International Journal of Antimicrobial Agents 52 (2018) 616–621

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Legal framework of antimicrobial stewardship in hospitals (LEASH): a European Society of Clinical Microbiology and Infectious Diseases (ESCMID) cross-sectional international survey

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ARTICLE INFO

Article history:
Received 21 November 2017
Accepted 18 July 2018

Editor: Dr Renu Bharadwaj

Keywords:
Legislation
Strategy
Antimicrobial stewardship
Hospitals
Europe

ABSTRACT

Antimicrobial stewardship (AMS) is the cornerstone activity in the combat against antimicrobial resistance. In order to ensure sustainable deployment and development of AMS, a strategic and regulatory framework needs to be provided by national healthcare authorities. Experts from 32 European countries, Israel and Turkey were invited to participate in a cross-sectional internet-based survey from October 2016 to May 2017 on the legal framework and mandatory components (structures, activities) of AMS in hospitals, i.e. components required by legislation or regulations. We collected data from 25 countries and two regions (in countries with federal health administration). Laws regulating AMS existed in seven countries and one region. Other health ministry regulations were applicable in 13 countries and one region. National strategies and/or action plans approved by ministries of health were in place in 13 countries and one region. Conversely, five countries and one region had no regulation of AMS in hospitals. Funding for AMS in hospitals was provided in five countries and one region. Eight countries and one region reported mandatory AMS structures and activities complying with the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) structure, policy and practice indicators. In 10/27 cases, however, the mandatory AMS activities were not being fully carried out. The survey showed heterogeneous legal frameworks for AMS in hospitals, and in many countries it was even lacking. The situation may be critical in countries with poor control of antimicrobial use and resistance. Recent international initiatives calling on policy-makers to address the threat of antimicrobial resistance could yield improvement.

1. Introduction

Antimicrobial stewardship (AMS) is defined as a coherent set of actions designed to use antimicrobials responsibly [1,2]. AMS interventions include multiple activities that involve a broad range of stakeholders ranging from individual prescribers to healthcare systems and supranational incentives and regulators. AMS has been historically driven by professionals who were aware of the problem and were willing to use their expertise to improve antimicrobial prescribing. However, to be effective, the wider healthcare community, the regulators, and the general public must recognise the need for and value of AMS [3]. For purposes of sustainable

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[1] (See Acknowledgements).

https://doi.org/10.1016/j.ijantimicag.2018.07.019
0924-8579/

deployment and development of AMS activities, a strategic and regulatory framework needs to be provided by national healthcare authorities [3,4]. Recent European guidelines for prudent use of antimicrobials in human health emphasise the responsibility of national authorities for developing, implementing and supporting the policies, actions and structures necessary to ensure the prudent use of antimicrobials. Their responsibilities include legislation, regulation and auditing [5]. Little information on the legislative regulations of AMS in hospitals is available. At the European Union (EU) level, reports on the implementation of EU council recommendations on the prudent use of antimicrobial agents in human medicine did not specifically describe legislation on AMS activities in hospitals [6]. Two reports, a study on successful implementation of AMS in hospitals in the UK, USA and France, and a global survey of AMS programmes in hospitals, pointed to the differences in legislation and underlined the need for legislative requirements and national standards for implementation of AMS [3,7]. The differences in legislative requirements for AMS between countries may reflect differences in healthcare systems and legislation in general [4], but also differences in health authorities' commitment to addressing the issue of antimicrobial resistance. In this survey, we aimed to provide more complete insight into the legislative and regulatory framework of AMS in hospitals in European countries, in Israel and in Turkey. Knowledge of these regulations may provide an opportunity to share good practices and may stimulate further research on the impact of specific legal frameworks on AMS, on the consequent quality of antimicrobial prescribing and, ultimately, on antimicrobial resistance rates.

2. Methods

2.1. Study design

Legal Framework for Antibiotic Stewardship in Hospitals [LEASH] was an ESGAP (European Society of Clinical Microbiology and Infectious Diseases – ESCMID – Study Group for Antimicrobial StewardshiP) international internet-based cross-sectional survey. It was conducted from the end of October 2016 until the beginning of May 2017.

2.2. Questionnaire

The 44-item questionnaire (13 questions, 31 sub-questions) in English (Appendix A) was developed by a multidisciplinary group of experts in infectious diseases, pharmacy and law, based on the literature [3,7–9]. It was finalised during an informal discussion between the authors of the survey and after pilot testing in a small group of invited experts that improved the clarity of the questions. The first part of the survey (nine items) addressed the legal documents on AMS programmes in hospitals at the national level such as laws, regulations (bill, resolution, executive order, decree, ministerial instruction…), strategies and action plans adopted by ministries of health. We were primarily interested in the situation on a nationwide level, but it was up to experts to provide regionwide information if the legislation on healthcare in the country was within the remit of regional authorities. In the second part, the questionnaire investigated the AMS structures and interventions that hospitals had to implement according to national/regional regulations (31 items covering 14 structures/interventions). We selected structures and interventions that were defined as core infrastructure, policy and practice indicators by the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) Expert Panel [10]. They covered funding, resources, surveillance activities, prescribing practices and evaluation. A question on provision of AMS education in hospitals was added. In the last part of the survey, we collected information on quality indicators for AMS programmes in hospitals reported on a national/regional level. The questionnaire referred to antimicrobials, but for the purposes of the survey the terms antibiotic and antimicrobials were considered synonymous. Factual questions were formulated concisely and used mostly dichotomous response scales (“Yes” / “No”). Additionally, a comment box was provided in most of the questions for a more detailed description of the situation. The web survey was hosted on the OneClickSurvey plaftorm [10].

2.3. Data collection

AMS experts from the 32 European countries, Israel and Turkey (Appendix B) were chosen from among the ESGAP executive committee members, ESGAP network and personal contacts. To ensure maximal reliability of the data, the experts were invited to discuss the topics addressed in the survey with other experts on AMS in their countries. A maximum of three experts per country were allowed to participate in the survey. The experts received an invitation letter and a link to the survey via email in October 2016, and a reminder in December 2016 if they had not answered within the first 2 months of the study. After closure of the survey, the country experts were contacted to review their answers and confirm their comprehensiveness, to check consistency of answers in cases of more than one answer by country, and to provide clarifications if needed.

Participation was voluntary and not compensated. Ethical approval was not required due to the design of the study.

3. Results

3.1. The regulations of AMS in hospitals

The experts from 26 out of 34 eligible countries responded to all questions in the questionnaire (response rate 76%). However, for Italy, responses were collected for two regions only, and not for the whole country; therefore, the results refer to 25 countries and 2 regions.

Nationwide regulations of AMS in hospitals in the 25 countries and 2 regions are presented in Table 1.

3.2. Mandatory AMS activities in hospitals

Surveillance of antimicrobial consumption in hospitals is mandatory in 15 countries (Austria, Bulgaria, Croatia, France, Germany, Hungary, Iceland, Ireland, Israel, Luxembourg, Romania, Serbia, Slovakia, Slovenia, UK – excluding Northern Ireland), and point prevalence studies of antimicrobial prescribing in hospitals are mandatory in Norway and Romania. Surveillance of antimicrobial resistance in hospitals is mandatory in 14 countries (Austria, Bulgaria, Croatia, France, Germany, Hungary, Iceland, Luxembourg, The Netherlands, Romania, Slovakia, Sweden, Turkey, UK) (Table 2).

Six countries or regions (Friuli Venezia Giulia (FVG), Germany, Ireland, The Netherlands, Switzerland, UK) reported that hospitals get special funding for AMS. Salary support for dedicated time for AMS activities is provided in the UK. In Romania, AMS activities are mandatory for infectious disease specialists in hospitals.

Some AMS structures were mandatory in seven countries/regions in our survey: formal organizational structure (body) in five (FVG, Serbia, Slovenia, Romania, UK), AMS teams were mandatory only in the Netherlands and in the UK, and AMS programmes in France, the Netherlands, and the UK.

Hospitals in seven countries/regions are mandated to carry out AMS interventions regarding prescribing practices; the types of mandatory interventions and regulatory bodies at the national/regional level are detailed in Table 3.

Table 1
Regulations of antimicrobial stewardship in hospitals on the national level in 27 participating countries/regions.

Country/region	Law	Regulation, signed by MoH*	Strategy, signed by MoH	Action plan including timeframe and responsibilities, signed by MoH	Other institution regulating AMS in hospitals**
Austria	-	-	-	+	-
Bulgaria	+	+	+	-	+
Croatia	-	-	-	-	-
France	-	+	+	+	+
Germany	+	+	+	+	+
Greece	+	-	+	-	-
Hungary	+	-	-	-	-
Ireland	-	+	-	-	+
Iceland	-	+	-	-	-
Israel	-	-	-	-	+
Latvia	-	-	-	-	-
Luxembourg	-	-	-	-	-
Malta	-	-	-	-	-
The Netherlands	-	-	-	-	+
Norway	-	-	+	+	-
Poland	-	-	+	-	+
Romania	+	+	-	-	+
Serbia	-	+	+	-	-
Slovakia	-	+	+	+	-
Slovenia	-	+	-	-	-
Spain	-	+	+	+	-
Sweden	-	+	+	+	-
Switzerland	-	-	-	-	-
Turkey	+	+	+	-	+
UK	+***	+	+	+***	+
Friuli Venezia Giulia (Italy)	+	+	+	+	-
South Tyrol (Italy)	-	-	-	-	-

+, the law/regulation/institution is present; -, no regulation/institution; AMS, antimicrobial stewardship; MoH, ministry of health.

* Documents adopted by the MoH such as bill, resolution, executive order, decree, ministerial instruction, guidelines.

** Bulgaria: Commission on Accreditation, Regional health inspectorate, National health insurance fund. UK: different authorities in each country (England, Northern Ireland, Scotland, Wales,). France: High authority for health. Germany: MoH. Israel: National infection control unit appointed by the MoH. Ireland: Health Information and Quality Authority. The Netherlands: SWAB (The Dutch working party on antibiotic policy), Healthcare inspectorate. Poland: The payer and the voluntary accreditation system. Romania: National Authority of Quality Management in Health. Turkey: Social security institutions.

*** Not in Northern Ireland.

Table 2
Regulatory authorities for antimicrobial consumption and antimicrobial resistance surveillance in hospitals in the 16 countries included in the survey.

Country/region	Regulatory authority for antimicrobial consumption surveillance	Regulatory authority for antimicrobial resistance surveillance
Austria	MoH	MoH
Bulgaria	MoH	National centre for Infectious and Parasitic Diseases
Croatia	MoH and Agency for Medicinal Products and Medical Devices	MoH
France	MoH through the system of indicators	MoH through the system of indicators
Germany	MoH through the Infection Protection Act	MoH through the Infection Protection Act
Hungary	National Public Health and Medical Officer Service (ÁNTSZ)	National Public Health Officer Service and The National Centre for Epidemiology
Iceland	Chief Epidemiologist, Medicines Agency	Chief Epidemiologist, University Hospital
Ireland	Health Services Executive	Health Services Executive
Israel	National Infection Control Unit appointed by MoH	
Luxembourg	MoH	MoH
The Netherlands		RIVM
Romania	MoH through County Public Health Service (executive service)	MoH through County Public Health Service (executive service)
Serbia	Medicines and medical devices agency of Serbia	
Slovenia	MoH	
Slovakia	Slovak institute of drug control	National reference laboratory for antimicrobial resistance
Sweden		Public health agency and regional infection prevention authorities
Turkey	Public health institute	MoH
UK	Different regulator in each country	Different regulator in each country

MoH, Ministry of health; RIVM, The Dutch National Institute for Public Health and the Environment.

3.3. Performance of mandatory hospital AMS activities

In 10 cases, even in countries/regions where the AMS structures and interventions were formally mandatory, experts reported that they were not (yet) completely carried out. The number of countries/regions with total or no/partial implementation of structures and activities as reported in the survey is presented in Fig. 1.

AMS activities in hospitals are reported as quality indicators at least once a year in 10 countries (Bulgaria, Croatia, Ireland, The Netherlands, Norway, Poland, Romania, Slovenia, Sweden, UK); in France reporting is biennial. The indicators are reported to the health ministries or related institutions (France, the Netherlands, Romania, Slovenia, Sweden, UK), national public health institutions (Bulgaria, Ireland, Norway, UK), or the payer (Poland, Croatia).

4. Discussion

In this study we investigated legislative framework of AMS in hospitals in 24 European countries and in Turkey and Israel. We examined the regulations enforced on the national or regional

Table 3
Mandatory antimicrobial stewardship interventions regarding prescribing in hospitals and the regulatory authorities at the national/regional level.

	Bulgaria	France	Romania	Serbia	Slovakia	Slovenia	UK*
Treatment guidelines based on local antimicrobial susceptibility to assist antimicrobial selection for common clinical conditions	-	MoH through the system of indicators	-	-	MoH	-	England: CQC/local commissioners (CCGs) Scotland: Regional Health Boards
Monitoring of antibiotic prescriptions compliant with guidelines	-	MoH through the system of indicators	-	-	Office for control of healthcare	-	England: see above Scotland: SAPG
Written policy that requires prescribers to document an indication in the medical record	MoH	-	-	-	-	-	England: see above Scotland: Regional health boards
Antimicrobial agents to be approved by a physician or pharmacist at initiation (e.g., pre-authorization)	-	Done in France for restricted antibiotics	MoH	Health Insurance Fund	-	-	England: see above, only for antibiotics defined by NICE Scotland: for specific 'protected' antibiotics only
Formal procedure to review the appropriateness of an antimicrobial at or after 48 h from the initial order (post-prescription review)	-	MoH through the system of indicators	-	-	-	-	England: CQC/Local commissioners (CCGs), Scotland: Regional Health Boards (after 72 h)
Audit or review surgical antimicrobial prophylaxis choice and duration	-	MoH through the system of indicators	-	-	-	-	England: see above Scotland: Regional Health Boards
Education in antimicrobial prescribing/stewardship	MoH	MoH through the system of indicators	-	MoH, Serbian Medical Chamber, Ministry of Education	Slovak Medical University Department for Chemotherapy	MoH	England: see above Scotland: NHS Education for Scotland

-, no mandatory activity; CCG, Clinical Commissioning Group; CQC, Care Quality Commission; MoH, Ministry of health; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; SAPG Scottish Antimicrobial Prescribing Group.
* Within Northern Ireland all items in Table 2 are carried out on a voluntary basis with no regulatory authority.

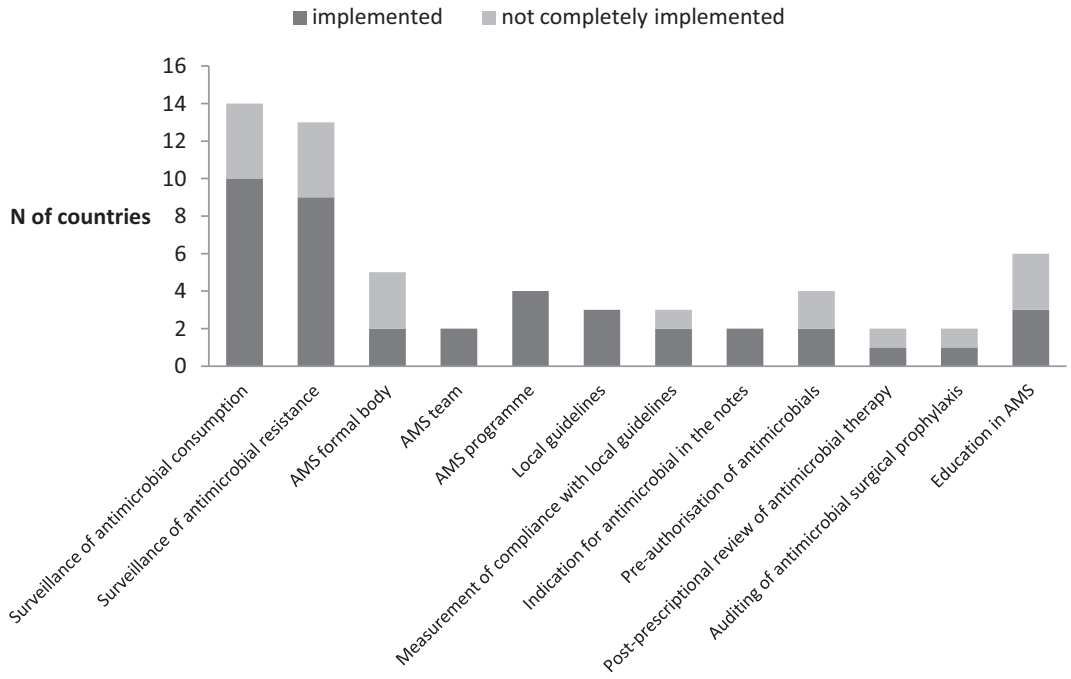

Fig. 1. Mandatory antimicrobial stewardship structures and activities in hospitals with respect to their implementation.

level in countries, if the experts reported that AMS was only regulated regionally. Roughly three-quarters of participating countries/regions reported having a document such as a law, regulation, strategy, or action plan adopted by the highest healthcare authority.

In 2000 Krcmery and co-authors reported that antibiotic policies were regulated at the ministerial level in the Czech Republic, Slovakia, Croatia and Russia. In Slovakia and the Czech Republic, laws mandated antibiotic committees, their structure, and restriction of antibiotics in hospitals [11]. In France, the first nationwide documents were approved at approximately the same time in the form of national strategy (2001) and guidelines issued by national agencies, but the first ministerial regulation on AMS in hospitals was enforced only in 2007 [9]. In the UK, AMS practices in hospitals have been mandated by the Health and Social Care Act since 2008. In the USA, the first legislative regulation of AMS in

hospitals was adopted in California in 2008 [3]. A modification of the infection protection act mandating antibiotic consumption surveillance and evaluation of local antimicrobial resistance was enacted in Germany in 2011 [8].

Enforcement of legislation relevant to antimicrobial resistance to be ensured by EU member states was mentioned in the EU Council conclusions on antimicrobial resistance in 2016 [13]. According to EU guidelines for the prudent use of antimicrobials in human health approved by European Commission last year [5], national, regional and local governments are responsible for the legislation necessary to ensure the prudent use of antimicrobials. In our survey, conducted at the end of 2016 and beginning of 2017, AMS in hospitals was required by law in seven countries and one Italian region, and by other types of ministerial regulations in 14 countries/regions (Table 1). Some countries remained without any legal regulations on AMS (11/27).

A strategy for prudent use of antimicrobials and its translation into an action plan have been recommended by the EU Council since the first recommendations in 2001 [12,14]. In 2015, all members of the World Health Assembly committed to the adoption of a national plan against antimicrobial resistance by 2017 [15]. Among the most recent European documents, the 2016 EU Council conclusions expected EU member states to have an action plan against antimicrobial resistance ready for mid-2017 [13], and the 2017 EU guidelines recommended the development of national strategies [5]. In our survey, 13 countries and 1 region of 27 respondents had a national/regional strategy pertaining to AMS signed by the Ministry of Health or corresponding regional authority. The corresponding action plan with responsibilities and timetables was approved in eight of them. Austria reported on having an action plan without a strategy as a separate document. Our results differ from the 2015 Report on the implementation of the 2001 EU Recommendations [7]: national strategies were reported in 20/29 countries and action plans in 21/29. The difference might arise from the definitions: in our survey, we were asking exclusively about the strategies and action plans signed by the Ministry of Health.

Lack of funding has been recognised as a major barrier to an AMS programme [16]. In our survey, only five countries and one region provided funding for AMS activities in hospitals, and salary support for AMS activities was provided only in the UK. In Europe, some funding covering AMS activity is also provided in Belgium [17]. This clearly shows that AMS is still performed only as an add-on activity, and is often far from being recognised as a vital part of hospital policy.

Eight countries and 1 region of 27 respondents reported having mandatory AMS structure or intervention that were included in the list of core TATFAR structure and process indicators [10]. Interestingly, education in AMS was the most commonly mandatory activity; it may, if properly implemented, yield long-term results [4].

Ten countries included in the survey provided a legal framework for the AMS activities in hospitals, but there were apparently problems with their implementation. Recently identified barriers to AMS programmes on the hospital level include the previously mentioned lack of funding, lack of dedicated personnel with expertise in AMS, lack of technology support, and relatively low priority [7,18,19]. In spite of expectations that legal frameworks would provide support for AMS programmes in hospitals, the identified implementation gap could be due to the same causes.

The legal framework in the countries included in the survey was heterogeneous, with differences even between the Italian regions included. In some countries, AMS activities seem well-regulated and performed (UK, France, Germany); in others, such as the Netherlands, there are fewer legislative requirements for AMS, but other structures exist such as non-governmental organizations involved in AMS activities on the nationwide basis. Because of the descriptive and cross-sectional nature of our survey, we did not decide to calculate statistical correlations between antibiotic use and resistance and the extent of legal frameworks. However, some interesting observations may be highlighted. France and the UK, which are countries with well-developed legal frameworks for AMS, were among the highest antibiotic prescribers in hospitals in the European System of Antimicrobial Consumption Network (ESAC-Net) [20], while the Netherlands, the country with only a few regulations, was the lowest. The level of antibiotic consumption in hospitals in France and in the Netherlands was different, but a decrease was observed in the last decade in France and an increase in the Netherlands. Very different resistance rates [21] may be observed in countries with well-regulated AMS, such as the UK and France, and the difference is even more pronounced in countries with few regulations, such as Norway and Greece or Croatia and Austria [22]. We did not examine other incentives or factors such as the activities of non-governmental organizations, hospital accreditation systems and reimbursement or the level of implementation of the legal framework that could influence the differences.

More legislation is needed for the control of antimicrobial use and resistance in some countries than in others. The legal framework of AMS in the countries may potentially reflect the development of the AMS in the past, the organization of healthcare, the legal system and specific sociocultural determinants. In addition, in some countries with high consumption levels and preoccupying trends in antimicrobial resistance, the legal framework has been developed as a response to the situation [3]. The results of our survey are discouraging if we mirror the situation to the EU Council documents published since 2001. TATFAR indicators that we measured in our survey also gave relatively poor results. However, TATFAR [10] indicators were established only in 2015 and it may take time for them to be required by law or regulation.

To the best of our knowledge, this is the largest international survey on this topic. The major drawback of our exploratory study is that the data were reported by the national experts and not derived directly from the original documents. We validated the data by discussion with the participants, but could not definitively exclude different understandings of the questions and the terms used in the questionnaire. The level of implementation of legal requirements was not systematically assessed, and the experts were only asked to provide their opinion. Additionally, we were unsuccessful in including all invited countries.

5. Conclusion

In conclusion, the legal frameworks of AMS in hospitals in Europe seem very heterogeneous and insufficient. More regulations are needed, especially in countries with high antimicrobial consumption and resistance. Special attention should be paid to the implementation of the regulations and the sustainability of AMS activities. Supranational action plans and policymaker commitment [15,23,24] are important drivers for the development of the AMS activities, but the approach should be adapted to local circumstances, i.e. epidemiological context and healthcare organization. Appropriate legal frameworks should ensure that the most efficient measures are implemented [10,25].

Acknowledgements

The LEASH study group: Franz Allerberger, Austria; Ria Benko, Hungary; Dag Berild, Norway; Robert Cunney, Ireland; Martine Debacker, Luxembourg; Aleksander Deptula, Poland; Uga Dumpis, Latvia; Oliver J Dyar, Sweden; Onder Ergonul, Turkey; Balint Gergely Szabo, Hungary; Cairine Gormley, UK; Malin Grape, Sweden; Thorolfur Gudnason, Iceland; Philip Howard, UK; Benedikt Huttner, Switzerland; Petros Ioannou, Greece; Ramona Ionescu,

Romania; Emma Keuleyan, Bulgaria; Viviane Knepper, Luxembourg; Diamantis Kofteridis, Greece; Tomislav Kostyanev, Belgium; Vladimir Krcmery, Slovakia; Botond Lakatos, Hungary; Roberto Luzzati, Italy; Jaap ten Oever, Sweden; Leonardo Pagani, Italy; José Ramón Paño Pardo, Spain; Mihaela Popescu, Romania; Mihaela Popovici, Romania; Mical Paul, Israel; Hege Salvesen Bix, Norway; Jeroen Schouten, the Netherlands; Jacqueline Sneddon, UK; Goran Stevanović, Serbia; Agnes Wechsler-Fördös, Austria; Katja de With, Germany; Vera Vlahović-Palčevski, Croatia; Peter Zarb, Malta.

The authors thank Jeffrey Arsham, a medical translator, for reading and reviewing the original English-language text.

Declarations

None.

Funding

No funding.

Competing Interests

None.

Ethical Approval

Not required.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2018.07.019.

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