BMJ

BMJ 2014;348:g1806 doi: 10.1136/bmj.g1806 (Published 27 February 2014)

VIEWS & REVIEWS

PERSONAL VIEW

We need a global system to help identify new uses for existing drugs

A centralised, worldwide system, similar to the existing "yellow cards" collected for adverse drug events, could amass the huge numbers of data needed, writes **Ricardo Borges**

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"Identification of potential therapeutic targets for new drugs" is a phrase commonly used in grant proposals in both basic and clinical research. Every year drug companies produce and patent hundreds of new drugs that have been assessed in preclinical tests. However, despite this enormous effort and cost, the number of new drugs in the formularies and available to clinicians is ever declining, and the general feeling is that this will persist.[1]

Many drugs are already used for therapeutic purposes that are different from those that were initially intended. Examples include the use of antidepressants as analgesics,[2] antiepileptics such as topiramate for migraine prevention,[3] antihistamine drugs as over the counter sleep aids, sildenafil for sexual impotence,[4] and methotrexate for arthritis.[5] Several drugs used to treat diseases of the central nervous system have other uses, after clinical improvements were seen that were unrelated to the disease originally targeted. Examples include promethazine[6] and imipramine,[7] and tetrabenazine and its derivatives, which were recently approved for chorea associated with Huntington's disease.[8]

Most of these drugs did not have to travel again that long, tortuous, and expensive road from their initial discovery in basic research, or from the early stages of clinical research, to get to the position where they are licensed for their new indication.

However, identifying new uses for old drugs is usually a serendipitous process, particularly in rare diseases, and most of these discoveries are the fruit of observations by isolated physicians who rarely communicate them to the scientific community (see, for instance, the US Food and Drug Administration's Rare Disease Repurposing Database[9]).

Indeed, the means to communicate such findings are limited. In contrast, a worldwide network communicates adverse effects of drugs and has allowed undesired activity to be detected early. This notification system, often known as the yellow card scheme, is well established in primary and secondary care,[10] although nowadays most reporting is online. This initiative has successfully collected dispersed, potentially dangerous side effects.[11] Data are collected from almost all interested parties, including nurses, patients, and patients' relatives.[12]

This system should be expanded to cover potential new therapeutic uses.[13] Such an initiative would collect and collate information about unexpected improvements in a patient receiving treatment for another condition, or about an unknown or unreported potential use of a drug.

This would be especially valuable for rare diseases, given the high cost of research and development and the smaller markets for commercial exploration that may discourage drug companies' investment.

Moreover, reaching a consensus about new treatments using established drugs can be difficult and requires a huge number of individual reports. The potential clinical benefits could be attained only via a system that centralises such communications.

Centralisation would also facilitate and encourage the sharing of such information. The system would have to take into account some legal considerations, such as intellectual property rights, because a doctor might claim discovery of a new application of a drug.

A system similar to the yellow card system but which collects adverse effects could help amass the data necessary to identify other potential uses of currently marketed drugs. Such a system might give a necessary boost to the industry's waning drug discovery programmes; hopefully it would also benefit patients, by increasing the clinical drug armoury.

Competing interests: I have read and understood the BMJ Group policy on declaration of interests and have no relevant interests to declare.

Provenance and peer review: Not commissioned; not externally peer reviewed.

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Cite this as: *BMJ* 2014;348:g1806