Learning From Social Media For Adverse Event Reporting

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Those interested in monitoring drug safety in the post-marketing setting have been exploring how best to capitalize on the vast amount of information available through social media platforms. While recent studies have suggested that social media may provide a useful source of additional information on patients' experiences after exposure to pharmaceutical and biotechnology products, they also highlight serious limitations on the use and interpretation of such data. As researchers continue to develop tools and methods to analyze social media data, it becomes necessary to consider how best to use those data and, perhaps more importantly, limitations to their uses in identifying and evaluating drug-induced adverse events ("AEs").

Using Spontaneous Reporting Systems to Report Adverse Events

Pharmacovigilance is the science of detecting and assessing the effects of marketed drugs post-regulatory trials and U.S. Food and Drug Administration approval. Ongoing monitoring is needed to identify and collect data on AEs that may not have surfaced in the tightly controlled environment of a clinical trial. Pharmacovigilance principally involves identifying and evaluating safety signals using data sources that are often referred to as "numerator-based," such as spontaneous adverse event reports and case

reports. These data record safety signals (the numerator) but not the underlying population of patients treated with the drug (the denominator).

The FDA and drug manufacturers collect information on patient experiences in the post-marketing setting through multiple sources, including spontaneous reporting system databases such as the FDA's Adverse Event Reporting System (FAERS). Such databases contain reports of suspected AEs that are submitted on a voluntary basis by anyone who wishes to do so (e.g., healthcare professionals, patients, family members or patient advocates). The accompanying data collection forms record specific information regarding the patient, the drug(s) and dosage to which the patient was exposed, the timing and nature of the AE, and the person submitting the report. If a drug manufacturer receives an AE report, it is required to submit the report to the FDA for entry into the FAERS database; often, that manufacturer will reach out to the originator of the report to obtain additional information concerning the circumstances giving rise to the report.

Using spontaneous reporting system databases, such as FAERS, to detect and evaluate statistical signals of potential drug-AE associations is considered good pharmacovigilance practice by the FDA as long as the statistical methodologies and signal evaluation processes are sound. These additional conditions are needed because such databases present serious limitations, including a high rate of under-reporting; unrepresentativeness; reporting generated by media coverage and journal publications; recall bias; and a large proportion of low-quality AE reports. Isolating true signals amid this noise is analytically challenging in these types of data.

Near-universal access to social media sites and applications offers the potential to collect many more unstructured reports of patient experiences following drug exposure. Indeed, one study of social media posts containing discussions of AEs ("Proto-AEs") found that "[t]here were nearly three times as many Proto-AEs found in Twitter data than reported to FDA by consumers."[1] This is because of the absence of restrictions on an individual's ability to air personal experiences with medications and treatments regardless of their accuracy via such social media sites as Twitter, Facebook, Google Plus,and Yelp (among others). Patients can also rate their medical experiences — actual or imagined — using many recently developed commercial sites such as Healthgrades.com, WebMD.com or AskaPatient.com. Furthermore, "influencers" with strong opinions could both elicit specific points of view from others or over-report their own perspective, thereby creating an unbalanced view of a specific product. This could, in turn, further bias reporting by others.

As a result of these potential biases, how to incorporate information from social media postings in the pharmacovigilance process and how to relate them to information from more conventional spontaneous reporting system databases, such as FAERS is a true quandary.

Comparison of Social Media Reports to FAERS

What is the quality of AE reporting on social media? Can these "data" be useful alongside or as an alternative to FAERS? A recent Analysis Group study[2] provides insight into such questions, highlighting potential opportunities afforded from social media sites as well as inherent limitations of such data sources, at least in their current state. The study also analyzed whether reporting patterns on social media are precursors of reporting patterns in FAERS, and whether they could accelerate the detection of signals for potential drug-related AEs.

To compare the information available from social media and conventional pharmacovigilance data sources, we collected reports of clinically important AEs pertaining to two drugs, Lipitor® (atorvastatin) and Meridia® (sibutramine), from the FAERS database and from AskaPatient.com, a patient support group website on which patients share and rate their experiences with different medications. Lipitor® is a heart medication that is widely considered relatively safe. Meridia® is a weight-loss drug ultimately withdrawn from the market by the FDA because of unforeseen cardiovascular problems including heart attacks and strokes.

Whereas AEs reported in FAERS had already been categorized based on standardized terms (i.e., according to the Medical Dictionary for Regulatory Activities, or MedDRA), reports in AskaPatient.com required manual screening to distinguish between positive and negative sentiment and to categorize AEs by type (e.g., muscle pain or cardiovascular AEs).

While there were similarities across the two data sources such as the types of AEs reported most often, patients reporting AEs through social media were significantly younger than those reporting through FAERS. Hence, AE reports from social media sources might better mirror those from conventional pharmacovigilance sources for drugs more frequently used by younger patients.

We also found that the percentages of reports categorized as serious for problems such as pain (in the case of Lipitor®) and cardiovascular AEs (in the case of Meridia®) were higher on FAERS than in social media. Overall, social media reports focused more often on less serious AEs that affect quality of life, such as itchiness and pain, while reports on FAERS tended to have more reports on serious problems, such as heart attack. This may reflect a higher proportion of medical professionals reporting through FAERS rather than social media.

Finally, social media AE reports helped predict the subsequent occurrence of FAERS reports for Meridia® but not for Lipitor®. As such, whether pharmacovigilance analysis of social media data can provide an earlier signal of potential drug-related AEs on a widespread basis remains uncertain.

Determining Appropriate and Efficient Uses for Social Media Reports

As of now, the FDA has not issued guidance on how and whether drug manufacturers should monitor and report AEs reported in social media. For example, should a drug manufacturer report to the FDA:

- All mentions of its products in social media that pertain to AEs?
- Only mentions of serious AEs (however defined)?
- Only those postings that identify the patient and describe the seriousness of the event in detail?

Alternatively, should drug manufacturers ignore social media postings because they are often incomplete, are anecdotal, are prone to herd effects and are too numerous to track and report on a systematic basis?

Furthermore, is it ethically appropriate for manufacturers to try to reach out to individuals posting on social media with vague reports of AEs to obtain more information at the risk of violating the patient's privacy?

Uncertainty around social media reporting could give rise to significant risks for manufacturers in terms of both compliance and potential liability. For instance, drug and biologic manufacturers could be taken to task by plaintiffs for ignoring online chats about drug AEs despite the absence of any plausible way for manufacturers to validate the accuracy of such reports. The inclusion of unverifiable self-reports from social media risks flooding the FAERS system with noise that could dilute the true safety signals. The dilemma for drug manufacturers is that online chats often lack scientific credibility even though, at times, they may contain useful adverse event information.

Our analysis of social media reporting suggests at least two conclusions relevant to litigation exposure. On the one hand, to the extent data from social media platforms could serve as an early signal from a broader patient population it could supplement conventional pharmacovigilance data sources. Although social media AE reports helped to predict FAERS reports for only one of the two drugs studied, the potential for such data to more quickly identify signals of potential drug-AE associations even among a subset of drugs may provide an important social benefit.

On the other hand, given the important differences in the types of information and AEs reported through social media and the inherent issues with their reliability, they should neither replace nor be considered additive to data from conventional pharmacovigilance sources such as FAERS. Doing so could dilute clinically important signals captured by the current FAERS system, overburden the pharmacovigilance community with non-life-threatening AEs that may not be clinically significant for patient safety, and result in scares that inappropriately lead to under-treatment that ultimately brings harm to patients.

As regulators continue to assess the use of social media data in the pharmacovigilance process, they should also consider and provide guidance about the types of social media reports that would constitute "reportable events" for entry into either FAERS or a separate database. Such guidance will be helpful for drug manufacturers as well as the pharmacovigilance (and legal) community on how to incorporate these new sources of data into their standard signal detection and evaluation processes, if at all.

As with any new data source, it is important to weigh the costs and benefits of constant active screening of social media, which currently requires manual review and categorization of posts. Given the large volume of social media posts, this represents a significant effort that may divert the resources of manufacturers, regulators, or other pharmacovigilance analysts from more reliable sources of AE reporting.

To address this tension, researchers are developing tools to automate the process of categorizing these types of data using natural language processing. These machine-learning algorithms can generate reliable predictions on the potential relevance and value of new postings based on past data. Although these new methods may one day alleviate the enormity of the undertaking given the ever-increasing volume of social media postings, they have had limited success so far in identifying credible drug safety signals.

Any FDA guidance about AE reporting based on social media data must ensure that clear and reasonable expectations are set around the collection, reporting and use of these data and that appropriate analytical techniques are developed and validated before they are relied upon as sources of information for adverse event detection.

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Endnotes

1 Clark C. Freifeld, et al., "Digital Drug Safety Surveillance: Monitoring Pharmaceutical Products in Twitter," Drug Safety (May 2014), 37:343.

2 Mei Sheng Duh, et al., "Can social media data lead to earlier detection of drug-related adverse events?", Pharmacoepidemiology & Drug Safety (December 2016), Volume 25, Issue 12.