



MISSION REPORT

ECDC country visit to Luxembourg to discuss antimicrobial resistance issues

29 May-2 June 2017

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This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Anke Kohlenberg.

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This report was sent for factual comments to the Ministry of Health, Coordination of the National Antibiotic Plan, Luxembourg.

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Contents

Abbreviations	iv
Summary	1
Rationale and purpose of the country visit.....	1
Conclusions	1
Options for action	2
1 Background	3
1.1 Rationale for country visits to discuss antimicrobial resistance issues	3
1.2 Purpose.....	3
2. Overview of the situation in Luxembourg.....	4
2.1 Antimicrobial resistance	4
2.2 Healthcare-associated infections.....	4
2.3 Antimicrobial consumption	4
3. Observations	6
3.1 Development of an Intersectoral Coordinating Mechanism (ICM)	6
3.2 Organised multidisciplinary and multisectoral collaboration at local level.....	6
3.3 Laboratory capacity	6
3.4 Monitoring of antibiotic resistance.....	7
3.5 Monitoring of antibiotic use	7
3.6 Antibiotic utilisation and treatment guidance.....	8
3.7 Infection control.....	8
3.8 Educational programmes on antimicrobial resistance	9
3.9 Public information related to antimicrobial resistance.....	9
3.10 Marketing-related issues	10
4. Conclusion and recommendations.....	11
Conclusions	11
Options for action	11
5. Annex	13
Assessment tool for ECDC country visits to discuss antimicrobial resistance issues	13
1. Development of an Intersectoral Coordinating Mechanism (ICM)	13
2. Organised multidisciplinary and multisectoral collaboration on local level.....	13
3. Laboratory capacity.....	15
4. Monitoring of antibiotic resistance	15
5. Monitoring of antibiotic usage	16
6. Antibiotic utilisation and treatment guidance	16
7. Infection control	17
8. Educational programmes on antimicrobial resistance	17
9. Public information related to antimicrobial resistance	18
10. Marketing related issues	18

Abbreviations

AMR	Antimicrobial resistance
ARHAI	Antimicrobial Resistance and Healthcare-associated infections Disease Programme
CPE	Carbapenemase-producing <i>Enterobacteriaceae</i>
DDD	Defined daily doses
EAAD	European Antibiotic Awareness Day
EARS-Net	European Antimicrobial Resistance Surveillance Network
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility testing
GNPIN	Groupe National de Guidance et de Prévention de l'Infection Nosocomiale
GP	General practitioner
HAI	Healthcare-associated infection
IC	Infection control
ICM	Intersectoral Coordinating Mechanism
ICU	Intensive care unit
LNS	Laboratoire National de Santé
MDRO	Multidrug-resistant organisms
MRSA	Meticillin-resistant <i>S. aureus</i>
PPS	Point prevalence survey
RDD	Recommended daily doses

Summary

Rationale and purpose of the country visit

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

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for and is carrying out, upon invitation from national authorities, country visits to specifically discuss and assess the situation of the country regarding prevention and control of AMR through prudent use of antibiotics and infection control. These country visits also help document how Member States have approached this implementation and ongoing national activities to support the European Commission in evaluating this implementation.

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

Following an official invitation by the Ministry of Health in Luxembourg, an ECDC team conducted visits and meetings to discuss AMR issues in the country with the overall objective of providing an evidence-based assessment of the situation in Luxembourg regarding prevention and control of AMR through prudent use of antibiotics and infection control. This country visit was conducted as a joint One Health AMR country visit together with a team from the European Commission's Directorate General for Health and Food Safety.

Conclusions

Antibiotic consumption in Luxembourg is at the EU average in hospitals, but higher than the EU average in the community. There may have been a small decrease in antibiotic prescriptions in the community since 2013 but this trend needs to be confirmed in the coming years. There has also been a 30% decrease in antibiotic prescriptions in children between 2006 and 2015.

The AMR levels in bacterial isolates from humans are at or below the EU average. According to The European Antimicrobial Resistance Surveillance Network (EARS-Net), the percentage of *S. aureus* bloodstream infections that are methicillin-resistant (i.e. MRSA) decreased slowly between 2012 and 2015. However, looking at the increasing trends of multidrug-resistant *Escherichia coli* from EARS-Net, there is a concern for more serious AMR problems in the future. Moreover, national experts and professionals are also concerned by the increasing number of cases of extended spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* in hospitals, and, in one hospital that we visited, by the increasing use of last-line antibiotics such as carbapenems, as well as the slow emergence of carbapenemase-producing *Enterobacteriaceae* (CPE).

There are multiple sources of data on AMR and on antimicrobial consumption at the national and local level in hospitals that are currently not consistently used by national and local experts for further analysis, and to implement and evaluate targeted interventions to prevent and control AMR.

Cross-border issues seem to have a greater importance in Luxembourg than in many other EU Member States. Firstly, patients are transferred across borders from Luxembourg to other countries and back to Luxembourg. These transfers could for example be necessary because certain medical procedures cannot be provided in the country, and this risks importing multidrug-resistant bacteria. Secondly, a large proportion of the population has connections with other countries and travels back and forth between Luxembourg and their country of origin. These persons may have different expectations about the need for antibiotics for common infections. Thirdly, medical doctors and other healthcare professionals usually train in neighbouring countries where they may be taught varied clinical and prescribing practices. While these cross-border aspects represent a challenge for Luxembourg, they could also be considered as an incentive to exchange best practices and foster cross-border collaboration.

Patients are often transferred between long-term care facilities and hospitals. As reported by acute care hospitals, long-term care facilities may represent an uncontrolled reservoir of multidrug-resistant bacteria.

Luxembourg is in a position to reverse the above-mentioned emerging AMR trends. In the past years, Luxembourg has implemented several good actions at the national or local level, often driven by personal initiative and efforts of a few dedicated professionals. This can be seen as the first phase of a process, which now needs official status, national coordination, enhanced collaboration, and support to ensure sustainability and meet future challenges.

Options for action

Based on the observations and conclusions, the ECDC proposes the following actions:

- Completion of the National Antibiotic Plan 2018–2020, in a One Health perspective in collaboration with the Veterinary Administration, to provide an overarching framework for all activities related to AMR prevention and control and ensure the continuity and sustainability of envisaged activities by providing adequate funding and staffing. In particular, there is a need to establish a permanent National Committee or Intersectoral Coordinating Mechanism (ICM) and a clearly defined role for the 'Groupe National de Guidance et de Prévention de l'Infection Nosocomiale' (GNPIN) as part of this ICM.
- Strengthening and centralisation of surveillance and response to AMR by creating a national epidemiological team responsible for:
 - Harmonising data collection activities providing a reference dataset and, possibly, tools to facilitate data collection in hospitals or for other providers (e.g. long-term care facilities);
 - Providing centralised and combined data analysis and reporting of AMR, antimicrobial consumption and healthcare-associated infections;
 - Defining events and multidrug-resistant organisms (MDRO) to be considered for mandatory notification;
 - Performing outbreak investigations and control activities;
 - Preparing one single comprehensive annual report.
- The minimum areas of expertise to be covered by this national epidemiological team are epidemiology, statistics and bioinformatics.
- Defining a list of a minimal set of indicators for antimicrobial consumption, AMR, healthcare-associated infections (HAI) and compliance to hand hygiene and identify proper benchmarks. When possible provide indications about the level of disaggregation of the analysis; for example, antibiotic use at community level by region, age, gender, type of patient (residents vs. non-residents), type of provider (generalist vs. specialist), etc. For some indicators it would be possible to set targets (e.g. antibiotic use in the community).
- Increasing the efforts into defining the epidemiology of CPE in Luxembourg and use of this information for the implementation of control measures.
- Review and take advantage of the multiple current sources of electronic data and implementation of the electronic patient record.
- Establishing national surveillance of surgical site infections.
- Review, update and dissemination of the national guidelines for prevention and control of MDROs.
- Providing national guidelines for treatment of common clinical infections and for surgical prophylaxis by developing (or updating existing) Luxembourg-specific guidelines or adapting guidelines from other countries and defining steps for their implementation.
- Coordination of regional/local initiatives and provision of a forum for exchange of best practices, experiences and materials, including guidance documents and software tools.
- Provision of education on AMR and antibiotic prescribing for medical doctors, for example by including them into a mandatory continuing professional education programme.
- Continuation of the national public awareness campaign on the prudent use of antibiotics, targeting not only the general public but also expanding and reaching other target audiences such as medical doctors, nurses and other hospital staff who have responsibility regarding antimicrobial treatment. Pharmacists also have an important role in reducing antimicrobial use and could be targeted by using ECDC's communication toolkit for the general public, focusing on self-medication.
- Continuation of the national campaign on hand hygiene, ensuring that the campaigns about prudent use of antibiotics and hand hygiene are in line and support each other.
- Implementation of education materials from e-Bug in schools in Luxembourg.
- Increasing the availability of infectious disease expertise in all hospitals.
- Involving long-term care facilities in the surveillance and control efforts for AMR.
- Enhancing cross-border collaboration on the prevention and control of AMR.

1. Background

1.1 Rationale for country visits to discuss antimicrobial resistance issues

In November 2011, the European Commission published a new 5-year **Action plan against the rising threats from antimicrobial resistance** with the aim to address AMR through the implementation of a coordinated approach in all concerned sectors (public health, animal health, food safety, environment, etc.), and strengthening and further developing EU initiatives against AMR and healthcare-associated infections (HAI) at EU and international levels. The new cross-sectorial approach was further strengthened in June 2012 with the adoption of the Council Conclusions on the impact of antimicrobial resistance in the human health sector and in the veterinary sector – a “One Health” perspective which call upon the Member States to step up measures on the prevention and control of AMR and HAI, and to develop inter-sectoral cooperation.

The mission of ECDC, 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 the official invitation by the Ministry of Health an ECDC Team was in Luxembourg from 29 May to 2 June 2017 to conduct visits and meetings to discuss AMR issues with the overall objective to provide an evidence-based assessment of the situation regarding prevention and control of AMR through prudent use of antibiotics and infection control.

1.2 Purpose

The Council Recommendation of 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 for a range of actions to be taken for its prevention and control. The Council Conclusions on antimicrobial resistance of 10 June 2008 reiterated this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for and is carrying out, upon invitation from national authorities, country visits to specifically discuss and assess the situation of the country regarding prevention and control of AMR through prudent use of antibiotics and infection control. These country visits also help to document how Member States have approached this implementation and deployed national activities, and support the European Commission in evaluating this implementation.

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

The country visit to Luxembourg was conducted as a joint One Health AMR country visit together with a team from the European Commission’s Directorate General for Health and Food Safety Unit F5. The ECDC team for the country visit consisted of Dominique L. Monnet, Head of ECDC’s Antimicrobial Resistance and Healthcare-associated infections (ARHAI) Disease Programme, Anke Kohlenberg, ECDC ARHAI expert, and two experts from EU Member States: Catherine Dumartin (France) and Carlo Gagliotti (Italy), as well as Andrea Nilsson (ECDC communication expert, only on 29-30 May 2017). At national level, the visit was coordinated for Luxembourg by Valérie Guérin, Coordinator of the National Antibiotic Plan, Ministry of Health.

2. Overview of the situation in Luxembourg

2.1 Antimicrobial resistance

For key indicator bacteria-antibiotic combinations reported to the European Antimicrobial Resistance Surveillance Network (EARS-Net), Luxembourg is among the Member States with levels of AMR below the EU/EEA population-weighted mean. However, time trends are not easy to determine as the proportions of resistant isolates fluctuate significantly from one year to another due to the low number of isolates reported for each bacterium.

Table 1. AMR of key indicator bacteria in Luxembourg, 2013–2015 (Source: EARS-Net)

Bacterium-antibiotic combination	2013			2014			2015		
	N	% R	95%CI	N	% R	95%CI	N	% R	95%CI
<i>Staphylococcus aureus</i> - meticillin	135	8.9	(5–15)	125	12.0	(7–19)	135	8.9	(5–15)
<i>Enterococcus faecium</i> - vancomycin	19	5.3	(0–26)	31	3.2	(0–17)	23	0.0	(0–15)
<i>Escherichia coli</i> - 3 rd -generation cephalosporins	301	10.6	(7–15)	368	12.0	(9–16)	347	12.7	(9–17)
<i>Escherichia coli</i> - carbapenems	295	0.0	(0–1)	368	0.3	(0–2)	347	0.0	(0–1)
<i>Klebsiella pneumoniae</i> - 3 rd -generation cephalosporins	53	34.0	(22–48)	66	34.8	(24–48)	60	28.3	(17–41)
<i>Klebsiella pneumoniae</i> - carbapenems	53	1.9	(0–10)	66	1.5	(0–8)	60	0.0	(0–6)
<i>Acinetobacter</i> spp. - carbapenems	1	**	(**)	6	**	(**)	7	**	(**)

N, number of tested isolates, %R, percentage of resistant isolates, CI, confidence interval, **, no percentage calculated.

2.2 Healthcare-associated infections

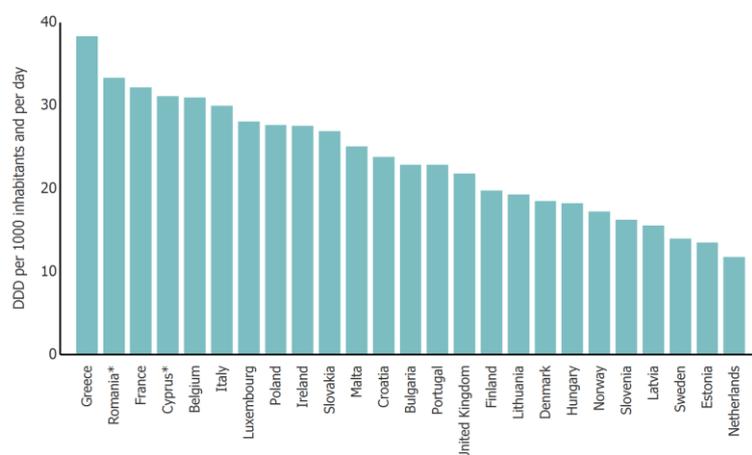
Nine hospitals participated in the ECDC point prevalence survey (PPS) in 2012 with a HAI prevalence of 5.4% among all admitted patients, with a 95%-confidence interval ranging from 3.6%–8.0%. The highest prevalence of HAIs was found in intensive care with 19.5%, followed by geriatrics with 11.6% and medicine with 5.3% of all admitted patients.

2.3 Antimicrobial consumption

Luxembourg is one of the Member States with a high consumption of antibacterials for systemic use, as reported for 2015 to the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) (Figure 2).

The trends in consumption of antibacterials for systemic use in the community and in the hospital sector are presented in Figures 3 and 4, respectively.

Figure 2. Overall (community and hospital sector combined) consumption of antibacterials for systemic use (ATC group J01), EU/EEA countries, 2015, expressed in defined daily doses (DDD) per 1000 inhabitants and per day (Source: ESAC-Net)



*country provided only total care data

Figure 3. Trend of the consumption of antibacterials for systemic use (ATC group J01) in the community, Luxembourg, 1997-2015, expressed in DDD per 1000 inhabitants and per day (Source: ESAC-Net)

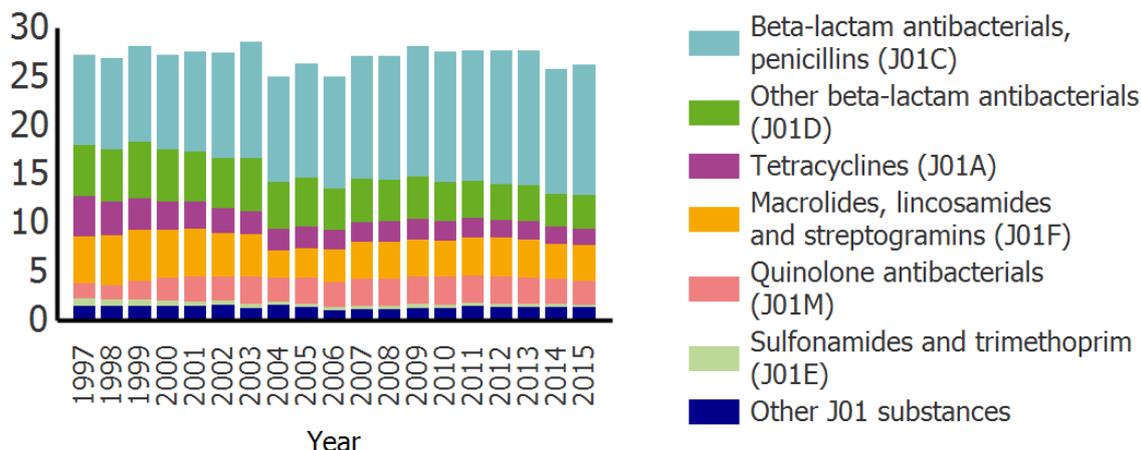
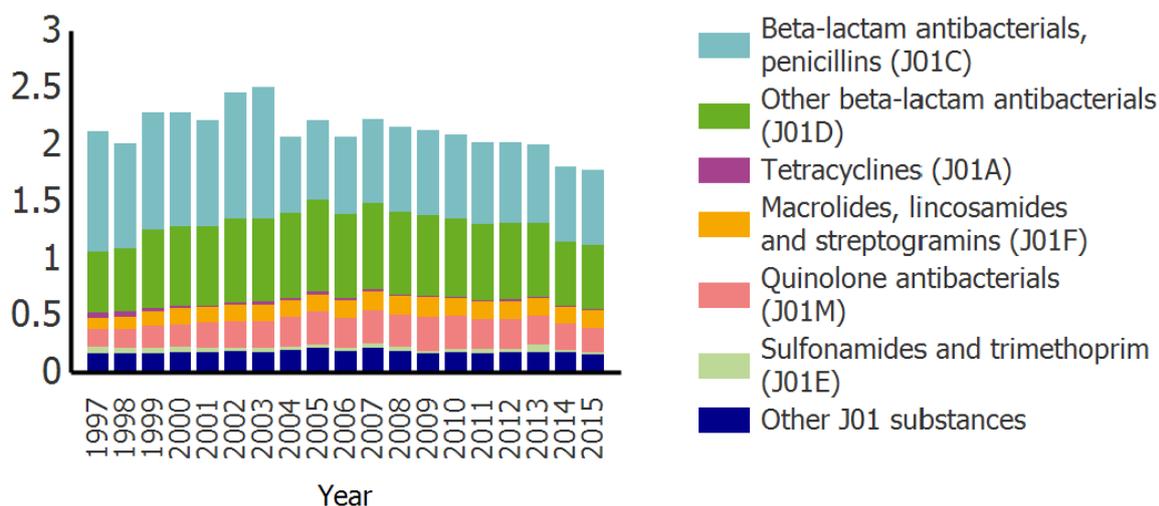


Figure 4. Trend of the consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, Luxembourg, 1997-2015, expressed in DDD per 1000 inhabitants and per day (Source: ESAC-Net)



3. Observations

3.1 Development of an Intersectoral Coordinating Mechanism (ICM)

Since 1997, the GNPIN has acted as a National Committee with a focus on the surveillance, prevention and control of HAIs. At the end of 2016, the Minister of Health and the Minister of Agriculture, Viticulture and Protection of Consumers, with support from the Minister of Environment, gave the mandate to the Health Directorate and the Veterinary Administration to develop a National Antibiotic Plan 2018-2022 in a 'One Health' perspective by the end of 2017.

The development of the National Antibiotic Plan is coordinated by a multidisciplinary Steering Committee currently acting as the ICM for AMR, with support by a Coordinator at the Ministry of Health. The development is performed by four multidisciplinary Technical Working Groups focusing on (a) prevention, communication and education, (b) treatment and diagnosis, (c) monitoring, and (d) research, respectively. The task of these working groups is to determine strategic priorities, objectives and interventions, activities, timetable and the need for resources. Every working group is led by a member of the Steering Committee. Most stakeholders are represented with the exception of the Ministry of Family Affairs and Integration, and of practitioners (in addition to representatives of professional associations). The GNPIN contributes to the work of these Technical Working Groups.

At the time of our visit, the Steering Committee had met twice, in March and April 2017, and the Technical Working Groups had met at least once (two meetings for the Technical Working Group on monitoring). As of May 2017, the general objectives and strategic axes of the National Antibiotic Plan 2018-2022 were determined, a preliminary assessment of the capacities, gaps, opportunities and threats had been performed, and the work on defining measures and activities had started. The objective is that the plan would be adopted by the Council of Ministers before the end of 2017.

3.2 Organised multidisciplinary and multisectoral collaboration at local level

Infection control (IC) teams as well as multidisciplinary IC committees existed in all visited hospitals. In addition, most of the visited hospitals had an antibiotic committee or equivalent. However, these teams and committees varied considerably between hospitals in the scope and extent of their multidisciplinary activities. For example, one hospital could not provide any systematic analysis of AMR and antimicrobial consumption data as a basis for interventions, while other hospitals had made considerable efforts into a detailed analysis of their data, development of local treatment guidelines and specialised software for better monitoring and steering of antimicrobial treatment.

There was, apart from an attempt to harmonise software for monitoring of antimicrobial consumption, no significant collaboration between different hospitals as well as between hospitals and long-term care facilities with regard to IC, especially for the control of MDROs and advice on antibiotic treatment. No national common approach to control of AMR and antimicrobial stewardship was identifiable.

All hospitals working with independent doctors reported a low level of participation of these doctors in any of the proposed activities, even if their participation would only require attendance of meetings for presentation of antimicrobial resistance or consumption data or training on local treatment guidelines. In the ambulatory setting, the general practitioner (GP) as well as the paediatricians who we met stated that there were regular meetings with peers to discuss different topics related to their specialty; however, these meetings did not include discussion on AMR and antimicrobial treatment.

3.3 Laboratory capacity

Microbiology laboratory capacity for standardised antimicrobial susceptibility testing is available at the National Reference Laboratory (Laboratoire National de Santé - LNS) and at the four visited hospital laboratories, which represent all microbiology laboratories operating in hospitals in Luxembourg. Laboratories are accredited or in the process of accreditation according to the ISO 15189/2012 and regularly participate in external quality assessment exercises. European Committee on Antimicrobial Susceptibility testing (EUCAST) standards are used for antimicrobial susceptibility testing. Laboratories have standard operating procedures and are staffed by medical and scientific microbiologists.

In the four hospital microbiology laboratories, the identification of bacterial species is performed using matrix assisted laser desorption ionisation-time of flight (MALDI-TOF) mass spectrometry, while the antimicrobial susceptibility tests are mainly performed by automated systems. Etest and disk diffusion tests are also used. All laboratories have facilities for computerised registration of specimens and practice selective reporting of antimicrobial susceptibility results. Computer-generated antimicrobial susceptibility data are downloaded from the laboratory information system of each of the four laboratories and transferred to local databases for analysis. In all the visited hospitals, the hospital IC teams has access to local AMR data from the microbiology laboratory.

Apart from working as a clinical laboratory performing routine testing for identification and antimicrobial susceptibility, the LNS provides reference services to the other laboratories for confirmation of resistance mechanisms, minimum inhibitory concentration dilution testing for colistin, vancomycin and teicoplanin, strain typing of healthcare-associated multidrug-resistant bacteria (e.g. ESBL-producing *Enterobacteriaceae*, CPE, methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococcus* spp.), typing of food-borne pathogens and *Neisseria gonorrhoeae*, mycobacterial detection and susceptibility testing. The LNS also has polymerase chain reaction (PCR) - equipment and capillary and whole genome sequencers to perform molecular typing and comparison of strains.

There is no National Antibiotic Committee, as recommended by EUCAST, in Luxembourg.

3.4 Monitoring of antibiotic resistance

At the national level, Luxembourg provides data for EARS-Net received from four hospital laboratories. Data collection is managed by the LNS. The LNS receives isolates from other laboratories for confirmation of resistance mechanisms and typing. There are national protocols for submitting MRSA isolates and isolates suspected to be CPE to the LNS, although it is not possible to assess the coverage of this system. The submission of isolates is not accompanied by epidemiological data. So far, there is no obligation at national level to report MDROs but a law is under discussion to make the reporting of clinical infections caused by MDROs mandatory.

AMR statistics, produced locally, were available in three hospitals and were, to some extent, used to inform treatment strategies. At the GP level, AMR data are not systematically available. The lack of Luxembourg-specific resistance data for common infections is perceived as an obstacle for more locally adapted antibiotic treatment.

3.5 Monitoring of antibiotic use

Information (reimbursement data) on antibiotic consumption in primary care is collected by the National Health Fund (Caisse Nationale de Santé). Data on antibiotic use in the hospital sector are collected at the hospital level (dispensing data) and collated at the national level by the National Agency of Medicines in number of units and then transformed into a number of DDDs. There is neither a harmonised methodology, nor a common tool to be used by hospital pharmacists to collect and analyse information on antibiotic use in their hospital. Due to this lack of a common approach, some hospitals have adapted French methods and tools to convert data into DDDs, whereas others prefer the German methodology and recommended daily doses (RDDs). Pharmacists are planning to define a common approach of measuring antibiotic use in DDDs or RDDs in relation to hospital activity expressed as number of patient-days. This could allow benchmarking by taking into account differences in clinical activity between hospitals. Hospital consumption data are generally fed back to the hospital antibiotic committee. National data on antibiotic consumption are reported by the National Agency of Medicines to the EU level through ESAC-Net.

The use of information on antibiotic use in the community could be improved, for example by active and individual feedback to prescribers of data analysed by age group, antibiotic class and specialty of prescribers. This feedback could include comments on trends and educational materials to increase knowledge. The prescribers (GP and paediatricians) who we met were interested in receiving such feedback.

Qualitative information on antibiotic use in hospitals has been collected during the ECDC point prevalence survey (PPS) in acute care hospitals in 2012 and through specific audits. The rate of surgical antibiotic prophylaxis lasting longer than the recommended duration was high in 2012 and is still an issue in 2017 in most of the hospitals that we visited. This issue could be addressed by specific activities at the national level such as updated national guidelines followed by an assessment of compliance with the guidelines.

There were examples of good practice in the visited hospitals. In one hospital, there was a system for electronic prescribing controlled by the pharmacist and nominative daily dispensation. In another hospital, the hospital information system links surgical room booking with the prescription of pre-operative prophylaxis. In contrast, in the other two hospitals pharmacists do not have information on antibiotic usage. The development of e-prescribing and electronic patient records at the national level represents an opportunity for improving the documentation of the indication for antibiotic prescriptions and including automatic reminders for the reassessment of the need for antimicrobial treatment after 2-3 days of therapy as well as controls to limit the duration of surgical antibiotic prophylaxis and of treatment of infections. This system could also facilitate the retrospective analysis of prescriptions and the collection of information for quality indicators.

3.6 Antibiotic utilisation and treatment guidance

No national guidelines exist for treatment of infections in hospitalised patients in Luxembourg. A summary guide had been distributed to practitioners with options for treatment of frequent infections in ambulatory care. This guide also highlights situations in which antibiotics are usually not needed. The visited GP as well as the paediatricians had this guide at hand in their office; however, they felt that the dissemination of the guide had been a one-time effort without follow-up and that more involvement of medical doctors, more background information on why certain antibiotics had been chosen and an update of the guide was needed.

All visited hospitals had guidelines on surgical prophylaxis and two hospitals had, in addition, developed their own guidelines for treatment of infections. One hospital had also measured compliance with the recommended treatment and dosing as described in the local guideline. In case of unavailability of guidelines or for infections not covered by guidelines, the Sanford guide and Up-To-Date were the most frequently cited sources of information, followed by guidelines from neighbouring countries.

In one hospital, revision of prescribed antimicrobial treatment in the wards was performed by a pharmacist. However, there was no systematic discussion of the pharmacist's findings with prescribers who instead received an electronic comment. Regular rounds with infectious disease, microbiology and pharmacology specialists to review treatment of complicated infections and resistance patterns did not take place in intensive care units (ICUs). Infectious disease (ID) specialists to assist in decision-making on antimicrobial treatment were only available in two hospitals, with very limited staffing, and were not able to cover the need for ID consultations. ID consultations were provided on request. The lack of ID expertise was perceived as an obstacle for optimal antibiotic use, especially for patients with difficult-to-treat infections.

In addition, the status of 'independent'ⁱ medical doctors in hospitals was considered to be an obstacle to more prudent use of antibiotics, not only by the hospital management but also by these doctors themselves. These 'independent' doctors have no incentive to participate in multidisciplinary teams and educational activities. Actions cannot be enforced by the hospital management to make these 'independent' doctors act as part of a community rather than as individuals without a common responsibility for antimicrobial use in hospitals. The 'independent' doctors also perceived the situation as being on their own in front of the patient rather than being part of a team with other colleagues and having a shared responsibility as a reason for overprescription of antibiotics in hospitals.

3.7 Infection control

Infection control activities are structured and organised in hospitals in Luxembourg. Each visited hospital has an IC committee and an IC team in place. IC teams are staffed with IC nurses, trained in neighbouring countries. However, a lack of clinical/pharmaceutical/microbiological dedicated time to perform the wide range of IC activities was mentioned in each of the hospitals that we visited. The part-time activity devoted by microbiologists and other physicians did not seem to be sufficient to cover the wide range of needed IC activities including training of healthcare staff, prevention, surveillance, reporting and environmental monitoring. Collaboration between IC teams and microbiologists is in place in hospitals as well as systems to alert IC teams on 'sentinel germs'. A specific software (Infectio) is used for this purpose in three of the four acute care hospitals that we visited.

Regarding prevention, hand hygiene is well integrated into care. The following are two examples of good practice:

- hand hygiene programmes in all hospitals include regular assessment of preconditions for appropriate hand hygiene and measurements of compliance with feedback to professionals;
- alcohol-based hand rubs are widely used and, in most hospitals, are available at the end of the patient bed or in close proximity.

ⁱ Independent doctors refers to those that are in private practice and not employed by the hospital and these doctors continue to treat and take the medical decisions for their patients in hospital.

The use of alcohol-based hand rub is monitored and used as a quality indicator for evaluation of the national hand hygiene campaign. Local guidelines on standard and additional precautions exist in all hospitals. In the hospitals that we visited, isolation facilities existed in ICUs and in the ID ward of one hospital. ICU rooms were generally large enough and well equipped.

All visited hospitals had guidelines for screening selected patients for MRSA carriage and for subsequent decolonisation procedures. Despite existing national guidelines, there was no homogeneous approach for MRSA screening and decolonisation. Similarly, screening for CPE was performed, but not always in accordance with the national guidelines.

Regarding surveillance, all hospitals use the methods of the Luxembourg Nosocomial Infection Surveillance System (Nosix) and participate in the ECDC PPS. Surveillance of HAIs in ICUs is ongoing and the results are used at hospital level. However, surgical site infections are not monitored in all hospitals due to barriers in the organisation of medical/surgical services. The GNPIN is well known by IC staff in hospitals, for its technical expertise as well as for its role in elaborating guidelines and performing surveillance of HAI with the Nosix system.

3.8 Educational programmes on antimicrobial resistance

Luxembourg does not have a university that offers medical or pharmaceutical studies apart from the first year of studies. Medical doctors and pharmacists therefore have to complete their medical degree in other countries, for example in Belgium, France or Germany, and agreements exist with some universities in these countries. Medical specialty training is offered for some medical specialties, but not for the full spectrum of medical specialties. As a result, the majority of medical doctors in Luxembourg do not have homogenous training and the government and medical boards have little influence on the curriculum of medical education. Two months before the ECDC visit, a decision was made to extend medical studies offered in Luxembourg from one to three years, and in the future to five or more years. It was also decided that, in the future, specialists in oncology and in neurology should be trained in Luxembourg.

For continuing professional education of medical doctors, seminars are offered either by professional societies or private organisations. Some of these seminars are sponsored either directly or indirectly by the pharmaceutical industry. The doctors who we met had not attended any seminar or workshop related to AMR or antimicrobial use. Continuing professional education is voluntary and there is no mandatory education that could be used to harmonise knowledge and promote a common standard. The hospitals with 'independent' doctors have the additional problem that they cannot mandate these doctors to attend training activities, for example on prudent antimicrobial use. As a result, there is a lack of control over the education of these doctors on AMR and prudent use of antimicrobials.

Hospital IC teams offer training on standard hygiene measures for newly employed healthcare staff. Training for nurses could not be evaluated.

3.9 Public information related to antimicrobial resistance

Luxembourg has implemented communication campaigns focusing on prudent use of antibiotics since 2006 and has participated in the European Antibiotic Awareness Day (EAAD) since 2008. Most of the activities take place on or around 18 November each year. Through its campaigns, the Ministry of Health has targeted mostly the general public and improvements are visible mainly through the results of the different Eurobarometer surveys on AMR throughout the years, in which Luxembourg is either on or above the European median in terms of knowledge and perceptions about antibiotics and about AMR. Materials such as posters, brochures, TV spots, checklists for doctors and patients have been developed and placed in key locations. Mass mailings have also been used to target GPs.

Public relations are relevant for the country and are well-managed, having close cooperation with national television and radio stations, as well as newspapers. National media tend to transmit the messages delivered by the Ministry in a coherent scientific way and seem to be good multipliers. This might also explain why the knowledge on AMR in the population is at a medium to high level. Press reviews and social media reports are produced each year after EAAD has taken place.

The visual design of the campaign is renewed every other year, but the content and messaging is the same. This approach could have a positive impact in terms of capturing the attention of the general public with new and attracting visuals every time a campaign takes place. Pre- and post-evaluation of these campaigns is currently not performed at national level.

Luxembourg also participates in the WHO's "SAVE LIVES: Clean Your Hands" hand hygiene campaign, and marks it each year on 5 May by developing its own materials and sharing them with hospital staff. The message of the campaign is "Propper Hänn, Sécher Hänn" (Clean hands, Safe hands). This is a good and necessary complement to the campaigns targeting prudent use of antibiotics, but there seems to be a missing link between the two campaigns.

3.10 Marketing-related issues

Independent drug information not supported by industry is not available, e.g. from a national database. Professionals rely on external sources of information such as international databases and drug compendia from neighbouring countries.

There is a Ministerial Act that defines the rules regarding advertising for medicines, gifts and sponsoring of professional and scientific meetings. There is another Ministerial Act defining a code of ethics for medical doctors. There is also a code of ethics for the pharmaceutical industry. Personal gifts from industry to physicians are legal as long as they are of low value and in relation with the professional activity of the prescriber. Sponsorship of educational symposia is legal only for the costs related to professional matters. However, the declaration by pharmaceutical companies of the value of gifts given to prescribers, and the declaration by prescribers of the value of gifts received from pharmaceutical companies is not mandatory.

4. Conclusion and recommendations

Conclusions

Antibiotic consumption in Luxembourg is at the EU average in hospitals, but higher than the EU average in the community. There may have been a small decrease in antibiotic prescriptions in the community since 2013 but this trend needs to be confirmed in the coming years. There has also been a 30% decrease in antibiotic prescriptions in children between 2006 and 2015.

The AMR levels in bacterial isolates from humans are at or below the EU average. According to The European Antimicrobial Resistance Surveillance Network (EARS-Net), the percentage of *S. aureus* bloodstream infections that are methicillin-resistant (i.e. MRSA) decreased slowly between 2012 and 2015. However, looking at the increasing trends of multidrug-resistant *Escherichia coli* from EARS-Net, there is a concern for more serious AMR problems in the future. Moreover, national experts and professionals are also concerned by the increasing number of cases of extended spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* in hospitals, and, in one hospital that we visited, by the increasing use of last-line antibiotics such as carbapenems, as well as the slow emergence of carbapenemase-producing *Enterobacteriaceae* (CPE).

There are multiple sources of data on AMR and on antimicrobial consumption at the national and local level in hospitals that are currently not consistently used by national and local experts for further analysis, and to implement and evaluate targeted interventions to prevent and control AMR.

Cross-border issues seem to have a greater importance in Luxembourg than in many other EU Member States. Firstly, patients are transferred across borders from Luxembourg to other countries and back to Luxembourg. These transfers could for example be necessary because certain medical procedures cannot be provided in the country, and this risks importing multidrug-resistant bacteria. Secondly, a large proportion of the population has connections with other countries and travels back and forth between Luxembourg and their country of origin. These persons may have different expectations about the need for antibiotics for common infections. Thirdly, medical doctors and other healthcare professionals usually train in neighbouring countries where they may be taught varied clinical and prescribing practices. While these cross-border aspects represent a challenge for Luxembourg, they could also be considered as an incentive to exchange best practices and foster cross-border collaboration.

Patients are often transferred between long-term care facilities and hospitals. As reported by acute care hospitals, long-term care facilities may represent an uncontrolled reservoir of multidrug-resistant bacteria.

Luxembourg is in a position to reverse the above-mentioned emerging AMR trends. In the past years, Luxembourg has implemented several good actions at the national or local level, often driven by personal initiative and efforts of a few dedicated professionals. This can be seen as the first phase of a process, which now needs official status, national coordination, enhanced collaboration, and support to ensure sustainability and meet future challenges.

Options for action

Based on the observations and conclusions, the ECDC proposes the following actions:

- Completion of the National Antibiotic Plan 2018–2020, in a One Health perspective in collaboration with the Veterinary Administration, to provide an overarching framework for all activities related to AMR prevention and control and ensure the continuity and sustainability of envisaged activities by providing adequate funding and staffing. In particular, there is a need to establish a permanent National Committee or Intersectoral Coordinating Mechanism (ICM) and a clearly defined role for the 'Groupe National de Guidance et de Prévention de l'Infection Nosocomiale' (GNPIN) as part of this ICM.
- Strengthening and centralisation of surveillance and response to AMR by creating a national epidemiological team responsible for:
 - Harmonising data collection activities providing a reference dataset and, possibly, tools to facilitate data collection in hospitals or for other providers (e.g. long-term care facilities);
 - Providing centralised and combined data analysis and reporting of AMR, antimicrobial consumption and healthcare-associated infections;
 - Defining events and multidrug-resistant organisms (MDRO) to be considered for mandatory notification;
 - Performing outbreak investigations and control activities;
 - Preparing one single comprehensive annual report.
- The minimum areas of expertise to be covered by this national epidemiological team are epidemiology, statistics and bioinformatics.

- Defining a list of a minimal set of indicators for antimicrobial consumption, AMR, healthcare-associated infections (HAI) and compliance to hand hygiene and identify proper benchmarks. When possible provide indications about the level of disaggregation of the analysis; for example, antibiotic use at community level by region, age, gender, type of patient (residents vs. non-residents), type of provider (generalist vs. specialist), etc. For some indicators it would be possible to set targets (e.g. antibiotic use in the community).
- Increasing the efforts into defining the epidemiology of CPE in Luxembourg and use of this information for the implementation of control measures.
- Review and take advantage of the multiple current sources of electronic data and implementation of the electronic patient record.
- Establishing national surveillance of surgical site infections.
- Review, update and dissemination of the national guidelines for prevention and control of MDROs.
- Providing national guidelines for treatment of common clinical infections and for surgical prophylaxis by developing (or updating existing) Luxembourg-specific guidelines or adapting guidelines from other countries and defining steps for their implementation.
- Coordination of regional/local initiatives and provision of a forum for exchange of best practices, experiences and materials, including guidance documents and software tools.
- Provision of education on AMR and antibiotic prescribing for medical doctors, for example by including them into a mandatory continuing professional education programme.
- Continuation of the national public awareness campaign on the prudent use of antibiotics, targeting not only the general public but also expanding and reaching other target audiences such as medical doctors, nurses and other hospital staff who have responsibility regarding antimicrobial treatment. Pharmacists also have an important role in reducing antimicrobial use and could be targeted by using ECDC's communication toolkit for the general public, focusing on self-medication.
- Continuation of the national campaign on hand hygiene, ensuring that the campaigns about prudent use of antibiotics and hand hygiene are in line and support each other.
- Implementation of education materials from e-Bug in schools in Luxembourg.
- Increasing the availability of infectious disease expertise in all hospitals.
- Involving long-term care facilities in the surveillance and control efforts for AMR.
- Enhancing cross-border collaboration on the prevention and control of AMR.

5. Annex

Assessment tool for ECDC country visits to discuss antimicrobial resistance 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.

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 Recommendations. 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 need for close cooperation from fields such as epidemiology, microbiology, clinical medicine, infection control, veterinary medicine, pharmacology, behavioural sciences, practitioners from different medical specialities as well as government departments and health care providers.

In the Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) and in the 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 organizations. There should be a group on the highest administrative level where representatives from regulatory bodies and professionals from the different sectors coordinate.

Tentative indicators

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 updated and structured data
- Provides support to local working groups.

2. Organised multidisciplinary and multisectoral collaboration on 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 with the rationale of using antibiotics appropriately.

A non-regulatory intervention that has indicated some influence on prescribing habits are local activities where practicing 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.

Time for practicing doctors is limited. 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

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 yearly.

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 yearly.

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. This can often not be done in all laboratories so a referral system to specialised laboratories should exist.

All laboratory work should regularly be quality assessed.

Tentative indicators

General

- Structures

- How many diagnostic laboratories are appropriately equipped for microbiological diagnostic work (minimum requirement: performance of gram-stain, aerobic 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 h of receipt of 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 h of receipt of diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 h of receipt of diagnostic specimen?
- What proportion of microbiological laboratories provides species identification of blood culture isolates to the submitting clinician?
- Who pays for sent in sample analysis?

Outpatients

- 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 h of receipt of diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 h of receipt of diagnostic specimen?
- Who pays for sent in sample analysis?

4. Monitoring of antibiotic resistance

Resistance patterns should regularly be followed. This should be done with a standardised method. The method should regularly be quality assessed.

To be able to guide prescribers in prudent usage of antibiotics, surveys of different clinical conditions should be done 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

- 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 standardised methodology in communities and hospital unites is on-going
- Data from hospitals and outpatient 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 to 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 regarded as sensitive, this kind of data can be used for the self assessment. Aggregated data may be used for local group discussions.

Tentative indicators

- 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. Still there is a need to find some common view on what is 'proper'. Guidelines are a way on 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 on 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. That is why systemic antibiotics are prescription-only medicines in EC.

Tentative indicators

- 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 bacteremia with sepsis (% of patients)?

7. Infection control

Healthcare and especially hospitals have historically been a main source of spread of epidemics. This has been shown for a wide variety of microbes. This was true with 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 is often poor.

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

Tentative indicators

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 standardised 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 antimicrobial resistance

The understanding of 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 relation 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

- Doctors have in their curriculum AMR as undergraduate course
- Hospital healthcare workers have some education on AMR
- Community healthcare 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 antimicrobial resistance

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 of the wider public are important.

Tentative indicators

- 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 do have an impact on prescribing habits irrespective of diagnosis or best practice. This should be discouraged.

Tentative indicators

- 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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