

UPPSALA REPORTS

— COVERING THE WORLD OF PHARMACOVIGILANCE —

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Pharmacovigilance

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INNOVATE

PLAY
AND TAKE
RISKS

BE THOROUGH
BUT FLEXIBLE



Our vision is a world where all patients and health professionals make wise therapeutic decisions.



IN THIS ERA OF ELECTRONIC COMMUNICATION, I must admit I take delight in receiving the occasional old-fashioned letter; a neatly folded piece of paper wrapped in an envelope, with a stamp and a handwritten address. There is something very attractive in anticipating its content while opening it, particularly if you know from the handwriting that the person who sent it is a good friend. This was the case when I recently received a letter from Ed Napke, a colleague and friend of many years. Ed was the inventor of the ingenious pigeon-hole system in Canada in the infancy of modern pharmacovigilance, and is still active as a consultant to UMC. Here is how his long and successful career in pharmacovigilance started:

The World Health Organization (WHO) asked member countries to set up a drug adverse reaction monitoring program and to make more stricter laws on drug manufacturers in the making of new drugs. It was a long story but Canada volunteered with 9 other countries to see if we could pool the data. This is where I came in. I was on my way to the University of California to do research on the effects of acceleration on humans and was asked to wait a year because the current researcher did not wish to return to South Africa and apartheid. My friend Dr J.M. offered me the job to take on the project which I agreed to. I thought it would take 2-3 years, instead it became my life's work 1963-1990.

What he wrote reminded me that many life-changing decisions seem to be the result of chance events. I certainly think that the world of pharmacovigilance has benefited from the chance taken by Ed Napke all those years ago. And, having lived for a bit, I have learnt to appreciate and make good use of opportunities that have come my way, many seemingly out of the blue.

It may seem as a paradox that I often argue for the benefits of proper work planning. I will continue to do so, but I want to make it clear that planning is just the means to achieve an end, not an end in itself. If we bury ourselves too deep in meticulous planning activities, there is a risk that wonderful new prospects may pass unnoticed. As so often, the challenge is to get the balance right; we must figure out in what circumstances careful planning is needed, and when a more open, relaxed approach

would be better. What is the right mix of rigour and flexibility no doubt varies from individual to individual, from situation to situation, and over time; but I do think we need both to thrive.

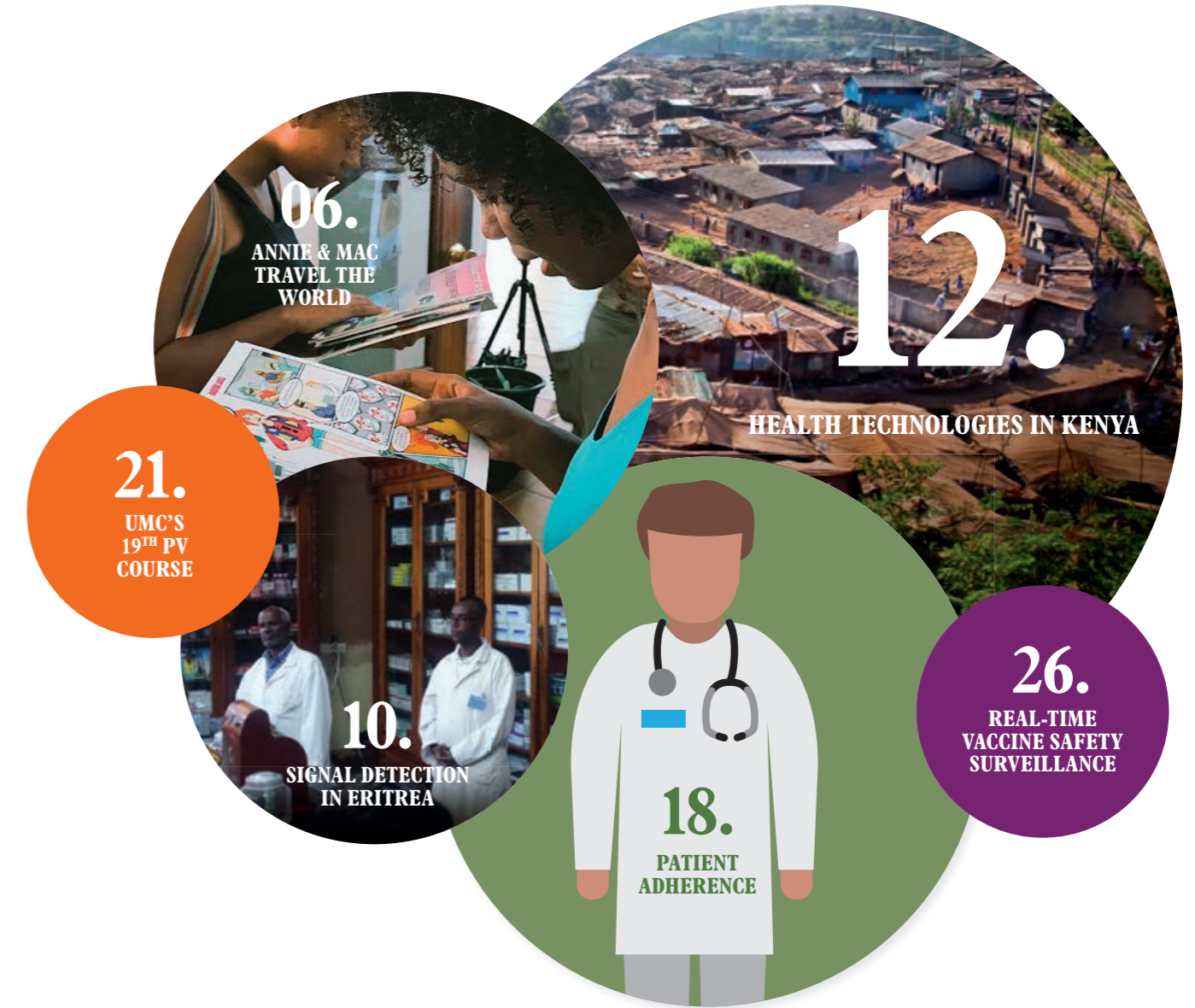
In the world of today, I am concerned that we build systems and organisations where fear of failure is a stronger driver than curiosity and open-mindedness; and I think there is too much emphasis on short-term productivity rather than long-term real gains. We do need good governance and work discipline to achieve results. But we also need to release creative forces for good and allow people to turn new ideas and chance findings into innovative solutions to the many problems we all face. This can only be done by actively encouraging some level of playfulness and risk-taking in working life. I am convinced that the world would be better for all of us if we left more space and room for people to sometimes veer into the unknown, and to try new things without fear of being punished if they get something wrong or don't achieve an immediate result.

P.S. IN CASE YOU WONDER – yes, I still have a physical tray in my office for incoming post. Apart from the odd contract, requiring my signature, it mostly fills up with glossy management magazines that I never ordered and promotional prospects from companies trying to entice me to join their next conference on drug development or to use their services for our next international meeting. If anyone knows where I can order a spam filter for such communications, do let me know.



Marie Lindquist
Marie Lindquist, Director

“We need to release creative forces for good and allow people to turn new ideas and chance findings into innovative solutions.”



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UPPSALA REPORTS *Covering the world of pharmacovigilance*

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KATHMANDU

Sharing knowledge to boost the Nepalese pharmacovigilance programme

UMC staff travelled to Kathmandu last spring to train pharmacovigilance colleagues in Nepal. What they found was a country that, despite the challenges it has had to face since a devastating earthquake two years ago, is determined to strengthen its pharmacovigilance activities.

IN LATE APRIL, UMC staff members Sara-Lisa Wargert, Therése Lundin and Gediminas Norgėla visited Kathmandu, Nepal to present a training course in pharmacovigilance. Course participants came from Nepal’s drug regulatory authority – the Department of Drug Administration (DDA) – and the country’s regional pharmacovigilance centres.

Over two days, UMC staff illustrated



basic topics in pharmacovigilance, including awareness raising and effective communication, and offered a hands-on training session on the VigiFlow system, which DDA uses as their national database for individual case safety reports. The training also touched upon data assessment and analysis, to highlight the importance of using the collected data to identify safety issues and act upon them, ultimately improving patient safety.

The course, set up in collaboration with the WHO Country Office in Nepal, is part of DDA’s recent effort to expand and strengthen the national pharmacovigilance system. Nepal is still recovering from a massive earthquake that hit the country in 2015 and killed 8,700 people, injured nearly 22,000 and inflicted enormous damage to the country’s infrastructure. Despite the burden this has placed on national authorities, DDA has lately begun to boost pharmacovigilance

activities in the country. In recent years, the number of regional centres set up to collect reports of adverse drug reactions increased and there are ten of them in the country today, mainly in teaching hospitals.

DESPITE THE CHALLENGING times, the health sector has developed in the past decade, according to Mr Narayan Prasad Dhakal, director general at DDA. Maternal and child mortality rates are decreasing and life expectancy is increasing. “Access to medicines and health facilities has improved a lot, both in the private and the public sector,” says Mr Dhakal. But many challenges remain. A major issue is anti-microbial resistance, which according to the director general is a widespread problem in Nepal. Staff from the regional centres confirm the need for urgent action in this area. DDA is currently planning to develop

increasing burden of non-communicable diseases and a larger elderly population, perhaps in need of multiple medicines, issues regarding rational use of medicines and their interactions are arising. “In terms of pharmacovigilance, it is very challenging now,” admits Mr Dhakal.

AN IMPORTANT STEP towards strengthening any pharmacovigilance system is to include it in the regulatory framework, a process which has now been initiated in Nepal. The Drug Act has been revised and is now being processed at ministry level. Step by step, the system for monitoring medicines safety is improving, and the director general is optimistic for the future.

“It is not only Nepal working in this area, a lot of countries are really focusing to improve pharmacovigilance. My

vision is that it [the pharmacovigilance programme] is implemented nationwide and that it is used even by the general public, the users of medicines,” Mr Dhakal says. “I see everything very positively.”

He stresses the need for international support, knowledge sharing and networking in the ongoing process. “This will really help us move this programme ahead,” he concludes.



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EL SALVADOR

A pharmacovigilance system is born

For many years, El Salvador lacked a national system for monitoring the safety of medicines. Thanks to the guidance of WHO and PAHO, the country has now begun to take a more active approach to pharmacovigilance. The Minister of Health has committed to develop the system, to protect the safety of the population when a drug is used.

So far, the pharmacovigilance undertaken was mostly in two public hospitals, each one following their own practices. El Salvador has had its own yellow reporting card for almost three decades, but there was no rigorous evaluation of the cases, and no national database to collect and store reports until recently.

In October 2016 a law was passed to

implement pharmacovigilance, leading to the opening of a new national pharmacovigilance office (Centro Nacional de Farmacovigilancia, CNFV). The same month new ‘Salvadoran Technical Rules for Pharmacovigilance’ were launched and with that legal document the CNFV aims to fulfil many critical indicators.

In March 2017 El Salvador started a two-week national pharmacovigilance sensitisation programme for healthcare professionals from the regulatory authority, hospitals, academia and industry. The UMC was present for one week to talk about the WHO Programme, to promote the use of the online reporting form connected to the management tool, VigiFlow, and for other contributions to the event.

It was an amazing experience to be at the launch of a national pharmacovigilance activity in a country, having been involved right from the beginning. More than 150 healthcare professionals participated with great enthusiasm during the whole training activity, in what is now the 127th member of the WHO Programme.



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Lourdes Jarquin and Elki Sollenbring with pharmacovigilance trainees in El Salvador.





ANNIE AND MAC'S ADVENTURES – Uppsala Monitoring Centre's comic book on pharmacovigilance – is currently being piloted in several countries and the feedback will be implemented in the coming number. “We have not completed the evaluation yet, but the response we received so far is very positive. We know that children in different parts of the world find the magazine fun and exciting, and at the same time they learn about medicines,” said Paula Alvarado, head of Global Communications at UMC. The organisation launched Annie and Mac's Adventures as part of its communication

efforts to drive behavioural change in relation to medicines. “Hopefully, the children will bring this new knowledge back to their homes and contribute to everyone's better understanding of the benefits and risks of medicines”. The comic is the first in a series aiming to explain medicines safety to a young audience. Written by Fredrik Brounéus and illustrated by Paul Crumacker, the story follows Annie and her pet hummingbird Mac on their heroic attempt to stop evil Count Erfeit from producing and selling fake medicines.

“We tell some of the best stories to each other every day. That's how we learn, share and build a community. Stories help us shape knowledge and remember it!”

“We tell some of the best stories to each other every day. That's how we learn, share and build a community. Stories help us shape knowledge and remember it!” added Alvarado. Children in Armenia, Cabo Verde, Jordan, Malaysia and Uganda received the first issue of the comic as part of an initial pilot phase. A second issue of the

comic is planned for autumn 2017 and will explore the topic of antibiotic resistance. Paula, Fredrik and Paul are now hard at work to incorporate feedback from the pilot countries and create new storyline and illustrations that are both educational and fun - a fine balancing act. UMC aims to publish two comic books per year. Story ideas are welcome!

▲ Young readers enjoying UMC's comic book in Uganda, Armenia, Cabo Verde, Malaysia and Jordan (clockwise from top left). **Photos:** Armenia, Scientific Center of Drug and Medical Technology Expertise. Cabo Verde, Paula Alvarado/UMC. Jordan, Jordan Food and Drug Administration. Malaysia, National Pharmaceutical Regulatory Agency. Uganda, National Drug Authority.

Interested? For more information, contact Paula Alvarado, UMC's head of Global Communications, on paula.alvarado@who-umc.org

“I think effective communication and management are very important for pharmacovigilance.”

IMPROVING *medicines safety* IN INDIA

How do you manage national medicines safety in a country as sprawling and diverse as India? Dr Kalaiselvan from the Indian Pharmacopoeia Commission sat down with Uppsala Reports for a Q&A on the challenges and progress in pharmacovigilance in the world's second-most populous country.

HOW WAS INDIA'S PHARMACOVIGILANCE SYSTEM ESTABLISHED?

– Before the Pharmacovigilance Programme of India (PvPI) was assigned to the Indian Pharmacopoeia Commission (IPC) in 2011, pharmacovigilance in the country was carried out in a scattered manner. Once it came to IPC, we started building a network among the stakeholders, we brought all the institutions and interested organisations under one umbrella, and we were able to build a strong network of communication with the stakeholders.

I think effective communication and management are very important for pharmacovigilance. We were able to learn from previous programmes why they had not been successful in India. It was a lack of communication, and the proper organisation was not there to coordinate the activities. So once the IPC assumed the responsibility for the PvPI, we started to invite different partners and stakeholders – particularly Uppsala Monitoring Centre and WHO. Then gradually we started identifying more regional adverse drug reaction (ADR) monitoring centres and were able to establish quality as well as quantity of reporting.

The most successful part of this programme is that we've been able to connect to the government properly. We've managed to convince our government and policymakers about the importance of pharmacovigilance.

WHAT ARE THE CHALLENGES TO PHARMACOVIGILANCE IN INDIA?

– In a country like India, there are a lot of challenges – particularly under-reporting. The cause of under-reporting is the work burden on doctors, who are over-loaded. They will not have the time to report. So we engage in a kind of solicited spontaneous reporting; we approach them and ask them for ADR reports.

Of course there is also a need to educate

and raise awareness about ADR reporting among the clinicians. In India, another challenge is that we need to empower the pharmacists – pharmacist empowerment is very much required to enhance ADR reporting.

WHO ARE THE MAIN REPORTERS OF ADRS?

– Doctors, pharmacists, nurses and consumers report ADRs in India. We get most reports from hospitals where we've set up ADR monitoring centres. We have established a system with one focal person in each of them. Then we have our PvPI staff working in every ADR monitoring centre. Through them the reports are coming from doctors and nurses.

HOW DO YOU WORK WITH THE NATIONAL AND REGIONAL CENTRES?

– The national coordinating centre comes under the Ministry of Health and Welfare, Government of India in Ghaziabad. That is the headquarters for pharmacovigilance. Under this umbrella, we have regional ADR monitoring centres in every state in India.

In order to provide regular training to the ADR monitoring centres, we've identified eleven regional training centres – including JSS Hospital in Mysore. So every year JSS organises at least one training programme for pharmacovigilance professionals in the region. Similarly, we have training centres in other parts of the country. It means that a person from Mysore, for example, doesn't have to travel to Delhi for training, they can attend the training at JSS. India is a big country – we cannot invite everyone to Delhi for each training. So in order to reduce expenditure and train more people we have set up these regional training centres.

WHAT'S NEXT FOR PVPI?

– In India we have more than 600 districts (which are administrative divisions of a state or territory). The Drugs Controller General of India, Dr G. N. Singh, is very keen on expanding the programme up to district level and we're planning to identify more

district hospitals that can be set up as ADR monitoring centres.

I'm very optimistic about the future. I'm very confident, because everyone is supporting us – UMC's support is there as well as WHO's support. And everybody is on board, we have very good communication channels, and a very effective system. Again, I want to stress that communication and good partnerships and working relationships are very important. So, I'm 100% confident and very optimistic that we are going to mature from being an emerging programme to an advanced one.



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PHARMACOVIGILANCE IN INDIA

India joined the WHO Programme for International Drug Monitoring in 1997. In 2016, 4.2% of all new suspected ADR reports submitted to WHO's global database of individual case safety reports, VigiBase, were sent by India, making them the sixth most active reporting country globally that year.

The Pharmacovigilance Programme of India was established in 2010 as the National Coordinating Centre for monitoring ADRs in the country, and came under the Indian Pharmacopoeia Commission. It falls under the Central Drugs Standards Control Organisation (CDSCO) of the Ministry of Health & Family Welfare (MOHFW).



WHO IS DR V. KALAISELVAN?

Dr V. Kalaiselvan (M.Pharm, Ph.D) is the Chief Scientific Officer at the Indian Pharmacopoeia Commission. He is responsible for managing the Pharmacovigilance Programme of India, and works with different partners in pharmacovigilance at national and international levels.

“The most successful part of this programme is that we've been able to connect to the government properly. We've managed to convince our government and policymakers about the importance of pharmacovigilance.”



Inside an old pharmacy in Asmara.

Home-grown signal detection sheds light on safety issues in Eritrea

Since 2015, Eritrea's National Pharmacovigilance Centre has carried out analysis of domestic adverse drug reaction reports, to better understand medicines-related issues in the country, and rely less on safety information from external sources.

SIGNAL DETECTION IS a challenge for many pharmacovigilance officers, especially those working in low- and middle-income countries. This was widely discussed during the 2014 National Centres meeting in Tianjin, China, where many representatives including myself voiced our concern at being unable to detect safety signals. Many countries with small national databases of reported adverse drug reactions (ADRs) and a limited pharmacovigilance workforce find it difficult to detect safety signals that primarily concern their domestic market.

In 2014, a public health programme manager in Eritrea expressed his satisfaction in seeing pharmacovigilance flourish and diffuse within the healthcare system, which improved the collection of reports of adverse effects from all parts of the country. The manager then asked if pharmacovigilance



“Weekly case-by-case assessment is the main strategy for signal detection in Eritrea, which helps detect safety signals even based on a single case report.”

was only about collecting and reporting ADRs. There was a concern that the national pharmacovigilance programme wasn't equipped to address all safety issues related to medicines in Eritrea. This motivated the centre to run a practical signal detection course from Uppsala Monitoring Centre staff in the country's capital Asmara in 2015.

Following this UMC course, the Eritrean National Centre (NC) detected two relevant safety signals of public health interest: artesunate/amodiaquine-induced extrapyramidal reactions in children and young adults, and a rapid diagnostic test for malaria that failed to detect malaria parasites. These signals gained much attention from the international community. In 2016-2017, six more safety signals were detected.

HAVING A SMALL national database of ADRs, it is impractical to look at statistical signals the way many high-income countries do. Instead, weekly case-by-case assessment is the main strategy for signal detection in Eritrea, which helps the NC detect safety signals even based on a single case report. The Data Processing (DPS) and Signal Management Sections (SMS) of the NC are the main players in checking completeness of ADR reports and quality of case assessment approaches. The DPS ensures that individual case safety reports (ICSRs) are as complete as possible and arranges routine causality and preventability assessment sessions. Once a potential safety signal is identified, it is the turn of the SMS to go for further signal assessment.

Another strategy is involving physicians in the case assessment process. Recently, the NC has recruited three volunteer pharmacovigilance medical officers to take part in the weekly case assessment sessions and signal detection processes.


UMC's search and analysis tool VigiLyze, which allows for country-specific views of data from WHO's global ICSR database VigiBase, has also been important in strengthening some safety signals.

ERITREA'S NATIONAL CENTRE routinely communicates with manufacturers and public health programme managers, and some of the signals identified by the centre have motivated regulatory action, such as product label changes, post-authorization safety studies, inclusion of the identified risk into boxed warnings, restriction in use and availability of the product, as well as the withdrawal of a product from the domestic market.

Previously, our regulatory decisions have relied on safety communications from big regulatory agencies, many of which are not relevant to our situation. Though most

of the safety signals identified by the NC are new adverse drug reactions, important safety issues encountered with inappropriate use and/or administration of medications and genetic variations have also been detected by using preventability assessment. Communications from the big regulators are less relevant for us as they are often related to new products, not available in Eritrea, where we use old drugs for different reasons.

To minimise or prevent the identified risks, the NC also communicates its findings to the international community, healthcare professionals, and other partners. In addition, the NC is carrying out epidemiological studies to further substantiate some of the identified safety signals.

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Mulugeta Russom, head of the Eritrean Pharmacovigilance Centre.

HEALTH INFORMATION TECHNOLOGIES IN RESOURCE-POOR SETTINGS

Internet penetration and mobile phone use stand at 90% in Kenya, but health clinics in the country's poor communities struggle to meet the basic needs of patients. UMC's Afifa Trad asks if health information technologies could support and improve primary healthcare in resource-poor countries.

A SHORT DRIVE out of Nairobi's city centre takes you to Kibera, an extremely poor community in the outskirts of the Kenyan capital, and home to around 250,000 people. The government owns this land but does not recognise the settlement. Despite its considerable size and vicinity to the capital, the 13 villages of Kibera lack even the most basic services and infrastructure, such as running water, paved roads and healthcare. Electricity is just being introduced in some parts, and sanitation remains a problem, with five or six households sharing a common toilet and bathroom.

There is a sense of congestion upon entering Kibera. Cars and old trucks drive on unmade, bumpy roads. People push around barrels with yellow plastic containers of fresh water for sale, vegetable stands are scattered along the streets, and barbershops and hairdressers take up every other shack.

On the walls surrounding the settlement, informative messages on drug abuse are painted in colourful graffiti.

Although basic services are not readily available in Kibera, internet access is easy to come by. In a country with an estimated population of 47 million, internet penetration stood at 90% by the end of last year, and the total number of mobile money accounts was around 32 million, according to the Communications Authority of Kenya. Low-income countries have undergone a rapid development of mobile infrastructure during the last decade. Due to the growing number of cell phone users, improved internet coverage, as well as the rising affordability of these technologies in resource-limited environments, health information technologies might just be the way to reach formerly under-served patients.

The expansion of mobile services might reduce administrative challenges and replace some traditional interactions with the healthcare system. Health information technologies could replace the costly development of traditional healthcare infrastructure and facilities, and offer the means to do follow-ups, monitor health-

“In a country with an estimated population of 47 million, internet penetration stood at 90% by the end of last year, and the total number of mobile money accounts was around 32 million.”

related activities, and facilitate data acquisition. They would also facilitate the analysis of behavioural trends in the use of healthcare resources, thus decreasing the workload and costs to the healthcare system.

MY VISIT TO the local health clinic in the Bombolulu village underlines the need to somehow bolster patient access to health services in Kibera. The clinic stands right in the centre of the settlement, surrounded by open sewage systems. From a hygiene perspective, it seems paradoxical to have a ▶

Photo: Getty Images.



“Mobile technologies have the potential to play a unique role in advancing healthcare, particularly in resource-limited or rural settings where communities have skipped the traditional development of healthcare infrastructure.”



Pharmacy in Kibera.

health facility in the midst of it all. The clinic is a satellite of the Shining Hope for Communities (SHOFCO) Main Clinic, located in another part of Kibera. It is privately funded and all medical staff operating there are locals. There are four other satellite clinics, and if referral is needed patients are assisted with fees for travel and admittance to the Kenyatta National Hospital or Mbagathi District Hospital in Nairobi.

Inside the clinic’s small, poorly lit consultation room, I meet Dr Anderson Kyalo, who explains how the clinic operates. The work there appears to be mainly paper based; patient records and what seem to be prescriptions are placed on his tiny desk by a colleague during our brief discussion. Dr Kyalo is the only doctor working this day and he expects to see around 50 patients. The clinic only treats outpatients and they provide no health services at night, nor are there any emergency wards in this part of Kibera. This poses a problem, Dr Kyalo says. The clinic is open 10 hours a day during the week and 8 hours on Saturdays. His colleagues are two community workers with some medical and health education, who conduct follow-ups through home visits and health talks with the patients. The rest of the staff consists of a pharmacist, a nurse, and a laboratory technician.

I T IS EVIDENT that there are many socio-economic and logistical challenges to optimum health and medicines safety in Kibera. However, if fully implemented and with staff trained for them, electronic and mobile health systems – so-called e-Health and m-Health – could supply the means to improve health management. In addition to providing user-friendly platforms for smooth communication between healthcare providers and patients, digital health technologies would benefit settings like Kibera in a number of other ways. Round-the-clock electronic access to medical sources would increase the availability of information at the point of care, and help clinicians keep up-to-date with best practices and treatment guidelines. Moreover, electronic handling of patient data could reduce the need for bulky paper documentation, and the use of clearly legible, electronic prescriptions could help avoid certain medical errors.



The health clinic in Kibera’s Bombolulu village.

“The expansion of mobile services might reduce administrative challenges and replace some traditional interactions with the healthcare system.”




A S I REFLECT on these issues, I continue my visit. Only a few minutes’ walk from the clinic stands the only registered pharmacy in this part of Kibera, where pharmacist Jorma Ojwang is at work. Like many healthcare workers in Kibera, Mr Ojwang is a former resident of the area. When asked why he chooses to work here, he shrugs his shoulders in resignation and answers, almost as if he has no choice: “This is my people, you know. I feel for them.” We discuss how the vulnerable population of Kibera afford

the medications they’re prescribed, and how access to medications and compliance to treatment are ensured when medicines are not in stock.

At the staff side of the pharmacy, between the shelves in the stockroom, two chairs are placed for occasional health talks and follow-ups with patients. Communication about adverse effects is straightforward and direct, according to Mr Ojwang. Patients are usually informed of what mild adverse effects might be expected with a certain type of drug. They are also made aware that they should come back to the pharmacy for further advice and dialogue before stopping their treatment altogether, if they experience a side effect. In case a suspected adverse effect becomes known to the pharmacist there are reporting forms available, but unfortunately they are locked away in a cupboard in the back of the pharmacy.

This is another area where health information technology could prove its value. By supplying novel health management tools, mobile technology could not only boost overall health education in Kibera but also improve patient compliance and reporting of adverse effects.

M OBILE TECHNOLOGIES HAVE the potential to play a unique role in advancing healthcare, particularly in resource-limited or rural settings where communities have skipped the traditional development of healthcare infrastructure, and leapt into modern technology. To achieve maximum impact, we need to take a fresh look at the opportunities and challenges lying ahead, and come up with innovative approaches tailored to the setting at hand. Sometimes we have no other choice than to walk down a bumpy road that no one has paved before us – in the most literal sense.

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Current safety concerns with HPV vaccination

Using adverse event cluster analysis – a novel data-driven approach to signal exploration – UMC and the Danish pharmacovigilance centre have researched the extent of safety concerns associated with HPV vaccinations.



Photo: Shutterstock

WITH THE PUBLICATION of “Current safety concerns with human papillomavirus vaccine: a cluster analysis of reports in VigiBase” in the journal *Drug Safety* this year, UMC contributed original research to the ongoing global conversation regarding safety signals for the human papillomavirus (HPV) vaccine.

Work on the topic of the HPV vaccine was initiated in the spring of 2015 when UMC researchers were contacted by the national pharmacovigilance centre of Denmark, the Danish Health and Medicines Authority (DHMA). UMC was asked to assist in interpreting a large local cluster of reports of postural orthostatic tachycardia syndrome (POTS) – a dysfunction of the autonomic nervous system – from a specialist clinic in Copenhagen. A physician there had noted a larger-than-expected number of referrals to the syncope clinic for young girls with a diverse set of symptoms, such as headache, dizziness, fatigue, vision disturbances and abdominal pain. After undergoing various tests of the autonomic nervous system many of these girls were found to have POTS. The DHMA requested UMC’s help to explore whether this syndrome was being reported from any other countries in the WHO Programme for International Drug Monitoring.

POTS HAS BEEN a poorly-understood and largely under-recognised diagnosis, as revealed in the relative paucity of published data regarding its pathophysiology and epidemiology. Prior to 2013, there had been only approximately 80 case reports of POTS received into VigiBase, WHO’s global database of suspected adverse drug reactions, for any medicinal product. A

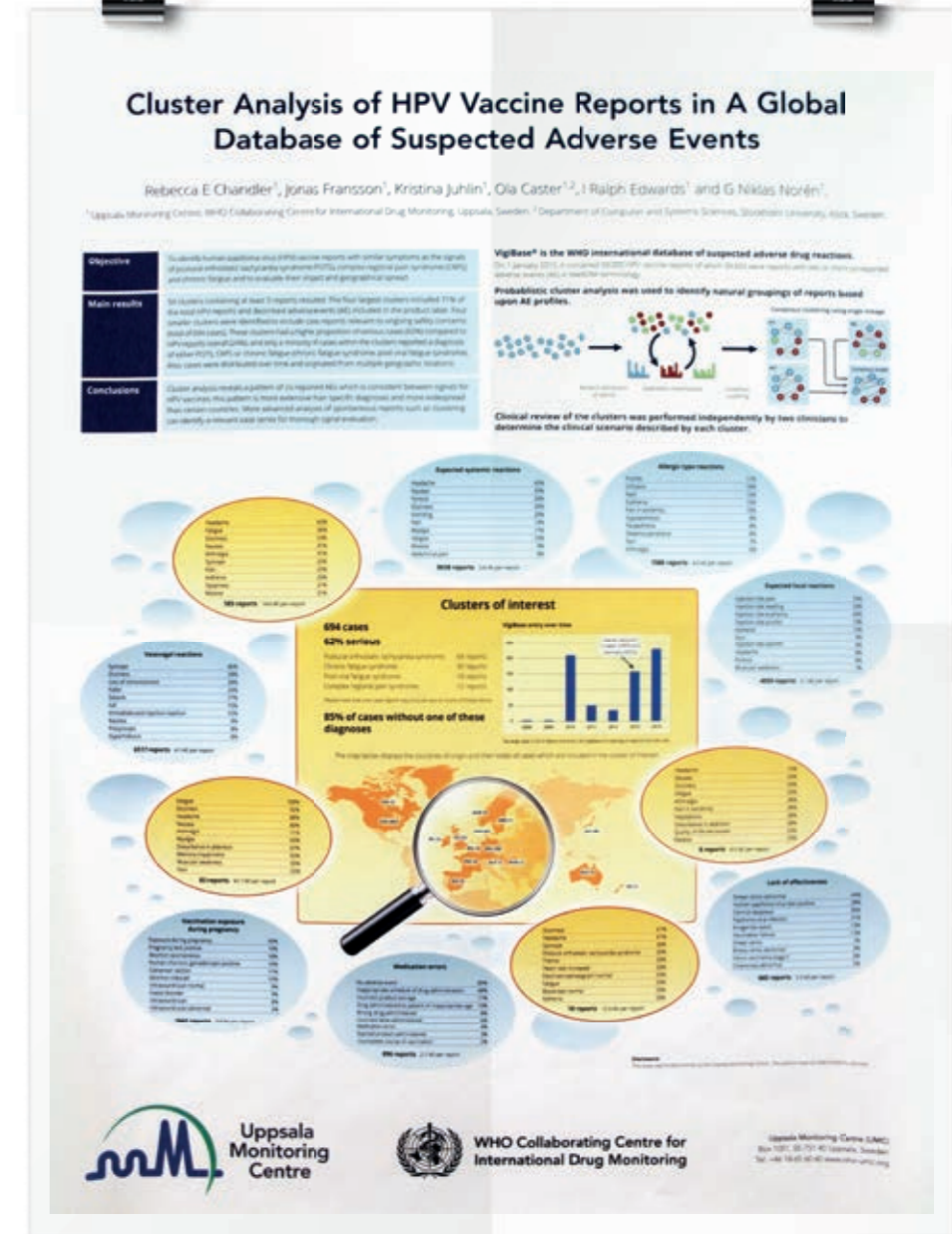
“New approaches to the analysis of spontaneous reports may better identify the relevant case series for thorough signal evaluation.”

review of the Danish case reports revealed that they included additional terms that were also found in many HPV vaccine reports in VigiBase from other countries.

Given the relative lack of awareness of POTS, UMC’s researchers speculated that traditional signal detection methodology – relying on disproportionality measures at the level of single drugs and adverse event terms – might not fully characterise this signal. The hypothesis was that different reporters might use different adverse event (AE) terms to describe similar conditions, and yet there could be enough overlap between these reports to identify subgroups of HPV vaccine reports with similar AE profiles. A novel data-driven approach to signal exploration, AE cluster analysis, was used to test this hypothesis.

The clustering algorithm targeted all HPV vaccine reports that included two or more adverse drug reaction (ADR) terms and had been received into VigiBase before January 1, 2015. It generated a total of 54 clusters containing at least five reports. The four largest clusters contained 71% of HPV reports in the analysis, and the case series defined by these clusters described ADRs that are included in the product label, namely local and systemic reactions, allergic/hypersensitivity reactions and vasovagal episodes. Four smaller clusters were identified that contained case reports relevant for consideration in assessment of the ongoing safety concern.

The most commonly reported AE terms were headache, dizziness, fatigue, or syncope; three of these four AE terms were reported in >50% of the reports in the clusters. These clusters had a higher proportion of serious cases compared with HPV reports overall (44-89% in the clusters compared with 24%). Only a minority of reports in the clusters included AE terms of diagnoses to explain these symptoms; however, the majority of all cases reporting POTS were included in these clusters.



TRADITIONAL STATISTICAL signal detection methodology, which is based upon disproportionality between single drug-AE pairs, highlights only those cases in which a diagnosis of interest, such as POTS, is reported. In contrast, in UMC’s analysis, reports with and without the diagnosis of POTS based upon the pattern of multiple reported AEs, were clustered together. This allowed for the identification of additional case reports which were relevant to further assessment of the signal.

One of the important messages from the

study is that new approaches to the analysis of spontaneous reports may better identify the relevant case series for thorough signal evaluation.

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READ MORE: Chandler RE et al, “Current safety concerns with human papillomavirus vaccine: a cluster analysis of reports in VigiBase”, *Drug Safety*, 2017.

Patient adherence as a part of pharmacovigilance

The expanding scope of pharmacovigilance from drug safety to patient safety in the last decades has brought attention not only to the inherent safety of medicinal products, but also to the way they are being used.

NOWADAYS, MEDICATION ERRORS are considered reportable in pharmacovigilance systems since they have the potential of leading to patient harm. One important aspect of medication errors concerns the failure of patients to adhere to treatment schedules as agreed with, or prescribed by, healthcare professionals.

WHO has estimated that adherence rates to chronic medicinal treatments is only about 50%. Non-adherence has been described as a silent epidemic and is estimated to play a role in 21-37% of preventable adverse drug events. Non-adherence can result in antimicrobial resistance, treatment failure, prolonged



hospitalisation, and increased costs for healthcare systems. It is also known that adverse drug reactions (ADRs) frequently result in non-adherence to medicine therapy. Other common reasons for non-adherence include the taste, form and route of administration of medicines, their cost, the length of treatment, forgetfulness, polypharmacy, patients' beliefs and communication breakdown between patients and healthcare providers.

A WHO review classifies factors contributing to non-adherence into five dimensions, namely: social and economic; healthcare team and system-related; therapy-related; patient-related; and medical-condition-related factors. Pharmacovigilance can contribute to our learning about these factors and influence them.

SOCIAL AND ECONOMIC FACTORS

Treatment failures are often reported in pharmacovigilance systems, and some may be due to non-adherence. In this perspective, non-adherence can be seen as an adverse drug event. Active pharmacovigilance follow-up of exposed patients can reveal how poverty, age, gender, illiteracy, cultural beliefs, self-medication and so on affect adherence to treatments.

In Ghana, an interactive text messaging service has been introduced to allow reporting of ADRs and promote adherence; most messages are linked to adherence issues, according to the country's Food and Drugs Authority (FDA). Systematic reviews of social media and websites managed by patient organisations can also

reveal important social or economic factors behind non-adherence.



reveal important social or economic factors behind non-adherence.

HEALTHCARE TEAM AND SYSTEM-RELATED FACTORS

Integrating pharmacovigilance in healthcare teams at all levels improves dialogue on agreed treatments and the risks involved. Patients should be offered easy means to report treatment outcomes to the healthcare team or the national pharmacovigilance system.

Patient adherence and learning about treatment-related problems were both improved in Ghana by including pharmacovigilance as a mandate for healthcare teams that managed mass-drug administration against tropical diseases. Ghana has also introduced an indicator-based pharmacovigilance assessment tool for hospitals with the objective of integrating



pharmacovigilance in the healthcare delivery system, according to the FDA. This has led to improved dialogue between prescribers, pharmacists and patients.

THERAPY-RELATED FACTORS

Pharmacovigilance can provide evidence on major ADRs that may occur during the agreed therapy, how to manage them, and when to report problems. Pharmacovigilance analyses of longitudinal patient healthcare records can provide forecasts on the likely persistence of problems that have been encountered. Such information builds confidence between healthcare professionals and patients.

PATIENT-RELATED FACTORS

Patients' motivation, anxiety, forgetfulness, misconceptions, cultural beliefs and taboos can all affect adherence. Open and correct information to patients about possible complications or possible ADRs associated with treatment should increase patient empowerment and motivation, and reduce their fear.

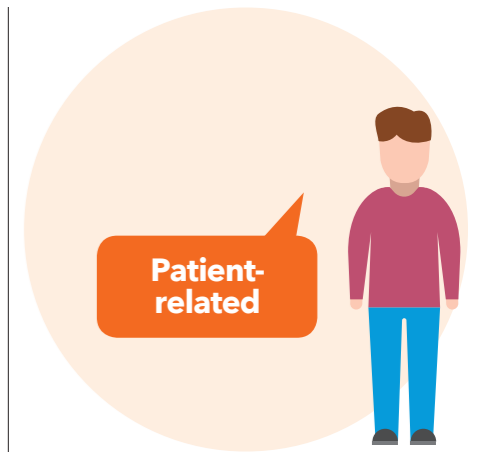
MEDICAL-CONDITION-RELATED FACTORS

It's not just vital to treat a diagnosis; understanding the challenges patients are facing is important for the provision of patient support as well. For example, HIV patients are often faced with multiple challenges, such as additional tuberculosis or viral hepatitis illness, comorbidities due to the ageing population, drug abuse and social stigma. Adherence to anti-retroviral treatment is fundamental for treatment

success and to avoid drug resistance. Pharmacovigilance studies, through active patient follow-up and mining of longitudinal health records, can reveal problems commonly associated with a particular condition, which can be important for the development of trust between healthcare providers and patients.

INTERVENTIONS INVOLVING pharmacists in medicines management – such as medication reviews, pharmaceutical care services, developing care plans and providing follow-up – are effective in empowering and motivating patients in adhering to their treatment. Clear communication about the risks that come with a certain treatment is inherent in pharmacovigilance, and an open dialogue is essential to building an atmosphere of trust. Such trust allows patients to share information about non-adherence and the reasons behind it. In this atmosphere of trust, patients and healthcare professionals can learn from each other.

In Lausanne, Switzerland, a patient-centred medication adherence programme has been established. It involves face-to-face patient interviews by pharmacists, objective measures of the actual medication intake with daily feedback from the treatment team to the patient, and then processing the results in medication adherence reports. Lessons learned from this activity include the critical importance of patient empowerment, the need to train the healthcare professionals involved to target



several of the factors mentioned above, and the importance of continuity of care.

Patient adherence issues should be regarded as adverse drug events, and therefore, it is important that non-adherence should become part of pharmacovigilance programmes, tackling this silent epidemic in the real world of pharmacotherapy.

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READ MORE:
World Health Organization, "Reporting and learning systems for medication errors: the role of pharmacovigilance centres", 2014.

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Finding patient narratives in VigiBase

UMC and the Dutch pharmacovigilance centre Lareb carried out a signal detection exercise specifically focusing on adverse drug reaction reports filed by patients, identifying both new signals and new details of known ADRs.

MEMBERS OF THE Research department at UMC joined with colleagues from the Netherlands Pharmacovigilance Centre Lareb to design and execute a signal detection exercise focused on adverse drug reaction (ADR) reports received directly from patients. Lareb is the WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting and has recognised patient reporting in pharmacovigilance since 2003; for its part UMC hoped to benefit from their experience and draw on their expertise to investigate if safety signals relevant to patient concerns could be identified in VigiBase, WHO's global database of suspected adverse drug reactions.

The signal detection exercise was prepared throughout the spring of 2016, with discussions about how traditional statistical signal detection methodologies could be adjusted to prioritise drug-ADR combinations whose case series included a significant proportion of patient reports. In addition to the routine review of product information intended for healthcare providers for information on the ADRs highlighted in the statistical screening, a decision was taken to also review the patient information leaflets, to ensure that patients are provided with adequate and understandable information on the ADRs.

In October 2016, a team from UMC travelled to the town of 's-Hertogenbosch in the Netherlands – home of Lareb – to assess a list of drug-ADR combinations

for potential signals. Over four days, the teams assessed a total of 212 drug-ADR combinations. As a result of this work, eight signals were communicated to the national pharmacovigilance centres in the WHO Programme for International Drug Monitoring.

TWO OF THE SIGNALS were new aspects of known ADRs, which were detailed in narratives in the patient reports. The patients' narratives provided important information on the severity of the ADRs as well as their impact on the patients' quality of life.

The first concerned genital itching and dapagliflozin. Dapagliflozin is of the class of oral medications used to treat type 2 diabetes, termed sodium glucose cotransporter-2 inhibitors (SGLT-2i). Itching in the genital area is a common non-serious adverse reaction for these types of drugs, which was known at the time of approval. However, from the patient reports it was identified that the itching could be so severe as to provoke discontinuation of the drug. The signal highlights the fact that some events can be characterised as non-serious in the clinical trial setting, but in the post-marketing period may manifest as severe events with a large enough impact on the patient's quality of life that discontinuing the medication is necessary.

The second signal was dry eyes and amitriptyline. A review of the product labelling for healthcare providers and the patient information leaflet revealed that only the term "anticholinergic effects" is included. While healthcare providers would be likely to understand that dry eyes are a manifestation of such effects, a patient would probably not. The signal recommends an update of the patient information leaflet to explicitly list eye dryness as an adverse effect.

THE EXPERIENCE WAS very valuable both as a face-to-face collaboration with one of the national centres in the WHO Programme, and in confirming that drug safety concerns of direct importance to patients can be identified in a global database such as VigiBase.



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10TH INTERNATIONAL PHARMACOVIGILANCE TRAINING COURSE

Uppsala Monitoring Centre welcomed 29 participants from 23 countries to its renowned annual pharmacovigilance course in Uppsala in May. The course offers two weeks of training focused on teaching the practical skills needed to run effective pharmacovigilance programmes.

Education



“The knowledge I obtained will guide me to improve pharmacovigilance practices in my country. It will help me put in my best effort to make Albania part of the big picture within the WHO PIDM, and contribute to patient safety worldwide.”

Dajana Roshi, MSc Pharmacy
Albania National Centre



“Fantastic, matched expectations! I hope the knowledge gained will be of great use to improve the quality of pharmacovigilance practices in Qatar.”

Pallivalappila Abdul Rouf, MPharm, MSc, PhD
Womens Hospital, Qatar



Education



“The course provided me with pharmacovigilance knowledge I did not have before, and this will definitely benefit the South African public.”

Mafora Florah Matlala, BPharm
Medicines Regulatory Authority,
South Africa



“The UMC pharmacovigilance training course was memorable, inspiring and well organised by a passionate and knowledgeable team. I left there motivated to develop pharmacovigilance in the Caribbean region.”

Rian Marie Extavour, RPh, PhD
Pharmacy Educator, Trinidad and Tobago

◀ Photos: Gediminas Norgėla and Göran Ekeberg for UMC.

Patient reporting is the future of pharmacovigilance

Patient-derived reports add a richness to our understanding of medicine safety that would not be achieved by relying on healthcare professionals' reports alone. Pharmacovigilance specialist Sten Olsson explains why.

I BELIEVE THAT direct patient reporting holds the key to the future of pharmacovigilance. While we keep struggling to convince healthcare professionals to report, often with little response, patients are usually happy to share their experiences if we provide a respectful environment for sharing information.

The reporting domain has undergone significant changes since the early days of pharmacovigilance. When I started working in the field, reporting was completely owned by physicians. The common perception was that since doctors are trained to make differential diagnoses - in other words to distinguish between the effects of the disease and the effects of the medicine - they should be the only ones to report. There was a great fear that random observations from lay people would distract and delay the uncovering of patterns of reactions to medicines, the first step to identify new signals. Today, when artificial intelligence is used to recognise patterns in big databases, random observations are much less distracting. In the early days however, data storage capacity was limited and it made sense to only store validated reports from trained physicians.

The physicians' reporting monopoly was challenged in the 1990s, when studies

showed that nurses' or pharmacists' reports are just as valid, and that there is little overlap between them. Perhaps not surprisingly, those studies indicated that members of different professional categories are more likely to report issues connected to their role. Whereas physicians mostly describe serious problems that require their intervention, nurses highlight issues that arise during patient care, and pharmacists tend to report problems related to the drug's dosage or its interaction with other medicines.

PATIENTS, ON THE OTHER HAND, contribute an additional level of information. They are often well educated and can make valid observations about their health status. We know from scientific studies that patients can teach us a lot about the impact of drug intake on quality of life. Patients are also more likely to report events that seem questionable to physicians, nurses and pharmacists. Healthcare professionals tend to refrain from reporting altogether if they cannot determine the cause, or possible cause, of the problem. Patients however are not inhibited by such concerns and their candour makes them valuable players in the identification of new signals.

Not only do patients contribute to

identifying novel adverse reactions, but they play an important role in confirming previously described ones. An old medicine taken by a new patient is in some ways a new medicine. A drug may have been on the market for several years and its adverse reactions well described, but that will not stop patients from reporting - the adverse reaction they experience will be new to them and if they are bothered by it, they will keep on reporting. Conversely, healthcare professionals limit themselves to reporting the most serious cases after medicines have been on the market for a couple of years. Patients' reports will better reflect the actual burden of medicine-related problems for society.

Involving patients in drug safety reporting has additional advantages. In many communities and in many countries, healthcare services and professionals are not easily accessible, or the costs of consulting them are prohibitive. Self-treatment with pharmaceuticals or traditional remedies is common in such settings and adverse consequences will rarely be reported to healthcare professionals. Electronic reporting via free messaging services or smartphone apps allows medicine users to report directly to the pharmacovigilance centres, bypassing the need to consult

expensive or inaccessible health facilities. Direct patient reporting systems have already been introduced in many low- and middle-income countries. They are more likely to reveal whether adverse reactions to self-treatment have manifested and whether the patient adhered to the treatment or not. Information on patient adherence is crucial to understanding treatment outcomes, but is often not shared with healthcare professionals. Reasons for lack of adherence may well be revealed in a direct patient reporting system, if the patient feels reassured that confidentiality will be maintained.

IF WE SUCCEED in mobilising patients worldwide into active reporting, we can create even bigger and more diversified databases of suspected problems associated with drug exposure. Combined with rapidly developing technology for data storage and analysis, such collections should lead to the earlier detection and a deeper understanding of the range of effects that medicines exert in different populations. A recent article referred to direct patient reporting as the 'renaissance of pharmacovigilance' and I couldn't agree more. We are only at the beginning of this exciting development in medicine safety, and I am looking forward

“If we succeed in mobilising patients worldwide into active reporting, we can create even bigger and more diversified databases of suspected problems associated with drug exposure.”

to seeing what the renaissance will bring.

A word of caution though. Focusing only on patient reporting might make health professionals feel redundant, which would be disastrous. If there is one thing we have learnt from decades of pharmacovigilance activities, it's that there is no single truth. We will always need the observational and analytical intelligence of trained physicians, nurses and pharmacists to understand why medicines occasionally cause harm and how to minimise that damage. Nurses, pharmacists, doctors and patients each hold a piece of the puzzle and only by placing the pieces together will we be able to see the big picture at last. Everyone - patients included - needs to be invited to the big round table of medicine safety.



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Härmark L et al, "Patient-reported safety information: a renaissance of pharmacovigilance?", Drug Safety, 2016.

Near real-time vaccine safety surveillance in the UK

A research team from the London School of Hygiene & Tropical Medicine and Public Health England is looking to implement a near real-time vaccine safety surveillance system using electronic health records in the UK.

VACCINE SAFETY IS extensively studied in clinical trials before a vaccine is approved. However, there is limited power to detect rare – but potentially serious – adverse drug reactions.

Post-licensure safety surveillance is thus required to ensure timely detection of potential safety signals. There are several methods to conduct post-licensing monitoring, including passive and active forms of surveillance.

In 2005, the Vaccine Safety Datalink (VSD) in the US proposed a new method to assess safety during post-licensing surveillance: near real-time vaccine safety surveillance using electronic health records. Unlike other methods, near real-time surveillance starts shortly after a vaccine is introduced into the market and data is checked at regular intervals, for example every week or every month. It uses sequential tests, based on the sequential probability ratio test that was developed by the mathematician Abraham Wald in the 1940s and is frequently used in industry and clinical trials.

Since its introduction in 2005 there have been several methodological developments, statistical tests made available, knowledge regarding the properties of these tests, and options to account for delays in data availability. There was particular interest in these methods around the 2009/2010 flu season, when the pandemic flu vaccine was introduced with limited safety information. This type of surveillance is now routinely used by the VSD

in the US, and has led to the identification of several safety signals, from which three were confirmed and resulted in changes in the vaccination recommendation. The three signals in question were for the measles-mumps-rubella-varicella combination vaccine and febrile seizures; the 2010/2011 trivalent inactivated influenza vaccine and febrile seizures; and the monovalent rotavirus vaccine and intussusception.

DESPITE THE WIDESPREAD use of this type of surveillance in the US, only a few other countries – including New Zealand and the UK – have implemented near real-time surveillance systems. This might be related to the need for readily available data from electronic health records, which is not collected or made accessible everywhere. In the UK there are several research-level electronic health records that can be used to perform near real-time vaccine safety surveillance. However, this type of surveillance has not been fully applied.

A research team from the London School of Hygiene & Tropical Medicine and Public Health England is assessing the possibility to implement a near real-time vaccine safety surveillance system using the Clinical Practice Research Datalink (CPRD). CPRD contains clinical data available in primary care, including information on diagnosis, vaccines administered in primary care, and referrals and feedback from secondary care. This data is generated from information that general practitioners enter in the software used in practice. CPRD currently contains information on over 4 million active patients.

CPRD DATA DIFFERS from other data sources already used to perform near real-time vaccine safety surveillance. Therefore it is necessary to assess whether it fulfils certain requirements to implement near real-time surveillance, and the best way to implement this type of surveillance. As mentioned, one of the key aspects of a near real-time system is access to timely data, and one of the first steps in the implementation process is to assess delays.

Delays in CPRD data can be due to either delays in making an initial diagnosis, in receiving feedback from other levels of care, or in data being made available to researchers. Data is made available to researchers on a monthly basis, which enables the construction of a system that looks at data every month.

The research team has also assessed delays caused by receiving feedback from other levels of care. For example, when a patient is diagnosed in a hospital it might take time before the general practitioner receives information about the diagnosis.

The assessment measured how long it takes for information such as diagnosis made in hospitals to be added to the CPRD data. This measurement was undertaken for outcomes of particular relevance to vaccine safety surveillance, i.e. outcomes that might be interesting to evaluate as potential adverse effects of a vaccine – such as Guillain-Barré syndrome, Bell's palsy, optic neuritis and febrile seizures. For these outcomes, the results indicate that most events recorded in CPRD occur within a month – a delay which is compatible with near real-time surveillance.

BASED ON THIS RESULT, the next step is to evaluate whether there is enough power to detect signals using CPRD. This will also include exploration of the best statistical tests to use to assess different pairs, and the options to account for previously identified delays. Preliminary results indicate that, using CPRD, there is power to detect large increases in risk for rare adverse drug reactions and increases in risk for more frequent adverse events. Further results of this work will enlighten the researchers on how to best use CPRD data to implement a near real-time vaccine safety surveillance system. The final results are expected to strengthen vaccine pharmacovigilance systems in the UK.

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Drug-name look-up in mobile apps made easier

The WHODrug country list look-up service is piloting a new channel for easier access to structured and quality-assured medicinal product information, tailored for use in mobile reporting apps and other data-collection tools by countries in the WHO Programme for International Drug Monitoring.

Paracetamol
Furosemide
Amoxicillin
Loratadine

Salbutamol
Ondansetron



USING STANDARDS from the start ensures improved quality, less manual work, and quicker processing of information throughout the entire pharmacovigilance system, from the patient to global drug safety systems and back.

When reporting suspected adverse drug reactions reliable identification of a medication used is vital. However, it is not enough to only know details about the medication suspected of causing a drug-related problem. It might be an unexpected medicine that is responsible for the problem or an interaction between two or more medicines. Therefore, reliable identification of concomitant medications is also important. In addition, for issues such as quality-related problems it is important to know the actual brand or trade name of the product – not only its active ingredients.

Even though pharmacovigilance professionals may all agree that it is important to have correct and detailed information about a patient's medicines, the use of quality-assured and standardised information sources for medicinal products hasn't been as widely adopted as it could be. However, good sources are available; within WHO's drug monitoring programme, information about medicinal products has been collected and structured in the global dictionary WHODrug since 1968. The dictionary is optimised for use within pharmacovigilance and clinical trials. It is available as text files and integrated in tools such as WHODrug Insight, VigiFlow and VigiLyze.

SEVERAL ORGANISATIONS have asked Uppsala Monitoring Centre for an easy way of getting access to a simple list of medicinal product names to include in e.g. mobile apps and various data collection tools. Rather than handling the complexity of the entire dictionary, which contains detailed information about products from around 130 countries, all they need is a small subset of WHODrug that is relevant for their region. In addition, new types of tools, using new technologies, also require new ways of accessing information.

In late 2016 UMC decided to address this need by providing easy access to subsets of WHODrug for usage within the Programme. A project was launched with the WEB-RADR project as a pilot user, and in February 2017 UMC successfully launched a web service that makes this possible.

The service makes a country-specific subset of WHODrug available, containing information about medicinal products with their trade names and active ingredients. There is no graphical user interface; instead the service is intended to be integrated in other tools, such as the mobile app developed in the WEB-RADR project. In this tool the service is used to present a list of medicinal products for the user to pick from. The selected product can then be used to retrieve news, get safety information, and report adverse events.

The new WHODrug service is up and running, servicing the mobile app developed in the WEB-RADR project. It will be evaluated within the scope of the WEB-RADR project and after evaluation, it will be decided if it should be offered for a broader use.



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Digital reporting made available to Montenegrin pharmacists

Pharmacists in Montenegro's public sector can now use a digital application as an easy and efficient way to report adverse effects directly to the country's Agency for Medicines and Medical Devices.

PHARMACISTS PLAY AN important role in post-marketing monitoring of drugs. They are both drug experts and the healthcare workers who are the most important link between patients and prescribers. The direct contact that pharmacists have with patients provides them with the opportunity to monitor the safety of treatment by reporting adverse effects, and to participate in the development of pharmacovigilance as an evidence-based scientific discipline. As the most important source of information for the efficient and safe application of over-the-counter medicines, pharmacists also play a key role in monitoring this category of drugs.

PREVIOUSLY, PHARMACISTS in the public sector in Montenegro could only report adverse effects by filling out a hard copy of the reporting form. However, in July 2016 the possibility to report digitally through the healthcare information system – which they use in their daily work – was introduced. The system links all pharmacies in the public sector to other participants in the health system, including the Agency for Medicines and Medical Devices of Montenegro (CALIMS). In this manner, the supply and consumption of medicines in pharmacies is monitored, which is essential for conducting analysis in the field of rational pharmacotherapy.

This digital application mimics the classical paper reporting form. After successfully entering data into the application, pharmacists send the report directly to CALIMS. The reports become automatically available to CALIMS's Pharmacovigilance Department, which is very important in cases when prompt regulatory action is needed.

Before officially commissioning the reporting application, CALIMS conducted training for pharmacists – the future users of the new reporting forms. Under the guidance of Pharmacovigilance Department employees, all trainees successfully tested the new application and showed great interest and willingness to use it.

The development of this digital application is one more step towards improving the cooperation between CALIMS and pharmacists, which will ultimately improve public health and patient safety.

ANOTHER DEVELOPMENT in Montenegro is the implementation of eReporting, which is available via the CALIMS website since March this year. The eReporting module allows national pharmacovigilance centres to collect reports of adverse effects directly from patients as well as healthcare professionals, which are then further passed

on to the WHO global ICSR database, VigiBase, via the VigiFlow management system. Amendments to the country's Law on Medicines envisage the possibility for patients to report directly to CALIMS, which has not been the case so far. In the near future, CALIMS expects that patients and healthcare professionals will use the online form.



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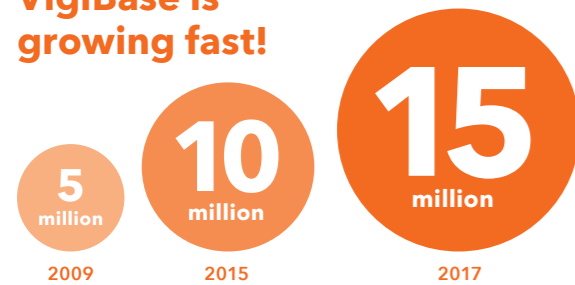
Nemanja Turković and Maja Stanković from CALIMS during training for pharmacists.

More transparency in clinical trial reporting

IN MAY 2017 some of the world's largest medical research funders and non-governmental organisations signed an agreement to implement WHO standards on reporting clinical trial results. About half of all clinical trials conducted today go unreported, often because the results are negative. Incomplete reporting leads to altered perception of the risks and benefits of vaccines, drugs and medical

devices, and it can even lead to use of suboptimal, if not harmful, products. The new standards will require all clinical trials to be registered in a publicly-available registry and the results to be disclosed within specified timeframes on the registry and/or by publication in a scientific journal. Most trials and their results will be accessible via WHO's International Clinical Trials Registry Platform.

VigiBase is growing fast!



15 million reports in VigiBase
The number of individual case safety reports in VigiBase surpassed 15 million in April 2017. "This is an impressive achievement by member countries in the WHO Programme! Their contribution is key to advancing global pharmacovigilance practices and for using data to improve patient safety," said Anki Hagström, the head of UMC's Global Services department.



UMC and ISoP have entered a three-year agreement to collaborate on pharmacovigilance training. UMC director Marie Lindquist and ISoP president Sten Olsson signed the agreement at WHO headquarters in Geneva in April.

Join the conversation on social media!

- Rebecca Chandler: Current Safety Concerns with Human Papillomavirus Vaccine: A Cluster Analysis of Reports in VigiBase®
- Uppsala Monitoring: Our #Pharmacovigilance comic has made the local news! @untse #safemeds #comicbooks #uppsala Find out more bit.ly/2qCjcFq
- Magnus Ekalo: WebRADR app for #ADRreporting now launched outside Europe; Burkina Faso now receives reports seamlessly from app to VigiFlow #mHealth
- Uppsala Monitoring: A delegation from the Zhejiang Centre for ADR Monitoring visited UMC last week to discuss the #pharmacovigilance system in China!
- Magnus Wåhberg: @UMCGlobalSafety has made Signals (possible Adverse Drug Reactions) from 2011 searchable as part of #VigiLyze. #pharmacovigilance #VigiBase



The WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) held its 14th annual meeting at WHO headquarters in Geneva in April.



Dr Tedros Adhanom Ghebreyesus is the new Director-General of WHO. The former Minister of Foreign Affairs in Ethiopia was elected by the World Health Assembly in May and began his five-year term on 1 July 2017.

Ecuador and El Salvador new WHO PIDM members



Ecuador and El Salvador joined the WHO Programme for International Drug Monitoring as its 126th and 127th full members in April.



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Vaccine Pharmacovigilance Fellowship

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Back to Basics in Pharmacovigilance

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www.dsru.org
@DSRUDrugSafety

10-14 September 2017

77th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2017

Seoul, Republic of Korea · International Pharmaceutical Federation (FIP)
www.fip.org/seoul2017
@FIP_org

25-27 September 2017

Advanced Pharmacovigilance

London, UK · Management Forum Ltd
www.management-forum.co.uk

26-28 September 2017

4th Annual Risk Management and Pharmacovigilance Summit

Vienna, Austria · Allan Lloyds
www.AllanLloyds.com
@AllanLloyds

4-5 October 2017

Risk Benefit Assessment in Pharmacovigilance

Fareham, UK · Drug Safety Research Unit (DSRU)
www.dsru.org
@DSRUDrugSafety

5 October 2017

An Essential Overview of Pharmacovigilance

London, UK · Management Forum Ltd
www.management-forum.co.uk

8-10 October 2017

17th Annual Conference of Society of Pharmacovigilance

Srinagar, India · Society of Pharmacovigilance, India (SOPI)
www.sopi.net.in

9-11 October 2017

Building Teratovigilance Capacity in Africa

Cape Town, South Africa · Centre for Infectious Disease Epidemiology and Research (CIDER)
www.buildingteratovigilance.co.za
@uctcider

10-11 October 2017

Uppsala Health Summit

Uppsala, Sweden · Uppsala University
www.uppsalahealthsummit.se
@Ua_HealthSummit

11-12 October 2017

Assessment and Medical Evaluation of Individual Case Safety Reports

Fareham, UK · Drug Safety Research Unit (DSRU)
www.dsru.org
@DSRUDrugSafety

15-18 October 2017

17th Annual Meeting of ISoP

Liverpool, UK · International Society of Pharmacovigilance (ISoP)
www.isoponline.org
@ISoPonline

24-26 October 2017

2nd Annual Risk Management and Pharmacovigilance America Summit

Boston, US · Allan Lloyds
www.AllanLloyds.com
@AllanLloyds

9-10 November 2017

Signal Detection and Regulatory Expectations

London, UK
Management Forum Ltd
www.management-forum.co.uk

4-6 December 2017

Pharmacovigilance

London, UK
Management Forum Ltd
www.management-forum.co.uk

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