

# From the EDITOR



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A pioneer in women's health issues and menopause research, in 1967 he established the Groote Schuur Menopause Research Clinic in Cape Town, the world's first such clinic. He was one of the three original founders of the International Menopause Society in 1976, of which he is Honorary Past President, and founded The North American Menopause Society in 1989.

He is the recipient of numerous national and international awards and research grants, and is still an active investigator with multiple grants. Dr. Utian has written over 200 papers related to the reproductive system in women and has authored five books on menopause and its effects on women. He is editor of *Menopause: The Journal of The North American Menopause Society*.

## Is Evidence-Based Medicine a Pipe Dream?

Sir William Osler (1849-1919) is credited with presenting the following observation during a commencement speech at Johns Hopkins Medical School: "As you complete your rigorous studies and graduate today, unfortunately I must inform you that half of what we have taught you is wrong. Even more unfortunately, we cannot tell you which half!"

In the concerted effort to enhance the quality and outcomes of contemporary health care, clinicians, other healthcare providers, medical societies, reimbursers and the rest have all scrambled to develop guidelines, clinical care-paths, protocols, "best practice of medicine" rules, and position statements. One of the most emphasized and current of these methodologies is the practice of so-called "evidence-based medicine."

The question I pose is this: Is evidence-based medicine really wishful thinking—a fanciful attempt at determining clinical practice on an Osler-defined shaky foundation?

### The Gold Standard

Evidence-based medicine attempts to determine the impact of a specific treatment on health outcomes, and it uses the randomized clinical trial as the gold standard—the best evidence available from a single study. In contemporary menopause management, the Women's Health Initiative (WHI) study, for example, has attempted to set itself up as the pinnacle of that achievement. Beyond the randomized controlled trial, structured meta-analyses of evidence from several randomized controlled trials of the same treatment, analyzed by organizations such as the Cochrane Collaboration, have been utilized to evaluate and rank the best current knowledge.

But it is not that easy! Despite our best  
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efforts, there are multiple flaws in our attempts to develop these evidence-based recommendations for health care. It must be asked why observational and randomized controlled studies so often come up with different answers.<sup>1</sup> The reasons can be manifold. For instance, randomized controlled trials apply to very carefully selected populations that have been rigorously screened for predetermined inclusion and exclusion criteria. These populations are invariably different from the general population, or the population most frequently presenting to the clinical practitioner with a certain problem. On the other hand, observational studies often include the appropriate population, but are then themselves so plagued by potential conflicting and confounding factors that the final observation may be quite imprecise.

The important step of translation from evidence-based recommendations to clinical practice is also imperfect.<sup>2</sup> This is not simplified by the notorious lack of reliability between a surrogate marker and a real disease outcome.<sup>3</sup> Randomized controlled trials utilizing surrogate markers are easier, quicker and cheaper to conduct than the long-term studies with larger populations that are necessary to determine outcomes. This can be particularly difficult when the prevalence of a problem is infrequent in the population being studied. Certainly, every effort needs to be made to make observational studies as credible as randomized controlled trials. Recommendations to achieve this goal exist,<sup>4</sup> but the purpose of this editorial is not to expand further on this issue.

**The Case Doesn't Fit**

The dilemma within organized medicine appears to be that in the absence of the perfect study (which, by definition, is virtually impossible to achieve), we attempt instead to try to “use evidence when the case doesn't fit.”<sup>5</sup>

Pertinent observations were made by a group of Japanese colleagues<sup>6</sup> who attempted to explain a waning interest in the concept of evidence-based medicine by clinicians. They

explained: “The main reason for evidence-based medicine not having been widely accepted in Japan seems to stem from an image problem. Evidence-based medicine was mainly promoted by public-health researchers and epidemiologists who had little knowledge of the clinical field, and only the techniques for literature searching and evaluation were emphasized. This concentration on theory resulted in criticism from clinicians that researchers were not involved with patients and were disregarding the value of experience and skill. However, the principle of evidence-

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based medicine is selection and execution of the optimum treatment plan based on scientific evidence, *and experience of clinicians is an important factor.*<sup>6</sup> (The emphasis is mine).

Suggestions have been made for a distinction to be drawn between *effectiveness* trials, which emulate clinical practice conditions, and *efficacy* trials, which feature well-defined study populations and highly specified interventions. Review of the literature reveals a paucity of the former and over-reliance on the latter.<sup>7</sup>

Other questions have also been raised about evidence-based medicine and quality clinical guidelines. For instance, guidelines need to be up to date, yet there is no published method for assessing whether an existing guideline is still valid. One evaluation found that three-quarters of the guidelines produced by the Agency for Healthcare Policy and Research were out of date, and recommended that guidelines be reassessed for validity every 3 years.<sup>8</sup>

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women regardless of their BMD values.

Our knowledge about urogenital health has greatly expanded in recent years. While we used to think that HT improved incontinence, we know now that hormones aggravate the condition. Recurrent urinary tract infections,



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however, do respond favorably to ET. I'd recommend a vaginal estrogen preparation; choices include estrogen creams, tablets and rings. Patient preference and cost both enter into the decision about what to recommend. If creams are used, it's important to remember that women often use more than is necessary.

I advise women to try to reduce the amount and frequency of application to the minimum amount that provides symptom relief.

"Sexuality problems" cover a lot of territory, so it would be important to take a very careful history to understand exactly what is troubling the patient. The primary sexual problem relieved with ET is vaginal dryness. If over-the-counter vaginal lubricants and moisturizers were not effective, I would prescribe vaginal estrogen.

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#### References

1. Grady D, Ettinger B, Tosteson ANA, et al. Predictors of difficulty when discontinuing postmenopausal hormone therapy. *Obstet Gynecol* 2003;102:1233-39.
2. Ockene JK, Barad DH, Cochrane BB, et al. Symptom experience after discontinuing use of estrogen plus progestin. *JAMA* 2005; 294:183-93.
3. Gordon S, Walsh BW, Ciaccia AV, et al. Transition from estrogen-progestin to raloxifene in postmenopausal women: effect on vasomotor symptoms. *Obstet Gynecol* 2004;103:267-73.
4. Haimov-Kochman R, Barak-Glantz E, Arbel R, et al. Gradual discontinuation of hormone therapy does not prevent the reappearance of climacteric symptoms: a randomized prospective study. *Menopause* 2006;13:370-76.
5. Grady D. A 60-year-old woman trying to discontinue hormone replacement therapy. *JAMA* 2002; 287:2130-37.
6. Grady D. Helping women stop postmenopausal hormone therapy [editorial]. *Menopause* 2006;13:323-24.

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#### An Excellent Objective

Our objective is excellent—to deliver the best and most current care to all patients. The solution remains problematic, but not insurmountable, provided we do the best we can with the most pertinent current knowledge. But if we are going to change practice and implement evidence, the hard work is to involve the best people, summarize the state of the science, recognize difficulties in achieving change, develop strategies and tactics for achieving change and, most essentially, create markers for measuring the efficacy of the outcome.

In getting to that point we certainly need to avoid *total* reliance on "data" or use of outdated methods. It is hoped that in this effort we can also narrow the gap between medical students' knowledge at the time of graduation and the best currently available information.

Where does this leave us with respect to pharmacotherapy for menopausal women post-WHI? I will attempt to address that issue in the near future. And what about my original question: Is evidence-based medicine a pipe dream? It's your call!

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#### References

1. Lawlor DA, Davey Smith GD, Kundu K, et al. Those confounded vitamins: what can we learn from the differences between observational versus randomised trial evidence? *Lancet* 2004;363:1724-27.
2. Grol R, Grimshaw, J. From best evidence to best practice: effective implementation of change in patient care. *Lancet* 2003;362:1225-30.
3. Grimes DA, Schulz KF. Surrogate end points in clinical research: hazardous to your health. *Obstet Gynecol* 2005;105:1114-18.
4. Vandembroucke JP. When are observational studies as credible as randomized trials? *Lancet* 2004;363:1728-31.
5. Flood AB. Making evidence-based decisions in medicine: (or more importantly) using evidence when the case doesn't quite fit. *Women's Health Issues* 2004;14:3-6.
6. Yokota T, Kojima S, Yamouchi H, et al. Evidence-based medicine in Japan. *Lancet* 2005;366:122.
7. Collins J. Which randomized controlled trials are relevant to clinical practice? *Obstet Gynecol* 2005;106:216-17.
8. Shekelle PG, Ortiz E, Rhodes S, et al. Validity of the ageing for healthcare research and quality clinical practice guidelines. How quickly do guidelines become outdated? *JAMA* 2001;286:1461-67.