The raging coronavirus disease-2019 (COVID-19) pandemic spurred discussions on the ethics of allocating respirators to needy patients. These discussions addressed not only respirators, but also extracorporeal membrane oxygenation (ECMO) machines, intensive care unit beds, and novel drugs that might be in short supply relative to the demand to save life. In this article, I focus on the allocation of respirators, ECMO machines, and similarly critical life-saving means. Some such means are interdependent of each other. It might be futile to connect a patient to a respirator when no ICU bed is available. Hence, a concrete life-saving modality needs abstraction into a unit of professionally arranged medical service and then be allocated to needy patients. I did not address the question of whether the exigencies of epidemics justify a compromise in the unit of service (e.g., mobilization of old respirators, placing ventilated patients outside the ICU). I also did not discuss the possibility of allocating second rate care (e.g., old respirators) to patients triaged out of standard care. In this focus article I offer a conceptual model for allocating a discrete modality of life-saving care in circumstances of shortage. Respirators in the COVID-19 epidemic are an example. I focused on the cultural context of Jewish law and the Israeli healthcare; yet, these findings may fit many other cultures and jurisdictions.

The leading value in the triage proposed is saving life, which pertains to any person with a long-term prognosis. In Jewish law, this means life expectancy beyond one year. If the person wants to fight for his or her life, quality of life does not affect care [1]. A second presumption is that a healthcare system cannot and must not prioritize the value of one life relative to another. Third, medicine must be rational and efficient; its efforts must correspond with chances of success. Last, medicine can quantify such chances.

The rationale of the proposed system is continuity with prevailing medical practice and similarity to ordinary (non-pandemic) experience of sickness and healthcare. It strives to separate the hopeless from the curable, granting every treatable person a real chance of cure. The scarcity situation will first eliminate excesses of medicine and then allocate respirators by a single scale, combining an evidence-based scoring system with risk-proportionate lottery.

The article is divided into two sections. The first is a socio-cultural framing of the problem, and the second is an outline of a triage for scarce respirators that accommodates a universal right to basic healthcare. As long as worry about contagion does not compel separate pools of ventilators (i.e., for the infected and non-infected), COVID-19 personal status is not a moral consideration.

Socio-cultural Background
Criticism of excessive use of invasive medical technologies and lamentation over the entrapment of patients by life-support has been a formative narrative of bioethics in affluent countries. The excesses of invasive care are attributable to three factors. The first is the overall medicalization of contemporary life and the

Allocation of Respirators in the Coronavirus Crisis in Israel: An Ethical Analysis and A Scheme for Triage

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ABSTRACT
This focus article is a reflection on the ethics of allocating respirators to patients in circumstances of shortage, especially during the coronavirus disease-2019 (COVID-19) outbreak in Israel. In this article, respirators are placeholders for similar life-saving modalities in short supply, such as extracorporeal membrane oxygenation machines and intensive care unit beds. In the article, I propose a system of triage for circumstances of scarcity of respirators. The system separates the hopeless from the curable, granting every treatable person a real chance of cure. The scarcity situation eliminates excesses of medicine, and then allocates respirators by a single scale, combining an evidence-based scoring system with risk-proportionate lottery.

The triage proposed embodies continuity and consistency with the healthcare practices in ordinary times. Yet, I suggest two regulatory modifications: one in relation to expediting review of novel and makeshift solutions and the second in relation to mandatory research on all relevant medical data and standard (as opposed to experimental) interventions that are influenced by the triage.

KEY WORDS: coronavirus disease-2019 (COVID-19), disaster medicine, Jewish medical ethics, respirators, triages
emergence of a risk-oriented society, which pushes healthcare to be on the safe side. The second is a conceptualization of the sacredness of life combined with defensive medicine that promotes the fight for life even when chances are grim and suffering enormous. The third is a set of legal, moral, and psychological factors that maintain hopeless and unwilling patients hooked to medical machinery.

Compared to other countries, Israel has gone a considerable length to regulate end-of-life care by democratic processes and ethical deliberations. Israel is the only country with primary legislation dedicated to the patient nearing death. However, 15 years after its enactment, its acceptance by the public and implementation by the healthcare system are skimpy.

Transparency and uniformity are not rife in Israeli healthcare. The Ministry of Health does not publish comparative morbidity and mortality data from its hospitals. Statutory committees on termination of pregnancy operate without coordination. Women who are rejected by one hospital committee are often accommodated by a different hospital [2]. This pluralism is not necessarily regrettable. However, even if uniformity and transparency are values worth promoting, it is unlikely that a uniform and transparent system of triage will be formulated and accepted during the COVID-19 crisis.

In this focus article, I delineate a system of triage that may be adopted and modified by all or some caring teams or hospitals. Some ethicists argue that individual choices of allocation must not be made by the responsible physicians, but by lay or mixed committees [3]. In Israel, the statutory ethics committees in relation to terminal patients do not convene. There is no reason to suppose that dedicated committees oversee individual decisions of triage. The caring team needs principles expressed in its own language and modes of reasoning as it may not comply with an external body or law telling it who to treat. Moreover, the centrality of medical criteria is essential to the capacity of medical teams to act on tough decisions, to be accountable for their practice, and to cope with moral distress [4].

Relative to other OECD countries, Israel is plagued by under-funding of its healthcare, with a low hospital beds to population ratio. Israeli culture is known for its fondness of creative improvisations. One example is the makeshift solutions adopted by the Israeli humanitarian mission to Haiti, following the 2010 earthquake. It allowed the field hospital to treat many more patients than other field hospitals with similar capacity; but it also raised questions on the clinical and ethical validity of the Israeli compromises and improvisations [5].

For many years, Israeli hospitals have been caring for ICU patients in ordinary departments. Israeli doctors are not asked to triage people for access to ventilators, but to triage patients on ventilators to either ICU or ordinary wards. Rooms of six ventilated patients inside a medical ward, often with doctors and nurses without formal training in their care, is not a rarity [6]. This practice is not necessarily harmful because elsewhere, many of the patients will not be given life-support at all. Recovery from such a compromised setting of care is not unusual either [7]. This Israeli practice seemed to infuse its healthcare system with resources for coping with the COVID-19 crisis better than other healthcare systems because so many Israeli doctors and nurses have some, sometimes rudimentary, knowledge and experience in the care of ventilated patients. Even if good clinical practice requires the abolition of this practice, is quite reasonable to accommodate ventilated patients outside of ICUs during an epidemic as many hospitals worldwide have been doing.

Considering the failure to bring the regulation of life-support into closure and the ubiquity of non-standardized care for patients on ventilators, any formal triage system for the COVID-19 crisis is unlikely to win immediate legitimacy. At least in Israel, we need an allocation system that grew from prevailing practice and was consistent with it.

Many authors and committees called for granting a priority to healthcare workers and other key actors in coping with the epidemic. Israeli law grants priority to holders of donor cards in the allocation of organs for transplantation [8]. The publicly available data does not include the number of people who were denied a transplant because a prioritized patient received the organ and died from organ failure while still waiting for transplantation. It is also possible that the Israeli legal system might grant priority to vaccinators over vaccination objectors in the allocation of respirators. However, in this focus article, I addressed resource allocation among all those who share equal moral and legal entitlements to care, not stratification of moral and legal entitlements. Moreover, while the organ prioritization system is not fully transparent, the system proposed would be committed to transparency in terms of morbidity and mortality. Without such a commitment, the system cannot meet the criterion of reversibility, which is central to rational and legitimate public policy [9]. Rationalization of the system, which should be conducted as research on human subjects, is key to legitimization.

**AN OUTLINE FOR A TRIAGE OF RESPIRATORS IN THE COVID-19 CRISIS**

The system proposed contains six inter-connected elements.

- A backbone of evidence-based medical scoring system
- Eliminating the psycho-cultural margins of extra-caution and vitalism
- Stratification of candidates as to grant every patient a chance while modifying the chance according to long-term survivability and the supply/demand ratio.
- A bi-directional but asymmetric triage, which means the criteria for allocating the respirator will be used for disconnecting it as well (reverse triage)
- An expeditious process for acceptance and dismissal of novel and makeshift practices
- A modification to the law regulating medical experimentation on human beings
While contemporary discourse uses the word triage for the allocation of scarce healthcare resources, historically, triage is a rational and fair system of efficient use of healthcare resources. Triage is an alternative to pandemonium, wastefulness, and injustice [10].

A decision whether to intubate a patient is first and foremost a decision about the good of the patient. It seems reasonable that the decision to determine how strong is the indication to intubate be based on the same criteria, either when the patient’s own good is at stake or when resources are scarce. The medical team first weighs the chances and burdens assuming resources are available, and only then honestly evaluates which need can be met. Indeed, in western and Jewish medical ethics, the category of extraordinary means has developed in relation to the burden of care, both on the individual patient and on society’s resources [11,12].

In the era of evidence-based medicine, there are many scoring systems for the stratification of the expected impact of care or prognosis under best care. The modified Acute Physiology and Chronic Health Evaluation (aka APACHE II) scoring system is a validated prognostication scale for ICU patients [13]. Its advantage over simplified scores (e.g., qSOFA) is its inclusiveness of many and diverse factors. This results in high resolution of stratification. Every patient’s score ranges between 1 to 34+ points, thus the chances that two patients with identical scores compete for a scarce resource are low.

When the gap in scoring is significant, it is easy to justify and to accept psychologically the allocation of a respirator to the clearly more promising patient. In the APACHE II scoring system, a 5-point difference is significant. The lower the APACHE II score, the better is the prognosis to recover from ICU. When the gap is tiny (e.g., 1-2 APACHE II points) physicians cannot claim that the patient with the extra points deserves the machine less, or that the patient shows inferior prognosis. However, whereas a big gap in a scoring system offers a substantive justification, when the gap is small, it can be used as a lottery, as an instrument of pure procedural justice, a heuristic of fairness. After all, granting the respirator to the patient who ranks one point more does not seem more reasonable or more legitimate [14]. The overall advantage of reliance on such scoring systems is the continuity of legitimization. It also shields the triage team from interference and bias.

As a first step, an APACHE II-like scoring system should be used to eliminate the margins, which contain patients with obviously grim prognosis; but at least in Israel, they are often intubated. The triage system will set a threshold within the range of 90% risk of mortality (i.e., APACHE II score > 35 points) beyond which patients will not be given artificial ventilation. Even though it is possible to justify heroic efforts to save such patients in ordinary times, there is no basis to suppose that no-treatment of such patients constitutes abandonment or killing. Rather, many believe it is wrong to intubate such patients even if resources are plenty. Healthcare professionals and the public should accept the fact that such patients die from disease, not from lack of treatment.

Depending on the supply/demand ratio, the margins may expand to exclude patients with lower (i.e., better) APACHE II scores. However, at a certain point it will become evident that the system excludes patients who deserve intensive care by ordinary medical standards.

If every patient with reasonable prognosis deserves access to lifesaving means, in a situation of dire scarcity, a system of stratification is implemented. According to this system, medically treatable patients will be divided into subgroups, deciles in the scoring system. Each decile will be granted a portion of respirators. An algorithm that responds to the overall balance of supply and demand will allocate each subgroup a quota, which does not reflect its size (number of patients) but its prognosis. For example, whereas 10% of patients may be in the lowest decile, they may be allocated only 2% of respirators, while the top decile, representing 10% of the patients might be allocated 15%. The division into deciles and the factoring (the relative slots allocated to each decile group) will be programmed into one scoring algorithm that will preserve at least 2% chances to every curable (2% is the range of futility). If there are a hundred old and frail patients who still stand chances of recovery, no fewer than two will be given respirators. Conversely, there might be 2% of those who have excellent prognosis of long-term survival who may not be given respiratory treatment.

The key factor in the system is the preservation of realistic chances of access to care for every patient who wants to fight for his or her life (or requests from his or her guardian) and who has a reasonable promise of cure. Because this is the principle guiding universal healthcare coverage, the triage system will only affect chances. Reasonableness will be determined by ordinary standards of good clinical practice in non-scarcity scenarios. The proposed system does not address extreme situations that cannot accommodate even this level of rationing.

Within this framework, whenever a patient arrives, the algorithm will determine whether he or she gets a ventilator by the pre-set chances correlated to his or her score. For example, a patient with excellent prognosis may have a 95% chance. One in a lower prognostic decile will have 85% and so forth. Thus, when rejection of curable candidates is inevitable, every patient, even the most promising one, will be subjected to a combination of medically justified criteria and lottery. Patients with excellent prognosis will have an excellent chance to gain the respirator, whereas those with relatively poor prognosis will have a low chance. The personal experience of patients and healthcare providers will be similar for all. It will constitute solidarity in fate and in promise. The whole population is at risk. Everybody faces scarce resources and everybody has a chance. Chances are a matter of prognosis with a component of luck. The absence of discrete categorization, such as absolute thresholds by age or other dominant parameter, is expected to ease the moral distress of healthcare professionals and might avert a sense of social disruption by the public.
In ordinary times, doctors have a special fiduciary duty to their patients. A cardinal implication of this special duty is a commitment not to abandon a patient for the sake of another. Consequently, many physicians do not disconnect patients who are still fighting for their lives for the sake of new patients with much better prognoses. In a medical environment in which disconnecting willing and hopeless patients with life support is still a taboo. Disconnecting during epidemics is likely to be quite difficult and needs special justification.

In times of epidemics, when the lives of everyone depends on joint action by the whole public, nobody can claim exclusive entitlement to life support. Consequently, in such difficult times, it is possible to argue that the public supply of respirators is only allocated conditionally and on presumed consent of sharing medical data that is essential for determining the outcome of the allocation system. Patients who fail to improve by objective prognostic scoring will be disconnected. To some, the rejection of a viable patient at the door, while keeping patients with much worse prognosis on ventilators inside, seems unjust and harmful. Rather, I contend, the patient deteriorating on a ventilator has been given a chance, whereas the one at the door has not.

However, the way in and the way out are not symmetric. Whereas a tiny gap in scoring may justify allocation of a respirator, disconnecting one may require a pre-set and significant deterioration in one’s score. When the score gap is very narrow, it makes sense to allocate resources by the logic of sheer luck. Yet, disconnecting patients must not be chance-guided. Reintroducing chance into ongoing medical care will obfuscate clinical practice and invite bias and moral distress. Society cannot expect healthcare professionals to risk their lives and stretch their personal resources for care that is subjected to arbitrary interruptions.

The proposed scheme of triage calls for two regulatory adjustments. An expeditious review process should decide whether to authorize improvised policies of care (e.g., homemade respirators, one machine for two patients, placement of ventilated patients outside ICU). Such modifications are justified because neglect of commitment to rational and safe practice is disrespectful of human dignity and an invitation to anarchy.

When the standard of care is evidence-based, it is possible and desirable to set uniform and universal clinical guidelines. However, because there is no controlled data and systematic information on strategies of triage and makeshift practices, there are no special reasons to expect uniformity. Rather, when different healthcare settings develop a diversity of organizational and clinical strategies, it will be possible to collect data and perform ad-hoc observational research that is crucial for improvement of care and the design of controlled studies. Current research ethics and Israeli law require an institutional review board (IRB) approval and patient/guardian informed consent to any systematic collection of clinical data for research purposes. It also requires such approval for experimental and novel treatments. In the current crisis, IRB processing might be too labor intensive and complicated. Hence, it is argued that the law must be amended to allow, actually mandate, analysis and observational monitoring of all treatment interventions in disaster settings. Such a policy is occurring de-facto during the mass vaccination of the Israeli population and with neither IRB authorization nor primary legislation [15]. Every practice that is ethical and legal without informed consent to research (e.g., any system or triage) should be subjected to monitoring analysis without such consent, yet with transparency to the public. It is also reasonable to suppose presumed consent to data monitoring by patients who are lucky to benefit from scarce life-saving resources.

**CONCLUSIONS**

Rationalization of healthcare, and especially the allocation of scarce resources, is a moral duty. Excellence in medical practice requires ongoing efforts to improve the scientific foundations of healthcare. Especially in times of crisis and scarcity, deterioration in quality and rationality of practice, as well as influences of political power, bias, and prejudice might run rampant. Hence, the triage system I proposed is simple and based on established scoring systems in common practice with few modifications or adjustments. The system is designed to fit the local healthcare environment, while still being valid and comparable to triage systems all over the world. It should serve as a template for ongoing ethical and medical discussions and refinements.

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**References**


Capsule

Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection

The immune response to SARS-CoV-2 is critical in controlling disease, but there is concern that waning immunity may predispose to reinfection. Zuo et al. analyzed the magnitude and phenotype of the SARS-CoV-2-specific T cell response in 100 donors at 6 months following infection. T cell responses were present by ELISPOT and/or intracellular cytokine staining analysis in all donors and characterized by predominant CD4+ T cell responses with strong interleukin (IL)-2 cytokine expression. Median T cell responses were 50% higher in donors who had experienced a symptomatic infection, indicating that the severity of primary infection establishes a ‘set point’ for cellular immunity. T cell responses to spike and nucleoprotein/membrane proteins were correlated with peak antibody levels. Furthermore, higher levels of nucleoprotein-specific T cells were associated with preservation of nucleoprotein-specific antibody level although no such correlation was observed in relation to spike-specific responses. In conclusion, the data are reassuring that functional SARS-CoV-2-specific T cell responses are retained at 6 months following infection.

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Eitan Israeli

Capsule

Building bridges in the brain

Some 200 million axons connect the right hemisphere to the left through the brain's corpus callosum. A malformed or absent corpus callosum causes neurological or cognitive deficits. During development, astrogia build a substrate for axons to use in crossing the interhemispheric fissure. Signaling by Netrin 1 (NTN1) and its receptor, Deleted in Colorectal Carcinoma (DCC), guides axons to the midline. Morcom and colleagues showed that NTN1 and DCC function even earlier to clear the path by regulating astroglial morphology and function. Without NTN1 and DCC function, astroglia that would normally build bridges across the interhemispheric fissure are unable to do so, and thus axons, no matter how well guided, struggle to build the corpus callosum.

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Capsule

Population-level lupus

Autoimmune diseases often show polygenic inheritance, making the identification of potential causal genetic variants difficult, especially across ancestrally divergent populations. Andreoletti and co-authors examined the transcriptomes of bulk immune cells from 120 systematic lupus erythematosus (SLE) patients of Asian and European ancestry. Disease-specific genetic signatures were revealed, as well as ancestrally associated differences in SLE molecular pathways and the role of gene expression variation in disease severity. Because SLE severity differs among populations, this study highlights the need to examine disease genetics in multiethnic cohorts for underlying differences and to explore the clinical treatment options for individuals of differing ancestries.

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