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# Not enough women included in some heart disease clinical trials

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Women are underrepresented in clinical trials for heart failure, coronary artery disease and acute coronary syndrome but proportionately or overrepresented in trials for hypertension, atrial fibrillation and pulmonary arterial hypertension, when compared to incidence or prevalence of women within each disease population, according to a study in the *Journal of the American College of Cardiology*.

Heart disease is the No. 1 killer of women and men. It represents a very significant health concern for women because it is often overlooked as a prominent health issue, plus the sex and gender differences in cardiovascular disease pathophysiology, clinical presentation and outcomes mean that treatments for men may not always work as well in women. Women being well-represented in clinical trials is important to determine possible gender differences in treatment responses.

In this study, researchers looked at the numbers of women and men who participated in cardiovascular trials submitted to the U.S. Food and Drug Administration supporting new drug application approvals. Between Jan. 1, 2005 and Sept. 15, 2015, 36 approvals for 35 drugs for acute coronary syndrome/myocardial infarction, atrial fibrillation, coronary artery disease including angina, heart failure, hypertension and pulmonary arterial hypertension, were looked at for the percentage of women enrolled.

"As we move into the era of precision medicine, that is assessing the impact of a wide range of patient and disease characteristics on drug

effects, it is imperative that clinical trial participants represent the full spectrum of patients for whom the drug will be prescribed," said Janet Woodcock, MD, senior author of the study and director of the FDA Center for Drug Evaluation and Research. "This will move us closer to our goal of providing the best information possible about the use of drugs for every patient."

Estimates for the participation of women were calculated by dividing the percentage of women among trial participants by the percentage of women in the disease population, with a range between 0.8 and 1.2 reflecting proportional representation. In total, the proportion of women enrolled ranged from 22 to 81 percent, with a mean of 46 percent.

The ratio for atrial fibrillation was 0.8-1.1, for hypertension it was 0.9, and for pulmonary arterial hypertension it was 1.4—all within or above the desirable range. Heart failure, coronary artery disease and acute coronary syndrome/myocardial infarction were all under the ratio level, at 0.5-0.6, 0.6 and 0.6, respectively. Researchers also looked at the gender differences in efficacy or safety and found little indication of clinically meaningful differences.

According to the researchers, previous studies have suggested that clinical trial inclusion and exclusion criteria disproportionately exclude women from cardiovascular studies; however, data in this latest study show that the lower enrollment of women reflects the lower number of women referred for pre-trial participation screening. Factors prior to screening, such as the identification of potential trial participants and the ability of a candidate to participate, may be more likely reasons for low enrollment of women.

"Based on this work, future research is needed to identify factors leading to under participation of women in cardiovascular clinical trials, particularly those occurring before screening," said Pamela Scott, PhD,

first author and Director of Research in the FDA Office of Women's Health. "Research is needed to better define barriers that limit participation of diverse populations, not only of women but of minority and older populations."

Limitations of the study are that it included only pivotal studies and does not reflect the inclusion of women in all studies reviewed by the FDA for new drug applications. Also, it is not required for new drug application submissions to include data on screening failures, so the ability to draw conclusions about the effects of screening criteria is limited.

In an accompanying editorial, Louise Pilote, MD, MPH, PhD, said that even though progress has been made in the fight against sex and gender disparities, there is more to be done.

"Patients, researchers and health providers can take action by addressing the alarming gaps in quality and equitable health care for women," Pilote said. "Our mandate as health providers and researchers should be to hone the energy and advance awareness that sex and gender in clinical trials really does matter."

Pilote added that "The lack of sex differences in efficacy and safety could be due to the exclusion of women who do not share the same pattern of disease as men."

Provided by American College of Cardiology