

Clinical Excellence Through Evidence-Based Practice: Fatigue Management as a Model

Victoria Mock, DNSc, RN, AOCN®, FAAN
2003 Oncology Nursing Society Distinguished Researcher Award

Introduction

by Ruth McCorkle, PhD, RN, FAAN

Victoria Mock, DNSc, RN, AOCN®, FAAN, was born in South Carolina to Geneva and James Mock. The family had three daughters—Tyke, Vicki, and Betsy—who grew up in a modest home; their parents worked hard to make ends meet. Vicki continues to be inspired by her mother. The three girls are strawberry blondes and loved the sun in their youth, but, as they have gotten older, they have come to realize that the sun can be harmful to them. After Vicki graduated from high school, she attended Duke University in Durham, NC, and obtained a bachelor's degree in nursing. Vicki worked as a staff nurse at Duke University Medical Center before relocating to San Francisco, where she earned a master's degree in medical-surgical nursing from the University of California, San Francisco. Her thesis was titled "The Deliberative Nursing Process and the Pain Experience of Patients." She was inducted as a charter member of the Alpha Eta chapter of Sigma Theta Tau. She left California to work as a faculty instructor in the College of Nursing at Wayne State University in Detroit, MI, and later relocated to Richmond, VA, where she worked as a staff nurse and faculty member. Vicki learned firsthand the experience of confronting cancer when she was diagnosed with melanoma and given a guarded prognosis. She knows the meaning of the experience for her patients and their families and has built her career on providing superb and empathic care that empowers patients to help themselves. After her own illness, she met her husband Quent while supervising student nurses who were caring for his mother, who was dying from breast cancer. He became her biggest supporter and recognized the remarkable sensitivities and potential that this highly gifted woman possessed. With his encouragement, Vicki had a singular focus to earn her doctorate as well as become a first-rate nurse researcher.

Vicki was enrolled in doctoral studies from 1982–1988 and graduated with a doctorate of nursing science in adult health nursing and nursing education from Catholic University of America in Washington, DC. Her dissertation was titled "Body Image in Women Treated for Breast Cancer" and subsequently was published in *Nursing Research*.

After completing the course work in her doctoral studies, she relocated to Boston in 1985 and joined the faculty at the School of Nursing at Boston University until it closed its doors in 1988; she taught at Boston College for the next six years. During that time, her program of research related to outcomes in women with breast cancer during treatment was launched. She

completed four grants associated with developing an exercise rehabilitation program for women while receiving treatment, supported by the American Nurses Association Foundation, American Cancer Society (ACS), Massachusetts Nurses Association, Boston College, and Massachusetts Department of Public Health.

In 1994, the School of Nursing at Johns Hopkins University in Baltimore, MD, recruited Vicki as the director of nursing research at Johns Hopkins Cancer Center, and she also assumed a joint faculty position in the School of Nursing. Since joining the faculty at Johns Hopkins, Vicki's research career has soared. Her program of research has been supported by ACS funds as well as an ACS Professorship in Nursing from the Mid-Atlantic Division, the ONS Foundation, and Johns Hopkins University, leading to her current, research-initiated grant, "Mitigating Cancer-Related Fatigue by Exercise," funded by the National Cancer Institute and the National Institute of Nursing Research. Her publications have established a solid foundation for the relationship of exercise and fatigue during breast cancer treatment. She generously has shared her knowledge with the profession at large through her presentations, publications, and leadership in various professional societies.

Vicki has worked hard to standardize her walking exercise intervention protocol. Two booklets have evolved from her research: *Every Step Counts: A Walking Exercise Program for Persons Living With Cancer* and *Managing Fatigue: A Guide for Individuals With Cancer*. One measure of success of any intervention protocol is the ability of investigators to replicate it across settings. She has been persuasive in encouraging a number of groups to test the program.

Since the 1990s, Vicki has developed a program of multisite research. In fact, every research study she has performed has been multisite. In this capacity, she has held steadfastly true to the scientific rigor required of advancing nursing as a science. Her commitment to this endeavor has meant meeting challenges with creative skills and perseverance. At the Fifth National Conference on Cancer Nursing Research, the keynote speaker, Ada Lindsey, RN, PhD, then dean of the School of Nursing at the University of Nebraska, cited Vicki's program of research as a model of the type of research needed most in oncology nursing: longitudinal, intervention testing, multisite, interdisciplinary, and focused on an identified research priority of the On-

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Digital Object Identifier: 10.1188/03.ONF.787-796

cology Nursing Society (ONS). Barbara Given, PhD, RN, FAAN, noted that prescribing moderate exercise to prevent high levels of fatigue during breast cancer treatment represents a paradigm shift for care providers whose typical recommendations to decrease activity reflected conventional wisdom. However, the results of Vicki's work and other research in the field has suggested that a change in clinical practice was indicated to provide evidence-based therapy for cancer-related fatigue. The innovative scientific basis of her research was recognized by the National Comprehensive Cancer Network (an association of the National Cancer Institute-designated comprehensive cancer centers), resulting in Vicki being the first nonphysician to be appointed chair of 1 of the 42 practice guideline panels. The recognition of her work and leadership for this activity is critical because these guidelines serve as models of care for patients who are undergoing cancer treatment.

Introduction

by Sharon Krumm, PhD, RN

Recognizing and honoring Victoria Mock, DNSc, RN, AOCN®, FAAN, as the 2003 Oncology Nursing Society (ONS) Distinguished Researcher is appropriate for many reasons. Ruth McCorkle, PhD, RN, FAAN, has written of the significant influence Vicki has had on the field of oncology nursing research, including multisite clinical trials research and her own focused research program related specifically to the management of fatigue. The scope of Vicki's influence is international and multidisciplinary, and her record of peer-reviewed publications is substantial and impressive.

I will reflect briefly on her influence on clinical nursing research and practice at Johns Hopkins Hospital and University in Baltimore, MD. In the mid-1980s, Linda Arenth, RN, MS, then the director of nursing for the Johns Hopkins Oncology Center and a visionary oncology nursing leader, first established the position of director of oncology nursing research for the center. Since 1994, Vicki has held this position, as well as that of associate professor in the School of Nursing at Johns Hopkins University, with a joint appointment in the School of Medicine. Linda envisioned that oncology nursing research would stand side by side with medical and basic science research and that oncology nurse clinicians would understand and apply research principles and findings to their practices. Recall the first time that you heard the terms correlational coefficient, statistical significance, descriptive design, quasi-experimental, factorial designs, and research variables. These are common terms to those whose careers are primarily in the area of research. Imagine adding them to the vocabularies of nurses whose primary careers are as clinicians, many without advanced degrees. So, here were Vicki's challenges: First, you have your own active, funded research program that withstands the test of your peers and medical and scientific colleagues; you publish and present the results of your research primarily in peer-reviewed journals and at national meetings; you teach a number of courses and assume leadership responsibilities within your school; you serve on university research committees; you lead hospital nursing research committees;

In her daily work, Vicki sets an example of how a researcher actualizes the role. She is a role model for multidisciplinary research. She has achieved exceptional credibility with physicians, nurses, and administrative staff. She has, in fact, been called by a senior nurse researcher, "one of the most talented and gifted nurse researchers with whom I have ever worked." Women with breast cancer will have better quality of care because of Vicki's influence and vision. It is a privilege to honor Vicki with the 2003 ONS Distinguished Researcher Award supported by Bristol-Myers Squibb Oncology, to acknowledge the outstanding work she has done, and to walk beside her as she continues to make future advances on behalf of our patients and families.

I would like to thank Sharon Krumm, PhD, RN, for cosponsoring the nomination of Victoria Mock, DNSc, RN, AOCN®, FAAN, for this award, and also to Marcia Grant, DNSc, RN, FAAN, and Barbara Given, PhD, RN, FAAN, for their letters of support.

you serve in national leadership positions; you volunteer for the American Cancer Society and other community organizations; you are active locally and nationally in ONS; you provide highly valued advice and counsel to administrators (and yes, sometimes we administrators do seek advice and counsel, and I have learned to always follow Vicki's advice); you consult with individuals and groups about their research interests; you advise and serve as investigator on studies that your colleagues initiate; you help nurses prepare abstracts about their projects and practices by providing encouragement and suggestions; you help nurses rehearse their presentations before actually speaking before small audiences such as faculty meetings or large, national meetings such as the ONS Congress; and, you do all of this with a calm demeanor, never becoming upset, patiently abiding the least intelligent of questions, and always, always offering a smile and word of encouragement. This is Vicki Mock.

For some, Vicki's curriculum vitae (CV) is so impressive that it almost is formidable. However, although her CV may list some of her accomplishments, and they are many and very worthy, it cannot really inform about the effect that she has on nurses and their clinical practice and professional development. As one nurse manager said, the smartest thing that we did in developing our new clinical program of inpatient and outpatient intensive bone marrow transplantation was to engage Vicki in the research team that formally studied the effects of the program. With Vicki's guidance, physicians, administrators, managers, and staff nurses studied and reported on the economic, social, and clinical outcomes of this program. Subsequently, again with Vicki's guidance and expert advice, staff nurses have furthered this work and continue to present their findings and incorporate them into their daily practices. Vicki guided staff nurses who studied the effect of acupuncture during infusion of bone marrow; an abstract about this work was presented at the 2003 American Society of Clinical Oncology meeting. Vicki also works with

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nurses and social workers to ensure that fatigue is addressed appropriately in patients, including taking time to personally meet and speak with patients and families in the fatigue “Meet the Experts” sessions. Can you imagine a more powerful role model for staff and advanced practice nurses? Vicki always is approachable and encouraging. She gives feedback in the most thoughtful and constructive manner, never criticizing or intimidating. At the same time, her attention to each detail results in presentations and publications of very high quality and infuses nurses who receive the feedback with a sense of pride and confidence that they would not have otherwise. One example of the respect that Vicki commands from oncology nurses at all levels was her nomination two years ago by the Greater Baltimore Chapter of ONS as Advanced Oncology Certified Nurse® of the Year. Vicki received the Johns Hopkins University Excellence in

Teaching Award last year, and her research speaks for itself in the quality and effect that it has had on clinical care.

Earlier, I listed some challenges faced in fulfilling Linda Arenth’s vision and how Vicki has made the vision come alive for us. The number of abstracts presented by Johns Hopkins nurses this year at the ONS 28th Annual Congress really is quite remarkable, especially considering the effect of the nursing shortage on staff nurses’ time for professional projects. This is a reflection of and a tribute to Vicki’s influence. In addition, two of Vicki’s former students received recognition for their research at this year’s Congress.

The staff nurses at Johns Hopkins are smiling because they know that Vicki’s selection as the ONS Distinguished Researcher for 2003 is so well deserved, and they, like those who have worked with her, honor her for all that she has accomplished and all that she represents.



Clinical Excellence Through Evidence-Based Practice: Fatigue Management as a Model

by Victoria Mock, DNSc, RN, AOCN®, FAAN

This article describes one example of many in which oncology nurse researchers have pursued a clinical problem passionately and contributed to the development of the science that ultimately led to changes in practice and improvement of outcomes for patients and families. The program of research, focusing on management of cancer-related fatigue (CRF), illustrates the contribution of oncology nursing research to clinical excellence through evidence-based practice.

Rutledge and Grant (2002) have defined evidence-based practice as “care that integrates best scientific evidence with clinical expertise, knowledge of pathophysiology, knowledge of psychosocial issues, and decision-making preferences of patients” (p. 1). The review and synthesis of scientific evidence are a relatively new focus in oncology nursing but are expanding rapidly, and nurses have been experts at the other components of evidence-based practice for many years.

Evidence-based practice begins with the identification of a clinical problem for which no effective treatment is readily identifiable. We conduct research to address the problem, synthesize the scientific evidence, integrate it with clinical expertise and other expert knowledge, and develop clinical practice guidelines. The guidelines are implemented, evaluated, and revised as new knowledge is developed and are used to guide clinical practice (see Figure 1).

The Problem of Cancer-Related Fatigue

Fatigue was determined to be a research priority by the Oncology Nursing Society (ONS) in 1991 (Mooney, Ferrell, Nail, Benedict, & Haberman), and more than a decade of research on this problem now is part of the scientific literature. The first national practice guidelines for CRF were published in 2000 (Mock et al.) by the National Comprehensive Cancer Network (NCCN) and revised in 2003 by the Cancer-Related Fatigue Practice Guidelines Panel (Mock et al., 2003). Several ONS nurse researchers serve on the multidisciplinary panel of experts. The guidelines are beginning to be implemented and evaluated in cancer centers in the United States.

CRF is defined by NCCN as a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning (Mock et al., 2003). The persistent character of CRF differentiates it from the fatigue of healthy individuals, which is normal, expected, and resolves with sufficient rest and sleep. Fatigue is a subjective experience, comparable to pain, and is best described by the person experiencing it. Recent evidence suggests that high levels of fatigue and other symptoms during cancer treatment can lead to significant reductions in usual functioning (Given, Given, Azzouz, & Strommel, 2001; Jacobsen et al., 1999; Mock, McCorkle, Ropka, Pickett, & Poniatowski, 2002; Nail, Beck, & Lindau, 2002), and researchers are uncertain whether patients regain full functioning when treatment is over (Bower, Ganz, & Desmond, 2000).

Fatigue is the most prevalent symptom of patients with cancer and has been reported to affect 70%–95% of patients receiving treatment with chemotherapy, radiation therapy, or biotherapy (Jacobsen et al., 1999; Robinson & Posner, 1992; Sitzia & Huggins, 1998). Fatigue remains a disruptive symptom in 17%–40% of disease-free cancer survivors (Andrykowski, Curran, & Lightner, 1998; Bower et al., 2000; Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998) and affects 85%–100% of patients in palliative care (Maughan et al., 2000; Stone et al., 1999; Wolfe et al., 2000).

Fatigue is a basic protective mechanism that is initiated to prevent damage to the organism when an imbalance exists between the demand for energy and the availability of needed resources (Aaronson et al., 1999). Patients with cancer may have additional demands to repair healthy cells damaged by chemotherapy and radiation therapy and decreased resources as a result of anorexia, nausea and vomiting, diarrhea, or changes in energy mechanisms, such as damage to mitochondria by cancer treatment. A reduced capacity to provide sufficient energy means that patients with cancer must use greater effort to perform usual activities, leading to high levels of fatigue.

Oncology healthcare professionals have come to accept CRF as expected and normal. Patients often are reluctant to report fatigue because they feel that it must be endured or that they should be able to manage it themselves. Healthcare providers frequently do not screen for fatigue because they are unaware of evidence-based treatments or of the distress and interference with functioning that accompanies fatigue. The result is that CRF frequently is underreported, underdiagnosed, and undertreated.



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funded, in part, by the following awards: American Cancer Society Professor of Oncology Nursing, Mid-Atlantic Division; American Cancer Society Massachusetts Division Behavioral/Psychosocial Research Award; American Nurses Foundation Scholar Research Award; Boston College Faculty Research Fellowship Award; Johns Hopkins University School of Nursing Exploratory Center for Pain, Fatigue, and Sleep Alterations in Cancer (National Institute of Nursing Research [1P20NR03278]); Massachusetts Department of Public Health Breast Cancer Researcher Development Grant; Massachusetts Nurses Foundation Research Award; and ONS Foundation (from an unrestricted Ortho Biotech donation) Multi-Institutional Fatigue Initiative in Research and Education (FIRE®) Competitive Grant Phase I and II Awards. As the recipient of the 2003 Oncology Nursing Society (ONS) Distinguished Researcher Award, supported by Bristol-Myers Squibb Oncology, Mock presented this article at the ONS 28th Annual Congress in Denver, CO.

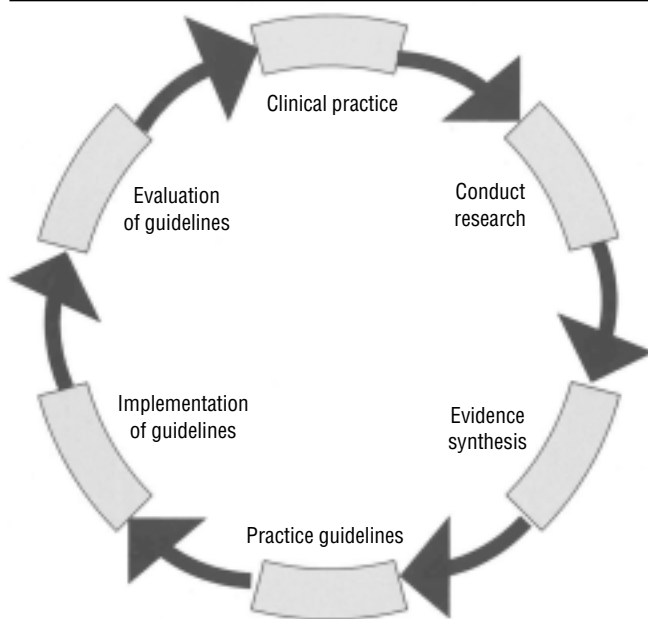


Figure 1. Evidence-Based Practice Model

This article describes a program of research to test one intervention—exercise—to manage CRF and encompasses four completed interdisciplinary studies. The fifth study currently is under way.

Conducting the Research

The program of research began in 1989 when a group of nurses identified a clinical problem. At that time, patients with breast cancer were being treated very aggressively with dose-dense and dose-intense protocols—combinations of powerful chemotherapy drugs resulting in severe side effects with much symptom distress and loss of functional status. We developed and tested a comprehensive rehabilitation program to support women through these aggressive protocols and facilitate their adaptation to breast cancer diagnosis and treatment.

The rehabilitation program included physiologic and psychosocial components. A literature review revealed a study by MacVicar, Winningham, and Nickel (1989) in which patients with breast cancer receiving adjuvant chemotherapy engaged in a laboratory exercise program that increased their functional capacity and functional status during treatment. An earlier report described beneficial effects on mood state and fatigue (MacVicar & Winningham, 1986). In our first study, we developed a protocol for a more moderate home-based walking exercise program that could be adjusted according to patients' symptoms from treatment and response to the exercise training. A support group led by an oncology advanced practice nurse was included as a component of the rehabilitation program to address the educational and psychosocial needs of the women with breast cancer.

The exercise intervention tested in all of the studies in this program of research is a moderate, symptom-limited, home-based, walking exercise program. Consenting patients are given an individually tailored exercise prescription to follow throughout their cancer treatment. The initial prescription is to walk briskly for 15–20 minutes per day, five to six days per week, at

a moderate intensity (target heart rate range of 60%–80% of maximum heart rate), but the program is modified by the patient's age, physical condition, and planned cancer therapy (Mock, Cameron, Tompkins, Lin, & Stewart, 1997). Each walking session begins and ends with three to five minutes at a slow pace as a "warm-up" and "cool-down" to protect the heart. Patients progress as tolerated to a maximum of 30 minutes for five to six days per week. Very debilitated or sedentary patients may need to begin at 5–10 minutes twice daily until they can tolerate longer sessions. Patients are contacted every two weeks to discuss their progress on the program and their side effects of cancer treatment. The exercise program is adjusted as indicated. Patients are taught how to exercise safely, including monitoring their pulse rate, and when to contact the oncology care team to report signs and symptoms (e.g., dizziness, chest pain). Patients are encouraged to walk with a family member or friend at a convenient location—neighborhood, shopping mall, or community exercise facility. Our patients have experienced no adverse events that could be attributed to the exercise program. The exercise program was developed in collaboration with an exercise physiologist, and each of the studies has included an exercise physiologist on the research team.

We obtained funding and conducted a pilot study of the program that subsequently was published in the *Oncology Nursing Forum* (Mock et al., 1994). Using an experimental design, 18 patients with stage I and II breast cancer receiving adjuvant chemotherapy entered the study and 14 completed. Women who were randomized to the rehabilitation program demonstrated improved physical functioning at the end of chemotherapy, as measured by performance on the 12-Minute Walk Test, and lower levels of fatigue and emotional distress, as measured by visual analog Symptom Assessment Scales (SAS), than a control group receiving usual care. The most prevalent symptoms reported were fatigue, sleep disturbance, and emotional distress. Although the potential benefits of the intervention were exciting, whether the benefits were the result primarily of the exercise, support group, or combination of exercise and support was not clear.

The second study tested the exercise intervention alone in a target population of patients with breast cancer receiving six weeks of external beam radiation therapy following conservative surgery (lumpectomy) because fatigue levels reportedly were high in this population. The hypothesis being tested was that patients with recurring breast cancer receiving radiation therapy who participated in the exercise program would have higher levels of physical functioning and lower levels of fatigue and emotional distress than women receiving usual care. We used an adaptation conceptual framework, the Roy Adaptation Model (Roy & Andrews, 1991), proposing that a more adaptive response to cancer diagnosis and treatment would be reflected in the hypothesized outcomes for the exercise group.

Fifty-two patients enrolled, and 46 completed the study. In this experimental design, participants were evaluated at baseline, after three weeks, and at the end of six weeks of radiation therapy. Although most exercise interventions need more than six weeks to demonstrate effects, post-test group comparisons in this study by multivariate analysis of covariance with pretest scores as covariates revealed significantly higher scores in the exercise group on physical function as measured by the 12-Minute Walk Test. Significantly lower fatigue scores, the most prevalent symptom, resulted on the Piper Fatigue Scale and SAS. Difficulty sleeping and anxiety scores

on the SAS also were lower for exercisers. The research report received the 1997 ONS Clinical Excellence in Nursing Research Award and was published in the *Oncology Nursing Forum* (Mock, Dow, et al., 1997).

In 1995, ONS contributed significantly to the development of the science of fatigue management through a competitive research mechanism, the Fatigue Initiative in Research and Education (FIRE®) Awards. This component of FIRE® offered funds for three individual one-year pilot projects and one three-year implementation project. Our team received a one-year FIRE® Phase I Developmental Pilot Award, as well as the FIRE® Phase II Implementation Award.

The FIRE® I study included the establishment of a multi-institutional team of nurse researchers and the standardization and feasibility testing of the walking exercise intervention at five sites. The study was guided by the Levine Conservation Model, an adaptation model in which fatigue is addressed as a component of Conservation of Energy (Fawcett, 1994; Levine, 1989). The study enrolled 50 patients with breast cancer during postsurgical radiation therapy or adjuvant chemotherapy who were stratified by type of treatment and randomized to the exercise program or usual care. Participants in both groups were given a booklet (Mock, Lubejko, Cameron, & Margolis, 1997) addressing ways to manage fatigue that did not include a structured exercise program. Participants in the exercise group also received instructions in the exercise program, including a booklet (Mock, Cameron, et al., 1997) and a video (Mock, Cameron, & Grimm, 1998), that were used to standardize the intervention across subjects and research sites. Outcomes measured at baseline and the end of cancer treatment included physical functioning, fatigue, and other symptoms, as well as quality of life.

Approximately 70% of the patients randomized to the exercise group were able to adhere to the walking program, but a diffusion-of-treatment effect occurred when 50% of the usual-care group exercised regularly during the study. Some of these patients had exercised before their diagnosis and decided to resume regular exercise. A compliance cohort model of data analysis was used to divide the sample into high-walk and low-walk groups with 90 minutes of exercise per week as the point of division (Mock et al., 2001).

Physical functioning as measured by performance on the 12-Minute Walk Test was significantly higher for the high-walk group compared to the low-walk group. Mean fatigue scores on the Piper Fatigue Scale decreased from baseline to end of treatment for the high-walk group whereas fatigue scores increased for the low-walk group, resulting in a significant difference between groups ($p < 0.01$). A similar result was observed on the fatigue subscale of the Profile of Moods States (POMS) scale. Emotional distress as measured by the POMS decreased for both groups from baseline to post-test, but these changes were very significant in the high-walk group ($p < 0.01$) and not significant in the low-walk group.

Quality-of-life scores on the Medical Outcomes Study (Short Form 36) varied among the subscales for the two groups over the course of cancer treatment. Self-reported physical-functioning scores were equivalent at baseline but decreased at post-test by 48% in the low-walk group whereas the high-walk group decreased only 16%. Social functioning increased for the high-walk group and decreased for the low-walk group ($p = 0.01$). Scores on the general health subscale showed a similar pattern.

A strong positive Pearson's correlation existed between symptoms of fatigue and emotional distress ($r = 0.83$, $p < 0.01$) in the sample at the end-of-treatment post-test. Moderate negative correlations existed between physical functioning and both fatigue ($r = -0.65$, $p < 0.05$) and emotional distress ($r = -0.64$, $p < 0.05$).

Reflecting on the phase I developmental study, we concluded the following. Longitudinal multisite research with patients experiencing a life-threatening diagnosis and onerous treatments is challenging in many respects. Recruiting and retaining subjects over a lengthy study are difficult, especially when the subjects are anxious, distracted, and experiencing multiple side effects of treatment. Patients are eager to receive any potentially beneficial treatment and reluctant to be randomized, so subjects often cross over and try the intervention. Symptomatic patients have difficulty complying with treatment protocols and study demands, and it takes years to complete the research. Lessons learned from the FIRE® I project were incorporated into the subsequent four-year, multisite, randomized clinical trial.

The second multisite study (FIRE® II) was conducted at the University of Pennsylvania, University of Virginia, Yale University, Greater Baltimore Medical Center, and the coordinating center, Johns Hopkins University. Many graduate and undergraduate students, as well as clinical nurses, were involved in the projects. More than 35 nurses received research training in the two projects.

In the FIRE® II project, 120 patients with breast cancer entered and 111 completed the study. Sixty-five percent were receiving radiation therapy and 35% receiving chemotherapy. Only sedentary women who had not been regular exercisers were eligible. Seventy-two percent of those randomized to the exercise group adhered to the program, walking a mean of 29 minutes per day for a mean of four days per week. This compared to a 50% adherence rate for healthy individuals beginning an exercise program (Dishman, 1998).

Crossovers also were a challenge in the results of this study because 40% of the usual-care participants exercised during their cancer treatment, an increase from their baseline sedentary level. Patients with breast cancer are eager to adopt any potentially beneficial self-care behavior, and this motivation presents important clinical implications for inclusion of exercise in standard care of patients with cancer (Demark-Wahnefried, Peterson, McBride, Lipkus, & Clipp, 2000).

Using a novel statistical approach to compare groups when nonadherence is present (Angrist, Imbens, & Rubin, 1996; Frangakis & Rubin, 2002), we identified and compared outcomes for the true adherers to group assignment in the two groups. Results indicated a significant difference between groups on the Piper Fatigue Scale scores. Fatigue levels for the exercise group decreased 0.85 units on the 0–10 point scale, whereas scores for the usual-care participants increased 1.17 for a difference between groups of 2.03 units. This demonstrated a clinically and statistically significant ($p = 0.03$) effect of exercise on fatigue. Emotional distress and difficulty sleeping were significantly lower in exercising subjects. Participants who exercised significantly increased their functional capacity ($p < 0.01$) and activity levels ($p < 0.01$), whereas non-exercisers experienced a reduction in both levels. The strong inverse relationship between fatigue and physical functioning was demonstrated by examining patients whose post-test fatigue scores were in the highest quartile of the entire sample

and those whose fatigue scores were in the lowest quartile (Mock et al., 2002).

Although physical functioning scores for these quartiles were equivalent at baseline pretest, participants with the highest post-test fatigue scores ($\bar{X} = 6.8$ out of a possible 10 on the Piper Fatigue Scale) reported a mean post-test physical functioning score of 66.5 (out of a possible 100) and a mean 12-Minute Walk Test score of 2,941 feet (number of feet walked in 12 minutes), whereas participants with the lowest quartile of post-test fatigue scores reported a mean post-test physical functioning score of 89.6 and a mean 12-Minute Walk Test score of 3,385 feet. This significant decrease ($p < 0.01$) in physical functioning seen in patients with breast cancer with high fatigue levels during treatment represents a considerable loss of ability to perform daily activities that may not be readily reversible when cancer treatment ends.

In summary, across the four studies reported here, a moderate home-based walking exercise program was effective not only in managing fatigue but also in maintaining physical-functioning levels during radiation therapy and chemotherapy in women with breast cancer. Exercisers also reported less emotional distress and less difficulty sleeping. An exercise program that prevents fatigue during cancer treatment may be more effective than interventions to manage high levels of fatigue once they have developed. Based on the results of these studies, we now have embarked on a four-year investigation of the exercise program with additional populations of patients with cancer and expanded physiologic outcomes and adherence measures.

Synthesizing the Evidence

Other teams of researchers have been studying exercise to manage CRF for patients in active cancer treatment. Table 1 contains a review of the published studies of exercise to manage fatigue during active cancer treatment. The investigations have included home-based programs (Schwartz, 2000; Schwartz, Mori, Gao, Nail, & King, 2001) and laboratory studies (Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; MacVicar & Winningham, 1986). The study findings were consistent and unequivocal. All of the studies demonstrated significantly lower levels of fatigue in individuals who exercised when compared to randomized controls, to subjects who did not exercise, or to baseline scores. This was true regardless of the type of exercise intervention, length of exercise program, type of cancer treatment, or cancer diagnosis.

The developing body of knowledge has profound implications for clinical practice in oncology nursing. Research shows that a high level of unmanaged fatigue leads to a significant decrease in physical functioning and increased symptom distress in patients receiving active cancer treatment. These changes inevitably lead to reductions in quality of life. Regular exercise at a moderate level during cancer treatment can help prevent deconditioning, high levels of fatigue, and other symptom distress.

Prescribing moderate-intensity exercise to prevent high levels of fatigue during cancer treatment represents a paradigm shift for healthcare providers whose typical recommendations to decrease activity reflect conventional wisdom (Foley, 2001). However, the results of these studies and other research in this field suggest that a change in clinical practice is indicated to provide evidence-based therapy for CRF. This low-cost, low-

risk walking exercise program easily was taught and monitored by oncology nurses and was well received by participants undergoing active cancer treatment. A diagnosis of cancer is a sentinel life event that frequently initiates a self-evaluation of current lifestyle. This offers a valuable opportunity for healthcare professionals to provide patient education regarding health promotion activities (Demark-Wahnefried et al., 2000). The home-based walking program is widely applicable, feasible, and acceptable to many patients with cancer as indicated by the crossovers in the FIRE[®] studies. Inasmuch as this moderate exercise program is similar to that demonstrated to promote positive health outcomes in all adults (Pate et al., 1995), continuing the program following cancer treatment offers the potential to improve health during survivorship.

Clinical Practice Guidelines

NCCN's clinical practice guidelines for management of CRF (Mock et al., 2003) are based on a synthesis of the evidence to date of effectiveness of interventions to manage fatigue. The guidelines also include expert opinion and identify standards for screening, evaluation, and management of fatigue in patients with cancer in active treatment, post-treatment follow-up, or palliative care.

Exercise and psychosocial support are interventions identified as having category-one evidence of effectiveness (Hadorn, Baker, Hodges, & Hicks, 1996). The guidelines recommend that all patients with cancer be encouraged to maintain an optimum level of physical activity, that patients consider initiation of an exercise program if they are in active treatment or in long-term follow-up, and that healthcare providers consider referrals to physical therapy, physical medicine, and rehabilitation therapy as appropriate for weak or deconditioned patients (Mock et al., 2003). The practice guidelines for fatigue management are being implemented at many cancer centers in the United States, and structured evaluation of the guidelines has begun.

Directions for Future Research: Development of the Science

The evidence supporting exercise programs to manage CRF is developing steadily, but some gaps in knowledge are readily apparent. We should target more diverse populations of patients with cancer, especially in relation to cancer diagnosis, ethnicity, socioeconomic status, age, and type of cancer treatment. Much of the work to date has used samples of well-educated white women with breast cancer. Few exercise studies have focused on fatigue in cancer survivors or in patients with recurrent disease or receiving palliative care, although some evidence exists that increasing activity levels is beneficial in these populations (Porock, Kristjanson, Tinnelly, Duke, & Blight, 2000).

The science would be stronger with more rigorous experimental designs and larger sample sizes; control groups, including healthy control groups; and attentional control groups as appropriate. Use of a select group of valid, reliable, and sensitive instruments to measure fatigue would facilitate comparison of outcomes across studies. More precise and comprehensive descriptions and standardization of exercise interventions would increase internal validity and permit replication of studies to determine reliability of clinical outcomes. Longitudinal designs

with follow-up assessments for a year or more after initiation of exercise would improve the understanding of exercise maintenance and effects of exercise on fatigue during the post-treatment survivorship period.

A fundamental need exists for greater emphasis on theory-based research with a focus on identifying and measuring the mediating mechanisms for fatigue interventions, such as changes in functional capacity or cytokine levels. Use of more objective measures of exercise variables, such as accelerometers and pedometers to measure activity, would increase reliability and validity. The science would be advanced by more comprehensive reporting of study results in regard to attrition rates, refusal rates, rates of adherence to exercise, and number and type of adverse events related to exercise.

We must address the essential issue of adherence before patients will be able to reap optimal benefits from exercise programs. What are the common barriers for patients with cancer, and what are the most effective methods for eliminating barriers? What are the best ways to make exercise programs safe and acceptable and help patients incorporate exercise into their busy lives? What types of exercise are most effective? Are there a minimum and maximum levels of exercise for safety and benefit?

Clinicians need evidence-based guidelines for exercise recommendations for different populations of patients. The NCCN practice guidelines for management of cancer-related fatigue (Mock et al., 2003) should be evaluated carefully in different clinical settings and revised as indicated by research findings.

Finally, further investigation regarding the effects of exercise on outcomes related to fatigue, such as mood state, sleep quality, functional status, and quality of life, is important. Other outcomes that have received little attention but have significant potential to be affected by effects of an exercise program on fatigue are patients' ability to return to work, the use of healthcare resources, symptoms related to hormone

deprivation, immune function during and following cancer treatment, and even survival.

In conclusion, much work has yet to be completed in investigating fully the effects of exercise on fatigue and related outcomes for individuals with cancer. However, the evidence is strong and the potential benefits yet unexplored are enticing.

I would like to extend my appreciation and gratitude to the many individuals with cancer who have participated in fatigue studies and shared their experiences and to the oncology clinical nurses who care for patients and serve as research collaborators. The Distinguished Researcher Award is a most prestigious honor, and it is humbling to have my work so recognized by peers. This work, encompassing more than a decade, would not have been possible without the unique significant support and contributions of numerous people and institutions. I am profoundly grateful for all the help that I have received from so many. Recognition is offered to a few below, but there are many others whom I would wish to thank. Unfortunately, there is not enough space to thank everyone personally, so to those who are not mentioned, I know you understand that your contribution is more than just appreciated.

Thanks to the members of the Oncology Nursing Society (ONS) and to the ONS Foundation that has steadfastly recognized how important research is to oncology nursing. Special thanks to ONS Chief Executive Officer Pearl Moore, RN, MN, FAAN; Gail Mallory, PhD, RN, CNAA, ONS director of research; and, of course, Bristol-Myers Squibb Oncology for its support of the ONS Distinguished Researcher Award. Much gratitude to the esteemed colleagues who not only supported me for this award but who have been mentors and collaborators for many years: Ruth McCorkle, PhD, RN, FAAN, Sharon Krumm, PhD, RN, Barbara Given, PhD, RN, FAAN, and Marcia Grant, DNSc, RN, FAAN. Considerable recognition should go to oncology nurse researchers who also have contributed to the science and have influenced my work: Lillian Nail, PhD, FAAN, Victoria Champion, DNS, FAAN, Betty Ferrell, PhD, FAAN, Marilyn Dodd, PhD, FAAN, Barbara Piper, DNSc, AOCN®, FAAN, and Karen Hassey Dow, PhD, FAAN. Grateful appreciation to Dean Martha Hill, FAAN, who has been my mentor and ardent supporter for 10 years at Johns Hopkins, and to Senior Associate Dean Anne Belcher, PhD, AOCN®, FAAN, who has been an enthusiastic committed oncology nurse leader and supporter for many years as well. Thank you to the invaluable research team members and colleagues on the two ONS FIRE® projects, the early Boston study teams, and the ongoing investigative team at Johns Hopkins University.

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