Does Adverse Event Reporting by Consumers Via Social/Online Media Platforms Impact the Drug Safety Profile?

By

Jaspreet Singh

Special Project

Submitted to the School of Health Sciences

Eastern Michigan University

In partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

In

Clinical Research Administration

April 16, 2020

Ypsilanti, Michigan

Acknowledgments

First and foremost, I would like to thank my parents who have supported me financially and emotionally throughout my life. I can only pray for their wellbeing and longevity.

I also would like to express my gratitude for Professor Dr. Irwin G Martin for his feedback on this project and for facilitating me in reaching milestones throughout this project. His ingenuity and constructive criticism on this project helped me to stay focused on my topic. Without his unconditional support, this project was not possible.

I am equally thankful and indebted to my advisor and Professor Dr. Stephen Sonstein for granting me admission into this wonderful program. This is an exceptionally well-organized and concrete curriculum and I feel fortunate to be a part of this program. Finally, I would like to thank my peers, library associates, my ESLN professor Ms. Kay Stremler for being supportive and guiding me in the right direction.

Abstract

Social media has become an active platform where consumers can report adverse events associated with drugs. Twitter and Facebook are the leading social media sites where most of the adverse drug events are reported. Websites such as patientlikeme.com are also used to identify the reported drug events. Through these reports, it is possible to improve a drug's safety profile.

The purpose of this research paper was, therefore, to attempt to evaluate the validity of adverse event reporting by consumers via social and online media platforms and to understand whether these reporting mediums, in any sense, affect or improve the safety profile of a prescription drug. The main methodology employed was an analysis of the latest data on the number of adverse drug events reported on social media sites. The second approach was to determine the social media site frequently used to report adverse drug events. Finally, the impacts of the adverse drug event reports on the drug safety profile and consumer feedback on how they reported from the events were determined.

The results show that ADRs posted on social media can be used to promote drug safety profile. Besides, the increasing use of social media to report adverse drug events increases its reliability in promoting drug safety. Key social media and online platforms used are Facebook, Twitter and PatientLikeMe.

Keywords: *social media, adverse events, Patientslikeme.com, Food and Drug Administration (FDA), drug safety, pharmacovigilance.*

Contents

List of Tables

Chapter One: Introduction

Background

The pharmaceutical arena is an extremely dynamic environment with stringent regulations and adherence to compliance standards enacted by regulatory agencies is of paramount importance [1]. Inarguably, the most volatile aspect of the pharmaceutical is pharmacovigilance, also known as drug safety [2]. Pharmacovigilance stands for proper detection, assessment, understanding, and reporting of adverse effects or any other possible drug-related problem [2] for an approved drug. After the thalidomide disaster in the early 1960s, regulations were enacted to require expedited reporting of all the serious adverse events and periodically non-serious reports to the FDA [3]. Under the current Federal Food, Drug and Cosmetic Act, all drug manufacturers are bound by law to report adverse events (AEs) to FDA [2]. This is usually done by pharmacovigilance groups -both in-house and contractual- which on the behalf of the manufacturing authorization holder (MAH), receive and process individual case reports received spontaneously from consumers, health care professionals, and specialty pharmacies and send them to regulatory agencies promptly [4]. The safety group also ensures that only reports which fit the criteria of reporting should be sent to FDA by triaging and determining whether a particular report meets the seriousness criteria and contain the basic 4 elements: i) An identifiable patient; ii) An identifiable reporter (the patient can report the adverse event on his behalf); iii) a suspect drug or a biological product, and iv) an adverse event (serious or fatal) [4].

Social media is among the latest technologies that play a critical role in the identification of adverse drug reactions and maintaining a high drug safety profile. Social media sites such as

Facebook and Twitter can improve the reporting of adverse drug reactions and useful information on drug safety [5]. Data from social media posts can be analyzed to determine how to report ADRs [5]. There is ongoing research on the role of social media in improving the level of drug safety [6]. However, there is inadequate research on the impact of the role of social media in promoting drug safety profile through the ADRs.

Purpose and Objectives of the Study

The purpose of this study is to determine if reporting adverse drug events on social media can help to promote drug safety profile. The growth of social media has had implications on many sectors including health care. With the number of adverse drug reports being made on social media, particularly Facebook and Twitter, it is important to consider the efficacy of social media as a reliable tool in promoting drug safety.

Objectives

The study seeks to address the following two objectives.

I. To determine if the social/online platform is commonly used to report adverse drug events.
II. To establish the impact of adverse drug events reporting through social media/online platforms on the drug safety profile.

Research Question/Hypotheses

Does Adverse Event reporting by consumers via Social/Online Media Platforms impact the Drug Safety profile?

Hypotheses

H#1: Social/online platform is commonly used to report adverse drug events.

H#2: Social media ADRs can promote the level of drug safety profile.

Literature Review

Maintaining a high level of drug safety is still a challenge in the pharmaceutical industry [3]. Before introducing any drug for clinical trials, several tests are done to ensure the level of safety is high [4]. The safety of any drug depends upon other factors as well which can be controlled, albeit, to a limited extent only [7]. The monitoring of drug effects and adverse events associated with a particular drug improves the level of patient safety. An adverse event under 21CFR 314.80 of FDA's regulations is defined as any adverse event in association with the use of a drug by a human (regardless being determined of a possible causality) involve the following: an adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action [8]. After the thalidomide disaster, FDA mandated reporting of all adverse events for all the approved drugs [9]. The MAH has specialized departments who handle the reporting of adverse events to the FDA. For instance, any death, life-threatening event (unlisted/unexpected/unlabeled), irrespective of its causality, should be submitted to FDA in 7 calendar days from the date of awareness of the event [10]. These timeframes are strictly followed by pharmacovigilance groups to update the FDA of any event signals. This type of reporting is often known as traditional reporting. It has assisted FDA in making real-time decisions in alerting manufacturers about their drugs or even recalling a drug based on the abrupt

signals which indicate that the drug is leading to more serious adverse events than had been anticipated. Many times, the manufacturers are advised to add a certain event in the drug labeling under the list of side-effects list so that the patients and the health care professional are well informed about the product and can establish the benefit vs. risks

The FDA has classified and divided the adverse events types, each of which has a multitude of different reporting patterns or requirements which the pharmacovigilance group has to adhere to. There are divided into 4 different types of groups- i) serious and unlisted, which means the event falls under the serious (death, hospitalization, a congenital defect, significant persistent disability/incapacity) and is not considered listed. By unlisted, it simply means not listed on the package insert or being considered labeled; ii) serious and listed; iii) non-serious and unlisted; iv) non-serious and listed [8,10]. Reporting of adverse events to different agencies fulfill the basic need of knowing more about the drug and what type of side effects patients are experiencing with these types of drugs. This is also known as post-marketing surveillance. So, this system of adverse event reporting has had success in reducing the second thalidomide to occur again. For instance, nomifensine (Merital®) which was indicated for depression was in the German market since 1976 and was prescribed to more than 10 million patients before its marketing began in the US in 1985. Initial side effects were recognized as long term reversible hypersensitivity or allergic reactions in the liver and causing hemolytic anemia and eosinophilia [9]. When FDA approved nomifensine, only 20 reported cases of hemolytic anemia were known and none of them were fatal. In the year 1985, when adverse event reports indicated that hemolytic anemia could be fatal, an extensive revision underwent in the labeling to reflect the seriousness caused by the drug [9]. On January 21, 1986, the manufacturer decided to withdraw

nomifensine from the market due to a high volume of hemolytic anemia cases being experienced [9,10].

Reporting of Adverse Events: Regulations and Law

The reports are made to FDA either by health care professionals directly or via manufacturer are called spontaneous reporting [6,11]. Reporting an adverse event whether it is associated with a particular drug or not by any health care professional is not essentially mandatory and falls under voluntary reporting. The manufacturers and distributors of FDA approved drugs or biologics, as well as medical devices, are bound by regulations to submit all the adverse event reports to the FDA on time. Under the FDC Act, the FDA has the right to analyze and evaluate the safety of the compound and when appropriate intervene and recommend appropriate steps for the manufactures to either amend the label of the drug or in extreme cases withdraw the NDA completely.

The Aggrandizement of Social Media

The use of social media in the pharmaceutical industry continues to grow at a high rate. With an exceeding amount of prescription drug advertising (also known as direct-to-consumer marketing), many patients and health care professionals have started utilizing media platforms to gain more insights about a particular product. The spontaneous reporting has acted as a catalyst in igniting the very open platform provided by the so-called social outlets.

Social Media and Adverse Effects

Social and online media has become a new tool which patients or consumers rely on to discuss, post, comment or criticize or tweet information regarding a particular drug. The consumers feel that reporting side effects and sharing their adverse experiences would help other concurrent patients with same or similar disease with intent to assist in improving the safety profile of the drug [13]. What consumers forget is that inadvertently or intentionally, they are inundating the social outlets with adverse events reports which often qualify for a true FDA report should a manufacturer of that drug happen to see or hear the incident. This reporting dilemma is itself divided into two groups. Some think that social media is going to replace the entire pharmacovigilance term since the number of reports which could be generated from only one source could be overwhelming. However, some argue that only a small percentage of the adverse event reports qualify to be real reports. They support their argument with factual numbers. Strangely, only one message was observed to contain all the four FDA required elements. Most of the reports often lack one or more than one required element. The big issue with these reports stems from the fact that the majority of the users wish to keep anonymous and at times, use a pseudo name which becomes very hard to relate and to comprehend who is the reporter and similarly the identifiable patient [13].

Despite this, the pharmaceutical industry has continued to broaden its reach by participating in different social media for pharmacovigilance [14]. The customers can post, ask questions about a product and many a time inadvertently (or intentionally) posts a side effect that they are experiencing which many times satisfies the criteria of a serious adverse event. The patients' posts on the pharmaceutical company's Facebook page, therefore, require a constant

observance of any kind of comment or discussion which may involve a company's drug and a reportable event [14, 15]. On the other hand, Twitter has a different social interaction in the sense that anybody can tweet by hash-tag. "Hashtagging" is simply a means of tagging that tweet with someone so that that hash-tag could be followed more often. Twitter also assists pharmaceutical companies to openly discuss current trends of industry with the means of tweets. A company representative can tweet about a new potential drug, which could cure a rare disease. Consumers can directly read the tweet and follow it so that others can also read what they are following. In providing more knowledge to other patients, the accident of posting some adverse event increases exponentially. The companies who board the comment of the image has been posted has to take into account the adverse event under good reporting practices and then convey the message to the appropriate pharmacovigilance team.

PatientsLikeMe (PLM)

Having inspired by their brother's real-life incidences, two brothers started this unique and challenging concept of improving millions of patients' lives who suffer from chronic conditions and other uncommon disease conditions. This platform intended to give freedom to all the patients anywhere in the world to share and post anything- symptoms of a disease, conditions, the treatment they are receiving, concurrent conditions, types of drugs they are taking, real-time side effects or adverse reactions they are experiencing, effects of drug reactions on their mood [17]. The widespread usage and availability of data in real-time have enabled the ALS patients to constantly participate and to share knowledge among other patients who are not aware of certain contraindications, drug-drug interactions, adverse effect awareness and any breakthrough technology that may alleviate them from experiencing more side effects. The PLM platform can be assessed by anyone and can be customized in a tailored fashion to give insight

about multiple patterns. The data can be organized into graphs and charts and assist patients in the quest to understand more about the specific condition [17].

Social Media Reporting

Despite the presence of numerous regulations, ensure each pharmaceutical company remains in compliance with reporting AE, it's quite unfortunate that there are very few which are enacted to regulate the social media reporting. There was a sense of ambivalence in the minds of pharmaceutical companies on how to tackle these peculiar situations [17]. The very first regulation was enforced by FDA in online media was in April of 2009 where it ensured the companies that efficacy of the products mentioned in the sponsored links should not advertise the efficacy without having clear and appropriate information about the risk factors of that particular drug [17]. The pharmaceutical companies enabled 'one-click' away information and had all the risk information about that product on the website which was linked to that brand. FDA did not like this idea and rejected the plea of such sponsored links. The FDA's rejection clarified that the companies should not assume anything regarding the regulations put in place of the online media. In the year of 2010, one of the leading pharmaceutical companies, Novartis, received an enforcement letter from the FDA for having a share function in its Facebook profile. This function had enabled any user to directly share the link of Tasinga product to their personal Facebook profile. Novartis was cited for excluding product risk information, having broadened the indications, the patient-generated online comments and the concern over adverse drug experience reporting on the Facebook personal page. The second most important challenge for any pharmaceutical company even if it becomes aware of an AE on a non-sponsored website is to identifiable factors. It is very hard to determine the causal link to determine the veracity of the event reported online to be adverse. Another difficulty in social media reporting is to make sure

every report has those aforementioned critical 4 elements. Sometimes, it becomes very hard to identify if the patient is a true reporter and how the AE's reported via online social media affect drug safety. The intent of this article is therefore to conduct an exploratory study and to analyze whether social and online media platforms improve or perhaps affect the safety profile of the drug.

ADRs on Social Media

Social media have been considered a research tool for most internet users. Usually, people search for information concerning health as well as commentary from other people about health or medical issues in their experience. Social media is an excellent source of literature on outbreaks of diseases, explanation of specific health characteristics [18]. Also, the users can find out more information about drugs basing on the information provided by other users after consumption. Furthermore, patients use online communities to discuss and adverse effects of treatment, such as drug interventions. In the long run, their conversations provide the most recent and free information.

Using social media has exposed individuals to information on the adverse effects of particular treatments. An example is a worldwide tragedy caused by thalidomide in the 1950s, which can only take as few as seven days for any researcher to come across it on social media [18]. Using a systematic review, researchers in this study explained the existing topic of the value of social media in relation to other means of obtaining data. This literature investigates the incidence and predominance of adverse effects data for healthcare interventions accessible through social media, including the corresponding power of social media as a source for adverse events data contrasted by different sources of data.

The findings indicate that most patients prefer sharing adverse events information on social media rather than filing the reports with any regulatory agency [18]. Furthermore, the research shows that social media is a more substantial source for data concerning symptoms or events with less severe symptoms rather than laboratory tests aberrations and other pressing adverse events that require proper medical care. Social media is a source for real-time, first-hand, and select adverse events shared online and also for determining the perspectives of patients. However, robust conclusions cannot be made based on these findings that social media data [18].

While existing systems have shown unsatisfactory performance regarding monitoring adverse drug events, social media presents opportunities for even updated data [19]. Social media data enables interested parties to access information such as what patients are saying or their views about specific drugs then respond appropriately. Studies have gone to the extent of using large-scale systems that mine data from Twitter to find adverse events in real-time based on tweets from users [19].

In their results, social media can be used by pharmaceutical companies as well as regulators to retrieve feedback from social media users. Also, the parties can use this information for further analysis and communication, as well as decision making. However, social media involves massive messages, tweets, and posts, which is, therefore, a challenge to the data mining process [19]. Hence, data must be critically analyzed and processed to exclude irrelevant and misleading information.

An example of the analysis process involves breaking down the messages into smaller bits for easier processing, and a message is treated as a single post, i.e., operated independently for simplicity [19]. In the analysis, information regarding mentions of drugs and the occurrence

of an adverse event in related tweets. Having filtered irrelevant information, the remaining almost real-time data proves social media to be efficient as a source for adverse drug events among patients.

In recent decades, the issue regarding safety in the process of using drugs and other pharmaceutical products has become an issue of concern. On the other hand, adverse reactions to treatment or drugs have called for a change in the way medical experts and practitioners manage medications [20]. Nevertheless, adverse reactions remain to be a common cause of illness, disability, or other times, death. Recent studies indicate the same results regarding the rising rates of deaths caused by these adverse reactions [20].

While technological advances have served as a means of controlling this problem, the recent trending approach is through consumer data. Information regarding personal health data is sufficiently available online and, more specifically, on social media [20]. Surprisingly, the data or rather approach of using social media data has not been fully exploited. The potential valuable information shared by patients is readily available on social media than through private health bodies.

Other sites are designed for only a given topic of discussion. For instance, specialized healthcare-centered social networks and forums have reduced the amount of effort required by the parties of interest to gain essential issues [20]. For example, some social networks can be designed to be used for explicitly sharing information on health topics, disease support, etc. On the other hand, others will allow the sharing of health-related experiences, such as prescriptions and their side effects. Also, others can correctly be used to compare the experiences of using

different medications to serve a similar purpose. Thus, social media data is deemed to become a future practice for vigilance in the medical field.

According to recent studies, adverse reactions due to using drugs have led to the need for post-usage surveillance of drugs by various established bodies. Social media has proven to be a domain for a tremendously growing storage of data [21]. It is in these social platforms where users share their views, opinions, and encourage or discourage others from using certain products or services. Also, studies indicate that 20% of patients tend to seek advice from watching or reading experiences and comments from other people on social media. More interestingly, social networks focusing on health issues attract many users, including health practitioners. Thus, social media is a unique source of health information, treatments, drugs, side effects, etc.

Scientists and data enthusiasts take the initiative to collect data from users who share information on social media after using the same treatments [21]. For example, people suffering from a common illness, using specific drugs, symptoms, treatments, or other similar characteristics, are the target for many information seekers. Regulatory authorities use social media to obtain necessary data for supplementing the current systems. The data can also be used to study people with everyday medical experiences such as drug abuse, symptoms, etc. [231]. User posts in social media provide details about the results of using the specific treatment and access to adverse drug events.

The study, in this case, provides a framework for adverse drug event detection from social media data. Other authors go to the extent of using multilingual text analysis engines, was to detect drugs and the occurrences of adverse events after consumption using social media data [22]. The first step is data collection. In this step, data can be categorized according to drugs or

other classification keywords. Secondly, data is filtered to remove irrelevant and misleading information. Finally, a statistical analysis of the extracted data can be conducted to analyze the harmful drugs [21].

Adverse drug events have become a rampant issue among patients, thus resulting in the need for mechanisms that can control or mitigate its occurrence [22]. Consequently, researchers have turned their attention to establishing viable approaches to curb this problem. The issue of health-related social media data usage in detecting adverse drug events arises to improve the safety of patients [22]. The detection of drug names, adverse events, prescriptions, among other critical identifying features is essential in establishing the occurrences of an adverse drug event.

Chapter Two: Methods

Study Design

The research methodology selected for this study is a systematic review. Social media sites have become effective in determining the number of adverse events concerning the use of drugs. Patients find it easy to report several drug events on social media platforms due to proximity to their phones than visiting the nearby healthcare facility. Nevertheless, there is a need to establish if social media can be reliable in promoting drug safety profiling based on adverse events reports. Thus, this study used a systematic review as the main research methodology to collect and analyze data related to the use of social media in reporting adverse events. Through the analysis, it was possible to identify the active role social media plays in improving the drug safety profile.

Source of Data/Search Criteria

Sources of data for this study was the articles selected from databases such as PubMed, Cochrane Library, and CINAHL. Google Scholar was used to widen the scope of the search and identify additional articles. The search process involved keywords – social media, adverse event reporting, Facebook and Twitter. These keywords ensured the articles identified related to the topic.

Inclusion Criteria

The inclusion criteria involved articles that related to the study topic. Besides, articles with a clearly described methodology and data analysis were included in this research. Furthermore, articles that described results to show how adverse events reporting contribute to drug safety were included in this systematic review. To determine eligible studies, each topic and

abstracts were screened. This screening ensured the article has relevant information about the study topic. Terms such as social media, adverse events reports, drug safety, Facebook and Twitter were searched on each article. Then, the methodology was also reviewed to establish how the researchers conducted their studies, and the approaches used led to the collection of relevant data.

Exclusion Criteria

Since some of the articles did not relate to the study topic, it was necessary to exclude them. For instance, articles that did not provide a clear description of the topic, aims, methodology, and results were not used for this study. Besides, outdated studies published more than 5 years ago were not considered. Those studies either had very limited correlation between the 'social media' and 'adverse event' terms. Besides, only articles published within the last 5 years have updated information related to the study topic.

Data Analysis

The study involved analyzing quantitative data presented in the articles selected by summarizing key posts on adverse events. Despite the study being a systematic review, the targeted articles had statistical information on the number of adverse drug events reported through social media platforms, particularly Facebook and Twitter. Analysis of these data helped to determine the social media site that recorded a high number of adverse drug events. The specific number of posts made on Facebook and Twitter were counted and compared across the social media platforms. Types of drugs reported to cause adverse events were also identified. Besides, specific types of adverse events reported were identified on each platform. This approach led to determination of the social media site with the highest number of posts on

adverse drug events, the most common adverse event and drugs with the highest reports on adverse events.

Chapter Three: Results

This chapter presents the results obtained from the databases and social media sides. The searched led to identification of 25 articles, which were used to get data on adverse events reported on social media. From the data retrieved, the use of social media on reporting adverse drug events is increasing at a steady rate. Besides, the social media posts have specific information on the drugs involved, and adverse events experienced.

Quantitative Results on ADEs Reported on Facebook and Twitter

Table 1 shows the number of followers on social media sites for five leading pharmaceutical companies.

Table 1: Top Five Pharmaceutical Companies on Facebook (2019 data)

Pharma company	**Pfizer**	**Merck**	**Novartis**	**Roche**	**Sanofi-Aventis**
Followers	373,751	83,315	362,522	116,199	56401
Option to report an Adverse event	No	No	Yes	Yes	No

Source – Retrieved from Facebook and Twitter pages on April 16, 2020.

Table 2 shows the number of social media posts and patient forums. The first column shows the drugs reported to have adverse events from the highest to the lowest events. The second and third columns have the number of posts made on Twitter and Facebook and the respective percentages. The fourth and fifth columns show the number of forum posts and the respective percentages.

Table 2: Facebook and Twitter Posts on Drugs and ADRs.

WEB-RADR substance(s)	No. of Twitter/FB posts	%	No. of patient forum posts	%
Methylphenidate	13,248	28.0	11,178	19.8
Topiramate	5190	11.0	4036	7.2
Diclofenac	4310	9.1	1081	1.9
Terbinafine	3706	7.8	1152	2.0
Levetiracetam	2927	6.2	1372	2.4
Vardenafil hydrochloride	2753	5.8	6023	10.7
Propofol	2268	4.8	435	0.77
Carbamazepine	1671	3.5	1191	2.1
Insulin glargine	1619	3.4	2752	4.9
Baclofen	1187	2.5	2740	4.9
Zolpidem	1152	2.4	2417	4.3
Clomipramine	950	2.0	844	1.5
Propranolol	830	1.8	2184	3.9
Zolmitriptan	651	1.4	207	0.37
Tamoxifen	597	1.3	3821	6.8
Total	43,059	91	41,433	73.54

Table 3 shows the analysis of ADR posts in Table 2 above and if they meet the criteria of adverse events. The data was analyzed based on each drug, number of posts and the adverse events associated. Besides, the information in each post was analyzed to determine if it has a correct description of drugs and associated adverse events.

Table 3: Information on ADR Posts on Facebook/Social media

Question	**Yes** ***n*** **(%)**	**Strengthen** ***n*** **(%)**	**Neutral** ***n*** **(%)**	**Weaken** ***n*** **(%)**
Does the post contain the correct drug?	594 (94.1)			
Does the post contain the correct medical adverse event?	462 (73.2)			
If the post contains the correct drug and medical event, is the medical event an actual adverse experience?	250 (39.6)			
Does the post relate the medical event to the drug of interest?	199 (79.6)[a]			
Is there evidence that the patient took the drug?	109 (43.6)[a]			
Is there information on latency?	24 (9.6)[a]	8 (33.3)	16 (66.7)	0 (0)
Is there a description of the course of the adverse event?	49 (19.6)[a]	11 (22.4)	36 (73.5)	2 (4.1)
Is there any mention/discussion in the post on risk factors (including lifestyle, medical history, comorbidity, indication) and/or co-medication?	33 (13.2)[a]	3 (9.1)	22 (66.7)	8 (24.2)
Does the post contain patient characteristics: age, sex,	7	1 (14.3)	6 (85.7)	0 (0)

Question	Yes *n* (%)	Strengthen *n* (%)	Neutral *n* (%)	Weaken *n* (%)
weight, height?	(2.8)[a]			
Is there any description as to whether/how the event affected the quality of life of the patient?	29 (11.6)[a]			

Table 4 shows how the posts on adverse events impacted the drug safety of social media users. The data was analyzed from the responses given by users who had seen posts on drugs and adverse events. The first column shows the effect whereas the remaining columns show the scale used to classify the responses.

Table 4: Impact of Social Media Posts on Drug Safety

	Not tried ever	No help whatsoever	Some assistance	Reasonable helpful	Extremely Helpful
Changed their medication for treatment	52%	11%	10%	14%	13%
Dosage change for a product	53%	13%	10%	14%	11%
Initiating new medication for the same treatment	43%	10%	10%	17%	20%
Stopping an old medication	56%	13%	10%	12%	10%
Comprehending the side effects of a drug	25%	6%	13%	21%	35%
Sought assistance from another person about his/her condition after taking a drug	38%	8%	13%	13%	28%

Table 5 shows the adverse drug events reported as obtained from the articles reviewed during the study. The first column has the general group of the disorders or events , the second column has

the specific drug events the third column has the count of the number of specific events and the fourth column shows percentage of events.

Table 5: Reported Adverse Drug Events.

OC	PT	Count	Percent
General disorders and administration site conditions	Drug ineffective	133	9.5
	Feeling abnormal	74	5.3
	Adverse event	57	4.1
	Fatigue	40	2.9
	Adverse drug reaction	37	2.7
	Drug effect decreased	20	1.4
	Other PTs	158	11.3
	Sum	519	37.2
Psychiatric disorders	Insomnia	59	4.2
	Hallucination	27	1.9
	Drug dependence	21	1.5
	Anger	20	1.4
	Euphoric mood	20	1.4
	Abnormal dreams	18	1.3
	Other PTs	205	14.7

OC	PT	Count	Percent
	Sum	370	26.5
Nervous system disorders	Somnolence	29	2.1
	Headache	17	1.2
	Memory impairment	16	1.1
	Amnesia	12	0.9
	Dizziness	11	0.8
	Convulsion	7	0.5
	Other PTs	69	4.9
	Sum	161	11.5
Injury, poisoning, and procedural complications	Drug dose omission	24	1.7
	Overdose	23	1.6
	Intentional product misuse	21	1.5
	Incorrect route of drug administration	8	0.6
	Extra dose administered	6	0.4
	Exposure during pregnancy	4	0.3
	Other PTs	35	2.5
	Sum	121	8.7

OC	PT	Count	Percent
Other SOCs	Sum	225	16.1
	Total	1396	100.0

Chapter Four: Discussion

Key Social Media Platforms for ADRS

Facebook

Facebook has been an easy way for consumers to post something they experience from a certain product. However, with the terms of conditions, removing consumer's posts, and prohibiting certain types of entries, it has become one of the controversial social media. There is no denying of the fact that with such massive total active users if the software could be developed which takes into account the adverse event reporting and for a certain product, it would be much easier to report an AE to FDA in even short amount of time with fewer resources from a dedicated traditional pharmacovigilance group. The safety of any drug with limited Facebook posts is hard to determine with these limited resources. Social media such as Facebook are for interaction, communication, and entertainment. The determination of a safety profile of a drug from Facebook is far from reality. At the same time, it should not be denied that with more and more consumers, healthcare professionals are getting prone to the use of social media; Facebook's role in improving the knowledge about a certain product cannot be denied. Product awareness is part of drug safety. With global sharing just one click away, the safety awareness of a certain product with the help of Facebook is apparent.

Twitter

Due to the explicit nature of the tweets, twitter messages can readily be deciphered and processed in real-time. Jiang et al. described an exemplary approach in mining twitter messages with the help of Natural Language Processing (NLP) by building Support Vector Machine (SVM) classifiers. A total of 2 billion tweets were taken into consideration and high-performance

supercomputers were utilized with a complicated mathematical algorithm. The main classification model was based on the textual as well as the semantic feature and drug-related tweets were taken into account depending upon the timeline of the total tweets. A different concept was generated called the bag-of-words. This model assumes the entry of text in a disorderly array of words.

PLM

From the above-mentioned results, it can be seen that Pharmaceutical companies have shown interest in the database organized by PatientsLikeMe. Some real examples of the mergers for some drugs will be discussed along with the validity of the side effects reported by consumers. Additionally, how the database would be difficult to handle soon as the number of patients increases will bring pressure and conflicts within this type of reporting.

The total number of patients was the active patients who are consistently following each other profile about how many times a dose is missed and what type of adverse effects one patient is encountering by taking a particular drug. The patients can also see what other drugs the patients are taking and for what indications. Additionally, patients can compare treatments and symptoms from other patients.

This likelihood of patients stopping drugs due to the fear of more adverse events reported for one drug and less for others could draw bias in requesting their primary physician to prescribe that drug which has fewer side effects reported on the website. Now, this information if before FDA can recall the drug which could potentially be fatal in the long term. Take the example of the second drug Duloxetine, out of total active patients of 4914, 980 have reportedly stopped taking the drug due to being ineffective. In the case of pregabalin, approximately one-

third of the patients have stopped taking the drug due to its severe side effects. The severe adverse effects vary from patient to patient, however. From this dataset, it could very well be inferred that there has been a growing trend in reporting adverse events directly on the social and online media and the events or effects reported directly correlate with the overall safety of the drug. The true nature of a particular drug in terms of its safety is hard to determine with such a small portion of reports. But the plethora of information provided in these reports is sufficient for other patients to decide whether they would like to continue the drug or not. Besides, the lack of constantly following up on other patients could be tiring and tedious and making a sound decision in terminating a particular drug is challenging. The equivocalness of the decision-making process often yields confusing results.

As seen in Table 2, the drug with the highest posts on Facebook/Twitter is Methylphenidate, forming 28% of the total posts [23]. The number of patient forums for this drug is 11,178, which is also the highest among all the drugs. Topiramate, Diclofenac, Terbinafine, and Levetiracetam are among the top 5 drugs reported to have high social media posts respectively at 11%, 9.1%, 7.8%, and 6.2% [23]. A total of 43,039 adverse drug reports were made on Facebook and Twitter, with the total number of patient forum posts being 41,433. These data show that social media has become a common platform for reporting adverse drug events.

As shown in Table 1, pharmaceutical companies have opted to use social media to interact with their clients. Through this interaction, it is possible to receive feedback on the adverse drug events, which patients experience. However, not all companies allow users to provide feedback or raise complaints on their social media platforms. For instance, Pfizer, Merck, and Sanofi-Aventis do not have an option for commenting on their social media

platforms. On the other hand, Novartis and Roche allow their clients to post on their Twitter or Facebook pages.

Accuracy of ADRs on Social Media

Although the number of adverse drug reaction reports is increasing on social media, it is important to establish their accuracy and relevance. Most consumers who report on adverse drug events probably have limited knowledge on the drugs and understand only the associated side effects or how they felt upon taking the medicines. Therefore, analysis of the specific reports is essential to establish if they relate to the adverse drug events. Table 3 provides a summary of the authenticity of the adverse drug events reported on Facebook and Twitter. As seen from the table, 94.1% of the posts contain accurate drug name whereas 73.2% has the correct medical adverse event [23]. However, only 39.6% of the events reported have actual adverse experiences. This shows that despite most of the drug events reported having accurate drug names or medical events, only a few are experienced by customers who report them. The table further shows that from the events reported, 43.6% of the patients took the drug [23]. This information indicates that the number of patients who take the drugs and report the adverse events to social media is increasing but has not reached the desired target (above 50%).

Another important consideration for the posts on adverse drug events reported on social media is the effect of the adverse events on patients. The posts should be analysed to determine patient characteristics, and risk factors such as lifestyle and medical history. This information helps to establish the relationship between the onset of adverse drug events and patient characteristics. From the data collected, only 13.2% of the adverse drug reports have mentioned on patients' risk factors such as lifestyle, medical history, comorbidity, indication, and co-medication. 2.8% describe the patients' age, sex, weight, and height [23]. 11.6% describe how

drug events affected the patient's quality of life. This data shows that despite many adverse drug events being reported, the information on patients' data or the impact of the drug is still inadequate.

Effectiveness of Social Media ADRs on Drug Safety

The essence of reporting adverse drug events on social media is to improve the level of drug safety. Drug manufacturers, healthcare providers and patients are interested in maintaining a high level of safety, hence rely on reports made on experienced adverse drug events [24]. Therefore, an analysis of customers' feedback on reported events can help to establish the efficacy of social media in promoting the required level of drug safety.

The data collected in this study show that social media used as a reliable source for pharmacovigilance. The use of social media in pharmacovigilance has been increasing particularly in the detection of ADRs [24]. The social media networks have been identified as real-life and rich sources of data. Thus, they can be used to help in the identification of safety issues and offer new insights on usage of medicine, which include medical errors, lack of efficacy and off label use. The social media reports also facilitate understanding of the role of including patients' concerns into the delivery of quality care. Most patients rely on social media as the available platform for contributing to the treatment process [24]. Through their reports on adverse events, health care providers can understand their important role in promoting their safety and that of other patients. Furthermore, medicine regulators and the pharmaceutical industry can rely on social media to access reports on treatment outcomes and ADRs [20]. The volume of social media data on ADRs can lead to regulated use of some medicines or a change in the treatment process for the benefit of patients. Besides, the data can help identify drugs to withdraw, reduce or change the dosage.

All the articles reviewed showed an increase in the number of adverse drug events reported on social media platforms. Facebook and Twitter are the leading social media platforms on which adverse drug events are reported. Although all the articles do not show the specific number of posts on ADRs, they hint that Twitter is the leading site where the adverse events are reported. Other sites include Linked In, YouTube and various health-related websites. The studies further identify specific drugs associated with adverse events, including drug abuse and reactions. In all the studies, the authors agree that social media can be used to enhance pharmacovigilance.

The findings show an agreement between information on ADRs obtained from social media and traditional sources. In 10,188 tweets collected on adverse drug events, some of the concept names used include allergic reactions, pain, dizziness, headaches, fatigue, and anxiety. When compared to the information available in drug databases, there was a close similarity with the adverse events reported in the tweets [23]. For instance, the majority of Twitter mentions were pain, fatigue and local injection site reactions at 10%, 17.2%, and 23.7% respectively. The top three events reported on Twitter were headache, skin/dermatologic site reactions and injection site reactions.

A similar study analyzed posts on Facebook and Twitter to determine if they relate to adverse drug events. The key objective of this study was to establish the effectiveness in mining social media data on promoting medicines safety surveillance. Through the applications programming interfaces (APIs) public messages posted on social media were retrieved. The authors managed to retrieve 2537 posts on cardiovascular events and rosiglitazone. Twitter had 98% of the posts whereas Facebook had only two posts. Based on the country of origin, two-thirds of the posts were from the US. All the posts affirmed a relationship between rosiglitazone

and onset of cardiovascular events. Then, another study found 2236 posts on the HPV vaccine and infertility with 85% of the posts from Twitter with Facebook having 23 posts. Google had 308 posts. More than half of the posts (567) were from the US. The data collected therefore shows that Twitter is the leading social media platform with the highest number of adverse drug events reported.

As shown in Table 5, the first category of social media ADRs is General disorders and administration site conditions. These 519 events are classified into ineffective drugs, feeling abnormal, adverse events, fatigue, adverse drug reactions, reduced drug efficacy, and other PTs [25]. Besides, a total of 370 psychiatric disorders were also reported to be associated with some of the drugs. These disorders include insomnia, hallucination, drug dependence, anger, euphoric mood, and abnormal dreams. The social media reports also identify 161 neurological disorders and 121 events related to injury, poisoning and procedural complications [25]. These findings show that social media sites are increasingly being used to report adverse events associated with various drugs or medical procedures.

Conclusion

The findings of this study show that social media plays an active role in reporting adverse drug events. Such reports can be used to improve the drug safety profile. The effectiveness and safety of any drug still depend upon the post-market surveillance program started by the FDA and the active participation of drug company manufacturers. Despite such rigorous regulations, there are still drugs that cause mishaps and at times on a larger scale. Therefore, through social media platforms such as Facebook and Twitter, it is possible to identify drugs with such mishaps.

The identified social media platforms where majority of the adverse drug events are reported are Facebook and Twitter. From the articles analyzed, Twitter has the highest number of posts on adverse events compared to Facebook. The implication is that chances of reporting adverse events associated with drug use are higher on Twitter than Facebook. Another key website in reporting drug events is https://www.patientslikeme.com/. On this website, patients report several incidences of adverse drug events.

Since many adverse drug event reports are made on social media, Facebook and Twitter could become effective in promoting drug safety profile. From the reviewed articles, most of the posts are made by patients or those in close contact with the patients who used the drugs. Some of the identified drugs are Avastin, Melphalan, Rupatadin, Tamoxifen, and Taxotere. Some of the leading adverse drug events are pain, cardiovascular events, headache, allergic reactions, and anxiety. Understanding the frequency of the drugs with adverse events and types of events can help in emphasizing adhering to the required guidelines thereby improving the level of drug safety profile.

References

1. Food and Drug Amendments Act of 2007, 2007. Retrieved from https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-administration-amendments-act-fdaaa-2007
2. Pitts, P.J., Le Louet, H., Moride, Y. and Conti, R.M., 2016. 21st century pharmacovigilance: efforts, roles, and responsibilities. *The Lancet Oncology*, *17*(11), pp.e486-e492.
3. Guthrie, Ellen. "Multiple Sclerosis Foundation - Examining The Safety Of Aspartame". *Msfocusmagazine.Org*, 2009, https://msfocusmagazine.org/Magazine/Magazine-Items/Examining-the-Safety-of-Aspartame.aspx. Accessed on April 20, 2020Provenzani, A., et al., Pharmacogenetic considerations for optimizing tacrolimus dosing in liver and kidney transplant patients. World J Gastroenterol, 2013. 19(48): p. 9156-9173.
4. Sarker, Abeed, et al. "Utilizing social media data for pharmacovigilance: a review." *Journal of biomedical informatics* 54 (2015): p. 202-212.
5. Heger, Monica. "Regulators move toward adverse event reporting via mobile apps." *Nature Medicine* 21.2 (2015): p. 104-105.Duclos, C., et al., Modeling, building and evaluating an ontology for the automatic characterization of adverse drug effects during pharmacovigilance. Stud Health Technol Inform, 2010. 160(Pt 2): p. 1005-9.
6. FDA. FDA adverse event reporting system. 2011; Available from: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070434.htm. Accessed on April 16, 2020.

7. Rehman, W., L.M. Arfons, and H.M. Lazarus, The rise, fall and subsequent triumph of thalidomide: lessons learned in drug development. Ther Adv Hematol, 2011. 2(5): p. 291-308.
8. "21 CFR 312.32 - IND Safety Reporting.". *Govregs.Com*, 2016, https://www.govregs.com/regulations/expand/title21_chapterI_part312_subpartB_section312.32#top. Accessed on April 20, 2020
9. Nomifensine withdrawn by manufacturer. FDA Drug Bull, 1986. 16(1): p. 7-8.
10. Inc., H.-R.P., Withdrawal of Merital, January 1986: Somerville, NJ: Hoechst-Roussel Pharmaceuticals Inc.
11. FDA. [cited 2012 30JUNE]; Available from: "Reports Received And Reports Entered Into FAERS By Year". *U.S. Food And Drug Administration*, 2015, http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070434.htm. Accessed April 20, 2020.
12. Golder, Su, Gill Norman, and Yoon K. Loke. "Systematic review on the prevalence, frequency and comparative value of adverse events data in social media." *British journal of clinical pharmacology* 80.4 (2015): 878-888.
13. Segura-Bedmar, Isabel, Ricardo Revert, and Paloma Martínez. "Detecting drugs and adverse events from Spanish social media streams." *Proceedings of the 5th international workshop on health text mining and information analysis (LOUHI)*. 2014.
14. Pappa, Dimitra, and Lampros K. Stergioulas. "Harnessing social media data for pharmacovigilance: a review of current state of the art, challenges and future directions." *International Journal of Data Science and Analytics* 8.2 (2019): 113-135.

15. Sarker, Abeed, et al. "Social media mining for toxicovigilance: automatic monitoring of prescription medication abuse from Twitter." *Drug safety* 39.3 (2016): 231-240.
16. *PatientsLikeMe*. PatientsLikeMe. Retrieved 6 April 2020, from https://www.patientslikeme.com/.
17. Lovells, H. (2009). *FDA enforcement of online advertising and promotional activities: emerging marketing opportunities come with legal and regulatory risk | Lexology*. Lexology.com. Retrieved 6 April 2020, from https://www.lexology.com/library/detail.aspx?g=026e6d4b-817c-4802-8a64-b7402c955e76.
18. Golder, Su, Gill Norman, and Yoon K. Loke. "Systematic review on the prevalence, frequency, and comparative value of adverse events data in social media." *British journal of clinical pharmacology* 80.4 (2015): 878-888.
19. Plachouras, Vassilis, Jochen L. Leidner, and Andrew G. Garrow. "Quantifying self-reported adverse drug events on Twitter: signal and topic analysis." *Proceedings of the 7th 2016 International Conference on Social Media & Society*. 2016.
20. Pappa, Dimitra, and Lampros K. Stergioulas. "Harnessing social media data for pharmacovigilance: a review of the current state of the art, challenges, and future directions." *International Journal of Data Science and Analytics* 8.2 (2019): 113-135.
21. Sarker, Abeed, et al. "Utilizing social media data for pharmacovigilance: a review." *Journal of biomedical informatics* 54 (2015): 202-212.
22. Segura-Bedmar, Isabel, Ricardo Revert, and Paloma Martínez. "Detecting drugs and adverse events from Spanish social media streams." *Proceedings of the 5th international workshop on health text mining and information analysis (LOUHI)*. 2014.

23. Caster, Ola, et al. "Assessment of the utility of social media for broad-ranging statistical signal detection in pharmacovigilance: results from the WEB-RADR project." *Drug safety* 41.12 (2018): 1355-1369.
24. Pierce, Carrie E., et al. "Evaluation of Facebook and Twitter monitoring to detect safety signals for medical products: an analysis of recent FDA safety alerts." *Drug safety* 40.4 (2017): 317-331.
25. Brosch, Sabine, et al. "Establishing a framework for the use of social media in pharmacovigilance in Europe." *Drug safety* 42.8 (2019): 921-930.