Misplaced allegations

As chairs of the Clinical Research Ethics Board (REB) at the University of British Columbia (UBC), we felt we should respond to the allegations made in *CMAJ*'s Holiday Review by Ian Scott and Cheryl Wilson,[1] both of UBC. Although there does appear to be a correlation between forest industry activity and the paper demands of research ethics boards, we suspect that this is more association than causation.

Nonetheless, we were concerned about the issue and conducted some further research. Ethics approval was not sought, because we could not afford to make the 20 copies required by our own REB. What we found is far more disturbing than the aforementioned association. Table 1 clearly shows what appears to be a strong association between the number of copies of ethics applications required by REBs and the number of Conservative Party of Canada plus Progressive Conservative (PC) members of Parliament from each province (Table 1). We are not sure how this factor has influenced the number of copies required by REBs, but we plan to find out. We also believe that the reason the PCs are still listed (at the time of writing, in mid-January 2004) as a separate entity in the House of Commons party standings,[2] despite recent reports of a merger with the Canadian Alliance, is to obscure this association.

Hence, for the foreseeable future, we plan to approve only research proposals that look into this issue. To expedite the process, we will require only 1 copy of any original research proposal that examines this disturbing trend. However, if the application comes from the Department of Family Practice at UBC, 40 copies will be required.

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Chair
Clinical Research Ethics Board
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Vancouver, BC
(Not on behalf of any of the other members of the UBC Clinical Research Ethics Board.)

References

1. Scott I, Wilson C. Understanding the number of copies of ethics applications required by faculties of medicine. *CMAJ* 2003;169(12):1297.
2. Party standings [online]. Ottawa: House of Commons; 2003. Available: www.parl.gc.ca/information/about/process/house/partystandings/standings-e.htm (accessed 2004 Jan 19).

Competing interests: Both Dr. McCormack and Dr. Loewen receive an honorarium for the work they do on the UBC Clinical Research Ethics Board.

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Table 1: Comparison by province of number of copies of ethics applications required by research ethics boards (REBs) and numbers of Conservative Party of Canada (CPC) + Progressive Conservative (PC) members of Parliament

Province	No. of copies required by REBs in each faculty of medicine	No. of CPC + PC members of Parliament*
British Columbia	20	25
Alberta	17	24
Manitoba	15	5
Nova Scotia	14	3
Ontario	13	3
Quebec	13	1
Newfoundland	11	3
Saskatchewan†	12	9

*According to data on party affiliations in the 37th legislature, as of Jan. 19, 2004.[2]
†Data from Saskatchewan were excluded from the analysis because that province refuses to participate in daylight savings time.

[One of the authors responds:]

We appreciate the desire of James McCormack and Peter Loewen to further understand the cause of the disparate number of copies of research applications required for submission to research ethics boards at different universities, as reported in our article.[1]

However, we were disappointed to learn that the Clinical REB at UBC has arbitrarily singled out our group and henceforth will be demanding 40 copies of any applications from the Department of Family Practice. In response, we plan to foster collaboration by seeking formal cross-appointments to the Faculty of Pharmaceutical Sciences for all members of our department, which we hope will lead to this unfair ruling being overturned. We wish to assure readers that the fact that members of the Faculty of Pharmaceutical Sciences get to personally experiment with all the great new drugs has nothing to do with our attempt to join this group.

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Reference

1. Scott I, Wilson C. Understanding the number of copies of ethics applications required by faculties of medicine. *CMAJ* 2003;169(12):1297.

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Sample size and study interpretation

Max Pittler and associates[1] report the results of a randomized double-blind crossover trial of the effectiveness of artichoke extract in preventing alcohol-induced hangovers. However, their sample size of 15 is too small. Even though the study had a crossover design, the standard deviations (SDs)

are too large for the results to have statistical significance (e.g., mean systolic blood pressure of 124.3 with SD of 17.7 mm Hg and mean diastolic blood pressure of 75.4 with SD of 10.9 mm Hg at baseline). Furthermore, the range of blood pressure measurements (as derived from the means and standard deviations presented in the article) indicate that the volunteers were not all that healthy.

Another problem relates to the study's power. Pittler and associates[1] state in the Methods section that there would be a power of 80% with 16 participants, but it is not clear if they recalculated the power on the basis of the 15 participants who actually completed the study. Also, the Methods section does not state the critical estimated scores of the 2 groups. The authors do admit a limitation relating to a possible type II error because of the small sample size. If this type II error was large, the authors are not justified in saying that "artichoke extract does not prevent the signs and symptoms of alcohol-induced hangover over and above placebo."

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Reference

1. Pittler MH, White AR, Stevinson C, Ernst E. Effectiveness of artichoke extract in preventing alcohol-induced hangovers: a randomized controlled trial. *CMAJ* 2003;169(12):1269-73.

Competing interests: None declared.

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[Two of the authors respond:]

We welcome the opportunity to restate important limitations of our study, which we discuss in our paper.[1] Frank Leung's main concern relates to sample size and its implications. The sample size of 16 for a power of 80% was calculated using an estimated standard deviation of 2.0 and an estimated mean difference of 1.5 cm on a 10-cm visual analogue scale. This mean difference was considered adequate in the expected and confirmed sample of moderately hungover individuals.[2] Because of the small sample size and the measurement variation, which proved larger than expected, we discuss in our paper the degree of uncertainty relating to the data and state that this might have obscured a possible true effect. Acknowledging the study's limitations and in the absence of any trend in favour of artichoke extract, we stand by our conclusion that "our findings do not suggest that artichoke extract is effective in preventing alcohol-induced hangover."

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References

1. Pittler MH, White AR, Stevinson C, Ernst E. Effectiveness of artichoke extract in preventing alcohol-induced hangovers: a randomized controlled trial. *CMAJ* 2003;169(12):1269-73.
2. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: What is moderate pain in millimeters? *Pain* 1997;72:95-7.

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Taking our vitamins

In Eric Wooltorton's article on vitamin and mineral supplements,[1] a footnote to Table 1 states that vitamin K has an anticoagulant effect. In fact, vitamin K promotes healthy coagulation, because it is a cofactor in a carboxylation reaction that is essential for the clotting process.[2] [A correction on this point was published previously.[3] — Editor.]

Vitamin K was excluded from this table because it "is not available in Canadian multivitamin preparations."[1] However, vitamin K is included in some multivitamins available in the United States. Given the popularity of cross-border shopping and the availability of products through the Internet, it is possible that many patients of *CMAJ* readers, or even the journal's readers themselves, are consuming vitamin K in supplement form.

Despite several trials evaluating vitamin K (vitamin K_1 [phylloquinone] and vitamin K_2 [menatetrenone]) for its effects on bone quality and density[4-6] and its usefulness in other contexts,[6] the toxic effects of even pharmaceutical doses of these 2 naturally occurring forms of vitamin K have not been identified.[8] In addition, at least one study, which evaluated the effects of large doses of vitamin K_2 (45 mg of menaquinone-4) on hemostatic activation, found no thrombotic tendency at high doses.[8]

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References

1. Wooltorton E. Too much of a good thing? Toxic effects of vitamin and mineral supplements. *CMAJ* 2003;169(1):47-8.
2. Vermeer C, Schurgers LJ. A comprehensive review of vitamin K and vitamin K antagonists. *Hematol Oncol Clin North Am* 2000;14(2):339-52.
3. Corrections. *CMAJ* 2003;169(4):283.
4. Iwamoto I, Kosha S, Noguchi S, Murakami M, Fujino T, Douchi T, et al. A longitudinal study of the effect of vitamin K_2 on bone mineral density in postmenopausal women: a comparative study with vitamin D_3 and estrogen–progestin therapy. *Maturitas* 1999;31(2):161-4.
5. Yonemura K, Kimura M, Miyaji T, Hishida A. Short-term effect of vitamin K administration on prednisolone-induced loss of bone mineral density in patients with chronic glomerulonephritis. *Calcif Tissue Int* 2000;66(2):123-8.
6. Somekawa Y, Chigughi M, Harada M, Ishibashi T. Use of vitamin K_2 (menatetrenone) and 1,25-dihydroxyvitamin D_3 in the prevention of bone loss induced by Leuprolide. *J Clin Endocrinol Metab* 1999;84(8):2700-4.
7. Takami A, Asakura H, Nakao S. Menatetrenone, a vitamin K_2 analog, ameliorates cytopenia in patients with refractory anemia of myelodysplastic syndrome. *Ann Hematol* 2002;81(1):16-9.
8. Fairfield KM, Fletcher RH. Vitamins for chronic disease prevention in adults. *JAMA* 2002;287(23):3116-26.
9. Asakura H, Myou S, Ontachi Y, Mizutani T, Kato M, Saito M, et al. Vitamin K administration to elderly patients with osteoporosis induces no hemostatic activation, even in those with suspected vitamin K deficiency. *Osteoporos Int* 2001; 12(12):996-1000.

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I commend Eric Wooltorton[1] for alerting Canadian physicians to the potential of health risks with excessive consumption of some vitamins and minerals. However, the recommended intakes listed in Table 1 of that article do not reflect dietary reference intake (DRI) values,[2] which should be used as the dietary standards for Canadians. Furthermore, there is no mention of