Questions:

1. The references of the publications presented during the webinar:

Risk factor signal detection:

Hopstadius, J., Norén, GN. Robust discovery of local patterns: subsets and stratification in adverse drug reaction surveillance. IHI '12: Proceedings of the 2nd ACM SIGHIT International Health Informatics Symposium January 2012 Pages 265–274. https://doi.org/10.1145/2110363.2110395

Signal:

Boyd, I. Ceftriaxone and Hepatitis in Patients 75 Years and Older. WHO Pharmaceuticals Newsletter. 2018, o. 6, p- 24. https://iris.who.int/bitstream/handle/10665/277447/WPN-2018-06-eng.pdf#page=24

VigiPoint:

Juhlin K, Star K, Norén GN. A method for data-driven exploration to pinpoint key features in medical data and facilitate expert review. Pharmacoepidemiol Drug Saf. 2017 Oct;26(10):1256-1265. doi: 10.1002/pds.4285. Epub 2017 Aug 16. PMID: 28815800; PMCID: PMC5656922.

VigiRank:

Caster O, Juhlin K, Watson S, Norén GN. Improved statistical signal detection in pharmacovigilance by combining multiple strength-of-evidence aspects in vigiRank. Drug Saf. 2014 Aug;37(8):617-28. doi: 10.1007/s40264-014-0204-5. PMID: 25052742; PMCID: PMC4134478.

VigiGroup:

- Norén GN, Meldau EL, Chandler RE. Consensus clustering for case series identification and adverse event profiles in pharmacovigilance. Artif Intell Med. 2021 Dec;122:102199. doi: 10.1016/j.artmed.2021.102199. Epub 2021 Oct 22. PMID: 34823833.
- Mitchell J, Yue QY. Appendicitis as a possible safety signal for the COVID-19 vaccines. Vaccine X. 2021 Dec;9:100122. doi: 10.1016/j.jvacx.2021.100122. Epub 2021 Nov 3. PMID: 34746743; PMCID: PMC8565092.
- Ekhart C, van Hunsel F, van Puijenbroek E, Chandler R, Meldau EL, Taavola H, Norén GN. Post-Marketing Safety Profile of Vortioxetine Using a Cluster Analysis and a Disproportionality Analysis of Global Adverse Event Reports. Drug Saf. 2022 Feb;45(2):145-153. doi: 10.1007/s40264-021-01139-y. Epub 2022 Jan 12. PMID: 35020178; PMCID: PMC8857005.
- Chandler RE, Juhlin K, Fransson J, Caster O, Edwards IR, Norén GN. Current Safety Concerns with Human Papillomavirus Vaccine: A Cluster Analysis of Reports in VigiBase®. Drug Saf. 2017 Jan;40(1):81-90. doi: 10.1007/s40264-016-0456-3. PMID: 27638661; PMCID: PMC5209415.

Web-RADR:

van Stekelenborg J, Ellenius J, Maskell S, Bergvall T, Caster O, Dasgupta N, Dietrich J, Gama S, Lewis D, Newbould V, Brosch S, Pierce CE, Powell G, Ptaszyńska-Neophytou A, Wiśniewski AFZ, Tregunno P, Norén GN, Pirmohamed M. Recommendations for the Use of Social Media in Pharmacovigilance: Lessons from IMI WEB-RADR. Drug Saf. 2019 Dec;42(12):1393-1407. Doi: 10.1007/s40264-019-00858-7. PMID: 31446567; PMCID: PMC6858385.

2. When is UMC planning to introduce courses on methods used in signal detection?

Methods used in signal detection is an important area where UMC could do more to support. UMC will think about this for the future. There are several courses available currently, touching upon different aspects and methods for signal detection.

PV management systems and terminologies
VigiLyze introductory course
Practical exercise in individual case causality assessment

3. We have a big challenge in signal detection with social media. How can we avoid online data biases that might come from groups reluctant to take medications or vaccines? Other difficulties are that posting and monitoring messages in social media are not a constant activity by professionals and patients, like passive surveillance. Is there any base line to compare with?

In the Web-RADR study, the possibility that false information might be planted in various fora as deliberate attempts to create biases, was not addressed. However, this is a serious issue if one relies on this technology to perform signal detection. With emerging technologies such as "generative AI", generation of enormous amounts of false information will be easy, and the issue you raise can be expected to become even more serious. There are not good recommendations on how to manage this issue. Another related issue is the quality of reports that is expected to be variable. In any case, at least for now, it is important to not completely automate the system but have some form of quality assurance made by humans.

4. Thank you for this interesting presentation and congratulations on the wonderful work done. It is an excellent example of the potential of using big data for public health. I have some questions regarding the sentiment analysis:
   Question 1: how were the following challenges addressed : - Representativity of posts - posts in multiple languages? - Access to social media posts (firewall, payments etc.) (especially now that the Twitter API will likely change) - ethical clearance to use such publications in a way they were not originally intended
   Question 2: how was the research method constructed: - Were most frequent words / linguistic groups first detected and then mapped to sentiments , OR - Were the linguistic groups of interest for specific emotions / sentiments first developed, and then targeted searching / social listening done ? - Was signal to be detected mapped to specific risk types ?

This answer concerns the PEEK platform.

Question 1: How the following challenges were addressed :

- Representativity of posts: Social media are naturally biased. However, for early warning this is less critical since it aims at discovering new facts with subsequent verification.

- Posts in multiple languages: We collect for the purpose of EWS posts in English, French, Spanish and Russian.

- Access to social media posts (firewall, payments etc., especially now that the Twitter API will likely change): We receive the data from a commercial provider of open-source data.

- Ethical clearance to use such publications in ways they were not originally intended: WHO does not use, divulgate, or share with external partners and stakeholders any personal information of people posting their experiences. The PVG Team divulgates posts corresponding to published articles in online journals and peer reviewed scientific journals. Until today, we have never used any social media posts in ways not originally intended.

Question 2: how the research method was constructed:

- Were most frequent words / linguistic groups first detected and then mapped to sentiments: Sentiment analysis was not our objective. We were aiming at fact detection. To that end we developed extensive taxonomies, also with the support of AI tools.
- Were the linguistic groups of interest for specific emotions / sentiments first developed, and then targeted searching / social listening done: Data collection was driven by the above-mentioned taxonomies targeting factual data, such as vaccines and medicines, as well as adverse events of special interest (AESIs).
- Was the signal to be detected, mapped to specific risk types: This was the task of the analyst after identification of the signal.

5. It would be important to amplify the narrative capture throughout spontaneous reporting

This is true. Narrative information is crucially important for signal assessment. Research at UMC tries to meet these needs by developing tools that allow PV assessors to optimize use of the narratives. One example in the presentation tried to illustrate that, where we developed a tool that allow PV assessors to perform intelligent searches in the narratives.

6. Can ADR detection from social media be reliable?

Like with other sources for signal detection, social media hold several limitations and pitfalls one needs to be aware of and take into consideration. Social media users are not necessarily representative of the population of interest. Furthermore, medicines discussed on social media might be in the spotlight for different reasons, and signals picked up via social media listening might be distorted (e.g., medicines used off label or treated population with concomitant conditions). Also, the risk of malicious reporting is potentially higher on social media (e.g., spread of misinformation).

7. Noticed that at least one of the links shown later in those slides were from well-known UK antivax sites. Would be interested to hear about the verification process for the sites/ content that is included in the 'signal detection', as we know there is a lot of misinformation.

An important number of posts that are picked in social media do not come from reliable sources and/or are not scientifically based. The social listening platforms presented during the webinar offer the possibility to categorize posts as “untrustworthy”. Pulsar platform integrated NewsGuard, a company that evaluates the credibility and transparency of news and information websites. They analyze content using apolitical journalistic criteria to give an understanding on the extent to which there is misinformation in the search. NewsGuard provides a nutrition label for each piece of content that allows to dive into instances to understand further the articles and content that may be spreading a false narrative. In addition, we have defined a list of sources that are known to favor conspiracy theories. All posts, however, undergo a rigorous analysis before further share with

relevant stakeholders. In the case of the anaphylaxis reaction following COVID-19 vaccination (example to which the question refers to), it was important to understand who posts the information and who spreads it. Negative claims about vaccine safety are inevitable, but the level and scale of response adopted should take into consideration resources and opportunity costs and the potential impact of the claim. For more information and additional resources, please visit Covid-19 vaccines: safety surveillance manual - Communication.

Comments:

- Important to be aware that most public LLMs are programmed to not talk about certain things; if you ask ChatGPT, BARD and others, to tell you about side effects of C-19 vaccines they are broadly blocked from talking about that topic
- For us there is a different between signal detection/ assessment and being aware of other sources of information for consideration during assessment and preparation of communications.
- The threat of misinformation and disinformation is exacerbated by AI content generation. We will need to be both vigilant and connected to follow and preempt these threats.
- Ethics cannot be lost in this 'new world'.