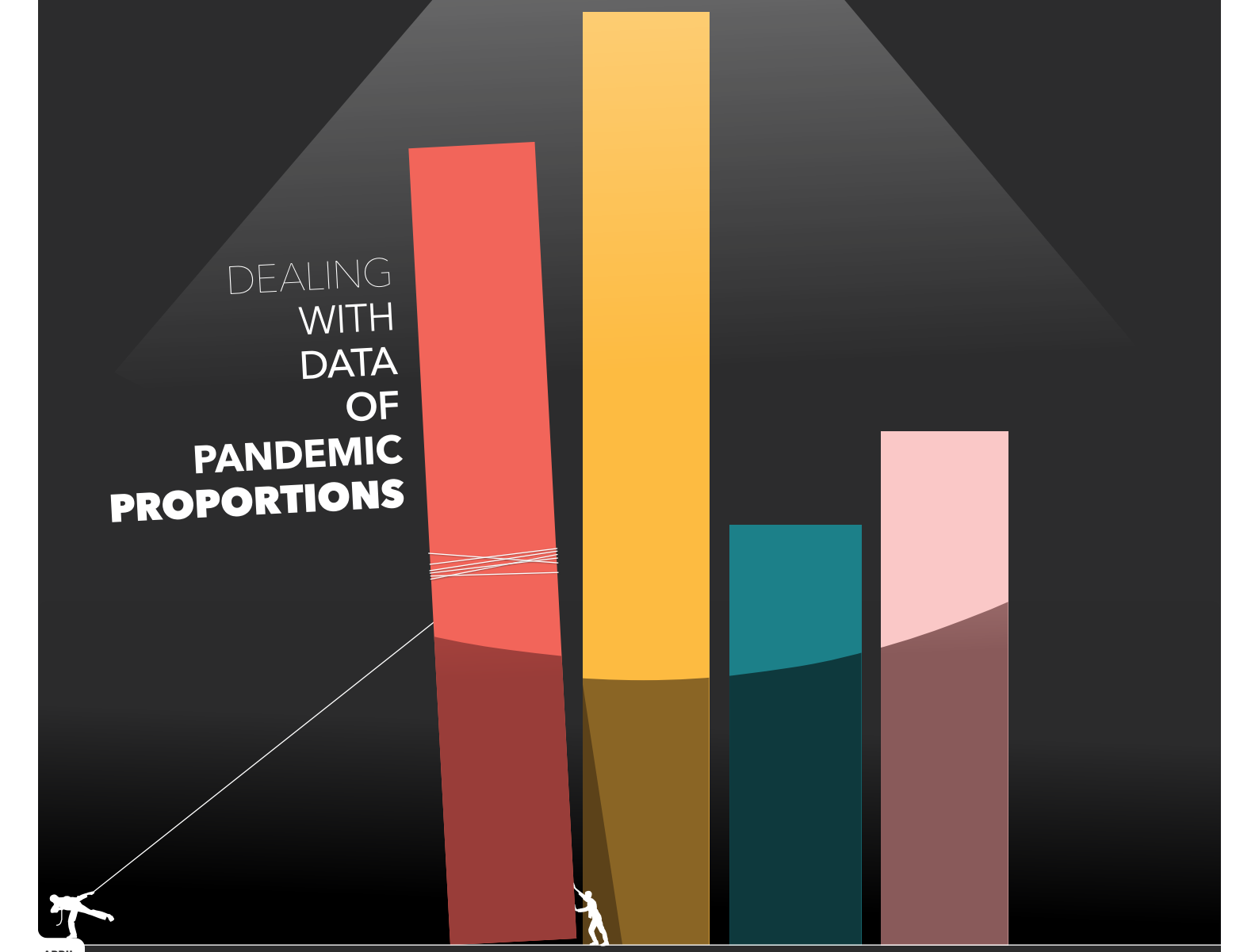
UPPSALA

REPORTS

COVERING THE WORLD OF PHARMACOVIGILANCE



DEALING WITH DATA OF PANDEMIC PROPORTIONS

APRIL 2023
ISSUE 87

COVID-19 VACCINE SURVEILLANCE

MEET THE NEW UMC DIRECTOR

WE REMEMBER TWO PV LEGENDS

Uppsala Monitoring Centre

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WHAT IS UPPSALA REPORTS?
Since 1996, Uppsala Reports has been the public voice of Uppsala Monitoring Centre, pursuing the mission and connecting the members of the WHO Programme for International Drug Monitoring.

From the editor

A turning point in UMC history

This issue marks many beginnings, but also some endings of chapters in the UMC story, starting with the magazine that serves as its scribe, *Uppsala Reports*, which now has a new editor. Although I am new to this role, I am not new to the magazine, having written for it before as a contributing editor. I have always loved telling stories, and to have been given the opportunity to play a part in continuing such an important one is an honour that I take on with much pride and enthusiasm.

That sentiment is also exemplified by Peter Hjelmström, UMC's new director. Peter comes to us with 25 years of experience spanning academia, healthcare, and the pharmaceutical industry. Although his career history is broad, Peter has always had one overarching focus: patient safety. We welcome him and his leadership to the UMC family.

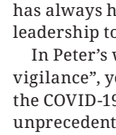
In Peter's words, UMC was "instrumental in building the field of pharmacovigilance", yet there remains much work to be done. To take one example, the COVID-19 pandemic and resulting global immunisation effort has left an unprecedented number of vaccine safety reports in its wake, requiring novel, innovative methods to deal with all that data. In this issue of *Uppsala Reports*, we feature three educational and inspiring stories on this topic, and we discuss some tools that UMC has specifically developed to help handle vaccine safety reports.

Lastly, it is with great sadness that we bid farewell to two heroes, not only in the UMC story, but in the greater story of pharmacovigilance: Barbro Westerholm and Ed Napke.

Barbro's life indeed reads like an epic: her origin story centres on the thalidomide tragedy that led to pharmacovigilance as a systematic practice. However, her legacy in pharmacovigilance is but a small part of her greater impact on human rights in Sweden.

And Ed Napke was a force to be reckoned with. While the term 'pioneer' tends to be overused in obituaries, it is the only way to describe Ed and his influence on pharmacovigilance. Ed is most famous for having developed the "pigeon-hole alerting system", a more visual way of aggregating case reports to detect signals. However, his theories and contributions continue to have a great impact on the world of pharmacovigilance.

What a time to begin a new chapter...



Alexandra Coutinho
Editor-in-chief

ILLUSTRATION: IWONA KAZIA KALITAN MŁODKOWSKA

Are you new to VigiFlow or VigiLyze?

Fast track your training with our online self-paced courses.

For those who are new to **VigiFlow**, we offer an introductory course in English, Spanish, and French which takes approximately one hour to complete. The course introduces new users to VigiFlow and its interface, illustrating how to enter and structure ICSRs in the system. For a more comprehensive understanding of VigiFlow, such as examining case processing, we have just released the intermediate course: "Enhancing understanding and improving workflow". This course is currently available in English and will soon be released in Spanish. It takes around 2–2.5 hours to complete.

If you are a new **VigiLyze** user or have limited knowledge of the tool, we encourage you to take the VigiLyze introductory course, available in both English and Spanish. This course takes approximately 1.5 hours to complete and aims to guide you through VigiLyze and its main functionalities to optimise the analysis of drug/vaccine safety data in your pharmacovigilance centre.

To enrol in a course, visit the relevant course page, click "Join waitlist" and create an account in the learning platform or log in to your existing account. Course applicants with VigiFlow or VigiLyze accounts will gain access to the course within 1–3 business days.

UMC also offers several other online courses open to the public sector. Visit the course catalogue to find out more: *learning.who-umc.org*

Announcing this year's #MedSafetyWeek!

Get ready for another annual medicines safety awareness week, taking place from 6 to 12 November 2023. The theme for this year is "Who can report? – How patients, doctors, and pharmacists contribute to pharmacovigilance."

Find out more by visiting our campaign website: *who-umc.org/medsafetyweek*

PHOTO: SHANNEN YOUNG

Peter Hjelmström joins UMC as new director

Uppsala Monitoring Centre (UMC), the WHO Collaborating Centre for International Drug Monitoring, is pleased to announce the arrival of its new director Peter Hjelmström.

After more than 25 years of experience within academia, healthcare, and the pharmaceutical industry, Peter Hjelmström brings with him a broad insight into the role of pharmacovigilance and patient safety.

Hjelmström has an academic background as a physician and scientist, with MD and PhD degrees. He was an associate professor at Karolinska Institute before joining the pharmaceutical industry where he has worked in various roles. He did his postdoctoral fellowship at Yale University.

He singles out UMC's heritage as a scientific leader, instrumental in building the field of pharmacovigilance, as being a key consideration in his decision to join UMC.

"It is a special organisation to be part of. It has achieved so much and has played a really important role in advancing patient safety globally since its foundation in 1978. That heritage, backed by the growing global member network of the WHO Programme for International Drug Monitoring and reinforced by continuous development of vital pharmacovigilance tools and services, together constitute a formidable platform for advancing medicine safety in the future and I am proud to now be a part of this organisation."

Speaking on behalf of the UMC Board, Chair Filippa Nyberg said: "We are very pleased that Peter accepted to become the next director of UMC. With his clinical and scientific background, extensive industry experience and focus on patient safety, Peter brings a rare skillset to the role. UMC is a strong organisation with a great history, and we believe Peter's leadership abilities are an excellent match for UMC's future development."

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WHO programme member updates

UMC is pleased to welcome **Yemen**, **Gabon**, and **Mauritania** as new full members of the WHO programme for International Drug Monitoring, and **Lesotho** and **Comoros** as new associate members. Mauritania, Gabon, and Comoros joined our ranks in January 2023, whereas Lesotho and Yemen joined in July and August 2022 respectively. Their membership brings the total number of WHO PIDM full members to 155, with 21 associate members.

All WHO programme members: *Bit.ly/WHOProgrammeMembers*

Welcome Yemen ...

...Gabon...

...Mauritania...

...Lesotho...

...and Comoros

ISTOCK

PROMOTING PHARMACOVIGILANCE IN AZERBAIJAN

Since it joined the WHO PIDM in 2010, Azerbaijan continues to prioritise the safe use of medicines.

Azerbaijan is a small country of around 10 million people bordered on the east by the Caspian Sea, neighbouring Iran, Turkey, Georgia, Russia and Armenia. Part of the WHO Euro region, it is an oil-rich nation with a strong artistic legacy, culture and customs. The capital, Baku, is one of the largest industrial, scientific and cultural centres in the region, and reflects the ethnic composition of the whole country.

In Azerbaijan, the national pharmacovigilance centre was established in 2017 within the Analytical Expertise Center (AEC) of the Ministry of Health (the national regulatory authority). It is responsible for formulating and implementing technical and operational guidelines, regulations and standards, setting up and coordinating pharmacovigilance systems at the national level, monitoring medicines safety, and identifying all changes affecting the benefit-risk balance.

The first pharmacovigilance activities in Azerbaijan were in 2010 when it joined the WHO Programme for International Drug Monitoring (WHO PIDM) as an associate member. The centre began submitting individual case safety reports (ICSRs) through VigiFlow to the WHO global database (VigiBase), and the current total number is 1,818. ICSRs are mainly received on medicines that are part of public health programmes, such as medicines for tuberculosis and AIDS. On 23 January 2018, the centre became the 130th full member of the WHO PIDM, further boosting pharmacovigilance activities in Azerbaijan.

Ensuring medicines safety in Azerbaijan is one of the AEC's primary responsibilities. UMC's web-based tools make it possible to actively monitor the safety of medicines marketed in Azerbaijan and take timely decisions based on safety signals. VigiFlow, being a web-based pharmacovigilance management system compatible with the ICH E2B (R2 and R3) guidelines for ICSR reporting, eases data entry options for ADR and AEFI reports. It uses integrated standardised medical terminologies such as WHODrug Global and MedDRA, and also supports the use of different causality assessment methods (such as WHO-UMC causality and Naranjo), and provides access to VigiLyze, where it is possible to perform signal detection by using disproportionality analysis and signal management. This online reporting tool gives us the confidence to continuously strengthen our collaboration within the WHO PIDM and to use VigiBase services.

Increasing global awareness of the importance of pharmacovigilance systems led the Azerbaijan government to call for legal reforms, which accelerated the revision of the law of the Azerbaijan Republic on medicinal products, and following that, the preparation of a "Regulation of Pharmacovigilance for Medicinal Products" in 2019. The regulation, developed to implement state control on the effectiveness and safety of medicinal products, defines a set of measures to detect, evaluate, and prevent adverse reactions and other undesirable consequences when using medicinal products. It applies to medicinal products' marketing authorisation holders (MAH) and all health institutions. Implementation has been supported by a set of guidelines for the conduct of pharmacovigilance in Azerbaijan, "Good pharmacovigilance practices (GVP)".

In connection with the implementation of pharmacovigilance activities provided by the 2019 regulation, both MAHs and health institutions must assign a person with a medical or pharmacy background to be responsible for pharmacovigilance. Since March 2022, public health institutions (hospitals and polyclinics) have undertaken active recruitment to the positions of responsible person for pharmacovigilance. Their duties and responsibilities include reporting ICSRs to the AEC's pharmacovigilance department, responding promptly in case of crises, and following up on ICSR reports.

The next stage will be crucial: working with responsible persons for pharmacovigilance assigned by health institutions. We plan to organise workshops and training for them and give them access to VigiFlow for reporting ICSRs. As a result, we believe that we will see a significant increase in the number and quality of ICSRs sent to VigiBase.

Besides that, with the support of experts from UMC, AEC has implemented an online reporting system. The UMC-developed online system for reporting ICSRs provides easy access to a simple, native language e-reporting form. Integration of the online reporting interface to the VigiFlow database makes it easy for national pharmacovigilance staff to collect ICSRs. Currently, we are working on preparing a video guide for reporters who will use the interface.

To ensure timely identification of suspected safety problems in medicinal products, we aim to enhance pharmacovigilance activities in health institutions across Azerbaijan. The continuous education, communication with healthcare professionals and MAHs, and workshops and campaigns will promote a reporting culture and encourage healthcare professionals and patients to report ICSRs.

Farid Hasanov
Head of Pharmacovigilance, Department of Analytical Expertise Center of the Ministry of Health, Azerbaijan

UMC MOBILISES OFFLINE APP FOR VACCINE ADVERSE EVENT REPORTING

Now vaccination field workers can collect reports on adverse events following immunisation (AEFI) using a phone, tablet, or laptop even in the remotest of locations.

UMC has launched a new offline app in partnership with the pharmacovigilance team at WHO for reporting possible side effects from vaccines.

Directly connected to UMC's VigiFlow data management system, the VigiMobile app makes it possible for immunisation field workers to collect AEFI reports electronically on their smartphones, tablets, or laptops, with or without an internet connection.

Vaccine safety surveillance is essential to the success of immunisation programmes. If safety concerns around vaccines aren't dealt with rapidly and correctly, they can dent people's confidence in vaccines and undermine vaccination programmes. But getting data to decision-makers quickly so potential safety issues can be investigated, understood, and managed is not always easy. According to WHO, there are several countries without an effective system for monitoring vaccine safety.

"Effective AEFI reporting is the first step in making sure vaccines are being safely administered," says Dr Madhava Ram Balakrishnan, Medical Officer Vaccine Safety at WHO. "In VigiMobile and VigiFlow for AEFI, we have a frontline system for monitoring vaccine safety right in the hands of the vaccinator and their supervisors. Such tools are particularly vital in countries where large parts of the population live in remote areas and essential to ensure the safety of vaccination programmes and see whether further public health or regulatory actions are needed."

In many countries vaccine monitoring and reporting is often paper-based due to traditional work practices, limited internet access, or high internet costs. This can delay information sharing and impact decision-making at district or state level where events or clusters of events may trigger more in-depth investigations.

Jenny Jansson Liikamaa, portfolio manager of pharmacovigilance offerings at UMC, says because the app is uniquely designed to capture structured vaccination and patient location data at time of reporting, VigiMobile can help investigators to pinpoint clusters of adverse events and make informed decisions based on actionable insights.

"Using their smartphone, tablet or laptop, immunisation workers can capture events as soon as they happen even when they are offline and queue them for sending later. They now have the confidence that in the unfortunate case of a rare serious adverse event, rapid reporting is possible in a few minutes. This reduces the risk of vital information being lost in the field and enables officials to respond faster to a serious event that demands urgent investigation and a rapid response."

UMC adapted VigiFlow to collect and analyse AEFI data during the coronavirus pandemic. Working closely with WHO, it set out to help national immunisation programmes and regulatory authorities meet the new guidelines around vaccine surveillance and safety monitoring. Before then VigiFlow had mainly been used by countries in the WHO Programme for International Drug Monitoring to collect and analyse reports of potential side effects from drugs. Now it has been customised to do the same for vaccines, with UMC successfully expanding its expertise in ICSR management to AEFI data.

"IN VIGIMOBILE AND VIGIFLOW FOR AEFI, WE HAVE A FRONTLINE SYSTEM FOR MONITORING VACCINE SAFETY RIGHT IN THE HANDS OF THE VACCINATOR AND THEIR SUPERVISORS"

READ MORE:

- AEFI reporting in the palm of your hand, anytime, anywhere *who-umc.org/pv-products/vigimobile/*
- WHO pharmacovigilance team web page *who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance*
- "VigiFlow boosts vaccine surveillance efforts", *Uppsala Reports*, 2021
- More on the WHO Programme for International Drug Monitoring *who-umc.org/about-the-who-programme-for-international-drug-monitoring/*
- About VigiBase – *who-umc.org/vigibase/*

LISTEN UP!

- Why we need vaccine surveillance systems, *Drug Safety Matters* podcast. Get it here: *http://bit.ly/3kqE18Q*

With VigiMobile, VigiFlow, and VigiFlow for AEFI, UMC can offer national immunisation programmes, national regulatory authorities, and national pharmacovigilance centres a one-stop shop for all their vaccine surveillance needs. This includes AEFI data collection, collation and identification of related safety events, and global information sharing.

Both VigiMobile and VigiFlow for AEFI use WHO's standard AEFI reporting form with the 25 core variables recommended by WHO for collecting AEFI data. As soon as reports have been sent to VigiFlow, immunisation programmes can also share them with WHO's global database of adverse event reports, VigiBase.

Zimbabwe is the first country to roll out the app, with other national immunisation programmes set to follow.

For more information, contact support@who-umc.org

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Ed joins UMC in celebrating 40 years of pharmacovigilance

PHOTO: GÖRAN EKEBERG

A THINKER OUTSIDE OF THE BOX

Canada's Dr Safety, Ed Napke, has died aged 99. The inventor of the pigeonhole "alert system" for adverse reactions was a fearless and determined campaigner for public health and the safer use of medicines.

Born in Lebanon in 1924, Ed Napke's family moved to Canada when he was very young. There he studied and went on to obtain a BSc at the University of New Brunswick in 1945, then his medical degree from the University of Toronto in 1951, and a public health degree in 1968.

A turn of fate took him down the path of ground-breaking research on adverse effects from medicines not related to active ingredients but triggered by excipient components, no doubt influenced by his broad view of the ways medicines, vaccines, and other chemicals might, on their own or by interacting with others, cause harm to individual people. He also understood the importance of recognising that the individual psychological, physical, and social circumstances of people at any time would be important in assessing the effects of medicines and chemicals. With adverse drug reactions he advocated not being limited to reporting single event terms, or even a collection of such terms, but recognised the importance of "syndromes", both in the medical sense, and in the way of finding collections and patterns in nature.

His research caused a stir in the research community; former

"To me adverse drug reaction monitoring is a commitment, not a job"

Members of the WHO Collaborating Centre advisory group outside its office at the MPA in Uppsala in the mid-80s

Dr Ed Napke strikes his characteristic smile in Dubrovnik, Croatia with Ralph Edwards and colleagues, 1985

The early years: Ed Napke and Ingebjörg Buajordet, the Scientific Director of the Pharmacovigilance Centre in Norway

UMC director Ralph Edwards wrote, in the preface to the 2009 UMC collection of Ed Napke's writings and thoughts, that he was "one of the pioneers in pharmacovigilance, and much else, whose work over the years has always brought the fresh air of innovation and controversy into medicine".

In the early 1960s, a friend asked Ed to join the Canada Food and Drug Directorate because of the post thalidomide drug regulations. In 1963, he and one other doctor began to medically review new drug submissions, which resulted in several visits to the US FDA, and in 1965 he created the Canada Adverse Drug Reaction Reporting Program within the drug regulatory body. He decided to expand monitoring from drugs to all products on the Canadian market and had inherited a fast expanding poisons control programme, and he renamed the ADR Reporting Program the 'Product Related Disease Division'. This was a farsighted move, the only other centre considering monitoring other chemicals as well as medicines was being developed in New Zealand by his friend and colleague, Prof Garth McQueen.

Ed would lead the Canadian pharmacovigilance programme until 1990. He continued work in the 90s and beyond as a keen founding member of the UMC's signal review panel, as well as co-author of an important and still cited paper on what might constitute a true signal from the aggregated data of case reports.

Over the years Ed held positions at McGill University's Psychopharmacology Division; Ottawa General Hospital; the Institute of Clinical Toxicology in Houston, Texas; the Memorial University of Newfoundland; and the Royal Ottawa Hospital Chronic Fatigue Syndrome programme. In 1971 he was made an honorary member of the National University of Buenos Aires in Toxicology, and in 1971 the Latin American Association of Toxicology made him a Correspondent Member. His long career truly reflects his declaration in *Uppsala Reports* 25 (April 2004), "to me adverse drug reaction monitoring is a commitment, not a job".

PHOTO: STEN OLSSON AND MARIE LINDQUIST

Ed's legacy lives on in the many people he has inspired through his work and research, such as Dr Viola Macolić Šarinić, a scientific officer at the European Medicines Agency and member of the WHO Advisory Committee on Safety of Medicinal Products. "[Ed Napke was a] Wonderful and brilliant mind serving public health, and at the same time a modest and kind human being. Ed Napke's name I came to know as a medical student and is one of those who inspired me to dedicate my professional life to pharmacovigilance. I also had the privilege to meet him in person when I became a pharmacovigilante."

Ed's outlook on disease prevention may best be summarised in his own words, written for the 2018 UMC anniversary book: "[We] must also return to the idea of preventing disease through good nutrition and exercise. Healthy bodies are cheaper, so we simply need to help people live better lives, with less fear. And I think that's a hopeful message for the future."

Edward Napke, 21 January 1924–13 February 2023

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READ MORE:

- I R Edwards et al, "Quality criteria for early signals of possible adverse drug reactions", *Lancet*, 1990.

AN ADVOCATE FOR CHANGE

We pay tribute to the life of a true advocate and agent of change in patient and medicines safety, Barbro Westerholm, who has died age 89.

Born and raised in Stockholm, she obtained her medical degree from the Karolinska Institute in 1959. While completing her PhD she joined the Swedish National Board of Health and Welfare in 1965 "to work with WHO and other countries following the catastrophe with thalidomide". She had been offered the drug during her second pregnancy – but had decided not to take it.

One of the pioneers of pharmacoepidemiology and pharmacovigilance, Barbro was heavily involved in the early stages of the WHO Programme for International Drug Monitoring and its prototype ADR terminology. Those early days of the programme nurtured a tight-knit family of individuals united around medicines safety concerns with a commitment to educate, communicate, develop methodologies, and listen to other countries' needs.

When in the mid-1970s WHO decided to focus on essential drugs and access to medicines and healthcare in developing countries rather than safety, Barbro became a key advocate for moving the drug monitoring centre to Sweden. Financial backing from the Swedish government and help with premises, together with the qualified staff who were recruited, culminated in the creation of Uppsala Monitoring Centre.

Barbro Westerholm presents at the 40th anniversary meeting for UMC in 2018

PHOTO: UMC

"EVEN IN TODAY'S DIGITAL AGE, PERSONAL CONTACTS ARE SO IMPORTANT"

Barbro remained fiercely dedicated to patient and medicines safety through the many initiatives she successfully led throughout her career. She was a medical adviser at the Swedish National Board from 1971 to 1974 and became its first female director general (1979 to 1985), where notably she had homosexuality dropped from the list of mental health diseases. She was also an adjunct professor of pharmacoepidemiology at the Karolinska Institute from 1986 to 1989, and medical director at Apoteksbolaget (the Swedish state-owned pharmacy) from 1985 to 1993. Her career further involved contributions to research such as investigations into the side effects of oral contraceptives.

She was elected to the Swedish parliament twice, from 1988 to 1999 and 2006 to 2022, and was awarded the Nordic Public Health Prize in 2009 for her work to fight discrimination against older people.

Barbro remained a steadfast friend to UMC and was a proponent of building good professional relationships; as she wrote in 2018: "Even in today's digital age, personal contacts [like these] are so important."

Barbro Westerholm
16 June 1933–13 March 2023

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READ MORE:

- *"Making medicines safer"*, Uppsala Monitoring Centre, 2018.
- History of Uppsala Monitoring Centre – *youtube.com/watch?v=Drog3Bpvhno*

EGYPT'S COUNTERFEIT MEDICINES:

GOING BEYOND THE SIGNAL

One recent case involving a potentially dangerous fake antibiotic drug has brought to the fore systemic weaknesses that can only be remedied by group action.

Substandard, also called "out of specification", and falsified (or counterfeit) medicines pose a real barrier to delivering high-quality health services, and are a significant contributor to longer hospital stays and deaths. These include branded and generic medicines that have failed to meet international good manufacturing practices, pharmaceuticals fraudulently produced with the wrong or no active ingredient, and poor quality products deliberately mislabelled to boost the ever-growing trade in medicines bought over the internet.

Antibiotics are among the most counterfeited medicines, particularly in poorly regulated developing countries, and contribute to driving high prevalence of drug-resistant pathogens with poor infection control. This could well lead to therapeutic failure that necessitates the prescription of broader-spectrum, relatively more expensive antibiotics. In Egypt untrained drug vendors have replaced pharmacists as the main source of medicines in most private retail pharmacies. Recently, safety issues stemming from counterfeit batches of Unictam 1500 mg vials by Medical Union Pharmaceuticals (MUP) were found in several provinces across Egypt.

Between 2 February and 17 April 2022, the pharmacovigilance department at MUP received 48 individual case safety reports (ICSRs) of suspected adverse reactions associated with Unictam. This led to a series of rapid investigations in 12 governorates, including Cairo, Alexandria, and the Nile Delta region. Aspects of this signal involved, among others, an increasing number of spontaneous reports submitted in a noticeably short period of time, the nature and prevalence of adverse drug reactions (ADRs), and the difference between adulterated and real pharmaceuticals with respect to product characterisation and impurity profiling.

ILLUSTRATION: MARTEN LEO

Along with some subtle differences in packaging and labelling, initial laboratory tests conducted on the seized counterfeits found that they contained a potentially harmful and unapproved substance of low quality, which did not meet the correct specification. At this point, nearly two-thirds of the documented cases of drug counterfeiting were hospitalised with symptoms of chest pain, haemoptysis, high blood pressure, syncope, and tachycardia. Healthcare professionals (HCPs) also took to social media to highlight the issue and voice their concerns over serious pregnancy-related complications in which one of the cases had experienced a miscarriage due to counterfeit Unictam administration.

For those patients who were unknowingly harmed by the counterfeit Unictam, the coverage for claims-made insurance policies ruled out unapproved products – including counterfeit medicines, with no financial protection against the costs of recalls sparked by such products.

> "We are assessing signals involving counterfeit medications at a broader level so as to help identify important potential risks, and to update our overall approach for managing risks"

Based on information corroborated by MUP, the relevant drug safety alerts that ensued have exposed the extent of the problem and led to calls for better harmonisation and coordination among pharmacovigilance stakeholders to ensure comprehensive implementation of regulatory and legal measures. Our findings require using a risk management approach to identify areas of exposure to counterfeit pharmaceuticals and provide for a national track-and-trace system in the pharmacy sector that would guarantee a reliable stock of authentic medicines all the way to patients. Poor supply chain management contributes to exhausted stocks that force patients to buy medicines of whatever sort outside the legitimate sales sector. This creates the possibility to infiltrate counterfeit drugs at every node of the entire distribution network.

It is clear that linking manufacturers directly to drug stores and hospitals, while bringing into force primary packaging serialisation to uniquely identify items at the unit level, will allow for a full audit trail and create a viable ecosystem of concerned stakeholders all with the same goal. From an overall perspective, advanced authentication and increased technological sophistication will set up successful anti-counterfeiting systems that make it easier for HCPs and patients to determine the legitimacy of suspect products by cross-referencing a unique product identifier in barcodes against a database.

Raising public awareness of the hazards connected to counterfeit medicines continues to be challenged by supply chain vulnerability and the risks arising from the presence of counterfeit drugs in unregulated markets. A pragmatic set of policies needs to be implemented to increase the availability of lowest-priced generics and to restore faith in genuine medicine, particularly in areas where the lure of affordable or unauthorised products tends to overwhelm the safety message. Switching of brands as well as loss of public confidence in the treatments they rely upon, and perhaps reputational damage, should be of concern to Egyptian pharmaceutical industry leaders as they position themselves to be among the primary pharmaceutical export markets in Africa and beyond.

Acknowledgements
The authors wish to thank Dr Hadir Rostom, President of the ISoP Egypt Chapter, for her support in undertaking the project; with a special thank you to those who collaborated to produce this piece of work.


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UNMASKING IN THE COVID-19 VACCINE ERA

First came the COVID-19 pandemic. Then came the COVID-19 vaccines. Then came millions of COVID-19 vaccine reports of suspected side effects. What are the implications of that?

New VigiLyze Therapeutic Scope setting enables unmasking

A recent update to VigiLyze lets users select drug- or vaccine-specific search and analysis. By default, all reports are included in the dataset, including drugs and vaccines. But with the new "Therapeutic Scope" setting, users can easily limit the scope to either vaccines or drugs. By controlling which reports are available for searches, users gain options for calculations and results, such as disproportionality values and report counts in the Qualitative and Quantitative areas.

ILLUSTRATION: MARTEN LEO

"WHAT IS IMPORTANT IS THAT WE STAY AWARE OF THE PROBLEM OF MASKING AND DO SOMETHING"

With the successful rollout of vaccines, starting barely a year into the pandemic, rigorous monitoring of their safe use immediately followed. Both regulators and WHO advocated for close monitoring and reporting of any potential adverse drug reaction (ADR), and this call was certainly adhered to: 2.9 million reports flooded into VigiBase during 2021, and an additional 1.7 million reports were entered during the first 10 months of 2022.

However, while these reports form a crucial asset in supporting the safe use of the vaccines, such a massive influx of reports does create an imbalance within VigiBase. "COVID-19 vaccine" is now, by far, the most commonly reported medicinal product type in VigiBase with 4.6 million reports (13% of the entire database). In a modest second place comes adalimumab with 650,000 reports, followed by etanercept with 570,000 reports (and both adalimumab and etanercept have been on the market for over 20 years).

Overall, the response to the call for reporting of COVID-19 ADRs must be considered a success. Nevertheless, when a single medicinal product makes up such a large proportion of the entire database, it will affect statistical signal detection, even when performed for other drugs. Let's take Bell's palsy as an example, where 87% of the 13,000 entries in VigiBase come from COVID-19 vaccine reports. It doesn't matter which measure of disproportionality you use, the expected counts for Bell's palsy will be inflated massively by the COVID-19 vaccine reports, which means that it will not appear as disproportionate for other drugs as long as the COVID-19 vaccine reports are in the way and hide the statistical signal. This effect is called masking, also known as cloaking, or competition bias.

Masking is not a new problem in pharmacovigilance. In 2013, UMC developed a method to uncover masking by identifying influential outliers. Earlier this year, we applied this method to all ADRs that have been reported for COVID-19 vaccine reports. What it basically does is compare the frequencies of an ADR with and without COVID-19 vaccine reports. If we see an increase by at least 50%, we consider the ADR masked. The method also applies statistical shrinkage to the calculation to get a more robust measure, limit the effects of random variability, and shift focus away from ADRs that are overall very rarely reported in the database.

Using this threshold, we identified 132 ADRs as masked by COVID-19 vaccine reports. Of these, 21 are on the EMA's list of Important Medical Events. Examples of reactions we see masked are sweating fever, Bell's palsy, vaccine breakthrough infection, hemiparaesthesia, myocarditis, and pericarditis. And notably, for some of these ADRs, a majority of the reports in VigiBase now relate to COVID-19 vaccine reports, as is the case with our example, Bell's palsy.

In a very interesting study made in VAERS, published in July 2022 in *Drug Safety* by Harpaz et al, we can see the opposite problem, how statistical detection of early COVID-19 vaccine signals in the very beginning of the vaccine rollout were delayed because of masking due to other drugs. For example, that study found that the statistical signals of myocarditis with Pfizer and Moderna vaccines were masked by smallpox vaccine. As more data accumulated, the Pfizer and Moderna vaccines then started to mask the signal from each other. This is also a very interesting piece of the puzzle, understanding that masking is not a static phenomenon, but something that evolves with the data. This study also teaches us that it might be especially important to consider masking when a new drug is introduced, or as long as there are few reports on that drug. Now the seesaw has flipped for the COVID-19 vaccines – signals are no longer masked from them but due to them.

So where do we stand now, knowing that 13% of VigiBase is made up of COVID-19 vaccine reports?

The large proportion of COVID-19 vaccine reports may hide or delay the detection of statistical signals of many ADRs when calculating disproportionality for other drugs. This is a problem that must be addressed. One way is to simply remove all COVID-19 vaccine reports when doing statistical signal detection for other drugs. Another way is to perform a method of unmasking, like the simple unmasking suggested by Juhlin et al 2013, which identifies any outliers and carries out a parallel analysis after they have been omitted. Regression analysis has also been proposed as a method to deal with the issue.

In the end, though, whichever method we choose is not that important. What is important is that we stay aware of the problem of masking (due to COVID-19 vaccines as well as due to other drugs) and do something.

Sara Vidlin
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READ MORE:

• Harpaz, R. et al, "Signaling COVID-19 Vaccine Adverse Events", *Drug Safety*, 2022.

• Juhlin, K. et al, "Outlier removal to uncover patterns in adverse drug reaction surveillance - a simple unmasking strategy", *Pharmacoepidemiology and Drug Safety*, 2013.

LISTEN UP:

• Unmasking data is the COVID-19 vaccine era, *Drug Safety Matters* podcast. Get it here: *http://bit.ly/3GexLZd*

Celebrating 30 years of learning

Uppsala Monitoring Centre has offered annual pharmacovigilance courses, both face-to-face and online, since 1993.

In that time, over 14,000 people from 168 countries have taken UMC courses in English and Spanish.

Many past course participants have gone on to advance pharmacovigilance in their own country, from founding national pharmacovigilance centres to becoming leading pharmacovigilance experts. Here are just some of them:

1993, Mariano Madurga
Ex-Head of Co-ordination Unit of Spanish Pharmacovigilance System (SEFV-H), Spain

1993, Rachida Soulaymani Bencheikh
Director of Morocco Poison Control and Pharmacovigilance Centre and Rabat Collaborating Centre, Morocco

1993, Niamh Arthur
Ex-Pharmacovigilance Manager, Health Products Regulatory Authority, Ireland

1995, Maia Uusküla
Head of the Department of Post-Authorisation Safety, Estonia

1996, Ambrose O Isah
Professor of Clinical Pharmacology and Therapeutics/Internal Medicine at the University of Benin, Nigeria

1999, Parthasarathi Gurumurthy
Director Pharmacovigilance & Clinical Trials, Botswana

1999, Priscilla Nyambayo
Head Pharmacovigilance & Clinical Trials at Medicines Control Authority, Zimbabwe

2001, Priya Bahri
Principal scientist at EMA, UK

2001, Martin Huber
Federal Institute for Drugs and Medical Devices (BfArM) and Vice-chair of the Pharmacovigilance Risk Assessment Committee (PRAC), Germany

2005, Wiltshire CN Johnson
CEO at the Pharmacy Board of Sierra Leone, Sierra Leone

2005, Adel Alharf
Vice President of the Drug Sector at SFDA, Saudi Arabia

2007, Helen Ndagije
Director of Product Safety at National Drug Authority and President of ISoP Africa Chapter, Uganda

2009, Manal Younus
Head of Iraqi Pharmacovigilance Center, Iraq

2011, Hadir Rostom
President of ISoP Egypt Chapter and co-founder and former head of the Egyptian Pharmacovigilance Centre, Egypt

2011, Victoria Nambasa Buhenya
Senior Program Officer at Health Product Safety AUDA-NEPAD and former manager of pharmacovigilance at National Drug Authority, Uganda

2012, Dr Juan Roldán Saelzer
Head of Pharmacovigilance Subdepartment, Department National Medicines Agency, Institute of Public Health, and board member of UMC, Chile

2012, Linda Hsien
Head of Pharmacovigilance Unit, Syria

2013, Naira Romanova
Head of the Pharmacovigilance department at the Scientific Centre of Drug and Medical Technology Expertise, Armenia

2013, James D K Goteh
Director of Pharmacovigilance & Clinical Trials at Liberia Medicines and Health Products Regulatory Authority, Liberia

2013, Mulugeta Russom
Head of Eritrean Pharmacovigilance Centre and member of WHO Advisory Committee on Medicines Safety, Eritrea

2014, Jaber Jaber
Head of RDU and Pharmacovigilance at Food and Drug Administration, Jordan

2016, Hussain Al Ramimmy
Director of Pharmacovigilance & Drug Information, MOH, Oman

2017, Mafora Florah Matlala
Pharmacovigilance Manager at the South African Health Products Regulatory Authority, South Africa

OPTIMISING VACCINE SAFETY SURVEILLANCE

IN THE NETHERLANDS

ZUBADA / ISTOCK

By utilising automated, web-based reporting forms and an efficient triage system, the pharmacovigilance centre Lareb enabled near real-time processing of over 200,000 COVID-19 vaccine AEFI reports.

Vaccine safety surveillance during a pandemic is challenging. In 2020, the global spread of the SARS-CoV-2 virus to pandemic proportions brought about the rapid development of vaccines to fight it. At the end of 2020 and beginning of 2021, the first COVID-19 vaccines became available for use in large, often population-wide, vaccination campaigns. Although large clinical trials had been conducted for these vaccines, there is still a risk that rare or previously unknown adverse reactions to the vaccine could still occur when administered at the scale of a global vaccination campaign.

As for any drug or vaccine that has been newly released to the market, risk groups for developing adverse events following immunisation (AEFI) are not yet well established, and potential

long-term effects are not yet entirely known. During large-scale vaccination campaigns, it can be difficult to differentiate between events that occur coincidentally within a plausible time frame after vaccination and those that are actually caused by the vaccine. Another consideration is that vaccines are biological products that need special storage conditions, so there is a risk of safety issues relating to incorrect storage or transportation of vaccine batches that may occur and need to be traced quickly before the vaccines are administered to large groups of people.

The spontaneous reporting system in the Netherlands is maintained by the pharmacovigilance (PV) centre Lareb. In the Netherlands, the COVID-19 vaccination campaign started on 6 January 2021, and a high volume of AEFI reports followed. To date, more than 234,000 reports have come in, with a total of more than 1,130,000 adverse reactions reported. Vaccinated people reported the majority of these adverse reactions themselves.

Since Lareb had expected a large volume of reports that needed to be processed and assessed within a short period, it developed a dedicated system to allow for near real-time processing of reports and vaccine safety monitoring. This started with a specific COVID-19 vaccine web-based reporting form with prespecified questions for case assessments. AEFI that were listed in the product information for the vaccine at the time of marketing authorisation were prespecified on the reporting form to enable faster processing. Vaccine brands could be chosen from a prespecified list as well. Closed questions specific to COVID-19 were also asked, for example whether the individual had been previously infected with COVID-19. By working with this structured reporting form, more than 33% of all incoming reports could be processed automatically in the first year of immunisation. Those who had been vaccinated were given a leaflet with information on their vaccine after each vaccination and this allowed them to fill in the batch number of their vaccine on the reporting form. When not known, and with permission from the reporter, batch numbers were retrieved from the national vaccination registry maintained by the National Institute for Public Health and the Environment (RIVM).

Lareb headquarters in Hertogenbosch

The remaining 67% of incoming reports that could not be automatically processed were triaged daily by a team of PV assessors with expertise in AEFI and signal detection. They selected high-priority cases based on the seriousness of the adverse event, listing them as an adverse event of special interest or signal value. These cases were then assessed by a team of dedicated vaccine experts. Brighton Collaboration case definitions were used for these assessments. In the first year of the COVID-19 campaign, 4% of cases were deemed high priority.

Case-by-case analysis of high-priority cases remained a driving force of the signal work. Daily signal detection meetings were held to discuss high-priority cases, for instance, those of thrombosis with thrombocytopenia syndrome (TTS) after vaccination with the Oxford/AstraZeneca vaccine.

Assessors could consult with an external clinical advisory board consisting of medical specialists working in clinical practice in fields such as immunology, haematology, and vascular medicine. As not all reports could be manually assessed, a custom-built line listing was made to review weekly vaccine data and reporting rates calculated from the number of reports received against vaccinations given in the Netherlands. These line listings could, for instance, focus on specific populations, such as teenagers and children. Although it was also incorporated as a feature in the line listing, the influence of such large amounts of COVID-19 vaccine AEFI data on disproportionality analysis was not known. Therefore, for the pandemic vaccination campaign, disproportionality was not used as a primary trigger for further analysis. In addition, a batch analysis was performed where reporting patterns of batches of the same brand of vaccine were compared. The batch analysis triggered no signal requiring action so far.

An automated standardised weekly report was generated by combining data from the spontaneous reporting system with that of a large cohort event monitoring study, which was started in early 2021 and involved monitoring individuals for six months following vaccination.

When much of your population is being vaccinated, it is important to consider the background incidence of clinical events of interest to identify potential signals. The background incidence rate of many potential events had already been mapped out in the European project ACCESS, so these were used for ”Observed/Expected” analysis of adverse events. Stratification of background incidences by age group and sex was also performed. Data on the vaccinated population were provided by the RIVM based on the Dutch vaccination registry. Additional background incidences specific to the Dutch population were provided on request by the PHARMO Institute based on electronic patient records of general practitioners as well as hospital data.

Following the initial COVID-19 immunisation campaign, booster vaccination campaigns were held using vaccines adapted to other strains of the virus. However, the SARS-CoV-2 virus has not been eradicated yet and may require future vaccination campaigns. It is important that national pharmacovigilance centres learn from the experience of the past two years and identify areas where innovation could help in future data management and signal detection.

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READ MORE:

- I Oosterhuis, et al, “Optimizing Safety Surveillance for COVID-19 Vaccines at the National Pharmacovigilance Centre Lareb: One Year of COVID-19 Vaccine Experience”, *Drug Safety*, 2023.
- A Kant, et al, “Description of Frequencies of Reported Adverse Events Following Immunization Among Four Different COVID-19 Vaccine Brands”, *Drug Safety*, 2022.

COVID-19 VACCINE SAFETY MONITORING:

HOW SAUDI ARABIA ROSE TO THE OCCASION

The challenges posed by the global immunisation effort against COVID-19 had the pharmacovigilance team in Saudi Arabia develop some innovative tactics to ensure vaccine safety for its citizens

The COVID-19 pandemic will go down in history as one of the most devastating pandemics ever. First identified in December 2019 in Wuhan, China, the SARS-CoV-2 virus was quickly identified as the pathogen responsible for serious respiratory distress in infected patients. The virus spread to many countries across the globe, forcing lockdowns and isolation at different levels. Public health authorities also turned to other public care strategies, such as hand washing, use of facemasks, physical distancing, and mandated travel to curb the outbreak. Just over a year later, vaccines from multiple pharmaceutical companies, such as Pfizer, Moderna, and AstraZeneca, were introduced as a more effective public health measure to curb the spread and catastrophic effects of the disease.

In Saudi Arabia, the first case was reported on 2 March 2020. As of 3 December 2022, 68,148,406 vaccine doses have been administered.

Vaccines are a necessary intervention in combating pandemics; however, ensuring their safety is vital. Therefore, pharmacovigilance plays an important role in monitoring the safety of COVID-19 vaccines throughout the world. In Saudi Arabia, a national pharmacovigilance plan has been in place since the beginning of the vaccination campaign in 2020.

Saudi Arabia’s active COVID-19 pharmacovigilance strategy was implemented in August 2020, following the introduction of COVID-19 vaccines. The pharmacovigilance executive directorate at Saudi Food and Drug Authority (SFDA) established a COVID-19 pharmacovigilance team, specifically focused on monitoring safety and quality of COVID-19 vaccines, including adverse events following immunisation (AEFI) monitoring and evaluation, reviewing and implementing vaccine risk minimisation measures (RMMs). Ultimately, the COVID-19 pharmacovigilance strategy in Saudi Arabia relied on passive spontaneous reporting of adverse events, and this raised some challenges which are worth reflecting upon.

Under-reporting in Saudi Arabia – Under-reporting is a rather common challenge with spontaneous adverse event reporting, posing a serious challenge for safety monitoring of COVID-19 vaccines. For example, healthcare professionals may not report certain adverse events, especially if they are not sure of the causal relationship between the vaccine and the adverse event. Adverse

events are also likely to be under-reported when the time to onset of event was delayed, which is common with AEFI, and may begin long after the vaccine has been administered and where recipients may not consider the vaccine as linked to the adverse event.

Causality assessment of AEFI reports – Assessing the potential causality relationship between an adverse event and the vaccine is limited by underreporting and missing information. Certain critical information such as differential diagnosis, laboratory results, imaging findings, patients' past and present histories, and outcome of the event can help assess the causality of the adverse event.

Lack of background rate – The absence of the background incidence rate of certain AEFI made it difficult to determine the trend of adverse events following the introduction of the COVID-19 vaccines. Without high-quality evidence and real-world data, the SFDA faced challenges to make rapid regulatory responses to some serious safety issues.

Transparency and clear communication of vaccine risks to the public – The lack of well transmitted information of vaccine risks has a lot of disadvantages. False information on vaccine risks circulate on the internet and social media, and many people believe this misinformation. This can increase vaccine hesitancy and may also affect people's reporting behaviours as they may ignore an adverse event and choose not to report it.

The public should be empowered with the right information, so they know how best to respond to adverse events. For instance, we published an official statement on the SFDA social media channels for the public about the possible risks of blood clots with the use of the Oxford/AstraZeneca vaccine following its suspension in certain European countries.

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Saudi Food and Drug authority

Fawaz Alharbi
Drug Safety and Risk Management Department Director, Executive Directorate of Pharmacovigilance,
Saudi Food and Drug authority

READ MORE:

- *COVID19.who.int*
- L Hazell, SAW Shakir, "Under-Reporting of Adverse Drug Reactions", *Drug Safety*, 2006.
- Y Albogami, H Alkofide, A Alrwisan, "COVID-19 Vaccine Surveillance in Saudi Arabia: Opportunities for Real-time Assessment" *Saudi Pharmaceutical Journal*, 2021.

7 LESSONS FROM THE PANDEMIC

Considering the limitations of the current COVID-19 pharmacovigilance system, there are opportunities to improve it for better monitoring of COVID-19 vaccine safety. These were the core steps taken by the SFDA to improve the COVID-19 surveillance system.

1 Strengthening the COVID-19 surveillance system – An active surveillance system differs significantly from a passive surveillance system as it uses real-world data against voluntary reporting. Active surveillance helps mitigate the limitation of under-reporting of AEFI. Therefore, the COVID-19 pharmacovigilance team, in collaboration with the Ministry of Health, conducted an active surveillance study to measure the cumulative incidence of AEFI of COVID-19 vaccines with different modes of action for three months after the first dose (from the first day of vaccination for seven days after the first and second doses, then biweekly for three months). The study also extended the duration of follow-up after vaccination for at least one year following immunisation.

2 Preparing a special form for reporting AEFI with COVID-19 vaccines – Reporting forms were modified to be more robust and effective for collecting more information that will help assess the causality of adverse events.

3 Facilitate reporting by designation of more than one channel for reporting AEFI with COVID-19 vaccines – Reporting lines are expanded to ensure that more AEFI are reported. Serious cases are followed up to gather critical missing information for better assessment. The SFDA launched a channel of communication with the Ministry of Health, National Guard Health Affairs, and Ministry of Defence Health Affairs, in addition to the regional pharmacovigilance centres to take up this responsibility. Furthermore, members of the general public who are eligible for vaccination will now be able to submit AEFI up to 90 days following vaccination via the Saudi Vigilance system and Sehaty application.

FEODORA CHIOSEA / ISTOCK

4 Change in evaluation process – All reported adverse events that focus on events of serious health risks are now pooled and assessed by the SFDA causality assessment committee in a timely manner. The SFDA personnel with biologics and vaccines expertise prepare comprehensive safety reviews for valid safety signals related to COVID-19 vaccines using several evidence sources, including literature, results of causality assessment of global cases and local cases, and stringent regulatory authority reviews. The SFDA Higher Pharmacovigilance Advisory Committee then conducts several meetings to extensively evaluate these reports to recommend the appropriate regulatory actions.

5 Engagement – For healthcare professionals, the SFDA conducted several workshops and distributed educational material illustrating pharmacovigilance practices regarding vaccine safety and reporting AEFI. The SFDA also disseminates information suitable for the general public on vaccine safety using appropriate channels.

6 Change in the regulator behaviour – A rolling submission process was adopted to accelerate the approval process of COVID-19 vaccines, and the vaccine's marketing authorisation holder is now required to submit RMMs at the time of application, such as a Healthcare Professional Guide and a Vaccine Recipient Guide. Moreover, the marketing authorisation holder is required to commit to monthly submissions of a summary safety report for six months following authorisation of their COVID-19 vaccine.

7 Collaboration and consultation – The SFDA joined the International Coalition of Medicines Regulatory Authorities (ICMRA) to exchange data and experiences related to AEFI with COVID-19 vaccines. This collaboration resulted in a change in the regulators' behaviour, at least initially, to focus on solving problems and finding ways to promote confidence in vaccine safety.

CONCLUSION

The SFDA has faced significant challenges in COVID-19 vaccine surveillance in Saudi Arabia. Therefore, the SFDA sought to strengthen the current surveillance system by adopting an active surveillance system approach and decentralising reporting channels to improve surveillance capacity. This will help to facilitate more rapid responses and help the SFDA to conduct well-informed benefit-risk assessments.
The experience from this pandemic and COVID-19 vaccination has also strengthened our pharmacovigilance system and prepared us for public health challenges that may arise in the future.

Disclaimer: *The views expressed in this paper are those of the author(s) and do not necessarily reflect those of the SFDA or its stakeholders. Guaranteeing the accuracy and the validity of the data is the sole responsibility of the research team.*

MEDICINES SAFETY TAKES ROOT IN LEBANON

Lebanon implemented its pharmacovigilance system and boosted safety reporting all while dealing with the effects of COVID-19. A glance at the 143rd country in the WHO programme.

Situated at the eastern end of the Mediterranean Sea, Lebanon has been making sound steps forward in medicines safety in recent years. Home to over six million people (although there is a large Lebanese diaspora, in the Americas especially), the official language of the country is Arabic, while French is formally recognised. Vast forests of cedar trees once covered much of Lebanon, hence the national emblem of the country and the centrepiece of its flag.

The establishment of a successful pharmacovigilance system is particularly difficult in resource-limited countries such as Lebanon. After becoming an associate member of the WHO Programme for International Drug Monitoring (WHO PIDM) in 2018, pharmacovigilance activities as core functions of the Ministry of Public Health (MoPH) were well underway when the COVID-19 pandemic began. Therefore, the implementation of an effective national pharmacovigilance system in Lebanon should be seen in the context of the effects of COVID-19.

The route to that success was initiated by establishing the legal groundwork with technical assistance from WHO offices. The Quality Assurance of Pharmaceutical Products Program (QAPPP) issued a series of regulations that facilitated the system's organisation and functions to further strengthen the framework for pharmacovigilance.

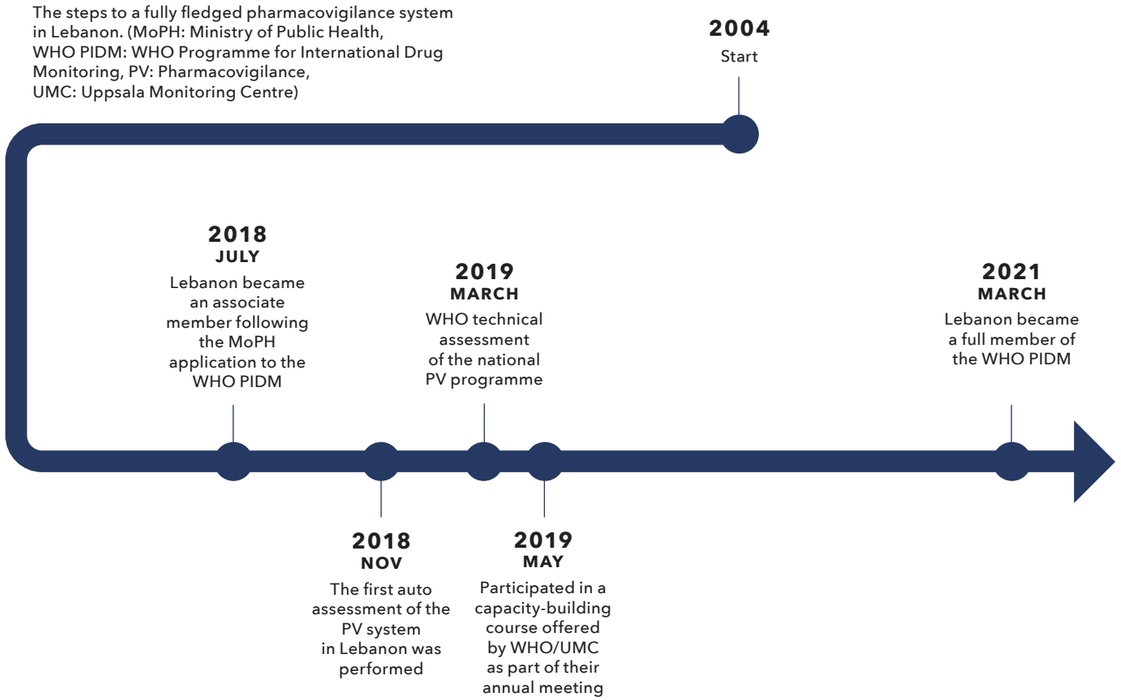
Under the supervision of the QAPPP within the Lebanese MoPH, the Lebanese National Pharmacovigilance Program (LNPVP) was created, and the national centre was admitted as a full member of the WHO PIDM in February 2021.

The infrastructure was defined by outlining all the stakeholders involved: policymakers, regulatory authorities, the pharmacovigilance operating entities, and the pharmacovigilance reporting entities. Once the legal framework, infrastructure, and human resources were in place, the QAPPP developed the means for reporting adverse events.

Patients, healthcare professionals and marketing authorisation holders (MAHs) can send reports either through the national adverse events reporting form, a landline hotline, or an e-reporting service. Reports are coded, analysed, and assessed at the LNPVP using VigiFlow, an electronic pharmacovigilance management database, and sent to the WHO global

A bustling city with a thriving pharmacovigilance system, despite all odds.

CARLOS HAIDAMOUS / ISTOCK



The steps to a fully fledged pharmacovigilance system in Lebanon. (MoPH: Ministry of Public Health, WHO PIDM: WHO Programme for International Drug Monitoring, PV: Pharmacovigilance, UMC: Uppsala Monitoring Centre)

database VigiBase. Staff members have been trained in data collection, and cleaning and coding of adverse events using MedDRA (Medical Dictionary for Regulatory Activities) terminology. Since active participation is vital from all stakeholders, HCPs and MAHs were made aware of the importance of reporting. In turn, the trained HCPs were responsible for educating patients on COVID-19-related AEFI, thus closing the loop with all relevant contributors to the post-marketing surveillance programme.

As a result of these initiatives, the LNPVP started receiving ICSRs, and thus became a full member of the WHO PIDM in 2021. Reporting during the COVID-19 mass-vaccination campaign greatly enhanced the system. The introduction of new reporting tools such as a national COVID-19 vaccine hotline (1214 Hotline), a vaccination module in the e-Governance platform in Lebanon, and an open-source toolkit for data collection and analysis in humanitarian emergencies (KoBotoolbox), boosted reporting from 20 to 100 weekly AEFI case reports. The effective screening of the AEFI reports resulted in a better classification and thus improved management of AEFI. Field visits to vaccination centres ensured compliance with operating standards, and a monthly report summarising AEFI findings was circulated.

LNPVP performed additional steps to strengthen the AEFI surveillance mechanism via signal detection and validation to identify signals associated with the Pfizer-BioNTech and AstraZeneca COVID-19 vaccines. This was hindered at many levels by the shortage of staff and lack of sustainable financial support. The response to COVID-19 coincided with a turbulent political and economic situation disrupting all of society including healthcare. Yet, despite these financial, political and technical difficulties the Lebanese pharmacovigilance programme established a rigorous safety profile, and in a short period received 7,000 case reports and 24,837 AEFI, following the administration of 5,134,093 doses of COVID-19 vaccines.

Currently, the pharmacovigilance team at the QAPPP is working on guidelines on good pharmacovigilance practice for MAHs. After strengthening the passive reporting system, the LNPVP is planning to establish an active surveillance system. Finally, with the vision of keeping the LNPVP up-to-date with technological advancements, the programme has recently adopted the safety app developed by MHRA as a new smart reporting tool. Pharmacovigilance is sending out strong branches across Lebanon for an evergreen future.

READ MORE:

- H Abbas, A Zeitoun, M Watfa, et al, "Implementation of a Pharmacovigilance System in a Resources-Limited Country in the Context of COVID-19: Lebanon's Success Story", *Therapeutic Innovation & Regulatory Science*, 2022.

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UMC REVAMPS MEDICINES SAFETY CYCLE

By putting the patient front and centre, UMC is helping countries in the WHO Programme for International Drug Monitoring to promote the safer use of medicines globally.

UMC is excited to announce the launch of a new communications resource to help explain the cycle of medicines safety.

The PV Cycle, now live on UMC's website in English, Spanish, and French, uses a visual narrative to take the reader through the different stages of the medicines safety cycle, with the patient at the centre of the story.

The PV cycle was promoted during *#MedSafetyWeek* in 2022 by UMC and many of the participating PIDM member countries, who requested a more in-depth explanation of medicines safety to complement the other materials we produce.

In our role at UMC we are often tasked with explaining why reporting side effects is important and what happens once a report is submitted. For this project we used an illustrated narrative to tell that story focusing on Lisa, a diabetic patient who experiences a side effect from her medication. Lisa's doctor submits a report on the side effect, and we follow the report and the decisions that are made throughout to protect patients from harm.

Visit the PV cycle page on UMC's website and keep an eye out for more content on UMC's social media channels, as we bring Lisa's story to the world.

READ MORE:

- How medicines safety works – *http://bit.ly/3GeaVBb*
- Cómo funciona la seguridad de los medicamentos – *http://bit.ly/3zyYmg5*
- Le cycle de PV – *http://bit.ly/3nKBAyZ*

Matthew Barwick
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Meet Lisa, your guide to the medicines safety cycle

ILLUSTRATION: IWONA KAZIA KALITAN MŁODKOWSKA ICONS: MÅRTEN LEO

ILLUSTRATION: MÅRTEN LEO

NEW UMC RESEARCH POSTERS

VigiBase, the world's largest database for adverse event reports, collects data from many sources. As a result, there is a risk that several records may be duplicates of the same adverse event. A thesis project by master's student Erik Turesson explores methods for identifying and "deduplicating" these reports, with a special focus on records for the COVID-19 vaccine. His research was presented at the annual ISoP meeting in November last year.

READ MORE:

• E Turesson, "Freetext Informed Duplicate Detection of COVID-19 Vaccine Adverse Event Reports", *DIVA Portal*, 2022.

• *who-umc.org/publications-library/research-posters*

UMC article wins journal award

A UMC article published last year on global safety monitoring of COVID-19 vaccines has been chosen as one of the best articles for 2022 by the scientific journal *Therapeutic advances in Drug Safety*. Awardees have been invited to present their work at the European Pharmacovigilance Congress in November 2023. Read the article here:

• A Rudolph et al, "Global safety monitoring of COVID-19 vaccines: how pharmacovigilance rose to the challenge", *Therapeutic Advances in Drug Safety*, 2022.

Research Corner series puts UMC's science in the spotlight

A new film series looks to shine a light on UMC's research and the people behind it.

We're pleased to announce the first in a new series of short films, presenting UMC's research to our global audience, in a new format. Research Corner – UMC's Science in the Spotlight puts our research and researchers in focus, with each episode in the series featuring a recently completed study: what was investigated and why, what were the findings, and what does it mean for pharmacovigilance.

For this first episode we teamed up with Daniele Sartori, pharmacovigilance scientist and PhD student at UMC and lead author of a paper on the evidence base and features of ADR reports that are used to support signals. Daniele sat down with us for a short interview to describe his research and assist us in producing some visualisations of his work.

Daniele had this to say about the new initiative: "From paper to film, the Research Corner captured my study from a different angle, personal, but to the point. As a researcher I'm not used to being in the limelight but overall, it was a great experience that will help to expand the outreach of my research to a wider audience."

The aim of this series is to promote our research in engaging bite-size chunks, giving the viewer an overview of the work and the people behind it, as a complement to more in-depth content on our channels and the academic papers themselves. We're excited to see who's next in the Research Corner series, so look out for future editions on UMC's channels.

Matthew Barwick
Communications Officer
& Video Producer, UMC
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READ MORE:

• D Sartori, "Signals of Adverse Drug Reactions Communicated by Pharmacovigilance Stakeholders: A Scoping Review of the Global Literature", *Drug Safety*, 2023

• Research poster on the review – *bit.ly/3TnxRn2*

WATCH IT:

• *youtube.com/watch?v=GhTmiGjLLyw*

On the PV agenda

27–29 April

• The Drug Hypersensitivity Meeting 2023

Verona, Italy
–European Academy of Allergy and Clinical Immunology (EAACI)

11–12 May

• Medication Safety in an Era of Evidence-Based Medicine

Rishikesh, India
–SoPICON

25–26 May

• Re-designing and Transforming PV for Augmenting Patient Safety

Mumbai, India
–DIA

27–29 May

• 15th China Forum on Drug-Induced Diseases and Safe Use of Medicines

Chengdu city, Sichuan province, China
–China Journal of Adverse Drug Reaction

1–2 June

• ISoP Mid-Year Symposium, in collaboration with Lareb Pharmacovigilance: Where science meets clinical practice

Leiden, Netherlands
–ISoP

5–9 June

• ISPE African Conference: 3rd Annual African Regional Interest Group Meeting

Cape Town, South Africa
–ISPE

7–9 June

• Medical Aspects of Adverse Drug Reactions

Whiteley, Fareham, UK
–DSRU

19–23 June

• Oxford Summer School 2023: Real World Evidence using the OMOP Common Data Model

Oxford, UK

2–7 July

• 19th World Congress of Basic & Clinical Pharmacology (WCP2023)

Glasgow, Scotland

–British Pharmacological Society & the International Union of Basic and Clinical Pharmacology

5 July

• WCP2023 - CIOMS meeting 'Guidance for Medicines Safety'

Glasgow, Scotland

–British Pharmacological Society & the International Union of Basic and Clinical Pharmacology

23–27 Aug

• International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE) 2023

Halifax, Nova Scotia, Canada

24–28 Sept

• FIP 2023 – Pharmacy building a sustainable future for healthcare – aligning goals to 2030

Brisbane, Australia

26–28 Oct

• ISPE 15th Asian Conference on Pharmacoepidemiology

Bangalore, India

6–9 Nov

• ISoP 2023 Annual Meeting

Bali, Indonesia

ISTOCK

UMC is an independent, non-profit foundation that works alongside the World Health Organization and other stakeholders to advance medicines safety. As a leader in the development of pharmacovigilance science and research methods, we explore the benefits and harms of medicines, and offer products and services used by health authorities and the pharmaceutical industry worldwide.

Uppsala Monitoring Centre