ECDC country visit to Spain to discuss antimicrobial resistance issues

15-19 February 2016
ECDC MISSION REPORT

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This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Alessandro Cassini, Expert, Antimicrobial Resistance and Healthcare-associated Infections.

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This report was sent for consultation to Dr Fernando Simón, Ministry of Health, Social Affairs and Equality, Spain.

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### Abbreviations

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<tr>
<td>AEMPS</td>
<td>The Spanish Agency of Medicines and Medical Devices</td>
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<tr>
<td>AMR</td>
<td>antimicrobial resistance</td>
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<tr>
<td>CPE</td>
<td>carbapenemase-producing <em>Enterobacteriaceae</em></td>
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<tr>
<td>CRE</td>
<td>carbapenem-resistant <em>Enterobacteriaceae</em></td>
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<td>EAAD</td>
<td>European Antibiotic Awareness Day</td>
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<td>EARS-Net</td>
<td>European Antimicrobial Resistance Surveillance Network</td>
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<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
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<td>ESBL</td>
<td>extended-spectrum beta-lactamase</td>
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<td>ESVAC</td>
<td>European Surveillance of Veterinary Antimicrobial Consumption</td>
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<td>HAI</td>
<td>healthcare-associated infection</td>
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<td>ICU</td>
<td>intensive care unit</td>
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<td>ICM</td>
<td>intersectoral coordinating mechanism</td>
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<td>IPC</td>
<td>infection prevention and control</td>
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<tr>
<td>LTCF</td>
<td>long-term care facility</td>
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<td>MDRO</td>
<td>multidrug-resistant organism</td>
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<td>MRSA</td>
<td>meticillin-resistant <em>Staphylococcus aureus</em></td>
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<tr>
<td>OTC</td>
<td>over-the-counter</td>
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<td>PPS</td>
<td>point prevalence survey</td>
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<tr>
<td>TB</td>
<td>tuberculosis</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Executive summary

Rationale and purpose of the country visit

A Council Recommendation dated 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat that AMR poses to human health and advocates a range of actions to be taken for its prevention and control. Council Conclusions on antimicrobial resistance (AMR) dated 10 June 2008 reiterate this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for country visits, which are carried out at the invitation of national authorities. These visits are designed to specifically discuss and assess the situation in the country regarding prevention and control of AMR through prudent use of antibiotics and infection control. The visits also help document how Member States have approached implementation of the Council Recommendation and deployed national resources in order to support the European Commission in evaluating implementation.

The main output of the visit is a report from ECDC provided to the national authority. To help ECDC ensure the consistency of the visits and follow up on progress, an assessment tool has been developed. The assessment tool includes ten topics which are regarded as the core areas for successful prevention and control of AMR, based on Council Recommendation 2002/77/EC and the Council Conclusions dated 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

Following an invitation by the Spanish Ministry of Health, Social Services and Equality, an ECDC team conducted visits and meetings to discuss AMR issues in Spain with the overall objective of providing an evidence-based assessment of the situation in Spain with regard to prevention and control of AMR through prudent use of antibiotics and infection control.

Conclusions

• According to the data available from the Spanish surveillance systems, the AMR situation in Spain poses a major public health threat to the country. The current levels of meticillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and Acinetobacter baumannii are high and are above the EU/EEA average. In addition, the rapid increase in carbapenemase-producing Enterobacteriaceae (CPE) over the past five years represents a new threat to the safety of patients in Spanish hospitals and other healthcare facilities. This is also a health security issue since CPE are resistant to almost all antibiotic classes, leaving only a few options for the treatment of infected patients.

• Antimicrobial consumption in primary care and hospitals is among the highest in the EU/EEA and during the visit the ECDC team saw evidence that infection prevention and control (hand hygiene, contact precautions, isolation, environmental cleaning) and environmental cleaning measures vary significantly among hospitals and units. This results in suboptimal control of multidrug-resistant organisms (MDROs) which are spread from patient to patient, either directly via the hands of healthcare workers or indirectly via the environment. This situation contributes to the development of outbreaks in hospitals, with a number of unidentified patients carrying MDROs such as CPE that may spread between hospitals and/or between wards within the same hospital.

• Although CPE and AMR in general are perceived as important issues by the health professionals we met, we noted that the high levels of CPE and AMR observed were sometimes accepted, as if they were unavoidable and health professionals felt that they had done everything they could – or everything within their remit and the limit of their resources - to control the spread of CPE. The emergency nature of responding to the threat represented by AMR in general, and CPE in particular, needs to be communicated and understood at all levels in the country, and especially by those working in hospitals and other healthcare facilities.

• Nevertheless, there is commitment and a willingness to discuss AMR issues both at the national level, in the Autonomous Regions that we visited, and among professionals. The fact that there is a broad, comprehensive, structured National Strategic Action Plan, with involvement of all the major actors including six ministries, is also an indication of the commitment to addressing AMR and prudent use of antibiotics in the country.

• There are numerous examples of good practice at regional and local level, and within professional societies. Moreover, the Ministry of Health, Social Services and Equality has been promoting and coordinating prevention and control programmes since 2008. There are also many surveillance and alert systems at national, regional and local level that provide a good picture of antibiotic prescription and generate excellent data to support a response to CPE and other AMR threats. However, it appears that in most cases data produced by these surveillance systems are not used to generate and evaluate targeted action. We also had the impression that there was a lack of clarity as to who was responsible and what needed to be done.
Based on these observations, ECDC’s team recommended the following actions:

- For each action in the National Strategic Action Plan, clearly indicate who is coordinating (person/position), which organisation is contributing, which Autonomous Regions are participating (the list of the latter will increase over time), set out clear deliverables and deadlines, and make this information publicly available on a website with regular, periodical updates on progress.
- The implementation of many actions in the National Strategic Action Plan relies on actions being taken by each Autonomous Region (and ultimately at the local level in each hospital, long-term and primary care facility in the country). Pledges of commitment by the political leadership of the Autonomous Regions are needed, with clear objectives, targets, deadlines and resources for implementation.
- The National Strategic Action Plan should include achievable targets for a selected number of outcome indicators that, when achieved, would clearly indicate how implementation of the Plan has an impact on AMR in the whole country.
- The commitment of the Autonomous Regions should extend to sharing tools, software and expertise (including infrastructural support) from successful initiatives with other regions and encouraging a culture of reciprocity of services and expertise between regions. A mechanism and platform (central, public repository) should be created to share examples of good practice, documents and tools that are produced by the Autonomous Regions that would be helpful to other regions. The mechanism/platform should also include initiatives from professional societies.
- A national hand hygiene programme, promoted by the Ministry of Health Social Services and Equality, in coordination with all the Autonomous Regions, started in Spain in 2008. However, its implementation and the level of compliance with hand hygiene practices in healthcare may vary among the Autonomous Regions. It is vital that Spain urgently evaluates the level and quality of the hand hygiene programmes implemented in hospitals and in the Autonomous Regions. This is an important step towards understanding the failures of previous programmes and assuring the sustainability of any future improvement. This will ensure that Spain fully implements the 2008-2009 WHO Guidelines for Hand Hygiene in Healthcare in all settings where healthcare is delivered. These Guidelines include a programme of education on the five moments and proper technique; availability of hand hygiene products at the point of care; a train-the-trainers approach to hand hygiene education and audit; regular compliance audits within all healthcare facilities; reporting and trend analysis of hand hygiene compliance, integral to and embedded within the patient safety culture of all settings where healthcare is delivered and coupled with the support of ongoing, high-profile national and regional information campaigns aimed at healthcare professionals and service users. Hand hygiene campaigns could also target the general public to promote awareness among all citizens (e.g. with messages highlighting the role of hand hygiene in the prevention of respiratory and gastrointestinal tract infections to reduce the need for antibiotics).
- Classify CPE and its control in Spanish healthcare as a public health emergency. For this, there should be an alert system that includes CPE as a communicable disease for which reporting is mandatory (with necessary epidemiological information and molecular typing information from the national reference laboratory). Mandatory reporting should be approved by all Autonomous Regions through the Interregional Council to ensure notification from local to regional level, and then from regional to national level. Health authorities at the national and regional levels and healthcare facility directors should be made accountable for achieving results (i.e. healthcare facility preparedness, implementation of information systems to identify cases - when transferred and on re-admission, reduction in the incidence of new cases, etc.)
• The creation of a national emergency response team of experts could support the Autonomous Regions in tackling emergency AMR situations, making use of field epidemiologists, expertise from the national reference laboratory and infection prevention specialists with competence in MDRO control to implement AMR control plans effectively.

• Incomplete data on human antimicrobial consumption in Spain is a threat to the representativeness of surveillance data and may impact evaluation of the National Strategic Action Plan’s implementation. Spain should acquire sales data on antibiotic consumption to include private prescriptions as well as the percentage of antibiotic sales without a prescription. Similarly, Spain should obtain data on antimicrobial consumption in the hospital sector and report them at EU-level to ESAC-Net. Sales data collected by the AEMPS could be used for this purpose, at national and regional level.

In addition:

• The mapping exercise of the National Strategic Action Plan should also define which resources are currently available or would be needed to implement the plan. At national level, there is a need for specific funding at least to start implementing the coordination of the actions. At local level, any savings that could be made from good practice (e.g. from prudent use of antibiotics), could be channelled into the reinforcement of prevention and control activities.

• Consider prevention and control of AMR and the prudent use of antibiotics as objectives in the contracts between the Autonomous Regions and hospitals and other healthcare facilities. It could also be considered as a point for accreditation of hospitals.

• Consider the funding necessary to make rapid point-of-care diagnostic tests more available to primary care doctors in order to aid in the prudent prescription of antibiotics at this level.

• Develop national guidelines for the prudent use of antimicrobial agents, including best practices for the diagnosis and identification of clinical situations where antimicrobial agents are not needed.

• Implement training on AMR and prudent use of antibiotics, at both pre-graduate and post-graduate levels, of all healthcare professionals involved in the prescription (doctors), dispensing (pharmacists) and administration (nurses) of antibiotics, as well as the laboratory diagnosis of infections that require antibiotic treatment (microbiologists).

• Given the extent and the scale of the threat posed by AMR in general and CPE in particular, it may be advisable to revisit the scope of practice of preventive medicine specialists in hospitals and scale up the number of these specialists specifically dedicated to infection prevention and control in Spanish healthcare.

• ‘Infectious Diseases’ are not recognised as a medical specialty, meaning that it is not possible to train specialists and this inevitably has an impact on the recruitment of infectious disease physicians in hospitals.

• Finally, to promote transparency towards stakeholders and the general public, the National Strategic Action Plan website (in preparation at the time of the visit) could include information on objectives and results achieved at national and regional level.
1. Background

1.1 Rationale for country visits to discuss antimicrobial resistance (AMR) issues

After the introduction of antibiotics in the 1940s, it soon became clear that antibiotic usage promoted the rise of antibiotic-resistant bacterial strains in common bacteria such as *Staphylococcus aureus* and *Mycobacterium tuberculosis* (TB). In the decades which followed, the increasing number of antibiotic-resistant strains could be managed thanks to the continuous availability of new antibiotics providing new means of treating patients infected with resistant bacteria. However, from the 1990s onwards, development of new antibiotics decreased and at the same time, the emergence of bacteria resistant to multiple antibiotics became an ever-increasing problem in clinical medicine. Treatment guidelines had to be rewritten and the need to take bacteriological samples for antibiotic susceptibility testing became essential.

Once a resistant bacterium has developed, it will spread from a colonised person to another person if appropriate hygienic precautions (e.g. hand hygiene, isolation) are not taken. The risk of resistant bacteria spreading is higher in crowded environments and even greater when people in the surrounding area are receiving antibiotics - a common situation in hospitals and other healthcare facilities.

Today, bacteria that are totally (or almost totally) resistant to antibiotics (i.e. untreatable with antibiotics) are spreading in Europe. This represents a patient safety issue.

In 1998, the Chief Medical Officers of the EU Member States recognised this evolving problem and took the initiative to arrange the first major conference on AMR, which resulted in the Copenhagen Recommendations (Report from the Invitational EU Conference on the Microbial Threat, Copenhagen, Denmark, 9–10 September 1998).

In November 2001, the EU Health Ministers adopted a Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC), which covers most topics of importance for the prevention and control of AMR. The Commission has to report back to the Council on progress in implementing the Council Recommendation.

In 2005, the European Commission reported to the Council on progress in Member States in the Report from the Commission to the Council on the basis of Member States reports on the implementation of the Council recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine (COM (2005) 0684). This states that ‘ECDC should be able to assist the Commission in the future preparation of implementation reports and of recommendation proposals.’

In June 2008, EU Health Ministers adopted Council Conclusions on antimicrobial resistance (AMR) that reiterated the call for action to contain antimicrobial resistance and called upon Member States to ensure that structures and resources for the implementation of the Council recommendation on the prudent use of antimicrobial agents in human medicine are in place and to continue with the implementation of specific strategies targeted towards the containment of the antimicrobial resistance.

In June 2009, EU Health Ministers adopted a Council Recommendation on patient safety, including the prevention and control of healthcare-associated infections (2009/ C 151/01), which further stresses the importance of combating AMR as a patient safety issue.

In April 2010, the European Commission published its second report from the Commission to the Council on the basis of Member States’ reports on the implementation of the Council Recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine. While acknowledging that Member States have made significant progress since 2003, this report highlights many areas where implementation is not optimal and identifies directions for future work.

In November 2011, the European Commission published a new five-year action plan against the rising threats from antimicrobial resistance with the aim of addressing AMR by implementing a coordinated approach in all those sectors concerned (public health, animal health, food safety, environment, etc.) and strengthening and further developing EU initiatives against AMR and HAI at EU and international levels.

Finally, the new cross-sectorial approach has been further strengthened with the adoption of the Council Conclusions on antimicrobial resistance of 22 June 2012 and the Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance of 17 June 2016.

ECDC's mission, as part of its Founding Regulation No 851/2004, is (i) to identify, assess and communicate current and emerging threats to human health from communicable diseases; (ii) in the case of other outbreaks of illness of unknown origin which may spread within or to the Community, the Centre shall act on its own initiative
until the source of the outbreak is known; and (iii) in the case of an outbreak which clearly is not caused by a communicable disease, the Centre shall act only in cooperation with the competent authority upon request from that authority. As part of this mission, ECDC may be requested, by the European Commission, a Member State, or another country to provide scientific or technical assistance in any field within its mission.

Following an invitation by the Spanish Ministry of Health, Social Services and Equality, ECDC conducted an assessment mission on 15-19 February 2016 to discuss antimicrobial resistance (AMR) issues in Spain, with the objective of providing an evidence-based assessment of the situation in Spain in relation to prevention and control of AMR through prudent use of antibiotics and infection control.

1.2 Purpose

Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat posed by AMR to human health and advocates for a range of actions to be taken for its prevention and control. Council Conclusions on antimicrobial resistance (AMR) of 10 June 2008 reiterated this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for country visits. At the invitation of the national authorities, these visits are undertaken to specifically discuss and assess the national situation regarding prevention and control of AMR through prudent use of antibiotics and infection control. The country visits also help document how Member States have approached implementation and deployed national activities and they support the European Commission in evaluating implementation.

The main output of the visit is a report from ECDC provided to the national authority. To help ECDC ensure the consistency of the visits and monitor progress, an assessment tool has been developed (see Annex 5.2 of this report). The assessment tool includes ten topics regarded as core areas for successful prevention and control of AMR based on Council Recommendation 2002/77/EC and the Council Conclusions of 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

Following an invitation by the Spanish Ministry of Health, Social Services and Equality, an ECDC Team country visit team conducted visits and meetings on 15-19 February 2016 to discuss AMR issues in Spain with the overall objective to provide an evidence-based assessment of situation in Spain regarding prevention and control of AMR through prudent use of antibiotics and infection control. The ECDC country visit team consisted of Dominique L. Monnet, who led the mission, and three experts from EU/EEA Member States: Dr. Karen Burns (Ireland), Dr. Catherine Dumartin (France) and Dr. Oliver Kacelnik (Norway), as well as Mr Giovanni Mancarella (ECDC, only on 15 February). At national level, the visit was organised and coordinated by Dr Fernando Simón, Spanish Ministry of Health, Social Affairs and Equality.

For the full list of national and regional experts met and the institutions and hospitals visited in three Autonomous Regions during the ECDC country visit, please refer to Annex 5.1 of the report.
2. Overview of the situation in Spain

2.1 Antimicrobial resistance (AMR)

Data on AMR in invasive bacterial isolates - mainly from bloodstream infections - are available from EARS-Net. From a European perspective, the present AMR situation in Spain is worse than in many other Member States. This observation applies to both multidrug-resistant Gram-positive bacteria (e.g. meticillin-resistant *Staphylococcus aureus* (MRSA), antimicrobial-resistant *Streptococcus pneumoniae*) and multidrug-resistant Gram-negative bacteria (e.g. *Escherichia coli*, *Klebsiella pneumoniae* or *Acinetobacter* spp.), as shown in data from EARS-Net and from the ECDC point prevalence survey (PPS) of HAIs and antimicrobial use in European acute care hospitals 2011–2012.

For carbapenem-resistant *K. pneumoniae*, the percentage of resistant isolates in bloodstream infections (EARS-Net) is still low compared with the Member States reporting the highest percentages, although it showed a statistically significant increase from 0.3% in 2011 to 2.3% in 2014 before stabilising at 2.2% in 2015.

The percentage of *Acinetobacter* spp. bloodstream infections with combined resistance to fluoroquinolones, aminoglycosides and carbapenems was very high (51.1% in 2014 and 41.5% in 2015; trends cannot be analysed because of the small number of isolates).

2.2 Healthcare-associated infections

Information on healthcare-associated infections (HAIs) from Spain for comparison with other EU Member States is available from the ECDC PPS on HAIs and antimicrobial use in European acute care hospitals 2011–2012. Fifty-nine acute care hospitals in Spain participated in this PPS in 2012, resulting in a mean prevalence of 8.2% for patients with at least one HAI (95% confidence interval: 7.5-9.1%), which was slightly above the EU/EEA average of 6%. In this ECDC PPS, Spain was one of the few countries that conducted a validation study. It showed a sensitivity above 90% for the detection of HAIs and confirmed the good quality of data from Spain. This is probably due to the country’s long experience with national point prevalence surveys of HAIs (EPINE) since the 1990s.

2.3 Antimicrobial consumption

On the basis of the ESAC-Net 2014 data, antimicrobial consumption in humans in the community (outside of hospitals) in Spain would be close to the EU average. These data are, however, based on reimbursed prescriptions whereas the data from most other Member States are based on sales at pharmacies. A study published in 2007 showed that this data source underestimated by approximately 30% the total antimicrobial consumption in humans in the community (*J Antimicrob Chemother* 2007; 60: 698-701). Once this correction was made, Spain appeared as one of the Member States with the highest consumption of antibiotics. Further studies have shown a correlation between antibiotic consumption and AMR (*Enferm Infecc Microbiol Clin* 2010; 28 (Supl 4): 1-3).

Data from ESAC-Net showed a small, but statistically significant, decreasing trend in antimicrobial consumption between 2010 and 2014 (when consumption was expressed as a number of packages - used as a surrogate for prescriptions - per 1 000 inhabitants and per day). Data from the Eurobarometer surveys confirmed this decreasing trend. In 2013, 38% (95% CI: 35–41%) of respondents indicated that they had taken antibiotics during the past year; a decrease of 15 percentage points compared to 2009 (53%, 95% CI: 56–62%). Nevertheless, the most recent Eurobarometer survey shows that this decrease may have been short lived since, in 2016, 47% (95% CI: 44–50%) of respondents indicated that they had taken antibiotics during the past year.

As indicated by the Eurobarometer surveys and similar to most other EU Member States, a large proportion of antibiotics in the community in Spain are taken for viral infections such as common colds, influenza and sore throats. These surveys also indicate that the level of knowledge of the general public about antibiotics and their ineffectiveness against viruses, including colds and influenza, is still below the EU average, even though it increased between 2009 and 2013.

In hospitals, the ECDC point prevalence survey of HAIs and antimicrobial use in European acute care hospitals (the only data available from hospitals in Spain) showed that on average 45% of patients in Spain’s hospitals in Spain received at least one antimicrobial agent, which was significantly above the EU average of 33% and the fifth highest for all EU Member States. In particular, more than 50% prescriptions for perioperative antibiotic prophylaxis exceeded one day, which would correspond to an excessive duration in most cases.

Finally, as reported in the ESVAC report 2014, antimicrobial consumption in food-producing animals in Spain in 2014 was the highest for all EU Member States.

In conclusion, the data on AMR and antimicrobial consumption in Spain indicate a situation that is worse than in most EU Member States.
3. Observations

3.1 Development of an Intersectoral Coordinating Mechanism (ICM)

There is a National Strategic Action Plan to reduce the risk of selection and dissemination of antibiotic resistance in accordance with a ‘One Health’ perspective. The Plan was adopted by a large coordination group in March 2014, and approved by the Interterritorial Council of the National Health System at its plenary meeting on 11 June 2014 and at the intersectoral plenary meeting of the Ministry of Agriculture, Food and the Environment on 8 July 2014. The Plan is structured around six priority areas: surveillance, control, prevention, research, training and communication. Measures and actions have been defined in each area, covering human and animal health.

Implementation of the Plan is coordinated by the Spanish Agency of Medicines and Medical Devices (AEMPS), with involvement of all Directorates-General of the Ministry of Health such as the Directorate-General of Public Health and the Directorate-General of Professional Arrangement.

As part of the plan, two large Coordination Groups have been formed:

- a Technical Committee, which is a multidisciplinary group composed of representatives of the official institutions and bodies, including six ministries and a number of scientific bodies and professional organisations specialising in human and animal health (nurses are not represented in this group);
- a Committee of Autonomous Regions, composed of representatives from the different Autonomous Regions.

The Coordination Groups meet twice a year. The coordination groups also have had joint meetings. It is unclear, which of these groups is the Intersectoral Coordination Mechanism for the country.

Although information about who (one identified person/position) was responsible for coordinating and implementing each action of the National Strategic Action Plan, which organisations are contributing, and which Autonomous Regions are participating in each group does exist, it is not publicly available. Patient groups or consumer associations are not involved in the subgroups in charge of communication and activities to raise awareness in the population.

Clear deliverables and deadlines for achieving these deliverables were not presented. A system of indicators to assess the implementation and the outcomes of the National Plan is under development.

There does not seem to be a specific national budget for implementing the actions in the National Strategic Action Plan.

3.2 Organised multidisciplinary and multisectoral collaboration at local level

During our short visit to Spain, we were presented with many examples of excellent organised multidisciplinary collaboration at all levels of the regional health systems (regional, district and primary care/hospital level). Some examples appear below.

- The Institutional Programme for the Prevention and Control of Healthcare-Associated Infections and Appropriate Use of Antimicrobials (PIRASOA) in Andalusia. This programme includes the monitoring 171 indicators on antibiotic use in primary care and hospitals and on infection prevention and control in hospitals, to provide information on achievements and shortcomings. It also includes activities on CPE laboratory diagnosis and control. Other Autonomous Regions have implemented similar antimicrobial stewardship programmes (PROA) in primary care and in hospitals.
- The Microbiological Surveillance Network from the Autonomous Region of Valencia (RedMIVA) for AMR surveillance and alert, in all healthcare facilities including long-term care facilities (LTCFs);
- ‘Resistencia Zero’ project in intensive care units (ICUs) promoted and coordinated by the Ministry of Health, Social Services and Equality in collaboration with Autonomous Regions, since 2008, and led from a technical perspective by the Spanish Society of Intensive Care Medicine, Critical Care and Coronary Units (SEMICYUC). This project and the previous ‘Bacteraemia Zero’ and ‘Neumonia Zero’ projects, include clinical bundles and activities performed according to patient safety methods in order to increase the safety culture among healthcare professionals. These projects have been very successful in terms of participation and promoting a decrease in HAIs and AMR in ICUs in Spain.
- A plan for prevention and control of infections due to CPE in the Autonomous Region of Madrid that was adapted and implemented at hospital level. This regional plan includes the review by health authorities of each local hospital plan to ensure that the planning and measures taken are in line with the recommendations.
- Mandatory reporting and alert system for CPE in the Autonomous Region of Madrid.
- In primary care, systems with electronic prescriptions with integrated guidelines, pop-up alerts; individual meetings and training with prescribers. Furthermore, these were tied to incentives for both the primary care centre and individual doctors.
• In primary care and in hospitals, financial incentives for prescribers to achieve targets related to prudent use of antibiotics through contracts between health authorities and healthcare facilities (as part of a general system of individual objectives related to activity/performance and quality of care).

These multidisciplinary programmes adopted a medical/clinical approach, with objectives regarding improvement of clinical outcomes together with process indicators such as quality and quantity of antibiotic use. They comprise educational measures (training, elaboration and dissemination of guidelines), feedback to prescribers, evaluation and development of an appropriate computerised system enabling education, access to information on individual prescribing data, etc. However, collaboration with private doctors and dentists is rarely mentioned.

In many instances, these initiatives have contributed to raising awareness about prudent use of antibiotics and AMR, to improving antibiotic prescribing practices and reducing the incidence of infections resulting from multidrug-resistant organisms (MDROs).

3.3 Laboratory capacity

The clinical microbiology laboratory that we visited was equipped to perform bacterial identification and antimicrobial susceptibility testing on bacteria from clinical microbiology samples and rapid identification of MDROs in accordance with current standards. This laboratory was accredited for a large number of tests.

In the hospitals that we visited, we saw evidence of timely delivery of preliminary and final laboratory results that influence patient care and implementation of infection control measures. This also applies to samples sent by primary care centres and LTCFs.

At the regional level, there was evidence in Andalusia that reference laboratory support was integral to PIRASOA activities. At national level, there is a reference laboratory, hosted by the Instituto de Salud Carlos III (ISCIII), performing confirmation of resistance mechanisms and molecular typing of isolates in order to understand and hopefully curb outbreaks.

3.4 Monitoring of antibiotic resistance

AMR surveillance is well developed at national, regional and local level. Spain participates in EU surveillance (EARS-Net) via a network of 40 sentinel hospitals covering about one third of the population in the country. These hospitals were selected according to the initial recommendations provided by the EARSS project when it started. Nevertheless, due to the small number of participating hospitals it is difficult to determine whether the results for Spain in EARS-Net are representative of the situation in the whole country.

There is no national AMR surveillance system other than that mentioned above.

Additional AMR data for healthcare-associated infections (HAIs) are available:

• for acute care hospitals from the yearly EPINE point prevalence surveys,
• for ICUs via the ENVIN-HELICS surveillance system.

Multidrug-resistant organisms (MDROs) such as CPE have been reported to the national reference laboratory on a voluntary basis since 2009. As of February 2016, it was not mandatory to report CPE and other MDROs to the national notification system for communicable diseases. Colistin resistance of CPE is not always reported.

In the absence of a consensus on how to screen patients exposed to a CPE-positive patient, the total burden of CPE (infected patients and colonised/carrier patients) is unknown.

At regional level, antibiotic resistance data are available through systems developed by health authorities (e.g. RedMIVa) or from laboratories at university hospitals that are reference laboratories for the region (e.g. in Andalusia, in relation to PIRASOA).

3.5 Monitoring of antibiotic usage

National data on antibiotic consumption in primary care are available and these data are reported to the EU through ESAC-Net. However, these data only relate to reimbursed prescriptions under the national health system, and do not include private prescriptions and antibiotics dispensed without a prescription. In one study from ten years ago, the authors concluded that this led to an underestimation of about one third of total antibiotics sales in primary care across the country. In February 2016, there was no recent study comparing reimbursement and sales data on antibiotics. Sales data reported by the pharmaceutical industry to the AEMPS are not used for surveillance or comparison with reimbursement data.

Data on antibiotic use in the hospital sector may be available in some hospitals and regions – for example, as part of the project ‘Surveillance of Nosocomial Infections in Hospitals in Catalonia’ (VINCat). However, in February 2016, these data were not compiled at national level.
Prevalence data on antibiotic use in patients at Spanish hospitals are available from the yearly EPINE point prevalence surveys.

In the Autonomous Regions that we visited, antibiotic prescription data are available per prescriber, with information on indication/clinical diagnosis. Healthcare centres and individual prescribers are given regular feedback on their antibiotic prescription level for selected indicators and meetings are organised with prescribers to discuss these results. These activities maintain a high level of mobilisation towards the prudent use of antibiotics among prescribers.

In veterinary medicine, a specific system - ESVAC-ES – has been developed and is used to report antimicrobial consumption data at EU level to the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project at the European Medicines Agency. The ESVAC-ES online system allows for reporting sales of antimicrobials by pharmaceutical companies, wholesalers, retailers and pharmacies. Its future development will include prescription of antimicrobials by veterinarians with access to information on available antibiotics (Vademécum). The database will then include information on prescribing veterinarian, farm, and species treated.

### 3.6 Antibiotic utilisation and treatment guidance

Discussions with experts during the visit indicated that the level of antibiotic dispensing at pharmacies without a medical prescription may have decreased, but we have not been shown data to confirm this.

There are no national guidelines for the treatment of infections. There are, however, guidelines in some of the Autonomous Regions and they have sometimes been integrated into the electronic patient journal system to appear when initiating a prescription.

We saw evidence of guidelines in primary care and in hospitals. Compliance of prescribers with the guidelines is assessed as part of the feedback given to family doctors in some of the regions. Training in relation to the guidelines is enhanced through counselling interviews based on case studies.

Rapid tests (e.g. diagnostics for Strep A tonsillitis) were generally not available at the primary care centres that we visited. This was mentioned by several family doctors as an area that through improvement could improve prescribing and patient care.

### 3.7 Infection control

In the hospitals that we visited, the components of an infection prevention and control (IPC) infrastructure were in place, including the presence of an Infection Control Committee and an infection control team from the preventive medicine department. Surveillance of HAIs, such as surgical site infections, or surveillance of HAIs in ICUs was implemented. However, the infection control team has a broad mandate including not only IPC but also vaccination of immunocompromised patients, and personnel and funding seems to be too stretched to provide adequate IPC services.

A national hand hygiene programme, promoted by the Ministry of Health Social Services and Equality, in coordination with all the Autonomous Regions, was launched in Spain in 2008. However, implementation depends on regional health authorities and the level of adherence and implementation may vary between the Autonomous Regions. During the visit, we saw no evidence of regional or local hand hygiene strategies. We were made aware of a previous national campaign that ended in 2012 and the levels of compliance with hand hygiene appear to be decreasing. Alcohol-based hand rub was available in the hospitals and units that we visited. However, its location and accessibility was highly variable, which in many instances did not promote good hand hygiene practices. We saw widespread evidence of healthcare personnel wearing wristwatches and hand/wrist jewellery in clinical areas. We also heard evidence of the need for culture change among healthcare professionals.

Hand hygiene programmes are one of the areas audited in teaching hospitals by the Ministry of Health Social Services and Equality and reports on hand hygiene performance indicators are available from the Ministry's website. These audits show that adherence to recommendations may vary among the Autonomous Regions. Some hospitals/units may perform periodic audits of hand hygiene practices or may monitor the volume of alcohol-based hand rub products, but without a clear strategy on how to use the results or plan action to improve compliance with hand hygiene practices.

In the hospitals and units that we visited, there was an awareness of the need for contact precautions in relation to MDROs, and the appropriate personal protective equipment was available for use outside of the rooms housing patients with MDROs. Nevertheless, in some of the high-risk areas visited, we saw patients requiring contact precautions who were not in single rooms and not separated from other patients. We also saw sub-optimal placements of patients and variability in the use of transmission-based information signs within units and between units. In the high-risk areas visited, implementation of hospital hygiene measures, and in particular the initiation of contact precautions for MDRO-positive patients to prevent cross-transmission to other patients, were delegated to preventive medicine and infectious diseases specialists. These precautions were not perceived as being part of routine patient management or the responsibility of each individual medical doctor, nurse and other healthcare professional.
In some of the hospitals and units that we visited environmental cleaning was sub-standard and to a level that could promote the persistence and facilitate the spread of MDROs.

Data from one Autonomous Region that we visited and from the ‘Resistencia Zero’ programme show that many patients are already MDRO carriers upon admission because they are transferred from another hospital or ward. This observation underscores the need for timely information on patient MDRO status for those transferred between healthcare facilities and between wards, for the rapid identification of MDRO carriage and implementation of contact precautions for confirmed MDRO carriers and patients at high risk of being MDRO carriers.

3.8 Educational programmes on AMR

At the hospitals and healthcare centres visited, there were good examples of hospital personnel training on AMR and the prudent use of antibiotics, for example:

- training during induction of new personnel;
- specific training on antibiotics for residents;
- training for primary care physicians.

There is no training on AMR or how to use antibiotics as part of the undergraduate education of medical doctors or pharmacists. There is one fee-based postgraduate course.

There is no specific training of nurses working in primary care health centres about prudent use of antibiotics although these nurses could play a role in educating patients, in particular those with chronic illnesses.

3.9 Public information related to AMR

Spain has participated in European Antibiotic Awareness Day (EAAD), each year since 2008, and is using the event to promote its activities, for example:

- A corporate video presenting the National Strategic Action Plan has been published and is still available on the AEMPS website to contribute to raising awareness of the population.
- The AEMPS often attends national scientific society congresses to promote the National Action Plan (25 attendances in 2015). Attendance includes an information stand, distribution of promotional material, and specific arrangements/symposia.
- Specific material (posters, brochures, ECDC antibiotic awareness material) was prepared and distributed to universities to be used for European Antibiotic Awareness Day.
- Merchandise items related to the National Strategic Action Plan against antibiotic resistance were distributed during European Antibiotic Awareness Day.

In the past, Spain has also organised several national campaigns to raise awareness regarding the prudent use of antibiotics. Some of the Autonomous Regions have also run such campaigns. It is worth noting the innovative use of magazines as a medium for engaging the public in one of the regions.

There is a good level of coordination of communication initiatives between the Ministry (Press office and Citizens Affairs department) and the Spanish Agency of Medicines and Medical Devices, especially as regards communication around the National AMR Strategy. There are further plans to involve the relevant services of the Ministry of Agriculture in the activities.

The Spanish Agency of Medicines and Medical Devices is also planning to create a specific website with all the relevant resources and material for the campaign.

3.10 Marketing-related issues

There is long-standing legislation in place to regulate the professional relationships between those who prescribe, dispense and market pharmaceutical agents. Implementation of the law is the responsibility of each Autonomous Region.

A code of practice also exists to provide guidance on financial relationships (e.g. gifts, sponsorship, etc.) A network of regional inspectors visit pharmacies and review prescribing and dispensing data to identify any irregularities or evidence of preferential prescribing.

Feedback from primary care physicians was that because most antimicrobials prescribed in primary care are generic drugs, there is little perceived presence of pharmaceutical representatives promoting antimicrobials in primary care. Feedback from the acute hospital setting indicated a perception that pharmaceutical representatives visited frequently and were particularly keen to meet with junior prescribers.
4. Conclusions and recommendations

4.1 Conclusions

- According to available data from the Spanish surveillance systems, the AMR situation in Spain poses a major public health threat to the country. The current levels of MRSA, ESBL-producing Enterobacteriaceae and Acinetobacter baumannii are high and are above the EU/EEA average. In addition, the rapid increase in carbapenemase-producing Enterobacteriaceae (CPE) over the past five years represents a new threat to the safety of patients in Spanish hospitals and other healthcare facilities. This is also a health security issue since CPE are resistant to almost all antibiotic classes, leaving only a few options for the treatment of infected patients.
- Antimicrobial consumption in primary care and hospitals is among the highest in the EU/EEA and during the visit the ECDC team saw evidence that infection prevention and control (hand hygiene, contact precautions, isolation, environmental cleaning) and environmental cleaning measures vary significantly among hospitals and units. This results in suboptimal control of multi-drug resistant organisms (MDROs) which are spread from patient to patient, either directly via the hands of healthcare workers or indirectly via the environment. This situation contributes to the development of outbreaks in hospitals, with a number of unidentified patients carrying MDROs such as CPE that may spread between hospitals and/or between wards within the same hospital.
- Although CPE and AMR in general are perceived as important issues by the health professionals we met, we noted that the high levels of CPE and AMR observed were sometimes accepted, as if they were unavoidable, and health professionals felt that they had done everything they could – or everything within their remit and resources – to control the spread of CPE. The emergency nature of responding to the threat represented by AMR in general, and CPE in particular, needs to be communicated and understood at all levels in the country, and especially by those working in hospitals and other healthcare facilities.
- Nevertheless, there is commitment and a willingness to discuss AMR issues both at the national level, in the Autonomous Regions that we visited, and among professionals. The fact that there is a broad, comprehensive, structured National Strategic Action Plan, with involvement of all the major actors including six ministries, is also an indication of the commitment to addressing AMR and prudent use of antibiotics in the country.
- There are numerous examples of good practice at regional and local level, and within professional societies. Moreover, the Ministry of Health, Social Services and Equality has been promoting and coordinating prevention and control programmes since 2008. There are also many surveillance and alert systems at national, regional and local level that provide a good picture of antibiotic prescription and generate excellent data to support a response to CPE and other AMR threats. However, it appears that in most cases data produced by these surveillance systems are not used to generate and evaluate targeted action. We also had the impression that there was a lack of clarity as to who was responsible and what needed to be done.
- The Spanish Agency of Medicines and Medical Devices (AEMPS) is in charge of coordinating the implementation of the National Strategic Action Plan and has set up a Technical Committee that involves six ministries. This includes all the Directorates-General of the Ministry of Health, such as the Directorate-General of Public Health and the Directorate-General of Professional Arrangement, as well as many scientific societies and professional organisations working with human and animal health. Moreover, tasks have been distributed to various working groups. However, this may have resulted in a dilution of responsibilities due to the fact that there are so many working groups.
- Spain is divided into 17 Autonomous Regions that are in charge of planning, managing and delivering health services. This is an obvious challenge when attempting to implement the National Strategic Action Plan. Consequently, a Committee of Autonomous Regions, composed of representatives from the different Autonomous Regions, was created to take this into account. This Committee of Autonomous Regions and the Technical Committee represent an opportunity to translate the success of the many initiatives taken at regional and local level, and by professional societies, into successful national initiatives that will ultimately help the National Strategic Action Plan to be realised. The regional implementation of the National Strategic Action Plan offers an opportunity to reduce the heterogeneity in the activities to control AMR developed by the different Autonomous Regions.

4.2 Recommendations

Based on these observations, ECDC’s team recommended the following actions:

- For each action in the National Strategic Action Plan, clearly indicate who is coordinating (person/position), which organisation is contributing, which Autonomous Regions are participating (the list of the latter will increase over time), set out clear deliverables and deadlines, and make this information publicly available on a website with regular, periodical updates on progress.
- The implementation of many actions in the National Strategic Action Plan relies on actions being taken by each Autonomous Region (and ultimately at the local level in each hospital, long-term and primary care facility in the country). Pledges of commitment by the political leadership of the Autonomous Regions are needed, with clear objectives, targets, deadlines and resources for implementation.
- The National Strategic Action Plan should include achievable targets for a selected number of outcome indicators that, when achieved, would clearly indicate how implementation of the Plan has an impact on AMR in the whole country.
- The commitment of the Autonomous Regions should extend to sharing tools, software and expertise (including infrastructural support) from successful initiatives with other regions and encouraging a culture of reciprocity of services and expertise between regions. A mechanism and platform (central, public repository) should be created to share examples of good practice, documents and tools that are produced by the Autonomous Regions that would be helpful to other regions. The mechanism/platform should also include initiatives from professional societies.
- A national hand hygiene programme, promoted by the Ministry of Health Social Services and Equality, in coordination with all the Autonomous Regions, started in Spain in 2008. However, its implementation and the level of compliance with hand hygiene practices in healthcare may vary among the Autonomous Regions. It is vital that Spain urgently evaluates the level and quality of the hand hygiene programmes implemented in hospitals and in the Autonomous Regions. This is an important step towards understanding the failures of previous programmes and assuring the sustainability of any future improvement. This will ensure that Spain fully implements the 2008-2009 WHO Guidelines for Hand Hygiene in Healthcare in all settings where healthcare is delivered. These Guidelines include a programme of education on the five moments and proper technique; availability of hand hygiene products at the point of care; a train-the-trainers approach to hand hygiene education and audit; regular compliance audits within all healthcare facilities; reporting and trend analysis of hand hygiene compliance, integral to and embedded within the patient safety culture of all settings where healthcare is delivered and coupled with the support of ongoing, high-profile national and regional information campaigns aimed at healthcare professionals and service users. Hand hygiene campaigns could also target the general public to promote awareness among all citizens (e.g. with messages highlighting the role of hand hygiene in the prevention of respiratory and gastrointestinal tract infections to reduce the need for antibiotics).
- Classify CPE and its control in Spanish healthcare as a public health emergency. For this, there should be an alert system that includes CPE as a communicable disease for which reporting is mandatory (with necessary epidemiological information and molecular typing information from the national reference laboratory). Mandatory reporting should be approved by all Autonomous Regions through the Interregional Council to ensure notification from local to regional level, and then from regional to national level. Health authorities at the national and regional levels and healthcare facility directors should be made accountable for achieving results (i.e. healthcare facility preparedness, implementation of information systems to identify cases - when transferred and on re-admission, reduction in the incidence of new cases, etc.)
- The creation of a national emergency response team of experts could support the Autonomous Regions in tackling emergency AMR situations, making use of field epidemiologists, expertise from the national reference laboratory and infection prevention specialists with competence in MDRO control to implement AMR control plans effectively.
- Incomplete data on human antimicrobial consumption in Spain is a threat to the representativeness of surveillance data and may impact evaluation of the National Strategic Action Plan’s implementation. Spain should acquire sales data on antibiotic consumption to include private prescriptions as well as the percentage of antibiotic sales without a prescription. Similarly, Spain should obtain data on antimicrobial consumption in the hospital sector and report them at EU-level to ESAC-Net. Sales data collected by the AEMPS could be used for this purpose, at national and regional level.

In addition:
- The mapping exercise of the National Strategic Action Plan should also define which resources are currently available or would be needed to implement the plan. At national level, there is a need for specific funding at least to start implementing the coordination of the actions. At local level, any savings that could be made from good practice (e.g. from prudent use of antibiotics), could be channelled into the reinforcement of prevention and control activities.
- Consider prevention and control of AMR and the prudent use of antibiotics as objectives in the contracts between the Autonomous Regions and hospitals and other healthcare facilities. It could also be considered as a point for accreditation of hospitals.
- Consider the funding necessary to make rapid point-of-care diagnostic tests more available to primary care doctors in order to aid in the prudent prescription of antibiotics at this level.
- Develop national guidelines for the prudent use of antimicrobial agents, including best practices for the diagnosis and identification of clinical situations where antimicrobial agents are not needed.
- Implement training on AMR and prudent use of antibiotics, at both pre-graduate and post-graduate levels, of all healthcare professionals involved in the prescription (doctors), dispensing (pharmacists) and administration (nurses) of antibiotics, as well as the laboratory diagnosis of infections that require antibiotic treatment (microbiologists).
- Given the extent and the scale of the threat posed by AMR in general and CPE in particular, it may be advisable to revisit the scope of practice of preventive medicine specialists in hospitals and scale up the number of these specialists specifically dedicated to infection prevention and control in Spanish healthcare.
- ‘Infectious Diseases’ are not recognised as a medical specialty, meaning that it is not possible to train specialists and this inevitably has an impact on the recruitment of infectious disease physicians in hospitals.
- Finally, to promote transparency towards stakeholders and the general public, the National Strategic Action Plan website (in preparation at the time of the visit) could include information on objectives and results achieved at national and regional level.
5. Annexes

5.1 Country visit team and people met during the ECDC country visit to Spain to discuss AMR issues

ECDC Team

- Dominique L. Monnet, Antimicrobial Resistance and Healthcare-associated Infections (ARHAI) Programme, ECDC, Stockholm, Sweden
- Karen Burns, External expert, National Focal Point for Healthcare-associated infections, National Focal Point (alternate) for AMR, National Focal Point (Alternate) for Antimicrobial Consumption, Dublin, Ireland
- Catherine Dumartin, External expert, CCLIN Sud-Ouest, Bordeaux, France
- Oliver Kacelnik, External expert, Norwegian Institute of Public Health, Oslo, Norway
- Giovanni Mancarella, External Communication Unit, ECDC, Stockholm, Sweden

(only on 15 February)

Persons met

Monday 15 February 2016

Meeting at the Ministry of Health, Social Services and Equality, Madrid: Legal framework, national and multisectoral strategies

Introduction

- José Javier Castrodeza Sanz, General Secretary for Health and Consumers, Ministry of Health, Social Services and Equality;
- Elena Andradas Aragonés, Director General of Public Health, Quality and Innovation, Ministry of Health, Social Services and Equality

Participants

- Ministry of Health, Social Services and Equality (MSSSI): Fernando Simón, Paloma Casado, Yolanda Agra, Berta Suárez, María José Sierra, Angel Luis Guirao García, Carlos Lens
- Ministry of Agriculture, Food and Environment (MAGRAMA): Luis F. Corbalán
- Spanish Agency of Medicines and Medical Devices (AEMPS): Antonio López Navas, Cristina Muñoz Madero, María Dolores Montero Corominas, Sara Sacristán Álvarez
- Instituto de Salud Carlos III (ISCIII): Manuel Cuéllar Estrella, Isabel Noguer, José Campos, Julio Vázquez, Carmen Varela, Pilar Gallego, Rosa Cano, Belén Aracil, Jesús Fernández Crespo
- Autonomous Region of Madrid: María Angeles López
- Spanish Society of Family and Community Medicine (SEMFYC): José María Molero García
- Spanish Society of General and Family Practitioners (SEMG): Mario Bárcena Caamaño
- Spanish Society of Preventive Medicine, Public Health and Hygiene (SEMPSPH): Francisco Botía Martínez
- University Hospital Puerta de Hierro, Madrid (also SEMPSPH): Ángel Asensio
- Spanish Society of Community Pharmacy (SEFAC): Pedro Gutiérrez Ríos
- General Council of Official Colleges of Pharmacists: Iván Espada
- Servicio Técnico, Tecnologías y Servicios Agrarios, S.A. (TRAGASTE): Amaya Sánchez

Presentations

- National context and introduction to the National Health System – Angel Luis Guirao García (MSSSI)
- Legal framework for the use of antimicrobials – Angel Luis Guirao García (MSSSI)
- National Committee for control of antimicrobial resistance and antibiotic use: Strategic plan – Antonio López Navas (AEMPS)
- Antimicrobial consumption and prescription in humans – María Dolores Montero Corominas (AEMPS)
- Antimicrobial use in animal health – Cristina Muñoz Madero (AEMPS)
- Antimicrobial resistance surveillance results – José Campos (ISCIII)
- Results of EPINE national survey: Hospital antimicrobial use and resistance – Ángel Asensio (SEMPSPH)
- HAI national surveillance system proposal – Pilar Gallego (ISCIII)
- Communication and awareness in Spain – Rosa Serrano Laguna (MSSSI)
- Prudent use of antibiotics awareness campaigns – Antonio López Navas (AEMPS)
- Communication and awareness strategies at ECDC – Giovanni Mancarella (ECDC)

Discussions with representatives of professional societies:

- Iván Espada (Consejo General de Colegios Oficiales de Farmacéuticos)
- Ángel Asensio (University Hospital Puerta de Hierro, Madrid, also SEMPSPH)
- Mario Bárcena Caamaño (SEMG)
- José María Molero García (SEMFYC)
Pedro Gutiérrez Ríos (SEFAC)

Discussions on communication and awareness campaigns:

- Angel Manuel Suarez Iglesias, Rosa Serrano Laguna (MSSSI)
- Eduardo Padilla León, Sara Sacristán Alvarez (AEMPS)

**Tuesday 16 February 2016**

**Visit to the Autonomous Region of Andalusia (Public health authorities and hospital)**

**Meeting at University Hospital Virgen del Rocío, Seville**

- Regional public health authority - Josefa Ruiz (Secretary General for Public Health and Consumers, Autonomous Region of Andalusia)
- Hospital authority - Manuel Romero (Director, University Hospital Virgen del Rocío)

**Presentations:**

- PIRASOA programme in hospital – José Miguel Cisneros (Director PIRASOA, University Hospital Virgen del Rocío) and Jesús Rodríguez Baño (Co-director PIRASOA, University Hospital Virgen Macarena)
- PIRASOA programme in primary care – Rocío Fernández Urrusuno (Pharmacy service, Aljarafe-Sevilla Norte Primary Care District)
- Andalusian reference laboratory for molecular typing of nosocomial pathogens and genotypic detection of antimicrobial resistance mechanisms – PIRASOA reference laboratory – Álvaro Pascual (Microbiology laboratory, University Hospital Virgen Macarena).

Also present:

Carmen Montaño Remacha and Javier Guillén Subirán (Epidemiologists, General Secretariat for Public Health and Consumers), María Aránzazu Irastorza (Integrated Planning Service, Andalusian Health Service),, , Rocio Álvarez (Infectious Diseases, University Hospital Virgen del Rocío), Javier Bautista (Pharmacy, University Hospital Virgen del Rocío), Fernando Simón (MSSSI), José Campos (ISCIII)

**Visit to University Hospital Virgen del Rocío, Seville**

Visit to intensive care unit

- Francisco Murillo Cabezas, Head of unit
- Catalina Martín Castaño, Head nurse

Also present: Fernando Simón (MSSSI), José Campos (ISCIII).

**Visit to community pharmacy, Seville**

- Antonio Morón, Community pharmacist

**Visit of primary care health unit Las Palmeritas El Juncal, Seville**

- Inmaculada Gabaldón, Director
- Ignacio Pajares, District medical director
- Eloisa Fernández Santiago, PIRASOA
- Manuel Ortega Calvo, District Health Officer

Also present: Fernando Simón (MSSSI), José Campos (ISCIII).

**Wednesday 17 February 2016**

**Visit to the Autonomous Region of Valencia (Public health authorities and hospital)**

**Meeting at University Hospital La Fe, Valencia**

- Regional public health authority – Ana María García (General Director of Public Health, Autonomous Region of Valencia)
- Hospital authority – Mónica Almiñana (Director, Hospital La Fe)

**Presentations:**

- Microbiological surveillance network in Valencia Community (RedMiVA) – Hermelinda Vanaclocha (Public Health Directorate, Autonomous Region of Valencia)
- Antimicrobial consumption surveillance system in the Autonomous Region of Valencia – Guidelines for antimicrobial use – Lala Buigues Pastor (General Directorate for Pharmacy and Healthcare Products, Autonomous Region of Valencia)
- ‘Resistencia Zero’ programme in the Autonomous Region of Valencia – Paula Ramírez (University Hospital La Fe)
- Strategies for the appropriate use of antimicrobial agents in primary care – Blanca Folch Marín (La Ribera Health Department, for the “Sociedad Valenciana de Medicine Familiar y Comunitaria”).
Also present: Eva Gonzalez, Dolores Gómez, Jose Luis López, Javier Perran, Hector Martínez, Jose Manuel Ventura, Emilio Monte Boquet, Eva Ronne Sanchez, Marta Montero Alonso (Hospital La Fe), Francisco González Morán (Public Health Directorate, Autonomous Region of Valencia), Fernando Simón (MSSSI), José Campos (ISCIII).

**Visit to University Hospital La Fe, Valencia**

Visit to clinical microbiology laboratory
- Jose Luis López Hontangas, Head
- Eva Gonzalez
- Dolores Gómez
- Javier Perran

Visit to intensive care unit
- Alvaro Castellanos Ortega, Head of ICU
- Paula Ramírez, Pdt of infection control committee
- Mario Guardiola Sabater, Nurse, Preventive Medicine

Visit to internal medicine unit
- Marta Montero Alonso

Also present: Fernando Simón (MSSSI), José Campos (ISCIII).

**Thursday 18 February 2016**

**Visit to the Autonomous Region of Madrid (Public health authorities and hospital)**

Meetings and presentations at University Hospital Ramón y Cajal
- Regional public health authority – María José Torijano Castillo (Sub-directorate of Epidemiology, General Directorate of Public Health, Autonomous Region of Madrid)
- Hospital authority – Agustín Utrilla López (Medical Director, University Hospital Ramón y Cajal), Fernando Roldán Moll (Deputy Medical Director, University Hospital Ramón y Cajal)

Presentations:
- Antibiotic use control policy at the Autonomous Region of Madrid – Ainhoa Aranguren Oyarzábal (Sub-directorate of Pharmaceutical Management, General Directorate of Public Health, Autonomous Region of Madrid)
- Action plan for prevention and control of carbapenemase-producing Enterobacteriaceae (CPE) – María Angeles López (Subdirectorate of Epidemiology, General Directorate of Public Health, Autonomous Region of Madrid)
- Microbiology laboratory implementation and standardization of CPE Action Plan – Rafael Cantón (Microbiology Laboratory, University Hospital Ramón y Cajal), on behalf of the technical group of experts that wrote the CPE Action Plan
- Infection control and antimicrobial stewardship at hospital level. Committees and interventions:
  - Infection control committee activities – Nieves López Fresneña and Cristina Díaz-Agero Pérez (Preventive Medicine and Public Health, University Hospital Ramón y Cajal)
  - Antimicrobial stewardship activities – Javier Cobo Reinoso (Infectious Diseases, President of Antibiotic Commission, University Hospital Ramón y Cajal)
  - Antimicrobial consumption. Prescription process and antimicrobial use data –
  - Teresa Bermejo Vicedo (Pharmacy, University Hospital Ramón y Cajal)
  - Antimicrobial resistance rates at University Hospital Ramón y Cajal – María Isabel Morosini and Rafael Cantón (Microbiology Laboratory, University Hospital Ramón y Cajal)
  - Zero programmes at ICU level – Joaquín Álvarez Rodríguez (Medical Coordinator of “Zero” programmes, Autonomous Region of Madrid, and Intensive Care Unit, University Hospital of Fuenlabrada).

Also present: Jenaro Astray Mochales (Subdirectorate of Epidemiology, General Directorate of Public Health, Autonomous Region of Madrid), María José Calvo Alcántara and José Manuel Izquierdo Palomares (Subdirectorate of Pharmaceutical Management, General Directorate of Public Health, Autonomous Region of Madrid), Ángela Rincón Caravilla (Preventive Medicine and Public Health, University Hospital Ramón y Cajal), (Patricia Ruiz Garbajosa (Microbiology, University Hospital Ramón y Cajal), Fernando Simón (MSSSI) and José Campos (ISCIII).

**Visit to University Hospital Ramón y Cajal**

Visit to intensive care unit
- Raoul de Pablo Sanchez, ICU nurse

Visit to infectious diseases unit (incl. TB isolation unit)
- Enrique Navas Elorza, Medical doctor

Also present: Fernando Simón (MSSSI).
Friday 19 February 2016
Preliminary report from the ECDC team to national authorities and stakeholders

- Ministry of Health, Social Services and Equality: Fernando Simón, Paloma Casado, Yolanda Agra, Berta Suarez, María José Sierra;
- Agency of Medicines and Medical Devices (AEMPS): Antonio López Navas;
- Instituto de Salud Carlos III (ISCIII): Manuel Cuenca Estrella, Isabel Noguer, José Campos, Julio Vázquez, Carmen Varela, Pilar Gallego, Rosa Cano, Belén Aracil;
- Autonomous Region of Andalusia: Carmen Montaño;
- Autonomous Region of Valencia: Hermelinda Venaclocha;
- Autonomous Region of Madrid: Jenaro Astray;
- University Hospital Puerta de Hierro, Madrid (also Spanish Society of Preventive Medicine, Public Health and Hygiene – SEMPSPH): Angel Asensio
- Spanish Society of Family and Community Medicine (SEMYC): Javier Muñoz Gutiérrez;
- Spanish Society of Community Pharmacy (SEFAC): Fernando Cantalapiedra;

Servicio Técnico, Tecnologías y Servicios Agrarios, S.A. (TRAGSATEC): Amaya Sánchez
5.2 Assessment tool for ECDC country visits to discuss antimicrobial resistance (AMR) issues

The mechanisms behind emerging AMR are complex. However, two main issues that stand out offering opportunity for control efforts are: the use of antibiotics and the epidemiological spread of resistant microbes.

The complexity of the problem makes it difficult to grade which interventions are most successful. Where interventions have been introduced few of them have been evaluated. This may partly be because few systematic interventions have been used.

The Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) lists a number of areas that have an impact on controlling AMR. Most of the following tentative indicators are based on the Council Recommendation. Some are based on experience from different countries. These indicators are either structure- or process-related. Outcome indicators are collected by dedicated surveillance networks.

1. Development of an Intersectoral Coordinating Mechanism (ICM)

Due to the complexity of the issue there is a need for coordination to make an interventional strategy work. There is also a need for close cooperation from fields such as epidemiology, microbiology clinical medicine, infection control, veterinary medicine, pharmacology and behavioural sciences. It also requires cooperation from practitioners working in different medical specialities as well as government departments and healthcare providers.

In the Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) and the World Health Organization (WHO) Global Strategy for Containment of Antimicrobial Resistance (WHO/CDS/CSR/DRS/2001.2) the establishment of a coordinating group is regarded as essential.

Member States have different administrative organisations. There should be a group at the highest administrative level where representatives from regulatory bodies and professionals from the different sectors coordinate.

Tentative indicators for 1

Structures
- Multidisciplinary composition
- Regular meetings
- Minutes from meetings
- National strategy plan available
- Defined governmental mandate
- Financially supported by government.

Functions
- Coordinates analysis of consumption and plans and supports interventions
- Proposes national objectives and policies
- Proposes, plans and supports interventions
- Provides policymakers, media and public with continues updated and structured data
- Provides support to local working groups.

2. Organised multidisciplinary and multisectoral collaboration at local level

One of the main elements for control strategies is to lower the selective pressure of antibiotics by restricting usage to appropriate indications. There is much evidence showing that antibiotics are overused. Prescribers need to be well acquainted with the AMR problem and the rational of using antibiotics appropriately.

A non-regulatory intervention that has had some influence on prescribing habits is a local activity whereby practising physicians discuss local data on consumption and bacterial resistance patterns, supported by epidemiologists, pharmacists and infection control. This proves to be an appropriate opportunity to revise local usage patterns, develop local guidelines (based on national guidelines) and organise local meetings with prescribers to promote rational use of antibiotics. In addition, topical issues can be discussed, such as problems related to MRSA or Clostridium difficile 027.

Practising doctors have limited time available. It is essential that there is a good collaboration with and support from the national/regional group to provide background data and help with scientific updates.
Tentative indicators for 2

General

Structures
- Are there local activities in some places?
- Are there nationally disseminated local activities?
- Are activities in hospitals and primary healthcare coordinated at the local level?

Primary health care

Structures
- Are there local activities in primary health care?
  - If yes:
    - Mostly multidisciplinary
    - Private practitioners are taking part
    - Have access to local surveillance data on AMR
    - Have access to local antibiotic consumption data
    - Have public funding
    - Meet regularly.

Functions

Primary areas of work are:
- Infection control
- Diagnostic practices/habits
- Analysis of local consumption and resistance data
- Educational activities
- Coordination of interventions
- Provide local guidelines
- Convene local meetings with prescribers at least once a year.

Hospitals

Structures
- Are there local activities in hospital health care?
  - If yes:
    - Mostly multidisciplinary
    - Have access to local surveillance data on AMR
    - Have access to local antibiotic consumption data
    - Have public funding
    - Meet regularly.

Functions

Primary areas of work are:
- Infection control
- Diagnostic practices/habits
- Analysis of local consumption and resistance data
- Educational activities
- Coordination of interventions
- Provide local guidelines
- Convene local meetings with prescribers at least once a year.

3. Laboratory capacity

Laboratory capacity is essential for many reasons:
- To be able to follow trends in antimicrobial resistance;
- To discover newly emergent resistant strains;
- To enable prescribers to make informed antibiotic choices. For this there is a need for timely feedback to clinicians.

It is important to characterise isolates that may have clinical importance. Often this cannot be done in all laboratories so a referral system to specialised laboratories should exist.

All laboratory work should be quality assessed regularly.
Tentative indicators for 3

General

Structures
- How many diagnostic laboratories are appropriately equipped for microbiological diagnostic work (minimum requirement: performance of gram-stain, aerobe culture and antimicrobial susceptibility testing)?
- What proportion of microbiological laboratories have at least one specialist clinical/medical microbiologist?
- Is there a formal referral structure to reference laboratories supported by public (alternatively through insurance system or equivalent) funding?
- Does a national external quality assessment scheme exist?
- Does an accreditation system exist for microbiological laboratories that requires regular QC and EQA?

Hospitals

Functions
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) via telephone or clinical rounds to the submitting clinician within the first 12 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) via telephone or clinical rounds to the submitting clinician within the first 24 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provides species identification of blood culture isolates to the submitting clinician?
- Who pays for the analysis of samples sent in?

Out patients

Functions
- What proportion of general practitioners can submit clinical specimen for microbiological investigation to an appropriately equipped microbiological laboratory within 12 hours?
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) to the submitting clinician within the first 24 hours of receiving diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 hours of receiving a diagnostic specimen?
- Who pays for sent in sample analysis?

4. Monitoring of antibiotic resistance

Resistance patterns should regularly be followed. This should be done using a standardised method. The method should be quality assessed on a regular basis.

To be able to guide prescribers in prudent usage of antibiotics, surveys of different clinical conditions should be carried out to define which pathogens and their susceptibility profiles for antibiotics. The resistance pattern may vary from area to area so local monitoring may be needed.

Data should be gathered nationally and internationally to follow long term trends.

Tentative indicators for 4

- Local, time limited studies have been performed
- Local continuous, monitoring is done in a few laboratories
- Are duplicates excluded?
- National monitoring with standardised methodology on clinically and epidemiologically relevant bacterial pathogens is on-going
- Country wide local monitoring with standardized methodology in communities and hospital unites is on-going
- Data from hospitals and out-patient settings are treated separately
- Data collection is financially supported by government
- Regular surveys of resistance patterns for pathogens in population based syndromes are performed
- Regular feedback of resistance patterns to prescribers and local groups is given.
5. Monitoring of antibiotic usage

As antibiotic usage is the driving force for emerging resistance it is important to monitor usage. Therefore, reliable surveillance systems of antibiotic consumption are essential to complement antibiotic resistance data and develop instruments for assessing effective strategies to foster appropriate antibiotic use in all European countries.

Current antibiotic use surveillance systems are mostly monitoring trends and shifts in usage patterns. However, to deepen our understanding of antibiotic prescribing, more detailed information is needed on patients’ age and gender, the prescriber, the indication and pathogen. Although prescriber data are felt as sensitive, this kind of data can be used for the self-assessment. Aggregated data may be used for local group discussions.

**Tentative indicators for 5**
- Are valid national data on outpatient antibiotic use available?
- Are valid national (or at least representative sample) data on hospital antibiotic use available?
- Is collection of data on antibiotic use legally supported?
- Is data collection financially supported by the government?
- Are data available per prescriber/clinical diagnosis/micro-organism?
- Is there regular feedback of prescription patterns to prescribers?
- Are anonymous data fed back to local groups?

6. Antibiotic utilisation and treatment guidance

Antibiotics should be used properly. ‘Proper use’ is a difficult term both in human and veterinary medicine. There is still a need to find some common view on what is ‘proper’. Guidelines are a way of agreeing locally or nationally.

Antibiotics allow treatment of serious bacterial infections. The largest volume of antibiotics is prescribed in ambulatory care. This use is increasingly recognised as the major selective pressure driving resistance, which in turn makes them ineffective. Therefore antibiotics should be used appropriately - i.e. (no) antibiotics for those who will (not) benefit from the treatment. In addition, unnecessary use of antibiotics requires more resources, motivates patients to re-consult and exposes them to the additional risk of side effects, whereas under-prescribing could be associated with higher risk of complications of untreated infections.

A ‘proper’ level of usage is difficult to define. The levels are mostly for following trends and shifts in usage patterns. With these data related to other data there might be a way of defining a ‘proper’ range of usage. One benchmark value at European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. Individual countries should position themselves and define their own benchmark. This should be based on the epidemiology of infectious diseases and national guidelines. A range of acceptable antibiotic use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Most guidelines define treatment for specific diagnosis. This means that the diagnosis has to be made correctly before guidelines are applicable.

That also means that antibiotic usage must be directed by medical diagnosis and decisions. This is why systemic antibiotics are prescription-only medicines in the European Union.

**Tentative indicators for 6**
- Availability of OTC (over-the-counter) antibiotics
- Availability of national treatment guidelines
- Availability of locally adapted treatment guidelines
- Has the compliance to guidelines been assessed?
- Defined standardised criteria for clinical diagnosis
- What is the rate of laboratory diagnostics use before deciding on use of antibiotics for sore throat (% of patients)?
- What is the rate of blood cultures before use of antibiotics for perceived bacteraemia with sepsis (% of patients)?
7. Infection control

Healthcare and hospitals in particular have historically been a major source of spread for epidemics. This has been shown for a wide variety of microbes – for example smallpox and early outbreaks of Lassa fever. A recent well-known example is SARS. Another very well-known bacterium that spreads in healthcare settings is MRSA.

All hospitals have defined procedures and hygienic principles although these may not always be based on the latest scientific knowledge. Implementation of guidelines and adherence to procedures is another problem. Surveys have shown that adherence to infection control guidelines many times is poor.

More and more people with complicated medical conditions are given home-based care. Many of them are elderly. Such patients may have indwelling catheters, a lower immunity and often use antibiotics. Infection control guidelines are difficult to follow in a home setting and many of the care staff have little or no training in infection control. Increasingly MRSA is reported to also be a problem in these settings.

Tentative indicators for 7

**General**
- Is there a national committee on issues related to infection control?

**Hospitals**
- Alcohol-based hand disinfection recommended for non-diarrhoeal disease
- Guidelines for hygienic procedures including standardized barrier precautions in >90% of hospitals
- Specific guidelines for MRSA in >90% of hospitals
- At least one infection control nurse/doctor per hospital
- Time allocated for infection control?
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in ICUs? (% of hospitals)
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in surgical wards? (% of hospitals)
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in internal medicine wards? (% of hospitals)
- Are there legal requirements for infection control system in hospitals?
- Is implementation of infection control practice regularly evaluated?

**Healthcare settings outside hospitals**
- Alcohol-based hand disinfection recommended for non-diarrhoeal disease
- Alcohol-based hand disinfection available in >90% of outpatient clinics
- Alcohol-based hand disinfection available in >90% of health care settings for elderly
- Guidelines for infection control are available for elderly and long term care staff
- Implementation of infection control practice in elderly and long term care is regularly evaluated.

8. Educational programmes on AMR

Understanding the problem with AMR is the basis for having an impact with interventional programmes. This can partially be achieved with educational programmes. Educational programmes should be an integrated part of undergraduate studies. All healthcare-related professionals need to have an understanding of the AMR problem.

‘Education’ in the context of AMR is more than just pharmacology of antibiotics or resistance patterns in microbes. It encompasses the relationship between microbes, antibiotics and the epidemiology of resistant strains. It describes the complex interrelation between all aspects brought up in this document.

Regular, repetitive, independent educational material best provided by locally-based colleagues in discussion groups seems to be one of the better success factors.

Tentative indicators for 8

- Doctors have in their curriculum AMR as undergraduate course
- Hospital health care workers have some education on AMR
- Community health care workers have some education on AMR
- Specific post-graduate courses for doctors in antibiotic resistance are provided
- Regular educational programmes in antibiotic resistance are provided for health staff
- It is compulsory for all prescribers to take part regularly in a session on AMR
- <60% of information on AMR is industry sponsored.
9. Public information related to AMR

Many prescribers blame patients for demanding antibiotics irrespective of their condition. This can only be changed if the public is well informed about what antibiotics can and cannot do. Hence, educational activities for the wider public are important.

Tentative indicators for 9

- No information provided
- Topic sometimes covered in media
- Some material for media and/or internet from official sources
- Occasional national campaigns
- Repeated, structured national campaigns
- Regular, structured information provided by professional bodies
- Public perception assessed.

10. Marketing related issues

Economics also have an impact on prescribing habits, irrespective of diagnosis or best practice. This should be discouraged.

Tentative indicators for 10

- Independent (not industry supported) drug information is available
- Ethical guidelines for interrelation between physicians and industry are in place
- Physician's prescriptions do not influence on physician's salary
- Personal gifts from industry to physicians are illegal.
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