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Cracking down on medical trials

Doctors need to have unbiased data on effectiveness of new drugs, says medical ethicist *Arthur Schafer*

North Americans consume a lot of pills: pills for high blood pressure, low libido, high cholesterol, acid reflux, arthritic pain, and depression.

We take prodigious quantities of pills because our doctors have been persuaded and have, in turn, persuaded us, that these pills work.

Doctors get their information about what works and what doesn't from a variety of sources, including what they were taught 20 years ago at medical school and what they were told last night by a paid consultant of some drug company after a fancy-free dinner.

Doctors are expected, however, to base their treatment recommendations upon the best scientific evidence available in the leading medical journals. We are supposed to be living in the era of "evidence-based medicine."

Unfortunately, when your doctor consults the medical journals she will likely discover only a thin slice of the relevant evidence, namely, the slice that makes new drugs look good. Those clinical trials which show the new drugs to be no more effective than older cheaper drugs are seldom submitted to the journals; hence, they remain unpublished and inaccessible to your doctor.

Here's an example. Let's say that 20 studies have been done of a new class of drug for high blood pressure. Now, suppose that of those 20 studies, six are positive (favourable to the new drug) and 14 are negative (showing that the drugs have dangerous side effects or work less well than older drugs).

One might naïvely think that this would be the end of the story. The new class of drugs would be consigned to the scrap heap of medical research, and the hunt would continue for a better, more effective treatment.

Suppose, however, that as a direct or indirect result of drug company influence, 12 of the negative studies are not published, while every positive study is published. Physicians who then attempt conscientiously to review the literature would find six positive but only two negative studies.

Since four out of six published studies seem to demonstrate that the new drug works well, drug company reps then spread the good word — along with quantities of free samples — to the medical community. The new drug is hailed as a medical breakthrough and rapidly becomes part of standard therapy.

This phenomenon of suppressing negative results is known formally as "publication bias." More colloquially, it's known as "the file drawer effect," because negative studies are hidden

away in a company's file drawer.

If the much-touted movement towards "evidence-based medicine" is to mean anything, then physicians need unbiased data on the clinical effectiveness, toxicity, convenience and cost of new drugs compared with available alternatives.

The pharmaceutical industry claims that when it sponsors drug trials the resulting data become its commercial property, to publish or to suppress as it sees fit. Critics argue that it's vital for doctors and patients to know the bad as well as the good news about new drugs in order to make proper health decisions.

Happily, rescue from this alarming situation is at hand. The International Committee of Medical Journal Editors (ICMJE) has just announced that in future it will refuse to publish the results of any clinical trial if that trial was not recorded at its outset in a publicly accessible registry.

The editors hope to compel drug companies to disclose all the data from the trials they sponsor. Publication bias would thus be eliminated.

For many years, health advocates have been warning that the current state of medical research isn't proper science so much as marketing through censorship or self-censorship. What seems finally to have spurred the medical journal editors into action was a lawsuit, brought by New York State Attorney-General Elliot Spitzer against the British pharmaceutical company GlaxoSmithKline.

The company was successfully marketing its anti-depressant Paxil for use by children and young people, even though the evidence from some of the clinical trials — which it refused to make public — indicated both that Paxil was no more effective than placebo AND that Paxil increased the suicidal tendencies of depressed children.

GlaxoSmithKline has not admitted wrongdoing, but it has agreed to pay a multi-million dollar settlement. It has also agreed, as have some other drug companies, that it will, in future, post more complete trial results on its website.

The ICMJE, however, is not impressed by the companies' deathbed repentance. As one editor asks: "Why would you put the fox in charge of the hen house?"

Perhaps it's time for governments, including Canada's, to compel companies by law to register all their results online in a not-for-profit database.

The next important step will be to tackle the bias that comes from having so many of our leading hospitals, universities and researchers sponsored by the pharmaceutical industry.

When your grandmother told you "he who pays the piper calls the tune" she knew whereof she spoke. If we want public science in the public interest we must pay for it with public funds, as we used to do before the trend towards "partnerships" with industry took hold.

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