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Report to Congressional Requesters

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WOMEN'S HEALTH

NIH Has Increased Its Efforts to Include Women in Research

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Contents

Abbreviations

AIDS	acquired immunodeficiency syndrome
HHS	Department of Health and Human Services
NIH	National Institutes of Health
ORWH	Office of Research on Women's Health
PHS	Public Health Service
WHI	Women's Health Initiative

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Health, Education, and
Human Services Division

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The Honorable Tom Harkin
The Honorable Barbara A. Mikulski
The Honorable Olympia J. Snowe
United States Senate

The Honorable Henry A. Waxman
Ranking Minority Member
Committee on Government Reform
House of Representatives

In the 1980s, public health leaders and advocates drew attention to inequities in the health research agenda and the fact that in particular women and minorities were being excluded from research studies. Many of the major research studies the National Institutes of Health (NIH) funded included only men, making it uncertain whether the studies' results applied also to women. NIH developed a policy to include women in research study populations, but in 1990, we found that NIH had been slow and ineffective in implementing it.[1] NIH began to take more comprehensive measures to increase research on health problems affecting women, and in 1993, the Congress passed the NIH Revitalization Act, which provided statutory authority and specific guidance for NIH to follow regarding research on women's health.[2]

In light of these developments, you asked us to assess NIH's progress in conducting research on women's health in the past decade. In response to your request, we have assessed NIH's progress in implementing its new guidelines on including women in clinical research, including the requirement that certain studies be designed to permit analysis of differences between women and men. We also provide information about the extent to which women are being included in clinical research that NIH funds, review the activities and accomplishments of the NIH Office of Research on Women's Health (ORWH) in promoting women's health

[1]*National Institutes of Health: Problems in Implementing Policy on Women in Study Populations* (GAO/T-HRD-90-38, June 18, 1990).

[2]Public Law 103-43.

research at NIH, and provide information about how much funding NIH has allocated to research on health issues that affect women.

To assess NIH's progress, we conducted work in several NIH institutes, centers, and offices, including the National Cancer Institute; National Heart, Lung, and Blood Institute; National Institute of Allergy and Infectious Diseases; National Institute of Arthritis and Musculoskeletal and Skin Diseases; National Institute on Aging; National Institute of Child Health and Human Development; ORWH; and Warren Grant Magnuson Clinical Center for intramural research. We also reviewed documents related to the review and approval of a sample of grants and cooperative agreements from the National Heart, Lung, and Blood Institute; National Institute of Allergy and Infectious Diseases; and National Institute of Arthritis and Musculoskeletal and Skin Diseases. We analyzed NIH's tracking data on the inclusion of women and minorities in clinical research, for NIH and for individual institutes and centers, and we analyzed NIH's data on expenditures on women's health. (For additional information on our methodology, see app. I.) We conducted our work between November 1999 and April 2000 in accordance with generally accepted government auditing standards.

Results in Brief

In the past decade, NIH has made significant progress in implementing a strengthened policy on including women in clinical research. It issued guidelines to implement the 1993 NIH Revitalization Act and conducted extensive training for scientists and reviewers. The review process for extramural research now treats the inclusion of women and minorities as a matter of scientific merit, which affects a proposal's eligibility for funding, and it appears that NIH staff and researchers are working to ensure that, when appropriate, study findings will apply to both women and men. The intramural research program now also implements the inclusion policy. NIH implemented a centralized inclusion tracking data system that is an important tool for monitoring the implementation of the inclusion policy. However, the data need to be more accurate and consistent. NIH is taking steps to improve the system, but ongoing training is needed to ensure the quality of the data. NIH has made less progress in implementing the requirement that certain clinical trials be designed and carried out to permit valid analysis by sex, which could reveal whether interventions affect women and men differently. We are therefore recommending that the Director of NIH ensure that NIH staff and reviewers implement this aspect of the inclusion policy, a recommendation with which NIH concurs.

More than 50 percent of the participants in clinical research studies that NIH funded in fiscal year 1997 were women, according to NIH. Even when studies with female-only or male-only protocols are removed from the data, the proportion of women enrolled exceeded 50 percent. Minority women were well represented, especially black and Asian and Pacific Islander women; however, the proportion of Hispanic women enrolled was below their proportion in the general population. There was some variation in enrollment levels by institute.

ORWH, established in 1990, has lead responsibility for ensuring that women and minorities are included in clinical research that NIH funds. Its budget grew from $9.4 million in fiscal year 1993 to about $20 million in fiscal year 2000. With input from the scientific and advocacy community, ORWH developed an agenda for research on women's health. ORWH uses its budget to leverage increased funding for research on women's health by the institutes and centers. It has carried out extensive training and education on the inclusion policy for staff members, investigators, and institutional review boards. However, ORWH has not conducted updated training on the data tracking system to ensure that its data are accurate and consistent.

Determining which NIH expenditures fund research that may affect women's health is complex and imprecise. NIH annually reports how much it spends on women's health, men's health, and conditions that affect both women and men. However, the nature of scientific inquiry makes it impossible to predict how research will affect specific populations, especially with regard to the basic research that receives a substantial portion of NIH resources, and we found inconsistencies in the methods NIH staff use to produce its expenditure estimates. Therefore, NIH's data on spending on conditions that affect women, men, or both should be interpreted with caution. According to NIH, spending on women's health conditions grew by 39 percent between fiscal years 1993 and 1999 when adjusted for inflation, in comparison with 23 percent and 27 percent increases, respectively, in spending on men's health and on research that affects both women and men. Using a different analytical approach, we found that NIH's total spending on diseases and conditions unique to or more prevalent in women grew more rapidly than NIH's overall spending from fiscal year 1993 to fiscal year 1999, but spending growth for specific diseases varied.

Background

NIH, the lead federal agency for medical research, is made up of 25 institutes and centers that had a total fiscal year 1999 budget of approximately $15.6 billion. NIH institutes and centers, each focusing on a particular research area such as cancer, infectious diseases, or heart, lung, and blood conditions, accomplish their missions chiefly through extramural and intramural research. Extramural research, constituting about 80 percent of NIH's budget, involves grants, contracts, and other funding awards to scientists who are employed outside the federal government and conduct research at their institutions. Intramural research, which represents about 10 percent of the NIH budget, entails government scientists conducting research in NIH's own laboratories, hospitals, and clinics or off-site at selected clinics and hospitals.

In 1986, NIH announced a policy of encouraging grant applicants to include women in study populations. However, in 1990 we found that NIH had been slow to implement this policy. Moreover, it had not been well communicated or understood within NIH or the research community, and it was applied inconsistently in research proposal reviews. In 1990, the inclusion policy applied only to extramural research, not to intramural research. Although the original policy announcement advised researchers to analyze findings by gender, NIH had done little to implement that part of the policy.

In response to criticism about the lack of progress on research on women's health, NIH took a number of actions. In 1990, it established ORWH in the Office of the Director to take the lead on women's health issues at NIH, and the following year, it launched the Women's Health Initiative (WHI), a large prevention study to examine the major causes of death, disability, and frailty in postmenopausal women. (See app. II.)

The 1993 NIH Revitalization Act required NIH to strengthen its previous policy on the inclusion of women and members of minority groups in clinical research supported by NIH.[3] The act contained provisions that required NIH to

- ensure that women and minority groups are included as subjects in clinical research except in cases in which it is inappropriate with

[3]Although the Revitalization Act addressed the inclusion of minorities as well as women, we focus in this report primarily on women.

respect to the health of the subjects or the purpose of the research or under circumstances that NIH's Director designates,
- conduct or support outreach programs for recruiting women and members of minority groups as subjects in clinical research,
- ensure that clinical trials that include women and minorities are designed and carried out in a manner sufficient to provide for the valid analysis of differences in effect for them,
- establish guidelines about including women and minorities as subjects in clinical research projects, and
- establish a data system to collect, store, analyze, retrieve, and disseminate information about women's health research that NIH supports or conducts.

In addition to strengthening the policy on inclusion, the Revitalization Act statutorily established ORWH, requiring it to carry out certain activities, and called for establishing the Advisory Committee for Research on Women's Health, a panel of nonfederal health practitioners, scientists, and other women's health experts. The act defined women's health conditions as conditions (1) unique to women or more serious or more prevalent in women, (2) for which the factors of medical risk or types of medical intervention are different for women or for which it is unknown whether such factors or types are different for women, or (3) for which clinical research using women as subjects or clinical data on women have been insufficient.

NIH Has Made Substantial Progress in Ensuring That Women Are Included in Studies but Less Progress in Encouraging Analysis by Sex

NIH's guidelines implementing the 1993 Revitalization Act strengthened its policies on the inclusion of women and minorities in clinical research. NIH conducted extensive internal training on the new requirements, educated the scientific community, and revised its application form for new grants. The review process for recommending extramural research proposals to fund now treats the inclusion of women and minorities as a factor that affects the scientific merit of a proposal, which in turn affects the likelihood that NIH will fund it. Moreover, NIH staff work with researchers to try to ensure that studies continue to meet the inclusion requirements as they proceed. The intramural research program now actively implements the inclusion policy as well. A centralized tracking data system provides information on the extent to which women are included in study populations, but there are some inconsistencies in the data, and updated training sessions have not been conducted. NIH has made less progress in implementing the requirement that phase III clinical trials be designed and

carried out to permit the analysis of whether interventions affect women and men differently.

NIH Issued Strengthened Guidelines and Trained Scientists and Reviewers

In March 1994, NIH published in the *Federal Register* new guidelines on including women and minorities as subjects in NIH-supported clinical research. They became effective in March 1994 for proposals submitted on or after June 1, 1994, and addressed all relevant provisions of the 1993 NIH Revitalization Act. In addition to continuing the NIH requirement to generally include women and minority groups in all NIH-supported biomedical and behavioral research involving human subjects, the new guidelines broadened the definition of clinical research to include all research involving human subjects, instructed reviewers to consider the planned study population when assessing the scientific merit of a grant proposal, and required that certain phase III clinical trials be designed to allow for valid analyses of differences by sex or minority status.[4] According to the new guidelines, cost is not an acceptable reason for excluding these groups from clinical studies. Furthermore, NIH must conduct or support outreach programs to recruit and retain women and minorities as subjects in clinical research.

To facilitate researchers' compliance with the inclusion policy, NIH revised its application form for new grants. The application for a Public Health Service (PHS) grant now contains instructions on compliance with the inclusion policy and displays the format for investigators to use to report data on the study population by sex and by racial and ethnic group. Applicants are instructed to report the composition of the proposed study population at the start of a project and report current enrollment data annually when they apply to continue a grant.

[4]The 1994 guidelines use "gender" rather than "sex." However, since scientists have begun to use the term "sex" to denote biologically based differences and "gender" to indicate culturally shaped variations between women and men, in this report we use "sex" when referring to analysis of different study results for women and men. For further discussion of this issue, see Jennifer R. Fishman, Janis G. Wick, and Barbara A. Koenig, "The Use of 'Sex' and 'Gender' to Define and Characterize Meaningful Differences Between Men and Women," in NIH, Office of the Director, Office of Research on Women's Health, *Agenda for Research on Women's Health for the 21st Century: A Report of the Task Force on the NIH Women's Health Research Agenda for the 21st Century,* Vol.1, *Executive Summary,* NIH publication 99-4385 (Bethesda, Md.: HHS, NIH, 1999).

After the 1994 guidelines were promulgated, NIH engaged in a series of activities to communicate the new policy to its own reviewers, program officers, and grants management staff, as well as to the broader scientific community. NIH trained more than 1,000 staff members on the inclusion requirements. The newly trained staff, in turn, worked closely with grant applicants in the research community to guide application development, submission, and review. NIH staff also presented information at professional meetings and in workshops with the chairs of institutional review boards.[5]

Study Demographics Now Affect Assessments of Scientific Merit and NIH Funding Decisions

NIH reviewers now routinely examine the planned study populations in extramural research proposals when evaluating their scientific merit. Initial review groups and study sections in NIH's Center for Scientific Review or the institutes and centers are responsible for determining whether grant applications for clinical research comply with NIH's inclusion policy. Under the guidance of a scientific review administrator, peer reviewers assess the scientific merit of proposals and assign an overall priority score to each application, which affects NIH decisions on studies to fund.[6] This score is supposed to reflect, in part, the level of adherence to the inclusion policy. Following the initial review, the scientific review administrator prepares a summary statement for each application, which is supposed to include all concerns about the research proposal, including any concern about the inclusion of women.

Our reviews of grant files and discussions with NIH program officers indicated that during the initial review process, NIH staff and many peer reviewers do pay attention to proposed study populations' inclusion of women. Most summary statements we reviewed at least mentioned the anticipated participation of women and minorities, and we found numerous instances of reviewers either noting that the level of planned participation was good or raising concerns about the adequacy of inclusion or strategies for recruitment and retention. We were not, however, able to assess the extent to which observations about study populations affected

[5]Institutional review boards are associated with a research institution or university and are responsible for implementing federal human subject protection requirements for research conducted at or supported by the institution or university.

[6]A scientific review administrator is an NIH staff member who serves as the primary contact with applicants during the initial phase of the peer review process until the conclusion of the first-level peer review process.

the priority scores given specific applications. In some instances, comments from individual reviewers submitted before the initial review group met identified concerns about the study population, but the final assessment of the initial review group was that the population was acceptable. This could have resulted from a difference of opinion among the reviewers or the investigator's having provided additional information that responded to those initial concerns.

NIH data indicate that in fiscal year 1997, first-level peer reviewers found that about 94 percent of the extramural applications with human subjects met NIH's standard for including women. If an application is found not to meet NIH's standard for inclusion, it receives an administrative "bar-to-funding." The bar-to-funding may be removed by NIH staff if additional information is provided or if the study design is modified. About 4 percent of the extramural applications with human subjects were found to be unacceptable in regard to the inclusion of women and received a bar-to-funding.[7]

When the review group identifies deficiencies in applications with respect to inclusion, NIH program staff explain to investigators the kinds of changes they need to make to their proposals so that the studies will comply with the inclusion requirements. We observed that some applicants have been requested to provide additional information about or improve strategies for including women before their applications were able to move forward.

Summary statements for applications recommended for further consideration are sent to the institutes and centers for review by their national advisory councils, which review research proposals not only for scientific and technical merit but also for their relationship to the institute's or center's mission, priorities, and research portfolio. Although the advisory council reviews are considered another element of NIH's process for ensuring the appropriate inclusion of women, most of the work of identifying and resolving problems related to inclusion occurs before the applications reach the councils. Council members are expected to consider a study population's inclusion of women when making a recommendation, but advisory councils typically focus on inclusion issues only when program staff flag problems as a result of the initial review process.

[7]The remainder of the applications, about 2 percent, were found to be unacceptable in regard to the inclusion of minorities and received a bar-to-funding.

Ensuring that women are included in research does not end with the initial approval of a grant. We found evidence that both investigators who have received funding and NIH staff continue to focus on inclusion issues after a study is under way. Investigators submitting annual progress reports sometimes call attention to problems with the recruitment of women and outline strategies for improving lagging enrollment. For example, they may say that they plan to concentrate all recruitment efforts in the coming year on enrolling women, outline planned outreach activities, or report that they will add new study sites that should provide greater access to the population whose enrollment is below target.

NIH program staff told us that when there is a large gap between planned and actual enrollment of women, they take steps to help investigators recruit more women. A National Heart, Lung, and Blood Institute official told us that he and other staff are consistently concerned about recruiting women to studies and clearly inform researchers when there is a problem. In general, NIH's approach is to work with researchers to expand recruitment strategies or identify reasons for difficulties in enrolling women. Often the research team pursues the necessary actions to improve enrollment, but a grant can be terminated if the enrollment pattern is not corrected.

NIH's Progress in Ensuring That Clinical Trials Can Analyze Differences by Sex Is Incomplete

Progress in carrying out the Revitalization Act's requirement that clinical trials be designed to permit analysis of whether interventions affect women and men differently has been less substantial than progress in implementing other aspects of the inclusion policy. NIH requires that phase III clinical trials include women in sufficient numbers to allow for the valid analysis of differences in intervention effects between women and men.[8] The agency limited the requirement to phase III trials because officials believed that the Congress had in mind studies that are well advanced on the biomedical research spectrum and that can contribute more immediately to the development of policy and standards of care than more

[8]To implement this policy, NIH developed a special definition of clinical trial to distinguish these trials from other types of clinical research that NIH supports. NIH defined clinical trial as "a broadly based prospective Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments." Phase I and phase II clinical trials are earlier phases of research in which interventions or treatments are tested in a smaller number of people.

basic scientific research.[9] As specifically authorized by the Revitalization Act, the guidelines also exempt certain clinical trials from this requirement. When substantial scientific data demonstrate no significant difference between women and men, NIH does not require that sex be considered in selecting study subjects but strongly encourages including women.

In practice, these guidelines leave room for interpretation as to when phase III clinical trials must be designed to allow for analysis by sex. A number of clinical trials whose files we reviewed were designed to include women but not in numbers large enough to allow analysis that would definitively measure different outcomes for women and men. For example, the target populations for certain trials related to acquired immunodeficiency syndrome (AIDS) or sudden cardiac death were based on prevalence data for the general population or the study's catchment area, which meant the goal for women's enrollment was in the 20 to 25 percent range. NIH program officers told us that for these and certain other studies, previous research indicated no reason to expect different outcomes for women and men, so the trials did not need to be designed for that type of analysis. They said, however, that the researchers would review data for each population subgroup, so that even if the studies were not designed to produce valid results separately for women and men, the researchers would recognize whether the data revealed differences that suggested the need for further study by sex.

Although the grant documents we reviewed provided strong evidence that NIH staff and reviewers routinely focus on studies' general inclusion of women, evidence as to whether they were taking care to implement the requirement related to analysis by sex was scant. For example, in discussing some of the phase III clinical trials we examined, program officers told us that under the NIH guidelines, they were exempt from the requirement. However, because the grant applications did not indicate plans to analyze the data by sex and the summary statements did not explicitly mention this issue, we were not able to assess whether reviewers had considered whether the studies should be designed to permit valid analysis by sex. Furthermore, when we reviewed requests for proposals and requests for applications for clinical trials that NIH issued, we found that while they instructed potential applicants that studies must include

[9]J. LaRosa, and others, "Including Women and Minorities in Clinical Research," *Applied Clinical Trials*, Vol. 4, No. 5 (May 1995), pp. 31-38.

women, they did not mention the need to design and carry out studies to permit valid analysis of outcomes by sex.

Because of the difficulty in determining from the available documents whether analysis by sex is occurring, we looked for evidence in the published literature. A study by the Society for Women's Health Research reviewed articles published in four major medical journals and found that only one-quarter to one-third of the non-sex-specific studies that included women analyzed data by sex of the subjects, with no significant change from 1993 to 1998.[10] However, even when scientists are performing such analyses, the results are not always published. NIH officials told us that when an analysis reveals no difference in outcome, journals publishing the analysis may omit this information because editors often discourage researchers from including "no news" information in their results. NIH officials also observed that because researchers who received funding after the new guidelines took effect are just now beginning to publish their study results, the amount of analysis by sex may increase.

NIH's Intramural Research Program Now Implements the Inclusion Policy

As required by the Revitalization Act, NIH's intramural studies also must comply with the inclusion policy. All the patients admitted to the intramural program are treated under a research protocol that one of NIH's 14 institutional review boards must review and approve. To approve a research protocol, a board must ensure that the selection of patients is appropriate. In the review process for the continuation of protocols, a board receives accrual data on the distribution of women and men for each of the intramural program's almost 1,000 research protocols. According to NIH, the boards play an active role in evaluating the inclusiveness of the intramural research designs and monitor the accrual data closely.

About 6 years ago, the intramural program developed and began implementing a new curriculum to train investigators that covers all aspects of clinical research practice, including NIH's inclusion policy. In addition, all newly appointed review board members are required to complete NIH's computer-based training on the protection of human subjects and a one-on-one orientation with the Office of Human Subjects Research that addresses the inclusion of women and minorities.

[10]Regina M. Vidaver and others, "Women in NIH-funded Clinical Research: Lack of Progress in Both Representation and Analysis by Sex in the Medical Literature," forthcoming in *Journal of Women's Health and Gender-Based Medicine*.

NIH's Centralized Tracking System Monitors the Implementation of Inclusion Policy but Needs Improvement

In 1995, NIH established an automated, centralized data tracking system to monitor demographic information on study populations and help assess whether the inclusion policy is being carried out. The Information Systems Branch of the Division of Research Grants developed this system in collaboration with ORWH, the Office of Research on Minority Health, the Office of Extramural Research, and the Office of Intramural Research, and it was designed to be compatible with NIH's existing data management system. Investigators manually submit data on their study populations to program staff at each institute, who either manually or electronically transmit them to the centralized tracking data system.[11] An NIH Tracking and Inclusion Committee, consisting of representatives from each of the institutes and centers and cochaired by the ORWH director and an NIH senior program official from a major institute, provides guidance on the tracking system and communicates tracking policies to the institutes and centers. Each year the committee reports on aggregate enrollment information in the tracking system. These data are generally about 2 years old because of the time it takes investigators to report and NIH staff to compile and process the data.

Not all research studies that NIH funds are entered into the tracking system. NIH officials have decided that ten different categories of studies do not need to report on the inclusion of women and minorities. These include basic research studies, studies involving only tissue or body fluid specimens, and very small studies. Also, if a study is part of a multicenter study or is funded by a supplemental grant, its data are presumed to be reported by its coordinating center or the parent study.[12] In fiscal year 1997, about 41 percent of NIH studies were tracked. Among the six institutes we reviewed, this percentage ranged from 13 percent of studies at the National Institute of Allergy and Infectious Diseases to 60 percent of studies at the National Institute of Child Health and Human Development. (See app. III.) The relatively small percentage of studies tracked at NIH overall and at

[11]There is no verification of the data that investigators submit on their study enrollment; however, falsifying these data would be a federal felony.

[12]The categories are (1) basic research; (2) studies in early stages of technology or methodology development; (3) studies with fewer than 10 participants; (4) multicenter projects, not at a coordinating center; (5) supplemental grants, when data are reported in the parent study; (6) unidentifiable gender and minority status; (7) awards made before implementing the revised inclusion policy; (8) substudy of existing reported population; (9) analysis of existing study data; and (10) only tissue or body fluid specimens are involved.

some institutes may in part reflect the fact that a majority of NIH research is nonclinical.

The inclusion data are subject to inconsistencies because of differing interpretations of which studies should be tracked. When the tracking system was first established, NIH staff involved in entering the data received training, but updated training has not been conducted. NIH officials told us that the system and the data derived from it have improved and have been refined and that the system is now capturing more meaningful information, such as enrollment targets. Some of the earlier data are being reconciled by the Office of Extramural Research, which is also transferring the system to a new NIH-wide data management system. NIH is also beginning to implement an electronic reporting system for applications that includes reporting the composition of study populations.

Women Are a Significant Proportion of Research Subjects

More than half of the participants in clinical research studies NIH funded in fiscal year 1997 were women, according to NIH's tracking data. Even when studies with female-only or male-only protocols were removed from the analysis, the proportion of women enrolled was greater than 50 percent. Minority women were well represented, especially black and Asian and Pacific Islander women; however, the proportion in Hispanic women enrolled was below their proportion in the general population. There was some variation in enrollment levels by institute.

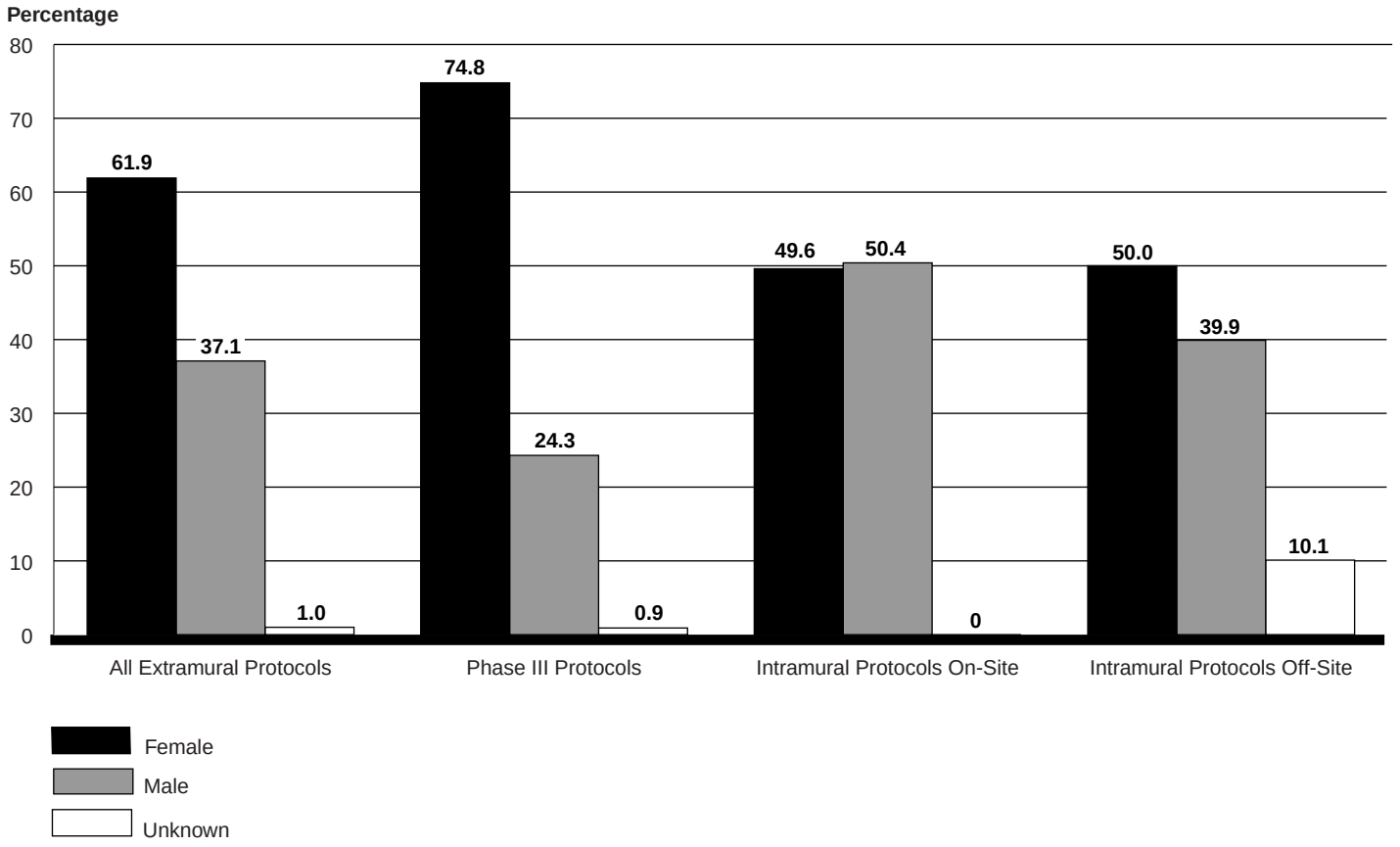
More Than Half of Study Participants Are Women, and Minorities Are Well Represented

NIH's tracking system indicates a large percentage of women enrolled in clinical research that NIH funds. Aggregate enrollment data for all extramural research protocols funded in fiscal year 1997 show that 61.9 percent of the study subjects were women and 37.1 percent were men. Phase III clinical studies funded that year included 74.8 percent women and 24.3 percent men. For intramural research projects, women represented about half of the study participants for both on-site and off-site protocols.[13] (See fig. 1.) When studies with female-only or male-only protocols were

[13]Where these percentages do not add up to 100, the remainder of study subjects were unknown.

removed from the aggregate extramural research enrollment data, the proportion of women enrolled was 52.1 percent.[14]

Figure 1: Aggregate Enrollment for NIH Extramural and Intramural Research, Fiscal Year 1997



NIH's data on the enrollment of minority women in extramural research projects indicate that blacks represented the largest proportion of minority women at 17.2 percent. Asians and Pacific Islanders represented 15.4 percent of women enrolled, and Hispanics represented 7.7 percent. (See

[14]Some studies restrict enrollment to women or to men because they focus on reproductive health, on diseases that affect women or men disproportionately or exclusively, or on the action of particular disease processes in only one or the other.

table 1.) These percentages compare favorably with the proportions of black women at 12.4 percent and Asian and Pacific Islander women at 3.6 percent in the general population; however, there is a larger proportion of Hispanic women in the general population, at 10.6 percent, than is represented in extramural research protocols at NIH.

Table 1: Enrollment of Minority Women in NIH Extramural and Intramural Research as a Percentage of Total Female Enrollment, Fiscal Year 1997

Type of research	American Indians and Alaska Natives	Asian and Pacific Islanders	Black, Not Hispanic	Hispanic	White, Not Hispanic	Other and unknown
All extramural	1.1	15.4	17.2	7.7	52.7	5.9
Extramural phase III	1.3	2.0	11.6	4.4	79.5	1.3
Intramural						
On-site	0.1	4.3	12.4	3.6	78.2	1.4
Off-site	0.2	55.3	3.8	0.5	38.4	1.8

NIH officials are cautious, however, about directly comparing enrollment data with national census figures. They believe that the goal of the NIH policy is to conduct biomedical and behavioral research in such a manner that scientific knowledge can be generalized to the entire U.S. population, not to satisfy proportional representation. NIH considers that the appropriate numbers of women or minority subgroups included in a particular study depend on the scientific question addressed in the study and the prevalence among women and minority subpopulations of the disease, disorder, or condition under investigation. Some studies, for example, would require a rate of minority participation higher than a group's presence in the overall population, and others would be sound with lower minority participation.

The Enrollment of Women and the Proportion of Studies Tracked Vary Across Institutes

When we examined the fiscal year 1997 distribution of studies by the percentage of women participating, most (52.5 percent) had enrolled between 30 and 60 percent women participants. Seventy percent of the studies had populations that were at least 40 percent women. (See table 2.) Among the six institutes we reviewed in detail, the range in aggregate enrollment of women in clinical research in fiscal year 1997 ran from the National Cancer Institute's highest at 70.9 percent to the National Institute of Allergy and Infectious Diseases' lowest at 48.1 percent.

Table 2: The Distribution of Fiscal Year 1997 Clinical Studies by the Percentage of Women Participants

Percent of women	Number of studies	Percent of studies
100	740	14.5
90 up to 100	45	0.9
80 up to 90	105	2.1
70 up to 80	196	3.9
60 up to 70	388	7.6
50 up to 60	1,115	21.9
40 up to 50	974	19.1
30 up to 40	586	11.5
20 up to 30	377	7.4
10 up to 20	224	4.4
1 up to 10	95	1.9
0	244	4.8
Total	5,089	100.0

Note: Excludes 74 studies in which it was not known whether the participants were women or men.

ORWH Helps Monitor Implementation of the Inclusion Policy and Develop NIH's Women's Health Research Agenda

ORWH has a mandate to ensure that women and minorities are included in clinical research that NIH funds, and it is specifically responsible for carrying out the guidelines on inclusion and coordinating the data tracking system. It conducted training and education on the inclusion policy when the policy first took effect but has not provided NIH staff with ongoing training on the data tracking system. ORWH took the lead at NIH in developing an agenda for research on women's health, obtaining input from individuals and groups outside NIH through numerous conferences, workshops, and its Advisory Committee for Research on Women's Health. ORWH has provided funding support to institutes and centers for women's health research that it considers important.

ORWH Played a Key Role in Implementing the Inclusion Guidelines

ORWH serves as a focal point for women's health research at NIH.[15] ORWH's estimated budget of about $20 million for fiscal year 2000 is a component of the budget of the Office of the Director. The ORWH budget more than doubled from fiscal year 1993 ($9.4 million) to fiscal year 1999 ($19.6 million), which was a 67 percent increase when adjusted for inflation. The size of ORWH's full-time-equivalent staff also increased, from 3 full-time-equivalent employees in fiscal year 1991 to 16 in fiscal year 1999. ORWH is required to prepare a report on its activities for the NIH director every 2 years. The most recent report, for fiscal years 1997-98, was still in draft in April 2000 and had not yet been published.

ORWH played a central role implementing NIH's 1994 guidelines on the inclusion of women and was responsible for some of the training and educational activities we described earlier in this report. For example, ORWH formed a task force in 1993 on the recruitment and retention of women in clinical studies; it also sponsored a public hearing following the publication of the guidelines. Recommendations from this hearing were incorporated into the planning of a scientific meeting, "Recruitment and Retention of Women in Clinical Studies," later that year, and in the fall of 1994, ORWH published a summary report.[16]

ORWH convened a meeting at NIH with institutional review board chairs from around the country after the 1994 inclusion guidelines were announced. The meeting focused on the role of board chairs in implementing the guidelines, discussed lessons learned during early implementation of the NIH policy, and suggested strategies for increasing the recruitment of women and minorities. In 1996, ORWH reconvened the board chairs to discuss their experience in implementing the guidelines.

To provide ongoing education and guidance to investigators as they consider scientific questions to research, appropriate study designs, and methods to facilitate the enrollment of study participants, ORWH published an outreach notebook in 1997, which is available on the Internet. This notebook provides advice on inclusion criteria in the form of a decision

[15]ORWH's mission also includes promoting the recruitment, retention, reentry, and advancement of women in biomedical careers. This report does not examine this aspect of ORWH's mission.

[16]NIH, *Recruitment and Retention of Women in Clinical Studies,* NIH publication 95-3756 (Bethesda, Md.: 1994).

tree, provides information on the key elements of the outreach process—such as understanding the study population and evaluating the efficacy of recruitment and retention strategies—and discusses a number of practical considerations. It describes the review criteria for including women and minorities and presents the format for the summary table of planned and actual enrollment.

In collaboration with the Office of Extramural Research, the Office of Intramural Research, and other components of NIH, ORWH is responsible for coordinating the collection and analysis of the inclusion tracking data and publishing reports with these data. ORWH organized and convened the NIH-wide Tracking and Inclusion Committee to ensure that uniform standards and definitions are used in reporting data on inclusion. However, as we indicated earlier, there have been inconsistencies in the reported data, and ORWH has not conducted updated training on the tracking system. The annual reports on the data have generally been limited to NIH-wide summary counts, with limited analysis.

The Revitalization Act also required NIH to establish a system of data on research on women's health, including a clinical trials registry, for health care providers, researchers, and the general public. ORWH worked with the National Library of Medicine to develop an NIH-wide clinical trials registry. In early 2000, NIH unveiled an Internet website listing all clinical trials sponsored primarily by NIH, and it plans to add studies from other federal agencies and the pharmaceutical industry later in 2000.

ORWH Collaborates Across NIH and With the Broader Scientific Community to Develop a Research Agenda

To develop a research agenda for women's health, ORWH has sought input from scientific experts and interest groups outside NIH. ORWH has sponsored or cosponsored with the institutes and centers numerous scientific conferences on women's health. Among the cosponsored conferences, topics covered since fiscal year 1993 include

- Directions for menopause research,
- Older women, health, and retirement: A demographic perspective,
- The recruitment and retention of minorities in clinical cancer research,
- African-American women's health care,
- The health of women with physical disabilities,
- Psychological and behavioral factors in women's health,
- HIV/AIDS in women: The changing face of AIDS,
- The U.S.-Mexico border and women's health,
- Neuroscience and endocrinology of fibromyalgia, and

- Research priorities in eating disorders.

One of ORWH's early actions was to convene a scientific workshop in September 1991 at which experts in the basic and clinical sciences, practitioners in women's health, and representatives of women's organizations developed recommendations for research activities in women's health, focusing on the major divisions of a woman's life span and the diseases and impairments that might affect her health and well-being over the course of her life. The deliberations and findings of that meeting were published as *Report of the National Institutes of Health: Opportunities for Research on Women's Health*.[17] According to the Director of ORWH, this report served as the basis for NIH's research priorities in women's health for 7 years.

In 1996 and 1997, ORWH and a task force of federal and nonfederal scientists and advocates convened three regional meetings around the country and a final national meeting to examine progress in research on women's health and to set an agenda for the future. Each meeting included a public hearing and a scientific workshop. Participants identified continuing or emerging issues, gaps in knowledge, and new models for designing and conducting research studies. The deliberations of these meetings were published in the 1999 report, *Agenda for Research on Women's Health for the 21st Century*.[18]

ORWH does not have a formal mechanism for monitoring how NIH's institutes and centers implement the women's health research agenda. Its primary means for collaborating with the institutes and centers is the Coordinating Committee for Research on Women's Health. The committee members, who are institute or center directors or, more commonly, their delegates, advise ORWH on NIH research issues regarding women's health and provide a liaison and a forum for communication among the institutes and centers and ORWH. ORWH now generally convenes committee meetings a few times a year to provide an opportunity for institutes and centers to share information on women's health research priorities and activities in their respective organizations. Representatives bring ORWH priorities back to their respective institutes and centers for consideration.

[17]NIH publication 92-3457 (Bethesda, Md.: Sept. 1992).

[18]*Agenda for Research on Women's Health for the 21st Century* is a six-volume report. Volume 1 is the executive summary, NIH publication 99-4385 (Bethesda, Md.: 1999).

Although ORWH does not fund research projects directly, it uses its budget to leverage funding for research on women's health by the NIH institutes and centers. From fiscal year 1991 through fiscal year 1999, ORWH provided almost $90 million to institutes and centers through various funding mechanisms such as making supplemental grants and cofunding studies. For example, one institute representative reported that funding assistance from ORWH led his institute to fund large-scale projects for women's health research. Some of the research projects that ORWH has cofunded have focused on reproductive health and sexually transmitted diseases, urological health, autoimmune diseases, occupationally related diseases and disabilities, physical disability in aging women, cancer, cardiovascular disease, depression, and violence.

The Advisory Committee for Research on Women's Health advises the ORWH director on appropriate women's health research activities for NIH to undertake and is charged with helping monitor compliance with the guidelines on including women in clinical research. To meet the Revitalization Act's requirement that the Advisory Committee issue a biennial report on its activities, it issues a report jointly with ORWH and the Coordinating Committee for Research on Women's Health.[19] Some Advisory Committee members have also taken an active role in ORWH conferences to develop the research agenda.

The ORWH director serves as co-study director of WHI with the National Heart, Lung, and Blood Institute director, receives periodic updates on the progress of the study's recruitment, and participates in WHI Advisory Committee meetings. In addition, the ORWH director serves as a member of WHI's Institute Directors Committee, which meets periodically to ensure communication among institutes and centers with an interest in WHI. A member of the ORWH Advisory Committee also serves as an ad hoc member of the WHI's Advisory Committee.

The Department of Health and Human Services (HHS) has an Office of Women's Health that serves as a focal point for women's health issues in the department by coordinating and promoting women's health activities across all HHS agencies. For example, the Office of Women's Health, along with ORWH, sponsored the Secretary's Conference to Establish a National

[19]See *Report of the Office of Research on Women's Health and of NIH Support for Research on Women's Health Issues, Fiscal Years 1995-1996*, NIH publication 99-4304 (Washington, D.C.: n.d.).

Action Plan on Breast Cancer. The conference involved collaboration with the National Breast Cancer Coalition, advocacy communities, scientific communities, and numerous components of HHS and other federal agencies.

NIH Spending on Women's Health Has Increased

It is difficult to estimate NIH's expenditures on research on women's health, in part because it is often not possible to predict who will benefit from research, especially basic research. NIH's estimates of expenditures for health conditions that affect women, men, or both women and men must therefore be interpreted with caution. According to NIH's estimates, NIH's spending on women's health conditions grew by 39 percent between fiscal year 1993 and fiscal year 1999, when adjusted for inflation, in comparison with 23 percent and 27 percent increases, respectively, in spending on men's health and on research that affects both women and men. Using a different approach, we found that NIH's spending on diseases and conditions unique to or more prevalent in women grew more rapidly than its overall spending, although this varied among specific diseases.

Determining the Amount Spent on Women's Health Is Difficult

NIH annually compiles a table that estimates expenditures for 124 specific disease categories. NIH classifies expenditures into three categories—spending on women's health conditions, spending on men's health conditions, and spending that affects both women's and men's health. Determining which NIH expenditures should be considered spending on women's health is challenging. The nature of biomedical research makes it difficult to predict the eventual uses of scientific findings and which segments of the population will benefit from particular studies. This is especially true for basic research, which is a substantial portion of the research that NIH funds. It is relatively easy to classify some expenditures, such as for certain research on ovarian cancer or prostate cancer, as related to women's health or men's health. Other expenditures, however, such as for certain cardiovascular research, could be divided between women's and men's health or placed in the category of spending that affects both. We found inconsistencies in the methods NIH staff use to produce the annual NIH expenditure table. For example, for clinical research that affects both women and men, some institutes use their data on the numbers of women and men enrolled in studies to place proportional

expenditures in the "women" and "men" categories. Others, however, enter the entire amount into the "both" category. One official noted that sufficient judgment is involved in making these decisions to suggest that even the same person might not make the same judgment twice.[20]

Spending on Women's Health Has Grown More Than Overall Spending

In light of the difficulties in assigning expenditures to the categories of women's health, men's health, and both, the following data must be interpreted with caution. NIH reported that it spent about $2.3 billion on women's health in fiscal year 1999, about 15.5 percent of total expenditures.[21] About 78.1 percent of expenditures that year fell into the "both" category, and about 6.4 percent went to men's health conditions. This distribution fluctuated to only a small extent from fiscal year 1993 through fiscal year 1999, but the share of total expenditures in the women's health category grew during that period while the proportions in the two other categories decreased (see table 3). When adjusted for inflation, spending in the women's health category grew by 39 percent from fiscal year 1993 to fiscal year 1999; during the same period, spending on men's health grew by 23 percent and spending on both grew by 27 percent.

Table 3: Percentages of NIH Expenditures for Research on Women, Men, and Both, Fiscal Years 1993-99

	1993	1994	1995	1996	1997	1998	1999
Women	14.3	14.5	16.1	16.0	16.2	16.0	15.5
Men	6.7	6.0	6.2	5.7	6.1	6.1	6.4
Both	79.0	79.4	77.6	78.3	77.7	77.9	78.1

We also analyzed NIH spending data using a different approach—comparing the growth in total NIH spending from fiscal year 1993 to fiscal

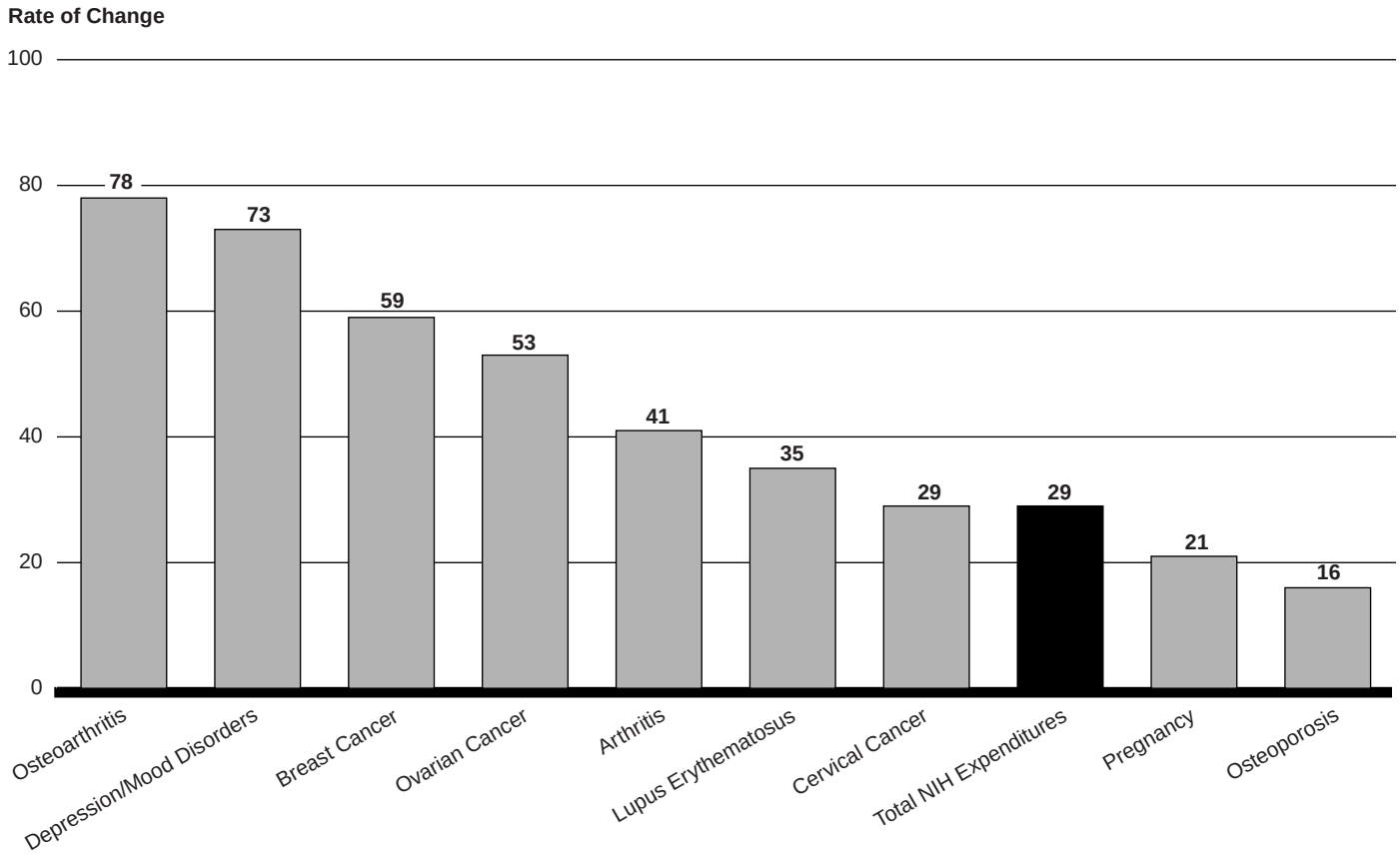
[20]One factor contributing to the inconsistencies is that NIH staff receive two sets of guidelines, one written by the HHS-wide Coordinating Committee on Women's Health and one by the NIH Coordinating Committee for Research on Women's Health, which differ in part.

[21]The total expenditure figures we are using in this report are the totals reported in the expenditure tables organized by the categories "women," "men," and "both." These figures may differ from other total expenditure figures NIH reports in other contexts, such as the annual budget justification, because the table figures do not include all NIH expenditures, such as buildings and facilities.

year 1999 with growth in spending on diseases and conditions that are unique to or more prevalent in women.[22] In the past several years, NIH's spending on these diseases and conditions has grown more rapidly than its overall spending. While overall expenditures, when adjusted for inflation, increased by about 29 percent from fiscal year 1993 to fiscal year 1999, adjusted expenditures for the conditions unique to or more prevalent in women grew by 37 percent. The rates of growth for specific women's conditions varied greatly. Adjusted spending on osteoarthritis and depression and mood disorders, conditions more prevalent in women, increased by more than 70 percent. Adjusted spending on pregnancy, at 21 percent, and osteoporosis, at 16 percent, however, grew more slowly than overall NIH spending. Adjusted expenditures on breast cancer and ovarian cancer grew by 59 percent and 53 percent, respectively. (See fig. 2.)

[22]These spending categories include the following diseases, conditions, and programs: breast cancer; cervical cancer; ovarian cancer; vaginal, uterine, and other reproductive cancers; contraception; infertility; female reproductive physiology; hysterectomy; endometriosis and leiomyomas (of uterus); pregnancy, pregnancy prevention, and maternal health; diseases related to DES exposure; menopause; hormone replacement therapy; incontinence; osteoarthritis; osteoporosis; thyroid diseases and conditions; violence; women as caregivers; depression and mood disorders; eating disorders; toxic shock syndrome; chronic fatigue syndrome; Sjogren's syndrome; temporomandibular disorders; fibromyalgia; urinary tract infections; arthritis; lupus erythematosus; multiple sclerosis; scleroderma; migraine; female genital mutilation; homeless women; WHI; and ORWH.

Figure 2: Rate of Adjusted Expenditure Growth for Selected Conditions and Total NIH Expenditures, Fiscal Years 1993-99



Note: 1999 expenditures have been adjusted to 1993 dollars.

Conclusions

An underlying goal of the 1993 NIH Revitalization Act and NIH's policy on including women and minorities in research is for every study funded by NIH to answer its research questions for as wide a segment of the population as is scientifically appropriate. NIH has made significant progress toward this goal. In contrast to our review of this issue 10 years ago, we found widespread awareness and understanding of most aspects of the policy, and many people in NIH and the research community are making concerted efforts to translate the policy into improved science.

For the policy to have its intended effect, however, NIH needs to expand its focus beyond simple inclusion and to ensure that, when it is scientifically

appropriate, researchers conducting clinical trials enroll populations and analyze study data in ways that enable them to learn whether interventions affect women and men differently. NIH staff, peer reviewers, and Advisory Council members should carry out this dimension of the inclusion policy as conscientiously as they attend to its other components. For example, when NIH initiates a phase III clinical trial through a request for application or proposal, unless NIH officials have determined that this particular trial is exempt from the requirement, the request should inform the applicants that they should design the trial to allow for a valid analysis of differences between women and men. As reviewers examine each application to receive funding for a phase III clinical trial, they need to explicitly consider whether the study should be structured to allow for analysis by sex. If the review group concludes that a particular trial should be exempt from this requirement—for example, because of previous research findings—noting this decision in the summary statement would increase confidence that NIH is implementing this aspect of the inclusion policy. Advisory Council members can carefully review these decisions to ensure that all research NIH funds is producing the scientifically appropriate information.

NIH's tracking system is an important tool for monitoring the implementation of the inclusion policy, and the system is beginning to capture more information, such as enrollment targets, that will help assess the policy's success. NIH's recent steps to improve the system and move toward increased electronic reporting should help improve the accuracy and timeliness of the data and improve the system's ability to measure progress. However, follow-up training on the requirements and purpose of the tracking system is needed.

Finally, NIH's data on spending on women's health must be interpreted with care. Determining which expenditures affect women's health is so complex and imprecise that it is easy to overstate or understate the extent of NIH's efforts. The nature of scientific inquiry makes it impossible to predict all the effects of research, and this is especially true for the basic research that makes up a large part of NIH's portfolio.

Recommendations to the Director of NIH

To strengthen the capacity of biomedical research to produce information on health applicable to all segments of the population, we recommend that the Director of NIH ensure that the agency implements the requirement that phase III clinical trials be designed and carried out to allow for the valid analysis of differences between women and men as fully as it implements other elements of the inclusion policy. Specifically, we

recommend that NIH appropriately communicate this requirement to applicants, that peer review groups explicitly determine whether each proposed phase III clinical trial is required to have such a study design, and that summary statements document the initial reviewers' decisions.

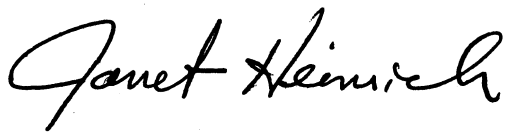
To improve the accuracy of NIH's tracking data on the inclusion of women and minorities, we recommend that the Director of NIH ensure that NIH staff who transmit data to the tracking system receive ongoing training on the requirements and purpose of the system.

Agency Comments

We provided a draft of this report to NIH for comment. NIH concurred with our recommendations. Regarding our recommendation to ensure that phase III clinical trials be designed and carried out to permit analysis by sex whenever appropriate, NIH said it will again emphasize to NIH staff and applicants that sex analysis should be included in research plans when it is scientifically justified and can be done in a way that protects the interests of study participants. The agency also indicated that it plans to take additional steps to implement the requirements related to phase III clinical trials. In response to our recommendation that ongoing training related to NIH's tracking system be provided, NIH said that its staff who transmit data to the tracking system will receive ongoing training and said that ORWH will work with the Office of Extramural Research to ensure that NIH staff are well informed about the data collection requirements of the current system. NIH also intends to conduct training on the tracking module in NIH's new grants administration system when it is implemented. Finally, NIH provided technical comments, which we incorporated where appropriate.

We are sending copies of this report to the Honorable Donna E. Shalala, Secretary of Health and Human Services, and to Dr. Ruth L. Kirschstein, the Acting Director of NIH; appropriate congressional committees; and others who are interested. We will also make copies available to others on request.

If you or your staff have any questions, please contact me at (202) 512-7119 or Helene Toiv at (202) 512-7162. Other major contributors are listed in appendix V.



Janet Heinrich
Associate Director, Health Financing
and Public Health Issues

Objectives, Scope, and Methodology

This report assesses the progress the National Institutes of Health (NIH) has made in implementing its 1994 guidelines on including women in clinical research, including the requirement that certain studies be designed to permit analysis by sex. The report also provides information about the extent to which women are being included in clinical research that NIH funded, reviews the activities and accomplishments of NIH's Office of Research on Women's Health (ORWH) in promoting women's health research at NIH, and provides information about how much funding NIH has allocated to research on issues that affect women.

To assess NIH's progress in implementing its inclusion policy, we interviewed officials in central NIH offices, six institutes—the National Cancer Institute; National Heart, Lung, and Blood Institute; National Institute of Allergy and Infectious Diseases; National Institute of Arthritis and Musculoskeletal and Skin Diseases; National Institute on Aging; and National Institute of Child Health and Human Development—and the Warren Grant Magnuson Clinical Center for intramural research. We also reviewed pertinent agency documents. We reviewed small judgmental and random samples of extramural clinical research grant files from the National Heart, Lung, and Blood Institute, the National Institute of Allergy and Infectious Diseases, and the National Institute of Arthritis and Musculoskeletal and Skin Diseases to assess adherence to the required procedures for ensuring that funded research complies with the policy to include women in study populations. We did not review any files involving intramural clinical research.

To determine the extent to which women have been included in clinical research supported by NIH, we analyzed NIH's tracking data for all extramural and intramural studies involving human subjects funded during fiscal year 1997, for NIH as a whole and for individual institutes. Fiscal year 1997 is the latest year for which data were available.

To assess the activities and resources of ORWH and its coordination and collaboration among NIH institutes and centers, we interviewed NIH's director and representatives to the Coordinating Committee and the Tracking and Inclusion Committee from the six institutes in our review. We examined ORWH's budget, mission, research agenda, and reports to obtain additional information on its resources and activities. To further examine coordination and collaboration issues, we interviewed individuals at other public and private agencies.

Finally, using the Department of Health and Human Services' (HHS) definition of health issues that affect women, we analyzed NIH's data on expenditures on women's health for fiscal years 1993 to 1999.[1] We compared NIH-wide and institute expenditures on women's health research with expenditures for research on men and on both women and men. We also analyzed NIH expenditures for conditions that are unique to or more prevalent in women. The Director of ORWH helped us identify the conditions to include in those categories. Finally, we interviewed NIH and institute and center budget officers about the methods they used to produce the data on expenditures on research on women's health.

We conducted our work between November 1999 and April 2000 in accordance with generally accepted government auditing standards.

[1]According to HHS, a health issue that affects women is a disease or condition that is unique to women, more prevalent in women, or more serious among women or that has different risk factors or different interventions for women.

Women's Health Initiative

The Women's Health Initiative (WHI) includes three research arms: (1) a large-scale randomized clinical trial to examine the effect of hormone replacement therapy, diet, and calcium and vitamin D supplementation in the primary prevention of cardiovascular disease, breast cancer, and osteoporosis in women; (2) an observational study to identify predictors of disease; and (3) a study of community approaches to enhance the development of healthy behavior.

WHI has reported significant progress since recruitment began in September 1993. The clinical trial is being conducted in 40 clinical centers nationwide and has enrolled more than 68,000 postmenopausal women between the ages of 50 and 79. This clinical trial has three components: a hormone replacement therapy trial, a dietary modification trial, and a calcium and vitamin D supplementation trial. The hormone component tests whether long-term therapy reduces coronary heart disease and fractures without increasing breast cancer risk. The final participant in this trial was enrolled in December 1998. The calcium and vitamin D component enrolls women who have already been in the hormone or dietary trials for up to 2 years.

The observational study, which will track the medical history of approximately 100,000 women, is designed to examine the relationship between lifestyle, health, and risk factors and specific disease outcomes. Women who joined this study fill out periodic health forms and also visit a clinic 3 years after enrollment. Participants are not required to take any medication or change their health habits. The observational study completed enrollment on December 31, 1998, and participants will be followed for 8 to 12 years.

The community prevention study, which began in October 1995, is a collaboration between NIH and the Centers for Disease Control and Prevention's National Center for Chronic Disease Prevention and Health Promotion. Eight community prevention centers have been conducting and evaluating efforts to encourage women, especially minority women, to adopt healthy behaviors such as improved diet, nutritional supplementation, smoking cessation, exercise, and early detection of treatable health problems. The goal is to develop model programs that can be implemented in communities throughout the United States. This study is expected to conclude in fiscal year 2000.

Percentages of NIH Studies Tracked and Not Tracked, Fiscal Year 1997

Tracking code	Description	NCI	NHLBI	NIAID	NIAMS	NIA	NICHD	NIH total
0	Must be tracked	31.88	31.58	13.24	20.40	40.64	60.11	40.66
1	Basic research, far removed from immediate clinical application	11.09	38.49	20.29	21.89	26.97	0.65	17.08
2	Early stages of technology or methodology development	7.52	5.64	0.87	4.23	4.19	1.85	3.87
3	Fewer than 10 participants	0.59	1.01	1.64	2.99	0.74	0.98	1.02
4	Multicenter project—not coordinating center	11.51	6.72	0.87	0.25	1.60	4.24	5.5
5	Supplement—data captured in parent award	2.98	5.77	3.38	3.73	3.69	4.13	4.05
6	Unidentifiable gender and minority	0.80	0.51	0	0.25	0.49	0.33	0.67
7	Awarded before implementing gender or minority policy	0.29	0	0.58	0.50	1.85	0	0.84
8	Substudy of existing reported population	2.98	0	1.93	2.24	2.83	0.11	1.73
9	Analysis of existing study data	2.90	3.55	6.96	1.00	8.87	7.28	3.48
10	Only tissue or body fluid specimens	21.42	0	46.28	40.30	4.19	13.04	16.36

Note: NCI = National Cancer Institute. NHLBI = National Heart, Lung, and Blood Institute. NIAID = National Institute of Allergy and Infectious Diseases. NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases. NIA = National Institute on Aging. NICHD = National Institute of Child Health and Human Development.

Comments From the National Institutes of Health

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

April 21, 2000

Janet Heinrich, Ph.D.
Associate Director
Health Financing and Public Health
U.S. General Accounting Office
Washington, DC 20548

Dear Dr. Heinrich:

The National Institutes of Health (NIH) appreciates the opportunity to comment on the Draft GAO report, *Women's Health: NIH Has Increased Efforts to Include Women in Research.*

We appreciate your recognition of the strong progress that has been made by the NIH in implementing the 1993 legislation mandating inclusion of women and minorities in clinical research and of the many impediments that have been overcome in doing so. There are a few minor items contained in the report for which we are providing comments/corrections. More general comments have been presented first, followed by responses to the recommendations in the report.

We hope that you find our comments to be valuable. If you have any questions, please contact me at 301-496-7322.

Sincerely yours,

Yvonne T. Maddox

Yvonne Maddox, Ph.D.
Acting Deputy Director

Enclosure

Responses to Specific Recommendations:

Recommendation #1

To strengthen the capacity of biomedical research to produce health information applicable to all segments of the population, we recommend that the Director of NIH ensure that the agency implements the requirement that Phase III clinical trials be designed and carried out to allow for valid analysis of differences by sex as fully as it implements other elements of the inclusion policy. Specifically, we recommend that NIH appropriately communicate this requirement to applicants, that peer review groups explicitly determine whether each proposed Phase III clinical is required to have such a study design, and that Summary Statements document the initial reviewer's decision.

NIH concurs with the above recommendation and will again emphasize to NIH staff and applicants that sex analysis should be included in a research plan whenever the issue is scientifically justified and can be done in a manner consistent with the overriding need to protect the best interests of study participants.

The NIH, through its Extramural Program Management Committee (EPMC), is developing strategies to enhance communication with the research community concerning the requirement for valid analysis of sex differences by intervention effects in Phase III clinical trials. Possible follow-up actions include republishing the NIH Guidelines on the "Inclusion of Women and Minorities as Subjects in Clinical Research" and drawing particular attention to the need for applicants to provide a justification when no data analysis by sex is proposed and requiring peer review groups to explicitly comment on the adequacy of the justification. In addition, since various Institutes/Centers (ICs)-specific review groups have developed separate how-to guidelines for applicants and reviewers, an appropriate NIH ad-hoc committee will review these and consider modifying and redistributing them as appropriate.

At peer review group meetings, the Scientific Review Administrators will address this issue in their introductory remarks to review groups considering Phase III clinical trials and ensure that reviewers comment on the adequacy of the justification in their verbal and written remarks. Attention will be given to applicant and reviewer requirements in new Program Announcements (PAs), Request for Proposals (RFPs) and Request for Applications (RFAs) to ensure that justification and appropriate language is included.

Finally, staff training regarding the inclusion guidelines will receive attention and the training curriculum revised to incorporate more effective strategies identified by the EPMC.

Recommendation #2

To improve the accuracy of NIH's tracking data on the inclusion of women and minorities, we recommend that the Director of NIH ensure that NIH staff who transmit data to the tracking system receive ongoing training on the requirements and purpose of the system.

We concur with the recommendation. The Director of ORWH will create an ad hoc committee composed of representatives of Institutes and Centers, the Office of Extramural Research (OER) and the Office of Intramural Research (OIR) to respond to this recommendation. In addition, the ORWH will work with OER, which maintains the tracking data system, to ensure that NIH staff are well-informed about the data collection requirements of the current system. When a new tracking module in the grants administration system (IMPAC 2) is ready for implementation, ORWH will collaborate with OER to develop and implement extensive training.

GAO Contacts and Staff Acknowledgments

GAO Contacts

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Anne Dievler, (202) 512-7006

Staff Acknowledgments

In addition to the persons named above, Nila Garces-Osorio, Brenda James, Darryl Joyce, and Katherine Tomber made important contributions to this report.

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