NCI COMMUNITY
CANCER CENTERS
PROGRAM

The Relationship between Participation in the National Cancer Institute's Community Cancer Centers Program (NCCCP) and Clinical Trials Activity

A special review as a part of the overall evaluation of the NCCCP

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Deliverables and dates:

As outlined in the analysis plan (Appendix 1), deliverables for this sub-contract were a slide deck summarizing findings and a formal report. The goal was to submit the written report to NCI and RTI on August 31, 2011. A summary of the findings was presented to the NCI and RTI project teams on August 17, 2011 and then the NCI in Bethesda, MD on September 26, 2011. Based upon this discussion, a number of changes were made to the data sources and analyses, and therefore the summary report. The draft summary report (version 1.0) was submitted on October 26, 2011. NCI reviewers suggested changes and clarifications. This current written report (version 2.0) is in response to those requests; the deliverable timeline was adjusted accordingly.

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DEFINITIONS AND ABBREVIATIONS

CCOP and MB-CCOP - The Community Clinical Oncology Program (CCOP) is a network consisting of 48 CCOP groups in 28 states, 16 Minority-Based CCOP groups in 12 states and Puerto Rico, and 12 Research Bases (9 NCI funded Cooperative Groups and 4 NCI-designated Cancer Centers). The groups provide the infrastructure to link more than 415 community hospitals and 3,675 community cancer specialists and primary care physicians with academic investigators in the Research Bases to conduct cancer prevention, control and treatment clinical trials. Of the 16 pilot sites, seven (7) are affiliated with the CCOP; three (3) are considered Lead/Institution of Record CCOP sites, and four (4) are Performance sites. Of the Performance sites, one is a MB-CCOP (minority-based CCOP) performance site. All CCOP sites in the NCCCP pilot were in place prior to 2000.

Clinical Trials Accrual – The number of patients enrolled in a given clinical trial. For the purposes of these analyses, we will only consider fully consented, enrolled patients, and not screening.

Clinical Trials Portfolio – The array of clinical trials at a given site. Analysis includes not only the number of trials open, but also the types of trials (e.g., phase, intervention under investigation, study Sponsor).

CTEP & CTEP Database – The Cancer Therapy Evaluation Program (CTEP) funds the NCI Cooperative Groups to conduct clinical trials. The CTEP database is a robust well-recognized repository of information about CTEP trials, and includes CTEP-sponsored therapeutic treatment trials and DCP-sponsored cancer control and prevention trials.

CTSU – NCI's Cancer Trials Support Unit (CTSU). The CTSU is a service of the NCI in support of a national network of physicians to participate in NCI-sponsored cancer treatment trials, cancer prevention and control trials and correlative science studies. The majority of these studies are sponsored by the NCI's Clinical Trials Cooperative Group Program.

Developmental NCCCP Site – A site which was chosen by one of the two lead hospital systems participating in the NCCCP pilot. These Developmental sites could be hospitals that did not meet the selection criteria for the NCCCP lead sites, yet had the potential to do so by the end of the pilot. There were 5 Developmental NCCCP sites where were included in the pilot and evaluated in this report.

FTE – Full-Time Equivalent; a way to measure a worker's contribution to a project.

Lead NCCCP Site – A site which was chosen for the NCCCP pilot based on their documented track record and maturity in specific capabilities anticipated as important for the NCCCP. They had to meet minimum requirements for number of clinical trials and patient accrual to be considered. There were 11 lead NCCCP sites which were included in the pilot and evaluated in this report.

IRB – An Institutional Review Board (IRB) is a committee that has been formally designated to review, monitor and approve biomedical research involving humans.

NCCCP - The National Cancer Institute (NCI) Community Cancer Centers Program began in 2007. The analysis will include only those 16 pilot NCCCP sites of which eleven (11) are considered Lead sites and five (5) are considered Developmental sites.

Open Study vs. Enrolling Study – A study may be open to enrollment but not actively enrolling patients for a variety of reasons (e.g., eligible patients not yet identified, physicians not aware of new trial for

patients, inadequate study staff to conduct trial.) Some primary analyses will include only those clinical trials with accrual data (i.e., open enrolling studies), and other analyses will include all open studies at a site (including non-enrolling studies.) Whenever possible, consideration of the overall clinical trials portfolio at a site will include description of all open studies and open enrolling studies.

PI – Principal Investigator. Each NCCCP site had a designated contact person who was formally identified as the Principal Investigator. This person was often an MD and was ultimately responsible for overseeing the conduct of all NCCCP activities.

Study Sponsor – The organization, agency, or company that funded the study. For the purposes of these analyses, Sponsor will include government (NCI, non-NCI NIH other, non-NIH government other), industry, philanthropy, other, and none.

Underserved Accrual – The number of patients enrolled in clinical trials that are from traditionally underserved populations. This includes racial/ethnic minorities: Black, Hispanic, Asian-American, American Indian, or other racial/ethnic backgrounds; the over age 65 population; and the rural-based population (for site-reported data only). As a note, The CTEP data reports on the elderly population as defined as "Age 65 and Over;" the site-reported data reported on patients "Over 65" with the exception of one site, which reported for "Age 65 and Over."

Other abbreviations used:
CEO – Chief Executive Officer
COO – Chief Operating Officer
CRA – Clinical Research Associate
IT – Information Technology
MD – Medical Doctor
NCI – National Cancer Institute
OMB – Office of Management and Budget
Pharm D – Doctor of Pharmacy degree
RN – Registered Nurse

EXECUTIVE SUMMARY

Background

In 2007, the National Cancer Institute (NCI) established the NCI Community Cancer Centers Program (NCCCP) of participating community hospitals, systems and their cancer centers to expand cancer research capacity and deliver the latest most advanced cancer care to more Americans in the communities in which they live. The pilot program, originally funded from 2007 to 2010, received additional funds through the American Recovery and Reinvestment Act of 2009 to expand the program to 30 sites in 22 states. This report focuses on the sites that received original pilot funds in 2007.

Initial funds supported a three-year pilot phase focused on creating a community-based platform for research initiatives, including basic, clinical, and population-based studies, across the cancer care continuum. A total of 10 organizations were originally funded: 8 individual hospitals and 2 system organizations, which altogether includes 16 hospitals. The 2 hospital system organizations each selected "Lead" sites to facilitate the implementation of the NCCCP within their system and to work with additional "Developmental" sites; these Developmental sites could be hospitals that did not meet the selection criteria, yet had the potential to do so by the end of the pilot. Seven of the 16 sites involved in the pilot program were also involved in the NCI's Community Clinical Oncology Program (CCOP). NCCCP goals include increasing patient participation in clinical trials, reducing healthcare disparities, and improving quality of care. Thus increase in research activity at community-based cancer centers is central to achievement of NCCCP goals.

Purpose

To evaluate the overall impact of the NCCCP pilot on clinical trials activity at participating community-based cancer centers, a study was designed to provide a global evaluation of the program's pilot phase (July 2007 to July 2010). Specifically, the evaluation assessed the clinical trials portfolio and accrual at sites participating in the pilot phase and explored the temporal relationship of sites' organizational characteristics to their clinical trial activities.

Methods

Two main outcomes were assessed:

1. Clinical trial **portfolio** (e.g., the number of open clinical trials at a site, phase of trial, breakdown of sponsor type [federal, industry, other], other research activities); and,
2. Clinical trial **accrual** (total accrual, accrual for underserved populations [racial and ethnic minorities, rural residents, age 65 and over]).

Data were drawn primarily from two sources:

1. The central NCI clinical trial database, housed within the Cancer Therapy Evaluation Program (CTEP), which captures information on clinical trials and accrual, and;
2. Data reported by NCCCP sites quarterly and yearly, which describe their on-the-ground staff and capabilities, clinical trials portfolio, and accrual.

These sources, both of which have limitations, contained complementary information that provided a more complete picture of clinical trials activity.

The evaluation compared performance in portfolio and accrual (a) across sites, (b) between NCCCP Lead and Developmental types, (c) between sites with and without CCOP affiliation, and (d) between CTEP data and site-reported data.

Results

Principal findings were the following[*]:

- During the pilot project period, sites comprising the NCCCP pilot network added Phase 3 studies to their clinical trials portfolios and increased the rate of participant accrual to Phase 3 trials at a higher rate than was observed for the overall CTEP database. The number of Phase 3 CTEP-sponsored trials launched nationally increased by 8% during the pilot time period, yet the NCCCP sites increased their local activations of these trials by 16%; accrual to Phase 3 trials increased by 30% nationally, and 133% in the NCCCP. Rates of change of Phase 1/2 trial activity was similar for both the nationwide and NCCCP assessments.
- Accrual increased among NCCCP sites overall. Lead sites contributed most to accrual, and showed the higher proportional increases in accrual, compared to developmental sites. Lead sites that were also CCOP sites contributed both the greatest accrual numbers at baseline and the greatest numbers to new accrual, but non-CCOP Lead sites demonstrated greater relative growth in accrual over the pilot period.
- Accrual of underserved populations increased across NCCCP sites. This increase was most dramatic among people age 65 and over. For racial and ethnic minority participants, the rate of increase in accrual was equivalent to, but not greater than the occurred at a rate commensurate with the overall increase in NCCCP accrual. Sites affiliated with the CCOP showed the most consistent relative increases in accrual of underserved populations, though their overall clinical trials activity did not increase.
- NCCCP Lead sites were engaged in a greater volume of clinical trials activity at the outset of the NCCCP pilot. Both Lead and Developmental sites increased the total number of open trials over the three-year period, but the relative proportional growth was greater among Developmental sites.
- Over the three-year pilot period, the Lead sites increased their portfolio of Phase 3 trials by 50% with little change in the number of Phase 2 trials. Developmental sites tripled the number of Phase 3 trials and also had little change in the number of Phase 2 trials.
- Clinical trials activity among CCOP sites participating in the NCCCP was at least partly declining over the three-year pilot, while sites not affiliated with the CCOP increased their activity; however, overall, the CCOP sites had the highest clinical trials activity at the outset of the program, so they were starting at a higher baseline.
- Trials conducted by NCCCP sites were predominantly NCI-sponsored Phase 2 and Phase 3 trials. The majority of Phase 2 studies were conducted by the more mature Lead sites.
- Accrual to Industry- and Other-sponsored trials rose over the three-year period. There was some increase in the median number of Industry-sponsored trials conducted, but generally this represented less than one-tenth of the overall activity.
- The number of "other research activities" increased each year in every category of activity (screening, early detection, diagnostic; ancillary; epidemiologic, observational, outcome; correlative).

Interpretation

Overall review of results indicates that the investment in the NCCCP program is stimulating additional accrual to clinical trials, including increased participation of underserved populations in the community. Many NCCCP sites increased their clinical trials activity, with most increases occurring in Phase 3 and NCI-sponsored trials. Patient accrual increased, especially in Phase 3 trials, and the overall patient per trial ratio increased. Performance improvements (i.e., increases in clinical trials portfolio and accrual outcomes) outpaced national trends.

[*] Reported as general findings; results at specific sites varied.

Nearly all sites increased their accrual to underserved populations in the racial/ethnic minority, rural, and/or age 65 and over categories. Sites also improved their other (i.e., non-clinical trial) research activity, such as accrual to biospecimen collection studies.

Differences emerged between Developmental and Lead sites in terms of performance, change in performance, and role. Lead sites, particularly those involved in the CCOP, evidenced a "maturation effect," that is, Lead sites with already-established research capacity had greater numbers of open trials, and higher accrual to trials, at the outset; due to this prior maturation, they exhibited lower growth in number of trials and accrual than did the less mature non-CCOP and NCCCP Developmental sites. Developing sites evidenced a "sequencing effect," that is, during the NCCCP pilot they accomplished numerous steps and infrastructure development tasks necessary to establish a functional research operation at their sites; their progress was apparent in greater numbers of open trials, but the timeframe of this evaluation was likely too short to detect impact on accrual. Lead sites served as a good example to the Developmental sites as they accomplished the requisite preparatory and infrastructure development steps.

BACKGROUND

The NCCCP Program and Site Designation

The National Cancer Institute (NCI) Community Cancer Centers Program (NCCCP) is a network of participating community hospitals, systems and their cancer centers that serves as a community-based platform by supporting basic, clinical, and population-based research initiatives across the cancer care continuum. In addition, NCCCP sites are directly contributing to the cancer research enterprise by: accruing patients to clinical trials; collecting high-quality biospecimens for research; expanding information technology through the use of electronic health records and participation in NCI informatics initiatives; and, collaborating with other NCI programs and related organizations, including the NCI Cancer Centers Programs, The Community Clinical Oncology Program (CCOPs/MBCCOPs), The Cancer Genome Atlas, the NCI Community Networks Program, the American Society of Clinical Oncology, and the American College of Surgeons' Commission on Cancer.

A core NCI goal for the NCCCP is to contribute to the NCI mission of evidence development and translation in the community oncology setting. Clinical trials are a fundamental aspect of cancer care, an important clinical option for patients, and the primary research mechanism that generates evidence on the clinical role of preventative or anti-cancer interventions. The NCCCP aims to provide cancer research treatments within the communities where the majority of patients live (i.e., 85% of cancer patients receive their treatments through community based hospitals) by involving more patients in clinical trials, providing them the opportunity to benefit from the latest therapies before they are available to the general patient population. The NCCCP sites are incentivized to build capacity to offer earlier phase trials (e.g., Phase II), with a goal of reducing the need for patients to travel to larger academic centers to access these trials. All patients should be considered as potential participants for trials at NCCCP sites, with a strong focus placed on reaching underserved populations, including racial/ethnic minorities, the elderly, those living in rural areas, and others who are typically underrepresented in clinical trials.

To achieve the program's stated aims, NCI established the NCCCP network of participating community hospitals, systems and their cancer centers. A total of 10 organizations were originally funded: 8 individual hospitals and 2 system organizations, which altogether includes 16 hospitals. The 2 hospital system organizations each selected "Lead" sites to facilitate the implementation of the NCCCP within their system and to work with additional "Developmental" sites; these Developmental sites could be hospitals that did not meet the selection criteria, yet had the potential to do so by the end of the pilot. Lead sites were chosen for their documented track record and maturity in specific capabilities anticipated as important for the NCCCP (which may be related to clinical trials capabilities, but not necessarily). Developmental sites were anticipated to learn and grow within the context of NCCCP activities through their participation in the NCCCP program. One system organization selected 2 Lead sites that met the selection criteria and added a Developmental site that is regionally based and encompasses 3 hospitals. The other system organization selected 1 hospital as its Lead site and 2 additional hospitals as Developmental sites. Even though the system organizations had multiple hospitals participating in the NCCCP, there was no additional NCI funding beyond what was awarded to the individual non-system organizations. Each of the 10 funded organizations was awarded approximately $500,000 annually to support the NCCCP activities.

Thus, the NCCCP started in 2007 with a total of 11 designated Lead sites and 5 Developmental sites; this corresponds with 10 organizations comprising 8 individual hospitals designated as "Lead" and 2 hospital systems, with 1 hospital system naming 2 "Lead" sites and the other naming 1 "Lead" site, and a total of 5 "Developmental" sites all associated with the 2 hospital systems.

Another important characteristic of the sites was their affiliation with the Community Clinical Oncology Program (CCOP). CCOP is a network for conducting cancer prevention, cancer control and treatment clinical trials by community medical practitioners. Of the 16 pilot NCCCP sites, 3 are also Lead/Institution of Record CCOP sites, and 4 are considered CCOP "Performance" sites. Of the "Performance" sites, one is a MB-CCOP (minority-based CCOP) Performance site. Since all of the Lead CCOPs affiliated with the NCCCP sites had been in operation for the past 10 years, these NCCCP sites had mature clinical trials infrastructure with many open and enrolling clinical trials prior to participating in the NCCCP program. One aspect of the analyses of the NCCCP program was therefore to examine whether the Lead and Performance CCOP sites within NCCCP performed differently (better or worse) than non-CCOP sites within NCCCP. Importantly, this report reflects an evaluation of the NCCCP program, and characteristics of NCCCP sites; it is not a comparison between the NCCCP program and other NCI programs (like CCOP).

A thoughtful evaluation program was built around the NCCCP pilot in order to determine if the overall goals of the program were being accomplished. While the NCCCP program evaluation included a range of questions relative to the various stated programmatic goals, a specific question and the focus of this current analysis is the association of the NCCCP investment and clinical trials activities at the 16 NCCCP pilot institutions.

METHODS

Evaluation of the Impact of NCCCP Participation on Clinical Trials Activity

This report is the summary of a global evaluation of the clinical trials activity of the NCCCP pilot period from July 2007 to July 2010. It includes an assessment of the clinical trials portfolio and accrual for the pilot sites, and a review of the temporal relationship of the organizational characteristics and clinical trial activities. In addition to summaries of activities, sites were considered in the context of their NCCCP Lead versus Developmental designation, as well as their CCOP affiliation. Two main outcome assessments were considered:

1. Clinical trial **portfolio** (e.g., the number of open clinical trials at a site, sponsor, types of trials [phase, intervention under investigation]); and,
2. Clinical trials **accrual** (total accrual and accrual for underserved populations [racial and ethnic minorities, rural residents, age 65 and over]).

The full analysis plan is provided in **Appendix 1**.

Data Sources and Limitations

The evaluation incorporates several data sources each of which has its advantages and limitations. The central NCI clinical trial database, housed within the Cancer Therapy Evaluation Program (CTEP), captures information on trials and accrual. Data cleaning is performed by the Cooperative Group lead. Sites accruing to CTEP trials submit their data on accrued patients directly to the lead Cooperative Group that is responsible for managing the data. Cooperative Groups are required to submit their data to CTEP on a quarterly basis and it is then stored on the CTEP database. Information in this database provides the most accurate view of actual accrual and trial characteristics for the trials reported in this system. Reports from the CTEP database do not, however, include trials that are open but not enrolling patients at a site (a substantial expense and drain on sites), studies that don't report to CTEP (like industry trials), and many correlative studies. Despite their limitations, CTEP data provide the cleanest dataset for a) comparisons between sites and b) comparison with national trends. An examination of CTEP data allows us to evaluate the NCCP specific contribution to cancer evidence development under NCI auspices - review of these data provides a "trial level lens."

Meanwhile, the NCCCP sites reported data quarterly and yearly about their on-the-ground staff and capabilities, trials portfolio, and accrual. The quality of these self-reported data likely improved over time as sites matured in their understanding of the questions and/or staff reporting information changed. For example, early in the NCCCP program sites may have misunderstood definitions or attributed study participants and trials to the wrong category. Subsequent reports could have improved (as local understanding of definitions improved), or worsened (through staff turnover). While the data were cleaned to improve accuracy, the fundamental limitations of the data remain. Still, these site-reported data provide important insights about the on-the-ground experience with the NCCCP, clinical trials activity, and changes over time –review of these data provide a "site level lens."

Data analyses include both "trial level" (i.e., CTEP) and "site level" (i.e., site-reported) comparisons, thus providing a summary of the NCCCP program's impact on clinical trials activity and maturation of experience on the ground. Another way to consider these two "lenses" is that site-level data enable a form of process evaluation using self-reported data, whereas the CTEP database supports an outcomes evaluation using a much larger administrative dataset.

Sites could participate in many different kinds of studies, including therapeutic treatment trials, cancer control and prevention trials, biospecimen collection /correlative studies, epidemiology studies, and other descriptive studies. Different study types require different levels of staff experience, confidence and expertise, on the ground, in order to successfully enroll participants and collect data. The changes in clinical trials portfolio at sites, by study type and phase, was considered, both in terms of change in complexity of trial type over time and related accruals. For example, a site may be very active in the Moffitt biospecimen collection study called Total Cancer Care; this may reflect high accrual but is a simple study to conduct. If this same site transitions to more therapeutic treatment trials, the accrual numbers may go down but the actual clinical trials workload for staff on the ground will increase and patient care may be more directly (and positively) impacted. In order to study these trends, some definitions were necessarily developed for the analyses.

The "NCCCP Clinical Trials Deliverables" were focused only on therapeutic, cancer control and prevention trials; these were the only types of trials considered specifically as "clinical trials." Therefore, for this report, all CTEP analyses of clinical trials portfolio and clinical trials accrual were performed for just these treatment, cancer control and prevention trial types. For the trial-level lens (i.e., CTEP database) the data include only those trials sponsored by CTEP (therapeutic treatment trials) or DCP (Cancer Control and Prevention). For the site-level lens (i.e., the site self-reported data) the data include all sponsor types, including NCI, Industry and Other- Sponsor (including Investigator-initiated trials, etc.) Therefore, when comparing the data specifically between the two databases, only the NCI-sponsored clinical trials from the site-reported data were used to compare to the CTEP clinical trials data.

Two further limitations should be noted when comparing the CTEP data to the site-reported data. The site reported data include all trials open, including those trials that are open but may not be enrolling patients. In contrast, the CTEP data only include trials with patient accrual. This may skew the results as open treatment trials with no accrual would not be counted in the CTEP reports. In addition, the site-reported data do not contain baseline data regarding the number of clinical trials or specific clinical trial accrual in the year prior to the evaluation period. Note, there was baseline data reporting a total accrual for all research activity, combining clinical trials with other research accrual described below. The first site-reported data specifically on clinical trials and accrual comes after the end of the first year of the program (designated Year 1). Therefore, analyses of the changes during the program using site-reported data are done using the data from the end of the evaluation period (designated Year 3), compared to Year 1. In contrast, the CTEP data do include a baseline year, the 12 months preceding the beginning of the NCCCP program in July 2007. Therefore changes during the evaluation period for trial-level data are done using data from the end of Year 3 compared to the baseline data for the number of clinical trials and number of patients accrued to those trials.

Since the CTEP database does not include other trial types apart from the treatment, cancer control and prevention trials mentioned above, the source for the remainder of study information was site self-reported data. The sites reported on all open studies and enrollment to "Other Research Activities" including studies in the following categories: Screening, Early Detection, Diagnostic, Epidemiologic, Observational, Outcome, Ancillary and Correlative Studies. Analyses of these other studies provide information on the impact of the NCCCP program on broadening the range of research activities at the site, and the perceived volume of clinical trials activity at a site.

The current landscape of clinical trials activities (accrual, number of trials, types of trials) nationally among NCI Comprehensive Cancer Centers, Cooperative Groups and NCI Research Bases, was also described, in order to set the NCCCP clinical trials activities within the context of other cancer-related clinical trials efforts. Analyses were performed to examine whether trends in change in clinical trials

accrual and portfolio among the NCCCP sites aligned with or differed from these national trends in clinical trials activity.

In summary, the evaluation of the NCCCP pilot program was done by comparing across sites, broken down by NCCCP Lead vs. Developmental types, by sites with CCOP affiliation versus sites without CCOP affiliation, and by CTEP data versus site-reported data. The clinical trial portfolio (number and phases of trials), clinical trial accrual, underrepresented population accrual, other research activities and enrollment, and comparisons to national trends were all examined as part of this evaluation report.

RESULTS

Overview

This summary of overall results is based on aggregate number of trials and patient accrual as reported using two different datasets. The number of NCI-sponsored trials (a subset of "All Trials") being conducted at the 16 NCCCP sites was described using data available through:

1. Cancer Therapy Evaluation Program (CTEP): The CTEP database is a robust, well-recognized repository of information about CTEP- and DCP-sponsored trials ("trial-level" called "CTEP Data"), and
2. Site-reported Information: Each site prepared information recorded by site personnel in response to requests from the NCCCP evaluation team and SAIC-F, an NCI subcontractor ("site-level" using "site self-reported data").

CTEP data generally reflect lower numbers of trials and activity than site-reported data because CTEP only presents NCI-sponsored trials (e.g., no Industry-sponsored trials), because data are focused on treatment, cancer control and prevention trials, and because studies without any accrual are excluded. CTEP data document a baseline before the NCCCP was initiated (true baseline); site-reported data were not collected until the Year 1 evaluation process was underway (i.e., a true baseline does not exist for this dataset).

Further details on specific individual sites are presented in Appendix 2. Because the data were positively skewed and thus not normally distributed, the results are reported as both the median as well as the actual counts by year where appropriate.

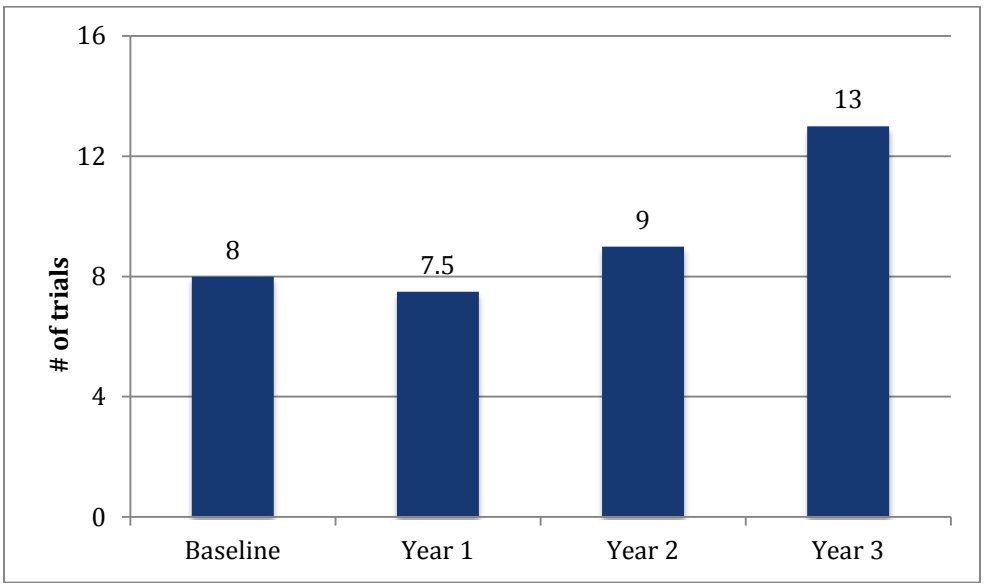
CTEP Data

Clinical Trials Portfolio - CTEP

Number of Trials

The median number of trials per site was 8 (aggregate=223, range 0-62) at baseline prior to initiation of NCCCP activities, 7.5 (aggregate=213, range 0-59) at Year 1, and 13 (aggregate = 263, range 0-58) at Year 3 (Figure 1). This reflects a 73% increase in the median number of trials per site between Years 1 and 3 (63% from baseline), with an 18% increase from baseline in the aggregate number of trials across the NCCCP program. As site-level data will demonstrate, the actual change at any individual site was variable.

Figure 1: Median Number of Trials (CTEP Data)



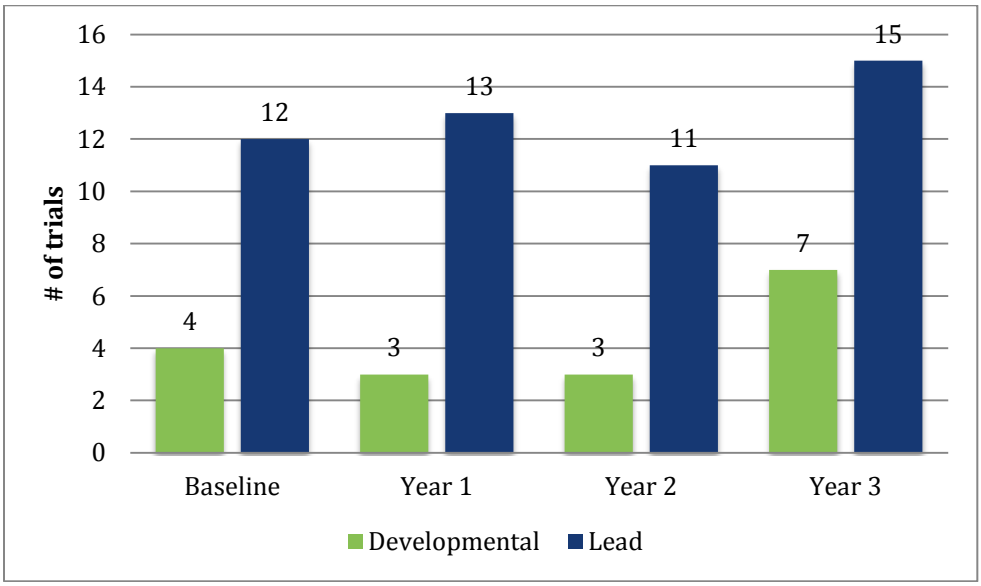
NCCCP Lead and Developmental Sites

All sites were designated as either a NCCCP Lead site (n=11) or a Developmental site (n=5) according to each site's organizational relationship and baseline capabilities (see Background). Based on this designation, there were considerable differences in the number of trials conducted during the evaluation period. For example, the median number of trials conducted at the Lead sites was 12 trials per site (aggregate=203, range 3-62) at baseline, 13 trials per site (aggregate=198, range 0-59) in Year 1, and 15 trials per site (aggregate=229, range 5-58) in Year 3. Over the three-year evaluation period compared to baseline, the median number of trials rose by 25% and the aggregate number of trials rose by 13%. By contrast, the median number of trials conducted by the five Developmental sites was 4 (aggregate=20, range 0-8) at baseline, 3 (aggregate=15, range 0-7) in Year 1, and 7 (aggregate=34, range 0-13) in Year 3. Over the three-year evaluation period for the Developmental sites, the median number of trials rose by 75% over baseline and the aggregate number of trials rose by 70% over baseline (Figure 2).

The overall interpretation is that, in general, Lead sites had a greater volume of clinical trials activity in place at the outset of participation in the NCCCP; while growth in the total number of open trials was witnessed for both Lead and Developmental sites, the relative proportional growth among Lead sites was more modest. The Developmental sites had little clinical trials activity reported at baseline and

demonstrated greater proportional growth over time. The most dramatic growth in the number of open trials for Developmental sites was in Year 3; because it is unrealistic to expect these sites to open trials and to demonstrate corresponding increases in accrual numbers in the same year, attributable increases in accrual are not likely to be evident until Year 4 (i.e., after this NCCCP program evaluation). Note that there were a small number of Developmental sites and an uneven distribution across these sites in the growth of the number of open trials, which may not be conveyed in the medians.

Figure 2: Median Number of Trials (CTEP Data) – NCCCP Lead & Developmental Sites



CCOP and Non-CCOP Sites

The Community Clinical Oncology Program (CCOP) is a network for conducting cancer prevention, cancer control and treatment clinical trials by community medical practitioners. A site can be designated as either a Lead CCOP or a Performance CCOP. Three sites were CCOP Lead sites, four were Performance sites, and nine were not affiliated with the CCOP program. All three of the NCCCP sites that are designated as Lead sites in the CCOP program were also designated as "Lead" in the NCCCP program. CCOP sites participating in the NCCCP pilot program reflect a small subset of the total CCOP program, and are not necessarily representative of CCOP sites more generally; observations relevant to this NCCCP clinical trials evaluation cannot be assumed to be applicable across the entire CCOP network.

Comparing CCOP sites and non-CCOP sites in the NCCCP, the median number of trials per CCOP site was 13 at baseline (range 0-62), 17 in Year 1 (range 0-59) and 20 in Year 3 (range 1-58), which is a 54% increase from baseline. The median number of trials per non-CCOP site was 7 at baseline (range 0-13), 5 in Year 1 (range 0-13) and 12 in Year 3 (range 0-25), which is a 71% increase (Figure 3). Comparing CCOP Lead and CCOP Performance sites for all CCOP sites in the NCCCP, the Lead sites had a 13% decrease over the period (median trials per site of 46 at baseline and 40 in Year 3) and the Performance sites had a 38% increase over the period (median trials per site of 8 at baseline and 11 in Year 3; Figure 4).

The overall interpretation is that, in general, clinical trials activity at CCOP sites was at least partly declining during the period of participation in the NCCCP program, predominantly for Lead sites, while

the non-CCOP sites were generally increasing their activity. In other words, CCOP sites may be near maximum saturation for current infrastructure and patient volume. This is consistent with observations across the whole CCOP program (and nationally, in generally) and is unlikely to be related to NCCCP participation.[†] It also is possible, however, that competing demands posed by other aspects of the NCCCP program diverted sites' energies and resources away from clinical trials and toward other deliverables. CCOP sites had higher median numbers of trials open at the beginning of the NCCCP project (median 13 for CCOPs versus median 7 across the whole program).

Figure 3: Median Number of Trials (CTEP Data) - CCOP & Non-CCOP Sites

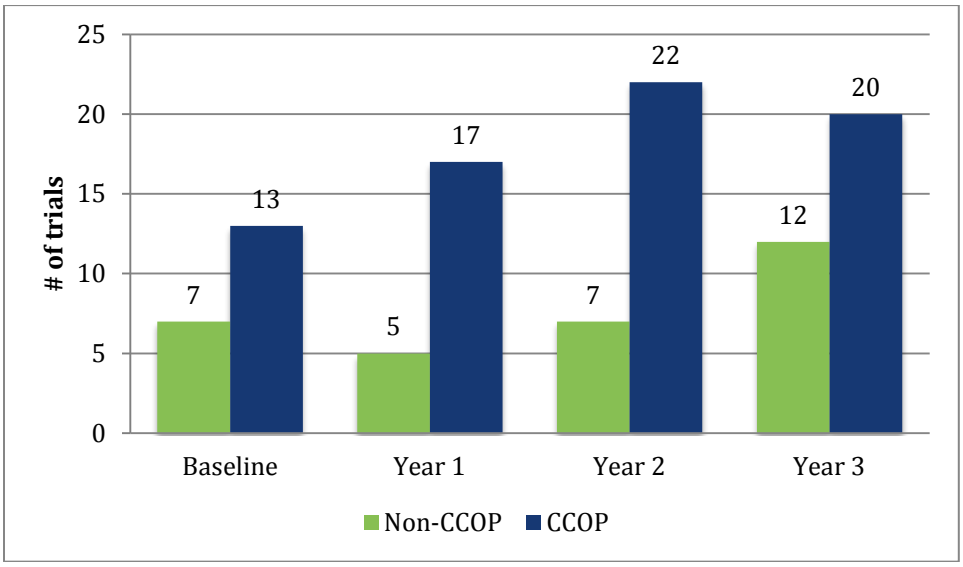
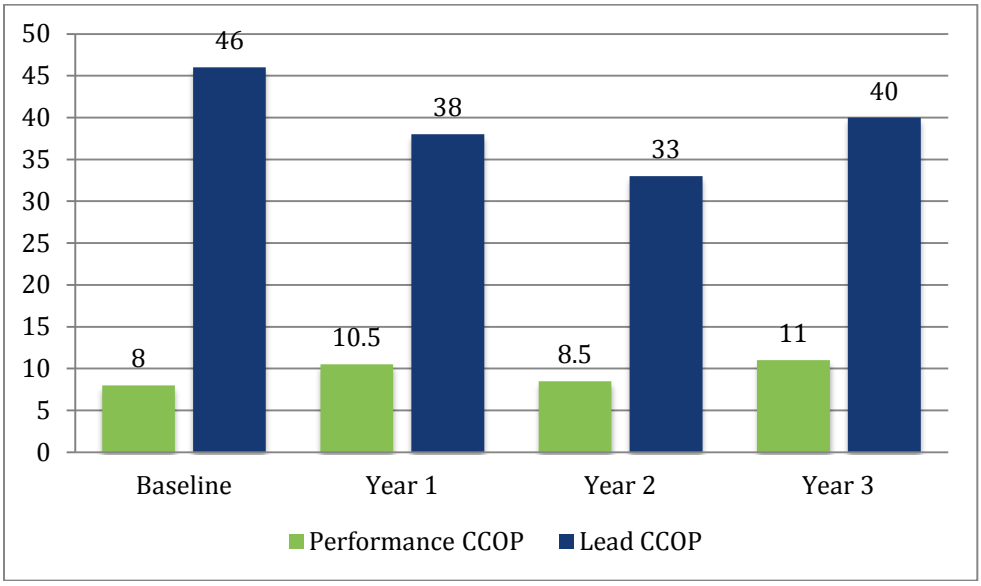


Figure 4: Median Number of Trials (CTEP Data) - Lead & Performance CCOP Sites



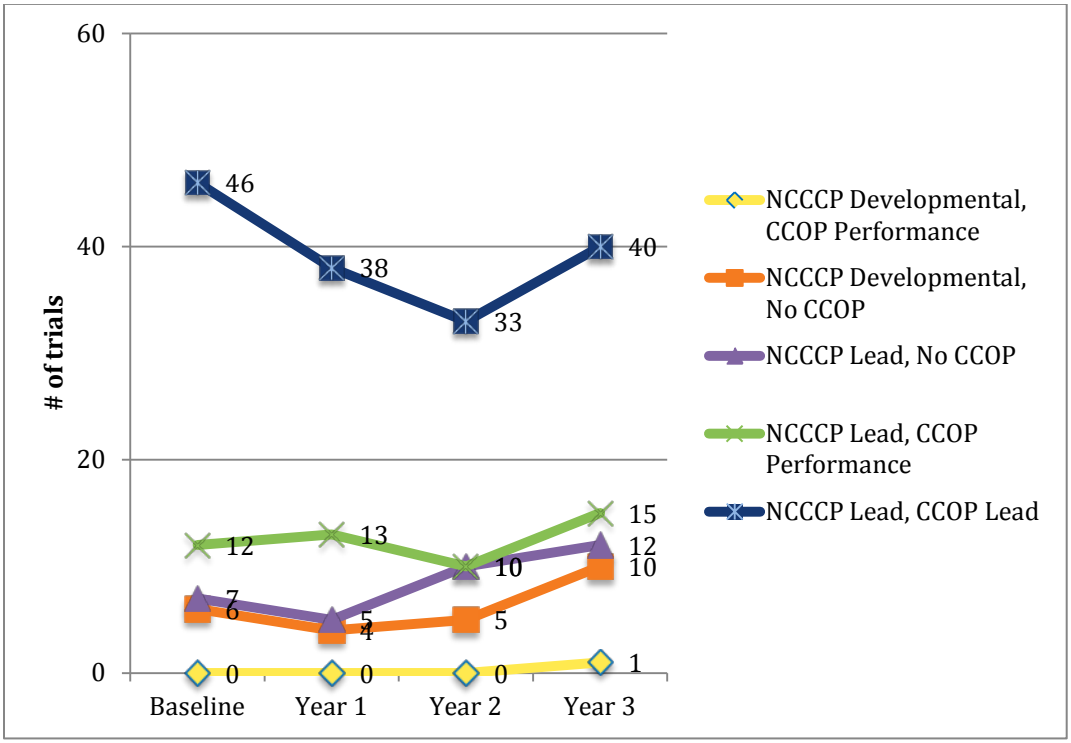
[†] Personal communication: Bryan Weiner, PhD, CCOP Program Evaluator, Teleconference on June 30, 2011.

Interaction Between Type of NCCCP Site and CCOP Status

Among the three sites that were designated as both CCOP Lead and NCCCP Lead, the median number of trials per site was 46 at baseline (range 26-62) and 40 in Year 3 (range 24-58; a 13% decrease). Among the three sites that were designated as NCCCP Lead and CCOP Performance sites, the median number of trials was 12 at baseline (range 4-13) and 15 in Year 3 (range 7-20; a 25% increase). There were five NCCCP Lead sites that were not a part of the CCOP program; for these sites the median number of trials was 7 at baseline (range 3-13) and rose to 12 in Year 3 (range 5-25; a 71% increase). There was a single center that was a NCCCP Developmental site and a CCOP Performance site. This site participated in no trials at baseline and one trial in Year 3. Finally, there were 4 NCCCP Developmental sites that were not participants in the CCOP program. The median number of trials performed at baseline was 6 (range 0-8); this increased to 10 in Year 3 (range 0-13; a 66% increase; Figure 5).

The overall interpretation is that Lead CCOP sites had substantially greater clinical trials activity at baseline which generally declined over the period of participation in the NCCCP program. Meanwhile, NCCCP sites without a CCOP affiliation showed the more marked relative increases in median numbers of trials over time regardless of whether it was a NCCCP Lead or Developmental site. The summary conclusion is that NCCCP non-CCOP and CCOP Performance sites have the most potential for growth for clinical trial activity.

Figure 5: Median Number of Trials (CTEP Data) - By Site Designation

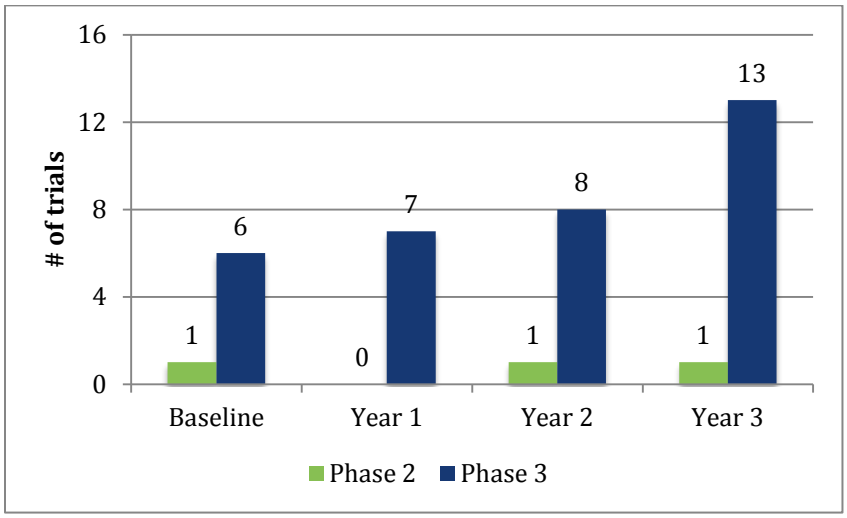


Portfolio by Study Phase

There were no Phase 1 CTEP-reported NCI-sponsored trials conducted during the evaluation period; Phase 1/2 trials were counted in the Phase 2 trial numbers. The median number of Phase 2 trials per site was one at baseline (range 0-22) and one in Year 3 (range 0-17). The median number of Phase 3 trials

was 6 at baseline (range 0-37), 7 in Year 1 (range 0-36), and 13 in Year 3 (range 1-39), a 117% increase from baseline (Figure 6).

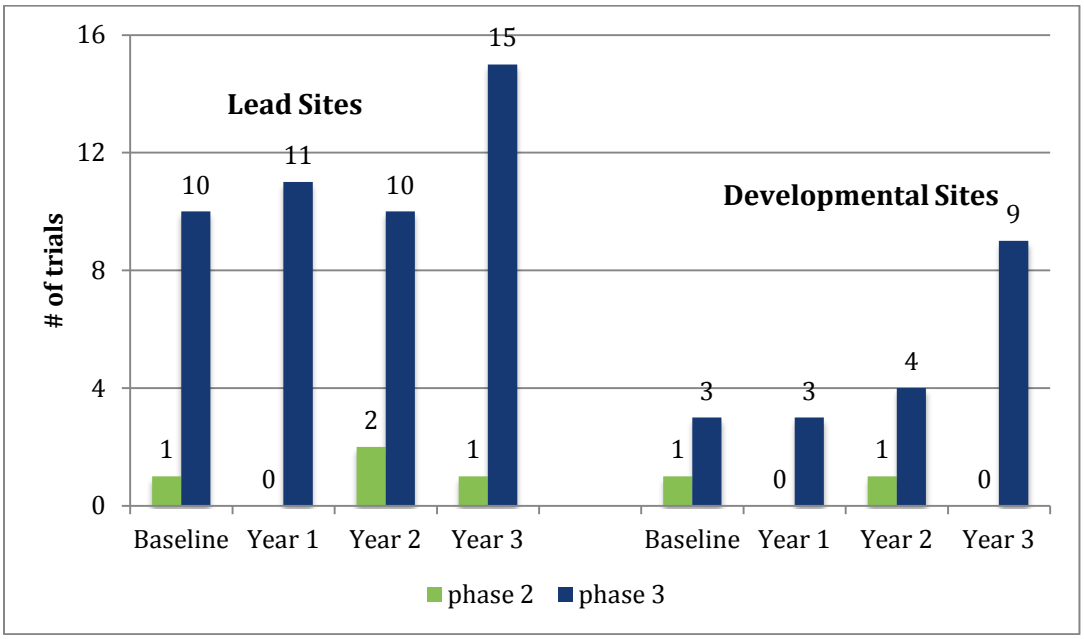
Figure 6: Median Number of Trials (CTEP Data) - By Study Phase



Phase 2 and Phase 3 trials by NCCCP Lead versus Developmental designation

Based on median number of trials, NCCCP Lead sites conducted two to three times as many Phase 3 trials compared to Developmental sites and about the same number of Phase 2 trials as Developmental sites. The Lead sites increased their portfolio of Phase 3 trials by 50% with little change in the number of Phase 2 trials. Developmental sites tripled the number of Phase 3 trials and also had little change in the number of Phase 2 trials (Figure 7).

Figure 7: Median Number of Trials (CTEP Data) - By Study Phase & NCCCP Designation



Phase 2 trials by site – When the proportional change in Phase 2 activity for each of the 16 sites is plotted, all five Developmental sites either had fewer trials or no change in the number of trials over the evaluation period. Four Lead sites increased their portfolio of Phase 2 trials, and the remainder had either no change or a decrease in the number of trials by the end of the evaluation period. The small number of Phase 2 trials implies that a net gain or loss of only a few trials would be interpreted as a substantial relative increase or decrease.

Phase 3 trials by site – In contrast with Phase 2 trials, all but two sites increased their portfolio of Phase 3 trials according to CTEP data. The most dramatic gains occurred at two Developmental sites, and half of all sites adding to their trials portfolio did so by at least 50%.

In the following figures, the same sites are represented in the same position to facilitate comparison in the changes in Phase 2 and 3 trial portfolios at the site level.

Information is presented as percent changes as this provides a practical normalized mechanism for comparison across sites. Numbers of trials are small and therefore proportions may appear large and inappropriately misleading. However, whenever only percentages are presented then information should be interpreted with caution.

The overall interpretation was that there was no overall change in the median number of Phase 2 trials (which hovered close to zero), according to CTEP data. The increases were in Phase 3 trials. Visual inspection of the relationship between the type of site (NCCCP Lead versus Developmental) by trial phase suggests that Phase 2 trials increased for some Lead sites but decreased for Developmental sites (Figure 8) while the Developmental sites most markedly increased their portfolios of Phase 3 trials (Figure 9). This is consistent with the fact that Phase 2 trials require a more sophisticated clinical research infrastructure and capability, which is more likely to be available in Lead sites. Whether Developmental sites would be able to shift their capabilities and increase their Phase 2 activities over time cannot be determined within the short three-year timeframe of this evaluation.

Also, proportional changes reflect wide-ranging changes from -300% to +333%. This is predominantly a reflection of small numbers of trials at baseline, and the fact that the addition of only a few trials can appear as a dramatic proportional change. Therefore, data must be interpreted with caution. Nonetheless, it is important to consider the dramatic site-level investment (or loss of investment) in order to achieve such relative changes; given this, proportional data were retained.

Figure 8: Proportional Change (Absolute Change) in Phase 2 Trials from Baseline to Year 3 (CTEP Data)

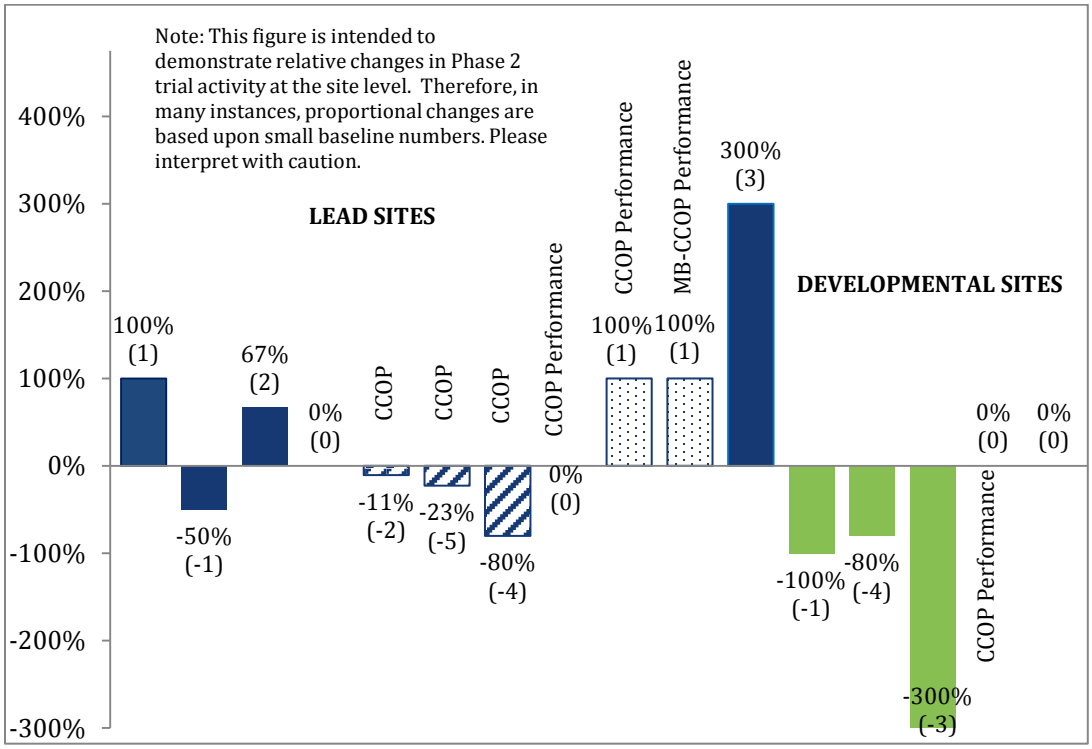
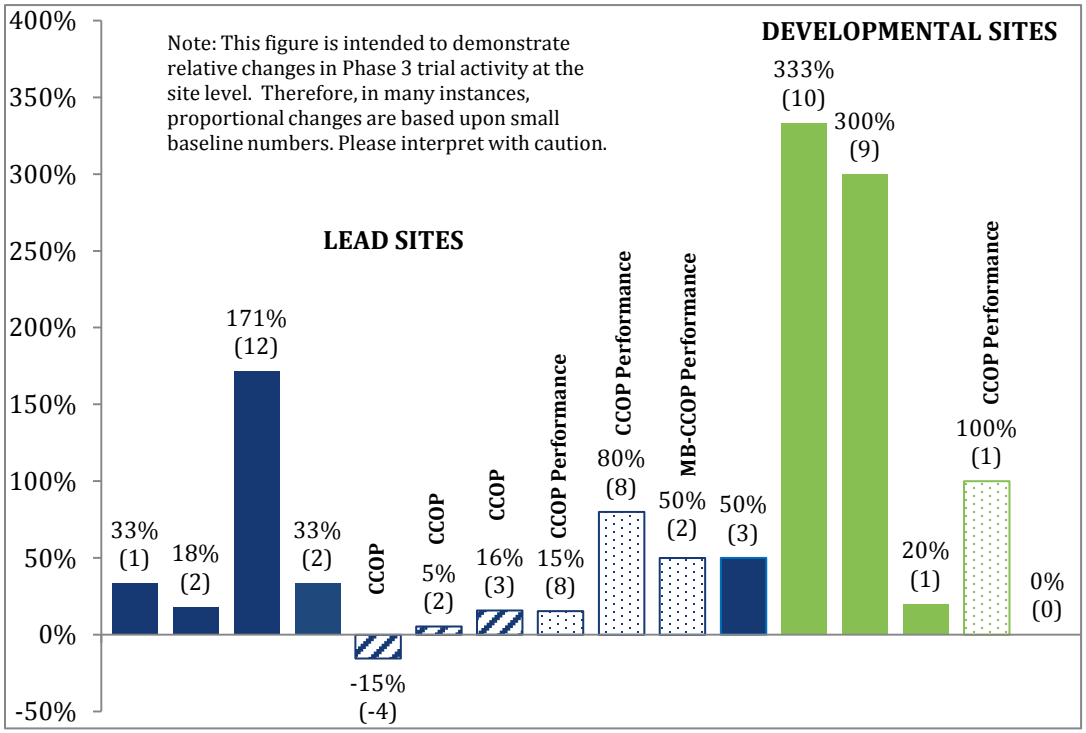


Figure 9: Proportional Change (Absolute Change) in Phase 3 Trials from Baseline to Year 3 (CTEP Data)

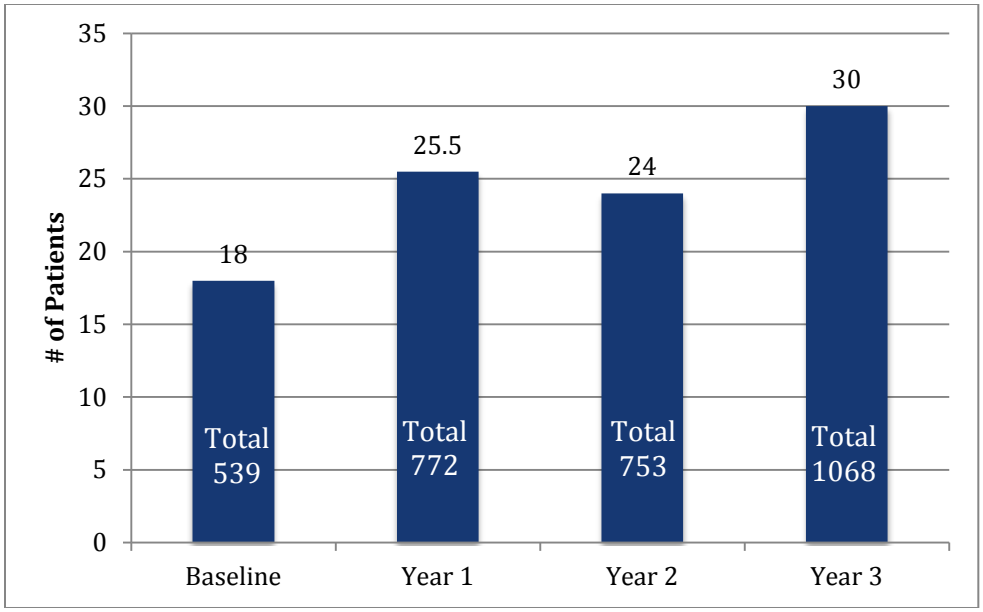


Clinical Trials Accrual – CTEP

Total Accrual

Each year there was a wide range of site-reported patient accrual by the 16 sites. At baseline, individual site accrual ranged from 0 to 203 patients. Total accrual across all NCCCP sites at baseline was 539 with a median of 18. By Year 3, the top of the range increased (0-501), the median increased to 30 (67%), and total accrual increased to 1068 (98%; Figure 10). The overall interpretation is that accrual across the NCCCP is increasing, and is doing so at a higher rate than the national average (see later sections in this report). CTEP data reflect a "trial-level" lens, which is the best way to reflect NCCCP activity compared to national activity.

Figure 10: Total and Median Accrual (CTEP Data)

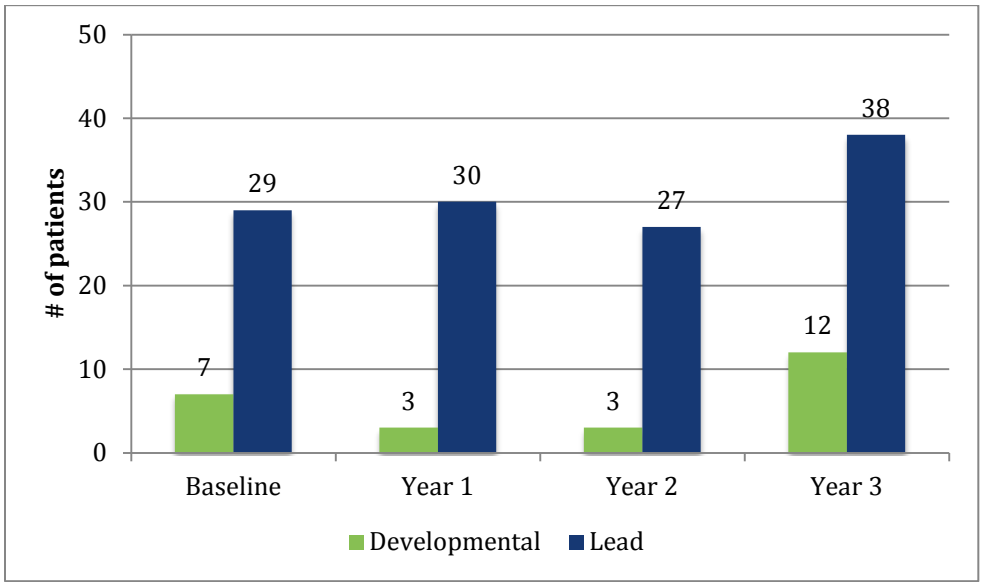


NCCCP Lead and Developmental Sites

CTEP data demonstrate that both NCCCP Lead and Developmental sites gained patients from baseline through Year 3. Lead sites had a relative increase of 31%, with a baseline median of 29 and range of 4-203, and a Year 3 median of 38 and range of 11-501. Developmental sites had a relative increase from baseline of 71%, with a baseline median of 7 and range of 0-23, and a Year 3 median of 12 and range of 0-26. Lead sites consistently accrued 3 to 4 times as many patients as the Developmental sites (Figure 11).

The overall interpretation is very consistent – according to CTEP data, accrual is increasing and the highest contributors to accrual as well as highest proportional increases in accrual are in the NCCCP Lead sites. This may be reflective of the sequencing effect observed in the site vignettes. Specifically, Lead sites have more open trials and more mature clinical research infrastructure at the outset, so are more poised to increase accrual over time. Developmental sites are predominantly focusing on getting their clinical research infrastructure organized, which first leads to more open trials with increases in accrual likely following later; in other words, it is likely too early to determine whether the Developmental sites will demonstrate positive changes in accrual as well.

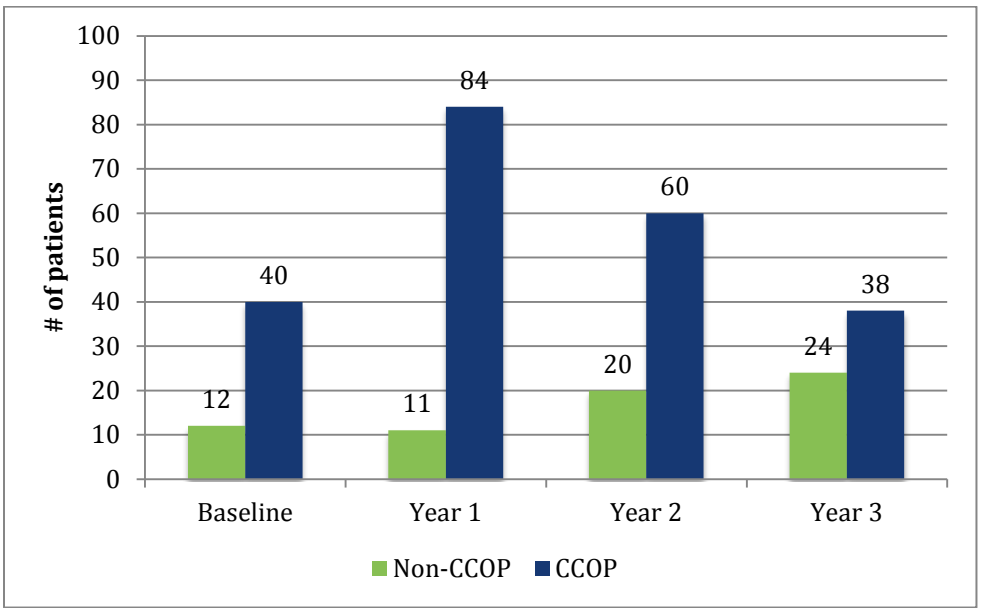
Figure 11: Median Accrual (CTEP Data) - NCCCP Lead & Developmental Sites



CCOP and Non-CCOP Sites

Comparing CCOP sites and non-CCOP sites, the median accrual per CCOP site was 40 at baseline (range 0-203), 84 in Year 1 (range 0-267) and 38 in Year 3 (range 1-501), which represents a 5% decrease. The median accrual per non-CCOP site was 12 at baseline (range 0-29), 11 in Year 1 (range 0-30) and 24 in Year 3 (range 0-48), which represents a 100% increase (Figure 12). The overall interpretation is that CCOP sites have substantially higher baseline accrual than non-CCOP sites, but that actual accrual is decreasing in CCOP sites and increasing in non-CCOP sites.

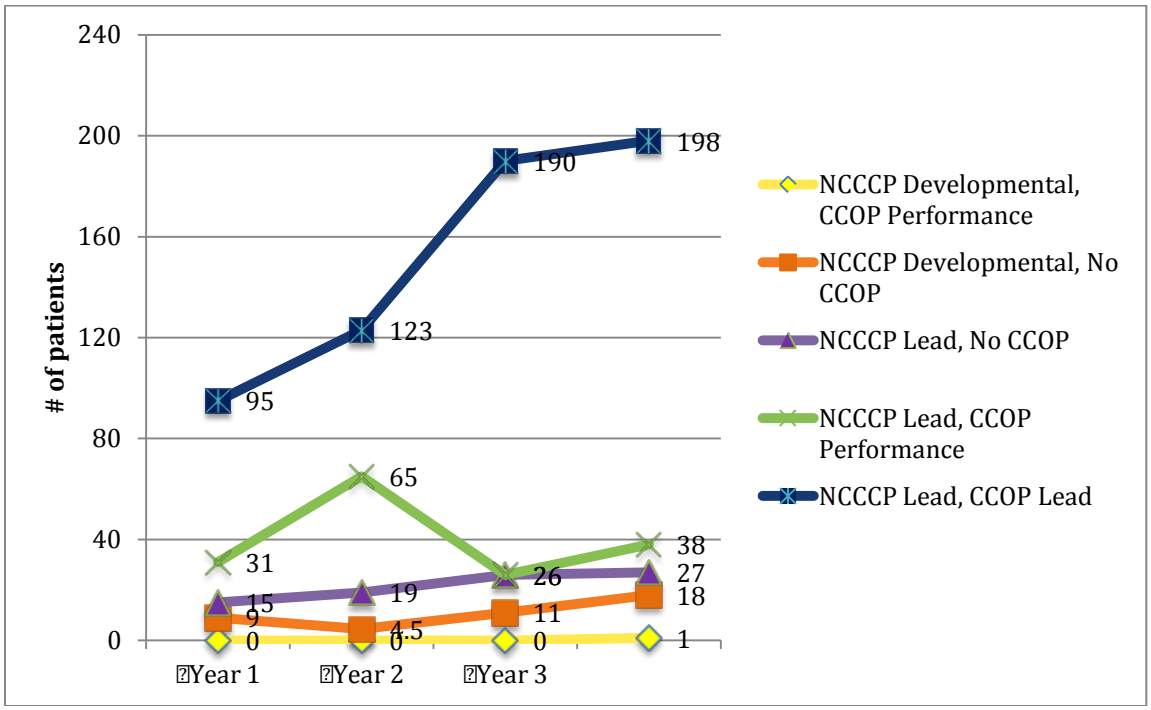
Figure 12: Median Accrual (CTEP Data) - CCOP & Non-CCOP Sites



Interaction between Type of NCCCP Site and CCOP Status

Among the three centers that were both Lead NCCCP and Lead CCOP sites, median per site accrual at baseline was 95 (range 40-203) and 198 in Year 3 (range 54-501), an increase of 108%. As the next section will reveal, this high and increasing median was being driven by one site. There were three centers that were NCCCP Lead sites and CCOP performance sites; their median accrual at baseline was 31 (range 6-42) and 38 in Year 3 (range 26-38), an increase of 23%. Five centers were NCCCP Lead sites that were not a part of the CCOP program. Their median accrual was 15 at baseline (range 4-29) and rose to 27 in Year 3 (range 11-48), an increase of 80%. There was a single center that was a NCCCP Developmental site and a CCOP Performance site. This site's accrual was 0 in Year 1 and 1 in Year 3. Finally, 4 NCCCP Developmental sites were not participants in the CCOP program. Their median accrual was 9 in Year 1 (range 0-23) and 18 in Year 3 (range 0-36), an increase of 100% (Figure 13).

Figure 13: Median Accrual (CTEP Data) - By Site Designation



At baseline, the CTEP data for each site showed that 14 of 16 sites had patients enrolled in clinical trials, with the largest accrual at the Lead NCCCP and CCOP sites (Figure 14). When % change in accrual over the evaluation period is plotted (Figure 15), only one CCOP site showed a marked increase in patient accrual with time. In most instances, there was an inverse relationship between the accrual at baseline and the proportional change in accrual over the three-year evaluation period. In the following figures, the same sites are represented in the same position to facilitate comparison.

The overall interpretation is that CCOP sites contribute the greatest numbers in actual accrual and also the greatest numbers at baseline, but that non-CCOP sites most consistently demonstrate relative growth in accrual over the NCCCP evaluation period. Both NCCCP Lead and Developmental sites were able to demonstrate relative growth in accrual. And, dramatically different experiences at a single site can lead to substantial swings in reported medians, potentially skewing interpretation of the results if individual site performance is not taken into consideration.

Figure 14: Accrual Per Site (CTEP Data) - Baseline

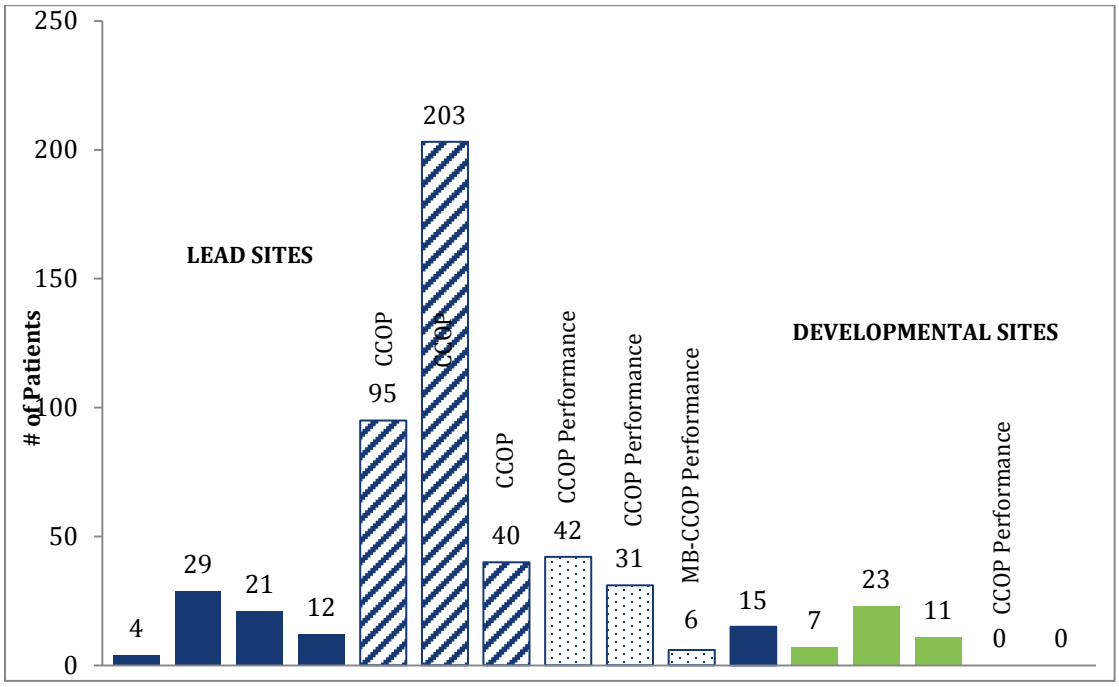
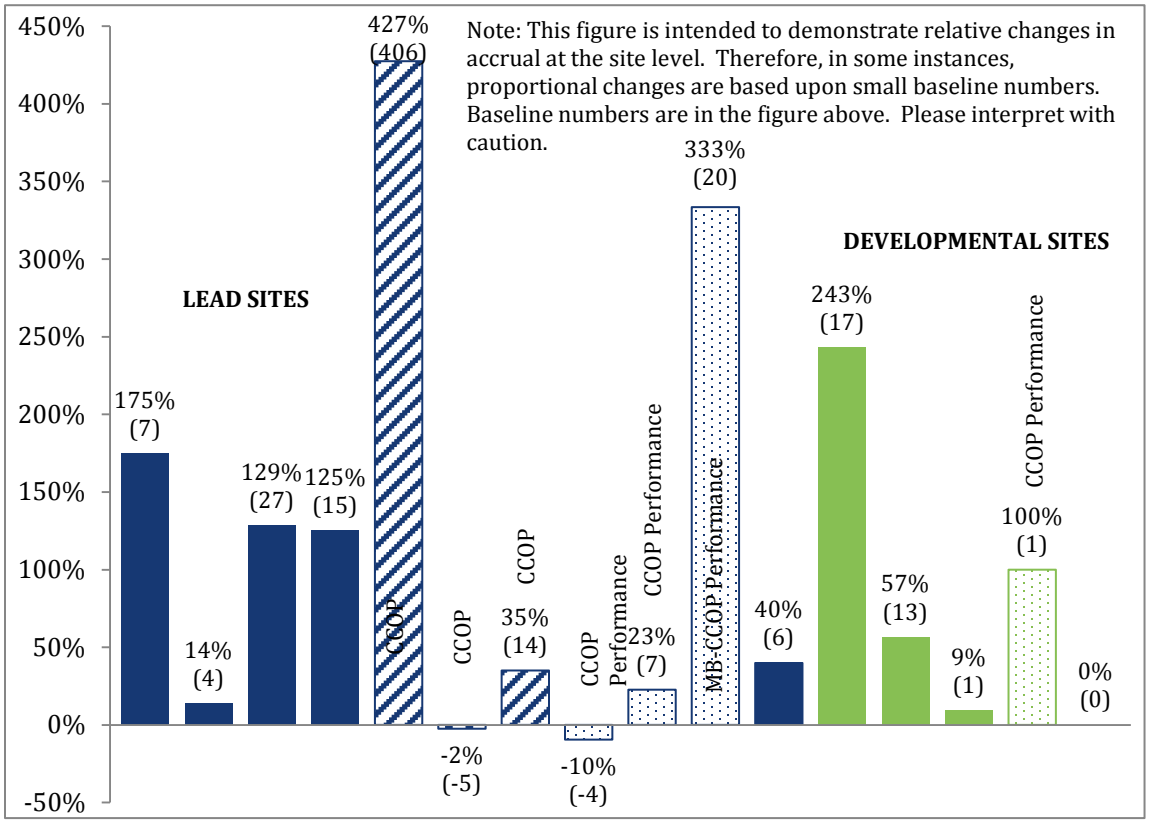


Figure 15: Accrual Per Site (CTEP) - Proportional Change (Absolute Change) from Baseline to Year 3

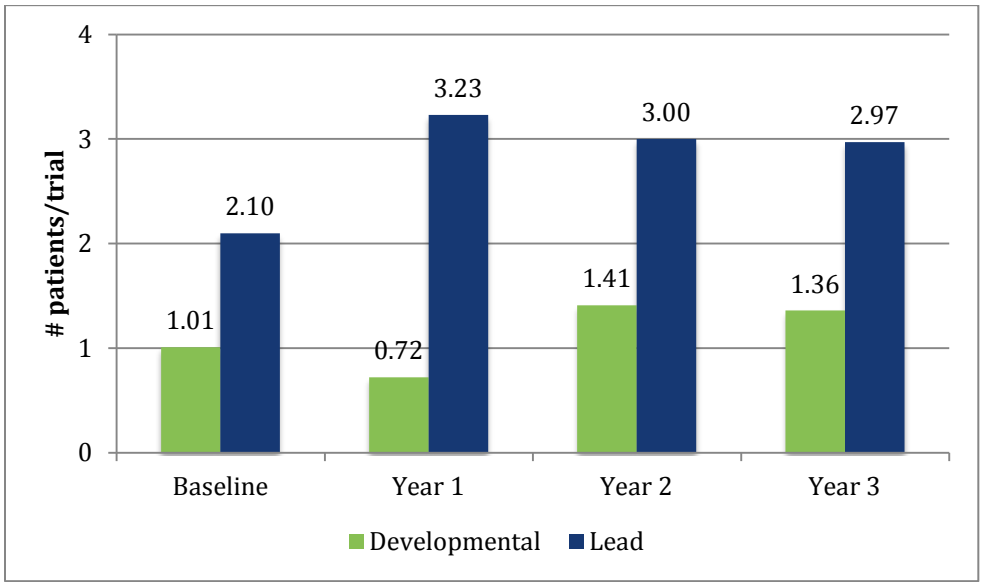


Average Accrual per Trial

The previous results focused on the number of trials or the number of patients. Also of interest is the average enrollment in trials (i.e., the number of patients accrued per trial being conducted). Across the whole NCCCP program, the average enrollment per trial at baseline was 1.80 (range 0-5.25), at Year 1 was 2.21 (range 0-8.13) and at Year 3 was 2.23 (range 0-12.53), a 24% increase. Developmental and Lead sites increased the average enrollment over the evaluation period, by 35% and 41%, respectively (Figure 16).

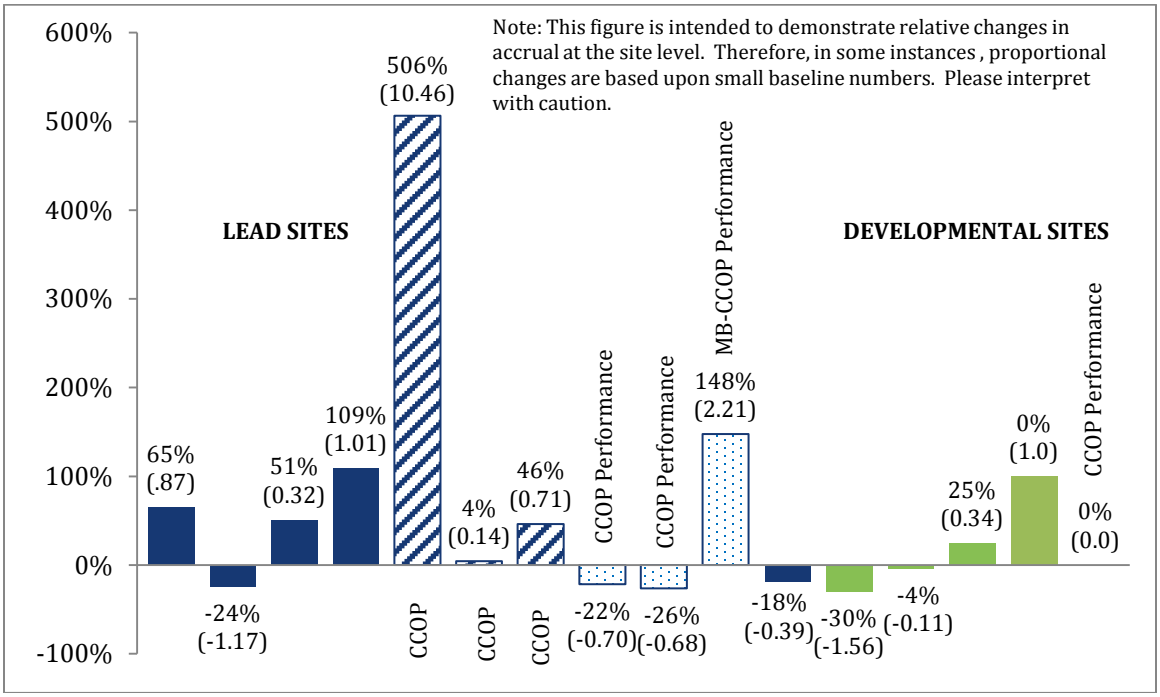
Lead sites increased their patients per trial in the first year and maintained that level throughout the three years while Developmental sites demonstrated a more gradual increase over time. This trend for NCCCP Lead sites to achieve accrual increases earlier than the Developmental sites may be another reflection of the sequencing effect observed in the site vignettes. Specifically, Lead sites have more open trials and more mature clinical research infrastructure at the outset, so are more poised to increase accrual earlier. Developmental sites are predominantly focusing on getting their clinical research infrastructure organized, which first leads to more open trials with increases in accrual likely following later.

Figure 16: Median Number of Patients per Trial (CTEP Data) - By NCCCP Lead & Developmental Sites



Based on the previous figure, one might assume that each site had a similar relative accrual over the 3 years. While 7 of the 11 Lead sites increased the patient to trial ratio, one site was clearly dominant. Furthermore, only a single Developmental site had increased its accrued patients to trials ratio over the evaluation period (Figure 17).

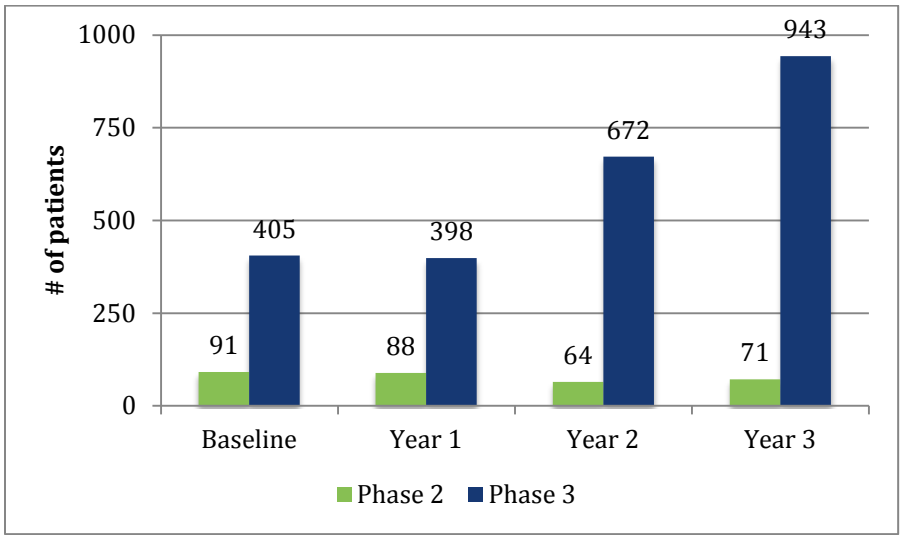
Figure 17: Proportional Change (Absolute Change) in Number of Patients per Trial from Baseline to Year 3 by Site (CTEP Data)



Accrual by Study Phase

As reported earlier, CTEP data showed that the number of Phase 3 trials increased over the evaluation period, whereas the number of Phase 2 trials stayed relatively stable. Not surprisingly, the total accrual to Phase 3 trials also increased from baseline (405) to Year 3 (943), an increase of 133%. Total accrual to Phase 2 trials decreased by 22% from 91 patients at Baseline to 71 patients accrued in Year 3 (Figure 18). The average enrollment in Phase 3 trials rose from 2.65 patients per trial at Baseline to 4.56 patients per trial in Year 3.

Figure 18: Total Accrual by Study Phase (CTEP Data)



Accrual of Underserved Populations

Accrual of patients of underserved populations increased yearly. As a note, the government's Office of Management and Budget (OMB) does not require collection of rural status for patients on clinical trials and this information is not captured in the CTEP system (although it is presented in the Site Self-reported Data section, later in this report, where sites self-defined the term "rural"). Therefore, CTEP data for underserved populations represent patients classified as "racial/ethnic minority" and those at or above age 65. People at or above age 65 were included since elderly individuals are frequently underrepresented in cancer clinical trials and were therefore a focus in the NCCCP clinical trials evaluation.

At baseline, CTEP data showed an accrual of 83 patients classified as "racial/ethnic minority" which rose steadily to 151 in Year 3 (Figure 19), an 82% increase. Total overall accrual during this period was 539 at baseline and 1068 in Year 3, a 98% increase. The relative increase in accrual for "racial/ethnic minority" was fairly consistent with the total accrual (15% of total accrual at baseline and 14% in Year 3), thus accrual of these patients rose in proportion with the increase in total accrual (Figure 20).

The accrual of patients classified at baseline as "age 65 or over" numbered 200 and rose to 641 in Year 3. This represents a 221% increase in accrual. The relative increase in accrual of patients "age 65 or over" was more than twice the relative increase in total accrual (37% accrual at baseline and 60% at Year 3) showing that enrollment of patients in this category was occurring more rapidly than for total accrual.

Figure 19: Accrual of Underserved Populations (CTEP Data)

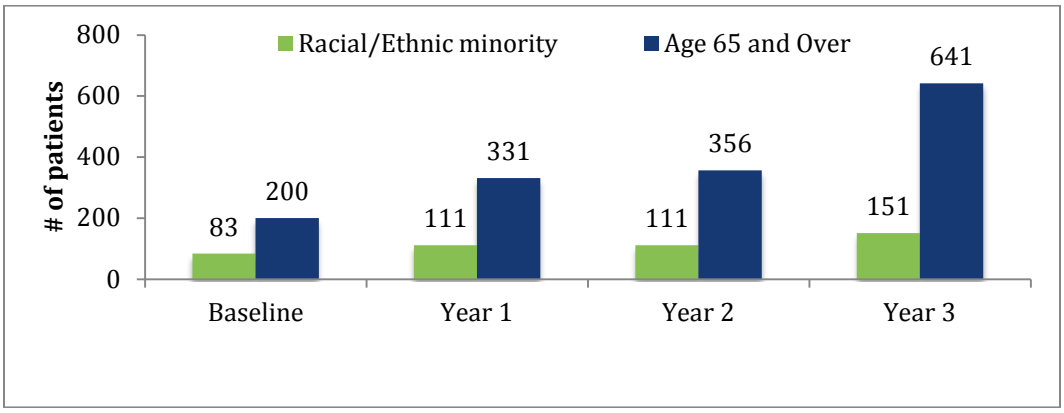
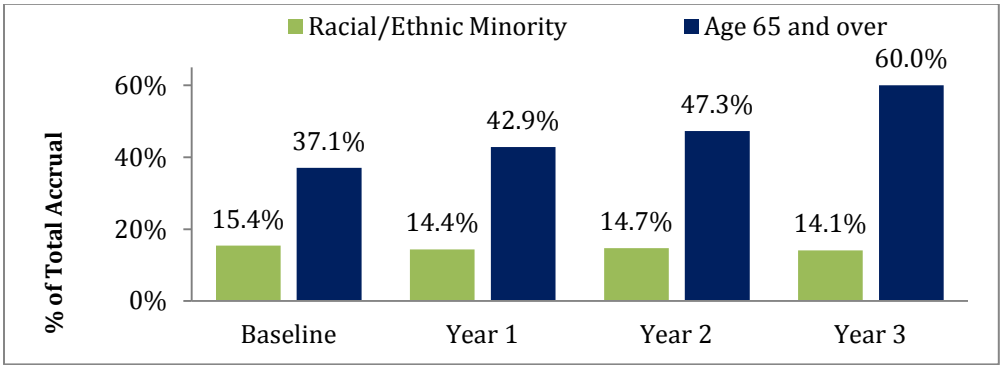


Figure 20: Accrual of Underserved Populations as a Proportion of Total Accrual (CTEP Data)



The relative change from baseline for each site shows a distinct pattern where a large fraction of accrual in "Racial/Ethnic Minority" occurred in two sites. This same pattern (albeit at 3 different sites) was evident for the "Age 65 or Over" patients (Table 1).

Table 1: Change in Underserved Accrual and Change in Proportion of Total Accrual by Site (CTEP Data)

(Note-Change in Proportional Accrual is in Brackets)

Site	NCCCP Lead or Developmental	CCOP Lead or Performance	Racial/Ethnic Minority	Age 65 or Over	Total Underserved Accrual
3	Lead	Performance	9 (22%)	14 (54%)	23 (76%)
14	Developmental		0 (0%)	17 (42%)	17 (42%)
16	Lead	Lead	40 (-6%)	365 (44%)	405 (38%)
15	Lead		9 (16%)	4 (3%)	13 (19%)
9	Lead	Lead	2 (2%)	13 (13%)	15 (15%)
6	Lead	Lead	11 (6%)	11 (7%)	22 (12%)
12	Lead		5 (9%)	5 (0%)	10 (9%)
2	Lead	Performance	3 (6%)	3 (1%)	6 (7%)
5	Developmental	Performance	0 (0%)	0 (0%)	0 (0%)
11	Developmental		0 (0%)	0 (0%)	0 (0%)
4	Lead	Performance	-6 (-14%)	2 (10%)	-4 (-4%)
1	Lead		-3 (-13%)	1 (-2%)	-2 (-15%)
10	Lead		-2 (-13%)	1 (-5%)	-1 (-18%)
13	Developmental		0 (0%)	-2 (-24%)	-2 (-24%)
8	Developmental		2 (-12%)	4 (-24%)	6 (-36%)
7	Lead		-2 (-66%)	2 (2%)	0 (-64%)

Visual inspection of the difference in accrual by site reflects the variable activity by site (Figures 21-24). The following figures reflect absolute accrual numbers and changes in accrual at a site over time; the same sites are represented in the same position to facilitate comparison. Most notably, 5 of 7 CCOP sites demonstrated positive shifts in accrual of underserved populations, which was most dramatic for people age 65 and over. Meanwhile, only 3 of 9 non-CCOP NCCCP sites demonstrated positive shifts in accrual of underserved populations, with two sites driving the majority of the activity. Also, consistent with the objectives of the Minority-Based CCOP site, this is the site with the greatest change in accrual of underserved populations.

The overall interpretation is that across the NCCCP, accrual of underserved populations is increasing, most notably among people age 65 and over. There is also increasing representation of racial and ethnic minority study participants, at a rate commensurate with the overall increase in accrual demonstrated in the NCCCP. NCCCP sites that are affiliated with the CCOP program see the most consistent relative increases in accrual of underserved populations; this is despite the fact that these CCOP-affiliated sites did not show consistent increases in overall clinical trials activity during this pilot program. The Minority-Based CCOP demonstrated most remarkable improvements; the site vignette suggests that organizational alignment at that site also likely had meaningful impact. When considered in summary with the site-reported data and vignettes, a reasonable conclusion is that the CCOP sites, which already demonstrated a high level of overall relative clinical research activity, were motivated by the NCCCP program to focus more intensively on accrual of underserved populations, aligned their internal focus accordingly, and enrolled more people of these backgrounds into clinical trials over time.

Figure 21: Total Accrual of Underserved Populations at Baseline by Site (CTEP Data)

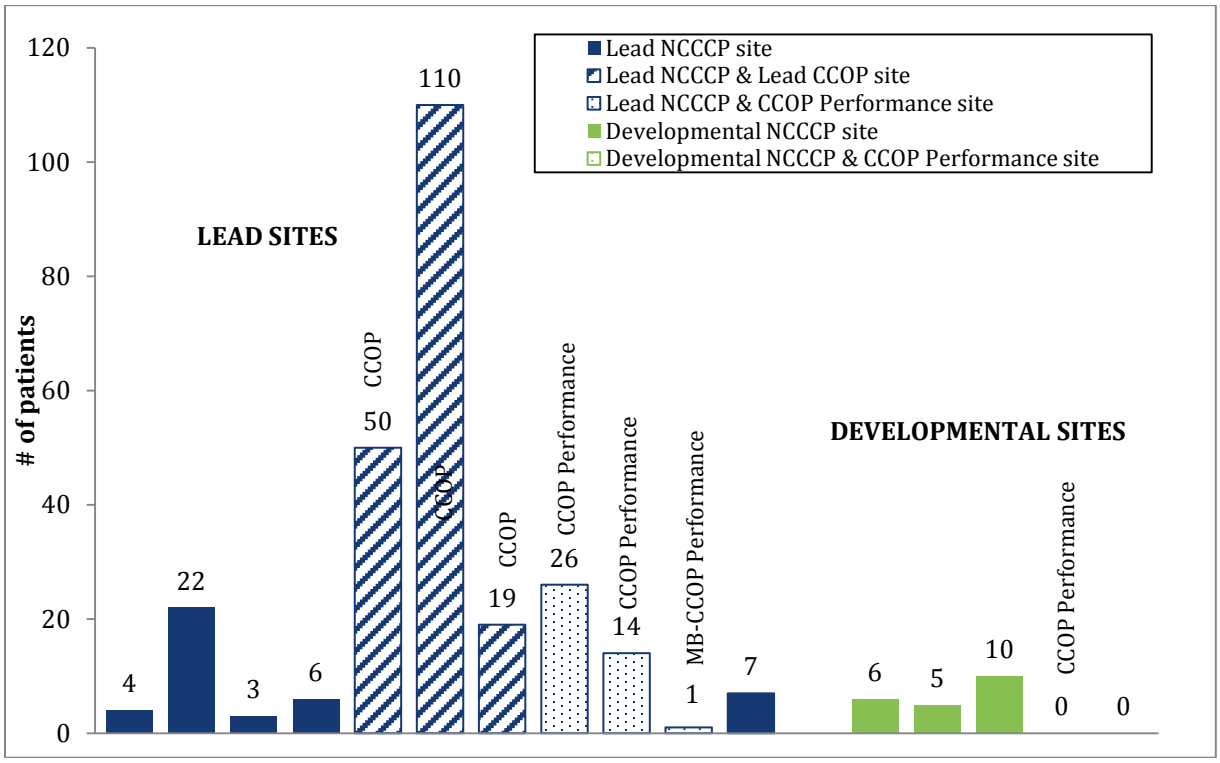


Figure 22: Proportional Change in % of Total Accrual of Underserved Populations from Baseline to Year 3 by Site (CTEP Data)

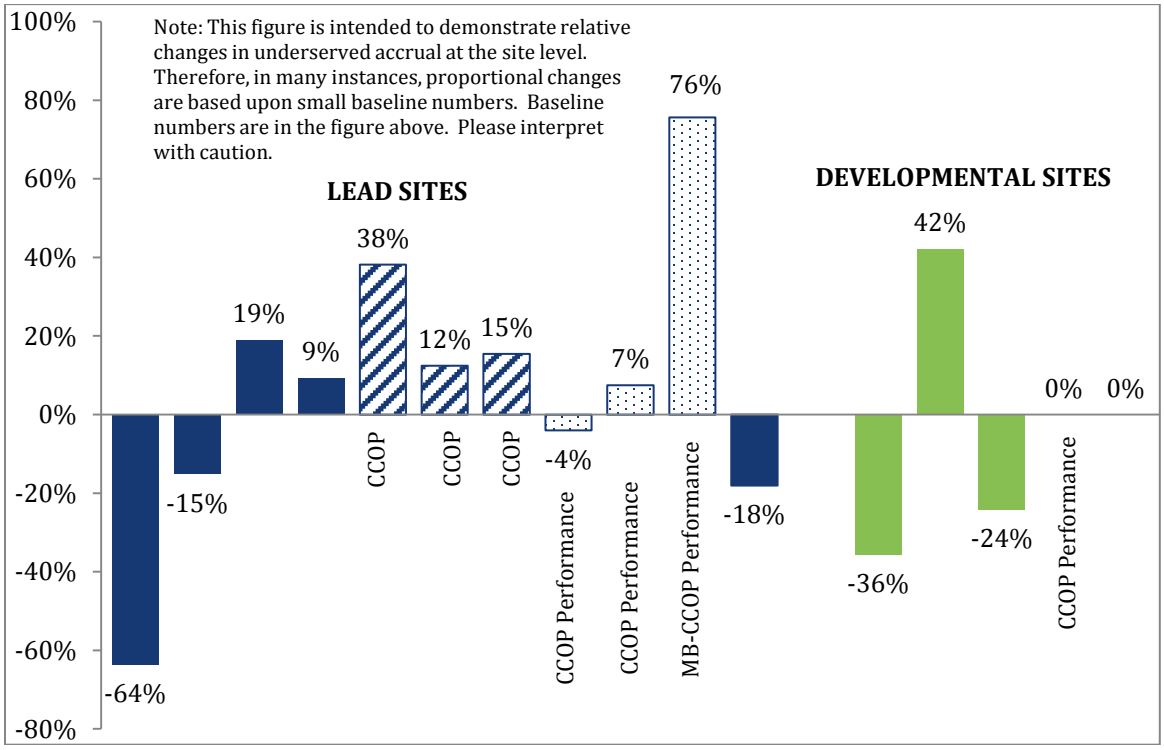


Figure 23: **Proportional Change in % of Total Accrual of Racial/Ethnic Minorities from Baseline to Year 3 by Site (CTEP Data)**

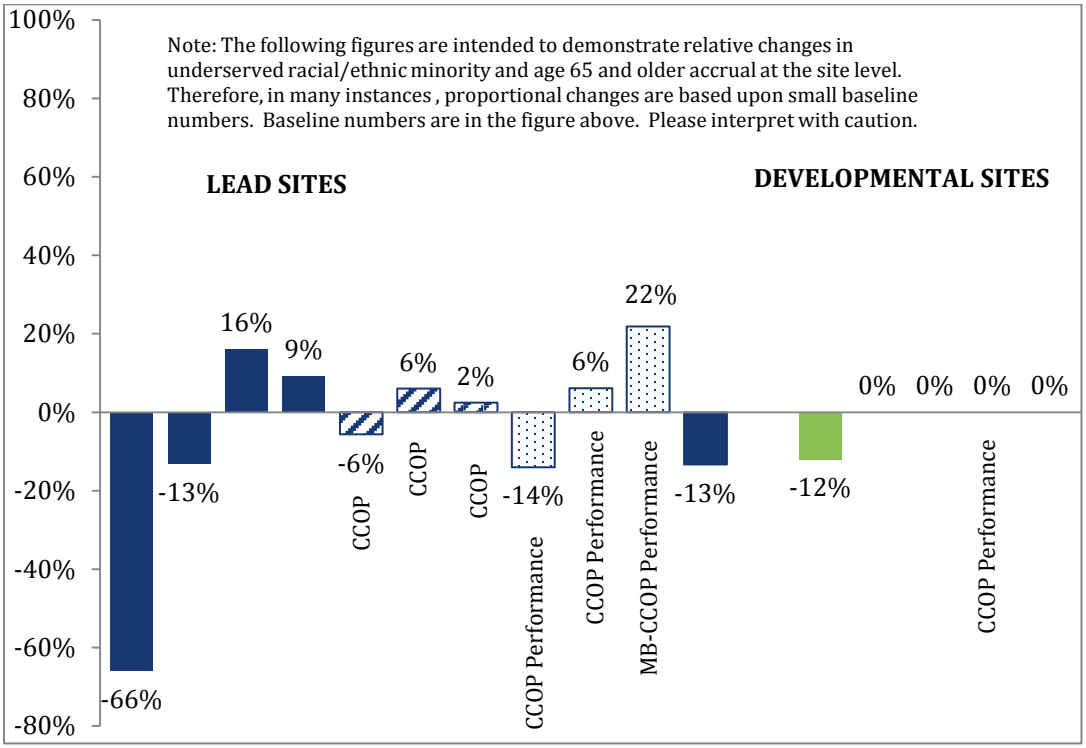
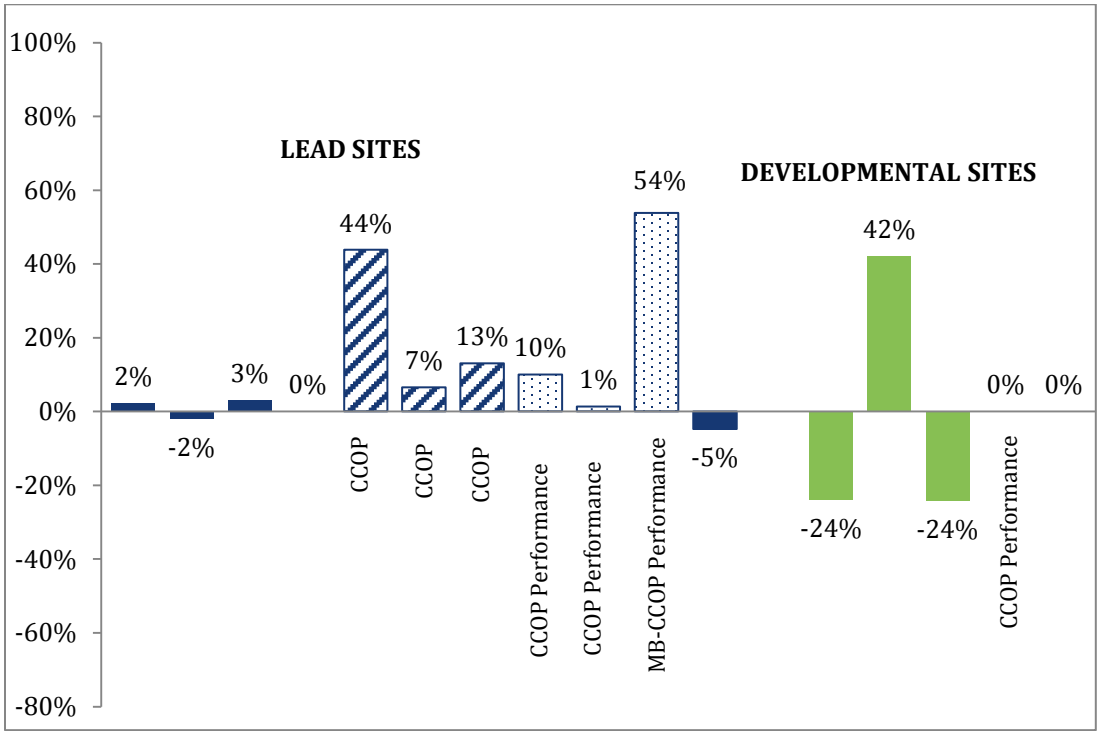


Figure 24: **Proportional Change in % of Total Accrual of People Age 65 and Over from Baseline to Year 3 by Site (CTEP Data)**



National Trends - Comparison Using CTEP Data

In order to set the NCCCP clinical trials activities within the context of other cancer-related clinical trials efforts, analyses were performed to examine whether trends in change in clinical trials accrual and portfolio among the NCCCP sites aligned with or differed from national trends in clinical trials activity. Importantly, the focus was on trends – namely, how did the trajectories reflecting change over time align or differ; while absolute numbers are presented here as they contributed to the trend calculations, the focus was not on the total numbers of trials and accrual but rather proportional change over time.

CTEP data were used to complete these calculations. The nationwide data includes information from all NCI Cancer Centers, Cooperative Groups, and DCP cancer control and prevention studies. It is assumed that the data from the NCCCP sites is also included as a part of this nationwide dataset. Since the NCCCP sites were not excluded for the national trends analyses, at least some of the national trend information reflects the influence of the NCCCP trend.

NCCCP site data was compared to total number of trials open in the national Cooperative Group network, not a comparison to non-NCCCP site data. There could be some concern that this analysis reflects a comparison of trial level data of the Cooperative Groups with site level data of the NCCCP sites. However, the goal was to focus on trends to facilitate broad general understanding of how NCCCP trial portfolio and accrual activity compared with what was happening nationally during the same period.

Number of Clinical Trials

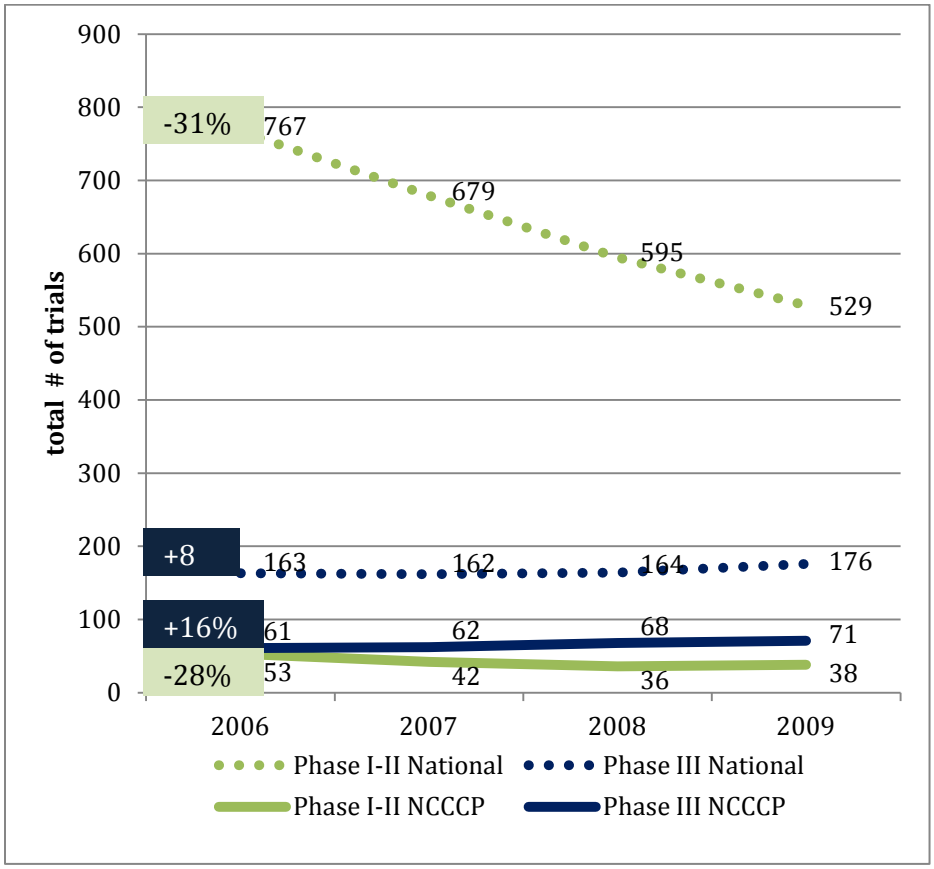
Phase 1/2 and Phase 2 trials (collectively called Phase 1-2) were grouped together and plotted with the Phase 3 trials over the evaluation period.

Over the evaluation period, the nationwide number of Phase 1-2 trials decreased by 31% while Phase 3 trials increased by 8%. During this time, the NCCCP sites showed a similar decline in Phase 1-2 trials with 28% fewer trials being conducted, but increased Phase 3 trials by more than 16% (Figure 25).

Reflected another way, at baseline, the NCCCP had 53 (7%) of the 767 Phase 1-2 clinical trials reported in CTEP open. At the end of the evaluation period, the NCCCP had 38 (7%) of the 529 Phase 1-2 clinical trials reported in CTEP open. At baseline, the NCCCP had 61 (37%) of the 163 Phase 3 clinical trials reported in CTEP open. At the end of the evaluation period, the NCCCP had 71 (40%) of the 176 Phase 3 clinical trials reported in CTEP open.

Overall, these data suggest that changes in number of trials open across NCCCP sites were generally consistent with national trends, although NCCCP sites added Phase 3 trials at a higher rate.

Figure 25: Number of Ongoing Therapeutic Trials Nationally and in the NCCCP over Time by Study Phase (CTEP Data)



Total Participant Accrual

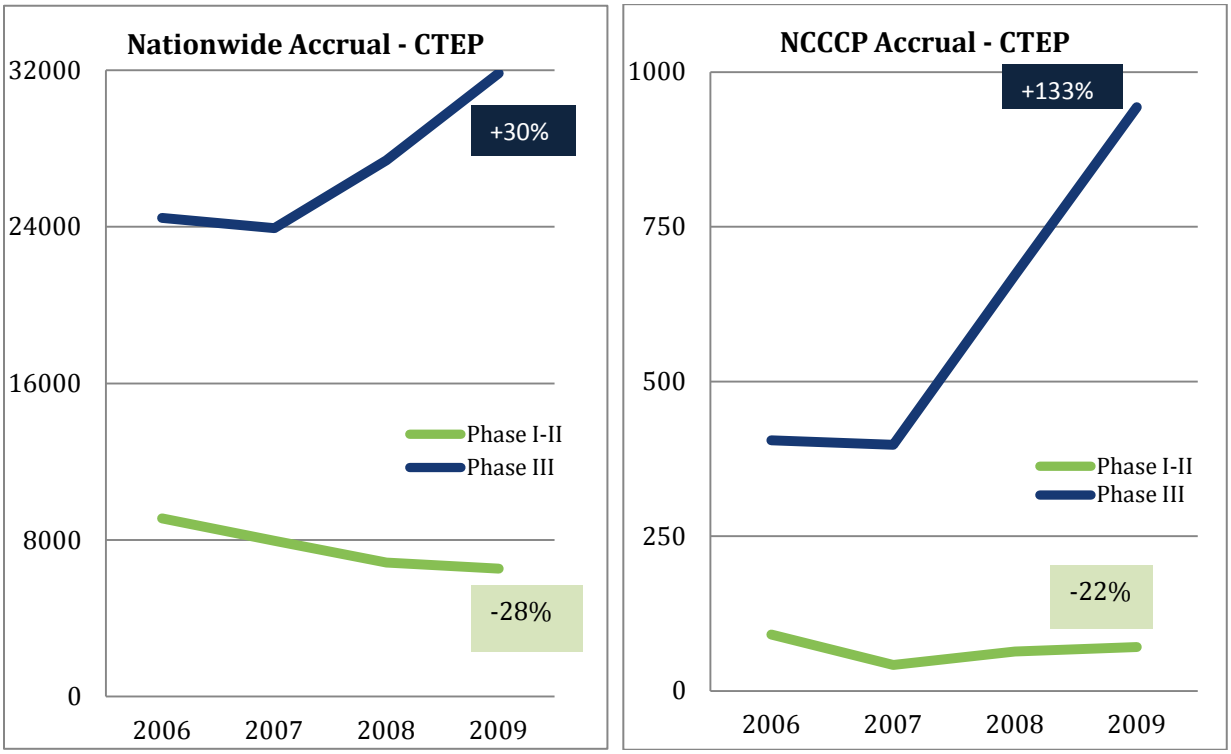
The CTEP data demonstrate that NCCCP sites contributed 539 (1.4%) of the 37,749 patients enrolled in studies reported in CTEP at baseline, and 1068 (2.5%) of the 42,217 patients enrolled in studies at the end of the evaluation period.

NCCCP sites performed better than nationwide sites during the evaluation period. Nationally, patient accrual decreased for Phase 1-2 trials (-28%) and increased for Phase 3 trials (+30%). In contrast, the NCCCP sites experienced a smaller decline in Phase 1-2 accrual (-22%) and a much greater increase in Phase 3 accrual (+133%; Figure 26).

In terms of absolute numbers, at baseline, the NCCCP had 91 (1.0%) of the 9097 patients enrolled in Phase 1-2 clinical trials as reported in CTEP. At the end of the evaluation period, the NCCCP had 71 (1.1%) of the 6539 patients enrolled in Phase 1-2 clinical trials reported in CTEP. At baseline, the NCCCP had 405 (1.7%) of the 24,462 patients enrolled in Phase 3 clinical trials as reported in CTEP. At the end of the evaluation period, the NCCCP had 943 (3.0%) of the 31,848 patients enrolled in Phase 3 clinical trials reported in CTEP.

Overall, these data suggest that NCCCP sites were contributing progressively more patients to Phase 3 trials over time than compared to the national rate. The rate of contribution to Phase 1-2 trials was consistent with national averages.

Figure 26: Nationwide and NCCCP Accrual over Time by Study Phase (CTEP Data)



Average Study Enrollment (Participants Per Trial)

The number of patients per trial is a metric that makes comparisons between sites with varying numbers more practical. Nationally, Phase1-2 trials averaged about 12 patients per trial across the evaluation period (July 2006-July 2010) with an increase of only 4%. Average study enrollment for Phase 3 trials rose from 150 at the start of the evaluation period to 181 at the end; a 21% increase. The relative NCCCP contribution to overall national study enrollment rose at a greater rate than observed generally, at 9% for Phase 1-2 trials and 100% for Phase 3 trials (Table 2).

Table 2: Average Study Enrollment Nationally and in the NCCCP over Time by Study Phase (CTEP Data)

Nationwide Sites	2006-2007	2007-2008	2008-2009	2009-2010	% change
Phase I-II	11.9	11.7	11.5	12.4	4%
Phase III	150.1	147.7	167.0	181.0	21%

NCCCP Sites	2006-2007	2007-2008	2008-2009	2009-2010	% change
Phase I-II	1.7	1.0	1.8	1.9	9%
Phase III	6.6	6.4	9.9	13.3	100%

The summary interpretation is that the NCCCP sites are changing their numbers of open trials generally in step with national trends, but that accrual is increasing across these sites faster than national trends. The 16 NCCCP sites are contributing about 2% of the national accrual to CTEP-reported clinical trials; this increased from 1.4% to 2.5% over the time period, accounting for an 80% change over time. Also, the NCCCP sites are predominantly contributing to Phase 3 trials, demonstrating more activity in these types of studies and more proportionally increasing activity over time. Participation in Phase 1-2 trials is generally similar to national trends.

Site Self-reported Data

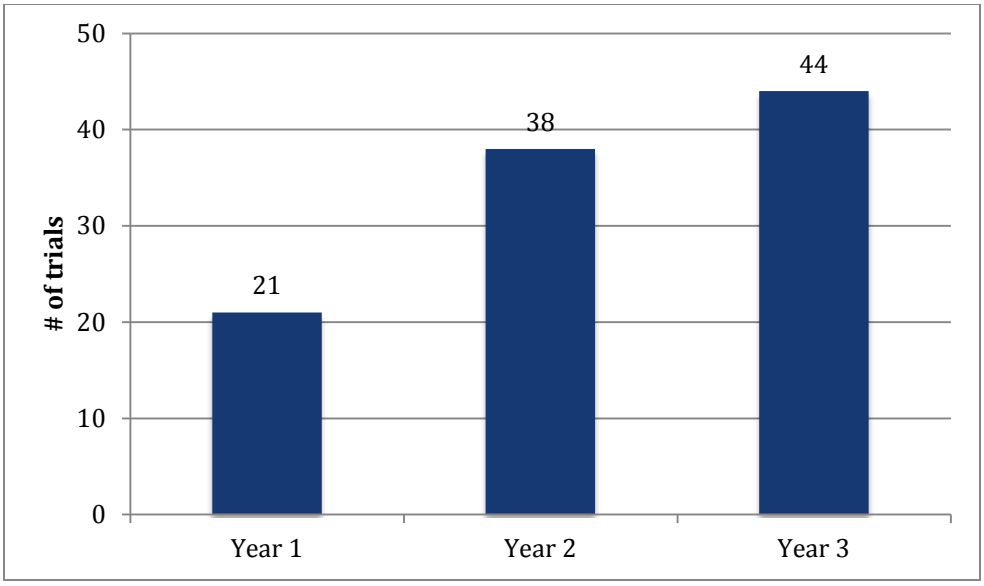
Clinical Trials Portfolio – Site-reported

The NCCCP sites reported data quarterly and yearly about their staff and capabilities, trials portfolio, and accrual. Limitations of these data are noted in Methods: Data Sources and Limitations, above. Despite their acknowledged limitations, these data furnish an important complementary view of the data extracted from the CTEP database. While CTEP data provide the most accurate view of actual accrual and trial characteristics for the trials reported in the NCI clinical trials system, the site-level data offer an "on-the-ground" view of the sites' clinical trials activities and performance.

Number of Trials

The total number of trials at baseline was unavailable. According to site self-reported data, the median number of all types of trials per site was 21 (aggregate=616, range 1-164) for Year 1, increasing to 44 (aggregate = 737, range 0-157) for Year 3. This reflects a 110% increase in the median number of trials per site between Years 1 and 3, with a 20% increase in the aggregate number of trials across the NCCCP program (Figure 27). This is consistent with the CTEP results showing the median number of trials increasing during the three-year evaluation period.

Figure 27: Median Number of Trials (Site Self-reported Data)



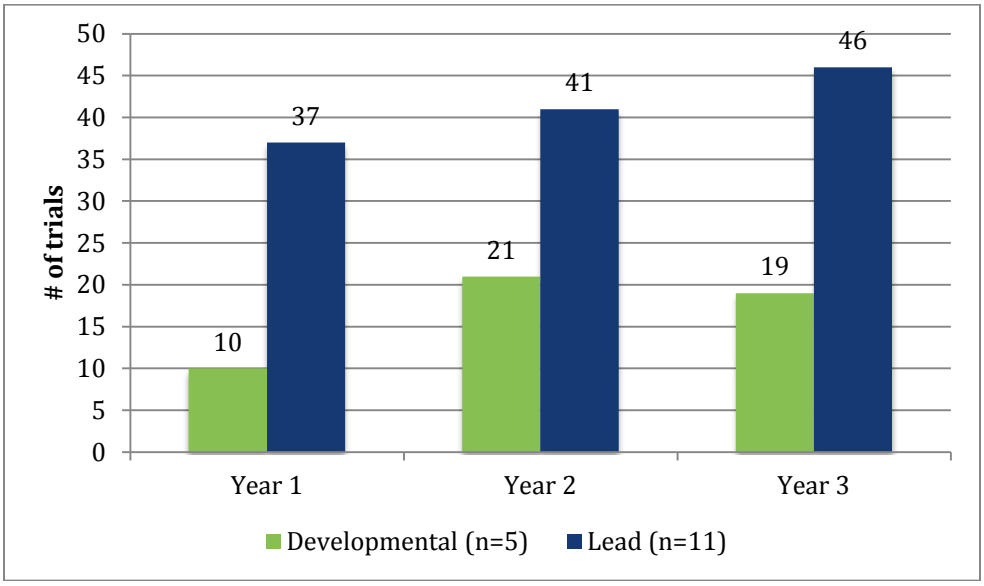
NCCCP Lead and Developmental

According to the site reported data, the median number of trials conducted at Lead sites was 37 trials per site (aggregate=578, range 1-164) in Year 1 that increased to 46 (aggregate=625, range 16-157) in Year 3. Over the three-year evaluation period, the median number of trials at Lead sites rose by 24% and the aggregate number of trials rose by 8%. The median number of trials conducted by the five Developmental sites was 10 (aggregate=38, range 1-15) in Year 1 and the median increased to 19 (aggregate=112, range 0-50) in Year 3. Over the three-year evaluation period for the Developmental sites, the median number of trials rose by 90% and the aggregate number of trials rose by 195% (Figure 28).

The overall interpretation is that, in general, Lead sites had a greater volume of clinical trials activity in place at the outset of participation in the NCCCP, per site self-reported data. While growth in the total

number of open trials was witnessed for both Lead and Developmental sites, the relative proportional growth among Lead sites was more modest. The Developmental sites had little clinical trials activity reported at baseline and demonstrated greater proportional growth over time.

Figure 28: Median Number of Trials (Site Self-reported Data) – NCCCP Lead & Developmental Sites



CCOP and Non-CCOP Sites

Comparing CCOP sites and non-CCOP NCCCP sites, the median number of trials per CCOP site was 47 in Year 1 (range 2-147) and 42 in Year 3 (range 8-157), a decrease of 11%. The median number of trials per non-CCOP site was 10 in Year 1(range 1-49) and 46 in Year 3 (range 0-66), an increase of 240% (Figure 29). Comparing CCOP Lead and CCOP Performance sites, the Lead sites had an 18% decrease over the period (median trials per site of 51 in Year 1-range 37-152 and 42 in Year 3-range 25-157) and the Performance sites had a 20% increase over the period (median trials per site of 35 in Year 1 – range 2-164, and 42 in Year 3 – range 8-85; Figure 30).

The overall interpretation is that, in general, site self-reported clinical trials activity at CCOP sites was declining during the period of participation in the NCCCP program. This is consistent with observations across the whole CCOP program more generally and is unlikely to be related to NCCCP participation, as described in the parallel section of this report describing the CTEP data. CCOP sites had higher median numbers of trials open at the beginning of the NCCCP project (median 47 for CCOPs vs median 21 across the whole program). CCOP Lead sites appear to be at maximum saturation, with reduction in trial numbers over time; CCOP Performance sites did show some growth.

Figure 29: Median Number of Trials (Site Self-reported Data) – CCOP & Non-CCOP Sites

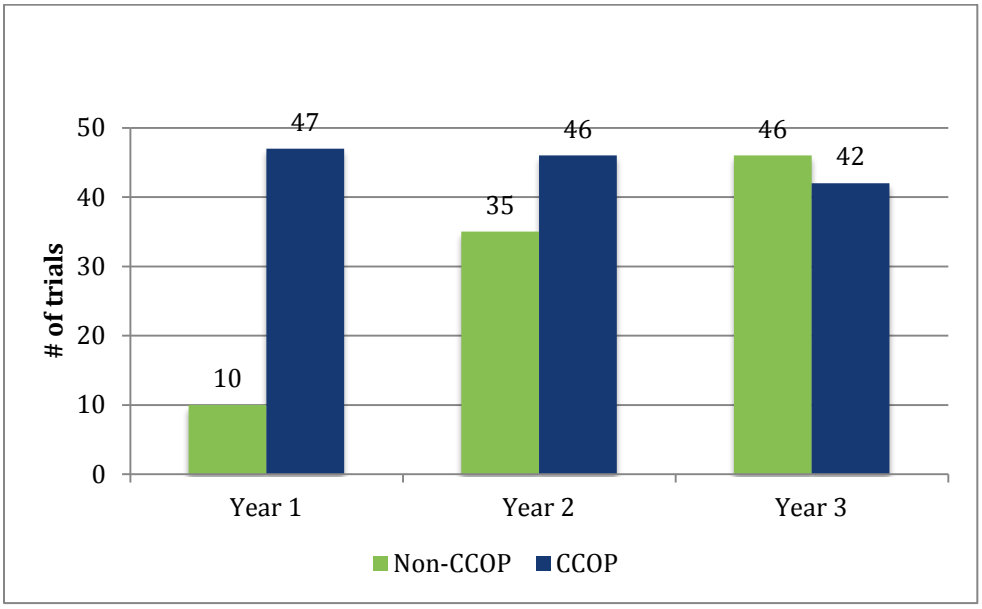
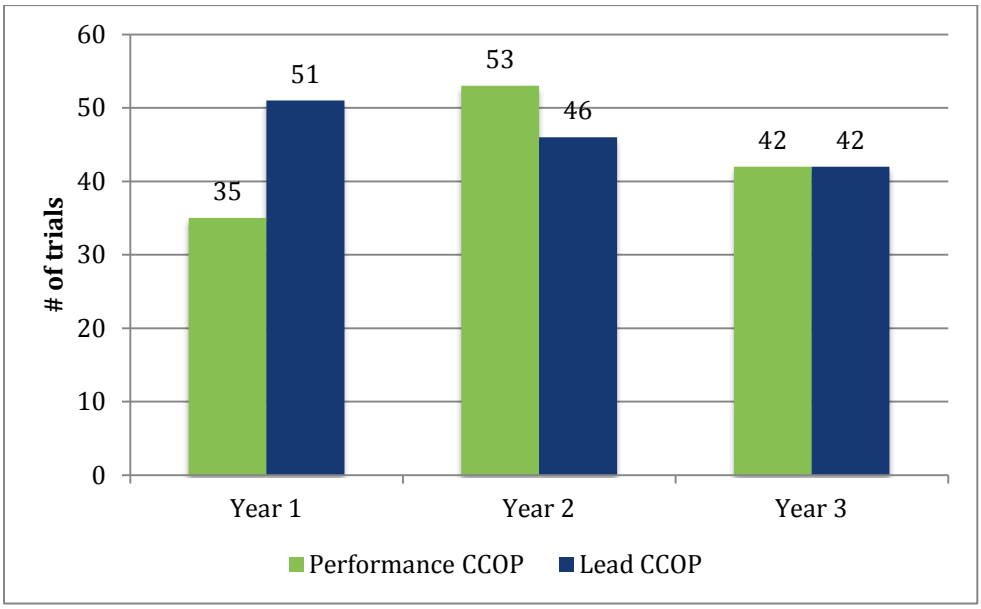


Figure 30: Median Number of Trials (Site Self-reported Data) - Lead & Performance CCOP Sites



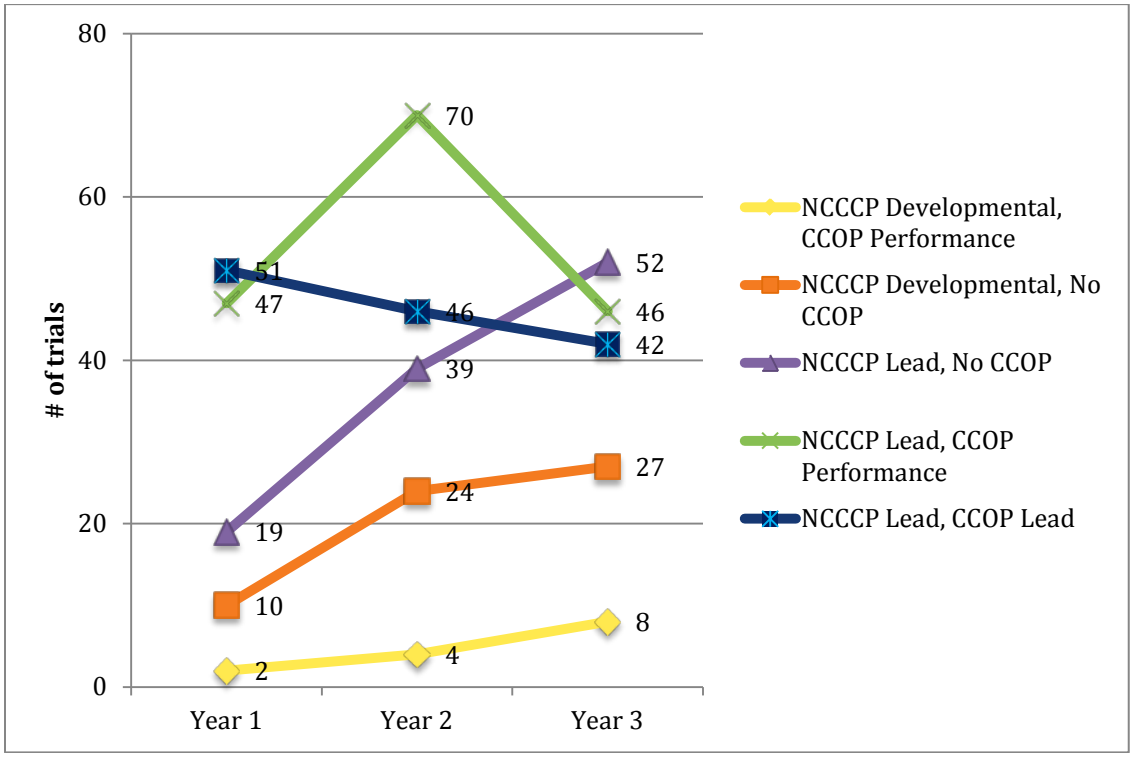
Interaction Between Type of NCCCP Site and CCOP Status

Among the three sites that were designated as both CCOP Lead and NCCCP Lead, the median number of trials per site was 51 in Year 1 (range 37-152) and 42 in Year 3 (range 25-157), a decrease of 18. Among the three sites that were designated as NCCCP Lead and CCOP Performance sites, the median number of trials in Year 1 was 47 (range 23-164) that spiked to 70 in Year 2 (range 35-139) before returning to 46 in Year 3 (range 37-85); overall, this reflects a 2% reduction from Year 1. There were five NCCCP Lead

sites that were not a part of the CCOP program; for these sites the median number of trials was 19 in Year 1 (range 1-49) and rose each year to 52 in Year 3 (range 16-66), an increase of 174%. There was a single center that was a NCCCP Developmental site and a CCOP Performance site. This site participated in two trials in Year 1 that doubled each year to eight in Year 3 (300% increase). Finally, there were 4 NCCCP Developmental sites that were not participants in the CCOP program. The median number of trials performed in Year 1 was 10 (range 1-15) and this increased each year to 27 in Year 3 (range 0-50), an increase of 170% (Figure 31).

The overall interpretation is that, in general, CCOP sites had substantially greater clinical trials activity at baseline which generally declined over the period of participation in the NCCCP program per site self-reported data. Meanwhile, NCCCP sites without a CCOP affiliation showed the more marked increases in median numbers of trials (all phases of trials) over time regardless of whether it was a NCCCP Lead or Developmental site. At the end of the pilot evaluation period, both CCOP sites and NCCCP Lead sites that were not CCOPs arrived at similar numbers of median trials per site, at 42-52 trials per site.

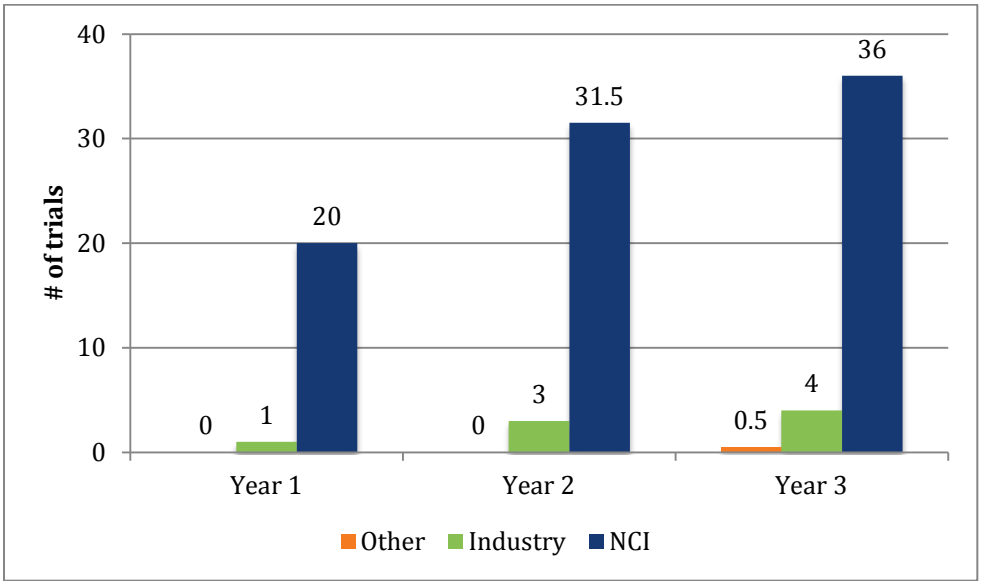
Figure 31: Median Number of Trials (Site Self-reported Data) - By Site Designation



Portfolio by Sponsor

Funds to conduct a trial came from a variety of sources. For the purposes of this report, site-reported trials were categorized as NCI-sponsored, Industry-sponsored, and a catch-all category of "Other" for all other trial sponsors. For all 16 sites, the median number of NCI-sponsored trials was 20 in Year 1 (range 0-132) and 36 in Year 3 (range 0-132). The median for Industry-sponsored trials was 1 (range 0-32) and 4 (range 0-20) in Years 1 and 3, respectively, and 0 (range 0-11) and 0.5 (range 0-5) for "Other" sponsored trials in Years 1 and 3 respectively (Figure 32).

Figure 32: Median Number of Therapeutic Trials by Sponsor Type (Site Self-reported Data)



NCI-sponsored trials – Overall, NCCCP Lead sites participated in two to four times as many NCI-sponsored trials when compared with the Developmental sites. The median number of trials conducted by the 11 Lead sites was 35 in Year 1 (range 0-132) and this increased to 38 in Year 3 (range 13-132) an increase of 9%. The median number of trials underway at the five Developmental sites was 8 in Year 1 (range 1-15) and this grew to 16 in Year 3 (range 0-45), an increase of 100% (Figure 33).

Figure 33: Median Number of NCI-sponsored Trials among NCCCP Lead & Developmental Sites (Site Self-reported Data)

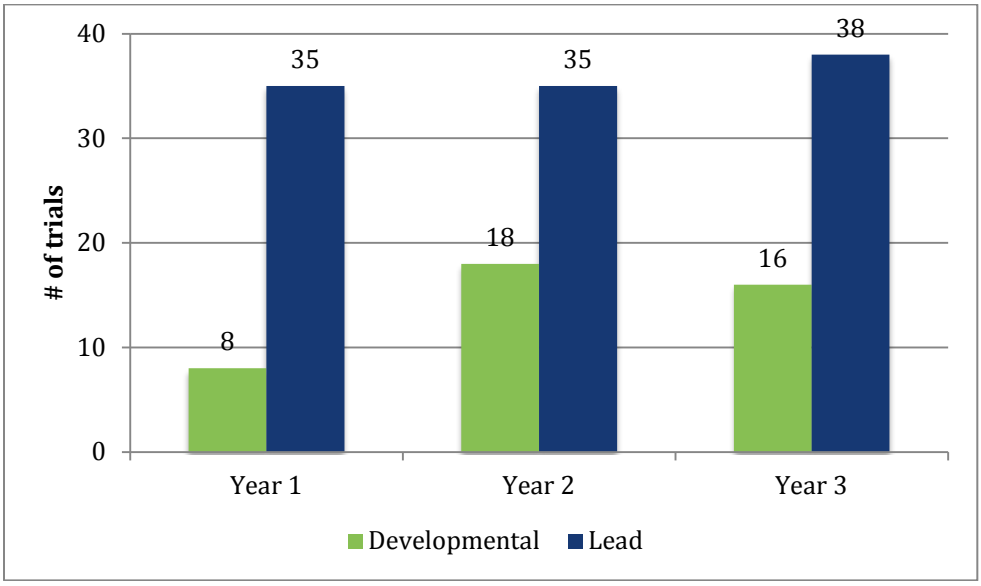
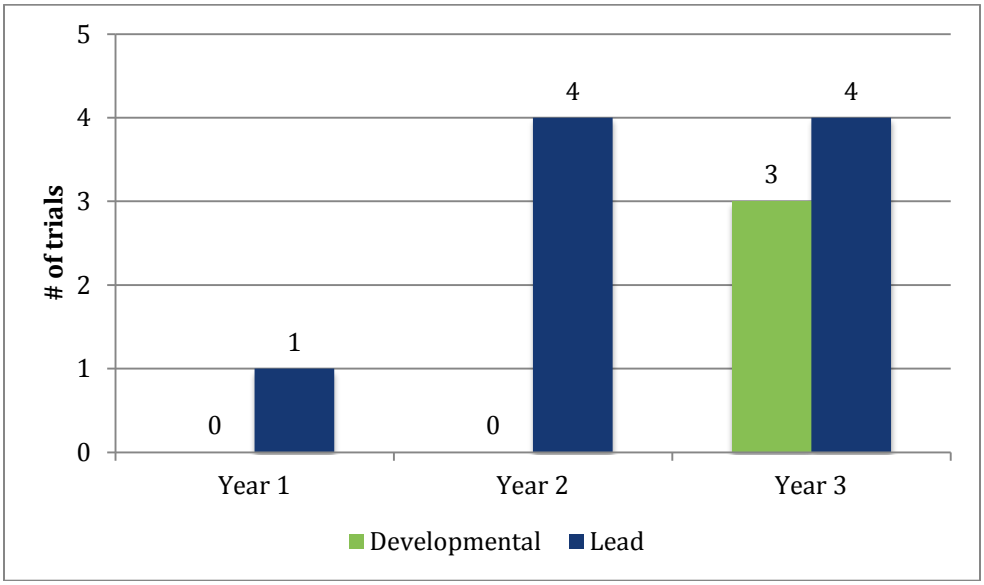


Figure 34: Median Number of Industry-sponsored Trials among NCCCP Lead & Developmental Sites (Site Self-reported Data)



Industry-sponsored trials – The number of Industry-sponsored trials at any site ranged from 0 to 32. The median number of trials conducted by the 11 Lead sites was 1 in Year 1 (range 0-32) and this increased to 4 in Year 3 (range 0-20). The median number of trials at the five Developmental sites was 0 in Year 1 (range 0-2) and this grew to 3 in Year 3 (range 0-9; Figure 34).

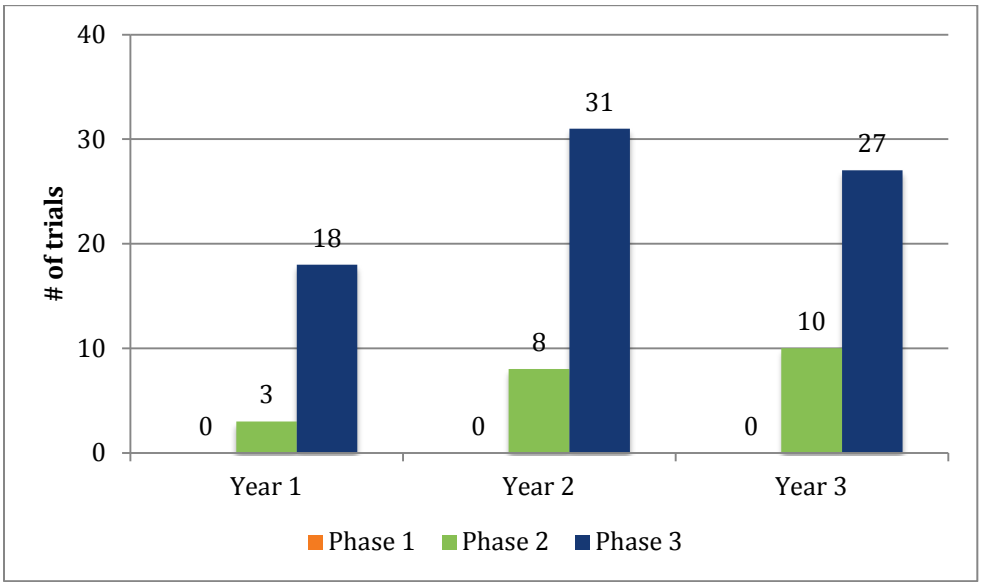
Other sponsored trials – There were few trials that were sponsored by "Other" sources. As most sites conducted no such trials, the median number of trials conducted was most often zero.

The overall interpretation is that, in general, per site self-reported data, the majority of the trials being conducted at these sites are NCI-sponsored. There was some increase in the median numbers of Industry-sponsored trials at median 3 trials per site, but overall this represented less than one-tenth of the overall activity.

Portfolio by Study Phase

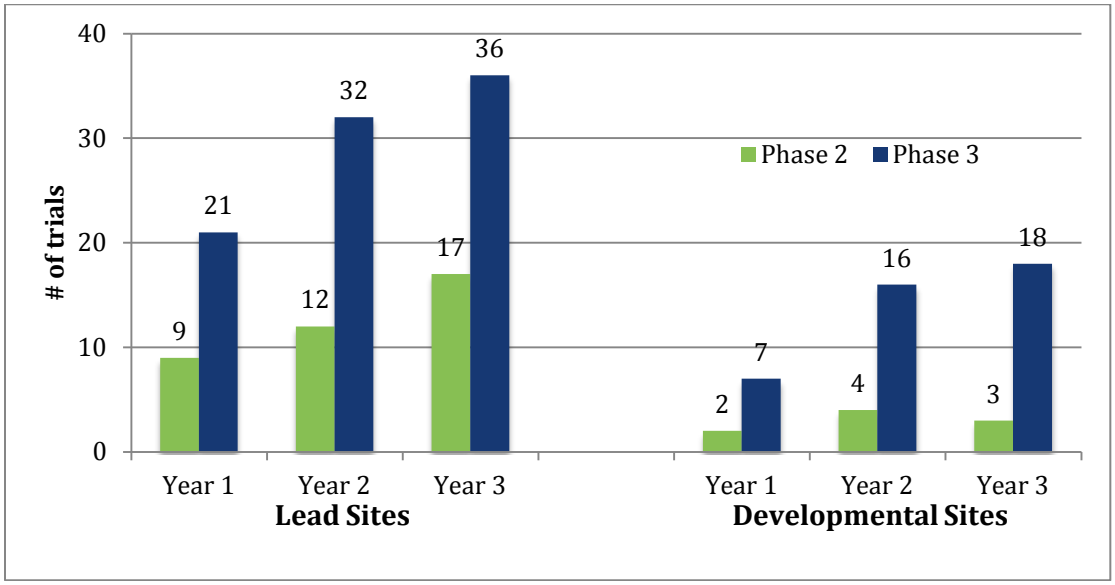
There were so few sites conducting Phase 1 trials that the median was 0 (range 0-5 across all years); subsequent discussion about trial phase will ignore Phase 1 trials. All sites conducted Phase 2 trials and 15 of the 16 sites conducted Phase 3 trials during the evaluation period. The median number of Phase 2 trials for Year 1 was three (range 0-71) and that rose to a median of 10 in Year 3 (range 0-62), an increase of 400%. The median number of Phase 3 trials in Year 1 was 18 (range 0-85) and this rose to 27 in Year 3 (range 0-82) an increase of 50% (Figure 35). Support for the largest fraction of these trials was NCI-sponsored. NCI-sponsored trials accounted for 67%, 62% and 60% of the Phase 2 trials reported by the sites for Years 1-3, respectively. NCI supported 94%, 87%, and 92% of the Phase 3 trials for Years 1-3 respectively.

Figure 35: Median Number of Trials (Site Self-reported Data) - By Study Phase



Phase 2 and Phase 3 trials by NCCCP Lead and Developmental designation – Based on median number of trials, NCCCP Lead sites conducted three to five times as many Phase 2 trials compared to Developmental sites and two to three times more Phase 3 trials than the Developmental sites (Figure 36).

Figure 36: Median Number of Trials (Site Self-reported Data) – By Study Phase & NCCCP Designation

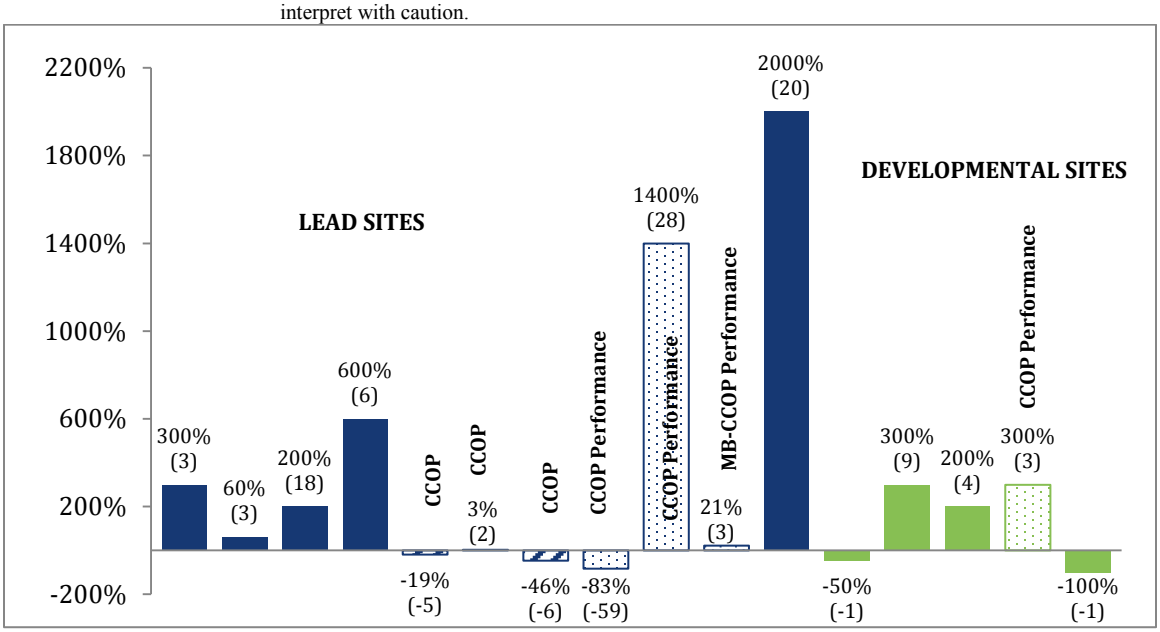


Phase 2 trials by site – All sites conducted phase 2 trials, and 11 of the 16 sites increased the number of Phase 2 trials they were conducting during the 3-year period. Eight of the 11 NCCCP Lead sites and three of the five Developmental sites reported an increase in the number of Phase 2 trials.

All three sites that had both NCCCP and CCOP Lead designation did not demonstrate substantial increase in the total number of Phase 2 trials, and two of three decreased numbers. All three of the NCCCP Lead sites that decreased their numbers of Phase 2 trials were CCOP sites. Meanwhile, among the CCOP vs non-CCOP sites, increase in Phase 2 trials was noted in four of seven CCOP sites and seven of nine non-CCOP sites (Figure 37).

Figure 37: Proportional Change (Absolute Change) in Number of Phase 2 Trials from Year 1 to Year 3 by Site (Site-reported Data)

Note: This figure is intended to demonstrate relative changes in number of Phase 2 trials at the site level. Therefore, in many instances, proportional changes are based upon small baseline numbers. Please interpret with caution.

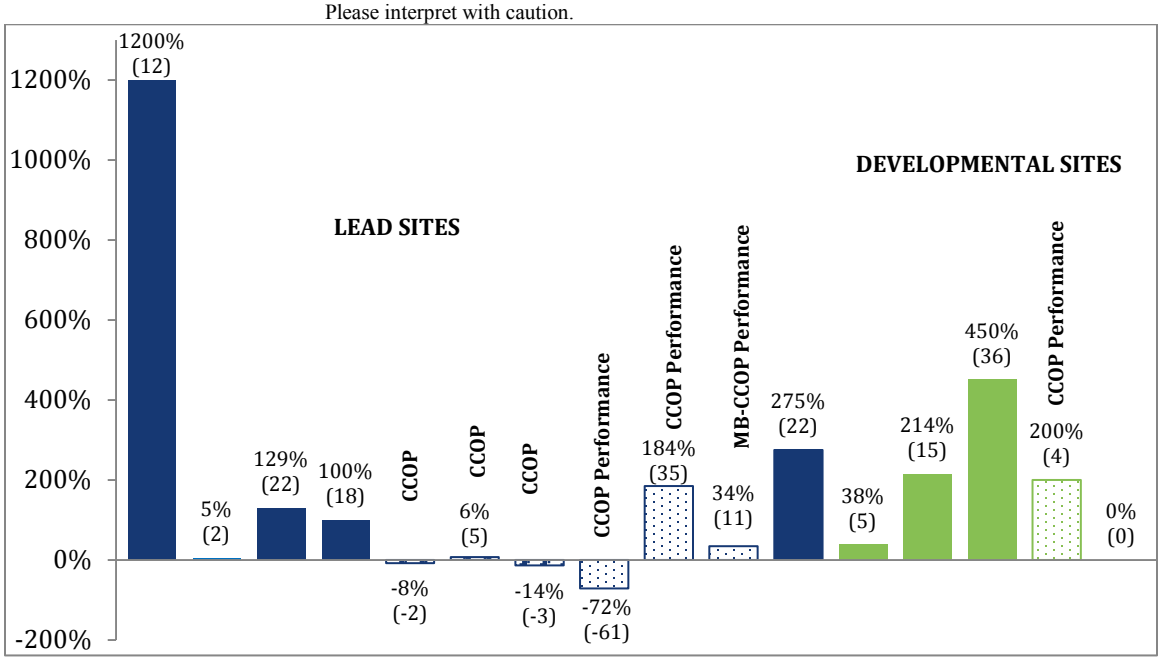


Phase 3 trials by site – A total of 15 of the 16 sites conducted Phase 3 trials during the 3-year period, and 12 of those sites increased the number of trials from Year 1 to Year 3. Seven of the 11 Lead sites and four of the five Developmental sites increased the number of Phase 3 trials. In the previous and following figures, the same sites are represented in the same position to facilitate comparison in the changes in Phase 2 and 3 trial portfolios at the site level. In general, sites that increased the number of Phase 2 trials also increased the number of Phase 3 trials.

Again, all three sites that had both NCCCP and CCOP Lead designation did not demonstrate substantial increase in the total number of Phase 3 trials, and two of three decreased numbers. All three of the NCCCP Lead sites that decreased their numbers of Phase 3 trials were CCOP sites. Meanwhile, among the CCOP vs non-CCOP sites, increase in Phase 3 trials was noted in four of seven CCOP sites and eight of nine non-CCOP sites (Figure 38).

Figure 38: Proportional Change (Absolute Change) in Number of Phase 3 Trials from Year 1 to Year 3 by Site (Site-reported Data)

Note: This figure is intended to demonstrate relative changes in number of Phase 3 trials at the site level. Therefore, in many instances, proportional changes are based upon small baseline numbers. Please interpret with caution.

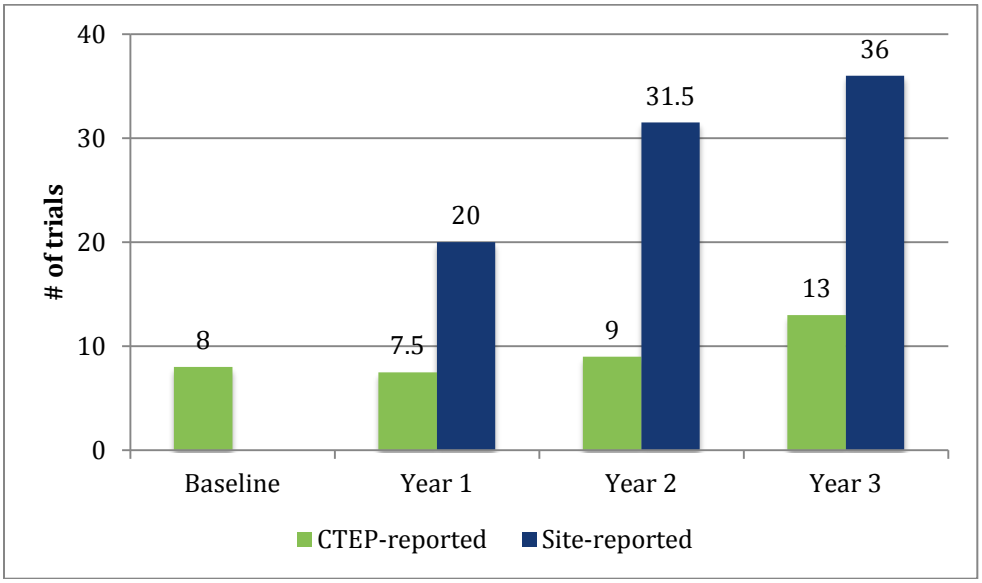


The overall interpretation is that the site self-reported trials conducted by NCCCP sites are generally NCI-sponsored Phase 2 and Phase 3 trials. Consistent with NCCCP goals, the number of Phase 2 trials increased over the project period. NCCCP Lead sites are more equipped to conduct Phase 2 trials than the Developmental sites, consistent with fact that Phase 2 trials require more sophisticated clinical trials experience and infrastructure; over time, with progressive maturation of their clinical research infrastructure, the Developmental sites have the potential to continue to increase their numbers of Phase 2 trials. Inspection of the relative changes in Phase 2 and 3 trials portfolios at the various sites demonstrates that sites with a dual designation of NCCCP Lead and CCOP were the most likely to have flat or negative changes in their portfolio. This suggests that the CCOPs were more likely to be at their maximal capability relative to their current level of clinical trials infrastructure, and that non-CCOP sites have the greatest potential for growth.

Number of Trials – Comparison of CTEP and Site-reported Data

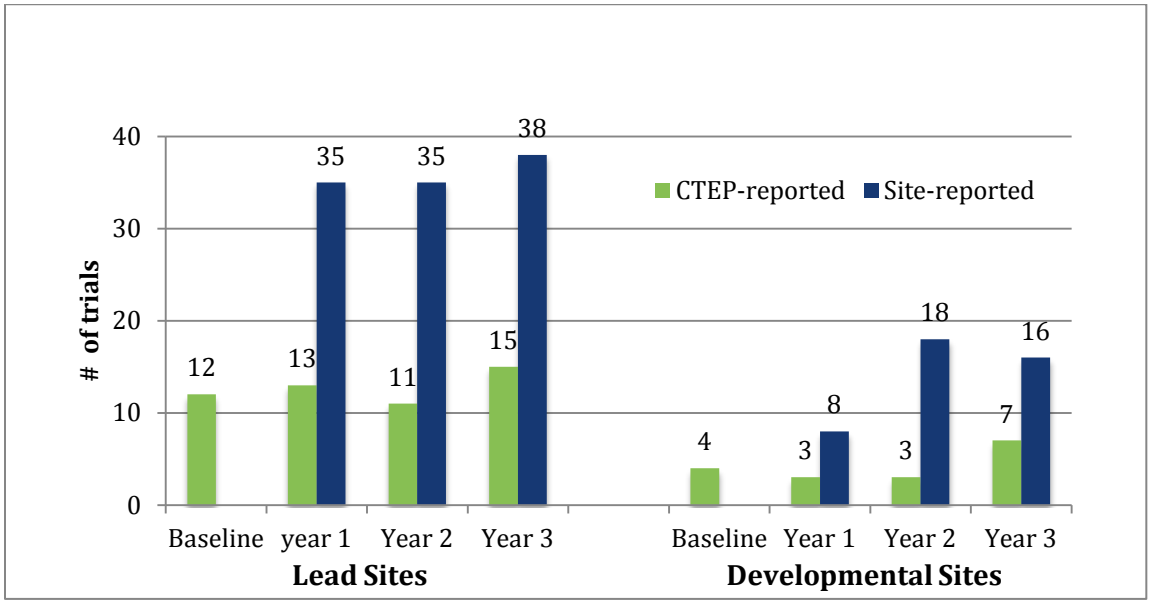
The CTEP database indicated a median of 8 trials per site were underway at baseline (range 0-62). In Year 1, the CTEP data indicated there was a median of 7.5 trials (range 0-59) underway at the each of the 16 sites and this grew to 13 by Year 3 (range 0-58), reflecting a 62% increase over baseline (73% increase over Year 1). Based on site-reported data, a median of 20 NCI-Sponsored trials were underway in Year 1 (range 0-132) and this rose to a median of 36 in Year 3 (range 0-132), reflecting an 80% increase over Year 1 (Figure 39).

Figure 39: Median Number of Trials per Site – Comparison of CTEP and Site-reported Data



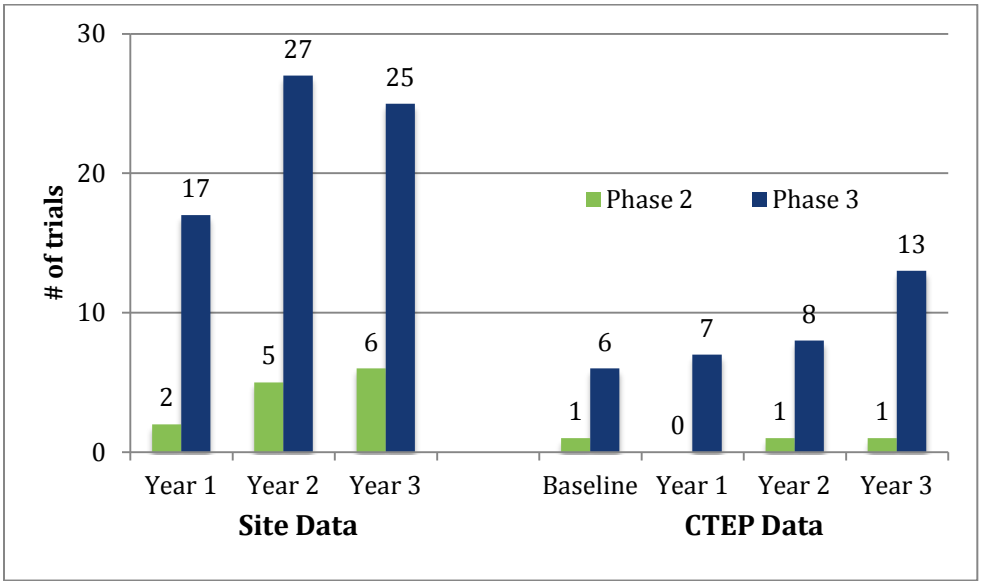
Similar trends are evident when data are grouped according to the site's NCCCP Lead or Developmental designation, although some variation in the relative increase in trial numbers is noted. CTEP data show that the number of trials increased by 15% and 133% for Lead and Developmental sites, respectively. Site-reported data indicate a 9% and 100% increase for Lead and Developmental sites, respectively (Figure 40).

Figure 40: Median Number of Trials per Site by NCCCP Designation – Comparison of CTEP and Site-reported Data



According to CTEP-reported data, there were no Phase 1 NCI-sponsored trials conducted during the evaluation period. For Phase 2 trials, the site-reported data indicated a 200% increase in trials, from a median of 2, range of 0-55 in Year 1, to a median of 6, range of 0-50 in Year 3. By comparison, the CTEP data showed an increase of only 1 trial from Year 1 to Year 3, and no increase in the median number of trials over baseline. For Phase 3 trials the CTEP data showed an 86% increase and the site-reported data showed a 50% increase (site-reported data: Year 1 median 17, range 0-75; Year 3 median 25, range 0-74; Figure 41).

Figure 41: Median Number of Trials per Site by Study Phase – Comparison of CTEP and Site-reported Data



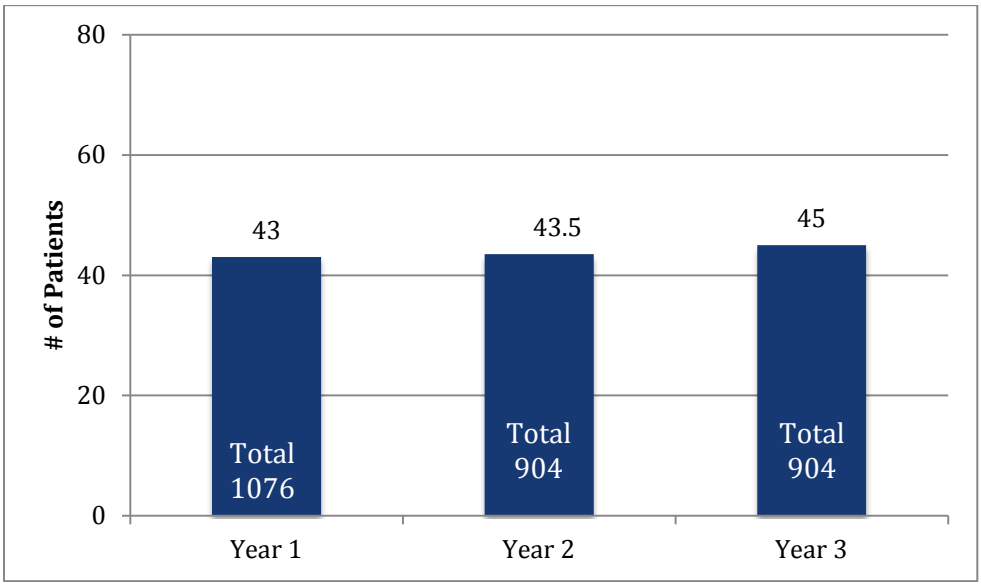
The overall interpretation was that the relative increase in the number of trials from Year 1 to Year 3 was similar using both the "site level" and the "trial level" views afforded by the site-reported and CTEP data, respectively. Evaluation of the data provided by the sites facilitated understanding of the perceived clinical trials activity and energy expenditure according to site staff. Evaluation of CTEP data provides robust comparison between sites, and with other national trends. An increase in the Phase 2 portfolio was an important NCCCP outcome; these changes were seen in site-reported data but not in the CTEP reported data. Discrepancies between the CTEP and site self-reported data are not entirely clear.

Clinical Trials Accrual – Site-reported

Total Accrual

Each year there was a wide range of site-reported patient accrual from all sponsors (NCI, Industry and Other) by the 16 sites. In Year 1, individual site accrual ranged from 2 to 254 patients. Total accrual for the year was 1076 with a median of 43. By Year 3, while the range was similar to Year 1 (0-251), the median increased slightly to 45 (+5%) and the total accrual fell to 904 (-13%; Figure 42).

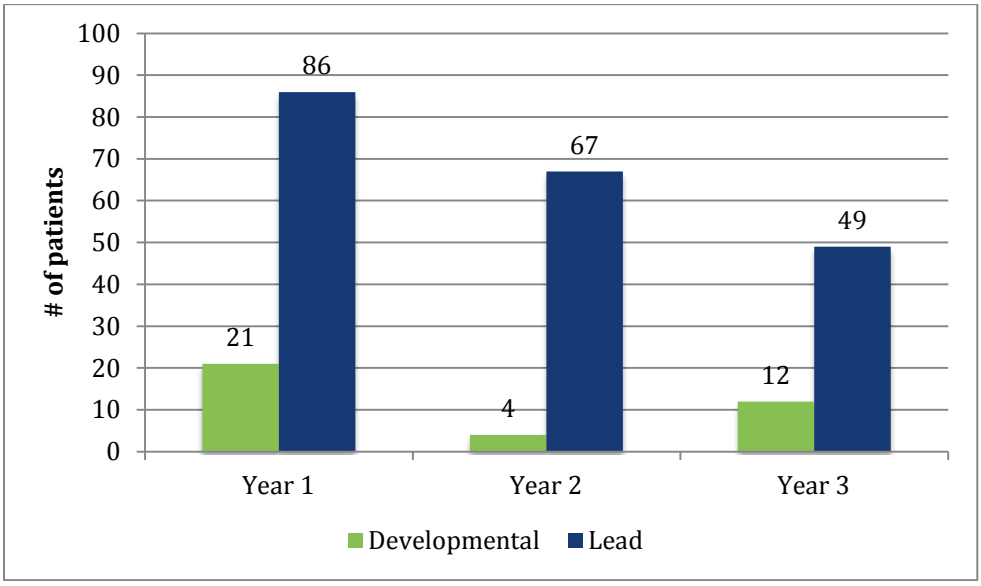
Figure 42: Total and Median Accrual (Site Self-reported Data)



NCCCP Lead and Developmental Sites

There was also a wide range of patient accrual between the 11 sites designated as NCCCP Lead sites and the 5 sites designated as Developmental. In Year 1, accrual reported by the Lead sites ranged from 3 to 254 patients with a total accrual of 968 patients and median per site accrual of 86. By Year 3, the range narrowed minimally (22 to 251) and the total accrual fell to 806 patients (-17%) with a median per site accrual of 49 (-43%). For the Developmental sites, the Year 1 range was 2 to 51 with a total accrual of 108 patients and median per site accrual of 21. By Year 3, the range was 0 to 62, the total accrual fell to 98 patients (-9%), and the median per site accrual fell to 12 (-43%; Figure 43).

Figure 43: Median Accrual (Site-reported Data) - NCCCP Lead & Developmental Sites



CCOP and Non-CCOP NCCCP Sites

Comparing CCOP sites and non-CCOP sites, the median accrual per CCOP site was 92 in Year 1 (range 2-254) and 83 in Year 3 (range 1-251), which is a 10% decrease). The median accrual per non-CCOP site was 27 in Year 1(range 3-97) and 32 in Year 3 (range 0-62), which is a 19% increase (Figure 44). Comparing CCOP Lead and CCOP Performance sites, the Lead sites had a 28% decrease over the period (median accrual per site of 141, range 88-254, in Year 1 and median of 101, range 85-251 in Year 3) and the Performance sites had a 49% decrease over the period (median accrual per site of 89, range 2-142 in Year 1 and median of 45.5, range 1-83 in Year 3; Figure 45).

The overall interpretation is that, while CCOP sites have substantially higher baseline accrual than non-CCOP sites, actual accrual is decreasing at CCOP sites and increasing at non-CCOP sites per site self-reported data.

Figure 44: Median Accrual (Site Self-reported Data) - CCOP & Non-CCOP Sites

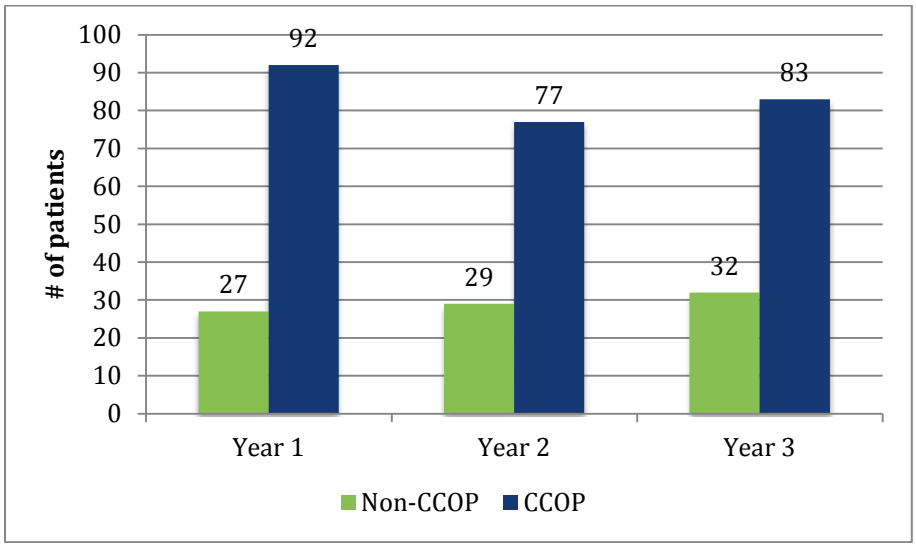
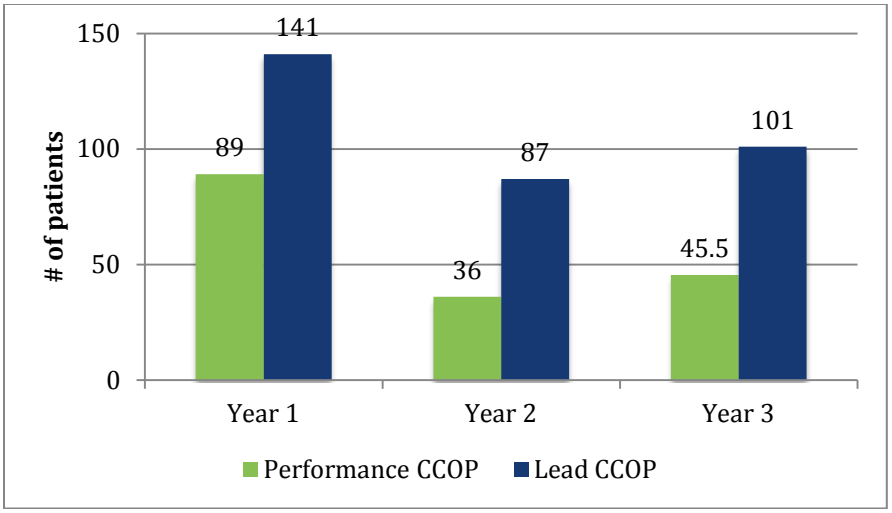


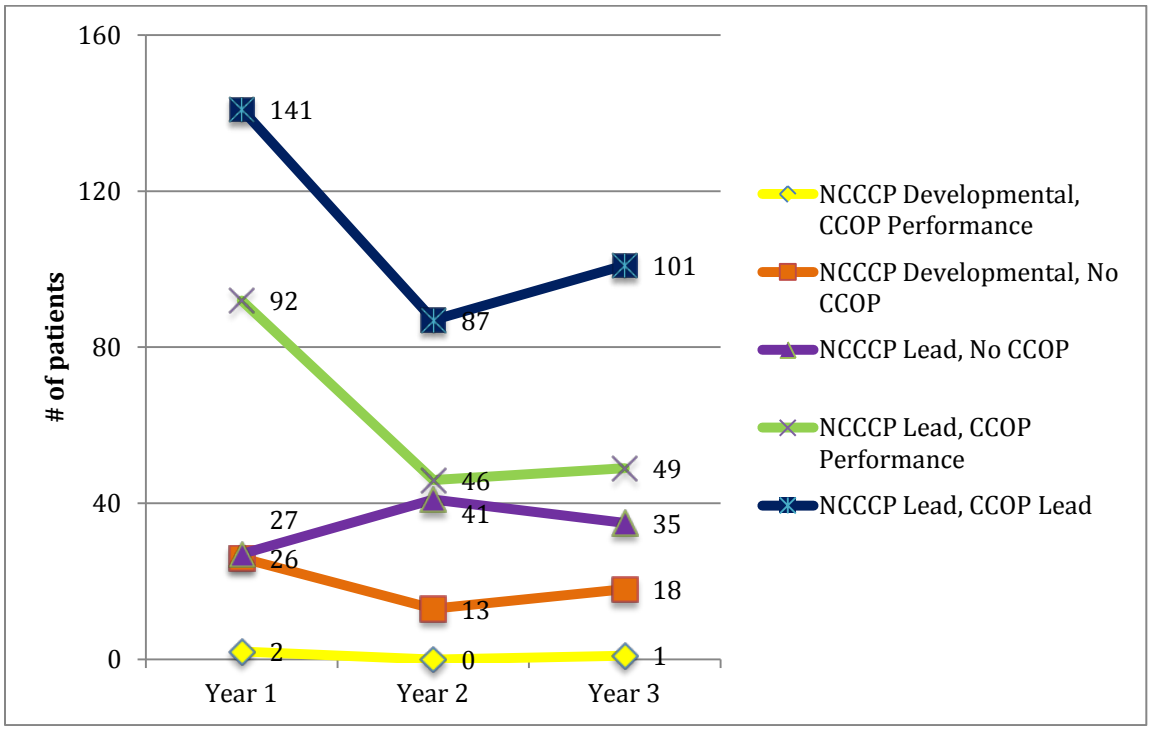
Figure 45: Median Accrual (Site Self-reported Data) - Lead & Performance CCOP Sites



Interaction Between Type of NCCCP Site and CCOP Status

Among the three centers that were both Lead NCCCP and Lead CCOP sites, median per site accrual in Year 1 was 141 (range 85-254) and 101 in Year 3 (range 85-251) which is a 28% decrease. There were three centers that were NCCCP Lead sites and CCOP performance sites; their median accrual in Year 1 was 92 (range 86-142), which fell to 49 in Year 3 (range 42-86) which is a decrease of 47%. Five centers were NCCCP Lead sites that were not a part of the CCOP program. Their median accrual was 27 in Year 1 (range 3-97) and rose to 35 in Year 3 (range 22-58), a 30% increase. There was a single center that was a NCCCP Developmental site and a CCOP Performance site. This site's accrual was 2 in Year 1 and 1 in Year 3. Finally, there were 4 NCCCP Developmental sites that were not participants in the CCOP program. Their median accrual was 26 in Year 1 (range 3-51) and the median was 18 in Year 3 (range 0-62) a 31% decrease (Figure 46).

Figure 46: Median Accrual (Site Self-reported Data) - By Site Designation



In Year 1, the records from each site showed that all 16 sites had at least two patients enrolled in clinical trials, with the largest accrual at the Lead NCCCP and CCOP sites (Figure 47). When proportional change in accrual over the evaluation period is plotted (Figure 48), the CCOP sites were more likely to reported reductions in patient accrual with time. In most instances, there was an inverse relationship between the accrual in the Year 1 and the percent change in accrual over the three-year evaluation period.

Figure 47: Accrual Per Site (Site Self-reported Data) – Year 1

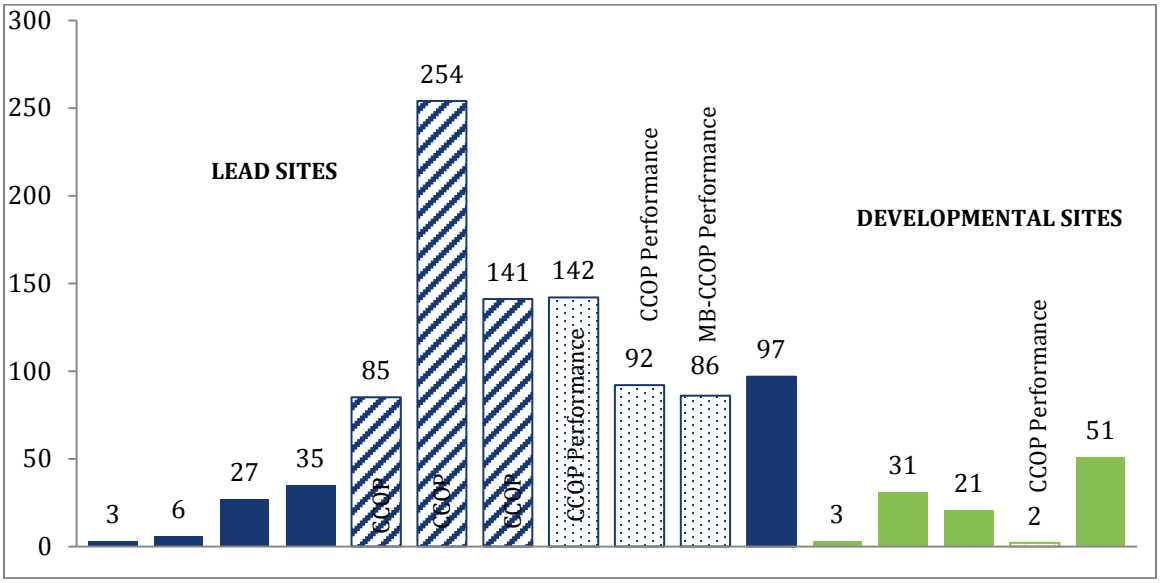
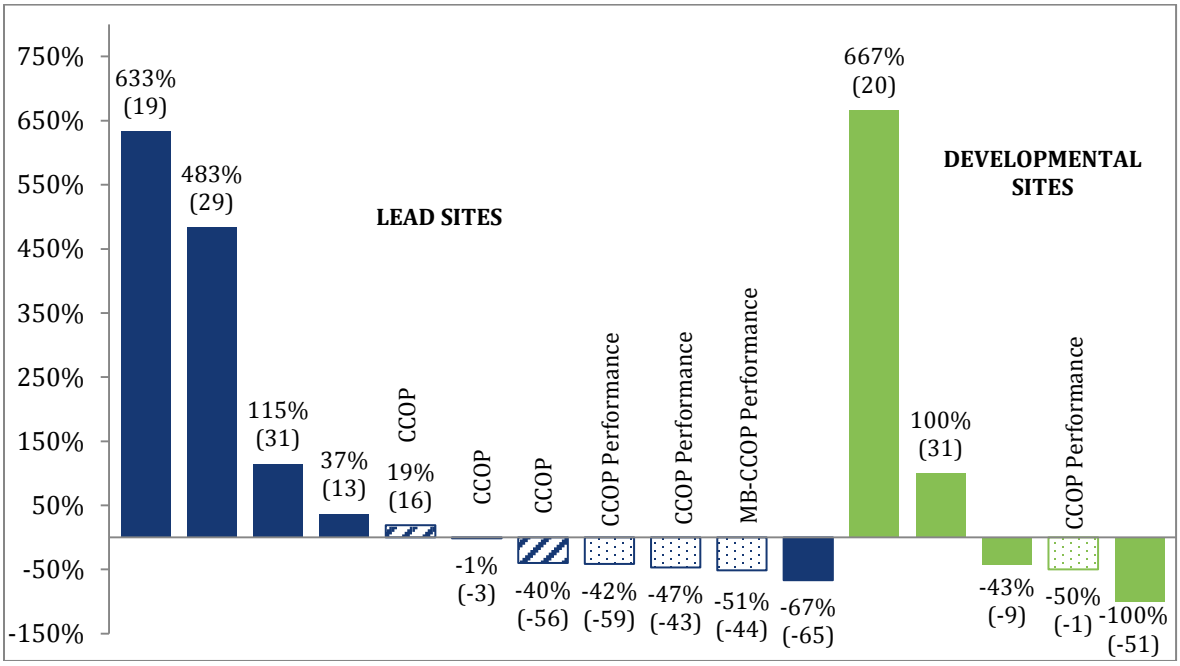


Figure 48: Accrual Per Site (Site Self-reported Data) - Proportional Change (Absolute Change) from Year 1 to Year 3

Note: This figure is intended to demonstrate relative changes in accrual at the site level. Therefore, in many instances, proportional changes are based upon small baseline numbers. Baseline numbers are in the figure above. Please interpret with caution.



The overall interpretation is that site self-reported accrual is decreasing for nearly all of the sites, except for the non-CCOP NCCCP Lead sites. One of the non-CCOP Lead sites and one of the non-CCOP Developmental sites had remarkable increases in accrual (>600%), but since these sites started off with few patients enrolled in trials (N=3) the actual contribution to overall accrual numbers is still relatively small. The CCOP sites demonstrated reductions in accrual, but had high levels of accrual at baseline, so these fluctuations have the most impact on NCCCP accrual numbers. Trends suggest that the CCOP sites are experienced clinical trials sites with higher accrual, but with reductions in accrual over time, suggestive of the same trends witnessed more globally in the CCOP program; they are likely good examples for NCCCP sites that are relatively new to conducting clinical trials and are trying to organize themselves to engage in more clinical trials activity. Non-CCOP NCCCP Lead sites reflect the group most poised to demonstrate positive increases in accrual; these are the sites prepared to increase accrual numbers by virtue of their increased number of clinical trials, the fact that they are not already saturated CCOP sites, and the fact that they are exposed to experienced CCOP sites through the NCCCP. NCCCP Developmental sites are likely focusing on opening trials and preparing for accrual but haven't really achieved demonstrable change in terms of accrual by the end of the evaluation period.

Accrual by Sponsor

When accrual is categorized according to the type of sponsor, data show that the reduction in accrual over time is attributable to relatively fewer patients being enrolled in NCI-sponsored trials (Figure 49). In looking at the change over time, there was a 24% reduction for NCI-sponsored trials from Year 1 (started at 982 patients enrolled or 91% of the total site-reported accrual in Year 1) to Year 2 (747 patients enrolled or 83% of total accrual) and a further 5% reduction from Year 2 to Year 3 (712 patients enrolled or 79% of total accrual). Accrual for trials supported by Industry sponsors and Other sponsors, while small in comparison with the number of patients involved in NCI-sponsored trials, both showed relative increases each year. From Year 1 to Year 2, accrual for Industry-sponsored trials increased by 49% (from 77 [7% of the total accrual] to 115 [13% of total accrual]) and another 30% increase in Year 3 (from 115 to 130 [14% of total accrual]). Accrual for trials supported by Other sponsors increased by 147% from Year 1 (17 patients) to Year 2 (42 patients) and by 48% from Year 2 to Year 3 (62 patients; Figure 50).

The overall interpretation is that, while the number of site-reported and CTEP documented NCI-sponsored trials is going up during the NCCCP evaluation period, site-reported accrual to NCI-sponsored trials is decreasing at a higher rate than for other sponsors. The reason for this is unclear. Perhaps it is a sequencing issue, reflecting the fact that trials need to be opened at a site before increases in participant accrual can be seen. Or this may be a data quality issue; sites were more accurate at reporting accrual in later years of the evaluation process and therefore data in later years is more accurate (with lower numbers). It is curious that the total number of patients reported in CTEP is higher than reported at the sites. Also, these observations may reflect a relative shift to Industry-sponsored activity. Or, most simply, it may reflect the fact that several large NCI-sponsored trials closed during the evaluation period, and site-level resources were therefore shifted to other studies once those trials were finished, requiring a start-up phase of restructuring those resources to the new trials.

Figure 49: Total Accrual by Sponsor Type (Site Self-reported Data)

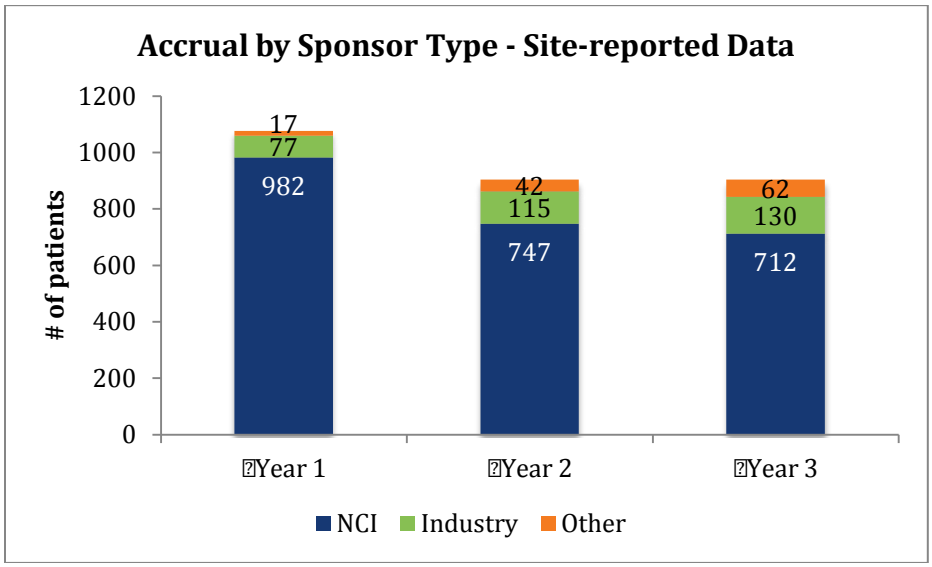
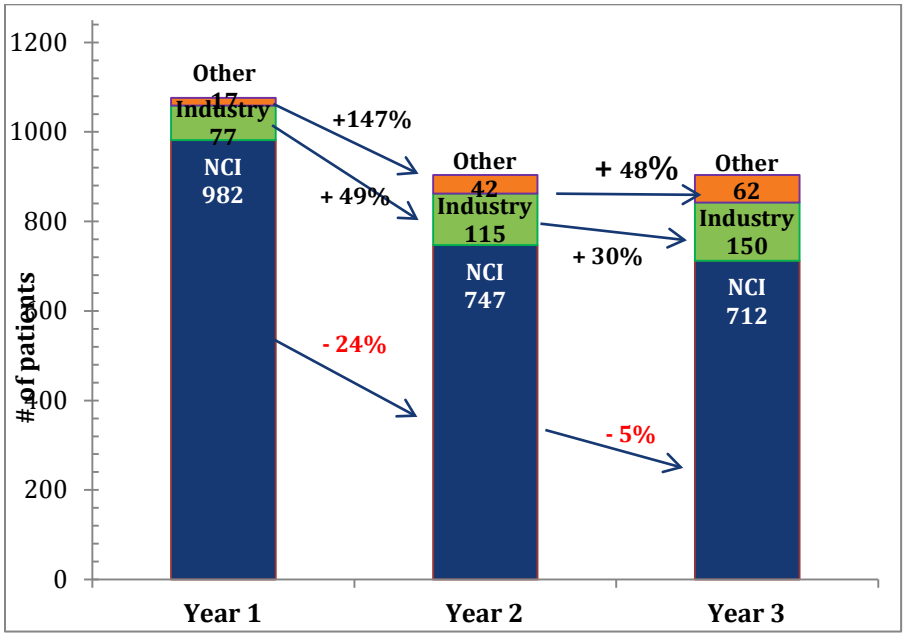


Figure 50: Total Accrual by Sponsor Type with Proportional Change over Time (Site Self-reported Data)

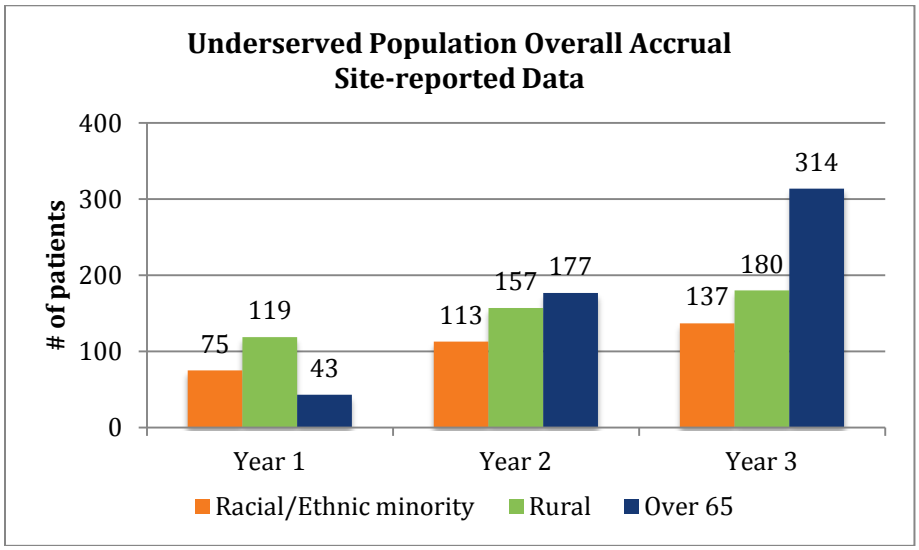


Accrual of Underserved Populations

According to site-reported data, there was a yearly increase in the accrual of patients in each category of underserved populations. The enrollment of patients classified as "racial/ethnic minority" increased 83% from Year 1 to Year 3. Similarly, there was a 51% increase in the enrollment of "rural" patients (site self-defined) and a 630% increase in the number of patients in the "over 65" category (Figure 51). It is important to keep in mind that prior to the start of the NCCCP pilot, many of the sites did not have a mechanism to capture ethnicity and some sites were still developing mechanisms to capture race. One

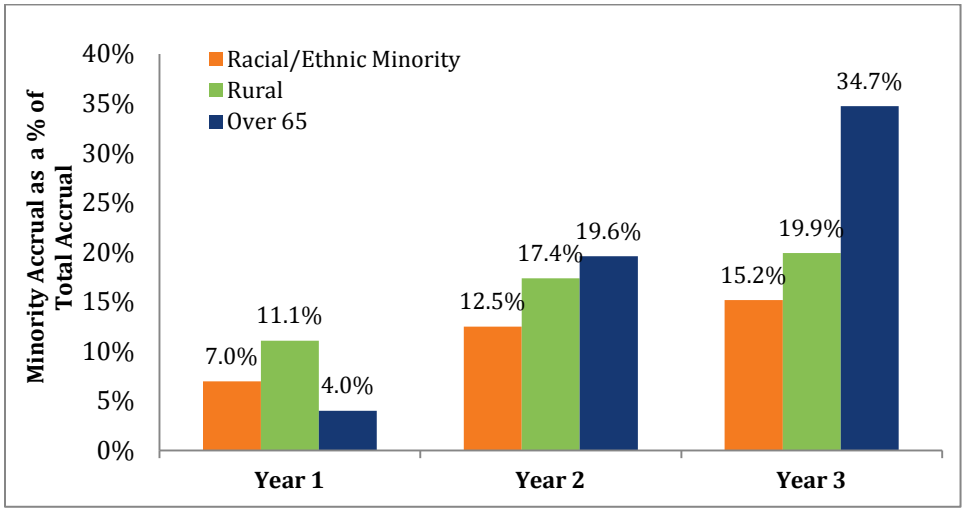
goal of the pilot was to have all of the sites report minority accrual according to OMB standards, which includes race and ethnicity. For some, this meant changing how their hospital system reported race and ethnicity, which was a formidable task. In the interim, sites were asked to report "minority" accrual which consisted of race only until the end of Year 3, when an online tool went into effect and both race and ethnicity were reported by all sites. Thus, some of the increase in the number of accrual to underserved populations may be initial reporting differences, a limitation of the self-reported data.

Figure 51: Total Accrual of Underserved Populations (Site Self-reported Data)



When the annual accrual of underserved patients is considered as a fraction of total accrual, underserved patients were increasingly represented each year. In Year 1, racial/ethnic minorities made up 7% of the total accrual. By Year 3, this group made up 15% of the total accrual. Rural patient accrual went from 11% of total accrual in Year 1 to 20% in Year 3. Patients who were over 65 years of age made up only 4% of the total accrual in Year 1, but in Year 3 were 35% of the total accrual. The increases were consistent across all sponsor types (Figure 52).

Figure 52: Accrual of Underserved Populations as a Proportion of Total Accrual (Site Self-reported Data)



The individual sites varied according to the relative change (Year 1 to Year 3) in accrual of patients from underserved populations (Table 3). For racial/ethnic minority patients, nine sites reported an increase in enrollment as a percent of total accrual. For rural patients, eight sites reported an increase in enrollment. For patients over 65 years of age, 12 sites reported an increase in enrollment as a percent of total accrual. As a note, some sites had no data for minority recruitment during just Year 1 and some reported no minority recruitment for the entire 3-year evaluation period. We considered "no report" to be 0 for the purposes of data analysis. It is unknown whether those sites did indeed accrue minority patients and didn't keep track of it or whether these sites actually had no minority accrual (Figures 53-56).

Table 3: Change in Underserved Accrual and Change in Proportion of Total Accrual by Site (Site Self-reported Data)

(Note – Change in Proportional Accrual is in Brackets)

Site	NCCCP Lead or Developmental	CCOP Lead or Performance	Racial/ Ethnic minority	Rural	Over 65	Total Under-served Accrual
3	Lead	Performance	7 (25%)	24 (57%)	22 (52%)	53 (135%)
14	Developmental		0 (0%)	40 (65%)	34 (55%)	74 (119%)
12	Lead		10 (16%)	0 (0%)	38 (79%)	48 (95%)
2	Lead	Performance	4 (12%)	8 (16%)	23 (47%)	35 (75%)
4	Lead	Performance	12 (17%)	0 (14%)	26 (31%)	38 (61%)
9	Lead	Lead	5 (6%)	-19 (10%)	37 (43%)	23 (60%)
6	Lead	Lead	15 (6%)	0 (0%)	74 (30%)	89 (36%)
7	Lead		3 (14%)	0 (0%)	4 (18%)	7 (32%)
1	Lead		9 (12%)	10 (-27%)	13 (37%)	32 (22%)
10	Lead		-3 (-3%)	1 (3%)	4 (13)	2 (13%)
13	Developmental		-3 (-14%)	-6 (0%)	3 (25%)	-6 (11%)
11	Developmental		0 (0%)	0 (0%)	0 (0%)	0 (0%)
15	Lead		4 (7%)	4 (3%)	0 (-14%)	8 (-4%)
8	Developmental		-1 (-33%)	0 (0%)	6 (26%)	5 (-7%)
16	Lead	Lead	0 (-2%)	1 (1%)	-13 (-20%)	-12 (-21%)
5	Developmental	Performance	0 (0%)	-2 (-100%)	0 (0%)	-2 (-100%)

Figure 53: Total Accrual of Underserved Populations at Year 1 by Site (Site Self-reported Data)

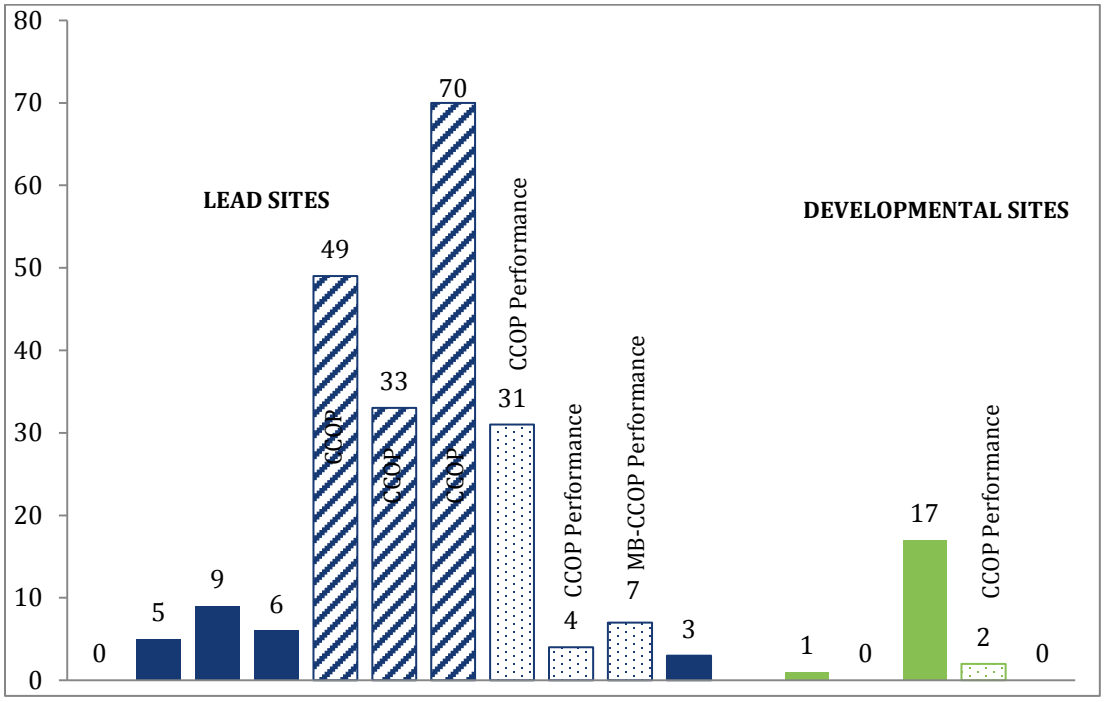


Figure 54: Proportional Change in % of Total Accrual of Underserved Populations from Year 1 to Year 3 by Site (Site Self-reported Data)

Note: This figure is intended to demonstrate relative changes in underserved accrual at the site level. Therefore, in many instances, proportional changes are based upon small baseline numbers. Baseline numbers are in the figure above. Please interpret with caution.

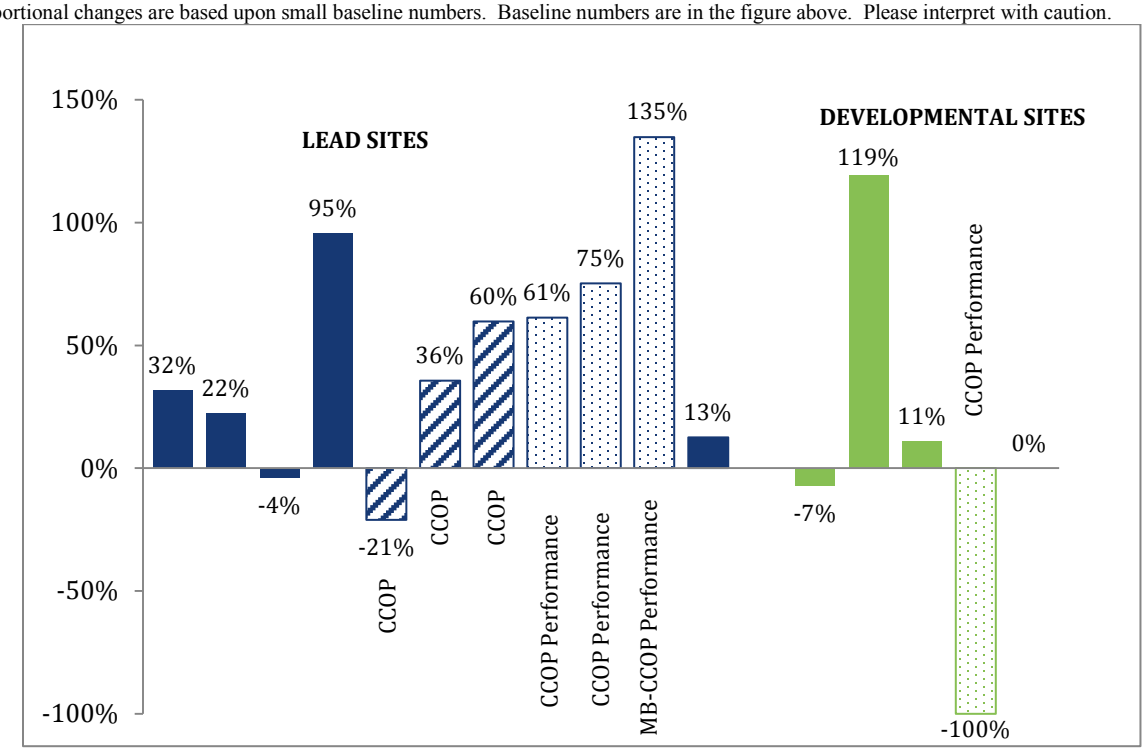


Figure 55: Proportional Change in % of Total Accrual of Racial/Ethnic Minorities from Year 1 to Year 3 by Site (Site Self-reported Data)

Note: These figures are intended to demonstrate relative changes in underserved accrual at the site level. Therefore, in many instances, proportional changes are based upon small baseline numbers. Baseline numbers are in the figure above. Please interpret with caution.

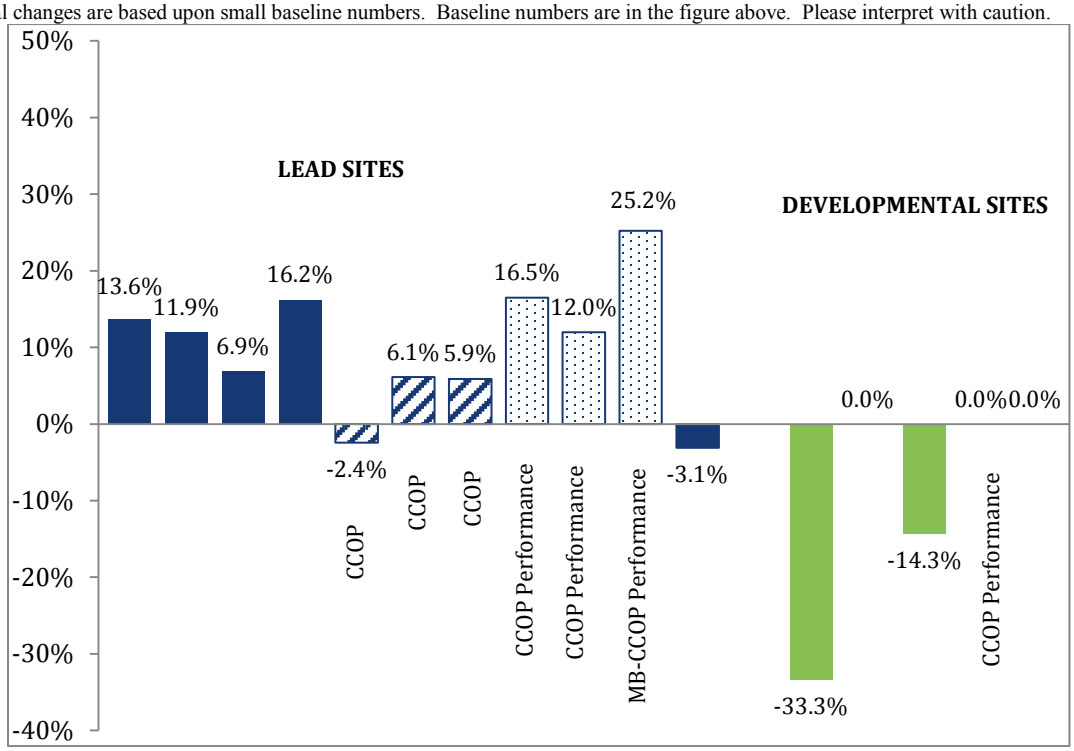
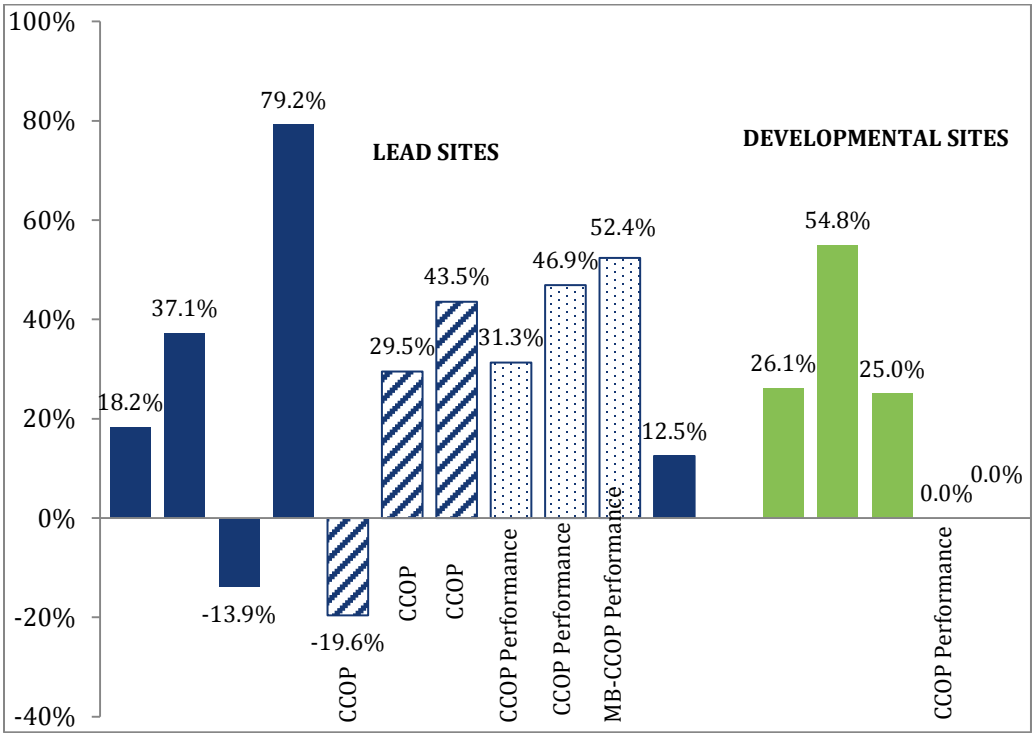


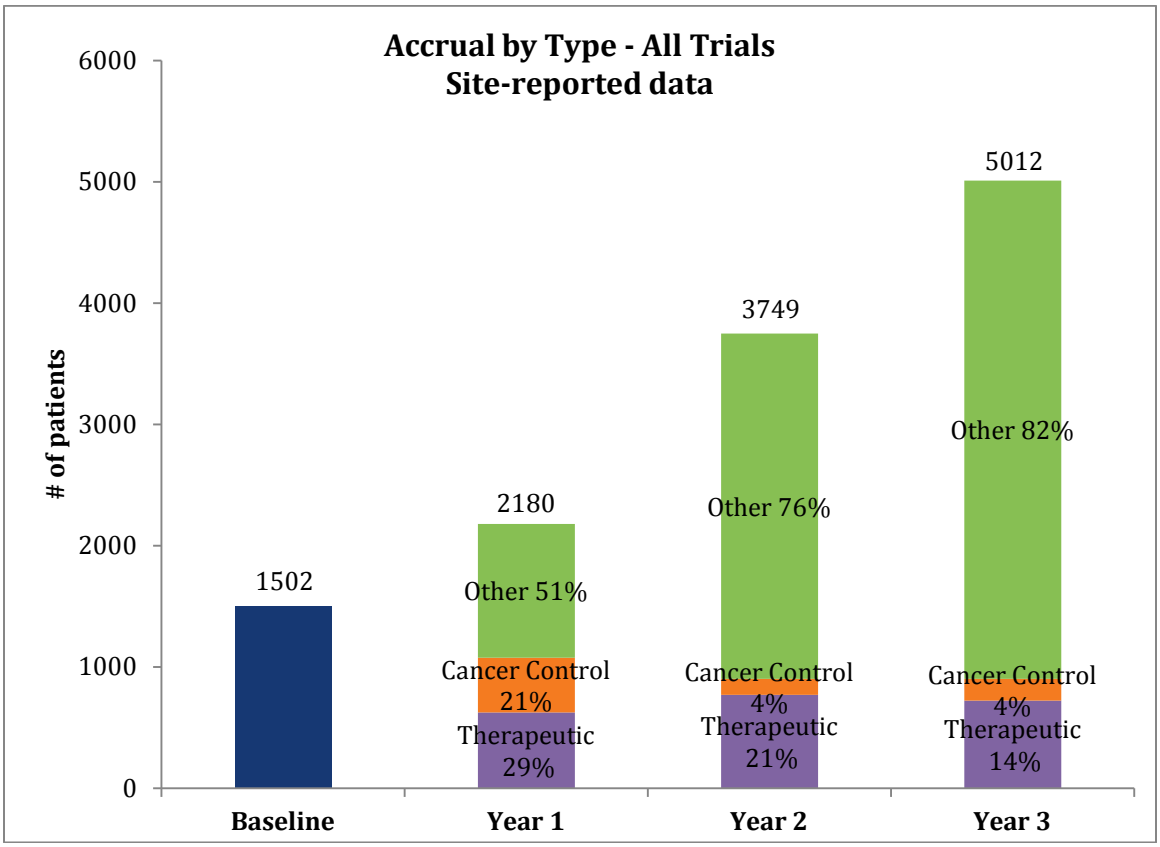
Figure 56: Proportional Change in % of Total Accrual of People over Age 65 from Year 1 to Year 3 by Site (Site Self-reported Data)



Total Enrollment for All Research Activity

Total patient enrollment at a site provides a reflection of the total research effort that that site is expending. This is across all study types and sponsors. Overall patient enrollment for all study types rose by 233% over the baseline of 1502 (note that sites reported a baseline total accrual for all research activity, not broken down by types of trials, for the calendar year 2006.) According to site self-reported data, during the three-year evaluation period, the relative fraction of total patient enrollment in Therapeutic and Cancer Control trials declined while patients enrolled in "Other" studies increased from 51% to 82% of total enrollment. "Other" includes enrollment from Screening, Early Detection, Diagnostic, Epidemiologic, Observational, Outcome, Ancillary and Correlative Studies (Figure 57).

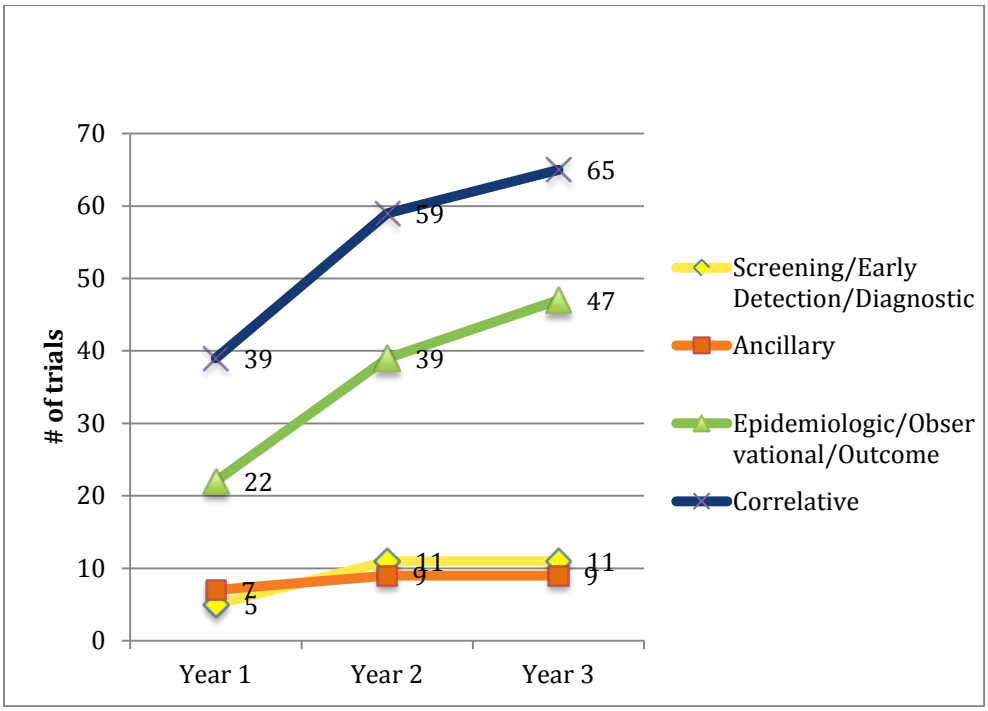
Figure 57: Total Accrual by Study Type (Site Self-reported Data)



Number of Other Research Studies

In addition to the increased patient enrollment, the number of studies in each category of "Other" research opportunities also increased each year. There were 73 total "Other" studies ongoing in Year 1, which rose to 132 studies in Year 3. Participation in the NCCCP program allowed the sites a broader range of research opportunities such as the Moffitt Total Cancer Care initiative (Figure 58).

Figure 58: Total Number of Other Research Studies for All Sponsors (Site Self-reported Data)



Patient Enrollment for Other Research Activities

There were a number of "Other" opportunities, but The Moffitt Total Cancer Care Initiative was a rich avenue for increasing a site's enrollment. Four sites reported substantial enrollment in Other Research Activities and three of these sites participated in the Moffitt Initiative the full three years showing enrollments of 487, 886, and 1531 patients. A fourth site began participation in the Moffitt Initiative late in Year 3, enrolling 104 patients in a brief period. Only one site reported substantial enrollment (309 patients) without participating in the Moffitt Initiative (Figure 59).

Comparison against a plot of change in Phase 3 trials by site based upon CTEP data shows that participation in the Moffitt program does not distract from participation in studies tabulated by CTEP (Figure 60).

Figure 59: Change in Number of Patients Enrolled in Other Research Activity from Year 1 to Year 3 by Site (Site Self-reported Data)

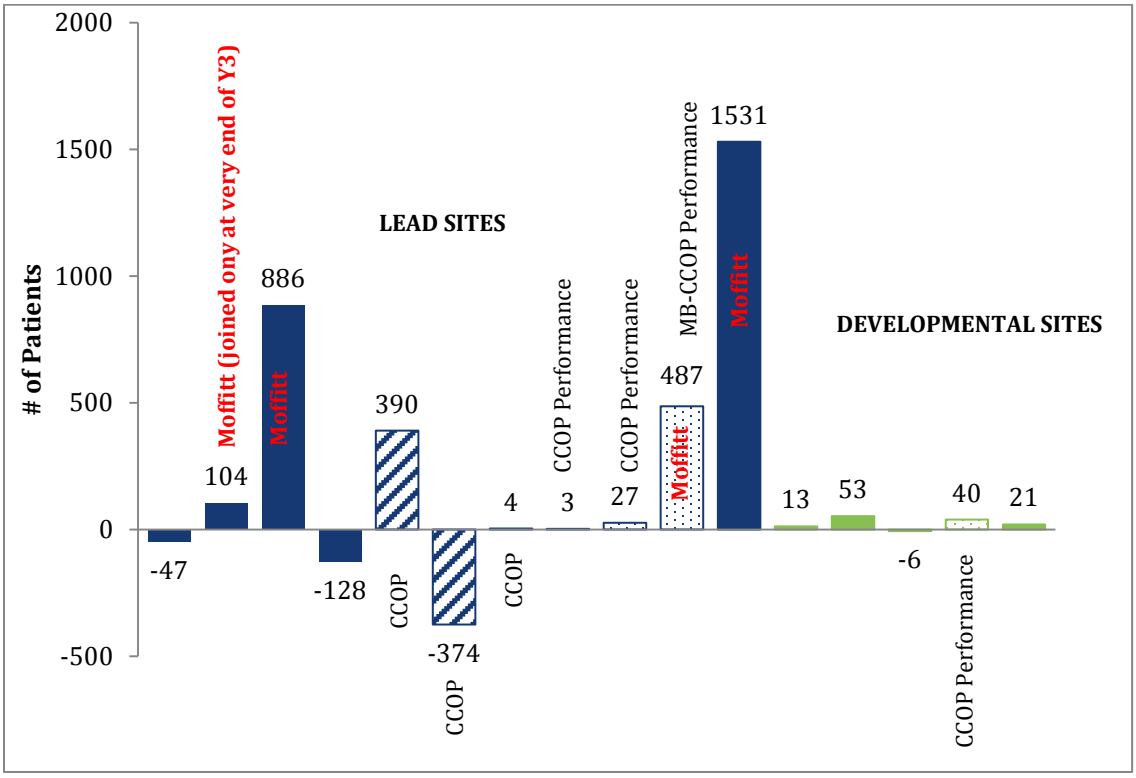
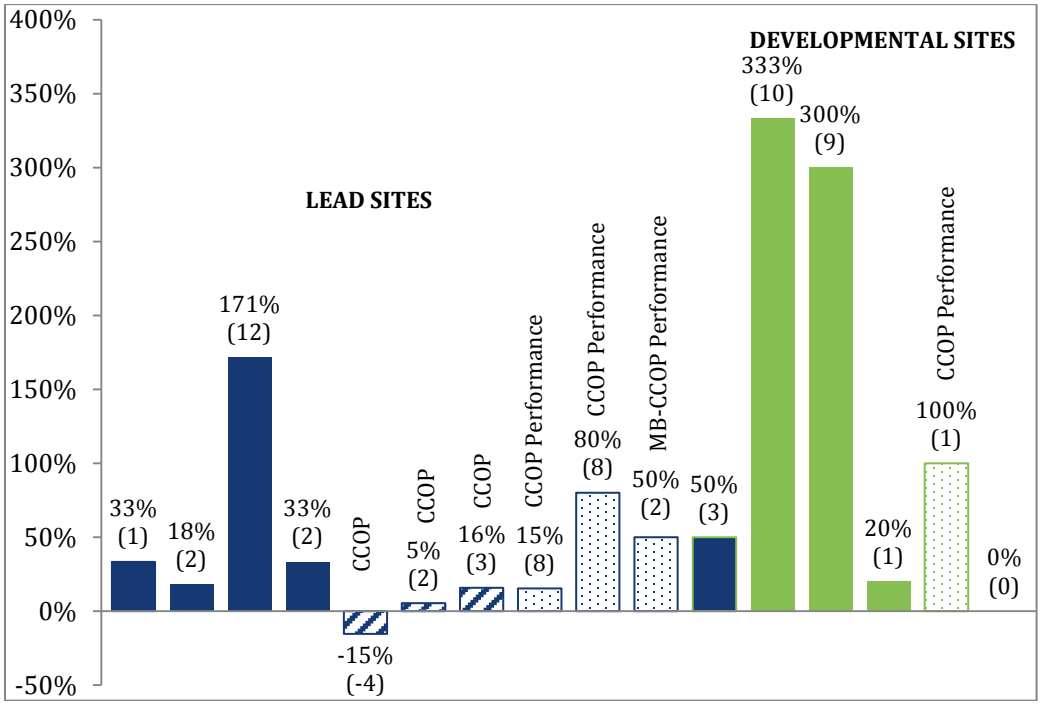


Figure 60: Proportional Change (Absolute Change) in Phase 3 Trials from Baseline to Year 3 by Site (CTEP Data)



Qualitative Analyses

One of the goals of the NCCCP evaluation was to examine which qualitative factors seem to be associated with the success of clinical trials activities at NCCCP sites. Sites were intentionally selected to be at different maturity levels at the start of the program; the developmental sites had limited capabilities and potential limited resources. Each site was unique in its implementation of the program activities and in the organizational changes that occurred during the pilot evaluation period. While the diversity among sites provided a rich backdrop of real-world clinical research scenarios in community settings, it also prevented aggregation and reporting of the qualitative data. Qualitative site information has therefore been summarized and presented by site in Appendix 2.

Certain contextual elements emerged as important considerations and possibly factors in determining the level and nature of research activity at sites. Examples include support of clinical trials on the part of cancer center leadership and hospital management, financial support of clinical trials and the configuration of this support (e.g., public/private partnership), staffing, and increases in physician participation in cooperative groups and other research activities. Key considerations were on-the-ground clinical trials infrastructure (e.g., IRB interaction, staff, PIs and physician arrangement), and institutional organizational dynamics (e.g., reporting structure between the cancer program and overarching institutional leaders, involvement and support of hospital management, and between the clinical trials program and the cancer program). Note that these factors are addressed more fully in the RTI Overall Evaluation Report as the main focus of this portion of the report is on the clinical trials quantitative data and their interpretation.

DISCUSSION

Initiated as a pilot program in 2007, the NCCCP is a network of community hospitals and their cancer centers created to expand cancer research capacity and to deliver the latest, most advanced, cancer care to more Americans in the communities in which they live. The purpose of the three-year pilot was to build a community-based platform to support a wide range of basic, clinical, and population-based research and approaches to care, centered on cancer prevention, screening, diagnosis, treatment, survivorship, and palliative care. The pilot included 11 designated Lead sites and 5 designated Developmental sites. Each of the 10 funded sites (or multi-hospital systems) received up to $500,000 per year to participate in the pilot. Sites were permitted to spend up to 60% of their budget on activities not related to Disparities; one of these other activity areas was Clinical Trials. Thus clinical trials constituted only a portion of the overall investment in and activity of the NCCCP; substantial contribution to the NCI's clinical trials mission was not one of the original main goals of the program, although NCI did seek to determine if a collaborative program such as the NCCCP could contribute to clinical research.

This report provides a global evaluation of clinical trials activity of the NCCCP pilot sites from 2007 to 2010. Primary outcomes were change in: (1) clinical trial portfolio (e.g., number of open clinical trials per site, sponsor, types of trials); and, (2) clinical trials accrual (total accrual, mean accrual per study, accrual from underserved populations). The experiences of individual sites provided qualitative snapshots of clinical trials experience "on the ground" over the pilot period; to illustrate key points in this section of the report, site vignettes are presented in text boxes. Site #14, below, exhibits the desired improvements in clinical trials portfolio and clinical trials accrual that were the primary outcomes of this study.

> *Site #14: Demonstration of the types of changes envisioned for the NCCCP program*
>
> Site #14, a Developmental NCCCP site with no CCOP designation, can be considered a site situated early in the learning curve. Over the pilot period, it achieved demonstrable and steady increases in portfolio and accrual, in step with median increases across the entire NCCCP. It is likely that multiple factors facilitated these improvements. The site had stable leadership and demonstrated stepwise increase in clinical trials infrastructure on-the-ground, likely enablers. It reported the addition of pharmacy and IT support, but the exact impact of these tools is unclear. (The new IT tools were likely rudimentary, as "Excel spreadsheets" was considered "the addition of IT.")

Two data sources, which provided complementary information, were used for the evaluation: (1) sites' quarterly and annual reports of trials and accruals from all sponsors and all trial types ("site-level" data), and (2) the CTEP database, which includes only NCI-sponsored trials, encompassing data from NCI Cancer Centers, Cooperative Groups, and DCP prevention and cancer control trials at NCI Research Bases ("trial-level" data). Although the CTEP data are generally considered more reliable and of better quality, the site-level data contained information, such as that regarding other sponsors and research activity, not contained in the CTEP database. Both sources of data were therefore useful to support the evaluation. The CTEP data also provided a national comparator against which to evaluate the performance of the NCCCP sites.

The use of two complementary data sources enabled us to validate several of our findings. For example, we found a similar relative increase in the number of trials open from Year 1 to Year 3 with both the site-level and the trial-level views afforded by the site-reported and the CTEP data, respectively. Evaluation of the data provided by the sites facilitated understanding of the perceived clinical trials activity and

energy expenditure according to site staff. Evaluation of CTEP data provided robust comparison between sites, and with other national trends.

At the gross level, the much larger pool of sites included in the national CTEP database (which generally represents the long-standing and large group of sites that have been conducting clinical trials for many years) conducted 3-5 times as many Phase 1-2 trials as Phase 3 trials, while the NCCCP sites conducted more Phase 3 trials than Phase 1-2 trials. *A first overarching observation reflects a "maturation effect." Long-standing, larger, research sites such as the NCI-designated cancer centers have the capacity to focus on the more difficult, labor-intensive, early-phase trials. By contrast, some of the local community-based NCCCP centers typically lack comparable infrastructure, resources, and experience; due to their level of research maturation, they are appropriately focused on less complex, later-phase trials.* This observation was also reflected in the site-level data, differences between CCOP and non-CCOP NCCCP sites, differences between NCCCP Lead and Developmental sites, and site vignettes. Site #6 represents those sites which have achieved a high level of research maturity; its metrics may not be as subject to change as those of less experienced sites, but its role in the network remains important.

Site #6: Impact of maturity on outcomes

Site #6 is both a Lead CCOP and a Lead NCCCP site, with stable senior leadership and organizational maturity. Its proportional increases in clinical trials numbers and accrual, at first blush, appear close to flat. However, all metrics are substantially higher than trans-program medians (>>300%). Interestingly, accrual dropped between Years 2 and 3 (site-reported and CTEP), and are generally stable from baseline. This mature site may be at its maximal accrual and clinical trials workload; the bouncing around between years may or may not be meaningful. Review of its data suggests that this site's real role may be in sharing experiences and expertise with other sites, providing clinical trials guidance to Developmental and other sites in the NCCCP and thereby improving overall research-related metrics.

Despite the short time window (three years) and limited funding of the pilot period, the sites participating in the NCCCP pilot improved their clinical trials activities, infrastructure and organization. The seven main findings of the evaluation are presented in Table 1, below; discussion follows the table.

Table 1: Principal Findings Regarding the NCCCP Pilot Sites' Clinical Trials Activity

	Main findings	Analytic results
1	Trends among NCCCP sites were generally better than those observed nationally in terms of total number of clinical trials opened within the NCCCP cohort.	Nationwide, from 2007-2010 the number of Phase 1-2 trials decreased 31% and Phase 3 trials increased 8%. Among NCCCP sites, Phase 1-2 trials decreased by 28% and the number of Phase 3 trials increased by more than 16%. Importantly, the difference here is rate of change trials opened across NCCCP sites compared with rate of change of trials opened nationally, not individual numbers of trials at any particular site.
2	The median number of trials per site, especially of NCI-sponsored trials, increased substantially across NCCCP sites.	Increases were 80% from Year 1-3 when calculated using site-reported data, or 62% from baseline to Year 3 using CTEP data. Site-reported data showed 200% increase in the median number of NCI-sponsored Phase 2 trials per site, and 50% increase in median number of Phase 3 trials per site. CTEP data showed an 86% increase over baseline in the median number of Phase 3 trials per site, but no change in the median number of Phase 2 trials.
3	Rates in increase in total accrual to Phase 3 trials was increased more substantially in the NCCCP cohort than across a broader national pool reflected in the complete CTEP database.	Nationally, patient accrual decreased for Phase 1-2 trials (-28%) and increased for Phase 3 trials (+30%). In contrast, the NCCCP sites experienced a smaller decline in Phase 1-2 accrual (-22%) and a much greater increase in Phase 3 accrual (+133%).
4	NCCCP sites increased their per trial accrual at a rate faster than national trends.	Nationally, mean annual accrual per trial increased by 4% for Phase1-2 trials and by 21% for Phase 3 trials during the evaluation period. The relative NCCCP rates were: 9% for Phase 1-2 trials and 100% for Phase 3 trials.
5	NCCCP sites' increase in accrual was largely attributable to trials not sponsored by the NCI, like the Moffitt Total Cancer Care biospecimen study.	Across sponsor types (federal, industry, other), site-reported data showed 5% increase in median patient accrual, but 13% decrease in total accrual. Accrual to NCI-sponsored trials fell by 27% from Year 1-3. Accrual to Industry-sponsored trials rose 69%, and accrual to Other-sponsored trials rose 265%. Baseline numbers for non-NCI studies were low, so relative proportional changes reflect exaggerated numbers and should be interpreted with caution.
6	Participating NCCCP sites increased accrual of underserved populations over the three-year study period.	Site-level data showed that accrual of racial/ethnic minorities increased from 7% of total accrual in Year 1 to 15% of total accrual in Year 3. Accrual of rural patients as a proportion of total accrual rose from 11% to 20%, and of patients age ≥65 from 4% to 35%, in Year 1 vs. Year 3.
7	Participating NCCCP sites increased their general research activity during the study period.	NCCCP participation may have prepared sites to participate in other research activities. For example, 4 sites were participating in the Moffitt Total Cancer Care Initiative by the end of the evaluation period; they collectively increased their enrollment in "Other Research Activities" from 45 patients in Year 1 to 3,008 patients in Year 3.

First, NCCCP sites performed better than national averages on the rate of adding clinical trials to the program portfolio. Nationwide, from 2007 to 2010 the number of Phase 1-2 trials decreased by 31%, while Phase 3 trials increased by 8%. By contrast, among the NCCCP sites, Phase 1-2 trials decreased at a slightly lesser rate (28% vs. 31%) while the number of Phase 3 trials increased by more than 16% (vs. 8%). Given this trend, the NCCCP sites' proportion of all Phase 3 trials is progressively increasing.

Trials conducted by NCCCP sites were predominantly NCI-sponsored Phase 2 and Phase 3 trials, with the majority of NCCCP Phase 2 studies being conducted by the more mature Lead sites. Consistent with NCCCP goals, the number of Phase 2 trials increased over the three-year pilot period; this increase in the Phase 2 portfolio was evident in site-reported data but not in the CTEP data. The reason for this difference is not clear. The pattern in locus of and increase in Phase 2 studies suggests that NCCCP Lead sites are better prepared to conduct Phase 2 trials than are Developmental sites; Phase 2 trials require more sophisticated clinical trials experience and infrastructure, which the Lead sites were more likely to possess.

Over time, if Developmental sites' clinical research infrastructure continues to mature, we might expect to see an increase in the numbers of Phase 2 trials at these sites. Conversely, we might expect to find a ceiling effect among well-matured sites. Inspection of the relative distribution of Phase 2 and 3 trials in the portfolios of NCCCP sites upholds this latter hypothesis. Sites with a dual designation of NCCCP Lead and CCOP were the most likely to have flat or negative changes in their portfolios – suggesting that the mature sites were more likely to have already established their research infrastructure and to be at or near their maximal research capacity (given the current extent of infrastructure available). The less-mature non-CCOP sites may have the greatest potential for growth with support of a program like NCCCP.

Second, the median number of trials per site, especially of NCI-sponsored trials, increased substantially across all NCCCP sites; increases were calculated as 80% from Year 1 to Year 3 using site-reported data, or 62% from baseline to Year 3 using CTEP data. Site-reported data showed an increase in both the median number of NCI-sponsored Phase 2 trials per site (200% increase over Year 1), and in the median number of Phase 3 trials per site (50% increase over Year 1). CTEP data showed an 86% increase over baseline in the median number of Phase 3 trials per site, but no change in the median number of Phase 2 trials. At least among mature sites, the pilot phase of the NCCCP appears to have allowed sites to reach a level of research activity comparable to that of their non-participating peers. At the end of the pilot evaluation period, both CCOP sites and NCCCP Lead sites that were not CCOPs arrived at similar numbers of median trials per site (42-52 trials per site). Discrepancies in site-reported versus CTEP results likely reflect differences in reporting; improved site-level reporting processes will improve reliability of the data over time and consistency of results. Nonetheless, the patterns are very similar.

When the maturation effect is taken together with findings with respect to clinical trial portfolio, a *second overarching observation emerges*, that is ultimately confirmed in the clinical trials accrual data, namely, that *there is a "sequencing effect" in which the sequential array of activities that must be completed, and of capacity development that must occur, in order to establish a productive research site determines what is possible with respect to increasing research activity and growth among inexperienced sites.* In this evaluation, it rapidly became clear that analysis of site performance must take into account the growth and maturational stage of the participating sites. First, a site must develop the organizational maturity of leadership and coordination in support of the NCCCP and its missions, including clinical trials. Sites without senior leadership or physician leadership have difficulty in initiating and completing trials. Site #3 illustrates the impact of supportive leadership on clinical trials activity, and more generally, in advancing a site along the path toward research maturity.

Site #3: Role of organizational leadership in sequencing effect

In Year 2, a new CEO was appointed at Site #3. This institutional leader took a keen interest in the NCCCP and was a frequent participant in meetings. The new leadership reorganized the organization's infrastructure in preparation for greater participation in the NCCCP. Year 3 data provide some early evidence of the positive impact of this restructuring. By Year 3, Site #3 demonstrated substantial reorganization of its clinical trials program, with growth in staff and physicians recruiting patients to trials; the timing of improvements suggest that the CEO's role was instrumental. In many ways it is appropriate to view this site's Year 3 data as its true Year 1, and to start the evaluation from there. Because of the timing of the reorganization, it might be too early to observe real changes by the Year 3 of the pilot.

The five sites selected as Developmental sites had clinical trials infrastructure and organization that was not well-developed; these sites had the opportunity to grow and learn from the more experienced Lead sites. Lead sites, presumably more mature with respect to research activities and capacity, showed correspondingly greater increases in the number of Phase 2 trials. The newer Developmental sites showed greater increase in Phase 3 trials.

In terms of adding numbers of trials to the portfolio, the sequencing effect can be best understood through acknowledging the multiple steps entailed in establishing a functional research infrastructure at such a site and then opening a trial. These steps include the following:

- Establish organizational infrastructure supportive of trials (e.g., provide space, secure initial funding for research staff)
- Hire research coordinator and other staff
- Train site investigator and staff
- Identify potential studies of interest
- Negotiate contract and budget
- Complete regulatory and IRB processes
- Develop recruitment and study conduct procedures
- Open the study at the site

  (These steps must be accomplished in order to add a clinical trial to a site's study portfolio. Note that to this point no patients have been enrolled yet.)
- Develop a recruitment plan
- Recruit and enroll the first patient

  (These steps must be accomplished in order to add initiate study accrual, and also for a trial to be reported as open at a site according to the CTEP database. Note that to this point only one patient has been enrolled in the trial.)
- Determine best mechanisms to conduct the trial
- Update the recruitment and retention plan, and the process for conducting the trial
- Enroll additional patients

  (These steps must be accomplished in order to complete enrollment in a specific trial. Note that site-level tasks are still not complete until the trial is fully closed out.)
- Perform data management tasks.
- Perform billing tasks
- Update the IRB as warranted
- Complete care on the trial and follow-up for all enrolled patients
- Close out the study (regulatory, data management, financial)

The performance of Site #13 may be representative of Developmental sites which – due to the sequencing effect and the many steps required before measurable impact on research activity can be detected – may not have shown improvements in clinical trials portfolio or accrual during the study period, despite significant internal progress toward research preparation.

> *Site #13: Time required to develop research capacity and demonstrate improvement*
>
> A Developmental site, Site #13 showed a clinical trials performance that initially appears poor throughout the NCCCP pilot period. However, closer inspection reveals a substantial increase in site-reported trials in Year 3. Although this may reflect a site-reported data error, it may also be due to the fact that the site has reported the additional trials as predominantly NCI-sponsored trials, which would not be captured in the CTEP database. (CTEP does not include clinical trials that have no patient accrual). This Developmental site may have taken the majority of the pilot period to develop internal study coordination capacity, and to learn from Lead sites in the NCCCP network. We would expect that the first signal of increasing clinical trials activity is a larger portfolio; this is the potential signal we are seeing in Year 3. Impact on accrual would not yet be observable at this point.

Third, the rate of change in accrual increased more at NCCCP sites than across all CTEP sites (i.e., benchmarked nationally). Analysis of CTEP data showed that NCCCP sites contributed 1.4% of patients (539 of 37,749) enrolled in studies reported in the CTEP database at baseline, and 2.5% patients (1,068 of 42,217) enrolled in studies at the end of the evaluation period. Most of this change occurred in Phase 3 trial accrual. Nationally, patient accrual decreased for Phase 1-2 trials (-28%) and increased for Phase 3 trials (+30%). In contrast, the NCCCP sites experienced a smaller decline in Phase 1-2 accrual (-22%) and a much greater increase in Phase 3 accrual (+133%). The rise in accrual at NCCCP sites outpaced the rise in number of trials, hence the average enrollment into Phase 3 trials increased from 6.6 patients per trial to 13.3 patients per trial.

Overall, NCCCP sites were contributing progressively more patients to Phase 3 trials over time compared to the national average. The rate of contribution to Phase 1-2 trials was consistent with national averages. The fact that total accrual decreased for nearly all of the NCCCP sites, except for the Lead sites that were not CCOP-affiliated, must be interpreted within the context of the national trends. One of the non-CCOP Lead sites and one of the non-CCOP Developmental sites had remarkable increases in accrual (>600%), but since these sites started off with few patients enrolled in trials (N=3), the actual contribution to overall accrual numbers is still relatively small. The CCOP sites demonstrated reductions in accrual, but had high levels of accrual at baseline, so these fluctuations have more impact on NCCCP accrual numbers than on CCOP numbers. Trends suggest that the CCOP sites in the NCCCP are experienced clinical trials sites with higher accrual, but with reductions in accrual over time, suggestive of the same trends witnessed more globally in the CCOP program; they may serve as helpful role models to NCCCP sites that are relatively new to conducting clinical trials and are trying to organize themselves to engage in more clinical trials activity. This yields *a third overarching observation: It is necessary to balance a view of the NCCCP (a) in aggregate, as an ecosystem of cancer-focused processes that ultimately support changes leading to meaningful increases in clinical trials activity, and (b) as a collection of individual sites, or of categories of sites with similar characteristics, with the characteristics of these sites informing how/if specific sites contribute to and/or gain from the ecosystem.*

Overall, the NCCCP Lead sites consistently accrued 3 to 4 times as many patients as did the Developmental sites. The highest contributors to accrual, as well as highest proportional increases in accrual, were among the Lead sites. This may be reflective of the sequencing effect (i.e., the fact that Lead sites have open trials and more mature clinical research infrastructure at the outset) and thus are more poised to increase accrual over time. Developmental sites must first focus on organizing and operationalizing their clinical research infrastructure, which leads first to more open trials and subsequently to likely increases in accrual. It may be too early to see whether the Developmental sites will demonstrate positive changes in accrual as well as increases in their clinical trials portfolios.

Non-CCOP NCCCP Lead sites reflect the group most poised to demonstrate positive increases in accrual; these are the sites prepared to increase accrual numbers by virtue of (a) their greater number of clinical trials, (b) the fact that they may still have room for growth, whereas mature CCOP sites may have already achieved a high and near maximum level of research activity feasible for their site, and (c) their exposure to experienced CCOP sites through the NCCCP. NCCCP Developmental sites are likely focusing on opening trials and preparing for accrual; due to the sequencing effect (see above), they have yet to achieve demonstrable change in terms of accrual. However, as exhibited by Site #16, it remains possible for even mature sites with large portfolio and high accrual at baseline to improve these metrics even further, with the support of a program such as NCCCP.

Site #16: Growth in research activity at a mature site

A mature Lead and CCOP site, Site #16 had a substantially greater number of trials open and accruing at baseline (CTEP treatment trials: site N=46, versus median N=8), with high performance persisting over the pilot period. Despite a small drop in number of trials over the three years, the number of patients accrued increased (CTEP data), suggesting that even Lead CCOP sites can see remarkable changes in accrual. The reasons are not readily apparent. The number of physicians at the site increased from 33 to 44, suggesting an increase in the total number of patients receiving care at the site, and therefore a potentially larger population of individuals screened. Exploration of circumstances at this site might help elucidate the types of on-the-ground changes that best support efforts to increase clinical trial enrollment.

Fourth, NCCCP sites are increasing their number of patients accrued per study at a rate faster than national trends. The average study enrollment (i.e., mean number of patients per trial) provides a metric of recruitment efficiency that allows for comparisons between NCCCP and non-participating sites. Nationally, Phase 1-2 trials averaged approximately 11.9 patients per trial at the beginning of the evaluation period and12.4 patients per trial at the end (July 2006-July 2010), an increase of only 4%. Average study enrollment for Phase 3 trials nationally rose from 150 patients per trial at the start of the evaluation period to 181 at the end, a 21% increase. The relative NCCCP trends demonstrate a greater rate in change of study enrollment efficiency: Phase 1-2 trials increased from 1.7 to 1.9 patients per trial (9% increase) and Phase 3 increased from 6.6 to 13.3 (100% increase). Thus, while the NCCCP sites are changing their numbers of open trials generally in step with national trends, they are increasing their accrual to studies faster than national trends. The 16 NCCCP sites are contributing about 2% of the national accrual to CTEP-reported clinical trials; this increased by 80% over the three-year period. The NCCCP sites are predominantly contributing to Phase 3 trials; participation in Phase 1-2 trials is generally similar to national trends.

CTEP data demonstrate that both NCCCP Lead and NCCCP Developmental sites gained patients from baseline through Year 3. Lead sites had a relative increase of 31% (medians: baseline=29, Year 3=38). Developmental sites had a relative increase from baseline of 71% (medians: baseline=7, Year 3=12). The increase in mean accrual to Phase 3 trials also spanned both types of NCCCP site, but closer inspection of the timing of those increases is illuminating. Both types of site showed an increase in average per trial enrollment over baseline (41% increase for Lead sites, 35% increase for Developmental sites, CTEP data), despite the fact that Lead sites had an average enrollment at least twice that of Developmental sites and that mean accrual among Lead sites is about 4 times that of Developmental sites (CTEP data). However, Lead sites increased their average enrollment in the first year and maintained that level throughout the three years of the pilot evaluation, while Developmental sites demonstrated a more gradual increase over time. The sites with the greatest Year 1 accrual (i.e., the well-established Lead sites with CCOP affiliation) were the sites most likely to exhibit a decrease in enrollment by Year 3. Sites with very little Year 1 patient accrual were the ones which showed the greatest increase by Year 3. Thus, NCCCP sites with a robust clinical trials program (such as those also involved in the CCOP) may have already reached the peak of their research capacity; the three years and modest additional funding may not have been sufficient to further increase their accrual rates.

Fifth, NCCCP sites' increase in accrual was largely attributable to trials not sponsored by the NCI. Upon examination of accrual by category of sponsor (federal, industry, other), NCCCP site-reported data showed a slight (5%) increase in the median patient accrual, but a 13% decrease in total accrual. Accrual to NCI-sponsored trials fell by 27% from Year 1 to Year 3. By contrast, accrual to Industry-sponsored trials rose by 69% and accrual to Other-sponsored trials rose by 265% over this time period. The overall reduction in accrual over time is thus attributable to relatively fewer patients being enrolled in NCI-sponsored trials. Accrual for trials supported by Industry and Other sponsors, while small in comparison with the number of patients involved in NCI-sponsored trials, both showed relative increases each year. Importantly, baseline numbers for non-NCI studies were low, so relative proportional changes reflect exaggerated numbers and should be interpreted with caution.

The reason for this pattern is unclear; four possible explanations are: (1) a sequencing issue, reflecting the fact that trials need to be opened at a site before increases in participant accrual can be seen; (2) a data quality improvement effect, in which sites were more accurate at reporting accrual in later years of the evaluation process and therefore data in later years is more accurate (with lower numbers); (3) a relative shift to Industry-sponsored activity, or; (4) closing of several large NCI-sponsored trials during the evaluation period, which could have caused site-level resources to be shifted to other studies once those trials were finished.

One of the stated goals of the NCCCP program was to extend the reach of clinical trials to underserved populations in participating sites' local communities; three categories of interest were racial/ethnic minorities, rural populations, and patients age 65 and over. A **sixth** major finding was that each participating site did succeed in increasing accrual from underserved populations over the three-year evaluation period. According to site-level data, accrual of racial/ethnic minorities increased from 7% of total accrual in Year 1 to 15% of total accrual in Year 3. Similarly, accrual of patients from rural populations rose from 11% to 20 % of total accrual; and of patients age ≥65 increased from 4% in Year 1 of total accrual to 35% of total accrual in Year 3. CTEP data (which document racial/ethnic and age, but not rural/nonrural, parameters) were consistent with these findings – accrual from racial/ethnic minorities increased by 82%, in step with the rise in total accrual, and accrual of patients age 65 and older increased by 221%, far outpacing the growth in overall patient accrual. These increases in accrual of underserved individuals were program-wide; site-level data showed increases at all but 2 Developmental sites in at least 1 of the 3 underserved population categories.

This yields *a fourth overarching observation – exposure to the NCCCP ecosystem yields improvements in accrual of underserved populations.* Historically, increasing minority accrual has been exceptionally difficult and a major area of focus for the NCI (e.g., the Minority-based CCOPs). The NCCCP focus on improved access of the underserved to care appears to have a corollary effect on minority accrual. This is most dramatic within the NCCCP sites that are also CCOP sites. These sites were less likely to demonstrate substantial increases in total numbers of patients accrued, but they were indeed the sites with most notable increases in minority accrual. A possible explanation is that these sites were at maximum capacity in terms of total participant accrual (given a relatively fixed infrastructure), but could adjust their internal recruitment processes in order to increase the proportion of people accrued from underserved populations. Sites #6 and #12 demonstrate the increases possible in minority accrual, potentially due to this emphasis within the NCCCP, at both CCOP and non-CCOP sites.

Site #6: Mature CCOP - Increase in accrual from underserved populations

Site #6, described previously, is both a Lead CCOP and a Lead NCCCP site. At first glance, their proportional increase in clinical trials numbers and accrual appears close to flat. But all numbers are substantially higher than trans-program medians (>>300%). Although their total accrual to clinical trials did not substantially change, their recruitment of patients from underserved populations did increase over the evaluation period, confirmed by both site-reported and CTEP data.

Site #12: Non-CCOP - Increase in accrual from underserved populations

A NCCCP Lead site with no CCOP affiliation, Site #12 showed increases in numbers of trials and patient accrual that were in step with the NCCCP medians. Remarkably, this site reported a 167% increase in clinical trial participation by racial and ethnic minorities. Similarly, in Year 1 it enrolled no patients over age 65 but in Year 3 it enrolled 38. The reasons for this improvement are unclear, but may include initial under-reporting of minority accrual. The site had a large clinical research enterprise with many enrolling physicians; the size of the enterprise itself did not increase substantially over the pilot period, but the number of enrolling physicians did increase. It would be useful to explore, at this site, the characteristics contributing to their substantial success in recruiting underserved populations.

A **seventh** major finding is that participating NCCCP sites increased their general research activity during the study period. The program afforded these community-based sites the opportunity to enhance their other clinical research activities (i.e., those in addition to Phase 1-2 and Phase 3 clinical trials). For example, 4 sites were participating in the Moffitt Total Cancer Care Initiative by the end of the evaluation period, and collectively had increased their enrollment in "Other Research Activities" (predominantly biospecimen and longitudinal data collection) to 3,008 patients in Year 3, compared to 45 patients enrolled in this category of study in Year 1. Across all sites as well, there were 81% more "Other" studies ongoing by Year 3 than in Year 1; these studies spanned the non-clinical trial categories of screening, biospecimen collection, correlative studies, epidemiology studies, and other descriptive studies. Thus, sites achieved another of the NCCCP goals – that of the sites expanding their trial portfolio and the types of research available to community-based cancer patients. The Moffitt program offered a mechanism through which NCCCP sites, as their research capacity grew through NCCCP participation, could become involved in additional (non-clinical trial) research activities. Sites #10 and #15 provide examples of how participation in the NCCCP worked synergistically with participation in the Moffitt program to increase overall research activity.

Site #10: Synergistic benefit of other research activity

A Lead NCCCP site, Site #10 participates in the Moffitt Total Cancer Care Program. According to CTEP data, this site's increases in numbers of trials and absolute participant enrollment over the pilot period were consistent with NCCCP medians. However, site-reported data demonstrate that the site had a dramatic increase in accrual activity related to the Moffitt program during this period. Moffitt participation appears to have encouraged high volume accrual and participation. It would be useful to learn from site physicians and leadership why participation in the Moffitt program seemed to add more value than accrual into NCI-sponsored trials. For example, this may reflect the differences in on-the-ground energy expenditure required to participate in a biospecimen program such as the Moffitt Total Cancer Care Initiative versus a Phase 2 or Phase 3 NCI-sponsored trial.

Site #15: Increase in accrual due to other research activity

As a Lead NCCCP site that was not in CCOP, Site #15 had overall clinical trials portfolio size and accrual to treatment trials that were slightly higher than the NCCCP medians. It achieved stepwise increases in portfolio and accrual over time, more than doubling both (per CTEP data). During the pilot period, this site exhibited a remarkable increase in other (i.e., non-clinical trial) accrual; it enrolled 888 patients in Year 3. This change occurred without commensurate reduction in clinical trial accrual. The large increase can likely be attributed to participation in the Moffitt Total Cancer Care Initiative, the impact of which is very evident by Year 3. It does not appear that participation in the Moffitt program impaired Site #15's ability to participate in the clinical trials activities valued highly by the NCI. Of note, this site increased its number of participating physicians from 3 to 9 over the pilot period. Site #15's performance suggests that a mature site can still have untapped clinical trials capacity. This capacity was harnessed to contribute more activity to NCI-sponsored trials, but even more impressively harnessed to contribute to the Moffitt biospecimen program.

Table 5 recapitulates the overarching observations that provide the context in which to consider this report's seven major findings. These observations have vital relevance to the design, timeframe, potential outcomes, and evaluation of future efforts to increase clinical trials activity at community-based cancer centers.

Table 2: Overarching Observations Regarding NCCCP Pilot Sites' Clinical Trials Activity

Maturation effect	Long-standing, larger, research sites such as the NCI-designated cancer centers have the capacity to focus on the more difficult, labor-intensive, early-phase trials. By contrast, the local community-based NCCCP centers typically lack comparable infrastructure, resources, and experience; due to their level of research maturation, they are appropriately focused on less complex, later-phase trials.
Sequencing effect	There is a sequential array of activities that must be completed, and a level of capacity development that must occur, in order to establish a productive research site. Where a site is positioned along this continuum determines what it can achieve with respect to increasing its research activity and growth.
Forest AND trees approach	It is necessary to balance a view of the NCCCP (a) in aggregate, as an ecosystem of cancer-focused processes that ultimately support changes leading to meaningful increases in clinical trials activity, and (b) as a collection of individual sites, or of categories of sites with similar characteristics, with the characteristics of these sites informing how/if specific sites contribute to and/or gain from the ecosystem.
Impact on disparities	Exposure to the NCCCP ecosystem yields improvements in accrual of underserved populations.

The trends and patterns identified through this evaluation point to several recommendations that may be useful in further evaluation, advancement, and refinement of the NCCCP. First, results of this evaluation are limited by the short timeframe of the evaluation period. While the maturation effect can be observed from baseline and across the three years of the pilot period, the sequencing effect implies that the impact of the NCCCP on certain outcomes – particularly those related to accrual – may not be observable within the study timeframe. Thus results reported herein should be viewed as preliminary, as they may not adequately capture the changes in accrual that will result from improvements in research capacity, increases in numbers of open clinical trials, and greater participation in other research activities, especially for sites that are relatively new to research, such as the Developmental sites.

Encouragement can be drawn from the fact that, while NCCCP CTEP data parallel national trends (e.g., decreases in Phase 1-2 trials and accrual, increases in Phase 3 trials and accrual), NCCCP sites fared better in general over the time period of the pilot. Additionally, the NCCCP pilot afforded sites more research opportunities overall (e.g., participation in the Moffitt Total Cancer Care Initiative) and contributed to underserved accrual in the community. Depending upon the goals of the NCI, these findings support a general observation that participation in the NCCCP ecosystem contributes to a mission of enhancing clinical trials activity in community settings.

Patterns in performance and performance change may indicate where future NCCCP attention and investment would be best directed. The CCOP-affiliated sites may have reached a saturation point in their research capacity (i.e., their workload for number of trials they can handle, and maximum patient

enrollment). Total accrual could therefore be better increased through the NCCCP by focusing support on sites that are not yet mature in their research activity. Evaluation results affirm that gains can still be made among mature sites, however, in increasing recruitment from underserved populations.

An important role emerged for mature (i.e., Lead) sites as mentors for Developmental sites. In general, the substantial clinical trials activities of the CCOP-affiliated Lead sites position them to mentor less experienced sites such as the Developmental sites, sharing best practices and role modeling actions. Additional reasons for the continued participation of mature sites in the NCCCP are their greater capacity for Phase 2 trials and for addressing their attention to accrual of underserved populations.

Similarly, it is likely that exposure to the NCCCP ecosystem as a whole, including the multiple parallel program goals (e.g., survivorship, quality, underserved populations), provided complementary elements that contributed to the increase in clinical trials activity. It would be hard to isolate any one ingredient, as these elements likely had synergistic impact on desired clinical trials outcomes such as minority accrual.

Discrepancies in performance, particularly in accrual, between Lead and Developmental sites underscores the point that, for sites new to clinical research, time is needed to establish infrastructure and processes. Sites must learn to organize and coordinate trials, to open them, to recruit and enroll patients, and to complete the multiple steps entailed in study conduct and regulatory compliance. To begin participating in clinical research, sites need to build considerable infrastructure, know-how, process and logistical pathways, and organizational capacity. These activities take time. They also take expertise, which could be cultivated at Developmental sites in the NCCCP through the mechanism of mentoring by Lead sites. Further study might examine areas in which mentoring succeeds, and reasons for that success, as well as factors associated with poor/unproductive mentoring.

CONCLUSIONS

A core goal of the NCCCP was to strengthen the clinical trials programs at participating community hospitals/hospital systems and their cancer centers. The 2007-2010 pilot phase included 16 hospitals (11 Lead sites and 5 Developmental sites), three of which were also Lead CCOP sites, and four of which were performance CCOP sites. Not surprisingly, these CCOP sites with already well-established clinical trial programs did not further increase their accrual or trial portfolio over the three-year period; they did, however, increase their accrual of underserved populations, and they likely served as good examples within the NCCCP ecosystem.

Many of the NCCCP pilot sites did enhance their clinical trials activity in meaningful ways. Most of the sites increased the number of ongoing Phase 2 and/or Phase 3 trials, especially NCI-sponsored trials. Patient accrual increased, especially in Phase 3 trials. The overall patient per trial ratio increased. Nearly all sites improved their accrual to underserved populations in racial/ethnic minorities, rural, and/or the age 65 and over categories. Sites also improved their other research activity (i.e., non-clinical trial research), fulfilling the NCCCP intention that participating sites become a research resource.

When compared to national trends over the three years of the pilot, outcomes of sites participating in the NCCCP program outpaced those of sites nationwide, in both number of trials and patient accrual. The 16 participating sites made impressive progress during this short pilot period, considering that strengthening of sites' clinical trials activity was only one of several goals of the NCCCP, and that sites were limited in the amount of their program funds that they could designate for clinical trials activities. These results give credence to the potential impact on clinical trials of a networked approach, wherein a centralized structure facilitates growth in sites' research programs and mature sites mentor inexperienced sites.

Results support a tiered approach to program goals, depending on the level of experience of the site. In this pilot, the more mature Lead sites focused on increasing the number and accrual to clinical trials, with marginal gains, but were likely able to share their best practices with the Developmental sites. Their limited ability to increase their clinical trials portfolios and accrual numbers reflects a level of maturity and saturation (i.e., approaching a ceiling on their capacity for trials and accrual), rather than poor performance. Performance of these sites might be better assessed through metrics that evaluate what they can still change, for example, accrual of underserved populations and mentoring of new sites. The less experienced Developmental sites, as they built their clinical trials programs over the three-year period, focused on establishing basic research organization and clinical trials infrastructure. These sites needed to sequentially attend to organizational features, research infrastructure, processes (e.g., protocol development, regulatory tasks), and development of in-house skills before they could open clinical trials and begin accrual. Once they established a functional research program, Developmental sites were positioned to improve their performance dramatically in terms of number of clinical trials and, subsequently, accrual. However, not all sites were equally performing, and some poorly performing sites were not able to meet the intended outcomes in the time provided by the pilot program.

In summary, despite the short evaluation period and the limited resources for sites' clinical trials activities, the NCCCP pilot supported progress in sites' clinical trials programs – as evidenced in their ability to open more clinical trials and to accrue greater numbers of patients to those trials. Investment in the NCCCP program appears to be resulting in achievement of a key goal, namely, inclusion in clinical trials of patients who may not be reached by other NCI programs (e.g., CCOP, NCI Cancer Center Program). Overall, this evaluation concludes that the NCCCP achieved its core goal with respect to clinical trials – to improve care for patients treated in community settings by (a) bringing more clinical trials to community-based settings, and (b) involving greater numbers of patients, and a greater diversity of individuals, in those studies.

APPENDIX 1: ANALYSIS PLAN

NCCCP Clinical Trials Data Analysis Plan – Version 3.0 – July 1, 2011

The National Cancer Institute (NCI) Community Cancer Centers Program (NCCCP) is a network of hospital cancer centers that serves as a community-based platform by supporting basic, clinical, and population-based research initiatives across the cancer care continuum. In addition, NCCCP sites are directly contributing to the cancer research enterprise by: accruing patients to clinical trials; collecting high-quality biospecimens for research; expanding information technology through the use of electronic health records and participation in NCI informatics initiatives; and collaborating with other NCI programs and related organizations, including the NCI Cancer Centers Programs, The Community Clinical Oncology Program (CCOPs/MBCCOPs), The Cancer Genome Atlas, the NCI Community Networks Program, the American Society of Clinical Oncology, and the American College of Surgeons' Commission on Cancer.

A core NCI goal for the NCCCP is to contribute to the NCI mission of evidence development and translation in the community oncology setting. Clinical trials are a fundamental aspect of cancer care, an important clinical option for patients, and the primary research mechanism that generates evidence on the clinical role of preventative or anti-cancer interventions. The NCCCP aims to provide cancer research treatments within the communities where the majority of patients live (i.e., 85% of cancer patients receive their treatments through community based hospitals) by involving more patients in clinical trials, providing them the opportunity to benefit from the latest therapies before they are available to the general patient population. The NCCCP sites are incentivized to build capacity to offer earlier phase trials, with a goal of reducing the need for patients to travel to larger academic centers to access these trials. All patients should be considered as potential participants for trials at NCCCP sites, with a strong focus placed on reaching underserved populations, including racial/ethnic minorities, the elderly, those living in rural areas, and others who are typically underrepresented in clinical trials.

To achieve the program's stated aims, NCI established a national network of participating community hospitals/hospital systems and their cancer centers. A total of 10 organizations were originally funded: eight individual hospitals and two system organizations, which altogether includes 16 hospitals. The two system organizations, each selected "lead" sites to facilitate the implementation of the NCCCP within their system to work with additional "developmental" sites. These developmental sites could be hospitals that did not meet the selection criteria, yet had the potential to do so by the end of the pilot. Even though the system organizations had multiple hospitals participating in the NCCCP, there was no additional NCI funding beyond what was awarded to the individual non-system organizations. Each of the 10 funded organizations was awarded approximately $500,000 annually to support the NCCCP activities. One system organization selected two lead sites that met the selection criteria and added a developmental site that is regionally based and encompasses three hospitals. The other system organization selected one hospital as the lead site and two additional hospitals as developmental sites.

Thus, the NCCCP started in 2007 with a total of 11 designated Lead sites and 5 Developmental sites. A thoughtful evaluation program was built around the NCCCP pilot in order to determine if the overall goals of the program were being accomplished. While the program included a range of questions relative to the various goals, a specific question and the focus of this analysis was the association of the NCCCP investment and clinical trials activities at the 16 NCCCP pilot institutions.

Amy Abernethy, MD, and colleagues at Duke University's Cancer Care Research Program (DCCRP) have been contracted to assist with a review of the clinical trials portfolio for the pilot NCCCP sites, and review the temporal relationship between organizational characteristics at the pilot NCCCP sites and

clinical trials activities. Within the context of this project, two main outcome assessments will be considered: clinical trials accrual (both total accrual and for underserved populations including racial and ethnic minority accrual) and the clinical trials portfolio [represented by the number of open clinical trials at a site, types of trials (phase, intervention under investigation, Sponsor)].

Since this program is still maturing and aggregate data are likely not informative, supplemental qualitative and quantitative analyses will be conducted to elaborate understanding, such as mapping of organizational changes and maturation of clinical trials capabilities over time within the temporal context of study accrual and portfolio. Key considerations will be on-the-ground clinical trials infrastructure (e.g., IRB interaction, staff, PIs and physician arrangement, contracting and financing know-how [when this information is available]) and institutional organizational dynamics (e.g., reporting structure between the cancer program and overarching institutional leaders, and between the clinical trials program and the cancer program). An aspect of the NCCCP program that will add richness to the qualitative data, but limit numbers for aggregate quantitative analyses is that sites were intentionally selected to be at different maturity levels at the start of the program and that the developmental sites had limited resources; this will be considered during all analyses.

This project incorporates several data sources each of which has its advantages and limitations. The NCCCP sites reported data quarterly and yearly about their on-the-ground staff and capabilities, trials portfolio, and accrual. These self-reported data were frequently erroneous and errors likely shifted over time; for example early in the NCCCP program sites may have misunderstood definitions or attributed study participants and trials to the wrong category, and these reports could have improved or worsened as categorical definitions were better understood or staff changed. To accommodate, the data were cleaned by SAIC-F and NCI to improve accuracy, but despite these efforts, the fundamental limitations of the data remain. Still, these site-reported data provide important insights for on-the-ground experience with the NCCCP, clinical trials activity, and change over time – review of these data provides a "site level lens." Meanwhile, the central NCI clinical trial database, housed within the Cancer Therapy Evaluation Program (CTEP), captures information on NCI trials and accrual; because it is cleaned at the trial level, attributing each participant to a study and then consolidating the study data to submit to the central CTEP database, it provides the most accurate view of actual accrual and trial characteristics for the trials reported in this system. However, the CTEP database does not include open but not enrolling trials (a substantial expense and drain on sites), non NCI-sponsored studies that don't report to CTEP (like industry trials), and many correlative studies. Despite its limitations, CTEP data provide the cleanest comparative data to allow comparison between sites, to national trends, and contribution of the NCCCP program to cancer evidence development – review of these data provides a "trial level lens." Planned analyses will include both points of view – site level and trial level – in order to provide a summary of the NCCCP program's impact on clinical trials activity and maturation of experience on the ground.

This analysis plan provides an overview of the evaluation planned for the clinical trials component of the NCCCP pilot program. Key sections include Objectives, Definitions and Assumptions, and Analytic Approach. Importantly, an iterative process is planned. The analysis plan will be serially updated as we learn from the data available. We welcome feedback on the analysis plan, its ongoing refinement, results, and interpretation and intend to update the plan within the scope and finances of this contract.

Name of Project	Specialized Analysis of NCI's Clinical Trials Data for the NCCCP Evaluation
Contacts/Key Stakeholders	*See "NCCCP Key Stakeholder Listing"*
Objective(s)	1. To evaluate the association of NCCCP participation on the clinical trials portfolio and activities at the pilot NCCCP sites over the 3 year period from program inception to the end of the initial evaluation cycle. 2. To evaluate what qualitative factors seem to be associated with the success of clinical trials activities at NCCCP sites.
Outcomes	The main outcomes of interest are: 1. Clinical Trials Accrual – total and for underserved populations 2. Clinical Trials Portfolio - including number of open clinical trials at a site, and types of trials (phase, intervention under investigation, Sponsor) A series of research questions will be explored in order to develop a better understanding of the relationship between NCCCP participation and the association on these outcomes over time. Various ways of presenting these outcomes are planned (e.g., ratio of accrual to cancer treatment clinical trials open with accrual), evaluated in cross section and over time. Planned analyses will use site-reported and CTEP data to reflect two points of view – site level and trial level – in order to provide a summary of the NCCCP program's influence on clinical trials activity and maturation of experience on the ground. Further, as we evaluate the site infrastructure (see research questions below) we will consider evolution in this infrastructure over time as a qualitative factor potentially explaining observations in trends in clinical trials accrual and portfolio.
Description of Research Questions	Evaluation questions include: • To what extent did the individual NCCCP sites improve their clinical trials outcomes sequentially over the course of the three year pilot study? • To what extent has participation in NCCCP led to building organizational capacity infrastructure to increase accrual to clinical trials? Examples of the elements to be considered are changes in center leadership support of clinical trials, financial support of clinical trials, staffing, increases in physician participation in cooperative groups and other research, accelerated IRB reviews, improvements to site tracking trial activity, and increases in clinical trials interactions with local community as they relate temporally to NCCCP participation. Key considerations will be on-the-ground clinical trials infrastructure (e.g., IRB interaction, staff, PIs and physician arrangement, contracting and financing know-how [when this information is available]) and institutional organizational dynamics (e.g., reporting structure between the cancer program and overarching institutional leaders, and between the clinical trials program and the cancer program). Analyses will be limited to available data, with a qualitative focus. • How do changes in the organizational mechanisms at the NCCCP sites relate to changes in clinical trials accrual and portfolio, qualitatively and quantitatively? • How do changes in the clinical trials infrastructure at the NCCCP sites relate to changes in clinical trials accrual and portfolio, qualitatively and quantitatively?

Description of Research Questions, cont.	• To what extent did the lead and performance CCOP sites (in NCCCP) perform differently (better or worse) than non-CCOP sites (in NCCCP), and what aspects of being a CCOP site seemed most influential in those differences? • Has the portfolio of trials at sites matured over time and how does this relate to accrual? Sites could participate in many different kinds of studies, including therapeutic treatment trials, cancer control trials, biospecimen collection /correlative studies, epidemiology studies, and other descriptive studies. Different study types require different levels of staff experience, confidence and expertise, on the ground, in order to successfully enroll participants and collect data. The changes in clinical trials portfolio at sites, by study type and phase, will be considered, both in terms of change in complexity of trial type over time and related accruals. For example, a site may be very active in the Moffitt biospecimen collection study called Total Cancer Care; this may reflect high accrual but is a simple study to conduct; if this same time transitions to more therapeutic treatment trials the accrual numbers may go down but the actual clinical trials workload for staff on the ground will increase and patient care may be more directly (and positively) impacted. These trends will be described quantitatively and qualitatively. • The current landscape of clinical trials activities (accrual, number of trials, types of trials) among the NCI CCOPs, NCI Comprehensive Cancer Centers, within the NCI CTEP overall, and nationally as represented by clinicaltrials.gov will be described, in order to set the NCCCP clinical trials activities within the context of other cancer-related clinical trials efforts. To what extent did the trends in change in clinical trials accrual and portfolio among the NCCCP sites align with or differ from these national trends in clinical trials activity?
Deliverables	1. Draft report and slide deck - 8/12/11 2. Final report – 8/30/11

Definitions and Assumptions	
Definitions	**NCCCP** - The National Cancer Institute (NCI) Community Cancer Centers Program began in 2007. The analysis will include only those 16 pilot NCCCP sites of which eleven (11) are considered Lead sites and five (5) are considered Developmental sites. **CCOP** - The Community Clinical Oncology Program (CCOP) is a network for conducting cancer prevention, cancer control and treatment clinical trials by community medical practitioners. Of the 16 pilot sites, three (3) are also Lead/Institution of Record CCOP sites, and four (4) are considered CCOP "Performance" sites. Of the "Performance" sites, one is a MB-CCOP (minority-based CCOP) performance site. All CCOP sites in the NCCCP pilot were in place prior to 2000. **Clinical Trials Accrual** – The number of patients enrolled in a given clinical trial. For the purposes of these analyses, we will only consider fully consented, enrolled patients, and not screening. **Clinical Trials Portfolio** – The array of clinical trials at a given site. Analysis includes not only the number of trials open, but also the types of trials (e.g., phase, intervention under investigation, study Sponsor). **Study Sponsor** – The organization, agency, or company that funded the study. For the purposes of these analyses, Sponsor will include government (NCI, non-NCI NIH other, non-NIH government other), industry, philanthropy, other, and none. **Open Study vs. Enrolling Study** – A study may be open to enrollment but not actively enrolling patients for a variety of reasons (e.g., eligible patients not yet identified, physicians not aware of new trial for patients, inadequate study staff to conduct trial). Some primary analyses will include only those clinical trials with accrual data (i.e., open enrolling studies), and other analyses will include all open studies at a site (including non-enrolling studies.) Whenever possible, consideration of the overall clinical trials portfolio at a site will include description of all open studies and open enrolling studies. **Underserved Accrual –** The number of patients enrolled in clinical trials that are from traditionally underserved populations. This includes racial/ethnic minorities: Black, Hispanic, Asian-American, American Indian, or other racial/ethnic backgrounds; the over age 65 population; and the rural-based population. **CTEP & CTEP Database** – The Cancer Therapy Evaluation Program (CTEP) funds the NCI Cooperative Groups to conduct clinical trials. The CTEP database is a robust well-recognized repository of information about CTEP trials.

List of Datasets and Indicators Planned for Utilization	**"NCCCP CT Analysis Information – Data from RTI" (sent May 17, 2011):** • NCCCP Baseline clinical trial data to RTI 2011-04-20.xlsx • NCCCP Clinical Trial Data to RTI 2011-04-13 FINAL for Duke (Verified) • NCCCP CT Analysis_Outcomes Matrix and Codebook_2011-05-06 • CurrentTrialsLog Inventory10Mar2011. xlsx **"NCCCP CT Analysis – Contextual Documents from RTI" (sent May 17,2011):** • NCCCP De-identified site numbers 2011-05-04.xlsx • NCCCPOncologyIssuesArticles CT.pdf • Recist_Implementation_ Matrix_Feb2010.doc • NCCCP Log Sites and Trials Open **CTEP Database – Data from RTI (sent May 24,2011):** • Revised NCCCP data.xls **NCCCP Organizational Factors – Data from RTI (sent May 20,2011):** • CT Analysis_Organizational_Factors_COPs_DATA_2011-05-20.xls • CT Analysis_Organizational_Factors_COPs_CODEBOOK_2011-05-20.xls

Data Limitations, Other Issues & Assumptions	• The data collected via the NCCCP quarterly reports is self-reported which may result in biases and misrepresentation. • Some of the NCCCP sites were less mature in their clinical trials programs, and therefore accrual data may not be as robust as one would expect over a three year period. As such, there may not be enough data to perform formal effectiveness analyses, and instead analyses will be made on a qualitative level. Developmental sites did not have to meet the baseline requirement of 25 patients accrued to clinical trials annually • It is assumed that final clinical trial data (provided to RTI as the conduit to Duke) includes clinical trials that are categorized in the most obvious way, only once. *Reference document: NCCCP Clinical Trial Data to RTI 2011-04-13 FINAL w Calculations for Duke* • It is assumed that there is no information regarding the specific types of clinical trials denoted in the baseline data. *Reference document: NCCCP Baseline clinical trial data to RTI 2011-04-20.xlsx* • It is assumed that CTEP accrual data may be different from self-reported accrual data. In addition, self-reported data include staffing information that is not found in CTEP data. *Reference document: NCCCP CT Analysis_Outcomes Matrix and Codebook_2011-05-06* • It is assumed that Y1 information from the baseline survey was administered Fall 2007, but that each item was representative of a distinct and potentially variable time period – such that counts per item can be confirmed, but time periods will be different for each data element. *Reference document: NCCCP CT Analysis_Outcomes Matrix and Codebook_2011-05-06* • Analyses will be performed to compare accrual to the number of cancer treatment trials open with accrual. However, the site reported data includes all trials open, including those with no accrual. In contrast, the CTEP only includes trials with patient accrual. This may skew the results as open treatment trials with no accrual would not be counted. • This list of assumptions will be continuously updated in order to document observations about the datasets and decisions made.

Analytic Approach

It is anticipated that the data analysis strategy will assume the following step-wise approach:

1. Exploratory
2. Descriptive
3. Inferential

Exploratory analysis will drive the future analysis and is anticipated to pinpoint problem areas in the data. Further, the following considerations will need to be addressed:

- Should outliers be included or excluded in the analysis?
- Is the data cleaned for consistency, and consistently cleaned?
- How much of the needed data are missing? How will this be handled?
- What do the distributions look like for each of the key variables/indicators/suggested hypotheses?

Following exploratory analysis, general descriptive statistics and graphical representation of trends longitudinally by site are anticipated to provide a powerful summary that will facilitate comparisons across sites and at group levels (i.e., CCOP sites, NCCCP sites, and national trends). Univariate, descriptive analysis will be used to describe the distribution, central tendency, and dispersion of investigated variables.

With regard to inferential statistics, the research questions will seek to drive investigation through: trends analysis (to find patterns over time); analysis of variance models (to compare averages for different groups), if appropriate; and multiple regression and correlation (to determine the strength of relationship between different variables within the data), only if appropriate (NOTE – we doubt that we will have adequate data to support these more definitive analyses at this time).

APPENDIX 2: SITE VIGNETTES

(Descriptions of the Quantitative and Qualitative Data for Each Site Individually)

NOTE: For this section site-reported data are presented prior to CTEP data in each vignette, because these vignettes reflect the site's perceived experiences and therefore the site-reported data provide the most accurate reflection of the on-the-ground experience

Definitions:

Total Number of Trials:

Site Self-Reported Data: The number of trials currently open at the site for the given year. It includes trials that are open but may not be enrolling patients. It includes all clinical trials of the following types: Treatment, Prevention, Symptom Management and Cancer Control, as identified by site personnel. Trials from all sponsor types are counted, including NCI, Industry and Other-sponsored trials. There was no site-reported data given as a baseline for these types of trials at any of the sites. Therefore, data from Year 3 are compared to the site reported data from the end of Year 1.

CTEP Data: The number of trials currently *enrolling* at the site for the given year. It does NOT include trials that are open but not accruing patients. It includes clinical trials that are sponsored by CTEP (Treatment trials) and DCP (Prevention, Symptom Management and Cancer Control trials). Baseline for these trials was reported for the year prior to the beginning of the NCCCP program (i.e., July 2006-July 2007).

Total Accrual:

Site Self-Reported Data: The number of patients enrolled in clinical trials for the given year. It includes only those patients enrolled in Treatment, Prevention, Symptom Management or Cancer Control trials, as identified by site personnel, across all sponsor types: NCI, Industry and Other-sponsored. There was no site-reported data given as a baseline for this specific type of accrual at any of the sites. Therefore, data from Year 3 are compared to the site reported data from the end of Year 1.

CTEP Data: The number of patients enrolled in clinical trials for the given year. It includes patients enrolled only in CTEP-sponsored treatment trials or DCP-sponsored Prevention and Cancer Control trials. Baseline for this accrual was reported for the year prior to the beginning of the NCCCP program (i.e., July 2006-July 2007).

Underserved Population Accrual:

Site Self-Reported Data: Sites reported the number of patients enrolled in trials who were from typically under-represented populations; specifically racial/ethnic minorities, rural populations and those patients above age 65. Some sites did not have the ability to report minority accruals in Year 1 or in some cases throughout the evaluation period. In addition, in the last quarter of Year 3 (and for all 3 years in the case of Site #16), some sites began reporting ethnic minority accrual separate from racial accrual. In these cases, the ethnic minority accrual was not counted in the racial/ethnic minority totals. For the rural patient population, NCCCP did not use a standard definition of "rural" choosing instead to let each site use its own definition. Finally, Site #16 reported accruals for patients "greater than and equal to age 65," rather than just "greater than age 65."

CTEP Data: For all sites, racial and ethnic minority accrual data were collected separately and included the following categories: Hispanic or Latino, Black or African American, AI or Alaska Native, Asian, NH or Other Pacific Islander, and More than One Race. The totals were combined for reporting of racial/ethnic minority enrollment. For the age population, accrual data included patients greater than or equal to age 65 at the time of enrollment. There were no rural populations recorded or collected in CTEP/DCP trials.

Other Research Activities:

Site Self-Reported Data: Sites reported on open trials and enrollment to all research activities ongoing at their site. This included studies in the following categories: Screening, Early Detection, Diagnostic, Epidemiologic, Observational, Outcome, Ancillary and Correlative Studies. The data for these studies have not been included in the number of trials and total accrual categories; rather they are reported on separately as "Other Research Activity" and "Other Accrual."

CTEP Data: The CTEP database does not collect nor include these studies or accrual in their data.

Site 1

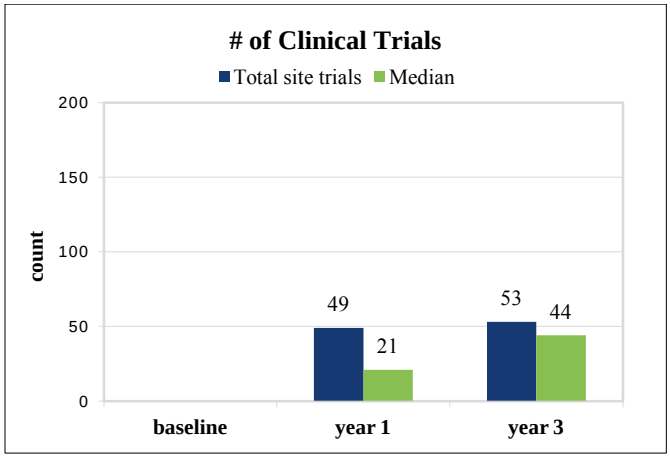
NCCCP Designation and External Relationships

This hospital is a Lead NCCCP site with no CCOP affiliation. They started supplying biospecimens in the 3rd year to the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

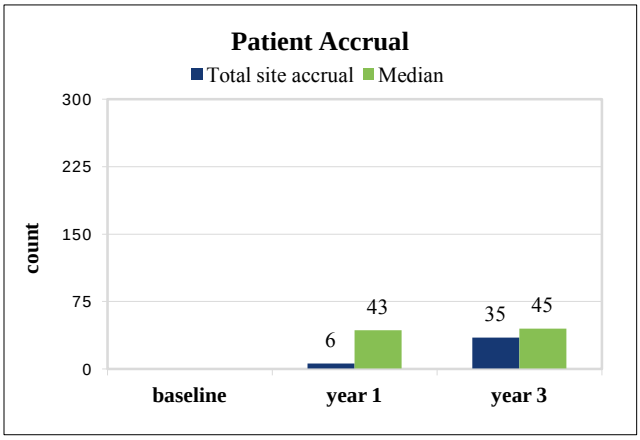
Trials Portfolio – Site-Reported Data

According to site-reported data, the total number of trials reported in Year 1 was 49, which increased to 53 in Year 3, representing an 8% increase in trials. The absolute number of trials was greater than the NCCCP median throughout the evaluation period, even though the proportional change from Year 1 to Year 3 was substantially less (8% vs. 110%).



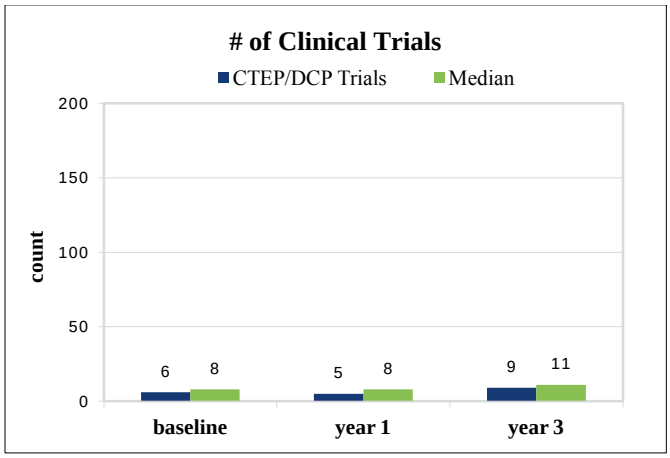
Accrual – Site-Reported Data

According to site-reported data, there were 6 patients enrolled in trials at Year 1, which increased to 35 in Year 3, representing a 483% increase in patient accrual. Participation in trials by racial and ethnic minorities increased from 1 in Year 1 to 10 in Year 3, representing a 900% increase. Rural participants numbered 4 in Year 1 and 14 in Year 3. The site reported no patients over 65 in Year 1 and 13 patients in Year 3. There were 6 reported "Other Research Studies" in Year 3, and the number of patients enrolled in those studies rose from 0 in Year 1 to 104 in Year 3.



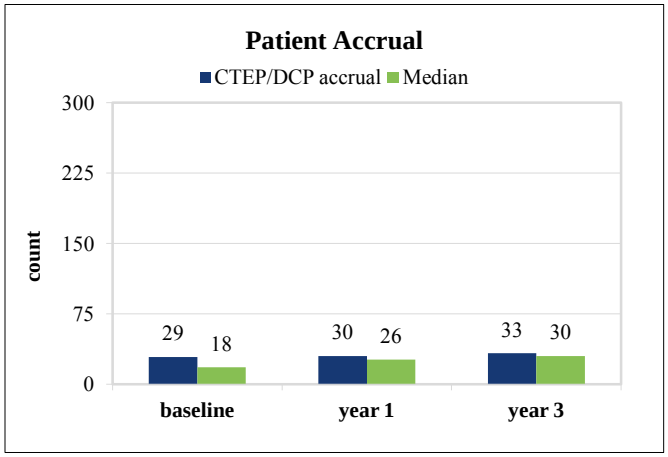
Trials Portfolio – CTEP Data

There were 6 CTEP/DCP trials underway at baseline, 5 in Year 1 and 9 in Year 3, reflecting a 50% increase over baseline by Year 3.



Accrual – CTEP Data

A total of 29 patients were enrolled at baseline, 30 in Year 1 and 33 in Year 3. This represents a 14% increase over baseline. The ratio of patients per trial was 4.83 at baseline, 6.00 in Year 1 and 3.67 in Year 3, which represents a 24% decrease from baseline. Participation in trials by racial and ethnic minorities decreased from 10 at baseline to 7 in Year 3. There were 12 patients aged 65 and over enrolled in CTEP/DCP studies at baseline and 13 patients in Year 3.



Comparison between Site-Reported and CTEP Data

In general, the trends observed in changes in number of clinical trials and accrual were similar using site-reported and CTEP data sources. Site-reported data reflected the accrual volume to the Moffitt biospecimens initiative in Year 3.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Hospital had a physician director (0.6 FTE) who reported to the Chief Executive Officer. The Hospital's leadership was part of the NCCCP structure. An outreach coordinator was in place at baseline as was an administrative director. According to site-reported data, at the final evaluation the physician director's role was revised to 0.12 FTE while adding the responsibility as the principle investigator, and a program manager was added who was a RN. A new research director that was a physician and a member of cancer center leadership was added by the end of the NCCCP evaluation period. In discussions with the RTI evaluation team, it was clarified that the site had a cancer center director that was a physician at the beginning of the NCCCP, but that this person left the role soon after the NCCCP project began. A non-medical executive director was responsible for administering the site until a new director was identified.

The overall FTE of the Center increased from 7.75 to 14. The number of physicians increased from 0.5 at baseline to 4 at the final evaluation. Other increases in staffing included one additional CRA, a full FTE pharmacist, and a social worker. At baseline, all 2 of 3 eligible physicians were enrolling patients. The final records show that 9 of 12 eligible physicians were enrolling patients.

At baseline and at the final evaluation, the Hospital had an IRB that met monthly. The Hospital did not provide IT support at baseline, but was providing this support at the final evaluation. This site was participating in CTSU trials at baseline and the final evaluation.

Comment:

Site #1 is a NCCCP Lead site without a CCOP affiliation that started participating in the Moffitt initiative by Year 3. This is an organization that underwent substantial leadership change over the 3-year evaluation period, and had a period of substantial distress at the top of the organizational hierarchy. Consistently, clinical trials activity lagged until Year 3 when increasing number of trials, accrual and participation in the biospecimen program is witnessed. Likely this site has residual clinical trials capacity that is cannot be tapped until after the interim period of organizational distress and realignment is overcome, which is therefore unlikely to be realized until after this NCCCP evaluation period is complete.

Site 2

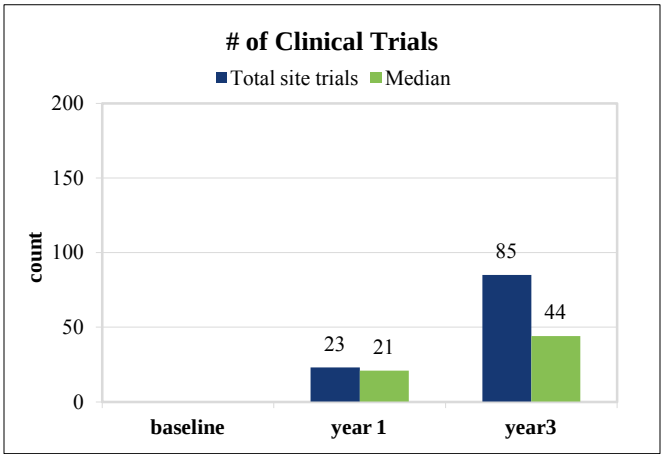
NCCCP Designation and External Relationships

This hospital is a Lead NCCCP site, and also designated as a Performance CCOP site. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

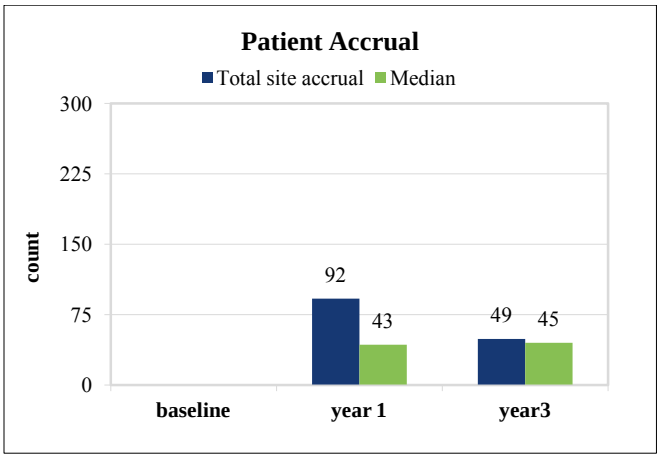
Trials Portfolio – Site-Reported Data

The site reported 23 trials underway in Year 1 which rose to 85 in Year 3, or a 270% increase. This increase in number of trials by Year 3 outpaced the median change across the NCCCP of 110%.



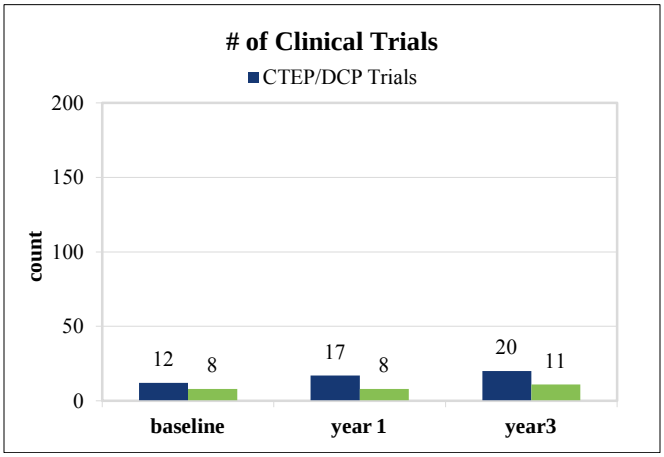
Accrual – Site-Reported Data

The site had 92 patients enrolled in trials at in Year 1 which declined to 49 in Year 3, or a 47% decline. This is in contrast to a relatively stable change in median accrual across the whole NCCCP (+5%) from Year 1 to Year 3. Participation in trials by racial and ethnic minorities increased from 4 in Year 1 to 8 in Year 3. There were no patients recorded over 65 in Year 1 and 23 in Year 3. There were no reported rural participants enrolled in Years 1 and 2; 8 enrolled rural participants were reported for Year 3. The number of "Other Research Studies" rose from 3 in Year 1 to 9 by Year 3, and "Other Accrual" increased from 9 in Year 1 to 36 in Year 3.



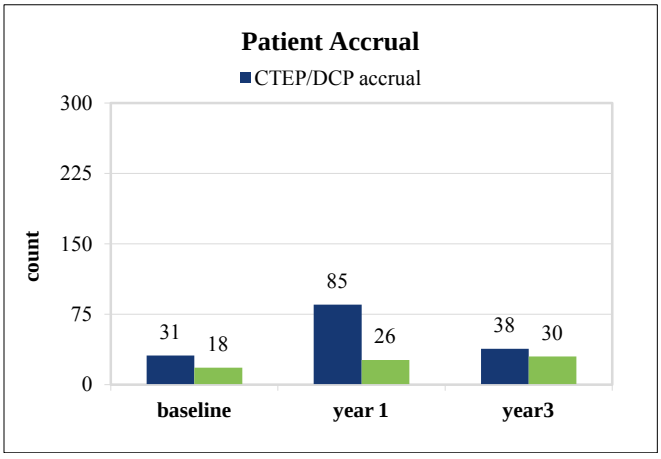
Trials Portfolio – CTEP Data

A total of 12 CTEP/DCP trials were underway at baseline, 17 in Year 1, and 20 in Year 3, or a 67% increase over baseline. The absolute number of trials and % change in trials for this site was greater than the median change (38% increase) for the whole NCCCP.



Accrual – CTEP Data

There were 31 enrolled patients at baseline, 85 in Year 1, and 38 in Year 3 in CTEP/DCP trials. This represents a 23% increase over baseline. The ratio of patients per trial was 2.58 at baseline, 5.00 in Year 1 and 1.90 in Year 3, which represents a 26% decrease from baseline. Participation in trials by racial and ethnic minorities doubled from 3 at baseline to 6 in Year 3. There were 11 patients aged 65 and over at baseline, which rose to 14 patients by Year 3.



Comparison between Site-Reported and CTEP Data

Both site-reported and CTEP data confirm an initial bump in accrual at the beginning of the NCCCP evaluation period, which dropped substantially by the end of the evaluation period. Both site-reported and CTEP data confirm an increasing clinical trials portfolio, above the median for the overall NCCCP.

Clinical Trials Infrastructure and Organizational Support

At baseline, the physician-director at this site held a 0.2 FTE appointment and reported to the Chief Operating Officer. The Center also had an administrative director. In Year 3, the only change to this organizational structure was raising the physician director from 0.2 to 0.5 FTE.

The overall number of FTE at the site contributing to clinical trials activity increased from 10.3 to 12.5 over the evaluation period. Two research nurse FTE and two nurse navigators FTE were added. An additional outreach coordinator as well as an additional trial coordinator was added. Throughout the evaluation period, 11 of the 12 eligible physicians were enrolling patients.

The site did not have an IRB at baseline, but had added one by the final evaluation. The IRB meets monthly. There was no IT support at baseline, but dedicated support was added over time including use of the CCOP's clinical trials management system.

Comment:

This NCCCP Lead and Performance CCOP site demonstrated variable activity during the NCCCP evaluation period. The reason for this is unclear. Progressively more trials were opened, including more CTEP-sponsored treatment trials, but accrual did not keep pace. This may be because changes in accrual lags behind the opening of trials, and the increased number of trials available in Year 3 will lead to future increases in patient participation (not represented here); however, it is likely too early to tell and, for now, explanations are lacking.

Site 3

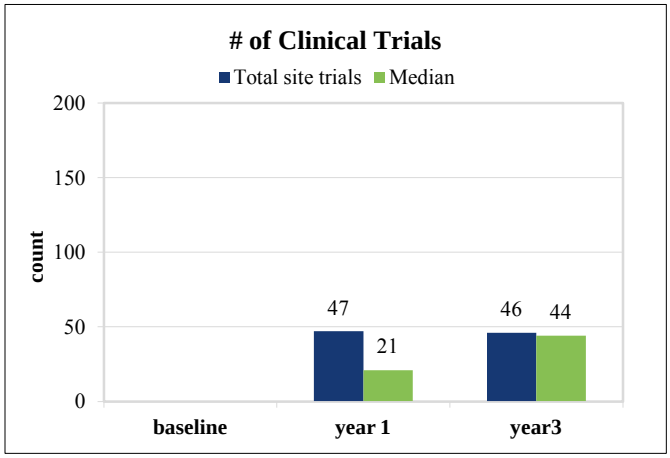
NCCCP Designation and External Relationships

This hospital is designated as a Lead NCCCP site and a Performance site for the state's MB-CCOP (Minority-Based Community Cancer Oncology Program). The date when this site joined the CCOP program was not stated in the site's report. They became a part of the Moffitt Total Cancer Care Initiative during the 2nd year of the NCCCP pilot program.

Clinical Trials Activity

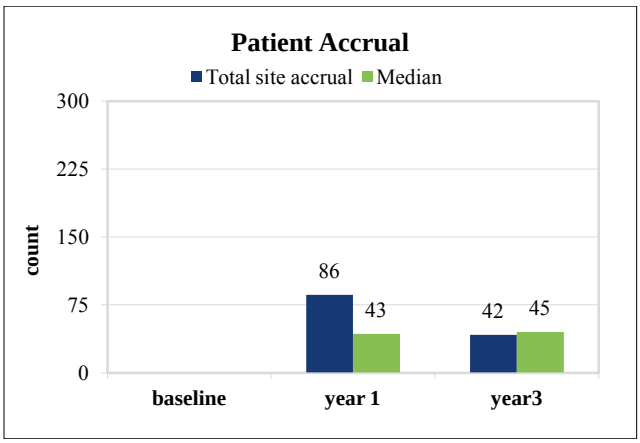
Trials Portfolio – Site-Reported Data

According to site-reported data, the total number of trials in Year 1 was 47 and the number of trials was 46 in Year 3, or a 2% overall decline. The absolute number of trials was above the median for the whole NCCCP, but the decrease from Year 1 was different from the median increase of 38%.



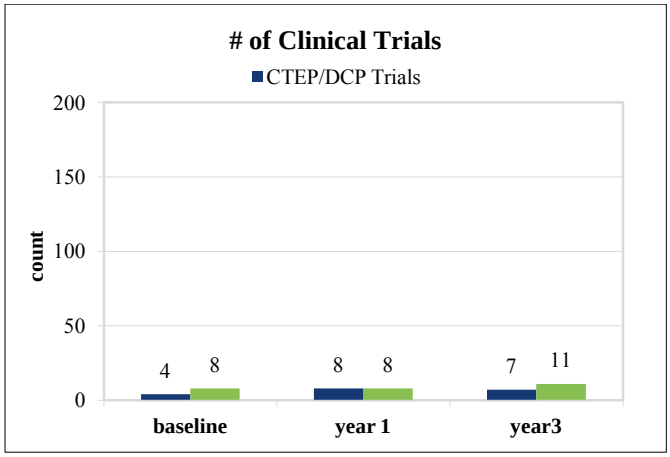
Accrual – Site-Reported Data

According to site-reported data, in the first year, 86 patients were enrolled in trials and this declined to 42 in Year 3, or a 51% decline. Participation in trials by racial and ethnic minorities increased from 7 in Year 1 to 14 in Year 3, representing a 100% increase. Rural participants numbered 0 in Year 1 and 24 in Year 3. There were no patients reported enrolled who were over 65 in Year 1 and 22 enrolled in Year 3. The number of "Other Research Studies" rose from 7 to 24 by Year 3, and "Other Accrual" increased from 32 in Year 1 to 519 in Year 3.



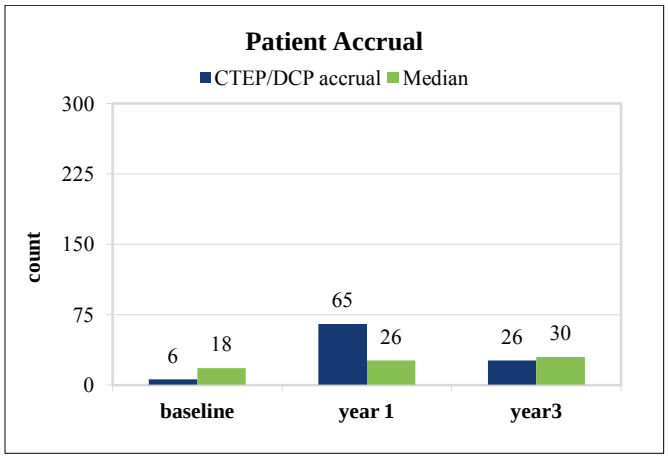
Trials Portfolio – CTEP Data

There were 4 CTEP/DCP trials underway at baseline, 8 in Year 1, and 7 in Year 3, reflecting a 75% increase over baseline by Year 3.



Accrual – CTEP Data

Six patients were enrolled at baseline, 65 in Year 1, and 26 in Year 3. This represents a 333% increase over baseline. The ratio of patients per trial was 1.50 at baseline, 8.13 in Year 1 and 3.71 in Year 3, which represents a 148% increase over baseline. Participation in trials by racial and ethnic minorities increased from 1 at baseline to 10 in Year 3, a 900% increase. There were no enrolled patients aged 65 and over at baseline, and 14 patients enrolled in Year 3.



Comparison between Site-Reported and CTEP Data

Comparison between site-reported and CTEP data can be misleading. Even when looking at treatment trials, sites are reporting all sponsors' treatment trials and CTEP/DCP trials are NCI-sponsored only. Nonetheless, both datasets demonstrate insubstantial change in the number of trials over time, and a decrease in patient accrual over time.

Clinical Trials Infrastructure and Organizational Support

The overall number of FTE at the site contributing to clinical trials activity doubled over the evaluation period from 5.25 to 10 FTE. The increase was made up by increasing the physician FTE from 0.25 to 1.0, reducing clinical research associates from 4.0 to 1.5, increasing research nurses from 1 to 5, and adding a nurse navigator, 0.5 FTE data manager and an outreach coordinator. Initially, 10 of 14 eligible physicians enrolled patients. The most recent report shows that seven of a possible 30 eligible physicians are enrolling patients.

The Medical Center did not have, and still does not have, an internal IRB, using instead a regional Board that meets monthly and is currently supported by weekly panel meetings. IT support for the Center was added during the course of the three-year period and participation in CTSU trials has ceased. There is no dedicated research pharmacy. Over the course of the three-year period, this Center invoiced only approximately 65% of the contracted amount, which may, in part, be reflected in the director assuming multiple management roles.

In year 2, a new CEO was appointed and took a keen interest in the program and was a frequent participant in meetings. The new leadership reorganized the infrastructure in preparation for greater participation in the NCCCP program. Early evidence of this restructuring is demonstrated in some of the Year 3 data. In many ways it is appropriate to view this site's Year 3 data as their true Year 1, and start the evaluation from there. Based on the reorganization, focusing on Year 3 might be too early to see real changes at this site.

Comment:

Overall, Site #3 demonstrated substantial reorganization of their clinical trials program, with growth in staff and physicians recruiting patients to trials; the timing of this suggests that the CEO's role was instrumental. Despite a drop in overall accrual to trials, there were increases in all three categories of underserved populations, which, considering its designation as a performance MB-CCOP, would be expected and welcomed. The large increase in "Other Accrual" can be attributed to participation in the Moffitt biospecimen collection that began in Year 2, and may have diverted resources and efforts from treatment clinical trials, resulting in a decrease in total trial number and patient accrual. The reorganization that took place in Year 2 (and likely with carryover effect into Year 3) may have had a delayed impact on clinical trials activity, as the decrement in accrual and trials portfolio in Year 3 likely reflects organizational change in the prior 12-18 months. The impact of the new organizational alignment and investment in treatment trials that took place in Year 2 would take an additional 12-18 months to be reflected in accrual.

Site 4

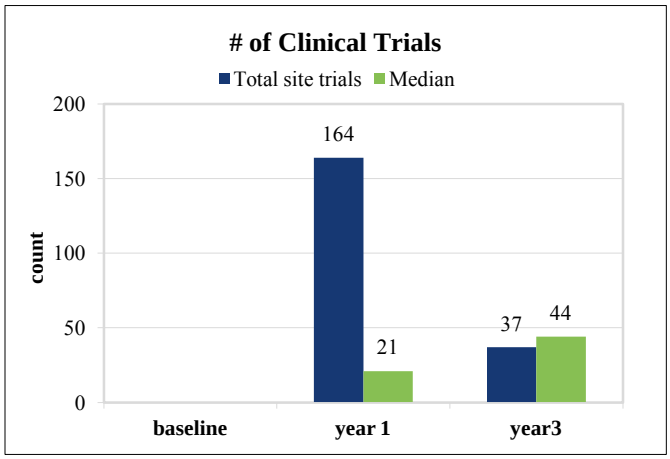
NCCCP Designation and External Relationships

This hospital is a Lead NCCCP site and designated as a Performance CCOP site. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

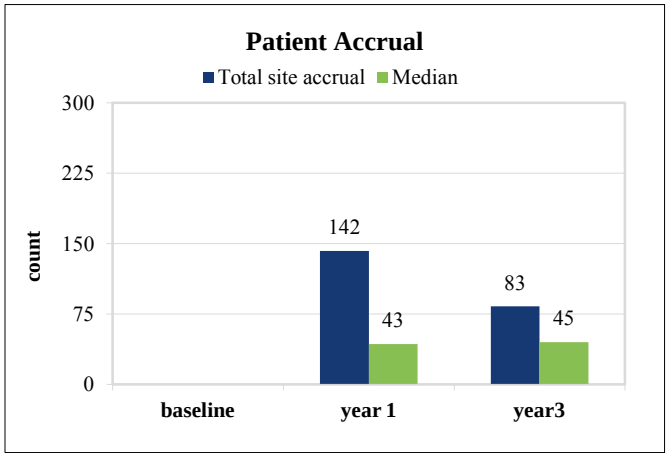
Trials Portfolio – Site-Reported Data

The total number of trials at baseline was unavailable, but 164 trials were underway in Year 1 that declined to 37 in Year 3, or a 77% decline.

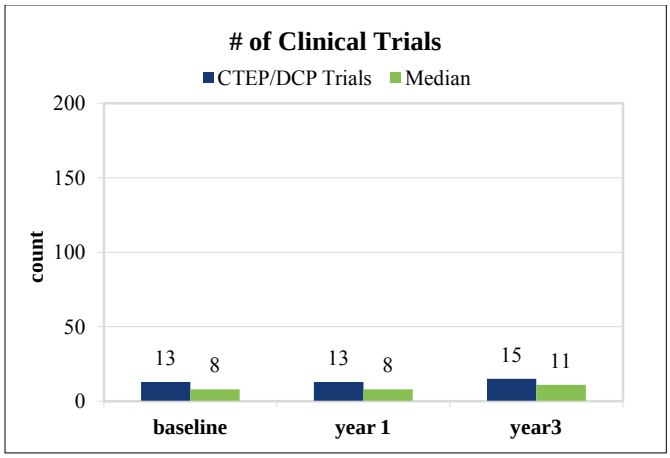


Accrual – Site-Reported Data

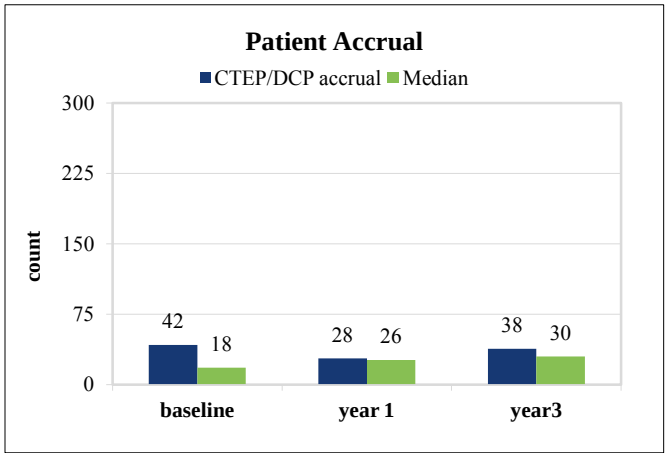
In the first year, the site reported 142 patients enrolled in trials and this declined to 83 in Year 3, or a 42% decline. Participation in trials by racial and ethnic minorities increased from 4 in Year 1 to 16 in Year 3. The number of rural participants numbered 27 in both Years 1 and 3. There were no patients over 65 in Year 1 and 26 in Year 3. The number of "Other Research Studies" doubled from 3 to 6 by Year 3, and "Other Accrual" increased from 12 in Year 1 to 15 in Year 3.



Trials Portfolio – CTEP Data
A total of 13 CTEP/DCP trials were underway at baseline, 13 in Year 1 and 15 in Year 3 or a 15% increase over baseline.



Accrual – CTEP Data
There were 42 enrolled patients at baseline, 28 in Year 1 and 38 in Year 3. This represents a 10% decline from baseline. The ratio of patients per trial was 3.23 at baseline, 2.15 in Year 1 and 2.53 in Year 3, which represents a 22% decrease from baseline. Participation in trials by racial and ethnic minorities decreased from 7 at baseline to 0 in Year 3. There were 19 enrolled patients aged 65 and over at baseline, and 21 patients enrolled in Year 3, an 11% increase.



Comparison between Site-Reported and CTEP Data
The site-reported data from Year 1 to Year 3 illustrates the relative decrease in the total number of trials (-77%). Despite having fewer trials active, the relative decrease in the total number of enrolled patients was smaller (-42%), making this site's increase in minority recruitment even more remarkable. The number of CTEP trials increased by 15%, but the number of enrolled patients decreased by 10%. Despite the decreasing number of trials, this site had more enrolled patients per treatment trial in Year 3 (2.24) than in Year 1 (0.87), nearly a 160% increase over Year 1. The corresponding ratios for Years 1 and 3 for CTEP/DCP projects were 2.15 and 2.53, a

4% increase. One reason behind the steep drop in the number of site reported trials and accrual is mentioned in the comment below.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Cancer Center's director/PI was a physician (0.15 FTE that increased to 0.20) who reported to the Chief Operating Officer of the hospital. The Center had an Executive Director and a Director of Research who were a RN and a MD respectively, but did not have an NCCCP Program Manager or an outreach worker devoted to cancer (both were added by the end of the pilot program). There were no other changes in the organizational structure.

The overall number of FTE at the site contributing to clinical trials activity increased from 13.25 to 17.7. The increase included 1 physician FTE, 2 research nurses, 2 data managers, and 0.25 Pharm Ds. At the beginning of the site's NCCCP participation, all seven physicians who were eligible did enroll patients. The most recent report shows that two new eligible physicians enrolled patients, thus all nine eligible physicians enroll patients.

The Hospital had an IRB at baseline that met twice a year, provided IT support for the Center, and participated in CTSU trials. There was no dedicated research pharmacy. The most recent report showed no other operational changes.

Comment:

During the three-year period of data collection, Site #4 was constructing a new cancer center that forced scaling back on research activities, especially during Year 3. Over 100 trials were closed or suspended, likely happening in Years 2 and 3 in anticipation of the construction. During this time, the site maintained or increased personnel and invoiced expenses, possibly in anticipation of being fully operational when construction is complete and being able to return to their pre-construction level of activity. Review of the site-reported vs. CTEP data suggests that their scaling back of clinical trials did not divert their activity away from trials most meaningful to the NCCCP program; the CTEP trials were relatively stable and the proportional accrual was stable across the evaluation period.

Site 5

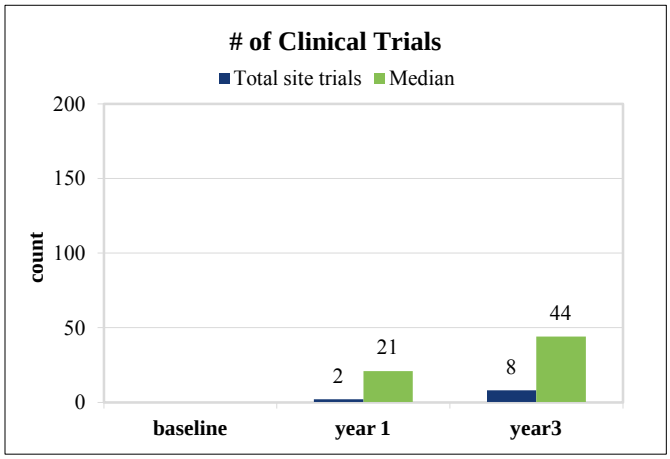
NCCCP Designation and External Relationships

This hospital is a Developmental NCCCP site that is designated as a Performance CCOP site. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

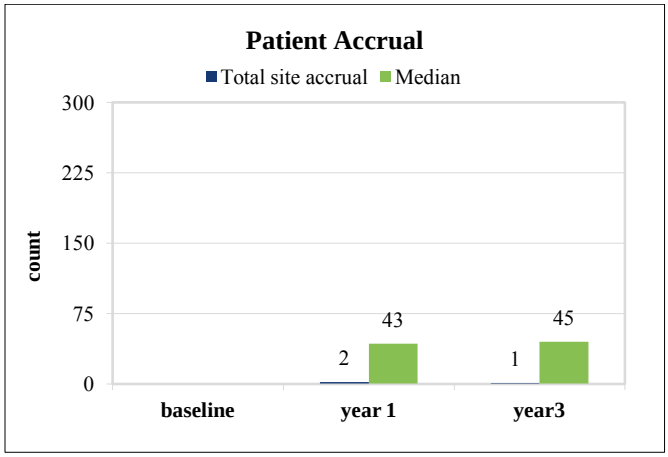
Trials Portfolio – Site-Reported Data

The total number of trials at baseline was unavailable, but 2 were underway in Year 1 that increased to 8 in Year 3, or a 300% increase. This was considerably below the medians for the overall NCCCP.



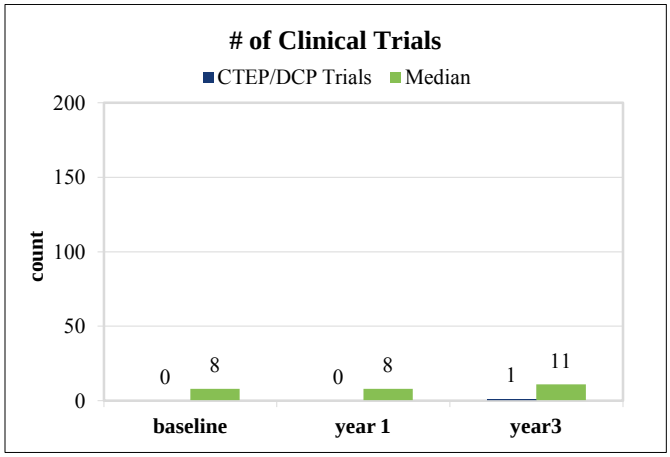
Accrual – Site-Reported Data

The site reported 2 patients enrolled in year 1 but dropped to 1 in year 3 or a 50% decrease. There were no racial/ethnic minority patients or patients over 65 participating in trials, as reported by the site. In Year 1 both enrolled "underserved" patients were from rural populations, but none were in the remaining years. There were no "Other Research Studies" underway in Year 1, but 5 were open by Year 3, with 40 patients enrolled that year.



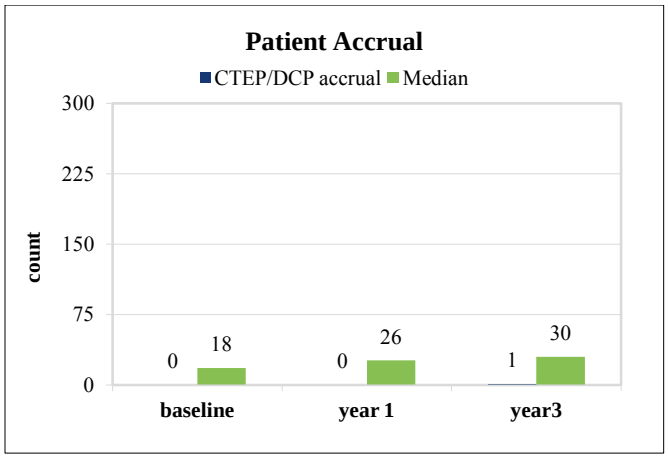
Trials Portfolio – CTEP Data

There were no CTEP/DCP trials underway at baseline and only 1 at Year 3.



Accrual – CTEP Data

There were 0 enrolled patients at baseline and only a single patient was enrolled in Year 3. The ratio of patients per trial could not be determined because there was zero accrual during this evaluation period. The single patient enrolled in Year 3 was not from an underserved population.



Comparison between Site-Reported and CTEP Data

Both site-reported and CTEP data confirm low clinical trials activity throughout the evaluation period.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that there was a single RN serving as the administrative director and a physician director (0.2 FTE) with no other infrastructure in place. There were no changes to this structure at the end of the evaluation period.

The overall FTE at this site contributing to clinical trials increased from 0 to 3.6. The increase included 1 physician FTE, 1 research nurse (0.8 FTE), a nurse navigator, and an outreach coordinator (0.8 FTE). Initially, 4 of 8 eligible physicians were enrolling patients. At the end of the evaluation period, 10 of 11 eligible physicians were enrolling patients.

The site has an IRB that meets twice a year.

Comment:

This Developmental site had low clinical trials activity throughout the NCCCP period, even though it was a Performance CCOP site. Both site-reported and CTEP data suggested activity below the mean, without real improvement over time. The reason isn't apparent, although the description of the administrative and organizational support suggests marginal leadership input. Notably, 4 of 8 physicians were enrolling patients at the beginning of the evaluation period and this increased to 10 of 11 by the end, but no related impact on clinical trials activity could be identified. This suggests that at least for this site, physician-level screening and enrollment for trials is not the only driving factor for accrual. The number of "Other Research Activities" and accrual increased from Year 1 to Year 3, suggesting that the site may have started with the relatively easier type of studies when developing their clinical research program.

Site 6

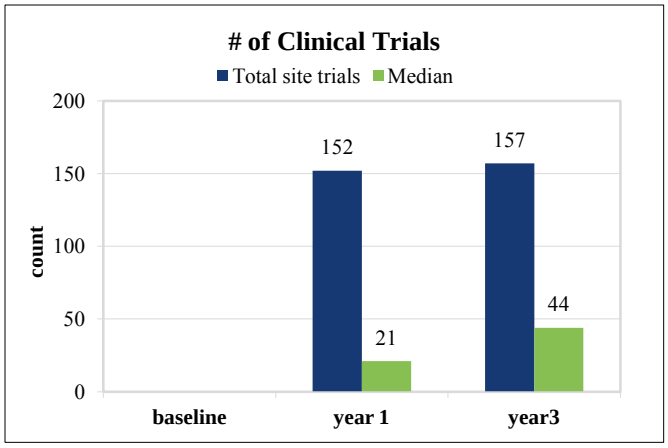
NCCCP Designation and External Relationships

This hospital is a NCCCP Lead site, as well as a Lead CCOP site. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

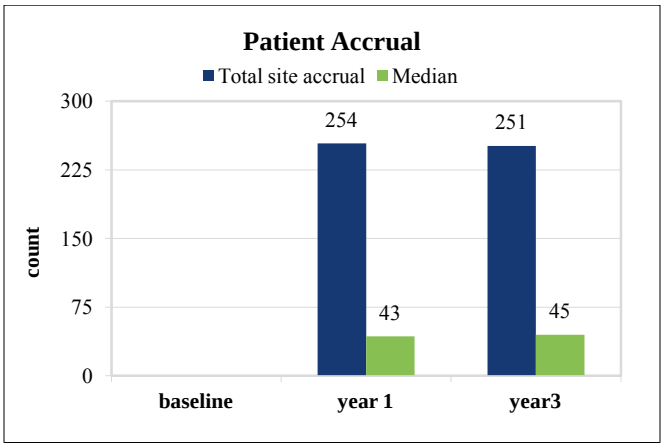
Trials Portfolio – Site-Reported Data

The total number of trials at baseline was unavailable, but 152 were underway in Year 1, rising to 157 by Year 3, reflecting a 3% increase over Year 1. The absolute number of trials open at this site during the entire evaluation period was considerably above the median number of trials open across all NCCCP sites.



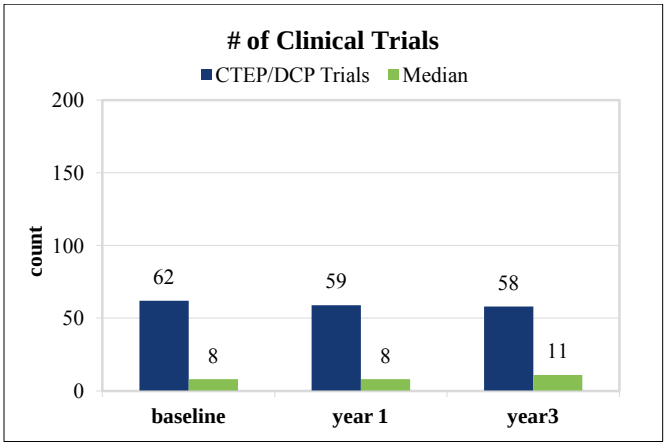
Accrual – Site-Reported Data

In the first year, 254 patients were enrolled in trials and this declined to 251 in Year 3, a 1% decrease from Year 1. Participation in trials by racial and ethnic minorities increased from 3 in Year 1 to 48 in Year 3. There were no rural patients enrolled during the evaluation period. There were no patients over age 65 in Year 1, 13 in Year 2, and 74 in Year 3. There were 22 "Other Research Studies" ongoing at Year 1, which increased to 30 in Year 3. However, "Other Accrual" decreased from 607 in Year 1 to 233 in Year 3.



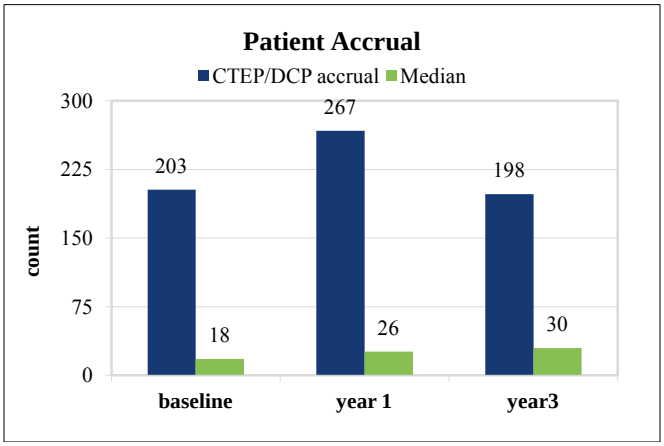
Trials Portfolio – CTEP Data

A total of 62 CTEP/DCP trials were underway at baseline, 59 in Year 1, and 58 in Year 3, or 6% below baseline. Total numbers of trials remained substantially above the NCCCP medians.



Accrual – CTEP Data

There were 203 enrolled patients at baseline, 267 in Year 1 and 198 in Year 3. This represents a 2% decline from baseline. The ratio of patients per trial was 3.27 at baseline, 4.53 in Year 1 and 3.41 in Year 3, which represents a 4% increase over baseline. Despite the slight decline in total accrual, the number of racial/ethnic minority patients increased from 34 at baseline to 45 in Year 3. The number of enrolled patients aged 65 and older rose from 76 at baseline to 87 in Year 3.



Comparison between Site-Reported and CTEP Data

Overall, the site-reported and CTEP data are very consistent; generally flat over the 3 years although much above the NCCCP medians in every category.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Cancer Center had a physician who was the fulltime Director/PI and reported to the Chief Executive Officer of the Hospital. The Center's structure also included a RN as NCCCP program manager, outreach workers, a Director of Research, and an executive director. This structure was in place at the end of the evaluation period.

The overall number of FTE at the site contributing to clinical trials activity increased from 68.5 to 73.55 over the evaluation period. The main increases included 2.5 physician FTE, 3.75 research nurse FTE, a Pharm D, and 5.25 outreach coordinator FTE. Initially, all 31 eligible physicians were enrolling patients. The most recent report shows that 31 of 32 eligible physicians enrolled patients.

The Hospital had an IRB at baseline that met 29 times a year, and now has 24 annual meetings. IT support, a dedicated pharmacy, and participation in CTSU trials were all in place at baseline and at the end of the evaluation period.

Comment:

Site #6 is both a Lead CCOP and a Lead NCCCP site. At first blush, their proportional increase in clinical trials numbers and accrual is close to flat. But all numbers are substantially higher than trans-program medians (>>300%). One curious finding is that site-reported and CTEP accrual dropped between Years 2 and 3, and are generally stable from baseline. This is a mature site, and they are potentially at maximal accrual and clinical trials workload, and the bouncing around between years may or may not be truly meaningful (i.e., this site likely needs to be evaluated within the context of averages across broad periods). Notably, although the total accrual did not substantially change, the recruitment of patients from underserved populations did increase over the evaluation period. The site has stable senior leadership and organizational maturity. Review of their data suggests that this site's real role is to be a mentoring site in the NCCCP, including as a clinical trials mentor to Developmental and other sites.

Site 7

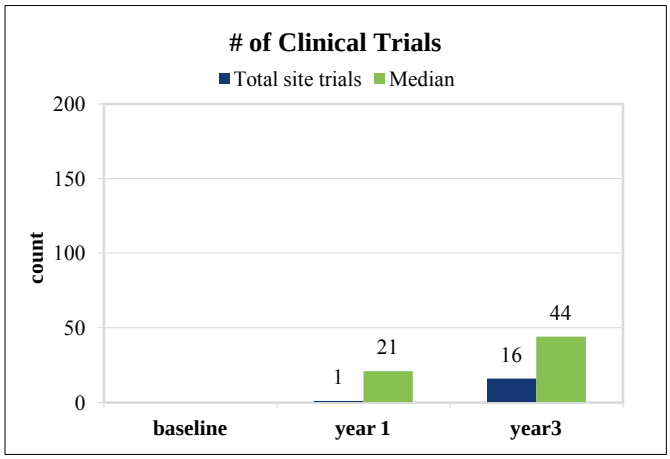
NCCCP Designation and External Relationships

This hospital is a Lead NCCCP site with no CCOP affiliation. The site does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

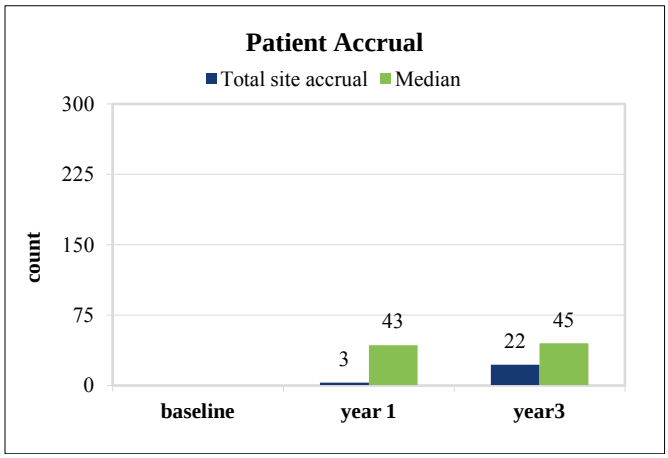
Trials Portfolio – Site-Reported Data

According to site reports, there was only one trial underway in Year 1 which increased to 16 trials in Year 3, a 1500% increase.



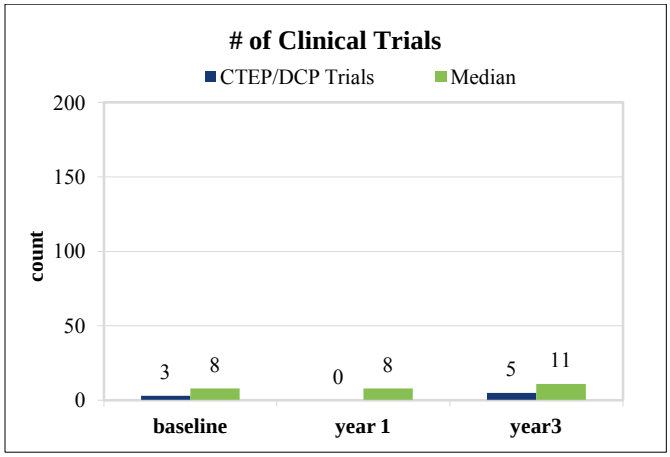
Accrual – Site-Reported Data

The site had 3 patients enrolled in the single trial in Year 1 and this rose to 22 patients in Year 3, a 633% increase. This site reported no recruitment from underserved populations in Year 1. It is unclear whether there was no specific enrollment, or if the site simply did not keep track of recruitment from underserved populations. There were two racial/ethnic minority patients enrolled in Year 2 and three in Year 3. Four rural patients were enrolled in Year 2 and none in Year 3. Three patients over 65 were enrolled in year 2 and four in Year 3. The number of "Other Research Studies" went from 2 to 4 from Year 1 to Year 3, and the "Other Accrual" decreased from 78 to 31 from Year 1 to Year 3.



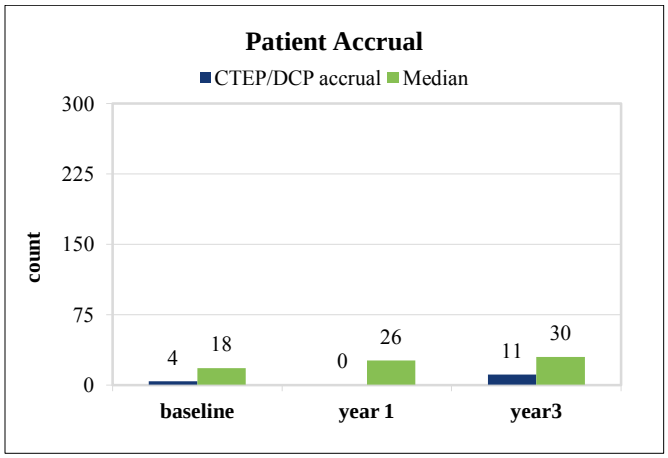
Trials Portfolio – CTEP Data

A total of 3 CTEP/DCP trials were underway at baseline, 0 in Year 1 and 5 in Year 3, or a 67% increase over baseline.



Accrual – CTEP Data

There were 4 enrolled patients at baseline, 0 in Year 1, and 11 in Year 3. This represents a 175% increase over baseline. The ratio of patients per trial was 1.33 at baseline, zero in Year 1 and 2.20 in Year 3, which represents a 65% increase over baseline. There were 3 racial/ethnic minority patients enrolled at baseline, which decreased to just 1 patient in Year 3. There was 1 patient aged 65 or above enrolled at baseline, which increased to 3 in Year 3.



Comparison between Site-Reported and CTEP Data

Both site-reported and CTEP data demonstrated consistent patterns of low accrual and numbers of trials below NCCCP programmatic medians, although both datasets showed increases in patient accrual and clinical trials over the three year evaluation period.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the site's director/PI was a physician (1.0 FTE) who reported to the Chief Operating Officer of the Medical Center. Also in place at baseline were a Director of Research and an administrative director. The only change to this structure was the reduction in FTE commitment by the Center's director/PI from 1.0 FTE to 0.4 FTE.

The overall number of FTE at the site contributing to clinical trials activity increased from 16 at baseline to 33.4 at the end of the evaluation period. The Center increased physician FTE (from 10.5 to 12), research nurses (from 1 to 2), Pharm D (from 0.5 to 1.0), data managers (from 0 to 2), outreach coordinators (from 0 to 6.8) and social workers (from 0 to 1). At baseline, seven of the 14 eligible physicians were enrolling patients. At the end of the evaluation period, 10 of 20 eligible physicians were enrolling patients.

Since baseline, the site has added an IRB that meets twice a year. Prior to this, they used an external IRB that met three times a year. IT support and a dedicated pharmacy have been added since baseline.

Comment:

Site #7 is a Lead NCCCP site that demonstrates few clinical trials and low accrual throughout the evaluation period, with overall numbers persistently lower than trans-program medians. They report a substantial number of individuals involved in clinical trials, however it appears likely that this site is counting personnel differently than other sites. At first blush, a Lead site might be expected to be a high performing clinical trials site since it is essentially a mentor site within the NCCCP program; but, this is a NCCCP Lead site, not a CCOP. Therefore, they don't necessarily have substantive prior clinical trials experience and might be more appropriately considered a "mentee" site in terms of clinical trials, rather than a mentor site.

Site 8

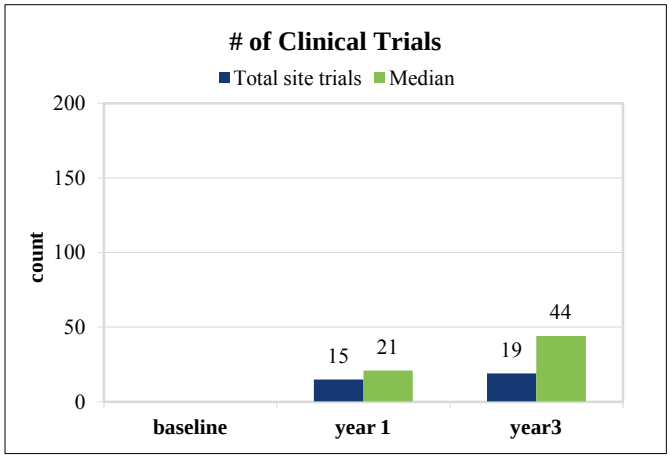
NCCCP Designation and External Relationships

Site #8 is a Developmental NCCCP site that has no CCOP affiliation. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

Trials Portfolio – Site-Reported Data

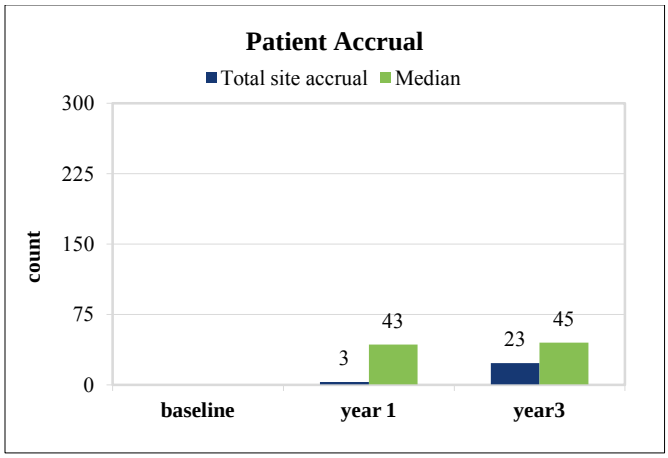
The site reported 15 trials underway in Year 1 and 19 in Year 3 or a 27% increase.



Accrual – Site-Reported Data

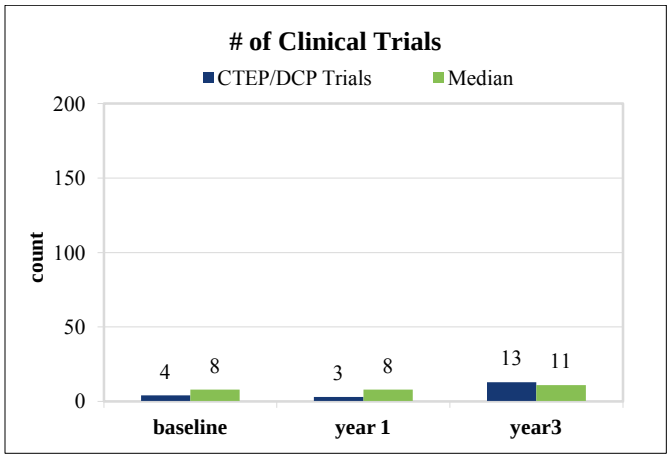
In the first year, 3 patients were enrolled in trials and this increased to 23 in Year 3, or a 667% increase. Participation in trials by racial and ethnic minorities did not really change, 1 in Year 1 to

0 in Year 3. There were no rural patients enrolled during any year of the evaluation period. The number of participants over age 65 numbered 4 in year 2 and 6 in year 3. There was one "Other Research Study" ongoing in Year 1 with one patient enrolled, and 2 studies underway in Year 3 with 14 patients enrolled that year.



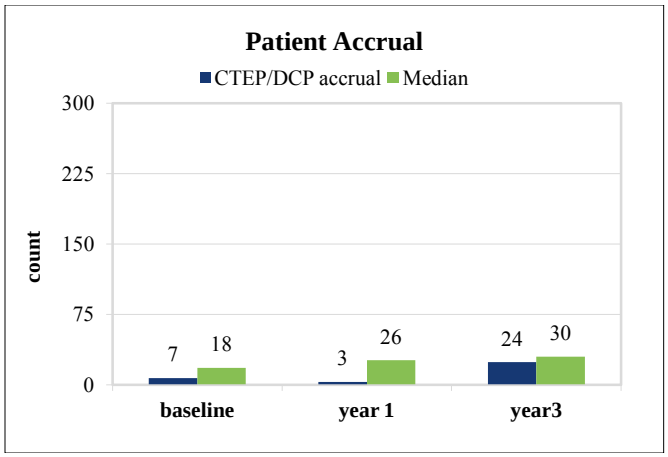
Trials Portfolio – CTEP Data

A total of 4 CTEP/DCP trials were underway at baseline, 3 in Year 1 and 13 in Year 3, or a 225% increase over baseline.



Accrual – CTEP Data

There were 7 enrolled patients at baseline, 3 in Year 1, and 24 in Year 3. This represents a 243% increase over baseline. The ratio of patients per trial was 1.75 at baseline, 1.00 in Year 1 and 1.83 in Year 3, which represents a 5% increase over baseline. There were 2 patients from the racial/ethnic minority population at baseline, which doubled to 4 patients in Year 3. At baseline, there were 4 patients age 65 or above enrolled in trials, which also doubled to 8 patients in Year 3.



Comparison between Site-Reported and CTEP Data

Over the evaluation period, this site's performance was generally below the median in all metrics. The picture of this site, however, is consistent between both site-reported and CTEP data. As the number of trials increased, the number of patients enrolled similarly increased.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Cancer Center's director was a physician (0.25 FTE). Other administrative support at baseline included a Program Coordinator and an administrative director; there were no changes at the final evaluation. According to discussions with colleagues at RTI, the physician Director was in an interim role, in private practice, and generally removed from the NCCCP site activities.

The overall number of FTE at the site focused on clinical trials increased from 5.7 to 10.45. The increase included 4 new physician FTE, and a doubling of 2 research nurse FTE. At baseline, 3 of 10 eligible physicians were enrolling patients. At the end of this evaluation period, 5 of 12 physicians were enrolling patients.

The Hospital does not have an IRB, instead participating with a regional Board that meets three times per year. Since baseline, the site has added IT support and a dedicated research pharmacy.

Comment:

The site was a Developmental site with a huge opportunity for improvement during the first 3 years of the NCCCP program, since at baseline there were only 4 CTEP treatment trials underway and only 7 patients enrolled. Indeed, progress was seen, in that the absolute number of trials and patients enrolled increased by >200% (CTEP data). However, there is clearly great room for improvement. Site #8 presents an interesting example of an infrastructure report that suggests substantial rearrangement and mobilization of the clinical research workforce "on the ground." Here we see more demonstrable positive impact on the number of clinical trials and enrollment by Year 3, but clearly substantial room for improvement. Is it too early to tell? This is possibly the case. Further, the site only had an "interim" physician Director who was reportedly quite removed from the site's NCCCP operations. As an interim role he/she may not have had the same level of authority or influence as someone permanent; the interim individual may not have

been able to generate the same level of enthusiasm and engagement to champion clinical trials activity and infrastructure development on the ground.

Site 9

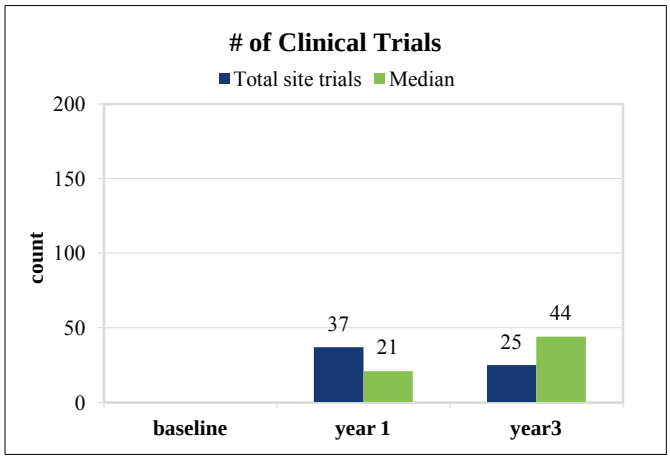
NCCCP Designation and External Relationships

This hospital is a Lead site in the NCCCP program and also a Lead CCOP site. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

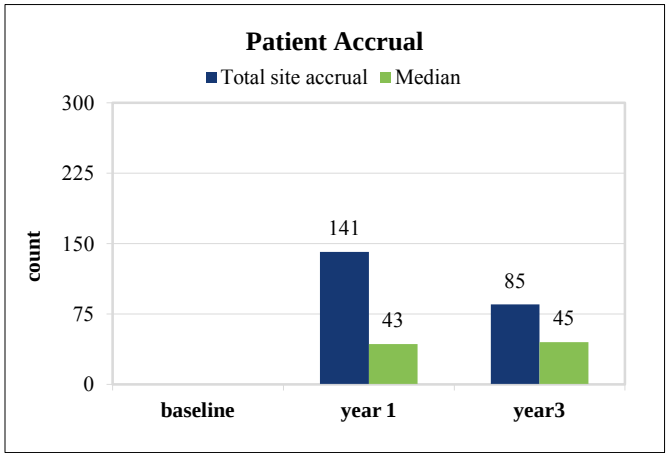
Trials Portfolio – Site-Reported Data

In the first year, the total number of trials underway was 37 which decreased to 25 in Year 3 or a 32% decline.



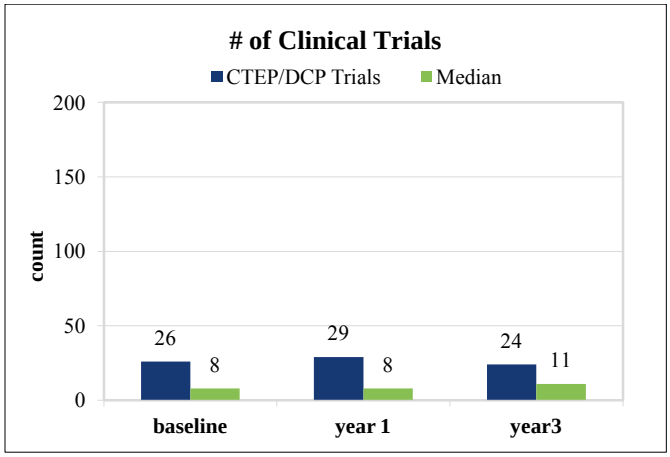
Accrual – Site-Reported Data

The site had 141 patients enrolled in Year 1 which declined to 85 in Year 3, or a 40% decrease. Participation in trials by racial and ethnic minorities increased from 0 in Year 1 to 5 in Year 3. There were no patients over age 65 in Year 1 and 37 in Year 3. The number of rural participants numbered 70 in Year 1 and 51 in Year 3. There were two "Other Research Studies" accruing just 1 patient in Year 1 and three studies in Year 3 enrolling 5 patients.



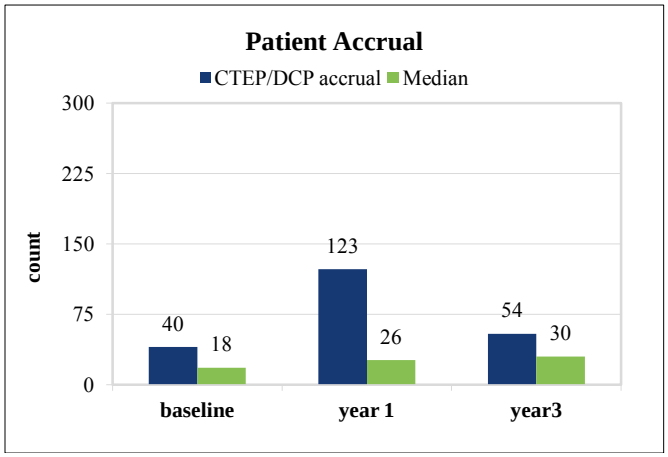
Trials Portfolio – CTEP Data

A total of 26 CTEP/DCP trials were underway at baseline, 29 in Year 1, and 24 in Year 3, an 8% decrease from baseline.



Accrual – CTEP Data

There were 40 enrolled patients at baseline, 123 in Year 1, and 54 in Year 3. This represents a 35% increase over baseline. The ratio of patients per trial was 1.54 at baseline, 4.24 in Year 1 and 2.25 in Year 3, which represents a 46% increase over baseline. Two patients at baseline were from racial/ethnic minority populations, and there were four such patients in Year 3. In addition, there were 17 patients aged 65 or older enrolled in trials at baseline, which rose to 30 patients in Year 3.



Comparison between Site-Reported and CTEP Data

Site-reported and CTEP data demonstrated consistent trends with absolute numbers above the program medians, but decreases in trials and patient accrual over the evaluation period.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Cancer Center's only administrative support was a program manager. The only change to this structure at the end of the evaluation period was the addition of an outreach worker specific to cancer.

The overall number of FTE at the site contributing to clinical trials activity increased from 31.3 to 43. Increases were seen for physicians (from 8 to 10), research nurses (from 11 to 18), nurse navigators (1 to 4), and data managers (0 to 1.5) while there were two fewer trial coordinators (from 9 to 7). At baseline, all 6 eligible physicians were enrolling patients. The final records show that all 7 eligible physicians were enrolling patients.

At baseline and at the final evaluation, the site had an IRB that met monthly. The hospital provided IT support, a dedicated pharmacy, and participated in CTSU trials. The site did not report a dedicated pharmacy at the final evaluation.

Comment:

Site #9 is both a Lead CCOP and a Lead NCCCP site. While accrual somewhat increased over baseline, overall clinical trials activities were generally stable between the beginning and end of the evaluation period. One curious finding is that the site-reported and CTEP accrual dropped between Years 2 and 3, and are generally stable from baseline. Individual trials of specific interest to the site may have opened and closed between Years 2 and 3, with recruitment increasing substantially and then waning; it isn't clear what happened. This is a mature site, and they are potentially at maximal accrual and clinical trials workload, and the bouncing around between years may or may not be truly meaningful (i.e., this site likely needs to be evaluated within the context of averages across broad periods). They have stable senior leadership and organizational maturity. Review of their data suggests that this site's real role is to be a mentoring site in the NCCCP, including as a clinical trials mentor to Developmental and other sites.

Site 10

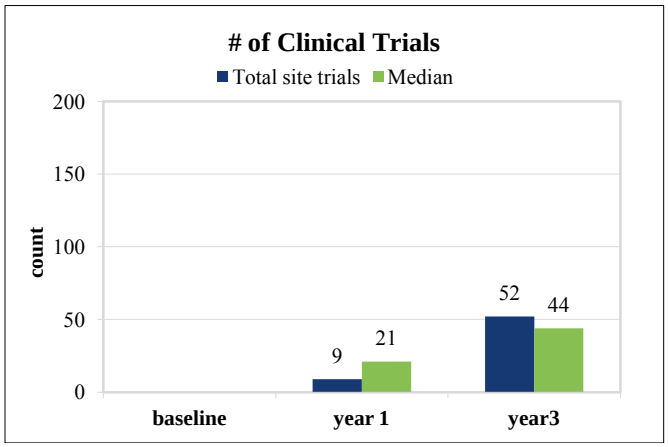
NCCCP Designation and External Relationships

This hospital is designated as a Lead NCCCP site with no CCOP affiliation. The hospital participates in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

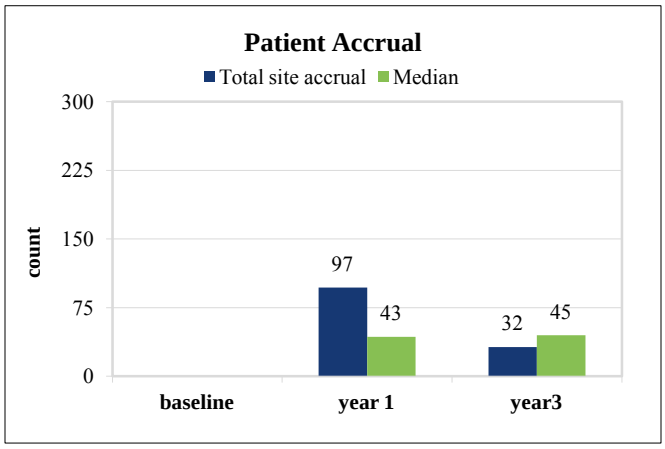
Trials Portfolio – Site-Reported Data

According to site-reported data, the total number of trials underway was 9 in Year 1 and 52 in Year 3, for a 478% increase.



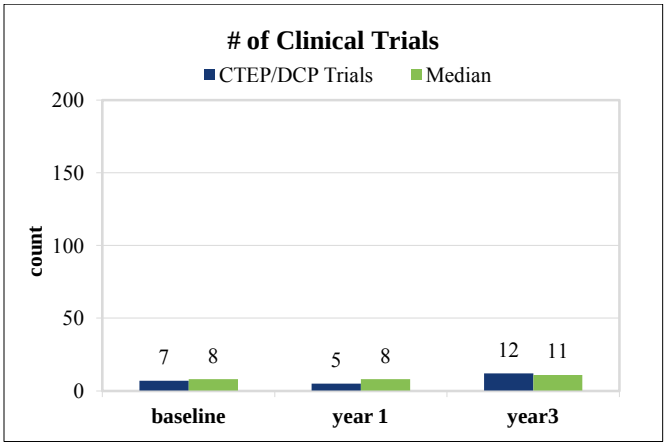
Accrual – Site-Reported Data

In the first year, 97 patients were enrolled in trials and this declined to 32 in Year 3, or a 67% decline. Participation in trials by racial and ethnic minorities decreased from 3 in Year 1 to 0 in Year 3. Rural participants numbered 0 in year 1 and a single patient in year 3. There were no patients over 65 in Year 1 and 4 in Year 3. There were 4 "Other Research Studies" ongoing in Year 1, which rose to 7 in Year 3; while "Other Accrual" increased considerably from 11 patients in Year 1 to 1542 patients enrolled in Year 3.



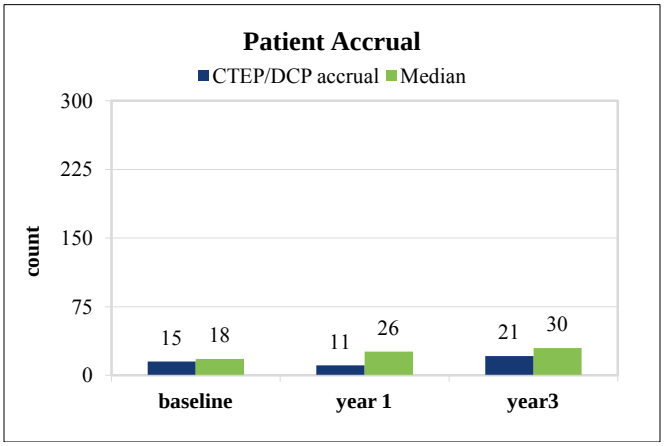
Trials Portfolio – CTEP Data

There were 7 CTEP/DCP trials underway at baseline, 5 in Year 1 and 12 in Year 3, reflecting a 71% increase over baseline by Year 3.



Accrual – CTEP Data

Fifteen patients were enrolled at baseline, 11 in Year 1, and 21 in Year 3. This represents a 40% increase over baseline. The ratio of patients per trial was 2.14 at baseline, 2.20 in Year 1 and 1.75 in Year 3, which represents an 18% decrease from baseline. There were 2 patients enrolled from the racial/ethnic minority population at baseline and none in Year 3. The number of patients aged 65 or above rose from 5 at baseline to 6 in Year 3.



Comparison between Site-Reported and CTEP Data

CTEP data reflects modest accrual lower than medians across the NCCCP, and increases in the trials portfolio at a rate consistent with the NCCCP. Site-reported data suggests that the trials portfolio was increasing at a more substantial rate than seen in the CTEP data, but that there was a dramatic shift in accrual by Year 3 over to the Moffitt Total Cancer Care Program.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the site had a physician/PI director (0.5 FTE) who reported to the Chief Operating Officer. The structure remained intact at the final evaluation.

The overall FTE of the Center increased from 46.5 to 52. While the number of physicians involved in clinical trials decreased from 33 to 27, there were 2 CRAs, a research nurse, and 2 outreach coordinators added to the staff. At baseline, all 32 of 59 eligible physicians were enrolling patients. The final records show that 62 of 83 eligible physicians were enrolling patients.

At baseline and at the final evaluation, the site had an IRB that met monthly. The Hospital provided IT support and participated in CTSU trials. The site did not report a dedicated pharmacy at baseline or the final evaluation.

Comment:

Site #10 is a Lead NCCCP site that participates in the Moffitt Total Cancer Care Program. According to CTEP data, in general, this site's increase in numbers of accruing trials and absolute participant enrollment over the evaluation period was consistent with medians across the NCCCP. However, review of site-reported data demonstrates that they had a dramatic increase in accrual activity related to the Moffitt program during the same time period. The overall interpretation is that the Moffitt participation is providing this site value in a way that encourages high volume accrual and participation; there was clearly capacity available at the site to contribute towards clinical trials accrual. It would be useful to learn from site physicians and leadership why participation in the Moffitt program appears to add more value than accrual into NCI-sponsored trials; this may reflect the differences in energy-expenditure on the ground to participate in a biospecimen program like the Moffitt Total Cancer Care Initiative versus a Phase 2 or Phase 3 NCI-sponsored trial.

Site 11

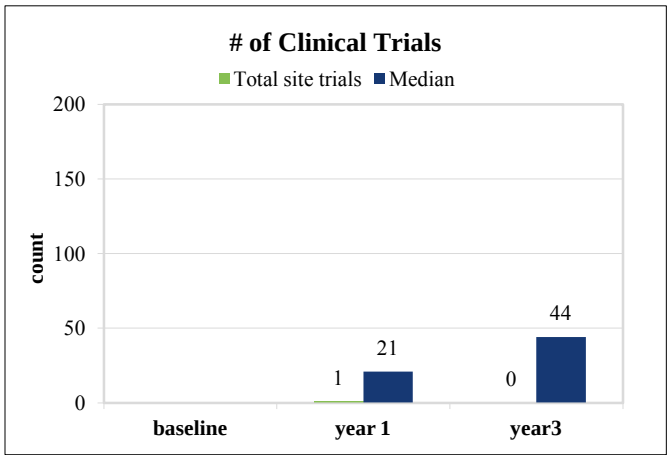
NCCCP Designation and External Relationships

Site #11 is a Developmental NCCCP site that has no CCOP affiliation. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

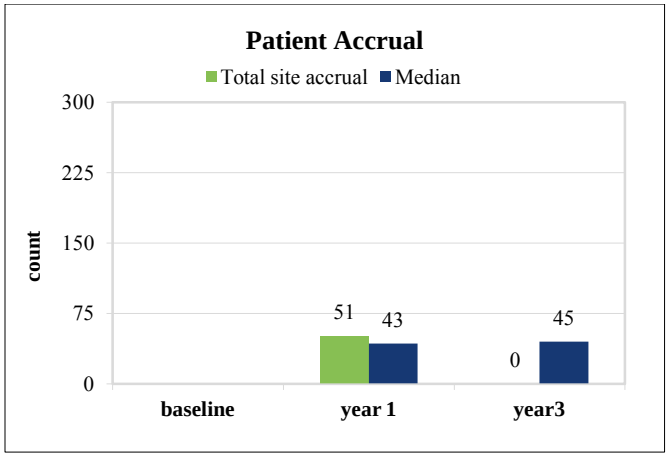
Trials Portfolio – Site-Reported Data

According to site-reported data, there was 1 trial ongoing in Year 1 and none in Year 3.



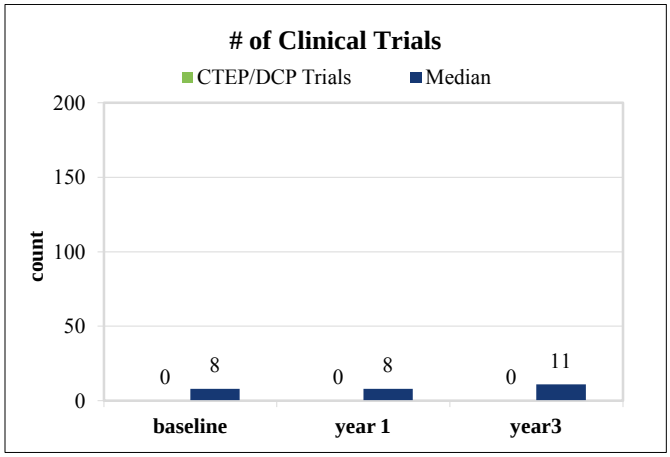
Accrual – Site-Reported Data

In the first year, 51 patients were enrolled in the single site-reported trial and this declined to 0 in Year 3 when no trials were open. Accrual of underserved populations was not reported. There were no "Other Research Studies" ongoing in Year 1, and 3 studies underway with 21 patients enrolled in Year 3.



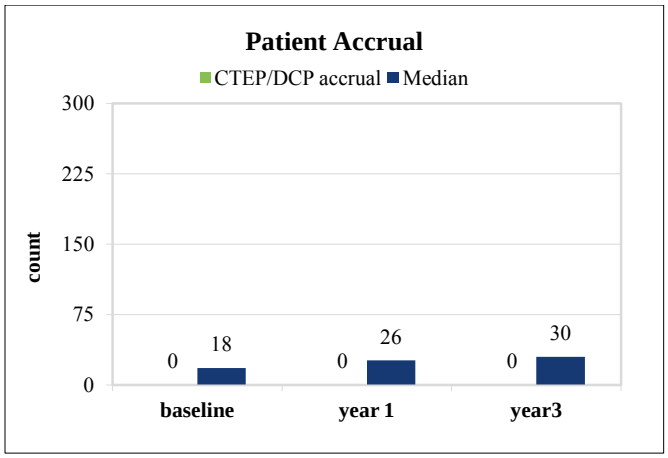
Trials Portfolio – CTEP Data

This site participated in no CTEP/DCP trials during this evaluation period



Accrual – CTEP Data

With no CTEP/DCP trials during this evaluation period, there was also no reported accrual and no minority accrual. The ratio of patients per trial could not be determined because there was zero accrual during this evaluation period.



Comparison between Site-Reported and CTEP Data

Over the evaluation period, this site's performance was below the median in all metrics. The site participated in a small number of trials with a limited number of patients and was involved in no CTEP activity during the evaluation period.

Clinical Trials Infrastructure and Organizational Support

At baseline, this site had only an NCCCP coordinator and a Director of Research. At the end of this evaluation period, the only personnel change was assigning 0.1FTE physician director.

The overall number of FTE at the site contributing to clinical trials activity increased over the 3-year period moving from 0.5FTE at baseline to 13 FTE in year 3. Much of the increase was in physicians (from 0 to 4), research nurses (from 0.2 to 5). At baseline, 5 of 6 eligible physicians

were enrolling patients and in year 3, 5 of the 12 eligible physicians were enrolling patients in trials.

The site had an IRB at baseline that met twice a year throughout the evaluation period and added IT support.

Comment:

Site #11 was a Developmental site with a huge opportunity for improvement through the NCCCP program, since there was no activity reported via CTEP at any time in the 3 years. This site presents an interesting example of an infrastructure report that suggests substantial rearrangement and mobilization of the clinical research workforce "on the ground" with unclear impact on clinical trials noted in the reports available to date. In fact, site-reported accrual dropped from 51 to 0 between Years 1 and 3. The true meaning of these changes in personnel in real terms is difficult to interpret, as at least some of the differences observed in the data between Years 1 and 3 are likely related to how the site is reporting the information rather than true changes in personnel and activity (e.g., the increase in physicians involved in trials is reported to go from 0 to 4, however the number of eligible physicians enrolling patients does not change, 5). This may be because they are still in the development phase, learning how to organize themselves to be successful, and how to report on their site. The noted changes do, however, suggest that further monitoring of the site for impact of these changes is warranted; it is likely too early to identify meaningful related changes in number of trials and accrual. This site does not appear to be focusing on trials that merit CTEP treatment trial reporting, and mentorship of this Developmental site is unclear.

Site 12

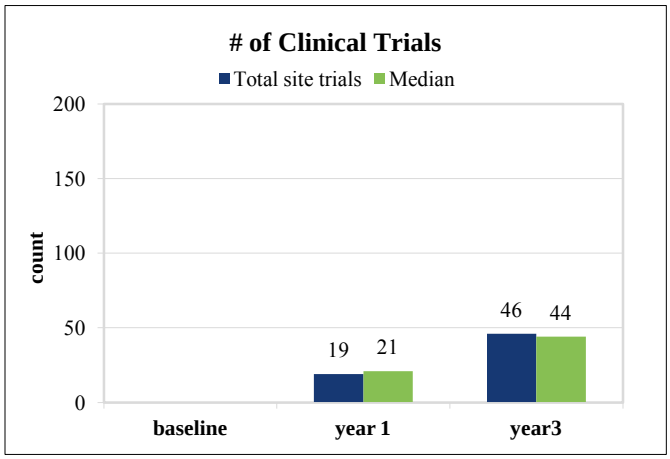
NCCCP Designation and External Relationships

This site is a Lead NCCCP site with no CCOP affiliation. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

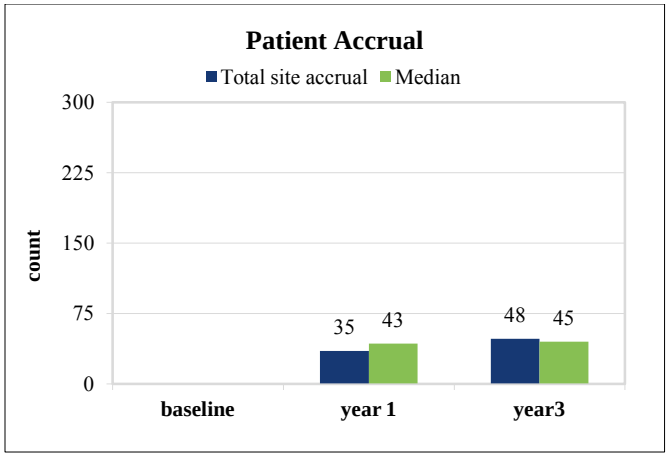
Trials Portfolio – Site-Reported Data

According to site-reported data, the total number of trials underway in Year 1 was 19 which rose to 46 in Year 3 for a 142% increase.



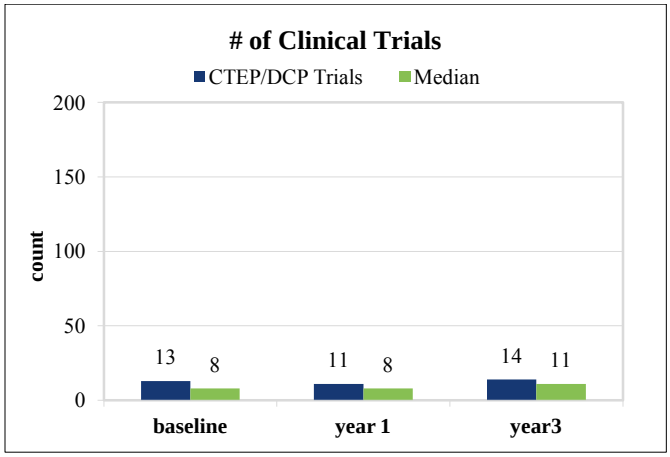
Accrual – Site-Reported Data

In the first year, 35 patients were enrolled in trials and this increased to 48 in Year 3, for a 37% change from Year 1. Participation in trials by racial and ethnic minorities increased from 6 in Year 1 to 16 in Year 3, representing a 167% increase. No rural participants were enrolled in any year of the evaluation period. There were no patients over 65 in Year 1 and 38 enrolled in trials in Year 3. There were 6 studies in the "Other Research Activity" category in Year 1, which rose to 16 in Year 3. "Other Accrual" however dropped from 267 patients in Year 1 to 169 patients in Year 3.



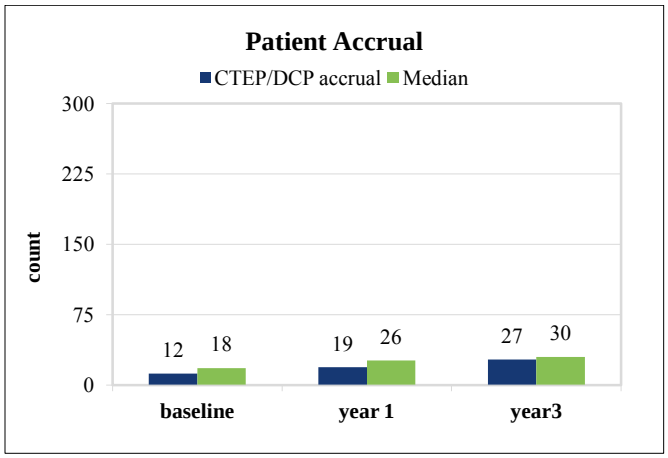
Trials Portfolio – CTEP Data

There were 13 CTEP/DCP trials underway at baseline, 11 in Year 1 and 14 in Year 3, reflecting an 8% increase over baseline by Year 3.



Accrual – CTEP Data

Twelve patients were enrolled at baseline, 19 in Year 1 and 27 in Year 3. This represents a 125% increase over baseline. The ratio of patients per trial was 0.92 at baseline, 1.73 in Year 1 and 1.93 in Year 3, which represents a 109% increase over baseline. There were 2 patients enrolled from the racial/ethnic minority population at baseline which rose to 7in Year 3. The number of patients aged 65 or above rose from 4 at baseline to 9 in Year 3.



Comparison between Site-Reported and CTEP Data

The pattern of change noted in site-reported and CTEP data are consistent, each reflecting increases in the number of clinical trials and accrual at the site consistent with medians.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Hospital had a physician director (0.8 FTE) who reported to the Chief Operating Officer and had in place an RN as its program manager. In addition, there was an RN as administrative director as well as an outreach coordinator. At the final evaluation the physician director's role was increased to a full 1.0 FTE. The remaining structure remained intact at the final evaluation.

The overall FTE of the Center changed little from 26.4 to 26 FTE. Changes to staffing FTEs included CRAs (+1), research nurses (-2.9), pharmacist (+1), Pharm D (-2), nurse navigators (+2), data managers (+2), and social workers (-0.5). At baseline, 5 of 25 eligible physicians were enrolling patients. The final records show that 21 of 57 eligible physicians were enrolling patients.

At baseline and at the final evaluation, the site had an IRB that met monthly. The Hospital provided IT support and was participating in CTSU trials at baseline and the final evaluation.

Comment:

Site #12 was a NCCCP Lead site with no CCOP affiliation. Increases in their numbers of trials and patient accrual were in step with the NCCCP medians as a whole, confirmed by both site-reported and CTEP data. The most remarkable finding for this site was their increase in site-reported accrual of potentially disadvantaged populations. Participation in trials by racial and ethnic minorities increased 167%, and in Year 1 there were no patients over 65 enrolled but 38 in Year 3. The reasons for this are unclear, but it is certainly much higher than other NCCCP sites. Interestingly they report a large clinical research enterprise with many enrolling physicians, but the size of the enterprise itself didn't increase substantially over the period (while the number of enrolling physicians did increase). It would be useful to conduct a specific evaluation at this site to understand characteristics contributing to their substantial success in recruiting underserved populations.

Site 13

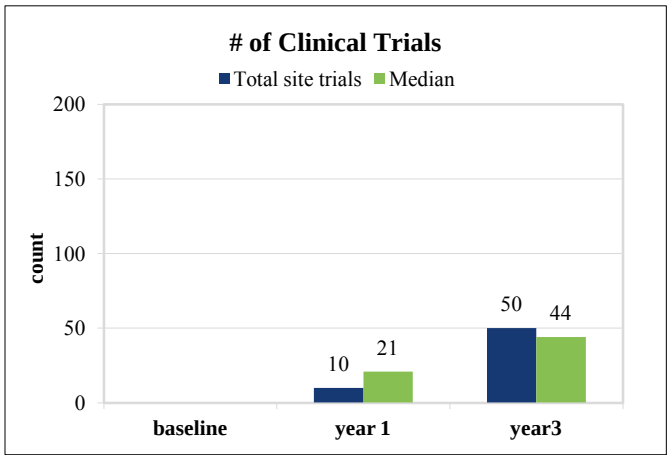
NCCCP Designation and External Relationships

This hospital site is a Developmental NCCCP site with no CCOP affiliation. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

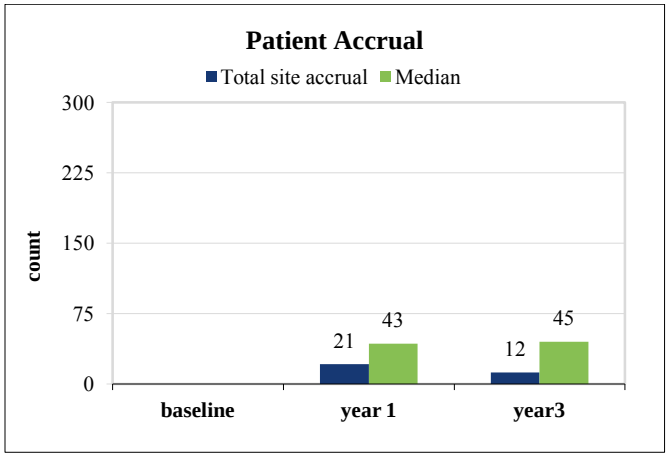
Trials Portfolio – Site-Reported Data

In the first year, there were 10 trials ongoing in Year 1 and 50 in Year 3, for a 400% increase.



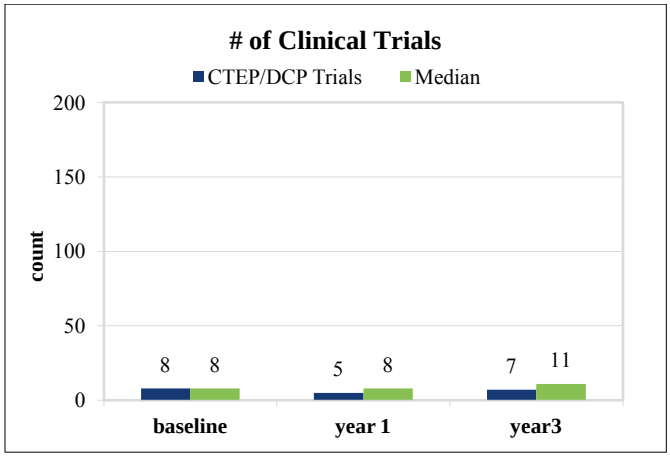
Accrual – Site-Reported Data

According to the site, 21 patients were enrolled in trials in Year 1 and this declined to 12 in Year 3, or a 43% decline. Participation in trials by racial and ethnic minorities decreased from 3 in Year 1 to 0 in Year 3. There were no patients over 65 in Year 1 and 3 in Year 3. The number of rural participants numbered 14 in year 1 and 8 in year 3. In the "Other Research Activity" category, there were 3 trials and 8 patients enrolled in Year 1, and 12 trials with 2 patients enrolled in Year 3.



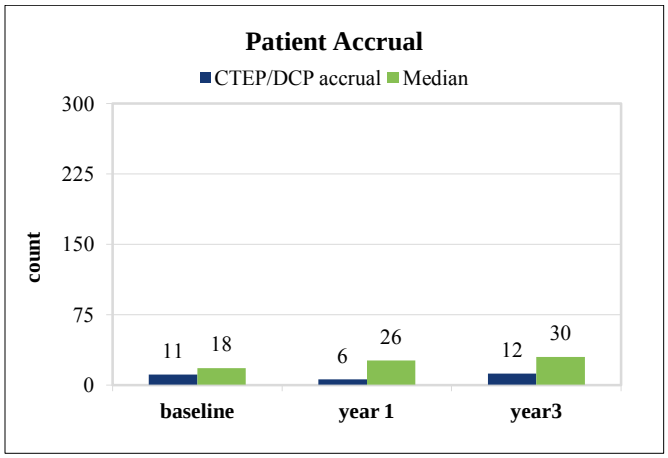
Trials Portfolio – CTEP Data

A total of 8 CTEP/DCP trials were underway at baseline, 5 in Year 1, and 7 in Year 3, or a 13% decrease from baseline.



Accrual – CTEP Data

There were 11 enrolled patients at baseline, 6 in Year 1, and 12 in Year 3. This represents a 9% increase from baseline. The ratio of patients per trial was 1.38 at baseline, 1.20 in Year 1 and 1.71 in Year 3, which represents a 25% increase over baseline. There were no racial/ethnic minority patients enrolled at baseline or in Year 3. The number of patients aged 65 or over was 10 at baseline and 8 in Year 3.



Comparison between Site-Reported and CTEP Data

This Developmental site showed some clinical trials activity at baseline, by both site-reported and CTEP data. However, overall the pattern was that of a decrease over the evaluation period. One interesting finding was the substantial increase in the number of site-reported clinical trials in Year 3; this was predominantly made up of an increase in NCI-sponsored trials, although similar increases in NCI-sponsored trials as reported by CTEP were not noted presumably because the trials were not accruing patients yet.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Cancer Center's director/PI was a physician (0% FTE that increased to 0.25). There were also a Director of Research and an RN Executive Director. This organizational structure remained consistent over the trial period.

The overall number of FTE at the site contributing to clinical trials activity increased from 3 to 6 over the evaluation period. All three eligible physicians were enrolling patients at baseline and the single physician added during the evaluation period also enrolled patients.

The site had an IRB at baseline that met twice a year, and there was IT support for the site. The most recent report showed no substantive operational changes.

Comment:

While the initial interpretation of the clinical trials performance of this Developmental site may be that of poor activity throughout the NCCCP period, the finding of a substantial increase in site-reported trials in Year 3 is interesting to consider. This may just be a site-reported data error. However, it might not be a data error, especially considering that the site has reported them as predominantly NCI-sponsored trials and CTEP data doesn't reflect clinical trials that aren't recruiting patients yet. This is a Developmental site and it may have taken the majority of the NCCCP period to get appropriately coordinated and learn from their Lead site mentors in order to increase clinical trials activity. We would expect that the first signal of increasing clinical trials activity is increasing portfolio, and this is the potential signal we are seeing in Year 3. It would be too early to see much impact on actual accrual.

Site 14

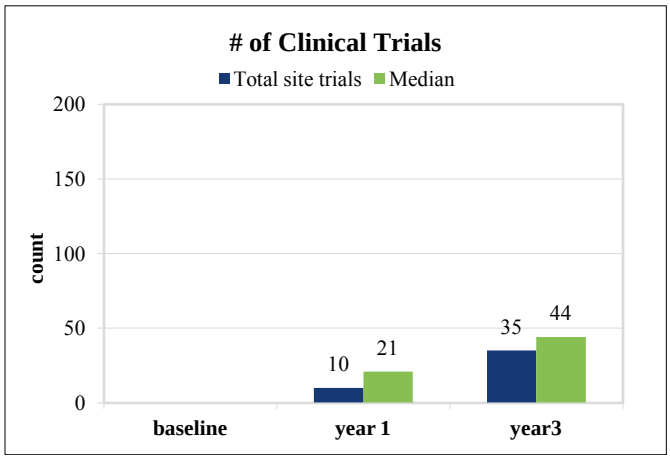
NCCCP Designation and External Relationships

This hospital is a Developmental NCCCP site with no CCOP affiliation. It does not participate in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

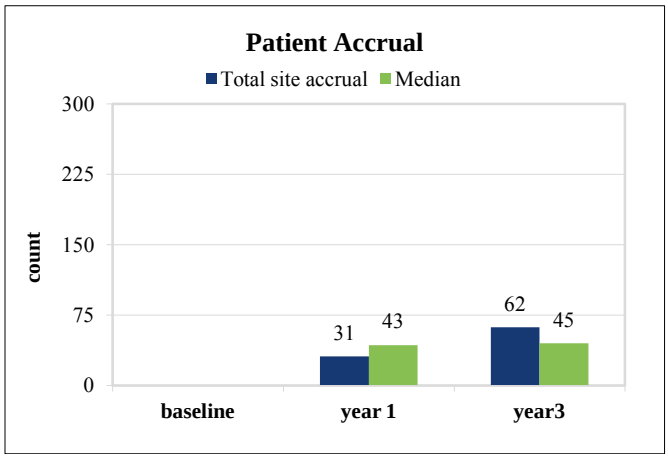
Trials Portfolio – Site-Reported Data

According to the site, there were 10 trials underway in Year 1 and 35 in Year 3, a 250% increase.



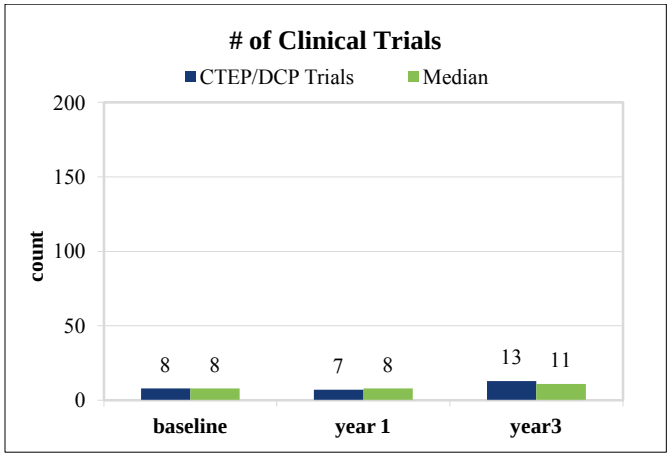
Accrual – Site-Reported Data

In the first year, 31 patients were enrolled in trials and this doubled to 62 by Year 3, a 100% increase. This site reported no underrepresented patients enrolled in Year 1. It is not known whether this was because the site did not track minority recruitment in Year 1, or whether it truly represents no patients enrolled from underrepresented populations. In Year 2, there was a single patient classified as a racial/ethnic minority and then none in Year 3. In Year 2 there were 27 patients enrolled who were over 65 years of age and this increased in Year 3 to 43 patients. The number of rural participants numbered 40 in both years 2 and 3. The number of "Other Research Studies" increased from 4 in Year 1 to 8 in Year 3, and "Other Accrual" increased from 27 in Year 1 to 80 in Year 3.



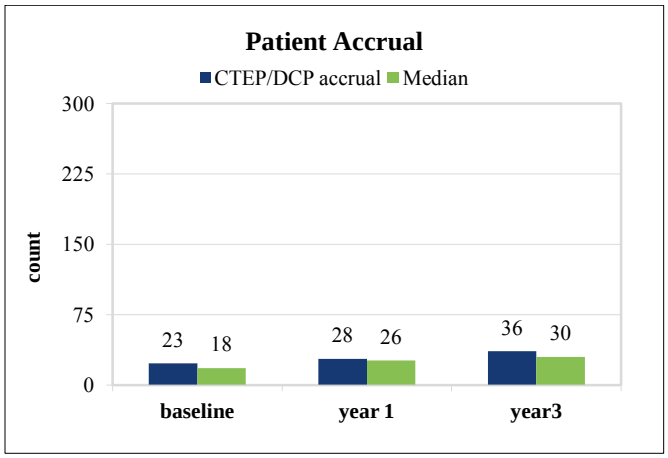
Trials Portfolio – CTEP Data

A total of 8 CTEP/DCP trials were underway at baseline, 7 in Year 1, and 13 in Year 3, a 63% increase over baseline.



Accrual – CTEP Data

There were 23 enrolled patients at baseline, 28 in Year 1 and 36 in Year 3. This represents a 57% increase over baseline. The ratio of patients per trial was 2.88 at baseline, 4.00 in Year 1 and 2.77 in Year 3, which represents a 4% decrease from baseline. The CTEP database showed no patients from racial/ethnic backgrounds were enrolled at baseline or in Year 3. There were 5 patients aged 65 or older at baseline, which rose to 23 in Year 3.



Comparison between Site-Reported and CTEP Data

Both site-reported and CTEP data supported increases in the clinical trials portfolio and accrual, which in general followed the pattern of median changes across the NCCCP program.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the site's director/PI was a full-time physician that by the end of the evaluation period had been reduced to 0.25 FTE allocated to the program. An administrative director supported the physician/PI director. Other than the change in the physician's designated load with the site there were no other changes to their organization.

The overall number of FTE at the site contributing to clinical trials activity increased from 8.9 to 12.0 FTE over the evaluation period. The increase was most evident in an added physician, two research nurses, two pharmacists, and minor reductions in load for a few support personnel (notably, this is more than 3.1 FTE, and the exact proportional distribution of the increase across these individuals is unknown). Initially, two of the three eligible physicians enrolled patients. The most recent report indicates that the addition of one physician showed that now three of the four eligible physicians were enrolling patients.

The site reports to an external IRB that met three times per year throughout the evaluation period. Neither IT support nor a dedicated research pharmacy was evident at baseline, but both were in place at the end of the evaluation period.

Comment:

Site #14 is a Developmental NCCCP site with no CCOP designation. Overall, this site demonstrates the types of changes envisioned for the NCCCP program. This site can be considered a "mentee" site. There are demonstrable and steady increases in portfolio and accrual across the evaluation time period, in step with median increases across the whole program (where the medians include Lead and Developmental sites). Facilitators of these changes are not clear. The site had stable leadership and demonstrated stepwise increase in clinical trials infrastructure on-the-ground, likely enablers. They reported the addition of pharmacy and IT support, but the exact impact of these tools is unclear (and the IT tools were likely rudimentary, as "Excel spreadsheets" was considered "the addition of IT").

Site 15

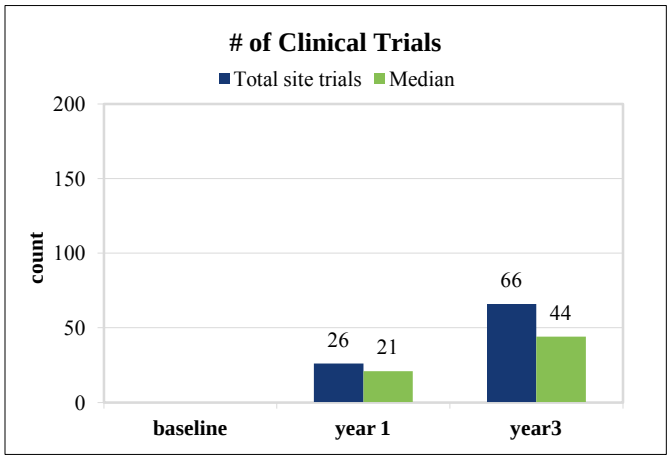
NCCCP Designation and External Relationships

Site #15 is a Lead NCCCP site with no CCOP affiliation. It participates in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

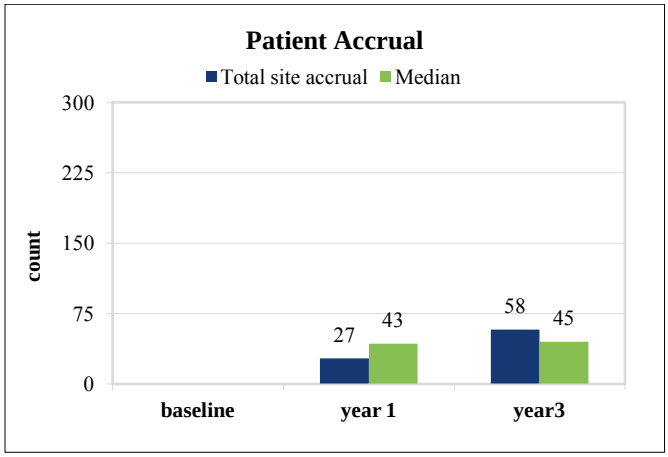
Trials Portfolio – Site-Reported Data

The total number of trials in Year 1 was 26 and in Year 3 there were 66 trials underway, a 154% increase in number of trials.



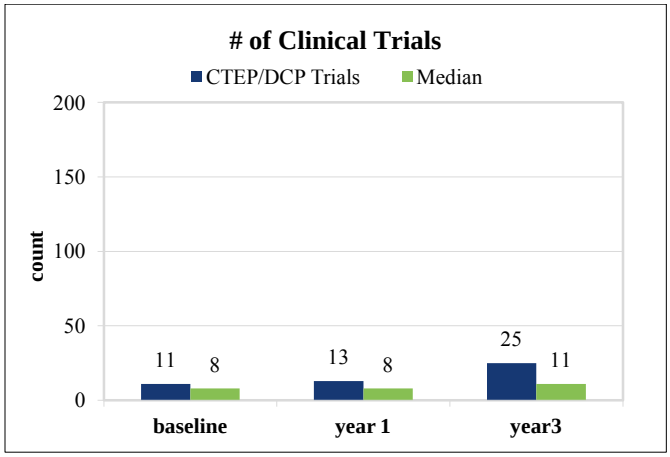
Accrual – Site-Reported Data

This site had 27 patients enrolled in trials in Year 1 and this increased to 58 in Year 3, or a 115% increase. Participation in trials by racial and ethnic minorities increased from 0 in Year 1 to 4 in Year 3. There were 7 patients over 65 in Year 1 and 7 in Year 3. The number of rural participants numbered 2 in Year 1 and 6 in Year 3. There were 4 "Other Research Studies" ongoing in Year 1, which rose to 6 in Year 3. Notably, the "Other Accrual" increased from 2 in Year 1 to 888 in Year 3, likely due to the impact of the Moffitt Total Cancer Care Initiative.



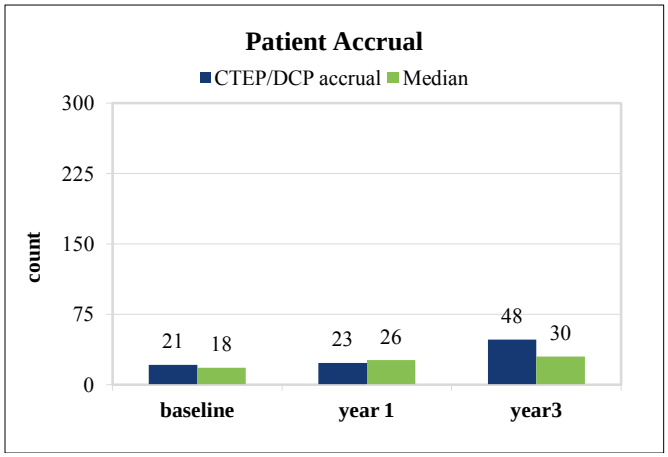
Trials Portfolio – CTEP Data

A total of 11 CTEP/DCP trials were underway at baseline, 13 in Year 1, and 25 in Year 3, or a 127% increase over baseline.



Accrual – CTEP Data

There were 21 enrolled patients at baseline, 23 in Year 1, and 48 in Year 3. This represents a 129% increase from baseline. The ratio of patients per trial was 1.91 at baseline, 1.77 in Year 1 and 1.92 in Year 3, which represents a 1% increase over baseline. There was one patient from the racial/ethnic minority population enrolled at baseline, which increased to 10 patients in Year 3. In the age 65 and over category, there were 2 patients at baseline, which increased to 6 patients in Year 3.



Comparison between Site-Reported and CTEP Data

Both the site-reported and CTEP data suggest general trends of the overall numbers of trials and accrual to be somewhat higher than the median across all sites. This Lead site had very high increases in site-reported "Other Research Accrual" in Year 3, that likely represents the impact of participant accrual into the Moffitt Total Cancer Care Initiative.

Clinical Trials Infrastructure and Organizational Support

Baseline records indicate that the Cancer Center's director/PI was a physician (0.25 FTE that increased to 0.50) who reported to the Chief Operating Officer of the hospital. The Center had an

Administrative Director, and a program coordinator. There were no other changes in the organizational structure over the evaluation period.

The overall FTE contributing to clinical trials at the site fell from 26.3 to 19 over the evaluation period, mostly from the loss of 2 trial coordinators and 7 research nurses. At baseline, 3 of 25 eligible physicians were enrolling patients. The final count was 9 of 28 eligible physicians were enrolling patients.

The site had an IRB at baseline that met three times a year. At baseline, there was a dedicated research pharmacy that was not in place in Year 3.

Comment:

As a Lead NCCCP site that was not a CCOP site, Site #15 had an overall clinical trials portfolio size and accrual to treatment trials that was slightly higher than the median across the NCCCP program and there was stepwise increases in portfolio and accrual over time (e.g., CTEP portfolio and accrual more than doubled). Overall, this site's most remarkable change during the program was its increase in other accrual (enrolling 888 patients in Year 3), without commensurate reduction in treatment trial accrual either by site-reported or CTEP data. The large increase can likely be attributed to participation in the Moffitt Total Cancer Care Initiative; the exact year that this began is uncertain, but it is likely in Year 1 or Year 2, as the impact is very evident by Year 3. Importantly, it doesn't appear that participation in the Moffitt program impaired Site #15's ability to participate in clinical trials activities valued highly by the NCI (as represented by CTEP activity). The other important observation for this site is that they increased the number of participating enrolling physicians from 3 to 9 over the evaluation period. In summary, this site's story suggests that of a mature site that still had untapped clinical trials capacity at baseline; the capacity was harnessed to contribute more activity to NCI-sponsored trials over the evaluation period but even more incredibly harnessed to contribute to the Moffitt biospecimen program.

Site 16

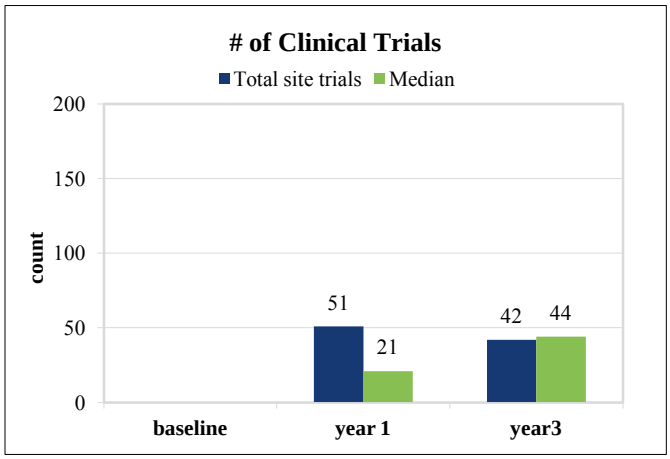
NCCCP Designation and External Relationships

Site #16 is designated a Lead NCCCP site and a Lead CCOP site that is not participating in the Moffitt Total Cancer Care Initiative.

Clinical Trials Activity

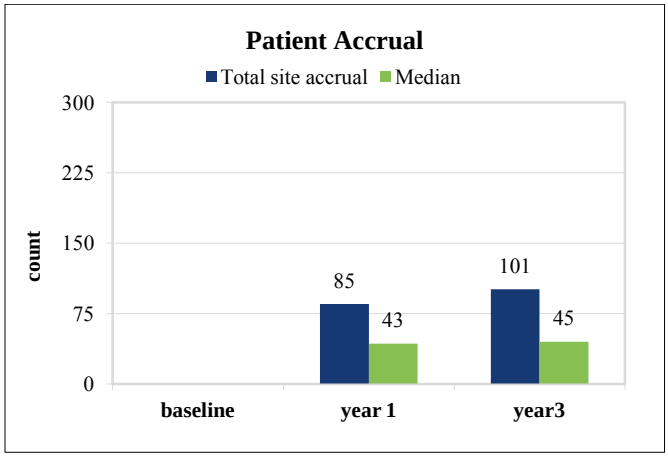
Trials Portfolio – Site-Reported Data

According to site-reported data, the total number of trials was 51 trials in Year 1 and 42 in Year 3, for an 18% decline.



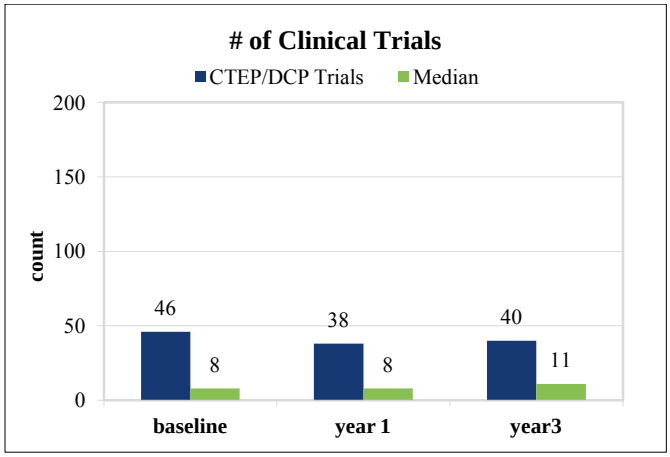
Accrual – Site-Reported Data

In the first year, 85 patients were enrolled in trials and this increased to 101 in Year 3, or a 19% increase. Regarding participation in trials by underrepresented populations, the only notable change over the 3-year period occurred in patients aged 65 years of age and over with 36 in Year 1 and 23 in Year 3 (note that this site used ≥65 rather than just >65 as its age criterion). There were 5 "Other Research Studies" underway in Year 1, and 6 in Year 3. "Other Accrual" increased from 19 in Year 1 to 409 in Year 3.



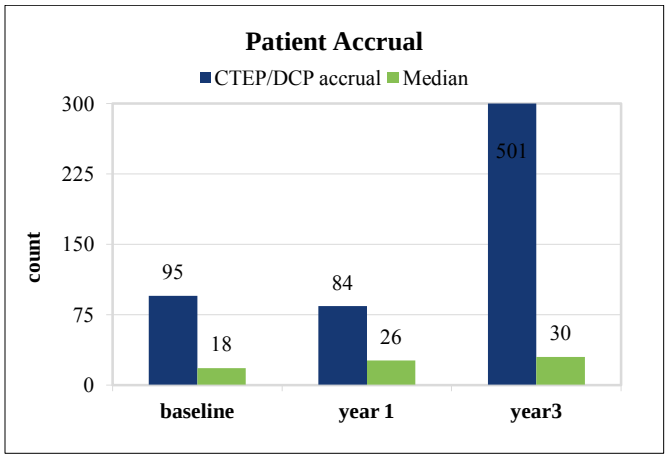
Trials Portfolio – CTEP Data

A total of 46 CTEP/DCP trials were underway at baseline, 38 in Year 1 and 40 in Year 3 or a 13% decrease from baseline.



Accrual – CTEP Data

There were 95 enrolled patients at baseline, 84 in Year 1, and 501 in Year 3. This represents a 427% increase over baseline. The ratio of patients per trial was 2.07 at baseline, 2.21 in Year 1 and 12.53 in Year 3, which represents a 506% increase over baseline. The number of patients from racial/ethnic backgrounds was 16 at baseline which rose to 36 in Year 3. In the "Age 65 or over" category, the number of patients enrolled increased from 34 at baseline to 399 in Year 3.



Comparison between Site-Reported and CTEP Data

Both the site-reported and CTEP data confirm decreases in the number of trials between Years 1 to 3; the relative decrease was similar from both the site and the CTEP databases. Despite the decreasing number of trials, this site enrolled nearly 20% more patients in trials by site reports and 427% more patients per the CTEP database. The number of trials was similar in Year 3 (site reported N=42 vs CTEP N=40), despite the fact that the site-reported data includes all sponsors. The difference in reported accrual (Year 3: site reported N=101 treatment; N=409 other accrual vs. CTEP N=501 treatment) is interesting and largely unexplained; one hypothesis is that, while the site matured in how it designated trials as treatment or not (presuming that alignment of trial categorization with CTEP suggests more appropriate designation), its internal assignments of clinical trials participants as in a treatment trial or not had not matured in the same way.

Clinical Trials Infrastructure and Organizational Support

Site #16 had a great deal of organizational infrastructure devoted to clinical trials in place at baseline. The overall FTE of the site increased from 33.75 to 37.5. The increase was the result of increases in the number of physicians (from 2 to 12), clinical research associates (from 2 to 4), nurse navigator (from 2 to 3) and social workers (from 1 to 2). To accommodate this increase in staff FTEs, there was a reduction in research nurses (from 19 to 11), data managers (from 3.25 to 1), and outreach coordinators (from 2 to 1). Initially, 20 of 33 eligible physicians enrolled patients. The most recent report shows that 22 of a possible 44 eligible physicians are enrolling patients.

The site had an IRB at baseline that met monthly and now, according to the latest report, meets twice monthly. The availability of IT support, a dedicated research pharmacy, and participation in CTSU trials evident at baseline continues to be present.

Comment:

This site is a mature Lead CCOP, which is evident in the substantially greater number of trials open and accruing at baseline (CTEP treatment trials: site N=46 vs median N=8) and persistence of these findings over the 3-year period. Despite a small drop in the number of trials over the three years, the accrual of patients in trials increased, as indicated by the CTEP data in particular. This suggests that even Lead CCOPs can see remarkable changes in accrual, although the reasons are not readily apparent. One interesting observation is that the number of potentially participating physicians at the site increased from 33 to 44, suggesting an increase in the total number of patients receiving care at the site, and therefore a potentially larger population of individuals screened. It would be useful to spend additional time with this site to learn what types of on-the-ground changes were most influential in increasing the number of patients enrolled in trials.

APPENDIX 3: PRESENTATION SLIDE DECK

NIH Publication No. 12-7945

August 2012