

## **Systematic review on the prevalence, frequency and comparative value of adverse events data in social media**

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# **Systematic review on the prevalence, frequency and comparative value of adverse events data in social media**

## **Abstract**

**Aim:** To summarize the prevalence, frequency and comparative value of information on the adverse events of healthcare interventions from user comments and videos in social media.

**Methods:** Systematic review of assessments of the prevalence or type of information on adverse events in social media. 16 databases and two internet search engines were searched in addition to handsearching, reference checking, and contacting experts. The results were sifted independently by two researchers. Data extraction and quality assessment were carried out by one researcher and checked by a second. The quality assessment tool was devised in-house and a narrative synthesis of the results followed.

**Results:** From 3064 records, 51 studies met the inclusion criteria. The studies assessed over 174 social media sites with discussion forums (70%) being the most popular. The overall prevalence of adverse events reports in social media varied from 0.2% to 8% of posts. 29 studies compared the results from searching social media to using other data sources to identify adverse events. There was general agreement that a higher frequency of adverse events was found in social media and that this was particularly true for 'symptom' related and 'mild' adverse events.

Those adverse events that were under-represented in social media were laboratory-based and serious adverse events.

**Conclusions:** Reports of adverse events are identifiable within social media. However, there is considerable heterogeneity in the frequency and type of events reported, and the reliability or validity of the data has not been thoroughly evaluated.

## **What is known about this subject**

Social media are commonly used to discuss health issues, including adverse events.

Social media are increasingly being used as a research tool.

Techniques have been developed to identify adverse events on social media.

## **What this study adds**

The prevalence of adverse events reports on social media varies from 0.2% to 8% of posts.

‘Mild’ and ‘symptom-related’ adverse events are over-represented in social media and ‘laboratory test abnormalities and ‘serious’ adverse events are under-represented compared to other data sources.

The question as to whether searching social media for adverse events data is a valuable use of resources resulting in improved patient outcomes remains unanswered. A cost-effectiveness analysis of all pharmacovigilance systems, including social media is urgently required.

## Introduction

Social media are commonly used to discuss health issues. 80% of internet users have searched online for health information and 34% have read someone else’s commentary about health or medical issues in the last 12 months (1).

Given these figures, it is unsurprising that social media have been discovered as a research tool. There is substantial literature on extracting information from social media to monitor disease outbreaks (2-15), health behaviors (16-19), and patient views (20-26).

Many patients choose online communities to discuss adverse effects of treatments, particularly drug interventions. This generates a large volume of unsolicited and up-to-date information. It has been suggested that by monitoring social media it would now take only five to seven days to be aware of the Thalidomide disaster (27). Despite public availability of these data, their appropriate role in pharmacovigilance has not been established nor are they routinely used for collecting adverse effects data.

The comparative value of social media in relation to other data sources (such as pharmacovigilance systems or clinical trials) is of interest. We need to know how adverse events data from social media compares to data from other sources in the type, range, frequency and timeliness of adverse events discovered. Information on social media may not be easily obtainable from other sources. With multiple questions which need addressing, research into the retrieval of information on adverse events from social media is particularly timely.

This systematic review summarizes research on, the prevalence, frequency and type of adverse events data for healthcare interventions available via social media and on the relative

value of social media as a source for adverse events data compared to other sources of data.

## **Methods**

The inclusion criteria were broad in order to provide an understanding of the volume and quality of the research in this area.

### ***Inclusion criteria***

The PICO for this systematic review was as follows;

Population: Any condition or disease type (chronic or acute) in any population

Intervention(s): Any type of social media , defined as any computer-mediated tools to create, share or exchange information, ideas ,pictures or videos in virtual communities and networks (such as message boards, social networks, patient forums, Twitter, blogs and Facebook).

Simple, non-social internet-based interventions (i.e. web 1.0) were excluded. Social media to recruit participants to a study or used exclusively by health professionals were excluded.

Comparators: Any other data source was eligible as a comparator, including no comparator.

Outcomes: Data on the type, frequency or prevalence of adverse events data were required.

A broad definition of adverse events was considered incorporating adverse events (where the likelihood of causation has not been measured), adverse effects (events likely to be associated with the intervention but can only be detected via laboratory tests) or adverse reactions (detected via signs and symptoms experienced by the patient). Any healthcare interventions were eligible.

Study Design: Any type of assessment was included.

### ***Exclusion criteria***

Population: None excluded

Intervention(s): Simple, non-social internet-based interventions (i.e. web 1.0) were excluded.

Social media to recruit participants to a study or used exclusively by health professionals were excluded.

Comparators: None excluded

Outcomes: We were primarily concerned with the properties of interventions under normal use. We therefore did not consider papers with the primary aim to assess events such as intentional and accidental poisoning (i.e. overdose), drug abuse, errors, or non-compliance.

Drug-drug interactions were not eligible where they were the primary objective of the paper due to the different techniques required in identifying interactions as opposed to adverse events.

Study Design: We excluded discussion papers, examples of posts from social media and technological papers which are summarized elsewhere [28].

### *Search methods*

16 databases covering a range of topic areas, including health and medical research, nursing, information and computer science, and grey literature (i.e. literature that is not formally published) were searched (Supplementary Table 1: Sources searched).

We undertook other supplementary methods which included searching two internet search engines, browsing internet blogs, handsearching journals, newsletters and conference proceedings, reference checking all included articles and related systematic reviews, and contacting experts in the field.

### *Search Strategies*

The database search strategies contained two facets – ‘social media’ and ‘adverse events’ (Supplementary Box 1: MEDLINE search strategy). A date restriction of 1996 onwards was placed on the searches as blogging first began in 1997. No language restrictions were placed on the searches, although financial and logistical restraints did not allow translation from all languages.

### *Data extraction*

Information was collected on the type of social media used (such as Twitter or Facebook), the adverse events and type of interventions searched for, the primary aim of the study as stated by the authors and the type and frequency of adverse events data identified. Details of comparator sources were noted along with any comparisons of the data collected. Lastly, data were extracted on the conclusions of the original investigators.

### *Assessment of methodological quality*

We did not stipulate any restriction on design of the included studies. As there is no relevant quality assessment checklist for these type of studies, we designed a bespoke tool based on five key areas to reflect potential risks of bias. These five key criteria were:

1. Search strategy to identify posts: How were the posts searched for? Were adequate search terms used? Searching social media is difficult due to the unstructured nature of the data. In particular, colloquial expressions/informal speech, misspellings, nicknames, the use of non-standard abbreviations used, different synonyms and different spellings make a comprehensive search impossible. However, attempts should be made to include numerous synonyms, spellings etc..
2. Selection of relevant posts: What methods were used in selecting relevant posts? For example, were double screening methods used for manual selection? Were computerized methods validated?
3. Definition of a report of an adverse event: Was there a clear definition of what constitutes an adverse report? (for example, the Food and Drug Administration (FDA) minimum criteria of an identifiable reporter, an identifiable patient, a reaction or event, and a suspected medicinal product)
4. Duplicate data: Did the researchers measure the amount of duplicate data? Were duplicate reports from the same user excluded?

### *Analysis*

It was anticipated that the included studies would be heterogeneous in nature as methods in this area are still under development. A narrative synthesis was therefore used.

### *Results*

The database and internet searches identified 3045 records, and these results were augmented

with studies identified from handsearching, reference checking, contacting experts, peer reviewers suggestions and studies already known by the authors (Figure 1 and Supplementary Table 2: Search results by database). Altogether 51 studies from 64 publications met the inclusion criteria

(Supplementary Table 3: Characteristics of included studies) (28-91).

There were 180 excluded studies based on the full-text papers (Supplementary Table 4: Excluded studies).

### *Baseline characteristics of studies*

#### *Social media*

Over 174 different social media sites were represented in the 51 studies. 71% (36/51) of the studies examined discussion forums, 10 looked at Twitter, five at Facebook, four at blogs, three at YouTube, one at RxISK and one at Treato (Figure 2). Three studies did not report the websites searched and seven studies looked at more than one type of social media.

#### *Discussion forums*

Of the 36 studies that looked at discussion forums six did not specify the forums searched, and one gave an incomplete listing. The most popular named forums were DailyStrength (six studies), WebMD (five studies), AskAPatient (five studies), MedHelp (four studies), ehealthforum (three studies), healthboards.com (three studies), PatientsLikeMe (three studies), and revolutionhealth (three studies).

The most popular disease specific patient forums were for cancer (five studies), depression (three studies), heart conditions (two studies) and diabetes (two studies). The number of forums searched ranged from one to 24, with an average of four forums searched in each study.

#### *Interventions*

Most studies looked at drug interventions (86%, 44/51), with only three looking at surgery (one with YouTube), two limiting by illness, and two looking for a medical device (both with YouTube). Of those studies that included drug interventions most assessed multiple drugs (84%, 37/44) whilst those studies assessing surgery or a medical device only evaluated one

intervention.

### *Adverse events*

90% (46/51) of the papers looked for any adverse events whilst only 10% (5/51) specified the adverse events they were looking for (withdrawal symptoms, SJS/TEN, fatal skin reactions/hypersensitivity, pain and sexual dysfunction).

### *Study validity*

A summary of the quality assessment of the 51 included studies is contained in Supplementary Table 5: Quality assessment of included studies.

#### Search strategy to identify posts

18 studies reported using a search strategy to identify the posts for sifting, 11 browsed a set of posts, 12 used some form of automation with a dictionary or lexicon to identify terms and 10 studies did not report how posts were retrieved.

Due to poor reporting it was difficult to ascertain the number of studies which conducted an adequate search strategy (for example, with an adequate range of synonyms, abbreviations and spellings) to identify a comprehensive or representative sample of posts from social media. Where search strategies were reported none could be considered comprehensive or highly sensitive on par with search strategies used in systematic reviews.

Of the 11 studies which simply browsed posts, five were browsed by at least two researchers, and in six cases it was unclear.

In the 12 studies which used medical dictionaries – all used multiple dictionaries and some adjusted them for the purpose of their research. With social media the use of colloquial terms is essential for an adequate search; this was recognized by eight of the 12 studies which either incorporated Consumer Health Vocabulary (CHV) or added their own informal terms.

### *Selection of relevant posts*

Methods used to select relevant posts varied between a solely manual approach (22 studies) to the use of automation (12 studies), with 17 studies not reporting on the methods used. Most



studies which used a manual approach used more than one researcher to select relevant posts (82%, 18/22); only two studies reported using only one researcher while two studies did not report the number of researchers. Automated methods are much more difficult to quality assess given the level of reporting. In addition, no common evaluation approach for automated methods exists and researchers design their own evaluation approaches (92). In this review, some studies used a manual check to verify results (for example, by comparing to manually annotated records) whereas others compared the results to known adverse effects often referred to as a ‘gold standard’ (identified from sources such as drug labels, pharmacovigilance or the published literature).

#### *Definition of a report of an adverse event*

The majority of the studies did not stipulate a clear definition of what constitutes an adverse report (76%, 39/51). However, seven studies stated that co-occurrence of a term for the drug and a term for an adverse event in the same post or in close proximity to each other were required for an adverse event report (four of these seven studies also carried out some form of manual checking). Five studies used the Food and Drug Administration (FDA) minimum criteria of; an identifiable reporter, an identifiable patient, a reaction or event, and a suspected medicinal product. The definition of an identifiable reporter varied – some studies accepted emails or screen names whereas others required full verified details.

In general, the included studies did not say how much clinical information was available in the media postings, or whether causality assessment (such as a Naranjo score) could have been performed (however difficult) to determine the likelihood of it being a genuine adverse effect/reaction.

#### *Duplicate data*

Only six studies reported that they used any measures to exclude duplicate reports. Yet 23 studies included more than one social media site – in these instances multiple posting may be a particularly pressing issue.

### *Primary aim of the included studies*

For the majority of the studies the primary aim was an assessment of the value of social media as an information source on adverse events, either in terms of patient experiences (such as, impact of adverse events on patients' lives and feelings), or the type or frequency of adverse events reports. 22% (11/51) of studies had a primary aim of developing methods used to mine social media for adverse events data but also presented their search results (31, 44, 46, 50, 54-56, 65, 78, 81-84, 91).

### *Frequency or prevalence of adverse events*

25 studies reported the frequency of reports of adverse events on social media. Although ideally the denominator should have been the total number of posts within the specified time frame, often a subset of posts or threads related to the intervention or illness were used. The variation in adverse event report frequency in social media was therefore wide ranging from 0.02% to 78% (Table 1). Obviously studies which calculated the percentage of adverse events posts as a proportion of all social media posts reported a lower prevalence than those with analysis restricted to intervention-related posts. However, there were clear differences between some of the types of social media. For example, the highest percentage of adverse event information was identified from YouTube videos, and disease specific forums generally had a higher frequency of adverse events than general health forums.

### *Comparisons against other data sources*

The majority of the studies (58%, 29/51) compared the data retrieved from social media to some other source of information. The most common comparator was to pharmacovigilance data (16 studies), followed by published trials (8 studies) (Table 2).

Comparisons were conducted either in terms of the list of adverse events compiled from either source (31, 35, 40, 45, 46, 50, 52, 54, 76, 84), a brief narrative comparison (30, 58, 72), a crude comparison of the number of studies and the number of posts (49) or some sort of comparison of frequency – either by a rank order (34, 35, 37, 41, 42, 87), by the percentage of adverse events posts (36, 53, 55, 63, 64, 68, 69), or by number of adverse event reports (56, 62, 78).

There was general agreement that there is concordance overall between adverse events mentioned in social media and those already documented in other sources (such as drug

labels or published trials). However, only seven studies reported on the actual percentage of adverse events identified in social media that are already documented elsewhere, this ranged from 57% to 99% (Table 2).

Those studies which compared the number of reports of specific named adverse events from social media to reports for the same adverse events from other sources generally agreed that the level of reporting in social media was much higher (34, 36, 42, 48, 51, 53, 58, 78).

### *More rapid identification of AEs compared to other data sources*

Only one study compared the timeliness of identifying adverse events from social media with other sources. This retrospective study compared the year that eight adverse events would have been detected using either social media or pharmacovigilance data (81-83). This paper found that social media detected FDA-alerted adverse events much earlier in six of the eight case studies. However, the precision or specificity of using social media was not indicated in this paper. This would have been particularly valuable given the potential for false positives from the large amount of adverse events reports in social media.

### *Types of adverse events in social media*

Some studies found that whilst some adverse events are over-represented in social media, other adverse events are under-represented as compared to events from sources such as pharmacovigilance systems, drug labels and the literature (Supplementary Table 6: Type of adverse event reported in social media in comparison to other sources). A higher frequency of adverse events in social media than in other sources tended to be reported for ‘unpleasant symptoms’ or adverse events classified as ‘mild’ (31, 34, 40, 42, 48, 54-56, 58, 62-64, 72, 87, 88).

Adverse events identified via social media but not documented elsewhere also tended to be ‘mild’ or related to ‘quality of life’ (31, 34, 42, 51, 55, 87, 88).

Under-represented adverse events on social media in contrast tended to include laboratory abnormalities (31) or effects requiring diagnosis from a healthcare professional (54, 72). Serious or severe adverse events were also under-represented in social media (31, 40, 55, 56,

62-64, 72). Severe adverse events were described by the users as 'severe' or were events requiring immediate clinical intervention (as defined in the papers).

Only three studies found some contradictory evidence of the higher incidence of reporting of 'mild' adverse events in social media. These studies reported a lower incidence of nausea and constipation (54), somnolence and dizziness (68), and headaches and nausea (62). One study also found lower rates of subjective adverse events in social media (60) and another reported on a laboratory value (high cholesterol) in social media which was not reported in other sources (31).

## **Discussion**

The large number of included and excluded studies in this review demonstrates the high level of attention that the utilization of social media for adverse events identification is receiving. There were only nine publications in the eight years spanning 2002 to 2010, but there has been a rapid increase recently, with 23 articles in 2014 alone.

Despite the disparate nature of the included studies, there are some key findings that merit further discussion. Numerous studies confirm that techniques are available to obtain signals of adverse events reported in social media. There is general concordance with other sources for the majority of adverse events. Social media are able to confirm known adverse effects/reactions and highlight novel or rare adverse events for signal generation/hypothesis testing, provide more detailed information on patient experiences and may possibly detect adverse effects/reactions earlier than pharmacovigilance systems, such as the current FDA system. Patients may find it easier to discuss their experience of adverse events on social media than to file spontaneous reports with regulatory agencies.

A different emphasis on the type of adverse events reported on social media was identified in the studies, which suggested that social media may be a better source for 'symptom-related' or less 'serious' (non-life threatening or not requiring hospitalization) than laboratory test abnormalities and 'serious' adverse events.

It is unclear though from the included studies whether trawling social media genuinely improves upon existing knowledge or would be a worthwhile use of precious resources. This

stems from important weaknesses in the methodological quality of the included studies, which means that robust conclusions cannot be drawn.

The biggest problem (particularly with automated or semi-automated methods) is that the purported adverse events may not be adverse events at all. Terms used to describe adverse events can also be used for indications of the condition being treated, beneficial effects (i.e. sleepiness can be a beneficial effect for someone with insomnia), or may not have been experienced by a patient. For example, within statements such as ‘Works to calm mania or depression but zonks me and scares me about the diabetes issues reported’ – diabetes is not an adverse event but an expressed concern (54). In one of the included studies ‘uterine cancer’ co-occurred 374 times with tamoxifen but most of the messages demonstrated only anxiety about taking tamoxifen because of this adverse event (31). In most studies attempts were made to eliminate false positive posts using algorithms, Natural Language Processing (NLP) or manual processes.

Reported abnormalities may have been caused by the disease rather than drug (e.g. confounding by indication). Although attempts were made to automatically classify a causal relationship it was particularly difficult to distinguish between symptoms that a drug is treating and the adverse effects/reactions it causes (69). Also, a major limitation is that the included studies did not really look at whether sufficient clinical detail is available to allow meaningful interpretation of the social media postings, or whether causality assessment was feasible. Although a number of studies acknowledged the potential for spam or non-genuine posting, they also recognized the difficulties of verifying posts [29, 31-33, 35, 36, 43, 44, 46, 48, 50, 52, 53, 60, 61, 66, 71, 72, 77, 84, 86]. Many authors thought that the problem of non-genuine posts may not be as large a problem as perceived because of site moderators, a lack of incentive or lengthy procedures to become a member of the site. One study found that 0.5% of posts were being spam and another study found that 6% of Facebook members were not real people.

Even if social media contains genuine posts, they may not reflect the true population of people who experience adverse events (for example, women and younger people are more likely to post on social media) and may be influenced by media report or individual biases.

Some of the included studies reported differences in frequency or type of adverse events in

comparison to more established data sources. Whether these differences genuinely reflect new adverse effects/reactions or more accurate frequencies of adverse effects/reactions is unknown as this was not tested or validated in any of the papers. We believe that there is currently very little robust data to justify the value of mining social media for previously unrecognized signals that might subsequently go on to become validated as genuine adverse drug reactions. Hence, we believe in a very cautious approach to social media postings which report adverse events that may or may not actually be related to drug therapy.

However, social media can provide more complete information on adverse effects/reactions considered important by patients, and aid researchers in understanding patient perceptions (32, 33). In one study, the authors proposed that frequency data should not serve as prevalence of the adverse effects/reactions but as measure of which symptoms may be the most salient to patients on a day-to-day basis (58). Street et al (93) suggested that social media can be used to inform Health Technology Assessments of interventions by gaining community perspectives, such as acceptability, social impact and potential uptake. They argue that social media can uncover a richer explanation of the issues involved with interventions to inform systematic reviews.(93) These conclusions could be relevant to reviews which incorporate adverse effects/reactions.

The next step for researchers may be to conduct prospective evaluations on how these data on adverse events from social media can give added value, particularly when directly compared to standard pharmacovigilance systems. Although many have discussed the value of this type of data for pharmacovigilance, the methods to incorporate these data into current systems are largely unexplored. In addition the ways in which data from social media can help inform primary and secondary research (such as clinical trials and systematic reviews) have not been developed (93). Social media could also be explored as a source to identify patient concerns on adverse effects/reactions and thus identify priority areas for further research (horizon scanning).

## **Limitations**

There are a number of limitations of this systematic review. First, the difficulties in searching for this type of study may have resulted in studies being missed. However, we did attempt to compensate for this by including a range of non-databases in addition to database sources.

There is great scope for selective outcome reporting or publication bias. Researchers may selectively choose to submit for publication positive findings about social media, whilst negative or null data are not disseminated.

There was a lack of detailed reporting of the output from searching social media in many of the studies. Although this was sometimes understandable given that the primary aim of some of the studies was the development of methods, this made assessment difficult.

The posts on adverse events may be sensitive to media reports, other people's posts and to other sources of information (such as drug labels) – yet this was rarely discussed.

Lastly, the most relevant question is whether the information from social media will help improve clinical practice or protect patients from harm. This was not addressed in any of the included studies.

## **Conclusions**

The limitations of searching social media for adverse events – such as the difficulties in searching, the large volume of irrelevant data, issues surrounding lack of validation, the danger of misinformation and duplicate reports were evident.

Although it is difficult to state the prevalence of adverse events reports in social media, it is quite apparent that a large volume of real-time, first hand experiences of adverse events are posted online. Social media may be a source for novel or rare adverse events and 'mild' adverse events and for ascertaining patient perspectives. The extent to which researchers searching social media for adverse events can lead to patient benefit, however, is unknown.

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### **Conflict of interest**

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare: GN and YL had no support from any organisation for the submitted work; SG had support from the National Institute for Health Research (NIHR) for the submitted work; SG, GN and YL had no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; SG, GN and YL had no other relationships or activities that could appear to have influenced the submitted work.



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## **Figures**

Figure 1: Flow diagram for included studies

Figure 2: Types of social media represented in included studies

## **Tables**

Table 1: Prevalence of adverse events reports by type of social media and denominator

Table 2: Comparison of adverse events in social media already documented elsewhere

## **Supporting Information**

Supplementary Table 1: Sources searched

Supplementary Table 2: Search results by database

Supplementary Table 3: Characteristics of included studies

Supplementary Table 4: Excluded studies

Supplementary Table 5: Quality assessment of included studies

Supplementary Table 6: Type of adverse event reported in social media in comparison to other sources

Supplementary Box 1: MEDLINE search strategy