A Multicenter Weighted Lottery to Equitably Allocate Scarce COVID-19 Therapeutics

To the Editor:

Shortages of new therapeutics to treat coronavirus disease (COVID-19) have forced clinicians, public health officials, and health systems to grapple with difficult questions about how to fairly allocate potentially life-saving treatments when there are not enough for all patients in need (1). Shortages have occurred with remdesivir, tocilizumab, monoclonal antibodies, and the oral antiviral Paxlovid (2).

Ensuring equitable allocation is especially important in light of the disproportionate burden experienced during the COVID-19 pandemic by disadvantaged groups, including Black, Hispanic/Latino and Indigenous communities, individuals with certain disabilities, and low-income persons. However, many health systems have resorted to first-come, first-served approaches to allocation, which tend to disadvantage individuals with barriers in access to care (3). There is mounting evidence of racial, ethnic, and socioeconomic disparities in access to medications for COVID-19 (4, 5).

One potential method to promote equitable allocation is to use a weighted lottery, which is an allocation strategy that gives all eligible patients a chance to receive the scarce treatment while also allowing the assignment of higher or lower chances according to other ethical considerations (6). We sought to assess the feasibility of implementing a weighted lottery to allocate scarce COVID-19 medications in a large U.S. health system and to determine whether the weighted lottery promotes equitable allocation.

Methods

In response to impending shortages of remdesivir in the spring of 2020, we developed a weighted lottery using an iterative multistakeholder process that included experts in bioethics, equity and inclusion, economics, medicine, and hospital operations. We engaged a community-based patient and family advisory committee during the lottery development process, who endorsed the final weighted lottery. The lottery's ethical goals were derived from policy recommendations from the Commonwealth of Pennsylvania Department of Health: *1*) to promote community benefit; *2*) to proactively mitigate health disparities in COVID-19 outcomes; and *3*) to ensure that all eligible patients have a chance to receive treatment and receive an individualized assessment. Pennsylvania guidelines do not permit direct consideration of race or ethnicity when allocating scarce COVID treatments (7).

To promote geographic equity, we redistributed the supply of remdesivir that was initially allocated solely to one large academic medical center in Pittsburgh, Pennsylvania, to all 21 University of Pittsburgh Medical Center (UPMC) hospitals in western Pennsylvania. To mitigate disparities and promote fairness, individuals from disadvantaged neighborhoods, defined as those with a score of 8, 9, or 10 on the state area deprivation index (ADI) (8), received a 25% increase in their chances above the baseline lottery chances (Table 1). Individuals who work in frontline essential jobs (e.g., healthcare workers, bus drivers, and grocery store employees) also received a 25% increase in their chances (9). To promote population-level outcomes, individuals who were expected to die within a year from an end-stage condition received 50% lower chances. When data emerged that individuals already receiving mechanical ventilation or extracorporeal membrane oxygenation (ECMO) were less likely to benefit from remdesivir, these individuals received 50% lower chances. A complete description of the ethical justification and operational details of the weighted lottery is freely available online (10).

We deployed the weighted lottery process during periods of shortage of remdesivir in the spring of 2020 across 21 hospitals in the UPMC health system. All patients who met the U.S. Emergency Use Authorization (EUA) criteria for remdesivir (11) were eligible and provided verbal informed consent before treatment. The UPMC quality improvement committee determined the weighted lottery to be a quality improvement project that did not require written informed consent because its primary purpose was to fairly allocate a scarce medical treatment within routine clinical care.

Daily, the allocation team received an automated report listing all patients admitted in the previous 24 hours with a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test result, then determined each patient's eligibility for remdesivir in consultation with the patient's physician. To minimize the time required of the treating clinical teams—who were strained by high patient volumes during pandemic surges—the lottery was performed by a member of the allocation team. They obtained the information needed for the lottery during brief telephone conversations with patients' attending physicians, which were already being conducted to determine whether the patient met the U.S. Food and Drug Administration's EUA criteria for treatment. Eligible patients from all 21 hospitals were entered into a single lottery each day, which was conducted by staff blinded to patient demographics at a coordinating center in Pittsburgh, Pennsylvania. Each patient was entered into the lottery only once. Baseline lottery chances were established each time a new drug shipment arrived, based on the drug supply and the projected caseload. To minimize the risk of unused drug supply, we set the baseline lottery chances slightly higher than the estimated chances from the prior week's supply and demand, which would lead to more rapid use of the drug supply. We also reassessed the lottery chances weekly based on actual use of the drug to adjust as needed to prevent incomplete use of the drug.

We used the electronic health record to ascertain the demographic characteristics of eligible patients. We collected feasibility data on the lottery process, including the proportion of days on which screening occurred, the proportion of eligible days on which the lottery occurred, and any deviations from the lottery protocol.

We used a Fisher exact test to compare the proportion of Black and White patients with each weighting attribute in the lottery. We determined what each patients' chances would have been in an unweighted lottery by dividing the number of available treatment courses by the projected number of eligible patients until the next drug shipment was expected to arrive. To determine whether the weighted

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Table 1. Weighting Factors in the Remdesivir Lottery

Weighting Factor	Specification
1. 25% increase in chances for patients from disadvantaged communities	Residing in a neighborhood in the three highest deciles of disadvantage quantified with the Area Deprivation Index
2. 25% increase in chances for frontline essential workers	As defined in publicly released guidance documents from the Commonwealth of Pennsylvania
3. 50% decrease in chances for patients expected to die within a year from an underlying end-stage medical condition	Clinical judgment of the patient's primary attending physician
4. 50% decrease in chances for patients with severe respiratory failure*	Patients with COVID-19 who required mechanical ventilation or extracorporeal membrane oxygenation at the time of evaluation

Definition of abbreviation: COVID-19 = coronavirus disease.
Hypothetical example of how a patient is entered into the weighted lottery: A patient is admitted with COVID-19 pneumonia and is requiring 4 L/min of supplemental oxygen via nasal cannula to treat hypoxemia. A hospital pharmacist, who is a member of the hospital's allocation team, receives a daily automated report of all patients in the hospital with COVID-19 who are receiving supplemental oxygen. She determines that this patient meets the U.S. Food and Drug Administration's emergency use authorization eligibility criteria to receive remdesivir. Based on the patient's home address, she determines that the patient lives in a highly disadvantaged neighborhood (Area Deprivation Index score = 9) She communicates by telephone with the patient's attending physician, who reports that the patient is a frontline essential worker (a nurse's aide in a skilled nursing facility) and does not have any end-stage medical conditions from which he is expected to die within a year. The pharmacist enters the patient into the centralized daily lottery. At the time the patient is evaluated for eligibility, the baseline lottery chances had been set at 50%, which was determined by dividing the number of eligible cases in the prior 7 d by the number of treatment courses available over the next 7 d. He receives a 25% boost in his chances because he is a frontline essential worker and a 25% boost in his chances because he is from a highly disadvantaged neighborhood. Therefore, his chance to receive treatment in the lottery is increased from the baseline chance of 50% to 75% ($[0.5 \times (1 + 0.25 + 0.25)] = 0.75 \times 100 = 75\%$). The central allocation committee uses a random number generator to select a number between 1 and 100. If the generated number is between 1 and 75, the patient will be allocated remdesivir (i.e., 75% chances in the lottery). If the number is between 76 and 100, the patient will not be allocated remdesivir. The randomly generated number was 11, so the patient was allocated remdesivir.
*This weighting factor was added when evidence emerged that remdesivir is less effective in patients with advanced respiratory disease.

lottery resulted in different allocation chances for individuals according to ADI status, essential worker status, end-of-life status, and receipt of ECMO or mechanical ventilation, we used the difference-in-differences method to compare each patient's actual weighted chances to what their chance would have been in an unweighted lottery (12). In a separate analysis, we also conducted a logistic regression to determine whether the weighting factors in the lottery (e.g., high ADI score, essential worker status, etc.). were associated with the expected increases or decreases in patients' treatment allocation.

Results

There were 55 courses of remdesivir available for 93 eligible patients during the 24-day period of drug shortage. The average age of eligible patients was 68 ± 15 years, 49% were female, 69% were White, and 30% were Black. Overall, 45% of eligible patients were from disadvantaged neighborhoods (68% of Black patients and 33% of White patients; $P = 0.003$), 20% were frontline essential workers (21% of Black patients and 20% of White patients; $P = 1.0$), 8% were receiving mechanical ventilation or ECMO (0% of Black patients and 11% of White patients; $P = 0.10$), and 9% were expected to die within a year from an end-stage condition (14% of Black patients and 6% of White patients; $P = 0.24$).

Feasibility metrics showed that the screening and lottery processes were conducted per protocol on 100% of eligible days. All patients who were allocated remdesivir in the lottery were offered remdesivir; all 55 treatment courses were allocated. Consistent with the goal of avoiding underuse of available drug, there were 3 days at

Table 2. Impact of Weighted Lottery on Equitable Allocation of Remdesivir

Attribute	Unweighted Lottery Chances	Weighted Lottery Chances	*P* Value*	Odds Ratio for Treatment Allocation†	95% CI†
Essential worker Yes (*n* = 19)	47%	60%	0.04	1.73	0.59–5.12
High ADI Yes (*n* = 41)	48%	57%	0.045	1.20	0.52–2.74
Near EOL Yes (*n* = 8)	42%	26%	0.01	0.44	0.10–2.04
Receiving MV/ECMO Yes (*n* = 16)	70%	57%	0.28	0.99	0.20–4.83

Definition of abbreviations: ADI = Area Deprivation Index; CI = confidence interval; ECMO = extracorporeal membrane oxygenation; EOL = end of life; MV = mechanical ventilation.
**P* value for difference-in-difference method testing whether, compared with an unweighted lottery, a weighted lottery significantly *1*) increased the lottery chances for patients with high ADI scores; *2*) increased the lottery chances for frontline essential workers; *3*) decreased the lottery chances for patients near the end of life (i.e., patients expected to die within a year from an end-stage medical condition); and *4*) decreased the lottery chances for patients receiving MV/ECMO.
†The odds ratios and 95% CIs were obtained from a multivariable logistic regression of allocation of remdesivir in the lottery on the four specific conditions tested simultaneously (essential worker [yes/no], high ADI [yes/no], near EOL [yes/no], and receiving MV/ECMO [yes/no]).

the end of the period of scarcity during which the drug supply was exhausted.

As summarized in Table 2, individuals from disadvantaged communities and those who were frontline essential workers had higher chances in the weighted lottery than in an unweighted lottery. Patients expected to die within 1 year and those already receiving mechanical ventilation/ECMO had lower chances. In multivariable analyses, we observed similar patterns, which did not reach statistical significance, with frontline essential workers and individuals from high-ADI areas having higher odds of treatment allocation. Overall, similar proportions of Black patients and White patients were allocated treatment in the lottery (61% vs. 59%; $P = 0.90$).

Discussion

We successfully implemented a weighted lottery to equitably allocate scarce COVID-19 therapeutics, which resulted in increased treatment allocation to groups that have been disproportionately impacted by the pandemic, decreased allocation to groups who are less likely to derive clinical benefit, and equal allocation to Black and White patients within the UPMC health system.

To our knowledge, this is the first use in clinical medicine of a weighted lottery to allocate scarce medical treatments. There are several important strengths to the weighted lottery process we developed. First, centralizing the lottery among 21 hospitals promoted geographic equity and reduced administrative burden. Using an automated case-finding process—rather than relying on physicians to identify and refer all eligible patients—promoted equity by preventing referral bias. The public legitimacy of the weighted lottery was enhanced by engaging diverse stakeholders in its development and by grounding the lottery-weighting factors in the ethical goals established by the Commonwealth of Pennsylvania.

In contrast to recent research showing racial disparities in receipt of scarce COVID therapeutics (4, 5), the weighted lottery resulted in equal access to treatment among Black and White patients. Although achieving equal access across racial groups is an improvement on the status quo, it does not mean equitable access was achieved. If equity requires that racial disparities in clinical outcomes are mitigated rather than merely not worsened—as was specified in Pennsylvania's allocation guidelines—then other strategies may be needed. Because the Commonwealth of Pennsylvania's guidelines disallowed direct consideration of race in the allocation framework, we used only "indirect" equity interventions—defined as interventions that do not directly consider individuals' race but are expected to narrow racial disparities (i.e., priority to patients from disadvantaged neighborhoods and to frontline essential workers). Our results raise important questions about whether the available indirect equity interventions will be adequate to achieve equitable allocation to the groups who have disproportionately borne the burden of the pandemic (13).

A potential limitation of our implementation strategy is that we relied on clinician judgment to determine whether a patient was expected to die within a year from an end-stage medical condition, which may introduce bias or inaccuracy. Future work should examine whether there are practical ways to rapidly incorporate validated mortality prediction models or expert consultation. We deployed the weighted lottery in a health system with extensive experience deploying systems-level initiatives across multiple hospitals. Our results may not be directly transferable to other settings without this experience.

We conclude that it is feasible to use a weighted lottery to allocate scarce COVID-19 treatments in the inpatient setting. The relevance of this weighted lottery goes beyond the current pandemic because it can be adapted to other situations of drug scarcity (e.g., supply chain disruptions). The specific lottery factors and weightings can be modified based on the clinical and ethical circumstances to promote equitable access to scarce treatments. ■

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COVID-19 and Risk of Oxygen-Dependent Chronic Respiratory Failure: A National Cohort Study

To the Editor:

Coronavirus disease (COVID-19) can impair gas exchange (1), but the risk of post-infectious oxygen-dependent chronic respiratory failure is unknown.

We performed a population-based, nationwide study of cumulative incidence, risk factors and clinical course of long-term oxygen therapy (LTOT) after COVID-19, using data from the SCIFI-PEARL (Swedish Covid-19 Investigation for Future Insights – a Population Epidemiology Approach using Register Linkage) study (2). We included all people in Sweden aged ⩾16 years with a laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection from January 1, 2020, until August 31, 2021, with no LTOT before the COVID-19 diagnosis. Data on LTOT start any time after COVID-19 until September 30, 2021, were obtained from the Swedish National Registry of Respiratory Failure (Swedevox) (3). In Sweden, home oxygen is prescribed strictly according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) criteria at specific respiratory units, using stationary and portable oxygen concentrators (3).

Risk factors for starting LTOT after COVID-19 were assessed using multivariable logistic regression. Severity of COVID-19 was categorized as mild (no hospitalization), severe (hospitalized without need of ICU), or critical (ICU care), age as 16–49, 50–59, 60–69, and ⩾70 years, and education as primary (compulsory school of 9 years), secondary (2–3 years beyond compulsory school), and tertiary education (university studies). COVID-19 comorbidity risk groups according to the National Board of Health and Welfare (4) included chronic heart, lung, and renal disease, type 2 diabetes with complications, obesity, and hypertension. Chronic lung diseases included chronic obstructive pulmonary disease (COPD; 85%), interstitial lung disease, cystic fibrosis, or chronic respiratory failure from other causes (4). Cumulative incidence of LTOT starts was compared among four periods: January–July 2020 (first wave); August–December 2020 (original SARS-CoV-2 variant of concern [VOC] with standardized COVID-19 treatments including corticosteroids and ventilation strategies [5]); January–March 2021 (alpha variant dominance); and April–September 2021 (delta variant and established mass vaccination in Sweden). In two merged periods—January–December 2020 and January–September 2021, including new VOCs and mass vaccination—differences in cumulative incidence and factors associated with LTOT were analyzed using chi-square tests, interaction analysis by period, and multivariable logistic regression.

In patients starting LTOT after COVID-19, frequencies of death, LTOT discontinuation due to improvement, and ongoing LTOT up to September 30, 2021, were calculated.

During the entire observation period of 21 months, 271 of 992,968 individuals with COVID-19 started LTOT. The overall cumulative incidence was 27 (95% confidence interval [CI], 24–31) per 100,000, decreasing over time from 81 (January–July 2020) to 28 (August–December 2020), 25 (January–March 2021), and 13 (April–September 2021). The difference between 2020 and 2021 was statistically significant: 38 (32–44) versus 20 (16–23) per 100,000, $P < 0.0001$, as was effect modification by first or second period on the associations of hospitalized COVID-19 infection and chronic respiratory disease, respectively, with LTOT start (data not shown).

Median time from COVID-19 confirmation to LTOT start was 46 (interquartile range [IQR], 30–83) days. Overall and in both time periods, the strongest independent risk factors for LTOT were severe or critical COVID-19, older age, and preexisting chronic respiratory disease (Table 1 and Figure 1). Lower educational level and female sex were associated with higher LTOT risk for the entire observation period, with similar point estimates in both periods (Table 1). In an

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