

**Adult Cancer Clinical Trials
in the Community Setting:
A Baseline Study to Examine
Patient Accrual**

Final Report

February 14, 2005

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Introduction

Access and enrollment to cancer clinical trials is a complex issue, and only an estimated 3 percent of adult cancer patients participate in clinical trials.¹ Obtaining representative participation is especially complex. In the early to mid 1990s, the number of minorities enrolled remained relatively stable, while enrollment of whites increased, and most patients came from higher socioeconomic areas of the country.²

Factors related to enrollment to cancer trials have been studied extensively, with particular focus on incentives and barriers both for patients and oncologists. For patients, the most common reasons for participating are hope for a better treatment outcome and altruism. Multiple barriers range from lack of knowledge and understanding, to concerns about costs and insurance problems, to additional travel and time commitments.^{2, 3, 4}

For many practicing and hospital-based oncologists, disincentives to participate continue to outweigh benefits. Common concerns are stringent protocol requirements, overall monetary costs, and time.^{5, 6} One study of cancer cooperative group physicians found that 80 percent of the patients enrolled from community hospitals were entered by only 10 percent of the active investigators.⁷

It is within this environment of clinical trials that the Medicare Prescription Drug, Improvement and Modernization Act (MMA) of 2003 is functioning. Further, within this environment, participation in clinical trials among community physicians will continue to be critical. The community oncologist is considered to play a key role in advancing cancer care through clinical trials.

Numerous professional, advocacy, and government organizations support and advocate involvement in clinical trials by community physicians. The National Cancer Institute (NCI), the American Society of Clinical Oncology, and the Coalition of National Cancer Cooperative Groups, for example, have funded studies looking at the issues surrounding trials and have implemented special initiatives such as NCI's Community Clinical Oncology Program. Many of these same organizations are now concerned that the impact of MMA may bring further disincentives and limited capabilities for oncologists to conduct trials, particularly in the community setting. Fewer clinical sites and fewer participants may be the end result.

In an effort to better understand and begin assessing the impact of Medicare reform, and other factors, on patient accrual to cancer clinical trials in the community setting, we conducted a descriptive baseline study on patient accrual for the four most common adult cancers in the U.S. -- breast cancer, prostate cancer, colorectal cancer, and lung cancer.

The primary purpose of the study was to assess the distribution of and level of patient accruals to clinical trials of investigational cancer care in the community setting as compared to other settings, primarily academic centers. The results of this study will contribute to future research to ascertain and assess trends in access and accruals to trials

in the community setting that could be attributed to changes to the Medicare program or other variables.

Specific research questions examined by the study were:

1. What is the relative distribution of trials conducted in the **community setting** as compared to other settings?
2. What is the distribution of patient accruals in trials conducted in the **community** as compared to other settings?
3. What are the sociodemographic characteristics of **community based** participants?

Methods

Study Inclusion Criteria

Because the universe of public and private adult cancer treatment trials is so broad and because of limitations in accessing confidential patient accrual data not publicly available, we used a set of a priori inclusion criteria to narrow the scope of the set of trials examined in this study. First, the scope of the trials were limited to U.S.-based Phase II and Phase III treatment trials for the four cancers with the highest incidence and mortality rates (breast, prostate, colon, and lung) in the adult population.⁸ These four cancer types (see Table 1) accounted for about 53 % of an estimated 1.37 million new cancer cases in the U.S. in 2004.

Table 1. Estimated New Cancer Cases in U.S. in 2004

Cancer Type	Number	Percent of All Cancer Cases
Prostate	230,110	16.8
Breast	217,440	15.9
Lung	173,770	12.7
Colon	106,370	7.8

Source: American Cancer Society, 2004

Second, because the study was intended to provide a baseline snapshot of clinical trials in community and academic settings, we limited the study to trials closed to enrollment in 2003. Thus, the study summarizes a select group of trials that ended prior to the enactment of MMA.

Third, because this was a small-scale study, trials were limited to those sponsored by NCI, the Federal government's lead agency for cancer biomedical research. These trials are conducted by academic researchers and community based oncologists around the U.S. in cancer centers, academic or teaching hospitals, and community hospitals and practices.

For purposes of this study, initially the community setting was defined as any site participating in NCI's Community Clinical Oncology Program (CCOP) or Minority-

based CCOP (MBCCOP). In short, CCOP and MBCCOP sites are groups of hospitals and/or private practices that apply for and receive grants for their participation in NCI-sponsored clinical trials. The CCOP program is a mechanism for disseminating cancer prevention and treatment research findings to the community level. Other settings were defined as non-CCOP and non-MBCCOP sites, which are primarily academic medical centers participating in NCI Cooperative Groups.

After closer review, we determined that CCOPs/MBCCOPs represent only a fraction of the universe of community sites. Specifically, most of the Cooperative Group systems collect and report data in three categories: CCOPs/MBCCOPs, academic institutions, and academic community based affiliates. Under this classification system, these affiliate sites represent more than half of the community sites. Therefore, the concept of community based sites was broadened to include CCOP, MBCCOP, and community based affiliates, with the definition being all community based private oncology practices or community hospitals conducting clinical trials. All other sites were classified as academic settings. Of note is the finding that NCI does not routinely collect and monitor data for these community sites collectively. Rather their centralized database only categorizes sites as CCOP/MBCCOP or Cooperative Group.

Data Collection

Secondary data analyses were conducted on an analytic dataset created with information derived from existing primary data sources. We used a four-step process to develop an analytic dataset of representative clinical trials meeting the inclusion criteria outlined above. To the extent possible, we maximized the use of publicly available clinical trials data.

In the first step, we conducted exhaustive searches of Physician Data Query (PDQ^R), NCI's comprehensive cancer clinical trials database, to identify and retrieve relevant trials and extract available required analytic data fields. Access provided by NCI to PDQ's back-end database, enabled the extraction of additional data fields not available through the publicly available PDQ. A sample of 88 protocols appearing to meet all of the study inclusion criteria was identified and retrieved from the database.

In step two, additional information, such as site location not found in PDQ was extracted from ClinicalTrials.gov, the federally sponsored website that provides public access to up-to-date information on federally and privately supported clinical trials for a wide range of diseases and conditions.

Third, NCI provided an additional set of trial- and site- specific data elements needed for analysis, but not available from PDQ or ClinicalTrials.gov. Specifically, we requested and received the data through a Freedom of Information Act (FOIA) request to NCI, which required this request/process because of the confidential nature of the data. Table 2 outlines the data elements requested of NCI:

Table 2. Trial- and Site- Level Analytic Data Elements

Trial-level	Site-level
PDQ Protocol Number	Site Organization Name
Cancer Type	Site City
Phase II or Phase III Trial Indicator	Site State
Accrual Start Date	Site Census Region
Accrual End Date	CCOP Indicator
Number of Sites	Minority-based CCOP (MBCCOP) Indicator
Length of Overall Enrollment Period in Days	Accrual Breakdown by: <ul style="list-style-type: none"> • Gender of Participants • Ethnicity of Participants • Race of Participants
Target Accrual Number	
Actual Accrual Number	

NCI provided an Excel file containing the combined protocol- and site-level information, which we converted to a SAS file for analysis. Trial-level and site-level information were linked through the PDQ Protocol Number. Data provided by NCI was also used to validate data retrieved from PDQ and ClinicalTrials.gov.

As noted, because the NCI data did not separate out all community based trials, as a final step, we consulted with staff at the Coalition of National Cancer Cooperative Groups and Eastern Cooperative Oncology Group to verify the definition and classification of all community based sites.

Analysis

The scope of the analyses were to compare and summarize available empirical data on the prevalence of cancer clinical trials in community settings (in comparison to other settings), their pre-2004 accrual rates, and characteristics of patients accrued to those trials in community settings. All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, N.C.). Results are summarized for each of the four cancer types (colon, lung, breast, and prostate). Percentages may not sum to 100 due to rounding.

Results

NCI located and provided data for 60 of the protocols through the ID numbers we submitted. After reviewing the NCI data, we eliminated an additional 15 trials from the sample because they did not fully meet our criteria. Consequently, subsequent analyses were restricted to a final sample of 45 trials that closed in 2003 (see Table 3). Thus, the trials in this sample included trials conducted through the Cooperative Groups systems, major cancer centers, and at the NCI.

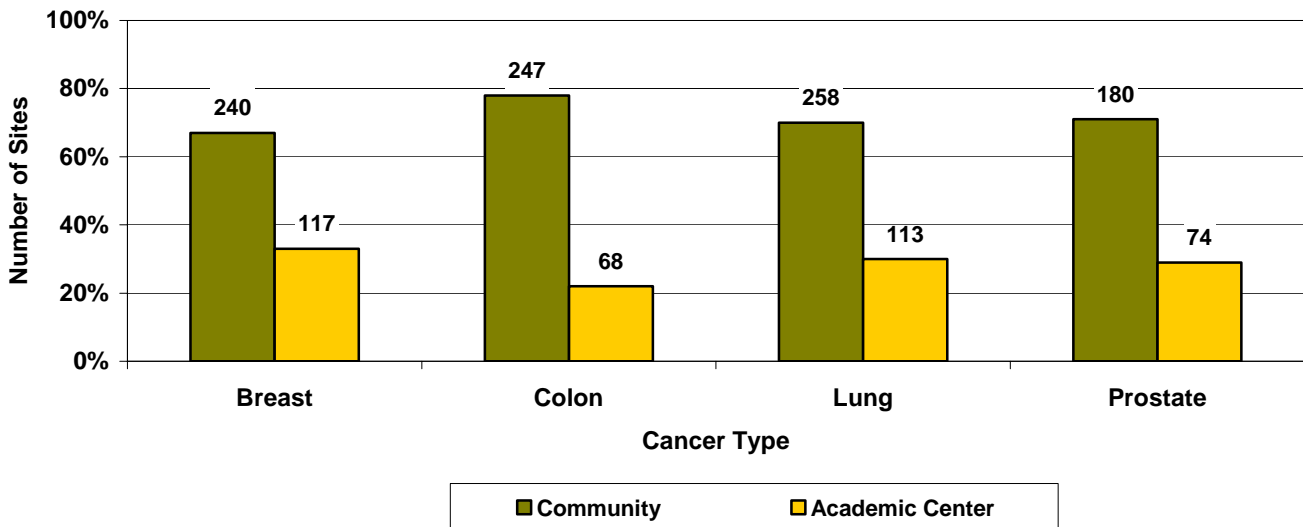
Table 3. Distribution of Trials by Cancer

Cancer	Number of Trials
Breast	12
Colon	7
Lung	16
Prostate	10
Total	45

Distribution of Sites and Trials in Community and Other Settings

Descriptive analyses revealed that 577 unique clinical sites participated in the 45 clinical trials. Of the 577 sites, 452 (78%) were community based and 125 (22%) were academic setting sites. Almost ¾ of the community based sites were community based affiliate sites (326, 72%) with the remaining sites representing CCOP and MBCOP sites (126, 28%). Figure 1 profiles the distribution of sites by cancer type and setting.

Figure 1. Distribution of Sites by Cancer Type and Setting

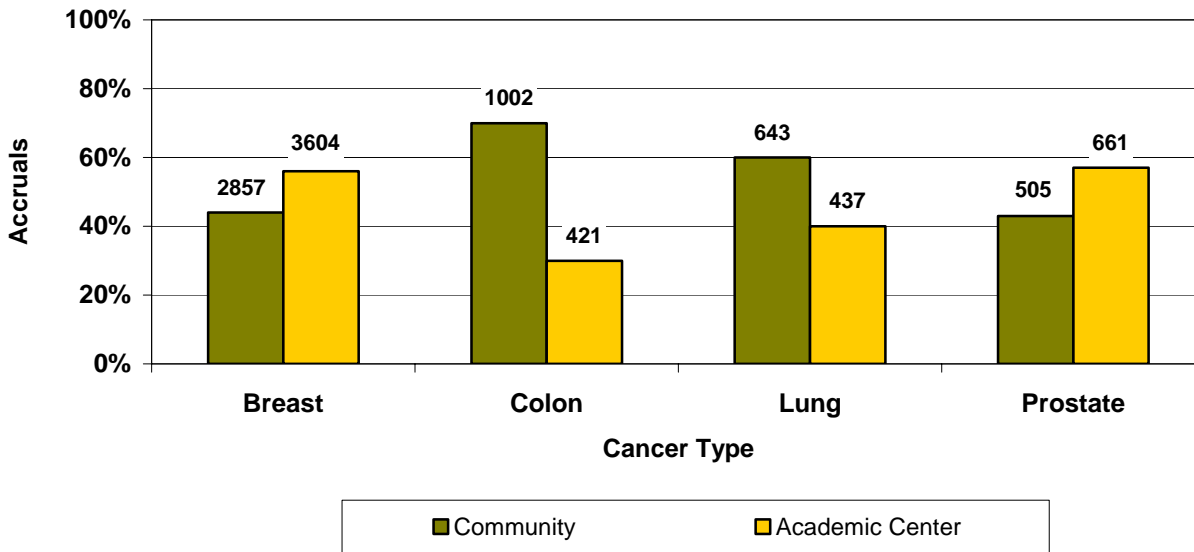


Distribution of Patient Accruals in Community and Other Settings.

Figure 2 compares accruals at community sites to accruals in academic settings by each cancer type. Overall, 10,130 participants were accrued to this set of 45 clinical trials. 5,007, or 49%, of the accruals occurred in the community setting, as compared to 5,123,

or 51%, from academic settings. Accruals to breast and colon cancer trials accounted overall for 77% of total community based accruals. However, the highest percentages of community patients by cancer type trials were accrued in colon and lung cancers, 70% and 60% respectively. Breast and prostate cancers followed with 43% and 44%.

Figure 2. Patient Accruals by Cancer Type and Setting



Sociodemographic Characteristics for Patients in Community based Trials

Site-level data allowed for characterization of patients participating in clinical trials in both community based and other settings. As shown in Table 4, patient populations were examined by four demographic characteristics: ethnicity, race, gender, and geographic location.

Of the total 5,007 community patients the vast majority were white (88%), 7% were African American and 3% Latino. Overall, the percentage of blacks at community sites (7%) is significantly lower than that at academic sites (11%) [Fisher’s exact test, $p < 0.0001$]. Both of these percentages are lower than the 12% of blacks in the U.S. population⁹.

Female patients comprised 70% of the community based accruals for the 45 trials. These numbers are skewed by the fact that so many women were enrolled in one breast cancer trial (Protocol ID=ACOSOG-Z0010). For non-gender specific colon cancer and lung cancer trials, the percentage of female patients (41% and 46%, respectively) at community sites is somewhat less than the percentage of females (51%) in the U.S. population.¹⁰

The findings by U.S. Census region illustrate the large percentage of community based sites in the Midwest (35%) and South (27%), followed by the Northeast (25%) and West (13%). Community patient accruals follow the same trend: 40% in the Midwest; 36% in the South, 15% in the Northeast, and 9% in the West.

Table 4. Demographics by Cancer Type and Setting

	Cancer Type																Total				Total	
	Breast				Colon				Lung				Prostate									
	Comm Site		Academic Site		Comm Site		Academic Site		Comm Site		Academic Site		Comm Site		Academic Site		Comm Site		Academic Site			
	n	%	N	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Ethnicity																						
Hispanic or Latino	77	3	73	2	28	3	19	5	6	1	5	1	17	3	42	6	128	3	139	3	267	3
Not Hispanic or Latino	2756	96	3488	97	957	96	394	94	623	97	421	96	488	97	612	93	4824	96	4915	96	9739	96
Not Reported/Unknown	24	1	43	1	17	2	8	2	14	2	11	3	0	0	7	1	55	1	69	1	124	1
Race																						
American Indian or Alaska Native	3	<1	3	<1	5	1	4	1	3	<1	0	0	1	<1	0	0	12	<1	7	<1	19	<1
Asian	47	2	86	2	14	1	7	2	6	1	5	1	5	1	12	2	72	1	110	2	182	2
Black or African American	216	8	354	10	62	6	36	9	29	5	78	18	53	11	87	13	360	7	555	11	915	9
Native Hawaiian or Other Pacific Islander	6	<1	4	<1	0	0	0	0	1	<1	0	0	0	0	1	<1	7	<1	5	<1	12	<1
White	2488	87	3051	85	878	88	349	83	592	92	348	80	442	88	553	84	4400	88	4301	84	8701	86
More than One Race	0	0	1	<1	0	0	0	0	1	<1	0	0	0	0	0	0	1	<1	1	<1	2	<1
Not Reported/Unknown	97	3	105	3	43	4	25	6	11	2	6	1	4	1	8	1	155	3	144	3	299	3
Gender																						
Female	2809	98	3531	98	414	41	167	40	298	46	198	45	0	0	0	0	3521	70	3896	76	7417	73
Male	40	1	68	2	587	59	251	60	345	54	239	55	505	100	661	100	1477	30	1219	24	2696	27
Unknown	8	<1	5	<1	1	<1	3	1	0	0	0	0	0	0	0	0	9	<1	8	<1	17	<1
Region																						
Midwest	872	31	1081	30	544	54	198	47	368	57	203	46	224	44	127	19	2008	40	1609	31	3617	36
Northeast	431	15	378	10	182	18	84	20	81	13	51	12	61	12	124	19	755	15	637	12	1392	14
South	1341	47	1423	39	208	21	82	19	125	19	101	23	142	28	232	35	1816	36	1838	36	3654	36
West	213	7	722	20	68	7	57	14	69	11	82	19	78	15	178	27	428	9	1039	20	1467	14
Total	2857	100	3604	100	1002	100	421	100	643	100	437	100	505	100	661	100	5007	100	5123	100	10130	100

Discussion

Overall, the results of this study provide informative, descriptive, snapshot information about the prevalence of and level of patient accrual to U.S.-based, NCI-funded adult cancer treatment clinical trials conducted in the community setting as compared to the academic setting.

Study results revealed that for the protocols examined, the majority, almost 78%, of the unique 577 adult cancer clinical trial sites were in the community setting. For each of the four cancer types examined, at least 2/3 of the clinical trial sites were in the community setting, ranging from 67% for breast cancer to 78% for colon cancer.

When patient accrual rates were examined, 49% of the total 10,130 (5,007) patient accruals across our study sample were in the community setting. With colon cancer and lung cancer, approximately 1/3 of the patient accruals occurred in the community setting.

When the sociodemographic characteristics of participants were examined, as may be expected, the vast majority of cancer clinical trial participants were white and non-Latino. Minorities, including African Americans and Latinos are underrepresented in the clinical trials in general, and more so at the community based sites.

In terms of geographic location, most community based sites were located in the Midwest and South. In fact, 76% of community based accruals occurred in these two Census regions.

In sum, this study presents a set of baseline information on patient accrual and the socio-demographic characteristics of community based sites that will contribute to future research designed to examine patterns of changes in the levels of clinical trials and accrual rates in the community setting attributable to changes in Medicare and other variables.

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