APRIL 2018 ISSUE 78

UPPSALA
REPORTS
COVERING THE WORLD OF PHARMACOVIGILANCE

MAPPING *the* HERBAL JUNGLE

Bhutan's PV progress • Uppsala Health Summit • Big data and causal dispositionalism • Managing MEs • Social media campaign • Better signal detection with vigiRank

THE MAGAZINE FROM UPPSALA MONITORING CENTRE
Uppsala Monitoring Centre

Director´s message

AFTER MY FATHER DIED LAST YEAR, I thought a lot about him and the role he played, and still plays, in my life. One of the most important things he taught me was that it is who you are as a person that matters – not where you come from, how you look, or what position you have in the world. And he never made me feel that there were things I couldn't do because I was a girl, not a boy. I knew that I was different from boys, physically, but I never felt branded negatively as the 'weaker sex'. Only much later did I fully appreciate how fortunate I was to be able to grow up thinking of myself primarily as a person, a human being who also happened to be a girl.

My view of a good world is where all of us are being seen, and valued, as the unique individuals we are. A world where we are appreciated in all our complexity, and where our choices are made based on ability and interest, not a category or label that we have been assigned by others.

Our ability to quickly categorise things around us is a basic instinct, a survival mechanism, and it was essential in a time when the ability to quickly identify danger was a matter of life or death. By classifying and grouping things, we make a complex reality more manageable. The problem is if we categorise in a way that is confining and excluding, and reduces reality too much – a simplistic reductionist approach easily leads to stereotyping, which can be anything from irritating to seriously damaging.

"By classifying and grouping things, we make a complex reality more manageable. The problem is if we categorise in a way that is confining and excluding, and reduces reality too much."

I have had many interesting discussions with Prof Ralph Edwards about the need for a paradigm shift in science, to complement the classic reductionist, often hierarchical approaches, with another way of thinking which better takes into account the complex and dynamic relationships which make up our world, and everything in it. It cannot be right to fit human beings into a few pre-defined categories when all of us have so many, often subtle, qualities, characteristics, and inclinations. And how can we find the unknown if we only look at what we already know?

A year ago, Ralph came back full of enthusiasm from a conference – a meeting of philosophers who were interested in causality assessment in pharmacovigilance. His own thinking about causality and complexity fit well into their theoretical philosophical framework, and as he explained to me what it was all about, I felt immediately that this was a track worth following. Like when we decided to develop our data mining methodology based on Bayesian probability – which can be defined as a reasonable expectation representing previous knowledge – the philosophy of complexity is intuitive and makes good sense. It is about "studying the dynamics of interactions rather than the static makeup of parts," as author Chris Lucas wrote. It doesn't necessarily make our job easier, but it allows us to be more nuanced in our analyses of how medicines affect individuals.

For those of you who are interested in digging a bit deeper into this, I have asked Ralph to introduce his thinking on causality, complexity and dispositionalism on page 28 in this issue of Uppsala Reports.

I find all these thoughts about complexity and causality fascinating, but quite challenging, too. So many questions, and no easy answers. It reminds me of another thing my father used to say: "never give up". Knowing me, I never will.

READ MORE:

R. Edwards, "Living with complexity and big data", Uppsala Reports 78, p. 28

C. Lucas, "The Philosophy of Complexity", calresco.org, 2005.

Marie Lindquist, Director

Uppsala Monitoring Centre

UPPSALA REPORTS *Covering the world of pharmacovigilance*

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ADDIS ABABA

ETHIOPIA FIRST TO USE UPDATED VIGIFLOW

In October 2017, the first version of the renewed VigiFlow was launched, and Ethiopia became the first country to go live with the new system.

THE LAUNCH PROMPTED UMC staff to visit Addis Ababa and the national pharmacovigilance centre (NC) in the Ethiopia Food, Medicine and Health Care Administration and Control Authority (EFMHACA), with the aim to train local personnel as well as to collect feedback for future VigiFlow training materials.

VigiFlow is used by more than 70 countries and the new version will gradually be rolled out to all of them throughout this year. UMC will contact each national centre to set up a timetable to start using the new version.

Since on-site visits to all users are not feasible, the Ethiopia experience and feedback from EFMHACA will be of great value when UMC prepares VigiFlow training materials, for example webinars, to be used by national centres.

ETHIOPIA HAS USED the old VigiFlow as their adverse drug reaction management system since they became a member of the WHO Programme for International Drug Monitoring in 2008.

Monica Plöen gives a VigiFlow demo.

With local conditions in mind – such as language, medical terminology, and the pharmacovigilance team's existing knowledge of VigiFlow – UMC's focus was to train NC staff how to optimise the use of UMC tools, i.e. VigiFlow and VigiLyze. They also gathered information from the NC staff regarding their pharmacovigilance work and processes.

The training was executed as a two-day workshop, with an agenda mixed with theoretical parts and hands-on sessions. The group looked at how Ethiopian data can be explored and analysed with the support of global data in WHO's database VigiBase through the search and analysis tool VigiLyze. Discussions on how to best capture the information from a case report in VigiFlow was illuminating for both UMC and national centre staff.

UMC received and documented instant feedback from the Ethiopian hosts on VigiFlow features that worked satisfactorily, but also on necessary further improvements to VigiFlow.

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VigiBase marches on to 17 million reports

In 2017, VigiBase received the largest number of individual case safety reports (ICSRs) since its establishment in 1967, with a positive reporting trend taking place in low- and middle-income countries.

The reports on adverse drug reactions in VigiBase, the WHO database of ICSRs, come from the 130 member countries participating in the WHO Programme for International Drug Monitoring. More than half of last year's reports originated from a handful of countries, namely the United States, Republic of Korea, United Kingdom, China and France.

Nevertheless, low- and middle-income countries, which constitute more than half the member countries in the WHO Programme, reached a notable milestone in 2017. A cumulative total of over 2 million ICSRs have been submitted by these countries. In fact, last year witnessed the largest contributions ever of ICSRs to VigiBase from the Asian, African and Latin American regions.

Latin America alone showed a 61% increase in the number of reports compared to the previous year. Significant contributors were Colombia, Mexico, Peru and Cuba. South Africa, Morocco, Egypt and Congo were the leading contributors in Africa and the continent recorded a 25% increase in the number of reports compared to 2016. The increase of reporting from Asian nations went up by 5% in 2017, and South Korea, China, Japan, and India, played a key role in the increase.

National centres are commonly faced with numerous challenges in their daily work. Yet increasingly they are going beyond merely gathering ICSRs, to investigating their data for potential signals. VigiBase, which is continuously updated with reports from member countries, allows for a timely identification of potential safety concerns.

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ATC/DDD Toolkit a gold standard for drug utilisation studies

Since 1996, the World Health Organization endorses the Anatomic Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) methodology as the gold standard for drug utilisation monitoring and research. The Toolkit and relevant resources are available online.

The WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway, developed the manual for the ATC/DDD Toolkit together with the WHO International Working Group for Drug Statistics Methodology. The WHO Medicines Safety group created the ATC/DDD online Toolkit, and the first version of it went live on WHO's website in March 2017. The Toolkit was created to be a comprehensive and user-friendly online resource for anyone interested in undertaking drug utilisation studies. It contains guidance on how to set up and use the international ATC/DDD methodology.

This methodology facilitates the presentation and comparison of drug consumption statistics at international, national, and regional levels irrespective of differences in nomenclature (both branded and generic), packing sizes, pricing, and customary dosages. Such methodology is useful for valid presentation and comparison of drug utilisation within and across countries to support better outcomes and quality use of medicines.

These kinds of studies are important because although medicines can provide substantial benefits they have the potential to harm patients, which can result in substantial costs. The level of expenditure on medicines varies between countries and it is important to be able to understand the patterns of use – for example, the types of medicines used and their quantity. Drug utilisation studies are essential for monitoring these patterns and trends, and for understanding their impact on the efficiency with which health outcomes are gained.

Test how much you know about the Toolkit with this quiz!
www.who.int/medicines/regulation/medicines-safety/toolkit_quiz/en/

Explore the Toolkit online
Through 10 chapters, the Toolkit will lead the user from the basics of the ATC/DDD methodology and its applications, to how to set up a drug utilisation study. Users can test their skills on the ATC/DDD methodology through the online quiz, and expand their knowledge through the literature recommended in the application. They can also sign up for the annual courses organised by the WHO Collaborating Centre for Drug Statistics Methodology.

READ MORE: www.who.int/medicines/regulation/medicines-safety/toolkit

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MYSORE

Asian and African pharmacovigilantes train in India

For the fourth year in a row, UMC joined forces with India's JSS University to train pharmacovigilance professionals from the Asia Pacific and African regions.

IN FEBRUARY 2018, 32 participants from 12 countries gathered in India for the 4th Asia Pacific Pharmacovigilance Training Course. The course, hosted by the JSS College of Pharmacy in Mysore, India, has been jointly organised by Uppsala Monitoring Centre and JSS University every year since 2015. It is modelled on UMC's two-week long International Pharmacovigilance Training Course in Uppsala, Sweden – taking place for the 20th time this year.

Although the Indian course was designed to develop pharmacovigilance knowledge and skills in the Asia Pacific region, recent years have seen an increasing number of participants from African countries. This year, more than a third of trainees came from Africa. Most participants worked for national pharmacovigilance centres, with a few representatives from pharmaceutical companies, hospitals and academia.

"This course gives a platform for people from different countries to come together," said Dr G Parthasarathi, dean for Global Engagement at JSS University and course organiser. "Participants get to know each other personally and professionally, and learn from each other. That will be of great value to them. I'm sure they will treasure that international collaboration."

LECTURES WERE delivered by UMC and JSS staff, and by external speakers from India and abroad, such as Dr Madhur Gupta from the WHO Country Office in India, Mr Sten Olsson from the International Society of Pharmacovigilance (ISoP) and Dr Frank May from the University of Queensland in Australia. The programme covered a wide range of topics, from creating a reporting culture to designing pharmacoepidemiology studies, and integrating pharmacovigilance in public health programmes. Workshop sessions on causality assessment and effective communications gave participants a chance to test their skills on practical cases and brainstorm solutions to problems they might be facing in their work. The agenda also included a visit to the regional pharmacovigilance centre at JSS University Hospital, where clinical pharmacists showed course students how they monitor and report adverse drug reactions.

"This course has been very beneficial to me," said Ms Chrissy Chulu, a pharmacist from the Pharmacy Medicines and Poisons Board in Malawi. "What I learned here – especially concerning medication errors and causality assessment – will definitely increase the scope of pharmacovigilance in our country. So this is the message I'm taking back home: we are going to work on this and it will help us a lot."

Course participants discuss test cases at a workshop.

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READ MORE: www.who-umc.org/education-training/education-training/

The next UMC pharmacovigilance training course takes place in Uppsala, Sweden, on 21 May–1 June 2018.

RIYADH

Advancing signal detection in Arabic countries

In an effort to put pharmacovigilance data to greater use, members of the Arab Pharmacovigilance Network exchanged notes on signal detection practices at their second regional meeting in Riyadh.

IN RECENT YEARS, several Arabic countries have developed robust processes to capture adverse drug reaction (ADR) data. A general trend in the region is devolving the collection of reports of adverse events to a more local level. The total of VigiBase reports coming from the region now exceeds 70,000 and with their expanding national databases, countries have been thinking about ways to make use of their data. When the Arab Countries Pharmacovigilance Network met in Saudi Arabia in October 2017, the investigation of safety issues was a general theme throughout the agenda. Signal detection practices across the region differ from country to country. In Saudi Arabia, a specialised team does the signal detection, whereas in other national centres case assessors undertake the entire process, from causality to signal evaluation.

Dr Amina Tebaa from Morocco's WHO Collaborating Centre for Strengthening Pharmacovigilance Practices, who was a speaker at the meeting, pointed out that signal detection with a modest number of reports should start with qualitative methods. But producing potential signals is only the means to an end, Amina underlined. The validation process requires more investigation to verify the signal, with analysis of good-quality cases and the use of statistical methods. Eventually, a signal should be brought to a national drug safety committee (if one exists), where the signal will be discussed and, once confirmed, acted upon. Action should include communication to all healthcare professionals, and preparation of a strategy to minimise the risk identified.

IN SAUDI ARABIA, the signal detection section has been operating since 2015. Three pharmacists are tasked with finding signals related to the 7,000 drugs approved in the Kingdom. In the early days, most signals originated from literature cases, as the local database did not contain enough reports. Today, signals still originate from screening the literature, but also from the national ADR database and media screening. Of the signals generated, known ones are excluded and the remainder are then ranked with an in-house signal prioritisation tool. Further investigation follows, sometimes by external reviewers, and ultimately regulatory action, if needed. In the near future, the Saudi Food and Drug Authority (SFDA) will improve signal dissemination and collaborate with academic institutions.

Dr Adel Alharf from the Saudi Food and Drug Authority. Photo: SFDA

"We will increase the communication of signals. You will start to see more signals in our newsletters locally and globally. We are also planning to increase our collaboration with research centres and universities. They could help refute or strengthen our signals by doing cohort studies," said Mohammed Fouda, head of the Signal Detection Section at SFDA, in his presentation.

THE ARAB GOOD VIGILANCE Practice Guidelines state that, while national medicines authorities are responsible for monitoring safety issues emerging from their databases, market authorisation holders are liable for signal detection and validation for their products. Several representatives from pharmaceutical companies were present at the meeting and were eager to learn more about signal detection and subsequent investigations.

Many agreed that there is a need to increase competence in signal detection in authorities and industry alike. Though few had seen Uppsala Monitoring Centre's online course on signal detection and causality assessment, it was a well-received initiative. Spontaneous reporting databases were recognised as a useful resource for signal generation, as were epidemiological methods for further investigation of signal hypotheses. Following the main meeting, a workshop explaining fundamental concepts in pharmacoepidemiology gained considerable attention.

Meanwhile, many Arabic countries do not operate national pharmacovigilance programmes at all. At the meeting, pharmacovigilance proponents from Kuwait and Lebanon told their stories about the emerging interest to establish pharmacovigilance systems in their countries.

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KAMPALA

Uganda welcomes the world to 40th annual meeting

In November 2017 the shores of Lake Victoria drew representatives from 60 national pharmacovigilance centres to the 40th annual meeting of the WHO Programme for International Drug Monitoring.

THE AFRICAN continent was well represented at the meeting, with over half of the attendees from the WHO African Region. Uganda has one of the more mature medicines monitoring systems in East Africa, an analysis of five key components of a regulatory system has shown. Recent developments have included the launch of online adverse drug reaction (ADR) reporting, implementation of targeted spontaneous reporting – which could be applied in all public health programmes, such as tuberculosis – and improved relationships with marketing authorisation holders (MAHs). A law has been passed to mandate MAHs for generics to nominate a person responsible for pharmacovigilance, which should increase reports.

To sustain its work, Uganda's National Drug Authority (NDA) is sponsoring staff to undertake postgraduate studies. Individual presentations at the meeting furthered the attendees' knowledge of activities in Uganda, with talks on the incidence of ADRs in anti-malarial treatment; on toxicity due to kanamycin in multi-drug-resistant tuberculosis; and on anaemia in clients eligible for highly active antiretroviral therapy (HAART) initiated on tenofovir, lamivudine and efavirenz as the preferred first-line antiretroviral therapy regimen.

Other presentations looked at the knowledge base of healthcare professionals related to ADR reporting behaviour at one of the 13 regional centres in Uganda, and collaboration in the introduction of bedaquiline to treat tuberculosis. The latter was complemented by views on the new anti-tuberculosis regimen from the Democratic Republic of Congo and the Pharmacovigilance Programme of India.

OTHER SESSIONS confirmed the intensive work being undertaken around Africa. Speakers from Burkina Faso and Zambia talked about mobile phone technology for ADR reporting, with substantial growth in the number of ADRs received in the former, and new access to safety news and reporting statistics for health workers and consumers in both.

In Nigeria, consumer reporting has boosted the quantity of reports received, although their quality is low. The Sierra Leone national pharmacovigilance centre described their involvement in combating antimicrobial resistance, and Togo the monitoring of therapeutic failures in artemisinin-based combination drugs.

Across Africa, regional – or supra-national groups – are springing up. The East African Community is one, covering Burundi, Kenya, Rwanda, South Sudan, Tanzania, and Uganda, and with a steering committee for medical agencies. In 2012 it produced guidelines which might eventually lead to mutual product approval recognition. The African Medicines Regulatory Harmonization (AMRH) is advancing the creation of an African Medical Agency, with a pharmacovigilance advisory group.

REGULATORY CHALLENGES in pharmacovigilance in low- and middle-income countries (LMICs) were in focus when Raj Long, of the Bill & Melinda Gates Foundation (BMGF), addressed the audience. Most LMICs, she said, can collect data and upload reports to VigiBase, the WHO global database of individual case safety reports (ICSRs), and are clearly motivated to improve their pharmacovigilance systems. Concerns relate to the continuing limited reporting in these countries, with reporting methods not necessarily suited to their setting, and their low capacity to analyse data. Moreover, few LMIC authorities react to signals received – most replicate what is done by more established authorities. This strategy fails when new medicines with limited safety data are introduced under their jurisdiction.

The 'Project Smart Safety Surveillance', launched by WHO and BMGF, aims to help LMICs identify, assess, and manage risks associated with new medical products, and is being piloted for tuberculosis, malaria, and rotavirus programmes. This project was further discussed in open sessions organised in connection to the annual meeting, where European and African stakeholders and the pharmaceutical industry gave their views on pharmacovigilance readiness in LMICs.

"Most LMICs can collect data and upload reports to VigiBase, and are motivated to improve their pharmacovigilance systems."

UMC's Tomas Bergvall discusses VigiLyze with Kenyan pharmacovigilance centre staff.

Dr Charlie Preston, an advisor at the Pan American Health Organization (PAHO), spoke about the difficulties of medicines regulation in the small, low-resourced states of the Caribbean Community (CARICOM). The region covers a population of 70 million, where some states have no regulatory authority, and few monitor drug safety and quality. A Caribbean Regulatory System (CRS) aims to reduce the reliance on reference authorities, and also targets pharmacovigilance and post-marketing surveillance. According to Dr Preston, the value of this sub-regional approach is evident in providing a database, analytical tools to countries that do not have them, and offering staff and technical support.

Meanwhile, the national pharmacovigilance centre in Croatia gave a round-up of recent advances in patient reporting and implementation of new technologies in ADR reporting. Their mobile app, launched in 2016, was featured on national TV news, boosting patient reporting. Campaigns have progressively lifted the reporting rate, especially from patients. Future plans include a closed IT system for health professionals, offering two-way communication, integrated with familiar clinical and hospital IT systems, thus allowing more direct reporting.

Tomas Bergvall and Dr Rebecca Chandler from UMC presented progress made in method development studies, research into medicines use data, and making better use of narratives in case safety reports – while respecting patient confidentiality – to make more detail available. Dr Chandler described two signal-detection exercises: One aimed at probing reports from patients, in collaboration with Lareb in the Netherlands. The other looked at covariates of individual attributes to see how VigiBase could be used for identifying risk groups of patients with an increased propensity to a given effect.

At the end Christoph Küng, Head of Division at Swissmedic, announced that the 2018 meeting, celebrating 50 years of the WHO Programme for International Drug Monitoring, would take place in Geneva, Switzerland, where WHO is headquartered, from 5–8 November 2018.

Geoffrey Bowring
Global Communications, UMC

READ MORE:

M. Wallberg, "Web-RADR goes Sub-Sahara", Uppsala Reports 77, 2017.

Caribbean Public Health Agency
carpha.org

See you in Switzerland in November!
The WHO Programme for International Drug Monitoring will host representatives of national pharmacovigilance centres at its 41st Annual Meeting in Geneva on 5–8 November 2018, when the programme also celebrates its 50th anniversary.

The International Society of Pharmacovigilance holds its 18th annual meeting in Geneva on 11–14 November. Register online: www.isop2018geneva.org

BHUTAN'S CLIMB TO MEDICINES SAFETY

The outlook is good for pharmacovigilance to progress upwards in Bhutan, Ms Tshering Choden, one of the country's five pharmacovigilance professionals, tells Uppsala Reports in this Q&A.

WHAT ARE THE CHALLENGES TO PHARMACOVIGILANCE IN BHUTAN AND WHAT CAN BE DONE ABOUT IT?

Being a small country, one constraint in Bhutan is that we have less manpower. Right now we are approximately 50 pharmacists in the country – with time I think there will be more. If we had more professionals who knew about the safety of medicines, we could expand pharmacovigilance activities in our hospitals, so having pharmacy professionals in hospitals is essential – they know what to do and have a knowledge of pharmacovigilance and adverse drug reactions (ADRs).

We have to build capacity with good education – we need more people to be trained in pharmacovigilance, and not only pharmacists. Previously we only focused on training pharmacy professionals, but if we want to have a good system in place in Bhutan, we should train all healthcare professionals, starting with nurses and doctors. We're now in the process of training all health workers – nurses, doctors, pharmacists, pharmacy technicians and health assistants – in all hospitals and primary healthcare units in Bhutan, on the importance of reporting ADRs, how to fill in the forms, and where to send the reports.

If we had more manpower I think we could make everyone report adverse effects. We could reach each household and learn about their knowledge of pharmacovigilance, and also talk to our healthcare professionals to check their knowledge of medicines safety. If we were all committed it would be really easy for us to report ADRs and we could strengthen pharmacovigilance activities in hospitals.

HOW ARE YOU WORKING TO IMPROVE PHARMACOVIGILANCE AT YOUR HOSPITAL?

One of the challenges we face at the Eastern Regional Referral Hospital is that most people have been unaware of pharmacovigilance. They don't think it's necessary to report ADRs because it's already written in the package leaflets – they think it's in the nature of the drug to cause the reaction, hence they don't report the ADRs.

Under-reporting is one of the biggest problems in under-developed countries. To encourage my colleagues to report, we made it mandatory in my centre to report ADRs, and they have to submit a minimum of three reports. We have free access to all the reporting forms in the hospital. I have distributed reporting forms to all the wards and explained to the staff how to report, what to write, and how they can submit to the reporting centres. I also developed a simple ADR notification form for my hospital, which led to increased reporting, and most of the staff in my hospital are aware of ADRs now.

WHY DO YOU THINK IT'S IMPORTANT TO SPREAD AWARENESS OF MEDICINES SAFETY?

Awareness of pharmacovigilance is very important because safety comes first in treatment. Without knowing the safety of the drug, we cannot treat the patient. Patients should know what pharmacovigilance means, what the effects of medicines are, and that there won't be any pharmacological effect without any side effects. And for healthcare professionals it's essential to know about pharmacovigilance when treating patients.

WHAT'S NEXT FOR MEDICINES SAFETY IN BHUTAN?

Bhutan has a very young pharmacovigilance system, so we are moving at our own pace to develop and to get our own place established for pharmacovigilance in the Ministry of Health. Everything needs time to fall into place. We are not in a hurry, we are not being so ambitious, but we are working on it and hope to strengthen the pharmacovigilance system in Bhutan.

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Pharmacovigilance in Bhutan

Bhutan, wedged between its giant neighbours China and India in the eastern Himalayas, became the 119th member of the WHO Programme for International Drug Monitoring in 2014. Here, 50 pharmacists see to the needs of the country's population of nearly 800,000, and the nation's medicines safety activities are primarily carried out by a total of five pharmacovigilantes at the national pharmacovigilance centre in the capital Thimphu and at three regional centres. Despite limited manpower, the country is making strides to educate more healthcare professionals on how to report adverse drug reactions.

Who is Tshering Choden?

Tshering Choden is a hospital pharmacist at one of Bhutan's three regional pharmacovigilance centres, the Eastern Regional Referral Hospital in Monggar. She is the pharmacovigilance contact person and has been a driving force behind increasing the amount of adverse drug reaction reports submitted at the hospital.

SEOUL

FIP pulls in the crowds and calls for change

Robotic dispensing is just one among many challenges reshaping the pharmacy profession as it negotiates the transition from a supply function to a priority of patient care. This year's FIP meeting explored the soul of pharmacy and how pharmacists should envisage and build their future.

MORE THAN 2,500 PEOPLE from 90 countries poured into Seoul in September 2017 for the 77th annual meeting of the International Pharmaceutical Federation (FIP, Fédération Internationale Pharmaceutique). With its theme of 'The soul of pharmacy', it had a strong philosophical thread, but there was also the usual packed programme of vivid reports of innovative practice and research from around the world.

'Soul' as a concept in ideal professional life was defined as "emotional or intellectual energy or intensity… depth, value, relatedness, heart and personal substance." The profession's commitment to the priority of the best interests of patients, proclaimed in the FIP Centennial Declaration of 2012, has long been established. Taking this a step further, a speaker from South Korea argued for the promotion of local pharmacies as "places of first resort for health advice and support, and for humane, engaged pharmacists."

EXPANDING AGENDA

A powerful example of radical practice was provided in a presentation about Pier Health Resource Centres in downtown east-side Vancouver, Canada. This group focuses on deeply disadvantaged areas of the state and, according to their account, has shown "massive growth in patient visits and prescription processing through empathetic, socially-engaged pharmacy services."

Other speakers outlined some of the pressing issues patients face where the profession has a great opportunity to improve health and quality of life: patient safety, adherence, women's issues, health literacy, back pain, polypharmacy, maternal health and mortality, elderly care, among many.

CHANGING DEMOGRAPHICS

Huge increases in the numbers of elderly people pose a threat to the sustainability of existing health and social care systems. In Korea in 2000, 7% of the population were over 65 years; it is predicted that in 2060, the figure will be 40%; by 2030 the average life expectancy of Korean women will be over 90 years.

With elderly people in Korea and everywhere being less and less cared for by their families, there is an ever-greater need for engaged and co-ordinated services in the community, with pharmacists playing a major part, to achieve the goals of personal functionality and independence, plus quality of life and prevention of harm.

PHARMACY AND THE REFUGEE CRISIS

Moving accounts of the work of small teams of pharmacists with refugees in Lebanon and Jordan were presented. With over half of the refugee population being under 18, and a quarter being women of child-bearing age, the health risks and needs were overwhelming, greatly intensified by the prevalence of disabling post-traumatic stress disorder in around a third of men and women.

In Sweden, refugee pharmacists have been welcomed into a dynamic integrative scheme of training and pairing with native professionals, giving hope to new arrivals and helping to address the national shortage of pharmacists.

A RICH AGENDA AND STERN PARAMETERS

Speakers presented information about new apps, film and video projects, adventurous graphics, and many other vital innovations. The chief at Google Health reminded everyone that attention spans were shrinking and that time available to grab attention on a digital device was now maybe as low as four seconds; three seconds the limit waiting for a website to load. Of 160,000 health apps available today, 36 account for around half of downloads, many of them quickly abandoned. There is current research to expand digital health to the four billion people not currently connected to the internet.

Healthcare, this man from the frontiers pointed out, does not compare well in terms of innovation and excitement with driving or online shopping; doctors and pharmacists are inevitably subject to unflattering comparisons.

Visionary pharmacists with soul clearly have an immense contribution to make in addressing multiple problems in all regions and countries of the world. The old paradigm of passive retailing and dispensing has to be transformed into dynamic, innovative, empathetic engagement with patients and communities, through mould-breaking technology and courageous personal effort. In Seoul, FIP was showcasing the vision and the methods to achieve that transformation.

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READ MORE:

FIP www.fip.org

Pier Health Resource Centres
www.pierhealth.ca

FIP Centennial Declaration 2012
Pharmacists and pharmaceutical scientists accept responsibility and accountability for improving global health and patient health outcomes by closing gaps in the development, distribution, and responsible use of medicines. Society can contribute to these objectives by supporting the advancement of pharmacy practice and the pharmaceutical sciences.

VIENTIANE & PHNOM PENH

Two days of medicines safety in Laos and Cambodia

Aiming to bolster pharmacovigilance competencies in the Asian region, Singaporean CoRE invited UMC to take part in workshops on medicines safety in Laos and Cambodia in August 2017.

THE WORKSHOPS were organised by the Centre of Regulatory Excellence (CoRE) at the Duke-NUS Medical School in Singapore. Part of CoRE's mission is to establish regional platforms and networks that will help boost skills and enhance collaboration in the ASEAN and Asia-Pacific region. To that end, the group organised two-day pharmaco-vigilance training workshops in Laos and Cambodia.

The three main topics at the training sessions were protecting public health through pharmacovigilance; engaging stakeholders to improve adverse drug reaction (ADR) reporting; and risk management planning. The workshops began with an introductory presentation on the topic, followed by an interactive session where participants discussed the challenges they face and brainstormed solutions suited to their own settings.

The introductory presentation was given by Adena Lim, the deputy director of the Vigilance and Compliance Branch within the Health Sciences Authority (HSA) in Singapore. She emphasised the crucial role that pharmacovigilance plays in protecting public health, and gave an overview of the work that transformed Singapore's ADR unit from the small operation it was when it started in 1993, to the multi-functional division it is today.

UMC's pharmacovigilance officer Deliana Aboka next talked about best practices for engaging stakeholders in improving ADR reporting. She underlined the importance of reporting and its societal impact, and also the benefits of optimising the workflow of ADR-report collection.

The second day had a presentation by Dr Jean-Christophe Delumeau, Board and Executive Committee member of the International Society of Pharmacovigilance (ISoP) and regional head of Pharmacovigilance Policy with Bayer. Dr Delumeau showcased a prototype mobile application designed as a risk-minimisation tool, offering information to the public on appropriate drug use, among other things.

THE OVERALL AIM of the workshops was to strengthen the capacity of the national pharmacovigilance centres, promote policy innovation, and enable positive changes through raising awareness about the importance of drug safety and ADR reporting among healthcare professionals.

At the event held in Laos's capital Vientiane, about 20 participants from the national pharmacovigilance centre and various public health programmes attended. The country has a population of almost 7 million and became a full member of the WHO Programme for International Drug Monitoring in 2015.

In Phnom Penh, Cambodia's capital, the workshop was ceremonially opened by Dr Or Vandine, the director general for health of the Cambodian Ministry of Health. She addressed the 80 participants with emphasis on the important role they play in protecting the population's health and she encouraged all to contribute to pharmacovigilance in their own settings. Many of the attendees were medical doctors practising outside the capital. Cambodia, with a population of over 15.5 million, joined the WHO programme in 2012.

The future of both countries lies in strengthening their pharmacovigilance structures and increasing their competence and capacity for analysing their own national data.

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Highlights from Uppsala Health Summit 2017. Photos: Uppsala Health Summit

UPPSALA HEALTH SUMMIT 2018: CARE FOR CANCER

At Uppsala Health Summit in Uppsala, Sweden on 14–15 June, international experts will gather to discuss how to provide better care for an increasing number of cancer patients and cancer survivors globally.

THANKS TO ADVANCES in treatment options, the chances of surviving cancer are better than ever before. However, cancer incidence is increasing and new forms of therapy are expensive. As a result, resource management and priority setting face major challenges. How can we ensure equitable access to diagnosis and treatment?

Each year, more than 8 million people worldwide die from cancer, and over 17 million people receive a cancer diagnosis. The number of new cases is projected to rise dramatically in the coming decades, especially in low- and middle-income countries, as a result of lifestyle factors such as smoking and poor diets, as well as chronic infectious disease. Already today, 70% of all cancer deaths occur in low-income countries where cancers are typically detected late and treatment options are few.

In May 2017, the World Health Assembly adopted a resolution on cancer requesting member states to develop national cancer plans, including prevention, and access to screening, diagnosis, treatment, and care.

Uppsala Health Summit will bring together a broad spectrum of expertise in the cancer community from across the globe, including scientists, private sector representatives, healthcare professionals, NGOs, and policy-makers. The meeting aims to put in motion a constructive dialogue and develop proposals on how to implement opportunities from science and innovation for more equal therapeutic access and better patient outcomes globally.

"Prevention by promoting a healthy personal lifestyle and reducing harmful external exposure is of course extremely important, but can only solve part of the problem," said Prof Lars Holmberg, Chairman of the Uppsala Health Summit Programme Committee.

"We also need to face the tough questions that arise with the fast-growing need for treatment and care. It's time to agree on guidelines and priorities that reflect the recent scientific advances, for example the opportunities around data, and work out ways we can make them benefit the individual patient," he said.

THE WORKSHOPS WILL address a broad set of critical topics, including biomarker development, precision medicine, drug repositioning, and how to prepare healthcare systems for more cancer survivors. The latter is the subject for the workshop prepared by a group led by Uppsala Monitoring Centre's Dr Birgitta Grundmark, oncologist and a member of UMC's research team.

"Worldwide, the number of cancer survivors is growing as access to efficient diagnostics and treatments improve. While this is a very positive trend, we also know that adverse effects both from the treatments and from the disease itself may appear later in life," Dr Grundmark said. "We need to prepare and improve national health systems' handling of this. Experiences from childhood cancer survivors will form the starting point for the discussions in this workshop."

How we improve care and treatment for children living with cancer today is one of the cross-cutting issues that will be an integral part of each workshop, along with patient involvement, equal care and global perspectives.

As always at Uppsala Health Summit, a plenary programme will guide and inspire the workshop dialogues. Confirmed speakers in plenary sessions include Dr Mariângela Simão, WHO assistant director-general for Drug Access, Vaccines and Pharmaceuticals; Prof Max Parkin of the Nuffield Department of Population Health, University of Oxford and the African Cancer Registry Network; and Prof Arnie Purushotham of the Tata Memorial Centre, Mumbai.

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UMC at Uppsala Health Summit 2017

Uppsala Monitoring Centre partnered with UHS for last year's summit on the topic of "Tackling Infectious Disease Threats – Prevent, detect, respond with a One Health approach". There, UMC's Dr Rebecca Chandler hosted a workshop titled "New Medicines and Vaccines: Monitor Safety in Emergency Situations?".

UMC's new podcast!

In the first episode of UMC's podcast, Dr Chandler draws on the UHS workshop to discuss pharmacovigilance in public health emergencies, issues of real-time safety surveillance, and public trust.

LISTEN: www.soundcloud.com/uppsalamonitoringcentre

NAVIGATING THE PLANT-NAMES JUNGLE

Inconsistent use of names for medicinal plants and plant-based drugs can have serious health consequences and impede efforts to analyse adverse reactions to herbal medicines. Kew Gardens' Medicinal Plant Names Services enables scientific rigour in the regulation, coding, and use of herbals.

MORE THAN 100 people in Belgium were prescribed slimming pills containing fang ji, a traditional Chinese medicine (TCM), in 1998. Severe nephropathy ensued, with most patients requiring dialysis. The clinic had dispensed the wrong product, unaware that 'fang ji' refers to TCM drugs derived from two different plants: *Stephania tetrandra* and *Aristolochia fangchi*. Subsequent reports demonstrated the same substitution had occurred in other countries. Ambiguity of herbal drug names is surprisingly widespread, the name 'ginseng' being associated with drugs derived from at least 18 plants with differing chemistries. Failing to deal with this ambiguity in labelling, regulation, and quality control clearly has serious health consequences.

Growing international use and trade in herbal products increases the urgency for professionals to address this issue. Pharmacovigilance professionals need accurate names for plant-based products to undertake effective signal analysis. Similarly, clinical trials must know which plant-derived drugs are taken by participants. Those writing monographs or framing regulations must be precise as to which plant is intended, and be aware of all its possible synonyms if they are to locate all relevant publications and adverse reaction records. Unambiguous labelling of plant materials and health records is the first step towards safer use and more effective authentication and quality control.

DIVERSITY OF MEDICINAL PLANTS

An astonishing number of medicinal plants are used worldwide, and international trade in herbal drugs and plant-based food supplements is growing. WHO estimated that the trade in TCM products alone was worth US$83 billion in 2012, and report that 90% of Germans use herbals. Although most formal healthcare systems continue to neglect them, a few countries are now integrating 'traditional' plant-based drugs into mainstream medicine, particularly to treat chronic conditions. Millions of people, especially in rural communities in parts of Africa, Asia and South America, nevertheless rely on traditional remedies for their primary healthcare needs.

Knowing exactly how many medicinal plants are used is complicated, as most plants are known by multiple

"Only 16% of medicinal species are under regulatory control, despite the popularity of herbal remedies."

names, causing double counting. In their 2017 State of the World's Plants report, Kew Gardens, a botanical research institute managing global taxonomic references, provided a reliable lower limit of 28,187 medicinal species cited in approximately 150 major pharmacopoeias and medicinal references.

This study also showed that only 16% of medicinal species are under regulatory control, despite the popularity of herbal remedies. Indeed, the number of species described within pharmacopoeias fell during the 20th century, with the Brazilian Pharmacopoeia, for example, citing 196 plants in 1926 but only 11 in 1996. Similar trends occur in European pharmacopoeias, despite recent inclusion of TCM plants. Why should this be? Several reasons exist. Some herbals simply fell out of favour as more targeted drugs became available. Gathering the scientific evidence required of modern monographs can also be a challenge when working with herbals, which are more complex than pharmaceutical drugs and consist of multiple chemicals with multiple potential targets. Nevertheless, such drugs often remain in widespread use despite their removal from pharmacopoeias.

Decocting pieces from *A. cimicifuga*. Photo: © Yulin Lin

Stephania tetrandra. A diuretic. Full scientific name: *S. tetrandra* S.Moore.

Aristolochia fangchi. Used to treat a number of conditions, but causing nephropathy when used at the concentration required of *S. tetrandra*. Full scientific name: *A. fangchi* Y.C.Wu ex L.D.Chow & S.M.Hwang.

Left: Fortaleza medicinal plant market in Brazil. Right: Kew Economic Botany Collection; TCM market in China. Photos: Andrew McRobb/ © Board of Trustees Royal Botanic Gardens Kew

THE PLANT-NAMES JUNGLE

Plants and the drugs derived from them are referred to using common, pharmaceutical or scientific names. Common names like 'ginseng' are part of everyday speech; they vary from place to place and their meanings may change over time. A plant called 'yarrow' in some places is referred to as 'millefeuille' or 'woundwort' elsewhere (synonyms). A name like 'bluebell' may refer to one species in England and another in Scotland (homonyms). The multiplicity of names and their inconsistent use across countries and disciplines cause considerable confusion.

Pharmacopoeias offer detailed technical descriptions of how to prepare herbal drugs and should be precise about which plant to use. Sadly, this is not always the case. Some pharmacopoeias use common names, and many others employ pharmaceutical names – often confusingly written in Latin – indicating the plant part or the preparation to be used (e.g. ginseng radix rubra). Pharmaceutical names are under no formal control and often refer to drugs derived from different plants in different pharmacopoeias, or even different editions of one pharmacopoeia.

Scientific plant names, in contrast, are formally controlled: their publication follows procedures established in the International Code of Nomenclature requiring, for example, that authors of new names cite the herbarium specimen(s) studied. These provide permanent physical evidence of the anatomy, chemistry, and DNA of plants carrying that name. Individual scientific names, written in full, are thus unambiguous and provide the only reliable way to refer to plants.

Obstacles exist, however, to using scientific names effectively. Non-botanists may be unaware of these issues, particularly the frequency with which plant nomenclature changes as understanding of taxonomic relationships improves. The misuse of scientific names by regulators, pharmacists, and pharmacovigilance staff can have serious consequences: ineffective regulation, misidentification, ambiguous publication, and even contradictory controls when regulators fail to appreciate that two names are synonyms for the same species.

THE SOLUTION

Kew's Medicinal Plant Names Services (MPNS) addressed this confusion by capturing all pharmaceutical, common and scientific names employed for herbal drugs in 150 major medical references, regulatory data sets and pharmacopoeias. Each name was mapped to Kew's botanical references to extract the current scientific name and all synonyms for each plant. MPNS can thus reliably count species and make links between pharmacopoeias that use different names for the same plant. The current version of MPNS, published in May 2017, contains 384,000 unique names for only 26,000 plants.

MPNS is updated regularly to reflect continuing improvement in Kew's taxonomies, and a portal enables users to search with any name familiar to them, be alerted to any ambiguity, discover which pharmacopoeias or references cite each plant, and check which plant parts and names are cited. Onward links provide additional information about the plants, such as chemistry, authentication details or illustrations, and permit comprehensive PubMed searches. Searching PubMed directly with a single scientific name will, on average, retrieve 10-15% of records about that plant. Searching PubMed via the MPNS portal, on the other hand, uses all scientific synonyms simultaneously and retrieves all records about that species, irrespective of which scientific names were used in the original publications, which is especially useful for research applications and for tracking adverse reactions.

BENEFITS FOR PHARMACOVIGILANCE

Since MPNS can link terminologies from different regulators, it is used by a new ISO standard: the Identification of Medicinal Products (IDMP), devised to harmonise specifications for all medicinal products. MPNS provides a controlled vocabulary for plant names and plant parts, and a web service updates the vocabulary periodically as plant names change. MPNS has worked with other health agencies to validate and enrich their plant data, and it offers training in designing workflows and IT systems reflecting best practice. MPNS continues to add medicinal sources from other countries and seeks partners to expand its coverage of food supplements, cosmetics and plants causing poisoning or allergic reactions.

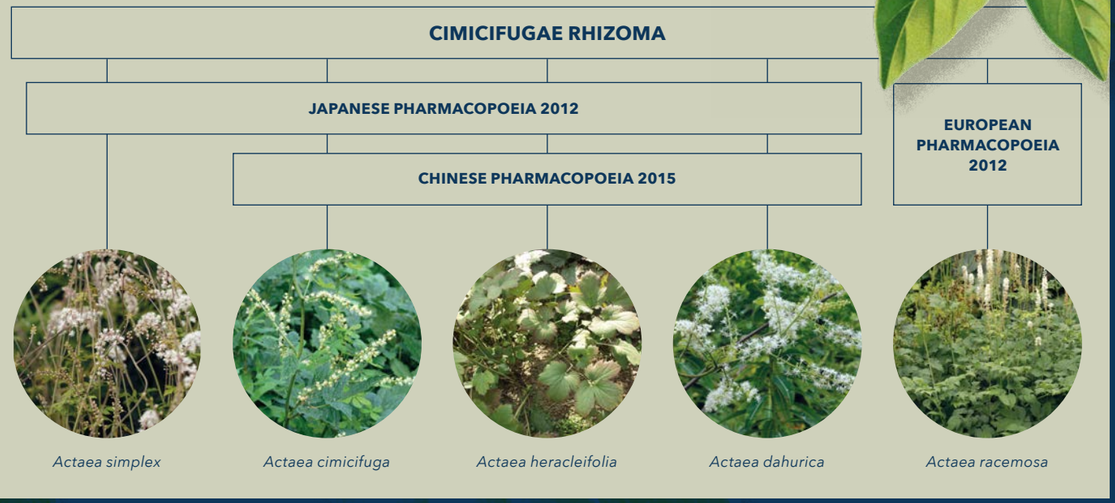
An old collaboration between Kew and Uppsala Monitoring Centre was reinvigorated by MPNS. For each of the approximately 4,000 different scientific plant names in the WHODrug dictionary, MPNS provided spelling corrections, the family name and the currently preferred scientific name and synonyms. This highlighted plants stored within VigiBase, the WHO global database of individual case safety reports, under multiple names, and enabled these to be linked to each other. The automatic validation saved effort, whilst increasing integrity and currency of plant data in VigiBase. Now UMC and MPNS wish to enrich VigiBase with full synonymy (so that users can find all relevant drug or adverse reaction records for signal analysis), enhance links to Kew's data, and allow plant names in VigiBase to be periodically refreshed.

Overall, MPNS is facilitating effective international

Dried whole rhizomes of *A. simplex*. Photo: © Yulin Lin

Ambiguity in pharmaceutical names

Confusion about plant names arises even in pharmacopoeias intended to ensure the quality and safety of herbal drugs. A single pharmaceutical name can refer to different species in different pharmacopoeias.



Pitfalls in using scientific names

Synonyms

1.6 million scientific plant names exist for 400,000 higher plants – 4 names per plant. Intensely studied medicinal plants have 14 synonyms on average (*Achillea millefolium L.*, or 'yarrow', has 70!) preventing you from finding all publications for any plant.

Changing names

10,000 changes to scientific plant names are published every year. Molecular and chemical studies offer new insights into plant relationships, requiring species to move between genera, be split, or merged.

Homonyms

4% of scientific names employ the same genus and species names, but were published by two authors independently to refer to two different plants. E.g. *Illicium anisatum Lour.* is star anise – a widely used condiment – while *Illicium anisatum L.* is a poisonous Japanese relative. Regulations citing *Illicium anisatum* with no author name are thus ambiguous.

Contradictory and incomplete references

Botanical databases offer alternative taxonomic opinions based upon different evidence, scope and purpose. Websites often copy data from others, but fail to update when the original is corrected. Rarely do these sources contain pharmaceutical or common names.

Best practice guidelines

1. Do not use common or pharmaceutical names alone.
2. Always use the full scientific name: genus, species, subspecies and author.
3. Use the currently preferred scientific name and be aware of all its synonyms.
4. When in doubt, consult the following resources in this order:
   i. Medicinal Plant Names Services
   ii. Plants of the World Online
   iii. The Plant List

communication about herbal drugs. Reducing effort and duplication amongst health agencies, through use of the tools and data described, can prevent repetition of tragic cases like the 1998 fang ji mix-up in Belgium. However, management of adverse reactions for traditional plant medicines not covered by pharmacopoeias remains imperfect. Ideally, reports would ensure authenticity of plant materials and cite the scientific name, plant part, and dosage employed. Traditional remedies are the primary source of healthcare for millions of people who deserve that we give as much attention to these remedies, as to herbal products optionally used in the West.

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READ MORE:

R. Allkin et al., "State of the World's Plants 2017, Chapter 4: Useful plants – medicines", Royal Botanic Gardens, Kew, 2017.

E. A. Dauncey et al., "Common mistakes when using plant names and how to avoid them", European Journal of Integrative Medicine, 2016.

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MUSCAT

Oman takes steps towards safer herbal medicines

In September 2017, a workshop on the regulation of herbal medicines was held in Oman. The event aimed to enhance herbovigilance measures in the country, to ensure safe, effective and good-quality herbal products on the Omani market.

Nawal Al Alawi speaking at the workshop. Photo: Khamis Al Saidi.

THE WORKSHOP, organised by the Directorate General of Pharmaceutical Affairs and Drug Control at Oman's Ministry of Health in collaboration with the World Health Organization, attracted around 50 participants from various health institutions, including public and private herbal medicine clinics. Current regulation of herbal medicines, medicinal plants and herbal products – including counterfeit ones – was reviewed.

Prof Souad Skalli, WHO consultant in pharmacovigilance of herbal medicines and research scientist at the Moroccan Poison Control and Pharmacovigilance Centre in Rabat, discussed international herbovigilance regulation. She also touched upon the Moroccan experience, where a herbovigilance system is already in place, including a national database of adverse events, and policies to regulate both raw herbs and finished herbal products.

Like other regulatory authorities around the world, the Omani Ministry of Health has become concerned with the use of herbal remedies and recognised the need for herbovigilance, especially since chemical substances are sometimes added to herbal medicines. In 2008, a new law mandated the registration of all products of herbal origin and their manufacturing companies, so that any herbal drug entering the country could be monitored and product safety standards ensured. In 2015, a separate herbal medicines section was established within the pharmacovigilance department at the Ministry of Health. To date, the section has registered 14 herbal medicine manufacturers and 60 herbal products.

"The Omani Ministry of Health has become concerned with the use of herbal remedies and recognised the need for herbovigilance."

The discussions at the workshop unearthed the many challenges still faced by Oman in the regulation of traditional medicines. The greatest challenge is to get healthcare professionals to report adverse events related to herbal products. Currently, herbal preparations are only available in private health facilities in Oman, whereas most reports of adverse events come from government-funded facilities where herbal medicines are not in use.

Collaborative efforts between academic institutions, research centres, and the media will play a vital role in creating awareness among healthcare professionals and the public. A reporting culture will need to be created, and should involve all those concerned – medical professionals, herbal practitioners and patients – so that a national dataset of safety reports can be built and better herbovigilance achieved.

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BETTER SIGNAL DETECTION WITH VIGIRANK

By factoring in the content and quality – not just the quantity – of adverse drug reaction reports, UMC's vigiRank algorithm reliably flags potential signals for further investigation.

SIGNAL DETECTION is at the core of Uppsala Monitoring Centre's mission, and scientific development in this area remains one of the organisation's hallmarks. The most recent UMC contribution to statistical signal detection in pharmacovigilance is vigiRank. Developed in 2014, vigiRank is a statistical method whose primary function is to help prioritise drug–adverse reaction pairs (or drug–drug–adverse reaction triplets) before manual clinical assessment. At UMC, such automatic first-pass screening of data in VigiBase, the WHO global database of individual case safety reports, was previously driven by disproportionality analysis – specifically, by one of its four common measures, the Information Component (IC). A large number of organisations worldwide employ disproportionality analysis for this purpose.

The major limitation, however, is that disproportionality relies solely on reporting frequencies: it counts reports for a given drug–adverse reaction pair, and compares that to an expected number. In contrast, vigiRank considers also the content of individual reports, and so better resembles the clinical assessment it is intended to support. For each drug–adverse reaction pair, vigiRank assesses five strength-of-evidence components: completeness, recency, disproportionality, availability of case narratives, and geographical spread. Moreover, while disproportionality analysis works as a hard filter – returning an unranked selection of drug–adverse reaction pairs to assess clinically – vigiRank provides a priority listing that can be followed from the top down, as far as resources permit.

When vigiRank was developed, its performance was first evaluated on a set of past safety signals. The results were encouraging; compared to the IC, vigiRank was better at predicting retrospectively which drug–adverse reaction pairs were to become signals. When put to practical use, the method was judged positively by UMC's signal assessors, too. Since then, vigiRank has replaced the IC in routine signal detection operations at UMC, but its impact on signal detection outcomes was only recently investigated.

IN A STUDY published in Pharmacoepidemiology and Drug Safety in August 2017, the UMC research team compared the first batch of drug–adverse reaction pairs prioritised by vigiRank in 2014, to an earlier dataset from the era of disproportionality analysis, selected with the same criteria. Of all the drug–adverse reaction pairs that were assessed, about 3% of those flagged by vigiRank turned out to be signals, compared to a mere 1% of those selected with the IC alone. In other words, vigiRank is more efficient than disproportionality alone at flagging potential signals in VigiBase.

As a natural but improved successor of disproportionality, vigiRank remains the fundament of automatic prioritisation in UMC's routine signal detection operations before clinical assessment. Reports or drug–adverse reaction pairs can be arbitrarily filtered to focus on specific subsets, and this is what UMC regularly does in its so-called 'signal detection sprints'. Previous sprints have focused, for example, on paediatric drugs, vaccines, patient reports, and regions of interest (Africa, Asia, Latin America).

So far, vigiRank has not been routinely available outside UMC. However, the algorithm is described in detail in a freely accessible scientific publication. The current implementation is tailored to VigiBase, and use in another database may require adaptations. UMC continuously strives to improve its services to the pharmacovigilance community, particularly for members of the WHO Programme for International Drug Monitoring. Concrete plans to increase support to local signal detection efforts within VigiLyze – UMC's search and analysis tool for VigiBase – are now taking shape, and there may be a role there for vigiRank. UMC hopes member countries will join in this exciting development.

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READ MORE:

O. Caster et al., "vigiRank for statistical signal detection in pharmacovigilance: First results from prospective real-world use", Pharmacoepidemiology and Drug Safety, 2017.

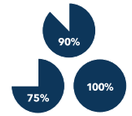
O. Caster et al., "Improved statistical signal detection in pharmacovigilance by combining multiple strength-of-evidence aspects in vigiRank", Drug Safety, 2014.

How does vigiRank work?

For each drug–adverse reaction pair, vigiRank computes a score based on these five components (in order of importance). The higher the score, the more likely the pair is to constitute a safety signal.

1. Completeness

How many informative reports are there for the drug-adverse reaction pair? This is calculated with UMC's vigiGrade method.



2. Recency

How many reports for this drug–adverse reaction pair were submitted in the last three years?

3. Disproportionality

Has the drug–adverse reaction pair been reported more often than expected? This is calculated with the Information Component (IC) measure of disproportionality.

4. Case narratives

How many reports contain free-text case narratives?

5. Geographical spread

How many countries have reported this drug-adverse reaction pair?

Brazilian hospital's early action system prevents medication errors

At the Hospital Estadual Sumaré, extra safety measures have been established to avoid medication errors, and an ME-prevention method based on the principles of signal detection is being investigated.

THE HOSPITAL ESTADUAL SUMARÉ (HES) is one of the hospitals of the University of Campinas (Unicamp), a public university in the state of São Paulo, Brazil. The hospital was opened in September 2000, and it is an important centre for education and in-service training for students from the School of Medical Sciences.

HES was the first public hospital in Brazil to be certified with a higher grade in the Brazilian accreditation system for healthcare units, and the first hospital outside of the state capitals to be certified by the healthcare standards organisation Accreditation Canada, again at a higher level. Quality management is an important part of the hospital's institutional culture. Following a recommendation by the regulatory authority of São Paulo, a pharmacovigilance commission was established in 2003 at the hospital, formed by a physician, a nurse, and a pharmacist. From the beginning, medication errors (MEs) were recognised as a specific issue that must be assessed separately from notifications related to suspected adverse drug reactions. Thus, several policies have been developed over the years, in order to reduce MEs at the hospital.

For each phase of the medicine-handling process – starting with purchase of products, through storage, prescription, drug dispensing from pharmacists, and finally drug administration – there are certain actions and safety measures that must be taken. For example, the qualification of suppliers is checked at the purchasing phase; 'high alert' drugs such as adrenaline and anesthetics are marked with a red label in the storage phase, and medicines are also sorted in a colour scheme by expiration date; the prescription phase calls for the use of standard prescriptions made according to medical protocols; and so on.

One action in particular should be highlighted: the prescription system for antimicrobial prophylaxis in surgery. There is a prescription protocol, but the physicians' rate of compliance with it was low – less than 50% – until 2011. The problem was that they were asked to prescribe using the drug name, but as doctors usually work in two

"HES staff are studying whether the methodology used to conduct signal detection in pharmacovigilance could be used for 'signal detection' to prevent medication errors in hospitals."

or more hospitals and each institution has its own protocol, inconsistencies occurred. At HES, a system was created where the physicians should prescribe the name of the medical procedure instead, for example cholecystectomy, which resulted in 100% compliance with the protocol.

TWO YEARS AGO, staff at HES discussed the introduction of a method to identify a risk and take early action to prevent MEs. This question is relevant because the assessment of the database is usually done by analysing the most frequent events. Focusing on this point, a pilot study was conducted, which became a research project.

In this project – which is still ongoing – HES staff are studying whether the methodology used to conduct signal detection in pharmacovigilance – namely the proportional reporting ratio methodology – could be used for 'signal detection' to prevent MEs in hospitals. To apply this methodology, all adverse events of one sector, e.g. the internal medicine ward, are compared with all adverse events of the other sectors. The pilot study was undertaken in 2015 on data collected between 2013–2014 and it was possible to identify a 'signal' for MEs. Now this methodology is promoted at HES using a database with more than 5,400 adverse events, excluding suspected adverse drug reactions, reported since January 2008. If the validity of this process can be proved, HES will start a prospective study.

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Surgical room at HES. Photo: Caius Lucillus

Colour coded medicines in the hospital pharmacy. Photo: Maurício Perroud

BOGOTÁ

AMERICAN PHARMACOVIGILANTES MEET IN COLOMBIA

For the last 14 years, pharmacovigilance specialists across the Americas have been gathering annually to share the latest in drug safety. Here is how the 2017 event unfolded.

THE 14TH INTERNATIONAL Pharmacovigilance Meeting of the Americas was held in August 2017 in Bogotá, Colombia. It was attended by around 320 people from academia, hospitals and pharmaceutical companies, from 14 Latin American countries and Canada. Among the participants were 45 members of the Red de Puntos Focales de Farmacovigilancia, a network of national pharmacovigilance centres in the Americas, and the meeting offered a chance to evaluate their annual activities. The agenda included round-table discussions to examine some of the challenges that the region, and the world at large, are facing in pharmacovigilance: management of adverse drug reactions related to off-label use of medicines, biotherapeutics, active pharmacovigilance, and the role of patients.

For the first time, the meeting was opened by Dr Shanthi Pal, medicines safety group lead at WHO. Dr Pal discussed issues relevant to the local audience, such as how drug regulatory authorities with limited pharmacovigilance capacity can deal with the launch of medical products. She proposed a strategy for pharmacovigilance in low- and middle-income countries, which should include the establishment of strong monitoring networks with a risk-based assessment perspective.

THE FIRST OF THESE meetings took place in Colombia in 2003. Sten Olsson, then WHO Programme expert at Uppsala Monitoring Centre, took part, together with Dr Albert Figueras, director of the Catalan Institute of Pharmacology in Spain; Dr Martín Cañás, professor in pharmacoepidemiology at Universidad Nacional de la Plata in Argentina; PAHO expert José Luis Castro; and Dr Mariano Madurga, former pharmacovigilance team leader at the Spanish Agency for Medicines and Medical Devices.

For the following eight years, under the leadership of Colombia's drug regulatory authority INVIMA (Instituto Nacional de Vigilancia de Medicamentos y Alimentos), Universidad Nacional de Colombia, the National College of Pharmacists of Colombia, and PAHO, the international meeting became the regional reference for rational use of drugs, pharmacotherapy news, and pharmacovigilance issues. Thanks to a PAHO initiative, the event then became the International Pharmacovigilance Meeting of the Americas, and it was decided it should be held in Colombia one year and in another American country every other year. Brazil, Peru and Panama took turns hosting the event between 2011 and 2017, and the next meeting will be held in Chile in 2018.

14 YEARS SINCE its inception, INVIMA director Javier Guzman emphasized "the value of the meeting as a regional public good." Mr Guzman expressed his pride in welcoming high-level speakers to Colombia, such as former ISoP secretary-general Ullrich Hagemann, UMC research pharmacist Elki Sollenbring, and Dr Madurga and Dr Figueras, among others. Claudia Vaca, professor at Universidad Nacional de Colombia – host of the event – and member of the Advisory Committee on Safety of Medicinal Products (ACSoMP), offered the audience a few words of advice. "Rescue essential medicines: they are known, simple and cheaper," she said. "Try to manage the financial burden of new drugs by closing the gap between high prices and limited public resources. Avoid fear-based vigilance of medicines and promote risk evidence-based monitoring."

Finally, as with every Colombian edition of the meeting, the 2017 one also included a valuable show of posters of local and regional pharmacovigilance initiatives. This activity was organised with the support of the recently created Colombian Pharmacovigilance Association, which contributed to the organisation of the meeting. Of the 27 posters presented, 14 were classified in the academic category and 13 in the experiences category. A team of four independent judges awarded prizes for the two best pharmacovigilance experiences to Silvia Salas Rojas, pharmacist at Tijuana Hospital Instituto Mexicano del Seguro Social in Mexico, for the work entitled 'Evolution of the General Hospital Tijuana's pharmaco-vigilance program'; and to Adriana Navarrerte, pharmacist at Clínica Medical S.A.S in Colombia, for the work entitled 'Detection and analysis of adverse drug reactions associated to parenteral anti-infective drugs in hospitalized patients'. The Colombian Pfizer Foundation raised funds to finance Adriana Navarrete's participation in UMC's annual pharmacovigilance training course in Uppsala.

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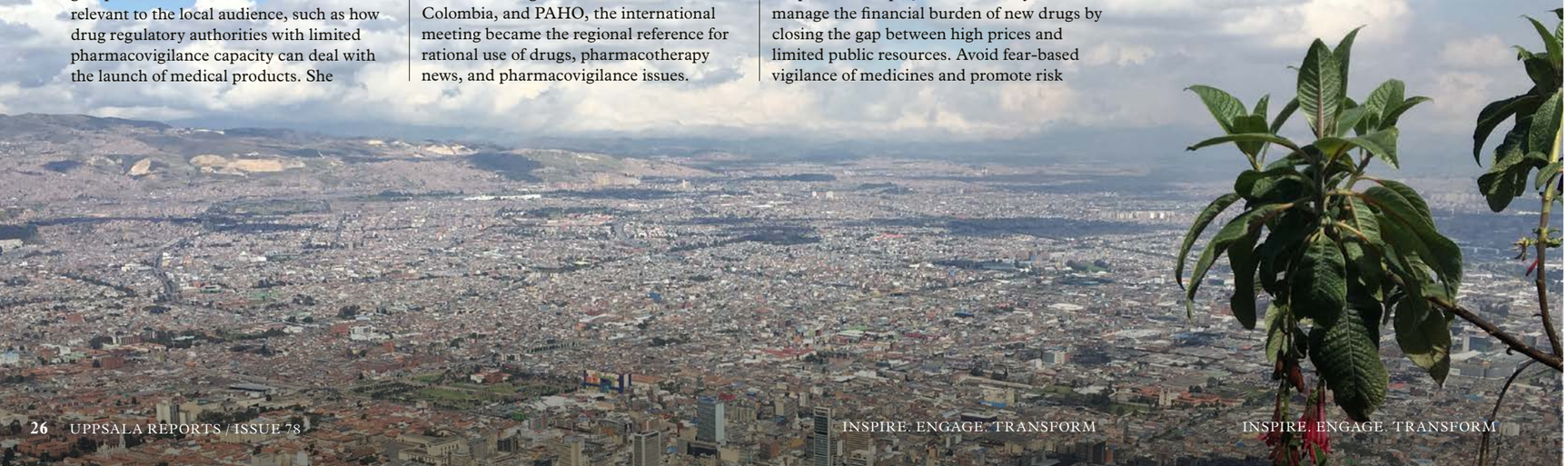

INSPIRE. ENGAGE. TRANSFORM

UMC and ISoP target regional challenges in Latin America

UMC and the International Society of Pharmacovigilance (ISoP) organised their fourth joint pharmacovigilance training course in September 2017 in Panama City – a choice of location that reflects the need to strengthen Latin American medicines safety.

UMC AND ISOP have a common aim to explore the benefits and risks of medicinal products, and share the primary objective to offer education in the field of medicines safety. In Latin America, there is scarce opportunity to take part in pharmacovigilance training. Though some theoretical courses have been offered in the last few years, workshops are not so frequent. That makes it difficult to turn theoretical knowledge into practice in daily pharmacovigilance activities.

The efforts of UMC and ISoP during the Panama course were thus focused on helping people to become more confident in their own knowledge, and reinforcing signal detection skills through hands-on exercises. Other workshops during the course focused on causality assessment and risk communication. The course was conducted by international and Latin American experts in pharmacovigilance, representing government, academia, and industry, and was designed to fulfill the needs of a diverse audience.

THE ATTENDEES CAME from different professional backgrounds, in both public and private institutions. That made the course the perfect meeting ground for regulatory agencies, pharmaceutical industries, and academia. A gathering like this is very rewarding because each participant can understand their own importance in the global pharmacovigilance process and the role of stakeholders.

Dr Martina Vlkova, part of ISoP's Course Organising Committee and associate director, head of QA at European PharmInvent Services, called the course "an excellent example of that it's possible to create a co-learning and co-practicing experience in the pharmacovigilance community in Latin America".

"I was delighted about the positive feedback from course participants and feel grateful for strengthening the bonds between the qualified and experienced course trainers and the participants from different target audiences. These bonds not only resulted in promoting and enhancing the safe and effective use of medicines in the region, but also the opportunity for fruitful discussions and questions arising from all participants from 12 countries and led to a higher level of their expertise and performance," she said.

This training course offered a great opportunity to strengthen pharmacovigilance activities and create a positive drug safety culture among healthcare professionals and patients in the region. More courses like this are necessary in Latin America to overcome technical difficulties, particularly as both old and new members of the WHO Programme for International Drug Monitoring need continuous training.

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Living with complexity and big data

In causal dispositionalism, the characteristics of both medicines and patients are considered when estimating probable beneficial or adverse outcomes of treatments. In this article, Prof Ralph Edwards discusses how this approach can be applied to causality in pharmacovigilance.

UMC HAS BEEN at the forefront of considering big data in pharmacovigilance. Since the mid-1990s we have been using disproportionality methods and developed tools, like VigiLyze, to extract useful information from the very large collection of individual case reports in the WHO global database VigiBase; with the aim to point to new potential problems related to medicines use, and to signal hypotheses of risk and harm. We have also been using similar approaches to analyse longitudinal healthcare records for over a decade, and been actively involved in several major public–private partnership projects that have sought to address the development and evaluation of methods for safety signal detection and refinement in longitudinal observational healthcare data, and, lately, patient-generated data in social media.

There is an ongoing debate on how to analyse and evaluate the data we gain from large data sets, and particularly what can we say about causality – after all, one is bound to find correlations by chance in vast amounts of data and with multiple analyses; but all this assumes that causality is a linear process which can be evaluated epidemiologically. Causality in real life, however, is usually multifactorial and complicated, and pharmacovigilance is concerned with data from complex healthcare systems in which multiple inter-relating factors evolve. The data we collect is affected by those changes over which we have no control.

IN "THE PHILOSOPHY of Complexity", author Chris Lucas writes that as a system "the parts are regarded as evolving in conjunction with each other in order to fit into a wider system environment, thus fitness must be measured in contextual terms as a dynamic fitness for the current niche, and not in relation to any imposed static function. The part structure will correlate to an external environment (giving a contextual fitness by structural coupling). This dependence upon environment contrasts with the isolated treatments of conventional science."

Furthermore, he writes: "We have a considerable bias towards simplification and in many situations will reduce a complex multidimensional issue to a one-dimensional form more conducive to an either/or decision. Complexity thinking looks to recognising the situations where this is invalid and to providing an alternative form of treatment that can better deal with these problems – the philosophy of complexity."

One different approach to causality in pharmacovigilance is causal dispositionalism and is applicable to complex data. This approach considers the innate characteristics (the dispositions) of both the medicinal product and the exposed patient – some property, state, or condition that, under certain circumstances, gives the possibility of some further specific state or behaviour. The relevant properties of the medicines would include its various pharmacological actions (pharmacodynamics), its distribution in the body (pharmacokinetics), and its interactions with other drugs. The relevant properties of the patient would include specific susceptibilities, such as genetics, age, sex, physiological state such as body weight or pregnancy, co-morbidities, drug–drug interactions, and social and environmental factors that have affected the patient.

"Let's be very broad-minded about what new value we can find in the multiplicity of big real-life data sets we can utilise to examine benefit and risk."

Consider a medication M, with a set of dispositions, $M[d_1]$, $M[d_2]$, and so on, known to be able to cause benefits and harms, and a patient P with dispositions $P[d_1]$, $P[d_2]$, and so on. We may then begin to investigate the probabilities that any M[d] will produce beneficial or adverse outcomes in a patient with any P[d], asking the questions 'how?', 'why?', and 'when?', using whatever information we have about the medicine M and the patient P to determine the benefit to harm balance.

This type of analysis is not merely probabilistic, but also takes into account the strength – the power – of M to affect P, as well as any outside factor that interacts with the causal link, e.g. drug–drug interactions. It also explicitly takes into account the power of P to respond to M. A disposition may be present but not become manifest until its power reaches a particular threshold, e.g. above a certain dose of a medication, in combination with, for example, a certain degree of renal function impairment in the patient.

Alternatively, a medicine with disposition $M[d_1]$ may have maximal effects in patient P_1 with dispositions $P_1[d_{2,3,4,5,6,7}]$, partial effects in patient P_2 with dispositions $P_2[d_{2\&7}]$, and partial or maximal effects in other patients P_n with, say, dispositions $P_n[d_2]$ or $P_n[d_{2,3,4,5,6,7,8,9}]$, but only in certain environment where the two extra dispositions d8 and d9 result in an additional influence, such as might occur when syncope from a vasodilator only happens when a susceptible patient is dehydrated.

TIME COURSES OF reactions can also be included in this type of analysis; Matthew Low has discussed the use of this approach in the diagnosis and management of a patient with back pain in a paper published last year in the Journal of Evaluation in Clinical Practice.

The Austin Bradford Hill observations on causation have been re-evaluated more broadly by Kristen Fedak et al. in the journal Emerging Themes in Epidemiology, and some of them can be interpreted in a dispositional way. We need to be able to relate them to real-life data. As Chris Lucas wrote: "Breaking away from the constraints of old-style scientific axioms (which nevertheless remain valid within their limited domains) allows us to explore an organic world that until now has been difficult to understand in overall terms. In such high-dimensional (multivalued) systems reductionist thinking proves inadequate, isolated single dimensional results do not predict real system behaviours. The co-evolutionary or epistatic nature of inter-related systems requires us to take a contextual approach, studying the dynamics of interactions rather than the static makeup of parts studied in more conventional science."

Let's be very broad-minded about what new value we can find in the multiplicity of big real-life data sets we can utilise to examine benefit and risk and thereby improve therapy.

Ralph Edwards
Senior Medical Advisor,
Uppsala Monitoring Centre

READ MORE:

C. Lucas, "The Philosophy of Complexity", calresco.org, 2005.

S. Mumford, "Dispositions", Routledge Encyclopedia of Philosophy, 2011.

S. Mumford, R. L. Anjum, "Getting Causes from Powers", Oxford University Press, 2011.

M. A. Low, "A novel clinical framework: the use of dispositions in clinical practice. A person centred approach", Journal of Evaluation in Clinical Practice, 2017.

K. M. Fedak et al., "Applying the Bradford Hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology", Emerging Themes in Epidemiology, 2015.

Prof Ralph Edwards at Uppsala Forum 2016.

SOCIAL MEDIA CAMPAIGN RAISES AWARENESS OF ADR REPORTING

Communications

Uppsala Monitoring Centre teamed up with medicine regulatory authorities in 27 countries to launch a social media awareness campaign on the importance of reporting adverse drug reactions.

IN NOVEMBER 2017, 27 countries across Europe, Latin America and Australasia ran a coordinated social media campaign to promote recognition and reporting of suspected adverse drug reactions (ADRs). The campaign formed part of the second ADR awareness week, and emerged from the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action project, whose first EU-wide awareness campaign ran in November 2016. The initiative was led by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK and Uppsala Monitoring Centre.

The objective of the campaign was to raise awareness among health professionals and patients about the importance of reporting suspected ADRs to their national pharmacovigilance centre. Regulators rely on ADR reporting to make sure medicines on the market are acceptably safe. Unfortunately, all reporting systems suffer from under-reporting, and the campaign was important to help strengthen the system.

"Our mandate as regulatory agencies is to promote awareness and health literacy among patients, to remind them to use drugs in the most appropriate and responsible way," said Mario Melazzini, director general of the Italian Medicines Agency (AIFA). "At the same time, we are providing patients with the right tools to play an active role in post-marketing surveillance of medicines. This is a universal mandate for all institutions in the health sector, and cooperation at the European level is crucial to disseminate and give greater resonance to key messages on these topics."

"Our efforts should not only raise awareness, but inspire people to take the step from awareness to action."

CAMPAIGN MATERIALS included a light-hearted and amusing series of animations produced by UMC, featuring funny cartoon characters whose unfortunate misuse of medicines leads to comical calamities.

"Humour and memorable characters are powerful storytelling elements that help question current behaviours and develop new, healthier ones," said Paula Alvarado, head of Global Communications at UMC. "We believe in pushing the boundaries of health communications to engage a wider audience and promote change. Our efforts should not only raise awareness – that is not enough – but inspire people to take the step from awareness to action."

The short animations were adapted for use in 19 European countries and New Zealand. Each country-specific version featured text in the local language, the logo of the medicine regulatory authority and a link to the national ADR reporting system. Seven additional countries supported the campaign by sharing non-tailored versions of the animations on their social media channels. Overall, the messages reached 2.3 million people on Twitter, Facebook, LinkedIn and YouTube, and resulted in 1,852 new ADR reports during the campaign week, an increase of 11% compared to the two months preceding and following the campaign.

"The eye-catching social media campaign helped us raise awareness of the importance of ADR reporting among young people, who are challenging to reach otherwise," said Svens Henkuzens, director of the State Agency of Medicines of the Republic of Latvia (ZVA). "This is a contribution to drug safety not only during the campaign, but also in the long term."

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READ MORE: M. Jadeja, "ADR reporting awareness on social media", Uppsala Reports 75, 2017.

27
participating countries

2.3 *million*
people reached on social media

1,852
new ADR reports during campaign week

11%
increase in ADR reporting during campaign week

Watch the animations on our YouTube channel!
www.youtube.com/c/UppsalaMonitoringCentre

Annie & Mac travel to Haiti

UMC's comic book pilot Annie & Mac's Adventures was run in two schools in Haiti – children can't wait for the final version to be released in spring!

Visitors from Morocco

Dr Latifa Ait Moussa and Afaf El Rherbi from the WHO Collaborating Centre in Rabat, Morocco (seated, centre), visited UMC in November 2017. They spoke to UMC staff to learn about our work, and explained how the Moroccan centre operates to build pharmacovigilance capacity in francophone and Arabic countries.

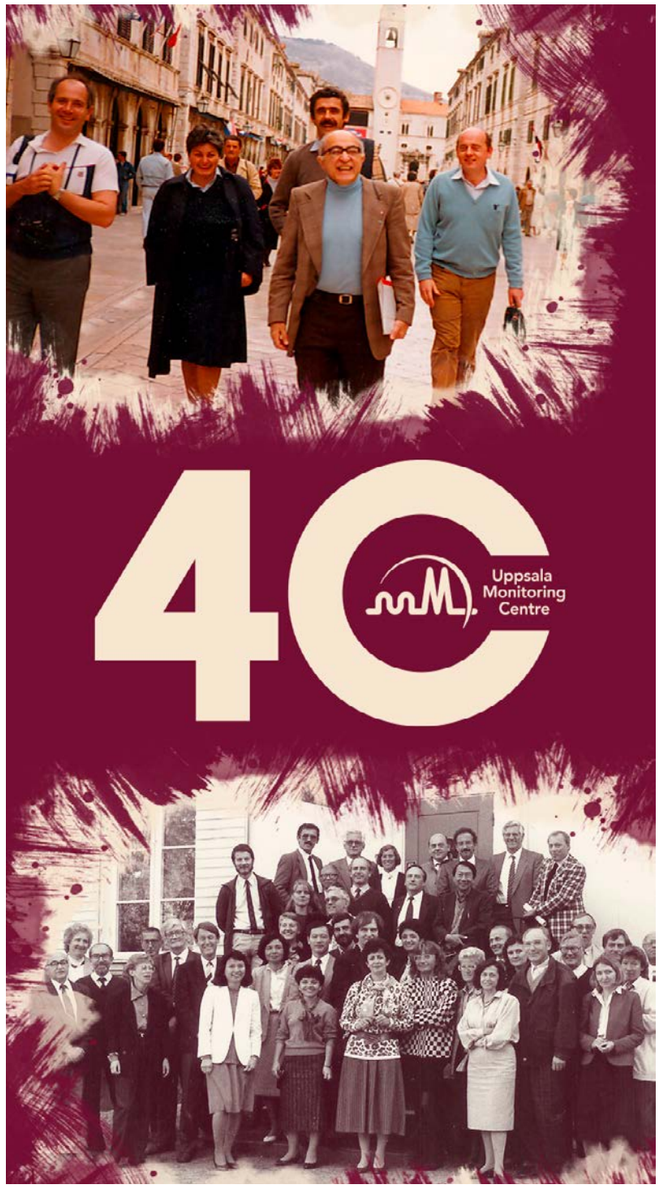
The 5th ISoP–UMC training took place in wintery Shenyang, China, in January. Over two days, 53 participants from Chinese regulatory, medical, and academic institutions learned about active surveillance, signal detection, and pharmacovigilance inspection.

Former UMC student Maarten van Eijk gets Meyler Prize

Maarten van Eijk, pharmacy student of Utrecht University who spent several months at UMC in 2017, was awarded the Meyler Prize for his Master's thesis 'Immunosuppressive antibodies and progressive multifocal leukoencephalopathy (PML): key reporting features and proposed search algorithm'. Congratulations Maarten!

New WHO PIDM members

Chad, Paraguay and Azerbaijan joined the WHO Programme for International Drug Monitoring as the 128th, 129th and 130th full members in January 2018. Papua New Guinea joined as the 131st full member in March 2018.



UMC is turning 40 years! What do these four decades add up to? Lots of commitment, lots of innovation, lots of ground-breaking science, and a world-wide collaboration network that has taken pharmacovigilance to where it is today. To mark the anniversary in May, we will publish a book showcasing some of the milestones in global pharmacovigilance, and release a documentary looking at various aspects of medicines safety in a handful of countries across the world. Keep an eye out for updates on our website and on social media!

Join the conversation on social media!

IN MEMORIAM

Dr Ana Maria Corrêa Nunes

(1947-2018)

IT IS WITH GREAT SADNESS that I write on the passing of our colleague and friend Dr Ana Maria Corrêa Nunes, on 24 December 2017.

Ana obtained her medical degree in Lisbon in 1972 and specialised in internal medicine and cardiology. After a few years of clinical work, she moved to the pharmaceutical industry and later to INFARMED, the Portuguese national medicines authority. But Ana's work went beyond the borders of Portugal.

I met Ana during her sabbatical in Uppsala in 1998 when she was working on the process of generating signals from international data. I had recently started a new job in the pharmacovigilance department of a company in Uppsala, and our meeting became the beginning of years of friendship, and sharing of knowledge and ideas. Ana later became a member of the UMC signal review panel.

Ana was the first secretary-general of the International Society of Pharmacovigilance (ISoP), and many of us know her from ESOP and then ISoP, and will treasure fond memories from those conferences. In 2005, Ana became a member of the Committee for Orphan Drugs at the European Medicines Agency, and a few years later she joined the ENCePP Steering Group.

Ana was devoted to her work, determined to do what was right, and improve the life of patients. However, she always found time for friends and family. She had great integrity and was very caring, and with a good sense of humour. Ana loved the arts, opera, fado, orchids and everything that was beautiful. She also became an expert in decorating cakes with sugar art.

It was a privilege for me to have been a part of Ana's life, which ended much too early. She passed away from a rare disease for which there is as yet no cure. Ana wanted us all to continue to improve pharmacovigilance and contribute to development of new treatments.

Christina Ström Möller

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Pharmacovigilance Meetings 2018

2–4 May 2018
Medical Aspects of Adverse Drug Reactions
Fareham, UK
Drug Safety Research Unit
www.dsru.org
@DSRUDrugSafety

15–16 May 2018
Signal Detection and Regulatory Expectations
London, UK
Management Forum Ltd
www.management-forum.co.uk

16–17 May 2018
Periodic Safety Reports: PSURs and PBRERs
Fareham, UK
Drug Safety Research Unit
www.dsru.org
@DSRUDrugSafety

21 May–1 June 2018
20th International Pharmacovigilance Training Course
Uppsala, Sweden
Uppsala Monitoring Centre
www.who-umc.org
@UMCGlobalSafety

4–22 June 2018
Pharmacovigilance Fellowship
Accra, Ghana
African Collaborating Centre for Pharmacovigilance
www.acc-afro.org

5–6 June 2018
Pharmacovigilance Conference
London, UK
Drug Information Association
www.diaglobal.com
@DrugInfoAssn

12–14 June 2018
Le congrès SFPT 2018
Toulouse, France
Société Française de Pharmacologie et de Thérapeutique
www.pharmacol-fr.org

19–21 June 2018
Pharmacovigilance
London, UK
Management Forum Ltd
www.management-forum.co.uk

20–21 June 2018
Big Data in Pharmacovigilance
London, UK
Drug Safety Research Unit
www.dsru.org
@DSRUDrugSafety

4–5 July 2018
Medication Errors
London, UK
Drug Safety Research Unit
www.dsru.org
@DSRUDrugSafety

22–26 August 2018
34th International Conference on Pharmacoepidemiology & Therapeutic Risk Management
Prague, Czech Republic
International Society for Pharmacoepidemiology
www.pharmacoepi.org

5–6 September 2018
Back to Basics in Pharmacovigilance
Fareham, UK
Drug Safety Research Unit
www.dsru.org
@DSRUDrugSafety

24–26 September 2018
6th ISoP–UMC Joint Pharmacovigilance Training Course
Guayaquil, Ecuador
International Society of Pharmacovigilance & Uppsala Monitoring Centre
www.isoponline.org
@ISoPonline

11–14 November 2018
ISoP 2018 Annual Meeting
Geneva, Switzerland
International Society of Pharmacovigilance
www.isop2018geneva.org
@ISoPonline

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www.youtube.com/c/UppsalaMonitoringCentre

Uppsala Monitoring Centre

Uppsala Monitoring Centre (UMC) is an independent non-profit foundation and centre for international service and scientific research. Our vision is a world where all patients and health professionals make wise therapeutic decisions in their use of medicines. Our mission is to support and promote patient safety through effective global pharmacovigilance practise.