

in  
the **red**  
**zone**

Antimicrobial Resistance:  
Lessons from Romania

european public health alliance



# In the Red Zone

## Antimicrobial Resistance: Lessons from Romania

Drug-resistant “superbugs” – more accurately described as bacteria resistant to antimicrobial drugs including antibiotics – pose a serious and urgent cross-border problem to European and global public health. As drug-resistant bacteria spread quickly and are not constrained by borders, European Union institutions must play an effective role in making sure that Europe’s health “safety net” is tight. Inaction, lack of resources or expertise in one country can swiftly become a public health catastrophe for the whole region and beyond.

This case study provides a compelling insight into the current AMR situation in Romania. On the basis of a series of expert interviews, the study was commissioned by EPHA to illustrate the urgent need for coordinated, well-resourced and effective EU policy action and programmes to tackle AMR. Whilst Romania is “in the red zone” in terms excessive antibiotic use and prevalence of several strains of drug-resistant bacteria, it is by no means an exception regarding inadequate funding for public health, health worker shortages, or lacking equipment and technology to safeguard patient safety: Many EU member states are facing similar challenges and risk tearing holes in Europe’s safety net.

Given large differences in the resources and capacities of national health systems, the EU can and must add value by ensuring that best practices, realistic targets and effective policies to contain AMR and stimulate responsible use of antimicrobials are taken up across the region. Dedicated resources and legislative measures need to be made available at both EU and national level: the EU does have the competence to do much more than it has under the AMR Action Plan 2011-2016<sup>2</sup>.

A follow-up EU AMR Action Plan is scheduled to be released by the European Commission in 2017. It will set out to advance the One Health approach and one of its strategic pillars will be to “support Member States and make the EU a best-practice region on AMR”<sup>3</sup>. The following recommendations should be included:

### **Recommendations**

The Romanian case demonstrates the challenges to health systems’ ability to combat AMR. If left unaddressed by policies, programmes and effective measures, resistant bacteria will continue to develop and spread. The report vividly underlines the difficulty of confronting multiple challenges at national level alone.

AMR is cross-border by nature and is an impending pan-European and global health security catastrophe as today’s antibiotics become ever less effective. It is in the self-interest of all European governments and institutions, in both health and economic terms, to ensure that our safety net spans all of Europe, and that it becomes as effective as possible in controlling the causes and reducing the prevalence of resistance.

A number of other recommendations can be extracted from the report, most of them relevant both at the European and national level. They include the following:

- Introduce rules in line with best practice for antimicrobial prescribing in medical offices
- Regularly update treatment guidelines on the prudent use of antibiotics in healthcare, protocols to support health workers, and up-to-date lists of which types of antibiotics can be safely prescribed under what circumstances; regularly update maps of resistance to major antibiotics
- Support use of rapid diagnostic tests
- Enforce existing legislation, including prescription-only dispensing
- Improve epidemiological surveillance and accurate data collection and reporting on AMR/HAI and antibiotics consumption (e.g. regular point prevalence surveys and meaningful performance indicators)
- Strengthen the role of multidisciplinary HAI control committees in hospitals and at national level and an adequate funding for infection control activities.
- Ensure long-term investments in health workforce education, training, remuneration and retention to ensure sufficient numbers of core functions and specialists
- Establish inclusive, multidisciplinary antimicrobial stewardship programmes
- Regulate promotion of antibiotics by the pharmaceutical industry that targets health professionals
- Scale up awareness-raising campaigns on prudent use of antibiotics and hygiene measures, including public education

### **EU policy recommendations**

On the basis of this report, EPHA makes the following EU policy recommendations:

- Deploy EU policies and programmes including legislation, to reduce drug-resistance, reduce excessive antimicrobial use and tackle other causes of AMR across all relevant sectors (human, animal, industrial, environmental)
- Expand the remit and resources of the ECDC, deepen the country visits and produce tailored targets and recommendations for Member States / regions
- Expand ECDC’s role in technical cooperation between the EU and Member States on AMR, including the take-up of best practices
- Include recommendations in the European Semester as a policy tool to motivate national progress on AMR and HCAI
- Design future EU funding opportunities and conditionalities to boost national policy and implementation capacity, improve facilities to tackle AMR and HAIs, e.g. use of rapid diagnostic tests, upgrade laboratory equipment, isolation units, etc.
- Identify EU experts to train inter-sectoral “AMR champions” at national level
- Develop a European curriculum for AMR, to be integrated into health workers’ education programmes.



# In the Red Zone

## Antimicrobial Resistance: Lessons from Romania

“I’d never heard of resistant bacteria before. Colectiv has brought them to the surface”, says Eugen Iancu, the father of Alexandru, one of 64 people killed as result of a fire that occurred during a concert in a crowded nightclub in Bucharest, Romania, on the night of October 30, 2015. Iancu was among the first to publicly speculate that some of the fire victims died not from the burns, but from hospital-acquired infections (HAIs). He recounts to EPHA that the idea came to him as he was trying to understand why his son and three other wounded who had been treated in the same hospital in Bucharest all died within a few days, three weeks after the fire. Fears about the infections that the victims were being exposed to were soon confirmed by the head of the intensive care unit of another Bucharest hospital<sup>4</sup>: “We had 27 hospitalized patients, out of which six died - three almost certainly ‘due to infections’”, Adrian Stănculea told journalists gathered at the Emergency Hospital for Plastic Surgery and Burns.

Alexandru Iancu, 22, died after suffering burns to 28% of his body - hands, chest and back - and to his airways. His father says that his medical file, which he received several months later, shows that the first treatment his son had received upon admission was a broad-spectrum antibiotic. Two days later, the first resistant bacteria, from the *Acinetobacter* species, was isolated from the intubation tube. He ended up with five antibiotic-resistant bacteria when he died, Eugen Iancu says. Despite having burns on more than 60% of his body, a wounded man in the bed next to Alexandru, who was later transferred to Belgium, has survived.

Talking about the eight victims from Colectiv who were transferred to Brussels, Serge Jennes,

the head of the burns unit at the Queen Astrid Military Hospital, later said in a report for Romanian television<sup>5</sup>: “All eight were carrying bacteria which were resistant to many antibiotics.



The 2015 fire at Colectiv killed 64 people. Several victims perished due to hospital-acquired infections.

Such a situation is unusual in Belgium during the first week. They had *Acinetobacter baumannii*, *Klebsiella pneumoniae*, one had MRSA, and others had *Pseudomonas aeruginosa* which was very resistant.”

Referring to the patients’ triage, which he had conducted in Bucharest, Jennes added: “I examined 90-100 patients; we didn’t talk about multidrug resistant bacteria at the time, but I noticed that an antibiotic was being administered,



which was unusual for two reasons: the timing – it was the seventh day - and the fact that it was colistin - which means that you’re dealing with multidrug-resistant bacteria: *Pseudomonas aeruginosa*, an *Acinetobacter*, or both.”

**At a conference in February 2016 at the Free University of Brussels, one of the slides being presented by Belgian specialists described the Colectiv victims that had been transferred to the Queen Astrid Hospital as “bacteriological bombs”<sup>6</sup>.**

### **Secret in Romania, well-known in Europe**

Although unfamiliar to the general public, the twin problems of HAIs and antimicrobial resistance (AMR) were well known in the Romanian health system. Vlad Voiculescu, the Romanian Health Minister between May 2016 and January 2017, said during a debate<sup>7</sup> in October that nosocomial infections were “an issue that healthcare workers certainly knew about. In the (health) system it was very well known.”

**However, according to a 2016 report<sup>8</sup> by the National Institute of Public Health (INSP), nosocomial infections are underreported and likely underdiagnosed, as the official reported incidence for 2014, 0.25% of discharged patients, is “25 to 30 times below the EU average.”**

The only figure in the “normal range” is 5.3%, Professor Alexandru Rafila, President of the Romanian Microbiology Society, tells EPHA, and comes from a validation study of the Point Prevalence Survey (PPS) of HAIs and antimicrobial use in European acute care hospitals<sup>9</sup>, carried out in 2011-2012 by the European Centre for Disease Prevention and Control (ECDC). In such circumstances, the human and economic burdens of infections caused by antibiotic-resistant bacteria – which result in an estimated 25,000 deaths and related cost of 1.5 billion eu-

ros in additional medical care and lost productivity per year in the EU<sup>10</sup>– cannot be accurately calculated for Romania. “I would only do this exercise when we have the first hospital that reports a 5% infection rate”, Rafila says, referring to currently unreliable reporting by hospitals. Referring to antibiotic-resistant bacteria, minister Voiculescu also said during a television program<sup>11</sup> marking one year since the fire that “they are not [only] a problem since Colectiv; the resistant bacteria that we have in Romania and that Romanian patients carry in hospitals abroad are already a known problem in many hospitals in Europe.”

**Annual data collected by ECDC’s European Antimicrobial Resistance Surveillance Network (EARS-Net) consistently places Romania among the problem countries:**

- For ***Klebsiella pneumoniae*** – which, according to ECDC, is a common cause of urinary tract, respiratory and bloodstream infections which, in the absence of appropriate prevention and control measures, can spread rapidly among patients in healthcare settings – the latest data<sup>12</sup> shows that Romania has the third highest resistance rate among 30 countries surveyed: 49.8% combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, compared to an EU / EEA average of 18.6%;
- 24.7% resistance to carbapenems, compared to just 8.1% in Europe.
- For ***Escherichia coli*** in 2015 – described by the ECDC as one of the most frequent causes of bloodstream infections and community- or healthcare-associated urinary tract infections –





resistance to third-generation cephalosporins was twice as high in Romania (26.8%) as in Europe (13.1%);

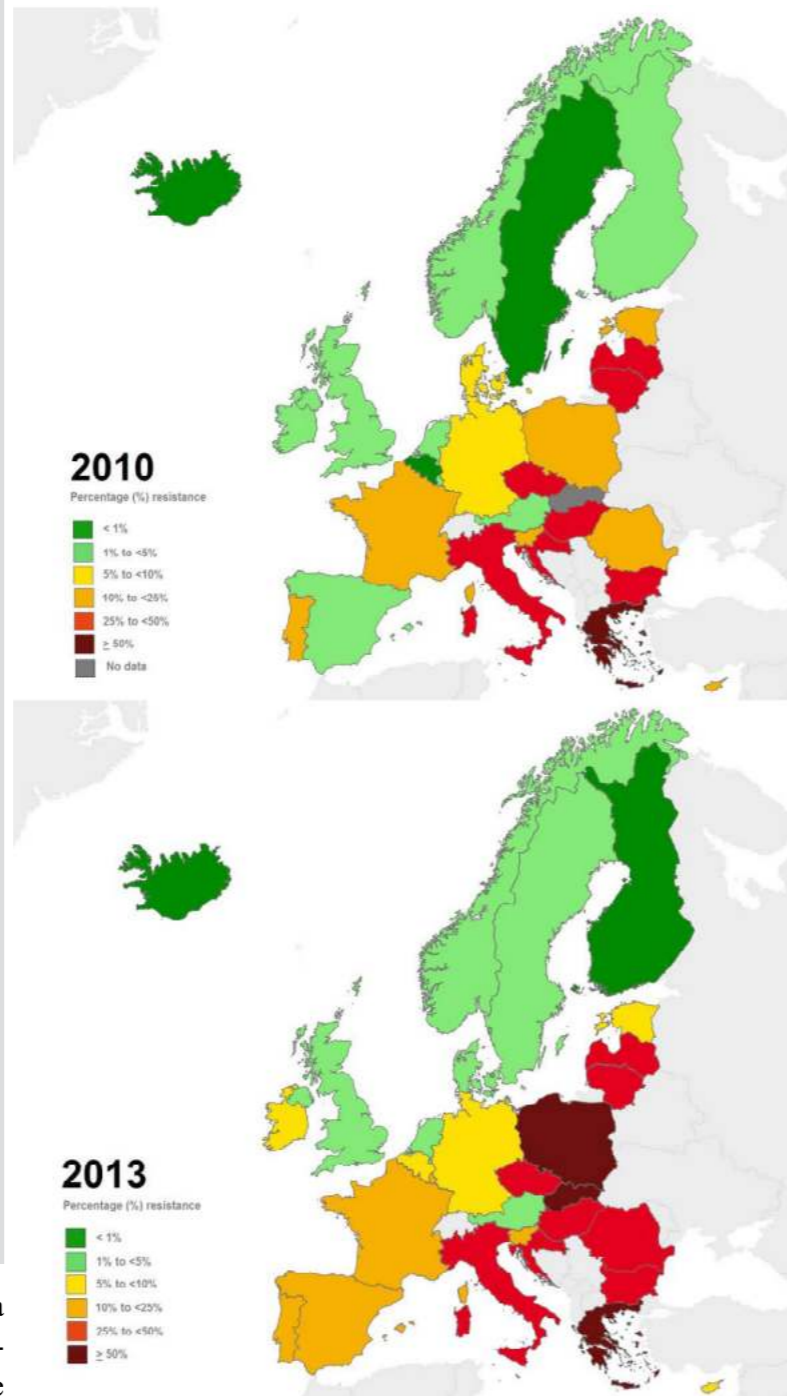
- The combined resistance of the bacteria to fluoroquinolones, third-generation cephalosporins and aminoglycosides is the third highest among the countries studied, 13.5% versus 5.3% for the EU / EEA;
- The combined resistance of **Acinetobacter** species – which, according to ECDC, cause HAIs such as pneumonia and bloodstream infections and often cause hospital outbreaks if appropriate preventive and control measures are not implemented – to fluoroquinolones, aminoglycosides and carbapenems in Romania is also the third highest in Europe, 76.9% in 2015; ECDC states that in countries where this type of combined resistance is higher than 50%, treatment options for such infections are seriously limited. The presence of Acinetobacter species in healthcare settings is seen as problematic, as it can persist and is difficult to eradicate.
- **Enterococcus faecium** resistance to Vancomycin– which ECDC says can cause endocarditis, bloodstream infections and urinary tract infections – in Romania is three times higher (25%), than the European average (8.3%) according to the latest data.
- Even when it comes to Methicillin-resistant **Staphylococcus aureus** (MRSA), which is considered the success story of European efforts against AMR, Romania is in a distant first place, with a 57.2% resistance rate, compared to an EU/ EEA average of just 16.8% in 2015.

In short, for these combinations of bacteria and antimicrobial groups reported to EARS-Net for 2015, Romania is among the top five countries with the highest levels of resistance.

“It is clear that you are in the red zone”, Dr Marc Sprenger, the former ECDC director, said in an interview<sup>13</sup> for the Romanian press on European Antibiotic Awareness Day (EAAD) 2014. “You see here (on the 2010 map) you are in the orange area, and here (on the 2013 map) you are

in the red area. So there is no progress. In general, the resistance in Romania is very high.”

**“It is clear that you are in the red zone”**  
**Dr Marc Sprenger,**  
**former ECDC director, 2014.**



*Klebsiella pneumoniae: percentage of invasive isolates with combined resistance to third generation cephalosporins, fluoroquinolones and aminoglycosides, EU/EEA, 2010 (top), 2013 (bottom)*  
 Image: European Centre for Disease Control ECDC

## Antibiotic consumption – from limited access to excessive use

“Antibiotic consumption in Romania has reached a very high level”, Gabriel Popescu, Infectious Diseases Professor and adviser to the Health Minister Voiculescu said at a press conference in November 2016.

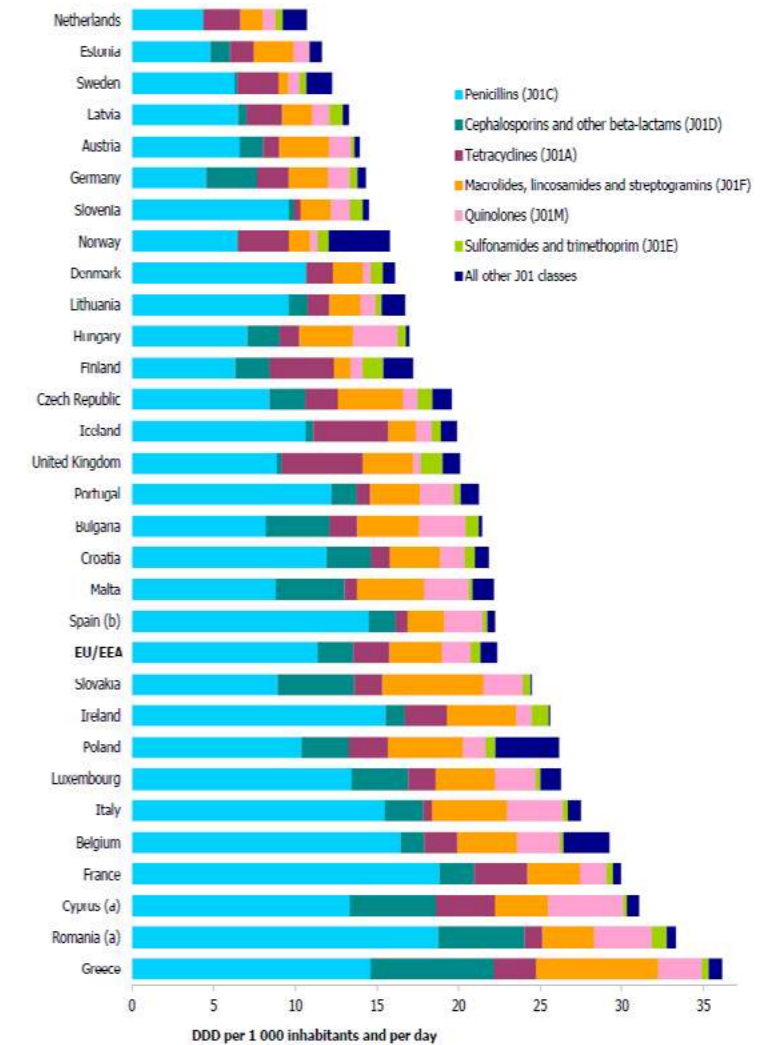
**Data<sup>14</sup> from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) show that Romania had a total consumption in the community and the hospital sector of 33.3 defined daily doses per thousand inhabitants and per day, the second highest in Europe.**

This means that “ on any given day more than 600,000 Romanians take antibiotics. It is a high level, which is reflected in the levels of bacterial resistance to antibiotics.” Increased antibiotic consumption in Romanian hospitals was confirmed by the ECDC Point Prevalance Survey. Although only 10 Romanian hospitals participated, local experts have noted that almost 50% of inpatients had received antimicrobial treatment, a level which was only surpassed by Greece.

Things have not always been so.

**“In 1990, we left the communist period with an unintended advantage: limited access to medicines meant that microbial resistance to antibiotics was limited to only the few types of antibiotics which had been available in Romania before 1989”, Gabriel Popescu explained.**

Marius Geantă, President of the Centre for Innovation in Medicine, a Romanian health policy think-tank, believes that it is in the 1990s that antibiotic prescribing and consumption habits



The EU/EEA bar refers to the corresponding population-weighted mean consumption.

*Romania had the second highest in Europe defined daily doses per thousand inhabitants and per day.*  
 Image: European Centre for Disease Control ECDC

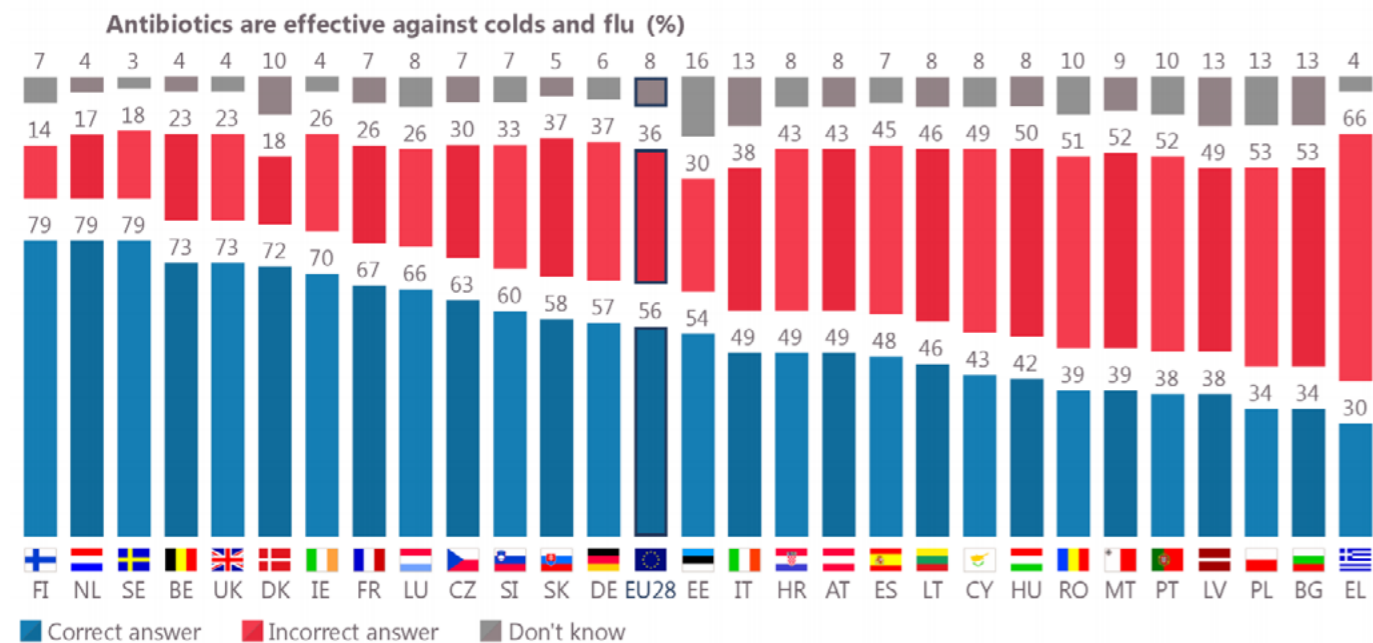
were created, leading to the current situation: “Infectious diseases were at the forefront at the time and were being quickly solved with antibiotics, whereas the way they were dispensed in pharmacies had been left unregulated for some time”, he told EPHA. He also speaks of those years as a “golden age for the pharmaceutical industry”, which was focusing heavily on antibiotic promotion, thus contributing to their oversized role.

One factor frequently incriminated for high antibiotic consumption in the country is poor public awareness.





QB4.2 For each of the following statements, please tell me whether you think it is true or false.



Correct Answer=False  
Total base (N=27,969)

51% Romanians believe that antibiotics are effective against cold and flu vs. 36% of Europeans,  
Image: Eurobarometer

### The 2016 Eurobarometer on AMR<sup>15</sup> confirms that Romanians' knowledge about the appropriate use of antibiotics is below the European average:

- 58% of respondents believe that they kill viruses, compared to an EU average of 46%,
- 51% believe that antibiotics are effective against cold and flu vs. 36% of Europeans,
- 79% know that unnecessary use of antibiotics makes them become ineffective compared to 84% in the EU,
- 62% know that taking them frequently has side effects vs. 66% in the EU.
- The average number of correct answers to the four questions was 2.1, placing Romania second lowest in the EU, on par with Bulgaria, Greece and Latvia and only ahead of Italy.

A survey conducted by the Romanian National Society of Family Medicine (SNMF) of a small number of its members attempted to describe part of the use of antibiotics in the community, which, according to ECDC, accounts on average for 90% of the total human consumption (as opposed to in hospitals). In an interview for EPHA, Sandra Alexiu, vice president of the Society, admits that

of all antibiotic prescriptions, a large proportion are given after a consultation with the family doctor: 34% for children and 22% for adults. Those requesting a prescription for antibiotics only after initiating the treatment themselves made up 20%. A further 13% of prescriptions were given for incorrectly initiated treatment (i.e. for non-bacterial diagnosis) at the emergency department or by other specialists. 11% of patients had received prescriptions for treatments from the pharmacy, without medical consultation.

In Romanian hospitals, Gabriel Popescu says, the Point Prevalence Survey (PPS) showed that “an important driver of consumption is perioperative antibiotic prophylaxis: in over 90% of cases, antibiotic administration was prolonged for more than 24 hours, whereas the general recommendation is for a single dose of antibiotic just before surgery and situations where this should be prolonged are well defined.” PPS data show that surgical prophylaxis was the indication for 16.3% of the prescriptions in European acute care hospitals – 42% in Romanian hospitals –, where it was prolonged for more than one day in 59.2% of cases.

Beside the high total antibiotic



consumption, another problem is the type of antibiotics being administered.

“The ratio between broad-spectrum antibiotics, which encourage bacteria to develop resistance, and narrow-spectrum antibiotics, has increased from six-to-one in 2011 to thirteen-to one in 2015”, Professor Popescu says.

Romania uses too many cephalosporins and quinolones, as well as ‘last-line’ antibiotics like carbapenems, which can trigger *Clostridium difficile* infections, a problem the country started to face in the past five years. According to ECDC, the *Clostridium difficile* infection is generally associated with previous antibiotic use and its clinical manifestations can vary from mild diarrhoea to life-threatening pseudomembranous colitis.

“A rational response would have been to see a drastic drop in consumption of second to fourth generation cephalosporins and of quinolones; on the contrary, we have a tendency to increase their consumption”. Almost 6,000 cases of *Clostridium difficile* infections and several hundred deaths have been reported in 2015, but these already high figures are likely understated, since they were reported by less than half of the country’s hospitals.

### Contagious deficiencies in infection control

Another reason for the increased AMR is the lack of screening procedures for patients who carry resistant bacteria and of capacities to isolate them from the rest of hospital patients, Professor Alexandru Rafila tells EPHA. He also observes another shortcoming – “handwashing: it is considered that everyone knows and does it, but it is not so.” Rafila notes that medical staff should wash their hands before and after examining each patient, but that this would “require an antiseptic dispenser close to the patient.”

The PPS found that Romania is among the lowest ranked countries in Europe when it comes to the number of single hospital rooms – a marker of the isolation capacity for patients with resistant bacteria - and alcohol hand rub consumption, as an indicator of hand hygiene.

In an interview with EPHA, Irina Brumboiu, an associate professor of epidemiology and president of the Romanian Society of Hospital Epidemiology, Prevention and Control of Nosocomial Infections, believes that in some sensitive areas, hospital staff do not fulfil duties rigorously. Hospital infections are thus favoured by “substantial deficiencies” in certain aspects of inpatient care, such as ensuring bodily hygiene, prevention of bedsores, and checking the catheters and intubation. Another issue that she identifies is the inadequate cleanliness of hospital wards and treatment rooms: “The cleaning lady checks (the list) saying that she cleaned everywhere, but the reality is different. The hygiene status of the wards and the treatment room is not in line with what is claimed to have been done.”<sup>16</sup> In addition, disorderly movement of medical staff between hospital departments favours contamination. Brumboiu believes that such practices are spreading between hospitals through informal contacts between healthcare workers: “this is a contagion phenomenon.”

A report<sup>17</sup> conducted in December 2015 at the request of the Ministry of Health to assess HAIs surveillance, prevention and control activities in the healthcare facilities in Bucharest where the Colectiv fire victims had been treated confirms and completes the picture of the problems in hospitals.

The report’s findings stated:

“1. Not all hospitals have the capacity to control the microbial circulation in the hospital.



2. The current equipment for some laboratories and/ or the laboratory outsourcing does not allow an effective work on infection control or monitoring of antibiotic therapy in every hospital.
3. There is no uniform, protocol-based approach in some sensitive activities: patient screening and isolation, cleaning/ disinfection depending on the risk area. Although there are many protocols, they are sometimes not known or observed, staff compliance is low, which indicates a need for thorough training, (...) focused on the major issues of the moment, e.g. antibiotic treatment and microbial resistance, antibiotic consumption, detecting the actual number of nosocomial infections in the unit.
4. The hospital Services for Prevention and Control of Nosocomial Infections have variable capacity to implement the recommendations they make, with economic considerations often being invoked as obstacles by the management.
5. The specialized staff needed for the control and prevention of nosocomial infections (microbiologist, epidemiologist, infectious diseases specialist) is lacking or insufficient. (..)

These shortcomings have various causes, have accumulated over time and are mainly due to the organization of health units, which is imposed by their architectural limitations and lack of medical staff.”

### **Expert Recommendations and Requests for Supporting Measures**

**Despite the fact that it is prohibited to dispense antibiotics in pharmacies without a prescription, the 2016 Eurobarometer showed that this is the way that 16% of Romanian respondents had obtained their last antibiotic course, above the European average of 7%, and only below Greece.**

Discussing the issue in a press conference, former Minister Vlad Voiculescu admitted that regulations are often not observed. “There is certainly a weakness of the state’s control capability”, he said, announcing his intention to take measures to strengthen control in pharmacies.

The true extent of antibiotics being dispensed by pharmacies without a medical prescription is not fully known at this time, Sandra Alexiu and Gabriel Popescu say, because doctors prescribe antibiotics not only on electronic prescriptions for drugs that are partly covered by the health insurance funds, but also on simple paper forms, for patients willing to pay full price. In order to compare the total amount of antibiotics being sold by pharmacies with those prescribed by doctors, simple paper forms could also be registered in a database, Popescu told EPHA. Another solution would be to introduce special prescriptions for antibiotics, the way Greece - the only country which surpasses Romania’s total antibiotic consumption— did for fluoroquinolones.

Professor Popescu too believes that promotional activities “in an area as hot as antibiotics” should be restricted one way or another. He points out that access to independent medical information for Romanian doctors, which is currently low and costly, should increase in order to balance the information coming from producers and distributors. Sandra Alexiu says that medical societies can regulate promotional activities in the conferences they organize, by setting up scientific quality standards for satellite symposia.

Sandra Alexiu says that family doctors often have to make decisions on prescribing antibiotics on the spot, because laboratory tests are either inaccessible to patients in rural areas or are not reimbursed because the available funds run out quickly in the first few days of the month. In addition, doctors do not have the funds to acquire point of care (rapid diagnostic) tests.

In addition to the points raised above, respondents to a small survey on the administration



of antibiotics have mentioned a number of tools that might support doctors in their work:

### **What could help doctors in their work? How EU support could make a difference**

- Rules in line with best practice for antibiotic prescribing in medical offices,
- Updated treatment guidelines,
- Regularly updated maps of resistance to major antibiotics and on optimal treatment for outpatient infections.
- Public education to reduce self-medication
- Better control of antibiotic dispensing in pharmacies
- Regulation of promotion of antibiotics in clinics, hospitals and pharmacies.

Marius Geantă, from the health policy think-tank, believes that in the past, professional societies have not given AMR the attention it deserved: “Looking at the agenda of relevant congresses, we see that it is antiviral therapy for HIV and hepatitis that had the large share – AMR used to be a secondary topic.” He thinks that the Romanian College of Physicians should now grant a large number of continuing medical education points to courses on this subject, so as to stimulate the participation of doctors. In 2016, the SNMF, together with Gabriel Popescu, created an accredited online course about patient adherence to antibiotic treatment, which proved popular with family doctors and might be extended and expanded in the coming years, Alexiu says.

### **Irina Brumboiu finds it necessary to improve epidemiological surveillance of resistant germs in hospitals**

which would connect the information collected from each case with the realities of the different hospitals so that the proposed

measures are adapted to each medical unit.

In addition, she thinks hospital managers should be involved in ensuring that staff actually fulfil work duties, judging by objective criteria.

### **Reality check**

Some interviewees pointed out limitations of simply copying approaches applied in other countries, and highlighted the importance of adapting the design of rules and programmes.

When it comes to both antibiotic prescribing by physicians and their dispense in pharmacies, Vlad Mixich, vice president of the National Medicines Agency at the time of the interview with EPHA, expressed reservations about the effectiveness of regulations: “You can pass laws, give sanctions. It’s useless - especially on this subject, because you’re interfering with the doctor’s independence and autonomy to practice, which is a delicate area legally and ethically. Precisely because of this, doctors usually have very little compliance to measures like these.” He cites the right to free health care enjoyed by law by pregnant women in Romania, to which many women, especially those from disadvantaged groups, do not have access to in reality; what’s more, despite hundreds of doctors being investigated on corruption charges in recent years, he points out that the practice of informal payments does not seem to have diminished. “This is a very difficult thing to understand in Western Europe: legally, on paper, things are the way they should be; but in practice, the law does not necessarily apply.” Mixich believes that better results could be achieved through behavioural interventions to physicians and pharmacists; these interventions would need to be properly prepared and tested by a team of well-trained people, who have the “luxury” to deal with the AMR topic for at least one year.





**“When I talk about the luxury of having a whole year for this, I’m thinking of the fact that in the last 27 years, the average mandate of a Romanian health minister was less than nine months”, says Mixich, who also mentions a chronic understaffing of the Ministry.**

Professor Popescu too explains that, in general, there are two major approaches when it comes to antimicrobial stewardship programs: the restrictions on prescribing, which have short-term results, but generate “escape mechanisms” after a few months - such as prescribing other last-line antibiotics instead of the ones being restricted, or giving antibiotics while the stewardship officer is not in the hospital - and the so-called “prospective audit” approach, involving discussions with the prescribing physician about alternatives to last-line antibiotics, which yield results after years of sustained efforts.

### **Recent progress - “Things are finally picking up”**

Recent years have marked some small improvements in knowledge about antibiotics, as well as in reporting of AMR and nosocomial infections. According to the latest Eurobarometer, Romanians reported the largest decrease in antibiotic consumption in Europe, 9 percentage points compared to 2013, while the share of those who had obtained them from a doctor increased by 4 p.p. The share of respondents who said they had taken the last course of antibiotics for a cold has decreased by 13 p.p., and that of respondents who had taken it for influenza by 11 p.p. The proportion of correct answers to each of the four questions about the proper use of antibiotics has increased significantly, while the average number of correct answers also increased from 1.5 in 2013 to 2.1 in 2016. As a result, Romanians are no longer the worst performers in Europe in this category.

Although there is yet no concrete evidence of this, Professor Alexandru Rafila feels that surgeons are being more careful about prophylactic antibiotic use, since the results of the PPS led to the adoption in 2013 by the Ministry of a Guide<sup>18</sup> dedicated to the issue. He also notes that the data representativeness on Romanian AMR levels improved in recent years, with the number of participating hospitals increasing from five to seventeen, while the number of invasive isolates being tested grew from a few hundred to nearly 1,800.

**“We’re starting to have a picture which is closer to the truth. The real picture will probably be when we have (data from) at least 50 hospitals, so that all counties are covered, and send a few thousand isolates. This requires that each hospital have certain technical facilities. But things are finally picking up”, Rafila concludes.**

In a press conference on European Antibiotic Awareness Day (EAAD) 2016, Roxana Șerban, coordinator of the nosocomial infections program at INSP, showed that after nearly two decades of official incidence rates for nosocomial infections declining, there’s been a slight increase in reporting since 2013. In the first nine months of 2016, the number of reported cases had risen by a quarter over the previous year, from 9,402 to 11,829. “Although not a spectacular result, it is nevertheless gratifying, because it means that medical staff became more aware and more responsible in admitting and reporting this type of infections. Admission is the first step to limiting this phenomenon and improving health care”, Șerban said.

### **Learning from tragedy: National measures**

When he became Minister of Health in May 2016, Vlad Voiculescu named<sup>19</sup> HAIs among the three priorities of his brief term. In July, a team of experts from ECDC visited Romania to discuss the topic, following which a number of short and medium-term actions were

identified. According to press releases from the Ministry of Health<sup>20</sup> and ECDC<sup>21</sup>, the first suggestion was to increase awareness of nosocomial infections and infection control measures, starting with hand hygiene, among hospital staff, patients, carers, and the general public.

#### **ECDC recommendations**

##### ***Awareness of the situation and infection control measures***

Increase awareness of nosocomial infections and infection control measures, starting with hand hygiene, among hospital staff, patients, carers, and the general public.

##### ***Encouraging HAIs reporting and implementing integrated epidemiological and microbiological reporting systems***

ECDC experts have recommended that hospitals be encouraged by the Government and the media to report HAIs in order to learn and improve their situation and that appropriate training be organised for the various categories of their staff. It was also suggested to implement integrated epidemiological and microbiological reporting systems, which could provide data for actions both at the hospital and the Ministry of Health levels.

##### ***Improving microbiology standards and protocols***

Another possible measure identified was improving microbiology standards and protocols to monitor nosocomial infections, as well as establishing a reference microbiological function to allow identification of unusual strains, confirmation of antibiotic susceptibility and epidemiological typing of bacterial strains involved in outbreaks.

##### ***Strengthening the role of multidisciplinary HAIs control committees***

Finally, the ECDC experts recommended strengthening the role of multidisciplinary HAIs control committees in hospital and at national level and an adequate funding for infection control activities.

A good part of these recommendations seem to be reflected in the actions tak

en by the Ministry of Health in late 2016. The main administrative measure was Order 1101<sup>22</sup>, regarding the rules for HAIs surveillance, prevention and control in hospitals, which entered into force in early October. Gabriel Popescu, the former minister’s adviser, explains that the order redefines the departments in charge of these activities in hospitals and clarifies the duties of each of the structure’s members. It stipulates that:

#### **Order 1101: the Ministry of Health takes action**

- For the first time, multidisciplinary hospitals must employ infectious diseases specialists, stating that there should be at least one such physician as well as an epidemiologist for every 400 hospital beds.
- The tasks of the infectious diseases specialist include developing the hospital antibiotic stewardship policy, which Popescu says had been seriously pursued in only a few hospitals prior to this Order.
- It also sets out the tasks, from managers to nurses, of all those playing a role in preventing germ transmission and in the appropriate use of antibiotics, thereby seeking to involve all hospital staff - not just the technical core - in these activities.
- In addition, all nosocomial infections will be reported weekly and in greater detail, which should increase the effectiveness of potential interventions;
- The Order also states a number of precautions in relation to colonized or infected patients.

Aurel Marin, MD, editor-in-chief of “Viața medicală”, a Romanian medical and health policy weekly newspaper, tells EPHA that introducing an explicit obligation for hospital staff to prevent nosocomial infections is useful, but believes that this would allow sanctions



to be applied in the event that such infections are reported. He also notes the requirement that every hospital employs at least one epidemiologist, even if Romania has very few such specialists - according to Alexandru Rafila, there are currently about 150 epidemiologists, some of whom do not even work in hospitals. While welcoming the creation of the leader positions for the antibiotic stewardship programs in hospitals, Marin comments that it “has no explicit possibility of approving or rejecting other doctors’ antibiotic prescriptions.” He also notes that the act does not mention regular AMR occurrence reporting. The Order provides that the position of leader for antibiotic stewardship programs should be occupied by an infectious diseases doctor or, if such a specialist is not available, by another clinician who has completed a training course in the field. But the journalist points out that there are few infectionists available for smaller hospitals, and that the Order does not specify whether the training courses for other clinicians will be organized by medical universities, what their minimum duration should be and how often they should be updated. Marin believes that antimicrobial stewardship could also be ensured by non-clinical specialists such as epidemiologists, microbiologists and pharmacologists, which however are not included in this Order. Finally, the journalist says that

**“(these) measures have not been tested in any pilot study and it is unknown how effective they will prove. In addition, they do not solve the problem of antibiotic overprescribing in primary care, and family doctors are in no way affected by the new Order. A significant share of antibiotic prescriptions, (which originate) from the GPs, are left unsupervised and unchecked.”**

The Ministry of Health also updated another Order<sup>23</sup> regarding measures for cleaning, disinfection and sterilization in health care facilities. Professor Gabriel Popescu says that it places a greater emphasis on education and hygiene, including hand hygiene, as measures to prevent microbial transmission. Aurel Marin,

however, notes the lack of a “systematic approach to ensure the hand hygiene of health-care workers”, as well as the importance given to biocides and to sterilization procedures “in the absence of data clearly indicating where the problems with nosocomial infections lie.”

One of the measures often being heralded in 2016 was a change in the management contracts for hospitals, in which one of the indicators used to be the number of nosocomial infections, which discouraged the reporting of actual data. “The (hospital) manager can be kicked out if it exceeds a certain level of nosocomial infections. So nobody had any interest to report the actual levels”, former Minister Vlad Voiculescu explained. This provision no longer appears in the draft Order<sup>24</sup> on performance indicators for public hospital management, which was put to public consultation in late 2016. The project establishes two essential indicators for obtaining a good final score: the level of specialized staff occupancy in the hospitals’ HAIs prevention services, as stated in Order 1101, and the rate of premises which comply from a sanitary and hygienic standpoint. According to the draft Order, the manager’s assessment would also include the screening rate of patients hospitalized in the ICU, oncology and haematology wards for germs with high epidemiologic risk, the amount of alcohol-based disinfectant being used, and compliance of the duration of perioperative antibiotic prophylaxis with the 2013 guidelines.

**In addition, an indicator will assess whether the hospital has conducted an annual point prevalence survey of HAIs and antibiotic consumption, which according to Gabriel Popescu, “could generate data much closer to reality.”**

## **Europe’s role**

**“There is the free movement of goods, capitals, people and services – but there’s also (the free movement of) treatment-resistant microorganisms. The first four are regulated through (European) directives, right? I think (the latter) should also be regulated one way or the other. I would not leave everything up to the Member States”, Marius Geantă says.**

On EAAD 2016, Amalia Șerban, a director in the Ministry of Health, expressed hope that **the AMR Nation action plan, which was requested by the EU Health Council Conclusions on AMR of June 2016, will be developed in 2017. The first step will be the setting up of an inter-ministerial committee by Government decision.**

The Romanian government has made a start with tackling HAIs, but the experts point out that changes will have to be structural and strictly supervised to ensure their effectiveness, perhaps with external support of expertise and resources.

As part of a 2016-2018 Strategic plan to prevent and combat nosocomial infections, adopted in April, steps have been taken in the second part of the year to increase the laboratories’ capacity to test for colonization with multidrug resistant bacteria, Professors Rafila and Popescu explain. As part of an integrated training conducted in December for doctors involved in HAIs control and prudent use of antibiotics in the most important 112 Romanian hospitals, microbiologists were trained on screening multidrug resistant germs and on standardizing the execution and interpretation of antibiotic susceptibility tests. In addition, investments were made to improve and standardize microbiology laboratories’ equipment.

**Another Ministry of Health Order<sup>25</sup>, which entered public consultation**

**at the end of 2016, plans to increase the capacity to isolate and treat patients who are colonized or infected with multidrug resistant microbes, by setting up infectious diseases wards, with dedicated rooms, staff and equipment in order “to limit the spread of germs from the infected / colonized patient to other inpatients and to reduce the risk of these germs crossing from the hospital in the community.”**

**Aurel Marin believes that, although they are welcome in theory, the recent steps to improve laboratory capacity “are symbolic and do not have a systematic and permanent nature.”**

Referring to measures regarding the capacity to isolate patients, he believes they will be hard to implement for small hospitals, which “will have difficulties in contracting the epidemiology and infectious diseases services, (and) have no real possibilities of executing bacterial cultures and antibiotic susceptibility tests.” In turn, Professor Rafila notes that ensuring the isolation and dedicated staff to treat patients with multidrug resistant germs will involve costs that might be difficult to bear for some hospitals.

In the long term, Professor Gabriel Popescu believes it is also important to educate the new generations of doctors: “for the first time this year, we have an optional course in the 4th year (of college) on AMR, prudent use of antibiotics, and the prevention of nosocomial infections. I also proposed that such a module be available during residency training for all specialties.”

**Aurel Marin, however, says that “today it is not information that’s missing, but best practice guidelines as well as therapeutic and prophylactic protocols. In addition, there should be a**





comprehensive list of antibiotics which can only be prescribed with the advice of an infectionist or pharmacologist.” He believes Romania needs “a strategic planning of healthcare workers’ competences, especially of the scarce specialties.” He warns that “in the absence of specialists, any kind of legislative measures will remain only on paper.”

Measures beyond infection control and workforce education become more complex to define and implement, but respondents outlined the kind of guidance that would help and highlighted especially the valued role of the European Centre for Disease Prevention and Control (ECDC):

“Health is not a (European) regulatory area, so I can’t say that I wish there was a European Directive to prevent colistin from being prescribed without (expert) advice, because this is not possible”, Professor Popescu says.

*He appreciates ECDC’s recent draft proposal for EU guidelines on prudent use of antibiotics and believes that a visit by the agency’s experts in March 2017 will be a very important step forward for Romania. The visit will focus on AMR and antibiotic use and is expected to produce a series of recommendations, like the previous one on nosocomial infections.*

*Aurel Marin, the medical journalist, also also considers that technical assistance provided to Romania by institutions like ECDC is important and thinks that it would be useful to implement strategies that countries like the Netherlands have successfully used to fight HAIs and AMR.*

*In turn, Alexandru Rafila believes that “ECDC should play a greater role and manage more consistent programs in the areas where Member States have problems.” He thinks that European experts should make an independent assessment, and then, alongside Romanian colleagues, develop a*

*multi-annual plan which could include legislative recommendations and regular reviews.*

*Sandra Alexiu, the vice president of the SNMF, says that having access to European funds to acquire point of care tests could be useful for doctors to fight AMR: “if I see a child with fever and very few other symptoms, I can find out quickly (with such tests) whether the infection is bacterial or not, (and) maybe in half the cases I would not treat with antibiotics.”*

Alexiu says that 90% of Romanian family doctors are self-employed and cannot access European funds. Organizations like SNMF also find it difficult to use such funds, which they could use to organize courses and write guidelines. Given that Romania should soon build three new regional hospitals with a European financial support of 150 million euros, Gabriel Popescu says that these should have the isolating capacities for patients colonized or infected with resistant germs that old hospitals are lacking. Both Aurel Marin and assistant professor Irina Brumboiu think there is a need for a

*European curriculum for university courses on combating HAIs and AMR, which should be mandatory.*

*Vlad Mixich, the former vice president of the National Medicines Agency, would like the EU to be involved with training the experts that should form a professional public policies unit in the Ministry of Health, which, he says, currently only functions on paper.*

He accuses the Romanian political parties of being irresponsible in the way they approached the subject of nosocomial infections – first by ignoring it, then by politicizing it – and believes that

*the European Semester could help by sending “extremely harsh” signals on AMR and HAIs.*

While acknowledging that the European Semester has so far adopted a cautious language on health issues, Mixich believes it is still the right tool to exert pressure on a Member State – “but it needs to be sharpened.”

## ***The Legacy of Colectiv: Awareness and Change***

In the final months of 2016, the Ministry of Health also launched two information campaigns. According to the Ministry’s website, the aim of the “Clean hands in hospitals” campaign is to increase awareness among the medical staff, patients and the public about the importance of hand disinfection in preventing HAIs. The campaign’s web page explains the proper hand washing technique and contains information about nosocomial infections and AMR. Another aim of the information campaign, according to the Ministry of Health, is to convince hospital managers to purchase disinfectant dispensers.

Another public awareness campaign, “No to random antibiotics”, promotes the appropriate use of antibiotics “by informing physicians and the lay public on the risk posed by their excessive and mistaken use.” A novel feature is the distribution of tens of thousands of boxes of pseudo-medicines, containing information specific to each group to whom they are addressed – patients, family doctors and hospital doctors. Funded by the Colectiv fire victims’ association, the campaign was launched exactly one year after Alexandru Iancu’s death. ■



## Methodology

The information contained in this report is the result of desk research and interviews (face-to-face and e-mail communication) undertaken during November-December 2016. It thus includes statements that were given verbally in response to targeted questions by the author, Mihail Calin. It also contains citations found in relevant media articles or that were provided at events.

In terms of scope, the case study does not aim to provide a comprehensive picture of the Romanian AMR situation but merely a snapshot of how key issues related to the sustainability of health systems can lead to the (cross-border) spread of AMR.

This report does not seek to discuss the veterinary or environmental causes of AMR but it is hoped that the healthcare gaps identified in this paper will also be discussed in relation to the many other aspects that expedite the development of AMR.

EPHA recognises that the issues discussed may well not present new information to policy makers, experts and other health stakeholders working in Romania. However, we hope that by reiterating them and placing them in a European, cross-border context, this paper can contribute to making a stronger case for EU involvement, support and resources to tackle AMR in order to protect public health across Europe and beyond.

## Author, Coordinators, Citation

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