original contributions

Overcoming Barriers to Clinical Trial Participation: Outcomes of a National Clinical Trial Matching and Navigation Service for Patients With a Blood Cancer

Maria Sae-Hau, PhD[1]; Kate Disare, MPH[1]; Margo Michaels, MPH[2]; Alissa Gentile, MSN, RN[1]; Leah Szumita, MS, RN[1]; Katherine Treiman, PhD, MPH[3]; and Elisa S. Weiss, PhD[1]

QUESTION ASKED: What factors are associated with clinical trial enrollment among patients served by The Leukemia & Lymphoma Society's Clinical Trial Support Center (CTSC), a unique, national nurse-led navigation service designed to mitigate multilevel clinical trial participation barriers that patients with a blood cancer and their oncology care providers face?

SUMMARY ANSWER: After controlling for other demographic and clinical characteristics, patients with Medicaid were significantly less likely to enroll than those with private or commercial insurance, and patients in treatment or maintenance were significantly less likely to enroll than those relapsed or refractory to most recent therapy.

WHAT WE DID: The approach and outcomes of the CTSC are described; the CTSC's nurse navigators assist patients with a blood cancer and their oncologists by identifying all appropriate trials based on clinical data and patient preference, facilitating informed and shared decision making, and minimizing enrollment barriers. New patient cases opened from October 2017 to October 2019 were analyzed (N = 906). A multivariate analysis among those with a known enrollment outcome (n = 537) was conducted to determine factors associated with enrollment, composed of variables significant in bivariate analyses (insurance, treatment status, Eastern Cooperative Oncology Group performance status, and urban or rural county of residence).

WHAT WE FOUND: The clinical trial enrollment rate was 16.1% among US patients with a blood cancer (n = 750) and 22.5% among the subgroup who had a trial search with a known enrollment outcome (n = 537). Multivariate analysis revealed that patients with Medicaid were less likely to enroll than those with private or commercial insurance (adjusted odds ratio, 0.054; CI, 0.003 to 0.899), and patients in treatment or maintenance were less likely to enroll than those relapsed or refractory to most recent therapy (adjusted odds ratio, 0.312; CI, 0.139 to 0.702). There was no significant difference in rate of enrollment between those seeking a first-line treatment option and those relapsed or refractory to their most recent treatment. Primary reasons for nonenrollment were preference for standard of care (66.3%) and patient passed away (16.1%) as opposed to logistical barriers.

BIAS, CONFOUNDING FACTOR(S), REAL-LIFE IMPLICATIONS

The population served by the CTSC was a group of individuals who have reached out to The Leukemia & Lymphoma Society for assistance. The findings may not be generalizable to other populations less engaged or among those with other cancer types. The population served was primarily White or Caucasian. The results may not represent the experiences of subgroups whose primary language is not English and who have varying cultural preferences and circumstances. Although bivariate analysis did not reveal significant differences in enrollment rates by race and ethnicity, this may be because of lack of variability within the sample and a high degree of missing data. There are numerous multilevel barriers to cancer clinical trial participation in the United States, and clinical trial navigation services at sites of care are limited. The findings capture the value of the CTSC in helping to mitigate clinical trial participation barriers that patients and oncology care providers face, and demonstrate the potential benefits of replicating this unique service model for patients with other cancer types. The findings highlight the need to increase opportunities for trial participation sooner after diagnosis and support the importance of policies that foster access to clinical trials among patients with Medicaid.

ASSOCIATED CONTENT

Appendix

Data Supplement

Author affiliations and disclosures are available with the complete article at ascopubs.org/journal/op.

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CARE DELIVERY

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abstract

PURPOSE There are numerous barriers to cancer clinical trial participation in the United States. This paper describes the approach and outcomes of The Leukemia & Lymphoma Society's Clinical Trial Support Center (CTSC), whose nurse navigators assist patients with a blood cancer and their oncologists by identifying all appropriate trials based on clinical data and patient preference, facilitating informed and shared decision making, and minimizing enrollment barriers.

METHODS Data on patients served from October 2017 to October 2019 were analyzed using bivariate and multivariate analyses to determine demographic and clinical characteristics associated with enrollment. Reasons for nonenrollment were examined.

RESULTS The CTSC opened 906 patient cases during this time frame. Among all US patients with a closed case (n = 750), the clinical trial enrollment rate was 16.1%. Among those with a known enrollment outcome after a trial search (n = 537), the enrollment rate was 22.5%. Multivariate analysis controlling for variables significant in bivariate analyses (insurance, treatment status, Eastern Cooperative Oncology Group performance status, and urban or rural residence) revealed that patients with Medicaid were less likely to enroll than those with private or commercial insurance (adjusted odds ratio, 0.054; CI, 0.003 to 0.899), and patients in treatment or maintenance were less likely to enroll than those relapsed or refractory to most recent therapy (adjusted odds ratio, 0.312; CI, 0.139 to 0.702). Primary reasons for nonenrollment were preference for standard of care (66.3%) and patient passed away (16.1%).

CONCLUSION The CTSC is an effective, replicable model for addressing multilevel barriers to clinical trial participation. The findings highlight the need to increase opportunities for trial participation sooner after diagnosis and among patients with Medicaid.

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INTRODUCTION

Addressing barriers to clinical trial participation is critical to accelerating progress toward more effective and less toxic cancer treatments[1] and to providing patients with access to novel therapies and treatment approaches. Approximately 20% of cancer clinical trials fail because of insufficient patient enrollment,[2] which hinders progress to improve cancer care. Numerous barriers to cancer clinical trial participation in the United States have been documented[3,4]; participation rates have remained low for many years, hovering at 8%[2] or less.[5] These barriers include *institutional and provider-related barriers* such as trial availability, staff and infrastructure capacity and capability, the quality and variability of provider communication, and ineffective patient identification and enrollment practices[6-12]; *barriers related to trial design* such as restrictive inclusion or exclusion criteria and lack of patient-centeredness[5,11,12]; and *patient-level barriers*, including awareness, self-efficacy, fear and mistrust, a preference to not lose control of treatment decision making, cost, and logistical concerns.[2,13-20] Barriers are even more pronounced—and participation rates are particularly low—for subgroups of patients of certain races and ethnicities, who live in rural areas, who are older or young adults, who are uninsured, and/or with low income.[2,10,14,21-29] Underrepresentation in trials may perpetuate disparities in outcomes and lead to limited generalizability in practice.[21,30-33]

Finding an appropriate clinical trial can be overwhelming for patients, and time and resource intensive

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for physicians. Clinical trial matching services are designed to help patients find suitable clinical trials. Patients provide information about their health status and diagnosis, which is compared with the eligibility criteria of open trials from a public or private database.[2] However, matching services can themselves present barriers[2]; to use these matching services effectively, patients must understand (1) the medical terminology related to their diagnosis and treatment; (2) the clinical research process; (3) specific trial attributes to determine their potential interest and eligibility; and (4) how to sort or refine search results.[34,35] Search results may inadvertently include inaccurate information[36] or may be limited in scope. They require significant health literacy skills[37-39] and self-efficacy[6,15,16] to initiate action around clinical trials, and they typically do not address logistical barriers or cost concerns.

Clinical trial patient navigation is a more patient-centered service that goes beyond matching. Over the past 10 years, some academic research centers have created internal navigation services that may focus primarily on trials within their institution but can extend beyond that institution as well.[40-43] Service scope tends to focus on increasing awareness, knowledge, and access to appropriately matched clinical trials, facilitating access to community resources such as connection to a care coordination nurse or social worker within the health care system, and improving communication between the patient and treatment team.[40] Studies have shown that these programs can increase patient awareness and knowledge about clinical trials[36,44] and participation in trials.[44] Several programs have also shown increased trial accrual and retention rates among underrepresented populations.[40,42,45-48] However, many patients do not have access to clinical trial navigation services at their site of care.

The Leukemia & Lymphoma Society's Clinical Trial Support Center

To address the need for better access to highly personalized clinical trial information among patients with a blood cancer, The Leukemia & Lymphoma Society (LLS) developed its Clinical Trial Support Center (CTSC) in 2016. It is a free, national, telephone-based, nurse-led navigation service for patients with leukemia, lymphoma, myeloma, myeloproliferative neoplasms, and myelodysplastic syndromes. The goal of the CTSC is not to have every patient served enroll into a clinical trial, but to increase awareness of opportunities to receive treatment within a clinical trial, facilitate informed and shared decision making with their oncologist about participating, and minimize barriers to enrollment if the patient decides that a clinical trial is right for him or her in collaboration with his or her health care team. The CTSC's patient-centered approach aims to provide care that is respectful of and responsive to individual patient preferences, needs, and ensures that patients' values guide all clinical decisions.

This paper describes the CTSC's comprehensive approach and clinical trial enrollment outcomes among patients served and seeks to shed light on the demographic and clinical characteristics associated with enrollment. Secondarily, it describes the patient demographic and clinical characteristics of those who initially chose to undergo, or not undergo, a search for appropriate clinical trials with assistance from the CTSC, as well as the reasons that patients chose not to enroll after receiving the results of a trial search.

The CTSC's Characteristics and Processes

The CTSC employs nurse navigators who are oncology nurses.[49] They are advanced practice nurses, nurse practitioners (both pediatric and adult), research nurses, and nurse educators, and they are supported by a coordinator. They undergo intensive and ongoing education in hematologic malignancy physiology, treatment methods, stem-cell transplantation, clinical trials, and genomics.

CTSC nurse navigators are assigned cases as they come in through LLS's website or Information Resource Center; patients self-refer or are referred by their oncology care team. The nurse navigators speak with a patient (or caregiver) to collect background information that will assist with conducting a targeted clinical trial search and to identify barriers to matching and enrollment. When working with a patient or caregiver, the nurse navigator focuses on seven comprehensive and essential service components described in Table 1, which were designed to surmount many of the multilevel barriers to enrollment described above. For example, increasing health literacy enhances patients' or caregivers' understanding of trial options and consent documents, and facilitates better communication with clinical trial investigators and staff. As needed, a language line is used to assist patients or caregivers who prefer to communicate in a language other than English.

METHODS

Retrospective analysis of secondary data was conducted with deidentified data from patient cases opened by the CTSC between October 2017 and October 2019. The study was reviewed by the Institutional Review Board at RTI International to ensure compliance with ethical principles (MOD00000870).

Data Collection

The CTSC routinely collected demographic and clinical information at the commencement of initial contact with the patient or caregiver, including insurance type, treatment status, and Eastern Cooperative Oncology Group performance status (ECOG PS).[50] Among those for whom a clinical trial search was conducted, enrollment status (ie, whether the patient enrolled in a trial with the help of the CTSC) and the primary reason for deciding to not enroll were documented by the nurse navigator based on follow-up with the patient or caregiver. In some cases, after a search was

TABLE 1. CTSC Patient-Centered Service Components

Component	Role of the CTSC Nurse Navigator
Medical history and status	Inquire about medical history and current medical status: disease markers and mutations, CNS involvement, ECOG PS, comorbidities, treatment history, treatment options discussed with the health care team, second opinions, and personal treatment preferences
Psychosocial factors	Inquire about emotional health, personal goals, values and beliefs, financial status, family support systems, and ability to travel or be away from home and employment for an extended period
Education about clinical trials	Provide plain language education to increase health literacy about clinical trial design and phases, considerations when choosing a clinical trial, the concept of risks and benefits, insurance coverage and typical costs of clinical trial participation, potential cost of travel and lodging, off-label use of medications when relevant, and expanded access and compassionate use programs when relevant
Personalized trial search and matching	Using ClinicalTrials.gov, conduct a search of clinical trials that are open for enrollment, or soon to be; curate an individualized list of trials for which a patient is potentially eligible by carefully reviewing the patient's medical and psychosocial history compared against trial inclusion and exclusion criteria
	Assemble in plain language a description of each clinical trial for which the patient is likely eligible and its contact information, which is sent via e-mail or mail to the patient or caregiver along with patient education materials; suggest that the patient discuss this list of trials with his or her treating oncologist
	Follow-up with each patient or caregiver after the trial list is provided to ensure that he or she understands the information; inquire about decision-making status or interest in obtaining more detailed information about a particular trial (early-phase results, articles, etc)
Decision support	Enhance self-efficacy by identifying strategies for communication about clinical trials with the treating oncologist and with insurance carriers to gain information that may help the patient decide if he or she would like to enroll in a particular trial
	Enhance health literacy by helping with interpretation of medical terminology and consent documents and with understanding the clinical research process
Assistance with connecting to clinical trial sites	Interact with clinical trial site staff (eg, principal investigators or research nurses) with patient's consent to help determine eligibility and facilitate connection to the site; speak with a trial sponsor to get the correct contact information of the trial, if industry-sponsored, or information about expanded access
Provision of ongoing support to resolve barriers to participation	Address all modifiable, logistical barriers to enrollment and participation that are uncovered to the extent possible using supportive resources offered by LLS, patient advocacy programs, and/or foundations; this may include financial assistance programs and community resources that assist with the cost of travel, lodging, and other urgent needs
	If a patient is denied insurance coverage, provide information and resources to maximize the likelihood of a successful appeal
	Encourage the patient to contact the trial sponsor or site during evaluation for enrollment to identify additional support that the trial sponsor or site may offer

Abbreviations: CTSC, Clinical Trial Support Center; ECOG PS, Eastern Cooperative Oncology Group performance status; LLS, Leukemia & Lymphoma Society.

conducted, the patient or caregiver did not respond to several follow-up attempts, so an enrollment outcome could not be determined. As there was no income or education data collected from patients, to supplement existing patient-reported data, socioeconomic status was classified using The Social Deprivation Index (SDI),[51] a validated county-level measure based on the American Community Survey. Census data and Centers for Medicare and Medicaid Services classification guidance were also used to classify patient residency into rural or urban counties.[52-54]

Data Analysis

Bivariate analyses examined patient characteristics associated with the outcomes of search and enrollment using Pearson chi-square tests, Fisher exact tests, and Kruskal-Wallis tests for the SDI score (two-sided; α of .05). Multivariate logistic regression determined factors associated with enrollment using adjusted odds ratios (AORs) and 95% CI. Variables examined in bivariate analysis were initial contact (patient or caregiver), patient sex, patient age, patient ethnicity or race, insurance type, primary diagnosis, treatment status, CNS involvement, travel considerations, ECOG PS, SDI, and urban or rural county of residence. Covariates were included in the multivariate model only if bivariate analyses showed significance ($\alpha \leq .05$). A penalized maximum likelihood estimation technique (Firth correction) was used. Analyses were conducted using SAS version 9.4.

RESULTS

Characteristics of Patients and Caregivers Served by the CTSC

From October 2017 to October 2019, 906 patient cases were opened (Fig 1). Among these, 92 cases (10.2%) were excluded because the case was still in progress at the time

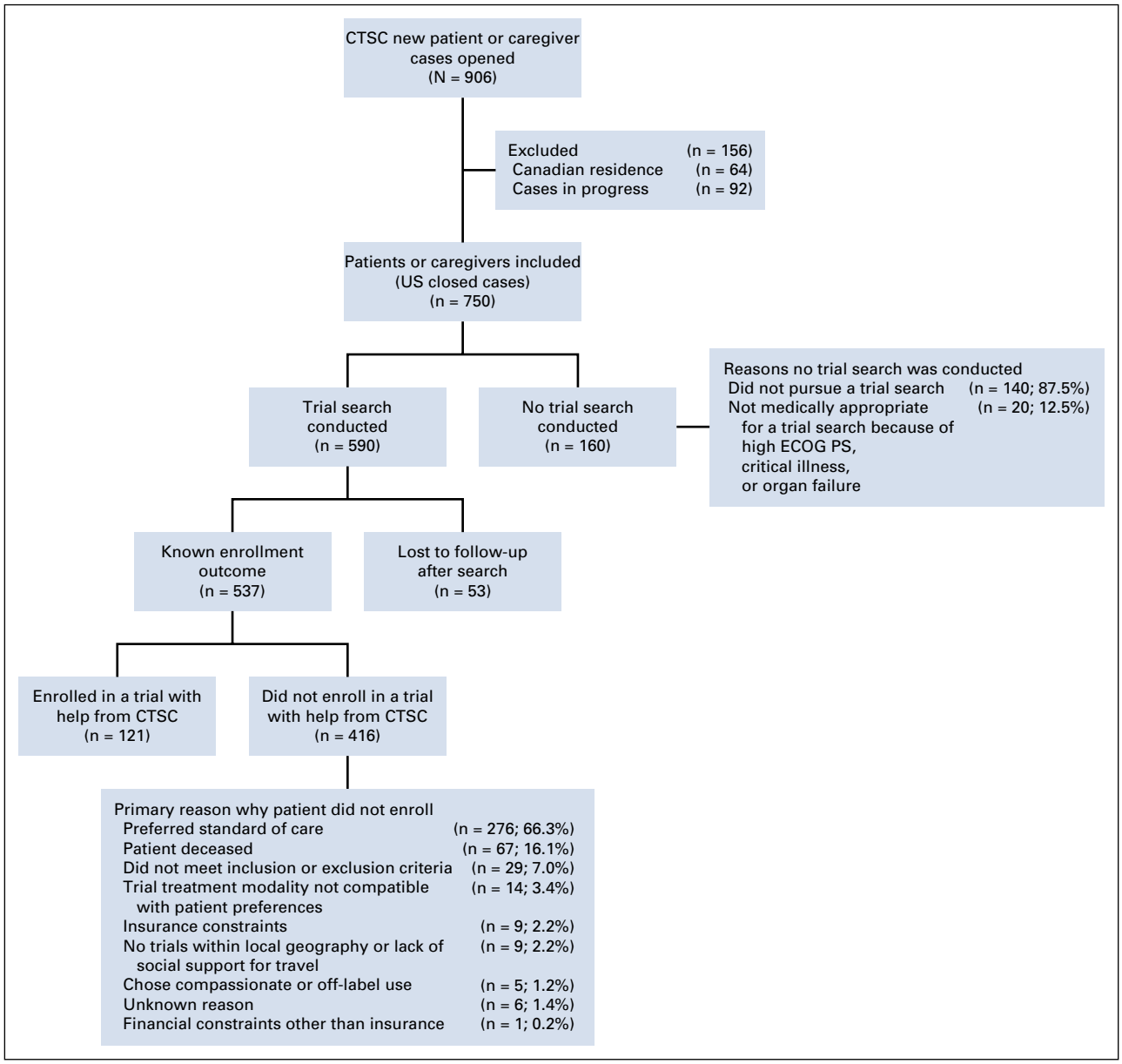

FIG 1. Characteristics of new referrals to the CTSC from October 2017 to October 2019. CTSC, Clinical Trial Support Center; ECOG PS, Eastern Cooperative Oncology Group performance status.

of analysis and 64 cases (7.1%) were excluded because the patient resided outside of the United States.

Of the remaining cases (n = 750), 590 patients or caregivers had a clinical trial search conducted and 160 did not. Of the 590 cases with a search conducted, 53 patients or caregivers were lost to follow-up, which leaves 537 cases with a known enrollment outcome. English was the primary language for all but three of the 537 cases, whose primary language was Spanish.

Table 2 shows the patient demographic and clinical characteristics for the following samples: total sample, those with a search, those lost to follow-up after search, and those with a search and known enrollment outcome. After having a trial search conducted, those who were lost to follow-up differed from those who had a known enrollment outcome by insurance type ($P = .002$) and treatment status ($P = .014$) (Table 2).

Among the 537 patients with a known enrollment outcome after a search, the average number of phone and e-mail interactions between a CTSC nurse navigator and any party (eg, patient, family member, treating health care provider, or clinical trial research staff) was 18.1. The majority of these interactions were with patients or caregivers (80.9%), followed by trial research staff (16.3%) and treating health care providers (2.3%). The average number of interactions for those who enrolled in a clinical trial was 25.0, and the

TABLE 2. Patient Demographic and Clinical Characteristics

Characteristic	Total Patient Sample, No. (%) (n = 750)	Patients With Search Conducted, No. (%) (n = 590)	Lost to Follow-Up After Search, No. (%) (n = 53)	Patients With Known Enrollment Outcome After Search, No. (%) (n = 537)	Lost to Follow-Up After Search Versus Known Enrollment Outcome (*P*)
Initial contact					.366
Patient	444 (59.2)	344 (58.3)	34 (64.2)	310 (57.7)	
Caregiver	306 (40.8)	246 (41.7)	19 (35.9)	227 (42.3)	
Patient sex					.278
Male	429 (57.2)	342 (58.0)	27 (50.9)	315 (58.7)	
Female	321 (42.8)	248 (42.0)	26 (49.1)	222 (41.3)	
Patient age, years					.115
0-19	26 (3.8)	21 (3.9)	0 (0.0)	21 (4.3)	
20-39	69 (10.2)	55 (10.3)	9 (19.2)	46 (9.4)	
40-59	195 (28.7)	145 (27.1)	10 (21.3)	135 (27.7)	
60-79	360 (52.9)	293 (54.8)	25 (53.2)	268 (54.9)	
80+	30 (4.4)	21 (3.9)	3 (6.4)	18 (3.7)	
Patient race or ethnicity					.394
White or Caucasian	416 (87.2)	330 (89.0)	32 (84.2)	298 (89.5)	
Black or African American	24 (5.0)	18 (4.9)	2 (5.3)	16 (4.8)	
Hispanic or Latino/a	21 (4.4)	14 (3.8)	3 (7.9)	11 (3.3)	
Asian	11 (2.3)	5 (1.4)	0 (0.0)	5 (1.5)	
Mixed race	3 (0.6)	2 (0.5)	1 (2.6)	1 (0.3)	
American Indian or Alaska Native	1 (0.2)	1 (0.3)	0 (0.0)	1 (0.3)	
Pacific Islander or Native Hawaiian	1 (0.2)	1 (0.3)	0 (0.0)	1 (0.3)	
Insurance type					.002
Private or commercial only	315 (47.2)	252 (47.3)	15 (30.6)	237 (49.0)	
Medicare	123 (18.4)	101 (19.0)	15 (30.6)	86 (17.8)	
Medicare plus private or commercial	117 (17.5)	90 (16.9)	6 (12.2)	84 (17.4)	
Medicaid	48 (7.2)	37 (6.9)	9 (18.4)	28 (5.8)	
Uninsured	30 (4.5)	24 (4.5)	1 (2.0)	23 (4.8)	
Medicare plus Medigap	19 (2.8)	19 (3.6)	3 (6.1)	16 (3.3)	
Military	16 (2.4)	10 (1.9)	0 (0.0)	10 (2.1)	
Primary diagnosis					.760
Leukemia	321 (42.9)	251 (42.6)	22 (41.5)	229 (42.7)	
Lymphoma	254 (34.0)	199 (33.8)	20 (37.7)	179 (33.4)	
Myelodysplastic syndrome	56 (7.5)	41 (7.0)	4 (7.6)	37 (6.9)	
Myeloma	88 (11.8)	72 (12.2)	4 (7.6)	68 (12.7)	
Myeloproliferative neoplasm	24 (3.2)	22 (3.7)	2 (3.8)	20 (3.7)	
Other blood cancers	5 (0.7)	4 (0.7)	1 (1.9)	3 (0.6)	

(continued on following page)

TABLE 2. Patient Demographic and Clinical Characteristics (continued)

Characteristic	Total Patient Sample, No. (%) (n = 750)	Patients With Search Conducted, No. (%) (n = 590)	Lost to Follow-Up After Search, No. (%) (n = 53)	Patients With Known Enrollment Outcome After Search, No. (%) (n = 537)	Lost to Follow-Up After Search Versus Known Enrollment Outcome (*P*)
Treatment status					.014
Watch and wait	34 (4.6)	30 (5.2)	7 (13.2)	23 (4.3)	
Diagnosed pretreatment	110 (14.8)	87 (15.0)	5 (9.4)	82 (15.6)	
On active treatment or maintenance	131 (17.7)	89 (15.3)	4 (7.6)	85 (16.1)	
Relapsed or refractory to most recent treatment	443 (59.8)	362 (62.2)	37 (69.8)	327 (61.8)	
Post-treatment or long-term remission	23 (3.1)	12 (2.1)	0 (0.0)	12 (2.3)	
CNS involvement					.621
Yes	45 (8.5)	35 (8.4)	3 (6.5)	32 (8.7)	
No	486 (91.5)	380 (91.6)	43 (93.5)	337 (91.3)	
Travel considerations					.787
Yes, willing to travel	524 (69.9)	422 (71.5)	39 (73.6)	383 (71.3)	
No, not willing to travel	66 (8.8)	48 (8.1)	5 (9.4)	43 (8.0)	
Unsure at this time	160 (21.3)	120 (20.3)	9 (17.0)	111 (20.7)	
ECOG PS					.153
0-1	537 (73.5)	424 (73.6)	35 (66.0)	389 (74.4)	
2	145 (19.8)	119 (20.7)	12 (22.6)	107 (20.5)	
3-4	49 (6.7)	33 (5.7)	6 (11.3)	27 (5.2)	
SDI score					.506[a]
Median (range 0-100)	41.0	40.0	42.0	40.0	
Urban or rural					.922
Urban	625 (88.9)	492 (88.7)	45 (88.2)	447 (88.7)	
Rural	78 (11.1)	63 (11.4)	6 (11.8)	57 (11.3)	
Total	750	590	53	537	

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; SDI, Social Deprivation Index.

[a]The Kruskal-Wallis H test did not show a statistically significant difference in mean rank SDI score between those who were lost to follow-up after search and those with a known enrollment outcome ($\chi^2(1) = 0.4428$, $P = .506$).

average number of interactions for those who did not enroll was 16.0. These interactions include follow-up support by phone or e-mail after a patient enrolled or did not enroll.

Likelihood of Clinical Trial Search

Among the 750 US patients and caregivers with cases not in progress at the time of analyses (ie, closed cases), 160 (21.3%) had no clinical trial search conducted. The most common reason for a nurse navigator not conducting a search (87.5%) was because the patient or caregiver chose not to proceed with one. For 12.5%, a search was not conducted because the patient was determined by the nurse navigator as not medically appropriate for a trial search because of high ECOG PS, critical illness, or organ failure.

Bivariate analyses were conducted to identify patient demographic and clinical characteristics associated with a clinical trial search. Patients who were on active treatment or maintenance at the time of referral were less likely to have a trial search than all other treatment statuses ($P = .001$). Those who were relapsed or refractory to their most recent treatment were more likely to have a trial search conducted than all other treatment statuses ($P = .004$). There were no other characteristics significantly associated with the likelihood of a trial search being conducted (Data Supplement, online only).

Likelihood of Clinical Trial Enrollment Among Those for Whom a Search Was Conducted

Among patients or caregivers who had a trial search with a known enrollment outcome (n = 537), 22.5% of patients enrolled in a trial with help from the CTSC (n = 121). Among all US patients or caregivers with a closed case (n = 750; Fig 1), 16.1% enrolled in a trial with help from the CTSC.

TABLE 3. Multivariate Logistic Regression Analysis of Enrollment by Patient Demographics and Clinical Characteristics Among Cases With a Known Enrollment Outcome After a Clinical Trial Search

Parameter	Adjusted Enrollment Odds Ratio (95% CI)
Insurance	
Private or commercial only (ref)	1
Medicaid	0.054 (0.003 to 0.899)
Medicare	0.592 (0.304 to 1.155)
Medicare plus private or commercial	1.059 (0.591 to 1.898)
Medicare plus Medigap	0.447 (0.105 to 1.900)
Military	0.216 (0.010 to 4.500)
No coverage or uninsured	0.412 (0.103 to 1.651)
Treatment status	
Relapsed or refractory to most recent treatment (ref)	1
Watch and wait	0.259 (0.066 to 1.022)
Diagnosed pretreatment	0.549 (0.275 to 1.098)
On active treatment or maintenance	0.312 (0.139 to 0.702)
Post-treatment or long-term remission	1.106 (0.279 to 4.377)
ECOG PS	
0-1 (ref)	1
2	0.580 (0.314 to 1.070)
3-4	0.311 (0.078 to 1.236)
Urban or rural	
Urban (ref)	1
Rural	0.526 (0.208 to 1.331)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; ref, reference.

Bivariate analyses were conducted to determine patient demographic and clinical characteristics associated with clinical trial enrollment. There were statistically significant differences in clinical trial enrollment rates by insurance type ($P = .005$), treatment status ($P = .010$), ECOG PS ($P = .037$), and urban or rural residence ($P = .026$; Appendix Table A1, online only). There were no significant differences in rates of enrollment by other characteristics. The primary reasons why patients did not enroll in a clinical trial with assistance from the CTSC are presented in Figure 1.

Multivariate Analysis

Multivariate logistic regression was conducted among patients who had a trial search with a known enrollment outcome. Controlling for factors significantly associated with enrollment in the bivariate analyses (treatment status, ECOG PS, and urban or rural residence), analysis results showed that compared to those with private or commercial insurance, patients with Medicaid were significantly less likely to enroll in a clinical trial with help from the CTSC (AOR, 0.054; CI, 0.003 to 0.899; Table 3). Additionally, patients who were on active treatment or maintenance at the time of referral were significantly less likely to enroll than those who were relapsed or refractory to their most recent treatment (AOR, 0.312; CI, 0.139 to 0.702).

DISCUSSION

This paper details the approach of a national, telephone-based nurse navigator-led service model that aims to reduce barriers to clinical trial participation among patients with a blood cancer and identifies patient demographic and clinical characteristics associated with enrollment. The findings suggest that this navigation service is effective at mitigating modifiable barriers to clinical trial enrollment. Among patients served in the United States with closed cases, the clinical trial enrollment rate was 16.1%. Among those for whom a search was conducted with a known enrollment outcome, the enrollment rate was 22.5%. While patients or caregivers assisted by the CTSC may be more open to clinical trial participation than the general population of patients with a blood cancer, these data do demonstrate the value of a comprehensive navigation program.

The CTSC predominately provided services to and conducted searches for patients relapsed or refractory to their most recent treatment, and the findings demonstrated that this group of patients was more likely to enroll onto a trial than those in active treatment or maintenance. Yet, there was no significant difference in rate of enrollment between those seeking a first-line treatment option (ie, in the diagnosed pretreatment category) and those relapsed or refractory to their most recent treatment after search. Collectively, these findings point to the importance of offering clinical trial options earlier in the disease spectrum for those who may be interested.[36,38,55]

This study found that after controlling for other factors that were significant in the bivariate analysis (urban or rural residence, treatment status, and ECOG PS), patients with Medicaid insurance were significantly less likely to enroll in a clinical trial than those with private or commercial insurance. Similar results were found in another national navigation study.[38] Factors contributing to this are likely complex; during the study period, Medicaid did not have a federal requirement to cover the cost of routine care within clinical trials, and clinical trial coverage depends on the state of residence.[56] For the minority of states that do provide coverage, state-based Medicaid insurance may limit the clinical trials a patient may be eligible for trials occurring within their state, although some patients are able to successfully appeal. The effect of Medicaid coverage may evolve in 2022, when a recently enacted federal law, The Clinical Treatment Act, requiring Medicaid to cover the cost of routine care within trials, will take effect. Some researchers have highlighted the need to better understand how outcomes among clinical trial participants with Medicaid are affected by external factors associated with insurance (such as quality of survivorship care).[57]

Intensive navigation was provided by CTSC nurses to help eliminate modifiable barriers to enrollment (an average of 25 phone or e-mail interactions for those enrolled). CTSC nurse navigators reduce patient-level barriers by providing education that addresses fears and dispels myths. They supplement site-of-care capacity by providing detailed information about trial status, eligibility, and the trial referral process beyond what may be available on ClinicalTrials.gov. They encourage the patient to take search results to their oncologist for conversation and help the patient create a list of questions to ask, which facilitates patient-provider communication and shared decision making. They connect patients to resources that assist with travel, food, and lodging costs, and insurance coverage and appeal. Even after addressing these modifiable barriers, preference for standard of care was the primary driver of nonenrollment; based on nurse navigators' experience, this was often because of provider recommendation and/or the known effectiveness of an approved therapy.

A disproportionate percentage of patients served by the CTSC identified as White or Caucasian, as compared to the general population. This further highlights the need for expanded and more effective outreach efforts to increase opportunities for clinical trial participation among other racial and ethnic groups, to help reduce disparities in access to novel therapies and treatment response.[2,21,30-33,45,58] Key lessons learned from the implementation of the CTSC include: the importance of having highly skilled nurses provide this service; maintaining deliberate focus on addressing multilevel barriers to accrual; leveraging technology to maximize comprehensiveness and relevance of trial searches; and giving patients or caregivers the tools they need to effectively communicate with their oncology care team about clinical trial options that are appropriate for them. Since the time the analysis was conducted, the CTSC has not only increased its service capacity by hiring more nurse navigators and enhancing the technological infrastructure, but also heightened outreach to underrepresented groups.

The population served by the CTSC was a group of individuals who have reached out to LLS for assistance. The findings may not be generalizable to other populations less engaged or among those with other cancer types. Moreover, the population served was primarily White or Caucasian. The results may not represent the experiences of subgroups whose primary language is not English and who have varying cultural preferences and circumstances. Although bivariate analysis did not reveal significant differences in search and enrollment rates by race and ethnicity, this may be due both to lack of variability within the sample and a high degree of missing data. At the time of data collection, race or ethnicity data were not systematically collected. Finally, this study was not able to control for comorbidities or individually reported socioeconomic indicators, which may differ from county-level data used in the analyses.

In conclusion, this paper describes the approach and outcomes of a free, national clinical trial matching and nurse navigation service for patients with a blood cancer, complementing the work of oncology care providers. Among US patients with closed cases, the clinical trial enrollment rate was 16.1%. Among those who had a trial search conducted and a known enrollment outcome, the enrollment rate was 22.5%. Given that clinical trial navigation services at sites of care are limited, the findings capture the value of this service in helping to mitigate clinical trial participation barriers that patients and providers face and demonstrate the potential benefits of replicating this model for patients with other cancer types. There remains a clear need to increase opportunities for clinical trial participation earlier in the cancer continuum, and the findings further support the importance of policies that foster clinical trial access among patients with Medicaid.

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Overcoming Barriers to Clinical Trial Participation: Outcomes of a National Clinical Trial Matching and Navigation Service for Patients With a Blood Cancer

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APPENDIX

TABLE A1. Bivariate Analysis of Enrollment by Patient Characteristics Among Those With a Known Enrollment Outcome After a Clinical Trial Search

Characteristic	Proportion Enrolled With Help From CTSC (% enrolled) (n = 537)	Proportion Not Enrolled With Help From CTSC (% not enrolled) (n = 537)	Difference Enrolled Versus Not Enrolled (*P*)
Initial contact			.975
Patient	70/310 (22.6)	240/310 (77.4)	
Caregiver	51/227 (22.5)	176/227 (77.5)	
Patient sex			.830
Male	72/315 (22.9)	243/315 (77.1)	
Female	49/222 (22.1)	173/222 (77.9)	
Patient age, years			.633
0-19	6/21 (28.6)	15/21 (71.4)	
20-39	12/46 (26.1)	34/46 (73.9)	
40-59	27/135 (20.0)	108/135 (80.0)	
60-79	60/268 (22.4)	208/268 (77.6)	
80+	2/18 (11.1)	16/18 (88.9)	
Patient ethnicity or race			.520
American Indian or Alaska Native	0/1 (0.0)	1/1 (100.0)	
Pacific Islander or Native Hawaiian	0/1 (0.0)	1/1 (100.0)	
Mixed race	0/1 (0.0)	1/1 (100.0)	
Asian	0/5 (0.0)	5/5 (100.0)	
Black or African American	1/16 (6.3)	15/16 (93.8)	
Hispanic or Latino/a	3/11 (27.3)	8/11 (72.7)	
White or Caucasian	71/298 (23.8)	227/298 (76.2)	
Insurance type			.005
Medicaid	1/28 (3.6)	27/28 (96.4)	
Medicare	13/86 (15.1)	73/86 (84.9)	
Medicare plus Medigap	3/16 (18.8)	13/16 (81.3)	
Medicare plus private or commercial	23/84 (27.4)	61/84 (72.6)	
Military	0/10 (0.0)	10/10 (100.0)	
Private or commercial only	68/237 (28.7)	169/237 (71.3)	
Uninsured	3/23 (13.0)	20/23 (87.0)	
Primary diagnosis			.064
Leukemia	53/229 (23.1)	176/229 (76.9)	
Lymphoma	48/179 (26.8)	131/179 (73.2)	
Myelodysplastic syndrome	7/37 (18.9)	30/37 (81.1)	
Myeloma	13/68 (19.1)	55/68 (80.9)	
Myeloproliferative neoplasm	0/20 (0.0)	20/20 (100.0)	
Other blood cancers	0/3 (0.0)	3/3 (100.0)	
Treatment status			.010
Watch and wait	2/23 (8.7)	21/23 (91.3)	
Diagnosed pretreatment	17/82 (20.7)	65/82 (79.3)	

(continued on following page)

TABLE A1. Bivariate Analysis of Enrollment by Patient Characteristics Among Those With a Known Enrollment Outcome After a Clinical Trial Search (continued)

Characteristic	Proportion Enrolled With Help From CTSC (% enrolled) (n = 537)	Proportion Not Enrolled With Help From CTSC (% not enrolled) (n = 537)	Difference Enrolled Versus Not Enrolled (*P*)
On active treatment or maintenance	9/85 (10.6)	76/85 (89.4)	
Relapsed or refractory to most recent treatment	88/327 (26.9)	239/327 (73.1)	
Post-treatment or long-term remission	3/12 (25.0)	9/12 (75.0)	
CNS involvement			.458
Yes	6/32 (18.8)	26/32 (81.3)	
No	83/337 (24.6)	254/337 (75.4)	
Travel considerations			.249
Yes, willing to travel	90/383 (23.5)	293/383 (76.5)	
No, not willing to travel	12/43 (27.9)	31/43 (72.1)	
Unsure at this time	19/111 (17.1)	92/111 (82.9)	
ECOG PS			.037
0-1	96/389 (24.7)	293/389 (75.3)	
2	18/107 (16.8)	89/107 (83.2)	
3-4	2/27 (7.4)	25/27 (92.6)	
SDI score			.527[a]
Median (range 0-100)	41.0	38.5	
Urban or rural			.026
Urban	105/447 (23.5)	342/447 (76.5)	
Rural	6/57 (10.5)	51/57 (89.4)	

Abbreviations: CTSC, Clinical Trial Support Center; ECOG PS, Eastern Cooperative Oncology Group performance status; SDI, Social Deprivation Index.
[a]The Kruskal-Wallis H test did not show a statistically significant difference in mean rank SDI score between those who enrolled and those who did not enroll ($\chi^2(1) = 0.4012$, $P = .527$).