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Commentary

A Five-Step Guide for Moving from Observational Studies to Interventional Research for Women Veterans

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Introduction

The Department of Veterans Affairs (VA) is devoted to the care of veterans, which historically have been primarily men. Over the last 30 years, however, the number of women serving in the active duty military has increased dramatically (Department of Defense, 1980; Department of Defense, 2010). Consequently, the VA health care system has experienced considerable increases in women veterans' enrollment and use, which poses challenges for VA health care providers to deliver gender-specific care within the traditionally male-focused system (Bean-Mayberry et al., 2010; Hayes, 2010). In response to the changing demographics of American veterans, the VA is expanding women's health care services and prioritizing women's health research within the VA health care system (Yano et al., 2006).

Observational studies documenting trends and describing concerns about the health and health care of women veterans have been documented extensively (Goldzweig, Balekian, Rolon, Yano, & Shekelle, 2006). Examples of gender differences include the greater burden of medical illness in veterans with post-traumatic stress disorder (Frayne et al., 2011) and lower use of smoking cessation medications among VA users (Sherman, Fu, Joseph, Lanto, & Yano, 2005). As the VA continues to accomplish key aspects of its women's health research agenda to address the unique needs of women veterans, there is substantial interest in moving the field toward intervention trials that operationalize what is known about health problems into testable strategies designed to improve, rather than describe, health outcomes (Yano et al., 2011). However, despite substantial progress in observational research in the past several years, interventional studies that seek to address women veteran's health care needs are lacking. A recent systematic review of the literature found that fewer than 3% of women's health studies conducted from 2004 to 2008 were clinical trials (Bean-Mayberry et al., 2010).

Based on an assessment of barriers faced by researchers interested in conducting women veterans' research, the dearth of interventional research among women veterans may be a result of such factors as knowledge gaps about women veterans (i.e., disease prevalence, utilization patterns, preferences) and barriers to their sufficient recruitment for trials given their small numbers in individual VA facilities (Yano et al., 2006). Furthermore, outside the VA, women veterans represent roughly 1 in every 100 women in the community, making them even harder to identify and recruit (Murdoch et al., 2006). Historically, most VA women's health researchers have been focused on generating basic knowledge about women veterans' health status, access, utilization, and quality, and, therefore, relied on expertise in secondary analyses of VA's large databases, survey design, and qualitative research (e.g., focus groups). These research activities have been essential to drawing an accurate portrait of women veterans' needs. However, transitioning VA women's health researchers to focus on interventions requires laying the groundwork for the steps necessary to design and rigorously test intervention strategies informed by previous observational research.

Because intervention development is a multidisciplinary process, this paper seeks to broaden researchers' understanding of the multiple factors present in intervention science and provide some common language to describe intervention development and testing. Specifically, this paper is designed as

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Table 1
Five-Step Process for Moving from Observational Findings to Interventional Research for Women Veterans

Key Tasks	Resources
Getting started	
Identify grant forms and key dates for submissions	VA Research and Development funding information: http://www.research.va.gov/funding/
Step one: Refine research question and develop an intervention strategy based on literature review	
Identify an observation that needs to be addressed with an intervention	PubMed: www.ncbi.nlm.nih.gov/pubmed/
Search for articles, systematic reviews, and meta analyses that relate to your observational finding	The Cochrane Collection: www.cochrane.org
Query the VA Women's Health Literature Database	VA Evidence-based Synthesis Program: http://www.hsrd.research.va.gov/publications/esp/
Look for VA-specific systematic reviews of your topic developed by the VA Evidence Synthesis Program	VA Women's Health Literature Database: http://www.hsrd.research.va.gov/for_researchers/womens_health/search.cfm
Based on existing research, refine your research question and intervention strategy	
Step two: Develop a conceptual model and preliminary intervention	
Create a conceptual model for your research	*Theory at a Glance* (National Cancer Institute, 2005) is a useful primer on behavioral theory (http://www.cancer.gov/cancertopics/cancerlibrary/theory.pdf).
Consider key predisposing and organizational factors unique to women veterans	*Conceptual models for health education research and practice* (Earp & Ennett, 1991) provides a description of conceptual models for intervention research.
Use the conceptual model to develop an intervention protocol	*Planning Health Promotion Programs: An Intervention Mapping Approach* (Bartholomew, Parcel, Kok, & Gottlieb, 2006) is a useful tool and provides instruction on developing intervention objectives that are theory-based and measurable. For information on the Women Veteran Program Manager position, see VHA Handbook 1330.02. To contact the Women Veteran Program Manager at your facility, visit http://www.publichealth.va.gov/womenshealth/
Step three: Pretest intervention	
Obtain IRB approval to contact potential pretest subjects	For detailed information on message development and pretesting, see *Making Health Communication Programs Work* (National Cancer Institute, 2002; http://www.cancer.gov/cancertopics/cancerlibrary/pinkbook/)
Examine existing VA-specific educational and other programmatic materials	The following sites show examples of VA resources that can be used in a pretest: www.va.gov/womenvet and www.prevention.va.gov
Using a small sample of the target audience, gather feedback on planned intervention material	
Amend your intervention materials according to pretesting feedback	
Apply for pilot funding (if available)	
Step four: Pilot test the intervention and make adjustments	
Using a sample of your target audience, pilot test a small-scale intervention typically at a single site	*Planning Health Promotion Programs: An Intervention Mapping Approach* (Bartholomew, et al., 2006) provides details on pilot testing interventions.
Adjust your intervention (as necessary) until confident that intervention is feasible to conduct and acceptable to the target audience	*Adapting evidence-based behavioral interventions for new settings and target populations* (McKleroy, et al., 2006).
Step five: Test the intervention in a randomized, controlled trial	
Determine the sample size necessary for study	For a list of recruitment strategies and advice on recruiting specific populations, see: *Recruitment for controlled clinical trials: literature summary and annotated bibliography* (Lovato, Hill, Hertert, Hunninghake, & Probstfield, 1997).
Plan large-scale recruitment efforts, allowing for changes when recruitment lags	For more information on the VA Women's Health Research Consortium or the Women Veterans' Practice-Based Research Network, see *Using research to transform care for women veterans: Advancing the research agenda and enhancing research-clinical partnerships* (Yano et al., 2011)
Contact the Women Veterans' PBRN for assistance with studies requiring multiple sites	
Apply for funding	
Launch trial	

a primer to accelerate the development of more intervention studies among women veterans. We propose and describe a five-step method by which researchers can move from observational findings to developing interventional research. Table 1 lists resources that may be helpful in developing intervention research among women veterans in VA and other public or private health care settings, while also providing examples of and resources for each step. Although we present these steps in a linear fashion, intervention development is an iterative process. In practice, intervention researchers move back and forth between steps as new information is gathered, created, and incorporated into intervention design.

Step One: Refine Research Question and Develop an Intervention Strategy Based on Literature Review

Observations made about women veterans in clinic or using VA databases are an important part of developing a research question. However, intervention research is an intelligence-gathering process that identifies possible strategy options to address compelling questions that can arise from these observations. To address clinical concerns through intervention efforts, it is important to know how others have addressed similar issues, including lessons learned, strategy mix used, sequence of strategies, and how those data can be used to choose

strategies for your research question. Therefore, an important first step is using prior research to refine the development of a research question and proposed intervention strategy. A thorough review of past research, including relevant systematic reviews, should yield 1) a better understanding of cognitive, environmental, and behavioral antecedents of the health issue and 2) evidence from previous interventions. Thus, prior research should refine your research question and inform your intervention development.

The VA has created specific resources that can help researchers to develop evidence-based intervention trials for women veterans. In 2004, the VA Office of Research and Development commissioned a systematic literature review to synthesize the research knowledge on women veterans' health issues. The results of this review are contained in a searchable literature database that is updated periodically. Also, the VA Health Services Research and Development Evidence Synthesis Program provides access to syntheses of health care topics prioritized as vitally important to health and health care of veterans. Links to these resources can be found in Table 1.

Step Two: Develop a Conceptual Model and Preliminary Intervention Design

Using information gathered in a careful review of the literature, the next step is to develop a conceptual model to guide research and intervention design for women veterans. Conceptual models serve two purposes: 1) Depict relationships among factors related to specified outcomes, and 2) guide development and conduct of the intervention. A conceptual model may be based on one theory or a combination of theoretical constructs.

Conceptual models should clearly outline proposed causal relationships among factors on which to intervene, as well as expected outcomes. When well-constructed, conceptual models serve as a parsimonious visual representation of complex relationships (Earp & Ennett, 1991). Models that are overly simplistic or overly complicated are not useful. When constructing conceptual models, it is important to consider factors 1) at different levels of influence (e.g., environment, policy, social network) on the problem to be addressed by the intervention (Stokols, 1996); 2) that cannot be changed by intervention, but may influence how participants respond to the intervention (i.e., predisposing factors); and 3) that influence the intervention itself (i.e., intervening factors). It is also important to consider relationships among intervening factors (i.e., does the intervention need to first influence one factor before it can influence another or will it influence the factors at the same time?).

When developing a conceptual model for an intervention specifically for women veterans, the following predisposing factors should be considered: Service era, branch of service, service-connection status (i.e., a disability recognized to be related to military service), and exposure to combat- and/or sexual-related trauma in the military. Furthermore, when developing interventions to be implemented in the VA health care system, it is critical to engage stakeholders in early phases of the study design and address VA organizational factors (e.g., presence of women's clinics, providers' experience with female patients). Every VA facility also has a full-time Women Veterans Program Manager who may be able to partner with researchers to ensure the intervention addresses patients' needs and will be supported by management, providers, and staff (Table 1).

Once a conceptual model has been developed, it is time to explicate specific intervention objectives and to optimize intervention strategies that will achieve those objectives within your target audience. Briefly, intervention objectives state clearly what intervention participants must learn or change to achieve the specified outcome. Selection of intervention strategies should be evidence-based and may be influenced by other contextual factors such as budget, site logistical issues, and expertise of the research team. To date, however, limited intervention research has been conducted with women veterans. Therefore, it is likely that researchers will need to consider evidence from interventions conducted with other groups (e.g., non-veteran women and male veterans) when selecting intervention strategies. Systematic processes for adapting existing evidence to the conditions and experiences of women veterans are needed.

It is important to get a general sense of both the formal and informal resources already available to the target audience on the specified topic. In many cases, it is possible to modify existing documents, programs, or materials. Search for publications, program plans, curricula, and websites previously developed by other researchers and organizations such as the Veterans Health Administration, the National Institutes of Health, and the Centers for Disease Control and Prevention, as well as state health departments. If resources are identified that coincide with objectives, contact developers and request permission to use or customize material. Developers may also serve as collaborators or consultants on intervention studies, if appropriate.

Step Three: Pretest the Intervention

The most effective intervention materials are those that fit the preferences and context of the target audience. Therefore, for patient-level interventions, the next step is to gather feedback from a small sample of women veterans similar to those you hope to reach with your intervention. For provider- or practice-level interventions, comparable steps should be taken with clinicians, staff, and/or health care managers. This feedback, called pretesting, allows intervention developers the opportunity to gather opinions from the intended intervention audience on select parts of the intervention (e.g., key message concepts, draft intervention materials) before pilot testing. Pretesting intervention materials can maximize intervention effectiveness through assessing whether intervention materials are appealing and easily comprehended by the intended target audience. In some cases, the examples available on the VA website can be used as pretest materials (Table 1). Always obtain Institutional Review Board (IRB) approval before making contact with any human subjects, even for pretesting purposes.

Step Four: Pilot Test the Intervention and Make Adjustments

The next step is to conduct pilot testing. A pilot study is a small-scale test of the intervention; it is a critical step in designing interventions for women veterans. Ideally, the same groups, organizations, or individuals who will carry out larger scale efforts are involved in testing the pilot. Also, the pilot should be tested with members of the intended target audience. Pilot testing an intervention allows researchers to directly test feasibility (e.g., process, logistics) and acceptability (e.g., participant recruitment, retention) of the proposed intervention. A small number of participants (20–30) are needed for pilot testing because the purpose of this step is to determine feasibility and acceptability and not intervention efficacy. The Women Veterans

Program Manager at your facility may be a helpful contact for recruiting pilot participants.

Pretesting and pilot testing are essential steps that allow researchers an opportunity to adapt and refine interventions before rigorous testing in randomized, controlled trials. Moreover, pretesting and pilot testing may help intervention developers avoid Type III errors, rejection of intervention effectiveness due to poor intervention design or inadequate intervention delivery. Table 1 provides resources to assist in applying for and writing small grants to fund pilot studies.

Step Five: Test the Intervention in a Randomized, Controlled Trial

Once you have established that your intervention is both feasible to conduct and acceptable for women veterans and other stakeholders, the final step in this process is to rigorously test the intervention in a randomized, controlled trial. Several key considerations should be addressed when developing trials of women's health interventions. First, when designing the study, serious consideration should be paid to which comparison condition provides an adequate test of the proposed intervention and advances the state of the science. For example, a randomized, controlled trial might compare an experimental intervention with a usual standard of care control (usual care is typically a minimal or no contact control group) or compare an experimental intervention with a previously studied effective intervention (a comparative effectiveness trial).

One of the greatest challenges of conducting intervention research is timely recruitment. Recruitment can be boosted through several strategies that have been identified as increasing recruitment rates. Examples of these strategies include offering incentives for participation (Paskett, DeGraffinreid, Tatum, & Margitic, 1996), using opt-out rather than opt-in recruitment procedures, open design (i.e., participants are not blinded to their study arm), and telephone reminders (Treweek et al., 2010; Table 1). It is advisable to develop contingency plans for when (not if) recruitment proves to be challenging. For example, when planning an intervention, allowing enough flexibility to quickly alter existing plans and implement new strategies when recruitment lags is essential (Lovato, Hill, Hertert, Hunninghake, & Probstfield, 1997).

Given the small number of eligible women at any one facility, researchers may need to conduct intervention studies across multiple VA medical centers and/or community-based outpatient clinics. To determine how many sites are needed to meet recruitment goals, VA researchers may follow local guidelines to conduct data pulls preparatory to research (i.e., review inpatient and outpatient records to determine the feasibility of conducting a particular research project). These local and national medical record databases may be accessed following local IRB policies. Access to these data is commonly limited to VA employees, although special permissions may be granted in certain circumstances to facilitate access among non-VA investigators. Engaging clinicians to participate in multisite intervention studies may also require protected time from clinical and administrative duties.

Once a study receives funding, assistance may be needed to facilitate adherence to site-specific human subjects' regulations (i.e., IRB approval), recruitment, and intervention delivery. Because of the size of the VA health care system and its accompanying research program, the VA has established a Central IRB for the conduct of multisite studies. Because most interventions among women veterans will have to be multisite to achieve sufficient sample sizes, use of the VA Central IRB is likely to be an essential adjunct to research in this arena.

Discussion

In an effort to bolster multisite research among women veterans, the VA Health Services Research and Development Service has funded establishment of the Women Veterans' Practice Based Research Network (PBRN). The PBRN is composed of a network of partnered VA medical centers with moderate to large volumes of women veteran patients and established investigators tasked with facilitating women veterans' research. To balance top-down research demands and bottom-up quality improvement needs, the Women Veterans' PBRN seeks to promote bi-directional collaboration between clinicians and researchers, facilitate multisite women's health research, and encourage a sense of community among women's health researchers. Because of the importance of educating investigators interested in women veterans' health research, the VA has also funded the VA Women's Health Research Consortium. The consortium provides education/training (e.g., cyberseminars), technical consultation, and mentorship, in addition to fostering collaborations, research–clinical partnerships, and dissemination. Combined, these two programs comprise the VA Women's Health Research Network, and are uniquely positioned to facilitate VA research in women's health by 1) identifying site coordinators in preparation for multisite trials, 2) providing specialized methods support (e.g., sample size estimates), 3) reviewing and providing feedback on protocols, and 4) assisting investigators of funded projects with issues related to complexities of multisite trials (e.g., central and local IRB, data security, privacy procedures).

The process of moving from observational research to interventional research is important to improve health care for women veterans. We have outlined a five-step process to guide researchers in developing rigorous testing intervention that address the needs of women veterans. We hope to facilitate an increase in the amount of interventional research conducted to meet the expanding needs of women veterans.

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