Given that numerous women who become pregnant will be exposed to medications during their pregnancies, it is important to establish whether these medications affect fetuses and pregnant women differently. To promote greater efficacy, as well as maternal and fetal health, medications should be tested in a small, representative sample of pregnant women, rather than continuing to prescribe these medications without more reliable information about their effects.

IMPROVING RECRUITMENT AND RETENTION OF WOMEN

Researchers cite many reasons for difficulty in recruiting women for clinical trials, including noncompliance, lack of incentive to seek alternative therapies, poor access to health care, lack of transportation, lack of child care, and mistrust of medical systems. These and other recruitment and retention issues can be mitigated in a variety of ways, including effective collection and use of comprehensive locator information, providing transportation or additional transportation compensation (e.g., gas cards, with IRB approval), the use of recruitment and retention specialists or participant trackers, and many others. NIH requires that all funded studies include an outreach plan for recruiting women as study participants, as well as strategies that address common barriers to study participation.

STRATEGIES FOR RECRUITING AND RETAINING WOMEN IN A CLINICAL TRIAL

Address Logistical and Financial Needs

- Maintain extended and flexible clinic hours.
- Provide at-home follow-up for participants.
- Offer childcare and transportation, or reimburse participants for these services.
- Reimburse study participants for their time and possible discomfort.

Advertise

- Network with emergency rooms, state and county assistance offices, primary care givers, and mental health centers.
- Post bulletin board ads in beauty salons, laundromats, churches, grocery stores, and gyms.

Staff Your Team Appropriately

- Train and hire more women investigators and educators to foster greater trust among female participants.
- Include women on your clinical trial staff, particularly women with the same ethnic or racial background as the target population.
- Sensitize staff members to the unique needs of women in clinical trials.

Involve the Study Participants

- Utilize input from previous women study participants when designing new clinical trials.
- Create a participant advisory board to give feedback on forms used, recruitment activities, study procedures, and other aspects of clinical studies.

Improve Communication

- Allow extra time to review the study's risks and benefits with female subjects if there are sex/gender-specific issues involved in study participation (e.g., medication trials).
- Inform participants about the study protocol, treatment, trial outcomes, and implications through meetings, newsletters, or other updates.
- Acknowledge the contributions of study participants in ways that are meaningful to them (e.g., certificates of appreciation or recognition).

FOR MORE INFORMATION

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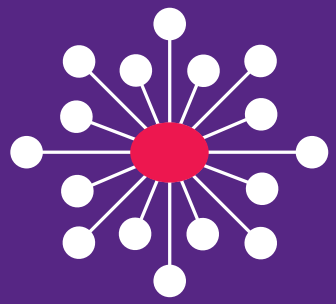
National Drug Abuse Treatment

Clinical Trials Network

Successfully Including Women in Clinical Trials

A Guide for Researchers



National Institutes of Health
U.S. Department of Health and Human Services

WHY INCLUDE WOMEN IN A CLINICAL TRIAL?

Federal regulation and National Institutes of Health (NIH) policy require that women, including women of childbearing potential, be included in all NIH-supported biomedical and behavioral research involving human subjects, unless there is a clear and compelling rationale that inclusion would harm the subjects or the purpose of the research.

Research has provided evidence of sex differences in many biological systems of the body. A woman's menstrual cycle, for example, can significantly change the effects of drugs. In addition to sex differences in biological systems, cultural expectations for both men and women have an effect on behavior, sense of self, and relationships.

While these differences may increase the challenge of implementing well-designed research studies, these findings also have strong implications for women's treatment. Simply put, research findings on efficacy and effectiveness of interventions derived from clinical trials that have used all-male samples are not necessarily applicable to women.

WHY CONDUCT GENDER ANALYSIS?

Including women in your research pro tocol is just the first step. Conducting a sex/gender analysis of your data is the next step. If sex differences have been shown to affect the course or impact of a treatment in early phases of research, then subsequent studies can be designed so that application of the treatment will benefit both men and women. In fact, any proposal submitted to NIH for a Phase III clinical trial must review the evidence to indicate whether clinically important sex/gen der differences in the intervention effect are expected. Researchers should consider known sex/gender differences in designing clinical trials and may wish to plan sample size and randomization strategies to be able to examine such differences in their analyses.

THROUGH GENDER ANALYSIS, WE KNOW THAT:

- Women who smoke are 20% to 70% more likely to develop lung cancer than men who smoke the same number of cigarettes.
- Approximately 30% to 50% of women in drug abuse treatment suffer from comorbid post-traumatic stress disorder—a rate that is two to three times greater than for men in treatment.
- After consuming the same amount of alcohol, women have a higher blood alcohol content than men, even allowing for size differences, and women metabolize alcohol differently.
- Medications can cause different reactions and have different side effects in women and men—even common medications such as antihistamines and antibiotics.
- During unprotected intercourse with an infected partner, women are 10 times more likely than men to contract HIV.
- Women are more likely than men to be daily users of cocaine, heroin, sedatives, and barbiturates.
- Depression is two to three times more common in women than in men, in part because women's brains produce less of the hormone serotonin.
- Women experience more challenges accessing treatment and staying in treatment due to child custody concerns, childcare issues, economic hardship, and stigma related to drug and alcohol use.
- Males and females relapse for different reasons.
- Males and females have different HIV progression.

MEETING THE CHALLENGE

Prior to the publication of NIH research guidelines issued in 1994, researchers often avoided including women in clinical trials. In addition to concerns about the effects of sex differences and hormonal fluctuations during menstrual cycles on study outcomes, researchers may be concerned about possible fetal exposure to drugs and long-term damage to women's germ cells, as well as difficulties with recruiting women. However, the importance of including women in our research far outweighs the challenges that can often be addressed.

REDUCING THE RISK OF FETAL EXPOSURE

Between 1977 and 1993, the Food and Drug Administration prohibited the inclusion of women of childbearing age in the early phases of research studies that tested new medications unless the woman had a life-threatening disease. However, recent laws and court decisions suggest that women should have the right to make their own risk-benefit choices about their pregnancies, as long as they are informed of all potential risks.

THREE WAYS TO MINIMIZE THE RISK OF FETAL EXPOSURE IN A CLINICAL TRIAL

1. Conduct thorough evaluations to assess whether the women of childbearing age that you are recruiting are unlikely to get pregnant—for instance, women using a reliable method of contraception, women whose partners have had vasectomies, and women who are not sexually active or are not active with male partners.
2. Include all available information regarding the potential risk of fetal toxicity and potential effects on fertility in the informed consent document and investigator's brochure. If no relevant information is available, the informed consent should explicitly note the potential for fetal risk.
3. Reduce the risk of fetal exposure through study design. By administering treatment during or immediately following a woman's menstrual period or after a pregnancy test, or by counseling women in trials about the need to use reliable forms of contraception, the risk to fetuses can be reduced.