Uncovering Treatment Disparities in Chronic Granulomatous Disease

Investigator
Morna Dorsey, MD, MMSc
Professor of Clinical Pediatrics, Step 1 Pediatrics
School of Medicine
550 16th Street
4th Floor
University of California, San Francisco
San Francisco, CA 94158

Co-Investigator
Christopher Scalchunes, MPA
Vice President of Research
Immune Deficiency Foundation (IDF)
Towson, MD 21204
443.632.2551
cscalchunes@primaryimmune.org

Co-Investigator/Study Coordinator
Tiffany Henderson, Ph.D.
Assistant Director of Survey Research
Immune Deficiency Foundation (IDF)
Towson, MD 21204
443-218-6412
thenderson@primaryimmune.org

Sponsors
Horizon Pharma
150 South Saunders
Lake Forest, IL 60045

Limitations exist in understanding real life practices surrounding medication use in patients with chronic granulomatous disease (CGD). Importantly, patients may not be receiving standard of care medications due to a variety of unknown factors and could highlight the need to educate physicians and families. The longevity and quality of life of patients with CGD has improved in large part due to the use of prophylactic medications such as trimethoprim-sulfamethoxazole,
itraconazole, and interferon gamma; bone marrow transplantation has greatly improved the longevity and quality of life as well. A recent analysis of results from the USIDNET database reveal surprisingly low rates of standard of care medication use in CGD. The goal of this study is to accurately identify rates of life-saving medication use, investigate impact on quality of life, and uncover barriers to use of these medications.

Although there is clinical data on over 380 patients with CGD in the USIDNET Registry, only 177 of those records were entered after the Registry required patient-consent for participation. Therefore, only those 177 patients are eligible to have their records updated on an ongoing basis, which is critical in assessing patient outcomes over time.

Additionally, much of the existing CGD data comes from a limited number of enrolling centers and may be skewed based on geographic and individual clinician biases. With the advent of IDF’s PI CONNECT program, patients are able to consent to participate in the USIDNET Registry online through the IDF ePHR, which allows the Registry’s reach to extend past the traditional enrolling centers. An added benefit of PI CONNECT is that the patients themselves can enter their own patient reported outcomes (PRO’s) that can be matched to their validated clinical data and used for research.

**Objective**

- Create a CGD specific web-based survey with a questionnaire created as a collaborative effort between: Horizon, IDF, USIDNET, PIDTC, clinicians, and patients to investigate quality of life and current medication practices of CGD patients.
- Analyze the survey data with goal of publishing a manuscript based on the survey data in a peer reviewed journal.

**Population and Sample Size**

The Immune Deficiency Foundation Patient Database will form the basis for sample selection for this study. Only persons who have attained the legal age for consent under the applicable laws of their jurisdiction are targeted as potential respondents.

- U.S. Residents
- Adult patient with PI (at least 18 years of age, at least 19 years of age in Alabama and Nebraska)
- Parent of a child with PI under the age of 18
- Valid e-mail address

Those under the legal age of consent for their particular jurisdiction will be screened out of the survey on the “Survey “Introduction Screen & Consent” page. This is the very first survey page potential respondents will view.

This survey’s potential respondent pool is about individuals. Given response rates for previous IDF surveys, it is possible 150 individuals could participate in the survey. Although this procedure will not result in a probability sample, even the minimum expected number of completed surveys would be adequate to provide good sampling precision for estimates of the target population.
In general, most researchers expect a maximum sampling error no greater than ± 5 percentage points at the 95% confidence interval for surveys reported in peer-reviewed journals. This level of sampling precision means that if the sample estimate is 50% (e.g., 50% of doctors prescribe medication X), then the true population value will fall between 45% and 55%, as demonstrated in 95 out of 100 repeated samples. We expect a minimum of 100 surveys that would give us and expected sampling error of +/- 9.8%.

Incentives

The majority of IDF surveys (i.e., online web-based surveys, mail surveys) are not incentivized. As a non-profit organization, IDF does not have the means to provide monetary compensation to our participants who complete our surveys. However, due to the length of the CGD Survey and in an effort to boost response rates, IDF will offer the opportunity for all participants who complete the CGD Survey to enter a raffle to win an Amazon.com eGift Card. IDF will purchase one $25.00 Amazon.com eGift Card, one $50.00 Amazon.com eGift Card and one $100.00 Amazon.com eGift Card. One household will be selected for each eGift Card. The random drawing for the eGift Cards will occur in November 2019. All participants will be made aware that they will not be eligible for the drawing if their survey is not completed by November 8, 2019.

Design of the Survey

The survey will contain, depending on a respondent’s answers, up to 185 individual questions. The questions are based on the respondent’s experiences and beliefs and will not involve or ask for any human subjects specific data. Question types for this project:

- Bivariate
- Multiple choice
- Multiple selection
- Scaled
- Open end text
- Open end numeric

Study Procedures

The survey will be performed electronically utilizing the Survey Monkey Software Platform. Security features of this software include enhanced SSL security and HIPAA compliant features.

Survey responses will be collected over secured, encrypted SSL/TLS connections. All other communications with the Survey Monkey website are sent over SSL/TLS connections. Secure Sockets Layer (SSL) and Transport Layer Security (TLS) technology to protect communications by using both server authentication and data encryption. This ensures that user data in transit is safe, secure, and available only to intended recipients.

User data is logically segregated by account-based access rules. User accounts have unique usernames and passwords that must be entered each time a user logs on. SurveyMonkey issues a session cookie only to record encrypted authentication information for the duration of a specific session. The session cookie does not include the password of the user.
SSL will be used to secure the transmission of survey data for analysis for this project. The survey data will be contained in a secured Immune Deficiency Foundation computer, accessible only by username and password.

IDF will send out an initial request to participate to all of the e-mails as described in the Population section of this document. Each e-mail address will be assigned its own unique survey URL. This unique URL serves two functions:

1. It will eliminate duplicate records, preserving data integrity
2. It will give IDF the ability to send a reminder e-mail only to non-respondents from the first e-mail.

The unique URLs are only linked offline to actual e-mail addresses that contain no other participant information. Two email reminders will be sent to non-respondents. After the second and third e-mail requests are sent to non-respondents, both lists will be permanently deleted. No more than three requests to participate in the survey will be sent to potential respondents.

- No personal identifying information will be collected in the survey.
- Once the project is complete the collected data will be permanently deleted from the Survey Monkey servers.

Statistical Analysis and Data Management

De-identified survey data will be analyzed utilizing the IBM SPSS 23.0 Statistical Software package. Descriptive statistics will be used to examine the distribution of key outcomes and predictor variables. Means and standard deviations will be computed for continuous variables and percentages for categorical variables. These data will be used to describe the study participants, address the descriptive research questions and inform further statistical analysis. All data will be stored indefinitely on a secured, encrypted IDF server.

Informed Consent

This survey, designed by Dr. Morna Dorsey from the University of California San Francisco and the Immune Deficiency Foundation (IDF), will focus on the experiences of those impacted by Chronic Granulomatous Disease (CGD). Funding for this project was provided by a scientific grant from Horizon Pharma.

The ultimate goal of the project is to better understand what it means to be an individual with CGD in the United States. The results from this survey will be used to create a manuscript for publication in a peer-reviewed journal. It will also be used to help educate physicians and researchers.

The entire survey should, depending on your answers, take approximately 35 minutes to complete.
It is possible that data obtained from this survey might be shared with other researchers or organizations conducting primary immunodeficiency research. In the event that this occurs, all personally identifying information will be removed in accordance with HIPAA regulations.

We do our best to keep your information confidential. Survey data is obtained and transmitted through a secure and encrypted process. All of your answers are grouped with all of the other answers, with none of your personal identifying information reported or used in the reporting. The sponsor, the Department of Health and Human Services, and Advarra’s institutional review board (IRB) may have access to the study data.

You may refuse to answer questions or discontinue the survey at any time. Deciding not to participate or choosing to leave the study will not result in any penalty or loss of benefits, not related to this survey, to which you are entitled from IDF or the CGD Foundation and it will not harm your relationship with IDF or the CGD Association. However, only surveys completed by November 8, 2019 will be entered into the lottery to receive either a $25, $50 or $100 Amazon.com eGift Card. Additionally, winning participants will be emailed within two weeks after the survey closes.

There is no cost to you. Also, there may be no benefit to you. But we hope your participation will help people in the future.

If you have any questions or concerns about this research, or your rights as a survey participant, please contact Christopher Scalchunes, Vice President of Research at IDF. He can be reached at: 1.800.296.4433.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Advisor
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046

- or call toll free:  877-992-4724
- or by email:      adviser@advarra.com
Please reference the following number when contacting the Study Subject Adviser: Pro00036845.

CONSENT: Please select your choice below.

Clicking on the "agree" button below indicates that:
• you have read the above information
• you currently live in the United States or in a U.S. territory
• you voluntarily agree to participate
• you are at least 18 years of age (you must be at least 19 years of age if you live in
  Alabama or Nebraska)

If you do not wish to participate in this survey, please decline participation by clicking on the "Disagree" button.

Agree        continue to INSTRUCTIONS 1
Disagree     SKIP TO END

FDA Regulation
This survey is not subject to FDA regulation and the results will not be submitted to the FDA.

Risk/Safety Information
There is no more than minimal risk associated with completing this study.

Monitoring/Reporting of AE/SAE
Though this study presents no more than minimal risk, any adverse events and serious adverse
events will be handled by Tiffany Henderson, Assistant Director of Survey Research at IDF.

Date of Study
We anticipate having the survey instrument out in the field by the third week of September 2019. 
Data collection would be closed by the beginning of November 2019.

Dissemination of Findings
A manuscript will be created to be submitted to relevant peer reviewed journals. We anticipate 
completion and submission of the manuscript by November 2020 It is also likely that an
Executive Summary based on survey findings will be created and completed by the end of April 2020. The results from the survey may be shared with various policy makers and insurance
organizations at any point in time after data collection is completed.