DESDE 1902
INSTITUTO DE HIGIENE E
MEDICINA TROPICAL
UNIVERSIDADE NOVA DE LISBOA

policy paper

Practical guide for the implementation of Antibiotic Stewardship Programs

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september 2015

INTRODUCTION

Antibiotics prescription is a complex process. Antibiotics are among the most prescribed and used drugs in clinical practice. However, it is estimated that 20-50% of antibiotics are improperly prescribed (1). The main consequence related with it overuse is the development of multi-resistant microorganisms (2). Antibiotic resistance leads to increased morbidity, mortality and costs associated to HealthCare Associated Infections (HAIs) (3, 4). The Centre for Diseases Control and Prevention (CDC) estimates that over two million people/year acquire an antibiotic resistant infection, and 23,000 die as a result of this infection. In Europe, it is estimated that 25,000 people/year may die with infections caused by resistant bacteria (5).

Antibiotic Stewardship Programs contribute to the optimization of antimicrobial therapy, ensuring the proper use (indication, dose and duration) and minimizing side effects (6). An adoption of these kind of programs leads to a reduction in the prevalence of antimicrobial resistance, costs and save lives (7).

These programs have been implemented throughout the world, and there are guidelines and recommendations in the USA (1, 8) and Europe (9, 10). In Portugal, antibiotics consumption is high (45.4% of patients in hospitals), when compared with Europe's average (35.8%), leading to resistance rates as high as 73.7% and 84.5% for certain microorganisms and infections (11–13). Portugal is even one of the European countries with higher antibiotic consumption rate in hospitals (Figure 1).

It is imperative to implement Antibiotics Stewardship Programs in Portuguese hospitals and develop effective strategies to prevent and control infections based on social, educational and cultural Portuguese reality (14). Direção Geral de Saúde (DGS) published already a recommendation on it (15).

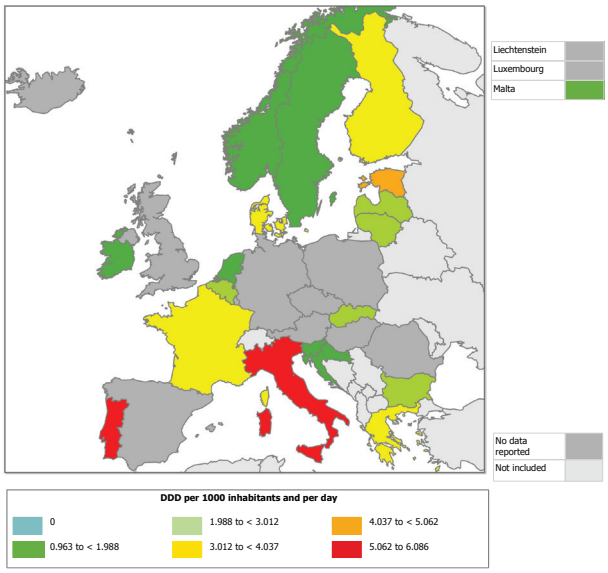

Figure 1. Antimicrobial consumption for systemic use in the hospital sector in Europe in 2012 (16).

AIM

Provide practical recommendations, based on evidence, for the implementation of Antibiotic Stewardship Programs in Portuguese hospitals in order to improve the quality of antibiotic prescription and contribute to better clinical outcomes. We also aim to complement the DGS campaigns: "Campanha de Precauções Básicas de Controlo de Infeção" of "Programa de Prevenção e Controlo de Infeções e Resistência aos Antimicrobianos" (www.dgs.pt/programas-de-saude-prioritarios.aspx).

GHTM Global Health & Tropical Medicine
CENTRO HOSPITALAR DE LISBOA OCIDENTAL, E.P.E.
FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA
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CORE ELEMENTS IN ANTIBIOTIC STEWARDSHIP PROGRAMS

The core elements described below are based on CDC and DGS recommendations (1, 15).

1. LEADERSHIP COMMITMENT

Leadership support and commitment is essential to the success of Antibiotic Stewardship Programs. This support can be expressed in several forms, including:

(i) Formal declarations supporting the efforts made to improve and monitor antibiotic use;

(ii) Include Antibiotic Stewardship Program activities in healthcare workers job description;

(iii) Ensure that healthcare workers involved in the Antibiotic Stewardship Program have enough time to participate in its activities;

(iii) Support training and education events;

(iv) Ensure the existence of human resources, money and informatic systems.

2. MULTIDISCIPLINARY TEAM

An efficient Antibiotic Stewardship Program needs a multidisciplinary team to support it (Figure 2).

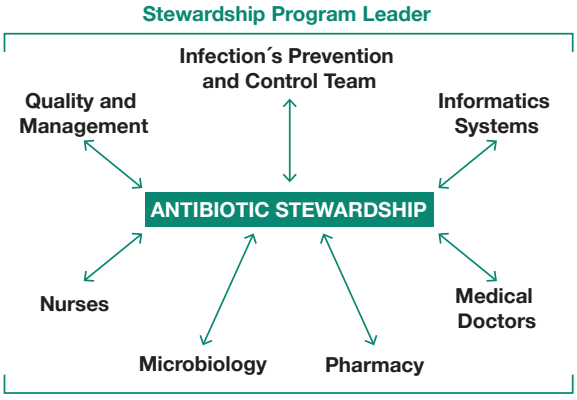

Figure 2. Multidisciplinary team for a hospital Antibiotic Stewardship Program

PROGRAM LEADER – it is advised to appoint a single leader responsible for the program. Experiences in other countries suggest a medical doctor as the best option. The leader must have expertise in infectious diseases and antibiotics prescription.

In addition, the success of the program is facilitated by the presence of the following working groups:

MEDICAL DOCTORS – as prescribers;

INFECTION'S PREVENTION AND CONTROL TEAM – their expertise in auditing, analyzing and reporting data are a great contribution to monitor and report resistance patterns, perform training and implement policies and strategies;

CORE ELEMENTS IN ANTIBIOTIC STEWARDSHIP PROGRAMS

Leadership Commitment
Ensure the existence of human resources, money and informatics systems. Support to training and education.

Multidisciplinary Team
Medical leadership with expertise in infectious diseases and antibiotic prescription. The working group should also include Medical Doctors, Infection's Prevention and Control Team, Quality and Management, Microbiology, Informatics Systems, Pharmacy and Nursing.

Situation Assessment
Identify problems and set goals. Create well targeted policies.

Interventions to improve antibiotics use
eg: take samples before begin antibiotic therapy; antibiotic review at 48 hours; prior authorization prescription; interventions driven and guided by the pharmacy; interventions for specific infections.

Surveillance
Monitor antibiotic prescription and resistance patterns to identify opportunities for improvement and evaluate the impact of implemented measures.

Report
Make periodic reports on antibiotic use, antibiotic consumption and resistance patterns, and disseminates them to healthcare professionals.

Educate
To train physicians on antibiotic resistance and optimization of antibiotic prescription; informing patients and the general public.

MICROBIOLOGY – as guiders for empiric treatment, creating, interpreting and communicating antibiotic resistance patterns;

NURSES – ensuring that cultures are performed in the right way and at right time (before starting antibiotics);

INFORMATICS SYSTEMS – in the integration of protocols and applications, to support clinical decision, in information systems;

PHARMACY – as distributors of pharmaceutical preparations and technical advice;

QUALITY AND MANAGEMENT – the proper use of antibiotics should be promoted for raising the medical quality, patients health, the management of resources and cost reduction.

The inclusion of health professionals (in full-time) to develop and manage these programs is advised. In small hospitals, health professionals in part-time or "outsourcing" can be a solution.

3. SITUATION ASSESSMENT

Before starting any intervention it is necessary to analyze the hospital's situation, characterize the problem and set goals. Policies and interventions should be adapted to the hospital reality.

It is advisable to obtain quantitative data as the number of infections, number of antibiotics used, and number of antibiotic resistant infections.

It is also necessary to establish priorities and communicate them properly to all hospital staff so that everyone feels part of the problem and the solution. It is recommended to elaborate a "driver diagram" that includes the general objectives and how to achieve them (Figure 3).

4. INTERVENTIONS TO INCREASE ANTIBIOTICS USE

The correct implementation of interventions to improve antibiotics use is essential. In addition, it is recommended to implement just one or two measures and only add new measures after the initial ones are well implemented and recorded.

See below some of the most used measures:

A) POLICIES FOR ANTIBIOTIC PRESCRIPTION – should include microbiological samples procediments, duration and type of treatment. The data should be based on evidence;

B) CLINICAL GUIDELINES – for infections treatment and prophylaxis should be available and adapted to local epidemiology;

C) TAKE SAMPLES FOR MICROBIOLOGICAL TESTS – before the beginning of antimicrobial therapy (when possible and relevant);

D) RE-EVALUATION OF THE ANTIMICROBIAL THERAPY AFTER 48 HOURS – in severe infections antibiotics are empirically prescribed (while the microbiological results are not available). A reassessment of the antibiotic therapy should be done after the initial 48 hours, combining the clinical course with the microbiology lab results;

E) PRIOR AUTHORIZATION PRESCRIPTION – existence of an expert in antibiotics and infectious diseases always available (eg: by telephone) to promote and advise the appropriate use of antibiotics, check the spectrum of activity, cost associated toxicity);

F) EXTERNAL AUDITS – antimicrobial therapy review by external experts is advised and effective (17);

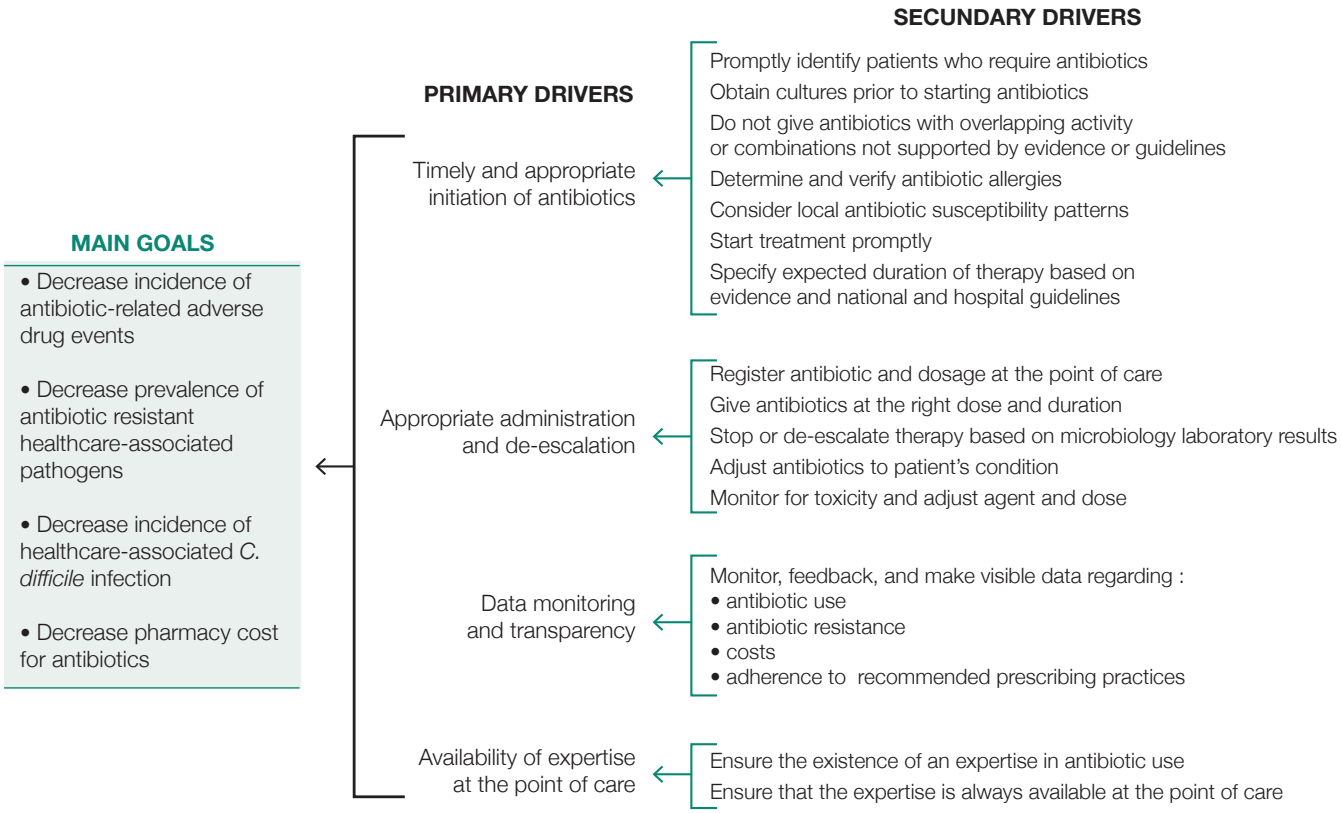

Figure 3. "Driver Diagram" example. Adapted from http://www.cdc.gov/getsmart/healthcare/implementation.html

G) PHARMACY-DRIVEN INTERVENTIONS
- Automatic changes from intravenous to oral antibiotic therapy (in appropriate situations);
- Dose adjustments in cases of organ dysfunction (except for the first dose);
- Dose optimization (when pharmacokinetics /pharmacodynamics is available);
- Automatic alerts when therapy might be unnecessarily duplicative;
- Time-sensitive automatic stop orders for specific antibiotic prescriptions (eg: surgical prophylaxis);
- Detection and prevention of drugs interaction;

H) AVAILABILITY OF GUIDELINES FOR SPECIFIC INFECTION
- Community acquired pneumonia;
- Urinary tract infections;
- Skin and soft tissue infections;
- *Staphylococcus aureus* methicillin resistant infections;
- *Clostridium difficile* infections;
- Culture-proven invasive infections.

5. SURVEILLANCE

Surveillance is essential to identify opportunities for improvement and assess the impact of the implemented measures. Surveillance should be applied both to the measures as to the results. The following items should be monitored:

A) ANTIBIOTIC USE - in days of treatment (DOT) or defined daily dose (DDD), but also the use of specific antibiotics and the use of antibiotics in different units;

B) LEVELS OF ANTIBIOTICS RESISTANCE - for pathogens isolated after admission and at the patient level (percentage of patients who develop infections by antibiotic resistant microorganisms);

C) PERIODIC REVIEWS AND INTERNAL AUDITS - of antibiotics use and infections treatment to determine the quality of antibiotics used: whether prescribers apply accurately the guidelines for diagnostic infections; document the statement; plan the duration of antibiotic therapy; perform relevant culture tests before starting the treatment; change the antibiotic selection based on microbiological results;

D) EVALUATE THE (direct and indirect) COSTS of the Antibiotic Stewardship Program.

Table 1. Measures for quality improvement of Antibiotic Stewardship Programs

Structural Indicators
• Availability of a multi-disciplinary team • Availability of guidelines for empiric treatment and prophylaxis • Availability of an educational program
Intervention
• Manage of antibiotics use in DDD and DOT • Compliance with acute empirical guidelines • Compliance with de-escalation guidelines • Compliance with intravenous vs oral use guidelines • Compliance with surgical prophylaxis guidelines • Compliance with specific infection guidelines
Results
• Rates of *C. difficile* infection • Surgical site infection rates • Antibiotic resistance surveillance • Readmission within 30 days • Complication rates • Treatment related toxicity • Mortality

Adapted from BioMérieux, Practical Guide to Antimicrobial Stewardship in Hospital. http://www.biomerieux-besmart.com/

6. REPORT

Communication is a key factor in an Antibiotic Stewardship Program. The report of the results should be clear, simple and must include the benefits of the program and of the measures adopted (Table 2).

Table 2. Template table for intervention results presentation

Measure	Begin of the Intervention	End of the Intervention
Number of patients surveyed		
Number of patients with antibiotic prescription		
Number of patients with single antibiotic prescription		
Number of prescriptions for parenteral antibiotic use		
Number of prescriptions compliant with local guidelines		
Number of surgical prophylaxis prescriptions with single dose		
Number of surgical prophylaxis prescriptions with one day duration		
Number of surgical prophylaxis prescriptions with more than one day duration		

Adapted from BioMérieux, Practical Guide to Antimicrobial Stewardship in Hospital. http://www.biomerieux-besmart.com/

It is recommended the **preparation of periodic reports** with information on the antibiotics use and consumption, and resistance patterns to broadcast them to doctors, nurses and other healthcare workers.

7. TRAINING

It is imperative **to train healthcare workers on antibiotic resistance and prescription optimization**, through workshops, presentations, posters, brochures and newsletters with regular updates on antibiotics prescription, resistance levels and specific procedures for infectious diseases. It is essential that the training is adapted to each profession. An evaluation process, in order to verify training process efficiency, is recommended.

It also recommended the existence of **informative and educational content for patients and general public**.

CONCLUSION

This document summarizes the best practices for the implementation of Antibiotic Stewardship Programs in the Hospital context. It results from literature review and our research experience in the Portuguese context (Projects: OSYRISH, FCT, PTDC/IVC-COM/5016/2012 and HAITool, EEA Grants, 000182DT3) specially at Hospital São Francisco Xavier (CHLO), Lisbon.

However, it should be noted that the management of antimicrobial resistance is a small part of the problem of healthcare associated infections. Factors such as the rate of occupancy beds, nurses ratio per patient, nurses working conditions and hand hygiene should be taken into account and will be addressed in future documents.

ADITIONAL RESOURCES

CDC (2014) Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services.

ARHAI (2011) Antimicrobial Stewardship: “Start Smart - Then Focus. Guidance for antimicrobial stewardship in hospitals (England).

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CHECKLIST FOR THE IMPLEMENTATION OF ANTIBIOTIC STEWARDSHIP PROGRAMS IN HOSPITALS

The checklist below is a systematic evaluation of the core elements for an Antibiotic Stewardship Program (1). This list should be verified by more than one member team in order to reach consensus.

1. Leadership commitment	
Has the hospital a formal written statement, from leadership, that supports the antibiotic stewardship program?	

2. Leadership	
Is there a medical doctor responsible for the antibiotic stewardship program?	

3. Multidisciplinary Team	
Does any of the staff below involved in the antibiotic stewardship program?	
• Medical Doctors	
• Infection's Prevention and Control Team	
• Quality and Management	
• Microbiology	
• Pharmacy	
• Informatics Systems	
• Nurses	

4. Actions to support optimal antibiotic use	
Is there a policy that requires prescribers to document the dose, duration, and indication for all antibiotic prescriptions?	
Are there recommendations, based on national guidelines and local susceptibility, to assist antibiotic prescription on common clinical conditions?	
Is there a formal procedure to review the appropriateness of all antibiotics 48 hours after the initial order?	
Do specified antibiotic agents need to be approved by the leader (medical doctor) prior to dispensing?	
Does the leader (medical doctor) participate on review courses of therapy for specified antibiotic agents?	

5. Pharmacy-driven interventions	
Are there automatic changes from intravenous to oral antibiotic therapy in appropriate situations?	
Are there dose adjustments in cases of organ dysfunction?	
Are there dose optimization (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility?	
Are there automatic alerts in situations where therapy might be unnecessarily duplicative?	
Are there time-sensitive automatic stop orders for specified antibiotic prescriptions?	
Does the Pharmacy participates in ward meetings?	

6. Infections specific interventions	
Are there specific interventions in place to ensure optimal use of antibiotics to treat the following infections?	
• Community-acquired pneumonia	
• Urinary tract infection	
• Skin and soft tissue infections	
• Surgical prophylaxis	
• Empiric treatment of methicillin-resistant *Staphylococcus aureus*	
• *Clostridium difficile* infections	
• Culture-proven invasive infections	

7. Monitoring antibiotic prescription, use, and resistance	
Does the hospital monitor the adherence to antibiotic use policies (dose, duration and indication)?	
Does the hospital monitor the adherence to facility-specific treatment recommendations?	
Does the hospital monitor the compliance of the specific interventions in place?	

8. Antibiotic use and outcome measures	
Does the hospital track rates of *C. difficile* infection?	
Does the hospital produce an annual antibiogram report?	
Does the hospital monitor antibiotic consumption at the unit/hospital by one of the following metrics:	
• By counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?	
• By number of grams of antibiotics used (Defined Daily Dose, DDD)?	
• By direct expenditure for antibiotics (purchasing costs)?	

9. Reporting information to staff on improving antibiotic use and resistance	
Does the antibiotic stewardship program share facility-specific reports on antibiotic use with prescribers?	
Has a current antibiogram been distributed to the prescribers?	
Do prescribers receive direct and personalized communication about how they can improve antibiotic prescription?	

10. Education	
Does the antibiotic stewardship program provide education to clinicians and other relevant staff on improving antibiotic prescription?	

Adapted from “Core Elements of Hospital Antibiotic Stewardship Programs”, CDC, www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf