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RESEARCH LETTER

Optimizing Safety Surveillance for COVID-19 Vaccines at the Swedish Medical Products Agency

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Dear Editor,

A vaccination campaign during a pandemic presents several challenges in view of pharmacovigilance. It calls for a rapid increase in resources to manage the large number of adverse drug reaction (ADR) reports, skills to prioritize, and a clarity in communication. Experiences from a single institution will not be implementable everywhere because of different national conditions but could serve as suggestions to solve mutual challenges. We report here the experiences from the Swedish Medical Products Agency (SMPA).

During 2021, the SMPA received 99,211 reports on suspected ADRs, which corresponds to a 12-fold increase in the average annual number of reports. Until 28 July, 2022, 103,788 ADR reports, whereof 82% were reported by consumers, have been received concerning COVID-19 vaccines following delivery of 22,794,815 vaccine doses to 7,856,715 individuals. During the previous mass vaccine program of the influenza type A/H1N1 with Pandemrix in 2009, there was a 50% increase in incoming ADR reports (4380 reports of 6.1 million vaccine doses) (Fig. 1).

The present situation has necessitated the SMPA to focus on the serious and unknown ADRs. First, the internal chain of command focused on decentralizing decision making close to the daily work so that the backlog of reports could be managed continuously and with a revised priority. Second, to unburden and speed up the handling of ADR reports, the technique of robotic process automation was used for registering and MedDRA coding certain data in the received reports, and to automatically retrieve information on batch numbers of vaccines directly from the Swedish national vaccination register. Unlike artificial intelligence processes based on learning, reasoning, and self-correction, robotic process automation processes are dependent on structured inputs and perform tasks based on pre-defined rules and logic. Third, the information considered necessary to be included in the ADR reports distributed to EudraVigilance was regularly re-evaluated based on the characteristics of the different reports and the size of the current inflow. For the national signal detection, disproportionality statistics of Swedish spontaneous reports in EudraVigilance were used. In addition, a case-by-case analysis was conducted to monitor serious unlisted ADRs. Fourth, a temporary administrative arrangement was started with the European Medicines Agency to support the case management and reporting to EudraVigilance.

However, the challenges related to a mass vaccine program is not only to manage the large number of reports, where the vast majority most likely will concern well-known ADRs. There is also the challenge to identify and verify the very uncommon ADRs that usually need complementary approaches for further analyses and confirmation. With experiences from narcolepsy and Pandemrix where the importance of conducting epidemiological studies was noted [1], the SMPA has, as a research project with ethical approval, set up a nationwide register-based study to detect and characterize suspected ADRs after COVID-19 vaccines [2].

Observed to expected analyses of safety concerns identified in the national signal detection work were evaluated using the aforementioned nationwide registers on hospitalizations and specialized out-patient care visits linked to the vaccination register [2]. Events occurring within a specified time window after immunization constituted the observed frequency. Pre-pandemic historical data from the same registers constituted the expected number, permitting a standardized morbidity ratio to be calculated. We hope that access to similar register data can be a part of our future regular pharmacovigilance. The preparedness enabled us to act rapidly

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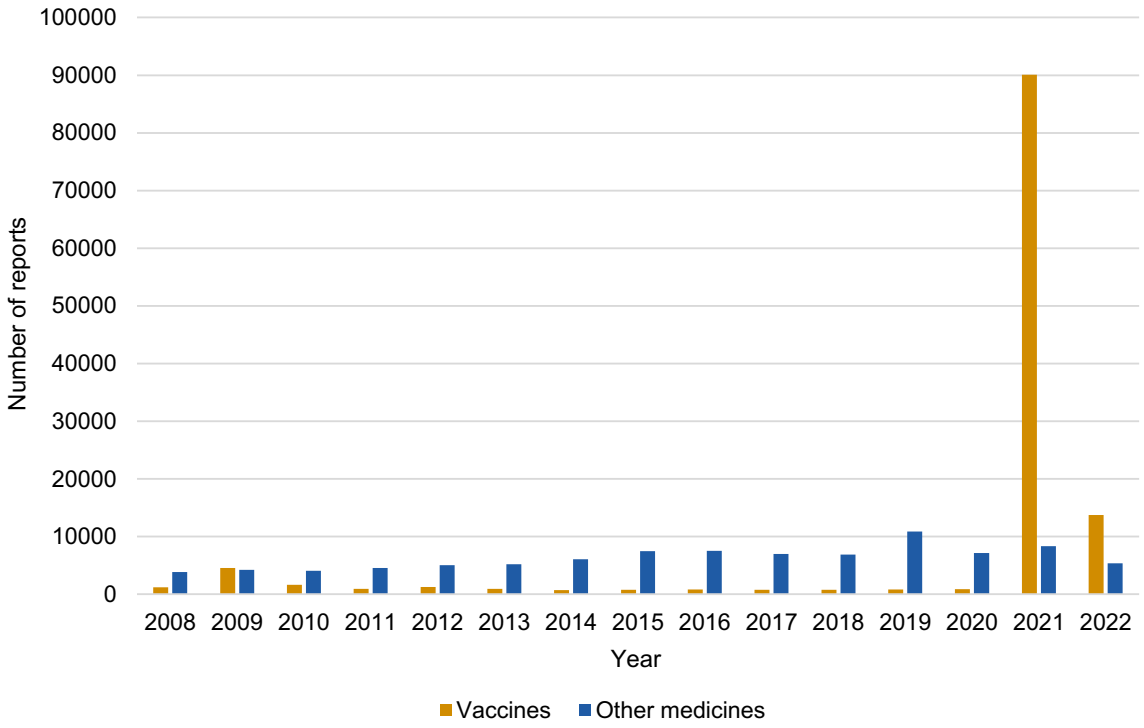

Fig. 1 Number of reports on suspected adverse drug reactions reported to the Swedish Medical Products Agency from 2008 to July 2022

and has hitherto generated information foremost regarding the risk of myocarditis in younger male individuals [3, 4].

A preparedness for future pandemic situations will most likely include a variety of measures of which some have been discussed by us and others [5, 6]. However, to improve the efficacy of the present daily pharmacovigilance activity, the robotic process automation technique and additional measures to facilitate the submitting of ADRs should be implemented immediately. The SMPA foresees a closer collaboration concerning epidemiological surveillance between data holders of health registries and the national competent authorities.

Declarations

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Conflicts of Interest/Competing Interests Anders Sundström reported participating in research funded by governmental agencies, universities, Astellas Pharma, Janssen Biotech, AstraZeneca, Pfizer, Roche, (then) Abbott Laboratories, (then) Schering-Plough, UCB Nordic, and Sobi, with all funds paid to Karolinska Institutet, outside the submitted work. Rickard Ljung reported receiving grants from Sanofi Aventis paid to his institution outside the submitted work; and receiving personal fees from Pfizer outside the submitted work. Karl Mikael Kälkner, Marja-Leena Nurminen, Maria Larsson, and Veronica Arthurson have no conflicts of interest that are directly relevant to the content of this letter.

Ethics Approval The study was approved by the Swedish Ethical Review Authority (2020-06859 and 2021-02186).

Consent to Participate The need for informed consent is regulated in the Swedish Act on ethical review in human research. An informed consent is waived by the Swedish Ethical Review Authority as this is a register-based study.

Consent for Publication Not applicable.

Availability of Data and Material Aggregated data of adverse drug reaction reports can be found at https://www.lakemedelsverket.se/sv/coronavirus/coronavaccin/rapporterade-misstankta-biverkningar-coronavaccin (in Swedish).

Code Availability Not applicable.

Author Contributions Drafting of the manuscript: KMK and RL. Analyses of number of spontaneous reports: ML. Critical revision of the manuscript for important intellectual content: all authors. All authors read and approved the final version.

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