Assessing Problem Areas in Referrals for Chronic Hematologic Malignancies and Developing Interventions to Address Them

Supporting Statement

Part B

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B. Collections of Information Employing Statistical Methods

This application contains a survey which requires statistical methods to select respondents and interviews and focus groups which do not. All three are presented below.

B1. Respondent Universe and Sampling Methods

Primary Care Provider (PCP) Survey

The cross-sectional sample for the survey will be drawn from the American Medical Association master file. A machine-readable file will be produced using eligibility specifications and used to generate mailing labels and to maintain control of data collection processes. To be eligible, a respondent must be a physician (DO or MD) in Massachusetts focusing on primary care specialty (general practice, family practice, internal medicine, pediatrics, or obstetrics/gynecology), and report at least 75% clinical effort. The sample size (250 mailed surveys, with an estimated response rate of 60%, for 150 completed) was selected to provide adequate precision on the proportion estimates for select response items, as well as providing adequate precision to generalize overall respondent referral behavior results to the population of primary care providers in Massachusetts. From the AMA master list of 8,400 PCPs in Massachusetts, 3000 names will be ordered. A random sample of 250 names will be taken to obtain at least 150 names (estimated response rate of 60%).

The resulting 150 completed surveys will provide adequate precision on the proportion estimates for select response items, as well as providing adequate precision to generalize overall results to the population of primary care providers in Massachusetts. In calculating the sample size, we have assumed that response would be dichotomized (i.e., referral vs. non-referral) for analysis purposes, although depending on response rates we may be able to use more than dichotomized responses. With 150 respondents, exact two sided 95% confidence intervals around the proportion of respondents who would refer patients under a set of circumstances would be no wider than ±8%. With 75 respondents (the number of respondents receiving each version of the vignettes), exact two-sided 95% confidence intervals on the same binomial variables would be no greater than ±11.3%. Additionally, given a total sample size of 150 primary care providers (PCPs), a two-sided Fisher's exact test will have at least 80% power to detect any given 30%

difference in the proportion of primary care physicians likely to refer patients depending on the specific vignette when alpha is 0.05.

Patient Interviews

A data analyst in the MD Anderson Cancer Center (MDACC) Office of Physician Relations will create a master file using MDACC data warehouse. This database is administrative only with no data from patient records, thus positioning the interviewer as an appropriate individual to call the patient. From 461,817 records in the database warehouse, patients meeting the following criteria will be identified for the master file:

- Over 18 years of age.
- Diagnosis of chronic lymphocyte leukemia (CLL), chronic myelogenous leukemia (CML), multiple myeloma (MM), or myelodysplastic syndrome (MDS).
- At least 6-9 months from first visit at MDACC.
- Either with or without previous treatment prior to arriving at MDACC.
- Have had the first MD Anderson appointment within six-nine months.

From this master file of an estimated 112 patients, patients will be entered into a tracking sheet and given a unique ID number. They will be randomly ordered and called in order until 18 interviews are completed. Data from this qualitative component of the study will not be used to generalize results to the respondent population. It will be used in the development of an intervention protocol following the Intervention mapping techniques.[10] No statistical methods were used to determine representativeness of sample or sample size for these qualitative activities.

Interviews with PCPs and Community Oncologists/Hematologists

A data analyst in the MDACC Office of Physician Relations will use the Involved Provider Database with an estimated 54,309 records to create a master file of providers meeting the following criteria:

- Primary care physician, community oncologists, and community hematologists.
- Referred a hematologic cancer patient with a diagnosis of chronic lymphocyte leukemia (CLL), chronic myelogenous leukemia (CML), myelodysplastic syndrome (MDS),

multiple myeloma (MM) and certain indolent types of non-Hodgkin's lymphoma (NHL) within the last year.

- Practice in Harris County or surrounding counties or rural areas.
- Have referred a patient to MDACC within two (2) years.

From this master file, 150 eligible physicians will be entered into a tracking sheet and given a unique ID number. They will be randomly ordered and called until nine (9) primary care physicians and 18 community oncologists/hematologists have been interviewed. Data from this qualitative component of the study will not be used to generalize results to the respondent population. It will be used in the development of an intervention protocol following the Intervention mapping techniques.[10] No statistical methods were used to determine representativeness of sample or sample size for these qualitative activities.

Primary Care Provider (PCP) Focus Groups

Focus groups are used for obtaining general background information about a topic of interest or generating research hypotheses that can be submitted to testing using more quantitative approaches. MDACC will be the primary institution responsible for recruiting primary care providers for the three focus groups of up to six participants each. After IRB and OMB approval, the MDACC data analyst in the Office of Physician Relations will use an extension of the list generated for the provider interviews with the restriction to primary care physicians only.

Once a list of the primary care providers meeting these criteria has been established as described previously, a sample of these providers will be chosen randomly by the analyst and entered into a tracking spreadsheet with a unique study ID number. This spreadsheet will be used by the focus group moderator while calling to inquire about participation in a focus group and to track contact with each physician. Two focus groups totaling 12 PCPs in addition to a pilot group to test the moderator guide will total three focus groups, which is the minimum required for saturation of ideas.[11] Data from this qualitative component of the study will not be used to generalize results to the respondent population. It will be used in the development of an intervention protocol following the Intervention mapping techniques.[10] No statistical methods were used to determine representativeness of sample or sample size for these qualitative activities.

B2. Procedures for the Collection of Information

The procedures for data collection for the survey, interviews and focus groups are described below.

Primary Care Provider (PCP) Survey

We propose a cross-sectional "postal" (mailed) survey. A cover letter (Attachment 7) describing the study and the questionnaire (Attachment 8) will be sent by Federal Express to the PCP's address. The cover letter will offer response options including returning the completed questionnaire by mail, completing the questionnaire via a secure web survey form, or completing via telephone interview. The packet will contain a pre-addressed, pre-stamped envelope for returning the study questionnaire. The packet will also contain a pre-paid, pre-addressed opt-out card (Attachment 9) that the subject can return if s/he does not wish to be contacted further about the study. Respondents will be informed that if they respond they will be offered $100 for their time. See Attachments 7-10 for the survey and supplemental materials.

DFCI will be responsible for designing and administering the system to generate questionnaires and to facilitate collection of data via a secure web survey option using the Illume Survey design and management system. Upon receiving the questionnaire, study staff will enter the responses into a password-protected Microsoft Access or MySQL database designed for this study using the coded identifier. As our questionnaire does not use standardized scales, no formal imputation procedures will be employed.

Prior to analysis, the computerized data will be cleaned by cross-referencing to the paper questionnaires. Missing data will be minimized through rigorous pilot testing to clarify questions on the survey. If missing data becomes a serious issue for certain survey items, an extra variable may be included in the analysis of those individual questions for "missing," and added as a covariate in any resulting regression models.

Reports will include 1) descriptive statistics (with confidence intervals) for our survey questions regarding the proportion of PCP's likely to suspect and/or refer when presented with different signs and symptoms as detailed in our survey, 2) how provider and/or patient characteristics

seem to affect these proportions, and 3) descriptive statistics (with confidence intervals) for the proportion of providers reporting different systematic referral practices and specific preferences, such as for the flow of information from PCP to specialist and back. Finally, logistic regression models and ordinal logistic regression models will be attempted to assess PCP and hypothetical patient covariates of referral using the case vignettes.

Patient Interviews

The interviewer will be a MDACC research staff member who will use the list generated from the administrative database to contact the patients by phone to invite them to participate in the study. At this time, the interviewers will give an overview of the project, invite them to discuss their potential participation in an interview, and if the patient is willing, tell what would be expected of him or her should he or she choose to participate in the interview.

If the patient agrees to participate in the interview, s/he will be given the option of having (1) a telephone interview during the initial contact or (2) a telephone interview at an agreed scheduled day and time. Official informed consent will be obtained when the patient and interviewer meet – via phone or in person – on the scheduled day and time, prior to beginning the interview. If the interview is done over the telephone, verbal consent will be obtained prior to beginning the interview. See Attachment 6 for the interview guide.

MDACC will audio record, de-identify, and transcribe tapes of interviews, and provide them to UTH for analysis. A set of appropriate codes will be developed for use in the qualitative analysis of the data. Qualitative analysis will be conducted using Atlas.ti. These data will complement the survey data in providing meaning to quantitative responses. Using the Intervention Mapping protocol,[10] these data will collectively determine the substance of an intervention prototype to increase timeliness of referral for hematologic cancers.

In-depth Interviews with PCPs and Community Hematologists/Oncologists

The interviewer will be a MDACC research staff member. This interviewer will use the list generated by the data analyst to contact the physicians by phone to invite them to participate in the study. At this time, the interviewers will give an overview of the project - including the

purpose and goal - and invite them to discuss their potential participation in an in-depth interview, including what would be expected of them if they choose to participate.

If the physician agrees to participate in the in-depth interview, they will be given the option of having (1) a telephone interview during the initial contact or (2) a telephone interview at an agreed scheduled day and time. Official informed consent will be obtained when the physician and interviewer meet – via phone or in person – on the scheduled day and time, prior to beginning the interview. If the interview is done over the telephone, verbal consent will be obtained prior to beginning the interview (see Attachments 4 and 12).

The in-depth interviews will be audio recorded and the tapes transcribed. The UTHSC Research staff will analyze this data, once the transcripts have been de-identified and provided by MDACC. A set of appropriate codes will be developed for use in the qualitative analysis of the data. Qualitative analysis will be conducted using Atlas.ti. No personal identifiers will be included in transcripts, and only the research team will have access to the transcripts. Tapes and transcripts will be kept in a locked file, only accessible by the Principal Investigator and Project Director. Tapes will be destroyed after they are transcribed; transcribed data destroyed one year after pubication. These data will complement the survey data in providing responses to aims one and two. Using the Intervention Mapping protocol, these data will collectively determine the substance of an intervention prototype to increase timeliness of referral for hematologic cancers.

<u>Primary Care Provider (PCP) Focus Groups</u>

The focus group moderator will be a MDACC research staff member. This moderator will use the generated list to contact the physicians by phone. At this time, potential participants will receive an overview of the project - including the purpose and goal - and an invitation to participate in a focus group with other primary care providers, including what would be expected of them if they choose to participate (Attachment 13). See Attachment 14 for the PCP focus group guide.

If the physician agrees to participate in the focus group, they will be given the option of several previously established days and times of focus groups to attend. Official informed consent will

be obtained when the physicians and moderator meet on the scheduled day and time, prior to beginning the focus group.

The focus groups will be audio recorded and the tapes transcribed. The UTHSC Research staff will analyze this data, once the transcripts have been de-identified and provided by MDACC. A set of appropriate codes will be developed for use in the qualitative analysis of the data. Qualitative analysis will be conducted using Atlas.ti. No personal identifiers will be included in transcripts, and only the research team will have access to the transcripts. Tapes and transcripts will be kept in a locked file, only accessible by the Principal Investigator and Project Director. Tapes will be destroyed after they are transcribed. These data will complement the survey data in providing responses to aims one and two. Using the Intervention Mapping protocol, these data will collectively determine the substance of an intervention prototype to increase timeliness of referral for hematologic cancers.

B3. Methods to Maximize Response Rates and Deal with Nonresponse

Primary Care Provider (PCP) Survey

Two weeks after the first mailing, we will send a follow-up postcard to all sampled PCPs (Attachment 9). If neither the study questionnaire nor the opt-out postcard has been returned by 14 days after the postcard reminder, we will send a second copy of the study questionnaire by Federal Express to the PCP, along with a reminder letter (Attachment 10). After an additional 14 days (six weeks since the original mailing), we will telephone non-respondents to verify receipt of the questionnaire and to try to obtain a response, either via telephone or via a web response. If we are unable to reach the PCP after three attempts at a phone call, we will leave a brief message asking them to call, but if we receive no response, we will consider this an "opt out." If requested by the PCP at any point in the process, we will mail a third copy of the questionnaire. Providers will be offered an incentive of $100 for completing the survey.

Patient In-depth Interviews

Six attempts will be made to contact each patient on the generated list: 2 daytime contacts, 2 evening contacts and 2 weekend contacts. Recruitment will continue until the desired number of respondents is attained. Patients will be offered a $30 incentive for participation.

In-depth Interviews with PCPs and Community Oncologists/Hematologists

Six attempts will be made to contact each potential respondent on the generated list: 2 daytime contacts, 2 evening contacts and 2 weekend contacts. Recruitment will continue until the desired number of respondents is attained. Providers will be offered a $50 incentive for participation.

Primary Care Provider (PCP) Focus Groups

Six attempts will be made to contact each PCP on the generated list: 2 daytime contacts, 2 evening contacts and 2 weekend contacts. Recruitment will continue until the desired number of respondents is attained. A light meal will be offered as incentive to participate.

B4. Tests of Procedures or Methods to be Undertaken

Primary Care Provider (PCP) Survey

A draft of the 34-item survey was developed jointly by the investigators using input from key informant interviews with three primary care providers (two community-based and one "academic") and two oncologists (one community-based and one "academic"). The survey requests that PCPs report their knowledge and preferences regarding management of patients with potential chronic hematological malignancies and also for personal and practice characteristics required for hypothesis testing. As there have been no prior surveys of hematological malignancy diagnosis practices aimed at primary care physicians, original individual items were constructed. The instrument includes two case vignettes, each of which has two versions. Vignettes were designed to vary sociodemographic covariates of the vignette "patients," namely race-ethnicity (vignette 1) and age (vignette 2). All PCP subjects will receive both vignettes that will be identical except for a change in one of those two parameters; each PCP will be randomized as to which version of each vignette he or she receives. The intent is to determine if altering the age or race-ethnicity description of a hypothetical patient affects PCP's likelihood to refer that patient to a specialist and/or diagnose a hematological malignancy.

The survey was piloted with five PCPs (a mix of RNs and MD/DOs), and cognitive debriefing was performed by study team members to identify ambiguous items. Pilot subjects were randomly selected from the master list of providers, using the same techniques that will be used

in the general survey. PCPs who participated in the pilot study received $200 for their time. After receiving a letter of invitation, participants were informed that their responses to the survey as well as to the cognitive debriefing questions afterward would be kept anonymous and detroyed after the questionnaire is finalized. The survey took 20 minutes to complete. In addition to probing about survey identified as problematic by the pilot subjects, each pilot subject was assigned a number of survey questions for detailed probing such that all questions were reviewed. Data from the survey questions answered by the pilot subjects will not be included in the final anlaysis. Modifications made resulted in the final survey. The final survey was submitted to and approved by the Dana Farber Cancer Institute (DFCI) IRB.

Pre-Testing of Interview Guides

Three interview guides were pre-tested: a patient interview guide, a primary care physician guide, and a hematologist/oncologist guide. We tested each guide three times using mock patients and mock physicians. The mock interviews were conducted over the phone so as to simulate actual experimental conditions. The interviewer went through the interview with a mock patient while two other research team members listened. After the interview was complete, the interviewee as well as the group provided feedback to the interviewer.

Pilot Testing of Interview Guides

Each of the three interview guides are being piloted with a maximum of 9 interviews per group. Changes to the interview guides for the full study (remaining 18 interviews per group) based on this pilot will be submitted to the IRB office, if applicable. No interview protocol to gather this information previously existed. All questions are newly developed for this study.

Primary Care Provider (PCP) Focus Groups

No focus group moderator's guide to gather this information previously existed. All questions are newly developed for this study.

B5. Individuals Consulted on Statistical Aspects and Individuals Collecting and /or Analyzing Data

Statistical sampling consultation was received from statisticians at the DFCI. The physician surveys are self-administered. Individuals collecting data for the patient, provider in-depth interviews and the focus groups will be MDACC staff. Data analyses will be performed by DFCI, University of Texas Houston and MDACC faculty. No contractors will be involved in data collection or analysis. Below is a list of individuals consulted on statistical aspects where applicable and individuals collecting or analyzing data.

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