

BARRIERS AND FACILITATORS TO PARTICIPATION OF MINORITIES IN CLINICAL TRIALS

Gerri L. Schmotzer, PhD

Objective: Historically, researchers have experienced difficulties with the recruitment of under-represented populations, especially for women and minorities to cancer clinical trials. This has led to marked health disparities among these groups. The purpose of this literature review is to investigate barriers and facilitators that provide explanations for the low participation rate of women and minorities in clinical trials.

Methods: A search was conducted for published work in medical and social research from 1995 to 2008 using computerized databases: PubMed, CINAHL, and PsycINFO. The following MeSH terms were used; clinical trials, minorities, minority groups, participation, recruitment, research subjects, and neoplasm. This netted a total of 43 articles, 22 of which were deemed appropriate for this article.

Findings: Most striking throughout the literature was that barriers to trial participation were reported at an appreciably higher rate than facilitators. Health care provider barriers were captured by two themes: physician triage and physician knowledge. Patient barriers to trial participation emerged as reports of fear, mistrust of the medical community and the burden associated with trial participation. Facilitators to trial participation included physician enthusiasm and good communication skills, a good provider-patient relationship, having a perceived benefit, and feelings of altruism.

Discussion: This review provides a background into women and minorities' participation in clinical research. Patient recruitment into clinical trials is a complex process and there is limited research exploring the optimization of study recruitment.

Conclusions: More information is needed to understand the issues surrounding the decision making process of the potential trial participant. (*Ethn Dis.* 2012;22(2):226–230)

Key Words: Clinical Trials, Minorities, Recruitment, Research Participants, Neoplasm

From New Mexico State University, School of Nursing.

Address correspondence to Gerri L. Schmotzer, PhD; New Mexico State University; School of Nursing, PO Box 30001, MSC 3185; Las Cruces, New Mexico 88003-8001; 575.646.8169; 575.646.2167 (fax); gschmotz@nmsu.edu

INTRODUCTION

Randomized clinical trials are a method of testing new cancer therapies and provide patients with opportunities to receive state-of-the-art treatment.¹ They are considered the gold standard for evaluating new medical treatments.² Ideally, clinical trials should advance medical treatment for all patients. However, for women and minorities, the US health care system has marked disparities in the cancer burden they experience,³ particularly with respect to the rate of morbidity and mortality.

Health disparities experienced by women and minorities are significant and defined by one National Institute of Health (NIH) working group as “differences in the incidence (new cases), prevalence (all existing cases), mortality (death), and burden of cancer and related adverse health conditions that exist among specific population groups in the United States.”⁴ To overcome these health disparities the National Institutes of Health Revitalization Act of 1993 working group published guidelines that would enhance the inclusion of women and minorities in clinical research.⁵ Apart from the obvious need for wider inclusion, the medical fact underlying the legislation was the noted failure in understanding differences in drug metabolism between sexes and among racial groups. The legislative presumption was that a research population that mirrored the population at large would better allow for the generalization of study results.⁶ The legislative goal was to advance medical treatment for all patients. However, recruitment of participants into clinical trials is an arduous endeavor with less than 3% of cancer patients

The purpose of this review is to investigate barriers and facilitators that provide possible explanations for the low participation rate of women and minorities in clinical trials with a specific focus on the field of cancer research.

enrolling in research studies.⁶ Furthermore, the enrollment barriers of under-represented populations have not been studied extensively, nor is much known about the strategies used for successful recruitment and retention of minorities into research studies.⁷

BACKGROUND AND SIGNIFICANCE

Developing effective new drug treatments is enhanced by the expeditious conduct of clinical trials. But new drug development in itself is a lengthy process. Although the US Food and Drug Administration has reduced its review time from a median of 22 months in 1992 to a median of less than 12 months in 1999,⁸ the average time to develop and test a new drug is 12–15 years.⁹ One major factor increasing this development time is full patient participation in clinical trials. Not only do clinical trials provide a process for testing new cancer treatments, they also

provide patients with optimal treatment during the trial period.⁶ But Cox et al¹⁰ argued that patients who do not participate in a clinical trial may receive inferior care whereas the results for those included are associated with an increase in survival time and appear to provide both psychological and emotional benefits.

Yet in the best of circumstances, clinical trial patient recruitment is a time consuming, multi-step process: the patient must be identified; the study aims, risks and benefits must be introduced and the standard of care discussed; the concept of randomization and placebo control needs to be covered; and the study procedures have to be outlined.¹¹ In addition to a lengthy complicated recruitment process, patients' misconceptions and/or lack of information about clinical trials may compound the inherent difficulty of recruitment.

Historically, researchers have experienced even greater difficulties with the recruitment of underrepresented populations, especially for women and minorities. To evaluate and enhance study participation from these populations, factors that facilitate or create barriers to study participation need further exploration.¹⁰ The purpose of this review is to investigate barriers and facilitators that provide possible explanations for the low participation rate of women and minorities in clinical trials with a specific focus on the field of cancer research.

FINDINGS

Review Strategy

A search was conducted for published work in medical and social research from 1995 to 2008. This initial year was selected because the implementation of the NIH Revitalization Act of 1993 guidelines specifically advocated inclusion of women and minority in current research. Searches were carried out using computerized

databases: PubMed, CINAHL, and PsycINFO. The following MeSH terms were used; clinical trials, minorities, minority groups, participation, recruitment, research subjects, and neoplasm. This combination of terms narrowed the findings and netted a total of 43 articles, 22 of which were deemed appropriate for this article. The articles selected included descriptive analysis of data from clinical trial participants and nonparticipants obtained by survey or questionnaire, focus group studies with potential clinical trial participants and health care providers, prospective data obtained from health care providers and two articles that analyzed the patient recruitment patterns of several studies. Articles were excluded if they were not in English, did not address research participation or recruitment, and did not represent an underrepresented group. For the purpose of this search, an underrepresented group was defined to include women, ethnic and racial groups, elderly and/or rural population, and individuals of low socioeconomic status. While the articles reviewed were diverse, several themes surfaced regarding study participation. Themes that arose included factors that created barriers or facilitated research study participation.

Barriers to Participation

Most striking throughout the literature was that barriers to trial participation were reported at an appreciably higher rate than facilitators. Health care provider barriers were captured by two themes: physician triage and physician knowledge. In one study¹² approximately one third of patients were excluded from trial participation prior to the physician reviewing protocol availability or eligibility criteria. Go et al¹³ reports their physicians "failed to present the option of participating in a clinical trial" 7.8% of the time. Thus, patients had no knowledge of the possibility of clinical trial participation. In addition, physician bias in selecting the best participant was also found. In two studies,^{14,15} physicians

anticipated logistical problems for the patient and therefore did not offer a clinical trial. Other reported triage mechanisms were: the patient was thought to be ineligible or had poor performance status;^{1,13} the patient was considered to have reduced long-term survivability; the patient was unable to understand study requirements; and the physician's own beliefs regarding the patient's preferences.¹⁴ Additionally preventing physicians from informing patients about clinical trials were assumptions about patient non-compliance¹ and thoughts the treatment risk was too great.¹⁵

In several studies¹⁶⁻¹⁸ physicians reported lacking the knowledge and awareness of available trials in their communities. As described in Hudson et al¹⁷ study, approximately "95% of primary care physicians, 84% of specialists, and 50% of oncologists" reported the lack of awareness or having insufficient information about open, accruing studies as a barrier to enrollment in clinical trials.

Emerging from this list of patient barriers to trial participation are several additional themes. Themes that emerged were patients reports of fear, the mistrust of the medical community and the extra burden associated with trial participation. Fear of randomization was a chief concern for patients who were asked to enter a clinical trial.^{13,17,19-21} In addition, patients were fearful of the concept of experimentation, did not want to be experimented on or feel like a "guinea pig."^{14,17,21,22} A correlated barrier was trust. Specifically reported by women and minority patients was a mistrust of the medical community, in particular mistrust of researchers and sponsoring agencies as opposed to physicians and nurses.^{16,21-25} Also reported was the fear associated with a perceived loss of privacy or lack of confidentiality.²⁵ Another barrier reported in several studies was the extra burden associated with participating in a clinical trial.^{1,12,13,16,23,26} Additional clinic visits coupled with the lack of transportation

to and from the research site, as well as the distance needed to travel to the clinic created an extra burden associated with their care for potential research participants. Moreover, the additional costs related to the study procedures not covered by insurance were reported. These issues combined placed an added burden on already stressed patients and decreased the likelihood of their study participation. Thus, time, travel, and extra costs were tangible significant barriers from the patient's perspective.

Factors that Facilitate Study Participation

Several factors were apparent from the literature as facilitators to trial participation. These include: physician enthusiasm and good communication skills, a good provider-patient relationship, having a perceived benefit, and feelings of altruism. Physician enthusiasm and communication regarding research was identified as one major facilitator. Familiarity and interest in clinical research were important in identifying potential study participants.⁷ The physician's good communication skills, the ability to answer questions and explain the study rationale enhanced the prospect of study recruitment.¹¹ Clinical research associates (CRA) reported in Wright et al's¹¹ study that creating a bond of trust, using an empathetic approach and personalizing the study information all helped to alleviate a patient's fear and misconceptions of study participation, and this multi-pronged approach was stressed repeatedly in their focus groups as a method to increase study participation. In addition, they found when physicians, who were likely to be the first to suggest trial entry, used communication approaches that acknowledged the difficulties patients faced during decision making, and this assisted study recruitment.²⁷ Another major facilitator to study entry included study participants and potential participants having a good relationship and a strong belief in the provider. Specifically this was

defined as trusting the physician,^{19,25} having a desire to please the physician,^{11,14} and the physician recommending or encouraging study entry.^{11,21,23}

Perceived benefit from study participation was the major facilitator for participants. Patients who perceived they would personally benefit from study participation were the most likely to report they would enter a research study. Perceived benefits included the desire to prolong life, hope for a cure and having terminal disease.^{11,14,21,25,27} Clinical research associates also indicated patients with these beliefs would be more likely to participate in a clinical trial. Another important patient consideration included the perception that the treatment they would receive as a result of trial participation would be better since they would get extra care and monitoring.^{7,14} In addition a patient's sense of altruism or the idea that their participation in clinical research would help others and/or benefit science facilitated trial entry.^{14,19,21,25,27}

DISCUSSION

This review provides a background into the multi-faceted phenomenon of underrepresented populations' participation in clinical research. The exclusion of these groups contributes not only to poor science but questions the equality of providing quality health care to the nation's varied populations. Reports from study participants regarding the clinical trial decision making process are scarce. In addition, there is little available information describing the characteristics of study participants and nonparticipants. Patient recruitment into clinical trials is a complex process and there is limited research exploring the optimization of study recruitment. Lack of knowledge concerning the facilitators and barriers of study participation means there is no way of knowing how the process can be improved.

Underrepresentation of vulnerable groups appears to be caused by a

number of factors. A greater understanding of the importance of provider and patient factors and their interactions influencing the process of clinical trial decision making is needed. Physicians have great influence over a patient's decision to participate in research studies and their attitudes are important when identifying potential participants. It is not clear if physicians' concerns about patient eligibility are due to comorbidities, a specific patient's health literacy, whether the protocol will be adhered to or a combination of these factors. A physician's communication style and explanation of the trial's goals and requirements considerably influences whether the patient will accept or decline entry into a clinical trial. While further exploration of physician attitudes regarding patient's beliefs is needed, the failure of a physician to offer a trial due to prior patient triage is inappropriate. A greater understanding of physician-patient factors and their interactions on influencing clinical trial decision making is needed. Patient's attitudes and their decision making process when faced with trial entry need further exploration. Participation in research appeals to the self-interest of the participant and enrollment appears facilitated when the patient has prior knowledge of the clinical trial process. Nonetheless, patients and researchers must be able to truthfully acknowledge research is not without risk and that while there may be some benefit, the pursuit of scientific knowledge is the primary purpose of research.

There have been few interventions designed to increase recruitment that have a positive impact on women and minority entry into clinical studies. Strategies are needed to reduce fear and mistrust of the medical community to help facilitate trial participation in these population groups. One way is to conduct education programs for professionals that address culture, race and class, create opportunities to work with vulnerable populations and incorporate

A major barrier identified was the increased costs associated with study participation.

ethics training to enhance skills that aid in reducing distrust.

A major barrier identified was the increased costs associated with study participation. While historically study related expenses have not been covered by insurance, recent changes with Medicare's extension of reimbursement includes coverage for standard of care costs associated with clinical trials.¹³ This initiative began in September, 2000. Also a number of state governments have passed laws that require health plans to cover the cost of routine medical care for clinical trial participants.⁴ Hopefully this will have a significant impact on the financial drawbacks of participation and help to alleviate some of the barriers women and minorities face due to financial considerations.

Another barrier identified was the fear of randomization. Randomization is a difficult concept to grasp. Patients may not understand the function of a clinical trial and the rationale for treatment allocation by randomization.^{19,28} It is not known whether patients decline a clinical trial because they do not understand the randomization concept or because they do understand this concept and they wish for their physician to choose the treatment. Prior studies suggest it is the former reason combined with either a too lengthy explanation of the concept or a poor explanation by trial personnel.^{19,29,30}

Recently, Wendler et al³¹ published a meta analysis that evaluated the claim that "racial and ethnic minorities are less willing to participate in health research." The specific aim of their analysis was to determine if, when

eligible and asked to participate in research, this population consented to participate less frequently than non-Hispanic Whites. The authors identified 20 research studies that reported the consent rates by race or ethnicity for over 70,000 individuals. They found that when invited to participate in a research study, minorities were no less likely than non-Hispanic Whites to agree to participate in clinic research. These findings challenge the widespread view that the major barriers to minority participation are not issues related to mistrust or the willingness to participate but whether they have access to entry into clinical research. Efforts are needed to ensure access for women and minorities and this places the burden directly on the research community. The findings from this review suggest more research is needed to ferret out the reasons underrepresented populations are not offered entry to research at the same rate as non-Hispanic Whites.

CONCLUSION

Efforts to increase minority participation need to focus on increasing access to research, not changing minority attitudes. Information gleaned from research on the barriers women and minorities confront can be used to develop, refine and conduct research protocols. Researchers have traditionally been rigid in the implementation of protocols. The reluctance of researchers to accommodate their target populations with flexible hours and/or schedules has contributed to the persistence of low rates that vulnerable population groups experience when participating in clinical research. Additionally, there remains a need for researchers to continue to establish and maintain trusting relationships within the communities they serve. Developing trust within minority communities can potentially advance the public's health and the health care of women and minorities in general. This beginning is a crucial step to

eliminating disparities in the health status of these population groups. One suggestion made by Ehrenberger et al³² is that the utilization of nurses, as patient educator and advocates, can play an integral part in increasing understanding of the research process and possibly increase patient participation in clinical trials, especially in vulnerable/ underserved and minority populations. Clinical trial nurses are in a unique position to identify and form partnerships with community groups and conduct educational sessions to disseminate readily available information on clinical trials. Additionally, nurses act as patient advocates, form a bond with their patients and are usually able to convey complex information in a manner that increases patient understanding. A clinical trial nurse is usually well informed and educated about a specific trial and this can improve information transfer and decrease patient anxiety about trial participation.^{11,29}

Unless women and minorities are routinely included in clinical trials, the scientific value of the results is not generalizable to these populations. Therefore, more detailed information is needed to understand the issues surrounding the decision making process of the potential trial participant. In addition, more research is needed to investigate the decision making process surrounding the issue of physician triage.

REFERENCES

1. Simon MS, Du W, Flaherty L, et al. Factors associated with breast cancer clinical trials participation and enrollment at a large academic medical center. *J Clin Oncol.* 2004; 22(11):2046-2052.
2. Hussain-Gambles M, Atkin K, Leese B. Why ethnic minority groups are under-represented in clinical trials: a review of the literature. *Health Soc Care Community.* 2004;12(5):382-388.
3. Bolen S, Tilburt J, Baffi C, et al. Defining "success" in recruitment of underrepresented populations to cancer clinical trials: moving toward a more consistent approach. *Cancer.* 2006;106(6):1197-1204.
4. National Cancer Institute. States that require health plans to cover patient care costs in clinical trials. 2002;http://www.cancer.gov/clinicaltrials/

- developments/laws-about-clinical-trial-costs. Accessed November 2, 2006.
5. National Institute of Health. NIH revitalization act of 1993. 1993; <http://grants2.nih.gov/grants/olaw/pl103-43.pdf>. Accessed November 2, 2006.
 6. Brawley OW. The study of accrual to clinical trials: can we learn from studying who enters our studies? *J Clin Oncol.* 2004;22(11):2039–2040.
 7. Connolly NB, Schneider D, Hill AM. Improving enrollment in cancer clinical trials. *Oncol Nurs Forum.* 2004;31(3):610–614.
 8. Food and Drug Administration. New drug application (NDA) process. <http://www.fda.gov/cder/regulatory/applications/NDA.htm>. Accessed October 2, 2006.
 9. Pharmaceutical Research and Manufacturers of America (PhRMA). What goes into the cost of prescription drugs? ...and other questions about your medication. 2005; http://www.phrma.org/index.php?option=com_content&task=view&id=382&Itemid=119. Accessed October 16, 2006.
 10. Cox K, McGarry J. Why patients don't take part in cancer clinical trials: an overview of the literature. *Eur J Cancer Care (Engl).* 2003;12(2):114–122.
 11. Wright JR, Crooks D, Ellis PM, Mings D, Whelan TJ. Factors that influence the recruitment of patients to Phase III studies in oncology: the perspective of the clinical research associate. *Cancer.* 2002;95(7):1584–1591.
 12. Lara PN Jr, Higdon R, Lim N, et al. Prospective evaluation of cancer clinical trial accrual patterns: identifying potential barriers to enrollment. *J Clin Oncol.* 2001;19(6):1728–1733.
 13. Go RS, Frisby KA, Lee JA, et al. Clinical trial accrual among new cancer patients at a community-based cancer center. *Cancer.* 2006;106(2):426–433.
 14. Grunfeld E, Zitzelsberger L, Coristine M, Aspelund F. Barriers and facilitators to enrollment in cancer clinical trials: qualitative study of the perspectives of clinical research associates. *Cancer.* 2002;95(7):1577–1583.
 15. Paskett ED, Cooper MR, Stark N, et al. Clinical trial enrollment of rural patients with cancer. *Cancer Pract.* 2002;10(1):28–35.
 16. Fouad MN, Partridge E, Green BL, et al. Minority recruitment In clinical trials: a conference at Tuskegee, researchers and the community. *Ann Epidemiol.* 2000;10(8 Suppl):S35–S40.
 17. Hudson SV, Momperousse D, Leventhal H. Physician perspectives on cancer clinical trials and barriers to minority recruitment. *Cancer Control.* 2005;12 Suppl 2:93–96.
 18. McCaskill-Stevens W, Pinto H, Marcus AC, et al. Recruiting minority cancer patients into cancer clinical trials: a pilot project involving the Eastern Cooperative Oncology Group and the National Medical Association. *J Clin Oncol.* 1999;17(3):1029–1039.
 19. Jenkins V, Fallowfield L. Reasons for accepting or declining to participate in randomised clinical trials for cancer therapy. *Br J Cancer.* 2000;82:1783–1788.
 20. Jenkinson C, Burton JS, Cartwright J, et al. Patient attitudes to clinical trials: development of a questionnaire and results from asthma and cancer patients. *Health Expect.* 2005;8(3):244–252.
 21. Robinson SB, Ashley M, Haynes MA. Attitude of African-Americans regarding prostate cancer clinical trials. *J Community Health.* 1996;21(2):77–87.
 22. Royal C, Baffoe-Bonnie A, Kittles R, et al. Recruitment experience in the first phase of the African American Hereditary Prostate Cancer (AAHPC) Study. *Ann Epidemiol.* 2000;10(8 Suppl):S68–S77.
 23. Brown DR, Fouad MN, Basen-Engquist K, Tortolero-Luna G. Recruitment and retention of minority women in cancer screening, prevention, and treatment trials. *Ann Epidemiol.* 2000;10(8 Suppl):S13–S21.
 24. Bruner DW, Jones M, Buchanan D, Russo J. Reducing cancer disparities for minorities: a multidisciplinary research agenda to improve patient access to health systems, clinical trials, and effective cancer therapy. *J Clin Oncol.* 2006;24(14):2209–2215.
 25. Freimuth VS, Quinn SC, Thomas SB, Cole G, Zook E, Duncan T. African Americans' views on research and the Tuskegee Syphilis Study. *Soc Sci Med.* 2001;52:797–808.
 26. Pasick RJ, Otero-Sabogal R, Nacionales MC, Banks PJ. Increasing ethnic diversity in cancer control research: description and impact of a model training program. *J Cancer Educ.* 2003;18(2):73–77.
 27. Wright JR, Whelan TJ, Schiff S, et al. Why cancer patients enter randomized clinical trials: exploring the factors that influence their decision. *J Clin Oncol.* 2004;22(21):4312–4318.
 28. Ellis PM. Attitudes towards and participation in randomised clinical trials in oncology: a review of the literature. *Ann Oncol.* 2000;11(8):939–945.
 29. Jenkins V, Fallowfield L. Reasons for accepting or declining to participate in randomised clinical trials for cancer therapy. *Br J Cancer.* 2000;82:1783–1788.
 30. Sood A, Prasad K, Chhatwani L, et al. Patients' attitudes and preferences about participation and recruitment strategies in clinical trials. *Mayo Clin Proc.* 2009;84(3):243–247.
 31. Wendler D, Kington R, Madans J, et al. Are racial and ethnic minorities less willing to participate in health research? *PLoS Med.* 2005;3(2):e19.
 32. Ehrenberger HE, Breeden JR, Donovan ME. A demonstration project to increase the awareness of cancer clinical trials among community-dwelling seniors. *Oncol Nurs Forum.* 2003;30(4):E80–83.