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TRANSFUSION

Use of a rapid electronic survey methodology to estimate blood donors' potential exposure to emerging infectious diseases: Application of a statistically representative sampling methodology to assess risk in US blood centers

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Background
Risk assessments of transfusion-transmitted emerging infectious diseases (EIDs) are complicated by the fact that blood donors' demographics and behaviors can be different from the general population. Therefore, when assessing potential blood donor exposure to EIDs, the use of general population characteristics, such as U.S. travel statistics, may invoke uncertainties that result in inaccurate estimates of blood donor exposure. This may, in turn, lead to the creation of donor deferral policies that do not match actual risk.

Study Design and Methods: This article reports on the development of a system to rapidly assess EID risks for a nationally representative portion of the U.S. blood donor population. To assess the effectiveness of this system, a test survey was developed and deployed to a statistically representative sample frame of blood donors from five blood collecting organizations. Donors were directed to an online survey to ascertain their recent travel and potential exposure to Middle East respiratory syndrome coronavirus (MERS-CoV).

Results: A total of 7128 responses were received from 54 256 invitations. The age-adjusted estimated total number of blood donors potentially exposed to MERS-CoV was approximately 15 640 blood donors compared to a lower U.S. general population-based estimate of 9610 blood donors.

Conclusion: The structured donor demographic sample–based data provided an assessment of blood donors' potential exposure to an emerging pathogen that was 63% larger than the U.S. population–based estimate. This illustrates

Abbreviations: BCO, blood collecting organization; EID(s), emerging infectious disease(s); IRB(s), institutional review board(s); MERS-CoV, Middle East respiratory syndrome-coronavirus; OMB, Office of Management and Budget; UNWTO, United Nations World Tourism Organization; USPHS, U.S. Public Health Services.

the need for tailored blood donor–based EID risk assessments that provide more specific demographic risk intelligence and can inform appropriate regulatory decision making.

Ensuring the availability of a safe blood supply is a public health responsibility that the U.S. Food and Drug Administration (FDA) shares with other agencies of the Department of Health and Human Services and with blood collecting organizations (BCOs). FDA's ability to react quickly and appropriately with effective public health policy depends on rapid and accurate assessment of the risk of transfusion-transmitted diseases and the potential impact of any change on the availability of blood. It is known that individuals donating blood in the United States differ significantly from the general population[1–3] in their demographics, travel and immigration histories, and behaviors. Therefore, the application of general population estimates to the blood donor population introduces uncertainties that can be avoided by focusing risk assessment strategies specifically on blood donors. When there is a rapidly evolving threat, it is vital that potential exposures of donors to emerging infectious diseases (EIDs) can be quickly and accurately assessed. In collaboration with five BCOs, FDA sought to develop a system to rapidly survey recent blood donors using donor contact information maintained by BCOs and then to aggregate and apply the survey results to properly represent the sampling frame and the risk to the donor population.

Middle East respiratory syndrome-coronavirus (MERS-CoV),[4] an EID endemic to Saudi Arabia, Qatar, United Arab Emirates, and Jordan, has the potential to spread to the United States through blood donors who have recently traveled to these countries. Cases of imported MERS-CoV were reported in Europe,[5] in Asia,[6] and in the United States.[7] MERS-CoV causes a severe acute respiratory illness with symptoms of fever, cough, and shortness of breath.[8] It has a high mortality rate and its transmissibility by blood transfusion is unknown.[8]

To model the risk of transfusion-transmitted MERS-CoV, knowledge of the number of blood donor travelers to endemic areas was required. A survey of blood donor travel to endemic areas would reduce uncertainty and improve the accuracy of risk estimates used to inform potential disease-specific donor deferral policies. However, many surveys do not leverage the demographic information of the population being sampled. For example, donors have been surveyed to determine motivations for donating blood,[1,9–12] but these studies are frequently performed by surveying a recent series of donors; although donor demographics may be recorded, this demographic information is not correlated with the demographics of all donors nor is it used to inform stratified sampling schemes.

This article reports on the development of infrastructure to rapidly collect information related to risks to the blood donor population. The work included establishing a statistical method for appropriately sampling donor populations from five different BCOs, assessing how effectively BCOs could disseminate online survey links to sampled donors and obtain responses, and analyzing the selected samples and respondents to determine how representative they were of the donor population. To further assess the effectiveness of this system, the results from a test survey done to estimate potential exposures to an EID (MERS-CoV) are presented. Developing this statistically validated system for sampling blood donors is essential for the acquisition of data that can be used in decision making.

1 | MATERIALS AND METHODS

A working group consisting of representatives from five U.S. BCOs, the FDA, AABB, and NORC at the University of Chicago developed the general protocol and method for this rapid response survey (Figure 1).

A survey to assess blood donor risk of exposure to MERS-CoV was developed with the assistance of the AABB Transfusion Transmitted Diseases Committee, submitted to the FDA Office of Blood Research and Review for input and approved by the Office of Biostatistics and Epidemiology. Figures 2A,B shows the survey landing page and question logic. Approval for the questionnaire and general protocol was obtained from the Office of Management and Budget (OMB)[13] and subsequently from the institutional review boards (IRBs) of the BCOs, NORC, and FDA.

The population and sample frame were defined in terms of blood donors at the five BCOs. The population of *interest* was defined as all allogeneic donors at least 18 years old with at least one date of donation in the calendar year 2013. However, to obtain rapid response to a Web-based survey, the sample frame or the subpopulation of donors from which the survey sample was drawn and, therefore, the population of *inference* was restricted to those donors in the population who provided both a means of rapid contact, that is, email or cell phone access, and permission for such contact. The sample

frame in this case was the list of all blood donors who could be selected into the sample and asked to respond to the Web survey.

The team spent significant time defining and constructing the sample frame. Each BCO had the demographic information of geographic location, sex, and age for their blood donors. In addition, information was available on the type of donation (apheresis or whole blood) and whether the donor was a first-time or repeat donor. Age was a required variable as the survey was restricted to individuals 18 years of age or older for purposes of consent. The auxiliary variables were used to evaluate the properties of the sample frame compared to the population of all blood donors and to evaluate the

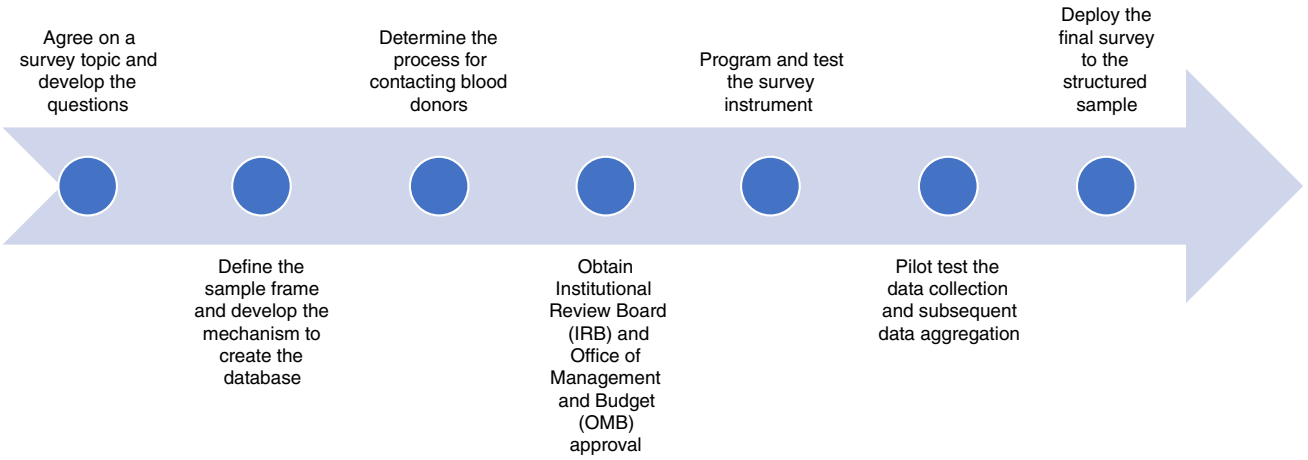

FIGURE 1 General study method [Color figure can be viewed at wileyonlinelibrary.com]

A

Welcome Screen and Consent Language

You have been selected at random from adults who donated blood in the past *[insert specific time period]*. The [Blood Center] thanks you for your past donation and invites you to participate in this short survey about your travel and health in the last month. The travel history of donors is important because of potential exposures to specific viruses, bacteria, and parasites that are not present in the US We are asking about your travel in order to characterize the travel history of blood donors in general and not specifically to characterize you. In fact, your responses will be anonymous, but will assist us and federal public health scientists in determining the potential US population exposure to a respiratory virus that has emerged over the past few years in the Middle East. No cases caused by this virus have been identified in the US[1] Your participation in this survey will help to assure a safe and adequate supply of blood for your neighbors and for you. Thank you, again, for being a blood donor—your donation has saved lives.

Participation is voluntary. Because you are one of a small number of people randomly chosen to participate, the survey cannot be accurate without you. The questions should only take about 5 minutes to complete. Your responses will be kept confidential and not disclosed to third parties. If you have any questions about the study, please call our toll free line at xxx-xxx-xxxx or send an email to xxxxx

FIGURE 2 A, MERS-CoV landing page. B, MERS-CoV donor questionnaire

B

[1] At the time of the survey, no imported cases of MERS-CoV had been reported; however, cases of imported MERS-CoV were reported on 2 May 2014 https://www.cdc.gov/media/releases/2014/p0502-US-MERS.html

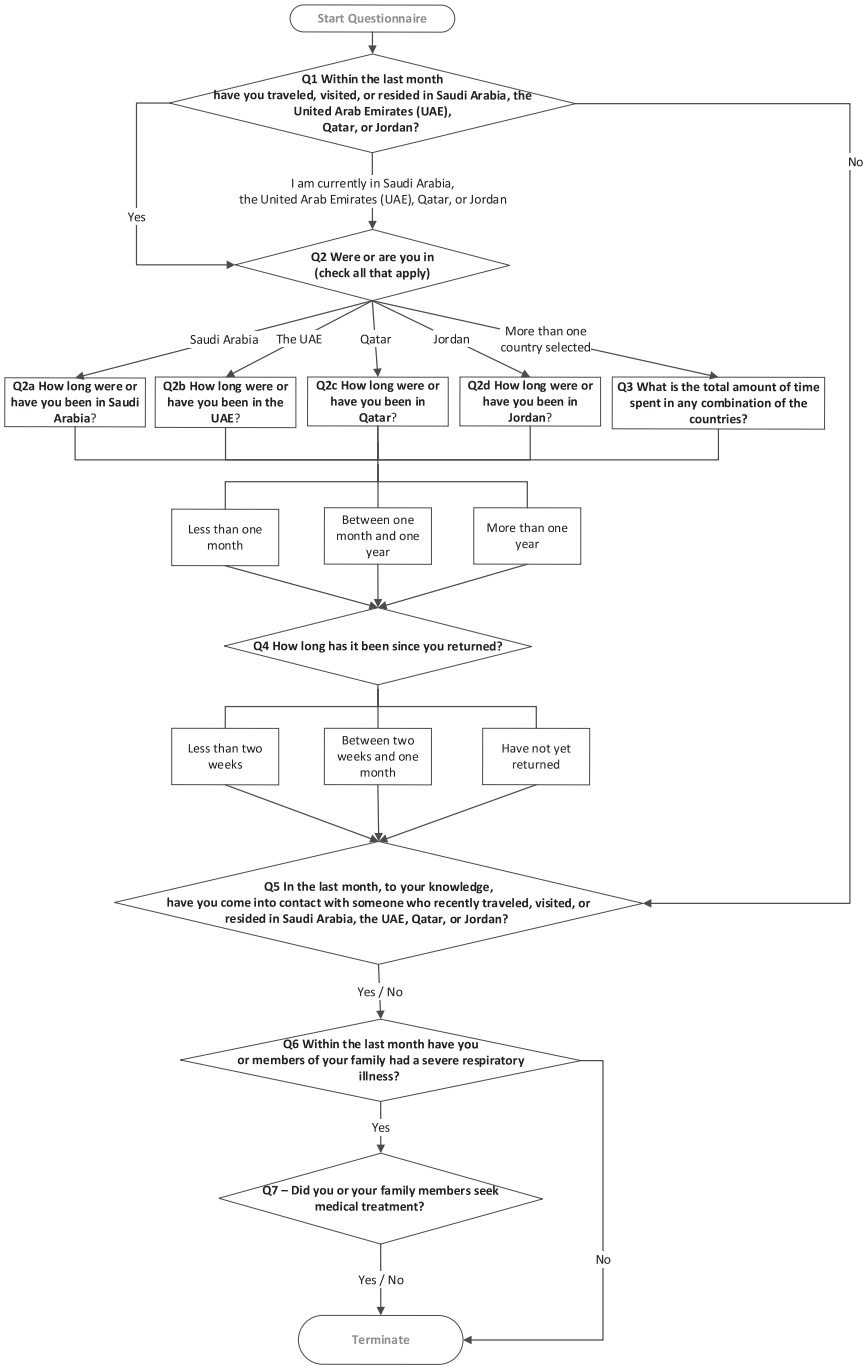

FIGURE 2 (Continued)

properties of the respondents compared to those of the sample frame.

The method for assembling the needed data items depended on the form and structure of the BCOs' databases. Each BCO worked independently to determine how the necessary data could be retrieved, formatted, and checked in a relatively quick time frame.

For four of the five BCOs, the sample frame was restricted to those donors in the population who provided an email contact. One BCO defined the sample frame as those individuals who provided an email address or allowed contact via a text message. One BCO inadvertently restricted their population to donors who had made more than one donation, that is, including only

repeat donors. This restriction may have increased this BCO's response rate but there was no evidence that the likelihood to travel was correlated with being a first-time vs repeat blood donor.

Each BCO independently developed and tested the Web-survey, based on the survey requirements (Figure 2). Data definitions and a uniform data format were developed. The survey was piloted to a small sample (596 responses) and each BCO collected responses and forwarded the deidentified data to NORC. Two critical issues were identified in the pilot. For one BCO the response could not always be linked to the donor's demographic information. This problem was corrected before fielding the full survey. The second issue was that some BCOs did not have the capacity to program the skip pattern so that the respondent did not see questions that were not applicable, resulting in a small percentage of the respondents providing inconsistent data. Some improvements to the questions were made to reduce the likelihood of such errors, but this problem occurred to some extent in the final survey.

Each BCO developed a random sample of donors selected from its sample frame to achieve the target of 1000 responses to the survey. This total of 5000 responses was intended to ensure adequate coverage of the demographic characteristics of the blood donor population. Donors were contacted, via email or text, and invited to respond to a Web survey. Each BCO ensured that a selected donor could respond only once to the survey and the respondent's demographic information was attached to the survey response. Because of the need for rapid response, there was little attempt to follow-up on nonrespondents to increase the response rate, although one BCO followed up with nonrespondents by email. Based on BCO and pilot experience, it was predicted that the response rate using this protocol could be as low as 10%. Therefore, BCOs sent Web survey invitations to an appropriately large sample of donors; 54 256 invitations were sent to valid email addresses or mobile devices.

Upon completion of the survey, anonymized data were provided to NORC. No personally identifying information was asked of the donors and potential identifiers (eg, age, location of residence) were suitably aggregated into classes or regions to minimize reidentification risk. The anonymized data were stored on a secure server at NORC and access was limited to the study team. Once the project was finalized, NORC deleted the individual data files received from each BCO. Donor risk was estimated based on the sampling method and survey results were compared with an estimate based on U.S. travel to the Middle East[14] to show the differences in uncertainty.

2 | RESULTS

2.1 | Response rates and patterns

A comparison of our blood donor population, the sample frame, and the respondents can be made by properties of sex, geographical location, and age. For example, females constituted 49% of the blood donor population, 50% of the sample frame, and 54% of the respondents.

Geographic results for the 10 U.S. Public Health Services (USPHS) regions are provided in Table 1. Comparing the sample frame to the population, USPHS regions 1 to 3 had the highest percentage of donors agreeing to be contacted by email (70%) and regions 6 and 7 had the smallest percentage (47%). Comparing the distribution between the respondents and the sample frame, the southwestern and western states, USPHS regions 6 and 7, 9, and 10, had relatively fewer respondents compared to the eastern and midwestern states (regions 1–5).

In general, the sample frame underrepresented the younger donors and overrepresented the older donors in the population (Figure 3). The youngest category displayed the greatest differences between population, sample frame, and response. This was partially caused by

TABLE 1 Distribution by geographic regions

USPHS regions[a]		Blood donor population	Sample frame	Respondents
1–3[a]	CT, DC, DE, MA, MD, ME, NH, NJ, NY, PA, RI, VA, VT, WV	14.6%	16.8%	17.3%
4	AL, FL, GA, KY, MS, NC, SC, TN	35.1%	33.7%	37.6%
5	IL, IN, MI, MN, OH, WI	22.1%	21.4%	23.6%
6 and 7[a]	AR, IA, KS, LA, MO, NE, NM, OK, TX	6.2%	4.7%	3.3%
8	CO, MT, ND, SD, UT, WY	5.5%	5.2%	4.7%
9	AZ, CA, HI, NV	13.2%	14.7%	10.9%
10	AK, ID, OR, WA	3.3%	3.5%	2.4%

[a]Some regions were combined to minimize the association of results with any specific BCO.

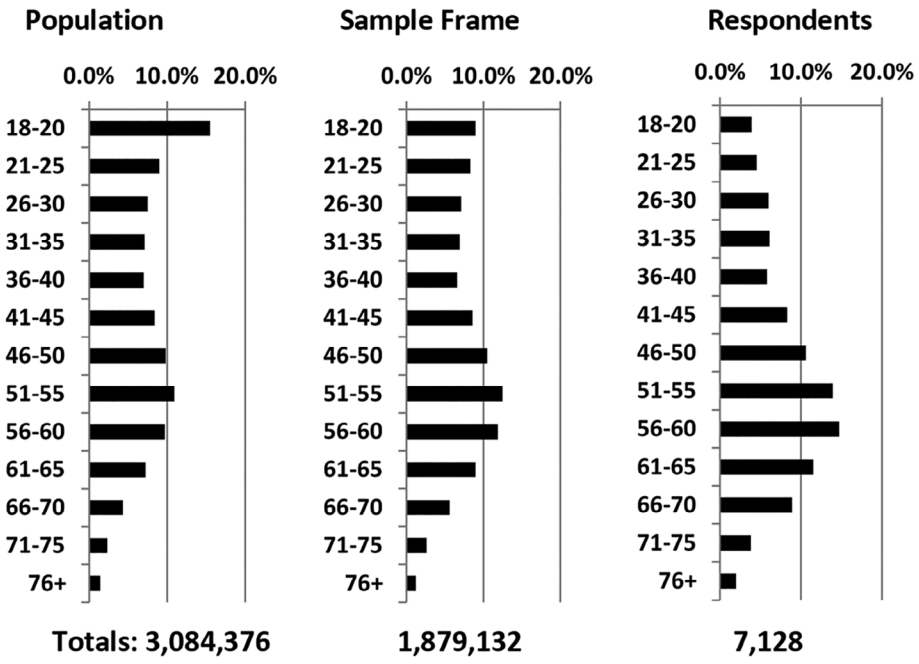

FIGURE 3 Distribution by age categories

some BCOs tabulating the youngest donor category as 16 to 20 years of age. The survey was later limited by OMB and IRB to adult donors (≥18 years old) for consent purposes. For these BCOs, the difference between the population and the sample frame included the elimination of 16- and 17-year-old donors. Nevertheless, when comparing the respondents to the sample frame, there was an even greater disparity in response by age. Ten percent of the donors in the sample frame were between 18 and 20 years of age, but only 4% of the respondents were in this age group. Fourteen percent of the respondents were 25 or younger compared to 28% in the sample frame, while 60% of the respondents were between 46 and 70 years of age, compared to the sample frame (46%).

Nineteen percent of the respondents were apheresis donors compared to 13% in the sample frame, and 11% in the population of all donors. Eight percent of the respondents were first-time donors compared to 13% in both the sample frame and the population.

TABLE 2 Countries visited by donors traveling to MERS-CoV–endemic areas

Question 2: Of these four countries, did you visit …?		
	Number of participants	
Response	Total	Responding (1) or (2) to Q1
Saudi Arabia only	1	0
UAE only	2	2
Qatar only	1	1
Jordan only	4	4
More than one	5	1
Missing	3	3
Did not travel to Middle East	7112	
Total	7128	11

2.2 | Survey results

Before discussing survey results, it is important to recall that the goal of this work is to examine means to quickly assess potential hazards to the blood supply. As such, the results are by necessity based on only those selected individuals who quickly respond to one survey request. Under the goals of the work, it is not feasible to send out reminders or perform other follow-up techniques to increase the response rates. The cost incurred is potential nonresponse bias in the results. However, we make simple adjustments to reduce and/or evaluate the potential nonresponse bias.

Starting with travel, Table 2 shows that relatively few (11/7128 or <1%) surveyed donors recently visited one or more of the countries in the Middle East where autochthonous MERS-CoV had been reported. Under the assumption that the 7128 respondents are representative of the 1.9 million donors, the proportion of donors who visited these countries was approximately 0.15% ± 0.09%; where the measure of uncertainty is calculated as twice the SE.

Despite the small percentage of travelers, the surveyresults indicate a possible relationship between age

and likelihood to travel (Figure 4). Stratifying and weighting by age, calculated using the age strata shown in Figure 3 and weighting by the stratum sample frame count divided bythe total number of survey responses in the stratum, results in an estimate of 4320 + 2938 of the 1,879,132 donors in the sample frame having traveled to these countries; or, as a proportion, 0.23% + 0.15%.

To further extrapolate the result with the assumption that the entire population of 6.8 million blood donors[15] are similar in their general properties across BCOs, yields an estimate that approximately 15,640 ± 10,200 (0.23% x 6.8 million) blood donors traveled to these countries. This estimate of error under-estimates the variability in the estimated number of donors who may have travelled to these countries, as it reflects only one source of variability. However, it does serve as a reminder that the estimate is based on a sample and it provides some sense of the potential variability.

For comparison, an alternate estimate of the number of donors impacted by travel to endemic areas is the approximate percentage of U.S. population that donates blood (3.3%) applied to the reported U.S. travel to Middle Eastern countries.[13] For 2014 (the year of our survey) the United Nations World Tourism Organization (UNWTO) reported 148 601 U.S. travelers from the United States to Saudi Arabia.[14] For Jordan, the number of U.S. travelers from the United States was 142 710; the number of 2014 U.S. travelers to the UAE and Qatar was not available. These data have been reported as outbound US travelers by the United States. Based on the 3.3% donor base of U.S. population, an estimate of the number of blood donors traveling in all of calendar 2014 to Saudi Arabia and Jordan alone would yield approximately 9610 donors as having traveled to these two, at the time, endemic MERS-CoV countries. This is notably less than the survey-based point estimate of 15 640 donors traveling within the past month.

The last three questions of the survey inquired about donor contacts with other travelers and respiratory illnesses. A larger number of donors reported contact with individuals who had traveled to the MERS-CoV–endemic areas (n = 134). Fewer respondents reported a severe respiratory illness for themselves or a family member (n = 94), with 79 respondents reporting having sought medical treatment. While none of these reported cases were related to the MERS-CoV outbreak, these response rates help establish an estimate of reported illness that can serve as a baseline for future surveys.

3 | DISCUSSION

This article describes the development of the tools and processes needed to rapidly survey blood donors. This included establishing a statistical method for sampling donor populations from five different BCOs; assessing how effectively BCOs could utilize electronic media to disseminate online survey links to sampled donors and get responses; and analyzing the results, the selected samples, and respondents to determine how representative they were of the donor population. To further assess the effectiveness of this system, we conducted a test survey to estimate potential exposures to an EID (MERS-CoV). We demonstrated that this goal can be achieved and identify here some areas for improvement.

While many blood centers survey their donors in the on-site postdonation environment, there is value and power to surveying blood donors using electronic media compared to paper-based or in-person methods. Although postdonation surveys can be convenient, paper-based or interview surveys can be costly, and the sample of donors may not represent the total population. Electronic surveys have disadvantages as well, and one surprising drawback that this survey showed was the reduced level of participation by one of the largest demographics of the blood donating population—the younger donor.

Even with such an outcome, the advantages to using the process of defining a sample frame and drawing a well-defined random sample compared to a convenience sample are substantial. The virtue of characterizing the sample frame and the respondents is that underrepresentation due to nonresponse can be identified and controlled initially through oversampling of the age cohort or, as here, addressed at the estimation stage by weighting the responses.

Rapid surveys have been used in other fields, including to ascertain immunization coverage[22] or attitudes,[23] however a convenience or random sample is most often applied. Stratified sample surveys have been employed using conventional platforms in other fields, including by email,[24] mail,[25] and in-person[26] or telephone interviews.[27] Novel survey approaches have also been explored, including the use of social networking sites[28] or WhatsApp,[29] but they are not uniformly stratified or rapid.

3.1 | Sample frame vs population of all blood donors

The goal of the rapid response survey is to quickly assess risk properties of blood donors to estimate potential hazards to the blood supply. While the response rate of 13% was a limitation, achieving a rapid response was our goal. There was no follow-up to the initial email survey request

and new donors were approached until the targeted number of responses was received.

Ideally, we would like to promptly receive responses from a random sample of all blood donors or of a targeted subpopulation of blood donors (eg, within a specific geographic region of known risk), but to achieve a speedy response, there must be a way to contact the donor quickly. Therefore, in this survey, the sample frame (the population of inference) was limited to those blood donors who have given permission to be contacted via email or text message. The assumption is that this restriction will not jeopardize the utility of the survey responses.

One of the advantages to a designed statistical sample is that an analysis of the properties of non-respondents can be made using auxiliary variables known for both the sample frame and the respondents. Estimates as used here, when correctly calculated based on a statistical sample with full response, are by design unbiased. When the response rate for a sample is low, one must be concerned about possible bias in the results if there is a correlation or connection between the likelihood of response and the variables being estimated by the sample (in this case, the likelihood of travel to specific areas). Christensen and colleagues[16] noted problems with low response rates in a national survey and the challenges to generalizing such data. Because we have auxiliary variables known for both the sample frame and the respondents, we can evaluate the potential for nonresponse bias, at least as measured by these auxiliary variables.

Generally, there were not significant differences in the demographics of those allowing email contact compared to all donors except for the fact that older donors were more likely to consent to email contact compared to younger donors (Figure 3). The results of the survey indicate a possible relationship between age and likelihood to travel (Figure 4), hence our age-weighted estimate. In future travel surveys, this information could be used to inform the sampling strategy.

It is not known why the response rate among young donors was comparatively low. This may reflect an attitude toward responding to surveys, the use of email in this population, the perceived usefulness of the survey, commitment to the act of blood donation, or some other factor(s) influencing survey response.

3.2 | Process

The team effort to develop the infrastructure needed to perform this survey resulted in a set of tools and skills that can be used for future rapid surveys of blood donors. The Web surveys were created and administered independently by each BCO and not all surveys were programmed to ensure adherence to the skip pattern. Therefore, the responses were not entirely consistent between questions and BCOs. For example, in Table 2, ideally only the 11 respondents answering "yes" to question 1 could have responded to the subsequent questions about which countries were visited. However, a total of 16 individuals indicated travel to these countries in questions 2 through 4. Such inconsistencies introduce additional uncertainty or error in the estimates. If these individuals did in fact travel to these countries, then the simple, unweighted, survey estimate would be 16 of 7128 or 0.22%, compared to 0.15% based on question 1.

Missing data items, while not impacting the overall results of the survey, were also a problem for specific

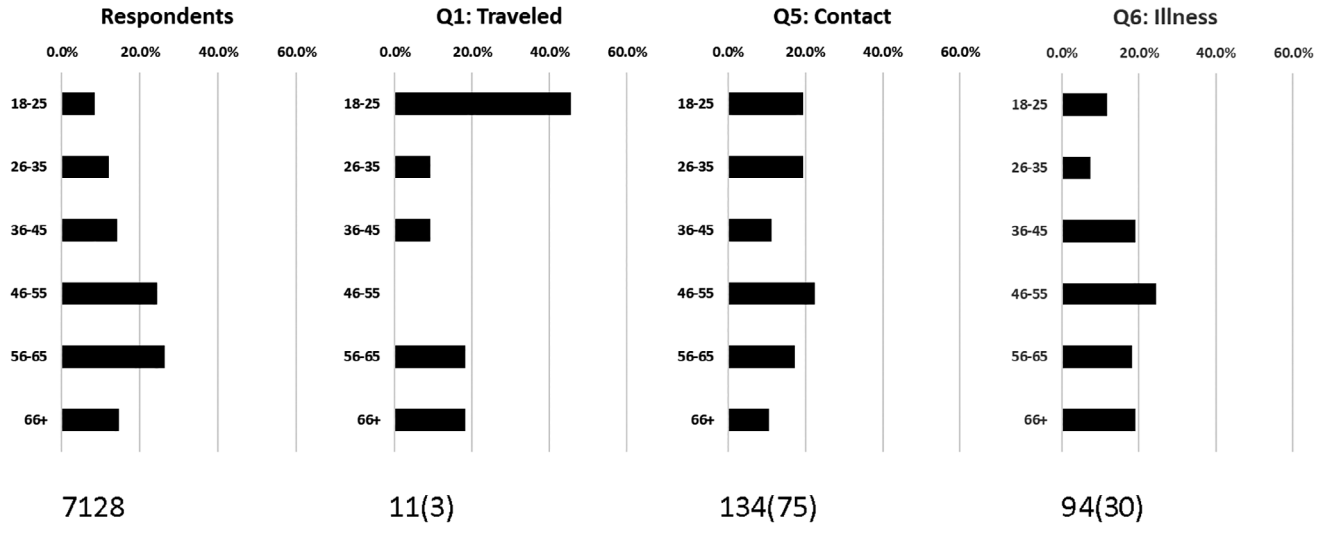

FIGURE 4 Age distribution of respondents to questions 1, 5, and 6. The number of missing responses is in parentheses

TABLE 3 Time spent abroad and time since return

Questions 2–4 for n = 11 participants responding (1) or (2) to Q1								
		Time spent abroad (Q2a &Q3)				Returned (Q4)		
Country	Participants indicating "yes" (Q1)	Less than 1 mo	Between 1 mo and 1 y	More than 1 y	Missing	Between 2 wk and 1 mo	Have not yet returned	Missing
UAE	2	2	0	0	0	2	0	0
Qatar	1	0	0	0	1	1	0	0
Jordan	4	2	1	0	1	2	1	1
Multiple	1	1	0	0	0	0	0	1
Missing	3	0	0	0	3	0	0	3

results. While the low number of respondents who had traveled to this area reduced the applicability of results for the length of time spent in the MERS-CoV–endemic countries (Table 3), the missing data associated with the responses to these questions further reduced its value. Of the 11 surveyed donors who reported travel to the MERS-CoV area, five said that their total time was less than 1 month, one said between 1 month and 1 year, and five were missing values. Question 4 asked how long it had been since they returned and five reported between 2 weeks and 1 month, one had not yet returned, and five responses were missing. The logic of the survey was designed to prevent moving on to the next screen in the absence of a response. In these few cases, this did not happen. More careful testing of the survey software and directing donors to a single survey instrument should reduce the incidence of missing data.

The small number of respondents having traveled to affected regions (n = 11) diminishes our ability to draw meaningful conclusions regarding the age distributions (Figure 4), countries of travel (Table 2), and time spent abroad and since return (Table 3). Nevertheless, of the six respondents who provided data, 80% (5/6) had recently traveled (within 14–31 days) to the area and one respondent was still in the country of interest. In addition, five of six for whom there were data spent less than 1 month abroad. The presence of missing data (from 5/11 reporting travel) further diminishes the ability to draw generalizable conclusions.

The time of year when a survey is performed can have an impact on the number of self-reported cases of severe respiratory illness. This survey was conducted during 2013 to 2014 influenza season, which may have increased the number of self-reported cases. The Centers for Disease Control and Prevention records[17] show a peak occurring at the beginning of 2014 with approximately 4.4% of visits for influenza-like illness in the United States with a somewhat linear decline to 2% (national baseline) over the next 10 weeks.[18] An estimate of the expected number of severe respiratory illness cases could be generated for comparison with the results if many assumptions were made.

3.3 | Comparison of survey estimate to an alternative

As described earlier, our age-stratified survey estimate that 15 640 blood donors traveled to the region in the month before the survey was 39% higher than predicted from the UNWTO report for calendar 2014 travel to just two of the MERS-CoV–endemic countries, suggesting that blood donor travel to these areas is much higher than that of the general population. Reasons for this difference may include that these two estimates do not consider the same population variables: the survey method estimates the number of recent travelers to any of the four countries, and the indirect method estimates the number of travelers over the entire year, but to only two of the four countries. While the UNWTO dataset may be of inconsistent reliability due to uneven reporting by countries, standardized definitions are used and the specific comparator travel data were provided by the US and as such, give an approximation of the US population's travel patterns.

There is also evidence that blood donors are healthier and more prosocial than non–blood donors[2,3,19,20] and these differences may lead to different, more frequent travel behavior.

Whereas the UNWTO travel surrogate is convenient, it provides no information about important exposure variables such as duration of stay in the endemic area. This survey allowed us to assess this information at another level of granularity, that is, less than 1 month, between 1 month and 1 year, and more than 1 year. The uncertainty with respect to travel to endemic areas was not

eliminated, but compared to the alternative means of estimating donor travel, this method provides increased assurance of accurate estimates.

In summary, this survey approach differs fundamentally from other reported studies[21] in two specific ways: (a) it establishes a methodology for BCOs to sample their donor populations in a statistically valid manner and (b) the data acquired can be used to help determine donor risk evaluation policies by both the BCOs and federal partners. The process to field the survey was long and difficult as many steps were required for agreement between AABB's Transfusion Transmitted Diseases Committee and FDA on the questions for the survey, for the merging of recruitment and donor record databases, for the development of the sample frames at each BCO, for the federal OMB approval, and for approval from the many individual IRBs. Even then there were operational challenges in implementing the survey. One of the key lessons learned was that centralizing the survey programming to a single source would preclude some of the individual BCO variations experienced when fielding the survey. It is also important that the survey process be repeated on a regular basis such that subprocesses be kept current, including generating sample frames and samples. An added benefit demonstrated by use of electronic surveys is the unusual circumstance that one of the donors surveyed was reached while still in the MERS-CoV region; a testament to the reach of the digital infrastructure.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest relevant to the manuscript submitted to TRANSFUSION.

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