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NIH Promulgates New Guidelines for the Inclusion of Women and Minorities in Medical Research

Jonathan M. Eisenberg†

Some medicines, such as penicillin, seem to benefit humans regardless of gender, race, or other demographic factors. However, other medicines and treatments have varying effects on people of different demographic groups. For example, we know that certain diet pills increase women’s, but not men’s, blood pressure; and that white people require larger doses of lithium to control mania than do African Americans.¹

If human-subject medical research (or “clinical research”) is conducted on people of one demographic group, such as white males, then the results may be applicable only to that group of people. For this medical research consistently to produce information useful for the prevention and treatment of all people’s health problems, it must take into account all relevant demographic factors.

The National Institutes of Health (“NIH”), part of the Department of Health and Human Services, is the main biomedical research agency of the federal government; the NIH also provides support for government-funded medical research done at private sites.² In March 1994, the NIH announced guidelines—applicable to all NIH-funded researchers—that demand the inclusion of “women and minorities” as subjects in clinical research.³ The

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1 At Last, Women, Minorities Count in Medical Research, USA TODAY, Mar. 11, 1994, at A12; Shari Roan, Sex, Ethnic Bias in Medical Research Raises Questions, L.A. TIMES, Aug. 3, 1990, at A1.
2 See Office of the Federal Register, National Archives and Records Administration, The United States Government Manual 1994/95, at 313 (1994). The government sponsors more than 90% of the medical research done in this country. In 1991, the latest year for which figures are available, there was $12.5 billion in medical research done in the United States, and the government funded nearly $11.7 billion of it. Researchers at private hospitals and universities often are funded through NIH grants. Statistical Abstract of the United States 1994: The National Data Book 110 (U.S. Dept. of Commerce, Economics and Statistics Administration, Bureau of the Census 1994). Meanwhile, medical research done by the NIH itself accounts for about 10% of all medical research done in this country. Philip J. Hilts, National Health Institutes to Revamp Criticized Research Program, N.Y. TIMES, May 5, 1994, at B11.
publication of these guidelines, in conjunction with 1990 guidelines, represents a significant step toward making medical research more effective at improving the health of all people.

However, the NIH may not have gone far enough. Specifically, it should have expressly insisted on the inclusion of female minorities as subjects in clinical research. Women's health statistics sometimes vary by ethnic group or by other demographic distinctions. For example, female breast cancer death rates vary tremendously based on ethnicity. The prevalence of overweight women also differs by ethnic group, as well as by socioeconomic status. The NIH's guidelines should acknowledge these differences among women and require medical researchers to study people with varying demographic factors to obtain more accurate and more widely applicable results.

I. History

For several decades, feminists have criticized the medical research community for ignoring women's health problems. Indeed, many "clinical trials"—important types of clinical research—excluded female subjects on one or several of the following grounds:

- men are considered to be easier to use in medical studies because their sex hormones do not vary cyclically to the same degree as women's;
- in certain diseases, such as coronary heart disease, where the frequency of occurrence may be lower for women than for men, the number of female subjects under study must be greater (as fewer women exhibit the disease), thereby increasing costs;
- women of childbearing ages may become pregnant during the course of studies and subject their fetuses to dangerous drugs or devices leading to birth defects (as was the case in the tests of Thalidomide and DES in the 1950s and '60s); and
- men, particularly white men, are said to be easier to recruit as subjects for studies.

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7 "A 'clinical trial' is a broadly based . . . 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." 59 Fed. Reg. 14,511.
8 LaRosa & Pinn, supra note 6, at 146; Harry Schwartz, Medicine Should Come First, USA TODAY, Mar. 11, 1994, at A12.
Regardless of the validity of these justifications for gender discrimination in clinical research, the result has been "startling gaps" in our knowledge of women's health, according to Bernadine Healy, M.D., former director of the NIH.\footnote{Bernadine Healy, Foreword to REPORT OF THE NATIONAL INSTITUTES OF HEALTH: OPPORTUNITIES FOR RESEARCH ON WOMEN'S HEALTH (1992).}

By the mid-1980s, the NIH was aware of this problem, but the initial commitment to change was debatable.\footnote{See Ruth L. Kirschstein, Research on Women's Health, 81 AM. J. PUB. HEALTH 291-93 (March 1991); LaRosa & Pinn, supra note 6, at 148.} Beginning in 1990, feminist activists and female members of Congress increased pressure on the NIH. In response, the NIH made several new efforts in women's health,\footnote{These efforts included the creation of the Office of Research on Women's Health within the Office of the Director of the NIH, and the launching of the Women's Health Initiative, a long-term, large-scale clinical study of mostly post-menopausal women. NAT'L INST. OF HEALTH, OVERVIEW: OFFICE OF RESEARCH ON WOMEN'S HEALTH (1994); NAT'L INST. OF HEALTH, WOMEN'S HEALTH INITIATIVE OVERVIEW STATEMENT (1994).} including promulgating its first set of guidelines for the use of women and minorities as clinical research subjects.\footnote{LaRosa & Pinn, supra note 6, at 148-49.} In 1994 the NIH revised these guidelines.

\section{The New Guidelines}

In the NIH Revitalization Act of 1993,\footnote{42 U.S.C. § 289a-2 (1994).} Congress required the NIH to include "women and minorities" as subjects in clinical research. The new guidelines were effective upon publication\footnote{59 Fed. Reg. 14,510.} and contain the following major provisions:

\begin{itemize}
  \item the NIH must ensure the inclusion of "women and members of minority groups and their subpopulations"—where "subpopulations" does not expressly include minority women\footnote{The guidelines' definition of minority subpopulations includes the following elements: "[e]ach minority group contains subpopulations which are delimited by geographic origins, national origins and/or cultural differences." For example, the minority group "Hispanic" includes people of "Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture or origin, regardless of race." Also, "[a]ttention to subpopulations also applies to individuals of mixed racial and/or ethnic parentage." 59 Fed. Reg. 14,511.}—in all NIH-funded, human-subject research, including clinical trials;
  \item the NIH will fund only those medical research projects that include women and minorities and members of their subpopulations—or that give an express scientific justification for the exclusion of these people;
  \item "[c]ost is not an acceptable reason for exclusion except when the study would duplicate data from other sources";
  \item "[w]omen of childbearing potential should not be routinely excluded from participation in clinical research";
  \item "[t]his policy applies to research subjects of all ages"; and
\end{itemize}
the NIH must initiate "programs and support for outreach efforts to recruit these groups into clinical studies."

Dr. Belinda M. Seto, an NIH senior advisor who is partially responsible for developing the guidelines, summarized the new guidelines' purpose: "Ultimately, we want researchers to do what is scientifically appropriate. We want them to ask the questions: Is there impact on women? On minorities? Think of them as additional parameters, like age."

On the whole, the new guidelines seem quite similar to the 1990 guidelines, although the new guidelines claim to "supersede and strengthen the previous policies." New items include: (1) the mention of minority subpopulations; (2) the statements dismissing arguments for exclusion of women or minorities based on costs; (3) the statement about including subjects of all ages; and (4) the mandated outreach efforts.

Indeed, the two sets of guidelines are so similar that Seto estimates that the medical researchers receiving NIH funding exhibited greater than ninety percent compliance with the new guidelines even before they were published because this community was already in compliance with the old guidelines. But ninety percent compliance does not mean that ninety percent of NIH-funded medical research projects actually include women and people of color as subjects. Rather, it means that ninety percent of these projects in their applications for NIH funding addressed the questions of inclusion of women and minorities as subjects.

However, if the researchers can justify the exclusion of women and people of color in a clinical trial to an NIH review board on scientific grounds they can still obtain funding. According to Seto, an example of a scientifically valid reason for excluding women and minorities from clinical research is that information about women and minorities with respect to the disease or drug being studied already is known, and it would be unnecessarily duplicative to conduct an inclusive study that would generate the same information. This example seems reasonable.

16 Id. at 14,508-14,511. To advance the outreach efforts, in August 1994 the NIH published a 37-page "Outreach Notebook" for researchers that explains, among other things, how to determine the extent to which women and minorities should be included in a clinical study and how to resolve ethical issues surrounding recruiting and retaining participants in studies. Some African Americans refuse to participate in government-sponsored clinical trials because of the memory of the horrifying "studies" of the sexually transmitted disease syphilis conducted in Tuskegee, Alabama, in the 1930s. There, researchers gave African-American men placebos rather than penicillin, a known cure for syphilis, to observe the long-term debilitating effects of this disease. See generally JAMES H. JONES, BAD BLOOD: THE TUSKEgee SYphilis EXPERIMENT (1981). Conceivably, further ethical issues would arise if the government offered to pay people of color to participate in clinical studies.

17 Telephone interview with Dr. Belinda M. Seto, senior NIH employee (Jan. 17, 1995).


19 Id.

20 Telephone interview with Seto, supra note 17.

21 These review boards are composed of independent medical scientists, not NIH scientists, but they award NIH funds. Telephone interview with Dr. Marvin Kalt, senior employee at the National Cancer Institute, an NIH institute (Jan. 18, 1995).

22 Telephone interview with Seto, supra note 17.
RECENT DEVELOPMENTS

III. CRITICISM OF THE NEW GUIDELINES

The NIH accepted public comments and criticisms about the guidelines for one year. At the time of this writing, the one-year period had not expired, but the NIH had received few comments and none that would prompt voluntary changes in the guidelines.

Those comments that have been received can be grouped into three categories:

1. Geography: Some researchers in states with ethnically homogeneous populations, such as New Hampshire and Oregon, complain of the unfeasibility of recruiting minorities to be participants in clinical trials.

2. Size: Researchers argue that they should not have to seek a gender and ethnic mix in their small-scale, exploratory studies, but only in subsequent large-scale studies based on the smaller studies.

3. Costs: Researchers continue to complain that the inclusion of women in clinical trials would greatly increase the costs of the studies.

Only the “geography” argument seems strong. Researchers in locations with ethnically homogeneous populations will indeed have a difficult time constructing ethnically diverse study populations. Perhaps the answer to such a researcher’s dilemma is that she be given NIH grants to study only (1) diseases or drugs that seem to affect all people similarly, or (2) diseases specific to the single ethnic group in the local population—and that she be denied funding to study diseases that affect people across the demographic spectrum. It is an unfortunate truth that such a researcher, because of her location, often will not be able to produce test results usable in the prevention and treatment of all people’s health problems.

The “size” argument seems particularly weak. How can a researcher reach an accurate preliminary understanding of a disease’s effects if she initially looks only at how these effects are manifested in a single demographic group? Additionally, how can a researcher be sure that she has designed a sound, large-scale clinical trial, involving diverse study populations, if the small-scale, preparatory work is based on a homogeneous study population?

The “cost” argument falls flat, too. If there exists any possibility that a disease or a medicine affects men and women differently, then the disease or medicine has to be studied with respect to both men and women. If a study is done of men only, then the results will be applicable to men only. A second study of women will be necessary. This is what happened with the 1980s study of the effect that regularly taking aspirin had on a person’s risk for a heart attack. Only men were studied; the result, that aspirin intake

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24 Id.
25 Telephone interview with Seto, supra note 17.
did cut the risk for a heart attack, was valid only for men.\textsuperscript{26} Another study was needed to conclude that women also benefited from regular aspirin intake.\textsuperscript{27} Two separate studies, one of men and the other of women, inevitably will cost more than a single study involving people of both genders.

An additional concern centers on the wording of the new guidelines. While the guidelines mention "women and minorities," they do not expressly mention "women minorities." Because women’s health statistics sometimes vary by ethnic group,\textsuperscript{28} the guidelines should explicitly state that NIH-funded clinical research must give particular, overt attention to women of color.

Asked about this omission, Seto answered that the term "women and minorities" includes by implication women of color; moreover, she said, the review boards that determine which NIH grant applications receive funding ensure that research proposals "reflect disease demographics" of all sorts, including gender, race, age, and socioeconomic status.\textsuperscript{29} Of course, if the review boards already function to ensure that all research proposals take into account relevant disease demographics, as Seto claims, one wonders why the guidelines needed to be written at all.

Dr. Marvin Kalt, director of external programs at the National Cancer Institute, is an NIH official listed on the new NIH guidelines as a contact person.\textsuperscript{30} When asked if the guidelines should list more groups of people than "women and minorities," such as low-income people or lesbians, Kalt responded that "you can’t get to the point of micromanaging research."\textsuperscript{31} Nonetheless, it is scientifically appropriate for researchers to consider additional demographic parameters when they design experiments. When they refrain from doing so, the NIH ought to play a larger oversight role to improve the research.

\textbf{IV. Conclusion}

The new guidelines represent a step in the right direction for medical science because they close some of the loopholes left by the 1990 guidelines through which researchers could continue excluding (white) women and minorities as subjects in clinical research. Now, neither additional costs of recruiting and using women and minorities in clinical trials nor women’s condition of pregnancy will justify the exclusion of these groups.

The next step is for human-subject medical research to take account systematically of all relevant demographic factors. This step must be taken,

\textsuperscript{28} See supra notes 4 and 5 and accompanying text.
\textsuperscript{29} Telephone interview with Seto, supra note 17.
\textsuperscript{31} Telephone interview with Kalt, supra note 21.
guided by either the force of government intervention or the medical research community’s own initiative, for only then will clinical research consistently produce information useful in the maintenance and improvement of all people’s health.