

**Author Affiliations:** Department of Medicine, Nephrology Associates of South Miami, Miami, Florida.

**Correspondence:** Dr Busse, Department of Medicine, Nephrology Associates of South Miami, 9193 72nd St SW, Ste 200, Miami, FL 33173 (jorgebusse@aol.com).

**Financial Disclosure:** None reported.

1. Winkelmayer WC, Liu J, Chertow GM, Tamura MK. Predialysis nephrology care of older patients approaching end-stage renal disease. *Arch Intern Med.* 2011;171(15):1371-1378.

---

*In reply*

We appreciate the comments of the letter writers, all of whom pointed toward an important, perhaps the most important, goal of earlier nephrology care, which is to slow the progression of chronic kidney disease. Our study<sup>1</sup> was not designed to investigate this question. Furthermore, these data should not deter any clinician from timely referral to a nephrologist. Our study merely pointed toward certain trends in practice patterns that are unproven and even potentially harmful, including earlier initiation of dialysis and injudicious use of erythropoiesis-stimulating agents. These trends may actually have obscured true advances on other care domains that would otherwise have led to measurably improved outcomes. Our article should serve as a wake-up call toward more rigorous testing of any nephrology-driven interventions and focus on practices that are shown to be both safe and effective.

Wolfgang C. Winkelmayer, MD, ScD  
Glenn M. Chertow, MD, MPH  
Manjula Kurella Tamura, MD, MPH

**Author Affiliations:** Division of Nephrology, Stanford University School of Medicine, Palo Alto, California.

**Correspondence:** Dr Winkelmayer, Division of Nephrology, Stanford University School of Medicine, 780 Welch Rd, Ste 106, Palo Alto, CA 94304 (wcw1@stanford.edu).

**Financial Disclosure:** None reported.

1. Winkelmayer WC, Liu J, Chertow GM, Tamura MK. Predialysis nephrology care of older patients approaching end-stage renal disease. *Arch Intern Med.* 2011;171(15):1371-1378.

---

## **Soy Isoflavone Supplementation in Menopausal Women**

**W**e would like to congratulate Levis and colleagues<sup>1</sup> for a well-designed study and thoughtful analysis on the effect of soy isoflavone supplementation on bone loss and menopausal symptoms. However, there are some issues with this trial that warrant further analysis and explanation.

Through 2 years, subject attrition rates were 18.8% with soy isoflavone and 34.1% for placebo ( $P=.008$ ). While the authors state that the baseline characteristics of the subjects who completed the trial were similar to those who withdrew, this explanation is inadequate. Were the reasons for study discontinuation available for comparison? It is unlikely that a discrepancy of this magnitude would occur by chance alone.

In regard to hot flashes, the assessment tool was the Women's Health Questionnaire (WHQ), consisting of 36 items that evaluate the physical and emotional health of middle-aged women.<sup>2</sup> Each question in the WHQ is graded as "yes definitely," "yes sometimes," "no not much," or "no not at all" and then simply dichotomized to "yes" or "no" responses. Next, the responses are scored and reported using 9 different domain scores including somatic symptoms, depressed mood, cognitive difficulties, anxiety/fear, sexual functioning, vasomotor symptoms, sleep problems, menstrual problems, and attraction. Why the domain scores are not presented, but the dichotomized results from an individual question of "I have hot flashes" are reported, is unclear.

This article would be strengthened by addressing some of the aforementioned issues. Assessment of the reasons for discontinuation and a sensitivity analyses may help to address the impact of disproportionate subject attrition on subject outcomes, particularly since intent-to-treat analyses were not used. Also, an analysis of the WHQ domain scores, not of the responses to individual questions, is encouraged.

Larry E. Miller, PhD  
Morgan E. Stewart, PhD

**Author Affiliations:** Sprim USA, San Francisco, California.

**Correspondence:** Dr Miller, Sprim USA, 235 Pine St, Ste 1175, San Francisco, CA 94104 (larry.miller@sprim.com).

**Financial Disclosure:** None reported.

1. Levis S, Strickman-Stein N, Ganjei-Azar P, Xu P, Doerge DR, Krischer J. Soy isoflavones in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. *Arch Intern Med.* 2011;171(15):1363-1369.

2. Wiklund I, Holst J, Karlberg J, et al. A new methodological approach to the evaluation of quality of life in postmenopausal women. *Maturitas.* 1992;14(3):211-224.

---

*In reply*

A total of 66 randomized participants did not complete the study (23 in the soy isoflavone group and 43 in the placebo group).<sup>1</sup> A comparable number of women in each group reported moving out of state, having a sick family member, a new job, or a desire to eat soy products as the reason to discontinue their participation. Although there was a marked difference in the proportion of participants who were no longer interested in participating in the study or were lost to follow-up (16 [19%] in the soy isoflavone group and 30 [34%] in the placebo group), we did not find any objective measures that could explain this difference.

At baseline, responses to all 9 different subscales in the Women's Health Questionnaire were similar between participants in both treatment arms.<sup>2</sup> At 12 months, scores in all domains were comparable between groups, except in the vasomotor symptoms domain where women in the soy isoflavone group had statistically significantly higher scores than women in the placebo group ( $P=.04$ ). At 24 months, scores in all domains were comparable in both groups.

We would like to take this opportunity to specify that the isoflavone content of the tablets is reported as aglycone equivalent, as already stated in the publication describing the study design and baseline characteristics of the participants.<sup>3</sup>

Silvina Levis, MD  
Ping Xu, MPH  
Daniel R. Doerge, PhD  
Jeffrey Krischer, PhD

**Author Affiliations:** Geriatric Research, Education, and Clinical Center, Miami Veterans Affairs Healthcare System, and Department of Medicine, Miller School of Medicine, University of Miami, Miami, Florida (Dr Levis); Department of Pediatrics, University of South Florida, Tampa (Ms Xu and Dr Krischer); and National Center for Toxi-

cological Research, US Food and Drug Administration, Jefferson, Arkansas (Dr Doerge).

**Correspondence:** Dr Levis, Department of Medicine, University of Miami, PO Box 016960 (D-503), Miami, FL 33101 (slevis@med.miami.edu).

**Financial Disclosure:** None reported.

1. Levis S, Strickman-Stein N, Ganjei-Azar P, Xu P, Doerge DR, Krischer J. Soy isoflavones in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. *Arch Intern Med*. 2011;171(15):1363-1369.
2. Hunter MS. The Women's Health Questionnaire: a measure of mid-aged women's perceptions of their emotional and physical health. *Psychol Health*. 1992; 7(1):45-54.
3. Levis S, Strickman-Stein N, Doerge DR, Krischer J. Design and baseline characteristics of the soy phytoestrogens as replacement estrogen (SPARE) study—a clinical trial of the effects of soy isoflavones in menopausal women. *Contemp Clin Trials*. 2010;31(4):293-302.

#### Call for Photographs

The Archives is seeking photographs to be included as fillers in our journal. We believe that our readers may be an excellent source of interesting and thoughtful photographs. If you would like us to consider your photography for publication, we invite you to submit your photograph to our Web-based submission site under the category Images From Our Readers at <http://manuscripts.archinternmed.com>. Please upload photograph submissions in .jpg or .tif format. Hard copy photographs are not acceptable. For more information please e-mail [archinternmed@jama-archives.org](mailto:archinternmed@jama-archives.org).