Clinical Trials: Considerations for Women and Ethnic Minorities

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician, behavioral health professional, or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families.

Previously acting as a faculty member at Capella University and Northcentral University, Dr. Yick Flanagan is currently a contributing faculty member at Walden University, School of Social Work, and a dissertation chair at Grand Canyon University, College of Doctoral Studies, working with Industrial Organizational Psychology doctoral students. She also serves as a consultant/subject matter expert for the New York City Board of Education and publishing companies for online curriculum development, developing practice MCAT questions in the area of psychology and sociology. Her research focus is on the area of culture and mental health in ethnic minority communities.

Faculty Disclosure

Contributing faculty, Alice Yick Flanagan, PhD, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for physicians, nurses, pharmacy professionals, social workers, counselors, and therapists who utilize clinical trial results to inform practice decisions or who care for patients who are or should be involved in clinical trials.

Accreditations & Approvals

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NetCE designates this continuing education activity for 5 ANCC contact hours.

This activity was planned by and for the healthcare team, and learners will receive 5 Interprofessional Continuing Education (IPCE) credits for learning and change.

NetCE designates this continuing education activity for 6 hours for Alabama nurses.

AACN Synergy CERP Category B.

NetCE designates this activity for 5 hours ACPE credit(s). ACPE Universal Activity Numbers: JA4008164-0000-22-012-H04-P and JA4008164-0000-22-012-H04-T.

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The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

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Disclosure Statement

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Course Objective

Clinical trials are considered the criterion standard of medical research, and participation in clinical trials provides treatment opportunities for a wide variety of patients. The purpose of this course is to increase the knowledge base of healthcare and behavioral health professionals about clinical trials, particularly the representation of women and racial/ethnic minorities in these trials.

Learning Objectives

Upon completion of this course, you should be able to:

1. Analyze the various components and types of clinical trials.
2. Outline the historical and sociocultural context of clinical trials.
3. Evaluate the sociocultural, medical, and scientific research milieu in order to better understand women's and racial/ethnic minorities' roles in clinical trials.
4. Discuss arguments and counterarguments for the inclusion of women and racial/ethnic minorities in clinical trials.
5. Identify barriers that contribute to the underrepresentation of women and racial/ethnic minorities in clinical trials.
6. Identify ethical issues specific to the inclusion of women and racial/ethnic minorities in clinical trials.
7. Discuss the role of healthcare and behavioral health professionals in the recruitment and retention of women and racial/ethnic minorities in clinical trials.

Pharmacy Technician Learning Objectives

Upon completion of this course, you should be able to:

1. Outline the history and context of clinical trials, including a review of the components of clinical trials.
2. Discuss the role of women and racial/ethnic minority participants in clinical trials.

INTRODUCTION

In medical research, clinical trials are considered the "gold standard" [1]. The primary purpose of a clinical trial is to accumulate scientific data examining the safety and effectiveness of new drugs, medical devices, and interventions. As of March 2022, U.S. clinical trials represented 32% of all clinical trials registered worldwide [122]. As of March 2021, a total of 409,120 clinical trials were registered at ClinicalTrials.gov (a database that includes private and federally run clinical trials worldwide), a 16-fold increase since 2005 [122]. Between 2001 and 2005, approximately 1 in 10 adults in the United States participated in a clinical trial [2]. According to a large-scale national survey conducted in 2005 with 2,261 adults in the United States, clinical trial participation has not significantly increased or decreased since 2001 [2]. Those who did participate in clinical trials prior to 2001 indicated that they did so because they wanted to play a role in advancing science. Since 2001, there has been a noticeable change in attitudes, as financial reasons are less of a motivating factor. In 2001, 51% of the participants said they participated in a clinical trial to earn money compared with 31% in 2005. However, this is not to say that financial incentives are not a reason for some to participate in clinical trials. In one study, 50% of the 1,194 participants who had participated in Phase 1 clinical trials reported annual incomes below the national average and had an unemployment rate three times the national average [13].

In 2001, 56% stated that they participated because they felt that clinical trials might offer them better treatments for their condition; however, this declined to 46% by 2005 [2]. In a large-scale study involving 68 countries and 12,427 adults, 84.5% felt clinical trials were vital in helping to discover new knowledge about medications [160]. However, only 41.0% were actually able to name a place where clinical trials were being conducted, and only 44.9% stated that clinical trials were men-

tioned as a treatment option by their physicians [160]. According to a study published in 2016, the top two reasons given for participating in clinical trials were to help advance medicine and to improve the quality of others' lives [139]. However, there is some evidence that distrust is growing. In 2019, 85% of participants indicated that they would be willing to participate in a clinical trial, but this had dropped to 49% in 2020 [46].

Overall, women and racial/ethnic minorities are under-represented in clinical trials, with official policies specifically excluding women of childbearing age for fear of potential adverse fetal effects [111]. In response to these trends, the 1993 National Institutes of Health (NIH) Revitalization Act was passed (and updated in 2000). The Act mandates the inclusion of women, ethnic minorities, and other minority groups in all human research, and the policy also requires official documentation of this demographic data [1; 3; 4]. The Act specifically indicates that cost is not considered a viable reason to exclude women and racial/ethnic minorities from clinical trials.

The goal of this course is to provide healthcare professionals, social workers, and other allied health professionals the information necessary to appropriately guide patients and clients who might be interested in participating in clinical trials. Many healthcare professionals and social workers also work in a setting where clinical trials are conducted, and they may have a direct role in shaping recruitment efforts. Consequently, it is important for professionals to understand the sociocultural factors that affect medical research and clinical trials in order to better understand the concerns and questions patients/clients may have.

CLINICAL TRIALS: AN OVERVIEW

Clinical trials are health and medical studies that test drugs, medical interventions, treatments, and devices using human participants, with the goal of producing new knowledge [5]. Clinical trials follow a specified, standardized protocol. Typically, there are three phases [6; 7]:

- Phase 1: A small number of subjects are recruited to test a new drug or intervention for the first time. The goal of this phase is to obtain preliminary information to document dosage and side effects.
- Phase 2: The drug or intervention is evaluated on a larger sample of subjects, and the goal is to examine the effects and side effects of the drug or intervention.
- Phase 3: The goal of phase 3 is to confirm the intervention's efficacy by comparing it to an existing intervention or standard treatment. Recruitment of very large sample sizes on a nationwide scale is necessary.
- Phase 4: After a drug is approved, researchers continue to monitor the drug's safety in the general population.

Depending upon the goal of the study, the type of clinical trial will differ. Types of clinical trials include [6; 7; 112; 148]:

- Treatment trials: To test new medications, devices, or interventions
- Prevention trials: To test interventions that focus on preventing the targeted disease from occurring
- Screening trials: To evaluate interventions that detect or screen certain diseases
- Quality of life trials: To test interventions that are intended to enhance the quality of life for those already diagnosed with certain medical conditions

- Diagnostic trials: To assess products and/or processes for the diagnosis of medical conditions.
- Behavioral trials: To test and compare behavioral interventions and processes intended to improve health outcomes

Medical scientists and researchers rely on clinical trials because the experimental research designs are the most rigorous research methods to infer cause and effect. The most basic design involves an experimental (intervention) group (i.e., the group that receives the treatment/medicine), a control group (i.e., the group who does not receive the treatment/medicine), and randomization of subjects to one of the two groups. Many trials include more than one experimental group, if different interventions or doses are being compared. Randomization refers to the process whereby human subjects are randomly assigned to one of the groups; in some cases, neither the researcher nor the subject is aware of the assigned group. The goal of randomization is to guarantee that there is no selection bias, which ensures that the groups are comparable [8]. Using such a design, it is the researcher's goal to determine if there are any statistically significant differences in disease experience between the groups. If there is, the researcher would infer that the intervention caused the difference.

When they are randomized, clinical trials may be referred to as single-blind or double-blind. Single-blind studies are those in which the subjects are not aware if they are in the intervention or control group. If subjects know they are in the experimental group and are being administered the medicine, for example, there is the possibility they will describe symptom reduction or other outcomes simply because they believe the medicine is working. A double-blind study is one in which the subjects, researchers, and all members of the research team are not aware of whether the subjects are assigned to the experimental group or the control group. The goal of either blinding type is to reduce bias.

Clinical trials often have specific inclusion and exclusion criteria, but the goal is ultimately to generalize the findings to the larger, specific population being tested [161]. Many have criticized clinical trials as having too strict inclusion criteria, effectively excluding those in need of the treatment [161].

CLINICAL TRIAL REGISTRIES

Clinical trial registries are not a new phenomenon; they have existed for decades [9]. These registries are database systems that list up-to-date information about different federally and privately funded clinical trials. They give the public information about both current and completed clinical trials. The public can access information about the purpose of the clinical trial, locations, and contact information. One of the main goals of these registries is to promote transparency in the conduction of clinical trials and their findings [113].

One of the largest registries in the world is ClinicalTrials.gov, which includes both national and international clinical trials [10]. ClinicalTrials.gov was started in 1999 by the National Institute of Health [113]. Within several years, many top medical journals would not review, accept, or publish manuscripts of clinical trials that were not included in this registry [114]. Today, registered clinical trials must also submit their findings [114].

Examples of other clinical trial registries include:

- National Cancer Institute (https://www.cancer.gov/about-cancer/treatment/clinical-trials)
- National Institutes of Health (https://clinicalstudies.info.nih.gov and https://www.nih.gov/health-information/nih-clinical-research-trials-you/list-registries)
- International Clinical Trials Registry Platform (https://trialsearch.who.int)
- CenterWatch (https://www.centerwatch.com)

HISTORICAL CONTEXT OF CLINICAL TRIALS

Testing the effectiveness of medical interventions using clinical trials is not necessarily a 21st century phenomenon. Research utilizing the scientific method (gathering measurable evidence to test a hypothesis) has been conducted for hundreds of years. During the Renaissance period, a surgeon named Ambroise Parè created a wound dressing by combining turpentine, rose oil, and egg yolk and compared this with the standard intervention being used at that time [11]. Although Parè did not have a control group or random assignment of subjects, in essence he was systematically observing the effects of his medicine. Later, others recognized the importance of having a controlled comparison group. In the early 19th century, John Snow compared cholera outbreaks by examining groups served by different water pumps in London [12]. In 1881, Louis Pasteur examined the effects of anthrax inoculations on two herds of animals [12].

James Lind conducted one of the more sophisticated clinical trial protocols in 1747 in his research regarding scurvy, which was very common at the time. He conducted his clinical trial on 12 sailors diagnosed with scurvy. The control group consisted of six men who were given a regular diet. The six men in the intervention group had a regular diet supplemented with citrus items. Lind observed that the group who received the citrus supplements was cured of or did not develop scurvy [11; 14]. As a result of Lind's study, in 1865, Claude Bernard wrote a textbook advocating the use of scientific methods to test the effectiveness of current standards of medical care [162]. In 1898, Johannes Fibiger introduced the alternate-allocation method for an antitoxin for diphtheria, which involved giving the antitoxin to every other patient [163].

The U.S. Food and Drug Administration (FDA) was founded in 1862 as a governmental regulatory body to monitor and control medical drugs and therapies. In 1906, the U.S. Congress passed the Food and Drugs Act, which prompted more clinical trials to ensure the safety of medical drugs before being released to the public [115].

By 1863, placebos were introduced. Austin Flint, an American physician, conducted an experiment to examine a treatment for rheumatism utilizing an herbal extract (the placebo) opposed to the standard treatment [14; 176]. By 1923, randomization was implemented into research designs [11]. One of the first examples of randomization was documented in a study of interventions for the treatment of tuberculosis. In this study, the researchers tossed a coin to determine which half of the 24 subjects would go to the intervention group [12; 162]. The goal was to produce experimental and control groups that were similar in patient characteristics to reduce bias [162].

Regulation of drugs in the United States began with enactment of the Pure Food and Drug Act of 1906 [176]. It did not allow for interstate commerce of contaminated and misbranded drugs. In 1938, the Food, Drug and Cosmetic Act was passed, which required drug manufacturers to provide proof of a drug's effectiveness and safety before marketing. This change was spurred by the deaths of 100 Americans, mainly children who died after taking sulfanilamide [177]. In 1962, Congress passed the Kefauvver-Harris Drug Amendment, which mandates that drug manufacturers test and demonstrate effectiveness and safety of the drugs using randomized controlled studies [176; 177; 198].

Clinical trials as they are known today, with randomization of subjects, a control group, and a double blind protocol, were introduced in the 1940s. The Medical Research Council trial to evaluate the efficacy of streptomycin in the treatment of tuberculosis was the first modern clinical trial to be published [11; 15; 115].

Clinical trials and research utilizing human subjects became infamous during World War II, when Nazis conducted experiments on Jews and other groups without their consent. These atrocities were brought to the public's attention in 1945 and resulted in the creation of the Nuremburg Code, which outlined basic ethical principles for the protection of human research subjects [16].

By the 1970s, the FDA had begun to require that pharmaceutical companies submit clinical study findings demonstrating the effectiveness of the drugs they produced. This heralded the regulatory structures in the pharmaceutical field now in use [163].

In 1997, Congress passed Section 113 of the FDA Modernization Act. This law required the National Institutes of Health to create a clinical trial registry accessible by the public and regulated by the FDA, and in 2000, ClinicalTrials.gov was introduced [164]. In 2020, all parties must submit the results of clinical trials for drugs and devices registered in ClinicalTrials to their databank [199].

Today, there is a focus on patient-centered clinical trials, in which patients are both research subjects and collaborators [140]. Patients are sought to help develop reader-friendly and informative consent forms as well as study protocols and designs [140].

SOCIOCULTURAL CONTEXT IN MEDICAL RESEARCH: A TIMELINE

A knowledge of the key events that have shaped clinical trials and medical research provides a brief sociocultural and historical context. This information can give insight into the justification for certain standards.

In the 1800s, it was common practice among surgeons and medical students to practice their skills on corpses, particularly of groups who were considered "outcasts," such as the poor, members of racial and ethnic minority groups, and slaves [55]. In the United States, the south typically opted to use African American corpses [55].

In 1845, Dr. J. Marion Sims purchased African slaves for gynecological experimentations relating to vesicovaginal fistula, a condition in which a hole develops between the bladder and the vagina, resulting from childbirth [56]. Dr. Sims's experiments with African slave women eventually raised questions about the recruitment of vulnerable populations and the ethical issue of autonomy and ability to provide informed consent [56].

In the 1870s, the Comstock Act was signed into law. This Act prohibited the publication of brochures about birth control and deemed the dissemination of contraceptives as obscene. The associated laws made research regarding contraceptives difficult to illegal [57].

The American Eugenics Society was founded in 1923 [58]. The main premise of the eugenics movement was the belief that degenerative genes bred harmful behaviors, such as poverty and alcoholism. Members of the eugenics movement were racial hygienists who believed that the genes of racial and ethnic minorities were inferior [58]. Many believed that forced sterilization would curb the proliferation of degenerative behaviors. Relatedly, in 1927 the United States Supreme Court Buck v. Bell case decision ruled that poor, unwed mothers could be sterilized without their consent. The motivation behind this decision was the perceived need to prevent the production of socially questionable offspring (again, a type of eugenics) [59].

Starting in 1932, the Public Health Service conducted a study of syphilis in African American men in Tuskegee, Alabama; this is now known as the Tuskegee Study. The goal of the study was to observe the men to determine how the disease progressed over time. However, none of research subjects were informed they had syphilis. Furthermore, when the study began, there was no cure for syphilis, and when penicillin became the accepted course of treatment in 1945, researchers did not inform the research participants of the available treatment. This allowed the research to continue, but obviously it had devastating effects on the study subjects [60].

Also starting in the 1930s, with the rise of the Nazi regime, medical experiments on human subjects without their consent was encouraged in World War II Germany. After the war ended, the Nuremberg Trial was held to investigate the war crimes committed by Nazi leaders [16]. Physicians and scientists who conducted these experiments were also tried. In 1964, the Declaration of Helsinki, a code of ethics for physicians and scientists conducting research with human research participants in clinical trials, was developed [141].

In the 1940s, Henrietta Lacks, an African American woman, was treated for cervical cancer. Although she died in 1951, cervical cells from one of her biopsies were taken and replicated for medical research without her consent or the consent of her family. Research using these cells (known as HeLa cells) have enabled significant medical advances, including cancer research, the polio vaccine, anemia treatment, and infectious disease processes. Despite the widespread use of these cells, Lacks' family has never been compensated for their use [200].

The first large-scale trial studying contraceptive use was conducted in Puerto Rico in 1956. The investigators argued that Puerto Rico was an ideal place to study contraceptives because Puerto Rico was less restrictive than the United States about birth control [57]. Other contraceptive clinical trials followed in Haiti, Mexico City, and Los Angeles [57]. Although these trials did not have trouble locating research subjects, they did experience high attrition rates and many of the follow-up interventions were difficult to implement because volunteer subjects did not show up [57]. One of the ethical issues that emerged out of these studies was the protection of the rights of vulnerable populations in research. This was highlighted in a 1960s trial conducted in San Antonio, Texas, studying the effects of contraceptives with impoverished Mexican women. The women came to the clinic for the sole purpose of obtaining birth control, but they were not informed of the possibility that they might receive a placebo [61]. The Comstock Act was finally overturned in 1971; however, there were still many legal restrictions on research on birth control, and arguments regarding what constitutes obscenity continue today [57]. Also in the 1970s, the deleterious effects of thalidomide, a drug prescribed to treat hyperemesis in pregnancy, on fetal development gained widespread attention [61]. Consequently, pregnant women were designated a vulnerable population in research by the U.S. Department of Health and Human Services [61]. In 1977, the FDA barred all women of childbearing age from the early phases of clinical trials due to the controversies that surrounded the damaging effects of thalidomide and diethylstilbestrol on fetal development [59].

At the height of the crack epidemic in the 1980s and 1990s, research policies disproportionately engaged in nonconsensual testing of African American pregnant women despite the fact that white pregnant women were equally likely to use crack [59].

In 1990, another controversial study with underlying racial bias and possible violations of informed consent was conducted on infants in Los Angeles [116]. An experimental measles vaccination was given to 1,500 African American and Hispanic infants, but parents were never told the vaccination was experimental. Although none of the subjects in this study were injured, similar studies conducted in Africa and Haiti resulted in a higher mortality rate among female infants, and the study was stopped in 1991.

A report by the U.S. Public Health Service Task Force on Women's Health Issues published in 1985 argued that the historical exclusion of women from research had compromised their health care [27]. This report prompted the National Institutes of Health to implement a policy to encourage inclusion of women in federally funded research. However, this policy was not enforced [27]. In 1990, the General Accounting Office issued a report indicating that women were under-represented in NIH-funded research. When women were included, the results were rarely analyzed by sex.

This report instigated the NIH Revitalization Act, which mandated the inclusion of women, ethnic minorities, and other minority groups in all human research [3; 27]. The NIH Revitalization Act had three main goals [165]:

- Ensure inclusion of women and racial and ethnic minorities in clinical trials
- Create the Office of Research on Women's Health
- Establish the Office of Research on Minority Health

The FDA issued its *Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs* in 1993. The guidelines no longer precluded childbearing-age women from participating in clinical trials [62]. Building on this, the Food and Drug Modernization Act of 1997 was implemented. It mandated that the FDA focus on issues related to the inclusion of racial and ethnic groups in clinical trials of new drugs [63]. Investigators submitting proposals for new drugs were required to collect data on race and ethnicity [63]. In 2012, the FDA Safety and Innovation Act was passed and requires the FDA to review and include data analysis related to sex, race, ethnicity, and age into their studies for drugs and devices [142].

With the implementation of the Affordable Care Act of 2012, there is renewed interest in reducing racial disparities in health care, including clinical trials participation. The Office of Minority Health was created to promote the participation of racial minorities in clinical trials and to ensure that race, ethnicity, and sex are considered in data analysis [143]. In 2015, the FDA's Center for Drug Evaluation and Research began to publish Snapshots, which include demographic information of research subjects who participated in clinical trials, with a goal of promoting greater public transparency [201].

SOCIETAL ATTITUDES ABOUT CLINICAL TRIALS

Historically, the common societal attitude toward clinical trials was that of skepticism. Given the atrocities that occurred during World War II and the Tuskegee Study in the United States, many felt that human research subjects should be protected and that research was dangerous [117].

Only about 5% of Americans have ever participated in a clinical trial, and attitudes toward clinical trials are mixed [202]. In a 2003 national survey of 1,000 adults 18 years of age and older about attitudes toward cancer clinical trials, 32% stated they would be willing to participate in a clinical trial if asked [17]. Attitudes were generally favorable and positive, but the study did find that many did not actually understand what participation in clinical trials entailed [17; 18]. In a qualitative study of 14 patients who had participated in clinical trials and 15 who had declined to participate, the majority expressed the belief that clinical trials were necessary for the advancement of medical knowledge [18]. In a separate study, when asked about motivations for participating in clinical trials, 60% of the research participants cited societal benefits [166]. Many acknowledged that their source of knowledge about clinical trials stemmed primarily or solely from the media. Interestingly, those who had declined participation in clinical trials were generally more cautious when it came time to make the decision. Both groups expressed unease about the randomization process in part due to the expectation to receive treatment [18]. This was confirmed in a qualitative study about cancer clinical trials. Participants were concerned that they would receive a placebo, rather than active treatment, viewing this as risky [144].

In a 2016 study, 28.7% of the participants stated they would be part of a clinical trial without any further information given, and an additional 32.7% stated they would join a clinical trial after they had been given more information about the study [167].

A 2009 study of 485 patients from the Mayo Clinic found comparable attitudes [15]. More than two-thirds were interested in participating in clinical trials, but 82% expressed some doubts because they were not familiar with how to access information about clinical trials. Others felt that clinical trials should be a last resort after other options have been depleted [168].

Motivations for participation in clinical trials vary. As noted, financial incentives have traditionally been a primary motivator. In a study of 136 healthy subjects who participated in a phase 1 clinical trial, participants indicated that financial benefits were the main reason they decided to participate [19].

Not surprisingly, there was a relationship between income and education and motivation to participate, as those individuals with lower income and education levels valued the financial incentives attached to clinical trials more than individuals with higher income and education levels. Others cited more altruistic motives, such as the hope to help further medical advances and to assist future patients [20; 21; 22].

In another study, researchers attempted to distinguish characteristics of those who were willing to participate and those who stated they were not at all willing to participate in clinical trials [23]. A total of 489 individuals in Pennsylvania were randomly selected to participate in a telephone interview. One of the strongest motivators for clinical trial participation was knowing a person who was ill. Age is another motivator; individuals between 35 and 64 years of age were more willing to participate than those 65 years of age and older [169]. Similarly, a survey study that explored the attitudes of clinical trials among 150 older people found that age was an impediment, with 25% reporting they were too old for clinical studies [145].

International studies on attitudes toward clinical trials yield similar results. In an Indian study, the majority of participants were not aware of clinical trials and the different phases of clinical trials and their only reported source of information was their physicians [118]. In a 2021 study, researchers evaluated public attitudes of 1,576 research participants toward COVID-19 clinical trials in Saudi Arabia and Jordan [203]. Almost three-quarters had heard of clinical trials before, and a bit more than half (56%) held favorable attitudes. The majority (80%) stated they would participate in a COVID-19 clinical trial in order to protect their family members, and 75% stated they would participate to help society and to restore it to some sort of normalcy.

CLINICAL TRIAL PARTICIPATION IN THE UNITED STATES

The issue of participant recruitment and retention in clinical trials is an ongoing problem for investigators. In a 2017 study, almost 75% of participants stated they did not know any family members or friends who had participated in a clinical trial [170]. When examining specific types of clinical trials, it was estimated that only 3% of all diagnosed adults diagnosed with cancer are enrolled in cancer clinical trials sponsored by the National Cancer Institute [24]. In total, research indicates that less than 5% of adults with cancer in the United States have participated in cancer clinical trials [168]. A study of 2,864 adults with human immunodeficiency virus (HIV) in the United States between 1996 and 1998 found that 14% had participated in a clinical trial study on an experimental medication [25]. These studies indicate that there is a large untapped population who could be recruited for clinical trial participation.

As discussed, starting in 1993 the NIH Revitalization Act mandated the inclusion of women, racial/ethnic minorities, the elderly, and other marginalized groups in medical research. Similarly, in 1993, the U.S. Food and Drug Administration (FDA) recommended researchers analyze and report their findings according to sex, age, and race. However, according to a Government Accounting Office report, about one-third of the applications for the study of new drugs did not adhere to these policy recommendations in 2002 [26].

WOMEN AND CLINICAL TRIALS

Since the implementation of the NIH Revitalization Act, many researchers have examined gender reporting and the inclusion of women in medical studies. Many have concluded there are still gender disparities and that progress has been slow [142]. Women are less likely than men to be enrolled in colorectal cancer, lung cancer, and surgical oncology clinical trials sponsored by the National Cancer Institute [204]. As recently as 2015, the U.S. Government Accountability Office maintained that gender differences must be taken into account in clinical research and [171]. A meta-analysis of randomized clinical trials of adult cardiac surgical procedures published between 2000 and 2020, identified 51 trials representing a total of 25,425 participants [205]. In 2000, 29.6% of the study sample were women, but this dropped to 13% in 2019. Similarly, a meta-analysis of five diabetes cardiovascular outcomes trials involving 46,606 participants found that women were underrepresented, comprising 28.5% to 35.8% of the population in each study [206].

In an analysis of oncology clinical trials, female research subjects represented 39% of all lung cancer trial participants, despite the fact that women have a higher prevalence of lung cancer [172]. This was also true of melanoma (35%) and pancreatic (40%) clinical trials. In a 2018 meta-analysis of randomized controlled trials published in American medical journals (782 studies in 14 journals), 15% of the studies had enrolled less than 30% women [173].

In 2013, a meta-analysis of 304 cancer clinical trials that included women found that more than 80% of the published studies reported a white sample and 60% of the participants were male subjects [146]. Concerns remain about gender and racial disparities in clinical trial participation.

In a 2011 systematic review of publications of phase III clinical trials, only 28% of the studies made any specific reference to gender [119]. However, there has been an increase in enrollment of women in these clinical trials as the average enrollment was 37% during this time period. Although it seems as if the NIH Revitalization Act has perhaps helped increase the enrollment of women, this has not appeared to have led to detailed reporting of the impact of the interventions on women nor "whether there is or is not a significant difference of clinical or public health importance between males and females in relation to the study variables" [119].

In another study, published NIH-funded studies in four leading medical journals in 1993, 1995, 1997, and 1999 were examined to determine if women were included and if the statistical analyses took gender into account [27]. Approximately one-fifth of the studies did not include women at all, and between one-quarter and one-third of the studies analyzed the findings by gender. The authors conducted follow-up telephone interviews with the original researchers of the published studies. Of the 18 researchers who were interviewed, 6 indicated that they did not analyze the data by gender because the sample size was too small for such an analysis. One researcher indicated that sex differences were well known in the topic area, and consequently, they decided it was not worthy of publishing.

A 2001 study examined patterns of enrollment by gender in randomized clinical trials by reviewing national and international studies published in the *New England Journal of Medicine* between 1994 and 1999 [28]. During this time, 120 randomized clinical trials met the eligibility criteria of the study. Of these studies, the authors found an average of 24.6% of participants were women, and only 14% of the studies analyzed the data based on gender. The authors concluded the Revitalization Act had minimal influence, both in the United States and internationally. Experts argue that much progress is needed in the area of recruitment of women. This includes making concerted efforts for inclusion and providing necessary resources (e.g., transportation, childcare, etc.) to make it more amenable for women to participate in clinical trials [27].

In a study of published articles on federally funded randomized control studies during 2004, researchers found that women were under-represented in these studies, comprising about 37% of the sample [29]. Gender was not taken into account in 87% of the studies, and 87% did not conduct any analysis by racial or ethnic groups.

A 2007 study focused on sex-specific reporting in articles on cardiovascular trials published in leading medical and cardiology journals during a six-month period from July to December 2004 [30]. The researchers found that three-quarters of the studies did not report differences in findings between male and female participants. Approximately 7% did not list the sex of participants, and 3% did not include women in their clinical trials [30].

RACIAL/ETHNIC MINORITIES AND CLINICAL TRIALS

By far, white, married, middle-class, and well-educated men are the largest segment of the population who participate in clinical trials and health-related research [31]. The NIH Revitalization Act of 1993 was implemented with the goal of changing this trend. This law has increased the number of minority participants in NIH-sponsored clinical trials, from approximately 1 million minority research subjects in 1995 to almost 15 million in 2016 [174]. However, this gain is almost entirely the result of greater number of trials and larger trials, as the rate of racial and ethnic minority participation has remained relatively level (36.7% in 1995 compared with 37.2% in 2016) [174]. One study examined the extent to which racial minorities were represented in U.S. vaccine clinical trials between 2011 to 2020 [207]. In total, 230 trials met the inclusion criteria, with a total of 219,555 research subjects. Nearly 78% of participants were White, 11.6% were Hispanic, 10.6% were Black/African American, 5.7% were Asian American, and 0.4% were Native American/American Indian.

Black/African Americans represent 12.3% of the U.S. population, but they only represented 9.7% and 9.8% in the Moderna and Pfizer COVID-19 vaccine clinical trials, respectively. Conversely, 73.6% of the U.S. population is White, but their participation rates in the Moderna and Pfizer trials were 79.4% and 81.9%, respectively [208].

In 20 health studies representing 700,000 participants that reported consent rates by ethnicity and race, researchers found that the consent rates did not differ significantly according to ethnicity and race [32]. However, they did find that in some studies, ethnic minorities were offered fewer opportunities to participate compared to their white counterparts. Relatedly, cancer clinical trials enrollment and participation among African Americans and Hispanics declined between 1996 and 2002 [33].

This pattern is observed in the many different types of clinical trials. For example, in clinical trials of HIV drugs, racial and ethnic minorities have traditionally been under-represented. A survey study of 266 HIV patients receiving services at an urban hospital indicated that racial and ethnic minorities were less likely to participate in HIV clinical trials compared to other HIV-diagnosed patients [34]. Latino patients were more likely to indicate that they were not informed about clinical trials. In a study of clinical trials for pulmonary diseases, only a modest increase in the inclusion of racial and ethnic minorities in non-NIH funded clinical trials was noted between 1993 and 2013 (1.1% to 3%, respectively) [165]. The largest increase was among Asians or Asian Americans (0.2% to 1.9%) [165].

Another issue is lack of reporting on participant race/ethnicity. In a meta-analysis of oncology clinical trials 2003 and 2016 (1,012 trials), only 31% reported race/ethnicity [172]. Among these trials, the majority of participants (83.4%) were non-Hispanic white, while 5.9% were black/African American, 5.3% were Asian/Pacific Islander, 2.6% were Hispanic, and 0.3% were Native American.

Racial and ethnic minorities also generally perceive that clinical trials are not necessarily targeted to them as a group. A focus group study found that African Americans and Native Americans felt that they did not fit into the typical profile of those who participated in clinical trials. They described typical study subjects as those from middle or upper socioeconomic brackets, holding at least a high school diploma, and being well connected in their communities [35]. Participants also fear being exploited and may refer to past atrocities (e.g., the Tuskegee study) [175].

In a 2014 meta-analysis, researchers found that less than 2% of the National Cancer Institute's clinical trials included racial and ethnic minority research subjects as their primary sampling [147]. Furthermore, only 20% of the randomized control studies in peer-reviewed oncology journals analyzed findings based on race and ethnicity. In FDA cancer therapy clinical trials conducted between 2008 and 2018, only 25% reported race subgroups in their analyses [209].

In a 2011 meta-analysis, researchers found that there was minimal improvement in reporting sex and race/ethnicity in clinical trial publications compared to 2004, with only 21% including outcomes data by race/ethnicity [120]. Among those that did report race/ethnicity data, African American and Hispanic research subjects were under-represented relative to their overall proportion in the U.S. population.

In a meta-analysis of trials funded by the National Institute of Mental Health (NIMH) between 1995 and 2004, the great majority (91.6%) reported gender and almost three-quarters of the studies reported race or ethnicity of participants [36]. But, more than half of the studies did not provide a complete breakdown of participants by race and ethnicity, and almost 90% of these studies only reported the number of white participants compared to non-white participants.

It should be noted that there is tremendous diversity within racial/ethnic groups, and race as a single primary variable to explain differences should be avoided. For example, when socioeconomic status or other demographic variables are taken into account along with race, race is no longer a significant variable [121]. In addition, acculturation and assimilation should be considered when analyzing the role of race and ethnicity.

In summary, clinical trial participation rates among women and racial/ethnic minorities and lack of full adherence to the NIH Revitalization Act should be concerns for all healthcare professionals. These disparities in research participation can lead to an imbalance in the distribution of benefits and opportunities among certain groups, a limited generalizability of scientific findings, and continued trends in health gaps among certain groups [37]. The discussion of whether their exclusion is problematic continues to be controversial.

CONTROVERSIES REGARDING WOMEN AND RACIAL/ETHNIC MINORITIES IN CLINICAL TRIALS

ARGUMENTS FOR INCLUSION

A number of arguments have been made for the inclusion of women and racial/ethnic minorities in clinical trials. They include, but are not limited to, demographic trends, enforcement of social justice, emphasis on evidence-based practice, and differences in experiences in health conditions.

Demographic Trends

As of 2022, the U.S. Census data show there are 164.8 million women in the United States, accounting for more than half of the U.S. population [210]. There is a larger proportion of women 35 years of age and older compared to men; however, the largest difference is among the older population, with women older than 65 years of age outnumbering their male counterparts by 5.5 million

and women 85 years of age and older doubling the number of men the same age [38; 210]. It is estimated that by 2060, women will outnumber men by nearly 3 million [210]. Census projections also indicate that, by 2043, ethnic minorities will be the majority in the United States. By 2060, it is believed 57% of the U.S. population will be ethnic minorities [39]. As these groups become larger sections of the American population, addressing their specific health issues will become a vital aspect of public health.

Evidence-Based Practice

In an era of evidence-based practice, in which clinical decisions are guided by empirical data, many argue that it is not possible to recommend interventions based on studies with samples of only men or white individuals [28]. It may not be possible to generalize or extrapolate the results to other groups when they have not been targeted for study. Furthermore, the interplay between genetics and the environment is important when attempting to understand the etiology of diseases [121]. Evidence-based knowledge must be used to guide the care of women and racial and ethnic minority groups in order to prevent harm [161; 201].

Ethical Practice

One of the basic ethical tenets in research is justice; researchers should ensure the benefits and costs of the research are distributed equally [40]. Studies consisting mainly of white men would then offer men and whites the benefits and expose risks to women and racial/ethnic minorities, as the extrapolated data would not yield complete and adequate information that could be generalized to women and racial/ethnic minorities [41]. Furthermore, it has been found that participants in clinical trials tend to benefit or have better outcomes compared to those who did not participate in clinical trials [42]. Patients who participate in clinical research tend to have greater opportunities to receive innovative services that might not be readily accessible under normal circumstances [43]. Thus, the issue of inequitable distribution of the provision of health care becomes a concern [42].

Disparities in Health Conditions

In general, women and racial and ethnic minorities are more likely to self-report poor health [178]. Gender and race/ethnicity impact the prevalence and experience of health conditions, with different groups reporting variances in symptomatology and screening practices [44]. Women are more likely to suffer an autoimmune disease and much more likely to report migraines compared to men [45; 46]. Even diseases that affect men and women at an equal rate may have sex-specific manifestations and risk factors. For example, diabetes is more likely to lead to heart disease in women than men [150].

Women are also at an increased risk for hypertension and diabetes during pregnancy; yet, reluctance to include pregnant women in clinical trials due to concerns about maternal and fetal health has made it difficult for physicians to recommend certain medications due to the paucity of data examining outcomes on pregnant women [47]. It is important to produce empirical data that indicate when medications may be used safely during pregnancy and/or breastfeeding.

Differences in experiences of health conditions are also evident among various racial groups. African Americans, for example, are 1.5 times as likely as non-Hispanic whites to have hypertension [48]. They are also 30% more likely to die from heart disease compared with their non-Hispanic White counterparts [211]. Native American/Alaskan Native adults are 2.3 times as likely as white adults to be diagnosed with diabetes, and Mexican American adults are twice as likely as white individuals to be diagnosed with diabetes [49; 50].

The four leading causes of death in the United States are cardiovascular diseases, cancer, stroke, and chronic lower respiratory disorders, but despite their widespread effects on public health, there is a gap in knowledge about gender and racial/ethnic differences in the progression and treatment outcomes for these diseases. This lack of true understanding limits the ability to develop effective preventive, diagnostic, and intervention guidelines [123].

There have been racial/ethnic disparities in severity of COVID-19. In the United States, there were 62 deaths for every 100,000 African Americans, compared with 26 deaths for every 100,000 non-Hispanic White Americans [212]. These differences in mortality are related to existing health disparities in other chronic conditions, including heart disease, diabetes, hypertension, and obesity. Furthermore, African Americans and other racial minorities experience greater adverse economic and structural barrier to optimal health care, such as poorer work conditions and insurance coverage [201].

Patterns of Healthcare Utilization

Generally, women seek and utilize healthcare services more frequently than men. In a study conducted in 2000, women had a higher average number of primary care clinic visits and used more diagnostic services compared to men throughout the lifespan [51]. For example, women have a higher share in costs in both long-term care and healthcare services than men, in part because they live longer [213]. However, the general trend is that both men and women of racial/ethnic minority groups tend to underutilize health services. Specifically, disparities in accessing medical care and services continue to exist among low-income women and women of color [151]. The reasons for this pattern of underutilization are complex and include factors such as distrust in the medical system, financial barriers, institutional discrimination, and cultural value systems about help seeking. Determining the exact cause of healthcare utilization and underutilization would require the inclusion of all groups in clinical trials.

Aversive Consequences

Continued exclusion of women and racial/ethnic minorities in clinical trials could have more aversive consequences. In general, women have 1.7 times the risk of developing an adverse drug reaction compared with men [179]. Women taking FDA-approved drugs experience higher blood concentrations and longer elimination times [214]. Pharmacokinetics are often able to predict women's tendency toward higher risks of adverse drug reactions. Pregnancy can also affect the metabolism of drugs. For example, pregnancy can impact the blood levels for antiviral medications, which can influence the appropriate dosage [180].

ARGUMENTS FOR EXCLUSION

Although there are clearly many arguments for the inclusion of women and racial/ethnic minority groups in clinical trials, there are reasons given for the exclusion of these groups. Some insist that the potential benefits do not outweigh the drawbacks.

Similarities Predominate

Those who believe women need not be included in clinical trials argue that men and women are essentially the same. These individuals generally assert that if there are biologic gender differences, they may be attributed to hormones. Because hormones do not necessarily affect the disease or intervention being studied, the gender of participants would not affect the findings [40].

Some with this viewpoint also maintain that race is not an important genetic factor in clinical trials, as inter-racial mixing has diluted any differences [52]. They argue that focusing on differences may lead researchers to reinforce stereotypes. They also argue that biologic differences are not at the heart of the argument; rather, differences are largely due to social issues [215].

Need to Protect

Historically, women have been excluded from clinical trials as a means of protection. In particular, women of childbearing age were excluded due to concerns of risks to potential fetuses [142; 181]. Some have argued that menstruating women should be excluded from clinical trials so as to mitigate the potential effects of fluctuating hormones on pharmacokinetics and pharmacodynamics [161]. This has continued to be used as a justification to exclude women of all ages [142].

Variations Predominate

This argument is the opposite of the belief that persons of various genders and racial backgrounds are similar. Some individuals argue there are more differences than similarities among subgroups, which leads to too many variations in studies' findings. From this perspective, the goal is to have a very "clean" study, with a homogenous sample, so any variation can be attributed to the intervention [46; 171]. Including women and racial/ethnic minorities in clinical trials would make interpreting the data more of a challenge; subgroups should be studied independently [40].

Gender Differences Not Significant

Some researchers argue that the question of whether there are differences in treatment efficacy between men and women is insignificant [124]. The proportion of treatment to which men and women respond differently is unclear, and it has been suggested that apparent differences may be attributed to other factors, such as gene expression [124; 142].

Lack of Clear Benefits

There are some who argue that the benefits of participating in clinical trials are overstated [53]. These individuals believe that it is important to note that participation in clinical trials is not long term and does not provide services or medication after the study is completed. Furthermore, medical care associated with a clinical trial is often not free [53].

Logistics and Costs

Recruiting, enrolling, and retaining women and racial/ethnic minorities in clinical trials can be difficult, and some argue that this can prevent important research from being completed [40]. In order to recruit and retain enough women and racial/ethnic minority participants to ensure there is enough statistical power to analyze, the sample size and resources necessary increase substantially. Some argue that women add complexity to studies, which ultimately increases the cost [142; 179]. In one study, adding the analysis of gender and race into the equation would have increased the cost of the study more than tenfold, from $115 million to $1.846 billion [54]. Furthermore, women are more likely to have competing domestic demands and responsibilities (e.g., child care) [182]. This would exacerbate the cost.

Legal Liabilities

Some researchers are concerned about the legal liabilities if participants are pregnant or become pregnant during the clinical trial. Many institutional review boards and investigators include pregnancy as an automatic exclusion criterion due to the fear of risks [47]. The main concern is that the intervention might affect the fetus or trigger a miscarriage, exposing the researchers and/or funders to potential legal action [40; 46].

BARRIERS TO PARTICIPATION IN CLINICAL TRIALS

In addition to institutional barriers, women and ethnic minorities experience their own barriers to participation in clinical trials. Personal fears and anxiety, mistrust, and cultural values can all affect willingness to enroll in scientific research.

FEAR AND ANXIETY

The perceived physical risks associated with injections, needles, and intrusive interventions can impede many from participating in clinical trials. Furthermore, many are concerned that ultimately there will be minimal personal benefits of participation [64]. In a survey of 1,256 research participants, the highest rated barriers involved fear and anxiety. Specifically, the participants feared potential side effects, expense not covered by health insurance, and ineffective treatment or placebo [152]. In a 2007 study, women expressed greater concern about the risks involved in clinical trials than men [65].

One of the prominent images associated with medical research is the research subject becoming a human "guinea pig" [175; 183; 216]. For example, one African American woman who was eligible for a smoking cessation clinical trial study opted not to enroll because she did not want "anyone playing with her mind" [66]. In a 2011 study of African Americans with HIV infection who had participated in a clinical trial, many stated that they were fearful of simply being treated like the subjects in the Tuskegee Study [125]. In another focus group study of Chinese immigrants and service providers, some Chinese immigrants from the community likened clinical trials to "experiments with animals" [67]. In fact, in some languages, the translated word for "clinical trials" is closer to the word "experiment," which unfortunately evokes fear in some patients [68]. This image is also associated with the general belief that certain groups are more vulnerable and more likely to be taken advantage of. In a cross-comparison study with 623 whites, 353 African Americans, and 157 Hispanics, women and racial minorities were more likely to believe that women are taken advantage of in biomedical research [69]. After controlling for socioeconomic status, African Americans were four times more likely and Hispanics were twice as likely as whites to believe that women are taken advantage of in medical research.

Finally, many individuals do not have a full understanding of clinical trials, and this can compound individuals' fears and anxieties. Research indicates that African Americans tend to have less subjective and factual knowledge about clinical trials compared with their white counterparts [184]. Factual or objective knowledge can be measured with questions with a specific answer, while subjective knowledge refers to a person's assessment of their own knowledge. A survey study found that deficits in subjective knowledge tended to predict declining to participate in clinical trials; lack of factual knowledge did not appear to affect participation [184]. In a study conducted in 2006 in an African American community, many participants misunderstood the concept of placebos [70]. Participants in the study conveyed that the use of placebos meant some people would not receive medication. They did not comprehend why the medication or intervention would be denied to patients who needed it for health concerns. This was also reported to be correlated with the atrocities committed in the Tuskegee Study [70].

MEDIOCENTRIC PRACTICES

The way that information is presented to research participants, with the use of technical language and jargon, can impede participation. Use of many unfamiliar technical, legal, and medical terms, for example, can foster anxiety and uncertainty. One study found that the largest barrier to women participating in a clinical trial was how well the study was explained [185]. It is important to remember that medical and legal terms and the many acronyms researchers use in their normal day-to-day professional vocabulary are not part of the language used by laypersons. These "unfriendly" terms end up excluding persons who have not been socialized in the medical profession [71; 185]. In a study of 353 breast cancer clinical trial sites, very few offered information in other languages and not all sites offered interpreting services for those with limited English abilities [153]. Minimal supplemental information was provided about the clinical trial. In a qualitative study, the majority of the Latino/a participants argued for materials in Spanish, written in a more reader-friendly manner [154]. For those not proficient in English, use of medical language can be intimidating, which can ultimately create a dichotomy of an "us" and "them" (i.e., researchers and participants) [185].

It is important to note that some terms have cultural connotations. The Spanish word *investigaciones*, for example, can be misconstrued to mean police investigation in some Hispanic cultures, particularly for those who come from more politically repressive countries [4]. Those who are undocumented may also be concerned enrollment in a clinical trial could trigger investigation of their legal status [217]. Clinical trials and health-related research studies are often conducted at medical

centers or academic institutions, which may be more convenient for researchers or sponsors of the research rather than the participants [71]. It is possible that this type of environment reinforces the "doctor culture," which could alienate research participants. Research studies and clinical trials are also based on the notion of medical individualism; however, for many cultural groups, family and social relationships are at the heart of decision-making, including decisions related to health [126]. Furthermore, the logistics and inconveniences associated with traveling to research sites may compound potential participants' fears.

The Consent Process

The goal of the consent process is to ensure that research participants understand the nature of the study and are able to make an informed decision whether to participate or not. However, many consent forms, particularly in clinical trials, are not easily comprehensible. Most consent forms are written at a college reading level; the average American reads at a fourth-grade reading level [72]. In one study of 287 adult participants in a clinical trial who had read and signed a consent form, approximately 75% of the participants did not understand the treatment discussed and half could not identify the risks and benefits of the study [73].

In another study of consent forms from HIV clinical trials, researchers found that the median length of a consent form was 22.4 pages, and the median reading level was grade 9.2, although this varied by section [127]. For example, the median reading level of the confidentiality section was grade 12.35. This is of particular concern because the average American's reading level is estimated to be at grade 4, which does not take into account persons for whom English is not their first language.

Many simply do not understand consent forms, and the long forms and complicated language may be a cause of suspicion among racial and ethnic minorities. Some believe that signing a consent forms means that they are waiving all of their rights [186]. Generally, low health literacy among many individuals is a barrier to clinical trial participation [216; 218].

Referral Systems and Communication Processes

Because most clinical trials take place at academic or medical centers, they may not be well-known by general practitioners. If physicians are unaware of trials, they will not refer their patients to them, and in many cases, direct referral is the sole way to access clinical trials [175]. Lack of patient-provider communication makes it difficult for clinical trials to recruit potential participants. At the same time, clinical trial investigators do not appear to make an effort to recruit hard-to-reach populations because of the costs and time associated [187].

Matched Researchers

In a study with African American and Hispanic individuals with HIV, researchers found that the decision to participate in a clinical trial was improved when the researchers and interviewers on the trial team looked like the research participants and spoke the same language [125]. This speaks to the importance of racial/ethnic matching [188].

This theme also surfaced in a qualitative study with Hispanic and Latino/a participants. Both groups reinforced the importance of racially diverse research teams. In addition, they suggested staff should be coached on how to communicate with diverse cultural groups [154].

MISTRUST

Experiences with negative and discriminatory practices in the healthcare system have bred institutional mistrust, and this can act as a barrier for racial/ethnic minorities participating in clinical trials. The distribution of smallpox-inoculated blankets to Native Americans, the forced relocation of Native Americans to reservations, slavery, medical experimentation on African slaves during the antebellum period, among many other studies, have resulted in mistrust on the part of women and racial/ethnic minorities toward government institutions and, by extension, government-funded research [74]. Fear that information will be withheld from them, general suspicion of the use of control groups, and wariness due to a repeated history of unethical practices continue to be bar-

riers to clinical trial participation [216]. Some have cited the theft of Henrietta Lacks' cells and withholding medical information as events that could recur [218]. In a systematic review of studies of racial and ethnic minority participation in clinical trials, 77% of the studies identified mistrust of the medical establishment and clinical trials [219].

Legacy of the Tuskegee Study

The Tuskegee Study has become a symbol for the historically discriminatory practices in medical research for many racial/ethnic minorities, particularly African Americans [75; 216]. Despite the fact that the Tuskegee Study was initiated more than 70 years ago and many African Americans are unable to describe the specific details of the study, many patients are able to associate the government's role in perpetuating the discrimination and abuse of African Americans [76]. In a focus group study, younger African Americans had heard about the Tuskegee Study and continued to express doubt about scientists and researchers [70]. However, some have suggested that the information that the public has about the Tuskegee Study may be based on perpetuated myths and inaccuracies [128]. In a 2011 study, although many of the study respondents had heard of or knew about the study, only a small portion could relate accurate details about the study [128]. For both white and African American participants, higher educational levels were related to a higher degree of detailed knowledge about the study.

Conspiracy Theories

In addition to historically accurate instances of discriminatory research practices, many conspiracy theories regarding clinical trials exist. These conspiracy theories generally refer to beliefs regarding genocidal plots orchestrated by the government and certain hegemonic groups to exterminate racial groups [74; 75; 77]. For example, some believe that the U.S. government deliberately invented HIV and crack to exterminate minority groups [75]. In a telephone survey study of African Americans, researchers found that almost one-third who participated believed that acquired immunodeficiency syndrome (AIDS) is a deliberate plot against blacks, and 30% of men and 24% of women agreed that HIV was produced in a government laboratory for this purpose [78]. During in-depth interviews, African Americans specifically linked conspiracy theories to HIV clinical trials, and by extension they associated participation with being expendable [79]. In a Texas-based study, more than 25% of African American participants and more than 20% of Hispanic participants reported believing conspiracy theories about HIV being a means of genocide for certain racial groups; fewer than 10% of Asian participants held the same beliefs [129]. In a study of 46 Native Americans, one-third (15) believed that HIV/AIDS was purposively created by whites, the U.S. government, or Christians to spread dominant "white" values [77].

Some individuals express concern regarding how research data will be utilized to portray their communities [80]. Some people have had negative experiences with researchers who collect data and leave immediately afterward without any interaction with the community [81]. As such, many communities view researchers with wariness, concerned that the research studies will have negligible outcomes or adverse results. For example, in one study of syphilis in a Native American community, identifying information about the community was released and the community was ultimately ostracized [82]. Another study on a Native American tribe and alcoholism led to a negative credit rating for the tribe. This type of behavior by researchers has resulted in many communities mistrusting researchers, fearing that the data will reinforce negative stereotypes [82].

CULTURAL VALUES

Some cultures adhere to the belief that language can dictate the course of events [83]. For example, in many Asian cultures, talking about illness or death is believed to bring about bad luck [84]. Within this context, it is understandable that some racial and ethnic minorities will be reluctant to participate in health-related research because of the emphasis on illness symptoms and discussion of risks [1; 85]. Furthermore, in Western industrialized countries, knowledge acquisition is viewed as a right, but in other cultures, community leaders serve as gatekeepers of knowledge [86].

Cultural differences in gender roles can compound the difficulties women experience participating in scientific research. Having to balance responsibilities of childcare, household-related tasks, and caring for other family members, ethnic minority women are more likely to not prioritize their own healthcare concerns [87]. Depending on the cultural group, assigned gender roles can play a prominent role in whether women will participate in health-related research. For example, due to a patriarchal culture, Korean men assume positions of authority and key decision making, and husbands or other male figures might "forbid" Korean women to participate in health-promoting activities, such as medical research [88].

Western society tends to place emphasis on medical interventions such as vaccinations, immunizations, and antibiotics. In part, this is a reflection of Western biomedical ethos, which is based on individualism and competitiveness [71]. However, many other cultural groups tend to have a more collectivistic and fatalistic orientation, whereby disease and illness are believed to be natural occurrences, not something to fight [71]. For example, some Americans' strong spiritual and religious convictions can impede participating in clinical trials if they adhere to the belief that healing belongs in the hands of God and that they should trust God's plan [216]. Being aggressive in seeking expensive and time-consuming procedures can be perceived as selfish, drawing attention to oneself and not focusing on the family or extended family system [68; 71]. This orientation could impede medical research participation.

Cultural beliefs can also affect an individual's view of specific health practices and treatments. When discussing participation in clinical trials that involve drawing blood, some Native Americans express concern that the blood samples would be saved after the individuals die; consequently, the person's soul would be unable to rest [89]. Similarly, some groups view tissue sampling as a violation of the human body, which is sacred and should remain in its natural state [90]. In Chinese culture, some believe that having blood drawn is a sign of disrespect to one's ancestors [92]. Some Asian cultures also believe that drawing or giving blood depletes the life source or life energy, negatively affecting health and vitality [92].

RIGOROUS EXCLUSIONARY CRITERIA

Clinical trials frequently have very specific and rigorous criteria for inclusion in and exclusion from enrollment. This is meant to be an added safety mechanism for research participants, but it can make clinical trials more inaccessible [186]. In addition, if certain exclusion criteria are more common among ethnic/racial minorities, this can lead to under-representation in trials. For example, African Americans often have higher incidences of conditions such as hypertension, heart disease, and diabetes compared to the general population, which can affect participation rates. If clinical trials require research participants to be in excellent health, racial minorities may be disproportionately excluded [130].

PRACTICAL LOGISTICS

Some barriers to clinical trial participation are purely logistical, such as not having access to technology, time, finances, or transportation to get to clinical trials for various tests and follow-up [219]. For example, in a study with Native American Indian college students, one of the barriers cited was distance of the study site [155]. Examining patients enrolled in trials registered between 1993 and 2014 in University of California San Francisco Clinical Trial Management System database, the median one-way trip to the trial location was 25.8 miles [189]. Individuals from low-income areas traveled a median 58.3 miles, compared with just 17.8 miles for patients from higher-income areas. As such, providing transportation to the study site is crucial, if possible [156]. Some individuals will not have telephones or Internet, so research staff will be unable to easily remind them of follow-up appointments [64]. Conflict with job responsibilities and the hours of operation of clinical trials make it difficult for many participants to attend the scheduled appointments [64]. Women's multiple roles may impede participation because they feel they do not have enough time. Lack of childcare is also often cited as a reason for not participating in clinical trials [64].

OVERVIEW OF ETHICAL ISSUES

In 1974, the National Commission for the Protection of Human Subjects was formed. In 1979, the Commission published *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. This report recommended that all institutions receiving federal research funding establish institutional review boards. *The Belmont Report* laid out three ethical principles to guide researchers to ensure that the rights of research participants are protected: respect for persons, beneficence, and justice.

RESPECT FOR PERSONS

The principle of respect maintains that all individuals are autonomous and that individuals with limited capacity to make autonomous decisions must be protected [93]. This ethical principle is translated into two practical applications in clinical trials. First, research participants must give informed consent; adequate information about the study must be communicated to participants so they can make an informed decision whether to participate in the study or not. In order to make an informed consent, participants must be able to comprehend the information provided. Researchers and practitioners should keep in mind the following questions:

- Is the information presented in a clear and organized manner?
- Is the information written at the appropriate reading level?
- For those whose English proficiency is limited, are consent forms translated in the targeted language?
- For those who cannot read, is the informed consent form provided in another format (e.g., presented orally, videotaped)?

For adult women of childbearing age, informed consent is based on the expectations that the woman will consider her own interests as well as the fetus's [94].

Informed consent in clinical trials is particularly important because many people mistakenly assume they will be assigned to the experimental or control group based on their own therapeutic needs [61]. In other words, many people believe they will receive treatment tailored to their medical condition if they participate in research [61]. Consequently, the language used on consent forms must be carefully scrutinized. For example, if researchers use the term "treatment" to mean "study procedures" or the term "patients" to mean "research subject," participants might assume that they are receiving certain treatments [61].

In a content analysis of placebo-related information in pamphlets and leaflets given to participants in clinical trials, 84% of the material stated that individuals had a 50% chance of receiving the placebo [131]. Placebo was often defined as a "fake" treatment made to look like the genuine medicine but containing no active ingredient. The pamphlets/leaflets focused on the benefits and risks of the treatment but rarely talked about benefits or risks from the placebo. If informed consent is considered a process (not just a single event), it is important for healthcare providers to continually communicate information about the study, definitions of terms, and possible benefits/risks to potential research subjects.

The second application of respect for persons is voluntary participation. Researchers and practitioners should consider the following questions [95]: Have research participants voluntarily agreed to participate in the study, without influence by any undue pressure or coercion? What is the relationship between the individual who presents the research information and the research participant? For example, do women or immigrants perceive that the healthcare provider is in a more powerful position that could adversely affect their healthcare services if they decide not to participate? Some may feel they will receive substandard services if they do not participate in the study [94]. In addition, the application of the ethical principle of voluntary participation must be placed in a cultural context. As discussed, autonomy, individualism, and self-determination are highly valued in Western societies, especially in the United States. However, in collectivistic societies, it is vital to remember that decision making is group-oriented and the patient may utilize another decision-maker who is accorded authority and respect (paternalism) [96]. Therefore, autonomy will have different connotations in cultures where paternalism is valued [95].

Finally, research participants should be treated with respect, with acknowledgement of their volunteered time and participation. At a minimum, this includes being informed of the findings, maintaining privacy and confidentiality, and having general welfare monitored and protected [220].

BENEFICENCE

Beneficence refers to ensuring that the beneficial outcomes of the study are maximized and the risks are minimized. This includes benefits to the research participant and benefits to the overall knowledge gained for science [97].

Benefits to participation in clinical trials can include [112]:

- Patients receive comprehensive and regular services from physicians, nurses, and other providers to whom they may not necessarily have access.
- Patients may access new treatment options that are not yet available to the public.
- The clinical trials treatment might be more effective than the standard treatment prescribed.
- Ultimately, patients are contributing to science and society.

Risks to participation in clinical trials can include [112]:

- The side effects to the clinical trials treatment may not be completely known and may be worse than the standard treatment.
- There is a time cost to patients. Patients are often required to be seen by members of the clinical trials team for evaluation as well as complete surveys, respond to interview questions, and participate in other aspects of data collection.
- There is an equal chance that patients will not receive the tested treatment.
- It is possible that the treatment in the clinical trial is less effective than the standard treatment.

Any adverse consequences should be clearly communicated in consent forms. If an adverse incidence does occur, there should be a mechanism in place whereby participants can convey the incident [190].

For women of childbearing age in clinical trials, unbiased information regarding the risks involved both to the individual and the potential fetus should be presented. Any explicit explanations about the responsibility to protect the fetus should be clearly stated in the consent process [98]. Ultimately, providers should review both the benefits and risks to patients and give them time to process the information and make a decision.

JUSTICE

As discussed, justice in clinical trials raises the question about who should receive the benefits and who should bear the burden of research [93]. It is important to ask who would benefit from the study—the research participants, the researchers, the sponsoring agencies/organizations, or those who have the medical condition [99]. It is also important to assess which groups will have an opportunity to access clinical trials and if any groups risk being marginalized [191]. If the study benefits everyone except the research participants, is that acceptable? What if a medication is too expensive for the participants to easily access after the experimental research is completed, or if the side effects of the intervention are painful [99]? Ultimately, injustice results in inequities, or the unfair distribution of benefits and burdens/risks due to structural factors [221]. These questions must be evaluated in order to adhere to the ethical principle of justice.

ROLE OF HEALTHCARE AND BEHAVIORAL HEALTH PROFESSIONALS IN CLINICAL TRIALS

When the goals and philosophies of the research team and the targeted sample community are aligned, recruitment and retention will be enhanced. This does not occur automatically; it takes concerted effort, time, and resources to build these relationships. Social workers, nurses, and other health professionals are in unique positions because they are often at the frontline of client/patient contact. They are not only facilitators but also advocates, ensuring that research participants are empowered and their rights are protected [94].

Providers should ask the following questions and have their patients consider the answers when considering if a clinical trial is a good option [191]:

- What are the outcomes with the current care that the patient is currently receiving? How would it compare with standard treatment?
- Would participating in the clinical trial increase the patient's survival to the extent it would not otherwise with the current care being received?
- What are the side effects of the clinical trial?
- Are there are other clinical trials?
- What does the patient want to do?
- Does the patient understand all the implications of participating (or not) in the clinical trial?
- Who is supporting the patient in the decision? Who is not?

GUIDELINES FOR RESEARCH RECRUITMENT

The term "hard-to-reach populations" has been used to categorize certain groups who are not easily accessed or served due to cultural, economic, and geographic factors. While some groups may be difficult to access, such as those in rural or frontier areas, others just may not have been the subject of outreach on the part of researchers [88]. There are several basic guidelines that might be helpful in recruiting women and racial/ethnic minorities to medical research. The first is having knowledge of the lifestyles of the group being targeted. Experts have emphasized the need for researches to understand the unique cultural and social practices of the group being targeted [88]. For example, when recruiting women to participate in a clinical trial, it may be important to offer evening and weekend hours in order to accommodate childcare needs, household responsibilities, and work schedules.

As noted, clinical trials and health-related research studies frequently take place at medical centers or academic institutions [71]. While these locations may be convenient to the researchers or sponsors, they may not be convenient to participants who are unfamiliar with the area or the local transportation system. The environment may be foreign and could potentially breed institutional distrust [71]. Healthcare professionals can play a vital role in mediating this perceived gap by facilitating access to clinical trials and resources and developing rapport with potential participants so they feel involved in the research process [64]. For example, in a study of Korean immigrants, study sites were located in areas where Korean Americans and immigrants frequented, such as ethnic grocery stores [88].

Word-of-mouth from individuals who are perceived to be trustworthy has been found to be the most effective recruiting method in underrepresented groups [100; 101]. In a cancer screening study targeted to older Filipino women, personal invitations from people whom the potential participants knew were a crucial factor in decisions to take part in the study [100]. This phenomenon was replicated in recruiting and retaining Hispanic research participants for a longitudinal study [101]. Initially, the researcher mailed flyers and conducted community presentations, but these efforts did not result in enrollment. However, when a community representative approached individuals one-on-one, enrollment increased. Some experts recommend message-mapping to ensure that communication to potential participants are evidence-based, intentional, systematic, and clear, using a variety of communication mechanisms [222]. Scripts are written and analyzed for clarity and comprehension. Key messages, with three to five supporting points, should be clearly communicated.

Collectivistic groups are more likely to value the process of relationship building, and this can be a key part of research outreach. In a study exploring differences in interactions of black and white patients with oncologists, black patients' interactions were briefer than their white counterparts [157]. There were also fewer mentions of clinical trials and less discussion about the nature of the various clinical trials offered. In a study that targeted Hispanic women for a dental disease prevention study, the cultural value of *personalismo* (or personal contact) was emphasized [102]. Direct, personal contact is beneficial for Latino/a participants because this type of communication reinforces cultural values regarding the importance of developing relationships that promote trust (*confianza*) and respect (*respeto*) ensue.

Maintaining frequent contact, actively listening to the women's stories, and sending birthday cards and handwritten, personalized messages helped participants to feel they were important, not simply trial subjects. In a study examining an intervention for African American female breast cancer survivors, researchers worked with African American churches to improve recruitment. Letters were written by church leaders linking African American women's faith, spirituality, and the intervention study as a ministry [132]. Because of African American culture's strong emphasis on spirituality and religion and integrating spiritual and religious dimensions to day-to-day life, invitation letters framed African American breast cancer survivors' participation as a way of helping others.

BUILDING RESEARCH PARTNERSHIPS/COLLABORATIONS

Healthcare providers can help communities regain trust in research by fostering and facilitating communication, consultation, collaboration, and partnerships in order to build public and community trust [158]. When COVID-19 became highly politicized, the importance of collaborating with a host of systems was highlighted to alleviate anxieties about the COVID-19 vaccine trial [223]. Messages and activities that represent trusted voices to the community should be coordinated. Therefore, strategies to develop collaborations with communities and leaders are key in recruiting women and racial/ethnic minorities into clinical trials [156; 192]. In some cases, gatekeepers maintain a strong presence in communities, particularly in some ethnic minority communities. In the Korean immigrant community, pastors, business owners, leaders from ethnic organizations, ethnic media outlets, physicians, service providers and advocacy organizations, and religious leaders can act as a conduit for research. Some may be more receptive to clinical trials, while others view research activities with more caution [88]. Developing partnerships with physicians and medical professional associations is also important [223]. In a focus group with Chinese participants, they mentioned that one motivating factor to participating in a clinical trial is a recommendation from their physician [159]. Consequently, it may be helpful for research team members to create a community asset map [88]. This involves highlighting specific resources within the targeted community and discovering the variety of individuals, organizations, social clubs, and businesses that would be helpful in recruiting research participants [223]. Additional word-of-mouth referrals or recommendations from the initial compilation of resources may be added to the profile. A continual examination of this map, including an assessment of any new cultural, social, and political forces that may have an impact, is highly recommended [88].

In a systematic review of previous clinical trials studies published with a focus on recruiting racial and ethnic minorities, community partnerships were effective in recruiting racial and ethnic minorities for clinical trials in 68% of the cases [133]. The retention rate was 65% for studies that mentioned data about retention. Individuals who have participated in clinical trials can also serve as recruitment partners, provide feedback on study design and consent forms, and present trial results to lay audiences [193].

Creative research partnerships should also be considered. Instead of one-sided research, collaborative projects, with creative or educational results, can be effective. For example, in one such project researchers forged a partnership with an African American sorority to recruit African American women for a genetics study [103]. The goal of this partnership was to educate African American women about the hereditary component of breast cancer and to increase African American enrollment in the national Cancer Genetics Network [103]. Although the partnership yielded very modest enrollment, the authors were confident that the lessons learned could lay the platform to building and improving future partnerships with other sororities. For example, they learned that rapid communication was crucial, as many volunteer organizations have competing interests [103].

Post-project engagement is just as important as pre-study planning [194]. Ideally, community partners could also help analyze and interpret the findings [192]. In a 2012 meta-analysis, community partners were discussed in the articles as assisting the researchers in interpreting the findings only 21% of the time [133]. However, community partners were involved in helping to develop the interventions more than 90% of the time. Partners may be less interested in the analysis phase due to perceived necessity for specialized skills, but this underscores the importance of engaging in a dialogue to help identify each parties' strengths and interests when it comes to the level of involvement.

The staffing of a research team should include a community representative [104; 192]. This individual would serve as an advocate and a facilitator for the community, bringing concerns, questions, and issues back to the research team. They could also serve as cultural consultants, which are also key to the success of researchers who desire to penetrate "hard-to-reach" communities. For example, consultants are often needed in research with Native Americans because there are specific processes that must be negotiated with tribal entities [104]. Lack of cultural competency and sensitivity of staff members has been identified as a barrier to clinical trial participation [222]. Clinical trial coordinators are the face of the study, and they implement a host of invisible "back office" activities to help recruit research participants. Being sensitive to cultural and logistical barriers can help make potential participants feel connected and appreciated.

In another study recruiting elderly African American women for cancer prevention control studies, researchers found that study helpers, local spokespersons, and familiar authority figures can legitimize the study and assist in improving recruitment [105]. Study helpers were local African American residents who accompanied the researchers conducting door-to-door canvassing. Doors were more likely to be opened when people saw familiar African American women from their own community [105].

Faith communities and churches can also powerful influencers with certain racial and ethnic minority groups. For example, the Dose of Hope program, designed to close gaps in health care utilization, relied on churches to disseminate the message of clinical trials to older African Americans [158]. Other community settings (e.g., barbershops, beauty salons) and events (e.g., health fairs, barbeques) can also be effective venues for recruitment [179].

MARKETING

Marketing strategies are also equally important. Community partners can be involved in all steps of marketing, including logo development, selection of media outlets, and targeted language [134]. Many assume community outreach and other racially and ethnically targeted marketing methods are more expensive and less effective, but this is not necessarily true. In a study of the effectiveness of smoking cessation outreach to African Americans, researchers found that the cost per research participant was $27 when using the community outreach method, $120 for advertisements on billboards, $940 employing ads on mass transportation systems, and $1,208 using newspaper ads [135]. They are also effective in achieving the desired outcomes of recruitment. One example of this method was the inclusion of an "Asian" themed greeting card along with the traditional marketing packet about the study; in this case, the researchers were specifically seeking Asian participants [224]. Those who received the greeting card were 4.5 times more likely to enroll in the study compared with those who received only the traditional marketing materials.

EDUCATION

Creating and promoting awareness about the overall value of clinical research is also important [106]. Community education should not simply be about telling people that clinical research is good for them [43]. Rather, it is more important to ask and listen to what the community values and needs. Furthermore, education regarding the various aspects involved in clinical trials, the logistics, and the processes is needed.

In regards to educational material, the consensus is that all instructions, brochures, flyers, and videos be culturally and linguistically appropriate.

Culturally appropriate logos, images, and colors are important as is informational content that is appropriately translated to the targeted group. Brochures, face-to-face presentations, and educational materials about the condition or intervention being studied should be conveyed in a culturally sensitive manner. Written materials may not be the best option for educational outreach. For example, researchers in one study disseminated a video to Hispanic women to reduce language barriers [104]. Creative approaches, such as videos, multimedia, and photos/images, may also be used to explain clinical trials [195]. When appropriate, information may be presented on social media platforms [194]. Instead of relying only on text, these approaches could facilitate greater comprehension of the study and higher retention levels [195]. In terms of directly speaking to women's participation, informational components may address the importance of women's participation in research to benefit not only an individual's health but the larger collective unit as a whole [106; 136].

Nurses, social workers, and other practitioners play key roles in educating patients and advocating for clinical trials [196; 197]. They can initiate conversations and answer questions, and they may also serve as liaisons between members of the research team and other healthcare providers [197]. Education for research staff regarding potential barriers to participation for women and racial/ethnic minorities may be helpful [192]. One study found that research site coordinators and research nurses held perceptions that minorities, and to a lesser extent women, were less likely to enroll in clinical trials because they were less interested in participation [107]. The research workers indicated their most effective interactions were with white men. They also stated they were less likely to enroll an individual who had missed previous appointments or did not speak English. Although it is true that racial and ethnic minorities are less likely to enroll in clinical trials, these views can ultimately affect recruitment decisions [107].

OVERCOMING LOGISTICAL BARRIERS

Assisting women and racial/ethnic minorities from their stated intention to participate to the actual execution of the decision involves addressing the practicalities and logistics of fitting the participation into day-to-day responsibilities [106]. As discussed, traveling to the research sites on multiple occasions for testing can be a burden, infringing upon research participants' time and finances. Furthermore, childcare is often a logistical barrier to participation, particularly for women. Social workers, nurses, and case managers can advocate for resources to deal with these logistical dilemmas and assist participants to coordinate necessary services, as convenience is key for enhanced research participation [52; 64; 219]. In some trials, childcare and transportation are provided to help with recruitment and retention of women research participants [134]. In another study of nutritional guidance for low-income mothers, participants were scheduled for follow-up interviews during times when they were already in the medical clinics for scheduled well-baby visits [137].

Compensation for the time spent traveling and engaging in study participation should be carefully considered [106; 188]. In one study, a several-phase incentive plan was designed to provide grocery gift cards in stages with gradual increasing amounts [137]. In addition, being culturally sensitive to the form of incentive is also important. In one study conducted in the Khmer community, community informants advised that monetary incentives in the form of checks may not be culturally appropriate because many of the targeted research participants worked primarily for cash [108]. In this case, grocery coupons were identified as more culturally sensitive compensation. At the same time, checks, grocery redemption cards, and any other incentive compensation that requires identification documentation for redemption may not be culturally sensitive, particularly for groups who are concerned about their immigration status [138].

Cash may be optimal, but if the funding agency of the study requires participants' social security numbers for tax purposes, this could be viewed as an impediment for some participants [138].

INFORMED CONSENT

Informed consent is a vital aspect of the healthcare system and of scientific research. While some immigrants may be reasonably fluent in English for day-to-day activities, they may be less comfortable communicating in English about healthcare issues [95]. Some individuals may sign a consent form without fully understanding the significance due to cultural belief systems about the role of authority figures. For example, a study of Japanese elderly research participants found that 40% had signed the consent form because they simply respected their physicians' authority and deferred to their decision making [83]. Furthermore, they perceived that not signing the form would be disrespectful. Given that loss of respect is a cultural value important to some immigrants, researchers should reiterate to research participants that a signature on the consent form is not binding [94]. In the United States, an individual signs the consent form, signifying he/she understands the information provided to him/her. However, in other cultures, community consent and decision making are advocated [149]. In patriarchal or male-dominated cultures, the male head (e.g., husband) may be the one to give consent for a female research participant [225]. Research that involves Native American Indian tribal groups or indigenous groups, the community leader, elders, grandparents, and/or other relatives provide consent (not the individual) [149].

It is incumbent upon the healthcare or behavior health professional to assess if the research participant has full understanding of the study and to encourage him or her to repeat the information on the form [94]. In a qualitative study that explored oncologists' communication styles and interactions with patients regarding cancer clinical trials, their role as educator was highlighted. Because the information is often complex and daunting, the oncologists spent time with their patients talking about the technical aspects of the clinical trial, side effects, and randomization [91]. In some cases, traditional written consent forms may need to be replaced with oral, video, audio, or even pictorial methods [225]. Thumbprints may also be permissible in lieu of the signature. Patient navigators, if available, can be beneficial in helping participants navigate through the healthcare system [224]. If there are language barriers, interpreters may be necessary. Having a diverse research team, including members who are proficient with the targeted study population's language, can also help overcome language and cultural barriers and assist with engagement and alleviating fears [186].

CONCLUSION

When researchers neglect the inclusion of marginalized populations and assume that findings from white male samples can be generalized to all groups, ethnocentrism can expand to institutions and even national policies. Ethnocentrism in research also surfaces when researchers compare women's or racial/ethnic minorities' health outcomes to those defined by the "normal" population [109].

The NIH Revitalization Act of 1993 was an attempt to include race consciousness in research in order to remedy past historical discrimination against women and racial and ethnic minorities in research [110]. While overall the inclusion of racial and ethnic minorities in research should reduce racial disparities, it is important for researchers to be careful about interpreting findings [110]. Biological or genetic interpretation of the data may not be possible, as the terms "race" and "ethnicity" are social categories. Ultimately, conducting clinical trials with women and racial/ethnic minorities requires cultural knowledge and sensitivity. Interpreting and applying findings of such trials also requires a basic knowledge of the trial process and awareness of historically exclusionary practices.

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