Statewide Cancer Clinical Trial Navigation Service

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Abstract

Purpose: Realizing that education and awareness are paramount in making clinical trials available to improve overall accrual rates, we sought to create a clinical trial navigation service to improve the accessibility of cancer clinical trials in Florida for physicians and patients. This study was undertaken to evaluate this service. We hoped to identify characteristics of our service that were effective in promoting clinical trial enrollment and to better understand barriers that prevented enrollment.

Methods: Qualitative and quantitative data were gathered to inform the evaluation. This information was drawn from semi-structured interview and focus groups as well as data from 6,350 patient questionnaires capturing diagnosis, stage, and treatment history. Quantitative data were analyzed by computing indices of central tendency and dispersion as well as frequency distributions. Qualitative data were analyzed using open coding to identify major themes representing the information.

Results: Our navigation system increased patient awareness of trials; however, this did not lead to an increase in trial enrollment. A key barrier to enrollment was the timing of the patient's awareness of a clinical trial opportunity. Often trial options were

realized after a treatment course was initiated. This frequently disqualified the patient from trial consideration. We identified factors underlying the critical role of how physician attitudes toward trials affect enrollment. We also found that government databases were incomplete. Twenty-five percent of clinical trials open in Florida were not listed with Physician Data Query or clinical trials.gov, and 15% to 22% were erroneously listed as having sites in Florida. Media efforts to increase patient awareness and use of the navigation service were transient. One-time educational programs did not have a long-term impact on clinical trial inquiries. Patients who spoke with clinical trial navigators were four times more likely to contact a matched trial site. Sharing a common database platform with various organizations increased the likelihood of patients finding trials near home. More than 82% of patients seeking information started their search on other Web sites.

Conclusion: Although we were able to overcome the barriers most commonly cited by patients, we found that taking a strictly patient-focused approach was not enough. Our results underline the critical role of health professionals in guiding patients to clinical trials, by including these options at a time when patients are likely to be eligible.

Introduction

History and Rationale

Florida leads the nation in cancer burden. This year, 101,920 Floridians will be newly diagnosed with cancer, and 41,660 will die as a result of cancer.¹ Research shows that ethnically diverse, low-income/low-literacy, and elderly populations are more likely to die as a result of cancer.¹ The minority population of Florida is 10% higher than the national average; 15.2% of residents live below the poverty level, and Florida has the largest elderly population in the nation (17.6%). Thirty-five percent of Floridians (5.6 million) are considered to be at high risk for cancer. Access to cutting edge research and treatment is vital to the population of Florida.

Clinical trials provide patients with cancer the highest quality cancer care available from leading physicians, yet only 3% of adults participate in clinical trials.^{2,3} Patients participating in these clinical studies have the opportunity to help physicians and researchers identify new medications and therapies to prevent, diagnose, and treat cancer while simultaneously receiving care that is as good as—if not better than—standard treatments. Clinical trials are critical components to advancing the fight against cancer. The standard treatments of today were the clinical trials of yesterday. Progress made through clinical trials has enabled patients with cancer to live longer, healthier lives. It

is critical that Floridians understand the importance of clinical trials.

Realizing that education and awareness are paramount to improving overall accrual rates,⁴ the Florida Dialogue on Cancer (Tampa, FL) created the Florida Cancer Trials (FCT) Board to oversee the creation, operation, and expansion of a clinical trials navigation service that would improve the quality, quantity, and accessibility of cancer clinical trials for patients, researchers, and practitioners. The primary objective of the board is to ensure equal access to clinical trials, giving with careful attention to the need for action at the community level and within diverse patient populations.

A board analysis of the National Cancer Institute (NCI) Physician Data Query (PDQ) and National Institutes of Health clinicaltrials.gov databases found that fewer than 25% of NCI-sponsored treatment trials were being reported as available in Florida. These findings prompted the board to create a statewide cancer clinical trials information system that would act as a centralized platform for all clinical research. Understanding the sociodemographic barriers that affect clinical trial awareness and accrual, the board agreed the ideal system would be a free Web- and phone-based navigation service.⁵⁻⁷ This platform would involve a grassroots effort for patients to match to appropriate clinical trials in their communities. The goal was

to have this single repository of available clinical trial information become part of the best practices of each cancer institution in identifying trials for patients. The system would be easily accessed by patients and physicians and serve to increase awareness of all clinical research being conducted in Florida.

This study was undertaken to evaluate this service. We hoped to identify characteristics of our service that were effective in promoting clinical trial enrollment and to better understand barriers that prevented enrollment.

Developing and Implementing Strategies

The FCT hosts a Web site—www.FloridaCancerTrials.com—with a complete, verified list of open trials for more than 100 cancers. The site allows patients and health care professionals to match to open trials throughout Florida through a single questionnaire. A toll-free number (1-800-584-9976) is provided to contact clinical trial navigators to help them through the education, matching, and referral process. The Web site, including all trial summaries, is available in Spanish, and clinical trial navigators are bilingual. A patient who finds a match receives an average of five follow-up telephone calls from the same clinical trial navigator, who provides basic clinical trial education and troubleshooting with trial sites when he or she encounters logistic or information barriers during the referral process.

To populate the database, the listing of trials available in Florida posted in the NCI PDQ and National Institutes of Health clinicaltrials.gov databases was imported into the FCT database. In November 2004, only 257 trials were listed for 40 cancer centers/hospitals in 27 cities across Florida. The board began an aggressive campaign, contacting all American College of Surgeons–approved sites, to organize a robust database of currently recruiting clinical trials and associated sites. A grassroots, community-based approach was developed whereby each participating hospital became a stakeholder in the collaborative enterprise. Currently, trials approved by the institutional review board of each hospital are updated on a monthly basis through ongoing contact. Easily understood patient-friendly trial summaries for all phase I to IV trials are written, translated into Spanish, and posted on the Web site.

In February 2009, 3,024 trials at 163 hospitals/private practices in 63 cities were listed. Each month, an average of 165 new trial/site combinations open, and 182 trial/site combinations close. Tremendous efforts have been made by all cancer centers and hospitals to expand the number of trials offered and increase the number of sites offering trials. This increases access to clinical trials close to home for all Floridians.

Methods

Data

This study was approved by the institutional review board at the University of South Florida (Tampa, FL). Information was collected from 6,350 patient profiles created through www.FloridaCancerTrials.com; 66% of the profiles were created by patients, 26% by family members, and 9% by health care pro-

viders. Semi-structured interviews and focus groups were held with top-level executives, clinical researchers, research nurses, clinical nurses, physicians, and intake staff at six cancer centers.

Analysis

Monthly reports on the number of trials loaded by trial site and city were monitored to analyze trends in database updating. These data consisted of raw counts of the number of trials added and the number of trials in the database at the end of each month. Disaggregation of the data by city and trial site provided trend information about the availability of trial information across the state.⁸

Counts of new Florida patients applying to trials and the total number of patients applying to Florida trials were analyzed by method of contact (ie, Web site, telephone center, and e-mail), patient geographic location, and trial location. Structured questionnaires captured patient diagnosis, stage, and treatment history. FCT staff conducts follow-up with patients seeking trials through this service. Follow-up consists of helping constituents troubleshoot difficulties while applying to trial sites, sending additional trials when appropriate, updating patient profiles with new treatment/staging information to rerun matches, and learning about outcomes of trial review. Because of the Health Insurance Portability and Accountability Act, there is no systematic, reliable method of tracking actual statewide enrollment; therefore, this information was not collected.

Surveys and interview protocols for site staff members were constructed to gather data on common methods of identifying patients for trial enrollment; enrollment of patients onto trials; usability, accessibility, and preponderance of database use; satisfaction with the database; and missing tools and services.

Both qualitative and quantitative data were gathered to inform the project and its evaluation. Quantitative data were analyzed by computing indices of central tendency and dispersion as well as frequency distributions. Qualitative data were analyzed using open coding to identify major themes representing the information. Because of the sequential nature of the project, data from each site were analyzed to inform implementation at subsequent sites. A final analysis of the similarities and differences among sites was conducted to address questions of project scalability and generalizability.⁸

Direct one-to-one comparisons of the trials listed in the FCT and PDQ/clinicaltrials.gov databases were performed on three different occasions (October 2006, April 2007, and December 2008). FCT staff extracted a list of all trials containing at least one Florida trial site from the databases. When a trial listed with PDQ/clinicaltrials.gov matched that in the FCT database, the trial was considered verified and open. When a trial listed with PDQ/clinicaltrials.gov was missing in the FCT database, the FCT placed up to three telephone calls to each site listed to confirm the status of the trial and the accuracy of the contact information.

Results

Finding 1: Government databases were incomplete. The most significant barrier to participation in clinical trials was the un-

Figure 1. Florida trials missing from government databases. (*) Confirmed by Florida Cancer Trials (FCT) through contact with Florida sites.

Figure 2. Trials erroneously listed by government databases as having sites in Florida. (*) Confirmed by telephone calls to Florida sites. FCT, Florida Cancer Trials.

availability of appropriate studies.⁹ To operate a referral service for Florida, accurate trial lists and contact information for each trial site are necessary. Twenty-five percent of clinical trials open in Florida were not listed with PDQ/clinicaltrials.gov (Fig 1), and 15% to 22% of clinical trials were erroneously listed by PDQ/clinicaltrials.gov databases as having sites in Florida (Fig 2).

Finding 2: One-time educational programs did not have a long-term impact on cancer clinical trial inquiries. Media efforts to increase consumer awareness and use of the FCT clinical trials navigation service were shown to be transient. An extensive and expensive media blitz was launched to promote the service. This included articles in 12 newspapers, stories on 26 television stations, spots on 55 radio stations, and online coverage on 15 online media outlets resulting in more than 7 million impres-

Figure 3. Web sessions on www.FloridaCancerTrials.com during period of focused media campaign, November to December 2004.

sions. Each peak in Web sessions corresponded to a local newspaper article or radio interview in a city or county (Fig 3).

Finding 3: Timing of searches was vital. The timing of a patient's search for clinical trials was vital to acceptance because of the restrictive eligibility criteria of most cancer clinical trials. In most cases, the timing of searches or the clinical profiles of patients varied by diagnosis. Four analyses illustrating the mismatch between the clinical characteristics of Floridians searching for cancer clinical trials and common eligibility criteria are as follows:

- Untreated patients were rare (Fig 4). One type of cancer clinical trial requires that patients enroll onto the trial before any treatment. The percentage of Floridians contacting the clinical trial navigation service before any treatment was low. Therefore, the proportion of patients potentially eligible for studies beginning before any treatment was quite low.
- Patients missed a window of opportunity to enroll onto neoadjuvant (ie, before surgery or radiation) studies (Appendix Fig A1, online only). Constituents visiting the clinical trial navigation site were often too late to consider enrollment onto studies requiring enrollment before surgery or radiation, including studies of tumor biopsies that must be collected during the first surgery.
- Patients may have been too ill to participate in clinical trials (Appendix Fig A2, online only). Physicians assess a patient's performance status when deciding whether it is safe enough to enroll that patient onto a cancer clinical trial. If the patient is too sick (eg, kidneys or liver not functioning properly), he or she will not be enrolled. The clinical trials navigators commonly heard patients express the misperception that cancer clinical trials were only for patients who had exhausted all other options.
- Patients looking for the next treatment option while receiving current treatment were not immediately eligible for trials (Fig 5). Some patients searched for trials to learn more about their options in case their current treatment was not successful or was successful for a limited period of time. No patient currently undergoing treatment is eligible to simultaneously enroll onto another treatment study. However, such patients were encouraged to return to the navigation service when they completed treatment.

Figure 4. Summary of Florida Cancer Trials patients from January 2005 to June 2007 showing percentage of patients with cancer untreated and therefore potentially eligible for neoadjuvant, adjuvant, or first-line advanced clinical trials.

Figure 5. Summary of Florida Cancer Trials patients from January 2005 to June 2007 showing percentage of patients with cancer receiving treatment and therefore currently ineligible for clinical trials.

Finding 4: Clinical trial navigators significantly increased conversion rates. Constituents who spoke with clinical trial navigators were four times more likely to follow up on their trial matches and contact matched trial sites (Appendix Fig A3, online only).

Finding 5: Physician attitude toward clinical trials affected enrollment rates.

- Physicians who did not believe in clinical trials were unlikely to refer patients to clinical trials.
- Some physicians referred patients only to specific trials, so referrals were dependent on the menu of trials open at the institution.
- Some physicians did not want to lose their patients to other physicians, so they were unwilling to refer even if they supported clinical trials. This even occurred within a clinic at a single center. In these cases, the physician assigned to the patient determined whether he or she is offered a clinical trial.
- Physicians at all centers were concerned that use of the general statewide FCT information service might steer their patients to other centers.

- Some physicians considered clinical trials the standard of care and prescreened 100% of their patients for clinical trials.
- Some physicians reported that the time needed to present a clinical trial option to a patient was too demanding given the time constraints.
- Some physicians reported that it was too time consuming to address patients' negative attitudes toward clinical trials (eg, fear of being a guinea pig, fear of receiving a placebo) given their stress level.

Finding 6: Cancer centers wanted to control enrollment but lacked the necessary tools. Some centers wanted to have their own staff prescreen and track enrollment of patients but had no tools readily available to support these activities.

Finding 7: There were no records of how many patients were matched to trials but did not enroll. Nor were there records of how many patients dropped out during the informed consent process, medical prescreening process, or final step of enrollment (perhaps with random assignment to one of two or three treatments).

Finding 8: Many physicians reported that it would be helpful if their patients were already aware of clinical trials before their first visit.

Finding 9: There were many opportunities to offer clinical trial information during patient visits. However, with a complicated process flow and high patient volumes, this was often overlooked. We were able to create a model for diagramming the patient flow through a cancer center or hospital. This facilitated collaborative discussions with each cancer center to identify the most logical point in time to offer patients education about or matching to clinical trials. Formalizing the intervention would eliminate sole reliance on the doctor remembering to inform patients about trials during initial visits (Appendix Fig A4, online only).

Finding 10: Customizing the clinical trials navigation service for a single cancer center greatly increased consistent use of the service. Two cancer centers (Shands HealthCare, University of Florida, Gainesville, FL, and Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL) piloted a private-label installation of the navigation service. This service featured matching to each institution's trials rather than the entire state database of cancer trials. These two services consistently generated far more traffic than the statewide, centralized service (Fig 6).

Finding 11: The sharing of a common database platform among organizations increased the likelihood of Floridians finding cancer clinical trials in Florida. Of the 2,759 patients who sought clinical trials in Florida during a 17-month period, 47% entered our Web site through various advocacy sites (eg, LIVESTRONG, the American Cancer Society, and 40 other groups), 17% through Web sites and call centers hosted by our vendor partner (EmergingMed, New York, NY) for cancer centers outside Florida, 9% through pharmaceutical Web sites and call centers operated by our vendor, and 9% through our vendor's Web site and its call center.

Figure 6. Profiles created for trial matching by source, July 2007 to November 2008.

Discussion

Although we were able to overcome the barriers most commonly cited by patients, enrollment onto cancer clinical trials has not increased significantly. Patients, for the most part, were already receiving treatment by the time they started their search for clinical trials. They were disappointed to find out that they were no longer eligible. Relaxing the requirements for enrollment to include comorbidities or prior treatment may increase enrollment rates.^{10,11} We decided that taking a strictly patient-focused approach was not enough. Coordination with health professionals needed to be addressed to successfully integrate the process of presenting clinical trials as a viable option for patients at a time when patients are likely to be eligible.

- A cancer center can only maximize clinical trial enrollment if every patient is matched to its portfolio of open, institutional review board–approved clinical trials.
- Patients are more likely to consider clinical trials if they (and their families) are educated about the basics of clinical trials—and dispelled of common misconceptions—soon after initial diagnosis.
- Cancer center staff may not have adequate time or manpower to educate all patients or match them to clinical trials. Our statewide navigation service has the staff, software, and business processes to provide these services in high volume at a substantially discounted price.
- Because we collect basic patient profiles as part of the matching process, we are able to work with centers to compare the match between their patient populations and the eligibility criteria of their clinical trials. For example, suppose we record that 80% of patients with colon cancer at a cancer center arrive for their first visit more than 8 weeks after initial surgery. This instantly tells the center that it is automatically too late to consider enrolling 80% of its colon cancer population onto neoadjuvant (must enroll just before surgery) or adjuvant studies (must enroll within 8 weeks after the surgery). This center would perhaps be best served by opening other types of colon cancer trials.

As a result of the findings listed above, we have created, revised, and launched three distinct services intended to increase the num-

ber of patients with cancer educated about and matched to cancer clinical trials in Florida. The three services include the following:

- Customized Web- and phone-based clinical trials navigation service targeting the trial program of each center.
- New patient education service providing outreach education for patients with cancer by bilingual clinical trial navigators either before or after their first visits to the cancer centers.
- Health professional matching and enrollment tracker enabling health professionals at a cancer center to quickly match new patients to the open trials at the center (via approximately five questions) and track matches on a center and statewide basis.

Recommendations

Offering a statewide database and centralized call center increases the likelihood of Floridians finding clinical trials close to home. Enhanced technology allows for an efficient and cost-effective means of rapidly providing individualized service to all cancer clinical trial sites in Florida. We found that patients know and trust health care centers in their local communities. This stresses the need to expand the availability of any statewide platform via multiple local portals. By using technology, we have positioned our service to provide a cost-efficient means of implementing clinical trials navigation for all community-based hospitals and medical centers in the state. This provides an incentive for each individual institution to participate and gain access to the same statewide database.

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