

Ethics of Outbreaks Position Statement. Part 1: Therapies, Treatment Limitations, and Duty to Treat

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Objectives: Outbreaks of disease, especially those that are declared a Public Health Emergency of International Concern, present substantial ethical challenges. Here we start a discourse (with a continuation of the dialogue in Ethics of Outbreaks Position Statement. Part 2: Family-Centered Care) concerning the ethics of the provision of medical care, research challenges and behaviors during a Public Health Emergency of International Concern with a focus on the proper conduct of clinical or epidemiologic research, clinical trial designs, unregistered medical interventions (including vaccine introduction, devices, pharmaceuticals, who gets treated, vulnerable populations, and methods of data collection), economic losses, and whether there is a duty of health care providers to provide care in such emergencies, and highlighting the need to understand cultural diversity and local communities in these efforts.

Design: Development of a Society of Critical Care Medicine position statement using literature review and expert consensus from

the Society of Critical Care Medicine Ethics committee. The committee had representation from ethics, medical philosophy, critical care, nursing, internal medicine, emergency medicine, pediatrics, anesthesiology, surgery, and members with international health and military experience.

Setting: Provision of therapies for patients who are critically ill or who have the potential of becoming critically ill, and their families, regarding medical therapies and the extent of treatments.

Population: Critically ill patients and their families affected by a Public Health Emergency of International Concern that need provision of medical therapies.

Interventions: Not applicable.

Main Results: Interventions by high income countries in a Public Health Emergency of International Concern must always be cognizant of avoiding a paternalistic stance and must understand how families and communities are structured and the regional/local traditions that affect public discourse. Additionally, the obligations, or the lack of obligations, of healthcare providers regarding the treatment of affected individuals and communities must also be acknowledged. Herein, we review such matters and suggest recommendations regarding the ethics of engagement in an outbreak that is a Public Health Emergency of International Concern. (*Crit Care Med* 2018; 46:1842–1855)

Key Words: disease outbreaks; ethics; experimental therapies; medical research; moral duty; public health

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The purpose of this position statement is to start the dialogue concerning the ethics of the provision of medical care, research challenges, and behaviors during a Public Health Emergency of International Concern (PHEIC) with a focus on the proper conduct of clinical or epidemiologic research, clinical trial designs, unregistered medical interventions (including vaccine introduction, devices, pharmaceuticals, who gets treated, vulnerable populations, and methods of data collection), economic losses, and whether there is a duty of health care providers (HCPs) to provide care in such emergencies, and highlighting the need to understand cultural diversity and communication with local communities in these efforts.

This dialogue continues in Ethics of Outbreaks Position Statement. Part 2: Family-Centered Care (1) with a specific focus on the provision of family-centered care in critical illness during a public health disaster. This report was constructed by literature review, and the Ethics Committee of the Society of Critical Care Medicine (SCCM) iteratively reviewed and approved the document during its development and approved the recommendations by expert consensus. Recommendations were further approved through the SCCM leadership team.

The Ebola epidemic presented enormous medical and ethical challenges. The epidemics of HIV and severe acute respiratory syndrome (SARS) previous to the recent Ebola epidemic and the subsequent Zika virus epidemic, all caused a significant highlighting of public concern and a demand for intervention. However, the ferocity of Ebola that shook the international medical community was exceptional (2, 3). SARS, although deadly, was more limited (4). Zika disease seems to be on its way to being relatively well controlled, understood, and mastered (5, 6). HIV, although fraught with social inaction, injustice, and prejudice, was an epidemic with highly educated activists who knew their disease, potential interventions, and the need of increased access to medical care (2, 7). Ebola, on the other hand, occurred in a considerably different environment. Ebola patients in West Africa generally could not provide valid individual informed consent and did not understand the various potential medical interventions; this was a problem of limitation to individuals' educational status and the rapid spread of the disease in an arena of extremely scarce resources (2). Here, we will review the ethics of therapies and the use of experimental interventions and conduct of research during a medical crisis/outbreak, treatment limitations, and the duty to treat versus the right to refuse to treat patients in the face of outbreaks. Each section will have search strategy and a background, which will be followed by recommendations to be considered by the medical and public health communities, generally.

I. THERAPIES: USE OF EXPERIMENTAL INTERVENTIONS IN MEDICAL CRISES

Search Strategy

PubMed MeSH and Google Scholar headings were searched iteratively for combination of disease outbreaks, clinical ethics, vaccine therapies, clinical trials (as a topic), informed consent, hemorrhagic fever, Ebola, and World Health Organization, resulted in 879 citations. The results were refined based on content and relevance as well as the identification of additional relevant citations through the review process. After deleting duplicates and those that were off topic, 72 were found to have information that informed this document. The following points are emphasized:

- Justification for experimental therapies in times of healthcare crises.
- Cautions of conducting medical research in times of a healthcare crisis.
- Recommendations.

Background

During an outbreak scenario, elimination of the disease from the community is of paramount importance; however, there is also a need to collect data with respect to epidemiology, drug efficacy and safety, and other treatment options. This is especially important with respect to an emerging pathogen or novel biochemical agent, in which case various stakeholders exist with differing priorities and needs that must be balanced. The perspectives of the various stakeholders may not share the same sense of urgency secondary to educational, economic, political, geographic, and/or social/cultural differences (8–13). Irrespective of the intervention, the question of who receives the therapy or vaccine and the order in which they are chosen will always arise and must always be tied to a therapeutic safety net and be based on sound ethical principles (14).

In a dangerous, large-scale emerging infection, the risk of contagion and the resultant morbidity and mortality must be significant enough to justify a novel or untested vaccination or treatment program. Such a justification includes the likelihood of transmission, the agent's severity, and/or its duration of effect (15). Although there are situations where emergency vaccinations or therapies have a low yield (high percentage of people already vaccinated or remote chance of an outbreak), diseases exhibiting high mortality in the face of no vaccines/therapies are exemplary situations where the rapid introduction of novel vaccines/therapies may be warranted when weighed against the risks of no treatments. Here, we will discuss the potential benefits and risks regarding experimental or untried therapies/interventions and the conduct of medical research in times of a healthcare crisis. There are gaps in knowledge regarding this area (the ethical issues of infectious disease), and the World Health Organization (WHO) has attempted to address them through their international repository for information sharing (16).

Justification for Experimental Therapies in Times of Healthcare Crises. *Life-saving medical interventions.* The world's recent experience with Ebola virus disease (EVD) has forever impacted the scientific, social, political, and economic communities' views of outbreak interventions and has brought to light the accompanying ethics of those interventions. In the case of an outbreak that is acutely devastating and has a high mortality rate, especially in a resource poor country, the WHO has declared that interventions which may have benefits, but whose efficacy is unknown and whose side-effects cannot be defined, may be initiated as long as the risks and benefits undergo continuous and simultaneous evaluation with sharing of data and provided that the population/government receiving the vaccine or clinical therapy are in agreement (12, 17, 18). Even before the recent Ebola epidemic, it was deemed ethically acceptable in the face of a life-threatening disease affecting thousands of people to provide the unquantifiable risk of unproven therapies (19). During the recent Ebola crisis, it became evident such a risk may be necessary because so many places in the world were at a significant disadvantage with respect to supplies, infrastructure, and preparation. As Briand et al (20) pointed out with regard to Ebola in Africa in 2014,

“Health services are understaffed, essential personal protective equipment (PPE) is in short supply. Capacities for laboratory diagnosis, clinical management, and surveillance are limited, and delays in diagnosis impede contact tracing. On top of these problems, health services are operating in a climate of fear and discrimination.”

Rapidly Gaining New Knowledge. Quality data acquisition and research are necessary in order to rapidly gain the benefit of new medical knowledge to help fight or prevent disease. In order for such data acquisition and research to take place during a crisis, several conditions need to be met. First, a valid research question must be formulated quickly, effectively, and accurately, and second, a sound research methodology must be employed. A simple, testable hypothesis is the most important component of successful conception and implementation for any therapeutic or vaccine intervention (21). If an intervention is not fully justified, ethical, and feasible, then agents of unknown efficacy should not be used without an organized framework for accurate and timely documentation of illness severity, clinical course, treatment details, adverse events, and clinical and nonclinical confounding factors (21). According to Muller-Nix et al (21), it is expected that a clinical trial performed during an outbreak has a valid comparison of cohorts treated in a different manner, which can then guide design of subsequent, more targeted trials, and interventions.

Decisions about the type of trial can stir debate. It is argued that rigorous evaluation through randomized controlled trials (RCTs) is the most accurate way to assess vaccines (8, 22–24), while at the same time not losing focus on the ethical requirements and implications of projects (9, 25). Nonetheless, in the face of an overwhelming infectious threat to a population, there must be an epidemiologic adaptation that favors speed and that in the presence of an ethical framework, can offer the best result, in the fastest manner, with the smallest kill of

scientific accuracy and precision. The WHO recommends that “A single data monitoring and oversight committee should have real-time access to all data. The study design should allow data to be evaluated in real-time to permit the adaptation of interventions as data becomes available” (12) (Table 1).

Suggestions have been made on the basis of WHO and the U.S. Food and Drug Administration (FDA) process and supporting documents, regarding unapproved interventions during a PHEIC (26). Singh (26) addressed the acceleration of drugs, devices, and products to the field through the utility of comprehensive regulatory mechanisms. He argued for time-sensitive access to unapproved interventions by: 1) emergency use of investigational new drug regulatory pathways, 2) investigational interventions through emergency use authorizations, 3) interventions through use of approved drugs for nonindicated uses, 4) investigational interventions through the partial lifting of suspended/halted clinical trials, and 5) use of investigational drug products when human efficacy studies are not ethical or feasible. This perspective stresses that: 1) in the face of death where there are a dearth of preventive, therapeutic, and diagnostic choices, unapproved interventions should be permitted; 2) regulatory threats/deficits in governments and their agencies must be altered/reissued in view of (1); 3) understanding governmental/FDA regulatory mechanisms may be helpful in responding to a catastrophic outbreak by providing effective guidance on regulatory adaptation to the threat; 4) vigorous monitoring and vigilance are needed in the creation and distribution of safe and effective products; and 5) a worldwide rapid deployment network is necessary for provision of these unapproved interventions. In view of the effects of a PHEIC on vaccine or therapeutic trials, the ethics of the trial design, and any unapproved interventions, require a serious consideration for the respect of persons, beneficence, and justice.

TABLE 1. Considerations on Potential Study Designs to Obtain Additional Scientific Evidence on Effectiveness and Safety in Public Health Emergencies of International Concern^a

The study design should minimize bias in evaluating the causal effect of the intervention. This must be balanced against demand for treatment, equity, and other ethical considerations.
Case reports, case series are valuable. However, unless there is a dramatic effect, validation of efficacy is limited without a control group.
Observational studies that have defined data collection protocols comparing outcomes between those who had a defined intervention and historical controls or a concurrent control group will be problematic in the interpretation of outcomes in regard to observed or lack of observed differences.
Randomized, placebo-controlled trials may not be ethical. Randomization into two different experimental therapies is more acceptable. Patients unwilling to be randomized can be followed as a control group that receive the usual and customary care. This improves the generalizability of the results. Here, there is a demand for true equipoise in regard to the relative value of the two treatments when compared with standard care.
Level of randomization or other method of allocation whether it is individual or cluster.
Multiple arms of treatments and different subgroups can be evaluated by adaptive randomized control trial designs.
It is very important to take in considerations between the differences in potential study designs for therapies, vaccines, and between prophylactic and therapeutic intervention groups.

^aAdapted from Box 2, WHO (12).

Cautions Regarding Conduct of Medical Research in Times of a Healthcare Crisis. Protection for vulnerable populations (individuals and governments). The protection of vulnerable populations should be at the forefront of medical/public health, social, and philosophical thought, and it is particularly noteworthy in regard to the conduct of research in times of crisis. Although medical ethics usually deals with the individual, this can present a different problem when the individual is the member of a nation with marginal economic viability inasmuch as cultural, ethnic, and religious differences must be respected and acknowledged (27). Providing experimental or unproven therapies in times of crises imposes risk. The possibility exists that large numbers of subjects will receive treatments of questionable efficacy and may lead to harm (21). During the SARS outbreak, an arguable failure to channel/focus limited resources into well-organized, standardized, controlled clinical trials resulted in misdirection of valuable resources into questionable applications of medical treatments (21). Muller-Nix et al (21) question whether clinical trials can be conducted during global outbreaks, and if so, what steps should be taken so that trials are appropriate and safe.

Respect for persons, or autonomy, is the quality or state of being independent, free, and self-directing (28). This concept applies to the ability to make an informed decision with regard to which activities one is willing or not willing to participate in. Informed consent for study participation requires four conditions: 1) understanding of the research interventions, 2) appreciation of the ramifications of the decision to either participate or not participate, 3) ability to reason through a decision, and 4) ability to make a choice and state it clearly. Outside influences are present but should not be unduly influential (29). A number of important considerations have to be mentioned in this context, especially with respect to outbreaks and/or epidemics (30). Key concepts to consider, especially in the setting of underdeveloped or developing nations, include: 1) assent requirements, including the elements of assent, assent protocols, age of assent, and a minor's ability to dissent (the American Academy of Pediatrics states that children's assent should not be sought unless their dissent will be respected); 2) parental permission requirements; 3) the presence of any financial incentives; 4) public, peer, or societal pressures; and 5) level of education and the ability to understand potentially complex concepts (31).

Autonomy becomes further complicated when a person or community is faced with near-certain death or disability when a physiologically crippling outbreak occurs, being forever mindful that the Western concept of autonomy may not translate to the area where the outbreak occurs. How can an individual or a community refuse? They can refuse, but this is difficult, especially when village elders, through culture and tradition, have powers to make or influence the thoughts of communities (11, 32). Additionally, besides accepting participation in a therapeutic intervention, there should be an understanding regarding participation in the "different types" of trial designs (8, 10, 12, 17, 19, 23, 33–36). These include

randomized control trials, cluster trials, stepped wedge/stepped role out trials, sequential analyses, parallel tracking, adaptive design, and block randomization within small centers with analysis matched by center. Investigators and clinicians must weigh whether the "standard of care provided" should follow the most advanced standards available globally, especially if the trial is being sponsored and/or carried out by nonlocal investigators (37). As described in the Belmont Report, HCPs have an ethical duty to provide beneficial interventions to the populations in which studies are being conducted (38, 39). Consequently, it is the duty of both the regulators and the investigators to ensure that treatments offered to study subjects have therapeutic potential.

The subject of children in therapeutic trials or vaccine trials typically generates much interest. They are a vulnerable population; they may be unable to or have a reduced capacity to consent (40–41). Although it is important to include children in therapeutic trials (44), there may reasons not to include them in vaccine trials (45). For instance, with regard to tuberculosis (therapeutic trials), children less than 18 years old represent a large percentage of this disease worldwide, and the number of pills they have to consume causes difficulties with respect to side effects, toxicity, and length of treatment (44). Their inclusion is important because: 1) they are vulnerable and (2) preserving a child's life will result in more significant disease reduction and more years of a healthy and economically productive span of life (15). However, with regard to vaccine trials, controversies may develop. Using an unvaccinated control population when an efficacious vaccine already is available is extremely controversial (45, 46). A WHO expert panel has delineated four situations in which a placebo may be used in vaccine trials (44). These include: 1) the need to assess complex toxic effects and tolerance in children, 2) research addressing a question relevant to the local health priorities, 3) the need for novel therapies, or 4) when there is a significant anticipation of adverse events from the disease or the coadministered medications. There may be times when cultural differences may impede this perspective in that some cultures may consider parturients and the elderly as having a higher social priority (45).

In regard to desperate and vulnerable populations and governments, respect for the local community must remain front and center. Advocacy for the local populace at the grass roots level is important. Supportive strategies must be presented to families, whether it is psychologic, medical, or nutritional, etc (48). Such advocacy can be from individual providers or from an intervening organization. Families of patients should be present and engaged by the individuals and organizations providing the outbreak support. Every effort should be made to ensure maintenance of family integrity throughout the crisis. Maintaining mothers and their children as an integral unit for care and support should be given unequivocal special consideration. In many resource-poor areas, lack of maternal support for a child can lead to poor health or even death (49, 50). Every consideration should be given to supporting mothers and their children in any research trial or provision of vaccine therapies.

Along with advocacy, cultural sensitivity and the engagement of community elders should not be overlooked. Many times, especially as it related to children, grandparents or community elders may be making or assisting in decisions, medical, social, digital (electronic big data medical formats), or otherwise (51–53). Furthermore, digital epidemiology, while an embryonic field, is moving to the research forefront rapidly (54). Its impact on local communities can have a substantial economic, social, and political impact. Key ethical challenges that this new research perspective brings will require involvement of elders and exquisite cultural sensitivity (55).

In this context, it is also of importance to clinicians, researchers, and critically ill patients that consent for treatment be appropriate. In disease outbreaks, events and illnesses may move quickly, and ill patients may not be able to provide consent. Scientist and clinicians realize the need for varied consent models, so they can increase their ability to be effective in future pandemic research endeavors (56). However in these situations, consent may be required from next of kin, or the community, and/or there may be need for the use of a deferred or waived consent model. The rapid evidence review of English language publications from 1996 to 2014 by Gobat et al (57) found that consent models using waived, deferred, third-party models seem to be broadly accepted; nonetheless, there needs to be more work done on epidemic/pandemic research consents. Some have also argued that use of alternative consent models may depend more on the capacity of patients than the urgency of the epidemic (58). Furthermore, consent may need to be obtained through various communications media, such as verbal (through translators or not) or by phone (57). Consent needs facile communication and mutual understanding between all stakeholders because myths and misconceptions must be addressed if any interventions are to be successful (59). Risks and benefits need to be made clear. The local community and culture must be understood well. Women's access to maternal medical services are often influenced by husbands, in-laws, traditional attendants, family, the community (52), and by religious leaders (51). The WHO Ethics Committee has reviewed studies done during the Ebola virus outbreak and has made some general recommendations in order to hasten approval of needed studies during pandemics (60). Also, a number of international groups have sought ethical approval for ICU data collection and have ethics policies in place, including the International Severe and Acute Respiratory Infection Consortium along with the Short PeRIod Incidence sTudy of Severe Acute Respiratory Infection (61).

Rushed or Poor Methodology and the Pitfalls of Data Misinterpretation. Care must be exercised during a crisis when considering vaccines in the early stages of development or other therapeutic interventions, especially when there are no current evaluations for safety and efficacy. In the setting of a need for speed in the presence of impending disasters, HCPs, researchers, and administrators must be cognizant of not inflicting harm. A rush to production of multiple vaccines to distribute to multiple countries may have to pass through

multiple ethics committees and even pharmacy and therapeutics and safety committees (12). The same can be said for experimental therapies. Here, much caution and care must be exercised. In a recent editorial in *Nature*, staff pointed out that the humanity of researchers is an enemy of robust science (62). Physicians and researchers have an obligation to be right, find patterns in everything, support truth, and ignore that which does not fit the evidence. There has been very poor reliability in regard to the analysis for bias in making medical decisions on current published studies (63), and although randomized clinical trials may be our best effort to analyze a problem, they are poor in regard to avoiding risk bias (64). A commentary, by Begley et al (65) in *Nature*, addressed the burden of irreproducible results (up to two of three survey respondents could not reproduce their published scientific results on at least one occasion) that is hampering the confirmation of medical evidence. Additionally, the work by Ioannidis et al (66) in regard to why most published research findings are false is appropriate to consider, as well as the study of Iqbal et al (67) that reported on a random sample of 441 biomedical journal articles from 2000 to 2014 in which only one study provided a full protocol and none provided all the raw data; studies that were replicated were very rare ($n = 4$). In this vein, the issue of the best methods in an outbreak scenario(s) should be addressed ahead of time by international consensus.

Potential for Unfair Allocation of Treatment and Preventive Resources. The concept of justice in a large devastating outbreak in poorer regions of the globe, such as the recent events related to EVD, easily comes to the forefront. Even if an experimental vaccine reached such an area, will it first go to the local population, or will it go to foreign workers from the West? How much vaccine exists for distribution? Will drug companies provide resources in such an endeavor to help the disadvantaged, even if the outbreak is not a threat to more affluent countries? In the end, ethical considerations demand that the countries affected need to have input into the plan for allocation of experimental interventions employing the same ethical principles that govern the allocation of other healthcare resources (47).

Regarding the subject of healthcare workers, it can be argued that their risk with regard to exposure to disease also makes them vulnerable, so under the rule of reciprocity (the concept of distributive justice), they may be vaccinated and treated because they are providing protection to the community through their care of the sick (68).

Appropriate Time or Personnel for Safeguards. Personnel treating infectious patients during an outbreak must be cognizant of their own safety at all times. An infected healthcare worker is a hazard to others and a lost asset of importance to the treating team. The type of PPE needed, and how to don and doff, it is extremely important (and can be found at a Centers for Disease Control and Prevention [CDC] website) (69). PPE is especially important when working with patients affected by a filovirus (Ebola and Marburg); a small inoculant is highly lethal. Using the recommended PPE can also cause an environmental hazard to the wearer. In tropical environments, PPE can cause impaired cooling, dehydration, unstable posture,

and loss of awareness and cognizance (70). Worker tolerance of the PPE wanes after 40 minutes of use. Staff training, a safe and well-engineered environment, treatments units that are appropriate to code, along with limited shift times and access restriction, are important safeguards (70–72). These criteria curtail patient contact/care time and necessitate the need for increased numbers of treatment personnel (70, 73). The economic aspects of an increased rate of consumption of supplies and the shipping/travel involved also need to be considered (70).

Recommendations. Recommendations in regard to global issues surrounding vaccine and therapeutic trials during a PHEIC/outbreak:

- 1) Create regulatory frameworks for expediting the science, research methodology, and technology in countries/regions where there are substantial pharmaceutical centers of research and production in order to fast track the development of vaccines and therapeutics required during a PHEIC.
- 2) Create legal standards or safeguards to address the emergent use of experimental therapies.
- 3) Create national or regional emergency ethics review boards. Such boards need to be given sufficient resources so as to eliminate any undue delays pertaining to the trial evaluation, revision, and approval process. Educational efforts should be made by the international community to create ethics review boards in every country. If this cannot occur initially, an effort to create regional ethics review boards encompassing multiple countries should be undertaken.
- 4) Facilitate international community agreement on the trial design approach to a PHEIC for vaccines and therapeutics, that is, RCT, adaptive, cluster, stepped wedge, while understanding that each outbreak situation may be different. Different regions' cultures and traditions should be taken into consideration.
- 5) Prioritize informed consent during PHEIC outbreak interventions, taking into consideration local custom, culture, the extended family and religious leaders as necessary. Additionally, deferred and waived consent should be considered.
- 6) Review and evaluate the use of placebo in vaccine trials or in therapeutic trials using children or adults through ethics committees and subject-area experts. Treat mothers and children as a unit, not separately.
- 7) Create a "Ready Team" of scientists/physicians/other support personnel available for insertion into the epidemic zone of a PHEIC through international agreement. However, insertion would only occur after approval of the host country and after consultation with international stakeholders. This process should occur in a rapid fashion. It would be to the world community's advantage if the composition of this team is addressed in advance to allow it to become a standing rapid medical deployment force. This is best addressed between the WHO and the CDC.
- 8) The Society of Critical Care Medicine should continue to publish articles where results are made publically available as studies are completed.
- 9) The Society of Critical Care Medicine should consider having an accelerated process for the evaluation of studies of critically ill PHEIC patients.
- 10) Specific emergency pathways for approvals during PHEICs should be considered, and the Society of Critical Care Medicine should play a role in contributing to recommendations to assist with ethical issues as they relate to critical care medicine.
- 11) Every effort should be made to understand what communities think about models of consent that may be employed during a PHEIC and how it equates with those of regulators.
- 12) Trialists should be encouraged to promote the premise that therapies that are successful will ultimately be made available to the community in which they were first tested.

II. TREATMENT LIMITATIONS IN EMERGING OUTBREAKS

Search Strategy

PubMed MESH and Google scholar headings were searched iteratively for combinations of ethics, (outbreak or pandemic or disaster or public health emergency or crisis), Ebolavirus, hemorrhagic fever, Ebola; duty to care and/or duty to treat and/or triage or allocation, or healthcare rationing resulting in 560 citations. Specifically, Ebolavirus and/or hemorrhagic fever, and/or ethics, and/or healthcare rationing yielded only four results. Here, the term "treatment limitations" encompasses the potential for rationing of care. The results were refined based on content and relevance as well as the identification of additional relevant citations through the review process. After deleting duplicates and those that were off topic, 34 were found to have information that informed this document. The following points are emphasized:

- The scarcity of resources and the resulting limitation of treatment.
- Treatment to those who are ill may be limited based on the risk of contraction of the disease risk by those who are providing the care.
- Recommendations.

Background

Emerging outbreaks and other public health crises are characterized by scarcity of resources, time-sensitive decision-making, substantial public health risk, and potentially increased health risks for healthcare personnel (74, 75). Crisis conditions may lead to alterations in the routine processes of medical care, such as difficulties with outbreak management and/or implementation of the most effective treatment options (76, 77) and can be ethically challenging and distressing if patients and/or HCPs desire the unavailable treatments (78). In this section, we discuss the limitations that may be necessary during outbreaks and the ethical justifications that have been offered for these limitations. Finally, recommendations are offered for ethically sound management limitations in future outbreaks and disasters.

Management/treatment option limitations (i.e., rationing) can be ethically sound with sufficient planning and organizational response to the outbreak or crisis event. Such planning should be based on the best available evidence, ethical reasoning, and relevant community values (74, 79). This planning includes the development of ethically sound management protocols. This “duty to plan” applies to the critical care community as well as other outbreak/disaster response care providers (78). The planning efforts of state and federal governments, as well professional organizations, are well documented (74, 77, 79, 80). Failure to plan and implement a well-organized response to a crisis may result in unjust and unfair resource allocations and a loss of public trust (81).

The Scarcity of Resources and the Resulting Limitation of Treatment. *Clearly defined goals are necessary.* Healthcare resources, like all resources, are allocated according to a system of rules inescapably grounded in ethical concepts. Disaster triage is an allocation system, applied in medical emergencies when demand for resources exceeds supply, and may result in some patients being denied intensive care services even if they may benefit from such services. The intensity of interventions depends on resources. Attempts had been made in 2013 to create models regarding the development of a putative epidemic of Ebola hemorrhagic fever. The model used preventive and emergency mass vaccination, vaccination of risk groups, a search for and isolation of cases, contacts, and quarantine (82). The experience gained from the Ebola crisis delineated the skill set required of public health professional for serious nontrauma-related public health emergencies (83). Clinicians that possessed these skills were few, at least initially, and the inadequacy of appropriately skilled clinicians became the “Achilles heel” of subsequent international events (83). Preparations for such a PHEIC required extraordinary support and resources and resulted in diversion of assets that could have been otherwise used in preventive health and other infectious disease activities (84).

A key aspect of triage that remains a challenge is the necessity of establishing clear and unambiguous goals for allocation decisions. Since the earliest battlefield descriptions of triage, the core ethical concept justifying decisions has been to provide the greatest good for the greatest number (85). And yet, there are different interpretations of the meaning of “greatest good.” (76, 86–88). It could be interpreted as maximizing survival or as reducing aggregate morbidity and maximizing aggregate health. In planning for future outbreaks, a primary goal of emergency medical systems has been the survival of as many patients as possible (76, 81).

Although published guidelines now advocate for maximizing survival, a number of alternative allocation schemes have been recognized and described that reflect different conceptions of “the greatest good.” These range from lottery schemes (where resource-inefficient communities recognize equal moral status for all) to the life-cycle principle that recognizes the value of being able to live through each life stage (76, 87). Although a full description of these alternative allocation principles is beyond the scope of this article, it is recognized

that each scheme may reflect moral values and intuitions that may resonate strongly in the communities where they may be applied. As such, an important component of the duty to plan is the engagement of the community to identify the values important in the allocation of scarce resources, thereby allowing clear unambiguous allocation systems reflecting those goals (74).

Ability to Operationalize Goals. In addition to establishing clear goals, it is necessary to develop effective triage protocols (81). However, clinical decision support systems face major challenges in successfully guiding allocation decisions to maximize the likelihood of medical benefit. Clinical decisions based on clinical judgment alone are prone to inconsistent application by triage officers (78), and there are concerns about the inadequate performance of existing scoring systems, based on mathematical modeling and the retrospective application of scoring systems to actual patients (89–91). Despite the clinical problems with triage protocols as they exist today, one unavoidable fact is that triage decisions will need to be made during an outbreak. Triage protocols transparently developed by expert groups, subject to revision as data become available, and fairly applied, will likely represent the best option for achieving the allocation goals. In situations where protocols are unlikely to perform better than chance, allocation systems using a lottery or a “first-come, first-served” scheme may be preferable (78).

Oversight by Triage Officers, State and Local Authorities. The duties of intensive care clinicians to treat individual patients with fidelity may conflict with a duty to triage care. A clinician may find it professionally, morally, and emotionally difficult to withhold potentially beneficial treatment from a patient under his/her care, even when following a properly established triage protocol. Consequently, the use of objective triage officers not involved in the direct treatment of individual patients has been recommended (88). Additionally, the use of clinical decision support systems (including triage protocols) may improve clinician performance and patient outcomes and has been shown to reduce the moral distress experienced by triage officers (81). It may be in the best interest of such officers to develop a plan that includes a clinical ethicist working with them in the emergency department and ICU to help address difficult decisions.

Treatment to Those Who Are Ill May Be Limited Based on the Risk of Contraction of the Disease Risk By Those Who Are Providing the Care (Public Health Imperative to Contain Spread of Disease). *Necessity of strict containment measures.* Emerging outbreaks from HIV to EVD have focused attention on the possibility that management options may also be limited based on public health concerns other than the scarcity of resources (4, 92). Similar to other outbreaks, the EVD outbreak was characterized by a highly transmissible virus, the potential for significant morbidity and mortality, and the lack of proven effective treatments (93). Additionally, the early phase of the U.S. response to EVD was notable for a lack of preparedness to treat infected and potentially infected patients in the majority of hospitals, a lack of readily available resources (and the training that must necessarily

accompany them) for preventing spread of disease to health-care workers and beyond, an initially incomplete understanding of the needed containment protocols, and elements of fear and panic that spread through the American populace (80, 94). Although some possible reasons for limiting treatments—such as fear, ignorance and prejudice—are ethically indefensible, others have stimulated vigorous discussion over the proper justifications for limiting treatments based on the risks to others (95).

Healthcare institutions, including regional and national governments, are obligated to provide care for patients but also have duties to HCPs and the public's health during emerging outbreaks, according to the principle of reciprocity (96, 97). Duties include effective planning before crises develop, the provision of adequate resources to care for the sick and injured as well as protection of healthcare workers, and the development of treatment protocols that may include limitations of management options during an outbreak (79, 98). It has also been argued that since HCPs accept significant personal risk during an emerging outbreak, they should receive high priority for vaccines and other effective treatments (99, 100). However, it should be noted that the CHEST consensus statement on pandemics and disasters has recommended that healthcare workers should not receive priority care over other infected individuals (77, 78).

In the recent experience with EVD in the United States, the marked transmissibility of the virus led to particularly strict containment protocols that substantially altered the usual processes of care for many hospitals. Some routine management tools (e.g., x-ray imaging and the full complement of laboratory tests) have been limited in hospital EVD protocols for the sake of containment. Similarly, the response time to urgent problems (e.g., cardiopulmonary arrest) is limited in many protocols by mandatory and lengthy PPE donning procedures. Protocols for invasive procedures (e.g., continuous renal replacement, endotracheal intubation) have been carefully designed for availability. These limitations and protocols restrict routine, but often nonessential management options, to prevent spread to HCPs and other patients and are acceptable under these conditions.

Limitations of Treatments With Low Probability of Benefit to the Patient. The determination of the medical appropriateness of treatments is unavoidably value-laden (101). The burden/benefit calculation depends on the values and priorities of patients and families. Therefore, physicians may sometimes provide treatment that they personally believe is unwarranted to provide benefit in order to honor the values of the patient (102). These determinations become more complex during emerging outbreaks when public health considerations play an important role in treatment options. In such circumstances, protocols may limit treatments that may otherwise be available to patients (such as cardiopulmonary resuscitation, extracorporeal membrane oxygenation, and major surgical and obstetrical procedures) if the benefits of the procedure are likely to be minimal and the public health impact is substantial (103–106).

Such determinations should be made on the institutional level in conjunction with hospital ethics committees, be open to public scrutiny, and would benefit from legal involvement in hospital preparedness planning (107). The potential for patient care to lead to significant morbidity and mortality for health-care workers and their contacts must be considered. Also, the public health imperative to contain transmission and protect the public, thereby constraining the individual rights of patients to request treatments that they believe may be beneficial to them, should be scrutinized. The recommendations for this section fall into two categories based on treatment limitations based on scarcity and those in regard to the risk of others:

Recommendations Regarding Treatment Limitations Based on Scarcity of Resources:

- 1) Recognize that no triage decisions are value-neutral. All allocation decisions are based in ethical values.
- 2) Establish clearly defined, unambiguous ethical principles that reflect the values and moral intuitions of the community when determining treatment limitations based on scarcity of resources.
- 3) Use protocols that incorporate expert opinion, valid and reliable scoring systems, and all available scientific evidence relevant to the particular outbreak/crisis in determining treatment limitations. In situations where no valid scoring system is available, it may be necessary to use a chance-based allocation scheme such as a lottery or first-come, first-served.
- 4) Excuse bedside clinicians from making triage decisions. Establish triage officers, or teams of triage officers, not involved in the treatment of individual patients, to be responsible for decisions to limit treatment, using properly designed triage protocols.

Recommendations Regarding Treatment Limitations Based on Risk to Others:

- 1) Identify appropriate reasons to limit treatment to patients in a public health crisis; clearly establishing that fear, ignorance, and prejudice is unethical and indefensible.
- 2) Mandate that healthcare institutions and government provide adequate access to care and resources in emerging outbreaks, as well as support and protection for HCPs who respond to the call to treat.
- 3) Clarify and educate the public that during emerging outbreaks and other crises, treatment options unlikely to benefit patients may be made unavailable to patients if the public health impact is substantial.

DUTY TO TREAT VERSUS RIGHT TO REFUSE: HEALTHCARE PROFESSIONALS' OBLIGATIONS AND RIGHTS IN THE FACE OF OUTBREAKS

Search Strategy

PubMed MESH and Google Scholar headings were searched iteratively for combinations of moral obligations, duty to treat, ethics, risk, and epidemics, resulting in 1170 citations. The

results were refined based on content and relevance as well as the identification of additional relevant citations through the review process. After deleting duplicates and those that were off topic, 40 were found to have information that inform this document.

Background

Emergence of deadly and highly contagious infectious disease epidemics in recent decades, along with refusal of some HCPs to treat patients, and lack of clarity in the language of the duty to treat during epidemics, have resurrected debates, legislative efforts, and legal actions to define such duty (108, 109). Are HCPs ethically or legally obligated to provide treatment, or can they assert the right to decline treating patients during outbreaks?

Some have argued that by entering the medical profession, HCPs have consented to face the risk of being exposed to patient illness. Therefore, they have an obligation to treat patients with an infectious disease (110). The question remains whether this obligation is absolute, or if there are circumstances under which refusal to treat is justified, such as level of risk or other considerations (20). The following are emphasized:

- The ethical duty to treat.
- The legal duty to treat.
- Recommendations.

The Ethical Duty to Treat. Healthcare professionals have a professional obligation to sick and vulnerable patients despite the personal health risk related to providing that treatment (95, 111–113). It has been argued that these duties are even more binding during crises such as outbreaks due to the specialized capabilities of HCPs (as in the case of training/special qualifications in treating critically ill patients with SARS, EVD, and influenza) (75, 113, 114). And yet, during recent outbreaks, questions have been raised about the limits of this duty to treat and what society and the healthcare community owe to the healthcare professionals called upon to care for these patients (94, 115, 116). If the health risks are substantially greater than the risks experienced during routine practice, the duty to care may be outweighed by individual rights of self-protection and duties to other persons such as family members or other patients (110, 115). The American Nurses' Association Code of Ethics asks nurses to balance a duty not to abandon those who need our care with a duty to self-care. Nurses are also encouraged to make decisions that do not compromise their own personal values and moral standards (117). Recognizing these competing obligations, volunteer clinicians may provide a resource to help fulfill the need for patient care, but this depends on availability. Once adequate safety practices are developed, reliance on volunteers may be professionally inappropriate and unfair (80, 118, 119). Reflecting on the SARS crisis, Reid (115) observed that HCP duties exist in a complex matrix of factors including societal support for healthcare institutions and providers, the particularities of healthcare crises including the magnitude and extent of the risk, and the distribution of risk within healthcare communities (120, 121).

Alexander and Wynia (122) found that only a narrow majority believes there should be a professional responsibility to treat (whereas a duty to treat does not come from a majority opinion; a duty is independent of opinion). The American Medical Association's (AMA) first written Code of Medical Ethics (the Code) in 1847 required physicians to treat patients during outbreaks "without regard to the risk to [their] own health (113, 118, 123)." This language remained essentially unchanged until 1957 and was removed by the late 1970s and then subsequently revised in response to the HIV/AIDS epidemic and the threat of bioterrorism. The current Code suggests that providers should balance the duty to treat patients with infectious disease with their duty to other patients, their own family members, and the family members of others in determining whether they should expose themselves to risk (118, 124, 125).

Historically, physicians' interpretations of professional guidelines have been based on their own value systems and assessment of risk (actual or perceived) (126). HCPs must be impartial in balancing the benefit to their patients against the risk to themselves, and the AMA has set guidelines for a minimum acceptable professional conduct regarding HCPs' duty to treat during outbreaks (118, 127, 128). The Code was originally set based on a three-part social contract, with reciprocal obligations among physicians, patients, and their communities (128, 129). This social contract required physicians to continue to treat patients despite the risk to their own health (113, 128). The same way that firefighters and police officers have an obligation to society even if it puts them in harm's way, HCPs have a duty to fulfill despite the risks involved. Physicians are granted special and privileged status by society, which comes with the risks associated with treating patients (129, 130). The question may arise as to whether HCPs should be allowed to define this threshold based on their own individual right to autonomy or whether HCPs' responses during outbreaks should be consistent with society's values and needs and not based on individual virtue (115, 131, 132). During HIV/AIDS epidemic, some suggested a new code of professional ethics to give physicians a moral context for the duty to treat based on both patients' and society's needs and understanding medicine as a moral and virtuous profession (133).

During the SARS epidemic, up to 30% of reported cases were of HCPs, some of whom died. Some HCPs also refused to work and were dismissed. Questions arose as to how to align the HCPs' obligations to treat patients with highly contagious and deadly infectious diseases with their right to refuse work and protect themselves (118). Healthcare professionals have responsibilities to their patients, family members, friends, other patients, as well as to themselves. The duty to treat and its scope should be defined in the context of these competing responsibilities, as well as to their autonomy and personal safety (119, 127, 134, 135). The fear in these situations is real and must be acknowledged by all stakeholders during a PHEIC. It is not only the fear of getting ill that is of concern but also of the post epidemic problems for HCPs, such as in the Ebola epidemic, post-Ebola syndrome, and post-Ebola posttraumatic stress disorder (136, 137).

The defined risk threshold in the workplace should be based on an HCP's expertise and specialty, implied and expressed consent, and an HCP's medical conditions (such as being immunocompromised or pregnant), etc. Factors, such as balancing the likely benefits of treatments to patients against the risks of exposure to an HCP, resource allocation, the HCP's duty to avoid harm, their competing obligations resulting from their multiple roles and responsibilities, and institutional implementation of necessary protections and safeguards for an HCP's health, are all important considerations to determine the scope and limits of the duty to treat during outbreaks (110, 129, 133, 138, 139). Once the threshold is set based on above factors, should the duty to treat be obligatory, overriding the autonomy of HCPs? If not, then the distribution of risk to HCPs will be unfair, as some, who decide to provide care, will be burdened by the refusal of those who choose not to treat patients (80, 128, 140, 141).

Another argument for the duty to treat during outbreaks is that HCPs simply have the skills and expertise to provide care (125, 129, 138). Society has invested in HCPs through education, thus implying a reciprocal responsibility. Furthermore, HCPs have assumed the risk by freely and knowingly choosing to enter the profession, so it is implied that they have agreed to treat despite the risks involved (125, 129).

To counter that argument, one survey of HCPs showed that although 80% of participants had some knowledge about risks when they enter the profession or during their education and training, over half of participants believed that there was a standard level of risk (SLR) beyond which the risk is not acceptable to impose the duty to treat unless protective measures were implemented. Interestingly, a minority of participants would have chosen a different profession had they been fully informed of risks. They also believed that there were certain diseases that would pose risks beyond SLR no matter what precautions were taken (142). As evidenced by this study, the definition of SLR and awareness of risk assessment by HCPs are limitations on using the concept of presumed consent or assumption of risk to establish the duty to treat (142). Some argue that specialty choice involving patient contact implies an agreement to accept a higher level of risk and exposure to potentially deadly infectious diseases (129), and some even imply that those who do not accept the inherent risk should not be allowed to practice medicine (80, 138).

As such, even though the AMA code of ethics is vague, an overwhelming majority of medical and ethics scholars believe that there is an ethical duty to treat patients during outbreaks, and the concerns for physicians' autonomy should not override that duty (113, 125).

The Legal Duty to Treat. The AMA's professional code of conduct is often recognized by courts and used as legal standard for states' Medical Board licensing, regulatory, and disciplinary functions as well as for setting the professional standard of care in medical negligence cases (125, 143).

The Americans with Disabilities Act (ADA) provides the primary legal framework to determine HCPs' legal duty to treat patients with a particular disease. Although the Supreme Court has determined physicians have a legal duty to treat patients

with HIV/AIDS under the ADA, the case law and its policy rationale could not be applied broadly to highly contagious and deadly infectious diseases such as Ebola or SARS (143). Under the ADA, HCPs can invoke the direct threat affirmative defense to refuse treating such patients. This is allowed when a patient's condition presents a "significant risk to the health or safety of others that cannot be eliminated by a modification of policies, practices, or procedures..." (139, 143, 144)

The Supreme Court held that the key word in this balancing test is whether the risk is "significant," which must be based on objective medical evidence and consensus (actual risk) and not physicians' individual good faith beliefs (perception of risk) (145). This means if a new highly contagious outbreak exists without prevailing consensus in the medical community of risk assessment, an individual physician's good faith assumption that the risk is significant (because the disease is deadly, highly contagious, and without effective treatments to benefit patients) may not absolve his/her legal duty to treat (143). Separately, using the specialist referral provision of the ADA, a physician can legally deny to treat a patient with a highly contagious disease and refer him to a specialist if he/she "lacks the experience or knowledge" to treat such diseases (143). Needless to say, this provision creates a quandary with specialties such as emergency medicine, critical care, and infectious disease.

The Emergency Medical Treatment and Active Labor Act (EMTALA) is another law that created a legal duty for hospitals to treat patients with highly infectious diseases in emergency situations. There is no "significant risk" or "direct threat" exception under EMTALA. However, physicians' legal duty to treat under EMTALA is contractual and only if they agreed to provide on-call emergency medicine services. Therefore, physicians are "free to negotiate" regarding their responsibilities to help a hospital's compliance with EMTALA (143, 146).

Finally, the Model State Emergency Health Powers Act proposed that during a public health emergency, states could require HCPs to "assist" with treatment of patients as a condition of their license to practice medicine (147). Since physicians and other healthcare professionals have property interests in their medical licenses, exercising such broad power by state without a due process would likely face constitutional challenges in court (143).

In a survey of Canadian HCPs, legislators, spiritual leaders, and members of the public, a majority believed that the duty to care should not be left to personal choice or individual ethics and morality but must be defined and codified by regulatory bodies and policymakers and with the inputs from the public (134). Physicians for most part have a legal duty to treat during outbreaks, and the right to refuse work only applies to the extent they could reasonably show unsafe working conditions and inadequate protection. Other considerations such as specialty, rural practice, and lack of access to other HCPs are among factors that determine a physician's legal obligation to treat patients during outbreaks (129).

HCPs are entitled to a safe work environment while fulfilling their duty to treat patients. HCPs, like any other

members of society cannot be forced to work against their will, but with some limited exceptions, have a legal duty to treat patients during emergencies and outbreaks. Their autonomy may only be recognized in balancing their competing responsibilities for self, family, and community with the benefits of treatment to the patients to whom they have a duty to treat.

Recommendations Regarding Professional Autonomy Versus Duty to Treat:

- 1) Establish early in the education and orientation process that HCPs have a duty to treat in the event of a public emergency when the available volunteer pool is not sufficient to meet the needs of the community.
- 2) Establish educational programs that highlight and address the fear HCPs may have in treating these patients, and how the risk is minimized with the use of safety/protective equipment.
- 3) Designate a greater duty to treat for specialists until education can be provided for others to develop specialized skills.
- 4) Set up volunteer pools of those willing to care for patients (Ebola) as long as such willing volunteers were sufficient in number for staffing, then those who were more hesitant do not necessarily need to be forced to provide care.
- 5) Although HCPs have autonomy in making decisions in regard to their personal situation as to whether they choose to provide care in an epidemic, such a consideration must be weighed against the patients' benefits in receiving treatment from the provider.
- 6) Ensure that institutions (not just clinicians) are aware of their responsibility to provide a safe working environment for all.

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