Barriers to Recruitment of Rural Patients in Cancer Clinical Trials

By Shamsuddin Virani, MB, BS, Lola Burke, MSIV, Scot C. Remick, MD, and Jame Abraham, MD

Mary Babb Randolph Cancer Center, Department of Medicine and School of Medicine, West Virginia University

Abstract

Purpose: The National Cancer Institute estimates that less than 5% of adult patients with cancer participate in clinical trials. This statistic has to improve in order for clinical trials to be more accurate and generalizable. Several studies have looked into the barriers to accrual among various patient subgroups. However, there are scant data regarding factors that act as barriers to accrual of rural patients. Our study aims to identify these barriers.

Patients and Methods: Among patients seen at the Mary Babb Randolph Cancer Center at West Virginia University, 1,000 were randomly selected to receive a questionnaire by mail. Data obtained consisted of demographic and clinical information, as well as awareness about clinical trials, willingness to participate, and factors influencing participation. Patients had 6 weeks to respond.

Results: Two hundred forty-one (24.1%) patients responded to the survey. Of these, 66.9% had heard about clinical trials, 19.6% reported that their health care team had discussed clinical trials, and 9.1% had participated in clinical trials. Respondents were more likely to be willing to participate in cancer prevention/screening trials than therapeutic trials. Regarding the decision not to participate in a clinical trial, patients cited discouragement from their oncologist, monetary burden, discouragement from family physician, commute, and lack of information as strongly or extremely influential factors.

Conclusion: Our findings specify the need for patient and physician education through community outreach programs. Oncologists should be trained to discuss clinical trials and to address concerns regarding their availability, utility, and accessibility. Financial counseling may play an important role in improving accrual rates as well.

Introduction

Clinical trials are increasingly defining the standards of modern health care. Therefore, it is important that these trials provide accurate information that can be generalizable to the applicable patient population. A method of increasing the power of a study is to increase the number of participants, which often proves difficult. Poor accrual of cancer patients in cancer clinical trials has been a chronic problem.[1]The National Cancer Institute (NCI) estimates that less than 5% of newly diagnosed adult cancer patients are enrolled onto clinical trials in the United States.[2-6]

Several studies have examined reasons for poor recruitment in cancer patients. Numerous factors have been identified, which are broadly divided into patient-, physician-, and protocol-related factors. Several subgroups, such as the elderly and racial/ethnic minorities, have been studied to identify particular hindrances to their accrual.[7-9]

Another important subgroup is patients living in rural areas. It is known that rural patients are more likely to be diagnosed with cancer at an advanced stage compared with their urban counterparts and are less likely to enroll onto a clinical trial.[2,10] However, little is known about the factors that prevent their accrual. This was evident from our literature search using keywords "cancer," "clinical trials," and "rural," which yielded few pertinent results. Our study aims to explore the factors that act as barriers to accrual of rural patient populations in clinical cancer trials. Once identified, steps can be taken to minimize the impact of such factors.

Patients and Methods

Data Collection

The study was conducted among cancer patients seen for diagnosis or treatment at the Mary Babb Randolph Cancer Center at West Virginia University Hospitals (Morgantown, WV) between 2001 and 2006. Written draft of the intent and proposed procedure of this study, including the questionnaire, was submitted to the West Virginia University institutional review board for review and validation. Formal approval was obtained before initiation of the study.

From all the patients seen at the facility, a list was compiled of patients who, according to clerical records, had clinical diagnoses of cancer. From this list of eligible patients, 1,000 were randomly selected and invited to participate. These patients were mailed a five-page questionnaire with a letter explaining the study. The questionnaire spanned over seven pages and consisted of 29 questions, including two Likert-scale tables; the remainder were multiple-choice questions. Participants were given 6 weeks to respond. There was no attempt made to contact nonresponders.

Data obtained in the questionnaire pertained to patient demographic information, clinical information, awareness of clinical trials, importance of clinical trials, willingness to participate, and factors affecting participation. No personal identifying information was collected or entered into the database. The demographics section included age, sex, ethnicity, level of education, and patient's ZIP code. Only categorical age data were analyzed. With regard to clinical information, we inquired about patients' subjective health status (ranging from poor to excellent), primary cancer site, stage of cancer, age at initial diagnosis, and current cancer treatment status. We also inquired about patients' insurance and key persons in health care decision making including self, family, family physicians, and friends. Respondents were allowed to mark more than one choice.

There were 13 questions regarding awareness of clinical trials. We inquired whether the respondents had heard about clinical trials in general and for their specific cancer type before receiving the survey. We further inquired whether the respondents had ever sought information or been provided information on clinical trials by their health care team and whether they were invited to participate or had participated in a cancer clinical trial. Respondents were also asked whether they were ever denied participation in a cancer clinical trial and, if so, what the reasons behind the denial were.

We asked respondents how willing they were to participate in cancer prevention/screening or a new therapeutic drug trial, with level of willingness graded from "very willing" to "not willing at all." We sought respondents' opinion regarding the ethics of cancer clinical trials and the notion that clinical cancer trials may increase their chances of living. We inquired whether or not doctors should refer patients to cancer clinical trials.

We also asked the respondents to rate how important clinical trials were to each of the following groups: oncologists and researchers, patients with cancer, people who may develop cancer, and themselves. Responses were rated on a four-point Likert scale ranging from "very important" to "not important at all."

After careful review of the clinical trials literature, we compiled a list of the 13 most commonly reported factors affecting clinical trial participation. Factors included discouragement from oncologist and family physicians, lack of discussion about clinical trials by an oncologist or family doctor, discouragement from friends and family, lack of information, prior bad experience with a clinical trial, lack of benefit, fear of adverse effects, prior denial from participation, monetary burden, excessive commute, and other medical conditions precluding participation. Respondents were asked how influential these factors were (or would be) in influencing their decision to participate in a clinical trial. Factors were rated on a five-point Likert scale ranging from "not influential at all" to "extremely influential."

Statistical Analyses

All questions had to be answered is order for the returned questionnaire to be considered analyzable and entered into the database. A total of 230 of the 241 questionnaires returned were considered eligible. Among the 11 ineligible questionnaires, reasons for exclusion included six respondents reporting that they had not been diagnosed with cancer, three questionnaires being returned because patients were deceased, and two questionnaires having missing pages.

Questionnaires were entered into the SPSS (version 14.0) database and analyzed. Statistical analyses included frequencies for categorical data and means and standard deviations (SD) for continuous data. Regression analysis was performed on some of the variables; data were analyzed with χ^2 testing after reduction into nominal variables.

Table 1. Patient Demographic Characteristics

Characteristic	No.	%
Total No.	230	
Sex		
Male	87	37.8
Female	143	62.2
Age, years		
< 45	18	7.8
45-54	38	16.5
55-64	64	27.8
65-74	53	23.0
75-84	47	20.4
> 84	10	4.3
Ethnicity		
African American	2	0.8
Hispanic/Latino	1	0.4
Native American	32	13.9
White	182	79.1
Other/unknown	13	5.6
Education		
< High school	9	3.9
High school	118	51.3
Undergraduate	53	23
Graduate	46	19.9
Other	4	1.7

Results

Of the 1,000 surveys mailed, 241(24.1%) were returned within the six-week period allowed. Of these, 230 (95.4%) were considered analyzable and were entered into the database for analysis. Respondents were 62.2% women (n = 143) and 37.8% men (n = 87). A large proportion of respondents (75.7%) were over the age of 55 years. Respondent demographics are described in Table 1.

Most respondents (67.8%) were no longer being treated for cancer; 22.6% were undergoing active treatment. Whereas some patients were not sure about their stage of cancer, a significant percentage (33.9%) reported that their cancer was in remission. Health status was self-reported as good or excellent by 44.7% of the respondents, and 29.1% rated their health as average.

The most common type of payer among respondents was government insurance (Medicare 52.2%, Medicaid 9.1%), followed by private insurance (36.5%). With respect to health care decision making, most participants reported that they themselves (83.4%), their families (67.8%), and their family doctor (61.7%) participated in their health care decisions. Table 2 lists the site, stage, treatment, and health status of the respondents as well as information about the insurance providers and key health care decision makers.

Most respondents (66.9%) had heard of clinical trials before receiving the survey. However, few (12.2%) had sought information on their own, and only 19.6% reported that their health care team discussed clinical trials with them. Previous partici-

Table 2. Health Care Information

Characteristic	No.	%
Cancer care status		
Currently being treated	52	22.6
Treated in the past	156	67.8
Other	22	9.6
Cancer type		
Skin	63	27.3
Breast	54	23.5
Prostate/bladder	22	9.5
Lymphoma	17	7.3
Leukemia	12	5.2
Ovarian	12	5.2
Lung	11	4.7
Colorectal	8	3.5
Head and neck	8	3.5
Endometrial	6	2.6
Testicular	3	1.3
Other	14	6.1
Cancer stage		
0	3	2.9
I	25	10.8
II	13	5.6
III	10	4.34
IV	12	5.2
Remission	78	33.9
Unknown	79	34.3
Other	10	4.2
Level of health		
Poor	17	7.4
Marginal	41	17.8
Average	69	30
Good	85	36.9
Excellent	18	7.8
Insurance provider*		
Medicare	120	52.2
Private	84	36.5
Self pay	38	16.5
Medicaid	21	9.1
Unknown	2	0.8
Decision makers*		
Self	192	83.4
Family	156	67.8
Family doctor	142	61.7
Friends	14	6.1
Other	9	3.9

*Respondents could choose more than one answer.

pation in clinical trials was reported by 9.1% of the respondents. Respondents had a positive outlook toward cancer clinical trials: one third thought that participating in a clinical trial would increase their chances of living, and a majority (70.4%) thought that doctors should refer patients to clinical trials. A majority (64.7%) of the respondents thought clinical trials were ethical; one third did not have a firm opinion about how ethical clinical trials are.

A majority of the respondents were at least somewhat willing to participate in a clinical trial, 70.3% in a therapeutic drug trial and 78.7% in a cancer prevention/screening trial. In a binomial regression that corrected for age, sex, and education, participants who believed that a cancer clinical trial would improve their chances of living were significantly more likely ($P < .001$) to be at least somewhat willing to participate in a clinical trial for a new cancer drug. Unfortunately, the belief that participation in clinical trials would improve the chances of living for patients with cancer did not correlate with whether or not respondents' health care providers discussed clinical trials with them.

With regard to their decision to participate in cancer clinical trials, patients cited discouragement by oncologist (59.8%), monetary burden (53.4%), discouragement by family physician (49.4%), commute (35.5%), and lack of information (35%) as strongly or extremely influential factors. Responses to these and the other factors are listed in Table 3. When asked to rate the importance of clinical trials, 92.4% of respondents rated clinical trials as being very important to oncologists and researchers, whereas 85.1% of respondents rated clinical trials as very important for patients.

Discussion

Randomized, controlled clinical trials are the research standard for evaluating the effectiveness of therapeutic interventions, because they minimize the risk of systemic errors. As mentioned above, poor accrual in cancer clinical trials has been a major cause for concern.[1]Less than 5% of the patients who receive the diagnosis of cancer participate in clinical trials.[2-6] This is especially true for the rural population. Studies have identified geographically based differences in disease stage at diagnosis, with rural patients receiving diagnosis significantly later than their urban counterparts. These differences have led to initiatives such as the Community Clinical Oncology Program (established 1985) and Reaching Communities for Cancer Care (established 1992).[11]

The US Census Bureau (2000) classifies rural areas as those located outside of an urbanized area or urbanized cluster.[12] Accordingly, 63.8% of West Virginia's population is classified as rural. Although available data suggest that rural patients are less likely to enroll onto a clinical trial compared with their urban counterparts, interestingly, 9.2% of the respondents to our questionnaire reported that they had participated in a clinical trial, which is higher than the national average.[2,10] In addition, most respondents had heard of clinical trials before receiving the survey. This could be secondary to education and counseling by the treating physicians or due to a selection bias, as the study was conducted among patients seen at a tertiary care center, who may have been referred there for consideration for enrollment onto a clinical trial for advanced disease. It is

Table 3. Factors Influencing Decision to Participate in Clinical Trials

	Not Influential at All		Not Very Influential		Moderately Influential		Strongly Influential		Extremely Influential	
Factor	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
My oncologist discouraged it	30	15.5	11	5.6	37	19.1	49	25.3	67	34.5
My oncologist did not discuss it with me	37	19.1	48	24.8	48	24.8	32	16.5	29	14.9
My family doctor discouraged it	28	16.3	15	8.7	44	25.6	49	28.5	36	20.9
My family doctor did not discuss it with me	52	30.4	34	19.9	48	28.1	19	11.1	18	10.5
Family/friends discouraged it	55	30.9	43	24.2	45	25.3	22	12.4	13	7.3
Other health problems	25	14.5	9	5.2	64	37.2	43	25.0	31	18.0
I am afraid the therapy will not work or there will be side effects	28	16.2	25	14.5	67	38.7	34	19.7	19	11.0
I don't feel there is enough benefit for me	35	20.7	33	19.5	50	29.6	35	20.7	16	9.5
I had past involvement in a clinical trial with bad outcome	58	43.6	12	9.0	21	15.8	25	18.8	17	12.8
I was previously denied participation in a clinical trial	72	56.7	21	16.5	15	11.8	9	7.1	10	7.9
I live far away from the clinic/hospital	46	29.1	23	14.5	33	20.9	30	19.0	26	16.5
Additional test costs and fee/not insured	27	16.8	15	9.3	33	20.5	42	26.1	44	27.3
I don't know enough about clinical trials	49	27.7	24	13.6	42	23.7	31	17.5	31	17.5

NOTE. Some respondents did not rate all of the above factors. Percentages were calculated on the basis of the total number of responses received.

even possible that individuals who completed the research questionnaire were more knowledgeable about and favorable toward clinical trials than those who didn't complete the questionnaire.

Most of our respondents think clinical trials are ethical, a third of the respondents think participation in clinical cancer trials may increase chances of living, and a majority think that doctors should refer patients to clinical trials when indicated. This is heartening to see, as it shows a positive outlook toward clinical cancer trials among the rural respondents.

However, our survey identified a few major barriers to participation in clinical trials, which include discouragement from oncologist/family doctors and lack of information from medical teams. Although clinicians strive to provide the best care for their patient, several studies have identified physician-related factors that affect patient accrual in cancer clinical trials. Such factors include incompatibility of the protocol with normal practice, problems with complying with the protocol, consent procedures, and/or time constraints.[3,5,11,13-18]

It has been suggested that physician barriers by could be alleviated through the use of reminders before the physician-patient encounter to discuss clinical cancer trials (eg, chart reminders, posters and brochures), allowing adequate time to discuss the study with potential participants, and flexibility with clinical scheduling.[3,5,6,11,14,16,19,20] Active engagement of nurses and certified research administrators in dispensing information improves patient understanding and hence accrual in cancer clinical trials. This may help to reduce burden on the physician in discussing clinical trials with their patients.[5,6,11,14,17]

Further, our study highlights the importance of involving primary care physicians, as they play a major role in screening for cancer—using diagnostic modalities to confirm the presence of disease—and in decision making regarding treatment options, including cancer clinical trials. Physicians, especially oncologists, should be trained to discuss clinical trial protocols and to address patient concerns regarding availability, utility, and accessibility of clinical trials as part of their training and through Continuing Medical Education.[11,16] Our study reiterated the fact that not only patients but also their family and often close friends are part of the decision-making process, as previously suggested.[16] Hence, discussions should involve family and, in appropriate instances, close friends because doing so will improve the physician-patient relationship and may positively influence willingness to participate in cancer clinical trials.

Almost half of the respondents were apprehensive regarding the additional cost associated with participating in clinical cancer trials. In two studies, Lara et al[6,11] have shown that patients with private insurance were less likely to be enrolled onto clinical trials compared with those with government-funded insurance. Although we did not find any significant correlation between the type of insurance and concern about additional cost, this is a potential area for investigation.

Availability of financial counseling can help in reducing such apprehension, thereby improving accrual.[6,11]Equally important is legislation such as California Law SB37 and a Commonwealth of Virginia Statute (SB 1235 HB 871 38.2-3418, 1999) requiring third-party payers to reimburse patient care costs related to cancer clinical trials.[20,21] Similarly, federal regulations such as the clinical trial coverage provision of the Patient Protection and Affordable Care Act (2010) can be of vital importance in improving participation in cancer clinical trials.[22]

Limitations

We surveyed patients who are being observed at a tertiary care center in West Virginia. A much larger and diverse study is needed for better representation of the rural population. Further, despite a good sample size, the questionnaire response rate was low. Some of the questions used a Likert scale, which has its own limitations.

A larger number of our respondents had participated in a clinical trial as compared with the national average. This could be a selection bias, as it is possible that some patients who were already on a clinical trial were referred to a tertiary care center for a second opinion or that patients were referred primarily for enrollment onto a clinical trial for advanced disease. It is also possible that the barriers to accrual in clinical trials are different for rural patients as compared with their urban counterparts. Perhaps, a larger controlled study is warranted to delineate such differences.

We noted that a larger proportion of our respondents had received higher education as compared with the state average. This could be because our immediate drawing area includes Morgantown, WV, which is a university town. Also, 13% of our respondents identified themselves as Native American, a proportion that is considerably higher than the US Census data for West Virginia (2000). This could possibly be due to the broad definition of the term "Native American" or perhaps due to migration, although less likely.

Summary

Our findings specify the need for patient education through community outreach programs and through educating physicians about cancer clinical trials. Physicians, especially oncologists, should be trained to discuss clinical trial protocols and to address patient concerns regarding availability, utility, and accessibility of clinical trials. There is a need for a concerted team effort involving physicians (primary care physicians and clinical oncologists), nurses, and certified research administrators in imparting knowledge about cancer clinical trials. Where appropriate, families and close friends should be part of the discussion, as they often play significant roles in health care decision making. Financial counseling may play an important role in improving accrual rates. In addition, legislative and public health policies should be formulated to support the cost associated with participating in clinical cancer trials.

Accepted for publication on December 17, 2010.

Acknowledgment

Supported by the Mary Babb Randolph Cancer Center, West Virginia University. Presented in part at the 44th Annual Meeting of the American Society of Clinical Oncology May 30-June 3, 2008, Chicago, IL, and at the Translational Research Cancer Center Consortium Meeting, February 21-22, 2008, Morgantown, WV.

Authors' Disclosures of Potential Conflicts of Interest

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: None **Consultant or Advisory Role:** Jame Abraham, Genentech (C) **Stock Ownership:** None **Honoraria:** Jame Abraham, Genentech **Research Funding:** None **Expert Testimony:** None **Other Remuneration:** None

Author Contributions

Conception and design: Shamsuddin Virani, Scot C. Remick, Jame Abraham

Administrative support: Jame Abraham

Provision of study materials or patients: Jame Abraham

Collection and assembly of data: Shamsuddin Virani, Lola Burke, Jame Abraham

Data analysis and interpretation: Shamsuddin Virani, Lola Burke, Scot C. Remick, Jame Abraham

Manuscript writing: Shamsuddin Virani, Scot C. Remick, Jame Abraham

Final approval of manuscript: Shamsuddin Virani, Lola Burke, Scot C. Remick, Jame Abraham

Corresponding author: Jame Abraham, MD, Mary Babb Randolph Cancer Center, P.O. Box 9300, Morgantown, WV 26506-9300; e-mail: Jabraham@hsc.wvu.edu.

DOI: 10.1200/JOP.2010.000158

References

1. Dilts DM, Sandler AB, Cheng SK, et al: Steps and time to process clinical trials at the cancer therapy evaluation program. J Clin Oncol 27:1761-1766, 2009

2. Sateren WB, Trimble, E, Abrams J, et al: How socio-economic, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. J Clin Oncol 20:2019-2117, 2002

3. Kornblith AB, Kemeny M, Peterson B, et al: Survey of oncologist's perception of barriers to accrual of older patients with breast carcinoma to clinical trials. Cancer 95:989-996, 2002

4. Kemeny MM, Peterson BL, Kornblith AB, et al: Barriers to clinical trial participation by older women with breast cancer. J Clin Oncol 21:2268-2275, 2003

5. Go RS, Frisby KA, Lee JA, et al: Clinical trial accrual among new cancer patients at a community-based cancer center. Cancer 106:426-433, 2006

6. Lara PN Jr, Higdon R, Lim N, et al: Prospective evaluation of cancer clinical trial accrual patterns: Identifying potential barriers to enrollment. J Clin Oncol 19:1728-1733, 2001

7. Grann VR, Jacobson JS, Troxel AB, et al: Barriers to minority participation in breast carcinoma prevention trials. Cancer 104:374-379, 2005

8. Paterniti DA, Chen MS Jr, Chiechi C, et al: Asian Americans and cancer clinical trials. Cancer 104:3015-3024, 2005

9. McCaskill-Stevens W, Pinto H, Marcus AC, et al: Recruiting minority cancer patients into cancer clinical trials: A pilot project involving the Eastern Cooperative Oncology Group and National Medical Association. J Clin Oncol 17:1029-1033, 1999

10. Gross CP, Filardo G, Mayne ST, et al: The impact of socioeconomic status and race on trial participation for older women with breast cancer. Cancer 103: 483-491, 2005

11. Paskett ED, Cooper MR, Stark N, et al: Clinical trial enrollment of rural patients with cancer. Cancer Practice 10:28-35, 2002

12. US Census Bureau. Census 2000 Urban and Rural Classification. http://www.census.gov/geo/www/ua/ua_2k.html

13. Tattersall M: Cancer clinical trial recruitment. Cancer 95:1397-1400, 2002

14. Tournoux C, Katshaian S, Chevret S, et al: Factors influencing inclusion of patients with malignancies in clinical trials. Cancer 106:258-270, 2006

15. Townsley C, Chan K, Pond G, et al: Understanding the attitudes of the elderly towards enrolment into cancer clinical trials. BMC Cancer 6:34, 2006

16. Townsley CA, Selby R, Siu LL, et al: Systematic review of barriers to the recruitment of older patients with cancer onto clinical trials. J Clin Oncol 23:3112-3124, 2005

17. Mansour EG: Barrier to clinical trials. Cancer 74:2672-2685, 1994

18. Giuliano AR, Mokuau N, Hughes C, et al: Participation of minorities in cancer research: The influence of structural, cultural, linguistic factors. Ann Epidemiol 10:S22-S34, 2000

19. Pinto HA, McCaskill-Stevens W, Wolfe P, et al: Physician's perspective on increasing minorities in cancer clinical trials: An Eastern Cooperative Oncology Group (ECOG) initiative. Ann Epidemiol 10:S78-S84, 2000

20. Lara PN Jr, Paterniti DA, Chiechi C, et al: Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials. J Clin Oncol 23:9282-9289, 2005

21. Hillner BE: Barriers to clinical trial enrollment: Are state mandates the solution? J Natl Cancer Inst 96:1048-1049, 2004

22. H.R. 3590, Patient Protection and Affordable Care Act. http://democrats.senate.gov/reform/patient-protection-affordable-care-act-as-passed.pdf