Women Abound in NIH Trials

A campaign that began in the 1990s to tip the balance toward female participants may have been more successful than people realize

SIX YEARS AGO, A *NEW YORK TIMES* COLUMNIST confidently stated that, before Bernadine Healy became director of the National Institutes of Health (NIH) in 1991, "women were usually excluded from clinical trials." It's a popular and tenacious view, but it's hard to find evidence for it. In fact, the current ratio of women to men in U.S.-government–funded trials is about 2-to-1.

It's true that until the 1980s, women of reproductive age were often excluded from trials, ostensibly to avoid harm to fetuses. The impression of male-dominated trials was reinforced by two large men-only heart trials launched in 1972 and 1981. In 1987, NIH formally made a commitment to include more women in research and followed in 1990 with the establishment of the NIH Office of Research on Women's Health. In 1991, NIH started the 15-year Women's Health Initiative, an intensive study of postmenopausal women.

These developments notwithstanding, many women argued that more attention was needed. In Congress, Representative Patricia Schroeder (D–CO) picked up the ball after one of her staffers called her attention to the two big male heart trials. "Because they were so big and expensive," in part, they provoked "outrage," says Adele Gilpin, a physician and lawyer at the Washington, D.C., law firm of Hunton & Williams. These pressures led to congressional passage of the 1993 NIH Revitalization Act, which further emphasized inclusion of gender considerations in research.

Despite all the hoopla, argues epidemiologist Curtis Meinert of Johns Hopkins University in Baltimore, Maryland, who has been following the issue for 2 decades, there is no evidence that women were getting short shrift. In 2000, he and Gilpin published a paper with data indicating more women than men had been in trials published in major journals between 1985 and 1995.

Meinert has since updated his figures once again (see chart, above). In an unpublished paper, he states that the ratio of female-only to male-only trials climbed in the past 10 years, especially in multicenter randomized trials for which, according to PubMed searches of English-language journals, the ratio in 2006 was 3.44-to-1. He also notes that according to statistics gathered by the Office of Research on Women's Health, of the 14.8 million people enrolled in 10,758 NIH research protocols in 2006, 64% were women.

Gender and Clinical Trials*

Published	Total	Male and Female %	Female only %	Male only %	F/M ratio	Unknown %
1991–1995	66,370	58.4	11.6	11.5	1.01	18.6
1996–2000	101,990	63.3	11.5	10.0	1.15	15.1
2001–2005	125,759	67.1	11.6	8.6	1.36	12.7
2006	31,114	68.9	11.7	7.4	1.58	12.0

*Counts from searching PubMed for "clinical trial," limited to publications involving human beings.

Meinert doesn't say whether the tilt toward women is bad for science. But he argues that "general perceptions have taken priority over data" in this subject. There's now a requirement that gender must be taken into account in every grant application involving human subjects. But in many cases, sex is much less relevant than other biological factors such as age, he says. He believes the regulations pertaining to women have "served to institutionalize a perception" that is "not supported by fact [and] that erodes public trust in an important enterprise." He also contends that a bias toward females has made it "politically risky to do male-only trials."

Vivian Pinn, director of the women's health office since 1993, says she doesn't buy the notion that political concerns have influenced the sex ratio in NIH-supported trials. She acknowledges that they feature "obviously a much larger percentage of women." But she believes that's probably justified given the complexity of female reproductive issues; male-only reproductive problems are mainly confined to the prostate. Plus, she says, the numbers also reflect studies that originally were men-only that are now being repeated in women.

Reproduction aside, says Pinn, there are "fewer conditions more prevalent in men than in women." Autoimmune diseases, for example, disproportionately affect women. And although heart disease occurs much earlier in men, she's not sure there's any difference in prevalence between the sexes. Finally, notes Pinn, if you look just at studies that include both sexes, the ratio only slightly favors women—roughly 53% to 46% in 2006. Phase III trials have slightly more men than women, she says.

Is the Office of Research on Women's Health still needed at NIH? Pinn still sees a role for it, mentioning in particular research on basic biological issues such as how sex may modify particular gene functions. At any rate, she adds, "looking at percentage of money spent on males versus females is not a good way to evaluate" research. **–CONSTANCE HOLDEN**

CREDITS (TOP TO BOTTOM): TIM PANNELL/CORBIS; SOURCE: CURTIS MEINERT

Published by AAAS