

COMMENTARY

Invisible Women: Exploring the need for greater enrollment of women in clinical trials

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Women are underrepresented in oncology clinical trials along with other groups including ethnic/racial minorities, the elderly and those of lower socioeconomic status. Increasing enrollment of women is important to increase data on proper use and efficacy of anti-cancer therapies in this subset of the population. Strategies should be adopted to increase enrollment of women in oncology clinical trials including older women and those that belong to racial and ethnic minority groups.

Historically, we have seen a vast underrepresentation of women in biomedical research, including cancer clinical trials.¹ As a result, data derived from a predominantly male population are commonly and perhaps inappropriately extrapolated for clinical use in women.¹ Between 2003 and 2016, women made up just 41% of participants in cancer clinical trials registered on clinicaltrials.gov website.¹ Of the 5,157 patients who participated in oncology trials that led the FDA approval of 17 new drugs in 2018, only 38% were women.² This lack of representation is not just limited to women; there are also longstanding disparities in cancer clinical trial enrollment of patients who belong to racial/ethnic minority groups, older patients, and patients with Medicaid/Medicare insurance. In a recent policy statement, The American Society of Clinical Oncology emphasized the urgent need for equity in trials with a goal to enhance access and representation in cancer research, and to improve overall cancer outcomes while upholding the principles of fairness and justice in health care.³ In this commentary, we seek to explore opportunities for greater enrollment of women in clinical trials.

In addition to lack of overall representation, there is heterogeneity in the enrollment of women in clinical trials across cancer subsites. Women have been found to be less likely to be enrolled in studies relating to colorectal cancer, lung cancer, and surgical oncology within National Cancer Institute (NCI)-sponsored trials compared to their male counterparts.² Another analysis of oncology trials in the United States from 2008 to 2020 shows significant sex gaps in bladder, head and neck, stomach, and esophageal cancers.⁴ However, women were found to be adequately represented in hematologic and pancreatic cancer trials when compared to male

participants.⁴ Older women and minorities have been found to be underrepresented when examining enrollment in trials studying breast and gynecologic cancers.²

Clinical trials provide the necessary data for the rational use of new drugs. If a subset of the population is underrepresented or excluded, important information on the proper use and efficacy of anti-cancer therapies in that subset will be lacking.¹ The importance of increasing the enrollment of women in clinical trials must be stressed as data generated in men does not necessarily correlate in women. For example, women have a 1.5-fold to 1.7-fold greater risk of developing an adverse reaction to a drug. In a study by Lee et al., it was reported that 8 of the 10 prescription drugs withdrawn from the US market between January 1997 and January 2001 posed a greater risk for women than men.² While data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program shows that a female's probability of being diagnosed with cancer is slightly lower than a male's probability, females suffer from lower cancer-specific 5-year survival rates.⁴ While there are myriad factors that determine cancer survival rates, this data also alludes to the importance of testing anti-cancer therapies in women in order to determine clinical efficacy in this patient population.

Barriers for enrollment of a greater number of women in cancer clinical trials must be broken down to accurately assess disease specific disparities and therapeutic efficacy of treatments across the entire population. Strategies for increasing recruitment of women to trials have varied. Some studies have pointed toward web-based registration of patients as well as patient education and community outreach specifically directed toward this underrepresented population. Targeting medical provider education on the availability and benefits of participating in clinical trials may also be essential to recruitment of underrepresented groups.¹ There are certain patient specific factors affecting women that can influence patients' willingness to enroll in clinical trials, including distrust of researchers, study burden, and inconvenience. As women are often the primary caregivers for their household, additional time burdens may discourage participation.⁵ Negative attitudes towards women as study participants from sponsors may also contribute, including misconceptions that women are more difficult to recruit and are more likely to be unwilling to participate in trials.² Along with education and awareness, trial design strategies including decreasing trial burden for women and tracking of enrollment by gender may also be effective in increasing enrollment. While significant strides have been made over the past several decades, there continues to be underrepresentation of women in cancer clinical trials with studies displaying broad variation of female representation existing among oncology intervention types, cancer sites, and funding sources. Increasing both provider- and patient-focused strategies to increase trial participation is inherently important in ensuring that anti-cancer therapies are effective in this population.

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