

The Millennium Series in Women's Health

Multidisciplinary Women's Health Research: The National Centers of Excellence in Women's Health

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ABSTRACT

Contemporary research increasingly needs to consider the value of a multidisciplinary approach in answering critical health questions. The current article outlines the need for multidisciplinary investigations specifically in reference to women's health, and addresses issues related to generating and sustaining interest in such an approach. In addition, the importance of resources and environment for facilitating multidisciplinary research and advocacy efforts for obtaining funding for this approach are discussed. Methodological issues pertinent to the operationalization of multidisciplinary research in women's health are also addressed, and lessons learned from the National Centers of Excellence in initiating multidisciplinary research in women's health are reviewed.

INTRODUCTION AND DEFINITIONS

THE NATIONAL CENTERS OF EXCELLENCE in Women's Health (CoE) were established in 1996 by the Office on Women's Health within the U.S. Department of Health and Human Services (DHHS). These centers were proposed as models for a new, integrated approach to clinical practice, education, and research related to women's health within academic health centers. One of the core components of the CoE program, united with advances in clinical services, teaching, public outreach, and the promotion of women in academic health careers, is the de-

velopment of multidisciplinary women's health research.

The purpose of this article is to highlight the need for multidisciplinary women's health research, the issues related to generating interest in and funding for such research, and some of the important lessons learned from the CoE experience. Paradigms for use in studying women's health are presented that illustrate the development of new approaches to gaining integrated knowledge in this area. Finally, key features essential to the development of a multidisciplinary study center based on the experience of the CoE model are provided.

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Multidisciplinary women's health research, used in its broadest sense, defines an investigational approach that fosters research across multiple disciplines for the purpose of generating a comprehensive and, ultimately, an integrated knowledge base on the health of women and the health implications of gender. This is the definition and model to which the CoE program subscribes. Multidisciplinary is often used interchangeably with other terms, such as interdisciplinary, transdisciplinary, or cross-disciplinary, and each can be used to capture the essence of collaborative efforts among disciplines to advance knowledge. For the purposes of this report, the term "multidisciplinary" is used primarily to describe an approach to research using more than one discipline that has as its basis the growth of knowledge in women's health and the development of structures that support the integration of such knowledge. This approach, supported by the CoE, seeks to advance research in women's health across the biomedical and social sciences, using a variety of scientific and clinical research strategies to answer questions relevant to women's health.

WHY IS THERE A NEED FOR MULTIDISCIPLINARY WOMEN'S HEALTH RESEARCH?

Every discipline is faced with the important and work-intensive task of increasing its knowledge base on the health and healthcare of women. To see the importance of fostering research on the health of women within many individual disciplines, one need only consider conditions that are more prevalent in women to find a broad-based list from different disciplines that includes such disorders as breast cancer, migraine, osteoporosis, depression and anxiety, and a variety of autoimmune diseases. Similarly, an examination of conditions that can manifest differently in women and men (and that may require different interventions), such as coronary disease, pain, and schizophrenia, illustrates the need for various disciplines to be concerned about sex-specific differences in healthcare. Further, a variety of interventions, within different areas of health service provision, can manifest possible sex-related patterns of outcome requiring investigation of sex-based approaches to care within those fields.

In addition to the need for sex-specific research and investigations on women's health within many disciplines, there is an increased under-

standing that effective solutions to health problems and healthcare issues require a multidisciplinary research approach.

To understand the need to integrate the efforts of multiple disciplines, one may consider how prevention and therapies might be enhanced by linking various biomedical and behavioral approaches to improve medical outcome and quality of life in the disorders and conditions listed, as well as for other syndromes. For example, in examining risk factors for diseases that are becoming more common in women, such as smoking, workplace stress, and human immunodeficiency virus (HIV) exposure, it is increasingly clear that these conditions are caused by and affect multiple variables that have traditionally been placed within different disciplines. The data on smoking alone show that (1) death rates from smoking-related diseases are rising for women, (2) lung cancer has surpassed breast cancer as the leading cause of cancer death in women, and (3) smoking among teenage girls continues to increase, and now one in four girls under the age of 18 smokes.¹ Rates of smoking or lung cancer, however, will not be affected by understanding only biological variables or solely behavioral variables. Similarly, in considering disorder-producing conditions that are more prevalent for women, such as domestic violence, childhood sexual abuse, and poverty, it is apparent that these conditions, the associated health consequences, and methods of prevention can be understood fully only when collaboration occurs across disciplines. Increasing evidence indicates that reproductive stage, menstrual cyclicality, and postmenopausal estrogen depletion affect a host of conditions and disorders, thus essentially dictating collaboration with disciplines that have expertise in these areas.

HOW TO GENERATE INTEREST IN MULTIDISCIPLINARY WOMEN'S HEALTH RESEARCH

Given the importance of multidisciplinary research in women's health, how does one stimulate its growth and help it to prosper? There are several key issues that must be engaged. The first issue is structural. Multidisciplinary research requires the resources and environment to attract investigators and conduct studies. Second, it is critical to build consumer-based and governmental support for women's health research be-

cause partnerships with these groups can assist in promoting targeted legislative backing for women's health research funding. Third, methodological advances are needed to permit simultaneous examination of biobehavioral systems and clusters of relationships. Fourth, new programs for multidisciplinary research need to be established and tested. These programs can be formulated in any number of ways, ranging from small initiatives, such as a newly organized set of pilot projects, to comprehensive research centers on women's health, such as the CoE made possible by funding from the Office on Women's Health of the U.S. DHHS. In succeeding sections, we explore each of these issues.

RESOURCES AND ENVIRONMENT

Overcoming administrative barriers

Central to the development of any multidisciplinary research effort in women's health is access to the resources necessary to support investigation and build new programs. Perhaps the most significant barrier to this access is the lack of an easily identifiable administrative locus for women's health research. Most academic medical centers and schools do not have women's health departments or divisions, so there often is no clear area of authority and responsibility for program development. This limits visibility and voice in internal power structures. Because resources are generally allocated along departmental or divisional lines, access to operating budgets, startup funds, staff, space allocation, and conference time may be limited. Furthermore, departments possessing resources may be reluctant to take money away from their core activities to fund women's health initiatives, and if they are willing to contribute, departments may not anticipate that credit will clearly accrue to them if the program is successful.

Another administrative barrier relates to the existence of few senior faculty members in the specific field of women's health. Because women's health is a relatively recent area of specialized investigation, few senior investigators have the academic preparation and experience to guide beginning scholars in this area. This means fewer mentors and less access to training or group grants (e.g., Specialized Centers of Research or Program Project Grants) for young investigators or trainees interested in studying women's health.

The situation also is compounded by the fact that women's health research is often conducted by female investigators, yet traditional academic promotion policies tend toward women being less likely to be promoted than their male peers. Thus, there are fewer female senior mentors.

The CoE program has attempted to address such administrative barriers by creating an identifiable, interdisciplinary, and coordinated locus for women's health activities in the academic health center and by promoting leadership development policies and opportunities for female researchers. The CoE program has required a strong commitment from the home institutions, reflected in allocation of resources and integration of the program within the institution's administrative infrastructure. In cementing this commitment, it has been found that partnership with an outside agency has been useful to broaden and clarify the objectives of each program within the institution. Developing a clear set of program objectives has been important for CoE programs to demonstrate the value these types of programs add to their home institutions in meeting these objectives. Regular reports are submitted to the administrative leadership that summarize progress in meeting program objectives and are helpful in internal marketing of the programs. These reports include such information as tallies of funded research projects in this area, new submissions for extramural funding, citations of women's research activities, and lists of publications. Many of the CoE have participated in successful fund-raising campaigns and have leveraged initial funding to obtain additional sources of funding for research activities and academic positions. Mentoring programs have been developed as part of the CoE programs to help align researchers in women's health for efficient career advancement and promotion and to highlight the importance of senior academic leadership in women's health research. Appointment of women's health researchers to prominent institutional roles via a program such as the CoE increases visibility and provides a platform from which to demonstrate the importance and relevance of women's health research initiatives.

Seed money for developing programs in women's health research

The experience of the CoE has demonstrated that institutions wishing to develop a women's health research initiative must be willing to pro-

vide seed money or in-kind resources for these programs. Even modest amounts of money and resources can attract new researchers to women's health topics. Any research effort, however, will eventually require external funding for effectiveness, longevity, and credibility. The effectiveness of seed funding in developing extramural support should be tracked and can be used to document the added value of women's health research programs. The CoE have found that seed money for pilot research programs and conferences related to women's health research is sometimes available from industry and foundations. Partnerships with preexisting formal structures that support women's health research (e.g., a cancer center) have been found to be useful and often ensure a longer-term commitment of resources. Such entities, devoted to women's health research within existing centers, can sometimes provide the additional benefit of commitments of space as a hub for part of the research effort. Overall, the experience of the CoE suggests that the most effective technique for securing resources involves each institution's identifying and developing those strategies that are most likely to succeed in its own culture and environment.

THE IMPORTANCE OF ADVOCACY EFFORTS TO SUPPORT FUNDING IN WOMEN'S HEALTH

In the case of women's health research, as in many multidisciplinary areas, traditional funding sources comparable to those in single specialties generally have not been developed. The Office of Research on Women's Health of the National Institutes of Health (NIH) is an excellent advocate for the importance of women's health research but has not had an extramural budget allowing significant funding for research in women's health. Furthermore, there is no readily identified, nationally accepted professional association to support women's health researchers in their professional careers. These all add up to funding gaps in women's health research, which will need to be addressed before the field can attract, support, and retain large numbers of investigators.

Because substantial funds are not allocated for women's health research, it is necessary to build them. Obviously, individuals will be powerful local advocates in their own institutions for creation of funding opportunities, but a larger effort is necessary. Advocacy is an important mechanism

to raise public, provider, and researcher awareness about the importance of women's health issues. Many constituencies need to be informed to create a widespread appreciation of the barriers to obtaining traditional funding sources for women's health researchers and of the need for special attention to funding concerns. These efforts should emphasize that advances in women's health and science are also advances in health knowledge for all.

Many existing consumer groups are deeply concerned with determining the causes and interventions for a wide array of disorders that preferentially affect women or for which there are sex differences in presentation and treatment. For example, grass roots advocacy groups for breast cancer and AIDS have dramatically increased public awareness of these diseases and enabled researchers to capture a greater share of the research dollar. The Society for Women's Health Research has formed a Women's Health Research Coalition that is an advocacy network of leaders within scientific and medical research. The Coalition has been a staunch advocate of greater funding and attention to women's health research and is actively seeking to influence federal spending. As noted previously, a number of government offices (e.g., the NIH Office of Women's Health Research, and the Office on Women's Health of the U.S. DHHS) also play essential roles in generating funding for research in women's health.

There are several success stories in regard to advocacy efforts for women's health research. For example, the Congressional Women's Caucus was instrumental in advocating for a review of NIH-funded research to determine if women were represented in clinical trials. The Caucus, in partnership with Representative Henry Waxman, who was chair of the House Subcommittee that oversaw the NIH, requested that the General Accounting Office (GAO) review NIH's implementation of its policy to include women in clinical studies. This review ultimately led to federal legislation requiring the appropriate inclusion of women and minorities in clinical trials.

METHODOLOGY ISSUES

Multidisciplinary programs in women's health research, by garnering the perspectives of researchers whose frames of reference are derived from studies of different mechanisms and systems, engender expanded scopes of research and

analysis. Systems, rather than individual outcomes, are explored, and clusters of parameters are considered or estimated. In reference to the efficacy of treatments or interventions across these systems, a focus on a single treatment effect can be considered self-limiting because effects can covary with outcomes across other systems. Consequently, within a multidisciplinary perspective, it is important to consider evaluation of outcomes ranging from chemical changes to more holistic influences on life quality.

Because responses to therapeutic interventions vary among individuals even for a single outcome measure, treatments have the potential to produce a range of effects, from beneficial to deleterious, across clinical populations.² When systems of measures rather than individual outcome measures are considered, the potential for variation in responses to medical interventions is increased. From this perspective, traditional approaches to understanding efficacy that have focused on a single mean effect for an average woman may obscure rather than clarify mechanisms of response. For example, with oral postmenopausal hormone therapy, it is expected that there will be a clustering of responses to outcome measures related to first-pass effects mediated by the liver (e.g., changes in lipid/lipoprotein, insulin, and glucose concentrations) and separate other clusters of outcome responses related to measures that reflect direct actions of estrogen on bones, arterial walls, and endometrial tissue.³ Heterogeneous responses to outcome measures within each cluster may be more tightly correlated than responses to outcome measures across clusters because of varying sensitivities and pharmacokinetics among women. Women deciding on the use of hormone therapy must weigh the potential for risks and benefits across these clusters of parameters.

Empirical methodologies

During the past decade, research on statistical methodology has made rapid progress in developing the means to model both heterogeneity among individuals and the complexity of systems of responses.⁴⁻⁶ These approaches have resulted in a more realistic understanding of patterns of data. For example, using new computer-intensive algorithms, Kirby⁷ modeled the full sequence of a cervical cancer screening process—a series of Pap smears at various times and of varying length followed by biopsies—in models that incorporate

diagnostic error rates, covariates, and heterogeneity among women. Each Pap smear and biopsy presents the chance of a false negative or false positive diagnosis that influences future screening and treatment. By addressing a complete system, rather than piecing together a collection of reductionistic models for individual smears and biopsies, such analyses allow the influences of different system components to be expressed and provide more realistic bases for contrasting screening recommendations.

Qualitative methodologies

An alternative scope of analysis involves qualitative methodologies. Such methodologies might include surveys, ethnographic interviews, interpretive techniques such as phenomenological or narrative analyses, or observational research. Qualitative research is used primarily to generate descriptions of complex human experiences. It differs from quantitative approaches by emphasizing the subjective nature of experience, which can be difficult to quantify. Qualitative methodologies assume that (1) experience is based on perceptions that differ for individuals and change over time, and (2) knowledge accrues additional meaning within a given situation or life context. Although specific qualitative methodologies differ, they usually emphasize interaction between the researcher and the participant and treat the participant as the best informant about her own experience and as an equal partner with the researcher. Thus, this approach to collecting data is believed by some to empower the individuals and communities participating in the research and be particularly appealing to a range of women participants. These methodologies also are seen as appealing to women because the study methods emphasize the social and life context of participants and frequently focus on understudied areas in women's health, such as women's responses to diagnosis and treatment, the sociocultural meaning of the proposed treatment, or the ability of women to gain access to therapies or services.

Conceptual links across disciplines

Women's health research extends scientific discussion across disciplines and requires the synthesis of ideas. Wilson⁸ uses the term "consilience" to describe this unification, a "linking of facts and fact-based theory across disciplines to create a common groundwork of explanation."^{8, p8} He em-

phasizes that consilience is important in order to apply what is currently known to multidisciplinary problems, and it is "the surest means of identifying the still unexplored domains."^{8, p298} Multidisciplinary research programs are developed to reinforce collaboration across disciplines, enhance discussion, and promote unified descriptions. This requires valuing and incorporating methodologies from different disciplines.

Each discipline will raise different questions from its unique disciplinary focus as a priority for inclusion in the research. Differences in beliefs about the role of the participant in the study, approaches to sampling, data elements to be included, analytical strategies, and interpretation of results will likely emerge among a multidisciplinary team. These teams may resolve these differences in several ways. One approach would be characterized as parallel work, in which each discipline carves out an area of focus, poses relevant research questions, and conducts a separate arm of the study. For example, a nurse scientist might investigate the experience of undergoing breast cancer treatment by conducting a phenomenological study using qualitative interviews and analysis with a subsample of participants in a randomized treatment study conducted by a physician scientist. An alternative technique is to develop an integrated study in which investigators from multiple disciplines merge their various approaches and design a multimethod study that all embrace, although each investigator might assume leadership for the part of the study most within her or his area of expertise.

Logistical and design issues

Experience in multidisciplinary research programs underscores the importance of standardized, well-defined protocols to ensure that methods are communicated and understood among investigators with varying backgrounds and that consensus in interpreting results can be fostered. In the design of programs, it is important for teams to reach consensus and discuss contingencies. Research databases need to be structured and documented to allow researchers to draw on their collective expertise.⁹ The challenges to integrating data are many, including differing protocols and data storage systems, issues related to data ownership, confidentiality requirements, insufficient documentation, difficulty in finding data resources, and time.¹⁰ The emergence of the

Internet and web-based communications software has made the sharing of data, documentation, and methodology much more efficient. Noting this, an expert panel convened by the National Science Foundation has called for the development of scientific collaboratories, that is, "integrated, tool-oriented computing and communications systems to support scientific collaboration,"¹¹ which may increase the efficiency of multidisciplinary research activities. Women's health research by its nature is a prime area for the development of such test bed collaboratories.

A consequence of increased complexity in modeling systems, rather than individual parameters, is that larger sample sizes are needed. As underlying models include increasing numbers of parameters, the ability (i.e., statistical power) to detect differences in individual outcome measures and relationships between pairs of outcome measures is reduced. The information necessary to characterize the complex system saps power from more precisely focused comparisons, so that larger clinical trials are necessary to demonstrate the efficacy of treatments. This is exemplified by the complexities encountered in the design of the large hormone replacement clinical trial of the Women's Health Initiative (WHI). This study contrasts placebo therapy with regimens of postmenopausal hormone replacement therapy (HRT) (estrogen therapy alone in women without a uterus; combined estrogen/progestin therapy in women with a uterus) with respect to the prevention of coronary heart disease events and osteoporosis-related fractures.¹² Because HRT may have a broad impact on women's health and metabolic systems, many secondary outcome measures and symptoms must be addressed. The team of investigators contributing to the design of the study included many experts in such diverse areas as hemostasis, lipidology, diabetology, psychology, and oncology. Inclusion of measures and outcomes across these disciplines has had several important effects on study design. First, by monitoring the relative efficacy of the interventions across these outcome measures, on which the time line of influences and the severity of the health consequences vary, global indices for pooling information across outcomes and time points were necessary.¹³ Second, the cost of data collection across the many outcomes of interest became significant and represented a major investment from the NIH. A complex computer system was required to manage the data

collection. Third, documentation of the trial procedures, with sufficient detail to convey practices across disciplines, is enormous. Finally, study administration across its many sites and disciplines became challenging and complex. Nonetheless, certain critical questions can be answered only by these types of larger-scale designs. Consequently, future plans for answering critical questions need to continue to be diligent in targeting areas that require this level of effort.

Summary of methodological issues

Although many approaches for organizing multidisciplinary research programs in women's health may be developed, it appears that several key methodological components can be identified that may add to their success. These include (1) models to characterize systems and clusters of interrelated outcomes and more sophisticated statistical methodologies to fit these models, (2) multiple innovative research methodologies that include both quantitative and qualitative approaches, (3) strategies for and use of computer communications systems to encourage data sharing as well as (4) standardization and documentation of methods, and (5) innovative strategies for monitoring safety across outcomes. The CoE have recognized the importance of these issues. They serve as forums for linking methodologists with other scientists and promote the communication necessary to develop consolidated approaches to research programs. The CoE also are developing registries of members that list the methodological expertise of researchers across disciplines to promote intramural and intermural collaborations.

MODEL PROGRAMS: LESSONS FROM THE COE

Resources and incentives

Keys to developing all multidisciplinary research programs, like the CoE, have roots in infrastructure, supportive climates, and rewards. The experiences of the CoE model suggest that all must be addressed for optimal success. First, a dedicated infrastructure must exist with several component parts. A director who actively supports research programs in women's health as well as the use of other resources, such as statisticians and research assistants, is an absolutely es-

sential component of this infrastructure. Space is another key component to this infrastructure, and space must be in a centralized location. A financial plan that allows faculty members to share resources and costs across academic units is also critically important.

Second, the climate for developing interdisciplinary research must be supportive. All faculty members must be given the same message that multidisciplinary research is valued. Verbal and nonverbal acknowledgment for this type of collaboration must be given at all levels of authority. Faculty members have to be given support for working together, and collaboration must be viewed as the desired model. Administrators should also be enlisted to participate in this model.

Finally, rewards are essential to foster the research effort. Faculty members may already understand that multidisciplinary research is viewed favorably by major granting agencies, such as the NIH, but rewards within an academic center are also needed. For instance, some schools provide a salary bonus to faculty members who compete successfully for NIH-funded grants. Special rewards also might be given when efforts are made to involve other disciplines. These could include travel monies or other incentives, such as protected research time. The CoE model has been instrumental in facilitating rewards of space and resources for interdisciplinary collaborations by requiring these as part of a CoE. The CoE model also has helped junior female faculty members by providing funds for support of these young investigators and requiring protected research time.

Program development

The CoE experience indicates that to develop a multidisciplinary effort, initial meetings need to be held with key persons identified in relevant disciplines. In the CoE example, efforts to identify all faculty members who are interested in research related to women are necessary. With the help of startup monies from a program such as a CoE-supported program, monthly multidisciplinary meetings around specific women's health topics can be held. Topics can range from tips on grant writing to assessment of outcomes from a multidisciplinary perspective. Time is needed to introduce each person's area of interest, and opportunities for local and national funding need to be discussed. Both before and after meetings, en-

couragement of interaction among faculty members from different disciplines is needed, and a CoE representative must take the initiative to link persons with similar research interests.

Program evaluation

Periodic evaluation of the status and progress of multidisciplinary programs is valuable. Procedures to track grant submission, publications, and other milestones are important to gauge the success of programs, assess their value, and publicize opportunities for researchers. Tracking procedures enhance the accountability of administrators of these programs and foster ownership among successful participating investigators.

Challenges

Change is not easy. The CoE experience clearly indicates that to build a multidisciplinary women's health research program, faculty members need the opportunity to learn to trust each other's unique perspective, value individual contributions, and share resources. For instance, faculty members can learn that involving a statistician can bring greater clarity to their work. Investigators can learn that behavioral proposals as well as clinical trials for medical treatment are of interest to NIH. Nurses can learn that psychologists can add new insights and theories to behavioral work. Everyone can learn that communication experts as well as programming experts can greatly enhance the quality of research. Faculty members also need to learn how to negotiate authorship and share the most valuable resource—study participants. These are the lessons of the CoE multidisciplinary and integrative model. Although the transition to true multidisciplinary efforts is not always smooth, the diversity added to women's health research, medical and behavioral science education, and clinical services across the entire health continuum is enriched by the contribution of diverse fields of inquiry.

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