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No more scavenger hunts

The recent media flap over antidepressants highlights the need for data to be transparent — and for a mandatory database of all clinical trials.

It was not the media's finest hour. When a study was released last week challenging the effectiveness of several popular antidepressant drugs, some news outlets, particularly in the United Kingdom, responded with headlines blaring 'the drugs don't work' — even though the drugs often do work. Yes, the study showed that the drugs often performed no better than a placebo. But what many of the media missed was that the placebo effect can be remarkably strong in psychological and neurological disorders, especially in mild depression. Doctors scrambled to assure patients that they should not abandon treatment.

Almost buried in the hubbub, though, was a more important story. To access the data needed for this study — a meta-analysis of 35 clinical trials — the researchers had to file a Freedom of Information Act request with the US Food and Drug Administration. And the information they finally received was incomplete: crucial data were missing for several studies that failed to find a significant benefit of the drug compared with the placebo. The missing data limited the analysis, and forced the researchers to abandon their investigation of two drugs altogether.

Such data chaos has become all too familiar in the world of clinical trials. And that fact, combined with recent scandals about antidepressants, diabetes drugs and cholesterol medications, has spurred an outcry to make clinical-trial registries mandatory.

That outcry has not been ignored — the past few years have seen dramatic improvements in data transparency. The International Committee of Medical Journal Editors took a valuable step forward in 2004 when it demanded that authors list and describe their clinical trials in an accepted registry. The number of clinical trials registered in the US National Institutes of Health database rose from 13,153 to 22,714 in a single month, and now stands at more than 52,000 trials spanning 153 countries. Other databases are also active, including an international trial registry hosted by the World Health Organization, which has declared the registration of all interventional trials a "scientific, ethical and moral responsibility".

That responsibility remains unfulfilled. The existing databases are neither comprehensive nor mandatory. Researchers in search of clinical-trial data still have to embark on a scavenger hunt through missing trials and incomplete database entries. Yet the taste of success has been enough to move some open-access advocates to the next step: asking for a description not only of a trial's protocol, but also its results.

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Critics argue that results databases could undermine the peer-review process, reveal competitive information or enable sloppy meta-analyses that set off public panics. They have a point: public registries are no substitute for peer-reviewed literature. But such results databases would still serve an important purpose — as repositories for the negative data that often go unpublished, but that can reveal a drug or treatment regime as ineffective. These data are crucial for meta-analyses, and could improve the design of subsequent trials. Despite reluctance by some pharmaceutical companies to participate, the registries could be helpful to them.

So what can be done to encourage recalcitrant investigators to deposit their data? Several prominent medical journals have removed one barrier by reassuring authors that depositing an abstract or table of results will not be considered 'prior publication'. Politicians in several countries have expressed interest in mandating clinical-trial registries, with some emphasizing the importance of depositing trial results as well. But true fulfilment of that moral responsibility will require international cooperation and enforcement by regulatory authorities — an unprecedented degree of organization and commitment. It is a daunting goal, but one worthy of the struggle. ■

Time to connect

More than ever, academics in Iran and in nations hostile to it should communicate with each other.

This week's address by Mohamed ElBaradei, director-general of the International Atomic Energy Agency (IAEA), to the 35 member states on the agency's governing board highlighted the urgent need for Iran to allow the agency broader inspection powers. But it also highlighted the importance of continuing constructive dialogue amid the bellicose words of national leaders.

There is plenty to alienate Western countries on the one hand and Iran on the other. Iranian President Mahmoud Ahmadinejad's threats against Israel, the nation's fatwa against the writer Salman Rushdie and current domestic violations of human rights are deplorable. But many in the West are ignorant of the depth of resentment, even among the most moderate Iranians, at Western foreign policy in the region. Particularly remembered are the 1953 overthrow by the United States and Britain of the elected government of Mohammed Mossadegh after he nationalized the Anglo–Iranian Oil Company, and the decades of despotic rule that ensued under the Shah.

Nevertheless, Iran's current hard-line leadership masks the county's rich veins of democracy, education and free thinking, which are more developed than those of most of its neighbours in the Middle East. Moreover, Iranian and US politics are both more diverse and pragmatic towards foreign policy than the respective presidents are.