Encouraging Blood Donation in Patients With a Blood Type in Short Supply – Part 2

Protocol and Statistical Analysis Plan

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Protocol

Scientific background

There has been a years-long national shortage of several blood types in the U.S., including in the Geisinger community. Previously, the study team collaborated with Miller Keystone, where Geisinger refers patients who wish to donate blood and from whom Geisinger receives blood for clinical purposes, on an outreach study to encourage blood donation in patients with needed blood types. The study demonstrated that, compared with a no-message control group, patient portal messages sent to patients with needed blood types increase patients' likelihood of attending donation appointments. However, results were ambiguous with respect to which of two message versions was most effective. One version, which stated that the patient had a needed blood type (blood-type message), caused a numerically, but not significantly, higher number of patients who attended appointments compared to the other version, which did not state that the patient had a blood type in need but rather informed the recipient of a general blood shortage (no-blood-type message).

Because Miller Keystone particularly values reaching new donors, the team ran a preregistered exploratory analysis to test whether the messages were differently effective for new donors compared to those who had previously donated at a Miller Keystone site. There was a significant interaction between previous donor status (previous donor, previous non-donor) and message type, such that previous non-donors were relatively more responsive to the blood-type message, while previous donors were more responsive to the no-blood-type message. However, the groups were uneven with respect to the number of patients that had previously donated. Moreover, when the analysis was limited to patients who opened their messages, this interaction effect disappeared: blood-type messages were still most effective in previous non-donors, and there was no difference in message effectiveness among previous donors. These follow-up analyses, and the unevenness of previous donors across groups, call into question the robustness of the interaction effect.

Objectives

The present study again tested whether the blood-type message is more effective than the no-blood-type message for patients with needed blood types overall, and separately for previous donors and non-donors. Messages in the present study were sent via email rather than via patient portal. Randomization occurred at the email-address level to one of the two message types to ensure everyone using the same email address received the same message (although each patient was sent an individualized message with their name; there was no no-contact control condition this time). Email addresses were excluded if they were shared by patients with different blood types. Randomization was stratified by whether all patients using the same email address are previous donors or not (email addresses shared by previous donors and non-donors were excluded).

Design

This study is a randomized controlled trial with 2 study arms.

Methods

Email addresses of patients enrolled in the study were randomized to the following arms:

1. No-blood-type message – a message that did not mention the patient had a needed blood type
2. Blood-type message – a message that mentioned the patient had a needed blood type

Randomization was stratified by previous donor status of all patients at an email address.

Power analysis

Our sample includes 40,486 patients with a total of 40,130 email addresses. 39,317 email addresses are associated with patients who are previous non-donors, and 813 email addresses are associated with patients who are previous donors.

Within the previous non-donor group, we will have 80% power to detect an increase in the primary outcome from 0.07% (the primary-outcome rate in previous non-donors who were sent a no-blood-type message in our previous study) to 0.16%, with a two-tailed alpha of .05.

Within the previous donor group, we will have 80% power to detect an increase in the primary outcome from 4.76% (the primary-outcome rate in previous donors who were sent a no-blood-type message in our previous study) to 9.87%, with a two-tailed alpha of .05.

Note that a portion of the sample will be excluded from analysis (e.g., those whose emails were not sent or bounced; see the *Analysis notes* section for details).

Project status

All emails have been sent. No outcome data have been extracted.

Statistical Analysis Plan

Primary outcome

Number of Participants Who Attended a Donation Appointment

Attended a donation appointment within 6 weeks of their message send date, regardless of whether they donated. This outcome includes patients who were unable to donate for

any reason (e.g., low hemoglobin) or patients who showed up to the appointment but decided to leave before donating.

[Time Frame: Within 6 weeks of the patient's message send date]

Question 1: Within patients who *are not* previous donors, do more patients attend donation appointments if they are sent the blood-type message compared with those sent the no-blood-type message?

Analysis 1: We will test the hypothesis that previous non-donors who are sent a blood-type message are more likely to attend a donation appointment than those sent a no-blood-type message. We will run an OLS regression with a binary predictor variable indicating whether patients were sent the blood-type message or the no-blood-type message.

Question 2: Within patients who *are* previous donors, do more patients attend donation appointments if they are sent the blood-type message compared with those sent the no-blood-type message?

Analysis 2: We will run *Analysis 1* including only patients who are previous donors.

Analysis notes

Whether or not a patient is a previous donor was determined by a data pull completed prior to randomization. Because the data on previous donors from this pull was used to stratify randomization, we will use this data pull to determine whether patients should be included in *Analysis 1* (previous non-donors) or *Analysis 2* (previous donors), even if we later learn the patient had previously donated (e.g., if they donated after the pre-randomization data pull but before the intervention began).

Analyses will be conducted on the email-address level. For each email address, if any associated patient attended a donation appointment, the email address will be "counted" as achieving the primary outcome. To ensure that our findings do not depend on patients who share an email address, we will also run the analyses above removing all patients who share an email address with another patient in the study.

All analyses will exclude patients who scheduled their appointment prior to their message send date.

Patients will be excluded from analysis if, according to our records, their emails were not sent (e.g., due to being unsubscribed from emails) or for whom our emails bounced.

Timeframes listed refer to the amount of time elapsed from the send date for a given patient. For instance, the primary outcome timeframe is 6 weeks; thus, for the purposes of this study, a

patient will be counted as having donated if they donated blood within 6 weeks of their message send date.

As a robustness check, we will rerun the analyses above on the subset of patients who open the messages, using a time frame of 6 weeks from the date each individual patient opened their message (rather than 6 weeks from the patient's message send date).

We will run an additional robustness check including only patients who scheduled an appointment within the 2 weeks following their message send date.

Recent work suggests that OLS regressions are appropriate in randomized experiments with binary outcome variables such as ours (Gomila, 2021).

Other prespecified outcomes

We will use the approaches described in *Analyses 1* and *2* above to evaluate the impact of the intervention on the other prespecified outcome measures listed in the pre-registration:

1. Number of Participants Who Successfully Donated Blood

   Attended a donation appointment within 6 weeks of their message send date and successfully donated, excluding patients who were turned away from or left their appointment without donating.

   [Time Frame: Within 6 weeks of the patient's message send date]

2. Number of Participants Who Scheduled a Blood Donation Appointment

   Scheduled an appointment within 2 weeks of their message send date.

   [Time Frame: Within 2 weeks of the patient's message send date]

3. Number of Participants Who Scheduled a Blood Donation Appointment

   Scheduled an appointment within 6 weeks of their message send date.

   [Time Frame: Within 6 weeks of the patient's message send date]

Additional exploratory analyses

1. Primary outcome in the full sample

We will run an OLS regression to test whether the primary outcome varies as a function of experimental group in the full sample, without dividing the sample by previous donor status.

2. New donors vs. previous donors

   We will run an OLS regression to test whether the primary outcome varies as a function of experimental group, a bivariate indicator for whether or not the patient previously donated blood, and the interaction between these variables.

3. Time to donation

   We will run regression models to test whether either intervention message influenced the timing (time elapsed since the message was sent) of donations.

4. Type of donation

   We will test whether there are differences in donation type (particularly whole blood and red blood cell donations) as a function of experimental group.

5. Demographics

   We will run regression models to test for main effects of several demographic factors on donation behavior, along with interactions between these factors and message group. These demographic factors may include binned age (18–24, 25–34, 35–44,45–54, 55–64, and 65+), sex, race, ethnicity, line of insurance (as a proxy for socioeconomic status), and Charlson Comorbidity.

References

Gomila, R. (2021). Logistic or linear? Estimating causal effects of experimental treatments on binary outcomes using regression analysis. *Journal of Experimental Psychology: General*, *150*(4), 700–709. https://doi.org/10.1037/xge0000920