Regulators move toward adverse event reporting via mobile apps

Tracking adverse events resulting from drugs once they are on the market has long been a tricky process. Although drug companies must notify the US Food and Drug Administration (FDA) of any adverse event reports they receive, patient and doctor reporting of these ill effects is voluntary.

It's perhaps no surprise, then, that studies have found that adverse events are both underreported and poorly reported, with most reported events falling in the category of generalized, non-serious symptoms that may not be related to the drug. For instance, a study last year found that only about 56% of drug reviews met criteria deemed important by the researchers, such as indicating in the title that the review assessed harmful side effects (*BMJ* **348**, f7668, 2014). An earlier 2006 meta-analysis of 37 papers concluded that 94% of adverse drug reactions were underreported, on average (*Drug Saf.* **29**, 385–396, 2006).

To simplify reporting and to better enable patients to directly report adverse events to regulators, the FDA and European regulators are increasingly turning to data collected from mobile apps and social media.

The FDA receives adverse event reports from drug manufacturers and also directly from patients and healthcare providers. It deposits those reports into the FDA Adverse Event Reporting System, which now includes around 9 million reports that have been submitted since 1969. However, according to an FDA spokesperson, "there is substantial underreporting" and in cases where a symptom or reaction is recorded "there is no certainty that the reported event was actually due to the product."

Some people complain about the significant lag time between when reports are submitted and when they become available to consumers, either through individual physicians, FDA-issued alerts, or updates to the drug label. The current system is "scarily broken," says Nabarun Dasgupta, chief data scientist at Epidemico, an informatics company spun out of the Boston Children's Hospital that develops consumer tools for monitoring public health, including MedWatcher, a tool for monitoring drug safety. MedWatcher, which launched in 2010, was one of the agency's first attempts to use an app to help with reporting. It aims to cover all approved drugs and devices and has information from clinical trials and manufacturer labels, and so far it includes around 1,400 adverse event reports submitted directly by patients. The app can be downloaded to a smartphone or used online to submit reports to the FDA about adverse events, to track drugs of interest, and to see what events others have reported.

Alexmillos / Alamy

Mobile malaise: Regulators try to tap into adverse event reporting by phone.

In 2012, the FDA began its Real-Time Application for Portable Interactive Devices (RAPID) program to create a mobile surveillance application to allow clinicians to input adverse drug reactions via photos, videos and medical records, as well as geo-mapping information to monitor such events during public health emergencies. The FDA is soliciting proposals from companies to use social media to monitor adverse events.

Social savvy

Europe's Innovative Medicines Initiative in September announced funding for WEB-RADR, a three-year project to use mobile apps and social media to gather information on potential adverse drug reactions. A consortium of academics, industry and regulators, such as the Medicines and Healthcare products Regulatory Agency in the UK, is participating.

Epidemico is developing these tools, but a handful of other companies exist, such as AdverseEvents, which created an online software platform for analyzing data on post-approval drug effects. And increasingly, the companies' products are demonstrating their ability to gather and sift through piles of data.

In an April study, Dasgupta and his colleagues published findings from Twitter data they collected on adverse events related to 23 medical products, showing that people's tweets more or less matched regulators' reports (*Drug Saf.* **37**, 343–350, 2014). Over seven months, they used software to collect Twitter posts that mentioned one of the products. From a sample of around 60,000 tweets out of a total of 6.9 million, they both manually curated and applied a keyword algorithm pinpointing 4,401 related to a potential adverse event. The paper noted that some products with widely known side effects had their own hashtags, such as #accutaneprobz for the acne medication Accutane (isotretinoin).

Epidemico is now working to update MedWatcher to automatically incorporate data from Twitter and Facebook and compare it to published information from a drug's clinical trials.

The right data

Simply increasing the amount of data gathered will not necessarily solve the problem of tracking adverse events, because many reported ill effects are not drug related.

Andrew Grey, an associate professor at Auckland University, says that in his field of osteoporosis, one of the main reasons for patients stopping an effective drug is what they perceive to be a side effect, but is often a general symptom that has nothing to do with the drug, such as lower back pain. In a study he published in August, he wrote that information about adverse events in commonly prescribed drugs is both "excessive" and "inconsistent" (*BMJ* **349**, g5019, 2014). Grey says that information collected online from social media or apps could potentially help, but it could also cause harm. "There's no way of verifying the causal nature of the relationship," he says.

Lisa Schwartz, a professor of medicine at the Dartmouth Institute for Health Policy and Clinical Practice, agrees that social media and patient-generated data are limited in terms of the conclusions that can be drawn, but notes that they are a good first step. "They're a good way to catch signals," she says, noting that academic scientists can then follow up on those signals with more rigorous studies.

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