

# Paying It Backward and Forward: Expanding Access to Convalescent Plasma Therapy Through Market Design

Scott Duke Kominers

Parag A. Pathak

Tayfun Sönmez

M. Utku Ünver

Working Paper 20-116



# Paying It Backward and Forward: Expanding Access to Convalescent Plasma Therapy Through Market Design

Scott Duke Kominers

Harvard Business School

Parag A. Pathak

Massachusetts Institute of Technology

Tayfun Sönmez

Boston College

M. Utku Ünver

Boston College

**Working Paper 20-116**

Copyright © 2020 by Scott Duke Kominers, Parag A. Pathak, Tayfun Sönmez, and M. Utku Ünver.

Working papers are in draft form. This working paper is distributed for purposes of comment and discussion only. It may not be reproduced without permission of the copyright holder. Copies of working papers are available from the author.

Funding for this research was provided in part by Harvard Business School. Kominers gratefully acknowledges the support of National Science Foundation grant SES-1459912, the Ng Fund and the Mathematics in Economics Research Fund of the Harvard Center of Mathematical Sciences and Applications (CMSA). Sönmez gratefully acknowledges the research support of Goldman Sachs Gives via Dalinc Ariburnu - Goldman Sachs Faculty Research Fund.

# Paying It Backward and Forward: Expanding Access to Convalescent Plasma Therapy Through Market Design\*

Scott Duke Kominers    Parag A. Pathak    Tayfun Sönmez    M. Utku Ünver<sup>†</sup>

May 2020

## Abstract

COVID-19 convalescent plasma (CCP) therapy is currently a leading treatment for COVID-19. At present, there is a shortage of CCP relative to demand. We develop and analyze a model of centralized CCP allocation that incorporates both donation and distribution. In order to increase CCP supply, we introduce a mechanism that utilizes two incentive schemes, respectively based on principles of “paying it backward” and “paying it forward.” Under the first scheme, CCP donors obtain treatment vouchers that can be transferred to patients of their choosing. Under the latter scheme, patients obtain priority for CCP therapy in exchange for a future pledge to donate CCP if possible. We show that in steady-state, both principles generally increase overall treatment rates for all patients—not just those who are voucher-prioritized or pledged to donate. Our results also hold under certain conditions if a fraction of CCP is reserved for patients who participate in clinical trials. Finally, we examine the implications of pooling blood types on the efficiency and equity of CCP distribution.

**Keywords:** COVID-19, convalescent plasma, vouchers

**JEL codes:** D47, C78

---

\*We thank Deniz Aktürk Erdem for bringing social media appeals for COVID-19 Convalescent Plasma to our attention.

<sup>†</sup>Kominers: Harvard Business School and Department of Economics, Harvard University; [kominers@fas.harvard.edu](mailto:kominers@fas.harvard.edu). Pathak: MIT Department of Economics and NBER; [ppathak@mit.edu](mailto:ppathak@mit.edu). Sönmez: Boston College, Department of Economics; [sonmezt@bc.edu](mailto:sonmezt@bc.edu). Ünver: Boston College, Department of Economics; [unver@bc.edu](mailto:unver@bc.edu). Kominers gratefully acknowledges the support of National Science Foundation grant SES-1459912, the Ng Fund and the Mathematics in Economics Research Fund of the Harvard Center of Mathematical Sciences and Applications (CMSA). Sönmez gratefully acknowledges the research support of Goldman Sachs Gives via Dalinc Ariburnu - Goldman Sachs Faculty Research Fund.

# 1 Introduction

Without therapeutic agents or vaccines for the novel coronavirus disease, COVID-19, the medical community has turned to a century-old therapy based on convalescent plasma.<sup>1</sup> In COVID-19 convalescent plasma (CCP) therapy, an infected patient receives a transfusion of plasma collected from a patient who has recently recovered from the disease. Plasma is extracted from the donor using an apheresis machine, which separates blood plasma from blood cells; the red and white blood cells are returned to the recovered patient through injection. When donated CCP is injected into an infected patient, antibodies in that CCP attack the virus. Subject to eligibility requirements, a recovered patient may be able to donate multiple units of CCP once she is free of disease.<sup>2</sup> Preliminary evidence suggests that plasma transfusions improve clinical outcomes (see, e.g., Duan et al. (2020), Shen et al. (2020), and Ye et al. (2020)), and broader trials of the therapy are ongoing. Moreover, on March 25, 2020, the U.S. Food and Drug Administration approved CCP therapy for expanded access—also known as “compassionate use”—when no other treatment is available.<sup>3</sup> And on May 1, 2020, Sheridan, 2020 reported that in the short run CCP therapy is the treatment of choice for COVID-19.

Yet CCP is a scarce resource. Estimates are inexact, but some suggest that present demand may be twice supply (Burch and Harmon, 2020). In the FDA’s National Expanded Access Treatment protocol, 5,968 patients have signed up to obtain convalescent plasma and only 2,576 have received it as of April 27, 2020 (Rubin, 2020).<sup>4</sup> As in the case of deceased-donor organ transplantation, the shortage is expected to be more severe for patients of certain blood types since CCP donors must be plasma-compatible with CCP recipients.<sup>5</sup> The number of units and times a donor can donate CCP is limited; current estimates suggest that a donor can donate between two and four units each time, for a maximum of three times, with a four-week wait between each donation.

Recognizing the necessity of increasing the supply of CCP and make it available to eligible patients in need, numerous medical institutions worldwide have sought to devise protocols to collect CCP from willing donors, which could then be made available to patients. On CCP distribution, Rubin (2020)

---

<sup>1</sup>Injecting sick patients with convalesced antibodies is a classic approach in immunotherapy. The first Nobel Prize in Physiology or Medicine was the 1901 prize for serum therapy (serum is the liquid left after coagulant elements are removed from plasma). Convalescent plasma treatment is often used during the outbreak of novel diseases when no other treatments are available; it was used, for example, during the 2003 SARS-CoV-1 epidemic, 2009-2010 H1N1 influenza virus pandemic, and 2012-13 MERS-CoV epidemic (EBA, 2020; Rubin, 2020). During the 1918 Spanish flu, fatality rates were cut in half for patients treated with blood plasma (see Luke et al., 2006 and Roos, 2020). Convalescent plasma has also been used to treat measles, influenza, and other infectious diseases.

<sup>2</sup>The current FDA emergency use authorization requires that before donating CCP, an individual who has recovered from COVID-19 must have a complete resolution of symptoms for at least 28 days, or no symptoms for at least 14 days and a negative lab test for active COVID-19 disease (FDA, 2020).

<sup>3</sup>The FDA has approved three criteria for administering or studying CCP: clinical trials, expanded access, and single patient emergency.

<sup>4</sup>The latest numbers are available at <https://www.uscovidplasma.org/>.

<sup>5</sup>An individual of blood type  $A$  has  $A$  antigens and anti- $B$  antibodies. An individual of blood type  $B$  has  $B$  antigens and anti- $A$  antibodies. An individual of blood type  $AB$  has neither antibody but has both antigens. An individual of bloodtype  $O$  has neither antigen but has both antibodies. An antibody present in the donor plasma attacks the associated antigen in recipient blood if present. Hence, donors of blood type  $AB$  (who have neither antigen) can donate their plasma to patients of all blood types; donors of blood type  $A$  can donate to patients of blood types  $A$  and  $O$ ; donors of blood type  $B$  can donate to patients of blood types  $B$  and  $O$ ; and donors of blood type  $O$  can only donate to patients of blood type  $O$  (Norfolk, 2013). (The plasma compatibility relation reverses the compatibility relation for solid organ donation, where blood type  $O$  is the universal donor and blood type  $AB$  is the universal receiver.)

states: “practically every day, another medical center announces plans to begin administering convalescent plasma to patients with COVID-19.” Blood donation centers such as those at the American Red Cross are being repurposed to collect CCP; at time of writing, more than 2,000 sites can accept plasma donations, and the Mayo Clinic has been named the lead institution in the U.S. to oversee the FDA’s expanded CCP access system.

By and large, access to CCP is uncoordinated. Donation efforts have thus far been based on outreach from physicians, hospitals, and local public health authorities.<sup>6</sup> Current disparities in CCP access depend on regional differences, socio-economic status, social-media appeals, and physician behavior (see, e.g., Aleccia, 2020). Harrison (2020) has emphasized the need for clear criteria for plasma allocation, so that the de facto allocation does not reduce to one based on awarding units to patients whose advocates “yell at hospital services the most.”

The absence of transparent and well-defined CCP allocation rules has important equity implications due to both blood type differences across ethnic groups and variation in COVID-19 exposure and testing driven by differences in socioeconomic status and health care access.<sup>7</sup>

This paper introduces and analyzes a market design approach to collecting and distributing CCP. We develop a steady-state continuum model that jointly incorporates donation and allocation of CCP. The crux of our mechanism is systematic utilization of dual *pay-it-backward* and *pay-it-forward* principles to increase the supply of CCP. Through the pay-it-backward principle, the system “pays back” a CCP donor for her potentially life-saving donation by giving her a number of vouchers that can be used to obtain priority for CCP therapy of her loved ones should the need arise. Through the pay-it-forward principle, a patient receives priority access for CCP therapy in exchange for a pledge to return the favor back by donating her own CCP in the near future, assuming she recovers and becomes eligible for plasma donation.<sup>8</sup> These features embed and formalize practices that are already informally embraced by some doctors in their attempt to increase the recruitment of CCP donors. For example, a pulmonologist interviewed in *JAMA* explained (Rubin, 2020):

“...blood collection centers generally do not permit donors to designate their blood for a specific patient. Instead, Brown said, she encourages people interested in making a designated donation to pay it forward and donate to replace the convalescent plasma used by their intended recipient.”

In our steady-state model of plasma donation, CCP donors may be given priority vouchers that can be used to give treatment priority to family members and other close associates; priority is also given to participants in clinical trials. The steady-state availability of CCP therapy is a function of

---

<sup>6</sup>There have also been several heart-wrenching appeals for CCP from family and friends of patients, often via the internet and through groups like Survivor Corps (see, e.g., Burch and Harmon, 2020).

<sup>7</sup>Kidney allocation policy has faced similar equity concerns. African-Americans make up a disproportionate share of renal failure patients of blood types *O* and *B* (Rettner, 2019), and the waiting times for kidneys with these two blood types are considerably higher than the waiting times for kidneys of blood types *A* and *AB*. In 2018, the numbers of deceased-donor transplants per 100 waitlist years for blood types *O* and *B* were roughly half the number for *AB* (OPTN, 2018, Figure KI 18).

<sup>8</sup>A similar feature exists in non-directed donor (NDD) chains in kidney exchange, where a patient receives a living-donor kidney before her incompatible donor donates a kidney to a patient in another incompatible patient-donor pair. Such an NDD chain becomes possible with the undirected initial donation of a Good Samaritan donor; the longest single-center paired kidney exchange of this form involved 101 donors and recipients (Pope, 2018).

the number of patients who have recovered (both through CCP therapy and by other means). We find that so long as the CCP replenishment rate is large enough to support the clinical trial, it is possible to treat all prioritized patients in equilibrium. The rate of treatment for non-prioritized patients becomes higher, as well. We characterize when it is possible to treat all patients—even those who are not ex ante prioritized—and show that so long as recovered patients are more willing to donate if they receive vouchers, introducing a voucher system strictly benefits non-prioritized patients. Overall treatment availability expands further if we prioritize patients who pledge to pay it forward by donating CCP once they have recovered: if patients who pledge to donate have an aggregate CCP replenishment rate that is more than one-for-one, prioritizing those patients increases the treatment rate for non-prioritized patients, irrespective of how many patients make pledge to donate ex ante. Most of our analysis works with a single blood type for ease of illustration. But we show how to combine that analysis with ideas from graph theory to identify the optimal cross-blood type CCP-pooling strategy to maximize an egalitarian treatment objective.

The remainder of this paper is structured as follows. Section 2 reviews some design considerations that might be relevant for practical implementation of our idea. Section 3 describes our model of plasma donation and distribution, specialized to the case of only one blood type. Section 4 examines the possibility of pooling multiple blood types, and reviews related literature. Section 5 concludes.

## 2 Market Design Considerations for Plasma Donation and Distribution

We envision a mechanism where only a portion of the CCP supply can be allocated through the two types of incentive schemes we introduce. We refer to that portion as the *incentivized CCP reserve*. The remaining portion is reserved for participants of clinical trials, as well as for any other patient group the central planner deems adequate; for simplicity, we refer to that portion as the *clinical trial CCP reserve*. The clinical trial CCP reserve is effectively exogenous—at any point in time, the clinical trial CCP reserve will be allocated to its beneficiaries.

The incentivized CCP reserve, meanwhile, is endogenous—depending on two different types of incentives. The first incentive we consider is the provision of a fixed number of vouchers to CCP donors, which can be later redeemed by patients of the donors’ choosing; we refer to this as a *pay-it-backward* incentive. These vouchers are of potential value to donors, because patients who arrive the system with a voucher have *first-tier priority* access for units in the incentivized CCP reserve.

The second type of incentive—which we call a *pay-it-forward* incentive—exploits the unusual feature of the CCP therapy that any patient who recovers becomes a potential CCP donor. Since each donor can supply CCP that is sufficient for the treatment needs of 2-4 patients each donation up to three times, this provides a unique opportunity to expand access to CCP: if we can use CCP to increase the recovery rate, and those recovered patients go on to donate CCP, then we can grow the CCP supply more than one-for-one. Thus, we propose to provide *second-tier priority* access to units in the incentivized CCP reserve to patients who do not have a voucher but who pledge to donate CCP in the near future, in the event that they recover. Any patient who is able to materialize her pledge through a CCP donation may also receive a number of vouchers, although not the same number provided to

donors of pay-it-backward incentives.

The priority tiers for access to treatment through the incentivized CCP reserve are then as follows:

1. *First-tier priority*: Patients who arrive with vouchers that are obtained in either way.
2. *Second-tier priority*: Patients who arrive with no voucher but who pledge to donate CCP upon recovery, subject to passing eligibility requirements.
3. *Third-tier priority*: Any other patient who is in need of CCP therapy.

Within each tier, ties are broken in a systematic way determined by the central planner.

Meanwhile, the allocation process in the clinical trial CCP reserve is fully regulated by the central planner.

## 2.1 Pay-it-Backward Incentives

Some donors are purely altruistic and they do not need any incentive to donate. But potential donors may at least in part wish to be able to donate to their loved ones. For these donors, the pay-it-backward incentive can be expected to be valuable because the voucher provides a medium of exchange that eases three frictions associated with donation. For example, consider a potential donor who wants to donate to a family member. She may not be able to donate to her intended recipient if any of the following three difficulties arise:

1. The donor and intended recipient are *time-incompatible*: by the point at which the beneficiary needs CCP, the donor is medically unable to donate.
2. The donor and intended recipient are *plasma incompatible*: the beneficiary has antibodies for antigens in donor blood that makes the donation medically impossible.
3. The donor and intended recipient are *location incompatible*: the donation is either difficult or impossible due to travel requirements.

The first friction occurs, for example, if potential donor might not be able to donate because she does not have enough antibodies remaining or is outside the 28-day window between donations; in this case, the voucher makes it possible for the donor to contribute to her loved one's recovery even after the donor would not normally be able to do so. The second friction occurs, for example, if the potential donor is of blood type O and her family member is of blood type A; here, the designated beneficiary can use her voucher to obtain compatible plasma. Finally, the third friction arises as when the donor and her preferred beneficiary are in different locations; this last issue is particularly salient in the case of COVID-19, since the pandemic has made travel even over medium distances quite difficult. While plasma can be stored, travel restrictions may prevent the donor's CCP from being transfused to a far away a beneficiary. A voucher would effectively bridge the distance gap, by enabling the donor to donate near her home, and then effectively "transfer" the resulting plasma treatment to her family member further away. By function as an in-kind medium of exchange, a voucher surmounts each friction; this should naturally result in greater overall donation. And because CCP donors can donate

multiple units of plasma, the resulting increase in CCP supply benefits the overall patient pool—not just voucher recipients.

There is a precedent for these types of vouchers in kidney exchange: A *voucher for a chronologically incompatible* pair (Veale et al. (2017)) involves giving a (typically young) patient priority for a future kidney transplant in exchange for a kidney donation from an older donor today; this mechanism is used when the donor is expected to be too old to donate when the patient will need a transplant. A relatively modest number of these intertemporal exchanges have been organized by the National Kidney Registry, which arranges kidney chains initiated by good-samaritan donors.<sup>9</sup> We anticipate a potentially more substantial role for vouchers in CCP donation, because the risk and potential negative consequences to the donor are much lower under CCP donation than for kidney donation.

## 2.2 Pay-it-Forward Incentives

The pay-it-backward principle just discussed rewards CCP donation ex post. The pay-it-forward principle, by contrast, gives an ex ante reward for a pledge to donate in the future conditional on recovery and eligibility; as we show in the next section, this too can be expected to increase the overall CCP supply, so long as a large enough fraction of the pledged donations are actually carried through.

It is thus essential to think about how many pledged donations will actually materialize. Some patients who benefit from pay-it-forward incentives may turn out to be unable to donate for medical eligibility reasons.

It is also possible that a patient may simply decide not to honor her pledge. This is an important practical issue, but one that appears to have been surmounted in non-directed donor chains in kidney exchange. In a non-directed donor kidney exchange chain, a patient receives a kidney based on the pledge that their donor will donate a kidney to another patient in the future. It is possible that after a patient receives a kidney, their donor may renege; however, in practice this occurs rarely.<sup>10</sup> And the incentive to renege on upfront pledges may be stronger for kidneys than for CCP, since kidneys are not regenerated, and require a much more invasive procedure for donation.

In our model, we allow for the possibility that a patient who pledges to donate in the future ends up not donating (for whatever reason); in the steady-state of our model, what we need is for the fulfilled CCP donation pledges to cover the flow of units used by the patients who pledge (both those who do and do not end up donating in the future).

Of course, since pay-it-forward incentives have not been used in CCP donation before, it is difficult to estimate what fraction of patients will end up fulfilling their pledges. But in any event, the CCP replenishment rate under pay-it-forward incentives depends on (i) the rate of pledge fulfillment, (ii) how many units of CCP each patient who does fulfill a pledge donates each time she does so, and finally (iii) how many times those patients donate; of these parameters, the only one recovered patients can control is (iii).

---

<sup>9</sup>These chains were introduced by Roth et al. (2006), and the proof of concept was documented by Rees et al. (2009).

<sup>10</sup>Cowan et al. (2017) report that only six donors reneged over the course of 1,700 transplants.



## 2.3 Price-Based Covid-19 Convalescent Plasma Markets

There is an active debate in economics and philosophy on the appropriate role of market-based mechanisms with compensation for human products used in medicine or medical research like kidneys, blood, blood products, sperm, breast milk, bone marrow, and other tissues.<sup>11</sup> Since, as far as we know, there is no current market where infected patients can buy CCP or where recovered patients can sell CCP, we do not consider this possibility as part of our model.

We briefly comment on how a price-based market for CCP might relate to these prior debates. Non-regenerative human products such as kidneys are at one extreme. The 1984 National Organ Transplant Act (NOTA) states “it shall be unlawful for any person to knowingly acquire, receive or otherwise transfer any human organ for valuable consideration for use in human transplantation,” and it is a near-universal norm that monetary compensation should play no role in kidney allocation. A 2007 amendment to NOTA, known as the Charlie W. Norwood Living Organ Donation Act, clarified that the language “valuable consideration” does not apply to human organ paired donation. Currently, live kidney donations are from unpaid volunteers with designated recipients.<sup>12</sup>

Regenerative human products like bone marrow and blood are at the other extreme—at present, there is compensation for some voluntary donors. A 2011 9th Circuit Court of Appeals ruled that NOTA’s ban on donor compensation does not apply to bone marrow. Meanwhile, for blood there is an active market, where in the US, patients pay \$334 per unit of whole blood to hospitals. US plasma donors are typically paid per donation, and plasma is aggregated and divided into parts to be sold to hospitals and drug companies (Slonim, Wang, and Garbarino, 2014). While there can be compensation, a donor of blood or blood products typically cannot designate a recipient.

Because CCP is a form of plasma, a natural question is whether a compensated market for CCP will develop. In our model, there is no option to pay to receive CCP or be paid for donating CCP, but a donor can designate the voucher in our model to particular patient in need. As a result, our model of CCP falls between the two extremes described above. We expect that in a crisis moment, there is unlikely to be an active compensated market for CCP (even though it may be impossible to fully prohibit resale of vouchers). If a price-based market does develop, society may deem it unacceptable. Even for a well-developed human product like blood, World Health Organization guidelines recommend that countries have 100% of blood donations come from non-remunerated volunteers due to social and ethical concerns (Slonim, Wang, and Garbarino, 2014). Perhaps more importantly, if vouchers attain monetary value, a significant concern is that some individuals may have an incentive to become sick in order to sell their CCP post-recovery, which seems ethically unacceptable.

## 3 A Model of *ABO*-identical Plasma Donation and Demand

To formalize our conceptual intuitions about the interaction between plasma donation and treatment, we develop a simple steady-state model of CCP donation and demand. In this section, we assume that each patient receives CCP from a donor of the same blood type.

---

<sup>11</sup>Some references are Arrow (1972), Becker and Elias (2007), Bénabou and Tirole (2006), Roth (2007), Sandel (2012), Satz (2012), and Titmuss (1970).

<sup>12</sup>There is an active literature in economics on kidney exchange beginning with Roth, Sönmez, and Ünver (2004, 2005b, 2007).

### 3.1 Paying it Backward through Priority Vouchers

We consider a CCP rationing system that sets aside some units of CCP for clinical trial patients through a *clinical trial CCP reserve*; the rest of the CCP supply is available to be distributed through our incentive schemes through the *incentivized CCP reserve*.

We first consider a pay-it-backward incentive scheme: We suppose that each individual who donates CCP receives  $v_X \geq 0$  *priority vouchers* that can be used to give treatment priority to a family member or other close associate.<sup>13</sup>

The novel feature of this incentivized CCP reserve is that while the clinical trial CCP reserve capacity is set as an exogenous parameter, the incentivized CCP reserve capacity will be endogenously determined at steady state as a function of certain population parameters as well as the priority voucher scheme in place. In particular, the incentivized CCP reserve will prioritize patient groups in the following order:

1. patients who have vouchers (we refer to these patients as *voucher-prioritized*); then
2. patients who do not have a voucher (*non-prioritized*).

Within each group priority group, CCP therapy is allocated based on a well-defined rule such as a point system or a lottery.

We contrast this system with one in which no vouchers are provided—i.e.,  $v_X = 0$ —in which, there is a set-aside reserve for clinical-trial patients and the rest of the CCP supply is rationed among the remaining patients, with all CCP being supplied through purely altruistic donation.

We consider a continuum flow model over (continuous) time and analyze the system at a steady state. Flow rates are defined as one-dimensional Lebesgue measures of sets of individuals that become available at each time.<sup>14</sup>

We suppose for now that there is a separate market for each blood type  $X$ .<sup>15</sup>

Let  $\tau_X$  be the flow clinical trial CCP reserve size. We assume that there is overdemand for the trial, so that a flow rate of  $\pi_X^t = \tau_X$  of patients participate.

At steady state we assume that there are patients who arrive to the medical system with the voucher-prioritized status; we denote the steady-state flow arrival rate of these patients by  $\pi_X^v$ . Each of these patients hold a voucher given to her by a CCP donor.

The remaining patients are non-prioritized; we denote their steady-state flow rate by  $\pi_X^n \geq 0$ .<sup>16</sup>

Some of the patients recover without any CCP therapy; we denote the flow arrival rate of these recovering patients by  $\omega_X$ .

The CCP therapy has steady-state arrival flow rate  $\gamma_X$ . We assume for simplicity that each patient who is treated recovers.<sup>17</sup>

<sup>13</sup>We introduce the pay-it-forward incentive scheme in the next section.

<sup>14</sup>We denote measures of sets, i.e., flow rates, with Greek letters, while we use Latin letters for numbers and proportions.

<sup>15</sup>In the next section, we generalize the analysis to allocate all four blood types of CCP in a single market. Thus, we carry the index  $X$  throughout our analysis in this section so as to anchor which parameters are functions of the blood type.

<sup>16</sup>We treat  $\pi_X^t = \tau_X$  as an exogenous parameter and  $\pi_X^n$  as a steady-state rate so that  $\pi_X^v$  is endogenously determined as a function of these and other population and voucher system parameters at the steady state.

<sup>17</sup>Our qualitative results are the same if only a proportion of treated patients recover and only a proportion of non-treated patients die.

We denote the service rates for clinical-trial patients, voucher-prioritized patients, and non-prioritized patients by  $s_X^t$ ,  $s_X^v$ , and  $s_X^n$  respectively; these are the proportions of the respective populations that are treated with CCP. The flow rates of recovery for each type of patient are then  $s_X^t \pi_X^t$ ,  $s_X^v \pi_X^v$ , and  $s_X^n \pi_X^n$ .

CCP can only be supplied by recovered patients. The flow rate of patients who can potentially provide CCP thus has four components:  $s_X^t \pi_X^t$ ,  $s_X^v \pi_X^v$ , and  $s_X^n \pi_X^n$ —all described in the previous paragraph—as well as patients who have recovered without CCP therapy, with flow rate  $\omega_X$ . We assume that recovering clinical-trial patients, recovering non-prioritized patients, and recovering patients using alternative treatment models donate CCP at the same rate  $p_X$ . We also make a simplifying worst-case scenario assumption regarding voucher-prioritized patients: we assume that voucher-prioritized patients who recover do not donate CCP.<sup>18</sup>

Thus, the steady-state CCP therapy supply flow rate is endogenously determined by

$$\gamma_X = p_X(s_X^t \pi_X^t + s_X^n \pi_X^n + \omega_X)k, \quad (1)$$

where  $p_X$  is the probability that a given recovered patient donates and  $k$  is the number of units of CCP that patient can donate.<sup>19</sup>

As mentioned before, each individual who donates CCP receives  $v_X \geq 0$  priority “vouchers” that can be used to give treatment priority to a family member or other close associate. Patients become voucher-prioritized if, and only if, some donor allocates one of her  $v_X$  priority vouchers to them; thus, we must have

$$\pi_X^v = p_X(s_X^t \pi_X^t + s_X^n \pi_X^n + \omega_X)q_X v_X, \quad (2)$$

where  $q_X$  is the proportion of vouchers actually redeemed. We will use  $r_X = q_X v_X$  to denote the average number of redeemed vouchers used per donor, which we call the *voucher redemption rate*. We refer to

$$p_X(k - r_X)$$

as the *replenishment rate* of the CCP therapy; this is the average amount of net CCP donated to the general pool per recovered patient.

Our first result states conditions that guarantee all prioritized groups have service rate 1, i.e.,  $s_X^t = 1$  and  $s_X^v = 1$ :

**Proposition 1.** *So long as the CCP replenishment rate is large enough to support the clinical trial, i.e.,*

$$p_X(k - r_X) \geq \frac{\tau_X}{\tau_X + \omega_X}, \quad (3)$$

---

<sup>18</sup>If we instead assumed that recovering voucher-prioritized patients donate at the same rate as the other patient groups, our Propositions 1, 2, 4 and 5 would all still hold, as donation by recovered voucher-prioritized patients increases the net CCP supply, and all four results provide sufficient conditions for a priority system to function under a minimum CCP supply. The qualitative conclusion of Proposition 3 that a voucher system is better than an altruistic donation scheme under Assumption 1, as well as the given sufficient condition, would also continue to hold.

<sup>19</sup>In the model we think of each donor as donating just once; however, the analysis is unchanged if donors can donate repeatedly and we take  $k$  to be the average total donations per-individual.

it is possible to ensure that all clinical-trial and voucher-prioritized patients receive CCP therapy, so that

$$s_X^t = 1 \quad \text{and} \quad s_X^v = 1. \quad (4)$$

*Proof.* The total flow rate of patients who are prioritized is given as  $\pi_X^t + \pi_X^v$ . To serve all of them, we need (4), i.e., that

$$\gamma_X \geq \pi_X^t + \pi_X^v \quad (5)$$

Substituting in (1) and (2), we see that (5) is equivalent to

$$p_X(\pi_X^t + s_X^n \pi_X^n + \omega_X)(k - r_X) \geq \pi_X^t \iff k - \frac{\pi_X^t}{p_X(\pi_X^t + s_X^n \pi_X^n + \omega_X)} \geq r_X.$$

In the worst-case scenario, the service rate for non-prioritized patients would be  $s_X^n = 0$ , yielding

$$k - \frac{\pi_X^t}{p_X(\pi_X^t + \omega_X)} \geq r_X$$

as a sufficient condition for (5); this is precisely (3) since  $\pi_X^t = \tau_X$  is the reserve size.  $\square$

We next turn our attention to the CCP therapy service rate  $s_X^n$  for non-prioritized patients, which takes the form

$$s_X^n = \frac{\gamma_X - s_X^t \pi_X^t - s_X^v \pi_X^v}{\pi_X^n}. \quad (6)$$

Assuming that (3) holds (i.e.,  $s_X^t = 1$  and  $s_X^v = 1$ ) we substitute (1), (2), and the reserve size  $\pi_X^t = \tau_X$  into (6) to find:

$$s_X^n = \begin{cases} \frac{\omega_X p_X(k - r_X) - \tau_X(1 - p_X(k - r_X))}{\pi_X^n(1 - p_X(k - r_X))} & \text{if } p_X(k - r_X) < 1 \\ +\infty & \text{if } p_X(k - r_X) \geq 1. \end{cases} \quad (7)$$

There is positive feedback: raising the number of patients who recover without CCP therapy,  $\omega_X$ , increases the steady-state service rate—and this effect is greater the larger the probability that recovering patients donate, and the more units they contribute to the system. Naturally, the service rate is also increasing in the replenishment rate.

We see from (7) that if the CCP replenishment rate is greater than 1, we will have an arbitrarily large amount of CCP available at steady state, so that all patients will be able to be treated. On the other hand, even if the replenishment rate is less than 1, we may still be able treat everybody and end up with finite but excess supply of plasma; this is characterized by (finite)  $s_X^n \geq 1$ .

We note in particular that so long as (3) holds, we have

$$s_X^n \geq 0,$$

which leads to the following corollary:

**Corollary 1.** *So long as the CCP replenishment rate is large enough to support the clinical trial (i.e., (3) holds), the flow recovery rate of non-prioritized patients,  $s_X^n \pi_X^n + \omega_X$ , is weakly higher than the rate that would arise absent CCP donation,  $\omega_X$ , even when all CCP-clinical-trial patients and voucher-prioritized patients are treated ahead of non-prioritized patients.*

From (7), we compute that  $s_X^n \geq 1$  whenever

$$p_X \geq \frac{\tau_X + \pi_X^n}{(\tau_X + \pi_X^n + \omega_X)(k - r_X)}. \quad (8)$$

We thus find:

**Proposition 2.** *Whenever (8) holds, it is possible to treat all patients—prioritized and non-prioritized—at steady-state. In particular, it is possible to treat all patients when replenishment rate is above replacement; that is, when*

$$p_X(k - r_X) \geq \frac{\tau_X + \pi_X^n}{\tau_X + \pi_X^n + \omega_X}.$$

### 3.1.1 Altruistic Donation vs. Incentivized Backward Donation

Additionally, we can think of  $p_X$  in terms of a supply curve  $p_X(\cdot)$  that is strictly increasing and differentiable as a function of the voucher redemption rate,  $r_X$ . Thus,  $p_X(0)$  refers to the altruistic donation probability (which is what would arise without any incentive scheme involving prioritization through vouchers).

We make the following assumption:

**Assumption 1.** The replenishment rate  $p_X(r_X) \cdot (k - r_X)$  is strictly increasing at  $r_X = 0$  (i.e.,  $p'_X(0)k > p_X(0)$ ).

Assumption 1 is fairly mild; it is satisfied if a sufficiently small percentage of recovering patients donate altruistically without any voucher scheme in place. Under Assumption 1, assuming an interior maximum  $s_X^* < 1$  (i.e.,  $s_X = 1$  cannot be achieved no matter what  $r_X$  is), our expression (7) for  $s_X^n$  implicitly defines the optimal  $r_X$  through the necessary first-order condition:

$$0 = \frac{ds_X^n}{dr_X} = \frac{d}{dr_X} \left[ \frac{\omega_X \cdot p_X(r_X) \cdot (k - r_X) - \tau_X (1 - p_X(r_X) \cdot (k - r_X))}{\pi_X^n (1 - p_X(r_X) \cdot (k - r_X))} \right],$$

so that we have

$$\frac{p'_X(r_X^*)}{p_X(r_X^*)} = \frac{1}{k - r_X^*}. \quad (9)$$

Observe that the  $r_X^*$  in (9) is also the value that maximizes the replenishment rate  $p_X(r_X) \cdot (k - r_X)$ .<sup>20</sup> Such an interior maximum exists for the service rate because the service rate is increasing in the replenishment rate and the replenishment rate is increasing at  $r_X = 0$  by Assumption 1 (and hence is positive at a small  $r_X \approx 0$ ); moreover the service rate falls back to 0 when  $r_X$  satisfies (4) with equality.

We summarize our findings with the following proposition:

---

<sup>20</sup>If there are multiple such values, we pick the one among them that achieves the highest service rate  $s_X^n$ .

**Proposition 3.** *Under Assumption 1, so long as the CCP replenishment rate is large enough to support the clinical trial, (i.e., (3) holds) the voucher redemption rate that maximizes the CCP service rate for non-prioritized patients satisfies  $r_X^* > 0$ —that is, using a voucher scheme strictly improves outcomes for non-prioritized patients.*

*Moreover, the service rate for non-prioritized patients  $s_X^n$  is strictly increasing in the CCP replenishment rate  $p_X(r_X) \cdot (k - r_X)$  and is maximized either*

- *at  $s_X^{n*} = 1$  by all voucher redemption rates  $r_X$  that satisfy (8), or*
- *at some  $s_X^{n*} < 1$  (if there is no  $r_X$  such that we can have  $s_X^n = 1$ ) by a voucher redemption rate  $r_X^* > 0$  satisfying (9).*

### 3.2 Paying it Forward through a Pledge of Future Donation

We now suppose that there is also a pathway some patients can use to gain priority for treatment, which is to pledge upfront to donate CCP upon recovery. We suppose that in addition to upfront treatment, we give such a patient  $v_X^f \geq 0$  vouchers after (and if) she donates CCP.<sup>21</sup>

As before, we set aside a reserve for clinical-trial patients with the flow capacity  $\tau_X$ . The rest of the CCP therapy is allocated within the incentivized CCP reserve, which now has three priority classes ordered as follows:

1. patients who have vouchers (whom we refer to as *voucher-prioritized*, as before);
2. patients who do not have vouchers but pledge to donate after they recover (*pledged* patients); and
3. patients not in any of the other categories (*non-prioritized* patients).

We denote the steady-state flow rate of patients participating in clinical trial by  $\hat{\pi}_X^t = \tau_X$ ; the flow rate of voucher-prioritized patients by  $\hat{\pi}_X^v$ ; the flow rate of pledged patients by  $\hat{\pi}_X^f$ ; and the flow rate of non-prioritized patients by

$$\hat{\pi}_X^n = \pi_X^n - \hat{\pi}_X^f \leq \pi_X^n.$$

We refer to the different types of patients' respective CCP therapy service rates as  $\hat{s}_X^t$ ,  $\hat{s}_X^v$ ,  $\hat{s}_X^f$ , and  $\hat{s}_X^n$ .

Then the total flow rate of recovering patients has four components:

- patients who participate in clinical trials, with a flow rate  $\hat{s}_X^t \hat{\pi}_X^t$ ;
- patients who are voucher-prioritized, with a flow rate  $\hat{s}_X^v \hat{\pi}_X^v$ ;<sup>22</sup>
- patients who have pledged to donate ex ante, with a flow rate  $\hat{s}_X^f \hat{\pi}_X^f$ ; and

<sup>21</sup>We may also count the treatment of the pledged patient herself as the upfront redemption of a voucher, in which case we would think of this patient as receiving vouchers to treat as many as  $v_X^f + 1$  patients, including herself.

<sup>22</sup>As before, we conduct a worst-case analysis under the assumption that patients who have vouchers do not become CCP donors upon recovery. Propositions 4 and 5 continue to hold if we assume voucher-prioritized patients also donate with probability  $p_X$  upon recovery.

- patients who are not part of clinical trials, do not have vouchers, and have not pledged to donate, with a flow rate of  $\hat{s}_X^n \hat{\pi}_X^n + \omega_X$ .

The total steady-state flow of CCP therapy is

$$\hat{\gamma}_X = (p_X(\hat{s}_X^t \hat{\pi}_X^t + \hat{s}_X^n \hat{\pi}_X^n + \omega_X) + p_X^f \hat{s}_X^f \hat{\pi}_X^f)k, \quad (10)$$

where  $p_X$  is the population probability to donate in return for vouchers (as in the prior sections) and  $p_X^f$  is the probability with which pledged patients donate upon recovery. We allow the possibility that some patients who pledge may not end up donating—perhaps due to medical ineligibility—so that  $p_X^f$  is expected to be less than 1. We only assume that pledging increases one’s probability of donation, so that  $p_X^f \geq p_X$ .

We assume that patients who decide to donate ex post each receive  $v_X$  priority vouchers to be used by their loved ones, as before. On the other hand, pledged patients possibly also receive a number of vouchers upon recovery and donation—if they they donate  $k$  units of CCP, they receive  $v_X^f$  vouchers. The  $v_X^f$  vouchers are only given after the pledged recovering patient “pays it forward” by donating CCP, which occurs with probability  $p_X^f$ .

Thus, the flow rate of voucher-prioritized patients  $\hat{\pi}_X^v$  satisfies

$$\hat{\pi}_X^v = p_X(\hat{s}_X^t \hat{\pi}_X^t + \hat{s}_X^n \hat{\pi}_X^n + \omega_X)q_X v_X + p_X^f \hat{s}_X^f \hat{\pi}_X^f q_X v_X^f. \quad (11)$$

As before, we will work with the voucher redemption rates

$$r_X = q_X v_X \quad (12)$$

for the patients who have not pledged ex ante but decide to donate upon recovery. Similarly, for pledged patients, we write:

$$r_X^f = q_X v_X^f. \quad (13)$$

The following proposition gives conditions under which we can fully serve all prioritized patient groups (i.e., so that  $\hat{s}_X^t = 1$ ,  $\hat{s}_X^v = 1$ , and  $\hat{s}_X^f = 1$ ):

**Proposition 4.** *Regardless of the pledged patient arrival rate  $\hat{\pi}_X^f$ , so long as we have*

$$p_X(k - r_X) \geq \frac{\tau_X}{\tau_X + \omega_X} \quad \text{and} \quad p_X^f(k - r_X^f) \geq 1, \quad (14)$$

*it is possible to ensure that all clinical-trial patients, voucher-prioritized patients, and pledged patients receive CCP therapy, so that*

$$\hat{s}_X^n = 1, \quad \hat{s}_X^v = 1, \quad \text{and} \quad \hat{s}_X^f = 1. \quad (15)$$

*Proof.* Clinical-trial patients, voucher-prioritized patients, and pledged patients are prioritized over non-pledged patients. Thus, by setting  $\hat{s}_X^t = \hat{s}_X^v = \hat{s}_X^f = 1$  and using (10) and (11), we see that all



prioritized patient groups can all be treated by CCP if

$$\hat{\gamma}_X \geq \hat{\pi}_X^t + \hat{\pi}_X^v + \hat{\pi}_X^f \iff p_X(\hat{\pi}_X^t + \hat{s}_X^n \hat{\pi}_X^n + \omega_X)(k - r_X) + p_X^f \hat{\pi}_X^f (k - r_X^f) \geq \hat{\pi}_X^t + \hat{\pi}_X^f. \quad (16)$$

To capture the minimum amount of CCP needed to treat all pledged patients, we consider the worst-case scenario in which no non-prioritized patients are treated, i.e.,  $\hat{s}_X^n = 0$ . Then necessary and sufficient conditions for (16) to be satisfied regardless of  $\hat{\pi}_X^f$  are

$$p_X(k - r_X) \geq \frac{\hat{\pi}_X^t}{p_X(\hat{\pi}_X^t + \omega_X)} \quad \text{and} \quad p_X^f(k - r_X^f) \geq 1. \quad (17)$$

Replacing  $\hat{\pi}_X^t$  with  $\tau_X$  in (17), we obtain (14).  $\square$

The first condition in (14) is the same condition as (3): The replenishment rate of the CCP obtained from initially non-pledged patients should be at least as large as is needed to support the clinical trial CCP reserve. The second condition in (14) requires that the replenishment rate of CCP obtained from pledged patients should at least cover those patients' own initial treatment in steady-state.

We now examine the CCP service rate for non-prioritized patients when (14) holds:

$$\hat{s}_X^n = \frac{\hat{\gamma}_X - \hat{s}_X^t \hat{\pi}_X^t - \hat{s}_X^v \hat{\pi}_X^v - \hat{s}_X^f \hat{\pi}_X^f}{\hat{\pi}_X^n}. \quad (18)$$

Expanding (18) assuming  $\hat{s}_X^v = 1$ , we find that

$$\hat{s}_X^n = \frac{\left[ p_X(\hat{s}_X^t \hat{\pi}_X^t + \hat{s}_X^n \hat{\pi}_X^n + \omega_X)(k - r_X) \right] - \hat{s}_X^t \hat{\pi}_X^t + \left[ p_X^f \hat{s}_X^f \hat{\pi}_X^f (k - r_X^f) \right] - \hat{s}_X^f \hat{\pi}_X^f}{\hat{\pi}_X^n}. \quad (19)$$

Solving (19) for  $\hat{s}_X^n$  (replacing  $\hat{\pi}_X^t = \tau_X$  and  $\hat{s}_X^t = 1$ ), we see that, assuming the pay-it-backward voucher replenishment rate does not on its own lead to infinite excess supply of CPP (i.e.,  $p_X(1 - r_X) < 1$ ),

$$\hat{s}_X^n = \frac{\omega_X p_X(k - r_X) - \tau_X(1 - p_X(k - r_X)) + p_X^f \hat{s}_X^f \hat{\pi}_X^f (k - r_X^f - \frac{1}{p_X^f})}{\hat{\pi}_X^n (1 - p_X(k - r_X))}. \quad (20)$$

Comparing (20) to (7), we see that non-prioritized patients are served at a weakly higher rate than they would be under a system that does not prioritize pledged patients whenever

$$\begin{aligned} & \frac{\omega_X p_X(k - r_X) - \tau_X(1 - p_X(k - r_X)) + p_X^f \hat{s}_X^f \hat{\pi}_X^f (k - r_X^f - \frac{1}{p_X^f})}{\hat{\pi}_X^n (1 - p_X(k - r_X))} \\ &= \hat{s}_X^n \geq \frac{\pi_X^n}{\hat{\pi}_X^n} s_X^n = \frac{\pi_X^n}{\hat{\pi}_X^n} \left( \frac{\omega_X p_X(k - r_X) - \tau_X(1 - p_X(k - r_X))}{\pi_X^n (1 - p_X(k - r_X))} \right). \end{aligned} \quad (21)$$

Thus, we find that  $\hat{s}_X^n \geq s_X^n$  when (14) holds, and conclude:

**Proposition 5.** *So long as (14) holds, besides treating every clinical-trial patient and voucher-prioritized*



patient ( $\hat{s}_X^t = \hat{s}_X^v = 1$ ), it is possible to treat every patient who pledges to donate CCP upfront ( $\hat{s}_X^f = 1$ ), while still raising the service rate for non-prioritized patients who have not pledged to donate.

## 4 ABO-compatible Plasma Donation

We now build on the analysis from the preceding section to allow patients receive donation from plasma-compatible donors.

In reality, there are four blood types  $O$ ,  $A$ ,  $B$ , and  $AB$ . Type  $AB$  plasma can be used to treat patients of all blood types; blood-type  $A$  plasma can be used to treat patients of blood types  $O$  and  $A$ ; blood-type  $B$  plasma can be used to treat patients of blood types  $O$  and  $B$ ; and blood-type  $O$  plasma can only be used to treat patients of blood type  $O$ . (Since CCP is a type of plasma, those same compatibility requirements are needed for CCP transfusion.) We let  $\mathcal{B} = \{O, A, B, AB\}$  be the set of blood types.

Under an ABO-identical treatment policy, non-prioritized patients of different blood types may be served in unequal service rates because the parameters  $\hat{\pi}_X^f/\pi_X^n$ ,  $\omega_X/\pi_X^n$ ,  $p_X$ , and  $p_X^f$  may vary based on blood type  $X \in \mathcal{B}$  even if the voucher redemption rates  $r_X$  and  $r_X^f$  are chosen to take these differences into account. The main reason behind this variation is that COVID-19 has different incidence depending on national/ethnic background, and the blood type distribution varies substantially as a function of background. Moreover, some blood-types may have excess supply of CCP while the others do not; for example, (8) may hold for some blood types while it does not for others.

We aim for an egalitarian service policy for CCP therapy with multiple blood types—thus we seek to make the non-prioritized patient service rates of different blood types as equal as possible without affecting efficiency.

We need to account for voucher holders possibly having different blood types from their original donors; we assume that their blood types are independently distributed from their donors'. Suppose  $b_X$  is the probability that a given patient is of blood type  $X$ . Let

$$r_X = b_X \sum_{Y \in \mathcal{B}} q_Y v_Y$$

be the voucher redemption rate for backward donation, and let

$$r_X^f = b_X \sum_{Y \in \mathcal{B}} q_Y v_Y^f$$

be the voucher redemption rate for forward donation.

We refer to the service rates for non-prioritized patients for each blood type  $X$  given in (20) as the ABO-identical service rate, and rephrase it here once more assuming all clinical-trial patients, voucher-prioritized patients and pledged patients are served, i.e.,  $\hat{s}_X^t = 1$ ,  $\hat{s}_X^v = 1$ , and  $\hat{s}_X^f = 1$ . Define

$$\sigma_X := \omega_X p_X (k - r_X) - \tau_X (1 - p_X (k - r_X)) + p_X^f \hat{\pi}_X^f \left( k - r_X^f - \frac{1}{p_X^f} \right) \quad (22)$$

$$\delta_X := \hat{\pi}_X^n (1 - p_X (k - r_X)) \quad (23)$$

for each blood type  $X$ . Here,  $\sigma_X$  is the *steady-state supply* of blood-type  $X$  CCP to be rationed to non-prioritized patients while  $\delta_X$  is the *steady-state demand* for CCP by non-prioritized blood-type  $X$  patients.

#### 4.1 Pooling for Plasma Treatment

Whenever,  $\delta_X < 0$ , which happens when the CCP replenishment rate for  $X$  is greater than 1, the blood-type  $X$  non-prioritized patients are self-sufficient, and we can distribute the remaining CCP to other compatible blood types to serve all of them.<sup>23</sup> Thus, assume that replenishment rate  $p_X(k - r_X) < 1$  for at least one blood type  $X \in \mathcal{B}$ , as otherwise all blood types will be self-sufficient and non-prioritized patients who survive donate enough CCP on net to supply future generations of patients.

Moreover, assuming  $p_X(k - r_X) < 1$ , we observe that  $\sigma_X$  is the numerator and  $\delta_X$  is the denominator of  $\hat{s}_X^n$  in (20)

$$\hat{s}_X^n = \frac{\sigma_X}{\delta_X}. \quad (24)$$

Another way the excess CCP of one blood type can be used for other blood types is that if  $\delta_X > 0$  and still  $\sigma_X > \delta_X$ . Suppose as an example, for  $\delta_O, \delta_A > 0$  we have,

$$0 < \hat{s}_O^n < \hat{s}_A^n. \quad (25)$$

Since blood-type  $O$  patients can receive blood-type  $A$  CCP, for an egalitarian CCP allocation, we can give some of the blood-type  $A$  CCP to blood-type  $O$  patients and increase the service rate for  $O$  patients and decrease the service rate for  $A$  patients. Let  $\sigma_{A \rightarrow O}$  be the resulting net transfer flow of blood-type  $A$  CCP to blood-type  $O$  patients.

Then, the new service rates of both types will be

$$s_O = \frac{\sigma_O + \sigma_{A \rightarrow O}}{\delta_O} \leq s_A = \frac{\sigma_A - \sigma_{A \rightarrow O}}{\delta_A}. \quad (26)$$

We can continue increasing the net transfer  $\sigma_{A \rightarrow O}$  until both service rates become equal, to sustain an egalitarian service rate among the two blood types. Either we will eventually have both service rates exceeding 1, and hence all of these patients are served, or we will end up with an equal service rate for  $A$  and  $O$  less than 1. Observe that the amount of CCP transfer from  $A$  to  $O$  that makes (26) hold with equality is

$$\sigma_{A \rightarrow O} = \frac{\sigma_A \delta_O - \sigma_O \delta_A}{\delta_O + \delta_A}, \quad (27)$$

which is strictly greater than 0 (by (25) and  $\delta_O, \delta_A > 0$ ) and strictly smaller than  $\sigma_A$  (as  $\delta_O, \delta_A > 0$ ).

---

<sup>23</sup>Relative to our model as presented in the previous section, this is the case in which we obtain infinite supply of blood-type  $X$  CCP in the steady-state.

This resulting service rate, what we call the *pooling service rate* for  $A$  and  $O$  is then

$$\hat{s}_{\{O,A\}}^n := \frac{\sigma_O + \sigma_A}{\delta_O + \delta_A} = s_O = s_A. \quad (28)$$

Observe that (28) treats patients as if  $A$  and  $O$  together form an “composite blood type” and yet the subsidy of CCP is one way: some blood-type  $A$  CCP is used to treat blood-type  $O$  patients, but blood-type  $O$  CCP is never used on blood-type  $A$  patients (as it would not be compatible).

As  $\sigma_A, \sigma_O, \delta_A, \delta_O > 0$ , we have

$$\hat{s}_O^n = \frac{\sigma_O}{\delta_O} < \hat{s}_{\{O,A\}}^n < \hat{s}_A^n = \frac{\sigma_A}{\delta_A}.$$

Additionally, if the service rate for  $B$ ,  $\hat{s}_B^n$  is larger than the pooled rate in (28) but lower than  $\hat{s}_A^n$ , we can further subsidize blood-type  $O$  patients and return some of the blood-type  $A$  CCP that was earmarked for  $O$  patients in (26) back to blood-type  $A$  patients.<sup>24</sup> Eventually, we would end up with a pooled service rate for the blood types  $\{O, A, B\}$ ; as long as  $\delta_B > 0$ , we would have

$$\hat{s}_{\{O,A\}}^n < \hat{s}_{\{O,A,B\}}^n = \frac{\sigma_O + \sigma_A + \sigma_B}{\delta_O + \delta_A + \delta_B} < \hat{s}_B^n.$$

## 4.2 Optimal Pooling

We now introduce a formal iterative pooling procedure to determine the service rates of non-prioritized patients when there are four blood types using the intuition just developed.<sup>25</sup>

For any  $\mathcal{X} \subseteq \mathcal{B}$  and any  $\mathbf{Y} \subseteq 2^{\mathcal{B}}$ , we define the following *compatibility set*:

$$\mathbf{C}(\mathcal{X}, \mathbf{Y}) = \{\mathcal{Y} \in \mathbf{Y} : \text{CCP of some type } Y \in \mathcal{Y} \text{ is compatible with patients of some type } X \in \mathcal{X}\}.$$

We construct a sequence  $\{\mathbf{B}^t\}$  iteratively such that each  $\mathbf{B}^t \subseteq 2^{\mathcal{B}}$  is a collection of subsets of blood types. We refer to each of these sets  $\mathcal{X} \in \mathbf{B}^t$  as *pooled* meaning that the service rates of all blood types in  $\mathcal{X}$  can be made equal either

- by treating patients of each blood type in  $\mathcal{X}$  with CCP of some compatible blood type  $X \in \mathcal{X}$  along with CCP of their own blood type, or
- by giving CCP of each blood type in  $\mathcal{X}$  to patients of some compatible blood type  $X \in \mathcal{X}$ .

The steps of the pooling construction are as follows:

### POOLING PROCEDURE:

**Step 0:** If  $\delta_X < 0$  for some blood type  $X$ , then we remove that blood type and all the blood types that blood-type  $X$  CCP be given to: all of compatible blood-type patients

<sup>24</sup>If  $\hat{s}_B^n > \hat{s}_A^n$ , then we would start with blood-type  $B$  CCP to subsidize blood-type  $O$  patients and then check later for further  $A$  CCP subsidy opportunities.

<sup>25</sup>The procedure discussed here subsumes a related procedure for use in kidney exchange that was proposed by two of the authors in a previous working paper (Sönmez and Ünver, 2015).

will be served in full by blood-type  $X$  CCP supply. We set the service rates for those blood types to 1. Let  $\mathbf{B}^0 \subseteq \{\{O\}, \{A\}, \{B\}, \{AB\}\}$  be the set of remaining blood types—where singleton sets  $\{X\}$  denote that no remaining types are pooled yet. We find all individual service rates  $\hat{s}_{\{X\}}^n$  as defined in (24) so that  $\hat{s}_{\{X\}}^n = \hat{s}_X^n$  for each  $\{X\} \in \mathbf{B}^0$ . We then continue to Step 1.

⋮

**Step  $t \geq 1$ :** Suppose  $\mathbf{B}^{t-1}$  is the collection of pooled blood sets determined in the previous step. For each pooled set  $\mathcal{Y} \in \mathbf{B}^{t-1}$ , let the service rate  $\hat{s}_{\mathcal{Y}}^n$  be as defined in previous steps. Suppose pooled set  $\mathcal{X} \in \mathbf{B}^{t-1}$  has the smallest service rate  $\hat{s}_{\mathcal{X}}^n$  among sets in  $\mathbf{B}^{t-1}$ . If  $\hat{s}_{\mathcal{X}}^n \geq 1$ , then all non-prioritized patients of blood types in every pooled set in  $\mathbf{B}^{t-1}$  are fully served, and we stop the procedure; otherwise, we continue.

- If  $\mathbf{C}(\mathcal{X}, \mathbf{B}^{t-1}) \supsetneq \{\mathcal{X}\}$ , let  $\mathcal{Y}$  be the set that has the largest service rate among all pooled sets in  $\mathbf{C}(\mathcal{X}, \mathbf{B}^{t-1}) \setminus \{\mathcal{X}\}$ . Then  $\mathcal{X}$  and  $\mathcal{Y}$  are pooled together; we replace  $\mathcal{X}$  and  $\mathcal{Y}$  with their union  $\mathcal{S} = \mathcal{X} \cup \mathcal{Y}$ , so that

$$\mathbf{B}^t := (\mathbf{B}^{t-1} \setminus \{\mathcal{X}, \mathcal{Y}\}) \cup \{\mathcal{S}\} \quad (29)$$

and the new service rate for  $\mathcal{S}$  (using definitions of  $\sigma_X$  and  $\delta_X$  in (22) and (23)) is

$$\hat{s}_{\mathcal{S}}^n := \frac{\sum_{X \in \mathcal{S}} \sigma_X}{\sum_{X \in \mathcal{S}} \delta_X}. \quad (30)$$

- If  $\mathbf{C}(\mathcal{X}, \mathbf{B}^{t-1}) = \{\mathcal{X}\}$ , then  $\mathcal{X}$  is not pooled with any other set. For each blood type  $X \in \mathcal{X}$  the final pooled service rate is set as  $\hat{s}_{\mathcal{X}}^n$ . We set

$$\mathbf{B}^t := \mathbf{B}^{t-1} \setminus \{\mathcal{X}\}. \quad (31)$$

If  $\mathbf{B}^t = \emptyset$ , then we stop by setting any final service rate greater than 1 to 1, otherwise we continue with Step  $t+1$ .

We illustrate the pooling procedure with an example:

**Example 1.** Suppose initially that

$$\hat{s}_{\{AB\}}^n < \hat{s}_{\{O\}}^n < \hat{s}_{\{A\}}^n < \hat{s}_{\{B\}}^n,$$

and the net demand is positive for each blood type, i.e.,  $\delta_X > 0$  for all  $X \in \mathcal{B}$ .

In Step 0, we let

$$\mathbf{B}^0 = \{\{O\}, \{A\}, \{B\}, \{AB\}\}.$$

In Step 1, the lowest service rate belongs to  $\{AB\} \in \mathbf{B}^0$ . There is no other blood-type CCP that

can be given to blood-type  $AB$  patients; hence,

$$\mathbf{C}(\{AB\}, \mathbf{B}^0) = \{\{AB\}\},$$

meaning that  $\{AB\}$  will be pooled alone with its service rate  $\hat{s}_{\{AB\}}^n$ . We set

$$\mathbf{B}^1 = \mathbf{B}^0 \setminus \{\{AB\}\} = \{\{O\}, \{A\}, \{B\}\}.$$

In Step 2, the lowest service rate belongs to  $\{O\} \in \mathbf{B}^1$ . We have

$$\mathbf{C}(\{O\}, \mathbf{B}^1) = \{\{O\}, \{A\}, \{B\}\}$$

as CCP of blood types  $A$ ,  $B$ , and  $O$  can be given to blood-type  $O$  patients. The highest service rate belongs to  $\{B\} \in \mathbf{C}(\{O\}, \mathbf{B}^1) \setminus \{\{O\}\}$ . As a result,  $\{O\}$  and  $\{B\}$  are pooled together as  $\{O, B\}$ : We set

$$\mathbf{B}^2 = \left( \mathbf{B}^1 \setminus \{\{B\}, \{O\}\} \right) \cup \{O, B\} = \{\{O, B\}, \{A\}\}$$

and find the new service rate for the patients in  $B$  and  $O$  as in (24) for  $\mathcal{S} = \{O, B\}$ . Here the key observation is that

$$\hat{s}_{\{O\}}^n < \hat{s}_{\{O, B\}}^n < \hat{s}_{\{B\}}^n,$$

which follows from the simple arithmetic relationship

$$\frac{a}{b} < \frac{c}{d} \implies \frac{a}{b} < \frac{a+c}{b+d} < \frac{c}{d}$$

(for  $a, b, c, d > 0$ ).

In Step 3, two cases are possible:

1. If  $\hat{s}_{\{O, B\}}^n < \hat{s}_{\{A\}}^n$ , then

$$\mathbf{C}(\{O, B\}, \mathbf{B}^2) = \{\{O, B\}, \{A\}\},$$

as CCP of blood type  $A$  can be transfused to patients of blood type  $O$ . Thus,  $\{O, B\}$  and  $\{A\}$  are also pooled together as  $\{O, A, B\}$  and

$$\mathbf{B}^3 = \left( \mathbf{B}^2 \setminus \{\{O, B\}, \{A\}\} \right) \cup \{\{O, A, B\}\} = \{\{O, A, B\}\}.$$

The procedure ends in the next step, as  $\mathbf{B}^3$  is a singleton. Thus, the pooled sets are

$$\{AB\} \text{ and } \{O, A, B\}.$$

2. If  $\hat{s}_{\{A\}}^n \leq \hat{s}_{\{O, B\}}^n$ , then

$$\mathbf{C}(\{A\}, \mathbf{B}^2) = \{\{A\}\},$$

as CCP of blood types  $O$  and  $B$  cannot be transfused to patients of blood type  $A$ . Thus,  $\{A\}$  is

pooled by itself and

$$\mathbf{B}^3 = \mathbf{B}^2 \setminus \{\{A\}\} = \{\{O, B\}\}.$$

The procedure ends in the next step as  $\mathbf{B}^3$  is a singleton, and the pooled sets are

$$\{AB\}, \{A\}, \text{ and } \{O, B\}.$$

### 4.3 Related Literature

To our knowledge, this is the first paper to bring a market design approach to CCP donation. That said, we build heavily on the market design literature for kidney exchange. Within that literature, our model is most closely related paper to that of Sönmez, Ünver, and Yenmez (2020), who introduced a dynamic continuum matching model to study the effects of incentivizing compatible kidney donor-patient pairs to participate in exchange by providing increased priority in the deceased-donor queue. Our application to CCP has several important differences from the Sönmez, Ünver, and Yenmez (2020) model. Most importantly, patients and donors are distinct in Sönmez, Ünver, and Yenmez (2020), whereas in our model they are the same population. The incentive schemes we propose directly exploit the fact that patients can go on to become donors; since this is not possible in kidney exchange settings, the incentive schemes proposed by Sönmez, Ünver, and Yenmez (2020) are naturally quite different.

Our voucher scheme does, however, have parallels in the work on intertemporal incentives in kidney exchange: Veale et al. (2017) report on a kidney voucher system where an older living donor of a young patient starts a chain of kidney exchanges through donation to an incompatible pair. Since the younger patient will likely need a kidney in the future, the patient receives priority for a kidney at the end of a similar future chain if her kidney fails. Since the donor is old, the window for donation is short and the scheme helps other pairs receive transplants through chain exchanges in the present and in some sense “insures” the initial patient paired with the donor. Akbarpour et al. (2019) study unpaired kidney exchange, where a patient  $i$  can receive a kidney from patient  $j$  and the system will remember that patient  $j$  has the right to receive a kidney in the future.

Since plasma is part of blood, our work is also related to research on the design of blood markets. Slonim, Wang, and Garbarino (2014) provide a recent summary, and show that providing donors some form of non-monetary incentive, such as a medal or trinket increases donation; this fact to some extent suggests that a non-monetary incentive, in the form of a voucher, may increase CCP donation rates. Heger et al. (forthcoming) have proposed introducing a registry for prospective blood donors. There is also precedent for the formation of a centralized plasma bank during a pandemic. Delamou et al. (2016), for example, have reported on the Guinean National Blood Transfusion Center, which involved donor mobilization and plasma collection, for Ebola therapy in 2015.

Last, we note that our continuum model is related to a growing literature in matching theory that considers large-market models. Large-market models oriented towards market-design applications include those of Kojima and Pathak (2009), Che and Kojima (2010), Abdulkadiroğlu, Che, and Yasuda (2011), Azevedo and Leshno (2016), Azevedo and Hatfield (2018), and Azevedo and Budish (2019). Our steady-state analysis is also related to recent models of dynamic matching markets, such as the work

of Ünver (2010), Anderson et al. (2017), Baccara, Lee, and Yariv (2018), and Akbarpour, Li, and Gharan (2020).

## 5 Conclusion

In this paper, we propose a market design approach to CCP donation and distribution. Plasma donors may be given priority vouchers that can be used to give treatment priority to their loved ones; priority is also given to participants in clinical trials. Our model illustrates important possibilities: if the plasma replenishment rate is large enough to support the patients in a clinical trial, it is possible to treat all prioritized patients in equilibrium. There is also a positive spillover on non-prioritized patients. Moreover, if recovered patients are more willing to donate if they receive vouchers, introducing a voucher system strictly benefits non-prioritized patients. Overall treatment availability expands further if we prioritize patients who pledge to “pay it forward” by donating plasma once they have recovered.

In the last two decades, collaboration between market designers and medical professionals has led to the development of organized kidney exchange clearinghouses around the world (see, e.g., Roth, Sönmez, and Ünver, 2004, 2005a,b), resulting in thousands of lives saved. Several of the key insights and tools in the kidney exchange literature have parallels with our proposed mechanisms for increasing CCP donation. For example, *non-directed donor chains*—one of the most successful innovations in kidney exchange (Roth et al., 2006; Rees et al., 2009)—involve “paying it forward.” In such a chain, each participating incompatible patient-donor pair first receives a kidney donation for their patient and at a later date their donor returns the favor by donating a kidney to another pair. These chains start with the gift of an altruistic donor, and can lead to quite long sequences of donations. Another life-saving innovation in kidney exchange involves “paying it backward” with a patient-donor pair where the patient is not ready for a transplant yet, and the donor will no longer be eligible for donation when the patient is expected to need a transplant in the future (perhaps due to donor age). Under a *kidney voucher* program, the donor donates today, and receives a transplant voucher for her donor in the future (Veale et al., 2017).

More broadly, suitably adapted market design innovations can assist with the novel challenges created by COVID-19. Given the fact that CCP is currently the preferred therapy for the virus, it is our hope that efforts that increase CCP supply can potentially save many additional lives.

## References

- Abdulkadiroğlu, Atila, Yeon-Koo Che, and Yosuke Yasuda (2011). “Resolving Conflicting Preferences in School Choice: The “Boston Mechanism” Reconsidered.” *American Economic Review*, 101(1), 399–410.
- Akbarpour, Mohammad, Shengwu Li, and Shayan Oveis Gharan (2020). “Thickness and Information in Dynamic Matching Markets.” *Journal of Political Economy*, 128(3), 783–815.
- Akbarpour, Mohammad, Julien Combe, Yinghua He, Victor Hiller, Robert Shimer, and Olivier Tercieux (2019). “Unpaired Kidney Exchange: Overcoming Double Coincidence of Wants without Money.” August 1, Stanford GSB Working Paper.
- Aleccia, JoNel (2020). “A desperate scramble as Covid-19 families vie for access to plasma therapy.” April 15, <https://www.nbcnews.com/health/health-news/desperate-scramble-covid-19-families-vie-access-plasma-therapy-n1183946>.
- Anderson, Ross, Itai Ashlagi, David Garmanik, and Yash Kanoria (2017). “Efficient Dynamic Barter.” *Operations Research*, 65(6), 1446–1459.
- Arrow, Kenneth J. (1972). “Gifts and Exchanges.” *Philosophy and Public Affairs*, 1, 343–362.
- Azevedo, Eduardo and Eric Budish (2019). “Strategy-proofness in the Large.” *Review of Economic Studies*, 86(1), 81–116.
- Azevedo, Eduardo and Jacob Leshno (2016). “A Supply and Demand Framework for Two-Sided Matching Markets.” *Journal of Political Economy*, 124(5), 1235–1268.
- Azevedo, Eduardo M. and John William Hatfield (2018). “Existence of equilibrium in large matching markets with complementarities.” University of Pennsylvania Working Paper.
- Baccara, Mariagiovanna, SangMok Lee, and Leeat Yariv (2018). “Optimal Dynamic Matching.” CEPR Discussion Paper 12986.
- Becker, Gary and Julio Jorge Elias (2007). “Introducing Incentives in the Market for Live and Cadaveric Organ Donations.” *Journal of Economic Perspectives*, 21(3), 3–24.
- Bénabou, Roland and Jean Tirole (2006). “Incentives and Prosocial Behavior.” *American Economic Review*, 96, 1652–1678.
- Burch, Audra D. S. and Amy Harmon (2020). “Will You Help Save my Brother?: The Scramble to Find Covid-19 Plasma Donors.” *New York Times*. April 29.
- Che, Yeon-Koo and Fuhito Kojima (2010). “Asymptotic Equivalence of Probabilistic Serial and Random Priority Mechanisms.” *Econometrica*, 78(5), 1625–1672.
- Cowan, N., H. A. Gritsch, N. Nassiri, J. Sinacore, and J. Veale (2017). “Broken Chains and Reneging: A Review of 1748 Kidney Paired Donation Transplants.” *American Journal of Transplantation*, 1–7.
- Delamou, Alexandre, Nyankoye Yves Haba, Almudena Mari-Saez, Pierre Gallian, Maya Ronse, Jan Jacobs, Bienvenu Salim Camara, Kadio Jean-Jacques Olivier Kadio, Achille Guemou, Jean Pe Kolie Maaïke De Crop, Patricia Chavarrin, Chantatl Jacquot, Catherine Lazaygues, Anja De Wegheleire, Lutgarde Lynen, and Johan van Griensven (2016). “Organizing the Donation of Convalescent Plasma for a Therapeutic Clinical Trial on Ebola Virus Disease: The Experience in Guinea.” *American Journal of Tropical Medical Hygiene*, 95(3), 647–653.



- Duan, Kai et al. (2020). “Effectiveness of Convalescent Plasma Therapy in Severe Covid-19 Patients.” *Proceedings of the National Academy of Sciences*, 117 (17), 9490–9496.
- EBA (2020). “Covid-19 and Blood Establishments.” April 25, <https://europeanbloodalliance.eu/covid19-and-blood-establishment/>.
- FDA (2020). “Recommendations for Investigational Covid-19 Convalescent Plasma.” U.S. Food and Drug Administration, <https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma>.
- Harrison, Sara (2020). “The Race to Get Convalescent Plasma to Covid-19 Patients.” *Wired*. April 27.
- Heger, Stephanie A., Robert Slonim, Ellen Garbarino, Carmen Wang, and Daniel Waller (forthcoming). “Redesigning the Market for Volunteers: A Donor Registry.” *Management Science*.
- Kojima, Fuhito and Parag A. Pathak (2009). “Incentives and Stability in Large Two-Sided Matching Markets.” *American Economic Review*, 99, 608–627.
- Luke, Thomas C., Edward M. Kilbane, Jeffrey L. Jackson, and Stephen L. Hoffman (2006). “Meta-Analysis: Convalescent Blood Product for Spanish Influenza Pneumonia: A Future H1N1 Treatment?” *Annals of Internal Medicine*, 145, 599–609.
- “The ABO System” (2013). *Handbook of Transfusion*. Ed. by Derek Norfolk. Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee, <https://www.transfusionguidelines.org/transfusion-handbook/2-basics-of-blood-groups-and-antibodies/2-4-the-abo-system>. TSO.
- OPTN (2018). “OPTN/SRTR 2018 Annual Data Report: Kidney.” Health Resources and Services Administration.
- Pope, Adam (2018). “Nation’s longest single-site kidney chain reaches 100.” *UAB News*. July 30, <https://www.uab.edu/news/health/item/9638-nation-s-longest-single-site-kidney-chain-reaches-100>.
- Rees, Michael A., Jonathan E. Kopke, Ronald P. Pelletier, Dorry L. Segev, Matthew E. Rutter, Alfredo J. Fabrega, Jeffrey Rogers, Oleh G. Pankewycz, Janet Hiller, Alvin E. Roth, Tuomas Sandholm, M. Utku Ünver, and Robert A. Montgomery (2009). “A Nonsimultaneous, Extended, Altruistic-Donor Chain.” *New England Journal of Medicine*, 360 (11), 1096–1101.
- Rettner, Rachael (2019). “What’s the Rarest Blood Type?” *Live Science*. April 1, <https://www.livescience.com/36559-common-blood-type-donation.html>.
- Roos, Dave (2020). “Before Vaccines, Doctors ‘Borrowed’ Antibodies from Recovered Patients to Save Lives.” *History Stories*. April 1, <https://www.history.com/news/blood-plasma-covid-19-measles-spanish-flu>.
- Roth, Alvin (2007). “Repugnance as a Constraint on Markets.” *Journal of Economic Perspectives*, 21(3), 37–58.
- Roth, Alvin E., Tayfun Sönmez, and Utku Ünver (2004). “Kidney Exchange.” *Quarterly Journal of Economics*, 119, 457–488.
- Roth, Alvin E., Tayfun Sönmez, and Utku Ünver (2005a). “A Kidney Exchange Clearinghouse in New England.” *American Economic Review: Papers and Proceedings*, 95(2), 376–380.

- Roth, Alvin E., Tayfun Sönmez, and Utku Ünver (2005b). “Pairwise Kidney Exchange.” *Journal of Economic Theory*, 125, 151–188.
- Roth, Alvin E., Tayfun Sönmez, and Utku Ünver (2007). “Efficient Kidney Exchange: Coincidence of Wants in Markets with Compatibility-Based Preferences.” *American Economic Review*, 97, 828–851.
- Roth, Alvin E., Tayfun Sönmez, M. Utku Ünver, Francis L. Delmonico, and Susan L. Saidman (2006). “Utilizing List Exchange and Undirected Good Samaritan Donation through “Chain” Paired Kidney Exchange.” *American Journal of Transplantation*, 6(11), 2694–2705.
- Rubin, Rita (2020). “Testing an Old Therapy Against a New Disease: Convalescent Plasma for Covid-19.” *Journal of the American Medical Association*. April 30.
- Sandel, Michael (2012). *What Money Can't Buy: The Moral Limits of Markets*. Farrar, Straus and Giroux.
- Satz, Deborah (2012). *Why Some Things Should Not be for Sale: The Moral Limits of Markets*. Oxford University Press.
- Shen, Chenguang et al. (2020). “Treatment of 5 Critically Ill Patients with Covid-19 with Convalescent Plasma.” *Journal of the American Medical Association*.
- Sheridan, Cormac (2020). “Convalescent serum lines up as first-choice treatment for coronavirus.” *Nature Biotechnology*. May 1, <https://www.nature.com/articles/d41587-020-00011-1>.
- Slonim, Robert, Carmen Wang, and Ellen Garbarino (2014). “The Market for Blood.” *Journal of Economic Perspectives*, 28(2), 177–196.
- Sönmez, Tayfun and M. Utku Ünver (2015). “Enhancing the Efficiency of and Equity in Transplant Organ Allocation via Incentivized Exchange.” Available as Boston College Working Paper 868.
- Sönmez, Tayfun, Utku Ünver, and M. Bumin Yenmez (2020). “Incentivized Kidney Exchange.” forthcoming, *American Economic Review*.
- Titmuss, Richard M. (1970). *The Gift Relationship*. Allen and Unwin.
- Ünver, Utku (2010). “Dynamic Kidney Exchange.” *Review of Economic Studies*, 77(1), 372–414.
- Veale, Jeffrey L., Alexander M. Capron, Nima Nassiri, Gabriel Danovitch, H. Albin Gritsch, Amy Waterman, Joseph Del Pizzo, Jim C. Hu, Marek Pycia, Suzanne McGuire, Marian Charlton, and Sandip Kapur (2017). “Vouchers for Future Kidney Transplants to Overcome “Chronological Incompatibility” Between Living Donors and Recipients.” *Transplantation*, 101(9).
- Ye, Mingxiang, Dian Fu, Yi Ren, Faxiang Wang, Dong Wang, Fang Zhang, Xinyi Xia, and Tangfeng Lu (2020). “Treatment with Convalescent Plasma for Covid-19 patients in Wuhan, China.” *Journal of Medical Virology*.