
Involving Communities as Partners in Cancer Clinical Trials

**Background Paper for the
Conference Series
*Communities as Partners in
Cancer Clinical Trials:
Changing Research, Practice
and Policy***

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I. Background and Context

Clinical trials help to move basic scientific research from the laboratory into treatments for people. By evaluating the results of these trials, scientists can find better treatments and ways to prevent, detect, and treat diseases like cancer.

Although about 20 percent of cancer patients are medically eligible for a treatment clinical trial¹ (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,³ who tend to have higher cancer mortality rates than the population as a whole. Studies have also found 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.^{4, 5}

Numerous structural, cultural, and linguistic factors negatively affect participation in clinical cancer research; many are clearly related to lack of knowledge and to underlying attitudes and beliefs on the part of the public as well as health care providers.⁶ According to one national survey, 75% of people with cancer would have been interested in participating in a trial, had they known it was available.⁷ Moreover, clinical trial investigators also report great difficulty in identifying appropriate patients for their trials. A 2005 Agency for Healthcare Research and Quality (AHRQ) Evidence Report/ Technology Assessment on cancer clinical trial recruitment⁸ confirmed what clinical trialists have known for years:

- There is substantial uncertainty about effective approaches for cancer clinical trials recruitment, especially among minority populations.
- There is a need for further investigation of effective communication and trust-building strategies, including research on the best approaches to disseminating information about clinical trials, both at community levels and at points of interaction with potential participants.

Why does this matter?

The low accrual rate in therapeutic cancer clinical trials has a profound effect on both the quality of research and the rate at which new scientific discoveries are made.⁹ Slow or insufficient patient enrollment in clinical trials significantly hampers trial completion and results in the occasional failure of clinical trials. It has been estimated that most clinical studies fail to enroll the required number of patients on time, increasing costs and delaying development of new treatments.^{10, 11} NIH policy mandates the targeted inclusion of minority groups and women in its funded research, underscoring the importance of adequate representation of all populations in clinical trials, so that we can learn about potential differences among groups and ensure the generalization of results.

Equally important to consider is how the low rate of clinical trial participation is a matter of social justice.¹² First, access to cancer clinical trials is a key quality measure for delivery of health care services; it is one of the established standards for the delivery of quality comprehensive cancer care.¹³ Some practitioners recommend trial participation as a means to receiving better overall treatment.⁸ Second, although it is largely assumed that minorities are uninterested in clinical research participation, a recent meta-analysis of numerous health research studies suggests otherwise. The study found that minority groups appear to be *as willing* to participate in research as whites; but are less likely to be *invited* to participate.¹⁴ Third, researchers who do not value the inclusion of minorities in their research may demonstrate less commitment to ensuring their participation.¹⁵

Finally, and somewhat paradoxically, many trials don't address the needs of the communities in which they are being carried out. Strict eligibility criteria often exclude patients with chronic conditions, which in turn exclude the elderly, members of minority groups, and patients with lower socioeconomic status from participating in trials.¹⁶ It is also important to consider who benefits from advances in research. Research advances often don't make the critical transition from controlled environments in research centers to widespread practice in hospitals, clinics and the broader community. Underserved groups have reduced access to health care advances because the treatments are often not affordable and/or are not effectively incorporated into practice by local health care providers. As Otis Brawley has suggested, equal access to clinical trials is "less a matter of scientific necessity than of social justice."¹⁷

So what can be done?

Experts continually recommend new community-based approaches for clinical trial outreach and accrual,^{18,19} noting that "success [in clinical trials accrual] will require sustained, aggressive action, and new partnerships between policymakers, healthcare professionals, professional societies, and underserved communities."²⁰ In its 2005 report, the President's Cancer Panel emphasized that "both trust ... and community participation are essential" to the success of clinical research. Others caution that the state of clinical research today "may hinge on the willingness and ability of the scientific community to actively engage study participants in every stage of research."²¹ Despite these calls for action, none of these recommendations have been meaningfully implemented and are largely absent from national policy forums and reports on reforming the clinical trial enterprise.²²

Central to many successful initiatives that seek to understand and improve the health of various subgroups – especially racial and ethnic minorities and low income people – are participatory models in which communities are actively engaged in the research process through partnerships with researchers.²³ A 2004 AHRQ Evidence Report suggests that the utilization of Community-Based Participatory Research* (CBPR) can improve

research quality, enhance intervention quality, improve outcomes, and enhance research recruitment efforts.²⁴ Use of community-based participatory approaches can help overcome distrust by fostering open and honest communication about the research process and engagement of participants in study planning and implementation. The CBPR approach views community participants as partners in the research process, rather than as subjects on whom research is conducted.²⁵ Although CBPR is a paradigm that has been more often demonstrated in public health research (health services, surveillance, health screening, behavioral interventions, etc.) than in clinical research,²⁶ we believe that the principles and approaches of CBPR can be systematically and integrally incorporated in every aspect of clinical research design and implementation.

Communities as Partners in Cancer Clinical Trials: Changing Research, Practice & Policy is a 3-part conference series designed to explore the potential of employing CBPR principles in therapeutic cancer clinical trials and to define an agenda for research, practice and policy. Convened by the Education Network to Advance Cancer Clinical Trials (ENACCT) and Community-Campus Partnerships for Health (CCPH), with core funding from AHRQ and the National Cancer Institute, the conference series will a) explore the potential links between incorporating CBPR principles into therapeutic cancer clinical trials and b) define an agenda for research, practice and policy for this field. The priorities developed through this conference series have enormous potential impact to change the way in which cancer clinical research is conducted at the local level and how it is funded.

This background paper is intended to serve two primary purposes. First, it serves as a primer on CBPR and the cancer clinical trial research system for the researchers, clinicians, staff, community leaders, patient advocates and other stakeholders who will be attending the conferences. Second, it lays out a vision for applying CBPR approaches to cancer clinical trial research and makes recommendations for implementing that vision. Respected representatives of these stakeholder groups were invited to write commentaries on the paper to enrich discussion at the first conference. These commentaries have been compiled into a separate document to accompany this paper.

II. What is CPBR and What Purpose Does it Serve?

There are multiple definitions for community-based participatory research (CBPR). We have chosen to highlight three commonly used definitions below:

“...a partnership approach to research that equitably involves, for example, community members, organizational representatives, and researchers in all aspects of the research process; with all partners contributing their expertise and sharing responsibility and ownership to enhance understanding of a given phenomenon, and to integrate the knowledge gained with interventions to improve the health and well being of community members.”²⁷

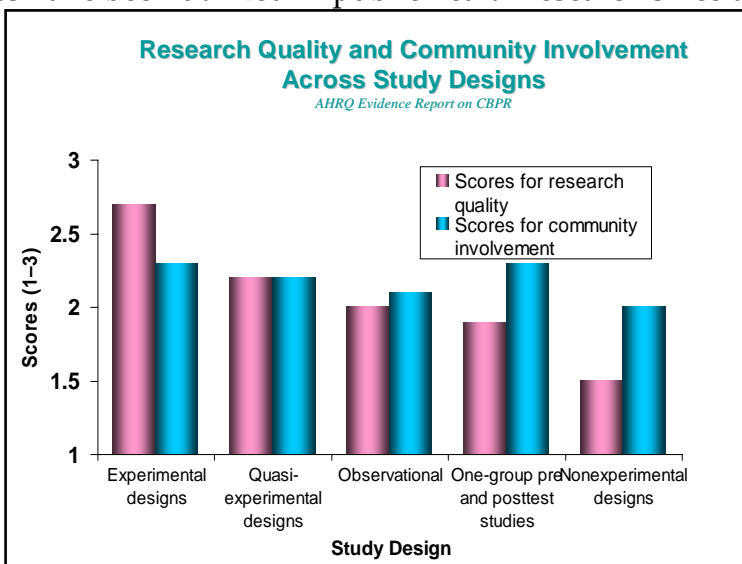
“A collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community and has the aim of combining knowledge with action and achieving social change...”²⁸

“Scientific inquiry conducted in communities in which community members, persons affected by condition or issue under study and other key stakeholders in the community’s health have the opportunity to be full participants in each phase of the work – conception, design, conduct, analysis, interpretation, conclusions and communication of results.”²⁹

The intent in CBPR is to transform research from a relationship where researchers *act upon* a community to answer a research question to one where researchers *work side by side with* community members to define the questions and methods, implement the research, disseminate the findings and apply them. Community members become part of the research team and researchers become engaged in the activities of the community. CBPR approaches have been utilized in public health research since the 1980s and notably in clinical research in HIV/AIDS since the mid-1990s.

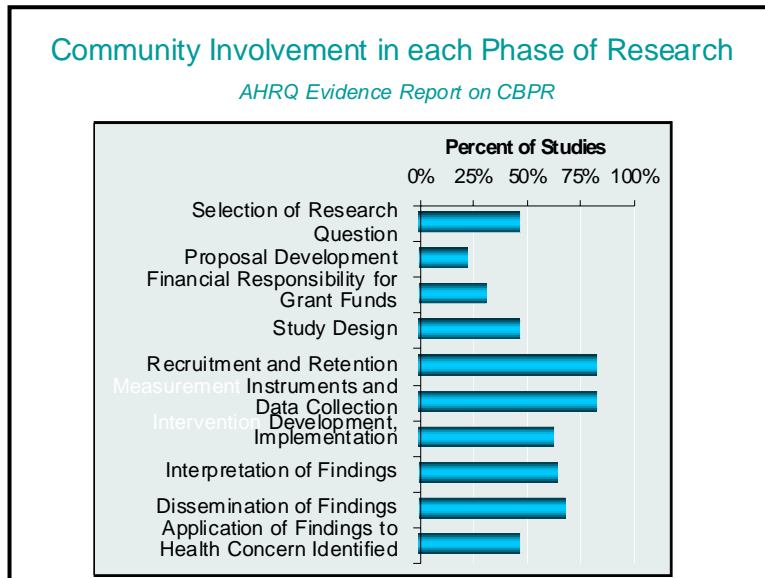
The previously cited AHRQ evidence report on CBPR demonstrated its application across a wide range of health issues and conditions, including general health concerns, environmental hazards, hypertension, heart disease and diabetes, and

HIV/AIDS. Seven percent of the studies identified focused on cancer screening and prevention. The authors demonstrated significant and comparable community involvement across all types of study designs. Of the 12 studies that implemented and



evaluated interventions, four were non-therapeutic randomized controlled trials

(RCTs); these included substance abuse prevention (Communities Mobilizing for Change on Alcohol^{30, 31, 32, 33, 34}); education for people with hypertension (East Baltimore Health Promotion^{35, 36, 37, 38}); cervical cancer prevention efforts (Health is Gold³⁹); and a psychosocial intervention for women with breast cancer (Sierra Stanford Partnership.^{40, 41}). The authors also found community involvement in each phase of research, with the greatest community involvement in participant recruitment and



retention, development of instruments and data collection.

Why take a CBPR approach?

There are several important reasons why more communities and researchers today are increasingly turning to CBPR approaches: ^{42, 43, 44}

- **There is a growing recognition that “traditional” research approaches have failed to solve complex health disparities.** Many research designs fail to incorporate multi-level explanations of health and the researchers themselves do not understand many of the social and economic complexities motivating individuals’ and families’ behaviors.
- **Significant community involvement can lead to scientifically sound research.** Researchers using participatory methods have found community input invaluable in the design and adaptation of research instruments that make the tools user friendly, applicable and culturally appropriate.
- **Research findings can be applied directly to develop interventions specific for communities.** The intended outcome of CBPR is not simply to find answers to complex social questions but to have those results provide information that can be used by the community to develop its own solutions.
- **Community members, wary of being “guinea pigs,” are increasingly demanding that research address their locally identified needs.** Traditional researchers often complain about the challenges in recruiting “research subjects.”

These challenges are often a result of community members feeling that all benefits accrue to the researcher (e.g., scholarly papers, promotion and tenure), while the community is left with no direct or sustained benefit.

- **CBPR approaches to research have the potential to enhance community interest in research by building greater trust and respect between researchers and communities.** There are a number of logistical, informational, attitudinal, cultural and socioeconomic barriers to the participation of individual community members in research, especially among persons of color.^{45, 46} These barriers include a common and pervasive distrust in both research and researchers, stemming from a history of abuse and exploitation in many areas (and not simply from the legacy of the US Public Health Service Syphilis Study in African Americans).^{47, 48, 49, 50, 51, 52} In considering research participation, women of color have specifically expressed the need to be treated respectfully and as individuals as opposed to just study subjects.⁵³ If the research design and methods actively engage community members in an equitable manner, trust is likely to build. A number of peer-reviewed journal articles have reported on the contribution that community-based participatory approaches can make to building trust and greater satisfaction among study participants, including in randomized control trial settings.^{54, 55}
- **Evidence is mounting that participatory models of health research are effective in bridging the gap that often exists between research and practice.**^{2, 56, 57, 58} Indeed, these models are essential to achieving the nation's health agenda, as articulated by the Centers for Disease Control and Prevention, the National Institute of Environmental Health Sciences, the National Institute of Nursing Research and the American Public Health Association, among others.^{59, 60, 61, 62}

Who is the “community” in CBPR?

There is no singular definition of community. Community can refer to a group that self-identifies by race, ethnicity, gender, sexual orientation, disability, illness, or health condition. It can refer to a common interest or cause, a sense of identification or shared emotional connection, shared values or norms, mutual influence, common interest, or commitment to meeting a shared need.⁶³ One common definition is *a group of people with diverse characteristics who are linked by social ties, share common perspectives, and engage in joint action in geographical locations or settings.*⁶⁴

In CBPR, questions such as “who is the community?” “who represents the community?” and “who speaks for the community?” are all critically important. Defining “community” in CBPR is often a search for answers to key questions such as those posed below:⁶⁵

- Are those who have a stake in the problem or issue being addressed at the table and involved in decision making roles?
- Are those most affected by the problem or issue being addressed at the table and involved in decision making roles?
- On whose behalf do patient advocates serve and speak?
- Do academic researchers have a responsibility to seek participation from all communities, or just work with the groups who are the most outspoken, or easiest, to work with?
- Is it legitimate or ethical for community members to come from only a few neighborhoods or social identity groups, thus benefiting some communities more than others?
- What if certain neighborhoods or communities are more outspoken, have greater community organizing skills, or are more comfortable negotiating with academic researchers than others?

Key Principles of CBPR

Developing community-researcher partnerships, which are successful in creating relationships and research initiatives that are locally relevant, takes time, skill and patience. A number of authors have advanced principles for CBPR. Drawing on nearly two decades of experience, Barbara Israel and her colleagues have identified eight key principles of CBPR that support successful research partnerships and are widely cited.⁶⁶ These partnerships:

1. Recognize community as a unit of identity
2. Build on strengths and resources within the community
3. Facilitate collaborative partnerships in all phases of the research
4. Integrate knowledge and action for mutual benefit of all partners
5. Promote a co-learning and empowering process that attends to social inequalities
6. Involve a cyclical and iterative process
7. Address health from both positive and ecological perspectives
8. Disseminate findings and knowledge gained to all partners

While principles are a useful guide, they should not be imposed upon a project or partnership, and they should be allowed to continually evolve to reflect changes in the research context, purpose and participants. The process of developing principles and making decisions about the partnership's characteristics is essential to building the infrastructure of the partnership itself.

Common Characteristics of Successful CBPR Partnerships

The *Examining Community-Institutional Partnerships for Prevention Research Group*, a CDC-funded collaborative, recently reported on the results of the project's aim to identify and

synthesize knowledge about CBPR partnerships, including the factors that contributed to success. The Group identified these common characteristics of successful CBPR partnerships:⁶⁷

1. Trusting relationships
2. Equitable processes and procedures
3. Diverse membership
4. Tangible benefits to all partners
5. Balance between partnership process, activities and outcomes
6. Significant community involvement in scientifically sound research
7. Supportive organizational policies and reward structures
8. Leadership at multiple levels
9. Culturally competent and appropriately skilled staff and researchers
10. Collaborative dissemination
11. Ongoing partnership assessment, improvement and celebration
12. Sustainable impact

It is important to note that there are very few reported applications of CBPR approaches in therapeutic clinical research. One randomized clinical trial identified in the literature, implemented by and with an aboriginal community in Australia for children with ear infections, employed a number of CBPR principles as outlined in sidebar and discussed in

Box 1 The Characteristics of Aboriginal Community-Controlled Health Research

- Setting the Research Agenda**
- Community-driven research is strategic and based on priority needs.
 - The power differentials between community-representative bodies and external research bodies are balanced.
 - The research focus is holistic and not just biomedical.
 - The generalisability of research findings is considered.
 - The capacity of community-controlled services is enhanced.
 - Multi-centre research involves national community-based leadership.
- Research Project Planning and Approval**
- Ethical clearance for Aboriginal health research is given by Aboriginal Human Research Ethics Committees.
 - The benefits and risks of the research to the individual and the population are carefully examined.
 - There is valid consent from community representative bodies.
 - The support that community bodies need for research to proceed is carefully appraised.
 - The trial interventions are sustainable.
 - The *time* required to plan and implement research is realistic.
 - The *cost* required to plan and implement research is realistic.
- Conduct of Research**
- There is no research without service while the problem of 'no service without research' is avoided.
 - Research coordinators have skills in cross-cultural communication and are respectful of community structures.
 - There is appropriate and informed client consent.
 - Local community-based leadership and communication networks are harnessed.
 - The approaches to data collection and management are flexible.
- Analysis, Dissemination and Application of Findings**
- The ownership of intellectual property is vested in community-representative bodies.
 - There is appropriate early community feedback.
 - Communities are enabled to document their experiences.
 - Research leads to actions promoting policy changes.

Box 1.⁶⁸ Defining these principles and specific approaches for therapeutic cancer clinical trials is a key objective of our conference series.

III. An overview of the therapeutic cancer clinical trial research system

Note: for a brief overview of how clinical trials work, see the Appendix.

As we consider the employment of CBPR principles and approaches, it is important to keep in mind the numerous systems and entities involved in cancer clinical research.

Cancer clinical trials can be run locally (in a single location or in a few institutions) or they may be run nationally (in a number of settings, including individual medical practices). Most cancer clinical trials are sponsored by governmental agencies (principally the National Cancer Institute), pharmaceutical and biotechnology companies.

National Cancer Institute: How trials are initiated and carried out

NCI sponsors a large number of clinical trials and has several programs that make clinical trials available to patients. These programs include the following:

- a) The **Clinical Trials Cooperative Group Program** brings researchers, cancer centers, and doctors together into networks called “cooperative groups.” These groups – 11 across the United States – identify research questions, and design and conduct multi-site clinical trials.⁶⁹ Each group is made up of a number of voluntary committees from member institutions which meet at least twice yearly. Each has administrative, data management, data coordination, and statistics staff at a central location. Among the 11 cooperative groups in the US, about 1700 member organizations⁷⁰ and 8000 individual investigators carry out multi-center, randomized phase 3 trials, as well as some phase 2 trials. Each year, the groups enroll some 20,000 new people in treatment trials.
- b) The **Community Clinical Oncology Program (CCOP)** makes clinical trials available in a large number of communities nationwide. Local hospitals affiliate with a cancer center or a cooperative group, which allows doctors to offer clinical trials within the community. The **Minority-Based Community Clinical Oncology Program** focuses on encouraging minority populations to participate in clinical trials.
- c) The **Cancer Centers Program** provides support to research-oriented institutions. These Centers develop their own research studies and also participate in cooperative group studies.
- d) The **Specialized Programs of Research Excellence (SPOREs)** bring together scientists and researchers to design and implement research programs that can improve prevention, detection, diagnosis, and treatment of specific types of cancer. SPOREs approach these goals through collaborative efforts within the individual multidisciplinary SPORE teams, inter-SPORE collaborations, partnerships with other NCI/NIH programs, and public-private partnerships with industry and non-profit organizations

Pharmaceutical industry trials: How trials are initiated and carried out

Today, a slight majority of cancer clinical trials are funded by the pharmaceutical industry. Pharmaceutical companies sponsor clinical trials to prove that their new agent works better than the standard treatment. This allows them to get Food and Drug Administration (FDA) approval to market the agent for a specific indication. They conduct their own research, often contracting with individual investigators, and also

fund investigator-initiated studies using their agents. Often the pharmaceutical industry collaborates on specific trials with government agencies.

Who is Involved in Therapeutic Cancer Clinical Research?

As we consider new ways to involve communities in the development and implementation of therapeutic clinical research, it is important to consider the entities involved. Five main entities enable patients to participate in clinical trials; their roles and responsibilities are described below.

a) Sponsors – such as government and pharmaceutical companies

Sponsors find qualified investigators, provide investigators with information and the drugs needed to properly conduct the trial, monitor progress, ensure compliance with government regulations, and file appropriate reports with the FDA.

b) The Food and Drug Administration and the Office of Human Research Protections

Drug studies in humans can begin only after an “Investigational New Drug Application” or IND is reviewed by the FDA and a local institutional review board (IRB). The FDA can approve the new agent for public use once a new drug application (NDA) is submitted with adequate data on safety and efficacy.

The US Code of Federal Regulations informs the role of local Institutional Review Boards (IRBs) in its charge to oversee medical research and protecting participants' safety and welfare. These regulations are enforced by two different Federal agencies:

- For clinical trials that are federally funded -- the Office for Human Research Protections (OHRP), an agency of the U.S. Department of Health and Human Services.
- For trials that are evaluating a new drug, medical device or other product that is subject to approval by the FDA --the FDA itself.

For clinical trials that meet both of the definitions above – both agencies enforce the regulations.

c) Institutional Review Boards

Before a proposed research study can begin enrolling people, the investigator must submit a detailed application to an IRB and the application must be approved. Federal regulations require that an IRB include at least five people of diverse occupations and backgrounds. At least one member must have primarily scientific interests, and another member must have primarily non-scientific interests. One member must be an institution outsider, not connected by a job or relatives to the institution.

The IRB reviews the application to ensure that:

- The risks to participants are minimized as much as possible.
- The risks are reasonable in relation to the anticipated benefits and the importance of the knowledge that may result.
- Participants will be selected fairly.
- There is a plan in place for seeking and documenting participants' informed consent and the consent document is both legally and ethically sound.
- If necessary, provisions have been made for monitoring the data collected to ensure the safety of participants as the trial progresses.
- Confidentiality and privacy provisions have been made.

Based on these considerations, the IRB approves or disapproves the clinical trial and notifies the investigator and the institution of its decision in writing. The IRB also must decide how frequently the trial should be reviewed once it is under way. Of note is that IRBs are not expected or required to assess the risks and benefits of the research to participants' communities or the broader community and most do not make this assessment.⁷¹

d) Clinical Research Team⁷² Interacting with Patients

Whether working on their own (investigator-initiated) trials or participating in a national cooperative group trial, doctors often serve as the “investigator,” advising patients on treatment decisions and presenting clinical trial opportunities to the patient.

A nurse or clinical research associate (CRA) explains the details of the trial to prospective study participants and, as part of the consent process, reviews the consent form. While patients are enrolled in the trial, they interact with other members of the team.

e) Data Safety and Monitoring Board

NIH-supported clinical trials require data and safety monitoring. Some clinical trials, especially phase III clinical trials, use a Data and Safety Monitoring Board (DSMB). A DSMB is an independent committee made up of statisticians, physicians, and in some cases, patient advocates. The DSMB ensures that the risks of participation are minimized, makes sure the data are complete, and stops a trial if safety concerns arise or when the trial's objectives have been met.

IV. How might CBPR principles and approaches be applied in therapeutic cancer clinical trial research?

Ensuring appropriate community representation

How can we ensure that the communities affected by the issue being studied are afforded ongoing and meaningful participation in therapeutic clinical trial design and

implementation? As noted above, the questions we must ask in order to define this group are more important than developing a singular definition. Who is entitled to speak for a community? Currently, many cancer advocates and survivors serve this role at the national and local levels. This representation, while important, is certainly not sufficient. As we seek to determine appropriate community representation, potential questions should include:

- Which groups are disproportionately affected by this cancer (as measured by incidence or mortality rates)?
- Which groups are at high risk for developing this cancer?
- Which groups tend to receive less than standard care for this cancer?
- Which organizations serve these groups at national or local levels?

Defining community participation

Central to the community's involvement is the question of influence. "Meaningful participation" should include the following characteristics: 1) it is systematic and required by the study sponsor(s); 2) the identification of appropriate community representatives is transparent; 3) the role and influence of the community members is genuine and clear; and 4) opportunities are provided for community representatives to play a role in approving protocols at national and local levels.

Enhancing community engagement

Recent reports on community engagement in genetics research have applicability in the cancer clinical trials arena. In a 2000 Federal report on the conduct of genetics research,⁷³ ten distinct recommendations were developed to enhance community engagement. Especially worth noting are the following: 1) Obtain broad community input for all phases of research; 2) Respect communities as full partners in research; 3) Facilitate the return of benefits to communities; 4) Ensure dissemination of accurate information to the media and the public; and 5) Provide sufficient funds for research and encourage community-researcher partnerships. These were further reiterated in a 2007 Federal report that recommends, in regards to a large population genetics study, that an assessment of the public's

Components of the cancer clinical trial research process

1. Oversight committee established
2. Research question(s) identified/concept developed
3. Trial designed (i.e., rationale, objectives, endpoints, eligibility, schema)
4. Consent form and process developed
5. Requirements for local research team developed
6. Trial submitted for approval and funding/peer review for scientific merit
7. Funding received/funds distributed
8. Trial "sign up" by local investigators
9. Institutional review board (IRB) approval and monitoring
10. Trial implementation at local level
 - Data collection protocols implemented
 - Communication of trial availability
 - Identification of potential participants
 - Screening and initial consent
 - Ongoing informed consent and communication
 - Participant retention
 - (in many cases) Data safety monitoring board (DSMB) monitoring
11. Data analysis and interpretation
12. Dissemination of findings
13. Translation of research into standard care provision

willingness to participate be made before any funding decision and that public engagement occur throughout all aspects and stages of the research process.⁷⁴

Developing community-based participatory clinical trials

A CBPR approach to clinical trials compels us to consider a new structural design to the entire clinical research enterprise – an ambitious undertaking, to say the least.

Separating the national cancer clinical research process into distinct components (see **attached Table One** and sidebar on page 14), we define how each works in the typical clinical trial research endeavor and how each could work within a CBPR framework.⁷⁵

What evidence is there (beyond published papers on individual CBPR projects) that *communities more broadly* want to engage as partners in clinical trial research? While difficult to quantify, there is evidence of interest on a number of fronts.

- *Community interest in enhancing access to cancer clinical trials through educational efforts*

The number of communities that applied for funding from the ENACCT Pilot Education Program is one indication of interest. Seventy-eight community coalitions throughout the U.S. vied for funding to implement comprehensive, community-centered outreach and education pilot programs that seek to enhance access and increase accrual to cancer clinical trials.

- *Community interest in participating in research*

Research!America poll data reveals that 60% of US adults greatly value clinical research and 63% would be likely to participate in a study, but only 6% indicate a doctor has ever made the suggestion.⁷⁶ The only nationwide study conducted to date on cancer clinical trials awareness confirmed that 80 percent believed that patients who participate in clinical trials benefit themselves and others and 80 percent said that they would consider a clinical trial if faced with cancer; and those who reported that they had a high level of understanding of the concept of a clinical trial were more positively inclined toward participation than were those with lower levels of understanding.⁷⁷

A recent meta-analysis 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, even though they appear to be asked less to participate less often.⁷⁸ Several experts have noted the harm in the common assumption that the public, especially people of color, are “distrustful” of research and research institutions, and therefore uninterested in participating in research. Rather, they note that it is the institutions' responsibility to engage in ongoing activities to gain people's trust^{79, 80} as a prerequisite for participation in research.

- *Growth in research advocacy*

Mostly volunteers affected by a disease, research advocates seek not only to change how research is conducted but also to influence decisions about what research should be funded. The literature has documented the important role of these patient advocates in clinical research study development and implementation, especially in HIV/AIDS,

and cancer research.^{81, 82, 83, 84} In cancer clinical research there is an increasingly visible role of advocates within a) National Cancer Institute-funded Cancer Cooperative Groups⁸⁵; b) US Department of Defense Research Programs⁸⁶ and c) California Breast Cancer Research Program.

In addition to assisting in clinical trial development and accrual, advocates participate in the strategic direction of Specialized Programs of Research Excellence (SPORE) projects and cores.⁸⁷ Research advocates have increased their influence in more than half of NCI's 56 SPORE sites nationwide.⁸⁸ Only 3 years after SPORE received initial funding, the advocates had become so important to its work that SPORE investigators included them as an official "core" of the SPORE program and provided them a small budget.⁸⁹

- *Community engagement in practice-based research networks*

A 2006 issue of the *Annals of Family Medicine* contains two editorials, a case study and an article on CBPR and practice-based research networks (PBRNs). The study by Westfall and colleagues surveyed PBRNs and found that more than one half have a method to engage community members and/or patients in their research.⁹⁰ While no PBRN reported full participatory methods, several reported active involvement by community members to generate research ideas, review research protocols, interpret results, and disseminate findings.

- *Community-driven policy and advocacy*

At least one CBPR-focused federal grant program – the Centers for Disease Control and Prevention (CDC)-funded Prevention Research Centers (PRC) – shows promise in this area. The community advisory boards of each PRC have banded together to form a National Community Committee, which brings a community perspective to policy and research decisions made about the program at the national level.⁹¹ Additionally, in 2004, the American Public Health Association (APHA) adopted a policy statement in support of CBPR that was spearheaded by the community-based leadership of the APHA Caucus on Community-Based Public Health.⁹²

- *Community interest in learning more about CBPR*

Between June 2004 and April 2007, more than 1,000 individuals from community-based organizations (CBOs) subscribed to a listserv devoted entirely to CBPR that is being co-sponsored by Community-Campus Partnerships for Health and the Wellesley Institute (of a 3,000 total subscriber base).⁹³ Nearly 20% of the 400 individuals who registered to participate in a January 2005 conference call on Federal CBPR funding were from CBOs. Among CBOs that participated in the call, the most frequently asked questions concerned building capacity to engage in CBPR partnerships with universities and serving as the lead applicant on CBPR grant proposals.⁹⁴

V. How are communities involved as partners in therapeutic clinical research?

As we move to consider how communities can be partners in clinical research, it is important to review specific examples of how clinical trial sponsors, institutions and individual investigators – whether in cancer or in other diseases – currently involve communities as partners in any aspect of clinical trial design or implementation. Two commonly reported ways in which community members have been involved in clinical research are through participation in Community Advisory Boards and through individual research advocacy activities. Efforts such as these have strong roots in the consumer movements of the 1960s and 1970s – the self-help, women’s health, patient rights, and environmental health movements – which advocated for changes in health care to maximize consumer participation in the control of such care.⁹⁵

Community Advisory Boards (CABs) are typically composed of community members who share a common identity, history, symbols and language, and culture.^{96, 97} An influential CAB reinforces the importance of community involvement in the decision-making process from the inception of a research study. At the national level, CABs can provide an opportunity for members of affected communities, especially clinical trial participants, to help in the design and implementation of clinical studies through ongoing interaction with researchers. CABs can provide a context for researchers and community members to discuss the intent, risks, benefits, and implications of research projects in a culturally appropriate manner.^{98, 99, 100, 101, 102}

At the local level, CAB members take information about research to their communities and relay community concerns to the researchers.¹⁰³ CAB members may also influence the informed consent process. Traditionally, the informed consent process focuses on the relationship between the researcher and the participant, each expecting that the decision about enrollment in clinical trials is an individual choice. Yet, community perceptions of research may guide individual action.¹⁰⁴ If the CAB has authentic connections to its community, its members can also transform attitudes about research.¹⁰⁵ Indeed, some have posited that the focus of the principles of ethical research outlined in the *Belmont Report*¹⁰⁶ need to be expanded to include an explicit respect for communities – perhaps through a CAB or other manner of gaining “community consent” – to supplement the individually-focused informed consent process.^{107, 108, 109}

Individual research advocates have been at the forefront of changing how cancer research is designed and implemented, and have taken on and expanded some of the roles often undertaken by formal community entities such as CABs. Similar to HIV/AIDS activists before them, cancer advocates participate in deciding what research should be funded and how it should be done. Their key activities are 1) to serve on the scientific merit review panels that make funding decisions about what research to support; 2) to advise on the scope of research studies and 3) to help design studies that

optimize patient participation. In the words of one advocate, “We don’t help accrue more patients to studies; we’re helping to make the studies more accruable.”¹¹⁰

One advocacy group, the National Breast Cancer Coalition (NBCC), has a Clinical Trial Initiative whose members work with research organizations to improve trial design and monitoring, increase access and accrual, educate the medical community and consumers, and promote initiation of breast cancer trials. The group only works with research organizations that meet specific criteria^a and its members must be able to provide meaningful input into study design and implementation.¹¹¹ In a widely cited effort,¹¹² NBCC members worked on the design and implementation of a Phase III clinical trial of the drug Herceptin®, helped design an expanded access program, served on various committees, and worked with grassroots organizations to raise awareness about the trial and facilitate patient accrual. However, in the past eight years, NBCC has been active with just five major clinical trials, which may suggest limited success in identifying clinical trial sponsors that meet the high NBCC partnership expectations, particularly in the area of advocate participation in research design and implementation.¹¹³

While these advocacy efforts have been and continue to be critically important in representing the needs of patients and in some cases broader communities, they are limited in their scope and thus insufficient in ensuring community participation in the conduct of clinical trials. Some have noted the “professionalization” of research advocacy and have questioned how well advocates represent “the community.”^{114, 115} In the end, however, all clinical trials are local; research takes place with individuals within a community through institutions. We must therefore consider this local community as we outline our vision for applying CBPR principles and approaches within clinical research.

The table below provides specific examples of community involvement at each phase of the clinical trial research process. These examples were identified through a review of literature and queries to the conference planning committee and several relevant listservs and should thus be considered illustrative but not exhaustive. It is important to note that these examples are largely drawn from therapeutic clinical research since this is the focus of the conference series. There are numerous examples of CBPR approaches used in other types of clinical research and public health studies that do not appear in the table.^{116,117, 118, 119}

^a The study must be designed to answer an important, novel question relevant to breast cancer; be well designed; be conducted ethically; adhere to commonly accepted guidelines for sponsorship, authorship, and accountability; have a mechanism to adequately address patient care costs; and adequately address NBCC’s concerns about the inclusion of a diverse population and inappropriate exclusion of specific populations.

TABLE 2: Examples of Community Involvement in the Conduct of Clinical Trial Research

Clinical trial research component	Example of community involvement
1. Oversight committee established	
2. Research question(s) identified/concept developed	<p>The “NACCHO ear trial” was a double-blind, multi-site randomized control trial for ear infections, a major case of hearing loss among aboriginal children. An indigenous, community-controlled health organization set the research agenda; planned the research; assembled the research team; gained approval; conducted the research and analysis; and disseminated application of findings.¹²⁰ Later, the study was judged the best clinical research article published in the Medical Journal of Australia in 2003.¹²¹</p>
3. Trial designed (i.e., rationale, objectives, endpoints, eligibility, schema)	<ul style="list-style-type: none"> • Cancer advocates are involved in local cancer centers and community advisory boards (CABs); the National Breast Cancer Coalition’s Clinical Trial Initiative with Herceptin, and four other major trials¹²² • Cancer advocates are involved in National Cancer Institute cooperative groups; each has patient advocates involved to some degree in trial design. • The National Institute of Allergy and Infectious Diseases (NIAID) has seven clinical research networks involving community members, with specific guidelines about membership, responsibilities, and how principal investigators must interface with the groups.¹²³ • Terry Beirn Community Programs for Clinical Research on AIDS has a national community constituency group, made of one member from each CAB. Members represent community issues – especially those of traditionally underserved groups - - on the scientific committees and protocol teams.¹²⁴ • Adult AIDS Clinical Trials Group (AACTG), the Pediatric AIDS clinical trials group (PACTG), the HIV Prevention trials Network (HPTN) and the IVI Vaccine Trials Network HVTN) each have Community Constituency Groups, which actively participate in network scientific committees and protocol teams, and have input in setting research agenda and scientific priorities.¹²⁵
4. Consent form and process developed	<p>Cancer advocates are involved in National Cancer Institute cooperative groups and local cancer centers and CABs.</p>

Clinical trial research component	Example of community involvement
5. Requirements for local research team developed	In order to receive funding announced through the 2006 NIAID request for applications for HIV/ AIDS Clinical Trials Networks, ¹²⁶ applicants needed to document meaningful community partnership; plans should include the establishment and maintenance of one or more CABs to represent the local population(s) impacted or threatened by HIV/ AIDS at the clinical research site(s) and present the research to be conducted to the community.
6. Trial submitted for approval and funding/ peer review for scientific merit	<p>The California Breast Cancer Research Program has a council that includes five breast cancer advocates, which provides vision, sets research priorities, and determines how funds are invested. ¹²⁷</p> <p>The Department of Defense Congressionally Mandated Research Programs have included consumers (explicitly defined as patients, survivors, and family members of people living with the disease under study) as full members on its peer review panels^{128, 129}and today remains the only federal agency to mandate consumer involvement. The program funds research in breast cancer, prostate cancer, ovarian cancer and other diseases.</p>
7. Funding received/funds distributed	None noted
8. Trial “sign up” by local investigators	In 1996, two CABs for AIDS treatment trials prevented two national trials from being implemented at the local sites, even though local investigators had “signed up” to participate. In both cases, the CAB expressed ethical concerns about study aims. ¹³⁰
9. Institutional review board (IRB) approval and monitoring	<p>In 2004, Siteman Cancer Center's Protocol Review and Monitoring Committee, through a subcommittee of local community leaders (Program for the Elimination of Cancer Disparities-PECaD) began a program requiring researchers to submit protocols for review and approval, as a separate but related part of IRB approval. The PECaD reviews each protocol’s recruitment and retention plan, as well as community relevance. It meets with investigators and reviews progress reports for minority accrual.¹³¹</p> <p>In 2003, Fox Chase Cancer Center developed a Recruitment, Retention, and Outreach Core facility, providing technical assistance to researchers in developing and designing recruitment and retention plans and materials; assists with implementation of recruitment plans; and educates patients and physicians regarding importance and availability of clinical trials. In addition to academics, the group includes outreach specialists, and advocacy groups with particular expertise in minority recruitment. As of 2006, it was utilized in prostate cancer screening, cancer control, and behavioral trials.¹³²</p>

Clinical trial research component	Example of community involvement
	<p>In 2000, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) developed the Health Partnership Program, which involves community partners representing various sectors of the African American and Hispanic/Latino communities of Washington, DC. A trained core group of partners meets regularly to review research proposals before they are submitted to the IRB. The contributions and comments of this core group have led to substantive changes in NIAMS research protocols.¹³³</p>
10. Trial Implementation at the local level	
a. Data collection protocols implemented	None noted
b. Communication of trial availability	<p>Cancer advocates are involved in local cancer centers and community advisory boards (CABs); the National Breast Cancer Coalition’s Clinical Trial Initiative with Herceptin, and four other major trials.</p>
c. Identification of potential participants	<p>Cancer advocate involvement in NCI cooperative groups and local cancer centers and community advisory boards (CABs)</p>
d. Screening and initial consent	<p>In AIDS vaccine prevention trials, in the mid -1990s, local CABs successfully advocated for compensation for trial-related injuries and full disclosure of information explaining the benefits and risks associated with trial participation, demanding a “patient bill of rights” for a particular trial and that the informed consent process be lengthened into several visits.¹³⁴</p> <p>The North Central Cancer Treatment Group created a core group of community advocates who are available to talk to candidates considering participation in a clinical trial. Advocates are trained about the clinical trial process and how to approach patients who have received a recent cancer diagnosis.¹³⁵</p> <p>The Vanderbilt-Ingram Cancer Center has a “Clinical Trials Mentor Program,” in which advocates (all former trial participants) mentor patients considering enrolling in clinical trials ¹³⁶</p>
e. Ongoing informed consent & communication	None noted
f. Participant retention	
g. Data safety monitoring board (DSMB) monitoring	<p>The University of Texas Health Science Center at San Antonio study included research subject advocates in the development of data safety and monitoring plans.¹³⁷</p>

Clinical trial research component	Example of community involvement
	The National Breast Cancer Coalition's Clinical Trial Initiative with Herceptin, and four other major trials.
11. Data analysis and interpretation	None noted
12. Dissemination of findings	None noted Cancer advocacy groups may discuss findings on their websites and at their national meetings.
13. Translation of research into standard care provision	None noted

VI. Barriers that Could Inhibit the Adoption of this Vision for Community-Based Participatory Clinical Trials

There are a number of significant barriers that could inhibit adoption of the vision we present in this paper:

- *Limited authority or integration of community members*

CABs can be viewed by researchers as auxiliary, or as “window-dressing;” it is important that CABs are given a meaningful role.¹³⁸ Dresser¹³⁹ argues that a research system that seeks to include community representation must do more, stating: 1) There must be a clearly defined role for community representatives, one universally implemented and accepted by all; 2) there must be training to help members make ethical judgments about research studies; 3) there must be a fair and open selection process; and 4) there must be meaningful implementation of the community’s role so that they do not just take token seats in the room.

- *Challenge of quantifying broad benefits of research*

While study participants and investigators can articulate the potential direct benefits of research (such as receiving a particular intervention), participants also expect their participation to benefit society as a whole, their particular communities (however defined), or other similarly affected persons. This broader concept of benefit is more difficult to measure, and it is harder to hold investigators accountable for its realization.¹⁴⁰

- *Limited funding for community participation*

There must be adequate support to build the capacity of community members to engage as research partners. Inequities in resources or in the means to control and distribute those resources can create tensions between community members and researchers. Resources allocated to the development and management of CABs tend to be limited and are often the first to be cut from study budgets when research priorities are considered.¹⁴¹ In government supported cancer clinical trials, the reimbursement rate is so low and labor costs are high, especially for recruitment efforts,¹⁴² that researchers are seldom able to seek community representation in their work. Further, with concerns over level or decreased NIH funding for clinical research, the community engagement “piece” is at risk of falling further down the list of priorities.

- *Additional time requirements for genuine partnerships*

Developing partnerships takes time, patience and ongoing commitment to a process. In one study, for example, developing and submitting a grant proposal to NCI using CBPR approaches took 10 months.¹⁴³

● *Difficulties in reforming a number of well-established systems and entities devoted to clinical research*

As we consider new ways to involve communities in the development and implementation of therapeutic clinical research, we are also challenged by addressing the well-established systems and entities described earlier in this paper. From the funding agency to the IRB to the work of the individual investigator, the work scope of many would need to be revised.

● *Reluctance to reform the traditional research design*

The NIH is an exclusive club with membership limited to the most specialized and recognized researchers and scientists, controlling many aspects of the national health services and clinical research enterprise, and with walls that are almost impenetrable to community.¹⁴⁴ Further, the pervasive sentiment that community participation in research comes at the price of scientific rigor, reliability and validity is a barrier to NIH “supporting” true CBPR, despite the identified advantages of the CBPR model. Academic researchers may also believe that community representatives lack the infrastructure and capacity to be full partners in achieving the research aims of the project.¹⁴⁵ Yielding power can be a problem; in one study, it was noted how university researchers were challenged when a particular health issue or research question was not prominent in the consciousness of the prioritized community.¹⁴⁶

● *Barriers to entry of new clinical trial investigators*

The barriers to enter the cancer clinical trial industry for new researchers are high. Such barriers include lack of consistency across practices for processes, need for research structure, and the need to comply with numerous regulations. In addition, there is little awareness of costs associated with cancer clinical trials.¹⁴⁷

● *A clinical trial workforce without CBPR training and experience*

The buy-in and participation of the “clinical trial workforce” is clearly critical to implementing this vision. This workforce includes oncologists/surgical oncologists/radiation oncologists – investigators who work on their own (investigator initiated) trials or choose to participate in a national cooperative group trial; research nurses, who are often oncology trained nurses, and clinical research associates. One barrier to realizing this vision is the knowledge, skills and attitudes of a clinical trial workforce that is at best unfamiliar and at worst deeply skeptical of CBPR approaches. CBPR researchers themselves have identified the need for ongoing training is needed, especially among researchers who were trained in the conventional investigator-initiated, hypothesis-driven model of conducting research. They emphasize the importance of providing CBPR training in a variety of venues and formats, “as very few researchers have undergone formal training to conduct CBPR.”¹⁴⁸

We need to consider that CBPR is not for every research study. CBPR requires a different set of values, skills and time frame than most research endeavors. Conducting research with underserved communities brings to the fore issues of power, race, class,

communication and respect. Not every researcher will agree with many of the values and principles that form the foundation of CBPR. Those who engage in CBPR must be committed to a participatory process, to community participation in the entire research process, and to delivering meaningful value and benefits to the community.

VII. Initial Recommendations for Practice, Research, Funding and Policy

Although the purpose of the first conference in the series is to develop a set of recommendations for practice, research and policy, the following are a start to realizing the vision of community-based participatory cancer clinical trials.

Recommendations for Practice

- *Communities need to participate meaningfully in trial design*

More attention should be focused on issues of trial design. If studies are not designed to address problems that are relevant to patients in minority and underserved communities, then even the best recruitment strategies will be ineffective. Similarly, trials that exclude patients with chronic conditions will preferentially exclude the elderly, members of minority groups, and patients with lower socioeconomic status, because they are more likely to have chronic conditions. There must be initiatives to design relevant and pragmatic trials, which meet the needs of local communities.

Community members need to be recognized for their unique role to the design and implementation of research studies, and research institutions should compensate them for their time and address barriers to their consistent participation (i.e., by providing childcare, transportation, parking). There should be clear expectations of community participation, which must occur early in protocol design, in research implementation and in plans for disseminating and sustaining new interventions into the community.¹⁴⁹ There must be training for community members to prepare them to participate meaningfully in this process, just as investigators need training on they ways to maximize this partnership.

- *Institutional/community partnerships need to be cultivated broadly and not be limited to any one trial*

Sufficient time should be allowed for relationships to be built with community members, including community-based providers, before accrual can begin. The period for building such relationships may take several years, but it would vary depending on the community and the existing relationships prior to initiation of the research. In addition, community partnerships need to have a broad focus, not on a singular trial.

● *Institutional commitment to building trust, diversity and cultural competency are needed*
Trust in clinical research – defined as an expectation of certain behaviors, such as reliability, competence, and power sharing – and community participation are essential to the success of clinical research.^{150, 151} There should be ongoing enhancement of the informed consent process to ensure a true understanding of risks and benefits, and involving advocates who can help explain study-related information and support participants.¹⁵² Similarly, an institutional commitment to diversity and cultural competency at all levels of the clinical trial workforce is needed.

Recommendations for Research

There are many unanswered questions about community participation in research, roles and impact of community involvement in the research process, and the model of community-based participatory clinical trial research we propose, as illustrated by the list below. Whenever possible, such studies should be linked to the implementation of cancer clinical trials, and include actual recruitment as a major outcome.¹⁵³

- What are effective strategies for engaging communities as partners in each of the phases of the cancer clinical trial process outlined above?
- What are effective approaches to delivering information about clinical trials, both at the community level and at the point of interaction with potential participants?
- What are effective strategies for recruiting underrepresented populations into cancer treatment and prevention trials and how can these be disseminated and applied in therapeutic trials?¹⁵⁴
- What are effective community-based approaches for clinical trial outreach and accrual?
- What are effective strategies for earning trust and community participation in cancer clinical trials?
- What is the impact of community participation on CABs, IRBs and DSMBs at national and local levels? What are the differences in a study's design, implementation, findings, dissemination and impact when community members serve on these bodies?
- What are community members' actual experiences of participating in clinical trials? What are community partners' actual experiences of participating as partner in clinical trials?
- What are the knowledge, skills and attitudes of the clinical trial workforce in community-based participatory approaches? What strategies for education and training are effective?

Recommendations for Funding and Policy

- *Supplement IRBs with community review mechanisms*

The principles of ethical research outlined in Belmont need to be expanded to include an explicit consideration of community consent and impact – perhaps through an entity such as a community advisory board or community review committee that can supplement the individual focus of the IRB and informed consent process.^{155, 156}

- *Improve funding for community participation*

There must be adequate support to build the capacity of community partners to engage in all aspects of research. Institutions and investigators are paid for their time, yet the predominant practice is that the community is not compensated for their time and efforts. Resources currently allocated to the development and management community engagement initiatives tend to be limited and are often the first to be cut from study budgets when research priorities are considered. Funding applications, including those from the NCI, can encourage or require investigators to subcontract to community based organizations as a way to incentivize participation, as the NIAID has done.

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IX. Appendices

Appendix A: Acronyms frequently used in this paper

AHRQ - Agency for Healthcare Research and Quality

APHA - American Public Health Association

CAB - Community Advisory Board

CBO - Community based Organization

CBPR - Community Based Participatory Research

CCOP - Community Clinical Oncology Program

CCPH - Community-Campus Partnerships for Health

CDC - Centers for Disease Control and Prevention

CRA - Clinical Research Associate

DSMB - Data and Safety Monitoring Board

ENACCT - Education Network to Advance Cancer Clinical Trials

FDA - Food and Drug Administration

IND - Investigational New Drug

IRB - Institutional Review Board

NBCC - National Breast Cancer Coalition

NCI - National Cancer Institute

NIAID - National Institute of Allergy and Infectious Diseases

NIH - National Institutes of Health

OHRP - Office for Human Research Protections

RCT - Randomized Controlled Trial

SPORE - Specialized Program of Research Excellence

Appendix B: A brief overview of cancer clinical research

Cancer clinical trials study scientific questions and try to find better ways to prevent, screen for, diagnose, or treat different types of cancer.

Types

There are several types of cancer clinical trials, the most common being prevention and treatment:

- a) **Prevention trials** test new approaches, such as medications, vitamins, or other supplements, that doctors believe may lower the risk of developing a certain type of cancer. Most prevention trials are conducted with healthy people who have not had cancer. Some trials are conducted with people who have had cancer and want to prevent recurrence (return of cancer), or reduce the chance of developing a new type of cancer.
- b) **Treatment trials** are conducted with people who have cancer. They are designed to answer specific questions about, and evaluate the effectiveness of, a new treatment or a new way of using a. These trials test many types of treatments, such as new drugs, vaccines, new approaches to surgery or radiation therapy, or new combinations of treatments.

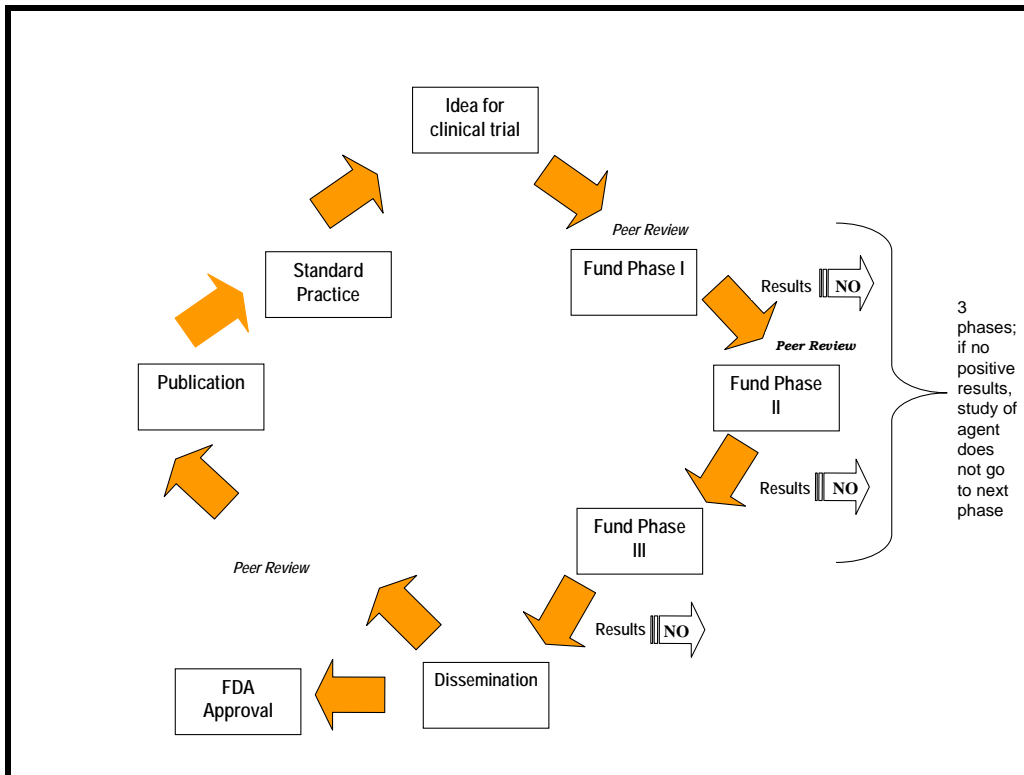
Eligibility criteria

Each study's protocol has guidelines for who can or cannot participate in the study. These guidelines, describe characteristics that must be shared by all participants. The criteria differ from study to study. They may include age, gender, medical history, and current health status. Eligibility criteria for treatment studies often require that patients have a particular type and stage of cancer.

Clinical Trial Phases

- a) **Phase I** trials are the first step in testing a new approach in people. In these studies, researchers evaluate what dose is safe, how a new agent should be given and how often. Phase I trials usually enroll a small number of patients and take place at only a few locations. If found to be safe, Phase I trials can determine a safe and appropriate dose to use in a phase 2 trial.
- b) **Phase II** trials study the safety and effectiveness of a new approach, and evaluate how it affects the human body. Phase II studies usually focus on a particular type of cancer, and include fewer than 100 patients. If found to be both safe and effective, Phase II trials can set the stage for a new approach to move into phase 3 testing.
- c) **Phase III** focus on learning how a new approach compares to standard treatment (the most widely accepted treatment, based on results of past research). Researchers want to learn whether the new treatment is better than, the same as, or worse than the standard treatment. In most cases, studies move into phase III testing only after they have shown promise in phases I and II. Phase III trials often include large numbers of people across the country.
- d) **Phase IV** trials are conducted to further evaluate the long-term safety and effectiveness of a treatment. They usually take place after the treatment has been approved for standard use. Several hundred to several thousand people may take part in a phase IV study. These studies are less common than phase I, II, or III trials.

In a best case scenario, the results of clinical trials will improve cancer care and will change standard practice. The figure below illustrates how this process works.



How clinical trials change research practice: A (overly) simple diagram

1. **Researchers develop a concept for a study, based on laboratory results or previous clinical trials.**
 - a. The concept is usually put forth for peer review at the institution or by the sponsor.
 - b. If it is a new agent, they apply to the Food and Drug Administration for an “Investigational New Drug (IND),” which gives permission to start a phase 1 trial. At this stage, the FDA decides whether it is reasonably safe for the company to move forward with testing the drug in humans. Drug studies in humans can begin only after an IND is reviewed by the FDA and a local institutional review board (IRB). The board is a panel of scientists and non-scientists in hospitals and research institutions that oversees clinical research.
2. **Phase I** trials evaluate safety. If found to be safe, Phase I trials can determine a safe and appropriate dose to use in a phase 2 trial. If a safe dose is not found, researchers stop investigating that agent.
3. **Phase II** trials study the safety and effectiveness. If found to be both safe and effective, the agent can move into phase 3 testing. If it is not found to be effective, researchers stop investigating that agent.
4. **Phase III** compares the new approach compares to “standard treatment.” If it is found the new approach is superior to standard treatment, several things can happen:
 - a. The results are disseminated through medical journals and conferences
 - b. The FDA can approve the new agent once a “new drug application” (NDA) is submitted.
 - c. The standard treatment can change as doctors use the new approach with their patients.

Patient Protection

- a) **Institutional Review Board (IRB)**
 All clinical trials that are federally funded or that evaluate a new **drug** or medical device subject to Food and Drug Administration regulation must be reviewed and approved by an IRB. Many institutions require that all clinical trials, regardless of funding, be reviewed and approved by a local IRB. The Board, which includes doctors, researchers, community leaders, and other

members of the community, reviews the protocol to make sure the study is conducted fairly and participants are not likely to be harmed. The IRB also decides how often to review the trial once it has begun

b) Data and Safety Monitoring Board

NIH-supported clinical trials require data and safety monitoring. Some clinical trials, especially phase III clinical trials, use a Data and Safety Monitoring Board (DSMB). A DSMB is an independent committee made up of statisticians, physicians, and patient advocates. The DSMB ensures that the risks of participation are as small as possible, makes sure the data are complete, and stops a trial if safety concerns arise or when the trial's objectives have been met.

c) Informed consent

Informed consent is a process by which people learn the important facts about a clinical trial to help them decide whether to participate. This information includes details about what is involved, such as the purpose of the study, the tests and other procedures used in the study, and the possible risks and benefits. Signing a consent form does not mean people must stay in the study. People can leave the study at any time – either before the study starts or at any time during the study or the follow-up period. The informed consent process continues throughout the study. If new benefits, risks, or side effects are discovered during the study, the researchers must inform the participants. They may be asked to sign new consent forms if they want to stay in the study.

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¹⁸ In its 2005 report, *Translating Research into Cancer Care: Delivering on the Promise*, the President's Cancer Panel made the following recommendations:

(Rec 17) Clinical and prevention research funders should require community participation early in protocol design and in research implementation.

(Rec 18) Research results must be shared with the individuals and communities that participate in clinical trials and other studies.

(Rec 19) Clinical and prevention research grantees should be required to include as part of the grant application a plan for disseminating and sustaining new interventions into the community.

(Rec 20) Existing community-based participatory research models should be evaluated to determine the potential for adopting them in other geographic areas and populations.

<http://deainfo.nci.nih.gov/ADVISORY/pcp/pcp04-05rpt/ReportTrans.pdf>

¹⁹ Two additional reports from the NIH and the NCI have stated similar concerns. In its 2005 report, *Translating Research into Cancer Care: Delivering on the Promise*, the President's Cancer Panel stated "Public distrust of medical research is firmly entrenched and is a significant obstacle to clinical trials participation; noted that both trust (an expectation of certain behaviors, reliability, competence, and power sharing) AND community participation are essential if research advances are to make the transition from the clinic to community." In its 2004 conference and subsequent report, *Public Trust in Clinical Research*, the NIH Director's Council of Public Representatives (COPR) stated "We need to find ways to integrate medical research into the primary health care delivery system. This solves several problems – including patient recruitment, dealing with access issues ... vesting practicing physicians, relying on known community leaders and partners, developing partnerships within the community to help with continuity of care, managing dropouts, etc. It also noted that to improve and enhance the state of clinical research, it is essential to build trust and relationships among all stakeholders. Among its many recommendations, the COPR recommended a number of actions be undertaken to help build trust through community partnerships.

²⁰ Christian, M. C., & Trimble, E. L. (2003). Increasing participation of physicians and patients from underrepresented racial and ethnic groups in National Cancer Institute-sponsored clinical trials. *Cancer Epidemiology Biomarkers & Prevention, 12, 277s-283s*.

²¹ Sung, N.S., Crowley, W.F. Jr, Genel, M., Salber, P., Sandy, L., Sherwood, L.M., Johnson, S.B., Catanese, V., Tilson, H., Getz, K., Larson, E.L., Scheinberg, D., Reece, E.A., Slavkin, H., Dobs, A., Grebb, J., Martinez, R.A., Korn, A., Rimoin, D. (2003). Central challenges facing the national clinical research enterprise. *JAMA. 2003 Mar 12;289(10):1305-6*.

²² In its 2005 final report, the National Cancer Institute's Clinical Trials Working Group (CTWG) outlined 22 strategic proposals for revamping the NCI's cancer clinical trials system and a five-year implementation plan to accomplish the changes. The report listed three proposals on patient outreach, recruitment and retention, with no mention of community-based efforts:

- Increase community oncologist and patient advocate involvement in clinical trial
- Design and prioritization to improve the rate of patient accrual, and better address practical and quality of life concerns in the design of trials.
- Increase patient and public awareness and understanding of clinical trials
- Increase minority patient access to clinical trials to improve the participation of underserved and underrepresented populations

²³ Israel, B.A., Schulz, A.J., Parker, E.A., Becker, A.B. (1998). Review of Community-Based Research: Assessing Partnership Approaches to Improve Public Health. *Annual Review of Public Health, 19, 173-202*

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* a collaborative research approach that is designed to ensure and establish structures for participation by communities affected by the issue being studied, representatives of organizations, and researchers in all aspects of the research process to improve health and well-being through taking action, including social change

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- ²⁹*Definition of CBPR. Federal Interagency Working Group on CBPR*. Retrieved 2007 from National Institute of Environmental Health Sciences Web site: <http://www.niehs.nih.gov/translat/IWG/iwghome.htm>
- ³⁰ Wagenaar, A.C. , Murray, D.M., Wolfson, M., et al. (1994) Communities Mobilizing for Change on Alcohol: Design of a Randomized Community Trial. *J Comm Psychology; Special Issue, 79-101*.
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- Evaluate patients for eligibility
 - Assist in the informed consent process
 - Ensure that protocol requirements are met
 - Write orders (with review and sign-off by a physician)
 - Ensure that follow-up tests are ordered
 - Notify the physician of dose modifications
 - Send specimens
 - Track patient visits and data due
 - Pull medical records
 - Complete data forms
 - Develop tools to facilitate efficient documentation
 - Develop and update reference guides (print and electronic) on clinical trial and protocol information

Develop a Research Team for Your Clinical Trial Program: Save Time and Physician Work, *Journal of Oncology Practice*, Vol 2, No 6 (November), 2006: pp. 296-297

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- ¹¹⁷ Freeman, E.R. et al.

The Healthy Public Housing Initiative (HPHI) was a multi-year research and service project; its focus on asthma and on pest management was motivated in large part by community concerns. Public housing residents were recruited, trained and hired to collect field data, to participate in development of policy recommendations and, to a more limited extent, to participate in data analysis, interpretation and publication.

Benefits of community consultation have been described in HIV/AIDS clinical research, genetics research, and international research.

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¹²⁴ *Add Your Voice: Opportunities for Community Participation in HIV/AIDS Research*. Retrieved March 2007 from NIAID website: http://www.niaid.nih.gov/publications/pdf/HVAD2005_addyourvoiceeng.pdf

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¹³¹ Conversation with Katherine Matthews, M.D, Assistant Professor, OB/GYN, Washington University in St. Louis, January 3, 2007

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