

The PIRASOA programme: design, structure, organisation and indicators of a comprehensive regional Institutional Programme for the Prevention and Control of Healthcare-associated Infections and Antimicrobial Stewardship for hospitals and primary care settings in Andalusia, Spain

Authors

María Dolores Rojo-Martín¹, Germán Peñalva², Carmen Pinto³, Inmaculada Salcedo⁴, Rocío Fernández-Urrusuno⁵, José Cabeza⁶, Juan de Dios Alcántara⁷, Olaf Neth⁸, Paloma Porras⁹, Javier Bautista¹⁰, José Garnacho-Montero¹¹, Rafael Sierra¹², Ángel Estella¹³, Carmen Lupión¹⁴, Elena Hevia¹⁵, Arantxa Irastorza¹⁶, José Luis Márquez¹⁶, María Luisa García-Gestoso¹⁷, Álvaro Pascual¹⁴, Jesús Rodríguez-Baño¹⁴, Raquel Valencia², María Antonia Pérez-Moreno², José Miguel Cisneros^{2*}, on behalf of the PIRASOA programme group

Affiliations

1. Department of Microbiology, University Hospital Virgen de las Nieves, Biomedical Institute of Granada, Granada, Spain
2. Department of Infectious Diseases, Microbiology and Preventive Medicine, Institute of Biomedicine of Seville (IBiS), University Hospital Virgen del Rocio, CSIC, University of Seville, Seville, Spain
3. Department of Pharmacy, Hospital de Guadix-Loja, Granada, Spain
4. Department of Preventive Medicine and Public Health, University Hospital Reina Sofia, Cordoba, Spain

5. Pharmacy Service, Primary Healthcare District Aljarafe-Sevilla Norte, Mairena del Aljarafe, Seville, Spain
6. Clinical Unit of Pharmacy of Granada, University Hospital San Cecilio, Granada, Spain
7. Primary Care Clinical Unit 'Luis Taracido', Bollullos Par del Condado, Healthcare District of Huelva Condado, Huelva, Spain
8. Department of Paediatric Infectious Diseases, Rheumatology, and Immunodeficiency, Institute of Biomedicine of Seville (IBiS), University Hospital Virgen del Rocio, CSIC, University of Seville, Seville, Spain
9. Primary Care Clinical Unit 'La Candelaria', Healthcare District of Seville, Seville, Spain
10. Department of Pharmacy, Institute of Biomedicine of Seville (IBiS), University Hospital Virgen del Rocio, CSIC, University of Seville, Seville, Spain
11. Department of Critical Care, University Hospital Virgen Macarena, University of Seville, Seville, Spain
12. Intensive Care Unit, University Hospital Puerta del Mar, University of Cadiz, Cadiz, Spain
13. Intensive Care Unit, Jerez de la Frontera Hospital, Jerez de la Frontera, Cadiz, Spain
14. Department of Infectious Diseases and Clinical Microbiology, University Hospital Virgen Macarena, Institute of Biomedicine of Seville (IBiS), University of Seville, Seville, Spain
15. Promotion of Rational Use of Medicines Service, Sub-Directorate of Pharmacy and Provisions, Directorate General of Healthcare and Outcomes in Health, Andalusian Healthcare Service, Seville, Spain
16. Department of Comprehensive Health Plans, Supporting Services of the Andalusian Healthcare Service, Seville, Spain
17. Primary Care Clinical Unit 'Puerta Este', Healthcare District of Seville, Seville, Spain

Corresponding author: José Miguel Cisneros, PhD

Phone: +34-955-01-21-85. E-Mail: jmcisnerosh@gmail.com

Abstract

Background

Antimicrobial Stewardship Programmes (ASPs) and Healthcare-associated Infections (HAIs) Programmes are recommended by scientific societies as a key intervention to fight against antimicrobial resistance (AMR), but their implementation and sustainability are not easy to achieve. Spain is among the European countries with the highest antimicrobial consumption, as well as high AMR rates; despite this fact, development of ASPs is scarce. In this scenario we designed and implemented a long-term comprehensive Institutional Programme for the Prevention and Control of Healthcare-associated Infections and Appropriate Use of Antimicrobials (PIRASOA) in both inpatient and outpatient care covering the whole Public Healthcare System of Andalusia, which is the most populated autonomous region in Spain with 8.4 million inhabitants.

Methods/design

This protocol describes the design, structure, organisation and indicators of the PIRASOA programme, as well as the methodology for its implementation development, data collection, assessment, feedback and continuity over time.

This education-based multifaceted programme with institutional support is divided in two sub-programmes integrated into daily clinical practice: the HAIs sub-programme, aimed at hospitals, and the ASP sub-programme, applied to both hospitals and primary care.

Conclusions

The PIRASOA programme is the first institutional comprehensive education-based programme integrated into daily clinical practice to prevent and control HAIs and to

optimise the use of antimicrobials implemented in the entire public healthcare system of an autonomous region in Spain, being among the first integral regional programmes in Europe. The assessment of antimicrobial consumption, clinical and microbiological indicators and reports are performed on a quarterly basis and are available for assessment and feedback in near real-time with only a three-month delay. The programme, started on 1 January 2014, has been adequately implemented in all public centres of Andalusia and it is committed to be integrated into daily clinical practice. Data collection is ongoing. Long-term results will be analysed and published from 2018 onwards.

Trial registration

Not applicable

Keywords: Healthcare-associated infections, antimicrobial stewardship programmes, antimicrobial resistance, antibiotic policy, infection control, antibiotic prescription, primary care, hospital infections

Background

Healthcare-associated infections (HAIs) are a major cause of morbidity and mortality, frustration for healthcare professionals and high public expenditure. Furthermore, HAIs are becoming more difficult to manage because they are increasingly being caused by multidrug-resistant bacteria (MDRB). Antimicrobials are a wide group of remarkably effective and complex drugs. Unfortunately, their effectiveness is decreasing rapidly due to increasing antimicrobial resistance (AMR) rates. The latest episode of this fight against MDRB is the worldwide dissemination of carbapenem-resistant Enterobacteriaceae [1]. Consequently, AMR also causes an increase in mortality, suffering and an economic burden. In addition, it is a threat to advanced medicine and to the sustainability of healthcare systems. Based on the ECDC estimates, 25000 patients die yearly in the European Union (EU) from MDRB-caused infections. These infections result in extra healthcare costs and productivity losses of at least 1.5 billion euros per year [2]. In this worrisome international scenario, Spain is one of the world's leading countries in antibiotic consumption per inhabitant and in incidence of infections caused by AMR [3].

On the basis of the above, scientific societies have published guidelines for developing institutional programmes to enhance antimicrobial stewardship [4-5]. Different nations and more recently the EU have produced documents for antimicrobial resistant strategies and for prudent use of antimicrobials [6-7].

Different local initiatives on infection control [8] and antimicrobial stewardship [9-11] have proven that it is possible to reduce HAIs and to improve the appropriate use of antimicrobials, but information about comprehensive ASP and HAI-control

programmes is scarce, particularly in the case of implementing those programmes in healthcare systems integrating both hospital and community care [12].

In Andalusia, the most populated autonomous region in Spain, the Andalusian Ministry of Health and Social Well-being approved the PIRASOA programme (Institutional Programme for the Prevention and Control of Healthcare Associated Infections and Appropriate Use of Antimicrobials), on 1 February 2013, in response to a professional initiative. The aim of this article is to describe the PIRASOA programme.

Methods/design

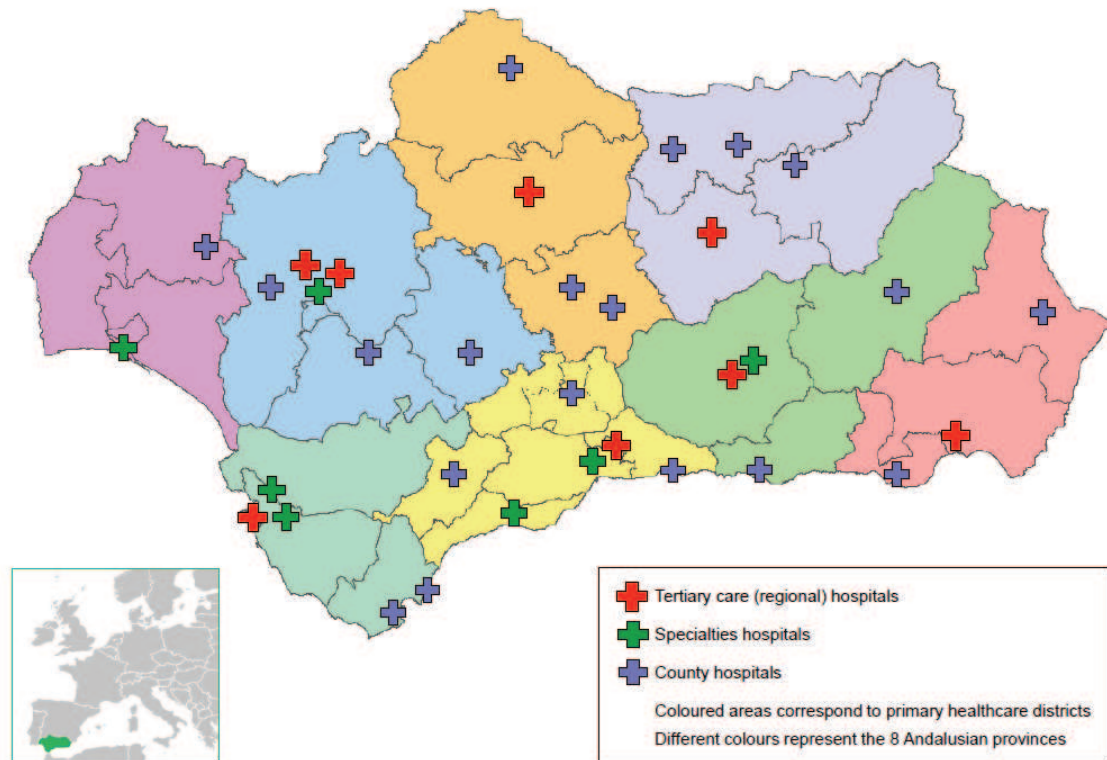
1. Objectives and features of the PIRASOA programme

The **overall objectives** of the programme are: 1) to reduce the incidence of HAIs, and 2) to optimise the use of antimicrobial drugs, both until reaching similar levels to those European countries with better indicators, in the entire Andalusian Public Healthcare System (SSPA). The SSPA serves a population of 8.4 million inhabitants, with a workforce of 93366 employees including 17182 physicians grouped in 982 clinical units distributed in 34 hospitals and 27 healthcare districts with a budget of 8683 million euros [13].

The **main features of the programme** are: 1) the scope of action is the SSPA, including both hospital and primary care settings ([Figure 1](#)); 2) it integrates the ASP and HAI sub-programmes in hospital settings and the ASP in primary care; 3) it is based on the professional leadership and on the scientific knowledge of the most involved specialities in the prevention, diagnosis, and treatment of infections; 4) it is carried out by multidisciplinary teams which work concertedly to achieve the programme goals; 5)

these teams are coordinated by the Medical Director of each healthcare centre within the frame of the hospitals Antimicrobial and Infections Committees. The composition of the teams will be detailed further below; 6) education is the key tool of the programme; 7) the outcomes are measurable and assessable, with clinical and efficiency objectives. Evaluation will be based initially on self-assessment in order to become comparable among centres further on and it will be carried out by means of a scorecard with shared standardised indicators which will allow for benchmarking; 8) it is organised around Clinical Units (CUs), -the basic organisational structures of the SSPA-, and the programme goals will be included in the management arrangements for each CU, as well as in the Contract-Programme signed between the Ministry of Health and Social Wellbeing of Andalusia and all healthcare centres of the SSPA; 9) the human and financial resources of the programme are those from the SSPA which should be prioritised to the necessities of the programme by the directors of each centre; 10) the dedication of the healthcare professionals to the programme is part of their everyday tasks because HAIs and ASPs are priority objectives for the CUs, hospitals, primary care districts, and the SSPA.

Figure 1. Map of the Andalusian Public Healthcare System (SSPA) hospitals and primary care settings



2. Organisational structure

The PIRASOA programme includes two sub-programmes: the HAI and the ASP, the latter being divided into two settings: hospital ASP and primary care ASP. The Primary Care in the Andalusian Public Healthcare System (SSPA) is organised in healthcare districts, local operational structures that comprise a certain number of healthcare centres or primary care practices.

The PIRASOA programme is based on a cross-sectional organisation with three interconnected levels (Table 1).

Table 1**PIRASOA organisational structure**

Andalusian Public Healthcare System	Local teams Hospital/Primary Care District	Clinical Unit
PIRASOA programme Coordinator	Medical Director (hospital) / Healthcare Director (primary care district)	Head of Clinical Unit
Scientific Committee	HAI and ASP teams ^a	Reference counsellors: physician and nurse
Pharmacists Specialists in preventive medicine Microbiologists Paediatricians General practitioners Intensive care physicians Infectious diseases consultants ^b Nurses ^c	<p><i>Hospital HAI local team</i> Coordinator: a specialist in preventive medicine Members: a microbiologist, an intensive care doctor, nurses^c, and an infectious diseases consultant^b Optional members: paediatricians, etc.</p> <p><i>Hospital ASP local team</i> Coordinator: a physician expert in antimicrobials Members: a pharmacist, a microbiologist, a specialist in preventive medicine, and an infectious diseases consultant^b Optional members: intensive care doctors, paediatricians, etc.</p> <p><i>Primary Care District ASP local team</i> Coordinator: a physician or a pharmacist Members: a general practitioner, a paediatrician, a pharmacist, and an epidemiologist</p>	
Reference Laboratory for Molecular Typing of Nosocomial Pathogens	Microbiologists	

^a adapted to each centre characteristics

^b specialists in Internal Medicine, experts in Infectious Diseases

^c HAI control nurses

2.1. Scientific Committee

The members of the Scientific Committee were selected from the scientific societies most involved in the prevention, diagnosis and treatment of infections [listed in [Additional file 1](#)]. The committee roles and responsibilities are: 1) to draw up the

programme; 2) to manage and coordinate it; 3) to work towards the implementation of the online communication systems, data logging, and assessment through a website; 4) to disseminate the programme; 5) to design and conduct the training plan of the programme; 6) to monitor and evaluate the results; 7) to analyse and disseminate the information and the knowledge generated; and 8) to assess quality control.

2.2. HAI and ASP teams

Local teams

The Medical Directors and the Healthcare Directors are the chairs of the PIRASOA programme at each hospital or primary care district, respectively. By agreeing with the Antimicrobial and Infections Commission, they are responsible for selecting the best-trained professionals to be members of the HAI and ASP local teams. The directors will meet regularly with the HAI and ASP team coordinators to facilitate the solution of problems and to verify that the programme is operating concertedly. The local teams composition is described in [Table 1](#).

The local teams are responsible for: 1) adapting the PIRASOA programme to their own hospital/primary care district, writing an operational document named 'local project' to be sent to the Scientific Committee when completed; 2) presenting the programme in the frame of the clinical sessions performed at every CU involved in HAIs and ASPs; 3) implementing the programme; 4) the proper fulfilment of the programme indicators; 5) evaluating the outcomes periodically; 6) the feedback of the information by means of regular reports.

Clinical Units

The hospital and primary care CUs are the settings where the PIRASOA programme has to be performed as a part of routine clinical practise. The heads of each CU have the responsibility for: 1) the correct development of the programme in their units, under the coordination of the HAls (hospital) and ASP (hospital and primary care district) local teams; 2) including the programme as an objective within the management arrangements of the unit; 3) selecting the referring professional or professionals of the CU who will perform the programme in cooperation with their local teams; 4) providing time available for the professionals of their CUs to carry out the programme tasks as a part of the scheduled work time.

2.3. Reference Laboratory

Molecular typing of clinically relevant multidrug-resistant bacteria in Andalusian hospitals is carried out in the Reference Laboratory for Molecular Typing of Nosocomial Pathogens, located in the Microbiology Service of the Hospital Virgen Macarena Seville, Spain. In this centre, resistance mechanisms, main circulating clones and clonal relationships of nosocomial multidrug-resistant bacteria are investigated.

The portfolio is shown in [Table 2](#).

Table 2

Reference Laboratory portfolio

Resistance mechanisms detection	Molecular typing
<p>Methicillin-resistance in <i>Staphylococcus aureus</i></p> <p>vanA and vanB genes in <i>Enterococcus spp</i></p> <p><i>cfr</i>-carrying <i>Staphylococcus spp</i></p> <p>Extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (TEM, SHV, CTX-M)</p> <p>Plasmid-mediated AmpC beta-lactamase genes (FOX, DHA, CMY)</p> <p>Mutations in regulatory genes of chromosomally encoded AmpC beta-lactamase expression</p> <p>OXY β-lactamases in <i>Klebsiella oxytoca</i></p> <p>Carbapenemases: – OXA-type carbapenemases in <i>Acinetobacter baumannii</i> – IMP, VIM, OXA-48, NDM, KPC (<i>A. baumannii</i>, <i>Pseudomonas aeruginosa</i>, Enterobacteriaceae)</p> <p>Mutational upregulation of efflux systems: MexABOprM (<i>P. aeruginosa</i>), adeABC (<i>A. baumannii</i>), acrAB (<i>Klebsiella pneumoniae</i>)</p> <p>Identification of mobile genetic elements (plasmids, integrons, transposons and insertion sequences)</p>	<p>Methicillin-resistant <i>S. aureus</i></p> <p>Linezolid-resistant <i>S. aureus</i></p> <p>Glycopeptide-resistant enterococci</p> <p>OXY-producing <i>K. oxytoca</i></p> <p>ESBL-producing <i>Escherichia coli</i> and <i>K. pneumoniae</i></p> <p>Carbapenemase-producing Enterobacteriaceae</p> <p>Multidrug-resistant <i>Serratia marcescens</i> and <i>Enterobacter spp</i></p> <p>Other multidrug-resistant Enterobacteriaceae</p> <p>Multidrug-resistant <i>A. baumannii</i> and <i>P. aeruginosa</i></p>

3. Healthcare-associated Infections sub-programme for hospitals

3.1. Objectives

1) to reduce the overall incidence of HAIs; 2) to diminish the incidence of HAIs due to MDRB; 3) to control the outbreaks of MDRB; 4) to generate knowledge about the clinical and ecologic impact of ASP; 5) to reduce HAI care spending.

3.2. Indicators

All the HAI indicators have been selected based on the international standards. A total of 74 indicators belonging to five groups were included: prevalence of HAIs in hospitals, incidence and incidence density (ID) of infection in the ICU, incidence and ID of the surgical site infections by categories, process assessment (hand hygiene, zero pneumonia in ICU, bacteraemia zero ICU and isolation measures) and ID incidence of global BMR infections (caused by *Clostridium difficile* and the most frequent MDR bacteria known as ESKAPE-pathogens). For the surgical site infections, each hospital must select four indicators as optional to report, according to its own casuistry, resources, and necessities. The rest of the indicators are considered mandatory. These indicators are described in [Table 3](#).

Table 3
Indicators from the Healthcare-associated Infections module for hospitals

Indicator	Definition	Features
Point prevalence-based indicators		
Prevalence of patients with nosocomial infection in current admission	No. of inpatients with nosocomial infection in current admission x 100/No. of inpatients	Yearly Mandatory
Prevalence of patients with nosocomial infections acquired in the hospital	(No. of inpatients with nosocomial infections acquired during their current admission + No. of inpatients with nosocomial infections acquired during a previous admission in the same hospital) x 100/No. of inpatients	Yearly Mandatory
Prevalence of nosocomial infections in the hospital	No. of nosocomial infections during the current admission x 100/No. of inpatients	Yearly Mandatory
Prevalence of nosocomial infections acquired in the hospital	(No. of nosocomial infections acquired during the current admission + No. of nosocomial infections acquired during a previous admission in the same hospital) x 100/No. of inpatients	Yearly Mandatory
Indicators for HAIs in the ICU ^a		
Incidence of catheter-related bacteraemia in the adult ICU	No. of patients with central venous catheter-related bacteraemia in the adult ICU x 100/No. of patients with central venous catheter in the adult ICU	Consecutive quarters Mandatory
Incidence density of catheter-related bacteraemia in the adult ICU	No. of central venous catheter-related bacteraemia in the adult ICU x 1000/central venous catheter-days in the adult ICU	Consecutive quarters Mandatory

Incidence of ventilator-associated pneumonia (VAP) in the adult ICU	No. of patients with VAP in the ICU x 100/No. of patients on mechanical ventilation in the adult ICU	Consecutive quarters Mandatory
Incidence density of VAP in the adult ICU	No. of VAP in the adult ICU x 1000/ mechanical ventilation-days in the adult ICU	Consecutive quarters Mandatory
Incidence of urinary catheter-associated urinary tract infection (UTI) in the adult ICU	No. of patients using urinary catheterisation in the adult ICU with urinary catheter-associated UTI x 1000/No. of patients using urinary catheterisation in the adult ICU	Consecutive quarters Optional
Incidence density of urinary catheter-associated UTI in the adult ICU	No. of UTI in patients using urinary catheterisation in the adult ICU x 1000/urinary catheter-days in the adult ICU	Consecutive quarters Optional
Indicators for surgical site infections ^b		
Incidence of SSI in heart surgery with sternotomy	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in heart surgery with sternotomy x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Mandatory
Incidence of SSI in colo-rectal resection surgery	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in colo-rectal resection surgery x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Mandatory
Incidence of SSI in complete hip prosthesis replacement surgery	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in complete hip prosthesis replacement surgery x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Mandatory
Incidence of SSI in complete knee prosthesis replacement	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in complete knee prosthesis replacement x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Mandatory
Incidence of SSI in laminectomy and spinal fusion surgery	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in laminectomy and spinal fusion x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Optional
Incidence of SSI in cholecystectomy	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in cholecystectomy x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Optional
Incidence of SSI in Caesarean section	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in Caesarean section x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Optional
Incidence of SSI in cataract surgery	No. of patients with SSI during the surveillance period (up to 30 days after surgery/365 days in case of implant placement or prosthesis) in cataract surgery x 100/No. of patients who underwent this surgery during the period	Consecutive quarters Optional
Process indicators		

Percentage of adherence to the hand hygiene indications ^c	No. of actions performed x 100/No. of opportunities	Quarterly Mandatory
Percentage of compliance of the preventive measures in Pneumonia Zero ^d	No. of patients on mechanical ventilation with all items affirmative in an observation x 100/No. of observations carried out in the quarter	Quarterly Mandatory
Percentage of compliance of the Bacteraemia Zero checklist ^e	No. of central venous catheters with all checklist items affirmative x 100/No. of CVC checklists performed in the quarter	Quarterly Mandatory
Percentage of compliance with contact precaution measures	No. of observations performed in patients with contact precaution measures indication and with all checklist items affirmative x 100/No. of observations performed in patients with contact precaution measures indication in the quarter	Quarterly Mandatory
Multi-drug resistant bacteria (MDRB) and <i>Clostridium difficile</i> indicators ^f		
Incidence density of inpatients with methicillin-resistant <i>Staphylococcus aureus</i>	No. of inpatients with methicillin-resistant <i>S. aureus</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with vancomycin resistant <i>Enterococcus</i>	No. of inpatients with vancomycin resistant <i>Enterococcus</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with ESBL <i>Escherichia coli</i>	No. of inpatients with ESBL <i>E. coli</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with carbapenemase-producing <i>Enterobacteriaceae</i>	No. of inpatients with carbapenemase-producing <i>Enterobacteriaceae</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with ESBL <i>Klebsiella pneumoniae</i>	No. of inpatients with ESBL <i>Klebsiella pneumoniae</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with multidrug-resistant <i>Pseudomonas aeruginosa</i> ^g	No. of inpatients with multidrug-resistant <i>P. aeruginosa</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with multidrug-resistant <i>Acinetobacter baumannii</i> ^h	No. of inpatients with multidrug-resistant <i>A. baumannii</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory
Incidence density of inpatients with <i>Clostridium difficile</i>	No. of inpatients with <i>C. difficile</i> infection/colonisation x 1000/No. of total stays during the trimester	Quarterly Mandatory

^a Data for infections which occurred in the ICUs were locally collected using a European-linked surveillance programme ENVIN-HELICS [20,21].

^b All the SSI indicators will be disaggregated for patient's risk SSI (0, 1, 2, and 3), following the CDC's National Nosocomial Infection Surveillance (NNIS) System Risk Index.

^c This indicator will be measured by using the WHO observation checklist [22].

^d This indicator will be assessed by using the Spanish "Zero-VAP" bundle checklist [23].

^e This indicator will be measured by using the "Bacteremia Zero project" checklist [24].

^f Duplicated bacterial strains in the same patient (isolation of the same pathogen, regardless of the collection site, with same susceptibility test results ≤ 365 days) will be not included in the

surveillance, as well as those samples from environment and colonisation screening (nasal smears, pharyngeal swabs, pressure ulcers, perianal or rectal smears, tracheostomy, etc.) as these outcomes will depend on the surveillance intensity of each hospital.

^g MDR *P. aeruginosa* will be considered those isolates resistant to ceftazidime and/or carbapenems (meropenem and/or imipenem).

^h MDR *A. baumannii* will be considered those carbapenem-resistant (meropenem and/or imipenem) isolates.

3.3. Actions

Actions to be undertaken by the **Scientific Committee** will be: 1) programme design and setup; 2) presentation to all the hospital teams; 3) inclusion as an economic objective within the Contract-Programme between the SSPA and hospitals; 4) comparative analysis of the evolution of hospitals outcomes; 5) specific training on demand; 6) dissemination of the overall results and knowledge; 7) support of the Epidemiological Surveillance System of Andalusia (SVEA) with the detection, study and control of alerts by MDRB.

Actions to be undertaken by the hospitals **HAI local teams**, in cooperation with the Scientific Committee, will be: 1) adapt the PIRASOA programme to their own hospital and write the operational document 'local project' to be sent to the Scientific Committee when completed; 2) presenting the programme in the frame of the clinical sessions performed at every CU involved in HAIs; 3) surveillance and fulfilment of the programme indicators; 4) support of the SVEA with the detection, study and control of alerts by MDRB; 5) training; 6) bundles; 7) regular evaluation of outcomes; 8) feedback of the information by means of regular reports.

4. Antimicrobial Stewardship Programme for hospitals and primary care

4.1. Objectives

1) to improve the correct use of antimicrobial drugs; 2) to improve the prognosis of patients with severe infections; 3) to reduce the adverse effects of the antimicrobials; 4) to reduce the antibiotic pressure; 5) to reduce the antimicrobial resistance; 6) to generate knowledge; 7) to reduce healthcare spending.

4.2. Educational interviews

ASPs must include regular assessment of the quality of antimicrobial treatments, both in hospitals and in primary care. The main activity of the ASP consists of a training programme directed towards all antibiotic prescribers in every hospital and primary healthcare centre based on Educational interviews (EIs), which are training activities based on the review of a real antimicrobial treatment between two physicians, an advisor and a prescriber. The methodology of the interviews has been previously described by us and implemented in a hospital setting [10]. Most recently, the EIs have shown their contribution to improve the quality of prescriptions leading to a sustained ecological and clinical impact, reducing the incidence and mortality of hospital acquired candidemia and multidrug-resistant bacteria bloodstream infections within an ASP in a tertiary-care hospital over a five-year period [11]. We have subsequently adapted the hospital EI to the primary care ASP.

The EI is held with the physician responsible for the antimicrobial treatment without prior warning. The EIs are carried out in a pedagogical way, as the main objective of the interview is to elevate the knowledge about infectious diseases treatments of all

the general practitioners and paediatricians in the centre, rather than to change any antimicrobial therapy. With this aim, the advisor reviews the antimicrobial treatment with the prescriber, examines the patient's clinical data and talks over the main aspects of the diagnosis and prescribed treatment following a purpose-designed questionnaire. Prescriptions are rated as 'appropriate' when all questions of the checklist have been evaluated positively. If one or more of the items were incorrectly accomplished, the prescription will be rated as 'inappropriate'. In order to make homogeneous recommendations, advisors will follow the criteria set out in the clinical guidelines of their own hospital or healthcare district based on the local epidemiological data, and on the best scientific evidence available. The acceptance of the programme is assessed by means of a voluntary anonymous questionnaire, in which the interviewed clinicians will give their opinion about the usefulness of the EI [10]. The satisfaction survey forms for hospitals and for primary care are given in [Additional files 2 and 3](#), respectively.

EIs for hospital settings

The EIs are carried out in each hospital by a group of clinical advisors, which will be selected from among doctors considered as local opinion-leaders in the management of patients with infectious diseases in each CU. In some cases, the clinical advisor could be a pharmacist. Each advisor will conduct EIs in his CU, randomly selecting a specific antimicrobial treatment previously prescribed. Structured interviews on target prescriptions (e.g. those including high-impact drugs or any lasting ≥ 7 days) can be performed as well. Three types of prescriptions are evaluated: perioperative prophylaxis, empirical, and targeted antimicrobial treatments. The EI form for hospitals is given in [Additional file 4](#). The number of EIs scheduled for each clinical unit will be

proportional to its antimicrobial consumption, requiring a maximum of one working hour per week. CUs with consumption below 50 DDDs will conduct one EI per week, units with consumptions between 50 and 100 DDDs will perform two, and those CUs with consumption beyond 100 DDDs will conduct three EIs per week.

EIs for primary care settings

This activity is carried out in each primary care practice by a clinical advisor, either a general practitioner or a paediatrician, who is selected from amongst doctors considered as local opinion leaders in the management of patients with infectious diseases in each healthcare centre. Each advisor conducts EIs in his centre, randomly selecting a specific antimicrobial treatment previously prescribed. Two types of prescriptions are evaluated: empirical and targeted antimicrobial treatments. The EI form for primary care is given in [Additional file 5](#). The number of EIs scheduled for each primary care practice will be proportional to the number of practitioners. The aim is a minimum of one EI a month per prescriber. Each primary care advisor will perform 3 to 5 EIs, requiring a maximum of one working hour per week.

4.3. Indicators for hospital ASP

All the ASP indicators are considered mandatory to be informed.

Hospital ASP indicators are divided up into process and outcome indicators. Clinical indicators assess the impact of the antimicrobial usage in terms of clinical outcomes. Antimicrobial consumption indicators allow hospitals to monitor their own consumption and to be compared with the others. These indicators are described in [Table 4](#).

Table 4

ASP indicators for hospitals

Indicator	Definition	Features
Process indicators		
Overall rate of inappropriate antimicrobial treatments	No. of inappropriate educational interviews (EIs) x 100/Total number of EIs	Quarterly Mandatory
Rate of inappropriate perioperative prophylaxis antimicrobial treatments	No. of inappropriate perioperative prophylaxis EIs x 100/Total number of perioperative prophylaxis EIs	Quarterly Mandatory
Rate of inappropriate empirical antimicrobial treatments	No. of inappropriate empirical EIs x 100/Total number of empirical EIs	Quarterly Mandatory
Rate of inappropriate targeted antimicrobial treatments	No. of inappropriate targeted EIs x 100/Total number of targeted EIs	Quarterly Mandatory
Clinical indicators for hospital ASP		
Mortality rate due to bloodstream infection by <i>Escherichia coli</i>	No. of patients with bloodstream infection by <i>E. coli</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>E. coli</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Pseudomonas aeruginosa</i>	No. of patients with bloodstream infection by <i>P. aeruginosa</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>P. aeruginosa</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Klebsiella pneumoniae</i>	No. of patients with bloodstream infection by <i>K. pneumoniae</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>K. pneumoniae</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Acinetobacter baumannii</i>	No. of patients with bloodstream infection by <i>A. baumannii</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>A. baumannii</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Staphylococcus aureus</i>	No. of patients with bloodstream infection by <i>S. aureus</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>S. aureus</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Neisseria meningitidis</i>	No. of patients with bloodstream infection by <i>N. meningitidis</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>N. meningitidis</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Streptococcus pneumoniae</i>	No. of patients with bloodstream infection by <i>S. pneumoniae</i> who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>S. pneumoniae</i>	Quarterly Mandatory
Mortality rate due to bloodstream infection by <i>Candida</i> spp.	No. of patients with bloodstream infection by <i>Candida</i> spp. who die within 14 days after diagnosis x 100/No. of patients with bloodstream infection by <i>Candida</i> spp.	Quarterly Mandatory
Mortality rate caused by community-acquired pneumonia ^a	No. of patients with community-acquired pneumonia who die within 14 days after diagnosis x 100/No. of patients with pneumonia	Quarterly Mandatory
Antimicrobial consumption indicators for hospitals		
Total antimicrobial drug expenses on inpatients	Euros spent in this budget line (ATC codes J01 and J02)	Quarterly Mandatory
Total antimicrobial drug expenses on outpatients	Euros spent in this budget line (ATC codes J01 and J02)	Quarterly Mandatory

Total antimicrobial drug expenditure	Euros spent in this budget line (ATC codes J01 and J02)		Quarterly Mandatory
Overall DDD/1000 OBD of antimicrobials ^b	Total DDD of antibiotic (J01) and antifungals (J02) a trimester x 1000/No. of total stays during the trimester		Quarterly Mandatory
DDD/1000 OBD of a certain antimicrobial drug ^b	Consumption (grams) of a certain antimicrobial drug a trimester x 1000/DDD of this antimicrobial drug x No. of total stays during the trimester		Quarterly Mandatory
Antimicrobials to be monitored for hospitals ASP			
amoxicillin	meropenem	linezolid	fluconazole
co-amoxiclav	doripenem	cotrimoxazole	voriconazole
cefadroxil	ciprofloxacin	clindamycin	posaconazole
cefazolin	levofloxacin	metronidazole	itraconazole
ceftriaxone	moxifloxacin	fidaxomicin	liposomal amphotericin B
cefotaxime	tigecycline	erythromycin	amphotericin B lipid
ceftazidime	colistin	clarithromycin	complex
cefepime	cloxacillin	azithromycin	amphotericin B
piperacillin-tazobactam	vancomycin	gentamicin	deoxycholate
ertapenem	teicoplanin	tobramycin	casposungin
imipenem	daptomycin		micafungin
			anidulafungin

^a The mortality rate caused by community-acquired pneumonia will be additionally broken down into CURB-65 scores 2, 3, 4 and 5.

^b The unit of measure will be the Defined Daily Doses (DDD) per 1000 occupied bed-days (OBD), following the Anatomical Therapeutic Chemical Classification (ATC/DDD) methodology [25]

^c Multi-drug resistant bacteria (MDRB) and *Clostridium difficile* indicators are described in Table 3.

4.4. Actions for hospital ASP

The hospital ASP actions to be undertaken by the **Scientific Committee** will be: 1) programme design and setup; 2) presentation to all the local teams; 3) inclusion as an economic objective within the Contract-Programme between the SSPA and centres; 4) comparative analysis of the evolution of the outcomes; 5) specific training on demand; 6) dissemination of the overall results and knowledge.

The actions to be undertaken by the hospitals **ASP local teams**, in cooperation with the Scientific Committee, will be: 1) adapt the PIRASOA programme to their own centre, and write the operational document 'local project' to be sent to the Scientific Committee when completed; 2) presenting the programme in the frame of the clinical sessions performed at every CU involved in antibiotic prescription or healthcare

centre; 3) inclusion as an economic objective within the management arrangements for each one; 4) programme implementation:

a) Updating of the local clinical practice guidelines for antimicrobial treatment, adapted to the local epidemiology. It is essential to update these guidelines with a participatory approach in order to be considered as their own contribution. The guidelines should be easily available online, either on the Internet, hospital's intranet or mobile devices [14].

b) Performance of EIs as a part of everyday clinical practice, as described previously in point 4.2.

c) Regular evaluation of the results of the indicators in a quarterly basis.

d) Feedback of the information to each CU or healthcare centre by means of quarterly reports.

4.5. Indicators for primary care ASP

In primary care, the potential impact of the ASP on the incidence of MDRB infections has to be assessed by means of MDRB indicators. AMR will be defined according to the reports on antimicrobial susceptibility provided by each health district's referral hospital laboratory of Microbiology. Measuring antimicrobial usage will allow healthcare centres to monitor their own consumption and to be compared with the others. All the primary care ASP indicators are considered mandatory to be informed. Every healthcare district will report them on a quarterly basis. These indicators are described in [Table 5](#).

TABLE 5

ASP indicators for primary care

Indicator	Definition	Features
Process indicators for primary care ASP		
Overall rate of inappropriate antimicrobial treatments in primary care	No. of inappropriate educational interviews (EIs) x 100/Total number of EIs in the healthcare district	Quarterly Mandatory
Rate of inappropriate empirical antimicrobial treatments in primary care	No. of inappropriate empirical EIs x 100/Total number of empirical EIs in the healthcare district	Quarterly Mandatory
Rate of inappropriate targeted antimicrobial treatments in primary care	No. of inappropriate targeted EIs x 100/Total number of targeted EIs in the healthcare district	Quarterly Mandatory
MDRB indicators for primary care ASP ^a		
Incidence Density of outpatients with methicillin resistant <i>Staphylococcus aureus</i>	No. of outpatients with methicillin resistant <i>S. aureus</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with co-amoxiclav resistant <i>Escherichia coli</i>	No. of outpatients with co-amoxiclav resistant <i>E. coli</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with ciprofloxacin resistant <i>Escherichia coli</i>	No. of outpatients with ciprofloxacin resistant <i>E. coli</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with ESBL <i>Escherichia coli</i>	No. of outpatients with ESBL <i>E. coli</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with ESBL <i>Klebsiella pneumoniae</i>	No. of outpatients with ESBL <i>K. pneumoniae</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with penicillin and cefotaxime resistant <i>Streptococcus pneumoniae</i>	No. of outpatients with penicillin and cefotaxime resistant <i>S. pneumoniae</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with erythromycin resistant <i>Streptococcus pyogenes</i>	No. of outpatients with erythromycin resistant <i>S. pyogenes</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with co-amoxiclav resistant <i>Haemophilus influenzae</i>	No. of outpatients with co-amoxiclav resistant <i>H. influenzae</i> infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Incidence Density of outpatients with ciprofloxacin resistant <i>Salmonella</i> spp.	No. of outpatients with ciprofloxacin resistant <i>Salmonella</i> spp. infection/colonisation x 1000/No. of inhabitants in the healthcare district	Quarterly Mandatory
Antimicrobial consumption indicators for primary care		
Total antimicrobial drug expenditure in primary care	Euros spent in this budget line (ATC codes J01 and J02) in the healthcare district during the trimester	Quarterly Mandatory
Overall DHD of antimicrobials in primary care ^b	Total DDD of antibiotic (J01) and antifungals (J02) x 1000/ No. of inhabitants in the healthcare district during the trimester	Quarterly Mandatory

DHD of a certain antimicrobial drug ^c	No. of packaging units sold of a certain antimicrobial drug x No. of pharmaceutical forms per package x grams of active ingredient in each pharmaceutical form x 1000/DDD of this antimicrobial drug x No. of inhabitants in the healthcare district during the trimester			Quarterly Mandatory
Antimicrobials to be monitored for primary care ASP				
amoxicillin	cefixime	clindamycin	azithromycin	
co-amoxiclav	ciprofloxacin	metronidazole	fosfomycin	
cefadroxil	levofloxacin	erythromycin	fluconazole	
ceftibuten	moxifloxacin	clarithromycin	itraconazole	
cefuroxime	cotrimoxazole			

^a Duplicated bacterial strains in the same patient (isolation of the same pathogen, regardless of the collection site, with same susceptibility test results ≤365 days) will be not included in the surveillance.

^b The unit of measure will be the DHD: Defined Daily Doses (DDD) per 1000 inhabitants, following the Anatomical Therapeutic Chemical Classification (ATC/DDD) [25]

^c The number of inhabitants to be considered in each healthcare district will be the number of individual public healthcare cards.

4.6. Actions for primary care ASP

The primary care ASP actions to be undertaken by the **Scientific Committee** will be: 1) programme design and setup; 2) presentation to all the primary care districts teams; 3) inclusion as an economic objective within the Contract-Programme between the SSPA and healthcare districts; 4) comparative analysis of the evolution of healthcare districts outcomes; 5) specific training on demand; 6) dissemination of the overall results and knowledge.

The Primary Care in the Andalusian Public Healthcare System (SSPA) is organized in healthcare districts, local operational structures that comprise of a certain number of healthcare centres or primary care practices.

The actions to be undertaken by the primary care **ASP local teams**, in cooperation with the Scientific Committee, will be: 1) to adapt the PIRASOA programme to their own healthcare district, and write the operational document 'local project' to be sent to the Scientific Committee when completed; 2) presenting the programme in the frame of

the clinical sessions performed at every healthcare centre; 3) inclusion as an economic objective within the management arrangements for each healthcare centre; 4) programme implementation:

a) Updating of the local clinical practice guidelines for antimicrobial treatment adapted to the healthcare district epidemiology.

It is essential to update these guidelines with a participatory approach, in order to be considered as an own contribution. The guidelines should be easily available online, either on the Internet, primary care intranet or mobile devices. Every general practitioner and paediatrician will have online access to the guidelines on their desk computer in every practice. The reference guidelines for primary care will be available in Spanish [14].

b) Performance of EIs as a part of everyday clinical practice, as described previously in point 4.2.

c) Regular evaluation of the results of the indicators on a quarterly basis.

d) Feedback of the information to each healthcare centre by means of quarterly reports.

5. External audits

External audits must be undertaken by the Scientific Committee. Two independent professionals of the audited hospital, who must be familiar with the PIRASOA registry, participate actively in the programme and belong to different specialties, will evaluate the concordance of the information. Annually, five hospitals will be randomly selected and four indicators will be chosen randomly for each hospital. The degree of data

concordance will be assessed through evaluation of the clinical documentation and all the necessary supplementary information. The reasons for the discrepancies will be discussed with the local teams in charge of the registry.

6. Training, monitoring and assessment

In order to connect the Scientific Committee and all the HAI and ASP teams, as well as to facilitate programme training, monitoring and assessment, a web-based online platform will be set up (<http://pirasoa.iavante.es/>). The PIRASOA online platform will be the main communication tool among all the local teams and the Scientific Committee. It will be used by the local teams for training and dissemination of the programme without prejudice to face-to-face communication between local teams and their respective clinical units and/or primary care centres. The EIs questionnaires templates for hospital ASP and primary care ASP, the survey questionnaires, and all supporting documentation will be available on the website.

Additionally, training of the local teams will be conducted through training courses and annual face-to-face sessions. Training modules will be structured as MOOC (Massive Online Open Courses) that reach a large number of participants since this methodology enables the development of training courses not only for clinical advisors, but also for all those clinicians or health professionals related to antimicrobial prescribing.

Monitoring and assessment will be performed by means of a Web application (Microsoft SharePoint), where a control panel with all the indicators will be available for the coordinators of the hospital and primary care local teams to upload their own data on a quarterly basis. The Scientific Committee will be responsible of analysing

data and time series, drafting the reports and providing quarterly and annual feedback, with a three-month delay. Feedback reports will allow each centre tracking their own progress as well as benchmarking with others with similar characteristics and complexity.

Implementation results

The programme, started on 1 January 2014, has been correctly implemented in all public hospitals and primary care centres of Andalusia and data collection is currently ongoing. Since the beginning of the programme the fulfilment of indicators has improved from 84% in the first quarter 2014 to 95% in the fourth quarter 2017 for primary care ASP; from 71% in the first quarter 2014 to 91% in the fourth quarter 2017 for hospital ASP; and from 81% in the first quarter 2014 to 92% in the fourth quarter 2017 for HAIs.

A total of 638 health professionals belonging to 34 hospitals and 27 primary care areas have participated in the PIRASOA programme as members of local teams. These professionals have incorporated the tasks of the programme into their daily clinical practice. Additionally, the programme has received funding to hire a lab technician who is working in the Reference Laboratory for Molecular Typing of Nosocomial Pathogens, located in the Microbiology Service of the Hospital Virgen Macarena Seville, Spain.

Hitherto, health professionals have performed 72529 EIs in primary care and 24934 EIs in hospitals (10848 EIs in tertiary care hospitals, 10432 EIs in specialities hospitals and 3654 EIs in county hospitals).

A total of 12 training courses with MOOC methodology have been conducted: two initial courses especially designed for the formation of local teams, with two modules corresponding to the different setting of the PIRASOA programme (primary care and hospital, including HAIs and ASP) that trained 554 health professionals; one course on the appropriate use of antimicrobials for the most frequent infectious diseases syndromes and six editions of a course on the appropriate use of antimicrobials in the hospital setting with 4605 professionals trained; two editions of a course on HAIs which trained 1410 professionals and one course on the optimization of the use of antimicrobials from community pharmacy (433 trained professionals). Additionally, the Scientific Committee holds three annual sessions with the hospital local teams and eight face-to-face meeting with the primary care local teams.

After 4 years, 16 quarterly reports with collected data, indicators and outcomes have been sent to all centres. The assessment of antimicrobial consumption, clinical and microbiological indicators and reports are performed on a quarterly basis and are available for assessment and feedback in near real-time with only a three-month delay. All reports are open and accessible to the public via the programme official website, downloads-reports section (<http://pirasoa.iavante.es/>).

Discussion

In this protocol, authors present the design and implementation of an institutional comprehensive education-based programme to prevent and control healthcare-associated infections and to optimise the use of antimicrobials implemented both in all public hospital settings and primary care practices in an autonomous region in Spain. To the best of our knowledge, this programme is among the first integral regional

programmes in Europe. Some authors highlight the need to develop and implement this type of comprehensive programmes, focused on a broader perspective, and involving multidisciplinary teams of healthcare professionals [10-12]. The results reflect that it has been implemented in a whole public health system with a high degree of compliance and a large number of training activities performed to improve antimicrobial prescriptions, infection control and data management.

It is important to emphasise the high degree of implementation and compliance achieved, over 90%. In this respect, institutional support from the SSPA as well as professional leadership have been essential to translate the programme into clinical practice both in hospitals and primary care settings of the entire public healthcare system.

Other initiatives have been implemented as cross-sectorial antibiotic stewardship networks in different healthcare settings at national, regional and local levels in other European countries like Sweden, France, Scotland and Cornwall (England), with diverse strategies such as educational resources, customised guidelines, pay for performance, pledge and public commitment, toolbox, and reporting [12,15-18]. A public reporting approach has been carried out since 2016 by Public Health England, making data available through a publicly accessible web tool [19].

PIRASOA comprises a specific bundle of measures. One innovative feature of the programme is its educational base, performed via structured EIs, which has previously been implemented [10] and proven its effectiveness at the local level [11]. Another innovative characteristic of PIRASOA is monitoring and data collection frequency on a quarterly basis, which leads to a near real-time assessment of antimicrobial consumption, clinical and microbiological indicators, feedback reports and public

dissemination available on a website since 2014. This frequency of follow-up on the programme outcomes, with only one-quarter delay, allows benchmarking in a more timely manner as well as motivates healthcare professionals to maintain achievements over time and to improve any identified weaknesses. The microbiology reference laboratory is an essential part of the programme to identify resistance mechanisms and clonal relationships. In addition, in order to monitor the incidence of multidrug resistant strains under emergency situations a new subprogramme has been developed since 2016 for the control of carbapenemase-producing *Enterobacteriaceae* in the Public Health System of Andalusia, named CarbaPIRASOA programme.

Henceforth, on the basis of experience gained with the programme's progress, we need to evaluate the impact that PIRASOA has had on use of antimicrobials and on microbial resistance both in hospitals and primary care settings. Work is being done on this objective.

Conclusions

The PIRASOA programme is the first institutional comprehensive education-based programme integrated into daily clinical practice to prevent and control HAIs and to optimise the use of antimicrobials implemented in the entire public healthcare system of an autonomous region in Spain, being among the first integral regional programmes in Europe. With this programme we want to join other success stories on ASP and contribute to improving them with the PIRASOA innovations, considering that the fight against AMR requires spreading through an entire healthcare system by means of integrating both hospital and primary care, ASP in conjunction with HAIs prevention

and control activities, novel educational activities like the EIs, and near real-time clinical indicators feedback on a quarterly basis to help achieve this aim.

The programme, started on 1 January 2014, has been adequately implemented in all public centres of Andalusia and it is committed to be integrated into daily clinical practice. Data collection is ongoing. Long-term results will be analysed and published from 2018 onwards.

Declarations

Ethics approval

Ethics approval has been received from the Care Ethics Committee of the University Hospitals Virgen Macarena and Virgen del Rocio.

Competing interests

The authors declare that they have no competing interests.

Funding

This study received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. JMC, JRB, and AP received funding for research from the Spanish Network for Research in Infectious Diseases (REIPI RD12/0015/0001 and REIPI RD16/0016), supported by Plan Nacional de I+D+i 2013-2016 and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Economía, Industria y Competitividad, co-financed by European Development Regional Fund “A way to achieve Europe”, Operative programme Intelligent Growth 2014-2020.

Authors' contributions

All the PIRASOA Scientific Committee members, JMC, MDRM, CP, IS, RFU, JC, JDA, ON, PP, JB, JGM, RS, AE, CL, EH, AI, JLM, MLGG, AP, JRB, and RV were involved in the programme conception and design. JMC, MDRM, GP, CP, and IS wrote the first draft of the manuscript. All the authors were involved in critical revision of the protocol for important intellectual content. All the authors approved the final version of the manuscript.

Acknowledgments

Other members of the PIRASOA programme group: the directors and coordinators of the local teams in Hospitals and Primary Care Healthcare Districts: Nieves Romero and Manuel Conde (Hospital Virgen del Rocío), Carlos Míguez, Pilar Retamar and M. Dolores del Toro (Hospital Virgen Macarena), José A. Mira, Juan E. Corzo and M. José Pérez-Lozano (Hospital Virgen de Valme), José A. Expósito and Eloy González-Barbero (Distrito Sevilla-Sur), Inmaculada Vázquez, Manuel Cámara and Ana Roldán (Hospital de la Merced and Distrito de Osuna), Rosauro Varo, Nuria Quintero and Mercedes González (APS bajo Guadalquivir), Rocío Hernández-Soto (Distrito Aljarafe-Sevilla-Norte), Javier Giménez, Juan Delgado and Sebastián Expósito (Hospital San Juan de Dios del Aljarafe), Ignacio Pajares and Elisa Fernández-Santiago (Distrito Sevilla), Reyes Alvarez, M. Carmen Gálvez and José R. Maldonado (Hospital Torrecárdenas), Francisco Delgado and Francisca Escabias (Distrito Almería Norte), Antonio González y Leticia Martínez (Hospital de la Inmaculada), José A. Hernández, M. Angeles Lucerna and Ana Lozano (Hospital de Poniente), Dolores Cueto and Francisco Peralta (Distrito Almería), Alfredo Ibáñez and Francisco Hernández de Haro (Distrito Poniente), Yolanda Santaella

and Carolina Payá (Distrito Campo de Gibraltar), Itziar Ramos and Montserrat Pérez-Pérez (Hospital de la Línea), Jesús Canueto and Jesús Dávila (Hospital Punta de Europa), M. del Mar Fernández and M. Dolores Pacheco (Distrito Jeréz Costa y Sierra), Salvador Pérez Cortés and Javier Jiménez (Hospital de Jeréz), M. Antonia Luquez and Rosa Ramos (Distrito Bahía de Cádiz-La Janda), María Rodríguez, Francisca Guerrero and Manuel Zarzuela (Hospital Puerta del Mar), José Egido, Estrella Figueroa and Patricia Jiménez (Hospital de Puerto Real), Antonio Llergo and Julián de la Torre-Cisneros (Hospital Reina Sofía), Elisa Lopera and Nieves Caro (Distrito Norte de Córdoba), Miguel A. Fernández and Estefanía López (Distrito Córdoba Sur), Yolanda Ortega and Justo Sánchez (Hospital Infanta Margarita), José Luis Zambrana and M. Pilar Fernández (Hospital de Montilla), José Nicolás García and Alfonsa Martín (Distrito Córdoba Guadalquivir), Fabiola Cabrerizo and Francisco Sánchez (Distrito Nordeste de Granada), Carmen Valero and Sara Pérez (Hospital de Baza), Cristina Sánchez, M. Carmen Ubago and Jesús Palomares (Hospital de Motril y Distrito Sur de Granada), Francisco Gallo and Sonia Anaya (Distrito Metropolitano de Granada), Marisa Serrano, José Hernández-Quero and Aurora Bueno (Hospital Campus de la Salud), Manuel García, Miguel Rosales and Juan Pasquau (Hospital Virgen de las Nieves), Inés Bonilla, Carlos Millán and Esperanza Quintero (Hospital de Río Tinto and Distrito Norte de Huelva), Carlos Gutiérrez, Alberto Cruz and Ignacio Suárez (Hospital Juan Ramón Jiménez and Infanta Elena), Lucía Carrión, Ana de Cos and Patricia Delgado (Distritos Condado Campiña and Costa de Huelva), Juan Carlos Fernández, Montserrat Gómez, and Juan Pedro Quesada (Hospital San Agustín and Distritos Norte and Nordeste de Jaén), Rosario Varela and Ricardo Villa-Real (Hospital San Juan de la Cruz), Aquiles Lozano, Daniel Fatela and Lourdes Ballesteros (Hospital de Andújar), Luis López, Rafael

Martínez and Carmen Herrero (Hospital de Jaén), Miguel Cerón and José M. Salmerón (Distrito Jaén and Jaén Sur), Juan Rios, M. Jesús Pérez and Diego Román (Hospital and Distrito Serranía de Ronda), Consuelo Hernández, Alberto Domínguez and M. José de Torres (Hospital de la Axarquía and Distrito Este de Málaga), Bárbara Torres, Rosa Garrido and José Ignacio Blanco (Hospital de Antequera and Distrito Norte de Málaga) Francisco Martos, Alfonso del Arco and Victor Fuentes (Hospital Costa del Sol), Francisco Pozo and Antonio Hernández (Distrito Costa del Sol), Bernardo Herrera and José Manuel Fernández (Distrito Guadalhorce), Miguel Angel Prieto, José María Reguera and Salvador Oña (Hospital Regional de Málaga), José Antonio Medina, Blanca O'Donnell and Enrique Nuño (Hospital Virgen de la Victoria). On behalf of them, our acknowledgment to the team of 638 healthcare professionals that comprise the PIRASOA local teams. We acknowledge Ian Brayshaw for the English language review.

References

1. Centers for Disease Control and Prevention (CDC). Vital Signs: Carbapenem-resistant Enterobacteriaceae. *MMWR Morb Mortal Wkly Rep.* 2013;62(9):165–70.
2. European Centre for Disease Prevention and Control (ECDC) and European Medicines Agency (EMA) joint technical report, 2009. The bacterial challenge: time to react.
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2009/11/WC500008770.pdf. Accessed 20 Jul 2014.
3. Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M. Achieving global targets for antimicrobial resistance. *Science.* 2016;353(6302):874-5. doi:

10.1126/science.aaf9286

4. Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;44:159–77.

5. Rodríguez-Baño J, Paño-Pardo JR, Alvarez-Rocha L, Asensio A, Calbo E, Cercenado E, et al. Programas de optimización del uso de los antimicrobianos (PROA) en hospitales españoles: documento de consenso GEIH-SEIMC, SEFH y SEMPSPH. *Enferm Infecc Microbiol Clin*. 2012;30:22.e1-22.e23.

6. Department of Health. UK five year antimicrobial resistance strategy 2013 to 2018. www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018. Accessed 14 Jan 2015.

7. European Centre for Disease Prevention and Control (ECDC). EU Guidelines for the prudent use of antimicrobials in human health. https://ec.europa.eu/health/amr/sites/amr/files/amr_guidelines_prudent_use_en.pdf. Accessed 3 Jul 2017.

8. Rodríguez-Baño J, García L, Ramírez E, Martínez-Martínez L, Muniain MA, Fernández-Cuenca F, et al. Long-term control of hospital-wide, endemic multidrug-resistant *Acinetobacter baumannii* through a comprehensive "bundle" approach. *Am J Infect Control*. 2009;37:715-22.

9. Lawes T, Lopez-Lozano JM, Nebot CA, Macartney G, Subbarao-Sharma R, Dare CR, et al. Effects of national antibiotic stewardship and infection control strategies on hospital-associated and community-associated methicillin-resistant *Staphylococcus*

aureus infections across a region of Scotland: a non-linear time-series study. Lancet Infect Dis. 2015;15(12):1438-49.

10. Cisneros JM, Neth O, Gil-Navarro MV, Lepe JA, Jiménez-Parrilla F, Cordero E, et al. Global Impact of an Educational Antimicrobial Stewardship Program on Prescribing Practice in a Tertiary Hospital Center. Clin Microbiol Infect. 2014;20(1):82-8. doi: 10.1111/1469-0691.12191

11. Molina J, Peñalva G, Gil-Navarro MV, Praena J, Lepe JA, Pérez-Moreno MA, et al. Long-term impact of an educational antimicrobial stewardship program on hospital-acquired candidemia and multidrug-resistant bloodstream infections: a quasi-experimental study of interrupted time-series analysis. Clin Infect Dis. 2017;65(12):1992-1999. doi: 10.1093/cid/cix692

12. Pulcini C. Antibiotic stewardship: a European perspective. FEMS Microbiol Lett. 2017;364(23). doi: 10.1093/femsle/fnx230

13. Andalusian Health Service - Servicio Andaluz de Salud .

<http://www.juntadeandalucia.es/servicioandaluzdesalud/principal/default.asp>.

Accessed 5 Jul 2017.

14. Servicio Andaluz de Salud. Guía de terapéutica antimicrobiana del área del Aljarafe.

<http://www.juntadeandalucia.es/servicioandaluzdesalud/guiaterapeuticaljarafe/guia>

[TerapeuticaAljarafe/](#) Accessed 7 Jul 2017.

15. Huttner B, Harbarth S, Nathwani D. ESCMID Study Group for Antibiotic Policies (ESGAP). Success stories of implementation of antimicrobial stewardship: a narrative review. Clin Microbiol Infect. 2014;20(10):954-62. doi: 10.1111/1469-0691.12803

16. Powell N, Davidson I, Yelling P, Collinson A, Pollard A, Johnson L, et al. Developing a local antimicrobial resistance action plan: the Cornwall One Health Antimicrobial Resistance Group. *J Antimicrob Chemother.* 2017;72(9):2661-5. doi: 10.1093/jac/dkx164
17. European Centre for Disease Prevention and Control (ECDC). European Antimicrobial Resistance Surveillance Network (EARS-Net). <https://ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/ears-net>. Accessed 25 Feb 2015.
18. European Centre for Disease Prevention and Control (ECDC). European Surveillance of Antimicrobial Consumption Network (ESAC-Net). <https://ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/esac-net>. Accessed 25 Feb 2015.
19. Johnson AP, Muller-Pebody B, Budd E, Ashiru-Oredope D, Ladenhein D, Hain D et al. Improving feedback of surveillance data on antimicrobial consumption, resistance and stewardship in England: putting the data at your Fingertips. *J Antimicrob Chemother* 2017; 72:953–956.
20. Suetens C, Savey A, Labeeuw J, Morales I; HELICS-ICU. The ICU-HELICS programme: towards European surveillance of hospital-acquired infections in intensive care units. *Euro Surveill.* 2002;7:127-8.
21. López-Pueyo MJ, Olaechea-Astigarraga P, Palomar-Martínez M, Insausti-Ordeñana J, Alvarez-Lerma F; ENVIN–HELICS Study Group. Quality control of the surveillance programme of ICU-acquired infection (ENVIN-HELICS registry) in Spain. *J Hosp Infect.* 2013;84:126-31.

22. World Health Organisation. Patient Safety checklists. Hand hygiene observation form. www.who.int/gpsc/5may/Observation_Form.doc. Accessed 20 Feb 2017.
23. Álvarez Lerma F, Sánchez García M, Lorente L, Gordo F, Añón JM, Álvarez J, et al. Guidelines for the prevention of ventilator-associated pneumonia and their implementation. The Spanish "Zero-VAP" bundle. *Med Intensiva*. 2014;38(4):226-36. doi: 10.1016/j.medin.2013.12.007
24. Palomar M, Álvarez-Lerma F, Riera A, Díaz MT, Torres F, Agra Y, et al. Impact of a national multimodal intervention to prevent catheter-related bloodstream infection in the ICU: the Spanish experience. *Crit Care Med*. 2013;41(10):2364-72. doi: 10.1097/CCM.0b013e3182923622
25. WHO Collaborating Centre for Drug Statistics Methodology. Norwegian Institute of Public Health. ATC/DDD Index 2017. https://www.whocc.no/ddd/definition_and_general_considera/. Accessed 5 Jul 2017.

Abbreviations

AMR: antimicrobial resistance; **ASP:** Antimicrobial Stewardship Programme; **CU:** Clinical Unit; **DDD:** Defined Daily Dose; **ECDC:** European Centre for Disease Prevention and Control; **EI:** Educational interview; **EU:** European Union; **HAI:** Healthcare Associated Infection; **MDRB:** Multidrug-resistant bacteria; **MOOC:** Massive Online Open Course; **PIRASOA:** Institutional Programme for the Prevention and Control of Healthcare Associated Infections and Appropriate Use of Antimicrobials; **SSPA:** The Andalusian Public Healthcare System; **SVEA:** Epidemiological Surveillance System of Andalusia

Additional material provided

Additional file 1. PIRASOA Scientific Committee. Format: pdf.

Additional file 2. Satisfaction survey form for hospitals. Format: pdf.

Additional file 3. Satisfaction survey form for primary care. Format: pdf.

Additional file 4. Educational Interview form for hospitals. Format: pdf.

Additional file 5. Educational Interview form for primary care. Format: pdf.

PIRASOA Scientific Committee

- **Andalusian Society of Microbiology and Parasitology:**

Dr. A. Pascual-Hernandez, Microbiologist

Dr. MD. Rojo-Martin, Microbiologist

- **Hospital Pharmacy:**

Dr. J. Bautista-Paloma, Pharmacist

Dr. J. Cabezas-Barrera, Pharmacist

- **Andalusian Society of Intensive Care Medicine:**

Dr. R. Sierra-Camerino, Specialist in intensive care medicine

Dr. J. Garnacho-Montero, Specialist in intensive care medicine

- **Resistance Zero Project coordinator for Andalusia:**

Dr. A. Estella-Garcia, Specialist in intensive care medicine

- **Nursing:**

Mrs. C. Lupion-Mendoza, Nurse infectious diseases department

- **Andalusian Society of Preventive Medicine and Public Health:**

Dr. R. Valencia-Martin, Specialist in preventive medicine and public health

Dr. I. Salcedo-Leal, Specialist in preventive medicine and public health

- **Andalusian Society of Hospital and Long-term care Pharmacy:**

Dr. CM. Pinto-Nieto, Pharmacist

- **Andalusian Society of Primary Care Pharmacy:**

Dr. R. Fernandez-Urrusuno, Pharmacist

- **Andalusian Society of Family Medicine:**

Dr. P. Porras-Martin, Family doctor

Dr. JD. Alcantara, Family doctor

- **Andalusian Society of Primary Care Paediatricians:**

Dr. ML. Garcia-Gestoso, Paediatrician

- **Hospital Paediatrics:**

Dr. O. Neth, Paediatrician

- **Andalusian Society of Infectious Diseases:**

Dr. J. Rodriguez-Baño, Specialist in infectious diseases

Dr. JM. Cisneros-Herreros, Specialist in infectious diseases

- **Sub-directorate of Pharmacy, Andalusian Health Service:**

Dr. E. Hevia-Alvarez, Pharmacist

- **Epidemiological Surveillance System of Andalusia (SVEA):**

Dr. B. Lopez-Hernandez, head of service

- **Andalusian Strategy for Patient's Safety:**

Dr. E. Moreno-Campoy

- **Andalusian Professional Dentists' Association:**

Dr. ML. Tarilonte-Delgado

- **Andalusian Professional Physicians' Association:**

Dr. C. Ortiz-Leyba

- **Andalusian Professional Pharmacists' Association:**

Dr. EJ. Garcia-Jimenez

- **Technical support, Andalusian Health Service:**

Dr. A. Irastorza-Aldasoro, Specialist in preventive medicine and public health

Mr. JL. Marquez-Diaz, Pharmacist

PIRASOA programme: Satisfaction survey form for hospitals

Date of the interview: _____

Hospital: _____

Clinical department: _____

Dear colleague:

We would appreciate your participation in this questionnaire. Knowing your opinion about the educational interview you have just received will help us to improve our stewardship programme.

Did you find the educational interview useful?

Yes

No

Do you have any additional comments?

Thank you for your cooperation,

The hospital PIRASOA local team

PIRASOA programme: Satisfaction survey form for primary care settings

Date of the interview:

Healthcare district:

Healthcare centre:

Dear colleague:

We would appreciate your participation in this questionnaire. Knowing your opinion about the educational interview you have just received will help us to improve our stewardship programme.

Did you find the educational interview useful? **Yes** **No**

Do you have any additional comments?

Thank you for your cooperation,

The primary care PIRASOA local team

PIRASOA programme: Educational Interview form for hospitals

Date of interview: Centre:

Clinical department: Episode number:

Advisor: Prescriber:

Antimicrobial agent(s) prescribed:

Clinical indication:

- Perioperative prophylaxis
- Diagnosis without microbiological confirmation
- Diagnosis with microbiological confirmation

Describe

Perioperative prophylaxis

1. Was prophylaxis indicated? Yes No
2. Was the chosen agent appropriate? Yes No
3. Was the administration timing appropriate? Yes No
4. Was the total number of doses appropriate? Yes No

Empirical antimicrobial treatment

1. Was empirical treatment initiation indicated? Yes No
2. Was the timing of treatment initiation appropriate? Yes No
3. Were microbiological samples collected?
 It was not indicated:
 Not performed
 It was indicated:
 Performed
 Not performed or incorrectly performed
4. Was the chosen agent appropriate? Yes No
5. Was the dosing appropriate? Yes No
6. Was the way of administration appropriate? Yes No
7. If other therapeutic measures were indicated, were they performed correctly?
 They were not indicated and not performed
 They were indicated and correctly performed
 They were indicated, but not correctly performed
8. Is the planned treatment duration appropriate? Yes No

Targeted antimicrobial treatment

1. Was antimicrobial treatment indicated? Yes No
2. Was the timing of the treatment initiation appropriate? Yes No
3. Was the interpretation of the microbiological results correct? Yes No
4. Was the chosen agent appropriate? Yes No
5. Was the chosen agent the most appropriate? Yes No
6. Was the dosing appropriate? Yes No
7. Was the way of administration appropriate? Yes No
8. If other therapeutic measures were indicated, were they performed correctly?
 - They were not indicated and not performed
 - They were indicated and correctly performed
 - They were indicated, but not correctly performed
9. Is the planned treatment duration appropriate? Yes No

PIRASOA programme: Educational Interview form for primary care

Date of interview: Healthcare District:

Healthcare centre/practice:

Advisor: Prescriber:

Diagnosis:

Antimicrobial agent(s) prescribed:

Empirical antimicrobial treatment

1. Was empirical treatment initiation indicated? Yes No
2. Were microbiological samples collected?
It was not indicated:
 Not performed
It was indicated:
 Performed
 Not performed or incorrectly performed
3. Was the chosen antimicrobial agent appropriate? Yes No
4. Was the dosing appropriate? Yes No
5. Was the planned treatment duration appropriate? Yes No
6. Has any intervention been done to improve patient's compliance and adherence to the treatment? Yes No

Describe it:

Targeted antimicrobial treatment

1. Was antimicrobial treatment indicated? Yes No
2. Was the interpretation of the microbiological results correct? Yes No
3. Was the chosen antimicrobial agent appropriate? Yes No
4. Was the chosen agent *the most* appropriate one? Yes No
5. Was the dosing appropriate? Yes No
6. Was the planned treatment duration appropriate? Yes No
7. Has any intervention been done to improve patient's compliance and adherence to the treatment? Yes No

Describe it: