meso or macro level, and selection criteria should be very clear to public and health care workers. On the other hand, triage in hospital medical care might be more difficult, if only because e.g. intensive care specialists will have to select persons on the basis of several factors. Separating allocation from care might even become impossible if allocation decisions will directly affect decisions to withdraw life-sustaining treatment – considerations that are almost taboo in regular clinical care (and for good reasons) but which might be justified in extreme scarcity and emergencies (see Chapter 4).

Given the importance of trust in allocation procedures, and government and health care institutions more general, there is one issue that requires careful consideration. Above it is argued that priority should be given to sustain the (public) health care system and to prioritize prophylactic or therapeutic antiviral treatment of health care workers. However, there are much more persons in roles essential for sustaining public health and societal life at large: members of government, police, key persons in public health policies, military forces, captains of industry, etc. Such persons might even require 'for the common good' prophylactic treatment with antivirals or first access to a new vaccine. Especially when resources such as antiviral drugs are limited, and public trust is vulnerable, one should be very reluctant with non-medical and non-public health criteria for priority setting. The more persons in 'essential roles' are given antiviral drugs for prophylaxis, the more this creates possibilities for favouritism, abuse and other inequities, which will further undermine public trust in health services and policies.

2.6 Practical implications

In preparation to a pandemic, governments and public health institutions should develop clear criteria and policies for distribution of scarce medical resources. These should take into account two basic principles:

(1) Efficiency: To maximize health benefits with given resources, preferably (though not necessarily) in terms of saving most lives.

(2) Equity: To avoid unjustified discrimination and unfairness. Equity also supports giving priority to groups who are at highest risk for influenza-related death, and to prioritize children and young adults.

These general principles and their specifications will often conflict. Moreover, cut-off points in group definitions (where to draw the line if young adults are given priority) will inevitably be arbitrary. Policies for priority setting will therefore be essentially controversial, which further underlines the need that there are

(3) fair and reasonable procedures for justification, public consultation, and enforcement of compliance (Accountability).

There are strong moral reasons to give certain groups priority access to protection and/or therapeutic treatment:

(1) Professionals like health care workers who are involved in saving the lives of many others, should be given priority access to protection against infection (protective equipment, chemoprohylaxis in early stages, and vaccination). This helps to prevent nocosomial infections and sustainment of health care functions. Sustainment of health care functions is also a strong reason for giving these groups priority access to antiviral treatment if they develop illness.

The group of 'life-savers' may further consist of cullers, vaccine developers and other professionals who are necessary in response to the pandemic. Moreover, fire-fighters and other professionals who are involved in saving many persons from non-influenza related death might be included as well. Obviously, this argument to protect life-savers can rapidly inflate, giving very large groups of persons special status. Moreover, criteria like these can be easily abused by groups who are in power and who consider themselves important and irreplaceable. During the societal disruption of a pandemic, governments should be very reluctant to implement a broad criterion for 'indispensable' roles that are eligible to priority protection, as this will undermine public trust.

(2) Some groups will have a relatively strong claim to life-saving interventions, and equity supports prioritizing them in pandemic response policies:
(a) Persons who get ill and need medical treatment have a stronger claim to antiviral drugs (compared to the healthy who are not in need). This supports using antiviral stockpiles for therapy instead of prophylaxis.
(b) Persons who are at high-risk to get severe complications and die from influenza may have a stronger claim to vaccination (if they are not yet ill) and antiviral treatment (if they get ill) compared to persons who are at lower risk and for whom these interventions are less urgent.
(c) The fair innings argument supports giving priority to saving the lives of the young rather than the old. This may apply to prevention (vaccination) as well as to treatment. The fair innings argument does not specify 'where to draw a line' between persons who are eligible to priority

access, and those who are not. Such a 'line' will always be rather arbitrary, and depend on availability of resources. Such arbitrariness is however no reason to reject age-criteria altogether.

3. Antiviral drugs

3.1 Background, circumstances & main questions

If there is no effective vaccine against pandemic influenza, the main pharmaceutical option is antiviral prophylaxis and treatment. Given the unpredictability of virus characteristics, there is no evidence that current antiviral drugs will be effective against pandemic influenza effectiveness (Jefferson 2006). However, many experts and public health organizations assume that they will be effective and can play an important role in response to a pandemic (e.g. Hayden 2001).

There are two classes of antiviral drugs: M2 inhibitors (amantadine and rimantadine) and neuraminidase inhibitors (zanamivir and oseltamivir). In this report oseltamivir will be used as main example, without implying that this should be the only choice. Antiviral drugs affect the ability of an influenza virus to replicate in an infected individual. In this way they help to reduce both the spread of the virus within an individual (and hence symptomatic disease) as well as transmission of the virus to other individuals. In principle therefore, these drugs can be applied as general (pre-exposure) prophylaxis, post-exposure prophylaxis and treatment of symptomatic patients. Antiviral therapy will still allow mild infection that actively immunizes the patient against the strain (Stiver 2003). However, supplies of antivirals are limited and production capacity cannot be easily increased when a pandemic does arise. Therefore, stockpiling in advance is the only option for ensuring adequate supply (WHO 2004).

Oseltamivir applied as *therapy* should start as early as possible after first influenza symptoms in a person for maximum therapeutic effectiveness. A normal therapeutic course against seasonal influenza infection will last for 5 days. The duration and dose of anti-viral therapy needed for pandemic influenza will have to be decided upon. Timely treatment reduces the average disease with one or two days, but more importantly, it will significantly reduce the chance that a person will suffer the severest (including fatal) symptoms. After recovery, the person will normally have acquired immunity against the virus. *Post-exposure prophylaxis* with oseltamivir is possible when started as soon as possible after exposure. A normal course will take 7-10 days. (WHO Drug Information 2005;19(4): 274-285). Finally, antiviral drugs can be applied as full preventive strategy, that is, as *prophylaxis prior to (possible) exposure*. This would require taking the drugs as long as there are risks of infection, which might be up to half a year or more. However, many persons taking prophylaxis might not get infected anyway. Stockpiling for pre-exposure prophylaxis therefore requires very large quantities of antivirals, involving costs up to almost 30 times as much as costs for treatment stockpiles (Lee 2006).

Given this background, several interrelated ethical questions arise for priority setting in preparation and response to an influenza pandemic. Should governments build stockpiles of antivirals – and how should such investments be related to other health care resources? This issue is connected to the question whether antivirals should be used for therapeutic treatment or for prophylaxis. The objectives of antiviral policies will affect the decisions about the magnitude of stockpiles, but also have important implications for how antivirals are to be distributed: which groups should be given priority? A final ethical issue to be discussed briefly is whether private purchase of antiviral drugs should be prohibited if this would undermine public health policies.

3.2 The use of antivirals in a pandemic: general objectives

As discussed before, one important goal in response to a pandemic is to slow down the spread of infection and mitigate effects of the pandemic in order to gain time for developing a vaccine. Theoretically, this goal could be accomplished by giving all persons within a population access to antiviral drugs as pre-exposure prophylaxis. Prophylactic strategies for all persons would obviously save most lives, and prophylaxis for high-risk groups only would still save a very large group. In most countries however, this will be unfeasible given the amount of drugs required. Moreover, if some countries could afford building extremely large stockpiles, this would reduce possibilities for other countries (especially low- and middle-income countries with less bargaining power) to purchase antiviral drugs required for a reasonably minimum stockpile, given limited production capacities. Hence, if some countries aim at maximum protection against pandemic influenza this will reduce the possibilities for other countries to develop a very basic protection, which is unfair.

On the other hand, prioritizing antiviral drugs for *treatment* of symptomatic patients can be well supported on the basis of the moral framework discussed in the previous chapter. Early symptomatic treatment may prevent further transmission and hence create individual benefits as well as public health benefits. Moreover, assuming fixed expenditures on antiviral drugs, symptomatic treatment will save more lives (hence is more cost-effective in this sense) than prophylactic treatment of high-risk groups (Lee 2006).

By preferring therapy over prophylaxis, priority is given to treating persons who are in immediate need, which can be well-defended from an egalitarian perspective. Finally, if high-income countries decide to create their stockpiles for primarily therapeutic and not fully prophylactic purposes, this leaves middle- and low-income countries more possibilities to create a reasonable stockpile as well – possibly with support and aid from high-income countries.

Giving priority to therapy does not imply that preventive use of antiviral drugs is to be avoided completely. Targeted mass geographic prophylaxis at the source of a pandemic can have enormous effects on global public health. It might at least delay further spread of an early pandemic, and even contain the outbreak of a new influenza virus at the source (Longini 2005). Such efforts are essential for the protection of public health throughout the world, and targeted antiviral policies at the source of a pandemic should be supported by all nations, coordinated and carried out by the WHO.

If containment at the source is impossible and global spread does happen, national governments can still further delay the spread by means of post-exposure prophylactic treatment of persons (health care workers, household contacts, and others) who have had close contact with first index patients. This also helps to support and sustain health care facilities during the very first period of a pandemic. Prophylactic use of antiviral drugs should however not take away the supplies which are needed (and reserved) for treating patients. In this way, antiviral policies can create optimal protection of public health and human life, while minimizing unfairness.

3.3 Stockpiles and availability of antiviral drugs

Several studies have indicated that in high-income countries, stockpiling antiviral drugs for therapeutic purposes can be cost-effective or even cost-saving (Ballicer 2005; Lee 2006). This supports current policies in many countries to create stockpiles. It is not obvious that stockpiling is also cost-saving in middle- and low-income countries where the "financial earnings lost per death" will be less than in high-income countries. Of course, this should not be considered a reason to refrain from stockpiling in low-income countries altogether. The economic evaluation of premature death should not be confused with its moral value. Many countries however will not be able to purchase antiviral drugs at all, either because of the price or because of limited supplies and production capacities.

For an adequate global response to the threat of a pandemic it will be essential that there will be sufficient production capacity and access to antiviral drugs. This applies to governments in high- and low-income countries alike, as well as to pharmaceutical industry. If stockpiling activities of high-income countries further decrease other countries' chances to get access to antiviral drugs, it would be fair if the former reserved parts of their antiviral resources for purposes of health aid for the developing world. Moreover, if low-income countries have access to antiviral drugs, this might further motivate them to develop and maintain influenza surveillance, which is essential for global public health. Finally, governments and pharmaceutical companies have a shared responsibility to improve availability and affordability of antiviral drugs.

Governments of low-income and middle-income countries should set clear priorities, and though antiviral stockpiles should not be created at the expense of already insufficient basic health care resources, many activities might be less important than the protection of public health. On the other hand, maintaining a stockpile is very costly because drugs may expire before the pandemic occurs. Moreover, prescription of drugs and monitoring patient compliance requires a basic health care infrastructure that will be useful and important at all times. Many countries should therefore give priority to creating and maintaining such health care infrastructure and not focus health care resources to antiviral stockpiling.

The availability of antivirals may further decrease if persons and companies start creating private stockpiles. If this undermines necessary public health policies, governments have strong reasons to interfere and prohibit private sale of antiviral drugs. On the other hand, such liberty-limiting interventions can only be legitimate if public health policies in such a country – including procedures and policies for distribution of antiviral drugs – are well-justified and fair.

3.4 Priority targets and groups

It is essential that there are international (WHO) stockpiles for geographical antiviral prophylaxis, as part of rapid response to a first outbreak of pandemic influenza, aiming to contain the outbreak at the source. On a national level, a country will ideally have a stockpile of antiviral drugs:

a) which is sufficient to treat all citizens who develop influenza symptoms. The attack rate of pandemic influenza is unpredictable and there fore there is no clear guideline for the size of a stockpile (it may involve having sufficient courses for 20-50% of the population);
b) which allows for post-exposure prophylaxis (health care workers, household contacts) when pandemic influenza is introduced in a population, aiming to delay further spread of the disease;
c) and which allow supporting public health interventions or medical aid in countries that have no or insufficient antiviral stockpiles.

Within a country, which groups should be given priority? On the basis of the objectives and principles discussed in this and previous chapter, these priority groups can be distinguished:

1. Post-exposure prophylaxis for health care workers, at least in the beginning of the pandemic. This may both delay further spread and nocosomial infection and prevent that the health care system will break down during the first stage of the pandemic.

2. Treatment of all symptomatic patients

If it is not possible to treat all symptomatic patients there are strong reasons to prioritize:

a) *Professionals who are essential for saving lives and who get ill themselves.* Persons whose professional role is necessary for the aim to save lives or those who are indispensable for the sustainment of the health care system can be given priority because this is can be expected to maximize health benefits. This priority group includes vaccine developers and health care professionals, and possibly cullers and decontamination workers. Some sub-groups may also be given priority for reasons of fairness and reciprocity if they run a disproportionate risk in their efforts to fight the virus and save lives.

b) *Symptomatic patients in pandemic high-risk groups who are at increased risk for severe disease and death.* Both the principle to save most lives and considerations of fairness support priority antiviral treatment for influenza patients at highest risk to die. High-risk groups for seasonal influenza are elderly persons and immune-compromised patients. However, a new influenza virus may result in a different mortality pattern, and in the first stages of an influenza pandemic it will be necessary to specify and redefine high-risk groups.

c) *Symptomatic younger adults and children* on the basis of the fair innings argument. Obviously this priority may conflict with the previous one (groups at highest risk to die) if the latter group will consist of elderly.

In times of drug scarcity it is tempting to treat more patients with a decreased dose or shortened course of antiviral drugs. This will easily facilitate the development of drug resistant virus strains, which is harmful to treated patients as well as to public health at large. Distributing reduced doses among a larger group therefore should not be considered as a fair and just response to scarcity.

4. Priority setting in medical care

4.1 Background, circumstances & main questions

Timely antiviral treatment will prevent severe symptoms and fatal illness in many patients. For numerous other patients however, antiviral treatment will not be available, and patients who are treated with antiviral drugs may still have insufficient benefit of such treatment. These groups will develop fever, suffer painful symptoms and develop respiratory problems. In a pandemic, large groups of patients will require intensive care, including mechanical ventilation, and far more will at least need basic relief of symptoms. The number of hospital beds, both in general wards and in intensive care units will be insufficient, and it is unlikely that patients who are admitted will recover rapidly and be discharged. To compare, during the SARS outbreak in Singapore, the average length of hospital admission of SARS patients was 18 days (Fowler 2003). The average stay of Toronto SARS patients in intensive care units was 10.5 days (Lew 2003). During an influenza pandemic similar hospitalizations will be necessary, but simultaneously the number of persons who develop serious respiratory problems or otherwise suffer from severe symptoms, will grow steadily.

For several weeks or months, hospitals and medical services of an affected area will be unable to accommodate all health care needs. In these circumstances it is inevitable that seriously ill patients (potentially large numbers) will not get necessary life-sustaining treatment or even will be deprived of basic relief of symptoms. Like in the case of scarce antiviral drugs and vaccines, decisions about priorities must be taken. Triage of hospital care – notably mechanical ventilation – will however be much more dramatic, given that patients have acute and severe need. Patients who are excluded from mechanical ventilation may decease in short time. Physicians and nurses will face deep and tragic dilemmas. Which patients should be given priority? Can or should special beds or departments for influenza be allocated, and how should such allocations be weighed against the availability of medical care for persons who suffer from ‘regular’ diseases or accidents? Should triage criteria apply only to withholding or also to withdrawing medical care?

4.2 Objectives and principles

Triage involves ‘sorting’ patients in groups: some are excluded from treatment, others are considered eligible for treatment. Treatment and non-treatment decisions are paramount in health care, and often patients are excluded from (even life-sustaining) treatment because the intervention is deemed medically futile (Lelie & Verweij, 2003). However, in extreme scarcity, exclusion criteria will be much more restrictive than standards of medical futility, also excluding patients for whom treatment is still considered necessary and useful.

Similar to judgements about medical futility, triage decisions should be based upon professional standards that are publicly justifiable. In this way, controversial and deeply troubling decisions are not left to the discretion or subjective assessment of individual care-givers. Priorities should be based upon general triage criteria that are reasonably acceptable to anyone. On the one hand this involves appeal to the basic normative principles discussed previously, maximization of health benefits (notably saving lives) and equity. On the other hand, criteria should be defined and specified on the basis of medical evidence about health needs and factors which determine the chance of recovery.

4.3 Triage of mechanical ventilation

In critical care, the primary focus is on saving lives by countervailing acute health crises. Triage decisions aimed at saving the most lives with limited resources will give less priority to patients who are expected to recover less easily. Though such implications will be harsh and controversial, the basic principle to save the greatest number of lives possible, can be reasonably justified to anyone.

A first step in a fair and efficient triage system is to exclude patients from treatment for whom mechanical ventilation is not considered absolutely necessary. Arguably such patients will not be admitted to intensive care in normal times either. From a medical point of view, all remaining candidates will now be equally worse off; that is, all require mechanical ventilation to survive.

A second step would be to formulate triage criteria aimed at ‘saving the greatest number’. Such criteria should be evidence-based where possible. So far little work has been done in formulating operational rules for triage in intensive care units in times of pandemic emergency. Hick and O’Laughlin (2006) have presented three tiers of (mostly medical) criteria, which impose stepwise more severe restrictions to access. The idea is that, when application of tier 1 criteria does not yet accommodate supply and demand, triage need to be more restrictive, hence the more strict tier 2 criteria will be applied in addition to tier 1 criteria. Tier 3 criteria will be even more restrictive.

One ***example*** of triage of mechanical ventilation in a pandemic (Hick & O'Laughlin, 2006)

Tier 1: Do not offer AND withdraw ventilatory support for patients with any one of the following:

1. Respiratory failure requiring intubation with persistent hypotension (systolic blood pressure <90 mm Hg for adults) unresponsive to adequate fluid resuscitation after 6–12 hours of therapy and signs of additional end-organ dysfunction (e.g., oliguria, mental status changes, cardiac ischemia)
2. Failure to respond to mechanical ventilation (no improvement in oxygenation or lung compliance) and antibiotics after 72 hours of treatment for a bacterial pathogen (timeline may be modified based on organism-specific data)
3. Laboratory or clinical evidence of R4 organ systems failing
    a. Pulmonary (adult respiratory distress syndrome, ventilatory failure, refractory hypoxemia)
    b. Cardiovascular (left ventricular dysfunction, hypotension, new ischemia)
    c. Renal (hyperkalemia, diminished urine output despite adequate fluid resuscitation, increasing creatinine level)
    d. Hepatic (transaminase greater than two times normal upper limit, increasing bilirubin or ammonia levels)
    e. Neurologic (altered mental status not related to volume status, metabolic, or hypoxic source, stroke)
    f. Hematologic (clinical or laboratory evidence of disseminated intravascular coagulation)

Tier 2: Do not offer AND withdraw ventilatory support from patients with respiratory failure requiring intubation with the following conditions (in addition to those in tier 1):

Patients with pre-existing system compromise or failure including:

1. Known congestive heart failure with ejection fraction <25% (or persistent ischemia unresponsive to therapy and pulmonary edema)
2. Acute renal failure requiring hemodialysis (related to illness)
3. Severe chronic lung disease including pulmonary fibrosis, cystic fibrosis, obstructive or restrictive diseases requiring continuous home oxygen use before onset of acute illness
4. Acquired immunodeficiency syndrome (AIDS), other immunodeficiency syndromes at stage of disease susceptible to opportunistic pathogens (e.g., CD4 <200 for AIDS) with respiratory failure requiring intubation
5. Active malignancy with poor potential for survival (e.g., metastatic malignancy, pancreatic cancer)
6. Cirrhosis with ascites, history of variceal bleeding, fixed coagulopathy, or encephalopathy
7. Acute hepatic failure with hyperammonemia
8. Irreversible neurologic impairment that makes patient dependent for personal cares (e.g., severe stroke, congenital syndrome, persistent vegetative state)

Tier 3: Specific protocols to be agreed upon by guideline development committee. Possibilities include:

1. Restriction of treatment based on disease-specific epidemiology and survival data for patient subgroups (may include age-based criteria)
2. Expansion of preexisting disease classes that will not be offered ventilatory support
3. Applying Sequential Organ Failure Assessment scoring to the triage process and establishing a cutoff score above which mechanical ventilation will not be offered

What if tiered criteria are not sufficient to accommodate demand and supply?

Tiered criteria however will not prevent situations where several patients satisfy all criteria. How to decide in such a case?

One approach is to give responsible physicians discretion to make such decisions, on the basis of their medical assessment of the situations of all candidates. This raises some problems. In the first place, it will be difficult to avoid bias, subjective judgements, or even prejudice. Even when choices are solely based on relevant medical conditions (e.g. B's blood pressure is lower than A's, and therefore A's prospects are considered slightly better) this will be rather arbitrary, given that both A and B have already passed strict exclusion and inclusion criteria. The differences between both patients will be too small to justify saving A and not B, and therefore such a choice can be neither clearly justified on grounds of 'saving the largest number', nor on fairness.

Two other approaches however can be justified from a fairness point of view. The first is to save the younger of two persons, on the grounds of the fair innings argument. A 25-year old person has had less of his life than a 50 year old person, and therefore the first might be considered to have a stronger claim to life-saving treatment. Again however, this argument loses force when age-differences between candidates are very small. Although a 25-year old has had more time of life than a 24-year old, the difference is too small to justify saving the latter and not the former.

A second approach opts for procedural fairness: if there are no relevant differences between two patients, then both should have an equal chance to get life-saving treatment. Such last-resort decisions could be based upon a lottery or possibly a 'first-in-line' procedure.

Special treatment for patients with influenza-related disease?

There are two remaining issues concerning the scope of triage procedures. The first is whether the criteria and procedures apply to influenza patients only, or to all patients who require mechanical ventilation. Though there will be pragmatic reasons for 'cohort care' and special wards and intensive care departments might be designated for influenza patients, scarcity will apply to all critical care departments. It would be unfair to treat influenza patients differently from ' regular' critically ill patients. The same criteria and procedures therefore apply to all patients. At the same time, some regions and hospitals may face different levels of scarcity, and, assuming that possibilities to transport patients between hospitals and regions will be limited, different hospitals and regions may have different 'tiers' of criteria in place.

Just withholding or also withdrawing treatment?

A second issue is whether triage criteria must be applied for decisions to withhold *and* to withdraw mechanical ventilation. This is a controversial issue, because if the criteria are also used for withdrawing treatment, it will imply that patients are extubated for whom ventilation could still be beneficial (although they would be expected to have a smaller chance of recovery within limited time). However, if the criteria are not used for withdrawing patients, ICUs may soon be full of patients whose conditions are much worse than those of patients who need ventilation and who do fulfil the triage criteria. As a result of that, the gap between supply and demand will grow further, forcing the hospital to apply further tiers of criteria that are even more strict.

Is there a moral basis for *not* applying the triage criteria to decisions about withdrawal of treatment? Many physicians and other health care workers may feel they have a duty not to abandon their patients, which means they can and should give priority to patients for whom they have already accepted responsibility.[4] Though there are good pragmatic reasons for such special obligations in normal circumstances (for example they support relationships of trust), in the context of a pandemic such considerations are less appropriate. If very large numbers of persons get infected and require care, health care workers can no longer prioritize patients who are already commended to their care. They should give equal attention to all who need it, and aim to save as many patients as possible – which applies to patients who are treated as well as to those who wait to be treated. This supports applying triage criteria to decisions to withhold *and* to withdraw treatment. In the context of a pandemic, this means that it can be justified that patients are extubated who may still benefit from such treatment.

The latter conclusion will be controversial in many if not all societies. It might be that health care professions and the public simply do not accept such decisions, even if these are rationally justified. An efficient triage policy may then not be sustainable, which could be a pragmatic reason for not applying the triage criteria to withdrawal of life-support.

4.4 Allocating hospital beds

Triage of mechanical ventilation raises clear and important dilemmas. However, in large parts of the world there is no intensive care available at all, neither in times of a pandemic, nor in 'normal' circumstances. There will however be a shortage of supply of regular medical care in the hospital as well. How should priorities be set in allocating hospital beds? This topic is in a way much more complex than allocating mechanical ventilation. Withholding ventilation for someone who needs it will normally lead to fatal complications within short term. If a sick patient is not given a 'regular' hospital bed, it is not as clear what the consequences will be – this depends on the treatment and care that can be offered when the patient is admitted.

[4] Note that the well-established thesis that there is no moral difference between withholding and withdrawing treatment is not the central issue here. That thesis normally applies to decisions about futile or non-beneficial treatment. In the current context however, treatment is not withheld because it is considered futile for this patient, but because more patients may be saved if this patient is not treated.

What sort of care can be given to influenza patients in a non-intensive care setting? Apart from treatment of bacterial superinfections, most forms of treatment will consist of symptom relief: paracetamol and other drugs to relieve pain and fever; intravenous rehydration; especially patients with prior pulmonary disease will get short of breath and may need airway medication, supplementary oxygen, and respiratory drainage. Patients may feel so ill that they require help with feeding, etc.

There will however not only be pandemic influenza patients – other diseases and accidents will be as common as always. Many patients will still need surgery, radiotherapy, cardiologic treatment, orthopaedic treatment, psychiatric care, etc. Hence, there will be a very broad range of different patients requiring hospitalization, and, depending on available resources there will also be a broad range of treatments that can be offered – though shortages of supply will be paramount. All hospital departments may face shortage of syringes, IV equipment, antibiotics, and even clean sheets and beds.

The maximizing principle for priority setting cannot be applied easily in such circumstances. Determining which priorities will produce most effect will be rather impossible, because the data that is needed to compare the effects of completely different forms of treatment in the special circumstances of a pandemic is not available. Moreover, many interventions do not 'compete' directly; hence it makes little sense to compare the cost-effectiveness of radiotherapy for certain cancer patients with primary care for influenza patients. Specialized wards, equipment, and staff cannot easily be given a different task, and cancer patients may not be helped by providing them with just a hospital bed and basic supportive care.

Some recommendations however are sensible and may find support on the basis of the maximization principle and the principle of equity.

1. To save lives and sustain the health care system it will be important to prevent nosocomial infections where possible. This supports assigning special wards or hospitals for influenza patients. Arguably, an influenza pandemic will also require the creation of a setting for giving influenza patients basic (non-specialized) supportive care and symptom relief.
2. Patients should be treated and cared for at home, by their family members, whenever possible. Priority in *non-specialized* hospital care and primary care beds should be given to patients who do not have family members who can give them the care they need.
3. In some cases regular treatment for e.g. a cancer patient, will be unsafe or insufficiently effective if a patient acquires influenza. In some specialized departments or treatment facilities (oncology, surgery, etc.) it may therefore be justified to give priority to *non-influenza* patients, and to postpone interventions for patients who do develop influenza. However, such a decision may be equally appropriate in a non-pandemic context.
4. All hospital departments will face scarcity and therefore need to set priorities more strictly. In many contexts there will be insufficient empirical basis for specifying criteria that aim at maximizing health benefits, given the broad range of patients, needs, and treatment possibilities that should be taken into account in such calculation. Setting priorities on the basis of medical need however – hence to prioritize patients who are worst off from a medical point of view – may be more feasible. Hence, like in 'normal' health care circumstances, there are good reasons for distributing hospital beds and medical care primarily on egalitarian grounds, that is, to give priority access to patients who need medical treatment most urgently.

4.5 Conclusions and recommendations for pandemic preparedness and response

Most influenza patients will require (at least) basic medical and nursing care and relief of symptoms. Many of them may be treated and cared for at home, with some support from nurses and general physicians. Such basic care requires adequate primary care facilities and infrastructure – which may not be available anyway in low-income countries, especially in rural areas. Developing and maintaining such infrastructures for primary care is a major priority for pandemic preparedness in those contexts, especially because such investments will be beneficial anyway, and not only during a pandemic.

In intensive care facilities, priority setting during a pandemic should focus on saving the most lives possible. This can be done by developing several tiers of successively more strict medical criteria for inclusion and exclusion of patients. Such criteria should be based upon medical evidence. Yet even when the most restrictive criteria are applied, there will still be situations where there are two or more patients eligible for one ICU. In such a case, it would be just either to give priority to the patient who is significantly younger, or to give all patients an equal chance to treatment by means of fair procedure (i.e. a lottery).

Allocating non-ICU hospital beds might seem slightly less dramatic, but ethical decision-making will be even more complex than in ICU settings. Though the general principles of maximization and fairness still apply, it is difficult to specify these in terms of clear guidelines for priority setting. Some practical recommendations are to avoid nosocomial infections by creating special departments for influenza patients and to give persons without family support priority access to basic care facilities. Considerations of equity further support the allocation of non-ICU hospital beds and medical care according to medical need.

Shortage of hospital beds, intensive care and medical facilities will create deep moral dilemmas for health care workers and the decisions and policies that need to be made will raise public controversy and anger, because the consequences of priority setting are acute. Very ill persons may be left without treatment and professional care if they do not get a hospital bed. Critically ill patients may die very soon if others are given priority access to mechanical ventilation.

In situations where basic life-support is scarce, the risk is great that vulnerable groups will be ignored easily and powerful persons and groups will be cared for first. From an ethical point of view however, equal persons must be treated equally. Developing clear and fair procedures for decision-making (chapter 2.5) is essential. As argued before, decisions about priority setting should not be made on a case by case basis, but as far as possible on the basis of prior established, general criteria that are publicly justified. This also decreases some of the burdens of responsibility for health care workers.

5. Vaccination

5.1 Background, circumstances & main questions

An effective vaccine will offer the best form of protection against pandemic influenza. Vaccination does not only protect the vaccinated individuals from getting ill, if sufficient people are immunized, this will also reduce further transmission of the virus within the population and hence prevent infections. Even if the vaccine is poorly matched to circulating virus strains, it may have large effects on a population level (Germann 2006; Ferguson 2006).

It is however not expected that such a vaccine will be available within 6 months after the start of a pandemic, and for large numbers of people this will be far too late. Even when a vaccine has finally been developed and approved, there will be insufficient production capacity to accommodate the enormous demand world-wide.

One difference with previously discussed interventions (antivirals and medical care) is that influenza vaccination can only be applied as preventative measure. Therefore, the target group consists solely of persons who have not yet been infected. Persons who have been infected with the pandemic virus strain and who recovered from illness or only had mild disease, will already have developed immunity and do not need vaccination. Timely antiviral treatment of symptomatic influenza patients does not obstruct such natural immunization.

Yet even when the virus has spread over the world for 6 months or longer, many persons will not be immune yet, and for them vaccination will offer the best form of protection – but it will be scarce. A second important difference with previous discussions is that vaccine supply, in contrast to antiviral drugs and medical care, will be increasing over time. Some high-income countries will aim to produce or purchase sufficient vaccines for all target groups, but not all groups can be vaccinated at once. The ethical question is then: which groups should be *first in line* to get the vaccine, and who should get it (several weeks or months) later? In low-income countries, again, supplies will be severely limited, and then the ethical problems of priority setting will be more like in the previous chapters: who should be vaccinated if not all can?

Vaccination against pandemic also raises a completely different issue. An effective vaccine against pandemic influenza will be quite different from current vaccines against seasonal influenza. Such newly developed vaccines however raise concerns about safety and therefore will be subject to strict regulations. Is it justified to streamline legal regulations for vaccine approval if such a new vaccine may mitigate a devastating pandemic? This issue will be discussed briefly in 5.3.

5.2 Ethical considerations for vaccination priorities

In the previous chapters it has been argued that giving priority to persons who are at high risk of acquiring lethal disease can be justified from the point of view of saving most lives, and from considerations of equity. In the case of vaccination however, other priorities may be also be efficient and fair, or even be preferable on grounds of equity.

First, vaccination programs can have a strong impact on virus transmission, yielding health benefits that go beyond the benefits of vaccinated persons. However, this is only possible if vaccination is targeted to groups that play an important role in transmission e.g. schoolchildren, Longini et al 2004), and it is well possible that this will not be a group that is at greatest risk of acquiring lethal disease. Possibly, vaccination of groups with highest mortality rates would save most lives, but this will offer less protection to the population as a whole.

Second, as argued before, an egalitarian approach would favour persons who are worst-off. Yet it is not obvious that persons who healthy now, but would be at high-risk to die if they got ill, are to be considered to be worst-off now and therefore have a stronger claim for vaccination. In a pandemic anyone (also persons in low-risk groups) face risk: anyone can develop influenza and may experience severe, even lethal complications. It would be unfair if persons at clear risk are not given access to vaccination at all, only because others run an even larger risk to lethal infection. Moreover, vaccination of high-risk persons may make them even *better-off* than persons in low-risk groups, hence, it is not obvious at all that prioritizing them would be fair.

From the point of view of fairness, the most equitable approach may therefore be a weighted lottery, in which all persons participate, but where higher risk increases one's chance to vaccination. In such a way, the chances to survive the pandemic could be spread more equitably (Cf. Taurek 1977, Broome 1984). Many pragmatic reasons may count against applying lottery procedures for life-protective interventions, and certainly it would be difficult to assign weights fairly. A different approach would be to take into account that – at least in some countries – the supplies of vaccine will increase over time. Though persons at highest risk may not have a stronger claim than others on vaccination *per se*, but given their increased risk protection is more urgent for them. Hence they have a stronger claim to be vaccinated first, assuming that others can be vaccinated later. Setting priorities over time may be a reasonable alternative to the weighted lottery. To conclude, if the increasing supplies of vaccine will be sufficient to vaccinate all persons in a population within a limited time, then it is reasonable to vaccinate high-risk groups first. If it is clear that not all can be vaccinated, fairness may require different vaccination priorities.

Third, by now it will be clear that there are also egalitarian ('fair innings') arguments for giving priority to children and younger adults. If young persons can also get ill and die, then vaccination protects their chances to live up to a reasonable life-span and have their fair share of opportunities in life. This supports (again) decisions to consider children as a priority group, but it might also give reasons to prioritize younger adults above the elderly. Assuming that elderly will be at high-risk, this direction might well conflict with considerations in the previous paragraph.

Finally, health care workers and other life-savers who are still not immune when a vaccine becomes available may be given priority access because that will produce indirect health benefits. Vaccination prevents both severe and mild disease and will therefore promote that health care workers continue their important work in a health care system that is already under severe pressure.[5]

5.3 Research and safety considerations

Developing a vaccine against pandemic influenza is of clear importance. An effective and useful vaccine against pandemic influenza will however be quite different from current vaccines against seasonal influenza. It will be necessary to induce sufficient immune response with a vaccine dose as small as possible – which would enable vaccinating much more persons than if larger doses or more injections per person are needed. Two possibilities to create sufficient response with low vaccine doses are to use whole (inactivated) virus instead of less reactogenic subvirion vaccines; or to use vaccines that contain adjuvants that boost immune responses (Nicholson 2003). Another relevant development is to enable vaccine production on the basis of cell cultures instead of on the basis of eggs which may be short of supply given that the pandemic influenza strain may originate from a bird flu virus.

The use of a new vaccine type however raises moral and regulatory issues about safety. What side-effects would be acceptable? Given the potential effects of vaccination on the spread of pandemic influenza and on mortality, even a relatively high frequency of side-effects, or the occurrence of some harmful effects, may still be acceptable. Evaluation of risks will however not be a simple calculation of aggregation of harms and benefits. For example, if there are concerns about the safety of a new vaccine, it will be problematic to vaccinate children for the common

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[5] It is less clear that such vaccine priority can also be based on reasons of reciprocity (cf. 2.5). If health care workers, while working for the common good, face disproportionate risk of infection, reciprocity supports giving them priority access to protection, in order to compensate for the increased risk. It would be unfair if their risk is higher than that of other, comparable citizens. However, fairness will not support reducing their risk far below that of other citizens – which is what effective vaccination might do. Cf. Murphy 2006.

good (as argued in the previous section). If there is significant risk in the vaccine, it is unfair to 'use' children and childhood vaccination to protect the population at large, especially given that most children will not be able to consent to vaccination. Arguably, although vaccine side-effects may be justified more easily in a pandemic, the safety requirements for a vaccine will be very strict, if only because, like in normal times, vaccination programmes will not be successful if people do not trust the vaccine to be safe (Verweij & Dawson, 2004).

There will also be many legal and regulatory issues before a new vaccine can be used to protect populations. If harmful effects are accepted more easily during a pandemic, it might be unfair to hold vaccine producers liable for all such effects. Hence, clear arrangements are necessary, if only to promote vaccine producers to develop effective means for immunization. A second issue concerns the approval of a new vaccine. All persons have a shared interest in regulatory policies that enable vaccine produces to bring effective and safe vaccines to the market as soon as possible. This should not preclude thorough assessment of vaccine safety. On the other hand, vaccine approval regulations throughout the world may be further harmonized and streamlined. For example, ideally formal approval of a vaccine in the USA would be sufficient for approval in Europe as well, and vice versa.

5.4 Conclusions and recommendations for pandemic preparedness and response

The discussion of influenza vaccination supports several, sometimes competing directions for priority setting.

1. Vaccinating children may be most effective in reducing transmission and hence in reducing the attack rate of pandemic influenza. Though such an approach may not save most lives, it does provide protection (external benefits) to the public at large. Hence, vaccinating children may offer all persons (who are not yet immune) within a population a prospect of benefit.
2. For persons in pandemic high-risk groups vaccination is more urgent than for persons who are at low risk of severe disease, but it is unfair to vaccinate only them if not all can be vaccinated. If the increasing supplies of vaccine will be sufficient to vaccinate all persons in a population within a limited time, then it is reasonable to vaccinate high-risk groups first. If it is clear that not all can be vaccinated, fairness may require different priorities.
3. Children and young adults have a strong claim to vaccination on the basis of the fair innings argument. (1) and (3) together give strong support to prioritizing children.
4. Health care workers and other 'life-savers' may be given priority access to vaccination, not on grounds of reciprocity, but in order to produce indirect health benefits.

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