

VIEWPOINT

An Ethical Framework for Allocating Scarce Inpatient Medications for COVID-19 in the US

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Viewpoint

As researchers and drug manufacturers work tirelessly to find effective treatments for coronavirus disease 2019 (COVID-19), the media and the public await any report of a promising therapy. The antiviral drug remdesivir recently received Emergency Use Authorization (EUA) from the US Food and Drug Administration (FDA) for treatment of COVID-19. Many other new or existing therapies are under investigation, and the FDA has committed to expedited approval of proven new therapies. With patients and clinicians desperate for effective treatments, each new therapy will be in high demand. The need is projected to exceed the available supply, even as manufacturers strive to increase production,¹ and shortages may be exacerbated by distribution problems and new waves of disease in the pandemic. When there is not enough of a new therapy available, frontline clinicians will need to rapidly identify which patients should receive it.

Recommendations have been published for the equitable allocation of COVID-19 therapeutics and vaccines around the globe, as well as the rationing of ventilators if necessary, but little information is available about rationing of new therapies.²⁻⁴ This Viewpoint

During a shortage, medications should be prioritized for indications for which peer-reviewed, randomized clinical trials (RCTs) have demonstrated efficacy and safety. Second, the choices of each patient should be respected. However, unlike conventional care, it may not be possible to follow the preferences of individual patients and their physicians when there is insufficient supply of a medication. Some patients who want the therapy and might benefit from it may not be able to receive it. Third, scarce medications should be allocated fairly, avoiding discrimination and mitigating health disparities. Fourth, allocation policies should be made transparent, accountable, responsive to the concerns of those affected, and proportionate to the situation, including the trajectory of the epidemic and the supply of medications relative to the need.

Goals of Therapies for COVID-19 Infection

Specific goals derived from this ethical framework can provide practical clinical advice. First, save the most lives in the short-term and near term. Although the primary goal is saving lives, additional goals may include reducing the duration of hospitalization or mechanical ventilation, or preventing new cases.

Second, decrease the disparities in COVID-19 case-fatality rates, which disproportionately affect African American and Latino communities.⁵ These differences are likely due to multiple factors including barriers to accessing health care, insurance status, income, primary language spoken, concerns about their own or household members' immigration status, and other social determinants of health.

Third, strengthen the community's ability to respond to the pandemic. Some workers in essential jobs are repeatedly exposed to individuals with infection or cannot practice physical distancing, including workers in retail, public transportation, and food processing; first responders including police and firefighters; and physicians, nurses, and other workers in hospitals and nursing homes. In some of these essential roles, persons of color predominate. In many instances, such workers are not provided with adequate personal protective equipment.

Fourth, preserve a supply of existing medications for patients with chronic illness who depend on them for non-COVID-19 indications.

Fifth, reserve enough of the drug to conduct additional well-designed clinical trials. In the long run, a stronger evidence base for COVID-19 therapies will save more lives.

Evidence-based, fair guidelines to allocate scarce drugs for COVID-19 could help physicians make difficult decisions

provides practical suggestions for clinicians and medical centers that are treating hospitalized patients with COVID-19 to consider when allocating proven parenteral therapies, such as remdesivir and other treatments that are under development, such as monoclonal antibodies, in a manner that maximizes benefit to patients, mitigates disparities, and adheres to ethical principles. Although ethical principles for allocating scarce resources during a pandemic are universal, their application to particular interventions, such as parenteral drugs or ventilators, depends on the clinical context and indications.⁴ The allocation of scarce outpatient drugs for COVID-19 is not addressed.

Ethical Principles to Guide These Decisions

In a public health crisis, broad ethical principles need to be balanced.⁴ First, reducing mortality provides benefit to the community as a whole. Benefit should be assessed using the best available evidence, and allocation policies should be revised as evidence develops.

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Practical Recommendations for Allocating a Scarce Drug

Guidelines for prescribing parenteral COVID-19 therapies when supply falls short of need should be developed by hospitals and professional societies.

First, allocation should be evidence based, with priority given to patient groups who have been shown to benefit in rigorous RCTs, such as those who meet the inclusion criteria of RCTs on which FDA authorization or approval was based. After approval, additional trials may support the drug's use in other conditions. If sound evidence emerges that certain patient groups have larger clinical benefits than others (eg, a lower number needed to treat to save a life), these groups should receive priority. While shortages exist, compassionate use beyond the evidence should be minimized.

Second, prioritization should not exclude patients based on age, disability, religion, race or ethnicity, national origin, gender, sexual orientation, or perceived quality of life.⁶

Third, for existing FDA-approved medications, patients already receiving the drug for other serious conditions, with good evidence to support such use, should continue to receive it.

Fourth, clinicians should base judgments about which patients might benefit the most or the least on rigorous evidence. For example, although older age, diabetes, hypertension, and coronary artery disease are risk factors for poor prognosis in COVID-19, predictors of poor prognosis do not necessarily predict response to a new treatment. Physicians should provide new therapies to patients with these conditions, unless evidence emerges that shows that they do not respond to the therapy or respond less well than patients without these conditions. Making inferences about the benefits of a scarce drug from anecdotal experience, observational data on disease trajectory, or post hoc subgroup analyses of small trials may be misleading and should not guide decisions during a shortage.

Fifth, random allocation, such as by lottery, is the fairest way to allocate a very scarce drug among eligible patients. A "first-come, first-served" approach should be avoided because it is not random and it disadvantages those who experience barriers to seeking care. Within a lottery, workers in essential jobs may be given some priority.

Sixth, clinicians will need support in having difficult discussions with patients who do not receive the drug and with their fami-

lies. Suggestions for how to respond to emotions such as concern and anger, and allegations of injustice, have been published.⁷

Implementation of Recommendations

Hospitals, as the institutions that provide parenteral drugs, should establish a multidisciplinary drug allocation committee tasked with developing guidelines for appropriate use of scarce therapies for COVID-19. Committees should include representatives from hospital medicine, infectious disease, critical care, pharmacy, nursing, administration, and ethics if available, as well as laypeople, including members of groups who experience health disparities. This committee should obtain feedback from clinicians, community leaders, and patient advocates, modifying the guidelines as appropriate; track the hospital's medication supply and utilization patterns; review emerging evidence on COVID-19 therapies; and communicate these guidelines to hospital leadership and clinical services. Even with a lottery, the committee should check that facially neutral policies for allocation do not in practice result in unfair disparities that harm groups that are already disadvantaged.

In addition, hospitals should promote adherence to guidelines, without unduly burdening clinicians. For example, prescribing criteria could be incorporated into the electronic health record, such as providing a checklist to document that the patient meets indications for the drug. A clinical pharmacist could review all new prescriptions for the drug for appropriateness and concordance with guidelines. Retrospectively, patterns of prescribing inconsistent with the guideline should be identified and addressed. Furthermore, hospitals should collectively work with government officials and pharmaceutical distributors to match supply with demand and improve the allocation process. Hospital leaders should also collaborate with insurers to ensure that out-of-pocket costs for effective drugs for COVID-19 are not a barrier for patients.

Conclusions

In summary, evidence-based, fair guidelines to allocate scarce drugs for COVID-19 could help physicians make difficult decisions. Transparent guidelines will help promote trustworthiness when not all infected patients can receive a medication that is in short supply.

ARTICLE INFORMATION

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