Evidence brief for policy
EVIPNet Europe
Number 10

Preventing antimicrobial resistance and promoting appropriate antimicrobial use in inpatient health care in Greece

Ioannis Kopsidas
Dimosthenis Theodosiadis
Christos Triantafyllou
Sotirios Koupidis
Andriani Fanou
Sophia Hatzianastasiou
Evidence brief for policy
EVIPNet Europe

Preventing antimicrobial resistance and promoting appropriate antimicrobial use in inpatient health care in Greece

Ioannis Kopsidas
Dimosthenis Theodosiadis
Christos Triantafyllou
Sotirios Koupidis
Andriani Fanou
Sophia Hatzianastasiou
ABSTRACT
The present Evidence Brief for Policy (EBP) drawn up in Greece within the framework of the WHO European Evidence-informed Policy Network was prepared by the National Public Health Organization, the Center for Clinical Epidemiology & Outcomes Research (CLEO), The Agency for Quality Assurance in Health S.A. and the WHO Country Office in Greece. This EBP was produced as a research-derived actionable tool, with a view to addressing the following pressing problems in hospital healthcare: a. the higher-than-EU-average rates of antimicrobial resistance (AMR) in hospital-acquired pathogens, b. the high prevalence of healthcare associated infections (HAIs), and c. the high consumption of advanced antimicrobials in hospitals. The working group defined the scope of the literature research, conducted a critical appraisal and review of the selected evidence, and carried out a series of meetings with key stakeholders in the field of clinical healthcare and health administration. The derived data, information and insights were used for the formulation of three options, that may be implemented in isolation or in conjunction to address the rising AMR and high incidence of HAIs in Greek hospitals. The proposed options pertain to: (1) Establishing an interconnected electronic AMR surveillance system in hospitals; (2) Establishing antimicrobial stewardship and IPC programmes in all hospitals; and (3) Implementing post-graduate educational programs for healthcare workers on prudent antimicrobial use and infection control in the hospital setting.

KEYWORDS
antimicrobial use, antimicrobial resistance, multidrug-resistance, hospital-acquired infections, hospital infection control, nosocomial infection surveillance, hospital care, Greece

Document number: WHO/EURO:2022-5837-45602-65411
© World Health Organization 2022
Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; https://creativecommons.org/licenses/by-nc-sa/3.0/igo).
Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: “This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition. Kopsidas I, Theodosiadis D, Triantafyllou C, Koupidis S, Fanou A, Hatzianastasiou S. EVIPNet evidence brief for policy: preventing antimicrobial resistance and promoting appropriate antimicrobial use in inpatient health care in Greece. Copenhagen: WHO Regional Office for Europe; 2022.”
Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization. (http://www.wipo.int/amc/en/mediation/rules/)
Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.
Sales, rights and licensing. To purchase WHO publications, see http://apps.who.int/bookorders. To submit requests for commercial use and queries on rights and licensing, see http://www.who.int/about/licensing.
Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.
General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
The mention of specific companies or of certain manufacturers’ products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.
All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.
The named authors alone are responsible for the views expressed in this publication.

Layout: Netra Shyam
CONTENTS

CONTRIBUTIONS AND ACKNOWLEDGEMENTS
ABBREVIATIONS AND ACRONYMS
KEY MESSAGES
EXECUTIVE SUMMARY
INTRODUCTION
  How this evidence brief for policy was prepared
THE PROBLEM
  How AMR occurs
  The burden of AMR
  Governance in Greece for human health care
  Inpatient settings – the obvious target for AMR in Greece
  Equity-related observations about the problem
THREE OPTIONS FOR ADDRESSING THE PROBLEM
  OPTION 1: Establish an interconnected electronic AMR surveillance system in hospitals
  OPTION 2: Establish antimicrobial stewardship and infection prevention/control programmes in all hospitals
  OPTION 3: Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting
IMPLEMENTATION CONSIDERATIONS
  Potential barriers
  Potential opportunities
REFERENCES
APPENDICES AND ANNEXES
  Appendix 1: Summary of systematic reviews relevant to Option 1 – Establish an interconnected electronic AMR surveillance system in hospitals
  Appendix 2: Systematic reviews relevant to Option 2 – Establish antimicrobial stewardship and infection prevention/control programmes in all hospitals
  Appendix 3: Summary of systematic reviews relevant to Option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection prevention and control in the hospital setting
Annex 1: Health-care legal framework: recent developments impacting antimicrobial use and antimicrobial resistance ......................................................................................................................... 76

Annex 2: Non-legislative complementary actions on antimicrobial use and antimicrobial resistance ................................................................................................................................................... 77

Annex 3: Key stakeholders involved in hospital AMR action plans in Greece ........................................................................................................... 78

Annex 4: Stakeholder and key informant interviews used as a source of information ............................................................................................. 79

Annex 5: Information derived from interviews with stakeholders ......................................................................................................................... 80

Annex 6: Summary of problems identified regarding the implementation of the national action plans ......................................................................................................................... 82
CONTRIBUTIONS AND ACKNOWLEDGEMENTS

The Evidence-informed Policy Network (EVIPNet) Europe (www.evipnet.org) – a regional arm of the global EVIPNet – promotes the use of health research in policy-making in countries of the WHO European Region. EVIPNet Europe promotes partnership at the country level between policy-makers, researchers and civil society to facilitate policy development and implementation through the use of the best available scientific evidence.

The antimicrobial resistance (AMR) programme of the WHO Regional Office for Europe and partners provides technical assistance and guidance to Member States on AMR at the national and regional levels, including supporting national AMR action plan development, facilitating intersectoral coordination, strengthening the surveillance of antimicrobial consumption and resistance, implementing infection prevention and control programmes, promoting antimicrobial stewardship, and supporting education, behavioural insight, advocacy and awareness campaigns.

The WHO Country Office in Greece has provided leadership and technical guidance.

AUTHORS

Ioannis Kopsidas, Center for Clinical Epidemiology and Outcomes Research
Dimosthenis Theodosiadis, National Public Health Organization
Christos Triantafyllou, Center for Clinical Epidemiology and Outcomes Research
Sotirios Koupidis, WHO Country Office, Greece
Andriani Fanou, The Agency for Quality Assurance in Health S.A.
Sophia Hatzianastasiou, National Public Health Organization

*Equal contribution

FUNDING

This evidence brief for policy and the training workshops to support the preparation of it were funded by the World Health Organization Regional Office for Europe (WHO/Europe).

This document was produced with the financial assistance of the European Union. The views expressed herein can in no way be taken to reflect the official opinion of the European Union.

CONFLICT OF INTEREST

The authors declare no conflicts of interest in relation to this evidence brief for policy. The funder had no role in the collection, analyses, interpretation or display of information and data presented in the publication.
MERIT REVIEW

The brief was reviewed by both local and foreign subject matter experts to ensure the validity, integrity as well as applicability of the evidence presented. The authors would like to thank the experts listed below for peer-reviewing and providing feedback on various drafts of this publication. Submitted for review to: The Hellenic Society for Infectious Diseases & The Greek Society for Infection Control, Independent AMR and evidence-informed policy-making consultants for WHO and peer-reviewed by the Estonian EVIPNet team.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMR</td>
<td>antimicrobial resistance</td>
</tr>
<tr>
<td>AMS</td>
<td>antimicrobial stewardship</td>
</tr>
<tr>
<td>AMSTAR</td>
<td>A MeaSurement Tool to Assess Reviews</td>
</tr>
<tr>
<td>AQAH S.A.</td>
<td>Agency for Quality Assurance in Health Société anonyme</td>
</tr>
<tr>
<td>ASP</td>
<td>antimicrobial stewardship programme</td>
</tr>
<tr>
<td>AWaRE</td>
<td>Access, Watch, Reserve (classification of WHO)</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CDI</td>
<td>Clostridioides difficile infection</td>
</tr>
<tr>
<td>CLABSI</td>
<td>central line-associated bloodstream infection</td>
</tr>
<tr>
<td>CLEO</td>
<td>Center for Clinical Epidemiology and Outcomes Research</td>
</tr>
<tr>
<td>COVID-19</td>
<td>coronavirus disease 2019</td>
</tr>
<tr>
<td>CRE</td>
<td>carbapenem-resistant Enterobacteriaceae</td>
</tr>
<tr>
<td>CSP</td>
<td>cloud service provider</td>
</tr>
<tr>
<td>DALY</td>
<td>disability-adjusted life year</td>
</tr>
<tr>
<td>DDD</td>
<td>defined daily dose</td>
</tr>
<tr>
<td>EBP</td>
<td>evidence brief for policy</td>
</tr>
<tr>
<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
</tr>
<tr>
<td>EMEA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>ESS</td>
<td>electronic surveillance system</td>
</tr>
<tr>
<td>ESVAC</td>
<td>European Surveillance of Veterinary Antimicrobial Consumption</td>
</tr>
<tr>
<td>EU/EEA</td>
<td>European Union/European Economic Area</td>
</tr>
<tr>
<td>EVIPNet</td>
<td>Evidence-informed Policy Network</td>
</tr>
<tr>
<td>HAI</td>
<td>health-care-associated infection</td>
</tr>
<tr>
<td>IC</td>
<td>infection control</td>
</tr>
<tr>
<td>ICU</td>
<td>intensive care unit</td>
</tr>
<tr>
<td>ID</td>
<td>infectious disease</td>
</tr>
<tr>
<td>IPC</td>
<td>infection prevention and control</td>
</tr>
<tr>
<td>IT</td>
<td>information technology</td>
</tr>
<tr>
<td>LoS</td>
<td>length of stay</td>
</tr>
<tr>
<td>MDR</td>
<td>multidrug-resistant</td>
</tr>
<tr>
<td>MRSA</td>
<td>methicillin-resistant S. aureus</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>NPHO</td>
<td>National Public Health Organization</td>
</tr>
<tr>
<td>OECD</td>
<td>Organization for Economic Co-operation and Development</td>
</tr>
<tr>
<td>PCU</td>
<td>population correction unit</td>
</tr>
<tr>
<td>PPE</td>
<td>personal protective equipment</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>YLD</td>
<td>years of healthy life lost due to disability</td>
</tr>
<tr>
<td>YLL</td>
<td>years of life lost to due to premature mortality</td>
</tr>
</tbody>
</table>
KEY MESSAGES

Antimicrobial resistance (AMR) comes at a significant cost both to patients and the health-care system. It is associated with increased morbidity and mortality, increased resource utilization and cost, guideline modification and increased hospital burden. Among European Union (EU) countries, Greece has consistently high rates of antimicrobial consumption and resistance. Greece also reports high rates of health-care-associated infections compared to the rest of the EU, and that is where infections with antibiotic-resistant organisms occur and use of last-resort antibiotics is high.

Three viable options to address the problem

- **OPTION 1**
  Establish an interconnected electronic AMR surveillance system in hospitals
  The use of electronic surveillance systems results in shorter times to detect targeted infectious diseases, improves the time and quality of data collection, and is associated with reductions in improper antimicrobial prescriptions, the cost of antimicrobials, adverse drug events and length of stay.

- **OPTION 2**
  Establish antimicrobial stewardship and infection prevention and control programmes in all hospitals
  Hospital-based antimicrobial stewardship and infection prevention and control (IPC) programmes, when implemented in combination, result in significantly fewer infections and decreases in antimicrobial consumption and costs. This benefit is higher in the critical care setting. Multimodal infection control practices, including surveillance, monitoring and feedback, have the greatest effectiveness in reducing hospital-acquired infections.

- **OPTION 3**
  Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting
  Multifaceted interventions combining education of physicians and nurses in a variety of venues and formats are successful in reducing inappropriate antimicrobial prescribing, decreasing the incidence of health-care-associated infections, as well as the incidence of antimicrobial-resistant bacterial infections.
Considerations for implementation of the three options

Human behaviour is affected by attitudes and beliefs, and this also applies to highly trained hospital personnel. Stakeholders expect quick results from the implementation of AMR and IPC programmes; however, habitual behaviours of health-care workers take time to change, and AMR and IPC take time to improve. Funding can be a major issue in many centres and a barrier to the implementation of antimicrobial stewardship programmes (ASPs).
EXECUTIVE SUMMARY

The problem

Antimicrobial resistance (AMR) comes at a significant cost to both patients and the health-care system. It is associated with increased morbidity and mortality, increased resource utilization and cost, and increased hospital burden.

Among European Union (EU) countries, Greece reports consistently higher-than-EU-average rates of resistance in hospital-acquired pathogens, such as *Klebsiella pneumoniae*. *Klebsiella pneumoniae* resistance to fluoroquinolones was highest in Greece (66.9%; EU/European Economic Area [EEA] average of 31.5%). According to the European Centre for Disease Prevention and Control (ECDC), 66.5% of *Klebsiella pneumoniae* isolates in Greece are resistant to third-generation cephalosporins, which are antimicrobials commonly used in hospitals, while the EU/EEA population weighted mean was 31.3%. Carbapenem resistance of *Klebsiella* isolates in Greece is 58.3%, seven times higher than the EU/EEA population weighted mean (7.9%).

**Greece also has a high consumption of antimicrobials.** In a 2020 ECDC report, antimicrobial consumption in defined daily dose (DDD) per 1000 inhabitants per day in Greece was at 34.1, the highest among EU countries. This is much higher in comparison with northern European countries, such as the Netherlands (9.5) or Sweden (11.8), and higher than other southern European countries, such as Spain (24.7) or Italy (21.7). At that time, the average total consumption in the EU/EEA was 19.4 DDD per 1000 inhabitants per day.

Finally, **Greece has the highest prevalence of health-care-associated infections (HAIs) among European countries** according to the most recent ECDC point-prevalence survey in the EU/EEA. On any given day, there are a minimum of 1821 patients in Greece who have at least one HAI, which accounts for 66 487 cases annually. Of note, HAIs in Greece are usually due to organisms resistant to antimicrobials and require treatment with last-resort antibiotics.

In 2015, an estimated median of 1626 deaths and more than 400 disability-adjusted life years (DALYs) per 100 000 population were attributed to infections with AMR bacteria in Greece, compared to under 200 DALYs per 100 000 population in the EU/EEA.

In November 2019, the National Public Health Organization (NPHO) published the *2019–2023 National Action Plan for the management of AMR in Greece within the One Health approach*, which identifies overall three urgent (out of six) priorities:

1. Surveillance: evidence is needed on the contextual conditions to inform and implement effective interventions. Therefore, reinforcement of the national surveillance of
nosocomial infections and the development of a surveillance system for the consumption of antimicrobials in the community is crucial.

2. Infection prevention and control (IPC): reinforcement of institutional bodies for IPC in hospitals, funding of interventions and development of yearly action plans are necessary.

3. Judicious antimicrobial use: a stewardship programme for prescribing practices needs to be enacted.

Although a number of activities have been initiated, there is a common understanding that the country still has a long way to go to achieve prudent antibiotic use in every layer of its health system, including hospital settings.

### Options for addressing the problem

Based on a review of the relevant scientific literature in English and Greek, and on stakeholder interviews, which were carried out to obtain insights and to identify potential local differentiators that would otherwise not appear in the literature, this evidence brief for policy (EBP) proposes three viable options for addressing inappropriate antimicrobial use in inpatient health care in Greece. Given the specificities of the national context, the proposed options could achieve the most significant improvement in antimicrobial use when implemented. The options could be implemented in isolation or, ideally, in combination, so that an additive effect can be achieved.

Evidence to support option 1 – Establish an interconnected electronic AMR surveillance system in hospitals – was found in five systematic reviews.

- The use of electronic surveillance systems results in shorter times to detect targeted infectious diseases and improves the timeliness and quality of data collection.
- Electronic surveillance systems for nosocomial infections and antimicrobial use are associated with reductions in improper antimicrobial prescriptions, the cost of antimicrobial use, adverse drug events and length of stay.

Evidence to support option 2 – Establish antimicrobial stewardship and IPC programmes in all hospitals – was found in nine systematic reviews.

- Hospital-based antimicrobial stewardship and IPC programmes implemented in combination result in significantly fewer infections, decreases in antimicrobial consumption and costs. This benefit is higher in the critical care setting.
- Multimodal infection control practices, including surveillance, monitoring and feedback, have the greatest effectiveness in reducing hospital-acquired infections.

Evidence to support option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting – was found in nine systematic reviews.
Multifaceted interventions combining education of physicians and nurses in a variety of venues and formats are successful in reducing antimicrobial prescribing for inappropriate indications, decreasing the incidence rates of HAIs and the incidence of antimicrobial-resistant bacterial infections.

**Opportunities for and barriers to implementation**

To decrease the levels of inappropriate antimicrobial use in inpatient health-care settings, policy options should be implemented as part of a comprehensive national health policy.

Regarding opportunities, the introduction of information technology (IT) in hospital settings could be accompanied by educational programmes for health-care workers on how to use the new technology. Moreover, learning to use new devices could be integrated into their daily work, and managers could place emphasis on how the technologies can improve daily clinical practices. It is very important for legislation in Greece to be updated, so that electronic patient data protection and appropriate authorized access can be harmonized.

Concerning the antimicrobial stewardship and IPC programmes, involving representatives of relevant clinical services in the development and implementation of evidence-based guidelines, providing opportunity for iterative feedback, and adding audits or continuous quality improvement cycles, could all improve adherence to treatment guidelines. Understanding the local prescribing culture, fostering an environment of appropriate prescribing, and increasing collaboration between infectious diseases physicians and pharmacists must also be promoted. The inclusion of all staff, including cleaning staff, porters, kitchen staff and other support staff, when implementing IPC guidelines would be very important for the proper implementation of infection control strategies.

Last but not least, at the national level, legislative modifications can be made regarding the education of medical residents. In Greece, there is currently no uniform core body of knowledge for residency programmes across the country. Therefore, introducing core competencies on infection control and antimicrobial use in clinical medical specialty training would ensure that new prescribers are familiar with the problem of AMR and the ways to administer antimicrobials judiciously.

Barriers to implementation have also been considered. For the national surveillance system of inpatient antimicrobial consumption and AMR to be digitized, an electronic database has to be developed first. This requires high investment in hardware (e.g. computers and other electronic devices), accompanied by sophisticated computer programs and special software. Currently, the majority of Greek hospitals, especially the ones not located in the capital, have outdated computer devices that may be unable to support the software needed for the digitalization of the surveillance system. Therefore, hospitals should be provided with new electronic equipment and IT specialists employed for the development of the database. This
process requires extra funding, which may be a limit to the implementation of an updated surveillance system, especially now that the Greek health system is devastated by the ongoing COVID-19 pandemic.

Regarding the barriers to implementing IPC guidelines, issues that Greek health-care workers have reported and are supported by the systematic review include: lack of guideline awareness, staff shortages, lack of training on IPC practices and use of personal protective equipment (PPE), and lack of isolation rooms. These issues contribute to poor guideline implementation. It has also been reported that patients sometimes feel isolated and stigmatized by the use of PPE, therefore physicians and nurses may find it difficult to use this type of prevention measure in such cases.

Potential opportunities include involving representatives of relevant clinical services in guideline development, as well as all staff in the implementation of evidence-based guidelines, which would provide opportunity for iterative feedback. Additionally, actions such as adding audits or continuous quality improvement cycles, as well as minimizing overcrowding, fast-tracking infected patients, restricting visitors, and providing easy access to handwashing facilities can all help health-care workers adhere better to IPC guidelines.

One of the most significant barriers is the anticipated difficulty of changing behaviour. Specifically, attending physicians often fail to update their knowledge on antimicrobial administration and infection control practices and tend to follow established patterns regarding patient care; therefore, inducing behaviour changes may be challenging. Resident physicians tend to copy the usual hospital practice and may not change their prescribing behaviour unless the guidance provided to them changes.
INTRODUCTION

Antimicrobial resistance (AMR) is a public health priority worldwide, including in Greece. A number of studies already highlight the current and future impact of this growing problem. Awareness of the AMR problem in Greece is rising and there is an increasing political interest in addressing this problem. In this context, this report was prepared to support decision-makers and ensure that the best evidence is available to them. The intention was to synthesize the available international and local evidence on the benefits, harms, costs and barriers to implementation of diverse available options while putting them in the context of the reality in Greece as expressed by the views and experience of local stakeholders. The goal is to support and contribute to the improvement of surveillance and infection prevention and control (IPC) practices to combat the AMR problem in Greece.

BOX 1: Background to the policy

This policy mobilizes both global and local research evidence about a problem, three options for addressing the problem, and key implementation considerations. Whenever possible, the policy summarizes research evidence drawn from systematic reviews of the research literature and occasionally from single research studies. A systematic review is a summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select, and appraise research studies and to synthesize data from the included studies. The EBP does not contain recommendations.

The preparation of the EBP involved six steps:

- convening a working group comprising representatives from the National Public Health Organization (NPHO), the Agency for Quality Assurance in Health Société anonyme (AQAH S.A.) and the Center for Clinical Epidemiology and Outcomes Research (CLEO);
- undertaking training on writing the EBP report;
- developing and refining the terms of reference for the EBP, particularly the framing of the problem, and three viable options for addressing it. This was done in consultation with the Steering Committee and a number of key informants and with the aid of several conceptual frameworks that organize thinking about ways to approach the issue;
- identifying, selecting, appraising and synthesizing relevant research evidence about the problem, options, and implementation considerations;
- drafting the EBP in such a way as to present concisely, and in accessible language, the global and local research evidence; and
finalizing the EBP based on the input of several merit reviewers, including the Hellenic Society for Infectious Diseases and the Greek Society for Infection Control.

The three options for addressing the problem were not designed to be mutually exclusive. They could be pursued simultaneously, or elements could be drawn from each option to create a new (fourth) option.

The policy was prepared to inform a policy dialogue at which research evidence is one of many considerations. Participants’ views and experiences and the tacit knowledge they bring to the issues at hand are also important inputs to the dialogue. One goal of the policy dialogue is to spark insights – insights that can come about only when all of those who will be involved in or affected by future decisions about the issue can work through it together. A second goal of the policy dialogue is to generate action by those who participate in the dialogue and by those who review the dialogue summary.

How this evidence brief for policy was prepared

This is the first evidence brief for policy (EBP) produced in Greece within the framework of the World Health Organization (WHO) Evidence-informed Policy Network (EVIPNet) Europe. It was developed by the NPHO, AQAH S.A. and CLEO. Box 1 summarizes the way this work was initiated and developed.

The evidence brief was submitted for revision to the WHO Regional Office for Europe, the Hellenic Society for Infectious Diseases and the Greek Society for Infection Control.

The authors analysed global and local evidence on the problem and policy options to address it, along with barriers to and opportunities for implementing the options (Box 2). The search for evidence focused on identifying systematic reviews of the effects of policy options and their implementation strategies (see Appendices 1–3). The authors also consulted other relevant single research studies, economic evaluations, key publications of major international organizations (e.g. European Center for Disease Prevention and Control [ECDC], Centers for Disease Control and Prevention [CDC], Organization for Economic Co-operation and Development [OECD], WHO) and finally government reports and the unpublished literature. The authors also acquired information from experts, stakeholders and key informants through interviews (see Annex 4). Their insights on the problem, the options for addressing it and implementation considerations were taken into account by the authors when writing and revising the EBP during its various development stages.

The approach to the review of the available evidence was performed in a systematic and transparent way (Box 2).
For the development of this EBP, various sources were used: international and local reports, and information from Medline/PubMed, Cochrane Library, Health Systems Evidence, Health Evidence and Google Scholar databases. Relevant grey literature was found by reviewing the websites of leading international and national organizations, such as the NPHO, WHO, ECDC, and CDC. Priority was given to research evidence that was published more recently, that was locally applicable (in the sense of having been conducted in the country), and that took equity considerations into account.

The information that was found on systematic reviews was organized in tables (see Appendices 1–3) that included the review, the year it was conducted, the focus and its key findings, the last year the literature was searched as part of the review and the rating of the overall quality of the review. The quality of each review was assessed using AMSTAR (A MeaSurement Tool to Assess Reviews), which rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to delivery, financial or governance arrangements within health systems. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e. the numerator and denominator) in mind. For example, a review that scores 8/8 is generally of comparable quality to a review scoring 11/11; both ratings are considered “high scores”. A high score signals that readers of the review can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the review should be discarded, merely that less confidence can be placed in its findings and that the review needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. Health Research Policy and Systems (in press)

In general, the quality of evidence was classified as follows:

- High 8–11 AMSTAR rating (points)
- Medium 4–7 AMSTAR rating (points)
- Low 0–3 AMSTAR rating (points)
THE PROBLEM

Antimicrobials – which include antibacterials, antifungals and antivirals – are medicines used to treat and prevent infections in humans, animals and plants. The discovery of antimicrobials almost 100 years ago revolutionized the way infections were treated and improved outcomes in surgery, oncology and obstetrics. In the US, in the first 15 years of antimicrobial use, mortality from any infection decreased by 75% (1).

However, Sir Alexander Fleming, who discovered penicillin, right from the beginning in his Nobel Prize speech, predicted the problem of AMR (2). AMR occurs when microorganisms no longer respond to antimicrobial agents. AMR is considered one of the most serious threats to global public health and is associated with increased morbidity, mortality and health-care costs (3). Without effective antimicrobials, common infections may be life-threatening, and treatments such as surgical procedures and chemotherapy will become riskier. It is estimated that about 33,000 people die each year as a direct consequence of an infection resistant to antimicrobials in Europe (4,5).

How AMR occurs

Even though AMR may emerge naturally as part of a microbe’s life-cycle, inappropriate antimicrobial use puts pressure on the natural evolution and survival mechanisms of microbes and accelerates the emergence of AMR.

There are two main drivers of AMR:

› First, the **consumption** of antimicrobials leads to the selection and reproduction of microbes already resistant to antimicrobials within a microbial population. At the same time, antimicrobials exert ecological pressure on microorganisms to survive by developing new resistant strains. The overuse of antimicrobials for human health care, either in the community, or in hospitals and other health-care settings, is a major driving factor for this problem. Antimicrobials can be misused in several ways:
  » when administered unnecessarily, for example, if used for illnesses that do not require antimicrobial treatment, such as viral infections;
  » when the antimicrobial used is not specifically targeted to the infecting pathogen, i.e. the antimicrobial given is of an unnecessarily “broad spectrum” and attacks a much wider spectrum of microbes than what is needed for the successful treatment of an infection (see Box 3);
  » when given for much longer periods of time than needed.
THE PROBLEM

BOX 3: Broad spectrum vs narrow spectrum antibiotics

Broad spectrum: antibiotics that are potent against a wide range of bacteria
Narrow spectrum: antibiotics that are potent against a small number of different bacteria.

Second, the transmission of antimicrobial-resistant microorganisms between humans, between animals, and between humans and animals: the use of antimicrobials in food-producing animals is part of the problem, as animals thus harbour resistant bacteria. Handling and consumption of these animals, or of vegetables contaminated with animal manure, can lead to the spread of resistant bacteria to humans. In addition, the antimicrobials used in animals are the same as those used in human medicine. In hospitals, humans treated with antimicrobials can become carriers of resistant bacteria, which they can spread to other patients through either direct contact or indirect contact with contaminated surfaces and objects.

The burden of AMR

AMR comes at a significant cost both to patients and the health-care system. It is associated with increased morbidity and mortality (increased length of hospital stays, need for isolation, surgery or intensive care unit [ICU] stay), increased resource utilization and cost (ICU beds, personal protective equipment [PPE] for the personnel), guideline modification (e.g. use of second-line agents with reduced efficacy and/or increased toxicity) and increased hospital burden (unit closures, surgery cancellations) (6).

In Europe, a study by Cassini et al. (7) estimated that an increase in the number of infections with antimicrobial-resistant bacteria from 239 238 (95% uncertainty interval [UI] 215 544–262 951) in 2007 to 602 609 (524 237–686 497) in 2015 was accompanied by an increase in the median number of attributable deaths from 11 144 (9999–12 407) in 2007 to 27 249 (23 544–31 471) in 2015 (7).

All age groups are affected, but the increased burden among adults is associated with ageing, which is important in the context of an ageing population in the European Union (EU)/European Economic Area (EEA). In 2015, the estimated age-standardized burden of carbapenem-resistant Klebsiella pneumoniae increased by 6.16 times in terms of the number of infections and number of deaths, while attributable deaths and disability-adjusted life years (DALYs) (see Box 4) were highest in Italy and Greece.

In 2015, among OECD countries, Turkey, the Republic of Korea and Greece had the highest average AMR rates estimated (around 35%), which were seven times higher when compared to Iceland, the Netherlands and Norway, which have the lowest proportions (around 5%) (8).
BOX 4: What are disability-adjusted life years (DALYs)?

Definition: One DALY represents the loss of the equivalent of one year of full health. DALYs for a disease or health condition are the sum of the years of life lost to due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health condition in a population.

Rationale: Mortality does not give a complete picture of the burden of disease borne by individuals in different populations. The overall burden of disease is assessed using the disability-adjusted life year (DALY), a time-based measure that combines years of life lost due to premature mortality (YLLs) and years of life lost due to time lived in states of less than full health, or years of healthy life lost due to disability (YLDs). One DALY represents the loss of the equivalent of one year of full health. Using DALYs, the burden of diseases that cause premature death but little disability (such as drowning or measles) can be compared to that of diseases that do not cause death but do cause disability (such as cataract causing blindness).

Among EU countries, Greece reports consistently higher-than-EU-average rates of resistance in *Escherichia coli* and *Klebsiella pneumoniae*. For instance, in 2017, *Klebsiella pneumoniae* resistance to fluoroquinolones was highest in Greece (66.9%; EU/EEA average of 31.5%) (4). In a recent ECDC report (9), 66.5% of *Klebsiella pneumoniae* isolates in Greece are resistant to third-generation cephalosporins, which are antimicrobials commonly used in hospitals. This is second only to Bulgaria (75.5%), while the EU/EEA population weighted mean was 31.3%. Carbapenem resistance of *Klebsiella* isolates in Greece is 58.3%, much higher than the second (Romania, 32.3%) and more than seven times higher than the EU/EEA population-weighted mean (7.9%) (Fig. 1). Additionally, *Pseudomonas aeruginosa's* resistance to fluoroquinolones (46.8%) is second to Romania (52.2%) and more than double that of EU/EEA population-weighted mean (18.9%) and for carbapenems, resistance is at 48.9% in Greece compared to the EU population-weighted mean of 16.5% (Fig. 2).

By 2050, according to the “Independent Review on Antimicrobial Resistance” commissioned by the UK Government, if policies to impede the spread of AMR are not implemented, AMR-related deaths are predicted to increase from the currently estimated 700 000 deaths per year to 10 million deaths globally per year, a number surpassing the 8.2 million deaths currently due to cancer, i.e. by 2050, one person may die every three seconds due to drug-related resistance (3).

In 2019, the CDC published the report *Antibiotic resistance threats in the United States, 2019*, estimating that at least 2.8 million antimicrobial-resistant infections occur in the United States every year, resulting in more than 35 000 deaths (10). An OECD model estimates that 2.4 million people may die in Europe, North America and Australia between 2015 and 2050, according to current AMR projections (8). This model forecasts the highest mortality rates in Greece, Italy and Portugal among OECD countries, while the highest absolute number of deaths are
FIG. 1. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to (A) third-generation cephalosporins and (B) to carbapenems in Greece vs EU/EEA population-weighted mean, 2019


FIG. 2. *Pseudomonas aeruginosa*. Percentage of invasive isolates with resistance to (A) carbapenems and (B) to fluoroquinolones in Greece vs EU/EEA European population-weighted mean, 2019

expected in France, Italy and the United States. The most recent studies show that over 33,000 people die every year in the EU due to infections from antimicrobial-resistant bacteria \((4,5)\).

In 2015, an estimated median of 1626 deaths and more than 400 DALYs per 100,000 population were attributed to infections with antimicrobial-resistant bacteria in Greece, compared to under 200 DALYs per 100,000 population in the EU/EEA \((7)\).

The OECD report estimates a global cost of US$ 100 trillion up to the year 2050 in terms of lost production due to AMR \((8)\). This number could be an underestimate due to new constantly emerging resistance, and to treatment complications related to the unavailability of effective antimicrobials. In 33 OECD and 28 EU countries, up to US$ 3.5 billion may be spent every year between 2015 and 2050 on AMR-related complications \((8)\).

Finally, annual global gross domestic product (GDP) may fall by 1.1% due to AMR in 2050, and this shortfall could exceed US$ 1 trillion annually after 2030. In a less moderate scenario, the annual GDP decrease may be 3.8% adding up to a US$ 3.4 trillion annual shortfall by 2030. Additionally, economic growth in low-income countries may be more severely impacted than in high-income ones, thus increasing global economic inequality \((11)\) (Fig. 3).

**FIG. 3. Substantial and protracted shortfalls in global economic output**

---

Drug-resistant infections: a threat to our economic future. Washington, DC: World Bank; 2017. License: Creative Commons Attribution CC BY 3.0 IGO
The role of health-care-associated infections (HAIs)

A health-care-associated infection (HAI) is an infection acquired in a hospital or other health-care setting. HAIs are recognized as a significant threat, as they are associated with increased morbidity, mortality and health-care costs. At a European level, it has been shown that HAIs in acute care hospitals are responsible for more deaths in the EU/EEA than all other infectious diseases under surveillance, including influenza and tuberculosis (12,13).

The surveillance of HAIs and AMR in Europe is mainly conducted by the European Antimicrobial Resistance Surveillance Network (EARS-Net), as well as through point-prevalence surveys coordinated by the ECDC. According to a point-prevalence survey in the EU/EEA (14), 8.9 million distinct HAIs occurred each year in acute and long-term care facilities. In acute care hospitals alone, there were 3.8 million patients with at least one HAI each year in the period 2016–2017. The prevalence of HAIs in the same population was 5.5%, which means that, on any given day, there were about 80 000 patients with at least one HAI in acute care hospitals in the 29 countries that participated. Carbapenem resistance, in particular, which signifies the ineffectiveness of commonly used antimicrobials, was detected in 6.2% of Enterobacteriaceae causing HAIs.

In Greece, according to the most recent ECDC point-prevalence survey in the EU/EEA (14), the prevalence of HAIs was 10%; the highest among participating countries. This means that, on any given day, there are at least 1821 patients in Greece who have at least one HAI, which accounts for 66 487 cases annually. In Greece, carbapenem resistance in Enterobacteriaceae causing HAIs was 43.7%, whereas Estonia, Finland, Iceland and Lithuania reported 0%, which indicates that the problem of AMR, at least as far as carbapenem-resistant Enterobacteriaceae (CRE) is concerned in Greece, is associated with HAIs in acute care hospitals.

Apart from the ECDC survey, studies that aimed to measure HAIs in Greece are few and usually restricted to one institution or unit, limited in duration, and inconsistent in terms of definitions, methods and outcomes, which makes it difficult to compare results and draw meaningful conclusions. Only a few studies were conducted in large collaborative Greek networks for device-associated infections (15–17) and surgical site infections (18). These studies measured the incidence of HAIs in Greece and showed that it is possible to have an impact with some low-cost interventions such as adherence to perioperative antimicrobial prophylaxis guidelines. For example, it is estimated that central line-associated bloodstream infection (CLABSI) rates were 6.02 per 1000 central line days in neonatal intensive care units, 6.09 per 1000 central line days in paediatric intensive care units, and 2.78 per 1000 central line days in paediatric oncology units, while it was 11.3 per 1000 central line days in adult ICUs (15). Also, an intervention based on education, audit and feedback improved the appropriate perioperative antibiotic prophylaxis and decreased surgical site infections from 6.9% to 4% in a study that was conducted in seven surgical departments of three major Greek hospitals (18).
Antibiotic consumption in Greece

In a 2020 ECDC report, antimicrobial consumption in defined daily dose (DDD) per 1000 inhabitants per day in Greece was at 34.1, the highest among EU countries. (See Box 5 for definition.) This is much higher in comparison with northern European countries, such as the Netherlands (9.5) or Sweden (11.8), and higher than other southern European countries, such as Spain (24.7) or Italy (21.7). At that time, the average total consumption in the EU/EEA was 19.4 DDD per 1000 inhabitants per day (9).

**BOX 5: Measures of antibiotic consumption**

Drug consumption can be expressed in cost, number of units, number of prescriptions or by the physical quantity of drugs. However, these can vary between regions and countries over time. This limits the comparison of drug consumption at an international level. To address variability in these measures between regions and countries, WHO developed a technical unit of measurement, the defined daily dose (DDD).

**Defined daily dose (DDD):** is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults.

**DDD per 1000 inhabitants per day:** Example: 10 DDDs per 1000 inhabitants per day can be interpreted as follows: in a representative group of 1000 inhabitants, 10 DDDs of the drug are utilized on average, on any given day of the year analysed. Odds ratio (OR) 10/1000 (1%) of the population are receiving this drug each day in that year.


In the **community**, consumption of antibacterials for systemic use was at 32.4 DDD per 1000 inhabitants per day, when the EU/EEA average was at 18.0, and higher than the second- and third-highest reported community consumption of 30.1 DDD per 1000 inhabitants per day in Cyprus and 24.0 in Romania. Looking at the ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and erythromycin expressed as DDD per 1000 inhabitants per day in the community, Greece was at 5.1 with the average at 2.8 and much lower than other countries such as Malta (20.0), Hungary (13.6) and Slovakia (8.3) (9). Part of the problem in the community seems to be the practice of obtaining antimicrobials without a medical prescription, which was possible until 2020.

In the **hospital sector**, Greece’s total consumption of 1.68 DDD per 1000 inhabitants per day is below the EU/EEA average of 1.77, and below that of other southern countries, such as Malta (1.99) and Italy (1.89). However, the proportion of advanced antimicrobials, namely glycopeptides, third- and fourth-generation cephalosporins, monobactams, carbapenems,
fluoroquinolones, polymyxins, piperacillin and enzyme inhibitors linezolid, tedizolid and daptomycin (DDD per 1000 inhabitants per day) is high at 50.8 compared to the EU/EEA average (33.7) and to other southern countries (Spain at 45.7 and Italy at 44.5) (9).

**The case of carbapenems and polymyxins**

Carbapenems and polymyxins are considered a last-line group of antimicrobials. They respectively belong to the Watch and the Reserve group of the WHO AWARe classification (19) (see Box 6 for definition) and are also respectively categorized as Critically Important and Highest Priority Critically Important Antimicrobials (HPCIA) for human medicine (20). There is a statistically significant positive association between the consumption of carbapenems and carbapenem resistance in invasive *K. pneumoniae* and *Escherichia coli* isolates (20).

**BOX 6: What is the WHO AWARe classification?**

The Access, Watch, Reserve (AWaRe) classification of antibiotics was developed by WHO to aid the reduction of AMR and to assist the development of antibiotic stewardship tools. Antibiotics are classified into different groups to make evident the significance of their appropriate use. It is intended to be used as a tool to better support antibiotic monitoring and stewardship activities globally.

**Access:** this group includes antibiotics that are active against a wide variety of commonly encountered susceptible pathogens. They also have a lower resistance potential than antibiotics in the other groups. Antibiotics in this group are recommended as first- or second-choice empirical treatment options for infectious syndromes.

**Watch:** antibiotics of this group have higher resistance potential and include most of the highest priority agents among the Critically Important Antimicrobials for human medicine. They should be considered a priority and key targets of stewardship programmes and surveillance. Some Watch antibiotics are recommended as essential first- or second-choice empirical treatment options for a limited number of specific infectious syndromes.

**Reserve:** antibiotics of this group should be considered a “*last resort option*” and should be reserved only for the treatment of confirmed or suspected infections due to multidrug-resistant organisms. Even though Reserve antibiotics should be accessible, their use should be customized to highly specific patients and settings, where all alternatives have either failed or are not suitable. They should be protected and considered priority key targets of national and international stewardship programmes to preserve their effectiveness.

**Source:** The 2019 WHO AWARe classification of antibiotics for evaluation and monitoring of use. Copenhagen: WHO Regional Office for Europe; 2019 (https://apps.who.int/iris/handle/10665/327957).

In a recent joint report by ECDC/EFSA/EMA (21) regarding the overall consumption of carbapenems in hospitals, Greece is second only to Malta and more than three times the
An asterisk (*) denotes that only community consumption was provided for human medicine. The population-weighted mean proportion (%) of the hospital sector from the 2017 total national consumption of carbapenems for EU/EEA countries providing data for both sectors is 94.4%. The weighted mean figure represents the population-weighted mean of data from included countries.

**Source:** Third joint inter-agency report on integrated analysis of consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals in the EU/EEA, JIACRA III. 2016–2018. ECDC, EFSA, EMA; 2021. Fig. 9, page 21.

weighted EU average (Fig. 4). Greece is first in terms of hospital consumption of very advanced antimicrobials, namely polymyxins, in humans among EU countries according to the same report (Fig. 5). In addition, looking at the population-weighted mean consumption of polymyxins, Greece showed a statistically significant increase during 2010 to 2019 among EU/EEA countries (9).

With regard to **food-producing animals**, Greece started participating in the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project only in 2015 (21).
**FIG. 5.** Population-corrected consumption of polymyxins in humans only, by country, in 29 EU/EEA countries in 2017

An asterisk (*) denotes that only community consumption data was provided for human medicine. The population-weighted mean proportion (%) of the hospital sector from the 2017 total national consumption of polymyxins for EU/EEA countries providing data for both sectors is 50.1%.

**Notes:**
1. The estimates presented are crude and must be interpreted with caution. For limitations hampering comparison of antimicrobial consumption by humans and food-producing animals, please see Section 14.
2. The weighted mean figure presents the population-weighted mean of data from those countries that were included.
3. There was no consumption of polymyxins in food-producing animals in Finland, Iceland and Norway.
4. There was no consumption of polymyxins in humans in Iceland and Lithuania.

**Source:** Third joint inter-agency report on integrated analysis of consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals in the EU/EEA, JIACRA III. 2016–2018. ECDC, EFSA, EMA; 2021. Fig. 32b, page 52.

According to the European Medicines Agency (EMEA), there was an increase of 59% in farm antimicrobial sales in Greece from 2015 (57.1 mg/population correction unit [PCU]) to 2018 (90.9 mg/PCU), in particular, for tetracyclines, aminoglycosides, pleuromutilins and amphenicols. (See Box 7 for definition.)
In conclusion, the inappropriate use of antimicrobials is prevalent not only in hospital and ambulatory settings, but also in agriculture. In the community, new recent legislation seems to have considerably lowered the phenomenon of over-the-counter administration without prescription. In agriculture and food-producing animals, the problem is not as profound as in the hospital setting; considering that as Greece has only recently started reporting to EU organizations, the surveillance landscape is most likely not as mature. Finally, hospital settings is where the problem of AMR and consumption of critically important antimicrobials is more profound as is evident from the above data. As such, even though AMR can be spread in the community and through the animal sector, this brief will specifically focus on addressing AMR in inpatient settings.

Regarding antimicrobial prescribing practices, a gap in education exists, as there is evidence that doctors do not receive adequate training about proper antimicrobial prescribing and are unfamiliar with its importance, which gives rise to prescribing errors in hospital inpatients (22). According to a cross-sectional study conducted in multiple hospitals in Spain, the majority of residents regarded AMR as a significant problem at national level; however, the training that they received about antimicrobials was inadequate (23). In Greece, residency programmes lack targeted education towards prudent antimicrobial use, with many of the new residents following the prescribing behaviours of their attendings, which may be outdated. Courses on antimicrobial use and proper infection control practices are not currently organized on a regular basis, but are rather ad hoc from certain scientific societies, such as the Hellenic Society for Infectious Diseases and the Greek Society for Infection Control.

**Governance in Greece for human health care**

Regulatory tools regarding AMR already exist in Greece; namely, a legal framework and a number of non-legislative actions involving several stakeholders (Annexes 1–3). According to the current legal provisions, all Greek public and private hospitals are required to participate in the National Action Plan for the control of AMR and HAIs in Greece. The National Action
Plan is based on the surveillance of nosocomial infections caused by selected drug-resistant bacteria, and the surveillance of the consumption of selected advanced antimicrobials, as analysed below.

**The National Action Plan "Procrustes" (24)**

The main national surveillance system regarding microbial resistance (named Procrustes) was introduced in 2010 by the NPHO under the auspices of the Ministry of Health. Until then, no data were available on a national level on the extent and spread of resistant pathogens (25).

The Procrustes Action Plan focuses on the surveillance of HAIs caused by the main antimicrobial-resistant pathogens involved in nosocomial infections, as well as monitoring the implementation of infection control measures in medical facilities according to the guidelines issued by the NPHO. Procrustes includes the following actions:

- establishment of a centralized national notification system for the mandatory notification of newly detected cases of infections caused by selected multidrug-resistant (MDR) pathogens in hospitals;
- evaluation of the burden of MDR infections in hospitals in Greece;
- implementation of infection control measures to attenuate the transmission of MDR pathogens in hospitals, including infection control bundles and geographical separation of MDR carriers and infected patients;
- evaluation of adherence to infection control bundles;
- communication links between hospitals and public health authorities.

The Plan was expanded to encompass antimicrobial use in hospitals and was made legally binding in 2014 by ministerial decree (Government Gazette FEK 388/B’ 18.2.2014). The new legislation:

- defined the competencies, role and work of infection control nurses in Greek hospitals;
- defined metrics for the surveillance of infection, AMR, antimicrobial consumption, and compliance of health-care workers with infection prevention practices;
- mandated that the evaluation of hospital administrators was to be linked to the effectiveness and efficiency of the reduction in hospital infection, antimicrobial use and AMR.

The 2014 Ministerial Decree requires that every hospital forms an infection control committee, with its task force consisting of an infectious disease specialist, a microbiologist and an infection control (IC) nurse. Moreover, it states that hospitals with up to 250 beds should

---

*a A simple set of evidence-based practices that, when implemented together, lead to the improvement of the reliability of their delivery and patient outcomes.*
have at least one IC nurse, while hospitals with more than 250 beds should have at least two IC nurses.

Each hospital is required to report to the NPHO monthly data regarding the incidence of bloodstream infections caused by five classes of drug-resistant bacteria (carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *Klebsiella pneumoniae*, carbapenem-resistant *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant Enterococci) along with the specific mechanisms of resistance.

Regarding AMS committees in Greece, a Ministerial Decree introduced in 2014 (FEK 388/B’ 18.2.2014) requires every hospital to form a Committee for Monitoring of the Consumption and Proper Use of Antibiotics. By law, the Committee consists of the pharmacy director, an infectious diseases (ID) specialist (if unavailable, a clinician who is a member of the Infection Control Committee) and representatives from the ICU, surgical wards and haematological/oncological wards. The role of this Committee is to monitor the compliance with treatment guidelines, prescription forms of advanced antimicrobials, surgical chemoprophylaxis forms, and the monthly consumption of antimicrobials. Moreover, the legislation states that the ID specialist (or the clinician of the Committee) should be exempted from other duties for two weeks every two months to engage in the work of the Committee.

Regarding antimicrobial consumption, each hospital reports monthly data on the use of selected broad-spectrum antimicrobials administered parenterally, e.g. carbapenems, piperacillin/tazobactam, vancomycin, etc. These data are then analysed by the NPHO and rates are calculated every 6 months and annually, and the results are then communicated to the hospital administration and Infection Control Committee, as well as to the Ministry of Health.

**Limitations in the implementation of the National Action Plan “Procrustes”**

The existing national surveillance programme has drawbacks that impede the surveillance of antimicrobial consumption and AMR. The data reported to the NPHO are collected in paper forms that are filled in manually by a member of the Infection Control Committee of each hospital and are afterwards sent to the NPHO via email or postal service, the latter if personal data are included. Given that this process is not automated and requires extra time from healthcare workers, not all hospitals are able to send all the data needed, and some of them do not participate in the surveillance system at all. One hundred eight out of 131 public hospitals, and 46 out of 130 private hospitals participate in the “Procrustes” surveillance system.

Moreover, these data are only about bloodstream infections caused by selected MDR nosocomial pathogens and do not incorporate hospital-acquired bloodstream infections by non-resistant pathogens, or other forms of HAIs, such as surgical-site infections and ventilator-associated pneumonias.
Additionally, although a legal provision exists, not every hospital has dedicated IC nurses, nor is there monitoring of physicians' compliance with infection control practices, while personal protective equipment (PPE) is not consistently provided in every hospital setting due to financial constraints. The Committee for the Monitoring of the Consumption and Proper Use of Antibiotics is not well established or is not operational in many Greek hospitals, public or private. Frequently, AMS committees are assembled but remain almost inactive, which limits the inspection of prescribing practices in hospitals. The barriers to the function of these committees can be traced at multiple levels, mainly staffing and allocated time shortage and education gaps.

Complementary surveillance systems

The national surveillance programme “Procrustes” is complemented by additional surveillance systems operating in parallel:

- WHONet Greece (Greek System for the Surveillance of Antimicrobial Resistance) monitors microbial susceptibility data uploaded by hospital microbiology laboratories. The system uses software developed by WHO and is jointly operated by the NPHO and the National School of Public Health with a scientific scope encompassing microbial resistance trends in medical and surgical wards, and ICUs, as well as the detection of hospital infection epidemics.

- Health insurance data registries, monitored by health insurance providers, hold important demographic data, which could be used to detect areas with increased risk of MDR infections and pinpoint unidentified equity issues. Greece has moved towards a single-payer health insurance modality since 2012, when the National Organization for the Provision of Health Services, which operates under the Ministry of Health (Greek acronym: EOPYY), replaced pre-existing health insurance funds. Antibiotic prescription is operated in partnership with the national e-Government Center for Social Security Services (IDIKA SA), supervised by the Ministry of Labour, Social Security & Social Solidarity. IDIKA also operates a number of clinical registries organized by type of disease or condition.

- Clinical data registries are usually organized per hospital clinic, with data stored on local hospital information systems/intranets.

Limitations of complementary surveillance systems

Clinical registry data are accessible by medical professionals of a particular hospital clinic, or of the entire hospital. There is no global intrahospital data-sharing, while interhospital data-sharing remains an exception. For example, although MDR pathogen notification is legally required when a patient colonized with resistant bacteria is transferred to another health-care facility, in practice this is only sporadically implemented. Through structured interviews with heads of Infectious Disease Committees, only one digital interhospital notification system was
identified concerning resistant pathogen colonization of transferred patients. The system was a locally operated initiative among a limited number of collaborating hospitals in southern Greece and was not functional in case a patient was transferred outside this local area.

Considerable overlap exists among the different surveillance systems, with little or no system interoperability, resulting in data fragmentation across different databases and preventing hospitals and health policy organizations from effectively utilizing valuable information.

In November 2019, the NPHO published the “2019–2023 National Action Plan for the management of antimicrobial resistance in Greece within the One Health approach”. It identifies overall these first three (out of six) priorities:

1. surveillance: reinforcement of the national surveillance of nosocomial infections and the development of a surveillance system for the consumption of antimicrobials in the community;
2. infection prevention and control: reinforcement of institutional bodies for IPC at hospitals, funding of interventions, development of yearly action plans;
3. judicious antimicrobial use: an inspection programme for prescribing practices is to be enacted.

Inpatient settings – the obvious target for AMR in Greece

As previously shown, HAIs in Greece

› have a high incidence and prevalence,
› are due to pathogens contracted within the hospital environment and, as such, are frequently resistant to antimicrobials,
› could require treatment with second-line and broad-spectrum antibiotics,
› are associated with high morbidity and mortality when caused by AMR pathogens.

The fact that Greece’s consumption of 1.68 DDD per 1000 inhabitants per day in hospitals is below the EU/EEA average of 1.77 might lead to the conclusion that another setting of antimicrobial consumption should be selected for an intervention. It is, however, the significantly high proportion of second- or last-line antibiotics prescribed (50.8 compared to the EU/EEA average of 33.7) that supports the decision to focus on addressing AMR in the inpatient setting in Greece.

Therefore, the joint and collaborative implementation of an IPC programme along with ASP in the inpatient setting is the logical target for any intervention aiming to address the problem of AMR in Greece.
Equity-related observations about the problem

Current AMR and antimicrobial consumption monitoring systems do not include racial, ethnic, gender or place of residence data. Therefore, the existing data do not allow for reliable equity-related observations regarding AMR in the hospital setting and nosocomial infections. Systematic disparities have been taken into account only with AMR prevention strategies in the community (26).

Given that preventable hospitalization is more prevalent within socially disadvantaged communities, an ensuing disproportionately high exposure to drug-resistant nosocomial pathogens would be expected. Communities with household overcrowding, a condition mostly prevalent among immigrant populations, have been shown to be colonized with more resistant bacterial strains (27). Database interconnection between AMR, antimicrobial usage and hospital records may help to capture the risks related to specific patient groups.
THREE OPTIONS FOR ADDRESSING THE PROBLEM

Considering viable options to address inappropriate antimicrobial use in inpatient health care, three options have been selected for more in-depth review:

› Establish an interconnected electronic AMR surveillance system in hospitals.
› Establish AMS and IPC programmes in all hospitals.
› Implement postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting.

Apart from an extensive literature review, stakeholder interviews were conducted (summarized in Annex 4) with a view to obtaining insights and identifying potential local differentiators that would otherwise not appear in the literature. These interviews made reference to a number of structural problems and fundamental administration errors, as well as to difficulties in implementing the existing regulatory provisions (summarized in Annexes 5 and 6). Combining the information from literature research and stakeholders’ interviews, the three options were formulated and are analysed in depth in this section. While each option can be implemented independently, combined implementation would likely have a greater impact on improving the use of antimicrobials in inpatient health care.

BOX 8: Mobilizing research evidence about options for addressing the problem

The available research evidence about options for addressing the problem was sought primarily from a continuously updated repository of syntheses of research evidence on governance, financial and delivery arrangements within health systems, and about implementation strategies that can support change in health systems. (Health Systems Evidence, www.healthsystemsevidence.org). The reviews were identified by first searching the database for reviews containing topic-related keywords in the title and/or abstract. The keywords included [Antibiot*, antimicrob*, antibacter*, overuse, consumption, prescr*, use, dispens*, Greece, Greek, Hellas]. Additional reviews were identified by searching the database for reviews addressing features of the options that were not identified using topic-related keywords. Additionally, a literature search was conducted in PubMed (pubmed.ncbi.nlm.nih.gov) with the same keywords.

The review authors’ key findings were extracted from the identified reviews. Each review was also assessed in terms of its quality (AMSTAR rating), local applicability (proportion of studies that were conducted in the country), equity considerations (proportion of studies that dealt explicitly with prioritized groups) and the review’s degree of focus on the issue. The overall evidence about the options was then summarized and relevant caveats introduced about the review authors’ key findings based on the quality, local applicability, equity and issue applicability assessments.
Attention was given to whether reviews contained no studies despite an exhaustive search (i.e. they were “empty” reviews) and whether reviews concluded that there was uncertainty about the option based on the identified studies. Being aware of what is not known can be as important as being aware of what is known. When faced with an empty review or with uncertainty or concerns about the review’s quality, local applicability of the review’s findings, or a lack of attention to equity considerations, primary research could be commissioned, or an option could be pursued, and a monitoring and evaluation plan designed as part of its implementation. When faced with a review that was published many years ago, an updating of the review could be commissioned if time allows.

No additional research evidence was sought beyond what was included in the systematic reviews. Those interested in pursuing a particular option may want to search for a more detailed description of the option or for additional research evidence about the option.

**OPTION 1: Establish an interconnected electronic AMR surveillance system in hospitals**

**OVERVIEW AND CONTEXT**

<table>
<thead>
<tr>
<th>Current status and limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance of selected HAIs is mandatory by law. However, the existing paper-based surveillance methods are burdensome as staff can spend up to 45% of their time undertaking surveillance, the application of definitions is subject to interpretation, and the identification of cases depends on effort (28).</td>
</tr>
</tbody>
</table>

**Proposed surveillance option**

The existing hospital surveillance system in Greece needs to be updated, expanded and digitalized in an interconnected way. Outdated analogue surveillance systems (e.g. paper-based) should be replaced by digital data management systems. For this reason, a national electronic platform should be developed, and data entry should be decentralized so that each hospital can upload data. To avoid redundancies in data collection, offline local surveillance systems (e.g. local hospital intranet systems) could be made compatible with the national data electronic registry platform. Database interoperability would provide the information necessary for actionable analytics, such as patient demographic information.

The national surveillance platform should provide timely reporting and allow hospitals to have real-time data on antimicrobial consumption, AMR, and infection prevention measures. This will also allow for benchmarking among hospitals and give the opportunity to evaluate and compare hospital data with other national hospitals.
Regarding the information collected, infection surveillance should be expanded to include, besides bloodstream infections and antimicrobials administered parenterally (e.g. intravenously), surgical site infections and ventilator-associated infections.

Incrementally, cloud-computed systems that can accommodate data from different platforms are being used in health-care data management as a means towards transactional scalability and universal access. The Ministry of Health is considering creating a hospital data cloud, a project that would provide solutions for data storage, protection from data loss, and access to big data, which would otherwise remain fragmented, stored in numerous inaccessible locations.

**EVIDENCE ON THE IMPACT OF OPTION 1**

Three systematic reviews reported that digital surveillance systems outperform manual ones in terms of utility, quality of collected data and time needed to detect nosocomial infections (29–31). This comes in line with the global challenge (32) to develop techniques that could provide accurate diagnostic information within a short time frame of clinical signs appearing, therefore allowing for more informed use of antimicrobial therapy at an early stage. Interconnected electronic databases for patient records, such as those using cloud computing, can reduce medical errors and allow data to be shared across multiple systems, which is lacking in many current health-care facilities in Greece (33). Such databases can also be developed for the surveillance of AMR and antimicrobial consumption within hospital settings.

A further systematic review (34) reported that electronic surveillance systems (ESSs) for nosocomial infections and antimicrobial use were associated with statistically significant reductions in the proportion of improper antimicrobial prescriptions, the cost of antimicrobials, the number of patients prescribed excessive antimicrobial dosages, adverse drug events, and length of stay (LoS), but not in mortality.

Another systematic review reported that few institutions or conventional public health surveillance systems include all types of infections, due to the costs of financial and human resources. As a result, the surveillance focuses on the most important infections, such as bloodstream ones, which is also the case in Greece’s surveillance system. An advantage of electronic surveillance is that, once the system is implemented, the size and comprehensiveness of surveillance is potentially independent of cost, as far as the electronic databases are concerned. Institution or regionwide surveillance is facilitated and may detect small outbreaks or those not included in the primary areas of interest. In addition, when the infection of interest is defined by the presence of a positive culture, electronic surveillance should have 100% sensitivity and may be higher than that of conventional surveillance, where errors may occur, especially when paper-based or passive reporting is used (31).

Regarding the operation of digital surveillance systems for inpatient antimicrobial use and AMR, individual data from each participating hospital can be centralized in electronic
platforms, analysed via specific algorithms, and the results produced may then be sent back to each hospital, via reports and alerts of potentially improper antimicrobial prescriptions (29). Antimicrobial resistance data-sharing with other national and regional institutions and linkage with a central reference laboratory for technical support should include individual as well as aggregate data in order to control for interhospital and interpatient variations (35). A summary of the key findings from the synthesized research evidence is provided in Table 1. A full description of the systematic reviews is presented in Appendix 1.

**TABLE 1. Summary of key findings from systematic reviews relevant to option 1 – Establish an interconnected electronic AMR surveillance system in hospitals**

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
</table>
| Benefits                  | - A systematic review of 110 studies found that using electronic surveillance systems could result in shorter times to detect targeted infectious diseases and improve data collection (29).  
- A systematic review found that electronic surveillance systems (ESSs) outperformed manual methods in monitoring and detecting HAIs where both methods were compared against a “gold standard”, and many methods detected HAIs with excellent sensitivity and specificity (30).  
- A systematic review found that electronic surveillance has moderate-to-excellent utility compared with conventional methods for detecting nosocomial infections (31).  
- A systematic review of high quality reported that electronic surveillance systems for nosocomial infections and antimicrobial use were associated with statistically significant reductions in the proportion of improper antimicrobial prescriptions, the cost of antimicrobials, the number of patients prescribed excessive antimicrobial dosages, adverse drug events, and length of stay, but not in mortality (34).  
- A systematic review found that electronic HAI detection systems use increasingly more electronic health records and patient data, as more data sources become available. As a result, systems tend to become more sensitive but less specific, though the increased availability allows systems to be tailored to the needs of health-care institutes’ surveillance programmes (36). |
| Potential harms           | - None found.                                                                                                                                                                                                |
| Resource use, costs and cost-effectiveness | - A systematic review reported that an electronic surveillance system could reduce the time taken to perform surveillance and improve timeliness and cost saving in reporting targeted infectious diseases (29). |
A systematic review reported that electronic surveillance of nosocomial infections is potentially inexpensive and efficient, as it utilizes data from existing databases after being collected for other laboratory, administrative or patient care purposes (31).

A systematic review reported that automated programmes for nosocomial infections reduced surveillance time by up to 61%. This may reduce cost and free up human resources from routine surveillance for proactive preventive efforts or outbreak investigation (31).

Driven by the increased availability of electronic patient data, electronic HAI surveillance systems use more data, making systems more sensitive although less specific (36).

Although electronic surveillance systems for nosocomial infections and antimicrobial use are associated with statistically significant reductions in the proportion of improper antimicrobial prescriptions, the cost of antimicrobials, the number of patients prescribed excessive antimicrobial dosages, adverse drug events and length of stay, there is little evidence of an effect on mortality (34).

According to the literature review, the surveillance systems for antimicrobial use and antimicrobial resistance in inpatient settings included the following components:

- collecting data: laboratory data were collected using electronic information technologies (such as WHONET), clinical data were uploaded in electronic databases or reported using web- or email- or mobile phone-based methods and pharmacy data were obtained via an electronic database (29);
- transmission, linkage and centralization of data: local data were submitted to the electronic databases of central offices via web-based methods, mobile phone applications, landline data transfers, and file transfer protocol (29);
- data analysis and reporting: some studies reported using specific software to capture abnormal activities of the targeted conditions, while others gave reports in the form of real-time early warnings. The reports and alerts of potentially improper antimicrobial prescriptions were sent either to the hospital’s pharmacy or the ID staff (29,34);
Table 1. contd

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(contd) Key elements of the policy option if</td>
<td>— follow up of index cases: GPS applications and records using mobile phones to capture the locations of index cases ( (29) );</td>
</tr>
<tr>
<td>tried elsewhere</td>
<td>— quality management system: a system that supervises the coordination and realization of quality objectives, which have been established ( (35) );</td>
</tr>
<tr>
<td></td>
<td>— data-sharing should be done with other national/regional institutions and linked with a national/central reference laboratory for technical support ( (35) );</td>
</tr>
<tr>
<td></td>
<td>— pathogens included in the system should be based on the local epidemiology and the major clinical impact attributable to a specific AMR profile. Data on ( Clostridioides difficile ) infections should also be included ( (35) );</td>
</tr>
<tr>
<td></td>
<td>— reporting frequency: annual reporting provides sufficient data to drive AMS, but in the presence of a new intervention or outbreak, a higher frequency might be considered ( (35) ).</td>
</tr>
</tbody>
</table>

| Stakeholders’ views and experiences           | ➤ During interviews with multiple stakeholders, the vast majority underlined the need for updating and digitalizing the existing HAI surveillance system of Greece, so that less time and effort are exerted on data entry and processing. |

**OPTION 2: Establish antimicrobial stewardship and infection prevention/control programmes in all hospitals**

**OVERVIEW AND CONTEXT**

The combination of high hospital consumption of advanced antimicrobials with a high prevalence of HAI supports the decision to focus on addressing AMR in the inpatient setting in Greece.

Despite existing comprehensive legislation for the management of the problem of AMR and HAI, implementation is hampered by difficulties in changing the organizational culture, a lack of administrative support, low acceptance among clinicians and limited resources \( (25) \).

HAI can be prevented with evidence-based practices, robust surveillance, essential infrastructure and human resources, and a change of culture at the institution, which effectively communicates the importance of IPC and patient safety \( (37) \). Considering the ways...
by which AMR occurs, there are two major areas of focus for the management, control and prevention of AMR (38).

- Judicious use of antimicrobials. This would include using them only when needed, using only the most appropriate agent for each infection and pathogen, and only at the correct dose and duration.
- Prevention of transmission of microorganisms, whether resistant or not; in the case of non-resistant microorganisms, the opportunity for development of resistance is lost.

AMS and IPC are evidence-informed approaches in the health-care setting.

**Antimicrobial stewardship programmes (ASPs)** entail monitoring and directing antimicrobial use at a health-care institution, thus providing a standard evidence-based approach to judicious antimicrobial use (39).

**Infection prevention and control (IPC)** is a practical, evidence-based approach, which prevents patients and health workers from being harmed by avoidable infection and by AMR (40).

AMS and infection control strategies exhibit synergistic effects when implemented concurrently (35,41–44). A joint 2018 policy paper (43) by the Association for Professionals in Infection Control and Epidemiology (APIC), the Society for Healthcare Epidemiology of America (SHEA), and the Society of Infectious Disease Pharmacists (SIDP) highlights the link between IPC and ASP and highly supports implementing them jointly and in collaboration. For example, combined IPC and ASP prevention bundles against *Clostridioides difficile* infection (CDI) resulted in a reduction of HAIs, given that ASP reduces antimicrobial drug consumption, which generates new CDI, while IPC practices prevent transmission of CDI (45,46).

According to the CDC, IPC and ASP in synergy resulted in an 18% reduction in the number of deaths caused by antimicrobial-resistant infections overall and by almost 30% in hospitals alone in the U.S. from 2013 to 2019, as a result of increased detection and surveillance capabilities, and action to rapidly identify, prevent transmission and innovate against resistance (10).

**Antimicrobial stewardship programmes (ASPs)** consist of coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents, including their choice, dosing, route and duration of administration (47,48). The benefits of such programmes include improved patient outcomes, reduced adverse events, including CDI, improvement in rates of antimicrobial susceptibility to targeted antimicrobials, and optimization of resource utilization across the continuum of care (49).

According to guidelines and recommendations from the EU, WHO and ECDC (32,50,51), AMS is an essential component of an integrated approach to health systems strengthening and should be universally implemented to ensure proper administration of antimicrobials. There are multiple interventions that can comprise an ASP, the ten most important of which are analysed in a practical guide published by WHO (52) and are briefly described below. A toolkit
THREE OPTIONS FOR ADDRESSING THE PROBLEM

Of interventions is described below, comprising interventions occurring prior to or at the time of prescription and those occurring after prescription. Each institution can select interventions adjusted to the local needs.

I. Interventions prior to or at the time of prescription

1. **Institution-specific guidelines for the management of common infections**: these include guidelines or algorithms specific for a certain institution, which can be adapted from national or international evidence-based guidelines to reflect local epidemiology, access to diagnostic testing and drug availability.

2. **Cumulative antibiograms**: reports that describe the proportion of isolates of a given microorganism that remains sensitive to recommended antimicrobial(s) based on in vitro susceptibility testing. They are useful in guiding empirical antimicrobial therapy.

3. **Pre-authorization of restricted antimicrobials**: clinicians obtain approval for the administration of specific antimicrobials before they are released from the pharmacy. Approval may be granted by AMS team members, pharmacists or infectious diseases physicians, including trainees.

4. **De-labelling of spurious antimicrobial allergies**: includes history-taking for dedicated antimicrobial allergy, with or without dedicated skin testing, to remove false antimicrobial allergy reports from patient records. It ensures that they do not receive overly broad antimicrobials or second-line therapies that are actually not necessary.

II. Interventions after prescription

1. **Prospective audit and feedback**: review of active antimicrobial use in individual patients and real-time recommendations for prescribers to optimize therapy.

2. **Self-directed antimicrobial reassessments by prescribing clinicians (antimicrobial time-outs)**: structured reminders or conversations that prompt clinicians to reassess an antimicrobial prescription.

3. **Antibiotic dose optimization**: individualized attention to patient characteristics that can influence the appropriate dose, interval and route of administration of an antimicrobial used in a given setting.

4. **Antibiotic duration**: selecting the appropriate duration of antimicrobial therapy.

Additional AMS interventions were identified during the literature search and are briefly described below:

- **Delayed prescriptions**: a prescription is issued by a health professional for use by the patient at a later date if their symptoms do not improve (26,53).

- **Formulary restrictions**: restricted dispensing of targeted antimicrobials on the hospital’s formulary, according to approved criteria. The use of restricted antimicrobials may be
limited to certain indications, prescribers, services, patient populations or a combination of these (54, 55).

- **Automatic stop orders**: automatically applied stop dates for antimicrobial orders when the duration of therapy is not specified. They can be individualized for specific antimicrobial classes, routes of administration and/or indications (55–57).

- **De-escalation of therapy**: the initial empirical antimicrobial(s) are stopped or reduced in number and/or narrowed in spectrum, based on microbiology results (58).

- **Therapeutic drug monitoring**: measurement of medication levels in blood (58).

- **Switch from intravenous to oral therapy** (58).

- **Bedside consultation**: visit by a health-care professional to an inpatient in another specialty for the purpose of consultation, treatment, counselling or advice (58).

Regarding the transmission of resistant pathogens within an inpatient setting and across different ones, it is common knowledge that infection prevention practices are necessary for controlling their spread. According to the *Global action plan on antimicrobial resistance* published by WHO, IPC programmes are a key strategy in containing AMR and preventing the spread of HAIs (59). Standard precautions, such as hand hygiene, use of protective equipment and respiratory hygiene/cough etiquette, should be followed for the care of all patients. Other types of precautions, such as contact, droplet and airborne precautions, should be implemented for the care of patients infected with drug-resistant pathogens.

According to WHO, the minimum requirement for IPC programmes in tertiary care includes at least one full-time trained IPC focal point (nurse or doctor) per 250 beds with dedicated time allocated (60). WHO has also published a practical manual for the implementation of effective IPC programmes (61). According to the manual, eight core components, including multimodal strategies, are necessary to improve IPC practices. These are as follows:

1. Introduction of an IPC programme with a dedicated, trained IPC team in each acute health-care facility
2. Development of IPC guidelines
3. IPC education and training
4. Data derived from HAI surveillance
5. Multimodal strategies
6. Monitoring/audit of IPC practices and feedback
7. Workload, staffing and bed occupancy
8. Built environment, materials and equipment for IPC.

**EVIDENCE ON THE IMPACT OF OPTION 2**

There is evidence that the implementation of ASPs in inpatient settings is associated with improved patient care and antimicrobial prescribing, reduced hospital costs and reduced
rates of AMR. A high-quality systematic review that included 221 studies (55), one of which was conducted in Greece, examined the effects of different inpatient AMS interventions and investigated the effect of two categories of interventions: restrictive (such as selective reporting of laboratory susceptibilities, formulary restrictions, expert approval prior to prescription and automatic stop orders) and enabling (such as audits and feedback, educational outreach through review of individual patients with recommendation for change, and circumstantial reminders targeted at doctors managing specific patients). Reminders in the form of posters or pocket cards summarizing antimicrobial policies were classified as environmental restructuring interventions. Other interventions were classified as structural and included: changing the records from paper to computerized forms and introducing new technologies for rapid microbiology testing or measurement of inflammatory markers. This systematic review found that the interventions contributed to improvements in prescribing practices and reduction in the length of stay and the duration of antimicrobial treatment, while the risk of death was similar between the intervention and control groups. Both enablement and restriction were independently associated with increased compliance with antimicrobial policies, and enablement enhanced the effect of restrictive interventions. Interventions were also effective in increasing compliance with prescribing guidelines, which reduces unnecessary treatment without increasing the risk of mortality (55).

A systematic review of high quality showed that AMS objectives, including the use of empirical therapy according to guidelines, de-escalation of therapy, a switch from intravenous to oral therapy, therapeutic drug monitoring, use of a list of restricted antimicrobials, and bedside consultation can lead to significant benefits for clinical outcomes, adverse events and hospital costs. Moreover, treatment according to guidelines and de-escalation of therapy had significant effects on reduction in mortality (58). Another systematic review on long-term care facilities reported that AMS strategies (mainly educational materials, educational meetings and guideline implementation) were associated with a 14% reduction in overall antimicrobial use (62).

Multiple systematic reviews reported that ASPs in inpatient settings substantially improve patient outcomes, including mortality, length of stay and readmission, and decrease colonization with MDR pathogens and the incidence of CDIs (63,64). The reduction in length of stay is not only beneficial for the patients themselves, but also for the health-care system, as it substantially decreases hospital expenditure and leads to cost savings (65). This is particularly important for the health-care system in Greece, which currently faces major financial challenges.

ASPs can be implemented in hospital settings with limited resources. A systematic review of medium quality regarding the introduction of such programmes in African countries reported that the interventions were associated with improved compliance with antimicrobial guidelines, appropriateness of prescribing, reduction in antimicrobial use and cost savings (66).

A systematic review of high quality found that multimodal infection prevention measures, surveillance, monitoring and feedback are the most effective interventions for reducing the
rates of HAIs (67). Another review of IPC programmes in long-term care facilities reported that behavioural change strategies using education, monitoring and feedback were successful in reducing the threat of HAIs, while the use of four or more elements of the WHO manual led to significant reductions in infection rates (68).

A summary of the key findings from the synthesized research evidence is provided in Table 2. A full description of the systematic reviews is presented in Appendix 2.

**TABLE 2. Summary of key findings from systematic reviews relevant to option 2 – Establish antimicrobial stewardship and infection prevention/control programmes in all hospitals**

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
</table>
| Benefits | - A systematic review of high quality reported that ASP practices (enabling and restrictive practices, as described above) are effective in increasing compliance with antimicrobial policy and reducing the duration of antimicrobial treatment. Lower use of antimicrobials probably does not increase mortality and likely reduces the length of stay. Enabling strategies consistently increase the effect of interventions, including those with a restrictive component (55).

- A systematic review of high quality revealed that the use of empirical therapy according to guidelines, de-escalation of therapy, switch from intravenous to oral therapy, therapeutic drug monitoring, the use of a list of restricted antimicrobials and bedside consultation (especially for *S. aureus* bacteraemia) can lead to significant benefits for clinical outcomes, adverse events and costs, although the quality of studies was generally low. Treatment according to guidelines and de-escalation of therapy had significant effects on mortality, although heterogeneity between studies was substantial (58).

- A systematic review of medium quality reported that AMS strategies, mainly educational materials, educational meetings and guideline implementation, were associated with a 14% reduction in overall antimicrobial use among different long-term care facilities (62).

- A systematic review showed that some types of ASP interventions (e.g. audit and feedback, guideline implementation and decision support) substantially improve patient outcomes, including mortality, length of stay, readmission or incidence of CDI. Most interventions were associated with improved prescribing patterns, as measured by decreased antimicrobial use or increased appropriate use. ASPs were generally associated with improvements in microbial outcomes, including institutional resistance patterns or resistance in the study population (63).
Table 2. contd

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
</table>
| (contd) Benefits | - A high-quality systematic review concluded that hospital-based ASPs result in significant decreases in antimicrobial consumption and costs, the benefit being higher in the critical care setting. Infections due to specific antimicrobial-resistant pathogens and the overall hospital length of stay improved as well (69).  
- A systematic review of medium quality reported that ASPs in African countries were associated with improved compliance with antimicrobial guidelines, appropriateness of prescribing, reduction in antimicrobial use and cost savings (66).  
- A systematic review concluded that ASPs reduced the incidence of infections and colonization with MDR Gram-negative bacteria, extended-spectrum ß-lactamase-producing Gram-negative bacteria, and methicillin-resistant *Staphylococcus aureus*, as well as the incidence of CDIs. It is notable that these programmes were more effective when implemented along with infection control measures, especially hand-hygiene interventions (64).  
- A systematic review of high quality reported that multimodal infection control practices, including surveillance, monitoring and feedback, had the greatest effectiveness in reducing hospital-acquired infections (67).  
- A systematic review regarding the benefits of IPC programmes in long-term care facilities found that behavioural change strategies using education, monitoring and feedback were successful in reducing the threat of HAIs. Studies using four or more elements of the WHO multimodal strategy reported significant reductions in infection rates (68). |
| Potential harms | - A systematic review raised concerns that the restrictive interventions of an ASP may lead to delay in treatment and a negative professional culture, because of breakdown in communication and trust between infection specialists and clinical teams. However, the evidence is of low certainty (55).  
- No study reported potential harms due to the implementation of IPC programmes in inpatient settings. |
| Resource use, costs and cost-effectiveness | - A systematic review of 146 studies reported that ASPs are associated with a decrease in length of stay (LoS) by 85% and antimicrobial expenditures by 92%. The average cost savings reported in the studies conducted in the US were US$ 732 per patient and similar trends were exhibited in European studies. The key driver of cost savings was from reduction in LoS (65). |
According to a high-quality systematic review, the implementation of ASPs reduced the overall antimicrobial costs by 33.9% (69).

A systematic review about the economic outcomes of four clinical best care practices (CBPs), including hand hygiene, hygiene and sanitation of surfaces, screening upon admission for carriage, and other basic and additional precautions, found that all were cost effective. The average yearly net cost savings from the CBPs ranged from CA$ 252,847 to CA$ 1,691,823, depending on the rate of discount (3% and 8%). The average incremental benefit–cost ratio of CBPs varied from 2.48 to 7.66 (70).

One systematic review of high quality involving 37 studies reported that reduced AMR over the long run is not testable within the limited time frame of most studies regarding the impacts of ASPs (63).

According to multiple systematic reviews, the following AMS interventions have been implemented in conjunction:

- use of empirical therapy according to guidelines (58)
- de-escalation of therapy (58)
- switch from intravenous to oral therapy (58)
- therapeutic drug monitoring (58)
- list of restricted antimicrobials (58)
- bedside consultation (58)
- educational materials and educational meetings (62).

A high-quality systematic review (55) included 221 studies, with a variety of different types of ASP interventions that are described below:

Educational:
- educational meetings
- dissemination of educational materials
- educational outreach

Persuasive:
- educational outreach by academia and recommendations for change

Restrictive:
- selective reporting of laboratory susceptibilities
- compulsory order forms
- formulary restrictions
- expert approval prior to prescription
- automatic stop orders

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resource use, costs and cost-effectiveness</td>
<td>➤ According to a high-quality systematic review, the implementation of ASPs reduced the overall antimicrobial costs by 33.9% (69).</td>
</tr>
<tr>
<td></td>
<td>➤ A systematic review about the economic outcomes of four clinical best care practices (CBPs), including hand hygiene, hygiene and sanitation of surfaces, screening upon admission for carriage, and other basic and additional precautions, found that all were cost effective. The average yearly net cost savings from the CBPs ranged from CA$ 252,847 to CA$ 1,691,823, depending on the rate of discount (3% and 8%). The average incremental benefit–cost ratio of CBPs varied from 2.48 to 7.66 (70).</td>
</tr>
<tr>
<td>Uncertainty regarding benefits and potential harms</td>
<td>➤ One systematic review of high quality involving 37 studies reported that reduced AMR over the long run is not testable within the limited time frame of most studies regarding the impacts of ASPs (63).</td>
</tr>
<tr>
<td>Key elements of the policy option if tried elsewhere</td>
<td>➤ According to multiple systematic reviews, the following AMS interventions have been implemented in conjunction:</td>
</tr>
<tr>
<td></td>
<td>➤ A high-quality systematic review (55) included 221 studies, with a variety of different types of ASP interventions that are described below:</td>
</tr>
<tr>
<td></td>
<td>Educational:</td>
</tr>
<tr>
<td></td>
<td>➤ educational meetings</td>
</tr>
<tr>
<td></td>
<td>➤ dissemination of educational materials</td>
</tr>
<tr>
<td></td>
<td>➤ educational outreach</td>
</tr>
<tr>
<td></td>
<td>Persuasive:</td>
</tr>
<tr>
<td></td>
<td>➤ educational outreach by academia and recommendations for change</td>
</tr>
<tr>
<td></td>
<td>Restrictive:</td>
</tr>
<tr>
<td></td>
<td>➤ selective reporting of laboratory susceptibilities</td>
</tr>
<tr>
<td></td>
<td>➤ compulsory order forms</td>
</tr>
<tr>
<td></td>
<td>➤ formulary restrictions</td>
</tr>
<tr>
<td></td>
<td>➤ expert approval prior to prescription</td>
</tr>
<tr>
<td></td>
<td>➤ automatic stop orders</td>
</tr>
</tbody>
</table>
Table 2. contd

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
</table>
| (contd) Key elements of the policy option if tried elsewhere | Structural:  
— reminders (physical) such as posters, pocket-size or credit card-size summaries or on laboratory test reports  
— new laboratory tests or rapid reporting of results  
Enabling:  
— audit and feedback  
— decision support through computerized systems or through circumstantial reminders, triggered by actions or events related to the targeted behaviour  
— educational outreach by review and recommend change |

According to a systematic review regarding clinical practice guidelines for creating an acute care hospital-based ASP, prior authorization and/or restriction policies should be considered essential for the development of an effective hospital-based ASP (71).

According to interviews conducted with ID specialists from 10 tertiary-care hospitals across the country, the implementation of both AMS and infection control programmes in each inpatient setting is considered necessary for reducing AMR in Greece.

**OPTION 3: Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting**

**OVERVIEW AND CONTEXT**

Education is a prerequisite for knowledge; therefore, educating health-care workers about prudent antimicrobial use and infection control practices should be one of the main elements of a national plan for reducing the levels of AMR and slowing its development.

According to the core competencies for IPC professionals published by WHO (72), education and training on IPC should be promoted both at the national and the facility levels. At the national level, a policy that all health-care workers should be trained in IPC should be accompanied by an approved IPC curriculum aligned with national guidelines. At the facility level, IPC education should be in place for all health-care workers, by using team- and task-based strategies that
are participatory and include bedside and simulation training to reduce the risk of HAIs and AMR. This can be done by providing training to all front-line clinical and cleaning staff upon employment on the facility IPC guidelines and standard operating procedures.

Option 3 is directly linked to option 2, as the development of both multidisciplinary programmes on AMS and infection control require proper training of health-care workers for them to have the skills needed for the successful implementation of the adopted measures.

**Evidence on the Impact of Option 3**

Most systematic reviews concluded that educational programmes should be multifaceted, combining both active and passive learning strategies. For example, training of physicians within small groups, implementation of interactive workshops regarding prudent antimicrobial prescribing and development of treatment algorithms (73–75), along with provision of audits and feedback on prescribing behaviour (76) proved effective in reducing the number of antimicrobials prescribed in the health-care facilities in which they were implemented. The education provided to prescribers should not only include general rules regarding antimicrobial use, but also incorporate online educational elements and information about local dispensing and resistance data (77), so that they are in concordance with the levels of AMR in Greece specifically.

As far as physicians are concerned, special attention should be given to new prescribers, because as they are less confident about their decisions regarding the medications prescribed, they might overprescribe (78). Moreover, registered nurses should also receive training regarding proper antimicrobial administration (74), as they play a major role in patient care.

Regarding IPC, multiple systematic reviews (79–81) reported that the systematic application of educational interventions targeting health-care personnel can increase their adherence to standard precautions for the control of HAIs and thus decrease their prevalence. Health-care workers have pointed out the lack of training they receive about how to use PPE properly, and find it problematic when training is not mandatory or does not include all hospital staff, such as the cleaning and kitchen staff (82). Therefore, mandatory training programmes on proper IPC practices should be incorporated into the curriculum of all health-care workers and supporting staff, not only medical and nursing staff.

A summary of the key findings from the synthesized research evidence is provided in Table 3. A full description of the systematic reviews is presented in Appendix 3.
TABLE 3. Summary of key findings from systematic reviews relevant to option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefits</td>
<td>▶ A systematic review of high quality (based on AMSTAR score) reported that physician education resulted in significant reductions in antimicrobial use (83).</td>
</tr>
<tr>
<td></td>
<td>▶ A systematic review suggested that active clinician education is more effective than purely passive education in reducing unnecessary prescriptions (73).</td>
</tr>
<tr>
<td></td>
<td>▶ A systematic review of high quality showed that a multifaceted intervention involving small group educational sessions and the provision of educational materials is generally acceptable to nurses and physicians in long-term care facilities and is associated with improvement of the appropriateness of antimicrobial prescribing (74).</td>
</tr>
<tr>
<td></td>
<td>▶ A systematic review found that antimicrobial prescription was reduced by 34.1% in a group of clinicians attending educational programmes concerning prudent antimicrobial use compared to controls. The number of inappropriate antimicrobial prescriptions was also reduced by 41% on average in the intervention group than in the control group (75).</td>
</tr>
<tr>
<td></td>
<td>▶ A systematic review of medium quality reported that clinician education about prudent prescribing of recommended antimicrobials for acute outpatient infections, alone or in combination with audit and feedback, resulted in improved antimicrobial prescribing by a median of 10.6% (76).</td>
</tr>
<tr>
<td></td>
<td>▶ A systematic review regarding factors that influence antimicrobial prescribing for uncomplicated acute respiratory tract infections in adult patients at the emergency department found that patients who visited an ED that provided education to health-care providers on the use of antimicrobials were less likely to receive antimicrobials (84).</td>
</tr>
<tr>
<td></td>
<td>▶ A systematic review of 39 studies regarding interventions to reduce antimicrobial prescribing in ambulatory care reported that multifaceted interventions combining physician, patient and public education in a variety of venues and formats were the most successful in reducing antimicrobial prescribing for inappropriate indications. One of the included studies demonstrated a sustained reduction in the incidence of antimicrobial-resistant bacteria associated with these interventions (85).</td>
</tr>
</tbody>
</table>
Table 3. contd

<table>
<thead>
<tr>
<th>Category</th>
<th>Key findings</th>
</tr>
</thead>
</table>
| (contd) Benefits | - A systematic review of medium quality reported that the systematic application of educational interventions targeting health-care personnel can decrease the rates of health-care-associated infections (HAIs). The beneficial effect of education was apparent in teaching and nonteaching institutions and in lesser-developed countries and developed nations (79).  
- A systematic review found that educational programmes for health-care workers improve their adherence to standard precautions for the control of HAIs (80). |
| Potential harms | - No systematic review provided information about harms or missed opportunity costs arising from educational interventions regarding prudent antimicrobial prescribing among health-care workers. |
| Resource use, costs and cost-effectiveness | - A systematic review reported that providing health-care workers with an educational meeting regarding proper antimicrobial use appeared to be more effective than audit/feedback but, on the other hand, was more labour intensive (83). |
| Uncertainty regarding benefits and potential harms | - A systematic review suggested that the effectiveness of educating clinicians, without combining it with other strategies, remains controversial, because several studies have shown no significant effect on the numbers of antimicrobial prescriptions after their education (75).  
- A systematic review of high quality assessed the effectiveness of IPC strategies in preventing transmission of methicillin-resistant S. aureus (MRSA) in nursing homes for older people. Intervention homes received detailed information on their baseline infection control scores via a written report and verbal feedback. Training on infection control, hand hygiene and decontamination of equipment/environment was also provided, and audits were given at specified time intervals. Although there was no change in MRSA prevalence between intervention and control sites, mean infection control audit scores were significantly higher in the intervention homes compared with control homes (81). |
| Key elements of the policy option if tried elsewhere | - Trials using active clinician education (e.g. workshops, meetings, etc.) demonstrated a trend towards greater effectiveness in reducing inappropriate antimicrobial prescribing than trials using only passive education techniques (73).  
- Interactive educational workshops and the introduction of specific treatment algorithms, which are reinforced by a local opinion leader, may produce the most effective changes in antimicrobial prescribing in long-term care facilities (74). |
Regarding the different types of interventions, education of physicians within small groups seems to be most often effective in reducing antimicrobial use (75).

According to a randomized controlled trial, a multifaceted educational programme managed to reduce antimicrobial prescription at the practice level in primary care and included the following components: a practice-based seminar reflecting on the practices’ own dispensing and resistance data, several online educational elements, and facilitator-based practice of consulting skills in routine care (77).

According to the literature, educational programmes about proper IPC practices in inpatient settings included the following interventions:
- Lectures (79)
- Classes (79)
- Video presentations (79)
- Posters (79)
- Questionnaires and fact sheets (79)
- Practical demonstrations (79, 81)
- Self-study modules with pretests and post-tests (79)
- Direct feedback (79, 81)
- Checklists and coloured cues (80)
- Infection control audits (81)

Active educational programmes (e.g. workshops) are more effective than passive ones (e.g. lectures). IPC training programmes involved the most common infections in inpatient settings, such as catheter-related bloodstream infections, catheter-associated urinary tract infections and ventilator-associated pneumonias. Promotion of hand hygiene was also an integral part of these programmes, while the control of MRSA spread was also attempted in some studies (79, 81).

Key informant interviews stressed that educational programmes regarding prudent antimicrobial use in the health-care setting should be of high quality and adjusted to the needs and level of knowledge of different health-care professionals. They also highlighted the need for ongoing education, with the focus on new prescribers.
IMPLEMENTATION CONSIDERATIONS

Potential barriers

**OPTION 1: Establish an interconnected electronic AMR surveillance system in hospitals**

For the national surveillance system of inpatient antimicrobial consumption and AMR to be digitized, an electronic database has to be developed first. This requires high investment in hardware (e.g. computers and other electronic devices), accompanied by sophisticated computer programs and special software (29). Currently, the majority of Greek hospitals, especially the ones not located in the capital, have outdated computer devices that may be unable to support the software needed for digitalization of the surveillance system. Therefore, hospitals should be provided with new electronic equipment and IT specialists employed to develop the database. This process requires extra funding, which may be a limitation to the implementation of the updated surveillance system (86), especially now that the Greek health system is devastated by the ongoing COVID-19 pandemic.

Regarding the uploading of data to the database, health-care workers have to familiarize themselves with the new material and acquire knowledge about common terminology, standardized methods, and corresponding data structures (87). A large number of infection prevention professionals have limited knowledge about IT (87) and, as a result, their workflow may be impeded by the combination of patient care with data entry (34). Some health-care professionals, especially older ones, report negative emotions of anxiety and concern while using technology (88), which can also impede the integration of digital means to everyday practice.

In addition, cyber security issues and challenges regarding the protection of patient data have to be addressed. The health-care industry is a prime target for medical information theft, as it lags behind other leading industries in securing vital data (89); therefore, confidentiality of patient information should be ensured during the development of digital surveillance. If cloud services are used for data storage and transfer, data can be bound by more than one law at the same time and each law may impose different requirements and consequences (33); therefore, legal issues should be addressed prior to introducing digitized surveillance in hospitals.

**OPTION 2: Establish antibiotic stewardship and infection prevention/control programmes in all hospitals**

Each hospital is legally bound to operate a Committee for the Monitoring of the Consumption and Proper Use of Antibiotics. Given that Greek hospitals are currently understaffed, ID specialists and clinicians are unable to allocate dedicated time for the Committee. As a result, it is perceived as an additional burden on an already overwhelming schedule. Furthermore,
the Committee has no executive role in discontinuing unnecessary antimicrobials or modifying the treatment in concordance with the guidelines. For this reason, it is considered by a lot of physicians as bureaucratic work with little actual clinical impact.

In addition, many prescribers are unaware of the magnitude of AMR, therefore do not understand the necessity of an ASP. Such a programme that controls the administration of antimicrobials and ensures compliance with guidelines may be regarded as a limitation to physicians’ clinical freedom (85) and can also create a negative professional culture between ID specialists and other physicians (55). At an administrative level, many jurisdictions still do not acknowledge the threat of AMR and prioritize other health-care demands, especially in the face of the ongoing COVID-19 pandemic.

Literature research provides further insight on potential barriers to the adherence of health-care workers to IPC practices and guidelines. According to a systematic review of high quality (82), health-care workers reported that rapidly changing local guidelines, lack of training regarding IPC practices and use of PPE, and lack of isolation rooms, all contribute to poor implementation of IPC guidelines, and the latter two are observed in Greece, too. They also pointed out that patients sometimes feel isolated and stigmatized by the use of PPE, therefore physicians and nurses may find it difficult to use in such cases. Health-care workers reported that they followed IPC guidance more closely when they saw its value, while the workplace culture also influences compliance with IPC guidelines.

**OPTION 3: Implementation of postgraduate educational programmes for health-care workers on prudent antibiotic use and infection control in the hospital setting**

Educating health-care workers about prudent antimicrobial use and infection control is a task that can face a number of challenges during its implementation. As far as attending physicians are concerned, they have already established their knowledge about antimicrobial administration and have deeply rooted beliefs regarding patient care, therefore changing them may be challenging (75). Regarding resident physicians, they tend to follow their attendings’ guidance and, because education is not a restrictive measure itself, they may not change their prescribing behaviour unless the guidance provided to them changes.

Apart from the above, organizing interactive workshops and lectures is labour intensive and requires a substantial amount of time (83). Moreover, these interventions need to be repeated on a regular basis for their results to be sustained and for them to be available to new health-care workers. The National Health System of Greece is currently understaffed, and physicians have no allocated time specifically for participation in educational seminars; therefore, the introduction of mandatory courses on prudent antimicrobial use and infection control may not be prioritized. Given that the implementation of such courses comes with extra costs, it may add to the financial burdens of the national health system.

The potential barriers for all options are summarized in Table 4.
TABLE 4: Potential barriers to implementing the proposed options

<table>
<thead>
<tr>
<th>Level</th>
<th>Option 1 – Establish an interconnected electronic AMR surveillance system in hospitals</th>
<th>Option 2 – Establish antimicrobial stewardship and infection prevention/control programmes in all hospitals</th>
<th>Option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipients of care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knowledge and skills</td>
<td>From patients’ perspective, no barrier to the implementation of an electronic surveillance system was found regarding aggregated antimicrobial consumption and resistance data.</td>
<td>Information directed to patients regarding the need for reduction in antimicrobial use and for the implementation of IPC guidelines is currently lacking (key informant interviews).</td>
<td>Patients generally consider antimicrobials to be necessary for treating all types of infections, therefore denying access to them may be considered as inadequate care (key informant interviews).</td>
</tr>
<tr>
<td>Attitudes regarding programme acceptability, appropriateness and credibility</td>
<td>As above</td>
<td>Some patients feel isolated, frightened or stigmatized when health-care workers use masks and other PPE (82).</td>
<td>In one study, doctors used delayed prescriptions to reduce antimicrobial use. Fewer patients in the delayed group reported to be ‘very satisfied’ with the quality of care provided than patients receiving standard care (26).</td>
</tr>
<tr>
<td>Motivation to change or adopt new behaviour</td>
<td>As above</td>
<td>A lot of patients have established, hard-to-change beliefs about the necessity of antimicrobials (key informant interviews).</td>
<td>There may be a lack of willingness to comply with the doctors’ orders, as they may be considered inappropriate (key informant interviews).</td>
</tr>
<tr>
<td>Providers of care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knowledge and skills</td>
<td>Doctors are increasingly being asked to incorporate new IT systems into their work, with little assessment of system usability or ways in which these systems may adversely impact their workflow or efficiency (34). Automation is complicated by limited access to the required clinical data and insufficient knowledge of automation within infection control specialists (87). Some health-care professionals reported negative emotions of anxiety while using technology (88).</td>
<td>Physicians want to prescribe what they think are the best medications for individual patients, which often means a broad-spectrum agent to protect against potentially resistant organisms, regardless of the ecological consequences (85). Barriers to physician adherence to practice guidelines include the lack of familiarity with the guidelines, which correlate with the volume of information, the time needed to stay informed and guideline accessibility (90). IPC strategies increase workload and fatigue of health-care workers (82).</td>
<td>Because medical professionals and adults have already established their knowledge, attitudes, and behaviours about antimicrobial use, it is difficult to change their deeply established views and behaviours (75). Studies have found that new prescribers may not be confident or even competent when prescribing, both by their own assessment and that of their supervisors (78).</td>
</tr>
<tr>
<td>Attitudes regarding programme acceptability, appropriateness and credibility</td>
<td>A misunderstanding of the technology’s purpose and feelings of difficulty and/or being uncomfortable are prejudices that may reportedly impede technology usage (88).</td>
<td>Physicians may consider prescribing recommendations a limitation to their clinical freedom (85). Restrictive interventions of ASPs may lead to delay in treatment and negative professional culture because of breakdown in communication and trust between infection specialists and clinical teams (low-quality evidence) (53).</td>
<td>Human behaviours are affected by attitudes and beliefs; therefore, close collaboration with behavioural and social scientists is required when developing an educational intervention programme (72).</td>
</tr>
</tbody>
</table>
### Level

| Option 1 – Establish an interconnected electronic AMR surveillance system in hospitals | Option 2 – Establish antimicrobial stewardship and infection prevention/ control programmes in all hospitals | Option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting |

### (contd) Attitudes regarding programme acceptability, appropriateness and credibility

| Resistance to change and older age negatively influence the degree of technology usage [88]. | ASPs, especially centrally planned ones, may include components of low relevance or low applicability for hospitals of different sizes or different specialist units (stakeholder interviews). | As human behaviours change over time, the educational messages must be repeated routinely [75]. Recommending an alternate behaviour using educational materials may not provide the physician with the tools to change a behaviour that is likely to be ingrained and multifactorial in origin [85]. |

### Motivation to change or adopt new behaviour

| Resistance to change and older age negatively influence the degree of technology usage [88]. | Inability to reconcile patient preferences with guideline recommendations, lack of outcome expectancy, lack of self-efficacy and inertia of previous practice, can all stand in the way of physicians following guidelines of care [90]. | As human behaviours change over time, the educational messages must be repeated routinely [75]. Recommending an alternate behaviour using educational materials may not provide the physician with the tools to change a behaviour that is likely to be ingrained and multifactorial in origin [85]. |

### Other stakeholders (including other health-care providers, community health committees, community leaders, programme managers, donors, policy-makers and opinion leaders)

| Knowledge and skills | If a cloud service provider (CSP) closes business, organizations may have to transfer services to a different CSP or move back to an in-house IT environment. Significant data transfer challenges can be faced during such incidents [33]. | There may be apathy towards the increasing threat of AMR, with many jurisdictions not prioritizing its minimization, when there are many other health-care demands requiring resources [71]. Health-care workers’ response to IPC guidelines is influenced by the level of support they feel that they receive from their management team, which may not be adequate [82]. Donors financing such educational programmes may be unfamiliar with the actual benefits for the health-care system that arise from their implementation (key informant interviews). |

| Attitudes regarding programme acceptability, appropriateness and credibility | During the implementation of electronic surveillance systems, difficulties can be faced in accessing and using data, as the data keepers may consider themselves to be data ‘owners’ and allowing a third party direct access to computer servers may be perceived as compromising data-keeper responsibilities [91]. | Providers frequently lack a thorough understanding of hospital cost structures. In most organizations, the large majority of costs in a hospital are fixed and cannot be reduced by shortening lengths of stay, reducing readmissions, etc. An ASP business plan will be interpreted as naive if the proposal calculates societal cost savings by reducing lengths of stay and claims it will thereby reduce hospital costs [92]. Stakeholders may expect quick results from these educational programmes; however, physicians’ habits take time to change and AMR takes time to improve (key informant interviews). |

| Motivation to change or adopt new behaviour | The risk of sensitive patient data being compromised is considered a reason behind slow adoption of cloud applications [33]. | An ASP business plan is not going to be funded just because it is important; an ASP will be funded if such funding does not harm existing operations that are equally, or more, important to the financial and operational stability of the health-care system [92]. The establishment of educational programmes targeting health-care providers requires additional time and effort (key informant interviews). |
### Health system constraints

<table>
<thead>
<tr>
<th>Level</th>
<th>Option 1 – Establish an interconnected electronic AMR surveillance system in hospitals</th>
<th>Option 2 – Establish antimicrobial stewardship and infection prevention/ control programmes in all hospitals</th>
<th>Option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection control in the hospital setting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Using an electronic database requires high investment in hardware (e.g. computers, mobile phones, other electronic devices), sophisticated computer programs and software, and well-trained personnel (29). Logistic barriers (e.g. geographical spread of hospitals) can affect communication and reporting by limiting access to laboratory services (35). Low-/middle-income countries (LMICs) are often characterized by small-scale laboratories, lack of appropriate training and absence of laboratory information systems (35). The lack of availability of clinical data in an electronic format can reduce the ability of electronic methods to detect HAIs (30). Cyber security issues should be taken into account when implementing an electronic surveillance platform, as the health-care industry lags behind other leading industries in securing vital data and therefore is a prime target for medical information theft (89).</td>
<td>Funding can be a major issue in many centres and a barrier to the implementation of ASPs (71). A lack of training about the infection itself and about how to use PPE may interfere with health-care workers’ compliance with IPC guidelines (82). A lack of isolation rooms and PPE of high quality contribute to poor implementation of IPC practices (82).</td>
<td>Educational meetings appeared to be more effective than audit/feedback and written patient information but, on the other hand, were more labour intensive (83).</td>
</tr>
<tr>
<td></td>
<td>Social and political constraints</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Legislation or regulations, corruption, political stability and technical capacities</td>
<td>The health-care industry is a prime target for medical information theft, as it lags behind other leading industries in securing vital data (89). As far as cloud services are concerned, data can be bound by more than one law at the same time and each law may impose different requirements and consequences (33).</td>
<td>Frequent changes in the leading positions at the hospital and ministry levels result in the development of new policies that may threaten the continuation of existing ones (key informant interviews).</td>
</tr>
</tbody>
</table>
Potential opportunities

To overcome the barriers mentioned above, a number of measures can be taken both at the hospital and the national level. The suggestions for each of the three options are listed below.

**OPTION 1: Establish an interconnected electronic AMR surveillance system in hospitals**

- The introduction of IT solutions in hospital settings should be accompanied by educational programmes for health-care workers on how to use the new technology. It is important to give health-care professionals sufficient time and resources to adapt to new technologies. Moreover, learning to use new devices should be integrated into their daily work, and managers should place emphasis on how the technologies can improve daily clinical practices. Regular educational updates, which take into account variations in competencies in digitalization among health-care professionals, should be organized.

- If cloud services are introduced, an integrated model to manage risks has been proposed by Ali, Warren, and Mathiassen. This model outlines three types of risks (services, technology and process-related risks) and four types of resolution (stakeholder engagement, technology development, innovation planning and control). Using this model, managers can profile their risk scenarios and possible responses to take advantage of innovation derived from cloud services.

- Legislation in Greece should be updated, so that electronic patient data are protected from unauthorized access. Any changes made should follow the General Data Protection Regulation (GDPR) introduced by the EU in 2016.

**OPTION 2: Establish antibiotic stewardship and infection prevention/control programmes in all hospitals**

- All hospitals should be staffed with the health-care workers needed for an ASP and an infection control committee, such as ID specialists, clinical pharmacists and IC nurses.

- Health-care workers who take part in such programmes should have dedicated time for its implementation and be exempted from other duties during this time.

- A training programme explaining the interventions introduced into each hospital setting should be included in the induction course of all new residents, so that they are familiar with the fundamentals of AMS and infection control and can clarify any existing misconceptions.

- The financial benefits of ASPs and IPC programmes should be thoroughly explained to the administration of the hospitals to ensure that they are adequately funded.

- Involving representatives of relevant clinical services in the development and implementation of evidence-based guidelines, providing opportunity for iterative feedback, and adding audits or continuous quality improvement cycles could all improve adherence to treatment guidelines. Understanding the local prescribing culture, fostering an environment...
of appropriate prescribing, and increasing collaboration between ID physicians and pharmacists are also suggested (63).

- Minimizing overcrowding, fast-tracking infected patients, restricting visitors, and providing easy access to handwashing facilities can all help health-care workers adhere better to IPC guidelines (82).

- The inclusion of all staff, including cleaning staff, porters, kitchen staff and other support staff when implementing IPC guidelines, is very important for the proper implementation of infection control strategies (82).

**OPTION 3: Implementation of postgraduate educational programmes for health-care workers on prudent antibiotic use and infection control in the hospital setting**

- At the national level, legislative modifications regarding the education of medical residents can be made. In Greece, there is currently no uniform core body of knowledge for residency programmes across the country. Therefore, introducing core competencies on infection control and antimicrobial use in clinical medical specialty training would ensure that new prescribers are familiar with the problem of AMR and the ways to administer antimicrobials judiciously.

- Regarding practising physicians, incentives could be given for their participation in relevant educational courses, such as continuing medical education/continuing professional development (CME/CPD) credits or other form of certification.

- Time should be allocated for these educational programmes, with doctors receiving days off during the days they participate in the courses.
REFERENCES


47. Society for Healthcare Epidemiology of America; Infectious Diseases Society of America; Pediatric Infectious Diseases Society. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS). Infect Control Hosp Epidemiol. 2012;33:322–7. doi: 10.1086/665010.


APPENDICES AND ANNEXES

The following tables provide detailed information about the systematic reviews identified for each option. Each row in a table corresponds to a particular systematic review. The focus of the review is described in the second column. Key findings from the review that relate to the option are listed in the third column while the fourth column records the last year the literature was searched as part of the review, and the fifth column a rating of the overall quality of the review.

The quality of each review has been assessed using AMSTAR (A MeaSurement Tool to Assess Reviews), which rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to delivery, financial, or governance arrangements within health systems. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e. the numerator and denominator) in mind. For example, a review that scores 8/8 is generally of comparable quality to a review scoring 11/11; both ratings are considered “high scores.” A high score signals that readers of the review can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the review should be discarded, merely that less confidence can be placed in its findings and that the review needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. Health Res Policy Syst; in press).

All of the information provided in the appendix tables was taken into account by the EBP’s authors in compiling Tables 1–3 in the main text of the EBP.
### Option element

<table>
<thead>
<tr>
<th>Focus of systematic review</th>
<th>Key findings</th>
<th>Year of last search</th>
<th>AMSTAR or SURE checklist (quality) rating</th>
<th>Proportion of studies conducted in Greece</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rattanaumpawan P, Boonyasiri A, Vong S, Thamlikitkul V.</strong> Systematic review of electronic surveillance of infectious diseases with emphasis on antimicrobial resistance surveillance in resource-limited settings. Am J Infect Control. 2018 Feb;46(2):139–46.</td>
<td>Electronic surveillance of infectious diseases</td>
<td>Information technologies can be used to facilitate the process of obtaining laboratory, clinical, and pharmacological data for the surveillance of infectious diseases, including antimicrobial-resistant (AMR) infections. Using electronic surveillance systems could result in shorter times to detect targeted infectious diseases and improve data collection.</td>
<td>2015</td>
<td>3/10</td>
</tr>
<tr>
<td><strong>Baysari MT, Lehnbom EC, Li L, Hargreaves A, Day RO, Westbrook JI.</strong> The effectiveness of information technology to improve antimicrobial prescribing in hospitals: a systematic review and meta-analysis. Int J Med Inform. 2016 Aug;92:15–34.</td>
<td>Effectiveness of information technology (IT) interventions on improving antimicrobial prescribing in hospitals</td>
<td>IT interventions took four main forms: (1) stand-alone computerized decision support systems (CDSSs), (2) decision support embedded within a hospital’s electronic medical record (EMR) or computerized provider order entry (CPOE) system, (3) computerized antimicrobial approval systems (CAAS), and (4) surveillance systems (SSs). IT interventions increased appropriate use of antimicrobials; however, no evidence of an effect was found when analysis included only studies with a quality score of five or above on the 10-point quality scale. There was little evidence of an effect of IT interventions on patient mortality or length of stay (LoS).</td>
<td>2015</td>
<td>7/9</td>
</tr>
<tr>
<td><strong>Pezzani MD, Mazzaferri F, Compri M, Galia L, Mutters NT, Kahlmeter G et al.; COACH working group.</strong> Linking antimicrobial resistance surveillance to antimicrobial policy in healthcare settings: the COMBACTE-Magnet EPI-Net COACH project. J Antimicrob Chemother. 2020 Dec 6;75(Suppl 2):ii2–ii19.</td>
<td>Summary of the evidence on how to collect, analyse and report AMR surveillance data to inform antimicrobial stewardship (AMS) teams providing guidance on empirical antimicrobial treatment in health-care settings</td>
<td>1. AMS team composition: involvement of a clinical microbiologist, pharmacist and infectious diseases specialist; in settings where they are not available, use the hub-and-spoke network model, in which a primary centre (hub) supports secondary centres with limited services (spokes). 2. Minimum infrastructure requirements for AMR surveillance: good laboratory practices and a quality management system 3. Organisms, samples and susceptibility patterns to report: the selection of pathogens should be based on local epidemiology and the major clinical impact attributable to a specific AMR profile, data on <em>Clostridioides difficile</em> infections should be included, antimicrobial susceptibility test data can be displayed using qualitative categories (susceptible/intermediate/resistant) or minimum inhibitory concentration (MIC).</td>
<td>2019</td>
<td>Not available</td>
</tr>
<tr>
<td>Option element</td>
<td>Focus of systematic review</td>
<td>Key findings</td>
<td>Year of last search</td>
<td>AMSTAR or SURE checklist (quality) rating</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------------------</td>
<td>--------------</td>
<td>---------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Option element</td>
<td>Focus of systematic review</td>
<td>Key findings</td>
<td>Year of last search</td>
<td>AMSTAR or SURE checklist (quality) rating</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>--------------------------------------</td>
</tr>
</tbody>
</table>
| de Bruin JS, Seeling W, Schuh C.  
Data use and effectiveness in electronic surveillance of healthcare associated infections in the 21st century: a systematic review. J Am Med Inform Assoc. 2014 Sep-Oct;21(5):942–51. | Description of recent trends in use of electronically available patient data by electronic surveillance systems for HAIs, and identification of the consequences for system effectiveness                                                                                                                                                                                                 | Electronic HAI surveillance systems use an increasing number of data sources, which are medico-administrative or clinical- and laboratory-based data. Trends on the use of individual types of electronic data established the important role of microbiology data in HAI detection, but also showed increased use of biochemistry and pharmacy data, and limited adoption of clinical data and physician narratives. The use of heterogeneous data sources leads to a higher system sensitivity at the expense of specificity. | 2011               | Not available                        | 0/26                   |
| Kruse CS, Frederick B, Jacobson T, Monticone DK.  
Cybersecurity in healthcare: a systematic review of modern threats and trends. Technol Health Care. 2017;25(1):1–10. | Identification of cybersecurity trends, including ransomware, and of possible solutions                                                                                                                                                                                                                                                                                                                                 | The health-care industry lags behind in security. Like other industries, the health-care industry should clearly define cybersecurity duties, establish clear procedures for upgrading software and handling a data breach, use VLANs and de-authentication and cloud-based computing, and train their users not to open a suspicious code. | 2016               | Not available                        | 0/31                   |
Healthcare professionals’ competence in digitalisation: a systematic review. J Clin Nurs. 2019 Mar;28(5-6):745–61. | Identification of key areas of competence for digitalization in health-care settings, description of health-care professionals’ competencies in these areas and identification of factors related to their competence                                                                                                                                                                                                 | Key competence areas on digitalization from a health-care perspective include knowledge of digital technology and the digital skills required to provide good patient care, including associated social and communication skills, and ethical considerations of digitalization in patient care. Health-care professionals need the motivation and willingness to acquire experience of digitalization in their professional context. Collegial and organizational support appear to be essential factors for building positive experiences of digitalization for health-care professionals. | 2017               | Not available                        | 0/12                   |
| Ali O, Shrestha A, Soar J, Wamba SF.  
Cloud computing enabled healthcare opportunities, issues, and applications: a systematic review. Int J Inform Manage. 2018;43:146–58. | Cloud computing in the health-care sector                                                                                                                                                                                                                                                                                                                                 | There is sufficient evidence to suggest that cloud computing can bring significant opportunities to the health-care sector. However, the issues related to the security and privacy of patient data and loss of control of data management to CSPs must be carefully evaluated, especially due to the strict regulations that govern the health-care sector. Cloud applications can enable access to multifaceted data for decision-making; however, using cloud computing for decision support in the health-care sector is a significant opportunity for researchers and practitioners. | 2018               | Not available                        | 0/88                   |
## APPENDIX 2. Systematic reviews relevant to Option 2 – Establish antimicrobial stewardship and infection prevention/control programmes in all hospitals

<table>
<thead>
<tr>
<th>Option element</th>
<th>Focus of systematic review</th>
<th>Key findings</th>
<th>Year of last search</th>
<th>AMSTAR or SURE checklist (quality) rating</th>
<th>Proportion of studies conducted in Greece</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E et al.</strong>&lt;br&gt;Interventions to improve antimicrobial prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2017;(2):CD003543.</td>
<td>Interventions to improve antimicrobial prescribing to hospital inpatients and investigation of the effect of two intervention functions: restriction and enablement.</td>
<td>Restriction was defined as “using rules to reduce the opportunity to engage in the target behaviour (or increase the target behaviour by reducing the opportunity to engage in competing behaviours)”. Enablement was defined as “increasing means/reducing barriers to increase capability or opportunity”. <strong>Results:</strong> 1. More hospital inpatients were treated according to antimicrobial prescribing policy with the intervention compared with no intervention. 2. The duration of antimicrobial treatment decreased by 1.95 days. 3. The risk of death was similar between the intervention and control groups, indicating that antimicrobial use can likely be reduced without adversely affecting mortality. 4. Antibiotic stewardship interventions probably reduce length of stay by 1.12 days. 5. Both enablement and restriction were independently associated with increased compliance with antimicrobial policies, and enablement enhanced the effect of restrictive interventions. 6. Enabling interventions that included feedback were probably more effective than those that did not.</td>
<td>2015</td>
<td>10/11</td>
<td>1/221</td>
</tr>
<tr>
<td><strong>Schuts EC, Hulscher MEJL, Mouton JW, Verduin CM, Stuart JWTC, Overdiek HWPM et al.</strong>&lt;br&gt;Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. Lancet Infect Dis. 2016 Jul;16(7):847–56.</td>
<td>Effects of antimicrobial stewardship objectives in hospitals and long-term care facilities on four patients’ outcomes: clinical outcomes, adverse events, costs, and bacterial resistance rates.</td>
<td>Empirical therapy according to guidelines, de-escalation of therapy, a switch from intravenous to oral treatment, therapeutic drug monitoring, the use of a list of restricted antimicrobials, and bedside consultation showed significant benefits for one or more of the four outcomes. Guideline-adherent empirical therapy was associated with a relative risk reduction for mortality of 35% and for de-escalation of 56%. Evidence of effects was less clear for adjusting therapy according to renal function, discontinuing therapy based on lack of clinical or microbiological evidence of infection, and having a local antimicrobial guide.</td>
<td>2014</td>
<td>11/11</td>
<td>0/146</td>
</tr>
<tr>
<td><strong>Wu JH, Langford BJ, Daneman N, Friedrich JO, Garber G.</strong>&lt;br&gt;Antimicrobial stewardship programs in long-term care settings: a meta-analysis and systematic review. J Am Geriatr Soc. 2019 Feb;67(2):392–9.</td>
<td>Antimicrobial stewardship interventions implemented in long-term care facilities.</td>
<td>The three most commonly implemented strategies were educational materials, educational meetings, and guideline implementation. Intervention labour intensity and resource requirements varied considerably among interventions. Meta-analysis of 11 studies demonstrated that antimicrobial stewardship strategies were associated with a 14% reduction in overall antimicrobial use.</td>
<td>2018</td>
<td>6/11</td>
<td>0/11</td>
</tr>
<tr>
<td>Option element</td>
<td>Focus of systematic review</td>
<td>Key findings</td>
<td>Year of last search</td>
<td>AMSTAR or SURE checklist (quality) rating</td>
<td>Proportion of studies conducted in Greece</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------------</td>
<td>--------------</td>
<td>---------------------</td>
<td>----------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Rennert-May E, Chew DS, Conly J, Guirguis M, Slobodan J, Fryters S et al.</td>
<td>Published clinical practice guidelines (CPGs) for the development of acute care hospital-based antimicrobial stewardship programmes (ASPs)</td>
<td>Prior authorization and/or restriction policies should be considered essential for the development of an effective hospital-based ASP.</td>
<td>2018</td>
<td>Not available</td>
<td>0/5</td>
</tr>
<tr>
<td>Wagner B, Filice GA, Drekonja D, Greer N, MacDonald R, Rutks I et al.</td>
<td>Effects of inpatient ASPs on patient, prescribing, and microbial outcomes</td>
<td>Few intervention types (e.g. audit and feedback, guideline implementation, and decision support) substantially impacted patient outcomes, including mortality, length of stay (LoS), readmission, or incidence of <em>Clostridium difficile</em> infection. Most interventions were associated with improved prescribing patterns as measured by decreased antimicrobial use or increased appropriate use. Where reported, ASPs were generally associated with improvements in microbial outcomes, including institutional resistance patterns or resistance in the study population.</td>
<td>2013</td>
<td>7/11</td>
<td>0/37</td>
</tr>
<tr>
<td>Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E.</td>
<td>Clinical and economic outcomes of hospital-based ASPs</td>
<td>Hospital ASPs result in significant decreases in antimicrobial consumption and cost, and the benefit is higher in the critical care setting. Infections due to specific antimicrobial-resistant pathogens and the overall hospital LoS are improved as well.</td>
<td>2015</td>
<td>9/11</td>
<td>0/26</td>
</tr>
<tr>
<td>Akpan MR, Isemin NU, Udoh AE, Ashiru-Oredope D.</td>
<td>ASPs in African countries</td>
<td>ASPs were associated with improved compliance with antimicrobial guidelines, appropriateness of prescribing, reduction in antimicrobial use and cost savings. Decrease in rate of surgical site infections and nonsignificant change in mortality and 30-day readmission rate were reported in two studies, respectively.</td>
<td>2019</td>
<td>5/10</td>
<td>0/13</td>
</tr>
<tr>
<td>Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S et al.</td>
<td>Effects of ASPs on the incidence of infections and colonization with antimicrobial-resistant bacteria</td>
<td>ASPs reduced the incidence of infections and colonization with multidrug-resistant Gram-negative bacteria, extended-spectrum β-lactamase-producing Gram-negative bacteria, and methicillin-resistant <em>Staphylococcus aureus</em>, as well as the incidence of <em>C. difficile</em> infections. ASPs were more effective when implemented with infection control measures, especially hand-hygiene interventions, than when implemented alone.</td>
<td>2016</td>
<td>Not available</td>
<td>0/32</td>
</tr>
<tr>
<td>Option element</td>
<td>Focus of systematic review</td>
<td>Key findings</td>
<td>Year of last search</td>
<td>AMSTAR or SURE checklist (quality) rating</td>
<td>Proportion of studies conducted in Greece</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------------</td>
<td>--------------</td>
<td>---------------------</td>
<td>------------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneu C.</td>
<td>Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review.</td>
<td>The majority of the studies showed a decrease in LoS (85%) and antimicrobial expenditure (92%) with the implementation of ASPs. The mean cost savings varied by hospital size and region (average cost savings in US studies: US$ 732 per patient). Similar trends were exhibited in European studies. The key driver of cost savings was from reduction in LoS. Savings were higher among hospitals with comprehensive ASPs, which included therapy review and antimicrobial restrictions.</td>
<td>2017</td>
<td>Not available</td>
<td>0/146</td>
</tr>
<tr>
<td>Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA et al.</td>
<td>Why don’t physicians follow clinical practice guidelines? A framework for improvement.</td>
<td>Multiple potential barriers to physician guideline adherence were identified, including awareness, familiarity, agreement, self-efficacy, outcome expectancy, ability to overcome the inertia of previous practice, and absence of external barriers to perform recommendations.</td>
<td>1998</td>
<td>Not available</td>
<td>0/76</td>
</tr>
<tr>
<td>Price L, MacDonald J, Melone L, Howe T, Flowers P, Currie K et al.</td>
<td>Effectiveness of national &amp; subnational infection prevention &amp; control interventions in high-income and upper-middle-income countries: a systematic review.</td>
<td>The interventions were categorized into the following types: multimodal, care bundles, policies, and surveillance, monitoring, and feedback. Evidence of effectiveness was found in all categories, but the best quality evidence was on multimodal interventions and surveillance, monitoring, and feedback.</td>
<td>2017</td>
<td>8/10</td>
<td>0/29</td>
</tr>
<tr>
<td>Lee MH, Lee GA, Lee SH, Park YH.</td>
<td>Effectiveness and core components of infection prevention and control programs in long-term care facilities: a systematic review.</td>
<td>Behavioural change strategies using education, monitoring and feedback were reported to be successful interventions for reducing the threat of healthcare-associated infections (HAIs). Generally, studies using four or more elements of the WHO multimodal strategy reported significant reductions in infection rates.</td>
<td>2016</td>
<td>Not available</td>
<td>0/17</td>
</tr>
<tr>
<td>Tchouaket Ngemeuleu E, Beogo I, Sia D, Kilpatrick K, Seguin C, Baillot A et al.</td>
<td>Economic evaluation, using a discount approach of 4 clinical best care practices (CBPs): hand hygiene, hygiene &amp; surface sanitation, screening upon admission for carriage, and other basic &amp; additional precautions</td>
<td>All studies demonstrated the cost-effectiveness of CBPs. The average yearly net cost savings from the CBPs ranged from CA$ 252 847 to CA$ 1 691 823, depending on the rate of discount (3% and 8%). The average incremental benefit–cost ratio of CBPs varied from 2.48 to 7.66.</td>
<td>2019</td>
<td>Not available</td>
<td>0/7</td>
</tr>
</tbody>
</table>
### Barriers and facilitators to health-care workers’ adherence to IPC guidelines for respiratory infectious diseases

<table>
<thead>
<tr>
<th>Option element</th>
<th>Focus of systematic review</th>
<th>Key findings</th>
<th>Year of last search</th>
<th>AMSTAR or SURE checklist (quality) rating</th>
<th>Proportion of studies conducted in Greece</th>
</tr>
</thead>
</table>
| 1. Barriers and facilitators to health-care workers’ adherence to IPC guidelines for respiratory infectious diseases | **Health-care workers felt**  
  - unsure as to how to adhere to local guidelines when they were lengthy, ambiguous or did not reflect guidelines;  
  - overwhelmed, as local guidelines were constantly changing and IPC strategies led to increased workload and fatigue;  
  - influenced by the level of support they felt that they received from their management team.  
  - Clear communication about IPC guidelines was seen as vital. Lack of training on infection itself and on PPE use was identified. It was a problem when training was not mandatory.  
  - A lack of isolation rooms, anterooms and shower facilities was identified as a problem. Other important practical measures include minimizing overcrowding, fast-tracking infected patients, restricting visitors, and providing easy access to handwashing facilities.  
  - A lack of PPE, and provision of equipment of poor quality, was a serious concern (need to adjust the volume of supplies as infection outbreaks continued).  
  - Health-care workers believed:  
    - IPC guidance is followed more closely when they see its value. Some felt motivated to follow the guidance because of fear of infecting themselves or their families, or because they felt responsible for their patients. Some found it difficult to use masks and other equipment when it made patients feel isolated, frightened or stigmatized.  
    - Masks and other equipment are uncomfortable to use.  
    - The workplace culture could also influence whether IPC guidelines are followed.  
  - Health-care workers pointed to the importance of including all staff, including cleaning staff, porters, kitchen staff and other support staff when implementing IPC guidelines. | 2020 | 6/9 | 0/20 |

Barriers and facilitators to healthcare workers’ adherence with infection prevention and control (IPC) guidelines for respiratory infectious diseases: a rapid qualitative evidence synthesis.  
### APPENDICES AND ANNEXES

#### APPENDIX 3. Summary of systematic reviews relevant to Option 3 – Implementation of postgraduate educational programmes for health-care workers on prudent antimicrobial use and infection prevention and control in the hospital setting

<table>
<thead>
<tr>
<th>Option element</th>
<th>Focus of systematic review</th>
<th>Key findings</th>
<th>Year of last search</th>
<th>AMSTAR or SURE checklist (quality) rating</th>
<th>Proportion of studies that were conducted in Greece</th>
</tr>
</thead>
</table>
| **van der Velden AW, Pijpers EJ, Kuyvenhoven MM.**  
Effectiveness of physician-targeted interventions to improve antimicrobial use for respiratory tract infections.  
Br J Gen Pract. 2012;62(605):e801–7. | Physician-targeted interventions to improve antimicrobial prescribing for respiratory tract infections (RTIs) | This review concludes that physician education reduces antimicrobial prescribing. Further research should focus on how to provide physicians with the relevant knowledge and tools, and when to supplement education with additional intervention elements. | 2009 | 2/10 | 0/58 |
| **Ranji SR, Steinman MA, Shojania KG, Gonzales R.**  
Interventions to reduce unnecessary antimicrobial prescribing: a systematic review and quantitative analysis.  
Med Care. 2008 Aug;46(8):847–62. | Quality improvement (QI) strategies to reduce antimicrobial prescribing for acute outpatient illnesses, for which antimicrobials are often inappropriately prescribed | QI efforts are effective at reducing antimicrobial use in ambulatory settings. Strategies using active clinician education and targeting the management of all acute respiratory infections (rather than single conditions in single age groups) may yield larger reductions in community-level antimicrobial use. | 2007 | 6/11 | 0/43 |
| **Fleming A, Browne J, Byrne S.**  
The effect of interventions to reduce potentially inappropriate antimicrobial prescribing in long-term care facilities: a systematic review of randomised controlled trials.  
Drugs Aging. 2013 Jun;30(6):401–8. | Interventions to improve the quality of, or appropriateness of, antimicrobial prescribing in long-term care facilities | Interventions in the long-term care setting involving local consensus procedures, educational strategies, and locally developed guidelines may improve the quality of antimicrobial prescribing. | 2012 | 8/9 | 0/4 |
| **Lee CR, Lee JH, Kang LW, Jeong BC, Lee SH.**  
Educational effectiveness, target, & content for prudent antimicrobial use.  
Biomed Res Int. 2015;2015:214021. | Educational interventions for promoting prudent antimicrobial prescribing | This review suggests that educational programmes regarding prudent antimicrobial use, focusing not only on clinicians, but also on undergraduate medical students, can lead to significant reductions in antimicrobial prescriptions. | 2014 | 4/11 | 0/28 |
| **Steinman MA, Ranji SR, Shojania KG, Gonzales R.**  
Improving antimicrobial selection: a systematic review and quantitative analysis of quality improvement strategies.  
Med Care. 2006 Jul;44(7):617–28. | Interventions effective at improving the prescribing of recommended antimicrobials for acute outpatient infections | Clinician education about prudent prescribing of recommended antimicrobials for acute outpatient infections, alone or in combination with audit and feedback, resulted in improved antimicrobial prescribing by a median of 10.6%. Clinician education alone was more effective than other interventions, however, confounding may partially account for this finding. | 2004 | 5/11 | 0/26 |
| **Brennan N, Mattick K.**  
A systematic review of educational interventions to change behaviour of prescribers in hospital settings, with a particular emphasis on new prescribers.  
Br J Clin Pharmacol. 2013 Feb;75(2):359–72. | Educational interventions to change prescribing behaviour, particularly among new prescribers | Among the 64 studies included, only 13% of interventions specifically targeted new prescribers. Most interventions (72%) were deemed effective in changing prescribing behaviour, but no particular type stood out as most effective. | 2012 | 5/11 | 0/64 |
<table>
<thead>
<tr>
<th>Option element</th>
<th>Focus of systematic review</th>
<th>Key findings</th>
<th>Year of last search</th>
<th>AMSTAR checklist (quality) rating</th>
<th>Proportion of studies that were conducted in Greece</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lim DW, Htun HL, Ong LS, Guo H, Chow A.</td>
<td>Factors associated with antimicrobial use for acute respiratory tract infections (uARTIs) in adults presenting at the Emergency Department</td>
<td>Patients with normal C reactive protein levels and positive influenza tests were less likely to receive antimicrobial treatment. Nonclinical factors associated with antimicrobial use were longer waiting time and perceived patient desire for antimicrobials. Patients attended by internal medicine physicians co-managed by house staff or who visited an ED that provided education to health-care providers on the use of antimicrobials were less likely to receive antimicrobials.</td>
<td>2017</td>
<td>Not available</td>
<td>0/12</td>
</tr>
<tr>
<td>Arnold SR, Straus SE.</td>
<td>Interventions to improve the selection, dose &amp; treatment duration of antimicrobials prescribed by health-care providers in the outpatient setting and evaluation of their impact on reducing the incidence of antimicrobial-resistant pathogens</td>
<td>Multifaceted interventions, where educational interventions occur on many levels, may be successfully applied to communities after addressing local barriers to change. Patient-based interventions and physician reminders show promise and should be further studied.</td>
<td>2000</td>
<td>7/11</td>
<td>0/39</td>
</tr>
<tr>
<td>Safdar N, Abad C.</td>
<td>Educational strategies of health-care providers for reducing health-care-associated infections (HAIs)</td>
<td>There was a statistically significant decrease in infection rates after intervention in 21 studies, with risk ratios ranging from 0 to 0.79. The beneficial effect of education was apparent in teaching and nonteaching institutions and in lesser-developed countries as well as developed nations.</td>
<td>2006</td>
<td>5/10</td>
<td>0/26</td>
</tr>
<tr>
<td>Moralejo D, El Dib R, Prata RA, Barretti P, Corrêa I.</td>
<td>Effectiveness of interventions that target health-care workers to improve adherence to standard precautions in patient care</td>
<td>1. Education may slightly improve health-care workers’ adherence to standard precautions and their level of knowledge. 2. Education with visualization of respiratory particle dispersion probably improves health-care workers’ use of facial protection, but probably leads to little or no difference in knowledge. 3. Education with additional infection control support may slightly improve health-care workers’ adherence to standard precautions, but probably leads to little or no difference in rates of health-care-associated colonization with MRSA. 4. Peer evaluation probably improves health-care workers’ adherence to standard precautions. 5. Checklists and coloured cues probably improve health-care workers’ adherence to standard precautions.</td>
<td>2017</td>
<td>Not available</td>
<td>0/8</td>
</tr>
<tr>
<td>Hughes C, Tunney M, Bradley MC.</td>
<td>Effectiveness of infection prevention and control strategies for preventing the transmission of methicillin-resistant <em>Staphylococcus aureus</em> (MRSA) in nursing homes for older people</td>
<td>At the end of the 12-month study, there was no change in MRSA prevalence between intervention and control sites, while mean infection control audit scores were significantly higher in the intervention homes compared with control homes.</td>
<td>2013</td>
<td>7/9</td>
<td>0/1</td>
</tr>
</tbody>
</table>
### ANNEX 1. Health-care legal framework: recent developments impacting antimicrobial use and antimicrobial resistance

<table>
<thead>
<tr>
<th>Year</th>
<th>Legislation</th>
<th>Main points</th>
</tr>
</thead>
</table>
| 2014 | Ministerial Decree issued by the Ministry of Health on Infection Control in hospitals: legal mandate for the implementation of the National Action Plan “Prokroustis” introduced in 2010 | - Establishment of a centralized national notification system for the mandatory notification of newly detected cases of infections caused by selected MDR pathogens in hospitals  
- Evaluation of the burden of MDR infections in hospitals in Greece  
- Implementation of infection control measures to attenuate the transmission of MDR pathogens in hospitals, including infection control bundles and geographical separation of MDR carriers and infected patients  
- Evaluation of adherence to infection control bundles  
- Communication links between hospitals and public health authorities  
- Antimicrobial stewardship |
| 2015 | Circular issued by the Ministry of Health: guidance for the implementation of infection control in hospitals | - Assembly and function of hospital Infection Control Committees and Committees for the Monitoring of the Consumption and Proper Use of Antibiotics  
- Annual hospital action plans for infection control, including dedicated budget |
| 2019 | Circular issued by the Ministry of Health on antimicrobial stewardship in hospitals | - Interhospital collaboration for antimicrobial stewardship and infection control purposes  
- Emphasis on stewardship regarding advanced antimicrobials and surgical antimicrobial prophylaxis  
- Provision for dedicated time allocated to personnel for infection control purposes |
| 2020 | State law issued on mandatory medical prescription for antimicrobials dispensed by private pharmacies | - Antibiotics must be electronically prescribed by a physician  
- Pharmacies may dispense antimicrobials only if a medical prescription is processed electronically  
- Clinical indication and dosage must be stated |
### ANNEX 2. Non-legislative complementary actions on antimicrobial use and antimicrobial resistance

<table>
<thead>
<tr>
<th>Year</th>
<th>Complementary action</th>
<th>Content</th>
</tr>
</thead>
</table>
| 2010–2019  | **National Guidelines** Issued by the National Public Health Organization (2010 onwards, year of last update stated) | ▶ Active surveillance for selected MDR pathogens in hospitals (active infections or patient carrier state, 2015)  
▶ Laboratory surveillance of MDR pathogens (2015)  
▶ Infection control measures for the prevention of MDR pathogen spread in hospitals (2015)  
▶ Diagnosis and treatment of infectious disease (issued in collaboration with the Hellenic Society for Infectious Diseases, 2015)  
▶ Interhospital transfer of patients bearing multi-resistant pathogens (2017)  
▶ Hand hygiene (in collaboration with the EU joint action on antimicrobial resistance, JAMRAI, 2018)  
▶ Use of antimicrobials in hospitals and antimicrobial stewardship (2019) |
| Since 2015 | **National cumulative report communication to hospitals & Central Government**         | ▶ Comparative hospital bloodstream infection rate (selected multidrug-resistant pathogens)  
▶ Comparative cumulative antimicrobial consumption  
▶ Comparative compliance with selected infection control measures  
▶ Hand hygiene implementation in participating hospitals |
| Since 2006 | **Collaboration with ECDC** The National Public Health Organization participates in the European Surveillance Reporting System (metadata analysis for public health action) | ▶ Annual sharing of antimicrobial resistance data in hospitals to the EARS Network (European Antimicrobial Resistance Surveillance Network)  
▶ Annual sharing of data on antimicrobial consumption in hospitals to the ESAC Network (Surveillance of Antimicrobial Consumption) |
### ANNEX 3. Key stakeholders involved in hospital AMR action plans in Greece

<table>
<thead>
<tr>
<th>Level of administration</th>
<th>Stakeholder</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Government</strong></td>
<td>Ministry of Health (main stakeholder)</td>
</tr>
<tr>
<td><strong>Local government</strong></td>
<td>Regional Health Districts (DYPE)</td>
</tr>
<tr>
<td><strong>National agencies</strong></td>
<td>Supervised by the Ministry of Health:</td>
</tr>
<tr>
<td></td>
<td>- National Public Health Organization (NPHO), which also operates the National Public Health Laboratory</td>
</tr>
<tr>
<td></td>
<td>- National Organization for Medicines (EOF)</td>
</tr>
<tr>
<td></td>
<td>- National Organization for the Provision of Health Services (EOPYY)</td>
</tr>
<tr>
<td></td>
<td>- National Healthcare Service (ESY), which operates State hospitals</td>
</tr>
<tr>
<td></td>
<td>Supervised by the Ministry of Labour, Social Security &amp; Social Solidarity:</td>
</tr>
<tr>
<td></td>
<td>- e-Government Center for Social Security Services (IDIKA SA)</td>
</tr>
<tr>
<td><strong>Academia</strong></td>
<td>National School of Public Health</td>
</tr>
</tbody>
</table>
## ANNEX 4. Stakeholder and key informant interviews used as a source of information

<table>
<thead>
<tr>
<th>Level/Jurisdiction (officials interviewed)</th>
<th>Field of consultative review</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Government, Ministry of Health</strong>&lt;br&gt;— Chief Health Administration officials&lt;br&gt;— Ministry consultants</td>
<td>▶ Health policy and health data management&lt;br&gt;▶ Health legislation, including legal framework for quality of hospital care and infection prevention&lt;br&gt;▶ Administrative division and jurisdictional boundaries in policy-making and policy implementation</td>
</tr>
<tr>
<td><strong>Regional Health Administration</strong>&lt;br&gt;(“Health Regions”, Greek acronym: DYPE)&lt;br&gt;— District Health Administration officials&lt;br&gt;— District Hospital Infection Control coordinators (newly appointed during the COVID-19 pandemic)</td>
<td>▶ Policy implementation regarding infection control programmes&lt;br&gt;▶ Management and organization of human resources in infection control in State hospitals&lt;br&gt;▶ Monitoring of quality of care&lt;br&gt;▶ Technology acquisition (laboratory capacity)</td>
</tr>
<tr>
<td><strong>National Public Health Organization</strong>&lt;br&gt;— Public Health and Nosocomial Infection experts&lt;br&gt;— Head Microbiologist and Biologist of the Public Health Reference Laboratory</td>
<td>▶ Guideline development and dissemination&lt;br&gt;▶ Information systems and health data management&lt;br&gt;▶ Communication of surveillance data on nosocomial infection&lt;br&gt;▶ European and International joint actions on Antimicrobial Resistance</td>
</tr>
<tr>
<td><strong>ECDC</strong>&lt;br&gt;— Public Health and Nosocomial Infection experts</td>
<td>▶ Surveillance, investigation of hospital outbreaks&lt;br&gt;▶ Infection control education&lt;br&gt;▶ Regulation and best practice communication</td>
</tr>
<tr>
<td><strong>Academia</strong>&lt;br&gt;— Medical and Nursing School Academic Staff</td>
<td>▶ Undergraduate and postgraduate instruction, research, ongoing education</td>
</tr>
<tr>
<td><strong>Professional bodies</strong>&lt;br&gt;— Medical and Nurses’ Association representatives</td>
<td>▶ Professional practice standards and professional education standards, professional accreditation&lt;br&gt;▶ Medical and nursing malpractice management</td>
</tr>
<tr>
<td><strong>Hospitals</strong>&lt;br&gt;— Hospital management&lt;br&gt;— Medical directors&lt;br&gt;— Infection control nurses&lt;br&gt;— Head of Infection Control Committee&lt;br&gt;— Head of Antimicrobial Stewardship Committee&lt;br&gt;— Head of Microbiology Laboratory</td>
<td>▶ Infection control budget and human resources&lt;br&gt;▶ Personnel knowledge capital and health-care worker professional development&lt;br&gt;▶ Patient records, microbial laboratory database&lt;br&gt;▶ Interprofessional collaboration (namely nurse–physician professional communication and chain of command perceptions)&lt;br&gt;▶ Technical infection control issues (e.g. isolation wards, cleaning and disinfection, waste management)&lt;br&gt;▶ Laboratory capacity for pathogen identification</td>
</tr>
</tbody>
</table>
## ANNEX 5. Information derived from interviews with stakeholders

<table>
<thead>
<tr>
<th>Field</th>
<th>Problems and barriers that underlie and impact fighting AMR in hospital settings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central and Regional Health Administration – organizational issues</strong></td>
<td>➤ Vague coordinating, supervisory and advisory functions over the hospitals&lt;br&gt;➤ High degree of concentration of hospital beds in the capital (43% of total beds, 35% of country population)&lt;br&gt;➤ Lack of continuity in strategic planning and implementation of measures (lack of consistency in health system values and direction of health-care reforms)&lt;br&gt;➤ Failure to solidify measures into a strategic framework&lt;br&gt;➤ Low uptake of European and International Joint Action programmes&lt;br&gt;➤ No established mechanisms to supervise and evaluate medical and nursing practices and assess the outcomes of care, or monitor the use of health resources</td>
</tr>
<tr>
<td><strong>Central and Regional Health Administration – transparency issues</strong></td>
<td>➤ Widespread political interference, particularly in appointing senior management staff&lt;br&gt;➤ Lack of objective monitoring processes and supervision mechanisms&lt;br&gt;➤ Abuse or perceived abuse of entrusted power by public officials in the public and private sector (petty corruption and informal payments)</td>
</tr>
<tr>
<td><strong>Hospital management</strong></td>
<td>➤ Funding problems, erratic cash flow&lt;br&gt;➤ Ineffective/outdated chain of command and line of reporting</td>
</tr>
<tr>
<td><strong>Digitalization and information management systems</strong></td>
<td>➤ Limited and erratic use of web-based platforms recently established by the Ministry of Health and EOPYY (National Organization for the Provision of Health Services, single-payer health insurance system)&lt;br&gt;➤ Fragmented data management, incompatibility of digital registries&lt;br&gt;➤ Outdated data filing system, extensive use of paper-based documentation&lt;br&gt;➤ Absence of electronic medical records</td>
</tr>
<tr>
<td><strong>Human resources</strong></td>
<td>➤ Unbalanced distribution of medical personnel and medical specialties: a general oversupply of doctors in the country coexists with medical understaffing in State hospitals&lt;br&gt;➤ Inadequate nursing staff in State hospitals despite a high number of nursing graduates&lt;br&gt;➤ Staff mix imbalances:&lt;br&gt;  ➤ Low nurse-to-physician ratio&lt;br&gt;  ➤ Ageing staff, surplus of senior staff, lack of junior staff&lt;br&gt;  ➤ Significant variation in skills, engagement, approach&lt;br&gt;➤ Slow recruitment processes, increasing restrictions on hiring personnel in the public sector&lt;br&gt;➤ Reduced replacement of retiring staff&lt;br&gt;➤ Non-renewal or delayed renewal of fixed-term contracts for temporary staff</td>
</tr>
</tbody>
</table>
### Field Problems and barriers that underlie and impact fighting AMR in hospital settings

<table>
<thead>
<tr>
<th>Field</th>
<th>Problems</th>
</tr>
</thead>
</table>
| **Organizational aspects of patient care** | - Low efficacy in preventing avoidable hospitalization  
- Fragmented chronic disease management, leading to frequent infectious complications and frequent readmissions  
- Hospital overcrowding:  
  - inefficient gatekeeping due to failure to implement the legal provisions for tiered primary care with gatekeeping function  
  - absence of a tiered referral system  
  - lack of hospice care  
  - inadequate availability of rehabilitation beds  
  - very limited and erratically available home-care services |
| **Guidelines and best practice**           | - Limited awareness of existing treatment guidelines:  
  - Despite (erratic) efforts by the Ministry of Health in collaboration with the medical societies to introduce clinical guidelines, their uptake and dissemination is limited.  
  - Low availability of local nursing protocols, low awareness of existing protocols (developed by the nursing faculties of Greek universities) and even lower consistent use of them  
- Lack of regular guideline revision  
- Antimicrobial overuse linked to:  
  - knowledge gaps  
  - perception of stewardship programmes as restrictive of the autonomy of the individual practitioner  
  - influence of pharmaceutical industry interests and supplier-induced demand  
  - fear of litigation (defensive medicine) |
| **Accountability**                          | - Culture of no accountability for low performance  
- Lack of objective staff evaluation  
- Professional advancement and other work benefits perceived as only loosely related to skill, commitment and effort |
| **Interprofessional collaboration**        | - Perceived low status and authority of the nursing profession in the hospital setting  
- Low levels of solidarity, mutual understanding and cooperation for solving daily in-clinic problems  
- Misperceptions on hierarchy and chain of command, lack of team-based models of work |
### ANNEX 6. Summary of problems identified regarding the implementation of the national action plans

<table>
<thead>
<tr>
<th>Field</th>
<th>Identified problems</th>
</tr>
</thead>
</table>
| Administration                      | ➢ Inconsistent administerial support  
 ➢ Staffing inadequacies  
 ➢ Nosocomial Infection Committee, Infection Control Nurse, and Antimicrobial Stewardship Committee established in hospitals, but no dedicated time or infrastructure allocated  
 ➢ No allocated budget in hospitals, despite existing legal provision |
| Infection control practices         | ➢ Great variability in the implementation of infection control and antimicrobial use practices, both interhospital and intrahospital  
 ➢ Variable consistency in adherence to infection control practices among physicians, nurses and auxiliary staff, plus intrapersonal variability inversely related to workload |
| Surveillance and reporting          | ➢ Erratic reporting plus significant delays in reporting  
 ➢ Extensive use of paper-based documentation  
 ➢ Data fragmentation in several databases, resulting in difficulty in accessing important information |
| Attitudes and perceptions           | ➢ Perceptions of medical practitioners regarding clinical autonomy undermine regard for rules on use of antimicrobials |
| Communication                       | ➢ Communication links between hospitals and public health authorities need to be strengthened |
| Education                           | ➢ Ongoing education needed |
MEMBER STATES

Albania
Andorra
Armenia
Austria
Azerbaijan
Belarus
Belgium
Bosnia and Herzegovina
Bulgaria
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Georgia
Germany
Greece
Hungary
Iceland
Ireland
Israel
Italy
Kazakhstan
Kyrgyzstan
Latvia
Lithuania
Luxembourg
Malta
Monaco
Montenegro
Netherlands
North Macedonia
Norway
Poland
Portugal
Republic of Moldova
Romania
Russian Federation
San Marino
Serbia
Slovakia
Slovenia
Spain
Sweden
Switzerland
Tajikistan
Türkiye
Turkmenistan
Ukraine
United Kingdom
Uzbekistan