Community Clinical Oncology Program Participation in the Breast Cancer Prevention Trial: Factors Affecting Accrual

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Abstract
Cancer prevention and control involves a diverse spectrum of activities that range from preventing the disease to providing rehabilitation to its survivors. The range of activities included within the definition of cancer prevention and control makes it difficult to determine factors that would predict accrual to specific cancer prevention and control trials. The participation of 36 CCOP organizations in the National Cancer Institute-sponsored Breast Cancer Prevention Trial (BCPT) presented the opportunity to assess the ability of Community Clinical Oncology Program (CCOPs) to enroll subjects in one of the nation’s first large-scale cancer prevention trials and to compare characteristics of CCOP accrual to the BCPT with factors associated with accrual by CCOPs to cancer treatment and other cancer prevention and control clinical trials. Although representing only 13% of participating health care organizations, CCOPs presently contribute nearly 30% of total BCPT accrual. Comparison of regression models representing accrual to treatment, cancer control, and chemoprevention (i.e., BCPT) protocols shows similar predictors between treatment and chemoprevention models. Cancer control models, however, did not share similar predictors. Thus, accrual to chemoprevention trials is associated, to a greater extent, with the characteristics that facilitate accrual to treatment trials rather than to cancer control trials. Results have implications for the planning and ongoing management of cancer treatment, control, and chemoprevention clinical trials.

Introduction
Cancer prevention and control research, a relatively new undertaking in oncology, has been defined as “the reduction of cancer incidence, morbidity, and mortality through an orderly sequence from research on interventions and their impact in defined populations to the broad, systematic application of the research results and includes research on cancer prevention and early detection” (1). Studies involving symptom management, behavioral interventions such as smoking cessation, early detection and screening, and chemoprevention all are within the realm of cancer control research. Thus, cancer control can be viewed as encompassing a diverse spectrum of activities that range from preventing the disease to providing rehabilitation to its survivors.

The range of activities included within the definition of prevention and control makes it difficult to determine factors that would predict accrual to specific cancer prevention and control trials (2). For example, do the same factors that predict accrual to treatment protocols also predict accrual to various types of cancer prevention and control trials? Prior analyses suggest that they do not (3). Unlike cancer treatment trials, cancer prevention and control research often requires access to individuals who are not in immediate need of medical care and may not have regular contact with a health care provider; thus, they fall outside the established bounds of the clinical trials network. In addition, successful participation in cancer prevention and control trials may be predicated on the establishment of linkages with primary care physicians who have greater access to the types of participants such trials may require. Finally, the number of subjects required to conduct a cancer prevention and control trial may be substantially greater than that necessary for the typical treatment trial due to reliance on cancer incidence as the end point for determining efficacy, as well as the greater statistical power needed to detect differences between treatment and control groups. These characteristics of cancer prevention and control research may place increased demands on participating organizations, particularly with respect to personnel resources. Recognizing the new and different challenges faced by clinical researchers in conducting cancer prevention and control trials, the NCI has focused efforts on developing a network of experienced researchers (4).

Participation in cancer prevention and control trials by organizational members of the CCOP has been mandated since 1987. The CCOP, a component of the NCI’s clinical trials network, was established in 1983 as an effort to conduct research available to cancer patients in their local communities, where an estimated 80% of cancer patients are treated (5, 6). The CCOP is comprised of three entities: (a) the NCI’s Divi-
CCOP Participation in the BCPT

Fig. 1. Location of CCOP organizations participating in the BCPT. Produced by the North Carolina Rural Health Research Program, Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill. 6/3/94.

The participation of CCOP organizations in the NCI-sponsored BCPT presented an opportunity to test the hypothesis that chemoprevention trials such as the BCPT are likely to be located on the treatment end of the cancer control spectrum because they employ clinical interventions that build on the traditional patient-physician relationship (7). Cancer prevention and control protocols are usually targeted at individuals who are not in need of immediate medical care. Chemoprevention studies, however, as a type of cancer prevention and control involve administration of chemical agents with the potential to slow the progression of cancer in humans, are targeted at high-risk individuals; thus, they are consistent with the more traditional patient-physician model associated with treatment (8).

A randomized clinical trial currently in progress in the United States and Canada, the BCPT is designed to assess whether the chemoprevention agent tamoxifen significantly reduces breast cancer incidence in women evaluated to be at high risk of developing the disease. Women enrolled in the BCPT must have a risk of developing breast cancer that is at least twice that of the general population (9). Every day for 5 years, approximately 16,000 participants will ingest either tamoxifen or placebo. Over the course of the study, they will be carefully monitored for toxicity, compliance, side effects, quality of life impacts, and other important clinical events, requiring frequent contact with health care providers. Many of the women recruited to the BCPT are identified through close relatives with breast cancer or the screening of biopsy or mammography records (10). The purpose of this paper is to: (a) assess the ability of CCOPs to accrue participants to the BCPT; and (b) compare the characteristics of CCOP accrual to the BCPT with the characteristics associated with CCOP accrual to cancer treatment and other cancer prevention and control clinical trials.

Materials and Methods

Data for this analysis are derived from two primary sources: (a) a larger evaluation of the CCOP program conducted by the Cecil G. Sheps Center for Health Services Research of the University of North Carolina and its subcontractor, the Survey Research Laboratory of the University of Illinois (Chicago, IL), under a contract from the NCI Division of Cancer Prevention and Control (11); and (b) BCPT accrual data supplied by the NSABP, the research base acting as the coordinating center for the trial. Data were obtained from CCOP grant applications, annual progress reports, a mail survey of key informants, and accrual databases.

Thirty-six CCOP organizations, which were part of the University of North Carolina evaluation, are participating in the BCPT. Fig. 1 shows the geographic locations of the participat-
ing CCOPs, which represent 13% of the health care organizations enrolling women in the BCPT. The analysis presented in this paper evaluates the BCPT accrual performance of as well as compares factors predictive of accrual by these 36 CCOPs for three types of protocols: (a) cancer treatment; (b) cancer control; and (c) chemoprevention, as represented by the BCPT.

The ability to enroll patients on NCI-approved research trials is an important indicator of individual CCOP performance. A credit or weight is assigned by the NCI for each patient enrolled to measure overall performance by CCOP organizations. Accrual credits earned per CCOP for patient enrollment on cancer treatment and cancer control research protocols during Phase II of the CCOP program (1987–1990) and accrual credits per CCOP for patient enrollment in the first 15 months of the BCPT are the dependent variables in the analysis. Data describing the CCOPs were gathered in 1990 and are used in the explanatory variables. Subanalyses of these data with baseline data for CCOPs participating in the BCPT indicated considerable stability in baseline characteristics, such as principal investigator tenure, research base affiliations, and component structure.

Models
Explanatory variables of interest included an array of structural, process, and environmental characteristics of the CCOP organizations. Fig. 2 presents a schematic outline of the major variable sets: the structure and process of the CCOP, the community within which it functions, and its interorganizational relationships.

The small sample size (n = 36) precluded the incorporation of all variables in a single model. Therefore, hierarchical regression modeling in which separate ordinary least squares regression models were constructed for structure, process, and environmental variables was used. Statistically significant variables from each model were then incorporated within a final integrated model. All regression models were subjected to rigorous diagnostic testing, including checks for appropriate functional form, multicollinearity, heteroscedasticity, specification error, and outliers. Detailed descriptions of explanatory variables used in the analysis are provided below.

Community Health Care Resources Environment
The patients, personnel, and facilities required by the participating CCOPs are made available by the local health care environment. The four indicators representing the local health care environment reflect the importance of a population base sufficiently large to provide eligible participants for enrollment in protocols, as well as the recognition that the practice of state-of-the-art medicine requires an infrastructure that provides at least a minimal set of resources to support the required activities of the CCOP. The indicators are potential patient market share, health care resources, rural versus urban location, and cancer incidence rate.

Potential Patient Market Share. The proportion of the patient market (i.e., the number of new cancer cases in a service area in a given year) to which a CCOP has access and the percentage of these cases being treated in CCOP-affiliated hospitals is a measure of the extent to which the CCOP organization provides coverage to its service area. Penetration of the service area increases the CCOP’s opportunity for accessing women within their local community.

Health Care Resources. To what extent does the CCOP’s local community provide the resources necessary for effective performance? This variable is measured by a population and distribution scaled index of population density, medical personnel (i.e., nurses), and medical facilities (i.e., medical schools and short-term general hospitals) in the CCOP’s service area. Data were taken from the Bureau of Health Professions Area Resource File.

Rural versus Urban Location. The definition of rural or urban location represents a continuum along which there is little agreement except at the extremes (12). However, along this continuum the challenges involved in the provision of health services, as well as the ability to assure access to state-of-the-art technology, differ. Although development of a CCOP provides an organizational mechanism to facilitate rural community access to state-of-the-art care, CCOPs located in rural areas may have greater difficulty in accruing patients to clinical trials. Data for this dichotomous variable were taken from the Area Resource File and reflect the percentage farm population in the CCOP service area.

Cancer Incidence Rate. CCOPs located in communities with higher cancer incidence rates may demonstrate greater accrual performance. Both census and Area Resource File data were used to construct this measure.

Interorganizational Environment
The CCOP’s relationships with the NCI, as well as its research base affiliates, provide a link to the larger research community. These linkages set the requirements and expectations to which
the CCOP must conform (13–15). The interorganizational environment is represented by three indicators, such as research base activity, agreement with NCI policy, and prior experience with CGOP.

**Research Base Activity.** Interaction between research bases and CCOPs involves more than the flow of protocols and accrual of patients, requiring the participation of CCOP physicians, nurses, and data managers in research base activities (16). The activity level of nurses was selected as an indicator of CCOP research base activity because of the critical role of nurses in identifying potential enrollees and alerting physicians to appropriate available protocols. The variable is measured by the total number of CCOP nurses attending one or more research base meetings each year. Data are taken from CCOP annual reports.

**Agreement with NCI Policy.** The primary function of the NCI in the CCOP clinical trials network is administrative oversight and the establishment of specific policies and guidelines for operation. The extent to which the attitudes and goals of key CCOP personnel concur with NCI program goals may facilitate CCOP activities, whereas disagreement over goals and policy may interfere with protocol accrual (17). An additive index of the level of agreement with general NCI program policy and administration is used to measure this variable. Data are taken from the Key Informant Survey.

**Prior Experience with CGOP.** The added experience of particular CCOP organizations in the NCI clinical trials network before establishment of the CCOP program as participants in the NCI-sponsored CGOP may predict a higher level of performance in subsequent protocol accrual under CCOP. This variable is a dichotomous indicator of whether the CCOP organization was a CGOP participant.

**Structure and Process**

Both structure and process are considered important components of professional behavior in the study of health services organizations. Structure and process provide the basic mechanics for achieving goals and accomplishing tasks. Dimensions of CCOP structure and process with the capacity to influence the accrual process are represented in five indicators, such as organizational size, organizational complexity, managerial control, staff allocation, and internal conflict.

**Organizational Size.** Size is often considered a major determinant of an organizational structure that influences performance through “economies of scale” and is recognized as a surrogate for resource availability (18, 19). Larger CCOPs may have greater flexibility in obtaining and allocating resources and, therefore, enhanced performance. Thus, a large number of formal components of a CCOP organization (i.e., the number of participating hospitals and/or group practices) may increase referrals to clinical trials and, therefore, facilitate accrual. CCOP size is measured by the number of hospital and group practice components formally participating in the CCOP.

**Organizational Complexity.** CCOP consists of both internal relationships (i.e., relationships among participating physicians, hospitals, and health maintenance organizations), as well as external relationships with research bases. The number and types of groups and individuals involved in both internal and external relations reflect a diversity that influences the management of the CCOP and its ability to accrue patients to clinical trials. Greater complexity may result in greater accrual performance. In this analysis, complexity is represented by two measures: (a) the number of medical specialties represented in the CCOP organization; and (b) the number of research base affiliations maintained by the CCOP.

**Managerial Control.** As the complexity of the CCOP organization increases, so does the challenge to successfully integrate the various components so that accrual performance is facilitated. Two structural mechanisms associated with managerial control are the degree of formalization within a CCOP and the extent to which decision making is centralized. Formalization refers to the extent to which rules and procedures are used to guide the CCOP’s activities, whereas centralization denotes the degree of control exercised over the organization’s decisions and daily activities by one individual or a small group of individuals. The appropriate level of formalization and centralization within an organization depends on the nature of the task being performed (20, 21). We hypothesize that greater formalization and centralization in the CCOP organization will facilitate protocol accrual. Data for the managerial control variables were derived from items on the Key Informant Survey.

**Staff Allocation.** Allocation of CCOP personnel to specific tasks is an important component of program performance. The CCOP’s ability to maximize accrual should be enhanced through the adequate staffing of key positions. We believe that allocation of data managers is critical to CCOP performance. Data managers are responsible for interfacing with research bases in the process of patient enrollment, as well as maintaining accurate records of patient treatment. The total number of hours/week worked by data managers in a CCOP was used as the measure of staff allocation. Data were obtained from CCOP annual reports.

**Internal Conflict.** The extent to which there is conflict among key members of the CCOP organization may negatively impact accrual performance. Data from the Key Informant Survey were used to construct an index measuring internal conflict.

**Results**

Results from descriptive analyses of 15 months of BCPT accrual data showed the 36 CCOPs collectively to be substantial contributors of subjects. These 36 CCOPs represent 13% of participating health care organizations, yet presently account for nearly 30% of total accrual. An average of 57.2 participants were enrolled per CCOP. Over the 15-month period, accrual per CCOP ranged from a low of 14 to a high of 180 subjects.

Results from ordinary least squares estimation of 12 regression models of CCOP structural and environmental characteristics are presented in Tables 1–4. A process model also was estimated but is not reported here because of poor model fit among all three dependent variables. Parameter estimates, standard errors, F statistics, and adjusted $r^2$ values are listed for each model. Table 1 shows results of models representing the CCOP’s community environment or relationships with NCI and research base affiliates. All three models demonstrate
adequate fit. Research base activity is the statistically significant predictor for both treatment and chemoprevention accrual but not for cancer control accrual. Prior experience in the NCI’s CGOP program and agreement among key CGOP members with NCI general policy toward the CCOP program are positive predictors of cancer control protocol accrual. Fifty-five % of the variance in treatment accrual is explained by the CCOP’s interorganizational environment. The model demonstrates lesser explanatory power for chemoprevention and cancer control accrual, at approximately 23 and 18% of variance, respectively.

Structural characteristics of the CCOP are presented in Table 3. Both treatment and chemoprevention accrual demonstrate adequate model fit but cancer control accrual does not. Organizational size and staff allocation are predictive of accrual to treatment and chemoprevention protocols. The structural characteristics model explains 61% of the variance in treatment accrual and 26% of the variance in chemoprevention accrual.

Finally, models integrating selected variables that describe structural, process, and environmental characteristics are shown in Table 4. Models representing treatment and chemoprevention accrual demonstrate adequate fit as measured by F-test and adjusted $r^2$ results, but the cancer control model does not. Research base activity is strongly predictive of treatment accrual, whereas organizational size and staff allocation are weaker determinants. Staff allocation is strongly predictive of chemoprevention accrual in the integrated model. Sixty-three % of the variance in treatment accrual and 35% of the variance in chemoprevention accrual are explained by the structural, process, and environmental variables incorporated in the integrated model. Although results suggest the availability of cancer control protocols to influence cancer control accrual and internal CCOP conflict to have a depressive effect on accrual to cancer control protocols, they should be viewed with some caution because of the poor fit of the cancer control model.

**Discussion**

The participation of 36 CCOPs in the BCPT, one of the nation’s first large-scale cancer prevention trials, presented a
Table 4 Predicting CCOP accrual to treatment, cancer control, and chemoprevention protocols with the integrated model

<table>
<thead>
<tr>
<th>Treatment protocol accrual</th>
<th>Cancer control accrual</th>
<th>Chemoprevention (BCPT) accrual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient market share</td>
<td>0.01</td>
<td>0.003</td>
</tr>
<tr>
<td>Centralization</td>
<td>12.62</td>
<td>–0.83</td>
</tr>
<tr>
<td>Size</td>
<td>10.11</td>
<td>0.16</td>
</tr>
<tr>
<td>Staff</td>
<td>0.53</td>
<td>0.12</td>
</tr>
<tr>
<td>Internal conflict</td>
<td>52.33</td>
<td>–32.05</td>
</tr>
<tr>
<td>Total</td>
<td>28.76</td>
<td>28.69</td>
</tr>
<tr>
<td>Intercept</td>
<td>53.19</td>
<td>38.69</td>
</tr>
<tr>
<td>F test (significance)</td>
<td>10.94</td>
<td>1.92</td>
</tr>
<tr>
<td>Adjusted</td>
<td>0.6303</td>
<td>0.1547</td>
</tr>
</tbody>
</table>

*a b, unstandardized regression coefficients.

*Statistically significant at 0.05 α level.

*Statistically significant at 0.10 α level.

*Statistically significant at p < 0.01.

*F test, global test of model significance.

*Adjusted r² coefficient of determination adjusted for model size.

unique opportunity to evaluate CCOP accrual performance in a specific clinical trial. Collectively, these CCOPs proved to be major contributors of subjects to the BCPT. A detailed comparison of models representing accrual to treatment, cancer control, and chemoprevention (i.e., BCPT) protocols by these 36 organizations showed similarities between treatment and chemoprevention models. Cancer control models, however, were not found to resemble either the treatment or chemoprevention models. Four statistically significant variables were shared in common between the treatment and chemoprevention models: patient market share, research base activity, organizational size, and staff allocation. In contrast, no statistically significant variables were commonly shared between either cancer control and treatment models or cancer control and chemoprevention models. These results clearly support our hypothesis that, along the broad continuum of cancer prevention and control research, accrual to chemoprevention trials is associated to a greater extent with characteristics that facilitate accrual to treatment trials rather than cancer control trials.

Although this analysis shows predictors of treatment and chemoprevention accrual to be analogous, they are not identical. Interaction of CCOP personnel with the affiliated research bases responsible for protocol design and monitoring was found to be a strong predictor of treatment accrual but not chemoprevention accrual. In contrast, results showed staff allocation as measured by data manager work hours to be a strong predictor of chemoprevention accrual but only weakly predictive of treatment accrual. As previously discussed, chemoprevention trials generally require sample sizes that are considerably larger than those needed in the typical treatment trial. In addition, participants are more likely to be drawn from healthy populations rather than a circumscribed population of cancer patients. Thus, in the conduct of a chemoprevention trial such as the BCPT, comparatively greater effort on the part of the CCOP organization through its data management staff may be required to recruit patients. Management of research base relations appears to be more critical in the conduct of treatment trials due to the CCOP’s ongoing reliance on its research base affiliates for new and multiple treatment protocols.

This analysis has implications for the planning and ongoing management of treatment, cancer control, and chemoprevention clinical trials. The importance of allocating sufficient personnel resources to treatment and chemoprevention trials is demonstrated. Our study also supports the contention that cancer prevention and control research is highly heterogeneous. Although we have identified many similarities among treatment and chemoprevention trials, there are determinants unique to each class of trial. Additional studies of a variety of cancer prevention and control research protocols are needed to better understand the complex dynamics of the accrual process in large-scale community trials. Particular emphasis should be placed on exploring the extent to which protocol availability, interest in cancer control research among investigators, perceived appropriateness of the protocol to the specific community, and finances, as well as other incentives for involvement in cancer control research, influence the successful conduct of these trials.

Acknowledgments

The authors wish to thank Brian Gallup for computer programming and Will McCann for manuscript preparation assistance. The authors also express their appreciation to Bernard Fisher, Walter Cronin, and Carol Redmond of the NSABP for data set access.

References


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