Current Practices in Clinical Research: A State of Social Injustice. *By Margo Michaels, MPH*

Equal "access to clinical trials is less a matter of scientific necessity than of social justice." – Otis Brawley

Although about 20 percent of cancer patients are medically eligible for clinical trials[1] (assuming availability of an appropriate trial), trial participation among adult cancer patients remains at about three percent.[2] This rate is even lower among people of color and the medically underserved, who tend to have higher cancer mortality rates than the population as a whole.[3] Although I am a strong believer in the importance of clinical research participation, I have long felt some serious concerns about how current practice in cancer clinical trials may violate ethical and moral principles at a community level.

The Belmont Report outlined three basic ethical principles of research that form the backbone of conduct of research in the US today: Respect for persons; Beneficence; and Justice. The report defines the principle of justice as fairness in w*ho ought to receive the benefits of research and bear its burdens.* A related concept is social justice, which can be considered "the foundation of public health."[4] As one health association stated, "Effective action to eliminate health inequities demands a perspective and conceptual framework grounded in values of social justice. Otherwise (we will)…continue to rely on…individual interventions, rather than transforming institutions that cause health inequities."[5]

In order to truly eliminate health disparities, we must meaningfully incorporate principles of justice and social justice in the design and conduct of clinical research. In this essay I will outline five concerns regarding current practices in cancer clinical research, how they affect underserved communities, and why they may violate the core principles of justice and social justice. I conclude with some proposals for policy that may help to address these concerns.

Concern #1: Although few cancer patients are offered the opportunity to participate in a clinical trial, certain populations are even less likely to be approached.

The color of your skin and the money in your pocket have a clear effect on clinical trial participation. Studies have shown that minorities with cancer are less likely to be offered participation in a clinical trial, that patients enrolled in clinical trials are significantly *more* likely to be insured, and that geographic areas with *higher* socioeconomic levels have higher levels of clinical trial accrual.[6, 7]

There are several reasons why we see low participation of minorities and other underrepresented groups in cancer clinical trials. First, like all cancer patients, they are generally unaware of clinical trials, and may be even less so due to their reduced access to specialty health care.[8] Many providers assume that minorities are unwilling to participate in research. Others simply avoid suggesting a clinical trial to them, out of concern that patients would be offended by the suggestion. However, a recent metaanalysis of numerous health research studies found that minority groups, particularly African-Americans and Hispanics, appear to be *as willing* to participate in health research as non-Hispanic whites. What the study did find were great differences in the number of individuals *invited* to participate.[9]

The Belmont Report states that the principle of fairness dictates "the selection of research subjects needs to be scrutinized in order to determine whether some classes … are being systematically selected." Given the data above, we must consider the likelihood that some classes are **being systematically excluded** from research studies and being stigmatized as groups who are unwilling to bear their fair share of the burdens required to improve medical care.

Concern #2: Disparities in cancer clinical trials participation has a direct relationship to the availability of quality health care.

Access to cancer clinical trials is one of the established standards for the delivery of quality health care and quality comprehensive cancer care (American College of Surgeons Commission on Cancer). Due to evidence that suggests research participation is associated with improved clinical outcomes, some practitioners recommend trial participation as a means to better treatment.[10] Moreover, participation in clinical trials increases access to state-of-the-art cancer care – a level of care inaccessible to many minority and underrepresented populations and a factor contributing to the unequal burden of cancer.

Concern #3: Institutions and investigators conducting cancer clinical trials do not take seriously their responsibility to engender public trust.

As noted elsewhere in this compendium, public distrust of medical research is a significant obstacle to clinical trials participation, particularly among ethnic minority groups in the US. This distrust can be traced to discrimination, disrespect, and the legacy of past abuses, such as the Tuskegee Syphilis Study.

This distrust may be exacerbated by current practices in oncology research today. For example, oncology care providers have had great difficulty recruiting ethnically diverse populations to clinical trials and in retaining their participation. Protocol development seldom considers the importance of culturally relevant recruitment and retention planning. These tasks are often left to nurses or research assistants who have few resources to effectively undertake culturally sensitive patient recruitment and retention efforts.[11, 12]

In a December 2005 interview with the *Washington Post*, Vanessa Northington Gamble, director of the Tuskegee University National Center for Bioethics, encouraged us to consider the "lack of trustworthiness" of medical institutions rather than saying that blacks are "distrustful" of the medical system. She prefers to speak of medical institutions' "lack of trustworthiness," to emphasize that it is the institutions' responsibility to gain people's trust."[8]

The onus must fall on all research institutions (and individual investigators) to create meaningful partnerships and trusting relationships with community groups. In its 2005 report, the Presidents Cancer Panel emphasized that" both trust (an expectation of certain behaviors, reliability, competence, and power sharing) and community participation are essential" to the success of clinical research. The panel advanced a number of recommendations for building trust and community participation in cancer clinical trials, including the expectation that community participation occur early in protocol design and in research implementation and that a plan for disseminating and sustaining new interventions into the community be in place.

Indeed, participatory models of research have become central to programs that seek to improve the health of minority communities and medically underserved populations.[13] By utilizing some of these approaches in clinical trial outreach, recruitment and retention, investigators can.[14,15]

"Experts have particularly emphasized the importance of community-based approaches, noting that 'success (in clinical trials accrual) will require sustained, aggressive action, and new partnerships between policymakers, healthcare professionals, professional societies, and underserved communities.'"

- Increase trust and bridge cultural gaps between partners
- Increase the possibility of overcoming the understandable distrust of research on the part of communities that have historically been the "subjects" of such research.
- Improve program design and implementation by facilitating participant recruitment and retention.
- Disseminate findings to all partners and involve them in the dissemination process, thereby ensuring ongoing partnership work.
- Create better informed and more effective practices for clinical trial education that are replicable and grounded in "real-world" experience.

Concern #4: The design of cancer clinical trial protocols doesn't necessarily reflect the needs of many local communities.

To participate in clinical trials, patients must be medically eligible and have personal circumstances, such as adequate finances/insurance coverage, flexibility in family and job responsibilities, and geographic proximity to allow them to participate. Strict eligibility criteria are a commonly reported barrier to trial participation, one that may disproportionately affect ethnic and cultural minorities due to co-morbidities. At a recent cooperative group meeting focusing on enhancing minority participation, investigators discussed their need to participate in trials that better fit the needs of their community. Not only were the exclusion criteria of most trials overly restrictive, but also many of the trials offered focused on cancer sites not commonly found in underserved communities. As one cancer center director stated, "…you …have to have clinical studies that are appropriate for your patient population and not appropriate only for the select, elite patients who may not represent all the issues that the average patient presents in oncology. This means that patients who are not in the best health should have available clinical studies."[11] We need to look objectively at eligibility criteria and ensure that they are broadened whenever and wherever possible.

Concern #5: The community being studied may not see the benefits of a trial in which it has participated.

The Belmont Report states that therapeutic advances must be available to those who can afford them and that the research should not involve groups unlikely to benefit from the new treatments. Sadly, underserved groups face less access to health care advances – regardless of who took part in the study – because the treatments are not affordable and/or are not effectively translated into practice by community cancer care providers. How can we ensure that research advances make the critical transition from the clinic to the community?

At the system level, we must develop easy ways for all practitioners, especially those who work with underserved groups, to incorporate new research findings into their care. Communities who are asked to support research efforts should consider obtaining assurances on the availability and affordability of any new medication that would be developed from their participation.

What can be done?

Addressing the challenges outlined above requires an ambitious multi-level approach to reform our policies and practices in clinical research design and implementation as well as the dissemination of new treatment modalities. At a minimum, this includes activities and responsibilities at the individual (community member or provider), community, and institutional levels so that we may build a critical mass of mutually supporting activities supporting a positive change. Experts have particularly emphasized the importance of community based approaches, noting that "success (in clinical trials accrual) will require sustained, aggressive action, and new partnerships between policymakers, healthcare professionals, professional societies, and underserved communities."[16] Table 1 illustrates some suggested activities to incorporate community based approaches to policies at the individual, community and institutional levels.

Table 1. Levels of recommended policy reform

Level of activity	Program design	Program Implementation
Individual (providers)	- Include community representatives in development discussions - Choose to participate in large Phase III trials only if they meet certain criteria for the community - Develop protocols with concrete recruitment and retention designs to include underserved groups	- Local providers have strong referral linkages with clinical trial investigators - Investigators implement research with culturally competent staff, including community representatives as partners
Individual (community members)	- Encourage community organization's participation in research design and implementation	- Consumers ask about clinical research opportunities when a loved one is diagnosed - Consumers demand that local physicians learn about local opportunities for referral to clinical research - Consumers make informed decisions when presented with options for clinical trial participation, reflecting on the facts about clinical research and how it impacts the individual and the community
Community	- Demand ongoing community education from all institutions conducting clinical research - Demand that any institution conducting cancer clinical research have available funding for indigent patients wishing to participate	- Communities become "informed consumers" when deciding whether or not to support clinical trials - Communities make informed decisions based on the evaluation of their collective experience - Communities become proactive, getting assurances that research benefits will be shared fairly
Institutional (cancer centers, CCOPs, hospitals)	- Require individual investigators to develop culturally appropriate recruitment and retention plans as a prerequisite for IRB approval - Begin the informed consent process with education in the community about clinical trials. - Only engage in large Phase III trials if they meet certain criteria for the community - Require meaningful community participation in protocol design and implementation	- Institutions make changes in IRB procedures - Institutions develop ongoing collaborative partnerships with community leaders/organizations
Institutional (funders)	- Encourage the development of protocols with concrete recruitment and retention designs to include underserved groups - Require concrete recruitment designs to increase access and participation of underserved groups - Require meaningful community participation in protocol design, implementation, and evaluation as full research partners - Require community education from all institutions conducting clinical research, giving community members control over their health and opportunities to self educate	Requests for Proposals will: - require community based participatory research practices (CBPR) - require appropriate education, outreach, recruitment, retention, and implementation practices

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