

Cancer Clinical Trials in North Carolina

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The field of oncology is entering a new and exciting period of discovery. For the first time, our understanding of tumor genetics and basic cell biology is leading to the rapid development of new therapies. Our ability to put these treatments to use, however, is dependent on our ability to study them in a scientific and controlled manner in clinical trials. North Carolina is a state with a very rich tradition of cancer research and patient care. We have 3 National Cancer Institute (NCI) Comprehensive Cancer Centers while 17 states have none at all. In addition, the state is the headquarters for the Southeastern Cancer Control Consortium (SCCC), the largest Community Clinical Oncology Program (CCOP) in the United States. The American Society of Clinical Oncology lists almost 600 physician members in the state and over 600 research studies are in place at nearly 250 sites. All in all, the state of North Carolina is clearly a leader in cancer care.

Yet, even with this great potential, we still struggle with the problem of enrolling North Carolinians with cancer in clinical trials. It is estimated that between 2% to 5% of the adult cancer population enrolls in cancer clinical trials nationally, and this estimate is widely cited.¹ However, this reflects only enrollment in National Cancer Institute trials and does not include studies sponsored by the pharmaceutical industry or developed locally at the university centers. Others have estimated that if all other treatment trials were included, the rate might be twice this estimate, if not higher. It is difficult, however, to confirm any of these estimates because there is a lack of reproducible methodology for measuring enrollment, a fact that

reflects the fragmented, decentralized nature of trial development and management outside of NCI trials. As a result of this system, obtaining a comprehensive estimate of total trial enrollment would require contacting many trial sponsors and having them voluntarily share their trial enrollment information—a task which is yet to meet with success.

Overall trial enrollment rates in North Carolina remain unknown, although enrollment estimates in NCI cancer treatment trials fall within the usual estimates of 2% to 5%. For the years 2002 through 2004, an average of approximately 2.5% of North Carolina adults diagnosed with cancer enrolled on NCI treatment trials.² This estimate has generally grown since the years 1995 to 1997, during which time approximately 2.1% of adults enrolled. This trend is favorable overall, but not all

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populations experience enrollment equally. For example, while analysis of minority enrollment is ongoing, there is evidence that African Americans enroll in trials at a substantially lower rate than do whites.¹ There is also wide geographic variation, with greater enrollment generally seen in more urban counties

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and those served by academic medical centers. Twenty counties experience adult enrollment rates of less than 1%, including multiple counties in the southern, eastern coastal, Appalachian, and western counties. An additional 38 counties, spread broadly across the state, experience enrollment rates of 1% to 2%.

While racial and geographic differences in enrollment rates are notable, it is challenging to understand the degree to which this variation represents a problem, given our lack of information on non-NCI trial enrollment, which is likely substantial. Understanding enrollment in NCI trials is important and illuminating, but it is not a comprehensive proxy for our overall understanding of clinical trials enrollment. Indeed, a great deal of informal reports in recent years have suggested that some practices are moving away from NCI trials to participate more in industry-sponsored trials or in networks exclusively devoted to these trials. Only by understanding the total picture of trial enrollment will we be able to identify true disparities in access to clinical trials, as well as the implications for cancer care quality and what needs to be done to resolve them.

The national situation for clinical trial awareness by both physicians and patients remains a problem. Even the SCCC has struggled with this issue. The SCCC does not have a way to evaluate the efficacy of its program of promoting clinical trials to the public, so it is unclear how well any particular form of clinical trial advertising functions to educate physicians and patients who may benefit from the trials. The Harris Interactive Study of 2000 showed that only 16% of the general population is aware that clinical trials are an option, but patients who are generally unaware of the clinical trials process nevertheless had a positive impression about clinical trials in general.³ Most patients who were on clinical trials rated their experience as positive and better than standard therapy. Only 26% of those who were aware that clinical trials were an option participated in a clinical trial. Of those that went on clinical trials 60% to 75% felt that their doctors told them about the trials and made a great effort to educate them to find a trial for them. Very few of the nonparticipants felt their doctor had taken such an effort.

The SCCC itself has used a variety of techniques including billboards with the slogan "Research Cures Cancer," colorful clinical trials brochures for the public, and media presentations in several of the large markets. This reaches a limited audience at best, and the total benefit of this effort in terms of accruals is unknown.

Slightly more than 50% of North Carolina residents live in rural areas, making the state one of the most rural in the nation.⁴ Across the country, more than 80% of patients with cancer receive their care in a community setting rather than at academic medical centers. This means that clinical research, if it is to be available to all North Carolinians, must be maintained in both the community and academic settings. At the present time, community practices are struggling to participate in research even as they face rising costs and declining reimbursement.

Most oncologists are involved in clinical trial enrollment as part of their fellowship training and understand implicitly that clinical trial data serve as the basis for the appropriate prescription of therapy. However, their enthusiasm may be tempered by the

"I have stage IV pancreatic cancer. I was diagnosed December 2, 2006. I was told I had 6 months to live. I'm now working on my 17th month. I feel like I'm a survivor each and every day. I have been working full-time since the start of April 2007. I got married July 28, 2007 to a former high school girlfriend."

*— Mitch
Pancreatic Cancer*

obstacles they face, especially in setting up a new site as part of a small practice or in an underserved area. A small office must devote a significant expenditure of personnel effort, time, and expense in setting up a clinical trial operation. The clinician must also spend extra time with patients explaining the trial, often to have the patient decline or to find that an interested patient is not eligible based on a technicality. In addition, oncologist offices face penalties if they have difficulty accruing patients to an open trial or if errors in data entry occur. Given these obstacles, it might be beneficial to have an apparatus that can reach out to oncologists in small offices and underserved areas to provide support and encouragement in hopes of yielding greater clinical trial availability to all cancer patients.

With this in mind, the states' cancer community has been working on the development of a new approach: a statewide repository for clinical trials in North Carolina. This would pull together clinical trials of all types—NCI trials, clinical trials looking at new drug development with industry sponsorship, trials developed within academic medical centers, and trials looking at cancer prevention and control. This single repository, accessible online by both physicians and patients, would raise awareness of clinical research and form the backbone for future collaborative efforts between university and community practice. It would also lead to our ability to track enrollments and look for gaps in clinical trial availability in different regions of North Carolina.

A statewide Web-based repository for clinical trials is not a novel idea. This model is in practice and undergoing evaluation in other states, most notably the state of Georgia. The Georgia Center for Oncology Research and Education (CORE) created a statewide Web-based repository for clinical trials several years ago and is currently in the process of refining the system and measuring outcomes. Their Web site is managed by the Georgia CORE and the Coalition of Cancer Cooperative Groups (CCCCG). The CCCC has been instrumental in providing both the infrastructure and the powerful search engine required to update an all-inclusive listing of trials. Although the CCCC automatically updates NCI-sponsored cooperative group clinical trials and those listed in the most well-known and comprehensive national search engines, they also coordinate regular communication with the performance sites in Georgia for quality control and

completeness (ie, to ensure that trials are listed with accurate details). The North Carolina Comprehensive Cancer Plan is considering collaboration with the CCGG and also has an ongoing relationship with the Georgia CORE to learn from and model their success.

A comprehensive listing of clinical trials in North Carolina and the surrounding areas will serve many purposes. It will allow university-based practitioners to help patients locate a clinical trial at a community practice close to their home. It will also allow community practitioners to help their patients find clinical trials in an academic setting. Further, clinical trials leaders in North Carolina will have the opportunity to better understand the landscape of research in the state, identify areas of need, and guide intervention design to increase clinical trial awareness and participation. A Web-based resource would allow patients and practitioners to search for clinical trials by variables such as tumor type or stage, trial ID, zip code, or prior treatment history. No login ID will be required and the service will be available at no cost to users.

The development of such a Web-based clinical trials repository, however, will have some challenges. The 3 NCI-designated cancer centers are required to submit trial accrual data to the NCI on an annual basis, making NCI data collection relatively easy, but the same is not true for the community cancer centers. Both the NCI-designated centers and the community-based trial sites include National Cancer Institute Cooperative Group studies as well as multiple institutional and pharmaceutical company sponsored trials. While each university has its own

cancer center specific Web site, the proposed statewide Web site would offer a single location that patients, families, and physicians could explore to find the most appropriate trials available at both the university and community-based locations. Many private practices and larger community hospitals have open trials but do not maintain a centralized database that lists all their open studies, making searching difficult for interested patients and families. The challenge with the proposed Web site will be to create incentives to encourage sites to submit all their data and maintain its accuracy so that the information is up to date and functional for those accessing the Web site.

This effort was originally intended to monitor the frequency with which patients were enrolled into studies. A centralized Web site would allow identification of open studies and active sites and could eventually provide a tool to track trial accrual at each site. This is not a trivial commitment on the part of the participating centers and again leads back to the issue of how to best encourage site participation. This might be accomplished by including it as a part of a state-designated "center of excellence in oncology practice" certification that could require a certain level of trial enrollment and submission of timely data to this Web site.

The development of a central Web site for North Carolina clinical trials will place clinical research back on the radar screen for private practices, serve as a common point of information, and raise patient awareness of clinical research as an added value to cancer care and a mark of quality for participating physicians and institutions. **NCMJ**

REFERENCES

- 1 Carpenter W, Corbie-Smith G, Weiner B, Psek W, Godley P. Increasing Cancer Clinical Trial Enrollment in North Carolina Communities. *National Cancer Institute Cancer Health Disparities Summit 2008: Eliminating Cancer Health Disparities through Science, Training, and Community*. Bethesda, MD; 2008.
- 2 NCI Clinical Data Update System.
- 3 Comis RL, Aldigé CR, Stovall EL, et al. A quantitative survey of public attitudes towards cancer clinical trials. Coalition of Cancer Cooperative Groups Web site. <http://www.cancertrials-help.org/CTHpdf/308-9.pdf>. Accessed July 17, 2008.
- 4 North Carolina Rural Economic Development Center Rural Data Bank, 2000 Census Data.