Vaccine confidence and vaccination delivery in the European Union

Stephanie Kohl

Recently, the European Commission published information on the vaccine confidence and the delivery of vaccination services in the European Union (EU). Both reports revealed the need for EU action to tackle on the one hand misinformation and the lack of awareness of the general public and on the other hand, the lack of coordination among Member States.

The vaccine confidence report underlined the crucial link between confidence and coverage rates. To better understand why immunisation rates are declining throughout the EU. Confidence of the public in the EU and among general practitioners in the Czech Republic, Estonia, France, Germany, Italy, Poland, Romania, Slovakia, Spain and the UK was surveyed. Since confidence varies from vaccine to vaccine, the report focused on measles, influenza and vaccines in general. Data show that the population group over the age of 65 years is generally more confident about the safety and importance of vaccination than those under the age of 65 years.

In conclusion, the report highlights that the recent measles outbreak should be used as an opportunity. Coordinated approaches should be taken to remind the EU population about the importance of vaccination and the danger of vaccine-preventable diseases.

The study on the organisation and delivery of vaccination services in the EU was prepared by the European Observatory on Health Systems and Policies. It is divided into three parts to provide a comprehensive overview on the current situation. It summarises information on vaccine uptake and vaccine-preventable diseases. In addition, it contains details on the systematic review of health system-related factors and their impact on vaccine uptake as well as country fiches that outline the organisation and delivery of vaccination programmes.

The combination of these three components provides on the one hand an insight on what has been achieved and on the other hand highlights areas where further improvement could be beneficial. Lack

of awareness and vaccine hesitance have been singled out as the main barriers for improved vaccine coverage. In relation to each country fiche, targeted actions were identified that could help a health system with the improvement of health coverage.

To drive forward the action at national level, the European Commission intends to put together a 'Coalition for Vaccination', which should bring together European associations of healthcare workers' and students' associations.

EU REPORT ON INEQUALITIES IN ACCESS TO HEALTHCARE

The European Commission released a study of national policies focusing on the inequalities in access to healthcare in Europe. The report covers the EU, the members of the European Free Trade Association (EFTA) and EU candidate countries. Findings show that inequalities in the access to healthcare continue to exist within countries and also in between different countries.

The conclusions and findings of the study concentrate on 10 key points. The first three relate to the funding of the public healthcare system and its coverage. Huge differences were found in the amount of public resources that are allocated to healthcare and the population that is covered. While in some countries nearly the whole population benefits for healthcare coverage, others are excluding a significant percentage of the population. Moreover, the report underlined that systems that are underfunded perform much worse than the EU average in terms of both access and inequalities in access.

High out-of-pocket payments for pharmaceuticals and waiting lists were mentioned as two findings that are raising concerns. Similarly, also the voluntary and occupational health insurance schemes that exist in several countries were named as a factor that may worsen inequalities. Several population groups, such as those with low income and migrants have significant difficulties in gaining access to healthcare. Ethnicity and residence status were reported as main hurdles.

Shortages of health professionals and the level of supply of health services were

mentioned as other key points. In relation to the outcome, it was highlighted that the access to healthcare is different for countries that are spending a similar amount of public money on healthcare. The report also stressed that inequalities in access to healthcare do not seem to be linked to the model of health system funding.

Recommendations to countries address the financing of the health system, health coverage, user charges, the availability of services, the voluntary health insurance and initiatives targeting vulnerable groups. On European level, the report highlights the importance of advancing the development of a roadmap for the implementation of Principle 16 of the European Pillar of Social Rights, which addresses the right of everyone to timely access to affordable, preventive and curative care of good quality.

ANTIMICROBIAL RESISTANCE IN THE EU: NEW EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL PUBLICATIONS

On 18 November, healthcare professionals across the EU celebrated the European Antibiotic Awareness Day (EAAD). Linked to this event, the European Centre for Disease Prevention and Control (ECDC) released new data on the antimicrobial consumption and the surveillance of antimicrobial resistance (AMR) in Europe in 2017.

The 2017 annual epidemiological report surveyed antimicrobial consumption data from 27 European countries (25 EU Member States, Iceland and Norway). The majority of these countries (22) reported both community and hospital consumption. Three countries (Austria, Germany and Iceland) only focused on community consumption, and two countries (Cyprus and Romania) reported total consumption in both sectors without differentiating between them. The Czech Republic, Greece and Slovakia were the EU countries that did not report antimicrobial consumption data for 2017.

Overall, the annual report highlighted that in the hospital sector no statistically significant change was observed when comparing information for the period 2013 to 2017. On average, 2.0 defined daily doses per 1000 inhabitants were consumed per day in the EU. An increase in consumption was found in the 2017 data of Croatia and Malta, while the consumption of Finland overall decreased.

The surveillance report which was also published ahead of the EAAD highlighted

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that the resistance levels of several bacterial species-antimicrobial group combinations remain high throughout the EU and the European Economic Area (EEA). In general, lower resistance percentages were reported by countries in the north, while higher percentages were reported in the south and east of Europe.

In particular, the study looked at *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter* species, *Streptococcus pneumoniae*, *Staphylococcus aureus* and enterococci. For *E. coli* and *K. pneumoniae*, combined resistance to several antimicrobial groups was frequent, and extended-spectrum beta-lactamase production was common. Resistance percentages were generally higher in *K. pneumoniae* than in *E. coli*. Carbapenem resistance was common in *P. aeruginosa* and *Acinetobacter* species, and at higher percentages compared with *K. pneumoniae*. For *S. pneumoniae*, it was reported that the resistance situation remained stable between 2014 and 2017. However, large intercountry variations were found. For *S. aureus*, the decline in the percentage of methicillin-resistant isolates reported in previous years continued in 2017. Among enterococci, the increasing trend of *Enterococcus faecium* resistance to vancomycin is a cause of concern.

NEW RULES IN THE VETERINARY SECTOR TO HELP BATTLE AMR

On 26 November, the European Council gave the green light for new rules on veterinary medicines and medicated feed. These new rules aim at improving the fight against AMR in the veterinary sector.

The new regulation on veterinary medicinal products repeals Directive 2001/82/EC. In line with the European Commission's One Health Approach on AMR, it will promote a prudent and responsible use of antimicrobials in the veterinary field. Moreover, the new regulation simplifies the marketing authorisation procedure for veterinary medical products in order to reduce the administrative burden for companies, especially small ones, strengthens pharmacovigilance and controls as well as improves the protection of the European consumers against the risk of the spreading of AMR through imports of animals and products of animal origin. The rules will become applicable in the next 3 years.

The new regulation on medicated feed that will repeal the outdated Directive 90/167/EEC aims at:

- bringing into action a ban on the preventive use of antimicrobials via medicated feed;
- restricting the veterinary prescriptions with antimicrobials;
- establishing harmonised limits for antimicrobials in ordinary feed.

In addition, it will set EU harmonised standards for manufacturing safe medicated feed and create a legal framework for safe manufacturing and distribution of medicated feed for pets.

THE STATE OF EUROPEAN HEALTH

On 22 November, the European Commission and the Organisation for Economic Cooperation and Development (OECD) issues their joint report '2018 Health at a Glance: Europe 2018—State of Health in the EU cycle'. The results which are based on information provided by the EU28, candidate countries and the EFTA countries provide an analysis of the state of health of EU citizens and the performance of EU health systems.

Overall, the report outlines that gains in life expectancy have slowed down and that large disparities continue to persist. In relation to health systems, it was underlined that 20% of health spending could be reallocated for better use. Optimisation are needed to reduce wasteful spending and to make health systems more effective and resilient. For the hospital sector, it was highlighted that many admissions could be avoided with better management of chronic conditions in the community. The report also puts a stronger emphasis on prevention and calls for improvements in the mental health sector. Preventive actions should tackle risk factors like smoking, alcohol and obesity as well as help with the reduction of premature mortality.

The publication of the report kicked-off the new state of health cycle. The second phase will commence in 2019 when the country health profiles of all EU countries are released by the OECD and the European Observatory on Health Systems and Policies. They will be presented alongside a companion report that offers conclusions. The current cycle will be concluded by a voluntary exchange with members states.

OECD: THE ECONOMIC BURDEN OF ANTIBIOTIC RESISTANCE

In light of the rising antibiotic resistance rates in Europe, North America and Australia, the OECD is warning about disastrous consequences for public health. Newly released data by the OECD on the

economic burden of antibiotic resistance revealed that 2.4 million people could die in Europe, North America and Australia until 2050 unless further action is taken.

Countries surveyed by this analysis include the EU28, Australia, Canada, Iceland and the USA. Southern Europe, in particular Italy, Greece and Portugal, will be severely affected by the growing resistance, leading to the highest mortality rates from AMR, if the projected trends continue to progress. Also the impact on quality of life was analysed by OECD. Children and elderly, as the most vulnerable groups, will be affected the most. In addition, the report highlighted the impact of superbugs on the overall health budget in the EU28 and OECD countries.

To counter the problem, the report lists five affordable policy solutions that could be implemented by governments. These include the improvement of hygiene measures, the implementation of stewardship programmes, the use of rapid diagnostic tests to help detect if an infection is viral or bacterial, delayed prescription and raising public awareness.

ECDC: NEW STUDY ON INFECTION DUE TO BACTERIA RESISTANT TO ANTIBIOTICS

Ahead of the EAAD 2018, the ECDC released a new study analysing the data from the European Antimicrobial Resistance Surveillance Network from 2015. The information was used to estimate the burden of five types of infections caused by antibiotic-resistant bacteria in the EU/EEA.

The results clearly indicate that the estimated burden of infections with antibiotic-resistant bacteria in the EU/EEA is substantial compared with that of other infectious diseases, and increased since 2007. Estimations indicate that around 33 000 people die each year as a direct consequence of an infection due to bacteria resistant to antibiotics. Adequate infection prevention and control measures, such as hygiene measures, could help lower the burden of disease due to healthcare-associated infections which currently make up 75%.

In particular, coordinated strategies to prevent and control antibiotic-resistant bacteria are needed. Given the great variation of results in the different EU/EEA countries, these measures also need to be tailored to the specific need of each EU country. Solutions are essential, especially since the study showed that 39% of the burden is caused by infections with bacteria resistant to last-line antibiotics

such as carbapenems and colistin. Antibiotics must continue to work, otherwise it is extremely difficult or, in many cases, impossible to treat infections.

EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES AND HEALTHCARE: CONSULTATION LINKED TO EUROPEAN PAEDIATRIC FORMULARY

The European Directorate for the Quality of Medicines and Healthcare has launched a public consultation on the first two pilot monographs and on two general texts for its European Paediatric Formulary. European pharmacists and paediatricians are invited to share their feedback on the draft monographs on hydrochlorothiazide oral solution and on sotalol oral solution.

The European Paediatric Formulary is a project created by the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and the European Pharmacopoeia Commission. It seeks to collect monographs on formulations for extemporaneous preparations that are currently described in national formularies centrally on European level. Overall, it aims at providing pharmacists and clinicians with specific formulations of appropriate quality to allow preparation when no licensed alternative is available on the market.

Monographs to be included in the European Paediatric Formulary are selected on the basis of criteria for inclusion and evaluation adopted by the CD-P-PH end of 2015. These include quality criteria, for example, that the preparation process is prescribed in a way to ensure reproducibility, and criteria for therapeutic relevance and clinical justification of the preparation, for example, following the therapeutic needs identified by the European Medicines Agency (EMA). The verification also includes the excipients to ensure they comply with Ph. Eur. requirements, are not harmful and suitable for their intended use.

EMA REPORT ON SALES OF VETERINARY ANTIMICROBIALS

In mid-October, the EMA released a report on the sales of veterinary antimicrobials. It shows that between 2011 and 2016, the sale numbers decreased across Europe by over 20%. This trend is partially attributed to the success of EU guidance efforts, including actions containing the 'One Health' action plan, and national campaigns that aimed at promoting the prudent use of antibiotics in animals. The report is a component of the EMA's

project on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC).

The study covers 2016 data collected from the EU28, Norway, Iceland and Switzerland and data from 25 EU Member States for the period 2011–2016. Even though sales of polymyxins went down by almost 40% and sales of quinolones declined by 13.6%, the situation is not homogenous across Europe. While 16 of those 25 countries that provided data for 2011–2016 saw a drop in sales of veterinary antimicrobials of 5% or more, six countries recorded an increase of >5% in sales during the same period.

The ESVAC project, which aims at harmonising the collection and reporting of data from EU Member States on the use of antimicrobials in animals, was launched in 2010. Each year, a report is produced which is used by risk assessors and risk managers in Member States as a reference for antimicrobial policies and for guidance on responsible use of antimicrobials.

RESOLUTION ON THE 'ONE HEALTH' APPROACH ADOPTED BY EUROPEAN PARLIAMENT

In mid-September, the European Parliament adopted a resolution addressing the growing threat posed by antibiotic-resistant bacteria. The resolution on a 'One Health' approach highlights the importance of the correct and prudent use of antimicrobials as an essential tool to limit AMR of humans, animals and aquaculture.

The resolution urges the European Commission and Member States to restrict the sale of antibiotics by healthcare professionals. In addition, incentives to prescribe them should be removed and firm action should be taken to address illegal sales and sales without prescription of antimicrobials in the EU. These actions should be supported by measures ensuring that consumers make well-informed choices. Another aspect taken up by the resolution is research and development. Investment in new substances should be stimulated and an EU priority pathogen list for both humans and animals should be drafted by the European Commission.

COMMISSION STAKEHOLDER CONFERENCE ON BIOSIMILAR MEDICINES

On 14 September, the European Commission hosted the fourth edition of its annual stakeholder event on biosimilar medicinal products to promote the exchange of knowledge and best practices in biosimilars' use and uptake. Topics addressed

during the event included the uptake of biosimilars in oncology, sustainable procurement practices and the improvement of the understanding of biosimilars through educational measures.

Representatives of public authorities, patients' organisations, healthcare professionals and pharmaceutical companies were among the participants. Dr Miguel Angel Calleja Hernández, President of the Spanish Hospital Pharmacy Association was among the speakers and outlined the views of hospital pharmacists.

During the event it was also announced that the 'information guide for healthcare professionals' is now also available in Dutch, French German, Italian, Polish, Portuguese and Spanish. This document which was developed jointly by the EMA and the European Commission ensures that healthcare professionals have access to realistic and unbiased information about the science and regulation-related biosimilar use.

UPDATES FROM THE EUROPEAN MEDICINES AGENCY

Launch of new website

At the end of September, the EMA launched a new version of its website to improve the user experience. Changes include an improved search, allowing users to find content easily and to filter their search results, a 'responsive' design for cleaner display on mobile devices, simpler URLs based on the location and title of webpages or documents and an updated visual design offering users a clearer reading experience and simpler navigation.

New paediatric action plan

To boost the development of medicines for children and adolescents, the EMA and the European Commission's Directorate-General for Health and Food Safety have adopted a joint action plan. This plan seeks to address the shortcomings outlined in the 10-year report on the implementation of the Paediatric Legislation (for more information see EU Monitor of 7 November 2017). The plan covers actions in the following five categories that should be implemented by 2020:

- ▶ identifying paediatric medical needs;
- ▶ strengthening cooperation between decision makers;
- ▶ ensuring timely completion of paediatric investigation plans (PIPs);
- ▶ improving the handling of PIP applications;
- ▶ increasing transparency around paediatric medicines.

PHARMACOVIGILANCE RISK ASSESSMENT COMMITTEE RECOMMENDS RESTRICTING THE USE OF QUINOLONE AND FLUOROQUINOLONE MEDICINES

Following a review of disabling and potentially long-lasting side effects reported with quinolone and fluoroquinolone medicines, EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended restricting the use of these medicines.

PRAC advised that all medicines containing a quinolone antibiotic should be removed from the market. In relation to the remaining fluoroquinolone antibiotics, PRAC recommended that they should not be used

- ▶ to treat infections that might get better without treatment or are not severe (such as throat infections);
- ▶ for preventing traveller's diarrhoea or recurring lower urinary tract infections (urine infections that do not extend beyond the bladder);
- ▶ to treat patients who have previously had serious side effects with

a fluoroquinolone or quinolone antibiotic;

- ▶ to treat mild or moderately severe infections unless other antibacterial medicines commonly recommended for these infections cannot be used.

Moreover, PRAC highlighted that fluoroquinolone antibiotics should be used with caution, especially when taken by the elderly, patients with kidney problems, patients who have had an organ transplantation or those who are being treated with a systemic corticosteroid. These patients are at higher risk of tendon injury caused by fluoroquinolone and quinolone antibiotics.

The PRAC's recommendations will now be sent to EMA's Committee for Medicinal Products for Human Use, which will adopt the Agency's final opinion.

PRAC confirms precautionary advice on HIV medicine dolutegravir

The PRAC confirmed its precautionary advice issued earlier this year on the use of dolutegravir in pregnant women and women who can become pregnant (for more information see EU Monitor of 24

May 2018). Recommendations include the use of effective contraception while taking dolutegravir and pregnancy testing before starting treatment.

The precautionary advice bases itself on the evaluation of preliminary results from a study which found cases of neural tube defects (birth defects of the brain and spinal cord) in babies born to mothers who used dolutegravir during pregnancy. As the study is still ongoing, a further assessment will be carried out once the final results become available next year.

Section 6: Education and Research

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