

Rapid Response Survey of Blood Donors in Support of Public Health

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Abstract

The objective of the study was to develop methodologies and infrastructure in order to quickly survey blood donors in situations where there could be possible exposure to transfusion transmissible pathogens or other potential hazards to the blood supply. The U.S. Food and Drug Administration (FDA) worked with five Blood Collecting Organizations (BCOs), NORC at the University of Chicago, and the American Association of Blood Banks (AABB) to develop sample frames, select samples, and administer web-surveys. This paper describes the general protocol, the response rates and the rapidity of response for two surveys. One survey addressed exposure to ticks and tick-borne infection and the second survey addressed exposure to the Hepatitis E virus.

Key Words: web survey, rapid-response, survey non-response, public health

1. General Protocol

The target population of blood donors was defined in terms of five Blood Collection Organizations (BCOs): the American Red Cross, BloodCenter of Wisconsin, Blood Systems, Inc., New York Blood Center, and OneBlood. In addition to demographic characteristics such as age, gender and geographic location, each BCO also has information on two other important characteristics of blood donors: 1) the type of donation made (whole blood or apheresis donation) and 2) whether the donor had made only one blood donation at this time (first-time donor) or had made more than one donation (repeat donor). Participation from BCOs was crucial because blood donors are a small portion of the adult U.S. population (less than 5%) with different demographics by education, age, gender, and socioeconomic status. General population surveys in the U.S. are not generalizable to blood donors. Accessing blood donors from the general

population would entail sampling 20 times more people (on average) in order to get the data needed for an appropriate risk assessment.

This study was approved, or an exemption was received, by all participating organizations' Institutional Review Board. Each BCO created the sample frame based on their blood donors, selected a random sample of blood donors, and contacted their donors. Initially the plan was that each BCO would also create and administer their own web-survey, and send the responses to NORC. NORC would de-identify, clean and aggregate the data so that responses could not be identified by BCO. The aggregated file would then be provided to FDA, the participating BCOs, and AABB.

An initial survey was conducted in 2014 to assess the potential risk of Middle East respiratory syndrome (MERS) infection based on recent travel of donors and any of their immediate contacts to the Arabian peninsula.¹ After the initial survey, the protocol was modified so that the selected donors were directed to one web-site managed by NORC. NORC tracked the responses and collected the data. The revised protocol was used for the subsequent surveys of donors on tick-borne infections and on Hepatitis E risk factors. The revision generally resulted in improved data quality and consistency. The potential disadvantage was that the demographic and donor information associated with the respondents must be collected from the respondents on the survey, rather than being provided by the BCO. However, the response rates to the demographic and donation questions on subsequent surveys were very high.

1.1 Population and Sample Frame

The Rapid Response Survey aimed to provide a snapshot of US blood donors through the collection of survey data from a statistically representative sample. The sample frame was developed based on the Blood Collecting Organizations (BCOs) blood donors who were 18 years of age or older and who donated blood in the previous year. The contact list of blood donors over the five BCOs provided coverage over all 50 states and included over 4 million individuals. The majority of the donors (88%) were donating whole blood; 68% had made repeated donations for the BCO and 20% were donors who had made one donation of whole blood at the time the population was evaluated. Only 12% of the blood donors were apheresis donors and these were almost entirely repeat-donors; only 1% of the population were first-time donors who had made an apheresis donation.

In order to ensure that the IRB age stipulation for consent was met, individuals with age unknown were excluded from the sample frame.² Due to the need to contact individuals quickly, the population of inference and the sample frame were restricted to those individuals who provided an email contact and contact permission. Over all donors with known age, 54% provided email contact permission.³ Due to an accidental change in the request for sample data, individuals with no information on gender were not subject to sampling. The sample frame definition was revised to reflect this unintentional change in the definition of the sample frame. With this further restriction, the sample frame

¹ The results of the initial survey will be reported elsewhere.

² The donors with age unknown represented only 2.5% of the population.

³ The comparison provided here is for the survey on tick-borne disease. The sample frame for the survey on Hepatitis E was slightly different (as time had passed) but the general properties were the same. For example, the sample frame for the Hepatitis E survey comprised 53% of the population.

contained approximately 2.1 million individuals, or 52% of the population of donors with known age.

Blood donors providing email contact and permission showed the following differences when compared to all blood donors who were at least 18 years of age and had recently made a donation:

- First time donors were less likely to provide email contact permission compared to repeat donors (32% versus 58%).
- Whole blood donors were less likely to provide email contact permission compared to apheresis donors (51% of whole blood donors allowed email contact versus 63% of apheresis donors). While there was also a correlation between type of donation and first-time vs repeat donors⁴, an analysis of variance indicates that both main effects and the interaction were significant factors in predicting the likelihood of being in the sample frame. Exhibit 1 shows the percentage in the sample frame for these two characteristics.
- The likelihood of being in the frame was generally higher for women than for men. Over all categories 54% of the women in the population were in the sample frame compared to 51% of the men. This pattern was consistent across the donor and donation categories as shown below.

Exhibit 1. Percentage of Donors Providing Permission for Email Contact
By Donor Type, Donation Type and Gender

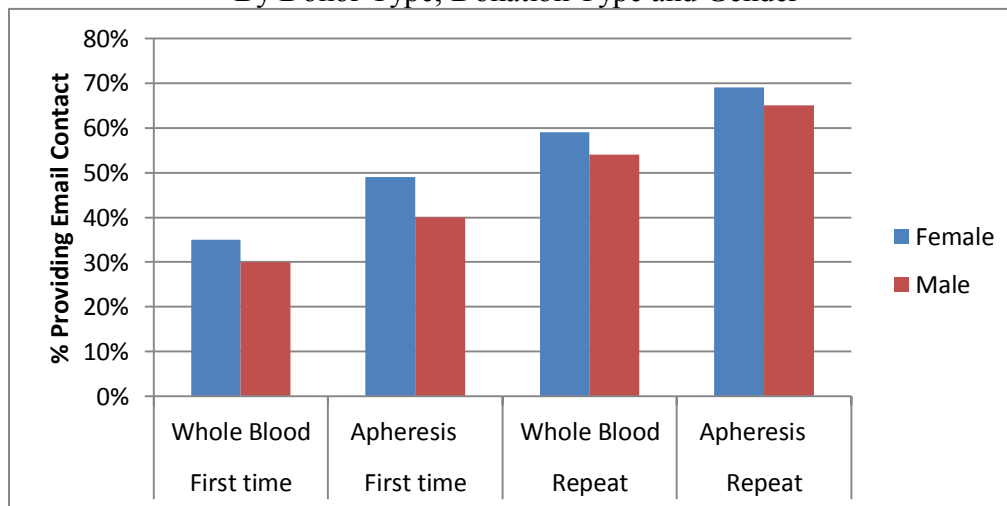
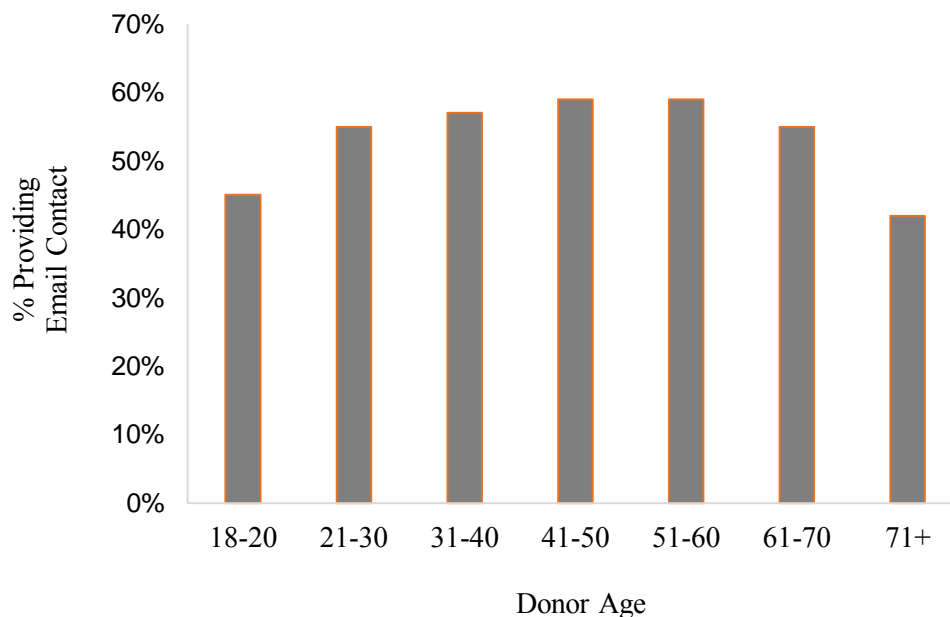


Exhibit 2 shows that the youngest donors and the oldest donors were less likely to be included in the sample frame compared to the other age categories. The same pattern is observed for subpopulations defined by donation type and donor type. These surveys were restricted to blood donors permitting contact via email which is probably not the preferred contact mechanism for younger donors. As discussed in the final section, the expectation is that the methodology would be expanded beyond email contact to include other electronic formats such as text messages.

⁴ Apheresis donors were much less likely to be first time donors compared to whole blood donors.

Exhibit 2. Percentage in Sample Frame, by Age Group

2. Response Rates and Characteristics of Respondents

2.1 Sample and Response

For each survey, the goal was to obtain a minimum of 5,000 completed surveys, with at least 1,000 from each BCO. Each BCO selected an initial sample, with the sample size based on the expected response rate for its donors. Sample replicates were constructed so that the email invitations could be sent out in waves, as needed.

A sample size of 65,359 blood donors achieved 5,769 responses for the tick-borne disease survey, and a sample size of 89,957 achieved 6,339 completed Hepatitis E surveys. The lower overall response rate in the second survey was due to one BCO accidentally sending out a much larger initial wave than intended, probably resulting in a process known as “cloudmarking.” That is, the reputation of the email address and domain used by the blood center was probably marked as “bad” either by a user or email providers’ internal systems, and many of the emails went to potential respondents’ junk mails. Cloudmarking is very common when using email blasts (i.e., sending many emails to many people at one time). Due to this initial failure, the sample size had to be increased for this BCO.

2.2 Donor and Donation Characteristics of Interest

There were five characteristics of the blood donors which were available on the BCOs’ source systems that were of interest in both surveys: gender, age, geographic location, type of donation, and whether the donor was a first time or repeat donor. The demographic characteristics may be associated with the survey topic (for example associated with types of behavior or likelihood of contagion). The donation

characteristics would be important for estimation or prediction of the potential effect on the blood supply. Therefore, it is important to evaluate both the demographic characteristics and the donation characteristics in terms of their association with the likelihood of response.

Each BCO provided NORC with the tabulation of the sample by demographic and blood donor characteristics. NORC collected the sample responses but could not identify the donor and therefore could not link the survey responses to the demographic information provided by the BCO. Therefore, the donation and demographic information were collected on the survey.

There was relatively little missing demographic information on the survey responses. The responses differentiated between 'Do not know' and 'Prefer not to Answer.' In each of the two surveys, less than 0.5% of the responders chose 'Prefer not to Answer' for any of these five questions. The largest number of 'Do not know' responses was to the question as to whether or not the last blood donation was whole blood or apheresis⁵. The expert opinion was that a blood donor making an apheresis donation would know this term and would know that they made an apheresis donation. If the donor replied that he/she did not know what type of donation was made, it was most likely a whole blood donation. Therefore, for purposes of analysis, the response 'Do not know' was recoded as 'Whole Blood.'

With this edit, the largest number of 'Do not know' responses in each survey was to the question regarding whether the person is a first-time or repeat donor. The relative number of 'Do not know' responses was much higher in the Hepatitis E survey due to a failure to clarify the intended sample frame target for this survey and to make necessary adjustments in the question for some BCOs. But the nonresponse rate was still very small for this question: 1% for the tick-borne survey compared to 2% for the Hepatitis E survey.

2.3 Analysis of the Characteristics of Respondents

Response rates were calculated by comparing the survey response data to the original sample tabulations. However, the tabulations of the selected sample by demographic categories were provided by each BCO and the respondent's demographic and donation information were collected on the web survey. Therefore, there were some discrepancies in the comparisons. For example, an individual tabulated as being 21-25 years old in the sample may refuse to provide age on the survey. Or an individual may have had their 26th birthday since the sample data were constructed. A first-time donor in the sample data may have made a second donation prior to taking the survey. The Appendix provides tabulations of the response rates and discusses the calculations and limitations of the data.

Exhibit 3 shows the response rates by the aggregated United States Public Health Service (USPHS) Regions. In both surveys, the lowest response rates were observed in Regions 1-4 and individuals in the southern region (Region 4) had a much lower response rate than any other area. The tick-borne disease survey was conducted in August and it was expected that the response rate might be low in Florida; the survey was initially delayed

⁵ For the tick-borne disease survey, 293 out of 5,769 did not know and for the hepatitis E survey, 390 out of 6,339 did not know whether their blood donation was whole blood or apheresis.

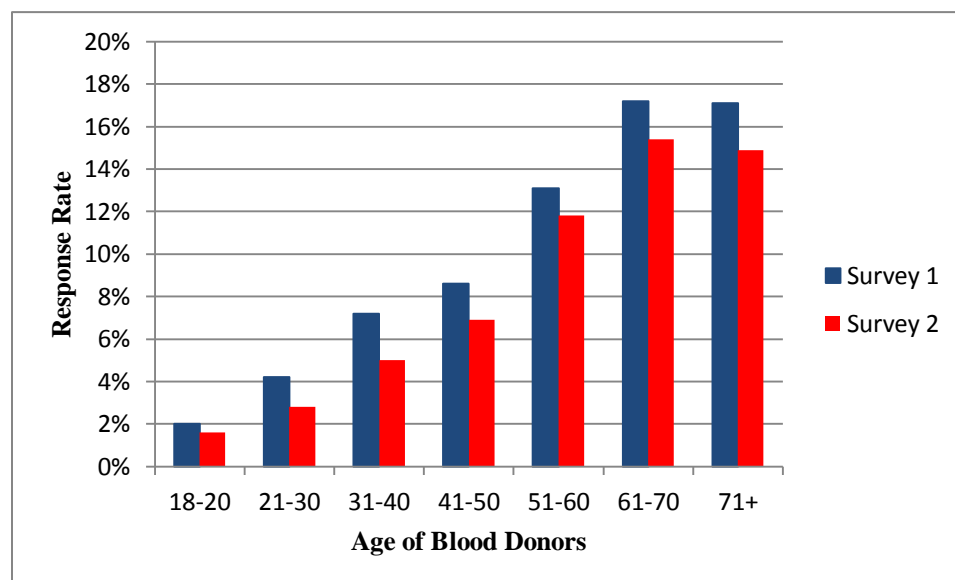
due to hurricane warnings. The even lower response rate for the Hepatitis E survey was due to the 'cloudmarking' problem discussed earlier.

Exhibit 3. Donor Survey Response Rates by Geography

	USPHS Regions	Tick-Borne Disease	Hepatitis E
1-3	CT, DC, DE, MA, MD, ME, NH, NJ, NY, PA, RI, VA, VT, WV	8.0%	9.7%
4	AL,FL,GA,KY,MS,NC,SC,TN	5.1%	2.5%
5-6	IL,IN,MI,MN,OH,WI	12.7%	17.1%
6-7	AR,IA,KS,LA,MO,NE,NM,OK,TX	10.0%	11.9%
8	CO,MT,ND,SD,UT,WY	13.8%	15.9%
9	AZ,CA,HI,NV	13.9%	18.4%
10	AK,ID,OR,WA	14.6%	16.6%
	Overall	8.8%	7.0%

In both surveys there was a strong association between age and likelihood of response, with younger donors being less likely to respond than older donors, as shown in Exhibit 4. The data are provided in the appendix.

Exhibit 4. Survey Response Rates by Age of Donor



There are several ways that the under-representation of the younger donors can be addressed. For the completed surveys, estimates can be made using weights to adjust for the nonresponse, as discussed later in this section. Future surveys should explore expanding the method of contact beyond email, to texting or whatever form of communication is currently being used. This would improve both the under-representation in the frame and could also improve the response rates.

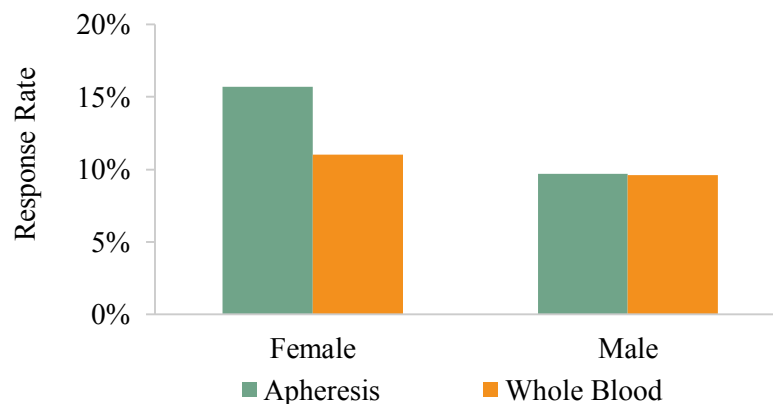
For both surveys, the following general patterns of response were found⁶:

- Repeat donors were much more likely to respond than first-time donors.
- Apheresis donors were more likely to respond than whole blood donors.
- Women were more likely to respond than men.

Less than 1% of first-time donors responded compared to 9-10% of the repeat donors. There were only 114 first-time donors responding to the tick-borne illness survey and 107 first-time donors responding to the Hepatitis E survey. Recall, however, that the comparison was made between the sample data which came from the BCO data and the survey response which occurred after the BCO data were tabulated. Therefore, some of the 'repeat' responses may have been 'first-time' donors at the time the sample data were compiled. However, there were insufficient first-time donor respondents for further analysis by type of donor.

The following discussion is limited to respondents to the tick-borne infection survey who provided complete demographic data and indicated that they were repeat donors⁷. The analysis of variance⁸ for the probability of response as a function of the four remaining demographic/donation characteristics indicated that the significant factors in the model for predicting the response rate were the main effects of gender, age class, and geographic region, and the interaction between donation type and gender. No other interaction terms were identified. The response rates by gender and type of donation are displayed in Exhibit 5.

Exhibit 5. Tick-borne Disease Survey: Response Rates for Repeat Donors
By Donation Type and Gender



Considering both gender and type of donation, female apheresis donors were the most likely to respond (15.7% response rate) compared to female whole-blood donors (11.0%)

⁶ The data are provided in the appendix.

⁷ As noted earlier, the exclusion of respondents with incomplete demographic data is very minor, removing only 108 of the 5,769 respondents to the tick-borne disease survey.

⁸ By location, the smallest sample was in Region 10 (fewer than 500) and there were very few apheresis donors (40) in the sample. Therefore these data were not included in the analysis of variance.

and to male donors of either donation type (9.7% for male apheresis donors and 9.6% for male whole blood donors). For male donors, the differences in response rate by donation type were not uniformly in the same direction, resulting in a significant interaction detected in the data. Further tabulations are provided in the appendix Exhibit A.4.

Generally, estimation should incorporate adjustments for the possible effects of the differential response rates. For estimating potential effects on the blood supply, it would certainly be important to include the effect of the differential response rates by type of donation and type of donor. In these examples, it is questionable that we can estimate properties of first-time donors in comparison to repeat donors; the respondents were almost all repeat donors. For characteristics such as the number of donors exposed to tick-borne infectious disease, to the extent that the non-respondents are similar to the respondents in terms of a characteristic of interest, the differential response rates will not bias the estimates. However, if the nonresponse is correlated with the characteristic of interest, then the differential response rate can bias the estimates if no adjustment is made.

For example, suppose that we did not have the population counts by age categories, but had collected age on the survey. The simple unadjusted estimate of the total number of donors under the age of 51 would be 759,000 donors (rounded to thousands). However, we know that in fact there were 1,336,000 donors 50 years of age or younger. The information on the population (or the sample) characteristics by age provides more precise information and the estimates would be calculated using this information, either by weighting the data or using ratio adjustments. In Exhibit 6 we compare the simple unadjusted sample estimates to the estimate when a weight is used which adjusts for age and region⁹.

As expected, for estimates of totals (e.g. total number of donors under the age of 51) the adjusted weight can provide much better estimates. When totals are known from the sample frame, similar estimates or even better estimates could be achieved without making adjustments to the weights, by using the known sample frame values to make ratio adjustments. However, this methodology is not available for all parameters of interest, and there is an advantage to the user to have the option of using relatively simple estimation techniques based on adjusted weights.

Exhibit 6. Sample Estimates with Adjusted and Unadjusted Weights

Characteristic of Interest	Sample Frame Value (Rounded)	Sample Estimates	
		Simple Weights	Adjusted Weights
Percentage of donors at risk	Unknown	28.0%	24.6%
Donors 50 years of age or younger			
Total number	1,336,000	759,000	1,322,000
Percentage of donors at risk	Unknown	24.3%	21.9%
Number of female donors	698,000	507,000	797,000

As an example of an unknown characteristic of interest, a donor at risk of tick-borne disease was defined as an individual who either lived in the area indicated or visited these

⁹ The basic weight was raked to the known totals for three age categories and for the Regions.

areas, and indicated at least moderate level of activity in areas frequented by deer. We do not know the true value for this parameter. For estimating this percentage, the adjusted weights resulted in slightly lower values.

Adjusting by only age and geography may not be sufficient. Additional adjustments should be considered, to include adjustments by gender and type of blood donation. Typically estimates should be calculated under at least two models related to nonresponse to evaluate the possible bias due to nonresponse.

3. Rapidity of Response

The goal of the project was to build a mechanism to collect information quickly. While the focus of this initial work was to develop the structure and the process, data were collected which allowed analysis of the speed of response. These data are described in this section.

Because each BCO selected its own sample and sent out the email invitations, the start time for the survey was different for different BCOs. In the Hepatitis Survey, four of the BCOs sent out their first invitation at approximately the same time (within the same week) (Wave 1). One BCO sent their first invitation approximately one month later than the others. However, there was only one closing date. Labeling the first day that an email invitation was sent as day #1, the last response was received on day #40. For three of the BCOs, a second wave (Wave 2) of invitations was required in order to obtain the desired number of responses. Having the survey open for such a long time period provided data on the percentage of the total response obtained 'quickly', i.e. in the first days after the email request is sent.

A more detailed description of the underlying response time data, and the complications, is provided in the appendix. The following table shows the cumulative response rates by BCO and Wave for the Hepatitis E Survey. In each case the time is measured from the first response and days are measured in terms of 24 hour periods after the first response.

Exhibit 6. Hepatitis E Survey Response Times: Cumulative Percentage

	Day 1	Day 2	Day 5	Day 7
BCO 1 – Wave 1	74%	86%	95%	98%
BCO 1 – Wave 2	81%	86%	94%	95%
BCO 2 – Wave 1	82%	90%	98%	99%
BCO 2 – Wave 2	81%	86%	93%	95%
BCO 3 – Wave 1	82%	91%	98%	100%
BCO 3 – Wave 2	73%	84%	92%	94%
BCO 4	72%	88%	95%	96%
BCO 5	55%	81%	96%	97%

As shown in Exhibit 6, in all cases, at least 94% of the total response was obtained within 7 days. Typically a rapid-response survey would not be fielded for more than 7 days. In order to make the response times consistent across the different BCOs, the data are truncated to those who responded within 7 days from the initial response.

For the tick-borne disease survey, the date and time of response were available for only a preliminary data set, covering four of the five BCOs. Similarly, for all such cases, over 95% of the total responses were obtained within 7 days and the data were truncated, for analysis, to those who responded within 7 days from the initial response.

Exhibit 7. Cumulative Distribution for Response, Data Restricted to Responses within One Week

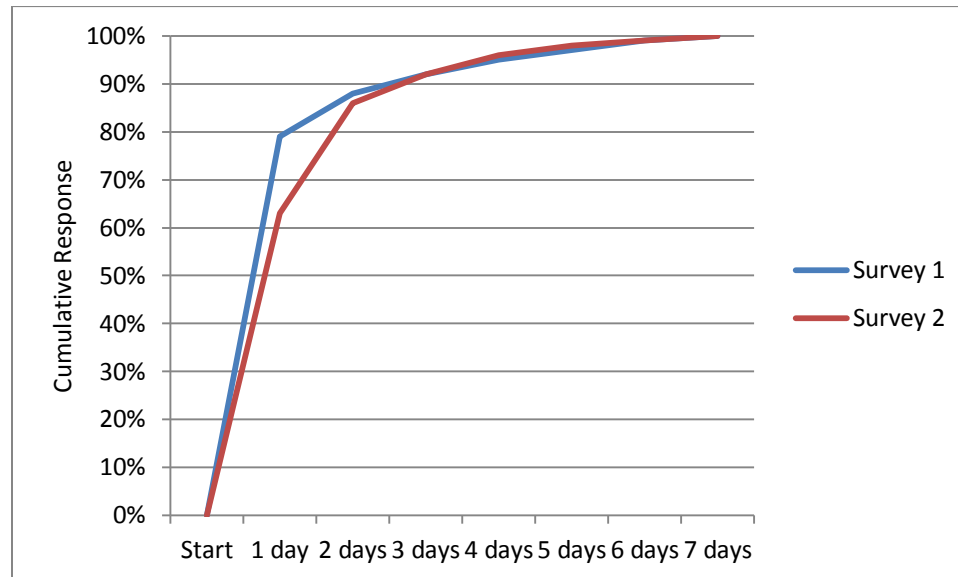


Exhibit 7 shows the results for the tick-borne disease survey (Survey 1) and the Hepatitis E survey (Survey 2), summarized over BCOs and waves. For each survey, over 85% of the responses had been received within 48 hours, and by the end of the third day, 92% of the responses had been received. (The data description and percentages are provided in the appendix.) These results indicate that a rapid response can be achieved for such a survey.

4. Summary and Conclusions

The project successfully developed and executed procedures to:

- create the appropriate sample frame for each BCO and provide the necessary tabulations,
- draw a random sample of blood donors from the sample frame,
- survey blood donors via an email contact, and
- provide the resulting response data, aggregated by broad geographic regions to provide BCO confidentiality

Furthermore, Exhibit 7 indicates that within 2-3 days one could have adequate response to the survey.

An alternative approach for surveying blood donors is to ask donors to fill out the survey, in person, when they come to make a blood donation. In the past this has been a paper survey, which does not allow for a rapid analysis of data. The consumable data acquisition methodology can be relatively rapid when tablets or other electronic devices

are used in order to collect and aggregate the responses. However, there are additional limitations to this approach.

Of most concern is that this methodology uses a convenience sample which does not have the properties of a random sample, and therefore cannot be said to be representative of all blood donors of interest. With the increasing problem of low survey response rates, it might be argued that the value of the random sample is diminished, especially with no opportunity to follow-up on non-respondents. However, the random sample, by providing representative coverage across all geographic regions, all ages, allows a more principled analysis of the potential sources of bias in the respondent data. It allows for adjustments to reduce the nonresponse bias. For certain survey topics, the limitation of the data collection to donors who are willing and *able* to donate blood at a particular time could significantly bias the estimates, for example in the case of an epidemic. Therefore the ability to rapidly survey across an entire, well-defined population has great analytic value.

While the methodology is now in place to repeat this process, this infrastructure to conduct such sampling may be at risk of loss over time. For some BCOs, the ability to define the sample frame and draw a sample appeared to be very similar to computations or processes already performed on a regular basis. For others, this ability to quickly construct the sample frame did not fit naturally into their normal operations. In order for this ability to be retained, each BCO would need to retain the methodology to refresh their sample frame on a regular basis and to sample from this frame.

In addition to retaining the progress made to-date, the following limitations should be addressed in the future.

There were certain types of donors that were under-represented in both the sample frame and the survey responses. Future improvements should be considered for those characteristics of most importance. Specifically, the youngest blood donors were much less likely to respond to the survey and they were also under-represented in the sample frame. The low response rates could be addressed by the use of sample weights in estimation, and in the future, the sample design could over-sample the younger donors. However, further research should be done to improve representation of the sample frame and the respondents. The first avenue to consider would be the expansion of the protocol beyond email contact, described next, which could improve both the representation of the sample frame and the respondents.

The process was limited to email contact. Further testing would be needed to determine whether the process would work as well, or even better, if contact were made using other contact options such as texting. Specifically, determining the best contact vehicle for the younger blood donors may improve both the sample frame coverage and the response rates for this subpopulation of interest.

First-time donors also appeared to be less likely to respond to the survey and, further, they were less likely to be in the sample frame. In the future, the sample design can be adjusted to over-sample the first-time donors to ensure an adequate number of responses. The survey response rate may not be as low as it appears because there was a reasonably long time gap between the definition of the sample frame and the survey. Therefore the data are also reflecting donors who changed status over this time period. If the sample frame is too “old,” it will not accurately represent first-time donors at the time of the

survey. This problem could be reduced by ensuring that the entire process, including developing the sample frame, can be accomplished very quickly. In addition, when it is critical to collect information from first-time donors, alternative methods could be considered, such as the collection of survey information at a sample of donation sites, as an auxiliary source of data.

Finally, the need for speed removes the ability to follow-up on even a sample of non-respondents. A parallel process is needed to provide weights which make at least basic adjustments for nonresponse.

Acknowledgements

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Appendix. Data Tables and Additional Discussion

A.1. Response Rates

Each BCO provided the complete tabulation of the selected sample by the five characteristics of interest: age, gender, USPHS Geographic Region, donation type, and whether the donor is a repeat or first time donor. The demographic and donation information for the respondents comes from the survey responses. Therefore, the respondent data will not necessarily match the tabulation of the sample. For example an individual tabulated as being 21-25 years old in the sample may refuse to provide age on the survey. Similarly, respondents may provide information that was not available on the frame. There will also be a few people whose characteristics have changed since the original tabulation of data. These changes should occur for a small number of individuals, so that the effect on the calculation of the response rates should generally be minor.

However, for three of the five BCOs, the Hepatitis E sample frame information was almost one year old, making some of the information less accurate. For the BCOs using the sample frame developed from the 2014 data file, the sample under-represents the youngest donors in 2016, as it misses those donors who were 16 and 17 in 2014 but would now be eligible. The other characteristic most likely to change with time is that first-time donors could have become repeat donors by the time the survey was administered. Therefore the response rates for the Hepatitis E survey are more likely to under-estimate the response rate for first-time donors, and over-estimate the response rates for repeat donors.

The following tables exclude survey respondents with missing data.

Exhibit A.1. Response Rates by Age

Age in Years	Tick-Borne Disease Survey	Hepatitis E Survey
18-20	2.1%	1.6%
21-30	4.2%	2.8%
31-40	7.2%	5.0%
41-50	8.6%	6.9%
51-60	13.1%	11.8%
61-70	17.2%	15.4%
71+	17.1%	14.9%
Overall	8.8%	7.0%

Exhibit A.2. Response Rates by Gender, Donor Type and Donation Type

Demographic Characteristic	Tick-Borne Disease Survey	Hepatitis E Survey
First Time donor	0.9%	0.5%
Repeat donor	10.5%	9.0%
Whole Blood donor	8.6%	6.9%
Apheresis donor	10.1%	8.0%
Female	9.6%	7.2%
Male	8.0%	6.9%

The following tabulations are restricted to the data from repeat-donor responses to the survey on tick-borne disease. The sample contained over 100 donors in each cell, unless otherwise indicated.

Exhibit A.3. Response Rates for Repeat Donors by Age
Tick-Borne Disease Survey

Donor Age	Repeat-Donor Response Rate				
	Overall	Female		Male	
		Whole Blood	Apheresis	Whole Blood	Apheresis
18-30	4%	6%	9%	3%	3%
31-50	9%	10%	14%	8%	8%
51+	16%	16%	21%	15%	16%
Overall	10%	11%	16%	10%	10%

**Exhibit A.4. Response Rates for Repeat Donors
By Location, Gender and Donation Type
Tick-Borne Disease Survey**

USPHS Region	Female		Male	
	Whole Blood	Apheresis	Whole Blood	Apheresis
1-3	9.8%	13.9%	7.9%	9.9%
4	8.4%	13.3%	6.1%	4.6%
5	12.7%	18.4%	12.5%	13.7%
6-7	10.7%	17.0%	11.2%	9.6%
8	15.0%	15.6%	16.9%	10.9%
9	15.8%	15.7%	17.9%	10.6%
10	15.0%	*	10.7%	*
Over All	11.0%	15.7%	9.6%	9.7%

*Fewer than 30 donors in the sample

A.2 Response Time

In each survey, the BCOs fielded the survey at very different times but the survey was closed at the same time for all. Therefore some BCO respondents had as long as 6 weeks to respond while for others, the website was open for only 10 days. The respondent data indicate the date and time of the response. For measuring time to respond, the time should be measured from the time the email invitation was sent. For each BCO the start date is known but not the exact time. Therefore the response times were measured from the first response on the start date.

Three of the five BCOs sent out a second wave of invitations when it was determined that the goal of 1,000 responses was not being met. For these BCOs, the first respondents classified as being in Wave 2 were those with response time on the first day of Wave 2 and in a cluster of respondents. For example, if on the day of the second wave there was a response at 04:00 and subsequently there were no responses until 10:00 and there were many responses between 10:00 and 11:00, Wave 2 was defined as starting at 10:00 and the response at 04:00 hours was considered to be a Wave 1 response. All responses occurring after the beginning of Wave 2 were classified as Wave 2. There will be some individuals classified as Wave 2 who were in fact invited in Wave 1, but the data for the two BCOs with only one wave indicate that there should be relatively few such cases: 96-97% of the responses were received within 7 days of the invitation.

The tick-borne disease survey response analysis was based on 3,752 responses out of the 5,769 final responses. Unfortunately, the data on the time of the response was retained only on preliminary data extracted part way through the entire time period. The response data include essentially complete response information for three BCOs and for one of two replicates for a fourth BCO. No response time data were available for the fifth BCO.

**Exhibit A.5. Cumulative Distribution for Response, by Survey,
Data Restricted to Response within One Week**

Survey	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Tick-Borne Disease	79%	88%	92%	95%	97%	99%	100%
Hepatitis E	63%	86%	92%	96%	98%	99%	100%