discouraging children from smoking until randomized trials in which large numbers of teenagers are assigned to smoking or nonsmoking groups showing that those who smoke experience greater long-term mortality rates. To extend this train of thought even further, we should presumably not ban drunk driving until randomized trials have demonstrated that it is dangerous.

Many of the preventive medical manoeuvres currently in use will never be supported by data from randomized trials. In the 3 examples outlined above, randomized trials would be unethical even if they were possible. The accumulated evidence from nonrandomized studies for the benefits of seat belts, the harmful effects of smoking and the dangers of drunk driving is so vast that further study would be in no one's best interest (except perhaps the tobacco industry).

The wearing of seat belts and the avoidance of smoking and drunk driving are measures that cannot conceivably be harmful. The nature of the evidence we require before advocating a preventive medical intervention depends on the nature of the intervention. A pharmacological intervention is vastly different from a lifestyle intervention, and the quality of the evidence we require may also be vastly different.

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Reference

1. Sackett DL. The arrogance of preventive medicine [editorial]. *CMAJ* 2002;167(4):363-4.

[The author responds:]

To the extent that Gabe Slowey and David Rapoport hold globally negative views on personal preventive measures and because Nicholas Forbath assigns me a nihilistic view of them, I disagree with all 3 of these correspondents.

During my clinical and health policy years I advocated and applied a wide array of personal preventive manoeuvres because I was dedicated, not to global conclusions about the value of preventive medicine, but to methods for generating level 1 evidence[1] as to whether its individual elements did more good than harm (by level 1 evidence I mean either systematic reviews of randomized trials or "all-or-none" evidence by which, for a universally fatal condition, an intervention was followed by survival or a less frequent adverse outcome was completely eliminated by the intervention). On that basis I advocated and practised the vigorous detection and treatment of certain levels of symptomless elevated blood pressure,[2] never ordered testing of prostate-specific antigen in a symptomless man, and changed my practice and teaching about treating hypercholesterolemia from a negative to a positive stance when the accumulating evidence from randomized trials of statin drugs showed that they did more good than harm.

In response to Mark Taylor, because the absence of proof is not the proof of absence, folks like me don't advocate abandoning established practices just because they haven't been tested in randomized controlled trials. Moreover, seat belt use satisfied the second criterion for level 1 evidence as soon as users began to survive auto crashes that were previously uniformly fatal. Importantly, however, when this same criterion is applied to another auto safety tradition, school-based drivers' education, the level 1 evidence shows that this intervention doesn't create better drivers, only younger ones, and its net effect appears to be harmful.[3]

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References

1. Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence-based medicine*. 2nd ed. Edinburgh: Churchill Livingstone; 2000. p. 173-7.
2. Sackett DL. The detection and treatment of hypertension in Canada: changing recommendations from recent research. *Clin Invest Med* 1978;1(3-4):171-4.
3. Roberts I, Kwan I, and Cochrane Injuries Group Driver Education Reviewers. School based driver education for the prevention of traffic crashes [Cochrane review]. In: The Cochrane Library; Issue 3, 2002. Oxford: Update Software.

Weighing the risks and benefits of tamoxifen

I read with interest Eric Wooltorton's article on tamoxifen for breast cancer prevention,[1] which directly followed a summary of the Women's Health Initiative (WHI) study on hormone replacement therapy (HRT).[2] The latter study was stopped early because the prespecified upper boundary for risk of breast cancer in the HRT group had been exceeded. To paraphrase Table 1 in Wooltorton's article,[1] it appears that, per 10 000 woman-years, tamoxifen was associated with 15 more cases of endometrial adenocarcinoma, 2 more cases of uterine sarcoma, 4 more cases of stroke and 5 more cases of pulmonary embolism (relative to placebo), for a total of 26 additional events or a 1.3% absolute risk increase over the 5-year period of the National Surgical Adjuvant Breast and Bowel Project (NSABBP). Tamoxifen was associated with fewer cardiovascular problems than reported for HRT in the WHI study,[2] but HRT did not cause any increase in endometrial cancer.

In the NSABP, the relative risk reduction for breast cancer among high-risk women who received tamoxifen was 49%.[3] Perhaps the Gail model for identifying women at high risk of breast cancer[4] could be modified to incorporate the known risks associated with tamoxifen, adjusted according to the patient's clinical characteristics, such as age, ethnic background and smoking status, to arrive at a net risk-to-benefit ratio. Without such a tool, it is difficult to get an accurate estimate of risk in clinical practice. A workshop has been held to quantify those risks,[4] and the next step would be to incorporate the findings into a tool for hand-held or personal computers. A woman's decision to take tamoxifen would still depend on the values she places on different outcomes, such as stroke or breast

cancer, but such a tool might help to estimate the risk–benefit ratio for her individual case.

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References
1. Wooltorton E. Tamoxifen for breast cancer prevention: safety warning. *CMAJ* 2002;167(4):378-9.
2. Farquhar D. Postmenopausal hormone replacement therapy for chronic disease prevention: results from the Women's Health Initiative trial. *CMAJ* 2002;167(4):377-8.
3. Fisher B, Costantino JP, Wickerham DL, Redmond CK, Kavanah M, Cronin WM, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. *J Natl Cancer Inst* 1998;90:1371-88.
4. Gail MH, Costantino JP, Bryant J, Croyle R, Freedman L, Helzlsouer K, et al. Weighing the risks and benefits of tamoxifen treatment for preventing breast cancer. *J Natl Cancer Inst* 1999;91:1829-46.

[Mitchell Gail responds:]

My colleagues and I have shown how to compare the risks and benefits of tamoxifen by combining 3 ingredients:[1] the absolute risks of breast cancer and other endpoints, such as stroke, in the absence of tamoxifen; the effects of tamoxifen on these background risks (from data in Fisher and associates[2]); and weights for comparing the various outcomes. We used weights of 1.0 for life-threatening outcomes (invasive breast cancer, stroke, pulmonary embolism, hip fracture and endometrial cancer), 0.5 for severe outcomes (in situ breast cancer, deep vein thrombosis) and 0 for other events. We pointed out, however, that a woman's own preferred weights could be used. Tables 10 to 12 in Gail and colleagues[1] indicate that the risks of tamoxifen outweigh the benefits in many women, especially older women in whom the risks from stroke and endometrial cancer are appreciable. Indeed, Rockhill and collaborators[3] estimated that only 2.3% of women in the Nurses' Health Study would experience a net benefit, according to Tables 10 and 11 in our study.[1] These observations reinforce the warnings outlined by Eric Wooltorton.[4]

Greiver suggests that the findings of Gail and colleagues[1] be incorporated into a computer-based tool. Until such a program, properly validated, is available, Tables 10 to 12 in that article provide useful indications of net risk or benefit.[1]

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References
1. Gail MH, Costantino JP, Bryant J, Croyle R, Freedman L, Helzlsouer K, et al. Weighing the risks and benefits of tamoxifen treatment for preventing breast cancer. *J Natl Cancer Inst* 1999;91:1829-46.
2. Fisher B, Costantino JP, Wickerham DL, Redmond CK, Kavanah M, Cronin WM, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. *J Natl Cancer Inst* 1998;90:1371-88.
3. Rockhill B, Spiegelman D, Byrne C, Hunter DJ, Colditz GA. Validation of the Gail et al. model of breast cancer risk prediction and implications for chemoprevention. *J Natl Cancer Inst* 2001;93:358-66.
4. Wooltorton E. Tamoxifen for breast cancer prevention: safety warning. *CMAJ* 2002;167(4):378-9.

Getting the word out

In recent correspondence, Greg Allen[1] and Eric Wooltorton[2] criticized the method that Health Canada used to communicate risks associated with droperidol, in particular the choice of addressees for the drug safety information letter.[3] Health Canada sent its letter[3] to chiefs of medical staff of all Canadian hospitals, otolaryngologists, retail pharmacies and other health associations. The letter included a request (printed in bold) that it be distributed to health care professionals in each institution, which was an attempt to ensure that the letter would reach all health care professionals who might be prescribing or dispensing injectable droperidol.

Health care professionals have a shared responsibility to acquire, communicate and incorporate new information to enable informed decision-making by patients, and these aspects of professional practice form part of provincial and territorial standards of professional practice. Nonetheless, concerns about the failure of health care professionals to read "Dear Healthcare Professional" letters and to incorporate new drug safety information into practice have been raised previously.[4]

Health Canada's Marketed Health Products Directorate agrees that physicians and other health care professionals must learn of any new drug safety information quickly. Recommendations arising from a workshop on this topic are posted at Health Canada's Web site.[5] In addition, several strategies such as toll-free telephone and fax lines for reporting of adverse reactions and an electronic mailing list have been implemented to facilitate communication of product-related risks between Health Canada and health care providers. (Readers may subscribe to various advisory mailing lists at www.hc-sc.gc.ca/hpb-dgps/therapeut/htmleng/adr.html).

Health Canada hopes that strengthening communication with health care professionals will stimulate spontaneous reporting of adverse reactions. Partnerships with stakeholders such as consumers, health care professionals, academia, industry and government are also important, as the responsibility for communicating drug safety information and incorporating new information into practice crosses jurisdictional lines.

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References
1. Allen G. Low-dose droperidol [letter]. *CMAJ* 2002;167(5):452.
2. Wooltorton E. Low-dose droperidol [letter]. *CMAJ* 2002;167(5):452.
3. Peterson RG. Cardiovascular toxicity with injectable droperidol. Ottawa: Health Canada, Therapeutic Products Directorate; 2002 Feb 12. Available: www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/advisory/tpd/droperidol_e.html (accessed 2002 Nov 8).
4. Jones JK, Fife D, Curkendall S, Goehring E Jr, Guo JJ, Shannon M. Coprescribing and codispensing of cisapride and contraindicated drugs. *JAMA* 2001;286;1607-9.
5. Summary report. Communicating Drug Safety