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Review Article

# Role of Social Media for Drug Safety Signal Detection

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**ABSTRACT**

Drug safety is an important factor considered during the drug discovery and development stages to develop safe and efficacious medicines for patients. Post-marketing surveillance is the commonly used method to obtain Adverse Drug Reaction (ADR) data of a marketed product through spontaneous reporting. In recent years, drug side effects are a major concern related to public health, increasing hospitalization and mortality rates. Social media has gained popularity in communicating and sharing every aspect of human life, including health-related information. The advantages of using social media to detect and report pharmacovigilance signals include the dissemination of data among healthcare professionals and stakeholders in a real-time and timely manner. The main objective of this review article is to explore the possible role of social media in the detection of a drug safety signal. It is observed from the extensive review that patients are seeking advice and getting information about health, disease, and medications from different social networks such as LinkedIn, Facebook, WhatsApp, Twitter, Pharmacovigilance Programme of India (PvPI) app, PubMed, MedHelp, PatientsLikeMe, etc It is concluded that social networks can be a useful tool for the detection of a drug safety signal. Thus, few limitations of traditional data sources or signal analysis suggested that these traditional signal analyses can be supplemented with data gathered from social media.

**Keywords:** Pharmacovigilance, Adverse Drug Reactions, Drug Safety, Signal Detection, Social Media.

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## INTRODUCTION

Data gathered during the pharmacovigilance operations such as individual cases and aggregate reports have a significant role in the identification of the drug's safety profile as well as the detection of novel effects that were not ruled out or discovered during the pre-approval phase (signals). The large amount of safety data acquired from everyday drug use is also useful in spotting even the most unusual events.[1] If the pharmaceutical industry receives any suspicious information about the safety signals then individual case reports and aggregate reports are sent to the regulators who evaluate the causality relationship with the drug and then make judgments about its safety concerns.[2] On the other hand, users of social media are open to sharing their experiences without validating and seeking guidance on particular content.[3] The rapid expansion of the internet provided the place for several online health enterprises to be available digitally, which attracted many patients to visit and search for medical information on these platforms. Earlier studies concluded that ADR reports which were not reported earlier may be verified from centralized reporting systems for patients' reports, and the quality of ADR reported by these systems was comparable to the ADRs reported by the health care professionals. As a result, these internet communities for health are a great place for patients to talk about the medications they're taking, resulting in a plethora of useful information for identifying possible ADRs.[4] On the performance of well-known statistical signal detection techniques for a diverse set of medications and adverse events on Twitter/ Facebook, certain data shows remarkable results.[5]

Social media establishes a better relationship between patients and healthcare professionals. Patient's health information is abundant and frequently available to the public; therefore, it is an unexplored source of post-market surveillance reports which could augment data from existing sources of pharmacovigilance data.[6] The internet is a great way to gather medication and device adverse event reports, especially from healthcare providers via different channels and methods. It also provides a quicker way for reporting and communicating new safety concerns/issues and enhances the amount of information available for evaluating the product's benefits and risks. Updated safety information should be communicated to stakeholders in a timelier manner. It also helps to accomplish a better relationship between companies and the community. The utility of various social media platforms for gathering information for the pharmacovigilance purpose

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is still in its initial stage. This review article's goal is to provide useful information about the role of various social media in the detection as well as reporting of ADRs. We'll go over the notion of drug safety signal detection, its traditional methods and limits, social media tools and techniques utilized in signal detection and their limitations, legal considerations of using this internet platform to detect drug safety signals, and future views, among other things.

## Drug Safety Signal Detection: Concept and Process

The primary goal of pharmacovigilance is to ensure patient safety by ensuring the safety of medicines. An important objective of National Pharmacovigilance Centers is to function as an early finder of any potentially harmful effects associated with the drugs, and this may be achieved through the perception of a signal. A signal may be speculation of a risk associated with a drug that is gathered from various viable sources.[7] According to the WHO, a drug signal is the reported information about the possible causal relationship between a drug and Adverse Drug Events (ADEs) which was unknown or incompletely documented earlier. More than one report is usually required to generate a signal.[8] Because of the involvement of complex or unexpected factors in the identification of individual ADRs, thus, it is very difficult to establish a conclusive correlation between a drug and an event due to the involvement of complex or unexpected factors. Earlier, there was a lack of advanced data supply or gathering for ADR reporting system.[9] Signals may be observed qualitatively and quantitatively (Figure 1). Qualitative signal observation is the result of a case-by-case evaluation of ICSRs (Individual Case Safety Reports) while the quantitative signal is obtained by machine learning or data mining methods that utilize databases of the world's genuine information compiled from various clinical trial phases, electronic health record, biomedical communications, pharmacological reports etc. Signals that are quantitatively or qualitatively recognized must be approved and confirmed by clinical conclusions and remarks. The points of signal detection are to prior find possible security concerns to differentiate higher-order association signals; to reaffirm signals that had previously been recognized from qualitative approaches; and to likely identify course impact security issues.[10] The development of computer technological innovation has drastically expanded the capacity to gather data compared with pharmacovigilance cases. It has made it conceivable to the selection of data and also creates pharmacovigilance signals with an effect on general well-being and restorative approaches. Vigibase, a worldwide dataset of ICSRs, has received spontaneous and other reports since 1967. A few nations acknowledge reports from drug organizations. Since 1978, VigiBase is governed by Uppsala Monitoring Center (UMC), and it contains more than 21 million ADRs database last year which increasing dramatically every year.[11] Therefore, it is important to ensure the security of the patients by confirming the safety of medicines. Every country has developed their own system of pharmacovigilance to detect, analyze and report ADRs associated with medicines using different reporting methods. Further, these ADRs are reported to the Uppsala Monitoring Center so that this information can be shared with the different stakeholders.

## Signal detection process

The origins of modern signals differ from those of previous signals. They could comprise all database information about the deployment of licensed medicinal products, such as quality, nonclinical, clinical, and pharmacovigilance information. Signals can come from all around, including spontaneous reporting and active-surveillance methods, non-interventional investigations, clinical trials, and other additional data sets (Figure 2).[12]

## Spontaneous reporting system

It is the voluntary method of ADR reporting where information about suspected ADRs is reported by the healthcare experts or consumers to the company, regulatory authorities, ADR monitoring centres or other organizations. For signal detection and processing, it employs a variety of strategies such as proportional reporting rationing, Bayesian, and other methods (Figure 3). Data mining procedures play a supportive role in the identification of unwanted events during the drug discovery phases and also use to look at drug-drug interaction.[13] However, spontaneous reporting is associated with limitations including underreporting and detailing of the particular event. This underreporting of ADRs can lead to potential threats through misleading outcomes which are occurred due to the non-presentation of real threats. Specific announcing is one more downside of this framework which might send a mixed signal of a danger that doesn't exist really.

## Prescription event monitoring

It is the process where the record of any suspected medication response, any modification in the laboratory findings of diagnosis parameters, and any unusual significant changes that occurred during the treatment is entered in the patient's medical file. Further, the conclusion drawn from these events is needed to be validated by experts and concerned hospitals. In most cases, our Lower-Level Terms (LLT) are proportionate to the favoured keywords used in the Therapeutic Lexicon for Administrative Exercises (MedDRA).[14] Both spontaneous reporting and PEM play an important role in signal observation. However, in contrast to the spontaneous reporting method (i) PEM collects all occasions in any case of the suspected causal drug connection, its reality or recurrence (ii) Report generated by general practitioners are not constrained to inquire for survey suspicion or causality.[15]

## Cohort event monitoring

It is a non-interference strategy for close monitoring of recently promoted drugs. Two primary kinds of signal observation

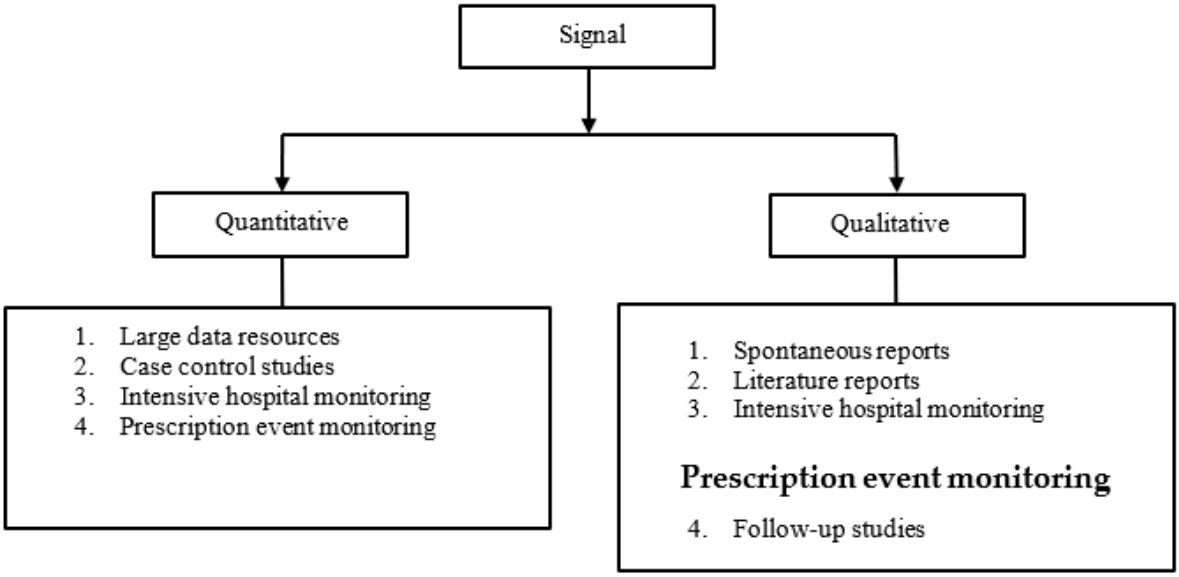


**Figure 1:** Types of Signals in Pharmacovigilance.

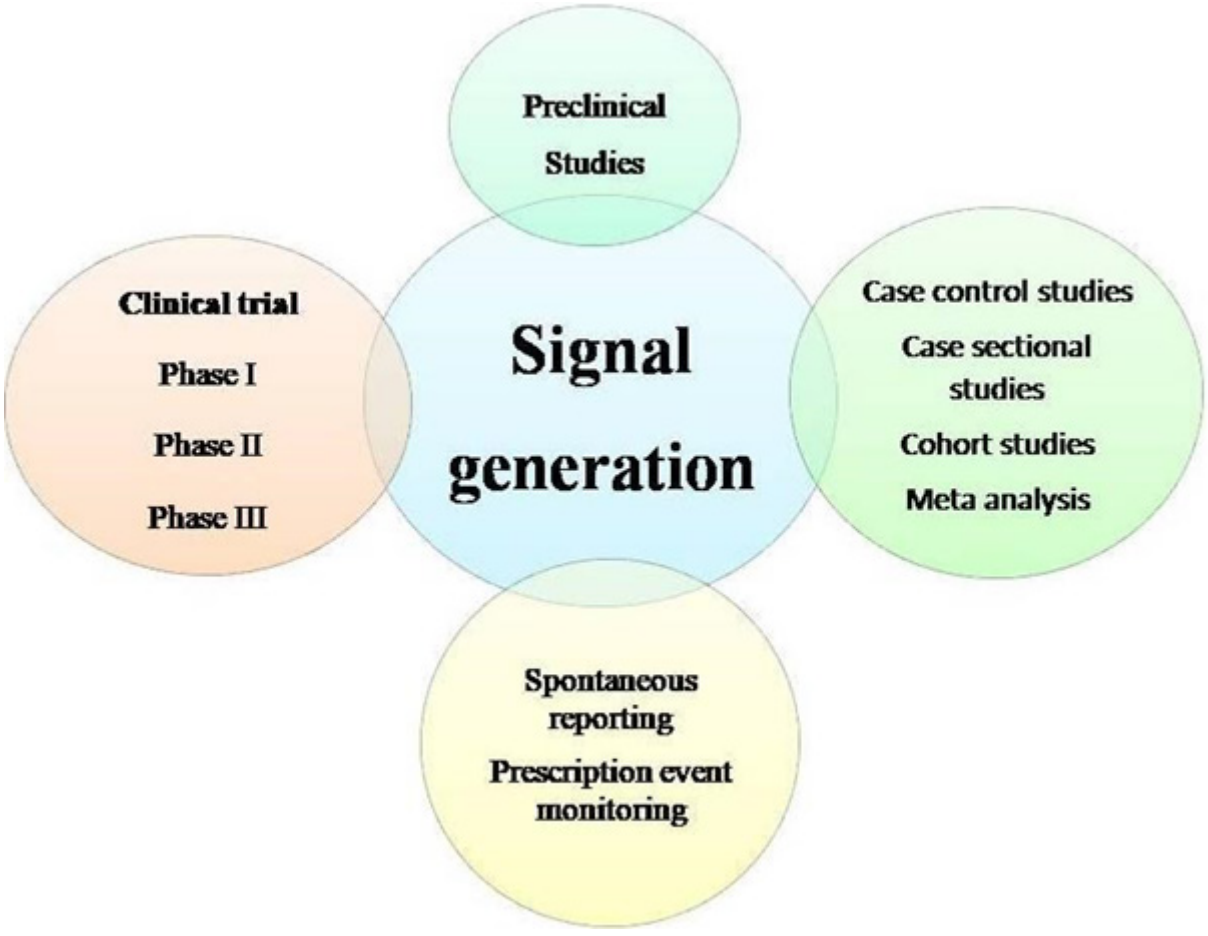


**Figure 2:** Sources of Signal Generation.[12]

strategies have been utilized on CEM (Cohort Event Monitoring)-qualitative and quantitative. Qualitative approach-Such evaluations consider a variety of realities when doing a case arrangement of quiet reports, for example, time to onset data, natural and pharmacological credibility depending on drugs information, the conceivable impact of related solutions, the part of fundamental sickness or co-morbidity, rechallenge and dechallenge data, and so on. Quantitative approach - Ordinarily, drug-event incident rates within the to begin with the month of presentation are analyzed and when compared to the equivalent occurrence statistics within the consequent 5 months.[16]

It is the procedure used to ensure the safety of marketed drugs. In India, PSUR submission by marketing authorization holders is mandatory to the CDSCO (Central Drugs Standard Control Organization) twice a year for the next two years.[17] The PSUR can be an incredible resource for locating unused safety signals. It intends to deliver updates on a pharmaceutical item's global compliance involvement to the qualified specialist at a specific point after the product's marketing authorization. In any case of promoting condition, PSURs must be submitted for all enrolled items. All items with similar active substances approved by one marketing authorization holder may be covered by a comprehensive report.[18]

## Pharmacoepidemiology resources

The names of several data collecting systems that have been used in an epidemiological observational study and as the application of the epidemiological methods to pharmacological issues are incorporated into the International Society of Pharmacoepidemiology (ISPE). The major types of databases include National databases for health care systems, databases that include Medical Insurance Claims e.g. All-Payer Claims Databases (APCDs), and Organization's Administrative Databases e.g. Medicare and Medicaid Services (CMS).[19]

## Electronic Healthcare Data (EHD)

Electronic healthcare information comprises of different provenances like EHRs (electronic health records), and regulatory or protection-claiming databases. Electronic healthcare information is a kind of longitudinal experimental framework where patients' therapeutic records are made from different frameworks in healthcare organizations. Many EHR areas are comprised of distorted information such as

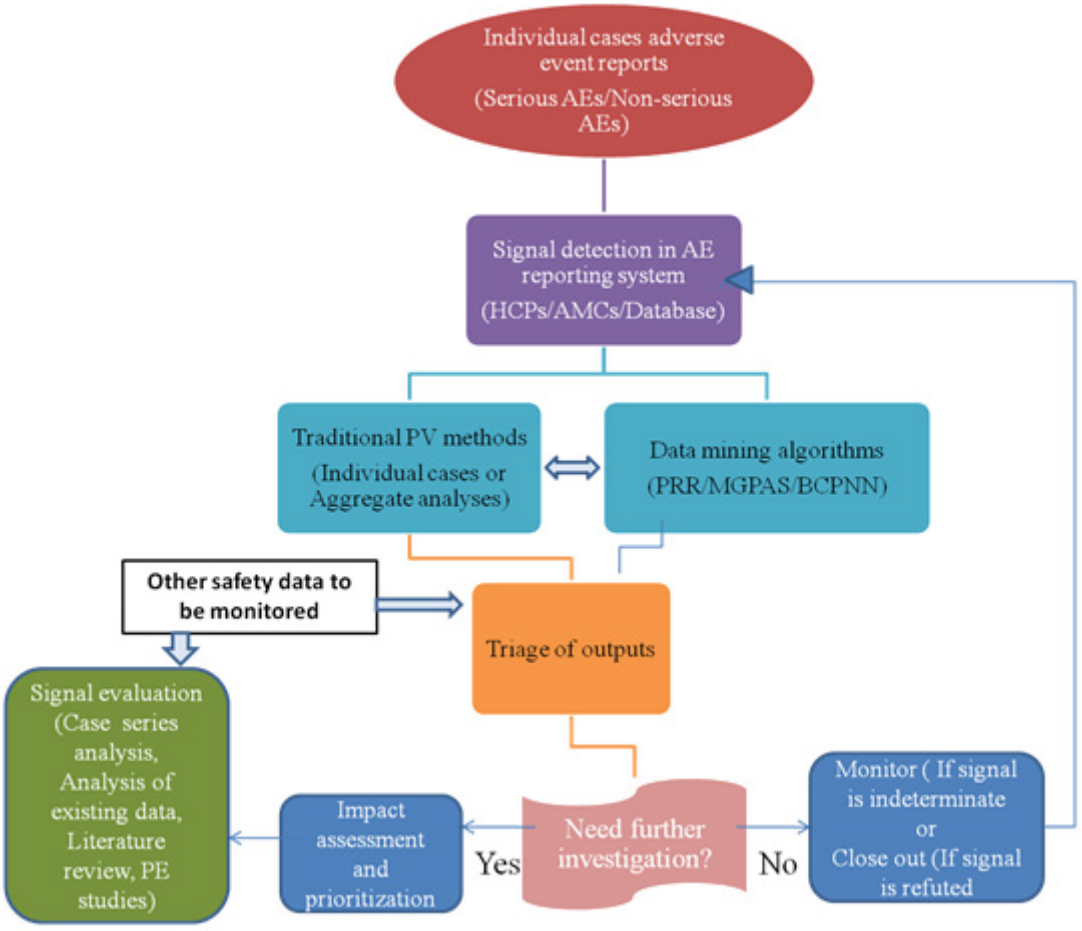


**Figure 3:** Signal Process Events in Pharmacovigilance System.[10] *Periodic safety update reports (PSURs).*

**Table 1: Various social media platforms, their role, advantages and limitations in drug safety signal detection.**

| Sl. No. | Social Media Platform | ADRs/Drug Safety Signal Detected | Study Description | Advantages | Limitations | References |
|---|---|---|---|---|---|---|
| 1. | Twitter | Rosiglitazone caused cardiovascular events such as Heart Failure and myocardial infarction<br>Infertility with the human papillomavirus (HPV) vaccine. | Studies were conducted by two French regional pharmacovigilance centres primarily at the Saint-Etienne College Clinic and second at the Georges Pompidou European Clinic in Paris with<br>2,537 tweets related to rosiglitazone and 2,236 posts related to the HPV vaccine. | Wide generality 98% compared to Facebook and Google plus. | Around 25% of tweets related to HPV communication showed a negative-sense.<br>Confinement of characters<br>Less enlightening than in unconstrained case reports.<br>Not suitable for old age person because this is a young platform<br>Misspelling. | 34 |
| 2. | Facebook | Insomnia, hallucination, drug dependence, euphoria<br>related with Methylphenidate, Topiramate, Levetiracetam, Propofol. | This study observed the number of posts constructed on Twitter and Facebook. | Facebook permits allocating of extended (i.e., boundless in length) posts, photographs, videos, and articles fluently. | Fewer chances of serious ADR reporting. | 35 |
| 3. | MedHelp | Diarrhoea, Nausea, Abdominal pain, constipation, Headache, and asthenia caused by Biaxin, Lansoprazole, and Luvox. | The study observed 3500 strings of negotiations by the Latent Dirichlet Allocation (LDA) model in the US. | Able to automatically expand the training data or statistics. | Themes of the customer ADR information among diverse kinds of drugs can be very different.<br>Tweets and blogs are distinctive in nature from gathering posts.<br>(MedHelp forums). | 36 |
| 4. | WhatsApp and e-mail | Incitement techniques to move forward with hospital-based announcing ADR. | This process is conducted in hospitals and community pharmacies to upgrade the inspiration of reporting rate and to decrease detailing tasks. | Frequent update messages might increment the chance of unfavourable drug response detailing. | Accessibility of asset individuals in each hospital setting requires economic-related help.<br>Persistent updates can be interpreted as an obtrusion.<br>Enhance the possibility of copied data and wrong detailing. | 37 |

| Sl. No. | Social Media Platform | ADRs/Drug Safety Signal Detected | Study Description | Advantages | Limitations | References |
|---|---|---|---|---|---|---|
| 5. | PVPI App | Azithromycin causes nasal mucositis, itching in the eyes, and a metallic taste.<br>2.Metoprolol, Atenolol, and Amlodipine cause rashes and epigastric pain, increased coughing, and pedal oedema. | To describe ADR at any time in any place in India NCC (National Coordination Centre) PvPI has developed an ADR PvPI application. | Encourage ADR detailing by healthcare professionals as well as consumers with the support of initiator reports and picture attachments.<br>It could be a paperless, basic, user-friendly, and rapidly evaluated app. | Patients may need restorative information and would in this manner likely not be able to form high-quality reports.<br>Due to a lack of awareness patients are not effectively included. | 38 |
| 6. | PubMed | Acetaminophen might cause intense liver damage. | PubMed is the widely used database of scholarly articles which is updated regularly. | Huge or large documented database. | Clamor and information deficiency. | 39 |
| 7. | PatientsLikeMe | In 2010 Italian considered lithium carbonate to have the capacity to moderate the advance of Lou Gehrig's disease. | These individuals are allowed to insert information on their circumstances, treatment history, side effects, and symptoms. | Comprehensive longitudinal record organized into tables and graphs or diagrams. | Want to make certain that statistics are no longer skewed with the aid of a person's ADRs being reported in more than one instance inside a single database.<br>They should have to make sure a positive degree of coordination between the reporting of an ADR with online affected person communities and reporting to regulatory authorities. | 40 |

discharge summaries, laboratory test reports, nurse reports, and non-distinguished unfavourable occasions.[20] From the aspect of PV (Pharmacovigilance), the most significant benefit of EHRs is their capacity to undertake dynamic observation based on real-time data. Merits of EHR as compared to Safety Summary Reports (SRSs) include non-inclusion of duplicate data, no effect due to under or over-reporting as they regularly determined naturally, giving reliable data on the majority of the subject's drug exposure period, clinically significant occurrences and profitable data on uncovered subjects without occasions, and much more total appraisal of medicines introduction and co-morbidity status. Thus, EHR frameworks could be useful to create safety signals prior to the spontaneous reporting framework.

## Biomedical literature

Biomedical writing may give useful medical information from pre-clinical, clinical, observational, and case studies which may be ignored in general pharmacovigilance practices because it focuses on codified and organized SRSs information. Further, drug interaction reports are commonly reported in scientific journals and special reports, making medical writing the most significant and effective source for drug-interactions observation.[21]

## Social Media: Tools, Techniques and Limitations in drug safety signal detection

The extraordinary reach of the web and social media over a long time has driven a progressive move in how individuals are interacting with each other nowadays. Within the scope of Web 2.0, social media programmes and apps are quickly

**Table 2: Advantages and Limitations of Classical methods of drug safety signal detection.**

| Sl. No. | Method | Drug safety signal detection study conducted | Advantages | Limitations /disadvantages | References |
|---|---|---|---|---|---|
| 1 | Spontaneous Reporting System. | RRA of Liver-related ADR in Children-Based on China's National Spontaneous Reporting System. | | Selective reporting and underreporting. | 12, 56 |
| 1.1 | Proportional Reporting Ratio (PRR). | Biases in pharmacovigilance databases affecting the proportionate reporting ratio (PRR): the case of Sertindole. | The underreporting of adverse events does not affect the PRR. | Besides, indeed if reporting is total, it is once in a while conceivable to count the denominator or fundamental populace of users, so not one or the other frequency rates nor dangers can be computed.<br>The PRR is calculated from 'numerator data' only. | 48, 57 |
| 1.2 | Reporting Odds Ratios (ROR). | Comparison of data mining methodologies using Japanese spontaneous reports. | The bias that is reflected in the PRR can be removed by using the ROR. | Inconstancy in detailing fractions over time and over categories of drugs and antagonistic events will still make inductions from such information risky. | 48, 58 |
| 1.3 | Bayesian methods. | Data mining study on antipsychotic medications and cardiac muscle disorders in international pharmacovigilance. | Allows to evaluate model parameters, create model predictions, and perform model comparisons.<br>each drug-AE combination. | Common restriction of these strategies lies in the fact that the end of attention is subjectively selected because it does not automatically evaluate the signal produced. it is troublesome to judge whether or not the created information is reasonable. | 52, 59, 60 |
| 2. | Prescription Event Monitoring | Four prescription-event monitoring studies, in general, practice looked at sedation with "non-sedating" antihistamines. | Allows comparison of the safety profile of drugs belonging to the same therapeutic group.<br>Evaluate signals generated by other systems or databases. | No method to determine non-prescription medications<br>Data collection is an operationally difficult task. | 61 |
| 3. | Periodic Safety Update Report (PSUR). | Impact of PSUR system: A preliminary trial in a tertiary care teaching hospital in Southern India. | Provide an assessment of a medical product's risk-benefit balance for reporting by MAH at specific periods during the post-authorization process. | The recovery of data from the data lock point (DLP) as well as the era of line arranging and outline layout, are frequently the most time-consuming and rate-limiting processes for high-volume PSURs.<br>Outcome and clinical preparation required for case classification, account composing, coding of ADR, therapeutic survey, and hazard evaluation as well as the genuine composing of the PSUR. | 18, 62, 63 |

| Sl. No. | Method | Drug safety signal detection study conducted | Advantages | Limitations /disadvantages | References |
|---|---|---|---|---|---|
| 4. | Comparative Observational Studies. | An assessment of diverse healthcare professionals' knowledge, attitudes, and practices about India's pharmacovigilance system. | Provides notifications of rare (AEs) in early clinical trials or pre-marketing research.<br>Important information is provided about risk groups, risk factors, and clinical aspects of known adverse drug reactions. | Difficult to control variables since no control over the environment.<br>Leading to an account for confounders and bias.<br>Furthermore, time-intensive and expensive to conduct observational studies. | 64, 65 |

accessed as the go-to frame of social interaction. Pharma firms use digital media to connect with patients and build awareness about ailments and treatments, clinical trial enrollments, and ongoing support programmes. Social media stages, by plan, can work to extend connections between companies and healthcare customers. From this technique companies specifically interface, capture and energize patients and customers to report more ADR which is going unreported. In a social media setting, patients are likely to be correspondents themselves, without any affirmation of information from Healthcare Professionals (HCPs).[22] Adverse Event (AE) detection in social media research focused on drug identification. Drugs are also represented as chemicals or brand names in AE pairs of individual publications, which is a prerequisite for using statistical signal detection techniques. Reports have demonstrated that there are 66.6%, 59.9%, and 53.6% of users of mobile phones, tInternetnet and social media respectively of the total population worldwide (Figure 4). There are various social media tools and platforms which are useful in the collection of information related to the drug-associated ADRs. These include WEB-RADR (Web-Recognising Adverse Drug Reactions), Apps, Websites, Posts on Facebook, Twitter, WhatsApp etc.[23]

## WEB-RADR

The Innovative Medicine Initiative (IMI) WEB-RADR which identifies ADRs is an example of a public-private partnership alliance supported by IMI. Various stakeholders such as European regulatory agencies members, pharmaceutical industry persons, academicians, patient groups and other interest organizations involve in the pharmacovigilance. The WEB-RADR association has examined the esteem, moral and security concerns of open, patient-generated security data from social media stages and counts an extensive dataset of posts from online communities such as Facebook, Twitter, Reddit, and Inspire The core signal detection analysis used the following "foreground" datasets: From March 1, 2012, to March 31, 2015, approximately 4.2 million tweets (65%) along with Facebook (35%) posts were gathered. In addition, 42,721 posts were collected from the 407 patient forums.[24] ŧAs part of WEB-RADR, the concept of AE identification on Twitter was built utilizing a natural language processing workflow.[25]

## Websites

There are numerous websites that provide vital information regarding drugs, diseases, medicines, and ADRs associated with the medicines. For example; theBody.com tells you the effects of various herbs and supplements, which are associated with one disease (e.g. HIV/AIDS). The App includes a feature called HealthTracker that patients can use to record and keep track of their lab results, prescriptions, and a log of their daily activities. HealthTalkOnline.org is a website that contains many thorough details of people's positive and negative experiences with diseases and treatments.[26] Data from social media sites were analyzed using a program called Epidemico's MedWatcher Social platform, posts with product names were included, if required. Bayesian classifier removes the spam and duplication which can be improved by manual correction. Patient's messages may be used to understand the usage of medications in real life including inappropriate use of medicines. Several pilot studies have suggested that social media could be used to assess specific research problems in the real world, for example the usage of social media during pregnancy, misuse, abuse, and even advantages. In addition, dictionaries that can capture more informal and informal terms need further development to enable the collection and analysis of meaningful data.[3]

There are different computer approaches through which we can also collect ADRs data. Ontologies deal with the traditional explanation of the meaning of a hypothesis whereas Semantic mappings are mappings among ideas used in assorted systems with identical explanations. Observational Health Data Sciences and Informatics (OHDSI, http://ohdsi.org/), repository explains creation of a worldwide information resource to collect and store

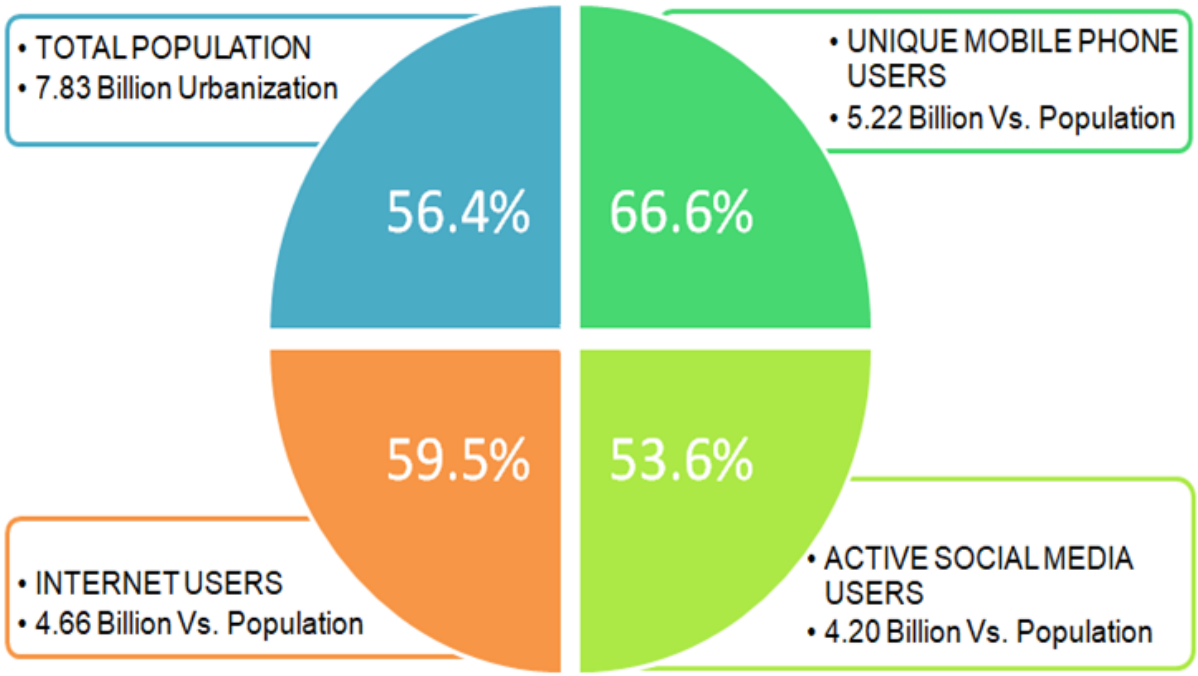


**Figure 4:** Social Media Users around the Globe.[23]

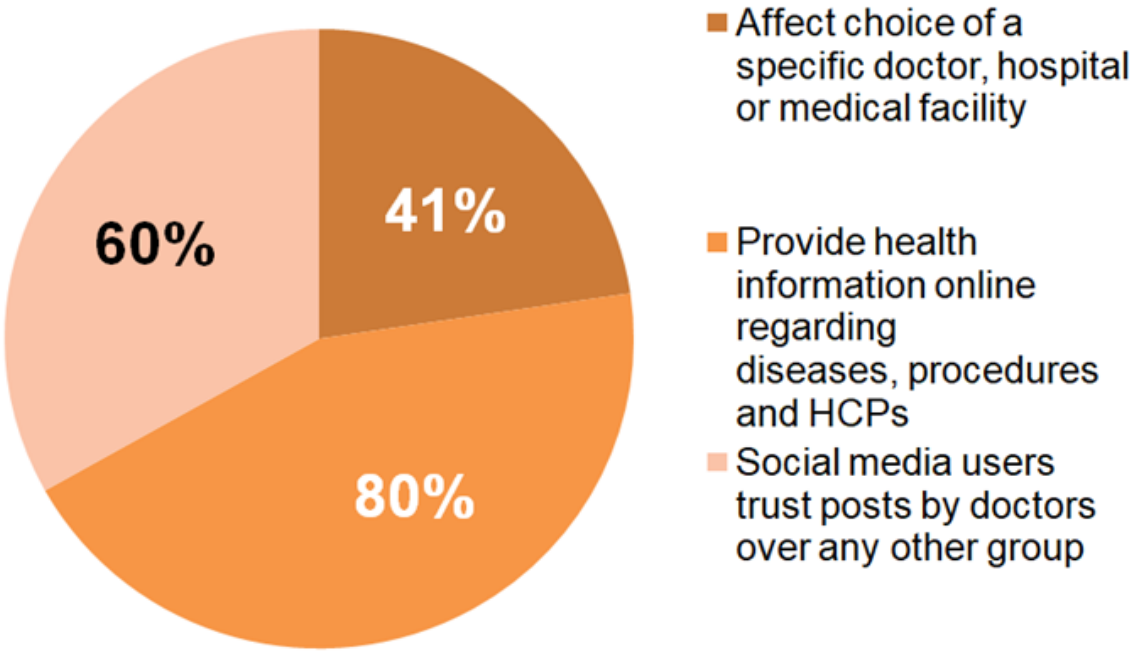


**Figure 5:** Contribution of Social Media in Healthcare.[30]

data for medicines from various electronic sources which are important for the safety of the drug.[27]

SAFER project (http://safer-project.eu/) is the webpage that creates a semantically upgraded stage for combinational signal observation by investigating assorted open-source signal detection methods, executions and freely accessible information. Taking into consideration the accessibility of different signal observation methods used as a source, (e.g. http://omop.org/MethodsLibrary, http://cran.rproject.org/web/packages/PhViD/, http://minisentinel.org/methods/methods_development/), open depot of connected information in connection with drug safety as well as activities for transparently displaying information about drug safety through programming workflow such as open FDA (https;//open.fda.org/), despite of many challenges,

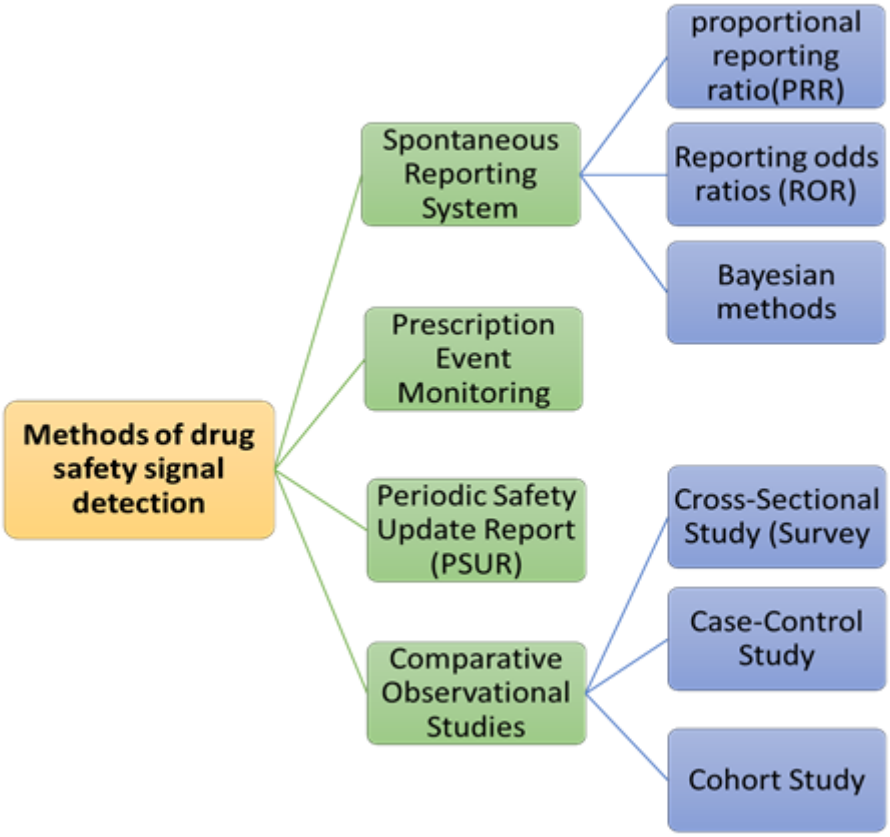


**Figure 6:** Methods of Drug Safety Signal Detection.[44]

consolidated detection of signals is attainable. PharmaMiner, is an implement pointing to strengthening computerized signal detection when using the Medical Dictionary for Regulatory Activities (MedDRA) to precise unfavourable events. The SALUS project (http://www.salusproject.eu/) built a semantic system and a committed toolkit to carry out this reason. The component of this toolkit encourages spontaneous reporting by pre-populating the individual forms with significant EHR information.[28]

## Posts on Facebook, Twitter, WhatsApp

Web community forums can be used to help doctors to collect and analyze useful health data, reliable and important data, and share it with patients, colleagues, and the general public. When considering interactions with patients, the amount of publicly available information and how this information could affect the patient should be considered. It is our perspective that composing a de-identified patient description employing tonnes of awareness on the various web community forums, comparable to the explanations distributed in books and treatment journals is not off-based in itself. Writing about certain patients and protecting their reputations can be more problematic than doctors realize, and potential privacy breaches have also been described in online posts on Twitter by medical students and by self-identified doctors.[29]

Due to the increasing popularity of social media platforms, it has become more prevalent for patients to share their health information (Figure 5). According to a survey conducted by the Pew Research Center, a number of caregivers and patients rely on social media to keep up with each other and share experiences. For example, caregivers (around 34%) and patients (around 20%) checked or observed someone else's comments or encounters on the internet. Furthermore, eleven percent of caregivers and six percent of patients share their interactions and attach their queries digitally. In relation to health monitoring, smoking cessation tendencies monitoring on Facebook, determining social groups user with frequent clinical experiences (such as drug usage), and keeping track of misconduct. Sharing information on their symptoms, treatments, and drug effects might provide valuable scientific data to both inpatients and the healthcare industry. Infectious/viral sickness monitoring can be advantageous by utilizing social media.[31]

Twitter gave the best number of (freely accessible) presents possibly significant on the two contextual investigations, we redressed an aggregate of 2537 posts in the US connected with rosiglitazone (anti-diabetic drug) and cardiovascular occasions including stroke and myocardial infarction, where most of the posts (around 98%) are addressing from Twitter. In addition, 41 and 2 posts were retrieved from Google+ and Facebook

respectively. Reposts or retweets post comprises only 10%. Despite the fact that Twitter has over 500 million subscribers, it was too 'juvenile' a source to utilize, especially for the contextual analysis on rosiglitazone. In May 2007, Twitter helped Avandia for less than a year at the time of the security alert given by the FDA (Food and Drug Administration) in its initial stage, still had not many supporters.[32]

The Healthcare system utilizes social media in different forms at various forums. Thus, these social media forums can be categorized into different including specialized healthcare social networks, generic social networking sites, and both specialized and generic which occupy 71.4%, 21.4%, and 7.2% of the total space of social media respectively. Further, specialized healthcare social networks and forums include MedHelp, Yahoo Groups, DailyStrength, WebMD, HealthBoards, ehaealthforum.com, diabetes.org, and others. While Facebook, Twitter, and Google+ are examples of generic social networking sites (Table 1).[33]

## Limitations of social media

Using social media to identify and report ADRs is also associated with certain kinds of limitations that should be taken into account. A few limitations are mentioned below.[41-43]

## Linguistic barrier in data collection

Sole-dependent groups need extensive training in statistics.

Risk of disclosure of patient information and personal data confirmation.

Quantification of accurate ADRs is difficult.

Incorporate obstacles with the validity, recency, uniqueness, recurrence, and striking nature of the information.

Information produced may consist of incorrect spellings, non-medical, and unclear terms describing health conditions.

Issues related to explanations due to an enormous amount of information.

Difficult to distinguish between people, but with the use of other personal assets, it may be easier.

Difficulty understanding the ethical issues raised by social media use.

Difficulty in ADR expression due to the involvement of complex wording.

## Classical methods of drug safety signal detection and their limitations

Clinical review of cases is used in conventional, qualitative approaches for signal detection. The large quantity of pharmaceutical items on the market necessitates the use of modern, quantitative ways to keep track of them.[44] There are various classical methods to detect drug safety signals such as qualitative signal detection, spontaneous reporting, PRO (Proportional Reporting Ratio), ROR (Reporting Odds Ratio), Bayesian methods, PEM (Prescription Event Monitoring), PSUR, Comparative Observational Studies, etc. (Table 2).

## Spontaneous Reporting System (SRS)

The SRS is generally considered a case reporting and case series type of method as it is often involved in the early discovery of novel, unusual, or serious ADR signals. Since the 1960s, voluntary investigating systems have been the primary origin of information for post-marketing pharmacovigilance. These are considered a passive method and comprise a survey of ADRs gathered voluntarily from HCPs (Healthcare Professionals), patients, and drug manufacturing industries, which are primarily managed by 'regulatory health agencies.' Yellow Card Scheme and MedWatch employed in the UK and USA respectively are examples of SRSs. Regulatory agencies of the USA and UK both employ SRS as active surveillance for a post-marketing survey of medicines. National pharmacovigilance systems depend significantly on spontaneous ADR reports provided by healthcare providers to ensure the safety of medicine after its market authorization. Healthcare workers and patients use spontaneous ADR reporting systems to notify any harmful effects to NCC which then, at that point, examine the ADRs, bringing about the detailing of speculation and the early location of signs. Further, ADR is sent to the UMC Uppsala. The concerned Institute may conduct more research to validate the safety signal or issue alerts and order manufacturers to incorporate the observed ADR in their pamphlets. The medicine may be withdrawn from the market if there are substantial ADRs.[45]

## Limitations of the spontaneous ADRs reporting systems

Absence of appropriate clinical subtleties on data, and auxiliary case audit is preposterous consistently.

Non-identification of every harmful effect as drug-induced events by healthcare professionals.

Selective and Under-reporting of ADRs-Under-reporting may occur because of an absence of information about the different parts of the voluntary investigating system due to a lack of awareness and knowledge about ADRs, pharmacovigilance, the criteria for reporting adverse events, and the ADR. This can result in ADR false positives and false negatives.[45]

## Non-reporting of real data due to misleading information.

### *Control data also isn't gathered like a component of an unexpectedly announced framework*

Despite the fact that spontaneous reporting is low-cost, it's not really the ultimate solution for post-market drug surveillance; however, we cannot ignore that it was and continues to be the primary tool for investigating early drug safety signals. The SRS is used to remove the majority of drugs from the market, demonstrating its effectiveness in detecting new safety signals[12] Various indicators including proportional reporting ratio, reporting odds ratio, and Bayesian theory-derived indicators are used in the spontaneous reporting data mining techniques (Figure 6).[46]

## Proportional Reporting Ratio (PRR)

It is the fraction to find all responses of interest using the total number of drug reports as the denominator (e.g. aids). This fraction can be compared to other drugs' values, and it is also possible to look at a comprehensive overview of adverse drug reaction reporting, with variations in the profile potentially representing signals. In a nutshell, it's the ratio of all recorded cases of an interesting event among those exposed to a given medication to the ratio of people exposed to all or several other medicines. It is also a Scale-Based Signal Generation Aid, which takes advantage of the huge database stability by calculating the proportions of specified reactions or collective reactions for drugs of interest, with many other drugs in the database representing the comparator. A proportional reporting ratio is the result of such a calculation.[47] PRRs have the advantage of being derived only from ADRs data collected spontaneously which are simple and easy to understand. If underreporting for the analyzed adverse event and all other adverse events reported in the database is of comparable magnitude, underreporting has no effect on the PRR.[48] One of the drawbacks of PRRs seems to be that exceptionally strong signals for a given drug can limit the numbers of the PRR for other drug-related signals. This is because a significant number of reports of a certain type substantially boost the drug's denominator. A recalculation of the PRRS that excludes those reports could be one way to address this issue.[47]

## Reporting Odds Ratios (ROR)

The ROR is the probability of a specific event occurring with your medical product versus the probability of the same event occurring with all other medicinal goods in the database. When the lower limit of the ROR's 95% Confidence Interval (CI) is greater than one, it is called a signal. The 95% confidence interval indicates the precision with which the ROR estimate was calculated. If the ROR is three, for example, the chances of this incident occurring with your pharmaceutical product are three times higher than the odds of this event occurring with all other reports in the database.[49] Biased estimation is a limitation of the PRR approach and can be resolved by applying a ROR with a set of predefined "control events" that can be used as a metric to evaluate the distribution of effects. Reporting rates are the same not only for "control events", but also for events that are of interest to a particular drug or other drugs. As a result, the ROR estimate may be preferred to the PRR measure for obtaining an impartial RR estimate.[46] Two sources of bias that are reflected in the PRR can be eliminated using the ROR. First, if the cases and controls are from diverse populations, it is more difficult to account for exposure dispersion. Second, a bias induced by incorporating cases in the denominator of the proportions used to calculate the PRR; this bias will be minor unless the instances evaluated account for a large proportion of all reported cases, but it will be completely eliminated if the ROR is used instead of the PRR.[48]

## Bayesian methods

Bayesian inference is a method of making inferences based on the probability distributions of unknown factors. On the other way, it is a process of fitting a theoretical model to observational data and abridging the results using the model's parameter probability distribution.[50] The Bayesian method was developed to generate signals in pharmacovigilance. It allows for estimating the model parameters, designing and building model forecasts, and performing model comparative studies.[51] The Bayesian Confidence Propagation Neural Network approach (BCPNN) and the Multi-item Gamma Poisson shrinker are also included (MGPS).[52]

## Prescription Event Monitoring (PEM)

It is a non-interventional proactive strategy for monitoring drug safety. It's a well-known post-marketing surveillance strategy for monitoring and ensuring the safety of newly marketed medicines for clinical use generally in 10,000 patients. A more targeted safety surveillance system known as Modified PEM (MPERM) is being implemented at the Drug Safety Research Unit in the United Kingdom. It is the combination of benefits of traditional PEM (which keeps track of the drug's overall safety as well as potential side effects) with safety concerns more focused on better understanding the known risks of the drug. Modified PEM extends by using enhanced data collection questionnaires that include a more comprehensive description of real-life drug usage, commitment to prescriptions, and focused assessment of occurrences requiring specific regulatory monitoring. Since it is impossible to detect all possible dangers for all prospective users during the medication research program, there may remain unanswered doubts about a medicine's safety at the time of marketing. Frequent pharmacovigilance, whether through self-reporting or extra-tailored post-marketing surveillance approaches like Prescription-Event Monitoring, is essential

and may raise the first suspicions of uncommon or rare safety problems (PEM)[53] Selection types have no effect on this type of monitoring and elimination criteria used in clinical trials, removing the possibility of selection bias. Patients or their doctors can then be addressed with a questionnaire to document any or all events. However, there are certain limits to this monitoring, such as the unknown percentage of unwanted side effects that go unnoticed by doctors[12]

## Periodic Safety Update Report (PSUR)

The International Conference on Harmonization (ICH) and the Council for International Organizations of Medical Sciences (CIOMS) have advised and provided recommendations on publishing regular safety updates on drugs. Subsequently, its applicability and utility in the current scenario of the pharmacovigilance programme have been reviewed and updated. It is widely accepted and gaining popularity as a standard worldwide in different countries such as European countries, Japan, and the USA. The PSUR contains information collected by healthcare professionals as well as consumers which is then communicated to the stakeholders in periodically manner.[18]

After getting a marketing license, Market Authorization Holders (MAHs) must keep an eye on their product's safety. As a result, they keep in continual contact with authorities to e The PSUR is among the most significant tools for MAHs and regulators to communicate once they have been approved. PSURs are meant to provide updated global experiences with the safety of a particular medicine. It comprises data from safety data from interventional, spontaneous reports, observational studies reports, and certain other relevant safety data. PSURs are intended to communicate, assess, and actively evaluate evolving safety data from all sources in relation to product exposure estimates, even if in general, the entire coverage of data sources may have limited.[54] Moreover, it is a summary report that is submitted to the regulatory authorities by the marketing authorization holder of a drug to report on the safety experience of the drug. The PSUR must be submitted to the authorities for all registered products.[12] PSURs must also be provided with applications to extend the first MA (marketing authorization) which is valid for 5 years in the European Union (EU). PSURs are created and assessed with significant resources by both regulatory bodies and MAHs. The results of these efforts, however, have not been clearly characterized.[55]

## Comparative Observational Studies

Spontaneous signal reports or case series can be validated using observational study techniques. These observational study designs may be categorized as follows:

## Cross-Sectional Study (Survey)

It is a study or survey that collects data from a cohort of patients at a moment in time or interval of time, independent of clinical condition or exposure. When data for serial time points can be obtained, it is utilized to look at the prevalence of disease at a single point in time or to look at patterns over time. In ecological analysis, these studies are also utilized to investigate the link between exposure and response. It's mostly used to collect information for surveys or ecological evaluations. There are some limitations, such as the inability to directly address the link between exposure and consequence.[12]

## Case-Control Study

This method identifies illness cases by selecting from the source population controls or patients who do not have the condition or event of interest. The odds ratio, which assesses the risk of disease, is used to compare the two groups' exposure status. This study is useful when a comprehensive relationship is present between drugs and adverse drug events or risk factors. The two groups' exposure status is then compared using the odds ratio. The odds ratio is a measure of how similar two groups are in terms of illness risk. It can be retrospective, descriptive, or observational type in order to identify the nature and extent of exposure. Other factors could confound the findings of these investigations.[55]

## Cohort Study

It's a prospective, observational study that tracks a group of people with similar features to see what kind of exposure they get and how much of it they get. In a cohort study, patients are followed over time to track the emergence of a disease or any suspected event in a group of people who are at risk for it. At each time of course and follow up the information about the use of medicine is accessed, and the incidence rate is calculated simultaneously. A special population (cohort of interest) is chosen based on the drug to be used and monitoring time duration, in many cohort studies. These studies are useful to calculate the prevalence rates of ADRs with relative risks and many ADRs can also be examined utilizing the same data source under the study. The main disadvantage is the time taken to reach an outcome of interest, as well as the effect of confounding variables, which calls their validity into question.[55]

## Legal aspects of using social media

The integration of digital information, specifically from social media, for the very same reason is known as digital public health surveillance. A lot of patients are engaging in social media sharing and posting health-related information.[43] Rather than focusing simply on spontaneously reported AEs which are underreported, social media-based collection of ADEs data is a proactive and patient-oriented approach, stating its strength and pros over

spontaneously reported AEs. Individuals may choose to disclose health-related information on social media, either inadvertently or on purpose, for a variety of reasons. Some require people to actively seek health information to be sought and disseminated it online in order for public health surveillance data to be collected.[66] Because it requires evaluating information in a free-text unstructured format, supervised learning is commonly used in digital surveillance systems to evaluate statistical properties with user-specified outputs.[67] There are ample posts and data available regarding the drug and associated ADRs but processing of the large data or text for the identification of adverse events on social media rely on machine learning tool such as Natural Language Processing (NLP). The aim of WEBRADR is to find out if social networks can make a scientific and public contribution to safety surveillance, as well as to assess the policy implications of using this secondary data. WEB-RADR collaborations will benefit from patient-generated drug safety data published from social media and patients' forums including a big dataset of posts from online patient groups such as Facebook, Twitter, Reddit, and Inspire. It generally investigates gender, ethics, and privacy matter. Different data sources have different qualities and applicability for PV.[24]

Studies have also been conducted to validate the usefulness of social media for drug safety signal detection since these platforms are also harboured or flooded with vague information. Because social media provides a potentially massive undiscovered source of data on direct patients' experiences that could be crucial for drug safety, it must be validated. Regulatory authorities believe that mining social media is a way to collect additional data in order to supplement existing systems that are already voluntary.[43]

- The FDA does not have any formal standards for pharmacovigilance on social media. The FDA, on the other hand, has issued guidelines for posting promotional materials and risk/benefit information on social media.
- ADRs via social media still can be reported to the FDA, despite the lack of official guidance. The ADR report must include a similar basic data set as the ABPI report (Association of the British Pharmaceutical Industry).
- Recently, the FDA issued a statement stating that social media ADR reports are scrutinized in the same way that other spontaneous reporting systems are scrutinized with a caveat that the reports might not always be of the highest quality.

For fear of creating an excessive number of adverse event reports that must be entered into business safety databases and reported to regulators, MAHs have been hesitant to deal with social media as a data provider for drug safety. Module VI17 of the Good Pharmacovigilance Practice Guidelines in Europe says "If MAH becomes aware of a report of a suspected adverse reaction described on any digital media that is not promoted by the company, the report should be evaluated to see if it is eligible for filing as an Individual Corps Safety Report (ICSR)".[3] There are chances to collect data from social media which are not directly related to humans. There are many reasons that may cause mistrust in public health information and intentions. As a result, particular behaviours or groups may be stigmatized as a substitute for the genuine underlying risk factors. Public trust is hampered by false alarms and missed cases by surveillance systems.

- In a clinical setting, reporting certain diseases is usually authorized by law, medical experts have their own set of ethics, and data is gathered specifically for health reasons. The Health Insurance Portability and Accountability Act (HIPAA) cover the medical data of medical institutions. While patients may expect that their medical information will be used by health agencies to track public health, it's not the case with social media.
- There is no legal need that social media data to be reported for public health purposes. There are also not any standard ethics for social media creators. Therefore, users might not anticipate their information being utilized to track public health trends. Data may be non-health related.
- Privacy concerns have recently been raised about social media sites and other online platforms.
- From a legal aspect, the Terms and Conditions cover consent, however, due to the intricacy of the text and the number of conditions, "informed consent" has been a source of concern.
- Despite measures such as the European Union's General Data Protection Regulation, the confidentiality and permission of online data collecting are in a state of flux. Because electronic information is mostly made up of non-health information, it's unclear if informed consent for individual-level health information can be violated.

The systems are under budget, but managing and analyzing the data requires automated procedures. These technologies could cost a lot of money to get started, and they'll need to be maintained on a regular basis to keep the algorithms fresh. Because the data obtained by these private companies is confidential, and there is no legal requirement that data be shared with public health, the companies' foundational algorithms must be updated on a regular basis, and permission can be changed at any time without notice.[3] If permission is denied, the funds allocated to the development of digital surveillance would be wasted. The implications of this can be that there is no guarantee that proprietary algorithms can be cancelled at any time and are not always replicable. Data demands regarding legal mandates may be an infringement of personal autonomy. Users contribute their data directly using Web-based

surveys in some surveillance systems, such as FluNearYou and Influenzanet.[66]

Because of concerns about access and privacy, the data available for pharmacovigilance is limited as society's use of social media grows. Furthermore, the unregulated nature of social media posts as well as the use of colloquial and nonmedical terminology makes systematic data mining difficult. The study found that there is not enough evidence that social media signal discovery matches other database systems or any other traditional method. Therefore, it is the need of hours to frame guidelines to consider the valid information gathered from social media thus it can be useful for the safety purpose of the medicines.[3]

### Future Perspectives

The internet is a great way to gather medication and device adverse event reports, especially from public healthcare providers. Traditional adverse events reporting data or data derived from health and reimbursement records have several advantages over social data. Social reports are more relevant because they are based on real-time data. Patients are more likely to be the reporters in a social media situation, without any validation from Health Care Professionals (HCPs). The credibility and source of these self-generated reports are important considerations. Furthermore, many elderly people do not utilize social media, which is significant because this produces a strong user bias for PV since this cohort is a big user of prescription drugs. To investigate the potential for detecting ADR through online healthcare forums, we suggested using association mining and Proportional Reporting Ratios (PRRs) to identify intriguing drug-side effect relationships. More robust statistical signal detection procedures may be necessary to account for the volatility of social media data sources. In the future, it will be necessary to address significant challenges such as identifying duplicate safety information in data arising from digital media, and multiple languages and how data collected from different languages waypoints to standard ADR, data protection and personal information protection issues, and data curation and cleaning.

## CONCLUSION

Patients' posts reveal how they utilize medications in their daily lives and how they are misused. They also share their own experiences with their medications and their effects in an attempt to elevate their quality of life. The statistical algorithms used to assess if an Adverse Event (AE) is being reported disproportionately in advanced systems are affected by biases in the data. The most challenging step is compiling a systematic glossary with consistent data, as a result, it is difficult to identify the accurate signals. Now the question arises whether social media monitoring is a good enough method for signal detection. In our opinion, more research is needed before it can be considered a stand-alone signal-detecting source. Until then, there may be some instances when social media data can be used to supplement traditional data sources or in signal analysis.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**ADEs:** Adverse Drug Events; **ADR:** Adverse Drug Reactions; **AEs:** Adverse Event; **AMCs:** Adverse Drug Reaction Monitoring (Pharmacovigilance) Centre; **APCDs:** All-Payer Claims Databases; **BCPNN:** Bayesian Confidence Propagation Neural Network; **CDSCO:** Central Drugs Standard Control Organization; **CEM:** Cohort Event Monitoring; **CIOMS:** Council for International Organizations of Medical Sciences; **CMS:** Centers for Medicare and Medicaid Services; **DLP:** Data Lock Point; **EHD:** Electronic Healthcare Data; **EHRs:** Electronic health records; **FDA:** Food and Drug Administration; **HCPs:** Healthcare providers; **HIPAA:** Health Insurance Portability and Accountability Act; **ICH:** International Conference on Harmonization; **ICSR:** Individual Corps Safety Report; **ICSRs:** Individual Case Safety Reports; **IMI:** Innovative Medicine Initiative; **ISPE:** International Society of Pharmacoepidemiology; **LLT:** Lower-Level Terms; **MAHs:** Market Authorization Holders; **MedDRA:** Medical Dictionary for Regulatory Activities; **MGPS:** Multi-Item Gamma Poisson Shrinker; **MPERM:** Modified PEM (Prescription event monitoring); **NLP:** Natural Language Processing; **OHDSI:** Observational Health Data Sciences and Informatics; **PE:** pharmacoepidemiologic; **PEM:** Prescription event monitoring; **PRR:** proportional reporting ratio; **PSUR:** Periodic Safety Update Report; **PV:** Pharmacovigilance; **PvPI:** Pharmacovigilance Programme of India (PvPI); **ROR:** Reporting Odds Ratios; **RRA:** Relative Risk Analysis; **SRSs:** Safety Summary Reports; **UMC:** Uppsala Monitoring Center; **WEB-RADR:** Web-Recognizing Adverse Drug Reactions; **WHO:** World Health Organization.

## SUMMARY

This manuscript discusses the importance of drug safety in drug development and highlights the role of social media in detecting adverse drug reactions. Social media is a real-time platform for patients to share their experiences and medication usage. It has the potential to complement traditional data sources for signal detection. Patients actively seek and exchange health-related information on various social networks, including LinkedIn, Facebook, and Twitter. The manuscript acknowledges the

challenges of data bias and the need for a systematic glossary in social media-based pharmacovigilance. It concludes that social media can be a useful tool for signal detection but requires further research to establish its reliability.

## REFERENCES


1. Pontes H, Clément M, Rollason V. Safety signal detection: the relevance of literature review. Drug Saf. 2014;37(7):471-9. doi: 10.1007/s40264-014-0180-9, PMID 24895178.
2. Malikova MA. Practical applications of regulatory requirements for signal detection and communications in pharmacovigilance. Ther Adv Drug Saf. 2020;11:2042098620909614. doi: 10.1177/2042098620909614, PMID 32313617.
3. Rees S, Mian S, Grabowski N. Using social media in safety signal management: is it reliable? Ther Adv Drug Saf. 2018;9(10):591-9. doi: 10.1177/2042098618789596, PMID 30283627.
4. Yang CC, Yang H, Jiang L, Zhang M 2012. Social media mining for drug safety signal detection. doi: 10.1145/2389707.2389714. Paper presented at the Proceedings of the 2012 international workshop on Smart health and wellbeing.
5. Caster O, Dietrich J, Kürzinger ML, Lerch M, Maskell S, Norén GN, *et al.* Assessment of the utility of social media for broad-ranging statistical signal detection in pharmacovigilance: results from the WEB-RADR project. Drug Saf. 2018;41(12):1355-69. doi: 10.1007/s40264-018-0699-2, PMID 30043385.
6. Pappa D, Stergioulas LK. Harnessing social media data for pharmacovigilance: a review of current state of the art, challenges and future directions. Int J Data Sci Anal. 2019;8(2):113-35. doi: 10.1007/s41060-019-00175-3.
7. [cited 2022]. Available from: https://view.publitas.com/uppsala-monitoring-centre/signal-detection-for-national-pharmacovigilance-centres-with-small-data-sets/page/1/.
8. Delamothe T. Reporting adverse drug reactions. Br Med J. 1992;304:465.
9. Garlapati S, Priyanka S. Cradles of signals for pharmacovigilance process. J Pharmacovigilance. 2014;3(1):e126. doi: doi \t "_blank" 10.4172/2329-6887.1000e126.
10. Ibrahim H, Abdo A, El Kerdawy AM, Eldin AS. Signal detection in pharmacovigilance: a review of informatics-driven approaches for the discovery of drug-drug interaction signals in different data sources. Artif Intell Life Sci. 2021;1:100005. doi: 10.1016/j.ailsci.2021.100005.
11. Bihan K, Lebrun-Vignes B, Funck-Brentano C, Salem JE. Uses of pharmacovigilance databases: an overview. Thérapie. 2020;75(6):591-8. doi: 10.1016/j.therap.2020.02.022, PMID 32169289.
12. Kumar A, Khan H. Signal detection and their assessment in pharmacovigilance. PharmSci. 2015;2(1):66-73. doi: 10.2174/1874844901502010066.
13. Suku CK, Hill G, Sabblah G, Darko M, Muthuri G, Abwao E, *et al.* Experiences and lessons from implementing cohort event monitoring programmes for antimalarials in four African countries: results of a questionnaire-based survey. Drug Saf. 2015;38(11):1115-26. doi: 10.1007/s40264-015-0331-7, PMID 26267842.
14. Heeley E, Wilton LV, Shakir SAW. Automated signal generation in prescription-event monitoring. Drug Saf. 2002;25(6):423-32. doi: 10.2165/00002018-200225060-00006, PMID 12071779.
15. Ferreira G. Prescription-event monitoring: developments in signal detection. Drug Saf. 2007;30(7):639-41. doi: 10.2165/00002018-200730070-00015, PMID 17604421.
16. Shibata A, Hauben M. Pharmacovigilance, signal detection and signal intelligence overview 14th International Conference on Information Fusion; 2011. p. 1-7.
17. Amale PN, Deshpande SA, Nakhate YD, Arsod NA. Pharmacovigilance process in India: an overview. J Pharmacovigil. 2018;6(2):259.
18. Klepper MJ. The periodic safety update report as a pharmacovigilance tool. Drug Saf. 2004;27(8):569-78. doi: 10.2165/00002018-200427080-00008, PMID 15154828.
19. Mann RD, Andrews EB. Pharmacoepidemiology of hormone therapy: an evolving picture. In: Pharmacovigilance. 2nd ed. John Wiley and Sons; 2007. p. 571-581DOI. doi: 10.1002/9780470059210.
20. Wysowski DK, Swartz L. Adverse drug event surveillance and drug withdrawals in the United States, 1969-2002: the importance of reporting suspected reactions. Arch Intern Med. 2005;165(12):1363-9. doi: 10.1001/archinte.165.12.1363, PMID 15983284.
21. Kostoff R. The extraction of useful information from the biomedical literature. Acad Med. 2001;76(12):1265-70. doi: 10.1097/00001888-200112000-00025, PMID 11739057.
22. Powell GE, Seifert HA, Reblin T, Burstein PJ, Blowers J, Menius JA, *et al.* Social media listening for routine post-marketing safety surveillance. Drug Saf. 2016;39(5):443-54. doi: 10.1007/s40264-015-0385-6, PMID 26798054.
23. Chaffey D, Ellis-Chadwick F. Digital marketing. 7th ed. uk: Pearson; 2019.
24. van Stekelenborg J, Ellenius J, Maskell S, Bergvall T, Caster O, Dasgupta N, *et al.* Recommendations for the use of social media in pharmacovigilance: lessons from IMI WEB-RADR. Drug Saf. 2019;42(12):1393-407. doi: 10.1007/s40264-019-00858-7, PMID 31446567.
25. Gattepaille L, Vidlin SH, Bergvall T, Ellenius J. Adverse event recognition in tweets: results from a WEB-RADAR project. Drug Saf. 2018;41(11):1160-1.
26. Edwards IR, Lindquist M. Social media and networks in pharmacovigilance: boon or bane? Drug Saf. 2011;34(4):267-71. doi: 10.2165/11590720-000000000-00000, PMID 21417499.
27. Boyce RD, Ryan PB, Norén GN, Schuemie MJ, Reich C, Duke J, *et al.* Bridging islands of information to establish an integrated knowledge base of drugs and health outcomes of interest. Drug Saf. 2014;37(8):557-67. doi: 10.1007/s40264-014-0189-0, PMID 24985530.
28. Koutkias VG, Jaulent MC. Computational approaches for pharmacovigilance signal detection: toward integrated and semantically enriched frameworks. Drug Saf. 2015;38(3):219-32. doi: 10.1007/s40264-015-0278-8, PMID 25749722.
29. Chretien KC, Kind T. Social media and clinical care: ethical, professional, and social implications. Circulation. 2013;127(13):1413-21. doi: 10.1161/CIRCULATIONAHA.112.128017, PMID 23547180.
30. [cited Jan 25, 2022]. Available from: https://www.creatopy.com/blog/social-media-healthcare/.
31. Nikfarjam A, Sarker A, O'connor K, Ginn R, Gonzalez G. Pharmacovigilance from social media: mining adverse drug reaction mentions using sequence labeling with word embedding cluster features. J Am Med Inform Assoc. 2015;22(3):671-81. doi: 10.1093/jamia/ocu041, PMID 25755127.
32. Coloma PM, Becker B, Sturkenboom MCJM, Van Mulligen EM, Kors JA. Evaluating social media networks in medicines safety surveillance: two case studies. Drug Saf. 2015;38(10):921-30. doi: 10.1007/s40264-015-0333-5, PMID 26242616.
33. [cited Jan 26, 2022]. Available from: https://asset.jmir.pub/assets/e07a095cbb59aaaa6e34f6a9d076b809.png/.
34. Lardon J, Bellet F, Aboukhamis R, Asfari H, Souvignet J, Jaulent MC, *et al.* Evaluating Twitter as a complementary data source for pharmacovigilance. Expert Opin Drug Saf. 2018;17(8):763-74. doi: 10.1080/14740338.2018.1499724, PMID 29991282.
35. [cited 2022]. Available from: https://www.emich.edu/chhs/health-sciences/programs/clinical-research-administration/documents/research/does-adverse-event-reporting-by-consumers-via-socialonline-media-platforms-impact-the-drug-safety-profile.pdf/.
36. Yang M, Kiang M, Shang W. Filtering big data from social media Building an early warning system for adverse drug reactions. J Biomed Inform. 2015;54:230-40. doi: 10.1016/j.jbi.2015.01.011, PMID 25688695.
37. Thota A, Sarkar S, Guptha S, Thota P. Stimulated adverse drug reaction reporting in pharmacovigilance: Indian Perspectives. J Pharmacovigilance Drug Res. 2021;2(2):13-8. doi: 10.53411/jpadr.2021.2.2.4.
38. Prakash J, Joshi K, Malik D, Mishra O, Sachan A, Kumar B, *et al.* "ADR PvPI" android mobile app: report adverse drug reaction at any time anywhere in India. Indian J Pharmacol. 2019;51(4):236-42. doi: 10.4103/ijp.IJP_595_18, PMID 31571709.
39. Natsiavas P, Maglaveras N, Koutkias V. A public health surveillance platform exploiting free-text sources via natural language processing and linked data: application in adverse drug reaction signal detection using PubMed and Twitter. In: Knowledge representation for health care. Springer; 2017. p. 51-67. doi: 10.1007/978-3-319-55014-5_4, PMID PubMed.
40. Gibson S. The role of the Internet in expanding consumer-driven adverse drug reaction reporting. Available at SSRN. SSRN Journal. SSRN Journal. 2012. doi: 10.2139/ssrn.2342008.
41. Sloane R, Osanlou O, Lewis D, Bollegala D, Maskell S, Pirmohamed M. Social media and pharmacovigilance: a review of the opportunities and challenges. Br J Clin Pharmacol. 2015;80(4):910-20. doi: 10.1111/bcp.12717, PMID 26147850.
42. Shrestha S, Palaian S, Shrestha B, Santosh KC, Khanal S. The potential role of social media in pharmacovigilance in Nepal: glimpse from a resource-limited setting. J Clin Diagn Res. 2019;13(3). doi: 10.7860/JCDR/2019/39979.12693.
43. Sarker A, Ginn R, Nikfarjam A, O'Connor K, Smith K, Jayaraman S, *et al.* Utilizing social media data for pharmacovigilance: a review. J Biomed Inform. 2015;54:202-12. doi: 10.1016/j.jbi.2015.02.004, PMID 25720841.
44. [cited 2022]. Available from: https://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.618567/.
45. Alomar M, Tawfiq AM, Hassan N, Palaian S. Post marketing surveillance of suspected adverse drug reactions through spontaneous reporting: current status, challenges and the future. Ther Adv Drug Saf. 2020;11:2042098620938595. doi: 10.1177/2042098620938595, PMID 32843958.
46. Ooba N, Kubota K. Selected control events and reporting odds ratio in signal detection methodology. Pharmacoepidemiol Drug Saf. 2010;19(11):1159-65. doi: 10.1002/pds.2014, PMID 20669233.
47. Evans SJW, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. Pharmacoepidemiol Drug Saf. 2001;10(6):483-6. doi: 10.1002/pds.677, PMID 11828828.
48. Rothman KJ, Lanes S, Sacks ST. The reporting odds ratio and its advantages over the proportional reporting ratio. Pharmacoepidemiol Drug Saf. 2004;13(8):519-23. doi: 10.1002/pds.1001, PMID 15317031.
49. [cited 2022]. Available from: https://allaboutpharmacovigilance.org/43-reporting-odds-ratio-ror/.
50. Ranjan A, Tripathi A, Saurabh A, KalaiSelvan V, Gupta R. Signal detection in pharmacovigilance: an application of subjective Bayesian inference. Adv Pharmacoepidemiol Drug Saf. 2016;5(207):2167-1052.1000207.

51. Prieto-Merino D, Quartey G, Wang J, Kim J. Why a Bayesian approach to safety analysis in pharmacovigilance is important. Pharm Stat. 2011;10(6):554-9. doi: 10.1002/pst.524, PMID 22140036.
52. Chen M, Zhu L, Chiruvolu P, Jiang Q. Evaluation of statistical methods for safety signal detection: a simulation study. Pharm Stat. 2015;14(1):11-9. doi: 10.1002/pst.1652, PMID 25329607.
53. Layton D, Hazell L, Shakir SAW. Modified prescription-event monitoring studies: a tool for pharmacovigilance and risk management. Drug Saf. 2011;34(12):e1-9. doi: 10.2165/11593830-000000000-00000, PMID 22077508.
54. Ebbers HC, Mantel-Teeuwisse AK, Sayed-Tabatabaei FA, Moors EHM, Schellekens H, Leufkens HGM. The role of Periodic Safety Update Reports in the safety management of biopharmaceuticals. Eur J Clin Pharmacol. 2013;69(2):217-26. doi: 10.1007/s00228-012-1317-3, PMID 22706615.
55. Mulchandani R, Kakkar AK. Reporting of adverse drug reactions in India: a review of the current scenario, obstacles and possible solutions. Int J Risk Saf Med. 2019;30(1):33-44. doi: 10.3233/JRS-180025, PMID 30175985.
56. Guo YM, Ge FL, Song HB, Xiong P, Jing J, Niu M, *et al.* Relative risk analysis of liver-related adverse drug reactions in children based on Chinese national spontaneous reporting system. J Pediatr. 2021;234:85-91. doi: 10.1016/j.jpeds.2021.03.044, PMID 33794217.
57. Moore N, Hall G, Sturkenboom M, Mann R, Lagnaoui R, Begaud B. Biases affecting the Proportional Reporting Ratio (PRR) in spontaneous reports pharmacovigilance databases: the example of sertindole. Pharmacoepidemiol Drug Saf. 2003;12(4):271-81. doi: 10.1002/pds.848, PMID 12812006.
58. Kubota K, Koide D, Hirai T. Comparison of data mining methodologies using Japanese spontaneous reports. Pharmacoepidemiol Drug Saf. 2004;13(6):387-94. doi: 10.1002/pds.964, PMID 15170768.
59. Haramburu AI, F Vol. I. Ahmed I, Haramburu F, Fourrier-Réglat A, Thiessard F, Kreft-Jais C, Miremont-Salamé G, *et al.* Bayesian pharmacovigilance signal detection methods revisited in a multiple comparison setting. Stat Med. 2009;28(13):1774-92. doi: 10.1002/sim.3586, PMID 19360795.
60. Coulter DM, Bate A, Meyboom RHB, Lindquist M, Edwards IR. Antipsychotic drugs and heart muscle disorder in international pharmacovigilance: data mining study. BMJ. 2001;322(7296):1207-9. doi: 10.1136/bmj.322.7296.1207, PMID 11358771.
61. Mann RD, Ferner RE, Pearce GL, Dunn N, Shakir S. Sedation with 'non-sedating' antihistamines: four prescription-event monitoring studies in general practice commentary: reporting of adverse events is worth the effort. BMJ. 2000;320(7243):1184-6.
62. [cited 2022]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vii-periodic-safety-update-report_en.pdf/.
63. Lokhande AK, Prabhu MM, Mallayasamy SR, Thunga G, Unnikrishnan MK. Impact of periodic safety update reporting system: A preliminary trial in a tertiary care teaching hospital of southern India. J App Pharm Sci. 2018;8(12):112-23. doi: 10.7324/JAPS.2018.81213.
64. Gilmartin-Thomas JFM, Liew D, Hopper I. Observational studies and their utility for practice. Aust Prescr. 2018;41(3):82-5. doi: 10.18773/austprescr.2018.017, PMID 29922003.
65. Bepari A, Niazi SK, Rahman I, Dervesh AM. The comparative evaluation of knowledge, attitude, and practice of different health-care professionals about the pharmacovigilance system of India. J Adv Pharm Technol Res. 2019;10(2):68-74. doi: 10.4103/japtr.JAPTR_4_19, PMID 31041185.
66. Aiello AE, Renson A, Zivich PN. Social media and internet-based disease surveillance for public health. Annu Rev Public Health. 2020;41:101-18. doi: 10.1146/annurev-publhealth-040119-094402, PMID 31905322.
67. Gavrielov-Yusim N, Kürzinger ML, Nishikawa C, Pan C, Pouget J, Epstein LBH, *et al.* Comparison of text processing methods in social media based signal detection. Pharmacoepidemiol Drug Saf. 2019;28(10):1309-17. doi: 10.1002/pds.4857, PMID 31392844.


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