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LETTER TO THE EDITOR

Comment on "Assessment of the Utility of Social Media for Broad-Ranging Statistical Signal Detection in Pharmacovigilance: Results from the WEB-RADR Project"

Cedric Bousquet[1] · Bissan Audeh[2] · Florelle Bellet[3] · Agnès Lillo-Le Louët[4]

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Dear Editor,

We read with great interest the article titled "Assessment of the Utility of Social Media for Broad-Ranging Statistical Signal Detection in Pharmacovigilance: Results from the WEB-RADR Project" by Caster et al., published online on 24 July 2018 in *Drug Safety* [1]. In that paper, the authors provide evidence that broad-ranging statistical signal detection on social media, such as Facebook and Twitter, is not worthwhile compared with other pharmacovigilance activities. More product–event combinations were detected in patient forum posts than in Twitter/Facebook, but detection was delayed in forums compared with VigiBase. The authors suggest that shortcomings of the adverse event recognition algorithms may partially explain poor signal detection performance, and we agree that additional efforts must be made to take into account the patient-specific terms that do not necessarily belong to the medical language. Nevertheless, these conclusions question the utility of any future work investigating knowledge extraction from social media for pharmacovigilance, by drug regulatory authorities or the pharmaceutical industry.

The experience of key pharmacovigilance stakeholders shows that taking into account patient reporting to health authorities is both valuable [2] and challenging [3, 4] to pharmacovigilance. Extracting patient feedback and reactions from social media was thus an appealing approach for pharmacovigilance for two main reasons. On the one hand, mentioning an adverse drug event in a post in social media requires less time for the patient than sending a formal report to a pharmacovigilance organization. On the other hand, social media is being used by a large portion of the population, and the volume of data that could be extracted from this resource was assumed to be significant compared with what could be obtained by reporting.

Starting in 2010, automatic approaches related to natural language processing [5] and machine learning on social media were proposed to support existing pharmacovigilance procedures. These automatic approaches aimed to overcome underreporting in pharmacovigilance, and to consider a new data source complementary to conventional means. Preliminary results showed that it is possible to automatically extract adverse drug events from social media [6]. The technical possibility and the opportunity to use social media for pharmacovigilance had given great hope [7, 8], but it now seems that the results obtained do not meet these expectations [9].

Although some studies reported negative or uncertain results regarding early detection of signals from social media compared with signals detected in an established pharmacovigilance database [10, 11], these studies were restrained to a limited number of drugs, adverse events and/or social media. This limitation means that such results could be the consequence of a random selection of parameters that led to unfavorable experimental conditions. Caster et al. implemented two reference sets with many drugs and controls, leaving little room for doubt about the hazard.

Even if we agree that, today, social media is not a 'first-line signal detection system', we must keep in mind that the 'virtual social media pharmacovigilance database' is not comparable with pharmacovigilance databases in terms of

✉ Cedric Bousquet
cedric.bousquet@chu-st-etienne.fr

1 SSPIM, Unit of Public Health and Medical Information, CHU University Hospital of Saint Etienne, Saint-Étienne, France

2 Laboratoire d'informatique médicale et d'ingénierie des connaissances en e-santé, LIMICS, Sorbonne Université, Inserm, Université Paris 13, 75006 Paris, France

3 Centre Régional de Pharmacovigilance, Centre Hospitalo-Universitaire, Saint-Étienne, France

4 Centre Régional de Pharmacovigilance HEGP, AP-HP, Paris, France

drug coverage and safety profile. First, non-serious adverse drug events are present in a proportion significantly superior in social media to those we can find in a pharmacovigilance database [12]. This observation is coherent with previous work [13] and with the fact that non-serious adverse drug events are not often reported by health professionals [14]. Second, social media are potentially important to evaluate drug use, as suggested by Bhattacharya et al. [11]. Indeed, patients report events with an impact on their quality of life, and therefore on their adherence to treatment. Third, patients who post messages on social media are mostly young adults [15], whereas case reports in pharmacovigilance databases usually relate to older patients [16]. Finally, drugs that are most often mentioned in social media are not necessarily the most prescribed, and drugs associated with the main concerns of follow-up in pharmacovigilance studies are not necessarily the most mentioned in social media.

This can have important consequences in constraining the scope of future studies to drugs that are the most frequently mentioned and the populations mainly represented on social media rather than relying on broad-ranging studies. We thus follow the position of Bate et al., who consider that future work should make it possible to establish for which populations, outcomes, or medicines signal detection from social media is best suited [17]. The Harpaz et al. dataset consists mainly of medically important events [18]. Adverse events in the Web-RADR dataset are not provided. Controls were selected within a list of product–event combinations identified by the manufacturer as validated signals. Since these signals were probably detected by means of spontaneous reports from health professionals, it is likely that this dataset was biased towards more medically important events than non-serious events generally described on social media.

We believe that the decision of pursuing or not pursuing research on social media for pharmacovigilance should not only be based on the performance of signal detection algorithms but should also take into consideration societal aspects related to the importance of patients' voice and expectations in improving drug surveillance. Indeed, regulatory agencies do not always respond in time to various emerging signals associated with patient complaints, which may lead to a loss of confidence of the patient toward the regulator [19].

For instance, in France between March 2017 and November 2017, more than 17,000 patients reported adverse events with levothyroxine reformulation [20]. This huge number of reports testifies the level of patients' complaints and feelings that health authorities have not met their expectations. While pharmacovigilance has historically favored serious and unexpected reactions, most patients' reports with levothyroxine described only expected and non-serious reactions, but, in this case, the significant number of patients concerned by these reactions required further attention.

In conclusion, the scientific interest of extracting knowledge from social media, the potential of using large-scale patient feedback in pharmacovigilance and drug-related research, and the impact of this type of research on patients' life quality and their adherence to treatments, lead us to believe in the importance of encouraging current and future research on social media for pharmacovigilance.

Compliance with Ethical Standards

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Conflict of interest Cedric Bousquet, Bissan Audeh, Florelle Bellet, and Agnès Lillo-Le Louët have no conflicts of interest that are directly relevant to the content of this letter.

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