

The Role of State Legislation and Policy in Addressing Disparities in Clinical Trials.

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For many diseases and disorders such as cancer, clinical trials have produced advances in therapy as well as prevention. These advances have occurred despite some considerable challenges, including a participation rate of only about 3–5% by cancer patients^{1,2}, particularly low participation by underserved groups (African American, uninsured, poor, rural)^{2,3} and a declining percentage of African Americans participating.³

In 1993, the National Institutes of Health (NIH) Revitalization Act (Public Law 103-43)⁴ was amended to require the inclusion of women and minorities in clinical and government sponsored human subject clinical research, including Phase III clinical trials. This Act states that cost is not an allowable reason for excluding minorities and that the NIH will support outreach efforts to fulfill this mandate.

Participation in clinical trials is influenced by patient, provider, structural and other factors. Some evidence suggests that slightly less than one-third (32%) of Americans would be willing to participate in clinical trials if asked, and, an additional 38% would be inclined to participate if asked but had some questions or reservations.¹ Therefore, additional factors other than patient intent or willingness seem to present barriers to participation in clinical trials. The following table summarizes several salient factors impeding participation:

The low participation rates in cancer trials by African Americans and other minorities may contribute to avoidable disparities in cancer, including substantially higher cancer incidence, morbidity and mortality rates.⁹ Ultimately, it is hoped that increased awareness and intensive educational programs which are guided

by research on trial barriers, increased availability of trials, and trial related policies will increase the access to and likelihood of participation in clinical trials by underserved patients.

Recent reports have focused on the policy implications and the role of state legislation in addressing access, reimbursement for and participation in clinical trials.¹⁰ This paper provides the author's views on the role of policy and state legislation in eliminating disparities in clinical trial participation.

Policy Role and State Legislation

One of the barriers to participation in clinical trials is the actual or perceived costs of participating anticipated by both patients and physicians.² Cost barriers can be a general concern as well as disparity population specific.

There are several challenges regarding health insurance coverage of clinical trials. In general, insurance companies make decisions regarding coverage for clinical trial participation based on two factors: the type of costs and the insurer's assessment of whether the care is "safe and effective", (i.e. treatment in the trial is established or investigational).¹¹

The NCI identifies two main types of costs associated with clinical trials: *patient care costs* and *research costs*. Patient costs are described as either "usual care costs" or "extra care costs." Usual care costs (the costs of undergoing treatment) are seldom questioned while "extra care costs" (additional tests and services associated with trial participation) are often not supported by the research sponsor and are frequently challenged by the health insurance provider. Research costs (administrative and staffing

Table I. Selected Examples of Factors that Impede Participation in Clinical Trials

Barriers to Clinical Trial Participation	Examples
Patient Factors or Demographics	<ul style="list-style-type: none"> minority² aging and rural² poor access to care² low socioeconomic status⁵
Patient/Community awareness, trust issues and history	<ul style="list-style-type: none"> mistrust of research / medical system⁵ fear of negative results/effects⁶ historical factors⁷; lack of information on available trials⁵
Physician and researcher barriers	<ul style="list-style-type: none"> reluctance to refer patients^{1,5} (fear of losing patients) lack of awareness / knowledge of clinical trials benefits⁶ doctor-patient communications lack of culturally appropriate researcher training to address patient concerns⁷
Infrastructure, design issues	<ul style="list-style-type: none"> lack of sufficient number of appropriate clinical trials; disqualification of patients¹ due to eligibility criteria lack of sufficient infrastructure to support trials in community settings²
Perceived or actual cost barriers	<ul style="list-style-type: none"> Patients may be reluctant to participate due to lack of insurance or fears of additional costs Physicians may be reluctant to refer patients due to real and perceived additional costs² Oncologists concern: lack of reimbursement for clinical and research costs⁸

costs) are typically not as much of a concern as they are generally fully covered by the institution or sponsor supporting the research.

Most insurance companies are reluctant to support the costs clinical trial that are considered “investigational” rather than “established.” Established treatments have typically been available long enough to be considered safe and effective. Generally, the insurance company will review the sponsorship of the clinical trial, the type of trial, (Phase III is more likely to be accepted than Phase I or II) as part of determining if it is investigational or established. Other factors which influence the decision to cover clinical trial costs are whether the treatment is “medically necessary,” if it is cost neutral, whether other treatment options are available, and the qualifications of the facility and staff.

Given this complicated set of circumstances, the role of policy and state legislation or regulation is emerging as an important consideration for increasing access, coverage and participation in clinical trials. In recent years a growing number of states, such as California, Louisiana, Maryland, and several others, have passed legislation and/or entered special agreements that require health plans to pay the cost of routine medical care provided during clinical trials.¹¹ In some cases, this also includes agreements with state Medicare and Medicaid to ensure coverage of clinical trial costs.

Policy and state legislative activities can cover a variety of areas, including:

1. Providing increased access to clinical trials by mandating coverage for clinical costs associated with trial participation.
2. Fostering informed consent and public disclosure of trial results and adverse events/errors that may occur.

Mandating coverage for associated costs

States increasingly have passed legislation to mandate coverage of costs, usually clinical costs associated with trial participation. This protects patients from the financial burdens of for uncovered blood work, x-rays and, even more importantly, clinical costs that result from diagnosis of unexpected medical conditions found during the course of the trial monitoring and not covered by the trial sponsor.

While an important step, state insurance mandates do not guarantee access to trials for the most vulnerable populations. In 1998 and 1999, Maryland passed state health insurance mandates into law including coverage of trial associated clinical costs.¹² However, after close review of the statute, these state mandates only cover 25% of the population. Further the American Cancer Society (ACS) reported that 60% of patients do not take part in clinical trials due to fears of having their insurance denied.¹² According to the American Society of Clinical Oncology (ASCO), this is a valid concern as denial for routine care costs were reported by oncologists as an obstacle to enrollment in clinical trials.¹³

Disclosure of adverse events and results

Some states support clinical trials registries as a tool for providing information on open trials, trial results, disclosure of errors and adverse events, moving beyond federally supported trial registries (i.e. state registries are increasing in interest to states).

Will removing insurance barriers through legislation and regulatory actions eliminate disparities in trial participation and enrollment?

The increase in state legislation and regulation on insurance coverage for clinical trials was an attempt to address the real and perceived cost barriers to trial participation. In the absence of such state policies and regulatory actions, cost barriers to trial participation would persist for the populations that are actually covered under state mandates. But studies reported by NCI and Yale University School of Medicine reviewed enrollment in cancer clinical trials prior to and after changes to policies on state and Medicare reimbursement designed to remove certain economic barriers to clinical trial participation. The studies concluded that removal of insurance coverage barriers will not, by itself, increase accrual or participation in cancer clinical trials.⁸ State policies were associated with an increase in Phase II but not Phase III trials.

A Case Study: Maryland Experience with Trial Availability and Participation Policy

Through the development of extensive community networks and partnerships locally, regionally, and within the state, Maryland has been able to significantly expand the availability and awareness of clinical trials in the state and to influence policymaking with regard to clinical trials. Support from key state policy makers and an ongoing technical assistance process were developed with elected officials. As part of a multilevel strategy, both qualitative and quantitative research has helped us to thoroughly understand existing attitudes toward clinical research and to identify specific barriers that may exist for participation. In addition, comprehensive community-based programs to educate both the general public and health providers have been undertaken, and efforts to support clinical trial infrastructure, including adding resources such as data collection tools and research staff, have been put in place. Some of these initiatives will be described below.

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1. *The University of Maryland Statewide Health Network (UMSHN) Baseline Health Survey.* The Maryland Statewide Health Network (The Network or UMSHN) is a regional and statewide, community-based infrastructure established in 2000 with support from Maryland’s Cigarette Restitution Fund Program to promote a broad range of prevention and control activities on cancer and other tobacco-related diseases (PI: CR Baquet). The overall goals of the UMSHN are: 1) to reduce morbidity and mortality from cancer and other tobacco related diseases; 2) to reduce or eliminate disparities in cancer deaths attributable to racial/ethnic, cultural, geographic, or socio-

economic barriers; and 3) to foster increased awareness and participation in clinical trials especially in community settings. The Network has established a central office and community regional offices across the state. These offices provide locations for ongoing community and physician educational programs, community-based research and sessions on available trials, human subject protections and best practices.

As part of this program, we implemented a major population-based telephone survey of households in Maryland. This comprehensive survey included self-reported information on health status and health behaviors as well as knowledge, barriers and attitudes regarding clinical trials.¹⁰

The analysis showed that of those asked to participate in clinical trials, African American and middle income respondents were significantly less likely to actually participate in clinical trials. Respondents who received information about clinical trials from their health care provider, who were knowledgeable about clinical trials, and those who had the time commitment were significantly more likely to participate in clinical trials. The lack of physician discussion about trials was also reported by the majority of study participants as a major reason for lack of patient interest in trials. These results support the need for increased targeted efforts to educate physicians, minority and rural patients and to provide the basis for development and implementation of community-based educational programs for both the general public and health care professionals.¹⁴

2. *Qualitative Focus Group Study of Mandated Health Care and Cancer Coverage in Maryland.*

A series of six focus groups were conducted across the state to determine awareness and understanding of Maryland's state legislative initiatives for assuring health benefits for specific diseases including cancer. These sessions revealed a number of important factors, including over half of participants were unaware or did not understand legislative initiatives in place in Maryland for mandated health coverage including the clinical trial coverage benefit. In addition, a number of participants were not aware that a governing body was in place that enacts laws to mandate insurers, health maintenance organizations, and non-profit health services. For both male and female participants, this lack of information about mandated benefits was considered a barrier for access to health care and clinical trial participation.¹⁵

3. *US Secretary of Health and Human Services National Best Practice Designation.*

In the fall of 2004, the University of Maryland School of Medicine and Eastern Shore Oncology, received a prestigious peer reviewed national "Best Practice" award from the US Secretary of Health and Human Services for a proven model to increase cancer trial availability and participation on the rural Eastern Shore of Maryland.¹⁶ With support from the Maryland Special Populations Cancer Research Network (PI: CR Baquet;

NCI U01 CA86249-03), the Maryland affiliate of the Susan Komen Foundation and the state, clinical trial availability and participation increased dramatically.

The Maryland Special Populations Cancer Research Network (MSPN) was one of eighteen five-year grants funded from 2000-2005 by the National Cancer Institute. Its primary goal was to reduce and eliminate cancer disparities in Maryland minority and underserved populations.

Increasing clinical trials availability was an essential component of MSPN. Through MSPN, UMSOM has provided education and clinical trials access to underserved populations in urban Baltimore City, and rural populations in Southern Maryland, the Eastern Shore, and Western Maryland. Clinical trials education has been provided to underserved communities, in urban Baltimore City, to tribal populations in rural Southern Maryland and along the rural Eastern Shore. In addition to the Best Practice designation, key accomplishments of relevance of MSPN that influenced clinical trials work conducted in Maryland included leverage of several million dollars in grant funding to support community programs, research and development of tools for technical assistance with key State policy makers.

Recommendations

While these initiatives have shown progress in increasing the knowledge and availability of clinical trials in Maryland and in other geographic areas, additional research, data reporting and state policy tracking initiatives could foster continued progress in clinical trials participation nationally. For example, although Maryland law mandates coverage for costs associated with participation in clinical trials, restrictions in application of this law make this benefit as well as other mandated health benefits only available to 25% of the insured population.

Recommendation: Specific and systematic research on the role of state and federal insurance mandates as a specific barrier to trial participation by health disparity populations would increase understanding of the role of this issue.

Recommendation: In addition, tracking population specific data on participation trends and barriers, the study of accrual and reasons for trial withdrawal (drop outs) by race and insurance status would lead to greater understanding of the specific issues that impact clinical trials accrual for both health providers and patients.

Recommendation: Finally, the development, adaptation, and dissemination of best practices which increase trial availability and trial participation is essential. Development of state policy and regulatory best practices is an important component of efforts to address disparities in trial participation. ●

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Table 1. Summary of Mandated Clinical Trials Coverage by State

State	Year	Services/Benefits Covered	Who is Required to Pay
Arizona	2000	Patient costs for Phase I-IV clinical trials	Hospital or medical service corporations, benefit insurers, health care service organizations, disability insurers, group disability insurers and accountable health plans
California	2000	Routine patient care costs for Phase I-IV cancer clinical trials	All California insurers, including Medicaid and other medical assistance programs
Connecticut	2001	Routine patient care costs associated with cancer clinical trials	Private insurers, individual and group health plans
Delaware	2001	Routine patient care costs for clinical trials for the treatment of life threatening diseases (conditions specified in the legislation)	Every group of blanket policy, including policies/contracts issued by health service corporations
Georgia	2000	Routine patient costs for Phase II-III prescription drug clinical trial programs for the treatment of children's cancer	Insurers and the state health plan
Illinois	1999, 2004	Routine patient care for approved Phase II-IV cancer research trial	HMOs and individual/group insurance policies to offer coverage to the applicant or policyholder. (2004: Plans may not be canceled or not renewed based on participation in a qualified clinical trial.)
Louisiana	1999	Patient costs for Phase II-IV cancer clinical trials	HMOs, PPOs, State Employee Benefits Program and other specified insurers
Maine	2000	Routine patient care costs associated with clinical trials	Managed care organizations and private insurers
Maryland	1998	Patient costs for Phase I-IV cancer treatment, supportive care, early detection, and prevention trials; Phase II-IV for other life-threatening conditions; Phase I on a case-by-case basis	Private insurers and other specified managed care organizations
Massachusetts	2002	Patient care services - all phases of qualified cancer clinical trials	All health plans issued or renewed after Jan. 1, 2003
Missouri	2002	Routine patient care costs for Phase III or IV clinical trials for the prevention, early detection, or treatment of cancer	All health benefit plans operating in the state
New Hampshire	2000	Medically necessary routine patient care costs for Phase I-IV cancer treatment trial for a life-threatening diseases	Private insurers and specified managed care plans
New Mexico	2002	Routine patient care costs for Phase I-IV cancer clinical trials	Private insurers, specified managed care plans, and Medicaid and other state medical assistance programs
North Carolina	2001	Medically necessary costs of health care services for Phase II-IV of covered clinical trials	All health insurance plans and teachers' and state employees' comprehensive major medical plan.
Rhode Island	1994, 1997	Coverage for new cancer therapies if treatment for Phase II-IV cancer clinical trial	Private insurers and specified managed care plans
Tennessee	2005	Routine patient care costs for Phase I-IV cancer clinical trials	All health benefit plans
Vermont	2001, 2005	Routine patient care costs for Phase I-IV cancer clinical trials	All health insurance policies and benefit plans, including Medicaid
Virginia	1999	Patient costs for Phase II-IV cancer clinical trials (case-by-base basis for Phase I)	Private insurers, specified managed care plans, and public employee health plans
West Virginia	2003	Patient costs for Phase II-IV clinical trial for treatment of life-threatening condition or the prevention, early detection and treatment of cancer	Individual/group insurers, health service corporations, health care corporations, HMOs, public employees insurance agency, Medicaid, and the children's health insurance program

Source: American Cancer Society. *Clinical Trials: State Laws Regarding Insurance Coverage*. Updated: 1/30/06. Accessed: 7/31/06. http://www.cancer.org/docroot/ETO/content/ETO_6_2x_State_Laws_Regarding_Clinical_Trials.asp.