FAST*facts*

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PHARMACOVIGILANCE

As many as one out of three drugs on the U.S. market may have safety issues, according to a recent study published in the Journal of the American Medical Association.[1] In the EU, the European Medicines Agency (EMA) reported in 2017 that as many as 200,000 deaths have resulted from preventable safety issues with drugs.[2]

These statistics highlight a key challenge of modern medicine: the need to track adverse events long after regulatory agencies have approved new drugs.

Q: What is "pharmacovigilance"?

Pharmacovigilance is the process of detecting, tracking, analyzing, and preventing negative side effects of drugs.[3] It allows manufacturers and regulators to continue studying drugs and their effects after the drugs are released.

Physicians and patients play a vital role in identifying and reporting patient responses. Data on patients are collected separately from drug companies, doctors, and governing bodies. Pharmacovigilance data can have many effects, from the simple communication of new data to the public or, in severe cases, a drug's removal from the marketplace.

The complexity of modern drugs such as biologics has intensified the need for pharmacovigilance. Biologic medicines are developed from living cells or tissue, and they may vary from batch to batch. They also vary from biosimilars, follow-on drugs that can offer similar benefit at a lower price. Biosimilars broaden patient options but also present the need for pharmacovigilance tools that differentiate similar but distinct drugs.

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Q: Aren't drugs proven safe before they reach patients?

Yes, but drug testing has limits. Once a drug advances past the clinical trial stage it may have been tested on 500-5,000 people.[4] With that number of participants, researchers cannot account for all the variables that might affect patients, such as their environment, lifestyle, or interactions with other drugs. Likewise, infrequent adverse events may not materialize during a clinical trial, even though they can pose problems once the drug is approved and available to a wider pool of patients.

Timeliness is important in medicine, but so is safety.

Scientists and regulators must balance the value a drug offers patients with the potential hazards it presents.

To understand why pharmacovigilance is important, consider the drug pergolide. Pergolide was created to help patients struggling with Parkinson's disease. Data on patient responses, however, soon linked it to serious heart valve damage and pulmonary fibrosis, and the FDA removed it from the U.S. market in 2007.[5]

Q: How does pharmacovigilance work?

Pharmacovigilance includes three basic steps:

1

Collecting information on adverse events, commonly called "side effects." Some adverse events are mild, while more serious adverse events can result in birth defects, disability, hospitalization, or death.

In the U.S., medical professionals can report these data through pharmacovigilance software programs. Patients tend to report their adverse events to their doctor or the drug company, which both report to the Food and Drug Administration (FDA).[6]

In the EU, patients have the option to self-report to national pharmacovigilance centers. In addition, both patients and physicians have the option to report directly to the drug manufacturer.[7] This capability provides the EMA with information about drugs quickly, allowing faster response times to adverse events.

Other countries may not track drugs as carefully. For example, Latin American governments typically lack robust systems for pharmacovigilance. Some instead have platforms known as medicine "observatories" that operate at the national level to monitor drug availability and accessibility.

2

Reviewing clinical data. As data on adverse events are collected, they must be carefully reviewed.

In the United States, the FDA monitors these data and flags products that have a high instance of adverse events using the FDA Adverse Event Reporting System. If enough safety risks are reported, the FDA will reevaluate the drug to determine if it should be removed from the market.[8]

In the European Union, this function is handled by the EMA. It sends collected data to the Pharmacovigilance Risk Assessment Committee, which monitors the safety of drug, to assess it and recommend regulatory action when required.[9]

Conversely, in Latin American many countries' drug safety authorities are instead focused on counterfeits and other quality-related issues.

3

Responding to clinical data.

If the FDA has a concern about patient safety, it may evaluate the drug further or take regulatory action such as updating a drug's label and/or communicating findings to the public.

Like the FDA, the EMA follows an escalating series of responses. It involves classifying problem drugs with suspected adverse events and monitoring data with a program called EudraVigilance. A committee of experts monitors safety signals from EudraVigilance and may recommend regulatory action as needed.[10]

Latin American governments rely mostly on international monitoring and consensus for decision-making related to any one drug's potential safety concerns. There are some regional efforts to harmonize drug safety regulatory capacity, such as the WHO/PAHO Pan American National Drug Regulation Harmonization effort. But national spending limitations make building effective reporting and data collection systems challenging.

Q: How can regulators get full and accurate information?

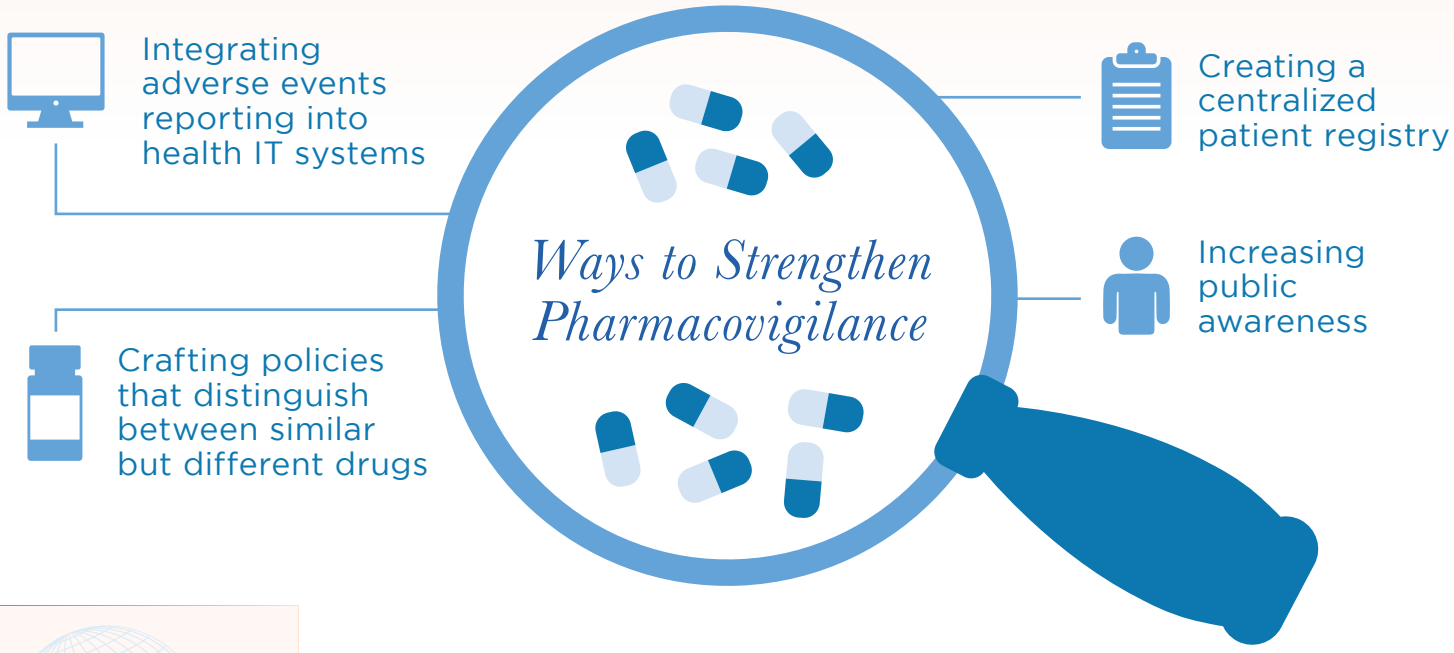
Collecting accurate, comprehensive data on adverse events is a challenge. Manual entry of patient records can result in errors. If pharmacovigilance systems don't fully integrate with modern electronic health records, vital information may go unreported.

Further complicating matters, data on patients are collected from separate entities. This translates to inefficiencies, duplicated data, or compromised data. It also means that regulators must sift through individual streams of information rather than a consolidated database.

A coordinated patient registry that centralizes data from all entities in one location would allow governing bodies to evaluate data more efficiently. Similarly, current protocols for quick communication between health care providers and national regulatory agencies such as the EMA or FDA could be strengthened and streamlined.

Another issue is accurately matching adverse events to similar but distinct drugs, as with biologic and biosimilars. As more biosimilars become available, patients may switch from one drug to another for either medical or cost reasons. Pharmacovigilance must help patients and physicians accurately trace any adverse events that arise as patients use and switch among these similar drugs.

Toward that goal, the FDA and the World Health Organization approved methods for creating distinct names for biologics and biosimilars.[11] As biological drugs become more common, regulators would do well to protect patient safety by continuing to craft policies that allow for accurate pharmacovigilance of these therapies.



Q: How do patients know how to report adverse events?

Overall, adverse events are underreported worldwide.[12]

Typically, patients who want to report an adverse event are directed to their doctor, who can then relay that information to a pharmacovigilance data system. However, since only five percent of doctors are estimated to participate in any pharmacovigilance system, this process can be inefficient at cataloging patient issues.[13]

In addition, the FDA runs an online voluntary reporting system called MedWatch, which permits medical professionals and the public to submit information about prescription and over-the-counter drugs, biologics, medical devices, and other medical products.[14] MedWatch also provides medication news, recall information, and drug labeling information.[15]

Still, the challenge with online applications isn't their utility so much as limited public awareness of pharmacovigilance. While these type of tools are helpful, they cannot fulfill their function if the patients do not know they exist.

To bolster public awareness of pharmacovigilance, the WHO's Uppsala Monitoring Centre has spearheaded initiatives such as the "Take & Tell" campaign. The campaign includes a catchy song meant to educate the public about the importance of pharmacovigilance. The jingle has been so successful it has been remarketed to Asian and South American markets.[16] This type of unorthodox outreach using new media is vital to engaging with the general public about pharmacovigilance.

Another way to improve patient reporting is to utilize non-traditional methods of gathering data from patient. For example, in 2013 a study showed that contacting patients to report side effects through text messages was effective in gathering data.[17]

Whatever the mechanism, increasing public awareness is critical to strengthening pharmacovigilance systems.

CONCLUSIONS

Since clinical trials cannot test for every variable, pharmacovigilance is needed to provide patients and providers with the most current, accurate safety data on drugs. With the rise of sophisticated drugs like biologics and the high-pressure demand for faster approvals, regulators must enhance pharmacovigilance practices. That includes tools that encourage fast, accurate reporting of adverse events and, for biologics and biosimilars, policies that clearly distinguish among similar drugs.

These efforts can help regulators find the balance between approving new drugs in a timely manner and protecting the safety of the patients who use them.

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