reply to 2 e-forms sent to the company.

It may be reasonable for a software distributor to prevent a user from downloading a book from one CD-ROM to several different handheld units. However, these programs, although sold on cheap media, cost the user more than the equivalent paper-based product, and the latter can be used for years without the need to purchase a new licence whenever one upgrades one's reading glasses.

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**Reference**

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As a busy clinician and regular user of a personal digital assistant (PDA), I was appalled to read, in Feisal Adatia and Philippe Bedard's article on handheld software,[1] that so many of my colleagues would choose ePocrates software as their drug reference of choice. It's bad enough that some software packages send advertisements along with the data, but what could possibly induce me to use "spyware" that tracks everything I look up?

Adatia and Bedard even remark that this software can track other Web sites visited by users of ePocrates. In other words, doctors are willingly giving marketers a picture of their prescribing habits and leisure activities every time they use this "free" program!

PDA users should know that a PDA version of another widely used print reference, the Tarascon Pocket Pharmacopoeia, has been available for beta-testing for nearly a year, free of charge (see www.tarasconpublishing.com/store/palm.asp). The Tarascon product has no spyware features and includes Canadian trade names, and during this beta-testing period the company is looking for input from users to make the program even better. Eventually there will be a nominal annual or monthly fee for updates — well worth it for the data and your privacy.

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**[The authors respond:]**

Software manufacturers use various means to protect their products from piracy, including registration codes. If problems are encountered when attempting to install software on a new device, the user should first try re-installing the software. If this fails, he or she can try re-installing the software using the same "hotsync" name as was used for the original handheld device. If the registration code is specific to the device hardware, the user should approach the company that sells or publishes the database and ask for a new version of the program or a new serial number, as David Openshaw tried to do. It is disconcerting that in Openshaw's case, there was no response from the distributor. We hope that all software companies come to realize the importance of word of mouth in a field as collegial as medicine.

In the area of pharmacopeias, ePocrates remains the most popular choice among physicians. This popularity is directly related to its availability free of charge. In addition, the ePocrates medication database is updated regularly and has a unique "multicheck" feature to look up drug interactions. However, other pharmacopeias provide a greater breadth of information, and some also include Canadian drug information.[1] We share Joseph Copeland's concerns regarding ePocrates' physician detailing practices. The ePocrates privacy policy[2] suggests that aggregate demographic and software usage records may be shared with third parties, but that personal user information, such as e-mail addresses and other contact information, is kept private. Ultimately, users must decide whether the benefits of this program outweigh the costs of disclosure.

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*Competing interests:* None declared.

## Investigating CAM

John Hoffer invokes homeopathy as an example of how medical scientists set a higher bar for proof of efficacy for complementary or alternative medicine (CAM).[1] Rather than describing this as a "complication," it might be better understood as an entirely appropriate response to extraordinary claims of any sort. "Evidence" of effectiveness can be found for any treatment, no matter how arcane. The question is how good the evidence is, in light of well-established scientific principles. In the case of homeopathy, we must ask whether chance and poor experimental design can explain positive results obtained in randomized controlled trials (RCTs) of homeopathy or whether RCTs with negative results (usually done by non-advocates of this type of therapy) but accompanied by a vast and well-established body of scientific evidence are in fact in error.

Hoffer also mentions St. John's wort and glucosamine as therapies of established efficacy. However, although positive RCTs of St. John's wort exist, the most rigorous studies (placebo-controlled and randomized, with proper case definitions and a treatment-responsive population) indicate no benefit.[2-6] Glucosamine enjoys the support of over 14 RCTs,[7] but critical reviewers will be concerned about the fact that almost all of these were conducted with funding from purveyors of this compound. Publication bias therefore appears to play a role.

Hoffer's call for funding to be directed to case reports and series on CAM therapies as a way of "grooming" them as candidates for RCTs may simply result in a situation in which nothing new is learned. Why? Because uncontrolled and nonrandomized trials are poorly suited for investigating the subjective or "soft" outcomes that CAM therapies so often promise to deliver. Randomization, placebo control and blinding limit the effect of precisely those biases that are likely to explain the "effects" of CAM therapies.

A brief glance through PubMed reveals a plethora of clinical CAM trials. The fact that so many have been done (over 2000 in the case of acupuncture) without producing any clear examples of valid new therapies not only indicates that research money is available but also that it might be better directed.

Why the evaluation of scientifically implausible therapies should be a priority of any magnitude remains an open question. One could argue that some funds should be spent to ensure that prevalent therapies be investigated for safety and drug interactions. Yet research funds are scarce as it is, and the public would be poorly served if money were deliberately funnelled into treatments already recognized as implausible.

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**[The author responds:]**

I applaud Lloyd Oppel's objection to wasting money testing highly implausible therapies, but it seems to me that he is missing the bigger picture. Important new ideas often seem implausible at their inception. The goal of therapeutic research should be to generate important, novel (and hence, at the outset, implausible) ideas, find out which of them may actually be correct, and then gather definitive evidence one way or the other. My article[1] outlined a practical, low-cost strategy for determining which complementary and alternative medicine (CAM) approaches are plausible enough to justify a thorough and fair evaluation.

Government and nongovernment funding agencies have taken the position that CAM merits evaluation. Furthermore, CAM may infuse important new ideas into medicine at a time when much of our mainstream therapeutic research agenda serves the pharmaceutical industry.

Glucosamine sulfate is a safe, inexpensive and potentially useful therapy for osteoarthritis[2] that is especially interesting because it is clinically plausible but biologically implausible. We recently proposed that sulfate, rather than glucosamine, could mediate its beneficial effects.[3]

Oppel cites 2 negative RCTs of St. John's wort in depression. The first was restricted to patients with severe, chronic depression, and its authors suggested that people with milder and less chronic disease might have done better.[4] In the second trial, also restricted to patients with major depression, St. John's wort fared no worse than the established treatment, sertraline.[5] One might conclude that severely depressed patients — especially those referred to specialty units and in whom standard antidepressants fail — are unlikely to respond to St. John's wort.

Oppel misunderstands my point about the role of plausibility in setting standards of evidence. If is often said that there is no difference between