
Gender Representation in Trials

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ABSTRACT: The perception is that women have been understudied relative to men. It has been sufficient to cause Congress to enact legislation to require that a clinical trial must be “designed and carried out in a manner sufficient to provide for a valid analysis of whether the variables being studied in the trial affect women . . . differently than other subjects in the trial.” We looked for evidence as to whether the perception has a basis in fact by looking at measures of gender-based research effort. Clinical trials, published between 1966 and 1998 in U.S. journals and indexed in MEDLINE, were classified by gender. Reports of trials ($n = 724$) appearing in five widely circulated medical journals (*Annals of Internal Medicine*, *British Medical Journal*, *Journal of the American Medical Association*, *Lancet*, and *New England Journal of Medicine*) in 1985, 1990, and 1995 were retrieved and read to obtain counts of the numbers of males and females represented in trials published in those journals. For reports of trials published in U.S. journals ($n = 100,455$), the percent involving males and females, males only, females only, and those where gender was not specified were 55.2%, 12.2%, 11.2%, and 21.4%, respectively. Counts of males and females represented in the reports of trials appearing in the five aforementioned journals were 355,624 and 550,743, respectively. We did not find evidence of systematic effort bias against females. *Control Clin Trials* 2000;21:462–475 © Elsevier Science Inc. 2000

KEY WORDS: *Clinical trials, clinical research, bias, gender, women’s health, legislation*

INTRODUCTION

The prevailing view is that the effort of the nation’s clinical research enterprise has been tilted in favor of men, and especially so in regard to clinical trials. We were interested in examining the extent to which the perception has a basis in fact, as seen by the gender mix represented in published trials. This report is an outgrowth of work of one of the authors on an Institute of Medicine Committee concerning ethical and legal issues relating to the inclusion of women in clinical studies [1, 2].

The Women’s Congressional Caucus, headed by Patricia Schroeder (Democrat; Representative; Colorado) and Barbara Mikulski (Democrat; Senator;

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Maryland), helped to focus attention on issues of equity in the research enterprise in the late 1980s and early 1990s [3]. It was energized, in part, by a report from a Public Health Service Task Force on Women's Issues concluding that: "The historical lack of research focus on women's health concerns has compromised the quality of health information available to women as well as the health care they receive" [1]. That conclusion led the National Institutes of Health (NIH) to issue instructions urging "applicants for grants and offerors for contracts to consider the inclusion of women in the study populations for all clinical research efforts" [4].

Issues of gender in research became a focus of discussion in U.S. Senate hearings for confirmation of Bernadine Healy as director of the NIH in March of 1991. Her intent, enunciated in those hearings, was to make women's health a central issue of her administration.

Testimony of representatives from the General Accounting Office (GAO) in Congress in 1990, as well as a 1992 GAO report on the Food and Drug Administration and drug testing, added to the climate of concern [5–8]. The testimony and report served to reinforce the perception that women and their diseases and conditions were understudied.

The NIH promulgated an *NIH Instruction and Information Memorandum* (Office of Extramural Research; 11 December 1990), the purpose of which was to remind applicants for NIH funding of the concern of Congress in regard to who is studied. However, the instruction was seen by Congress as being "too little too late" and served to increase the resolve of Congress to act.

The restiveness of Congress was increased by a measure of moral outrage directed at NIH because of its role in funding several large-scale, male-only, heart trials in the 1970s and 1980s, principally, the Coronary Drug Project (CDP) [9–13], the Coronary Primary Prevention Trial (CPPT) [14, 15], the Multiple Risk Factor Intervention Trial (MRFIT) [16, 17], and the Physicians' Health Study (PHS) [18–22]. The CDP was a secondary prevention trial. The other three were primary prevention trials.

The MRFIT and PHS, in particular, came to be viewed as "smoking guns" serving to prove the existence of bias and as providing prima facie evidence of a lack of distributive justice [23]. Of the two, the PHS became a cause célèbre because it involved only male physicians. Female physicians were not studied, even though they represented about 10% of the total population of physicians in the age range of interest (40 to 85 years of age on enrollment).

Indignation was increased by a misunderstanding of figures contained in a report prepared by the NIH Advisory Committee on Women's Health Issues [24]. It provided data on expenditures for female-specific or female-related diseases or conditions as a percentage of total NIH expenditures (12.2% and 13.5% for fiscal years 1986 and 1987, respectively). In the absence of corresponding figures for males, it was assumed that the complement of the figures (87.8% and 86.5%, respectively) were the corresponding figures for males.

Figures reported since 1988 have been for women and men. The ratio of expenditures (F/M) was 2.20 in 1988 and 2.62 in 1998, the last year for which we have data. The ratio has ranged from a low of 1.79 (1991) to a high of 2.81 (1996).

The perception that trials have favored men and their diseases and conditions has been strong enough to have caused the 103rd Congress to require that the

director of the NIH ensure (for trials involving diseases or conditions common to men and women) that such trials be “designed and carried out in a manner sufficient to provide for a valid analysis of whether the variables being studied in the trial affect women or members of minority groups, as the case may be, differently than other subjects in the trial” [25].

The “valid analysis” requirement contained in the act was translated into a set of guidelines issued by the NIH [26]. The rationale for the guidelines is contained in a publication by Freedman et al., inclusive of comments by various writers [27].

METHODS

Results summarized herein are based on counts obtained from MEDLINE using the Ovid Technologies search engine. The database, at the time of the searches (mid-1999), contained some 9.6 million citations to publications (1966 through 1998); 7.3 million to English language publications and 3.9 million citations to U.S. English language journals. Citations to U.S. English language journals were pruned to 1,997,100, corresponding to full-length reports containing original research results and indexed as involving human beings [i.e., bearing the Medical Subject Heading (MeSH) “human”]. The pruning was done by excluding publication types such as abstracts, letters, editorials, interviews, news reports, review articles, errata, meta-analyses, treatment or practice guidelines, consensus reports, and proceedings of meetings.

The resulting data set was searched for reports of clinical trials. A “clinical trial” in the vernacular of MEDLINE is a preplanned clinical study of the safety, efficacy, or optimum dosage schedule of one or more diagnostic, therapeutic, or prophylactic drugs, devices, or techniques in humans selected according to predetermined criteria of eligibility and observed for predefined evidence of favorable or unfavorable effects [28]. The database contained citations to 100,455 trials. Trials, as a percentage of all citations, ranged from a low of 1.8% (1966) to a high of 9.7% (1996).

A “randomized controlled trial” in MEDLINE is defined as a clinical trial that involves at least one test treatment and one control treatment, with concurrent enrollment and follow-up of the test- and control-treated groups and in which the treatments to be administered are selected by a random process, such as the use of a random-numbers table. Treatment allocations using coin flips, odd-even numbers, patient social security numbers, days of the week, medical record numbers, or other such pseudo- or quasi-random processes are not truly randomized and a trial employing any such techniques for patient assignment is designated simply a controlled clinical trial [28]. About half of all trials counted were indexed as randomized controlled trials (52,027 of the 100,455).

A “multicenter study” in MEDLINE is defined as a controlled study performed by two or more cooperating hospitals or services [28]. Joining that dataset with the one for clinical trial produced a dataset of multicenter clinical trials. However, because indexing for multicenter study is spotty until the mid-1980s, we chose to limit counts related to multicenter clinical trials to publications appearing after 1985 and to augment the identification process by expanding the multicenter study dataset to include citations having multicenter, multi-center, multicentre, multi-centre, or multisite in the title or author field

of a citation. The dataset contained 10,190 such citations for the time period 1986 through 1998, 13.2% of all clinical trials in that time period.

The “explode” mode of identification (a mode in which an article is included if it is tagged with any MeSH term of lower order in a hierarchical tree with the selected MeSH term at the apex) was used in creating counts of trials by disease area. The explode mode, for example, as applied to the MeSH term “heart diseases,” would include citations tagged with the MeSH term “myocardial ischemia” even though the MeSH term “heart diseases” might not be appended to the citation. The “focus” feature of MEDLINE was invoked as well. Selection of articles was based on those where the specified MeSH term, or a downstream MeSH term, was tagged in MEDLINE as being a primary focus of the report cited.

Counts of trials by gender category are based on logic allowing one to limit, join, and exclude subsets of citations using the MeSH terms “male” and “female.” For example, the count of female-only trials was obtained via a “limit to female” statement followed by a “not male” statement to purge the set of citations having male as a MeSH. Counts for trials involving both males and females were made by generating sets of citations via the statements “limit to male” and “limit to female,” joining the sets to produce a set of citations that had gender designated, and then excluding male-only and female-only trials. Counts for “no gender” trials correspond to citations for reports having neither male nor female as a MeSH.

RESULTS

Figure 1 is based on counts of trials by year, from 1966 through 1998, as classified by the gender mix of the populations represented in the trials. In 1998, 65.3% of the 8903 trials identified involved males and females, 10.1% involved males only, 10.7% involved females only, and the remainder, 13.9%, could not be classified as to gender mix. The percentages plotted in Figures 1A and 1B are for articles indexed to “clinical trial.” The percentages in Figures 1C and 1D are for articles indexed to “randomized clinical trial.” The corresponding percentages by decade and for the 3-year period 1996–1998 are given in Table 1.

The percentages plotted in Figure 2 and reported in Table 2 are by disease category for articles indexed to “clinical trial.”

The counts of trials in Tables 3 and 4 are for citations to manuscripts published in the *Annals of Internal Medicine*, *British Medical Journal*, *Journal of the American Medical Association*, *Lancet*, and *New England Journal of Medicine* in the years of 1985, 1990, and 1995. MEDLINE does not provide counts of persons studied. Hence, the only way that counts such as those represented in Tables 3 and 4 can be obtained is by retrieving and reading manuscripts. The counts in Table 3 are restricted to reports where the gender of persons studied was indicated (603 of the 724 manuscripts reviewed; see last line of each panel of Table 4 for counts of trials by gender mix). The classification by disease or condition area of focus for Table 3 was made by us when reading the articles.

Overall, for the 724 trials represented, 60% involved both males and females (Table 4). There were more female-only than male-only trials (12.5% compared

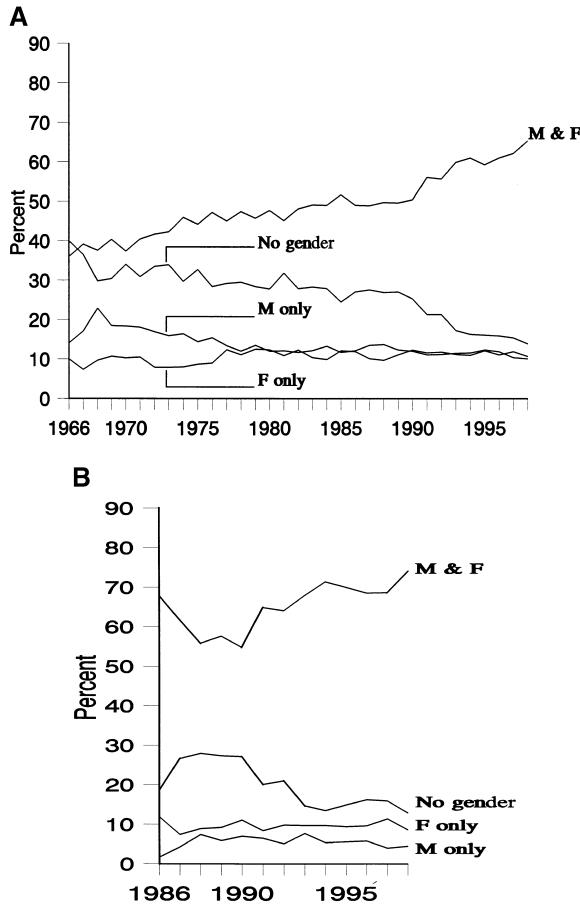


Figure 1 Clinical trials by gender mix as indexed in MEDLINE. (A) Clinical trials; (B) Multicenter clinical trials; (C) Randomized clinical trials; (D) Randomized multicenter clinical trials. Results are limited to English language publications appearing in the U.S. journals and after exclusion of abstracts, letters to the editor, review articles, and other publication types not containing original results. Results are also limited to publications involving human beings and are exclusive of publications involving human beings and animals.

to 10.8%). The ratio of female-only to male-only trials was 1.00, 1.00, and 1.53 for 1985, 1990, and 1995, respectively.

The results in Table 4 are suggestive of a tendency for smaller trials to be male-only. Phase of trial is rarely reported. Hence, we cannot say whether that tendency is due to a concentration of male-only phase I and II drug trials in the < 100 sample size stratum. Female participants outnumbered males 1.55 to 1 in all trials combined and in neoplasms trials 13.63 to 1 (Table 3). For heart disease trials, males outnumbered females 3.66 to 1. Overall, the median sample

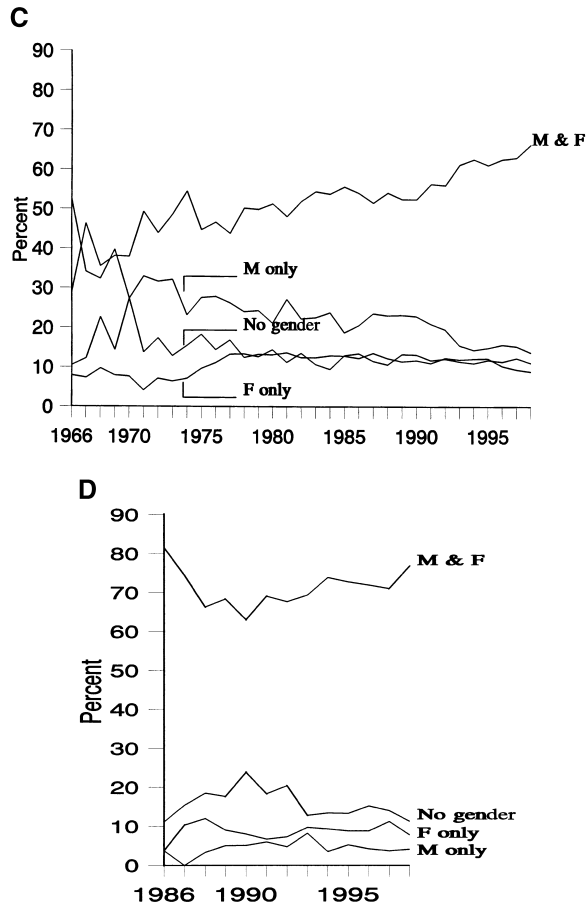


Figure 1 (Continued).

size of the trials counted was 118 for two-gender trials, 45 for male-only trials, 180 for female-only trials, and 86 for trials where gender was not specified.

DISCUSSION AND OBSERVATIONS

Overall, we find little to support the perception that females have been underrepresented or understudied in trials or that there is an effort bias in favor of males [29]. The counts represented in Table 1, even in the decade preceding the one in which Congress acted, are not suggestive of systematic understudying of females in trials.

However, that said, one must also recognize that there is a certain futility in trying to prove the absence of representation biases in trials. One obvious shortcoming here is in the need to rely on published trials as an indicator of who is studied. For example, the gender mix represented in published trials could be different than that in unpublished trials if more small trials are male-only and are also less likely to be published—a form of publication bias related to the gender of who is studied [30].

Table 1 Gender Mix Represented in Trials Published in U.S. English Language Journals

	Total	Percentages				
		No Gender	Male and Female	Male Only	Female Only	Female Only/ Male Only
Clinical trials						
1966–1975	7,401	32.8	41.1	17.0	9.0	0.53
1976–1985	15,993	28.1	48.1	12.6	11.2	0.89
1986–1995	50,389	21.0	55.6	12.0	11.4	0.95
1996–1998	26,672	15.1	62.8	10.8	11.3	1.05
Total	100,455	21.4	55.2	12.2	11.2	0.92
Multicenter clinical trials						
1986–1995	6,339	19.1	65.2	6.1	9.6	1.57
1996–1998	3,854	14.9	70.5	4.7	9.9	2.11
Total	10,190	17.5	67.2	5.6	9.7	1.73
Randomized clinical trials						
1966–1975	1,008	30.4	44.9	16.9	7.8	0.46
1976–1985	7,476	23.0	51.8	13.1	12.1	0.92
1986–1995	29,316	18.7	57.4	12.0	11.9	0.99
1996–1998	14,228	14.8	64.0	9.5	11.7	1.23
Total	52,028	18.5	58.2	11.6	11.8	1.02
Multicenter randomized clinical trials						
1986–1995	3,716	16.0	70.1	5.3	8.6	1.62
1996–1998	2,698	13.4	73.4	4.0	9.2	2.30
Total	6,414	14.9	71.5	4.8	8.9	1.85

The representation mix could be distorted as well if the no-gender trials were predominantly male only. Though such a possibility cannot be ruled out, indications are against it. One would expect the ratio of female-only to male-only trials to change over time as a function of the decline in the fraction of no-gender trials if such trials were primarily of one gender type. It does not.

Contrary to popular belief, the majority (64%) of heart trials involve both males and females (Table 2), though many more of the single gender trials are male only (13.9%) than female only (0.08%).

The concentration of male-only heart trials has been used to suggest that it has worked to the disadvantage of females in that the benefits of trials have accrued differentially to males. Benefit has many dimensions and hence is difficult to measure. However, at least with regard to mortality, the evidence of differential benefit is lacking. The ratio of mortality rates for white males compared to those for white females ranged from a high of 2.99 for persons aged 45–54 to a low of 1.10 for persons 85 or older in 1950. The corresponding ratios for 1990 were 3.40 and 1.15, respectively [31].

The male-female differentials in 1990 remain and in fact have increased relative to 1950. The ratios of mortality rates over all decades of life from 25 to the end of life for both white and black males, relative to white females, are consistently greater than that for 1950. The largest differential for white males was 3.74 for persons aged 35–44 and 8.77 for black males relative to white females, also for persons aged 35–44.

The differences seen for heart disease and Human Immunodeficiency Virus disease are in directions consistent with male-female disease burden. That is

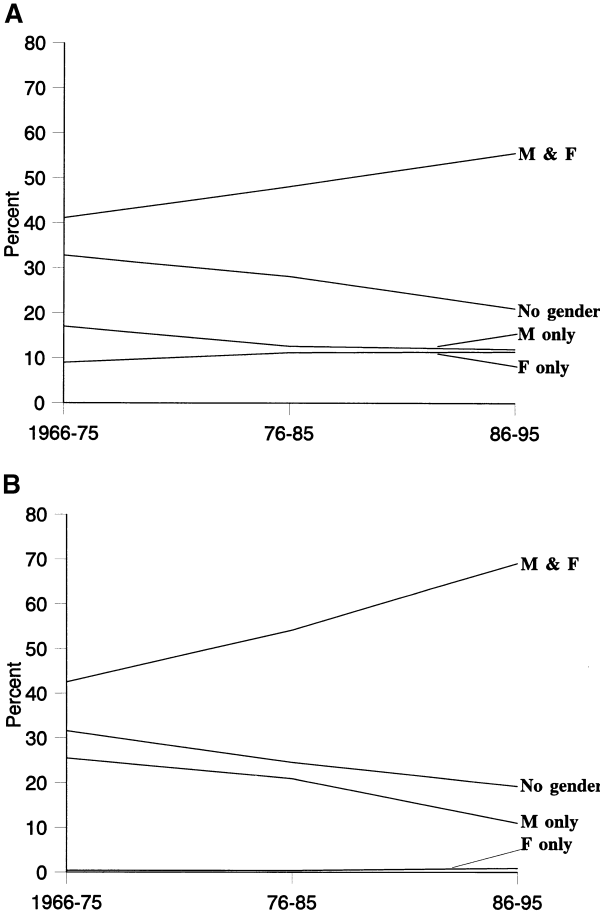


Figure 2 Gender mix of clinical trials by disease area: (A) All; (B) Heart; (C) Neoplasms; (D) All other areas. English language publications in U.S. journals, classified by disease area based on MEDLINE index terms as detailed in text.

not the case for neoplasms. Female-only trials outnumber male-only trials 2.56 to 1. The difference is not accounted for by the differential in breast versus prostate trials. In fact, the ratio of female-only to male-only trials is increased (3.16 to 1) if breast and prostate trials are removed.

The estimate of gender representation here is based on counts of single-gender trials. An alternative measure is counts of males and females studied in trials, but, as already noted, those counts are not provided in MEDLINE. The best we can do is to make such estimates based on counts from the 724 papers read in relation to producing Tables 3 and 4. There was a total of 906,367 persons represented in the 603 trials providing counts by gender (Table 3). The ratio of females to males was 1.55 to 1. The corresponding ratio for heart trials (105 with gender mix specified) was 0.27 and 13.63 for the neoplasms trials (80 trials providing counts). The corresponding ratios, based on counts of single-gender trials, are 1.15, 0.04, and 3.43, respectively.

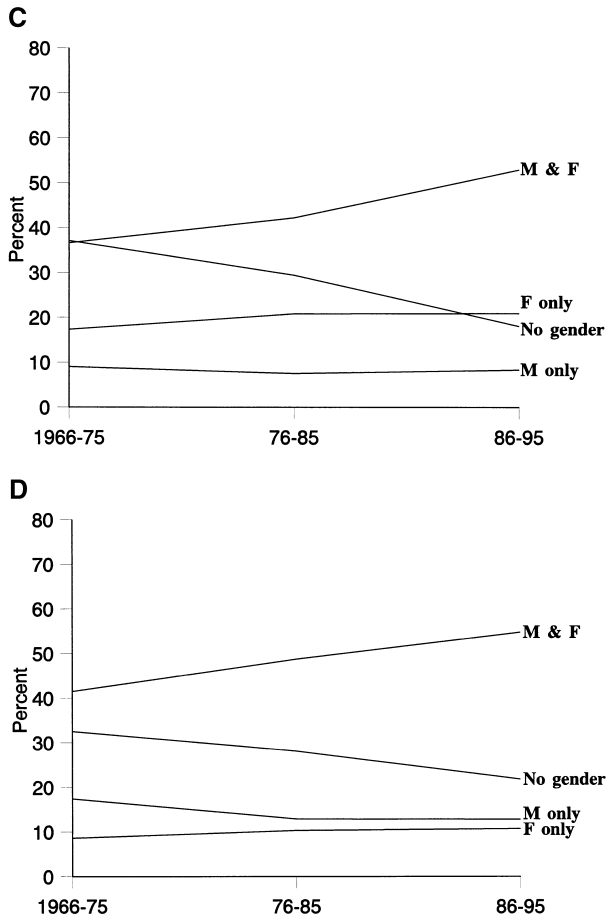


Figure 2 (Continued).

An issue that cannot be addressed with information in MEDLINE has to do with the reason for trials being male or female only. No doubt, the reasons are varied and have to do with access, convenience, logistics, or disease demographics. Indications are that more of the female-only trials are legitimately female only than the male-only trials are legitimately male only. Evidence of this tendency can be seen in the trials reviewed for Tables 3 and 4. Of the 90 female-only trials represented in the tables, all but nine were read by us as legitimately female only compared to just 19 of the 78 male-only trials.

Trends and Impact

There are relatively few conditions or diseases that are uniquely male or female, except for those dealing with reproduction and male and female anatomy. Hence, the hope for the future is for more broadly inclusive trials and fewer arbitrarily single-gender trials because, by and large, treatments that work do so without regard to gender or ethnic origin.

Table 2 Gender Mix of Clinical Trials by Disease Area in U.S. English Language Journals

	Total	Percentages				Female Only/ Male Only
		No Gender	Male and Female	Male Only	Female Only	
Clinical trials						
All areas						
1966–1975	7,401	32.8	41.1	17.0	9.0	0.53
1976–1985	15,993	28.1	48.1	12.6	11.2	0.89
1986–1995	50,389	21.0	55.6	12.0	11.4	0.95
1996–1998	26,672	15.1	62.8	10.8	11.3	1.05
Total	100,455	21.4	55.2	12.2	11.2	0.92
Heart disease						
1966–1975	275	31.6	42.5	25.5	0.4	0.02
1976–1985	1,138	24.5	54.1	20.9	0.4	0.02
1986–1995	3,894	19.2	69.0	11.0	0.9	0.08
1996–1998	1,814	13.5	77.3	7.1	2.1	0.30
Total	7,121	19.0	67.7	12.1	1.1	0.09
Neoplasms						
1966–1975	579	37.1	36.6	9.0	17.3	1.92
1976–1985	2,476	29.4	42.2	7.5	20.8	2.77
1986–1995	7,275	18.0	52.9	8.3	20.9	2.52
1996–1998	3,716	11.6	57.0	10.4	21.0	2.02
Total	14,046	19.1	51.4	8.7	20.8	2.39
All areas except heart and neoplasms						
1966–1975	6,547	32.5	41.5	17.4	8.6	0.49
1976–1985	12,379	28.1	48.7	12.9	10.3	0.80
1986–1995	39,220	21.8	54.7	12.8	10.7	0.84
1996–1998	21,142	15.9	62.9	11.2	10.3	0.92
Total	79,288	21.0	56.0	12.5	10.5	0.84
Breast						
1966–1975	49	2.0	2.0	0.0	95.9	
1976–1985	353	1.7	4.2	0.8	93.2	
1986–1995	817	5.5	3.2	0.2	91.1	
1996–1998	451	5.3	5.1	0.0	90.2	
Total	1,670	4.6	3.9	0.3	91.3	
Prostate						
1966–1975	28	0.0	3.6	96.4	0.0	
1976–1985	93	0.0	4.3	95.7	0.0	
1986–1995	406	0.0	1.7	98.3	0.0	
1996–1998	277	0.0	2.5	97.5	0.0	
Total	804	0.0	2.4	97.6	0.0	
Breast and prostate						
1966–1975	77	1.3	2.6	35.1	61.0	1.74
1976–1985	446	1.3	4.3	20.6	73.8	3.58
1986–1995	1,223	3.7	2.7	32.8	60.8	1.85
1996–1998	728	3.3	4.1	37.1	55.5	1.50
Total	2,474	3.1	3.4	31.9	61.6	1.93
HIV and AIDS						
1986–1995	1,003	25.2	46.6	24.0	4.2	0.18
1996–1998	704	21.7	58.1	15.3	4.8	0.31
Multicenter clinical trials						
All areas						
1986–1995	6,339	19.1	65.2	6.1	9.6	1.57
1996–1998	3,854	14.9	70.5	4.7	9.9	2.11
Total	10,193	17.5	67.2	5.6	9.7	1.73

(continued)

Table 2 (Continued)

	Total	Percentages				Female Only/ Male Only
		No Gender	Male and Female	Male Only	Female Only	
Heart						
1986–1995	885	17.3	75.7	6.6	0.5	0.08
1996–1998	439	15.5	78.8	3.9	1.8	0.46
Total	1,324	16.7	76.7	5.7	0.9	0.16
Neoplasms						
1986–1995	1,274	15.6	56.2	10.3	17.9	1.74
1996–1998	732	10.4	60.5	8.2	20.9	2.55
Total	2,006	13.7	57.8	9.5	19.0	2.00
All areas except heart and neoplasms						
1986–1995	4,180	20.6	65.7	4.7	9.0	1.91
1996–1998	2,683	16.0	71.9	3.9	8.2	2.10
Total	6,863	18.8	68.1	4.4	8.7	1.98

The focus on gender is likely to have the opposite effect. The trend, even before Congress acted, has been toward more multicenter female-only trials. They outnumbered male-only multicenter trials 1.57 to 1 in 1986–1995 and 2.10 to 1 in 1996–1998 (Table 1). The corresponding ratios for 1986–1992 and 1993–1998 are 1.58 to 1 and 1.81 to 1, respectively.

Science reports that “Ten years after its scathing report on the National Institutes of Health’s failure to include women in clinical research, the General Accounting Office (GAO) has concluded that the NIH is doing much better” [32]. Better compared to what? The reality is that, at least with regard to trials, it is perhaps the scathing report that may be in question. Even as far back as 1979, the last year the NIH maintained its inventory of clinical trials, evidence was against the perception. Of the 986 trials listed as ongoing at the time of the inventory, 80.5% involved both males and females. Among the remainder, there were many more female-only trials (15.2% of the 986) than male-only trials (4.3%) [33].

It is tempting to attribute changes in the gender mix of trials to the events of the 1980s and early 1990s aimed at increasing effort on females, but caution is in order. The biggest change in the mix of published reports occurred prior to those events. The ratio of female-only to male-only trials jumped from 0.53 for the decade 1966–1975 to 0.89 for the following decade.

On Perception

In some sense, perception is more important than fact. Perception becomes reality and truth. Beliefs, right or wrong, underlie many of the actions we take and the behaviors we exhibit. The disconnect of perception from fact would be only an interesting curiosity if it did not also have serious consequences. In the case of clinical research, and clinical trials in particular, the perception that the publicly funded research enterprise of the nation has favored one gender group over the other serves to erode a public trust essential to a healthy and robust clinical research enterprise. It leads, inexorably, to apportioning effort along gender lines where the emphasis shifts from our being seen as

Table 3 Enrollment by Gender in Trials Published in 1985, 1990, and 1995^a

	Two-Gender Trials		One-Gender Trials		All Trials		No. of Trials
	Males	Females	Males	Females	Males	Females	
All areas							
1985	11,169	7,664	10,709	169,466	21,878	177,130	115
1990	62,574	32,689	41,782	133,856	104,356	166,545	227
1995	217,223	145,255	12,167	61,813	229,390	207,068	261
Total	290,966	185,608	64,658	365,135	355,624	550,743	603
Heart							
1985	5,020	3,231	8,083	0	13,103	3,231	14
1990	40,135	14,676	38,715	0	78,850	14,676	42
1995	102,380	36,515	8,154	875	110,534	37,390	49
Total	147,535	54,422	54,952	875	202,487	55,297	105
Neoplasms							
1985	986	569	2,033	168,347	3,019	168,916	16
1990	3,232	3,222	273	46,526	3,505	49,748	29
1995	12,815	13,501	1,020	45,313	13,835	58,814	35
Total	17,033	17,292	3,326	260,186	20,359	277,478	80
Neoplasms less breast and prostate							
1985	986	569	1,954	0	2,940	569	8
1990	3,232	3,222	43	337	3,275	3,559	23
1995	12,815	13,501	20	686	12,835	14,187	25
Total	17,033	17,292	2,017	1,023	19,050	18,315	56

^a Reported in the *Annals of Internal Medicine*, *British Medical Journal*, *Journal of the American Medical Association*, *Lancet*, and *New England Journal of Medicine*.

Table 4 Gender Mix Represented in Reports of Trials^a

	Total No. of Reports	Percentages				
		No Gender	Male and Female	Male Only	Female Only	Female Only/Male Only
1985						
<i>n</i> < 100	81	19.8	58.0	16.0	6.2	0.39
<i>n</i> ≥ 100	63	20.6	54.0	6.3	19.0	3.02
Total Trials	144	20.1	56.3	11.8	11.8	1.00
1990						
<i>n</i> < 100	145	17.9	51.0	16.6	14.5	0.87
<i>n</i> ≥ 100	134	19.4	57.5	10.4	12.7	1.22
Total Trials	279	18.6	54.1	13.6	13.6	1.00
1995						
<i>n</i> < 100	105	15.2	67.6	11.4	5.7	0.50
<i>n</i> ≥ 100	196	12.2	67.3	5.6	14.8	2.64
Total Trials	301	13.3	67.4	7.6	11.6	1.53
1985, 1990, 1995						
<i>n</i> < 100	331	17.5	58.0	14.8	9.7	0.66
<i>n</i> ≥ 100	393	16.0	61.8	7.4	14.8	2.00
Total Trials	724	16.7	60.1	10.8	12.4	1.15

^a Based on identification of trials in *Annals of Internal Medicine*, *British Medical Journal*, *Journal of the American Medical Association*, *Lancet*, and *New England Journal of Medicine* via MEDLINE followed by reading of article to classify trial as to sample size and to obtain information on gender mix of study population.

persons, happening to be male or female, to males and females entitled to their fair share of a limited resource. It is hard to imagine how, as males or females, we will be better served by that kind of preoccupation.

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