Clinical Relevance of Gender

Women’s Health Research and Health Leadership: Benchmarks of the Continuum

Vivian W. Pinn, M.D.

Dr. Pinn is Director of the Office of Research on Women’s Health, National Institutes of Health. Direct correspondence to her at Office of Research on Women’s Health, National Institutes of Health, 6707 Democracy Blvd., Suite 400, MSC 5484, Bethesda, MD 20892-5484; 301-402-1770 phone; pinnv@od1tm1.od.nih.gov.

Bringing the appropriate attention to research on women’s health is a process that has evolved in tandem with our understanding and acceptance during the past four decades of women as individuals with rights and roles in society equal to as well as different from those of men. Thanks to the leadership of many, recent progress has been made in women’s health research. That evolution during the past fifteen years can be characterized by the following concepts:

• expanded concepts of women’s health,
• policies for and research on sex-gender comparisons,
• addressing health disparities among various populations,
• setting research priorities and approaches, and
• advancing women’s roles in health research, health policy, and health careers.

Each of these benchmarks has influenced the others, but taken individually, they can provide a framework for describing areas of progress.

Expanded Concepts of Women’s Health

Traditionally, women’s health has been thought primarily to be that of the reproductive system during reproductive years. Little attention was given to other areas of women’s health, and research was primarily defined for women in terms of the reproductive system. In the late 1980s, women’s health advocates began to question this approach and the resulting gaps in knowledge about women’s total body systems across the lifespan. They questioned whether it was scientifically sound to consider men the norm for women when evaluating medical interventions. At that time, the assumption was that clinical applications derived from studies conducted on men would have the same applications for women. Historically, women had not been routinely included in biomedical research studies, in part because of an interest in protecting them from risks, especially pregnant women or women of childbearing age. The risks seemed unwarranted given the general belief at that time that women and men did not differ significantly in response to treatment in most situations.

Advocates of women’s health brought their questions—along with demands for funding to address gaps in women’s health research—to women legislators, and from that point on, tremendous changes in how government-sponsored research addresses health issues of women have resulted. The resulting benchmarks were fundamental to moving the continuum forward: 1) the establishment in 1990 of the Office of Research on Women’s Health (ORWH) in the Office of the Director of the National Institutes of Health (NIH) of the U.S. Department of Health and Human Services, and 2) the strengthening of the NIH grant-funding policy to require that women and minorities be included in all NIH-supported clinical research studies (unless exclusion could be justified according to a number of criteria).

The purpose of the ORWH is to stimulate and encourage meritorious research on women’s health, including the role of sex and gender in health and disease, and to ensure that women are appropriately represented in clinical research studies. The ORWH collaborates with the scientific, health professional, and advocacy communities to develop the NIH agenda for research on women’s health. The ORWH implements the agenda through collaborative projects with the multiple institutes and centers of the NIH. The ORWH also has the responsibility to develop
opportunities for the recruitment, retention, reentry, and advancement of girls and women in biomedical careers and to encourage both men and women to pursue women’s health research.

The NIH revised its inclusion policy in 1994 to mandate that women and minorities be included in all NIH-supported clinical research studies. The result is a policy that the NIH would not fund any grant, cooperative agreement, or contract, nor would it support any intramural project, to be conducted or funded in fiscal year 1995 and thereafter that did not comply with this policy. The shift in policy from protectionism and exclusion of women to one of broad inclusion of women of all ages in research studies with appropriate human subject protections is a benchmark that has been pivotal in the scientific approach to women’s—and men’s—health research.

Policies for and Research on Sex-Gender Comparisons

In setting the NIH agenda for women’s health research and including women in clinical trials, two basic facts are fundamental: 1) men and women are different, and 2) not all women, or all men, are the same. Therefore, women’s health research today has basically two approaches: to determine sex-gender influences on health and disease, and to study the many determinants that result in health disparities between different populations of women (and men). A further important distinction exists, and that is in the concepts (and terms) of “sex” and “gender.” The 2001 Institute of Medicine report Exploring the Biological Contributions to Human Health: Does Sex Matter? urges scientists to use these terms consistently, defined as follows:

Sex: The classification of living things, generally as male or female, according to their reproductive organs and functions assigned by chromosomal complement.

Gender: A person’s self-representation as male or female, or how that person is responded to by social institutions based on the individual’s gender presentation. Gender is rooted in biology and shaped by environment and experience.

This report recommends investigating natural differences between sex and gender in genetic variability, disorders of sex differentiation, reproductive status, and environmental influences to better understand human health. It also proposes the monitoring of sex differences and similarities for all human diseases that affect both sexes. These recommendations provide scientific impetus to consider sex differences in basic biomedical studies in addition to clinical research.

Research to date has in fact deepened and broadened our knowledge of how a number of diseases and conditions affect women differently from men, including the presentation, outcomes, and responses to interventions for heart disease; the manifestations and progression of HIV/AIDS; experience of pain and response to pain therapies; clinical features and management of depression; the prevalence and care of diabetes, especially type 2 diabetes; musculoskeletal diseases such as osteoarthritis, osteoporosis, and sports injuries; and autoimmune diseases such as lupus, multiple sclerosis, thyroid diseases, and rheumatoid arthritis.

An important illustration of progress that has evolved from sex-gender research is that of cardiovascular diseases (CVD). CVD accounts for about 45 percent of deaths among women, more than 250,000 deaths each year; it is the most common cause of death of women, as well as of men. A 2003 review of the studies on coronary heart disease (CHD) in women reports that much of the research in the preceding twenty years on the diagnosis and treatment of CHD either excluded women entirely or included only limited numbers of women and minorities. As a result, many of the tests and therapies that are used to treat women for CHD are based on studies conducted predominantly of men. Even in studies that include women, the published research often does not provide findings specific to women; only 20 percent of the articles reviewed for that project provided separate findings on women. Therefore, it is a benchmark that, in the past ten years, many clinical trials have been initiated to better define risk factors, prevention, and treatment of coronary and cardiovascular diseases specific to women.

We now know that women and men often have different signs and symptoms, outcomes, and responses to interventions for heart disease. For example, women have a worse prognosis following a heart attack than do men, partly because of older age at the time of the heart attack and also because of
multiple risk factors. We have only recently learned from the Women’s Health Initiative that hormone therapy for menopausal women in this study did not prevent cardiovascular disease and may even increase a woman’s risk for cardiovascular disease.\(^5\)

In contrast, for osteoporosis, our knowledge about women is greater than about men. The incidence of osteoporosis is increasing in both men and women, and the proportion of women with osteoporosis far exceeds that of men: 89.7 percent for women, 10.3 percent for men. Consequently, most research has been done among Caucasian women. In a sex-gender approach to research, we need to clarify such basic elements as the risk for fractures relevant to bone size for men and women and whether the same bone mineral density criteria for diagnosis and fracture risk determined in studies of women are appropriate for use with men.\(^6\)

These are only two examples of many important advances in scientific knowledge derived recently from sex-gender research. Overall, we have achieved a benchmark in pursuing our understanding of the genetic, environmental, hormonal, and other causative pathways of diseases in males and females and of gender-appropriate medical care.

### Addressing Health Disparities Among Various Populations

Disparities in disease prevalence, health outcomes, disabilities, and premature deaths exist for some population groups. Those disparities occur between the sexes, between subpopulation groups within the sexes, and between and among racial-ethnic groups. Multiple factors contribute to those disparities, including biology, genes, hormonal milieu, environment, behavior, race-ethnicity, access to health care, and differences in sex, education, and poverty.

It is an important benchmark in women’s health research that now women—and women of all population groups—must be included in research supported by the NIH. The intent of the inclusion policy is to ensure that scientific norms for health, disease, treatments, and other medical interventions are applicable to all populations (men and women and diverse racial-ethnic groups), based on scientific evidence established by studying those populations.

In other words, are there biological or other differences in effects based upon sex or race? Are there differences in natural history of disease or response to interventions based upon racial heritage?

### Setting Research Priorities and Approaches

The expanded concept of women’s health across the lifespan, the recognition and support of the need for sex-gender comparisons, and the policy to understand and address disparities in health and health care all underlie recent, current, and future health research priorities and approaches. Each year, the ORWH considers the continuing gaps in knowledge from the NIH agenda and reviews newly emerging scientific concepts to determine specific areas of research priorities for new initiatives or increased focus.

In the ORWH’s fiscal year 2005 research priorities, many research opportunities are described in terms of overarching themes. Basic, translational, behavioral, and clinical research in women’s health, especially applied to sex-gender differences, are of particular interest. These research priorities are not an exclusive list of research areas important to women’s health; other innovative or significant research submissions are also considered. Currently, two special emphasis areas have been identified: genetics-pharmacogenomics, and prevention and treatment. The genetics-pharmacogenomic area covers the role of confounding factors, including sex, on the function of genes and genetic polymorphisms in disease and health. Specific topics include sex chromosomal differences; critical windows of susceptibility; genetic, molecular, and cellular bases for action of pharmacologic agents; and the impact of lifespan (including pregnancy) on pharmacokinetics, pharmacodynamics, drug efficacy, and adverse effects of therapeutic agents. The prevention and treatment area covers basic biological factors and the effects of risk behaviors and intervention. Specific topics include identifying and validating biomarkers; the effects of diet, hormones, exercise, weight, alcohol, substance abuse, violence, and the like; the relationship of reproductive factors to susceptibility and protection; development, testing, and validation of preventive and curative strategies; and the effects of biological, behavioral, cultural, social, economic, and environmental factors.
Interdisciplinary Research Approach

In identifying future priorities for gender-appropriate health research and health care, interdisciplinary research can serve as a foundation for integrated medical care of women. With the support of many of the NIH institutes, the ORWH has initiated two large-scale programs to promote interdisciplinary research: Building Interdisciplinary Research Careers in Women’s Health (BIRCWH), and Specialized Centers of Research (SCORs) on Sex and Gender Factors Affecting Women’s Health. These initiatives are benchmarks in the continuum of enhancing research and careers in women’s health across multiple disciplines. These programs benefit both women’s and men’s health through sex-gender research, interdisciplinary scientific collaboration, and support for young investigators in a mentored environment to become independent investigators doing research in women’s health.

In an interdisciplinary mentored environment, the BIRCWH program pairs senior investigators with junior researchers who have recently completed clinical training or postdoctoral fellowships and who are beginning basic, translational, clinical, or health services research related to women’s health. During the process of developing the women’s health research agenda, needs were identified to expand support for interdisciplinary collaborations and for developing career opportunities for researchers in women’s health. To date, the ORWH has funded twenty-three centers, and eleven new and continuing awards were made in 2005. One of those focuses on oral health and its impact on cardiovascular and endocrine health and pregnancy outcomes.

A SCOR is envisioned as a national resource associated with one or more major medical complexes and dedicated to furthering the interdisciplinary research effort on women’s health or sex-gender factors to translate basic research into clinical application. Currently, there are eleven SCORS. Examples of research areas are pharmacologic response differences, pain in women and men, substance abuse, urinary tract (incontinence) and irritable bowel syndrome, and pregnancy loss. Especially relevant to oral health is the SCOR at the University of Maryland, which is studying neuronal mechanisms that underlie sex differences in pain sensitivity, in particular for visceral and temporomandibular pain.

Women’s Health Research in Oral Medicine

The complexity of content areas involved in the study of women’s oral health implies the need for interdisciplinary collaborations to integrate knowledge and practices. Women’s oral health comprises multiple content areas, including oral influences on systemic health, systemic influences on oral health, societal influences on women’s health, gender influences on health risk, oral diseases affecting the most women, diseases more common in women than in men, and women and the health care system. As stated in the surgeon general’s report on oral health, “Associations between chronic oral infections and other health problems, including diabetes, heart disease, and adverse pregnancy outcomes, have also been reported.” For example, pilot clinical trials have shown that periodontal disease management reduces the risk of low-birthweight and premature babies.

Furthermore, as reported at the First International Women’s Leadership Conference, “Women dentists are often asked to advise and counsel their patients regarding women’s health issues such as obesity, osteoporosis, sexually transmitted diseases, hormone replacement therapy, breast cancer prevention and therapy, and others.” A recommendation in the American Dental Association’s The Future of Dentistry states, “The dental profession should take the lead in convening all members of the health care community in developing a plan to incorporate appropriate oral and systemic health care concepts into the respective curricula.”

Examples of oral diseases or conditions that men and women experience differently are temporomandibular joint (TMJ) disorders and orofacial pain, Sjögren’s syndrome, salivary gland dysfunction, burning mouth, alterations in taste, and pregnancy-associated oral changes. The NIH is supporting a number of research approaches for TMJ disorders: developmental biology, genetics, and proteomics of TMJ structures; inflammation and TMJ pain; TMJ disorder comorbidities; bioimaging; bioinformatics; development and improvement of animal models; and a TMJ implant registry. A greater percentage of women than men report experience with chronic orofacial pain: 6.9 percent vs. 3.6 percent. Orofacial pain is a major condition that affects quality of life; it is associated with sleep deprivation, depression, and multiple adverse psychosocial outcomes. Not only do women experience pain differently than do men, but women also respond differently to anesthesia.
and pain medication; therefore, it is important in the management of pain conditions for practitioners to have tested information about the choice of medicines and dosages.

**Advancing Women’s Roles in Health Research, Health Policy, and Health Careers**

The ORWH’s mandate includes developing opportunities for the recruitment, retention, reentry, and advancement of girls and women in biomedical careers and encouraging both men and women to pursue women’s health research. To bring new insights and initiatives to women’s health issues, it is desirable to benefit from the potential of women to contribute to scientific research and medical practice and have gender diversity in careers that affect health research, health care, and health policymaking.

Fortunately, in the past decade or so, we have been experiencing increases in opportunities for women to enter science and health professional careers, and women are taking advantage of those opportunities, as is illustrated in Figure 1. In dental schools, first-year enrollments of women slowly increased from a few percent in 1970 to 42.4 percent in 2004. The number of women in advanced dental education programs increased from 18 percent in 1984 to 35 percent in 2003.

While these statistics are an encouraging benchmark, a second set of statistics is disappointing: faculty and leadership demographics do not reflect student demographics, a situation resulting in a paucity of women mentors and role models. In U.S. dental schools in 2002, for example, six of fifty-five deans were women (11 percent); in 2003, ten of

---

*Data from 1980-1981 are unavailable*


**Figure 1. Women in schools for selected health professions, 1980-81 and 2002-03**
fifty-six (18 percent) were women. Representation of women on medical school faculties does not reflect leadership and decision making positions at an equitable level (see Figure 2). The issue of women in biomedical careers is not solely recruitment and entry (pipeline), but also providing, supporting, and encouraging opportunities for retention and advancement in those careers.

Once women have entered a career path, they often encounter attitudes and practical obstacles to continuing or advancing in their careers. Those attitudes include insensitivity to gender, sex discrimination, sexual harassment, and racial bias. While there are differences between men and women in brain structure, no evidence shows any difference in general intelligence. Brain size does not predict intellectual performance, and men and women perform similarly on IQ tests. Recent public discussions about women in science have brought attention to how an underlying bias against women has contributed to factors preventing them from making deserved gains and that has required them to outperform men to be recognized as adequate to the job.

The ORWH conducted a nationwide study in 1994 to identify the barriers to women’s advancement in biomedical careers and identified several: lack of female role models and mentors, dual family and professional responsibilities, lack of parity in rewards such as career advancement and salaries, sex discrimination and sexual harassment, lack of gender sensitivity, and special needs of minority women. A recent article in *Science* reviewed the issue of women in science and attributed the problems to pipeline issues, climate, unconscious bias, and balancing family and work.

**Overcoming the Barriers**

How can we overcome the barriers? In a personal communication, Shirley Malcom, Ph.D., director of education and human resources programs at the American Association for the Advancement of Science, outlined three essential steps: 1) identify barriers and determine ways to overcome them, 2) assert affirmative behaviors, and 3) devise methods to result in systemic changes. The NIH has been taking those steps, in collaboration with many organizations and institutions, for the past decade. A Colloquium on Career Paths for Women in Health Sciences: A Global Perspective, sponsored by the ORWH, the Fogarty

---

**Figure 2. U.S. medical faculty by gender and rank, 2005**

International Center, and the National Institute of Environmental Health Sciences in October 1993, addressed perpetual problems and responsible solutions. The meeting participants identified a number of critical needs and potential solutions:

- collect and publicize data to change perspectives and policies related to women in science, especially regarding documentation of gender biases, salaries, promotions, responsibilities, and mentoring;
- move plans into action, taking into account cultural or political loopholes for gender biases;
- make women aware of equity issues and recognize the role of women leaders;
- provide guidance to individuals through one-on-one mentoring, electronic mentoring networks, and formalized programs at the job site;
- make leadership part of the educational curriculum;
- collaborate regionally among organizations to overcome gender biases;
- centralize and share information on policies, priorities, and best practices for career advancement; and
- evaluate programs and efforts.

Over the years, in developing career initiatives, the OR WH has recognized and incorporated the roles of professional societies, institutions, and individuals. Career development initiatives focus on interdisciplinary research, mentoring, reentry and bridging careers, and collaboration with professional societies. Specific programs include the following:

- Building Interdisciplinary Research Careers in Women’s Health (BIRCWH)
- Women’s Reproductive Health Research Career Development Centers
- ORWH Office of Intramural Training and Education Programs
- ORWH Reentry Program
- WISH-net (http://wishnet.od.nih.gov/)
- AXXS-ORWH (www4.od.nih.gov/axxs)
- ORWH Office of Science Education Programs

The ORWH Reentry Program was developed in 1992 as a pilot program to help fully trained scientists (women and men) reestablish careers in biomedical or behavioral science after taking time off for family responsibilities. The program has now expanded across the NIH and is supported by all NIH institutes and centers. This program provides administrative supplements to existing NIH research grants to support full-time or part-time research in a program to update scientists’ existing research skills and knowledge. It is anticipated that, at the completion of the supplement, the scientist will be in a position to apply for an NIH or career development (K) award or for a research award.

AXXS is an initiative of NIH women scientists, the ORWH, the National Academy of Sciences, and the American Society for Cell Biology. The program is designed to help scientific societies encourage women to enter scientific fields, develop effective programs to build careers, facilitate mentoring, identify ways to overcome barriers, share strategies for promoting careers, and develop products that can be used with each scientific discipline.

Career Issues for the Future

In November 2004, the ORWH convened a roundtable, “Looking to the Future,” at which participants discussed progress in women’s health research and challenges in the future. The following needs were identified regarding career issues and will help to guide future initiatives:

- Understand the academic environment and the threat to young researchers. The costs of medical school and liability insurance are high and rising, and many young people who begin in research do not continue, especially women and minorities.
- Training for women and minorities is needed in practical matters: how to negotiate a contract, what to ask for, how to arrange work to lifestyle needs, how to be pregnant and not jeopardize advancement.
- Mentors of all levels and both genders are needed for young people.
- Complacency and insensitivity to career issues for women and minorities are beginning to characterize some younger scientists; this trend should be counteracted.
- Unconscious gender-based assumptions and minority stereotypes are deeply embedded in the patterns of thinking of both men and women. Therefore, women and minorities and their work seem to consistently receive lower evaluations (by both men and women evaluators). The effect has impeded progress toward academic leadership by these needed groups.

Conclusion

Individuals and institutions can all be change agents to improve the field of women’s health, whether in research, educational, or health care set-
tings. There are benchmarks of progress during the past fifteen years, and we have opportunities to create and perpetuate even more successful initiatives. We must challenge the system, use new technologies for information exchange, and develop collaborative partnerships. By doing so, the next several years of this century will witness new benchmarks of success in addressing women’s health and achieving career opportunities and advancement for women in biomedical careers.

REFERENCES