



Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Consensus document

Antimicrobial stewardship in hospitals: Expert recommendation guidance document for activities in specific populations, syndromes and other aspects (PROA-2) from SEIMC, SEFH, SEMPSPGS, SEMICYUC and SEIP[☆]



Emilia Cercenado^a, Jesús Rodríguez-Baño^{b,*}, José Luis Alfonso^c, Esther Calbo^d, Luis Escosa^e, Aurora Fernández-Polo^f, Julio García-Rodríguez^g, José Garnacho^h, María Victoria Gil-Navarro^{i,j}, Santiago Grau^k, Carlota Gudíol^l, Juan Pablo Horcajada^m, Nieves Larrosaⁿ, Carmen Martínez^o, José Molina^p, Xavier Nuvials^q, Antonio Oliver^r, José Ramón Paño-Pardo^s, María Teresa Pérez-Rodríguez^t, Paula Ramírez^u, Pedro Rey-Biel^{v,w}, Pablo Vidal^x, Pilar Retamar-Gentil^b

^a Servicio de Microbiología Clínica y Enfermedades Infecciosas, Hospital General Universitario Gregorio Marañón, Departamento de Medicina, Facultad de Medicina, Universidad Complutense de Madrid, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Madrid, Spain

^b Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario Virgen Macarena, Instituto de Biomedicina de Sevilla, CSIC, Departamento de Medicina, Universidad de Sevilla, Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Sevilla, Spain

^c Servicio de Medicina Preventiva, Hospital General Universitario de Valencia, Departamento de Medicina Preventiva y Salud Pública, Universidad de Valencia, Spain

^d Unidad de Enfermedades Infecciosas, Hospital Mutua de Terrassa, Universidad Internacional de Cataluña, Barcelona, Spain

^e Servicio de Pediatría hospitalaria, enfermedades infecciosas y tropicales, Hospital Universitario La Paz, Instituto de Investigación IdIPAZ, Madrid, RITIP (Red de Investigación Translacional en Infectología Pediátrica), Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), SEIP (Sociedad Española de Infectología Pediátrica), Madrid, Spain

^f Servicio de Farmacia, Hospital Infantil Vall d'Hebron, Vall d'Hebron Institut de Recerca, RITIP (Red de Investigación Translacional en Infectología Pediátrica), PROA-NEN, Barcelona, Spain

^g Servicio de Microbiología, Hospital Universitario La Paz, IDIPAZ, Departamento de Microbiología, Universidad Autónoma de Madrid, CIBERINFEC, Spain

^h Unidad Clínica de Cuidados Intensivos, Hospital Universitario Virgen Macarena, Sevilla, Spain

ⁱ Unidad de Farmacia, Hospital Universitario Virgen del Rocío, CSIC, Instituto de Biomedicina de Sevilla (IBiS), Sevilla, Spain

^j Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Sevilla, Spain

^k Departamento de Farmacia, Hospital del Mar, Universidad Pompeu Fabra, Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Barcelona, Spain

^l Servicio de Enfermedades Infecciosas, Hospital Universitario de Bellvitge, Instituto Catalán de Oncología (ICO), Instituto de Investigación Biomédica del Hospital Universitario de Bellvitge (IDIBELL), Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Barcelona, Spain

^m Servicio de Enfermedades Infecciosas, Hospital del Mar, Instituto Hospital del Mar de Investigaciones Médicas (IMIM), Universidad Pompeu Fabra, Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Barcelona, Spain

ⁿ Servicio de Microbiología, Hospital Universitario Vall d'Hebron, Universitat Autònoma de Barcelona, Vall d'Hebron Institut de Recerca (VHIR), Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Barcelona, Spain

^o Servicio de Microbiología, Hospital Universitario Miguel Servet, Zaragoza, Spain

^p Unidad Clínica de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Hospital Universitario Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBiS), CSIC, Universidad de Sevilla, Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Sevilla, Spain

^q Servicio de Medicina Intensiva, Hospital Universitario Vall d'Hebron Barcelona Hospital Campus, Shock Organ Dysfunction and Resuscitation (SODIR) Research Group, Vall d'Hebron Institut de Recerca (VHIR), Barcelona, Spain

^r Servicio de Microbiología y Unidad de Investigación, Hospital Universitario Son Espases, Instituto de Investigación Sanitaria Illes Balears (IdiSBA), Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Palma de Mallorca, Spain

^s Servicio de Enfermedades Infecciosas, Hospital Clínico Universitario Lozano Blesa, Instituto de Investigación Biosanitaria Aragón, Departamento de Medicina, Universidad de Zaragoza, Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Zaragoza, Spain

^t Unidad de Enfermedades Infecciosas-Departamento de Medicina Interna, Hospital Álvaro Cunqueiro, Complejo Hospitalario Universitario de Vigo, Instituto de Investigación Sanitaria Galicia Sur (IIS Galicia Sur), Vigo (Pontevedra), Spain

^u Servicio de Medicina Intensiva, Hospital Universitario y Politécnico la Fe, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Valencia, Spain

^v Departamento de Economía, Finanzas y Contabilidad, ESADE, Universidad Ramón Llull, Barcelona, Spain

^w Departamento de Economía, Finanzas y Contabilidad en ESADE, Universidad Rey Juan Carlos, Madrid, Spain

^x Unidad de Cuidados Intensivos, Complejo Hospitalario Universitario de Orense, Orense, Spain

[☆] The complete consensus document is available as [Appendix A](#) in Supplementary Material.

* Corresponding author.
E-mail address: jesusrb@us.es (J. Rodríguez-Baño).

ARTICLE INFO

Keywords:

Antimicrobial stewardship
Antimicrobial stewardship in ICU
Antimicrobial stewardship paediatrics
Antimicrobial stewardship
oncology–haematology
Antimicrobial stewardship clinical
syndromes
Antimicrobial stewardship emergency
Diagnostic stewardship

ABSTRACT

In 2012, The Spanish Societies of Infectious Diseases and Clinical Microbiology (SEIMC), Hospital Pharmacy (SEFH), and Preventive Medicine, Public Health and Healthcare Management (SEMPSPGS) lead a consensus document including recommendations for the implementation of antimicrobial stewardship (AMS) programs (AMSP; PROA in Spanish) in acute care hospitals in Spain. While these recommendations were critical for the development of these programs in many centres, there is a need for guidance in the development of AMS activities for specific patient populations, syndromes or other specific aspects which were not included in the previous document or have developed significantly since then.

The objective of this expert recommendation guidance document is to review the available information about these activities in these patient populations or circumstances, and to provide guidance recommendations about them. With this objective the SEIMC, SEFH, SEMPSPGS, the Spanish Society of Intensive Care Medicine (SEMICYUC) and the Spanish Pediatric Infectious Disease Society (SEIP) selected a panel of experts who chose the different aspects to include in the document. Because of the lack of high-level evidence in the implementation of the activities, the panel opted to perform a narrative review of the literature for the different topics for which recommendations were agreed by consensus. The document was open to public consultation for the members of these societies for their comments and suggestions, which were reviewed and considered by the panel.

© 2022 Published by Elsevier España, S.L.U. on behalf of Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica.

Programas de optimización del uso de antimicrobianos en hospitales: guía de recomendaciones de expertos para actividades en poblaciones específicas, síndromes y otros aspectos (PROA-2) de la SEIMC, SEFH, SEMPSPGS y SEIP

RESUMEN

En 2012, las Sociedades Españolas de Enfermedades Infecciosas y Microbiología Clínica (SEIMC), Farmacia Hospitalaria (SEFH) y Medicina Preventiva, Salud Pública y Gestión Sanitaria (SEMPSPGS) lideraron un documento de consenso que incluía recomendaciones para la implementación de Programas de optimización del uso de antimicrobianos (PROA) en hospitales de agudos en España. Si bien estas recomendaciones fueron críticas para el desarrollo de estos programas en muchos centros, actualmente es necesario establecer unas guías para la implementación de las actividades de los PROA en determinadas poblaciones de pacientes, síndromes clínicos y otros aspectos específicos que no se incluyeron en el documento previo o que desde entonces se han desarrollado significativamente.

El objetivo de esta guía de recomendaciones de expertos es revisar la información disponible acerca de esas actividades en estas poblaciones o circunstancias de pacientes y proporcionar unas recomendaciones que sirvan de guía sobre ellas. Con este objetivo, la SEIMC, la SEFH y la SEMPSPGS, así como la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC) y la Sociedad Española de Infectología Pediátrica (SEIP), seleccionaron un panel de expertos que eligieron los diferentes aspectos a incluir en el documento. Debido a la ausencia de evidencia de alto nivel en la implementación de las diferentes actividades, el panel optó por realizar una revisión narrativa de la literatura de los diferentes aspectos, en los que las recomendaciones se acordaron por consenso. El documento se abrió para consulta pública a los miembros de estas sociedades para sus comentarios y sugerencias, que fueron revisadas y consideradas por el panel.

© 2022 Publicado por Elsevier España, S.L.U. en nombre de Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica.

Palabras clave:

Programas de optimización del uso de
antimicrobianos
PROA
PROA en UCI
PROA pediátrico
PROA en oncología-hematología
PROA en urgencias
PROA en síndromes clínicos
PRODIM

Antimicrobial stewardship in specific populations

Guidance recommendations for antimicrobial stewardship programs in critically-ill patients admitted to Intensive Care Units (ICUs)

Structured antimicrobial stewardship programs (AMSP) should be implemented in all ICUs.

AMSP in the critical care setting should be led by an expert ICU staff member and implemented by a collaborative and multidisciplinary team including, infectologists, microbiologists, pharmacists, preventive medicine specialists and other specialists as needed.

Specialists of preventive medicine will form part of AMSP, for the coordination of outbreak control actions and other preventive measures to implant (patient hygiene, asepsis and antisepsis measures in taking samples, etc.) for invasive procedures device monitoring, for surveillance and monitoring of surgical prophylaxis, and for control of environmental biosafety in controlled environment rooms in order to minimize infection transmission and prevent the appearance of outbreaks of environmental origin.

The design and implementation of AMSP in critically ill patients should consider the specificities of this patient population. Infection severity, organ dysfunctions and changes in pharmacokinetics should be taken into account. Therapeutic drug monitoring, if available, is helpful for dose adjustments in ICU patients.

Collaborative, non-compulsory interventions including audit and feedback should be prioritized. De-escalation and shortening of treatments should be the main targets.

AMSP in critically ill patients should be fueled by real-time microbiological information and clinical microbiologists support.

Updated knowledge of the local epidemiology is mandatory to design the antibiotic policy.

Guidance recommendations for antimicrobial stewardship programs in haematological patients

AMSP should be developed by a multidisciplinary team including haematologists, infectious diseases experts, microbiologists, preventive medicine specialists and pharmacists.

Patterns of antimicrobial prescription and antimicrobial resistance should be monitored periodically.

The implementation of screening samples to detect colonization by multidrug-resistant organisms (MDRO) may be considered, at least in patients at highest risk.

Antimicrobial prophylaxis, empirical and streamlined therapy for febrile neutropenia should be protocolized considering local epidemiology and different patient risk profiles. Adherence to recommendations should be measured.

On-demand availability of infectious diseases experts, clinical microbiologists and pharmacists should be warranted, at least for the most complex cases, and also specialists in preventive medicine in order to control outbreaks or isolation.

Periodical, regular, multidisciplinary rounds are recommended.

Guidance recommendations for antimicrobial stewardship programs in solid cancer patients

Specific local guidelines for the treatment of the most frequent infectious syndromes in patients with solid tumors (not only febrile neutropenia) based on local epidemiology, must be developed by the AMSP team and oncologists. Implementation of clinical pathways is more complex but also useful.

The AMSP should include availability of infectious diseases specialists for consultation.

Continuous active training on appropriate antimicrobial use must be implemented.

Interventions specifically targeting febrile neutropenia, antifungal stewardship or biomarker-based algorithms may have a limited impact on patients with solid tumors and should not be prioritized.

Research is needed regarding optimal duration of antimicrobial treatments or the clinical impact of rapid diagnostic tests in this setting.

Guidance recommendations for antimicrobial stewardship programs in patients near the end of life

To develop local protocols with criteria helping in the identification of patients who will most probably benefit from antibiotics (i.e. improvement in survival or symptom relief while maintaining the quality of life) and those in which avoiding futile treatments, developed by palliative care experts and the AMSP team. The antibiotics and routes to be used in the most frequent syndromes and rules for early stopping should be included.

A multimodal approach targeting physicians, patients and care-givers' perceptions is also recommended. Availability of consultation to palliative care and infectious diseases specialists is recommended.

Research is needed about the optimal approach for developing and implementing AMSP in palliative care.

Guidance recommendations for antimicrobial stewardship programs in children

The AMSP team should include an expert paediatrician in infectious diseases and antimicrobial use for the activities in paediatric population.

Overall, the principles of AMSP in adults are applicable to children; however, two aspects must be considered: (a) local protocols for antimicrobial use in children should not be simple dose-adjusted transcriptions of protocols for adults but be specifically developed, and (b) evidence for some interventions is more limited in children than in adults.

The fact that viral infections are more frequent as cause of acute respiratory infections in children should be outlined, and availability of appropriate diagnostic methods must be considered in order to help avoiding the unnecessary use of antibiotics.

For monitoring antimicrobial consumption, days of therapy (DOT) per 1000 patient-days is the preferred indicator.

Guidance recommendations for antimicrobial stewardship programs in patients attended at emergency departments (ED)

Multidisciplinary antimicrobial stewardship team with knowledge of the specific barriers for implementation of AMSP in the local ED must be formed.

Local empirical treatment guidelines with input from local epidemiology must be available for ED faculty.

Appropriate training for the basic aspects of infectious diseases diagnosis and treatment must be provided.

Specific appropriate clinical outcome indicators and evaluations of quality of prescriptions must be measured.

The coordination activity of preventive medicine specialists with primary care doctors or community centres or residences, responsible for the continuity of antibiotic treatments, will be essential. This activity will make it possible to change the antibiotic when the patient has attended the ED where he has received the antibiotic of choice and has gone home.

If individualized data on antibiotic prescriptions are not automatically available, pooled data weighted by the number of patients attended at the department (daily defined doses [DDD] per 100 patients admitted in the observation area, DDD per 100 patients discharged from de ED) may be considered.

Antimicrobial stewardship for specific syndromes and surgical prophylaxis

Guidance recommendations for antimicrobial stewardship programs in community-acquired pneumonia (CAP)

Increased adherence to CAP guidelines must be an objective of AMSP. Indicators for the measurement to adherence of the principles of treatment of CAP must be implemented.

Empirical therapy in CAP must be locally protocolized according to guidelines, considering patients' severity and local epidemiology.

Adherence to early antibiotic de-escalation, switch to oral therapy and short courses of therapy must be objectives of AMSP. Barriers for the implementation of these two strategies may be overcome by appropriate educational interventions.

Research regarding the effectiveness of rapid diagnostic molecular tests as a stewardship tool in CAP is needed; however, these techniques should be considered in advanced AMSP with evaluation of results.

The use of procalcitonin is useful to improve antibiotic use in patients with CAP, and may be incorporated as an aid tool together with appropriate clinical workout.

Guidance recommendations for antimicrobial stewardship programs in urinary tract infections (UTI)

Empirical antimicrobial therapy in UTI should be based on local guidelines. These guidelines should take into account local bacterial resistance rates, individual risk and severity of infections.

Antimicrobial stewardship teams should provide advice for optimizing directed therapy in UTI caused by MDRO.

Interventions to avoid the inappropriate use of antibacterials in asymptomatic bacteriuria must be implemented.

Interventions to improve adherence to short treatments according to specific type of infection and patients characteristics must be implemented.

Audits with feedback in selected patients or targeted microorganisms may be considered.

Guidance recommendations for antimicrobial stewardship program in vascular catheter-related bloodstream infections (VCA-BSI)

Promote the appropriate diagnosis and management of VCA-BSI by providing adequate training and adherence to guidelines.

Specifically, appropriate duration of therapy of VCA-BSI should be promoted.

Bacteraemia programs, in which unsolicited advice and follow-up is provided for all patients with bacteraemia (or at least for high risk patients and pathogens) should be implemented; measurement of adherence to quality-of-care indicators is recommended.

Guidance recommendations for antimicrobial stewardship programs in surgical antimicrobial prophylaxis (SAP)

Local adaptations of guidelines for SAP in all procedures performed in the hospital, agreed with surgeons and anaesthesiologists, should be available. The local guidelines must include the antibiotics of choice and alternatives, as well as the appropriate timing, dosing and duration of antibiotic prophylaxis. It is important to enhance other prophylactic measures and their implementation carried out by preventive medicine specialists.

Training about the principles of SAP should be provided to all staff involved.

Regular audits about adherence to local guidelines using standardized indicators must be performed, and feedback provided.

Specific interventions to improve SAP must be considered according to local resources and problems detected.

Other aspects of antimicrobial stewardship programs

Guidance recommendations for antimicrobial stewardship programs in aspects related to routes and ways of administration of antimicrobials

The different routes for antimicrobial administration, and the different modes of intravenous perfusions should be considered in local protocols; AMSP must include activities aiming at providing the most appropriate way to administer antibiotics to the patients.

Timely switch to oral therapy when indicated must be an objective for AMSP, and activities encouraging this practice should be implemented; they should include actions to avoid longer treatments once the oral route is started.

Infusion pumps facilitate the correct administration of intravenous antimicrobials and must be used in circumstances in which

extended or continuous perfusions are considered critical for the patient. Handling of these devices must be carried out by trained personnel.

Implication of nurses in AMSP is key in order to assure an appropriate administration of antibiotics.

Guidance recommendations for antimicrobial stewardship programs in aspects related to new antimicrobials

AMSP should promote the inclusion of new drugs in hospital formularies according to local needs and best evidence, in order to provide patients with the best available therapy in infections caused by MDRO.

AMSP should include local consensus guidelines including specific indications of use of new drugs according to the best available evidence and local epidemiology.

AMSP should implement non-compulsory interventions as auditing and feedback to facilitate the adherence to the established guidelines.

AMSP should monitor and evaluate the data concerning the outcomes of patients treated with new drugs, development of resistance to them and their impact in the overall epidemiology of MDRO.

Guidance recommendations for application of social sciences and behavioural change in antimicrobial stewardship programs

Antimicrobial stewardship interventions should be designed considering knowledge from behavioural and social sciences and should employ behaviour change techniques. Whenever possible, behaviour experts should be part of antimicrobial stewardship teams.

The prescribing behaviours that are intended to be changed should be precisely defined, and barriers and promoters should be analyzed locally.

Behaviour change techniques (BCTs) should be selected taking into account the main determinants of the desired and/or undesired behaviours. The interventions must combine several BCTs.

There are several behaviour's change theories and models that can be applied in the field of AMS. One of the most frequently adopted models for AMS is the behaviour change wheel.

It is advisable to conduct process evaluations of ongoing interventions in order to learn why they fail or succeed.

Guidance recommendations for e-tools implementation in antimicrobial stewardship programs

Whenever possible and feasible, e-tools should be included in AMS interventions to facilitate guidelines, clinical pathways and post prescription review.

The efficacy and safety of AMS e-tools should be validated through cluster randomized control trials or adequately controlled quasi-experimental designs.

AMS e-tools should be available for prescribers. Social media may be considered as tools to disseminate the AMSP resources.

Diagnostic stewardship

Guidance recommendations for diagnostic stewardship

Diagnostic stewardship principles should be part of any AMSP.

The adequacy of laboratory test requests and correct handling of specimens should be promoted among the activities of the AMSP.

Rapid microbiological diagnostic techniques for the adequate samples and patients, and rapid identification and susceptibility testing from positive blood cultures should be implemented and

associated with rapid active reporting and antimicrobial stewardship interventions.

The use of rapid viral diagnostic testing for respiratory pathogen should be promoted in the appropriate settings.

Non-culture-based fungal markers in patients with haematological malignancies at risk of invasive fungal infections must be implemented and associated with appropriate interpretation criteria to both improve diagnosis and facilitate adequate use of antifungals.

Fast-track protocols for selected patients (critical or immunocompromised patients) must be designed and implemented.

Provide cascade or selective reporting instead of over-reporting all tested antimicrobials.

Provide periodical data on cumulative antimicrobial susceptibility for optimizing empirical therapy, with appropriate stratification of data whenever possible.

Surveillance programs of multidrug-resistant pathogens for the detection of outbreaks and emerging new clones must be implemented.

Funding

This document has not received any kind of funding.

Conflict of interest

No conflicts of interest to disclose: JR-B, JLA, ECalbo, LE, AFP, JGR, JG, MVGN, SG, CG, CM, JM, JRPP, MTPR, PRB, PV.

EC has participated as a speaker at scientific meetings sponsored by Pfizer, MSD and Shionogi.

JPH has participated in advisory boards and as a speaker at scientific meetings sponsored by Pfizer, MSD, Menarini, Angelini, and Zambon.

NL has participated as a speaker at scientific meetings sponsored by Accelerate Diagnostics, bioMérieux, Menarini, MSD, Pfizer, and Shionogi.

XN has participated as a speaker at scientific meetings sponsored by Pfizer, Gilead, and MSD, and in advisory boards for Gilead.

AO has participated as a speaker at scientific meetings sponsored by Pfizer, MSD, and Shionogi.

PR has participated as a speaker at scientific meetings sponsored by Pfizer, MSD, Novartis, Menarini, Gilead, Becton-Dickinson, and Shionogi.

PRG has participated as a speaker at scientific meetings sponsored by Biomérieux, Shionogi, and MSD.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.eimc.2022.05.005](https://doi.org/10.1016/j.eimc.2022.05.005).