datasheets and reference texts is not always known, and it can be very difficult to determine how real a particular threat is. Prescribers are therefore forced to grapple with the curious conundrum that quantitative efficacy data from a high quality systematic review have to be weighed up against adverse effects data of uncertain origin and indeterminate frequency.

It would clearly be impractical to carry out exhaustive safety analyses for every treatment decision. Instead we should focus on recognizing the specific occasions (table) on which we need to look beyond datasheets and reference texts. As an example, most prescribers would think twice before recommending aspirin in either of the first two scenarios in the table. Do the cardiovascular benefits outweigh the gastrointestinal harms?

This question can be addressed in an evidence based manner by using the method of Glasziou and Irwig to estimate the absolute benefit and harm according to the patient's risk profile.[6] Here, the reduction in cardiovascular events and associated increase in gastrointestinal hemorrhages is calculated by using data from systematic reviews and observational studies of aspirin therapy.[7] The benefit:harm tradeoff across a range of risk levels can then be summarized graphically to help bedside prescribers decide whether aspirin therapy is warranted or not.

Precise estimates of harm are important when the available drugs have equal efficacy but there are potentially valuable differences in the rates of adverse effect—for example, when deciding between a selective cyclo-oxygenase 2 inhibitor and another analgesic (table). The treatment decision here may hinge on which agent offers the more attractive safety profile. While single trials may not have sufficient power to distinguish adequately between the drugs, a meta-analysis may show small but significant differences in complication rates of ulcers.[8]

The therapeutic challenge in the listed scenarios lies not in the recognition of new adverse reactions, but in having enough data to guide the management of well established safety concerns. Drug safety researchers must now move beyond their traditional focus on the detection of adverse reactions and face the new hurdles of characterizing known reactions in greater detail. After all, Bottiger argues that most deaths related to adverse reactions are not from rare, new, or unexpected complications but are due to well recognized reactions.[9] We would be able to manage these adverse reactions better if we had information on their frequency, dose responsiveness, time course, and patients' susceptibility factors.[10] Most importantly, we also need to ensure that safety evaluations are based on data that are of the same high standards required in the assessment of therapeutic efficacy.

Are these realistic goals? Probably yes, some say, but only if we can remove the dogmatism that prevents a happy union between evidence based medicine and traditional pharmacovigilance.[11] In making the best treatment decisions for our patients, it is time that we tackled the weaknesses of the existing data and moved the science of drug safety forward.

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RAPID RESPONSES FROM BMJ.COM

Following is an edited excerpt from a Rapid Response generated by this editorial. It can be read in its entirety at http://bmj.bmjjournals.com/cgi/eletters/329/7456/7.–Editor

Loke has highlighted the importance of knowing the frequency of a side effect of a drug. In 1995 the Council for International Organizations of Medical Sciences (CIOMS)[1] advised that drug companies should report adverse reactions in terms of frequency. I wrote to 120 drug companies in 1996 to see if they could do this and the majority (45 out of 46 replies) [indicated] that at that time they could not.[2] I repeated my survey in 2002 and received 27 replies from 50 letters to drug companies. Twenty-one of these companies stated that their current policy was to follow the guidelines. Seven of these companies stated that they could provide such information for new products only, at present, and would review older drugs at the time of license renewal. Companies that could not follow the CIOMS guidelines stated that such information was at present unreliable due to under-reporting of adverse drug reactions and not knowing the number of patients taking the drugs in question. It appears that drug companies can now provide this information and drug information textbooks should now request and publish this information.

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