

being younger and having fewer traditional coronary risk factors.

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Placebo tribulations

Charles Weijer's¹ recent indictment of the Canadian research review process is unsupported. On the basis of the meagre information given, it is impossible to determine whether the protocol in question violates the *Tri-Council Policy Statement (TCPS)*.² That guideline enunciates a strong presumption against placebo use when "standard therapies" are available. It does not state an exceptionless rule, and, indeed, the policy discusses some of the exceptions. Demonstrating that the protocol violates the TCPS statement is crucial to Weijer's accusation that Canadian researchers, research ethics boards (REBs), universities and federal funding agencies are shirking their responsibilities.

Health Canada cannot dictate decisions on particular cases to REBs, but nothing is wrong with it promulgating general policy on research ethics. The passage Weijer quotes contains nothing but statements of general principles. Not a single one of them is objectionable, idiosyncratic or even at odds with the TCPS statement. I know of no national or international guideline that specifies that the judicious use of placebo controls in clinical trials is un-

ethical. (There is, of course, great controversy over what counts as a judicious use.) Benjamin Freedman agreed with the TCPS that REBs should reject trials with inconclusive designs.³

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In his commentary, Charles Weijer imposes interesting and challenging questions regarding placebo-controlled clinical drug trials.¹ However, it is unfortunate that he chooses to make negative and unsubstantiated assertions about for-profit research ethics boards (REBs), lumping them all together.

He states that the failures of university teaching hospital REBs are attributed to "lack of clarity ... regarding the need for adherence to the *Tri-Council Policy Statement*" while for-profit REBs are assailed because of "obvious conflicts of interest doing ethics reviews." Why is the latter an "obvious" conflict of interest? Getting paid for work does not necessarily compromise judgement.

We would suggest that the members of most for-profit REBs are guided, or should be, by the same ethical standards as are the members of university teaching hospital REBs. For example, the members of the latter are subject to the same conflicts of interest because university teaching hospitals receive "overhead" funds whenever a study is done at that institution. Moreover, the voting members of university teaching hospital REBs regularly review studies submitted by their colleagues and thus potentially have more conflicts of interest than do the members of for-profit REBs. Our institutional review board

(IRB) is totally independent, without a research arm, and is well positioned to pass judgement on the merits of a particular study. We are completely independent of outside pressures and able to consider the safety of the patient foremost, providing the study has scientific merit.

We would like to point out that our IRB rejected an unethical study involving an angiotensin-converting enzyme (ACE) inhibitor versus an angiotensin-II blocker versus placebo in diabetics with proteinuria, although 7 Canadian university teaching hospital boards approved it. Only 1 university teaching hospital REB rejected it. What's even more worrisome is that this particular study had been running for more than 2 years before it was sent to us, and each of the approving university teaching hospital REBs had extended the approval. None shut it down despite incontrovertible evidence of the ACE inhibitor's nephroprotective effect during the continuing review period.

We also restricted approval of a study with a new thrombolytic agent to 3 months due to safety concerns, although a university teaching hospital REB approved it for 1 year. Why did we restrict it? Because we knew of an exsanguinating hemorrhage with the study compound that occurred at the hospital REB's sister hospital. The bleeding could not be stopped, and the case was discussed during the university's cardiology department rounds. Despite this occurrence, the REB apparently did not review their approval or require changes to the consent form, despite information from their own investigators that the study drug might cause life-threatening bleeding.

How do we know about the hospital REBs' decisions? Because in each instance we were told by the sponsor or the principal coordinating investigator when we refused to approve these studies that "you are the only one to refuse!"

In several other cases, we have rejected unethical studies that other REBs have not (see the complete letter at www.cmaj.ca).

Weijer should also consider the well-publicized ethical problems at presti-