

Surveillance for control of antimicrobial resistance

Evelina Tacconelli, Frangiscos Sifakis, Stephan Harbarth, Remco Schrijver, Maaïke van Mourik, Andreas Voss, Mike Sharland, Nithya Babu Rajendran, Jesús Rodríguez-Baño, on behalf of the EPI-Net COMBACTE-MAGNET Group*



Antimicrobial resistance poses a growing threat to public health and the provision of health care. Its surveillance should provide up-to-date and relevant information to monitor the appropriateness of therapy guidelines, antibiotic formulary, antibiotic stewardship programmes, public health interventions, infection control policies, and antimicrobial development. In Europe, although the European Antimicrobial Resistance Surveillance Network provides annual reports on monitored resistant bacteria, national surveillance efforts are still fragmented and heterogeneous, and have substantial structural problems and issues with laboratory data. Most incidence and prevalence data cannot be linked with relevant epidemiological, clinical, or outcome data. Genetic typing, to establish whether trends of antimicrobial resistance are caused by spread of resistant strains or by transfer of resistance determinants among different strains and species, is not routinely done. Furthermore, laboratory-based surveillance using only clinical samples is not likely to be useful as an early warning system for emerging pathogens and resistance mechanisms. Insufficient coordination of surveillance systems of human antimicrobial resistance with animal surveillance systems is even more concerning. Because results from food surveillance are considered commercially sensitive, they are rarely released publicly by regulators. Inaccurate or incomplete surveillance data delay a translational approach to the threat of antimicrobial resistance and inhibit the identification of relevant target microorganisms and populations for research and the revitalisation of dormant drug-discovery programmes. High-quality, comprehensive, and real-time surveillance data are essential to reduce the burden of antimicrobial resistance. Improvement of national antimicrobial resistance surveillance systems and better alignment between human and veterinary surveillance systems in Europe must become a scientific and political priority, coordinated with international stakeholders within a global approach to reduce the burden of antimicrobial resistance.

Burden of health-care-associated infections and antimicrobial resistance

Health-care-associated infections and antimicrobial resistance are growing threats to public health and the provision of health care worldwide. However, their scale is difficult to quantify because of the high heterogeneity of data collection and reporting and the absence of surveillance systems, particularly in low-income and middle-income countries.¹⁻⁷ This paucity of information substantially limits coordination of approaches and comparability of the effectiveness of interventions. This Personal View focuses on European surveillance systems to define the status, main limitations, and unmet needs of health-care-associated infections and antimicrobial resistance.

In Europe, the burden of antibiotic resistance is established primarily through the European Centre for Disease Prevention and Control (ECDC) point-prevalence surveys, the European Antimicrobial Resistance Surveillance Network (EARS-Net), and national institutions or networks (table 1; figure). In the 2011–12 hospital point-prevalence survey, meticillin resistance was reported in 41% of invasive *Staphylococcus aureus* isolates, vancomycin resistance in 10% of enterococcal isolates, third-generation cephalosporin resistance in 33% of all Enterobacteriaceae isolates, and carbapenem resistance in 81% of *Acinetobacter baumannii* isolates. Antimicrobial resistance is also increasingly detected in community-acquired infections, although variation between countries is evident.⁸

Findings within the past decade of antimicrobial resistance in animals and the food chain portend further

increases in antimicrobial resistance in human beings. Resistance to ampicillin, quinolones, tetracyclines, and sulphonamides has frequently been detected in salmonella and *Escherichia coli* isolates from broilers,

Key messages

Short-term priorities

- Agreement on surveillance goals, definition, and measures of antimicrobial resistance, involving representatives from academia, public health, and the pharmaceutical industry, stakeholders, and clinicians
- Development of European data sharing policy encouraging and enabling surveillance systems to provide barrier-free and timely access to key national data on antimicrobial resistance

Long-term priorities

- Creation of a platform in which representatives from public health and the pharmaceutical industry collaborate to maximise the value of existing and future epidemiological efforts in Europe
- Ministerial involvement to include surveillance of resistance in the political agenda and define dedicated resources
- Implementation of a harmonised surveillance system that links European clinical, epidemiological, radiological, and microbiological data
- Increase in coverage and representatives of antimicrobial resistance surveillance systems in animals and the food chain
- Connection among surveillance systems in human beings, animals, and the food chain

Lancet Infect Dis 2018;
18: e99–106

Published Online
October 25, 2017
[http://dx.doi.org/10.1016/S1473-3099\(17\)30485-1](http://dx.doi.org/10.1016/S1473-3099(17)30485-1)

*Members of the EPI-Net COMBACTE-MAGNET Group are listed at end of paper

Division of Infectious Diseases, Tübingen University Hospital, DZIF Center, Tübingen, Germany (E Tacconelli MD, N B Rajendran PhD); US Medical Affairs Evidence Generation, AstraZeneca Pharmaceuticals LP, Gaithersburg, MD, USA (F Sifakis PhD); Infection Prevention and Control Service, University Hospitals of Geneva, Geneva, Switzerland (S Harbarth MD); VetEffect, Bilthoven, Netherlands (R Schrijver MD); Department of Medical Microbiology and Infection Control, University Medical Center Utrecht, Utrecht, Netherlands (M van Mourik MD); Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, Netherlands (A Voss MD); St George's University of London, London, UK (M Sharland MD); Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario Virgen Macarena, Sevilla, Spain (J Rodríguez-Baño MD); Instituto de Biomedicina de Sevilla, Sevilla, Spain (J Rodríguez-Baño); and Departamento de Medicina, Universidad de Sevilla, Sevilla, Spain (J Rodríguez-Baño)

Correspondence to:
Dr Evelina Tacconelli, Division of Infectious Diseases, Department of Internal Medicine, Tübingen University Hospital, 72076 Tübingen, Germany
evelina.tacconelli@med.uni-tuebingen.de

Surveillance system or institution	
National	
Austria	National Reference Center for Nosocomial Infections and Antimicrobial Resistance (NRZ)
Belgium	The Scientific Institute of Public Health (WIV-ISSP)
Bulgaria	Bulgarian Surveillance Tracking Antimicrobial Resistance (BuSTAR)
Croatia	Intersectoral Coordination Mechanism for the Control of Antimicrobial Resistance (ISKRA)
Croatia	Croatian Institute of Public Health (CIPH)
Cyprus	National antimicrobial resistance surveillance system
Czech Republic	National Institute of Public Health (NIPH)
Denmark	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP)
Finland	Finnish Study Group for Antimicrobial Resistance (FIRE)
France	The National Observatory of the Epidemiology of Bacterial Resistance to Antibiotics (ONERBA)
Germany	Hospital surveillance system for nosocomial infections (KISS)
Germany	Antibiotic Resistance Surveillance (ARS)
Germany	Surveillance of antibiotic use and bacterial resistance in intensive care units (SARI)
Germany	Monitoring antibiotic resistance in Niedersachsen (ARMIN)
Greece	Greek System for the Surveillance of Antimicrobial Resistance (GSSAR)
Hungary	National Nosocomial Surveillance System (NNSR)
Ireland	Health Protection Surveillance Centre (HPSC)
Italy	Regional surveillance system for intensive care units (SITIER)
Italy	National surveillance systems for post-surgical infections (SNICH)
Italy	Prospective surveillance of nosocomial infections in intensive care units (SPIN-UTI)
Italy	Surveillance of antibiotic resistance—National Institute of Health (AR-ISS)
Lithuania	Surveillance of antibiotic resistance—Institute of Vilnius
Netherlands	Infectious Disease Surveillance and Information System for Antibiotic Resistance (ISIS-AR)
Norway	Norwegian surveillance system: health-care-associated infections module for surgical site infections; antimicrobial drug resistance module; communicable diseases (FHI)
Portugal	Antibiotic Resistance Surveillance Programme in Portugal (ARSIP)
Romania	Sentinel surveillance system of nosocomial infections and antimicrobial resistance
Slovakia	Slovak National Antimicrobial Resistance Surveillance System (SNARS)
Spain	Estudio Nacional de Vigilancia de Infección Nosocomial en Servicios de Medicina Intensiva (ENVIN-UCI)
Sweden	Annual resistance monitoring and quality control programme (ResNet)
Sweden	Swedish surveillance of antimicrobial resistance (Svebar)
Switzerland	Swiss Centre for Antibiotic Resistance (ANRESIS)

(Table 1 continues in next column)

Surveillance system or institution	
(Continued from previous column)	
Switzerland	CA-MRSA surveillance system (CA-MRSA)
Regional	
Italy	Regional (Emilia-Romagna) surveillance of antibiotic resistance and intravenous antibiotic usage (LAB)
Italy	Regional (Toscana) surveillance of antibiotic resistance (SART)
Spain	Regional surveillance system (Asturias; SVPCIP)
Spain	Regional surveillance system (Galicia; SVIN)
Spain	Regional surveillance system (Catalunya; VINCat)
Spain	Prevention and control of nosocomial infections and inappropriate usage of antibiotics (PIRASOA)
Switzerland	Prevention and control of nosocomial infections (HPCI)
UK	Welsh Healthcare Associated Infections Programme (WHAIP)
UK	Health Protection Scotland (HPS)
UK	Public Health England (PHE)
UK	Public Health Agency (PHA)

CA-MRSA=community-associated-meticillin resistant *Staphylococcus aureus*.

Table 1: National and regional surveillance systems of antimicrobial resistance

strains have been reported over the past decade.¹¹ Furthermore, an association between antimicrobial consumption in food-producing animals and resistance in human bacteria has been reported for the first time by the ECDC, European Food Safety Authority, and European Medicines Agency.¹²

The need for improved surveillance

Surveillance is essential to all aspects of the management of health-care-associated infections and antimicrobial resistance because it provides the necessary information to develop and monitor therapy guidelines, antibiotic formularies, antibiotic stewardship programmes, public health interventions, infection control policies, and novel antimicrobials and vaccines. The key part played by surveillance starts with the development of both algorithms for empirical antibiotic therapy and stewardship programmes. Active monitoring of antimicrobial resistance is essential for effective antibiotic stewardship, supporting appropriate antimicrobial use that optimises patients' clinical outcomes while minimising unintended effects of antibiotics, including toxicity and the emergence of resistance.¹³ Monitoring should be combined with the availability of local-level, hospital-level, and community-level data. Knowledge of up-to-date surveillance and cohort data improves public health not only at the local level (clinical outcomes for patients), but also globally (antimicrobial resistance rates in hospitals and communities). Moreover, data from global surveillance systems provide information on new and concerning trends of antimicrobial resistance and allow policy makers at the national and international levels to design new strategies to counter the threat.

artificially fattened turkeys, and meat.^{9,10} Within the past year, extended-spectrum β -lactamase-producing strains have been isolated in Europe, and colistin-resistant

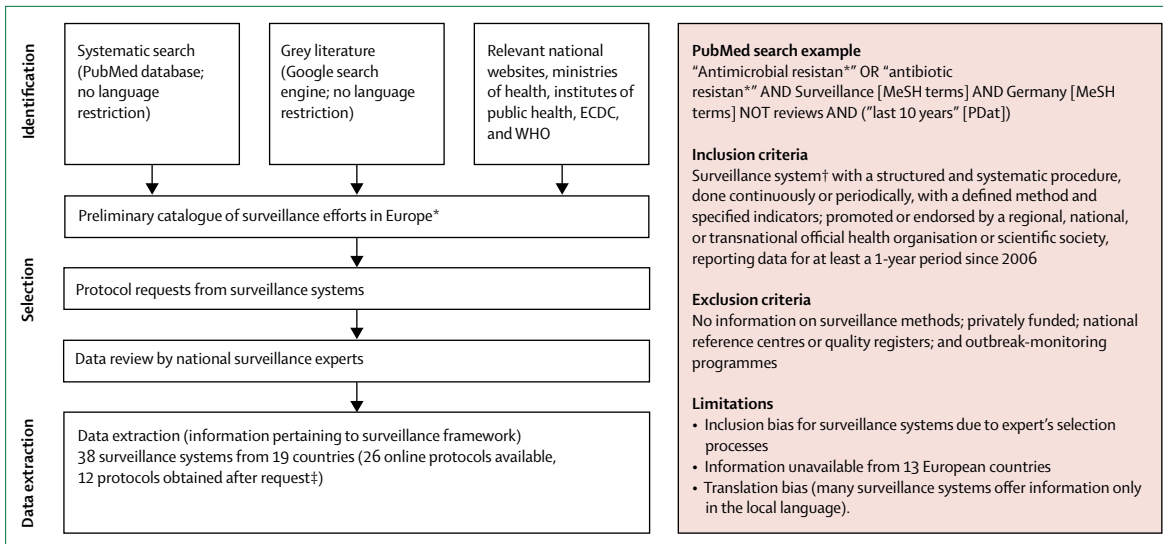


Figure: Mapping of national surveillance systems in Europe

Relevant websites and national surveillance experts are selected on the basis of expert advice from the European Committee of Infection Control of the European Society of Infectious Diseases and Clinical Microbiology (EUCIC). ECDC=European Centre for Disease Prevention and Control. *Europe includes the 28 European Union member states and the four countries from the European Free Trade Association. †A surveillance system was defined as a structured and systematic procedure to measure the prevalence or incidence cases of antimicrobial resistance. ‡Bulgaria, Cyprus, Czech Republic, Estonia, Iceland, Latvia, Liechtenstein, Luxembourg, Malta, Poland, Romania, and Slovenia.

European surveillance data are publicly available from the ECDC and many national cohorts.¹⁴⁻¹⁶ EARS-Net, the largest publicly funded antimicrobial resistance surveillance system in Europe, was established in 1998 by the European Commission and has been coordinated and funded by the ECDC since 2010.¹⁷ This network, which substantially improved the quality of surveillance data in Europe, provides yearly reference data on antimicrobial resistance; however, the system is adversely affected by the heterogeneity among European countries (ie, variations in the organisation of health-care systems, health-seeking behaviour, reimbursement strategies, and local indications for blood sampling). Since antimicrobial resistance has emerged as a substantial threat, many national surveillance systems have also been implemented in Europe (table 2).

Limitations of these national surveillance systems can be grouped into three categories: structural problems, laboratory-based surveillance issues, and insufficient co-ordination with animal and food surveillance systems (panel). Structural problems are manifold. Generally, the national surveillance efforts in Europe are still fragmented and heterogeneous. Many local and national systems for data collection on health-care-associated infections and antimicrobial resistance have different goals and little or no coordination, harmonisation, or information sharing with international networks. Inadequate standardisation of epidemiological definitions, samples and data collected, settings included, microbiological testing methods (including susceptibility testing), and data sharing policies are potential obstacles to reliable and informative collaborative surveillance. Table 2 provides the main

characteristics of 24 national and 14 regional antimicrobial resistance surveillance systems active in 19 European countries. Almost half of these systems do not report whether guidelines from the European Committee on Antimicrobial Susceptibility Testing or Clinical and Laboratory Standards Institute are used to define resistance—a clear definition of antimicrobial resistance is provided for only a third of the systems. Although point-prevalence surveys and laboratory-based surveillance can provide comprehensive information, these results are often published years after data collection, reducing their utility in clinical, institutional, and regulatory decision making and targeting of resources and research priorities. Only 3% of the surveillance systems in Europe provide real-time access to resistance data (table 2).

Inherent limitations of the methods also challenge adequate interpretation of the data. Laboratory-based systems have many limitations. First, the microbiological results reported usually have no associated relevant epidemiological, clinical, or outcome data. Thus, these systems provide no information on the identification of at-risk patient populations, types of infections, sources (ie, community-onset, health-care-associated, or hospital-acquired infections), treatment failure, or real burden of disease associated with health-care-associated infections and antimicrobial resistance. Second, genetic typing and characterisation is not routinely included for all relevant isolates or mechanisms of resistance; this testing would help to establish whether trends of antimicrobial resistance are caused by the spread of resistant strains or by transfer of resistance determinants among different strains and species.¹⁸ Third, sample

	Number of systems (%)
Coverage	
National	24 (63%)
Regional	14 (37%)
Population	
Inpatient or outpatient	20 (53%)
Inpatient	10 (26%)
Laboratory	5 (13%)
Not specified	3 (8%)
Time of reporting	
Yearly	23 (61%)
Quarterly	3 (8%)
Monthly	2 (5%)
Real time	1 (3%)
Mixed	5 (13%)
Not specified	4 (11%)
Modality of reporting	
Individual data	3 (8%)
Comparative data	13 (34%)
Pooled data	19 (50%)
Mixed data	1 (3%)
Not specified	2 (5%)
Quality audits	
Done	22 (58%)
Resistance definition criteria	
EUCAST	12 (32%)
CLSI	1 (3%)
Local	2 (5%)
EUCAST or CLSI	7 (18%)
EUCAST, CLSI, or local	3 (8%)
Not specified	13 (34%)
Outcome	
Prevalence	14 (37%)
Incidence	7 (18%)
Prevalence or incidence	9 (24%)
Others	8 (21%)
Clinical data*	
Reported	17 (45%)
Reported coverage of microorganisms	
MRSA	32 (84%)
VRE	30 (79%)
CR <i>Pseudomonas aeruginosa</i>	24 (63%)
CR <i>Acinetobacter baumannii</i>	25 (66%)
CR <i>Klebsiella pneumoniae</i>	23 (60%)
<small>EUCAST=European Committee on Antimicrobial Susceptibility Testing. CLSI=Clinical and Laboratory Standards Institute. MRSA=metillin-resistant <i>Staphylococcus aureus</i>. VRE=vancomycin-resistant enterococci. CR=carbapenem resistant. *Includes antibiotic use in 15 countries (40%), invasive procedures in seven (18%), comorbidities in two (5%), previous hospitalisation in four (11%), and travel history in one (3%).</small>	
Table 2: Major characteristics of 38 national and regional surveillance systems in Europe	

collection might introduce biases that reduce external validity, prevent measurement of the effect of health-care-associated infections or antimicrobial resistance

within an institution or a community, and prevent prediction of future trends. Differences in the frequency and distribution of sampling among physicians, institutions, and countries, and the inclusion of screening isolates instead of the inclusion of only clinical isolates, undermine how representative the data are. In some settings, sample collection is considered best practice only for the more severe infections or those not responding to first-line treatment. In these cases, rates of antimicrobial resistance might be inflated, and use of these data could lead to an inappropriate choice of therapy and increased resistance and health-care costs. Conversely, under-reporting of health-care-associated infections and antimicrobial resistance might occur if samples are not routinely collected, and reliance on laboratory-based surveillance underestimates the incidence of clinically relevant health-care-associated infections. However, because samples are probably collected from affected sites in a subset of patients, laboratory-based surveillance of only clinical samples is not likely to be useful as an early warning system for emerging pathogens and resistance mechanisms, which are more likely to be first detected as colonisation in samples such as sputum or urine.¹⁹

High-quality surveillance of antimicrobial resistance in animals and the food chain is essential for the understanding of and prediction of trends in antimicrobial resistance and mechanisms in human beings; however, surveillance in these areas is also inadequate. In their report¹² exploring associations between consumption of antimicrobials and antimicrobial resistance in human beings and food-producing animals, the ECDC, European Food Safety Authority, and European Medicines Agency emphasised major limitations of the available evidence and highlighted the need for enhanced combined surveillance. Few European countries have implemented national antimicrobial resistance surveillance programmes for animals or food, and these systems have limited goals (table 2). The systems were set up to monitor resistance mainly in salmonella, *Campylobacter jejuni*, and *E coli* as required by the European Commission's mandate, and only a few monitor resistance in klebsiella and *S aureus*. Even in countries where such systems have been established, insufficient coordination with human antimicrobial resistance surveillance systems limits the data's applicability to human beings. More importantly, existing surveillance systems do not provide any alert or explore the exchange of resistance determinants between the pathogens of human beings and animals in either direction. Data collection in animals is directed mainly towards treatment of disease and less towards detection of resistance to either veterinary or human drugs. The data largely cover veterinary pathogens and antibiotics, so although there is some overlap with human diseases, they are difficult to interpret with regard to human health or are not at all relevant. Furthermore, food and animal surveillance have the same structural problems as human

surveillance systems—namely fragmentation, insufficient standardisation and coordination, and reporting delays. Results from food surveillance are usually not released publicly and can be difficult to obtain from regulators because they are considered commercially sensitive.

Effect on patient care

The limitations of surveillance systems substantially affect patients' care and outcomes. Inadequate and delayed reporting of surveillance data leads to suboptimal empirical prescribing and overprescribing that jeopardise the outcome for the individual, increase risk of transmission among patients treated in hospital and those in the community, and further drive the cycle of antimicrobial resistance development. In a meta-analysis of 27 studies,²⁰ the rate of inappropriate antibiotic therapy in patients with severe infections ranged from 14% to 78%, and more than half of the studies had an inappropriate prescribing rate of more than 50%. Successful empirical therapy of bacterial infections requires knowledge of the potential microorganism and related patterns of susceptibility. Surveillance should thus provide up-to-date information to the clinician to establish a patient's risk for resistance in a specific setting. Because of the increase in globalisation (including refugee movements, international travel, and medical tourism), geographical and temporal changes in antimicrobial resistance should be closely monitored and the data should be available in a timely manner. New molecular tests should also be included to increase the understanding of traceability and spread of new antimicrobial resistance threats. Furthermore, an ideal surveillance system would correlate these data with demographic and clinical data. Surveillance data should be easily accessible, continuously updated, and detect the emergence and spread of previously uncommon or completely novel types of resistance.

In addition to the deleterious effects on patient treatment, inadequate surveillance data hamper efforts in other areas; they can put uninfected patients being treated in hospital and individuals in the community at risk when infection control measures needed to stop the spread of antimicrobial resistance are delayed or incorrectly targeted. Data that are not representative reduce the understanding of antimicrobial resistance and complicate the implementation of agricultural, food industry, and environmental regulations to reduce transmission via animals, food, and water. Inaccurate or incomplete surveillance data inhibit the identification of relevant target microorganisms and populations for research and revitalisation of dormant drug discovery programmes. The wrong targets might be chosen and individuals in academia and industry might be loath to commit scarce resources when the data are of uncertain quality. In particular, inadequate or partial surveillance data are an obstacle to the translational approach in research that is considered the sole pathway for development of new and clinically effective antibiotics.²¹

Panel: Limitations of antimicrobial resistance surveillance in Europe

Structural problems

- Differing objectives
- Insufficient coordination and sharing of information
- Inadequate standardisation of data collected and methods of microbiological testing (including susceptibility testing), and data sharing policies
- Delay in publication and insufficient publication for food surveillance data

Laboratory-based surveillance issues

- Insufficient associated and relevant epidemiological, clinical, and outcome data
- Genetic typing and characterisation not routinely included
- Biases introduced by sample collection protocols

Insufficient coordination between human, animal, and food systems

- Data collection in animals directed at disease eradication and not detection of resistance to either animal or human drugs
- Coverage of only veterinary pathogens and antibiotics in animal and food surveillance systems

The way forward

Because of the pressure of increasing antimicrobial resistance, several initiatives have been launched in Europe in the past few years to address the limitations of existing surveillance systems. The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project of the European Medicines Agency, which since 2009 has collected and reported data on sales of veterinary antimicrobials, has recently announced its strategy for improved surveillance over the next 5 years. ESVAC's goals include expansion of data collection to all countries in the European Economic Area (bolstered by a new regulatory requirement), transition to ongoing annual reporting, standardisation and harmonisation of data collection, automation of data analysis and presentation, database linkage, and integration of animal, food, and human data.²²

The Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) network is a joint initiative of the WHO Regional Office for Europe, the European Society of Clinical Microbiology and Infectious Diseases, and the Dutch National Institute for Public Health and the Environment. CAESAR is a network of national surveillance systems for antimicrobial resistance and includes all countries of the WHO European Region that are not part of EARS-Net. The second annual CAESAR report was published in November, 2016.²³ 20 countries are participating in CAESAR and six have submitted national surveillance data to the CAESAR database.²³ In 2015, WHO launched the Global Antimicrobial Resistance Surveillance System project to improve surveillance of seven antibiotic-resistant bacteria in member states. The surveillance report based on the 2016 data should be made publicly available by July, 2017.²⁴

The European Survey on Carbapenemase-Producing Enterobacteriaceae project was funded by ECDC in 2013 with the goal to reduce gaps in the diagnostic capacity

and heterogeneity of national surveillance and reporting standards in Europe. The network completed a multicentre study of the prevalence of carbapenemase-producing Enterobacteriaceae in European countries and showed that challenges in the establishment of continent-wide enhanced sentinel surveillance for antimicrobial resistance can be overcome.²⁵

For EPI-Net see
<https://www.combacte.com/about/epi-net/>

EPI-Net was launched in 2015 to contribute to the improvement of surveillance for health-care-associated infections and antimicrobial resistance in Europe within the COMBACTE-MAGNET project and the New Drugs for Bad Bugs (ND4BB) programme. ND4BB is a programme of the Innovative Medicines Initiative: a joint undertaking of the European Union represented by the European Commission and the European Federation of Pharmaceutical Industries and Associations to accelerate development and patient access to new medications to address the antimicrobial resistance crisis in Europe.²⁶ The major innovation of this new project is the creation of a network of representatives from all sectors involved in surveillance (including stakeholders, clinicians, public health, academia, and the pharmaceutical industry) to build consensus and drive funding without duplication efforts. EPI-Net is generating a database that maps all active surveillance programmes in human beings, animals, and food to identify strengths, limitations, areas for mitigation or improvement, and possible linkages. Short-term goals include implementation and testing of semi-automated surveillance systems in European countries to test feasibility and data sensitivity. Long-term goals include a central data repository that for the first time will include different sources of data (ND4BB studies, individual hospitals, and national networks) and produce standardised indicators with real-time data access and evaluation of the cost-effectiveness of connected sentinel laboratories for human beings and animal data.

Many initiatives, such as the Center for Disease Dynamics, Economics & Policy's Global Antibiotic Resistance Partnership and ReAct—Action on Antibiotic Resistance, have started with a special focus on low-income and middle-income countries, providing support in establishing policies and action plans in addition to collecting surveillance data on antimicrobial resistance.²⁷ The Center for Disease Dynamics, Economics & Policy's online tool, ResistanceMap, offers prevalence data from such countries.²⁸

For The Center for Disease
Dynamics, Economics & Policy's
ResistanceMap see <http://www.cddep.org/garp/home>

A call to action

Timely and targeted dissemination of surveillance data should be an essential component of efforts to combat the threat of antimicrobial resistance. Development of a reliable, comprehensive, and sustainable surveillance network of health-care-associated infections and antimicrobial resistance is needed to adequately support all stakeholders and physicians involved in patient care. The development requires involvement of national and international medical and veterinary societies,

environmental advocates, health-care systems, and representatives from academia, the pharmaceutical industry, and governments. Collection of high-quality surveillance data, timely analysis, and wide dissemination will enable various stakeholders to commit the resources and take the actions necessary to combat the spread of antimicrobial resistance. No country or professional group can achieve this goal without more extensive collaboration, and such collaboration will reduce the burden of health-care-associated infections and antimicrobial resistance and provide both health and economic benefits worldwide.

The incessant tide of threats posed by health-care-associated infections and antimicrobial resistance cannot be stopped without improvement of surveillance systems in all WHO regions. Specific programmes should be developed and financed in every region on the basis of existing network structures. At the European level, two short-term priorities are urgent in our opinion. First, agreement among major stakeholders involved in surveillance projects at national and international levels on goals of antimicrobial resistance surveillance and on definitions and standardised measures to increase comparability of data and feasibility of international projects. Second, agreement on data policy and sharing. These achievements would allow increased and simplified transmission of data and thus definitively contribute to the development of automated systems for antimicrobial resistance alerts. Long-term goals should include the development of an automated linkage of routine surveillance data with other databases containing relevant clinical data (such as treatments and outcomes) and epidemiological data to provide large integrated patient-level datasets and a definition of the burden of antimicrobial resistant infections in different patient settings and communities. Surveillance systems of antimicrobial resistance in animals and the food chain should be enhanced, and connection among these surveillance systems and those in human beings, including agreement on key human and veterinary pathogens and antibiotics should be monitored and periodically updated on the basis of trends in antimicrobial resistance. To achieve this goal, major scientific stakeholders should work together with legal experts to provide recommendations to European policy makers. Involvement of governance is essential to achieve effective data-linkage of patients among different platforms (ie, microbiological, clinical, and epidemiological data). The connection would benefit the quality and comparability of surveillance data and the implementation of infection control measures and procedures to reduce the spreading of resistant strains in Europe (ie, patient-patient transfer among countries). This process can be pursued only if the creation of dedicated funding is included in the political agenda to help countries implementing necessary changes in their surveillance systems.

The homogenisation of surveillance systems in Europe should represent only the first step of a more articulated approach to the improvement of the quality and coverage of global surveillance for antibiotic-resistant bacteria.²⁹ Recently WHO underlined the difficulties in defining the burden of antibiotic resistance because of the absence of surveillance systems active at the global level and called for efforts to improve the systems particularly in low-income countries and in community settings.⁷

Conclusions

This era of escalating antimicrobial resistance presents an urgent need for improvements in surveillance to optimise empirical therapy, drive antimicrobial stewardship and infection control measures, and inform development of new drugs and vaccines. Without such improvements, it will be difficult—almost impossible—to substantially reduce the medical and economic burdens imposed by antimicrobial resistance. New initiatives (including ESAC, CAESAR, European Survey on Carbapenemase-Producing Enterobacteriaceae project, Global Antimicrobial Resistance Surveillance System, the Center for Disease Dynamics, Economics & Policy's ResistanceMap, and EPI-Net) can improve the fragmentation, heterogeneity, time lag, and other inadequacies of existing surveillance but cannot achieve the necessary advances on their own. Global coordination of initiatives and political involvement should be pursued and not be further delayed.

Contributors

ET, FS, JR-B, and AV developed the first draft of the paper. SH, RS, MvM, MS, NBR, and the EPI-Net COMBACTE-MAGNET Group provided critical review and revisions. All authors approved the final version of the manuscript.

EPI-Net COMBACTE-MAGNET Group

Julia Bielicki, Marlieke de Kraker, Sumanth Gandra, Petra Gastmeier, Kim Gilchrist, Achilleas Gikas, Beryl Primrose Gladstone, Herman Goossens, Hasan Jafri, Gunnar Kahlmeter, Frank Leus, Christine Luxemburger, Surbhi Malhotra-Kumar, Giuseppe Marasca, Michael McCarthy, María Dolores Navarro, María Nuñez-Nuñez, Abdel Oualim, Jessica Price, Jérôme Robert, Harriet Sommer, Maja von Cube, Cuong Vuong, Irith Wiegand, Anne Therese Witschi, and Martin Wolkewitz.

Declaration of interests

FS is an employee of AstraZeneca Pharmaceuticals LP. SH reports grants from IMI Brussels and Pfizer during the study and personal fees from DNA Electronics, Bayer, and GlaxoSmithKline outside the submitted work. MS reports grants from GlaxoSmithKline, Pfizer, and Cubist outside the submitted work. JR-B reports grants and personal fees from AstraZeneca and personal fees from Merck, InfectoPharm, Achaogen, and Basilea outside the submitted work. All other authors declare no competing interests.

Acknowledgments

This Personal View is based on the discussion during the first annual meeting of the EPI-Net project in Tübingen in December, 2015. We thank Sergey Romualdovich Eremin (WHO, Geneva, Switzerland) and Nicola Thompson (Centers for Disease Control and Prevention, Atlanta, GA, USA) for the active participation and contribution to the meeting. We thank the Innovative Medicines Initiative Joint Undertaking for supporting the EPI-Net COMBACTE-MAGNET project (grant agreement number 115737), resources of which include financial contribution from the European Union Seventh Framework Programme (FP7/2007–2013) and European Federation of Pharmaceutical Industries and Associations

companies in-kind contribution. We thank the European Society of Infectious Diseases and Clinical Microbiology and the European Committee on Infection Control for suggesting experts in epidemiology. We thank the following experts, Lisbeth Kyndi Bergen, Lubos Drgona, Vincent Jarlier, Elisabeth Presterl, Mario Poljak, and Oana Sandulescu, for their suggestions. We are grateful to the following surveillance experts for providing protocols and data information: Rossella Buttazzi (Agenzia sanitaria e sociale regionale Emilia Romagna, Italy), Fortunato D'Ancona (Istituto Superiore di Sanità, Italy), Carlo Gagliotti (Agenzia sanitaria e sociale regionale Emilia Romagna, Italy), Jari Jalava (National Institute for Health and Welfare, Finland), Stefan Kuster (SWISSNOSO, Switzerland), Ines Noll (Robert Koch Institute, Germany), Christiane Petignat (Prevention and control of nosocomial infections, [HPCI], Switzerland), Alberto Ricciardi (Agenzia sanitaria e sociale regionale Emilia Romagna, Italy), Gunnar Skov Simonsen (Norwegian surveillance system for antimicrobial resistance, Norway), and Walter Zingg (University of Geneva Hospitals, Switzerland). We also thank Anne McDonough, a professional medical writer, for providing medical writing services.

References

- 1 Department of Health Antimicrobial Resistance Strategy Analytical Working Group. Antimicrobial resistance empirical and statistical evidence-base: a report from the Department of Health Antimicrobial Resistance Strategy Analytical Working Group. 2016. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/553267/AMR_EBO_2016.pdf (accessed Dec 16, 2016).
- 2 Ammerlaan HSM, Harbarth S, Buiting AGM, et al. Secular trends in nosocomial bloodstream infections: antibiotic-resistant bacteria increase the total burden of infection. *Clin Infect Dis* 2013; **6**: 798–805.
- 3 Watkins RR, Bonomo RA. Overview: global and local impact of antibiotic resistance. *Infect Dis Clin North Am* 2016; **30**: 313–22.
- 4 Tacconelli E. Antimicrobial use: risk driver of multidrug resistant microorganisms in healthcare settings. *Curr Opin Infect Dis* 2009; **22**: 352–58.
- 5 de Kraker ME, Stewardson AJ, Harbarth S. Will 10 million people die a year due to antimicrobial resistance by 2050? *PLoS Med* 2016; **13**: e1002184.
- 6 Gandra S, Barter DM, Laxminarayan R. Economic burden of antibiotic resistance: how much do we really know? *Clin Microbiol Infect* 2014; **20**: 973–80.
- 7 WHO. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Feb 27, 2017. http://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf?ua=1 (accessed June 12, 2017).
- 8 European Centre for Disease Control and Prevention. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012. July, 2013. <http://ecdc.europa.eu/en/publications/publications/healthcare-associated-infections-antimicrobial-use-pps.pdf> (accessed Dec 16, 2016).
- 9 Lazarus B, Paterson DL, Mollinger JL, et al. Do human extraintestinal *Escherichia coli* infections resistant to expanded-spectrum cephalosporins originate from food-producing animals? A systematic review. *Clin Infect Dis* 2015; **60**: 39–52.
- 10 Kluytmans JA, Overdeest IT, Willemsen I, et al. Extended-spectrum β -lactamase-producing *Escherichia coli* from retail chicken meat and humans: comparison of strains, plasmids, resistance genes, and virulence factors. *Clin Infect Dis* 2013; **56**: 478–87.
- 11 Schwarz S, Johnson AP. Transferable resistance to colistin: a new but old threat. *J Antimicrob Chemother* 2016; **71**: 2066–70.
- 12 European Centre for Disease Prevention and Control, European Food Safety Authority, European Medicines Agency. ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals. *EFSA J* 2015; **13**: 4006–114.
- 13 Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; **62**: e51–77.

- 14 Nationales Referenzzentrum für Surveillance von nosokomialen Infektionen. Kurzbeschreibung des Moduls ITS-KISS. <http://www.nrz-hygiene.de/surveillance/kiss/its-kiss> (accessed Dec 16, 2016).
- 15 Public Health England. English surveillance programme for antimicrobial utilisation and resistance (ESPAUR): report 2016. November, 2016. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/575626/ESPAUR_Report_2016.pdf (accessed Dec 16, 2016).
- 16 Observatoire National de l'Epidémiologie de la Résistance Bactérienne aux Antibiotiques (ONERBA). Rapport d'activité 2013–14. <http://onerba.org/publications/rapports-onerba/> (accessed Dec 16, 2016).
- 17 European Centre for Disease Prevention and Control. European Antimicrobial Resistance Surveillance Network (EARS-Net). <http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx> (accessed Dec 16, 2016).
- 18 WHO. Antimicrobial resistance: global report on surveillance. June, 2014. http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748_eng.pdf?ua=1 (accessed Dec 16, 2016).
- 19 Koontz FP. Microbial resistance surveillance techniques. Blood culture versus multiple body site monitoring. *Diagn Microbiol Infect Dis* 1992; **15** (suppl 2): S31–35.
- 20 Marquet K, Liesenborgs A, Bergs J, et al. Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis. *Crit Care* 2015; **19**: 63.
- 21 Tacconelli E, Peschel A, Autenrieth IB. Translational research strategy: an essential approach to fight the spread of antimicrobial resistance. *J Antimicrob Chemother* 2014; **69**: 2889–91.
- 22 European Medicines Agency. Draft ESVAC vision and strategy 2016–2020. April 7, 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2016/04/WC500204522.pdf (accessed Dec 16, 2016).
- 23 WHO. Central Asian and Eastern European Surveillance of Antimicrobial Resistance: annual report 2016. 2016. http://www.euro.who.int/__data/assets/pdf_file/0009/323568/50646-CAESAR-Annual-report-2015-web-15-11-2016.pdf?ua=1 (accessed Dec 16, 2016).
- 24 WHO. Global antimicrobial resistance surveillance: manual for early implementation 2015. http://apps.who.int/iris/bitstream/10665/188783/1/9789241549400_eng.pdf?ua=1 (accessed May 24, 2017).
- 25 Albiger B, Glasner C, Struelens M, et al. The European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) working group. Carbapenemase-producing Enterobacteriaceae in Europe: assessment by national experts from 38 countries, May 2015. *Euro Surveill* 2015; **20**: 30062.
- 26 Kostyanov T, Bonten MJ, O'Brien S, et al. The Innovative Medicines Initiative's New Drugs for Bad Bugs programme: European public-private partnerships for the development of new strategies to tackle antibiotic resistance. *J Antimicrob Chemother* 2016; **71**: 90–95.
- 27 ReAct. The global threat of antibiotic resistance. <https://www.reactgroup.org/antibiotic-resistance/the-threat/> (accessed June 12, 2017).
- 28 Center for Disease Dynamics, Economics & Policy. About ResistanceMap. <https://resistancemap.cddep.org/About.php> (accessed June 12, 2017).
- 29 Núñez-Núñez M, Navarro MD, Palomo V, et al. The methodology of surveillance for antimicrobial resistance and healthcare-associated infections in Europe (SUSPIRE): a systematic review of publicly available information. *Clin Microbiol Infect* (in press). DOI:10.1016/j.cmi.2017.07.014.