A Multiclass, Multiproduct Covid-19 Convalescent Plasma Donor Equilibrium Model

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Outline

Motivation

Covid-19 and Convalescent Plasma Therapy

- During the Covid-19 pandemic one treatment that has been implemented to treat critically ill patients, especially when and where vaccines were not available, is that of convalescent plasma therapy.
- In 2020, the United States Food and Drug Administration (FDA), in partnership with academics and industry, began a nation-wide effort to facilitate the development of two investigational therapies: one on convalescent plasma treatment and the other on hyperimmune globulin.

NEWS | 01 May 2020

Convalescent serum lines up as first-choice treatment for coronavirus

Antibodies from blood donated by people who recovered from the illness and hyper-immunoglobulins are becoming treatments of choice for COVID-19, with recombinant polyclonal antibody approaches to follow.

Cormac Sheridan

Motivation

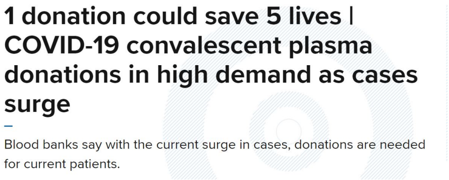
Convalescent Plasma Donation

- In the United States the FDA maintains strict guidelines for convalescent plasma donor eligibility.
- In some cases, individuals who are not eligible to donate plasma for direct treatment due to safety concerns, such as Hasidic women who have recovered from Covid-19, can still choose to donate for hyperimmune globulin creation.

Motivation

Convalescent Plasma Donation

- The nonprofit blood banks and hospital blood programs have been seeking convalescent plasma for clinical trials conducted by research groups and for treatment of severely ill patients.
- Profit-making companies also started collecting this potentially life-saving product for manufacturing hyperimmune globulin, supplying blood samples to laboratories and test manufacturers with monetary compensations.
- As a result an interesting market for convalescent plasma emerged.
- This market involves multiple players with different objectives and a limited donor pool.



1 donation could save 5 lives | COVID-19 convalescent plasma donations in high demand as cases surge

Blood banks say with the current surge in cases, donations are needed for current patients.

Motivation

Concerned by the competition between nonprofit and profit-making organizations Farrugia et al. (2020) wrote:

We apprehend that potential CP donors who may approach the community blood sector for altruistic reasons may be deflected to the commercial sector through the high remuneration offered. This may be accentuated during this period as the traditionally low-resource population of paid plasma donors may be further augmented through the difficult economic situation, as occurred in previous economic crises.

Market For Blood Plasma From COVID-19 Survivors Heats Up

May 11, 2020 · 5:00 AM ET

JONEL ALECCIA

FROM KHN

Contributions

- It is important to study the behavior of donors in this competitive scenario that can also help government agencies prepare for future waves of the Covid-19 pandemic or other infectious disease outbreaks.
- In this paper, we develop a novel multiclass, multiproduct donor model for convalescent plasma donations.
- To the best of our knowledge this is the first model to capture competition between nonprofit organizations and for profit organizations for the collection of convalescent plasma.
- Based on the study on donor behavior conducted by Evans and Ferguson (2013), we assume that the blood or, in this case, the convalescent plasma donor population is not homogeneous and can be separated into several classes on the basis of their motivation as well as appropriate fit for a specific product.
- The model is an equilibrium model and consists of different classes of recovered Covid-19 survivors who meet the criteria for donating convalescent plasma for one or more of the plasma products.

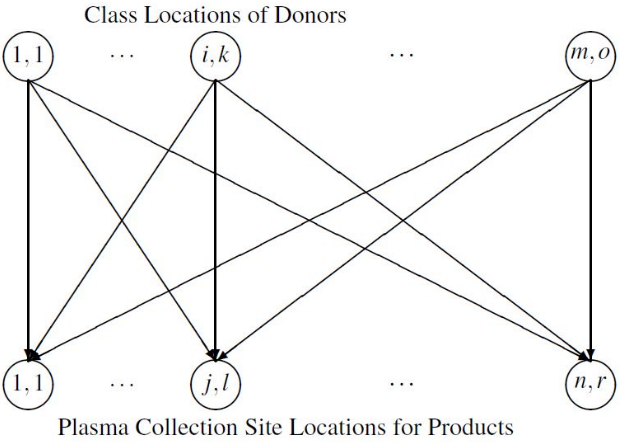
Literature Review - Some References

Charitable Donations and Donor Behavior: Toyasaki and Wakolbinger (2011), Kessler and Roth (2012), Saxton and Zhuang (2013).

Human Migration Models: Nagurney (1989, 1990), Causa,Jadamba, and Raciti (2017), Nagurney and Daniele (2021), Nagurney, Daniele, and Cappello (2021).

Blood Supply Chains: Nagurney, Masoumi, and Yu (2012), Lacetera, Macis, and Slonim (2013), Masoumi, Yu, and Nagurney (2017), Dutta and Nagurney (2019), Nagurney and Dutta (2019), Cheraghi (2020), Kominers et al. (2020).

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model



The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

- The model consists of m locations at which recovered Covid-19 individuals are located with a typical such origin location denoted by i.
- There are also n locations at which the convalescent plasma is collected that the donors need to go to, with a typical such destination location denoted by j.
- We denote a convalescent plasma product by l and there are r such products.
- There are o different classes of convalescent plasma donors, with a typical class denoted by k.

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

Notation	Definition
Q_{ij}^{kl}	the donation flow of convalescent plasma for purpose l of class k donor from location i to collection site j. The $\{Q_{ij}^{kl}\}$ elements for all i, j, k, and l are grouped into the vector $Q \in R_+^{mnor}$.
$\bar{Q}_i^k$	the nonnegative amount of convalescent plasma from potential donors of class k at location i; $k = 1, \ldots, o$; $i = 1, \ldots, m$.
$U_{ij}^{kl}(Q)$	the utility perceived by class k at location i to donate convalescent plasma at location j for product/purpose l; $i = 1, \ldots, m$; $j = 1, \ldots, n$; $k = 1, \ldots, o$; $l = 1, \ldots, r$. We group all the utilities into the vector $U(Q) \in R^{mnor}$.
$c_{ij}^{kl}(Q)$	the generalized cost of class k at location i to go to location j to donate product l of their convalescent plasma, which includes financial cost, time, and risk of class k for $i = 1, \ldots, m$; $j = 1, \ldots, n$; $k = 1, \ldots, o$; $l = 1, \ldots, r$. We group all the generalized costs into the vector $c(Q) \in R^{mnor}$.
λ_i^k	the nonnegative Lagrange multiplier, in effect, associated with the available amount of convalescent plasma potentially to donate by class k located at location i; $i = 1, \ldots, m$; $k = 1, \ldots, o$. We group all the Lagrange multipliers into the vector $\lambda \in R_+^{om}$.

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

The convalescent plasma donations must be nonnegative, that is,

$$Q_{ij}^{kl} \geq 0, \quad \forall i, j, k, l.$$

We define the feasible set $K \equiv \{(Q, \lambda) |$ such that $Q \in R_+^{mnor}$ and $\lambda \in R_+^{om}\}$. Note that the feasible set K is closed and convex.

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

The full statement of the governing equilibrium conditions is given below.

Definition

A vector of multiclass, multiproduct convalescent plasma donations (flows) and a vector of Lagrange multipliers $(Q^*, \lambda^*) \in K$ are in equilibrium if they satisfy the equilibrium conditions: for each class k; $k = 1, \ldots, o$ and each product l; $l = 1, \ldots, r$:

$$c_{ij}^{kl}(Q^*) \begin{cases} = U_{ij}^{kl}(Q^*) - \lambda_i^{k*}, & \text{if} \quad Q_{ij}^{kl*} > 0, \\ \geq U_{ij}^{kl}(Q^*) - \lambda_i^{k*}, & \text{if} \quad Q_{ij}^{kl*} = 0, \end{cases}$$

and

$$\bar{Q}_i^k \begin{cases} = \sum_{j=1}^{n} \sum_{l=1}^{r} Q_{ij}^{kl*}, & \text{if} \quad \lambda_i^{k*} > 0, \\ \geq \sum_{j=1}^{n} \sum_{l=1}^{r} Q_{ij}^{kl*}, & \text{if} \quad \lambda_i^{k*} = 0. \end{cases}$$

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

We now provide a deeper interpretation of the equilibrium conditions. Specifically, we note that they can be rewritten as follows: for each class k; $k = 1, \ldots, o$ and each product l; $l = 1, \ldots, r$:

$$\lambda_i^{k*} \begin{cases} = U_{ij}^{kl}(Q^*) - c_{ij}^{kl}(Q^*), & \text{if} \quad Q_{ij}^{kl*} > 0, \\ \geq U_{ij}^{kl}(Q^*) - c_{ij}^{kl}(Q^*), & \text{if} \quad Q_{ij}^{kl*} = 0. \end{cases}$$

From the above expressions, we can see that, for, a given class at an origin location, the utility minus the generalized cost is equalized for all plasma product / destination choices that are selected; that is, for those for which there is a positive volume of convalescent plasma donated. And that difference between the utility and the generalized cost exceeds the analogous values for the not selected options; that is, those with zero convalescent plasma donations (flows).

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

Theorem: Variational Inequality Formulation

The vectors of convalescent plasma donations (flows) and Lagrange multipliers satisfy the equilibrium conditions if and only if they satisfy the variational inequality problem: determine $(Q^*, \lambda^*) \in K$ such that

$$\sum_{i=1}^{m}\sum_{j=1}^{n}\sum_{k=1}^{o}\sum_{l=1}^{r}\left[c_{ij}^{kl}(Q^*) - U_{ij}^{kl}(Q^*) + \lambda_i^{k*}\right] \times \left[Q_{ij}^{kl} - Q_{ij}^{kl*}\right]$$

$$+\sum_{i=1}^{m}\sum_{k=1}^{o}\left[\bar{Q}_i^k - \sum_{j=1}^{n}\sum_{l=1}^{r} Q_{ij}^{kl*}\right] \times \left[\lambda_i^k - \lambda_i^{k*}\right] \geq 0, \quad \forall (Q,\lambda) \in K.$$

An Extension to Include Capacities

We let cap_j denote the maximum amount of plasma donations that can be handled at collection site j and we let $\mathcal{S}$ be the set of such sites j. Assume that there are $n_{\mathcal{S}}$ elements in the set $\mathcal{S}$. Also, we introduce the Lagrange multiplier γ_j for each collection site $j \in \mathcal{S}$ and we group the Lagrange multipliers γ_j into the vector $\gamma \in R_+^{n_{\mathcal{S}}}$.

We define the feasible set
$K^2 \equiv \{(Q, \lambda, \gamma) | \text{ such that } Q \in R_+^{mnor}, \lambda \in R_+^{om}, \gamma \in R_+^{n_{\mathcal{S}}}\}$.

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

Definition: The Capacitated Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Conditions

A vector of multiclass, multiproduct convalescent plasma donations (flows) and vectors of Lagrange multipliers $(Q^*, \lambda^*, \gamma^*) \in K^2$ are in equilibrium if they satisfy the equilibrium conditions: for each class k; $k = 1, \ldots, o$, each product l; $l = 1, \ldots, r$, for donors at i; $i = 1, \ldots, m$, and for $j \in \mathcal{S}$:

$$c_{ij}^{kl}(Q^*) \begin{cases} = U_{ij}^{kl}(Q^*) - \lambda_i^{k*} - \gamma_j^*, & \text{if} \quad Q_{ij}^{kl*} > 0, \\ \geq U_{ij}^{kl}(Q^*) - \lambda_i^{k*} - \gamma_j^*, & \text{if} \quad Q_{ij}^{kl*} = 0, \end{cases}$$

whereas for each class k; $k = 1, \ldots, o$, each product l; $l = 1, \ldots, r$, for donors at i; $i = 1, \ldots, m$, and for $j \notin \mathcal{S}$:

$$c_{ij}^{kl}(Q^*) \begin{cases} = U_{ij}^{kl}(Q^*) - \lambda_i^{k*}, & \text{if} \quad Q_{ij}^{kl*} > 0, \\ \geq U_{ij}^{kl}(Q^*) - \lambda_i^{k*}, & \text{if} \quad Q_{ij}^{kl*} = 0, \end{cases})$$

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

Definition: The Capacitated Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Conditions

and for $j \in \mathcal{S}$:

$$cap_j \begin{cases} = \sum_{i=1}^{m} \sum_{k=1}^{o} \sum_{l=1}^{r} Q_{ij}^{kl*}, & \text{if} \quad \gamma_j^* > 0, \\ \geq \sum_{i=1}^{m} \sum_{k=1}^{o} \sum_{l=1}^{r} Q_{ij}^{kl*}, & \text{if} \quad \gamma_j^* = 0, \end{cases}$$

holding for all j, that is,

$$\bar{Q}_i^k \begin{cases} = \sum_{j=1}^{n} \sum_{l=1}^{r} Q_{ij}^{kl*}, & \text{if} \quad \lambda_i^{k*} > 0, \\ \geq \sum_{j=1}^{n} \sum_{l=1}^{r} Q_{ij}^{kl*}, & \text{if} \quad \lambda_i^{k*} = 0. \end{cases}$$

The Multiclass, Multiproduct Convalescent Plasma Donor Equilibrium Model

Variational Inequality Formulation of the Capacitated Model

A vector of multiclass, multiproduct convalescent plasma donations (flows) and a vector of Lagrange multipliers $(Q^*, \lambda^*, \gamma^*) \in K^2$ satisfy the above equilibrium conditions if and only if they satisfy the variational inequality problem: determine $(Q^*, \lambda^*, \gamma^*) \in K^2$ such that

$$\sum_{i=1}^{m} \sum_{j \in S} \sum_{k=1}^{o} \sum_{l=1}^{r} \left[c_{ij}^{kl}(Q^*) - U_{ij}^{kl}(Q^*) + \lambda_i^{k*} + \gamma_j^* \right] \times \left[Q_{ij}^{kl} - Q_{ij}^{kl*} \right]$$

$$+ \sum_{i=1}^{m} \sum_{j \notin S} \sum_{k=1}^{o} \sum_{l=1}^{r} \left[c_{ij}^{kl}(Q^*) - U_{ij}^{kl}(Q^*) + \lambda_i^{k*} \right] \times \left[Q_{ij}^{kl} - Q_{ij}^{kl*} \right]$$

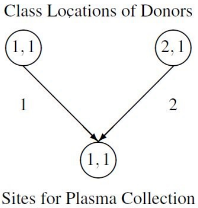
$$+ \sum_{j \in S} \left[cap_j - \sum_{i=1}^{m} \sum_{k=1}^{o} \sum_{l=1}^{r} Q_{ij}^{kl*} \right] \times \left[\gamma_j - \gamma_j^* \right]$$

$$+ \sum_{i=1}^{m} \sum_{k=1}^{o} \left[\bar{Q}_i^k - \sum_{j=1}^{n} \sum_{l=1}^{r} Q_{ij}^{kl*} \right] \times \left[\lambda_i^k - \lambda_i^{k*} \right] \geq 0, \quad \forall (Q^*, \lambda^*, \gamma^*) \in K^2.$$

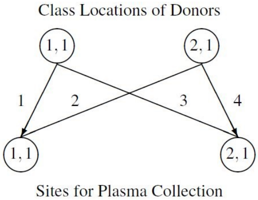
Numerical Examples

- We applied the **modified projection method** to compute solutions to numerical examples of increasing complexity.
- The examples, although stylized, are inspired by the Covid-19 outbreak in New York City, the areas that have been affected, the number of recovered patients, and also the availability of collection sites for convalescent plasma products as of May 2020.

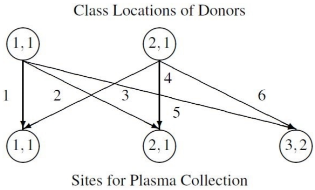
Numerical Examples



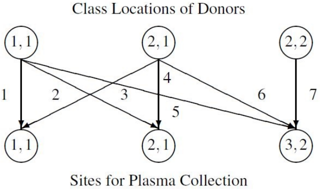
Network Topology for Example 1



Network Topology for Example 2



Network Topology for Examples 3 and 4



Network Topology for Examples 5 and 6

Numerical Examples

- Example 1 consists of a **single class of donor at two locations**. There is a **single collection site** for convalescent plasma which we associate with a **nonprofit organization**.
- In Example 1 we see that the donors at both origin locations choose to donate all their available convalescent plasma. We saw this in practice, that those who have recovered from Covid-19 are seeking to give back and help others through donations of convalescent plasma.
- Example 2 is constructed from Example 1 and has the same data but with the **addition of new data to handle a new collection site for convalescent plasma for another nonprofit organization**.
- With the new collection site, the **donors at the first origin location now donate all their convalescent plasma to the new collection site**.
- The **donors at the second origin site** donate the majority of their plasma to **the new site**. Again, all the available plasma is donated and the Lagrange multipliers are positive.

Numerical Examples

- Example 3 has a **single class of donors, two origin locations, and three collection locations**, with one being a for profit one **collecting for another product**.
- The **donors at origin location 1** now donate all their convalescent plasma to the **for profit collection site**. The **donors at the second origin** location donate the **majority of their convalescent plasma also to the for profit collection site**.
- Clearly, the **nonprofits lose** in terms of convalescent plasma donations due to the **competition from the profit organization**.
- Example 4 is a variant of Example 3 where we assume the donors at the second origin location are now a bit embarrassed by those in their community in that they are donating so much convalescent plasma to the for profit organization and modify their utility function associated with donating to the for profit accordingly.
- We see a **positive amount of convalescent plasma that is being "switched"** from being donated to the **for profit organization to the nonprofit one at the second collection site**.

Numerical Examples

- Example 5 has the same data as Example 4 but now we introduce a new class 2 that is not able to donate their convalescent plasma for direct infusion into Covid-19 patients but, rather, can still donate for another product managed by the for profit organization at its collection site 3.
- From the results we see that now **class 2 does not donate all of the convalescent plasma that it can** and, hence, the associated **Lagrange multiplier is equal to** 0.00.
- In Example 6 we introduce **bound on location 3 collection site capacity**.
- We see that now there is a **positive amount of convalescent plasma donated by class 1 and origin location 2 to nonprofit collection site 1** and **an increase in convalescent plasma donations from this class and location to collection site 2**.
- Because of the capacity on collection site 3, the volume of plasma donations there decreases from donors of class 1.
- Class 2, which is unable to donate for immediate transfusion purposes, again, donates all of its plasma to the for profit site 3.

Conclusions

In this paper, we developed a multiclass, multiproduct equilibrium model to study the behavior of convalescent plasma donors in the Covid-19 pandemic.
Some of the insights gained from the numerical examples, although stylized, are:

- It is important to make the experience of donating convalescent plasma as positive as feasible since a decrease in a utility function fixed term can impact donations.
- Care should be taken when a for profit moves in since convalescent plasma donors may shift their donations from nonprofit organizations to a for profit one.
- Proximity matters and convenience of collection sites.
- Availability of labor needed for the collection process during the pandemic and capacities of the collection sites play an important role. Organizations collecting convalescent plasma need to have the resources to collect from the donors.

Thank you!

This work is dedicated to all essential workers, including: healthcare workers, first responders, freight service providers, grocery store workers, farmers, and educators, who sacrificed so much in the Covid-19 pandemic. We also recognize all those who have suffered from Covid-19 and memorialize those who perished from this disease.