Hormone relacement therapy

The arrogance of preventive medicine

David L. Sackett

ß See related articles pages 357, 361, 377 and 387

Preventive medicine displays all 3 elements of arrogance. First, it is *aggressively assertive*, pursuing symptomless individuals and telling them what they must do to remain healthy. Occasionally invoking the force of law (immunizations, seat belts), it prescribes and proscribes for both individual patients and the general citizenry of every age and stage. Second, preventive medicine is *presumptuous*, confident that the interventions it espouses will, on average, do more good than harm to those who accept and adhere to them. Finally, preventive medicine is *overbearing*, attacking those who question the value of its recommendations.

Although one could level these same accusations against the "curative" medicine delivered to symptomatic patients who seek health care, the 2 disciplines are absolutely and fundamentally different in their obligations and implied promises to the individuals whose lives they modify. When patients sought me out for help with their established, symptomatic diseases, I promised them only to do my best and never guaranteed that my interventions would make them better. Although many of my interventions had been validated in randomized trials,[1] the need to intervene in rapidly advancing, life-threatening disorders forced me to use treatments justified only on the basis of past experience, expert advice, and the first principles of physiology and pharmacology.

But surely the fundamental promise we make when we actively solicit individuals and exhort them to accept preventive interventions must be that, on average, they will be the better for it.[2] Accordingly, the *presumption* that justifies the *aggressive assertiveness* with which we go after the unsuspecting healthy must be based on the highest level of randomized evidence that our preventive manoeuvre will, in fact, do more good than harm. Without evidence from positive randomized trials (and, better still, systematic reviews of randomized trials) we cannot justify soliciting the well to accept any personal health intervention. There are simply too many examples of the disastrous inadequacy of lesser evidence as a basis for individual interventions among the well: supplemental oxygen for healthy premies (causing retrolental fibroplasia), healthy babies sleeping face down (causing SIDS), thymic irradiation in healthy children, and the list goes on.

To this sad list we must now add estrogen plus progestin when given to healthy postmenopausal women under the presumption that they will be protected against cardiovascular disease. The Women's Health Initiative randomized controlled trial, as reported in the July 17 issue of *JAMA*,[3] was stopped when it became clear that the participating women's risk of cardiovascular disease went up, not down, on active therapy. This damage began to develop soon after randomization, and after a mean follow-up of 5.2 years the trial was stopped for harm. In human terms, the 8506 women treated with estrogen plus progestin had about 40 more coronary events, 40 more strokes, 80 more episodes of venous thromboembolism and 40 more invasive breast cancers than the 8102 women assigned to placebo. Given the frequency with which this treatment is prescribed to postmenopausal women worldwide, hundreds of thousands of healthy women have been harmed.

As with other disasters, there are heroes and villains in this piece. First place among the heroes is shared by each of the 16 608 women who agreed to collaborate in the estrogen-plus-progestin portion of the Women's Health Initiative randomized trial. Second come the investigators, clinical collaborators, and members of the data safety and monitoring board, followed closely by the reviewers and members of the US National Heart, Lung, and Blood Institute who saw to it that a rigorous, adequately funded trial was designed, executed and stopped when the answer to the study question became clear (Canadian Institutes of Health Research, please note).

What about the villains? Who is to blame for the widespread application of this and the other harmful "preventive" interventions that cause disability and untimely death? I suggest that we not waste time blaming the manufacturers of "preventive" drugs and devices, for they are pursuing profit, not health, and anyone who looks to their print advertisements and television spots for health guidance arguably deserves whatever harm comes to them (according to the *New York Times*[4] the company that supplied the study drug has already sent 500 000 "Dear Doctor" letters stressing the symptomatic benefits of their combination). Nor, I suggest, should we blame "demanding" patients who insist on receiving some bogus preventive intervention of unknown efficacy, for they are simply doing their best to improve their lives in an "evidence-vacuum."

I place the blame directly on the medical "experts" who, to gain private profit (from their industry affiliations), to

satisfy a narcissistic need for public acclaim or in a misguided attempt to do good, advocate "preventive" manoeuvres that have never been validated in rigorous randomized trials. Not only do they abuse their positions by advocating unproven "preventives," they also stifle dissent. Others, who should know better than to promote "preventive" manoeuvres without clinical trials evidence, are simply wrongheaded. When a 1997 systematic review of 23 trials of postmenopausal hormone therapy concluded that this treatment substantially increased the risk of cardiovascular disease,[5] the attack on its results included a public announcement from a prominent editorialist: "For one, I shall continue to tell my patients that hormone replacement therapy is likely to help prevent coronary disease."[6]

Experts refuse to learn from history until they make it themselves, and the price for their arrogance is paid by the innocent. Preventive medicine is too important to be led by them.[7]

Dr. Sackett is with the Trout Research & Education Centre at Irish Lake, Markdale, Ont.

Competing interests: None declared.

Acknowledgements: I thank Iain Chalmers, Brian Haynes, Klim McPherson, Andrew Oxman and William Silverman for their comments on the initial draft of this commentary.

References

1. Ellis J, Mulligan I, Rowe J, Sackett DL. Inpatient general medicine is evidence based. *Lancet* 1995;346:407-10.
2. Sackett DL, Holland WW. Controversy in the detection of disease. *Lancet* 1975;2:357-9.
3. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288(3):321-33.
4. Petersen M. Company sends letter to retain hormone sales. *New York Times* 2002 Jul 11. Sect A:21.
5. Hemminki E, McPherson K. Impact of postmenopausal hormone therapy on cardiovascular events and cancer: pooled data from clinical trials. *BMJ* 1997; 315:149-53.
6. Naylor CD. Meta-analysis and the meta-epidemiology of clinical research. *BMJ* 1997;315:617-9.
7. McPherson K. For and against: public health does not need to be led by doctors. For. *BMJ* 2001;322:1593-4.

Correspondence to: *Dr. David L. Sackett, Trout Research & Education Centre at Irish Lake, RR1, Markdale ON N0C 1H0; fax 519 986-9951; sackett@bmts.com*