

# Antimicrobial stewardship programs an overall approach

**Jeroen Schouten**

*Intensivist and senior researcher*

*Chair ESGAP (ESCMID Study Group on Antimicrobial Stewardship)*



**ESGAP**

ESCMID STUDY GROUP  
FOR ANTIMICROBIAL  
STEWARDSHIP

European Society of Clinical Microbiology and Infectious Diseases

Center for Infectious Diseases

**Radboudumc**

---

# Definition AMS

*Appropriate antimicrobial stewardship includes **optimal selection, dose, and duration of treatment** as well as control of antibiotic use...it will prevent or slow the emergence of resistance among microorganisms*

**IDSA 1997**

---

# Definition

*AMS refers to the multifaceted approach that **healthcare organizations** have adopted to optimize prescribing*

*Essentially, antimicrobial stewardship advocates the use of the most suitable antibiotic in the context of the presenting clinical condition and specific patient*

**Charani 2010**

## Dia 3

---

### JS1

Conceptualises AMS as an approach to optimizing prescribing; how is AMS different from other approaches to optimize prescribing?

Focus on quality of care; does not place any emphasis on the societal problem of resistance in the case of prescribing for an individual patient

Jeroen Schouten; 16-3-2017

---

# Definition

*‘Stewardship’ describes careful or responsible management of a valued entity entrusted to one’s care. Antimicrobial agents should be viewed as a shared resource that must be managed with an eye to preservation of their use for future generations...*

**van Schooneveld, 2011**

## Dia 4

---

### JS2

presents AMS as a strategy, but then defines it as interventions with a specific purpose and methods; perhaps 'defined as' would be better replaced by 'consists of'

Describes what 'stewardship' means (have not identified any other articles that do this)

Jeroen Schouten; 16-3-2017

---

# Goals of AMS

1. to achieve the best **clinical outcomes** related to antimicrobial use
2. to minimize **toxicity** and other adverse events
3. to limit the selective pressure on bacterial populations that drives the **emergence** of **antimicrobial-resistant** strains
4. reduce excessive **costs** attributable to suboptimal antimicrobial use

**IDSA 2012**

## Dia 5

---

### JS3

so if we want to study interventions related to AMS we need to know what the relevant outcomes are that we strive for

Jeroen Schouten; 2-4-2018

---

# Goals of AMS

“to provide safe and effective antimicrobial therapy whilst safeguarding its effectiveness for future generations”

**Aryee, 2014**

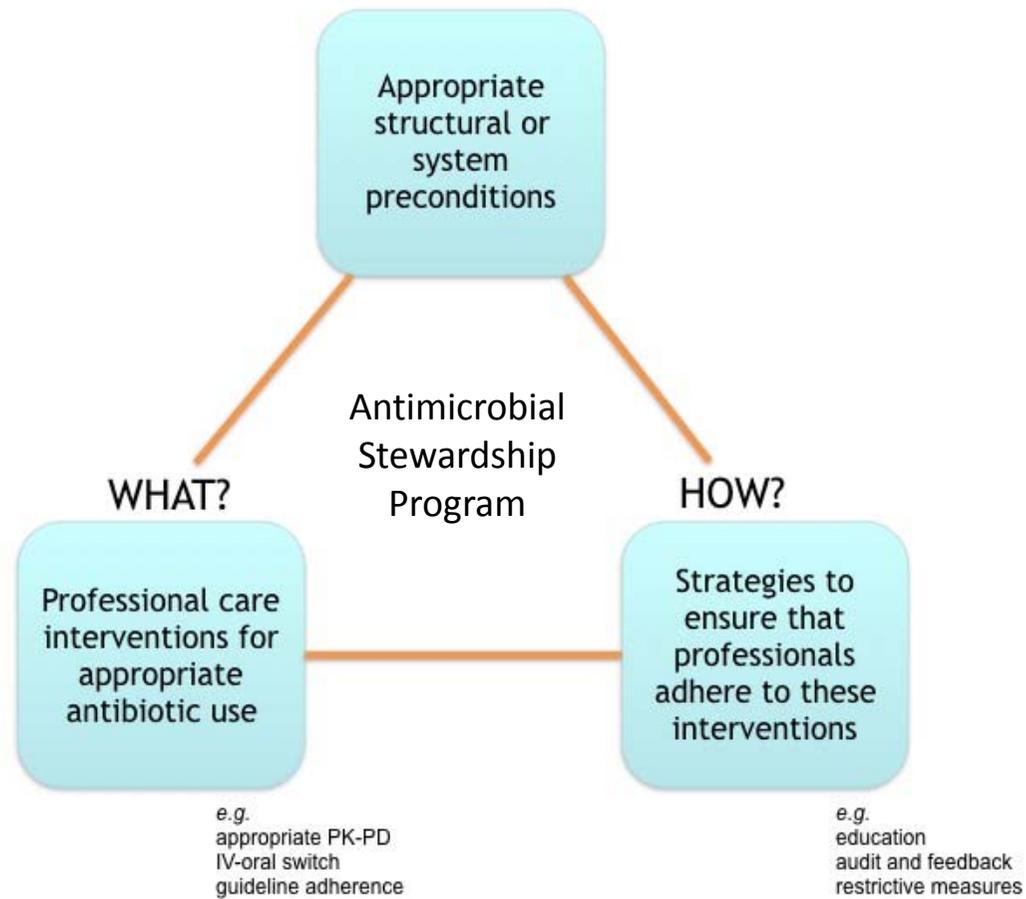
**Dia 6**

---

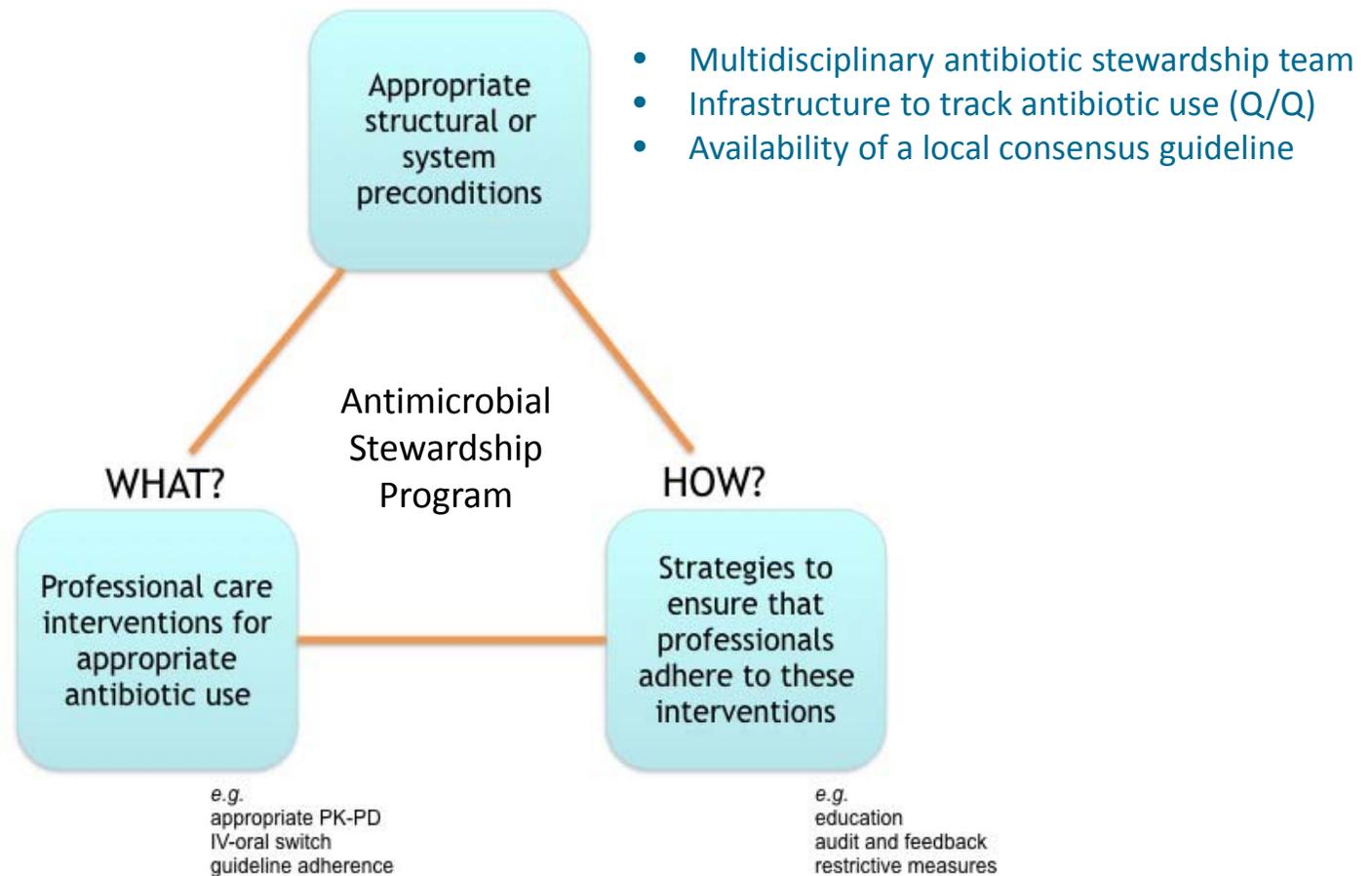
**JS4**

so this would need to be the talisman for our research!

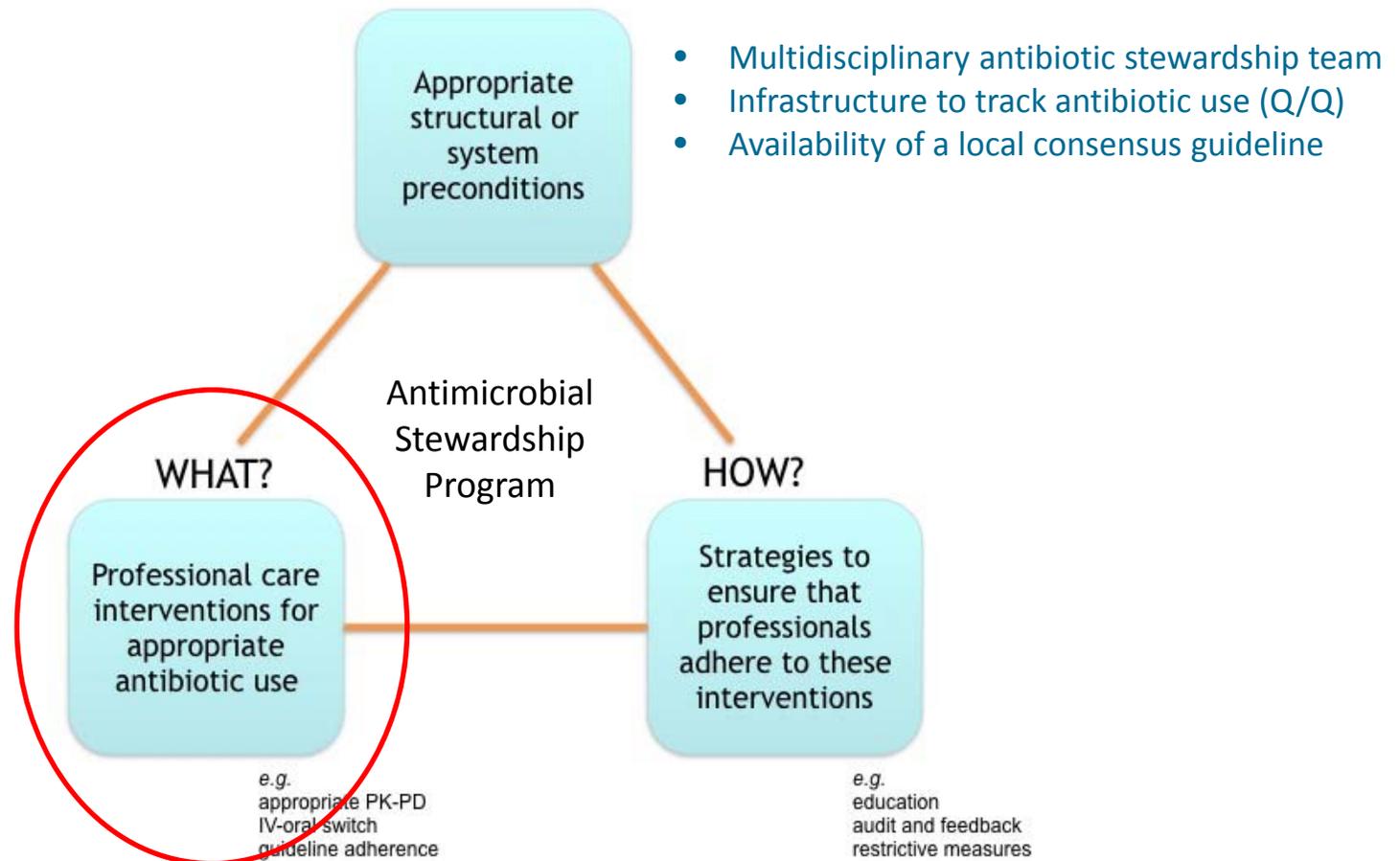
Jeroen Schouten; 2-4-2018



Schouten, Intensive Care Medicine, 2015



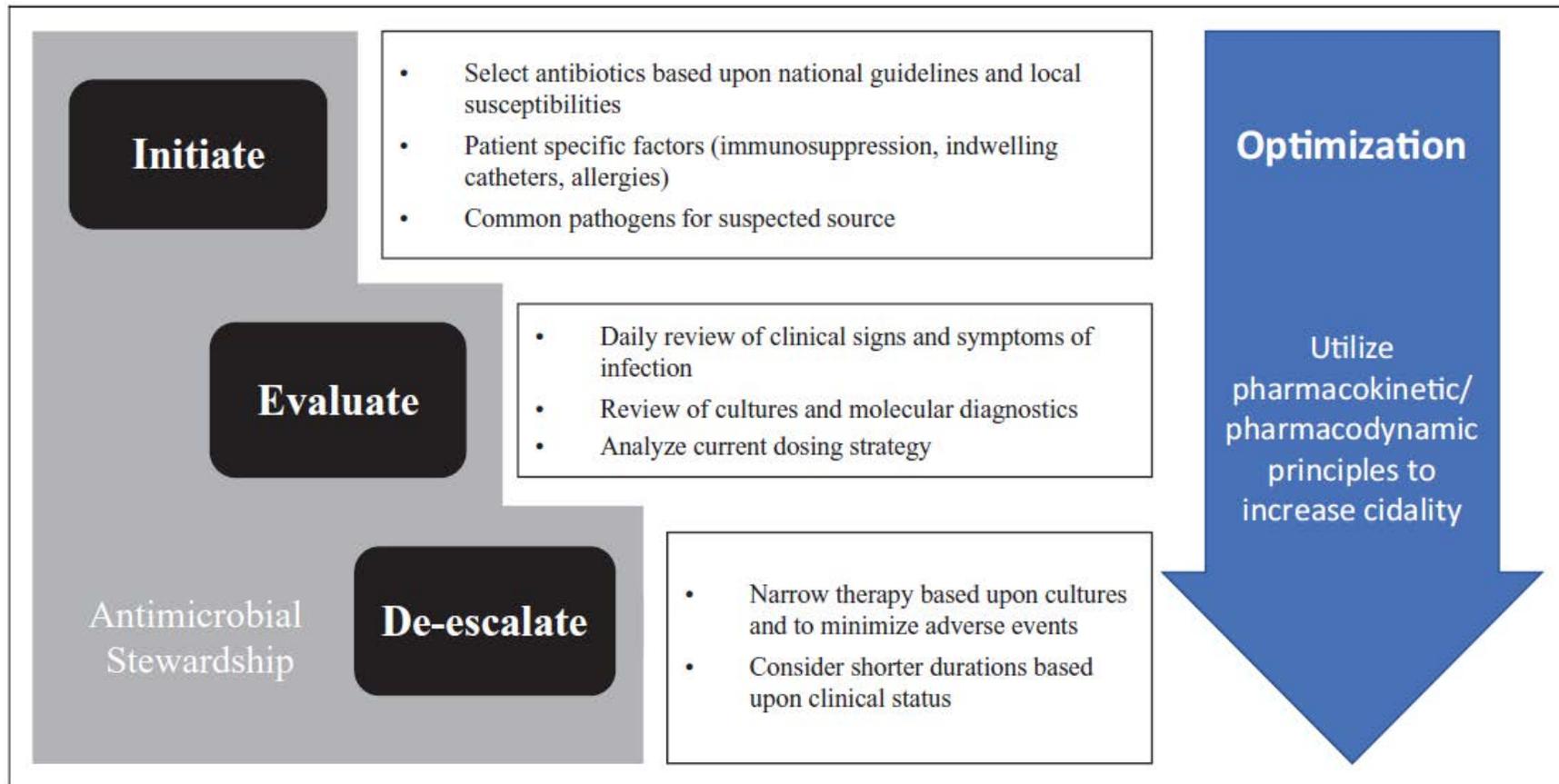
Schouten, Intensive Care Medicine, 2015



Schouten, Intensive Care Medicine, 2015

---

# The 'what'



Campion, J Int Care, 2018

# The 'what'

Articles

## Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis



*Emelie C Schuts, Marlies E J L Hulscher, Johan W Mouton, Cees M Verduin, James WT Cohen Stuart, Hans W P M Overdiek, Paul D van der Linden, Stephanie Natsch, Cees M P M Hertogh, Tom F W Wolfs, Jeroen A Schouten, Bart Jan Kullberg, Jan M Prins*

### Summary

**Background** Antimicrobial stewardship is advocated to improve the quality of antimicrobial use. We did a systematic review and meta-analysis to assess whether antimicrobial stewardship objectives had any effects in hospitals and long-term care facilities on four predefined patients' outcomes: clinical outcomes, adverse events, costs, and bacterial resistance rates.

*Lancet Infect Dis* 2016  
Published Online  
March 2, 2016  
[http://dx.doi.org/10.1016/S1473-3099\(16\)00065-7](http://dx.doi.org/10.1016/S1473-3099(16)00065-7)

**Methods** We identified 14 stewardship objectives and in Embase, Ovid MEDLINE, and PubMed. Studies v outcomes in patients in whom the specific antim findings in patients in whom the objective was or w risk reductions with relative risks and 95% CIs.

**Findings** We identified 145 unique studies with evidence was generally low and heterogeneity bet empirical therapy according to guidelines, de-esc therapeutic drug monitoring, use of a list of restri showed significant benefits for one or more of th associated with a relative risk reduction for morta

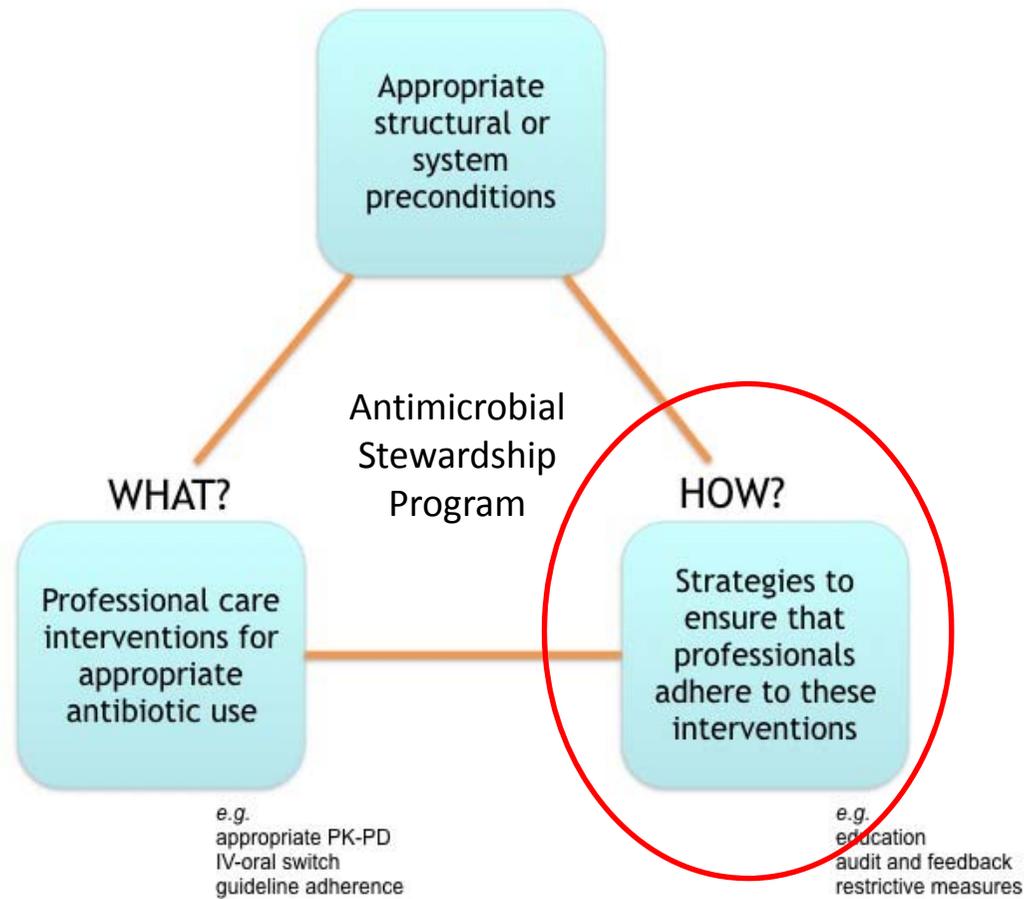
**Empirical therapy according to guidelines**  
**De-escalation of therapy**  
**Switch from intravenous to oral treatment**  
**Therapeutic drug monitoring**  
**Use of a list of restricted antibiotics**  
**Bedside consultation**

---

# The 'what': Dutch quality indicators

1. Performance of blood cultures prior to starting antibiotics: percentage of patients in whom at least two sets of blood cultures were performed 48 hours before until 24 hours after start of empirical systemic antibiotic therapy on ICU.
2. Adequate performance of antibiotic concentration levels: percentage of patients in whom a level was performed timely and at the correct indication
3. Performance of surveillance cultures during SDD and SOD: percentage of patient in whom -during their ICU stay at least one surveillance culture was performed for the presence of resistant GNB
4. 'Resistance meeting': how many times per year does a face-to-face meeting take place between ICU and Dpt of ID / Microbiology regarding the development of resistance in the ICU

Dongelmans, NICE 2017



Schouten, Intensive Care Medicine, 2015

---

# The 'how'

The HOW of antibiotic stewardship describes **recommended strategies** to ensure that professionals apply these professional care interventions in daily practice

These are **behavioural change** interventions

---

# The 'how'

## *Restrictive interventions*

- prior authorisation for selected (classes of) antibiotics
- restricted formulary
- automated antibiotic stop order

## *Persuasive (enabling) interventions*

- education
- feedback
- reminders
- decision support systems

**JS9**

We defined restriction as 'using rules to reduce the opportunity to engage in the target behaviour (or increase the target behaviour by reducing the opportunity to engage in competing behaviours)'. We defined enablement as 'increasing means/reducing barriers to increase capability or opportunity'.

Jeroen Schouten; 21-3-2018

---

# The 'How'



## **Interventions to improve antibiotic prescribing practices for hospital inpatients (Review)**

Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, Gould IM, Ramsay CR, Michie S

Now this would be considered the bible of interventions to improve AB prescribing practice

It actually shows that

-any intervention could work in the right circumstance: One size does not fit all

-education most used but least effective needs to be accompanied

-feedback should be accompanied by

Jeroen Schouten; 15-3-2018

---

## Davey et al. 2017



221 studies/120 interventions

- Persuasive (enabling) interventions
  - Restrictive interventions
- 
- Both enablement and restriction are effective
  - Effect size of e.g. dissemination of educational materials varied between -3.1% and 50,1%
  - Enabling interventions enhanced the effect of restrictive interventions
  - Enabling interventions that included feedback are more effective

---

## Davey et al. 2017



**Any** behavioral stewardship intervention might work to improve professionals' antimicrobial use

**How** then to select -from this menu of effective interventions- those interventions that might work best in a specific setting (e.g. hospital or ward)?

---

# Model for planning change <sup>JS7</sup>

<sup>JS8</sup> 1. Define 'good quality care'



2. Analyse current performance of this 'good quality care'



3. Analyse factors influencing the provision (or not) of 'good quality'



4. Develop a quality improvement strategy based on this diagnosis



5. Develop plan, execute, evaluate this improvement strategy

## Dia 19

---

**JS7**

this is where quality of care research comes in and where we try to apply the principles of the model for planning change or IMPLEMENTATION strategy That means that in our research we will first try to define what appropriate care is.

Jeroen Schouten; 4-4-2018

**JS8**

this is actually working towards more evidence in the WHAT of AMS; these are primary studies looking at the effect of interventions (such as deescalation, early withdrawal etc on relevant goals as described before such as mortality, costs and resistance

Jeroen Schouten; 4-4-2018

## Model for planning change

1. Define 'good quality care'

2. Analyse current performance of this 'good quality care'

### DIAGNOSTIC PHASE

3. Analyse factors influencing the provision (or not) of 'good quality care'

4. Develop a quality improvement strategy based on this diagnosis

5. Develop plan, execute, evaluate this improvement strategy

# Framework for implementation of AMS

## 1. Define appropriate antibiotic use

## Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis



Emelie C Schuts, Maaike E J L Hulscher, Johan W Mouton, Cees M Verduin, James W T Cohen Stuart, Hans W P M Overdijk, Paul D van der Linden, Stephanie Natsch, Cees M P M Herthog, Tom F W Wolfs, Jeroen A Schouten, Bart Jan Kullberg, Jan M Prins

### Summary

**Background** Antimicrobial stewardship is advocated to improve the quality of antimicrobial use. We did a systematic review and meta-analysis to assess whether antimicrobial stewardship objectives had any effects in hospitals and long-term care facilities on four predefined patients' outcomes: clinical outcomes, adverse events, costs, and bacterial resistance rates.

**Methods** We identified 14 stewardship objectives and did a separate systematic search for articles relating to each one in Embase, Ovid MEDLINE, and PubMed. Studies were included if they reported data on any of the four predefined outcomes in patients in whom the specific antimicrobial stewardship objective was assessed and compared the findings in patients in whom the objective was or was not met. We used a random-effects model to calculate relative risk reductions with relative risks and 95% CIs.

**Findings** We identified 145 unique studies with data on nine stewardship objectives. Overall, the quality of evidence was generally low and heterogeneity between studies was mostly moderate to high. For the objectives empirical therapy according to guidelines, de-escalation of therapy, switch from intravenous to oral treatment, therapeutic drug monitoring, use of a list of restricted antibiotics, and bedside consultation the overall evidence showed significant benefits for one or more of the four outcomes. Guideline-adherent empirical therapy was associated with a relative risk reduction for mortality of 35% (relative risk 0.65, 95% CI 0.54–0.80,  $p < 0.0001$ ) and for de-escalation of 66% (0.44, 0.30–0.66,  $p < 0.0001$ ). Evidence of effects was less clear for adjusting therapy according to renal function, discontinuing therapy based on lack of clinical or microbiological evidence of infection, and having a local antibiotic guide. We found no reports for the remaining five stewardship objectives or for long-term care facilities.

**Interpretation** Our findings of beneficial effects on outcomes with nine antimicrobial stewardship objectives suggest they can guide stewardship teams in their efforts to improve the quality of antibiotic use in hospitals.

**Funding** Dutch Working Party on Antibiotic Policy and Netherlands National Institute for Public Health and the Environment.

### Introduction

Although the benefits of antibiotic use are indisputable, misuse and overuse of antibiotics have contributed to antibiotic resistance, which has become a serious and growing threat to public health.<sup>1,2</sup> Patients with infections caused by resistant bacteria generally have an increased risk of poor clinical outcomes and death and use more health-care resources than patients infected with non-resistant bacteria of the same species.<sup>3</sup>

Of all antibiotics prescribed in acute-care hospitals, 20–50% are either unnecessary or inappropriate.<sup>1,4</sup> Hospitals worldwide have been incorporating antimicrobial stewardship into hospital policy, with the goal of improving the quality of antimicrobial use. The primary goal of antimicrobial stewardship is to achieve optimum clinical outcomes and ensure cost-effectiveness of therapy while keeping to a minimum unintended consequences of antimicrobial use, including toxic effects, selection of pathogenic organisms, and the emergence of resistance.<sup>5</sup> The characteristics of antimicrobial stewardship programmes vary<sup>6</sup> but

generally consist of a range of interventions that can be selected and adapted to fit the infrastructure of any hospital.<sup>9</sup>

In stewardship programmes, two sets of interventions should be distinguished. The first relates to recommended care at the patient level (stewardship objectives), such as treating patients according to the guidelines or taking cultures of blood and from the site of infection. The second set relates to recommended strategies for achieving the stewardship objectives, such as restrictive (eg, formulary restriction) and persuasive (eg, education and feedback) strategies, to improve appropriate antimicrobial use. The evidence for the second set of interventions has been systematically reviewed,<sup>1</sup> but the yields of individual stewardship objectives do not seem to have been assessed.

We did a systematic review and meta-analysis to summarise the current state of evidence of the effects of antimicrobial stewardship objectives on patients' clinical outcomes (eg, mortality and length of stay [LOS] in

Lancet Infect Dis 2016

Published Online

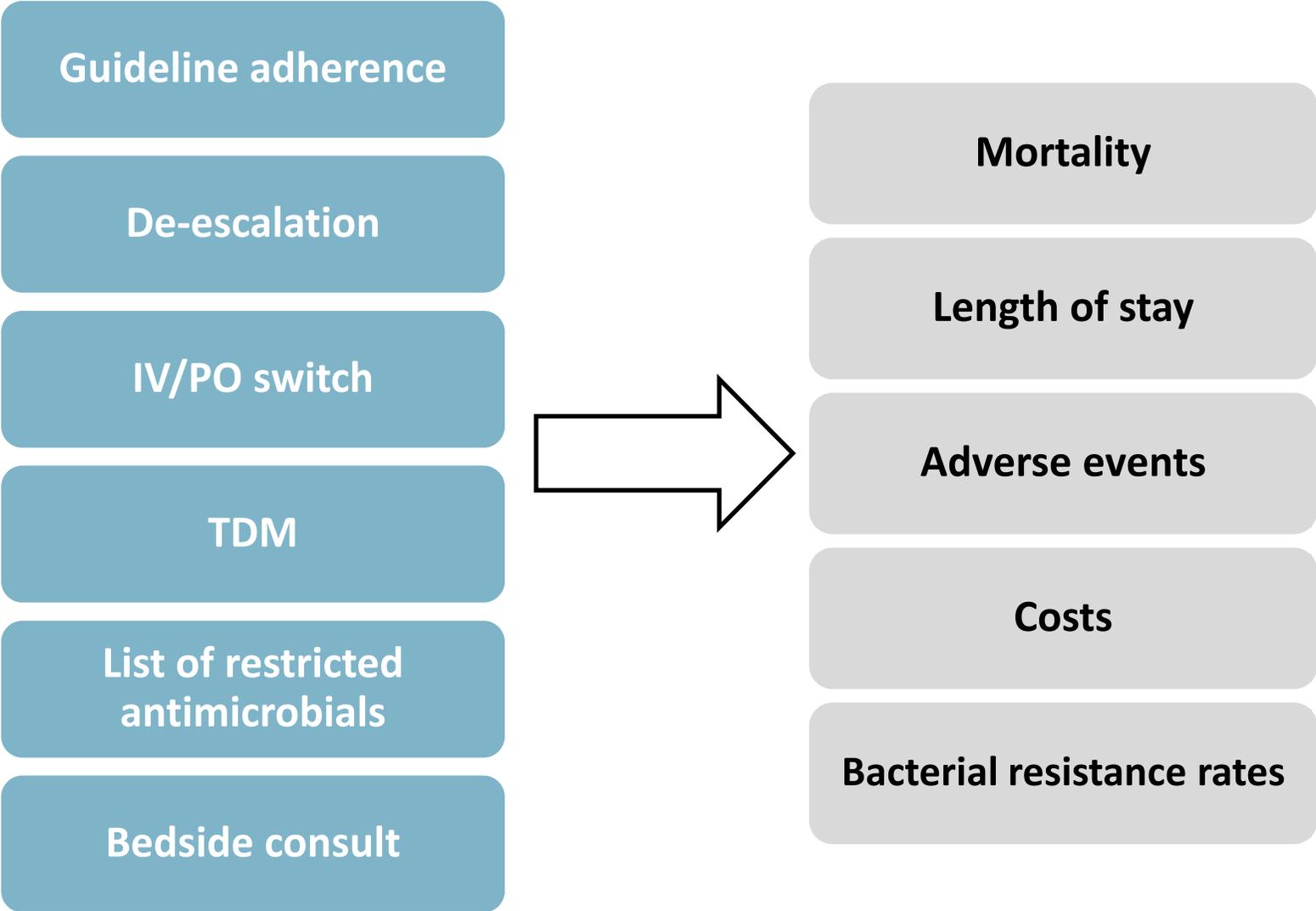
March 2, 2016

[http://dx.doi.org/10.1016/S1473-3099\(16\)00065-7](http://dx.doi.org/10.1016/S1473-3099(16)00065-7)

See Online Articles

[http://dx.doi.org/10.1016/S1473-3099\(16\)00099-2](http://dx.doi.org/10.1016/S1473-3099(16)00099-2)

Department of Internal Medicine, Division of Infectious Diseases, Centre for Infection and Immunity Amsterdam (CINIMA), Academic Medical Centre, Amsterdam, Netherlands (E C Schuts, EJC, Prof M Prins MD), Scientific Institute for Quality of Healthcare, Radboud Institute for Health Sciences (Prof M E J L Hulscher PhD), Department of Pharmacy (S Natsch Pharm D), and Department of Internal Medicine, Centre for Infectious Diseases (Prof B J Kullberg MD), Radboud University Medical Centre, Nijmegen, Netherlands, Department of Medical Microbiology and Infectious Diseases, Erasmus MC, Rotterdam, Netherlands (Prof J W M Outen MD), Department of Medical Microbiology and Infection Prevention, Amphia Hospital, Breda, Netherlands (C M Verduin MD), Department of Medical Microbiology, Medisch Centrum Alkmaar, Alkmaar, Netherlands (J W T Cohen Stuart MD), Department of Hospital Pharmacy, Medical Centre Haaglanden, The Hague, Netherlands (J W P M Overdijk Pharm D), The Hague Hospitals Central Pharmacy, The Hague, Netherlands (J W P M Overdijk), Department of Clinical Pharmacy, Tergooi Hospital, Hilversum, Netherlands (P D van der Linden Pharm D), Department of General Practice and Family Care Medicine, VU University Medical Centre, Amsterdam, Netherlands (Prof C M P M Herthog MD), Department of Paediatric



# Framework for implementation of AMS

INVITED ARTICLE **QUALITY IMPROVEMENT**

Trish M. Perl, Section Editor

## 1. Define appropriate antibiotic use



## Quality Indicators to Measure Appropriate Antibiotic Use in Hospitalized Adults

Caroline M. A. van den Bosch,<sup>1</sup> Suzanne E. Georfings,<sup>1</sup> Stephanie Natsch,<sup>2</sup> Jan M. Prins,<sup>1</sup> and Marlies E. J. L. Hulscher<sup>3</sup>

<sup>1</sup>Department of Internal Medicine, Division of Infectious Diseases, Academic Medical Center, University of Amsterdam, and Departments of <sup>2</sup>Clinical Pharmacology and <sup>3</sup>Scientific Institute for Quality of Healthcare, Radboud University Medical Center, Nijmegen, The Netherlands

**Background.** An important requirement for an effective antibiotic stewardship program is the ability to measure appropriateness of antibiotic use. The aim of this study was to develop quality indicators (QIs) that can be used to measure appropriateness of antibiotic use in the treatment of all bacterial infections in hospitalized adult patients.

**Methods.** A RAND-modified Delphi procedure was used to develop a set of QIs. Potential QIs were retrieved from the literature. In 2 questionnaire mailings with an in-between face-to-face consensus meeting, an international multidisciplinary expert panel of 17 experts appraised and prioritized these potential QIs.

**Results.** The literature search resulted in a list of 24 potential QIs. Nine QIs describing recommended care at patient level were selected: (1) take 2 blood cultures, (2) take cultures from suspected sites of infection, (3) prescribe empirical antibiotic therapy according to local guideline, (4) change empirical to pathogen-directed therapy, (5) adapt antibiotic dosage to renal function, (6) switch from intravenous to oral, (7) document antibiotic plan, (8) perform therapeutic drug monitoring, and (9) discontinue antibiotic therapy if infection is not confirmed. Two QIs describing recommended care at the hospital level were also selected: (1) a local antibiotic guideline should be present, and (2) these local guidelines should correspond to the national antibiotic guidelines.

**Conclusions.** The selected QIs can be used in antibiotic stewardship programs to determine for which aspects of antibiotic use there is room for improvement. At this moment we are testing the clinimetric properties of these QIs in 1800 hospitalized patients, in 22 Dutch hospitals.

**Keywords.** quality indicator; quality improvement; antibiotic treatment; appropriate antibiotic use; antibiotic stewardship.

The World Health Organization signaled the emergence of antibiotic resistance, along with the steady decline in the discovery of new antibiotics, as a major health threat for the coming decade. To help control antibiotic resistance, better use of current agents is warranted and a decrease in inappropriate use of antibiotics is necessary [1].

Antibiotic stewardship is an active interprofessional effort by multidisciplinary teams to optimize clinical outcome while minimizing unintended consequences

of antibiotic use, including the emergence of resistance [2]. Literature shows that stewardship programs can decrease incorrect antibiotic use and reduce healthcare costs without negatively influencing the quality of care provided [2]. An important requirement for an effective stewardship program to set priorities and focus improvement is the ability to measure the appropriateness of hospital antibiotic use.

Guidelines on the management of infections describe, by definition, appropriate antibiotic use [3]. Adherence to such guidelines improves clinical outcome, is correlated with a lower rate of development of resistance to antibiotics, and lowers costs [4–8]. Available guidelines and international literature can be used to systematically develop precise parameters, so-called quality indicators (QIs), to measure the appropriateness of antibiotic use [9–11]. The European Surveillance of Antimicrobial Consumption developed QIs to measure appropriate outpatient antibiotic use in Europe [12]. However, at

Received 6 February 2014; accepted 11 September 2014; electronically published 26 September 2014.

Correspondence: Caroline M. A. van den Bosch, MD, Department of Internal Medicine, Division of Infectious Diseases, Academic Medical Center, University of Amsterdam, Room T4-132, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands (c.m.vandenbosch@amc.uva.nl).

Clinical Infectious Diseases® 2015;60(2):281–91

© The Author 2014. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.  
DOI: 10.1093/cid/ciu747

# Framework for implementation of AMS

1. Define appropriate antibiotic use

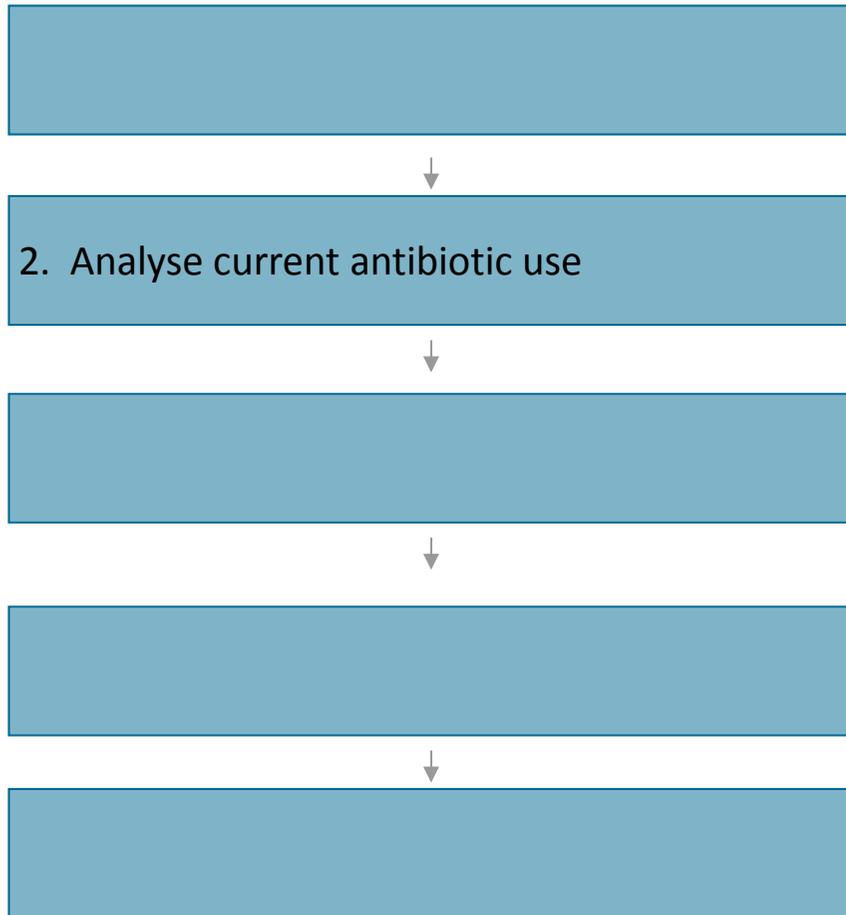


Table 1. Quality Indicators for Antimicrobial Stewardship in the Emergency Department

| STEWARDSHIP PREREQUISITES  |
|--|
| 1. An antibiotic stewardship program that comprises measuring and improving antibiotic use should also cover the ED (QI 1)   |
| 2. A local antibiotic guideline should be present in the ED of the healthcare facility (QI 2) <ul style="list-style-type: none"> <li>- The local guideline should correspond to the national guideline but should be adapted based on local resistance patterns (QI 3)</li> </ul>  |
| 3. Essential antibiotics as defined by local antibiotic guidelines should be stocked in the ED (QI 4)  |
| 4. Antibiotics in stock in the ED should not be beyond the expiration date (QI 5)  |
| 5. Antibiotics should be adequately conserved and handled in the ED (QI 6)   |
| DIAGNOSTICS  |
| 6. Diagnostic microbiological tests relevant for the site of infection should be collected in the ED preferably before antibiotic administration (QI 7)  |
| EMPIRICAL TREATMENT  |
| 7. Antibiotics should be prescribed in the ED according to local antibiotic guidelines or according to national guidelines when no local guidelines are available (QI 8) <ul style="list-style-type: none"> <li>- Dosing and dosing interval of antibiotics should be prescribed in the ED according to guidelines (QI 9)</li> <li>- The route of administration of antibiotics given in the ED should be compliant with guidelines (QI 10)</li> <li>- Timeliness of administration of antibiotic therapy and prophylaxis in the ED should be compliant with guidelines (QI 11)</li> </ul> |
| 8. When prescribing antibiotics in the ED, the following should be taken into account: <ul style="list-style-type: none"> <li>- Relevant* results of previous cultures and susceptibilities (QI 12) *as defined by the local or national guidelines</li> <li>- Previous antibiotic use (QI 13)</li> <li>- Allergy status (QI 14)</li> <li>- Contraindications (QI 15)</li> </ul>   |
| 9. Antibiotics prescribed by an ED provider for an admitted patient should be initiated while the patient is in the ED (QI 16): <ul style="list-style-type: none"> <li>- In patients with sepsis or septic shock, administration of antibiotics should be initiated promptly in the ED aiming to reduce that time to as short a duration as feasible (QI 17)</li> </ul>  |

---

# Framework for implementation of AMS



## Different dimensions

### *Metric*

Quantity of antibiotic use indicators  
Quality of antibiotic use indicators  
Proxy indicators

### *Level of analysis*

National level  
Hospital level  
Ward level

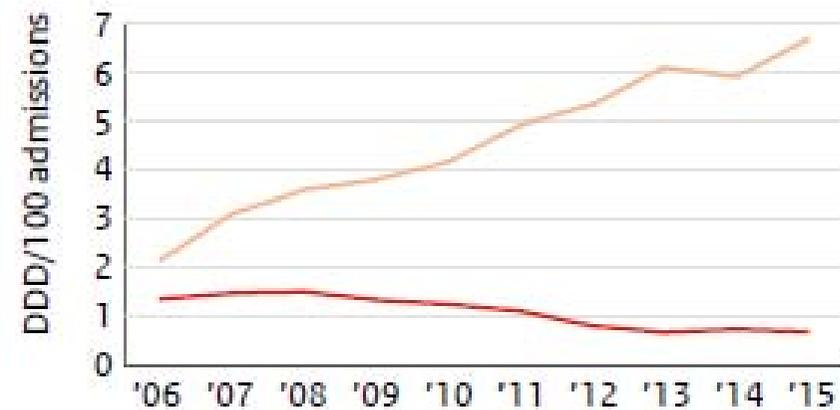
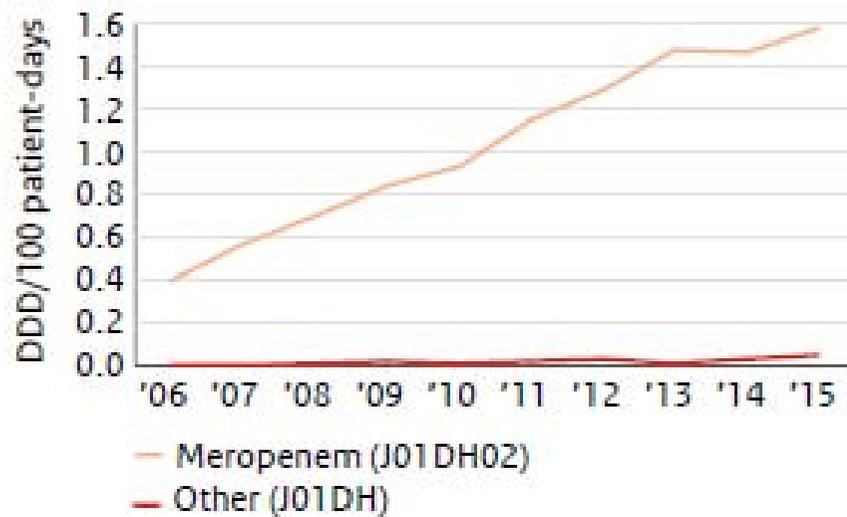
### *Timing*

Day-to-day tracking  
QI projects / Audits

Selection is dependent on particular setting and goals of an ASP

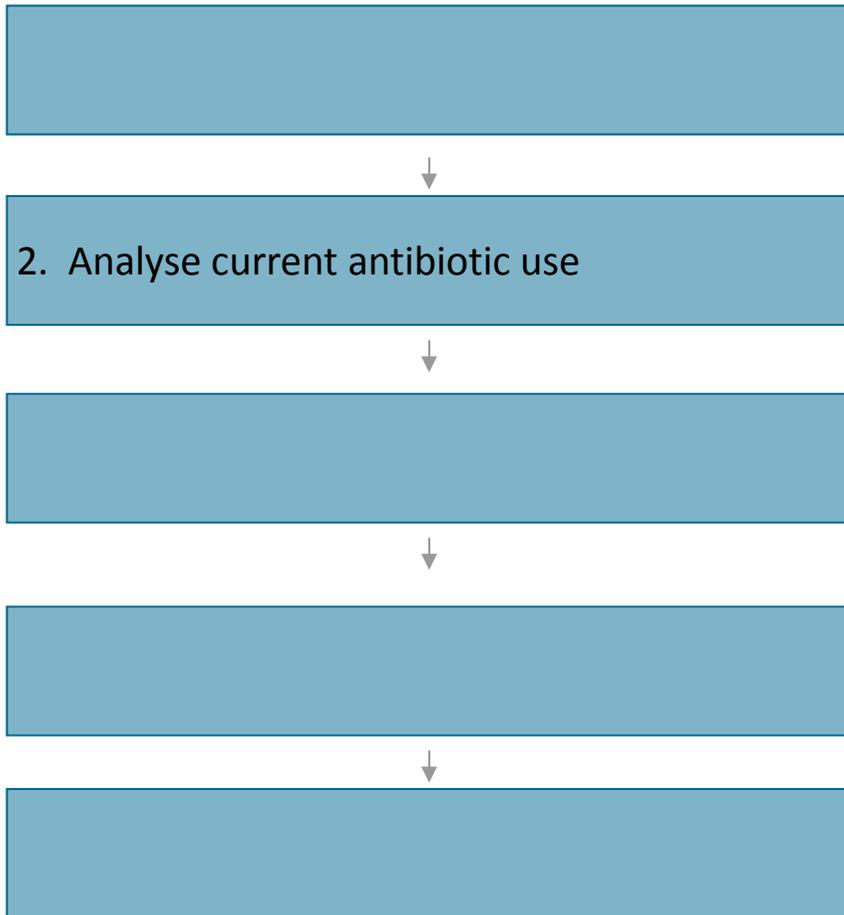
# Framework for implementation of AMS

Quantity of Use indicators  
National level



NethMAP

# Framework for implementation of AMS



Spoorenberg et al. *BMC Infectious Diseases* (2015) 15:505  
DOI 10.1186/s12879-015-1257-5



RESEARCH ARTICLE

Open Access



## Appropriate antibiotic use for patients with complicated urinary tract infections in 38 Dutch Hospital Departments: a retrospective study of variation and determinants

V. Spoorenberg<sup>1\*</sup>, S. E. Geerlings<sup>1</sup>, R. B. Geskus<sup>2</sup>, T. M. de Reijke<sup>3</sup>, J. M. Prins<sup>1</sup> and M. E. J. L. Hulscher<sup>4\*</sup>

### Abstract

**Background:** Appropriate antibiotic use in patients with complicated urinary tract infections can be measured by a valid set of nine quality indicators (QIs). We evaluated the performance of these QIs in a national setting and investigated which determinants influenced appropriate antibiotic use. For the latter, we distinguished patient, department and hospital characteristics, including organizational interventions aimed at improving the quality of antibiotic use.

**Methods:** A retrospective, observational multicentre study included 1964 patients (58 % male sex) with a complicated urinary tract infection treated at Internal Medicine and Urology departments of 19 Dutch university and non-university hospitals. Patient characteristics were extracted from medical charts. QI performance scores were calculated using previously constructed algorithms. Department and hospital characteristics were collected using questionnaires filled in by an internal medicine physician and a urologist. Regression analysis was performed to identify determinants of QI performance. Clustering at department and hospital level was taken into account through inclusion of random effects in a multi-level model.

**Results:** Median QI performance of departments varied between 31 % ('Treat urinary tract infection in men according to local guideline') and 77 % ('Perform urine culture'). The patient characteristics non-febrile urinary tract infection, female sex and presence of a urinary catheter were negatively associated with performance on many QIs. The presence of an infectious diseases physician and an antibiotic formulary were positively associated with 'Prescribe empirical therapy according to guideline'. No other department or hospital characteristics, including stewardship elements, were consistently associated with better QI performance.

**Conclusions:** A large inter-department variation was demonstrated in the appropriateness of antibiotic use. In particular certain patient characteristics (more than department or hospital characteristics) influenced the quality of antibiotic use. Some, but not all antibiotic stewardship elements did translate into better QI performance.

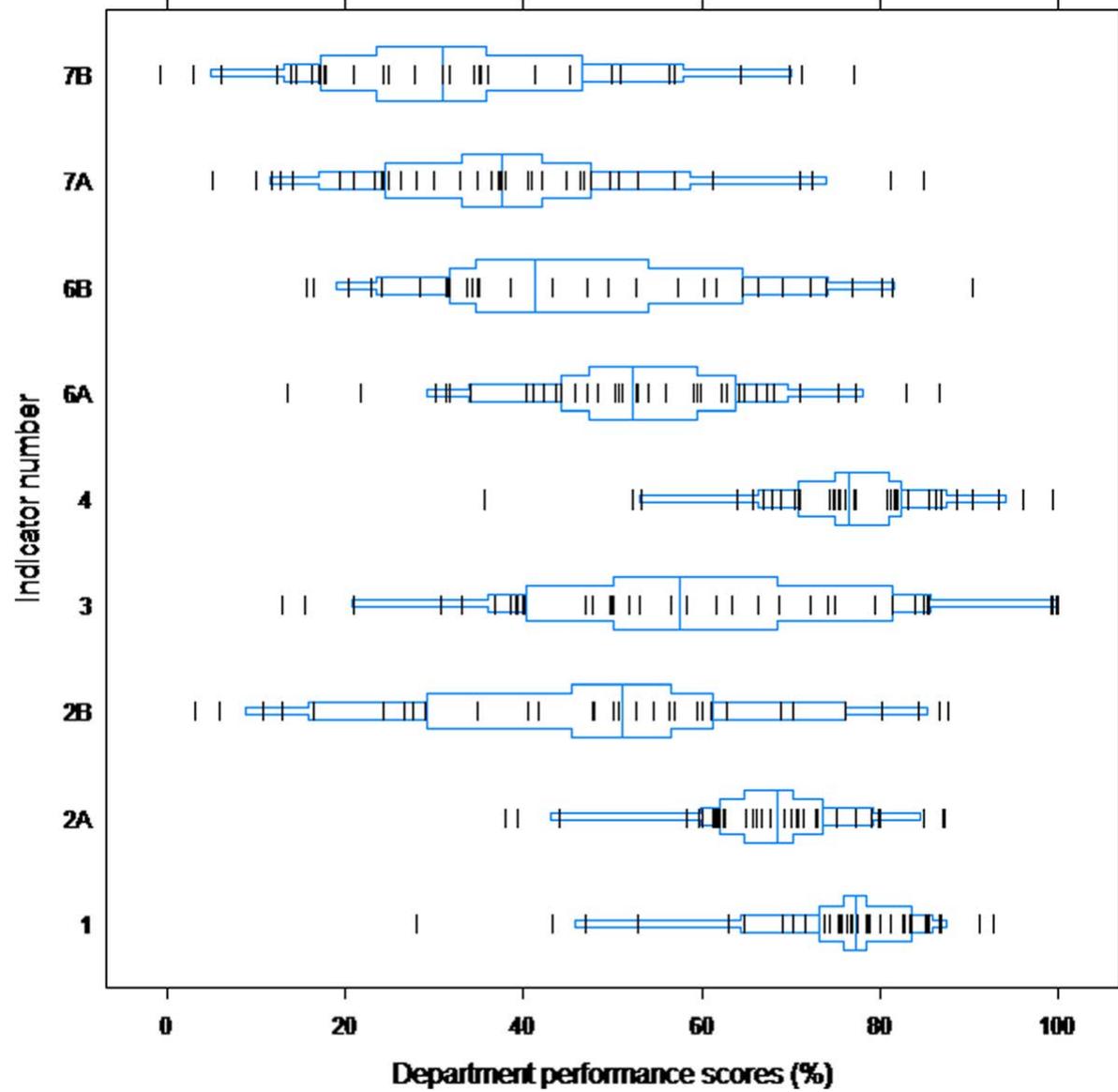
**Keywords:** Antibiotic use, Urinary tract infection, Quality indicator, Guideline adherence, Antibiotic stewardship, Determinants

\* Correspondence: vspoorenberg@mc.nl, m.hulscher@quimc.nl  
<sup>1</sup>Department of Internal Medicine, Division of Infectious Diseases, Centre for Infection and Immunity Amsterdam, Academic Medical Centre, Amsterdam, The Netherlands  
<sup>2</sup>Scientific Institute for Quality of Healthcare, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands  
Full list of author information is available at the end of the article



© 2015 Spoorenberg et al. **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Streamline treatment  
Switch from iv to oral



# Framework for implementation of AMS

Berrevoets et al. BMC Infectious Diseases (2017) 17:565  
DOI 10.1186/s12879-017-2673-5

BMC Infectious Diseases

RESEARCH ARTICLE

Open Access



## Monitoring, documenting and reporting the quality of antibiotic use in the Netherlands: a pilot study to establish a national antimicrobial stewardship registry

Marvin AH Berrevoets<sup>1,7\*</sup>, Jaap ten Oever<sup>1,7</sup>, Tom Sprong<sup>2</sup>, Reinier M van Hest<sup>3</sup>, Ingeborg Groothuis<sup>4</sup>, Inger van Heijl<sup>5</sup>, Jeroen A Schouten<sup>6</sup>, Marlies E Hulscher<sup>6,7</sup> and Bart-Jan Kullberg<sup>1,7</sup>

### Abstract

**Background:** The registry. This registry stewardship activities by antimicrobial stewardship pilot study we aim

**Methods:** We performed validated stewardship objectives (11 process of care recommendations and 3 structure of care recommendations) the A-teams monitored and documented in individual patients. They provided, where possible, data to compute quality indicator (QI) performance scores in line with recently developed QIs to measure appropriate antibiotic use in hospitalized adults for the period of January 2015 through December 2015

**Results:** All hospitals had a local antibiotic guideline describing recommended antimicrobial use. All A-teams monitored the performance of bedside consultations in *Staphylococcus aureus* bacteremia and the prescription of restricted antimicrobials. Documentation and reporting were the best for the use of restricted antimicrobials: 80% of the A-teams could report data. Lack of time and the absence of an electronic medical record system enabling documentation during the daily work flow were the main barriers hindering documentation and reporting.

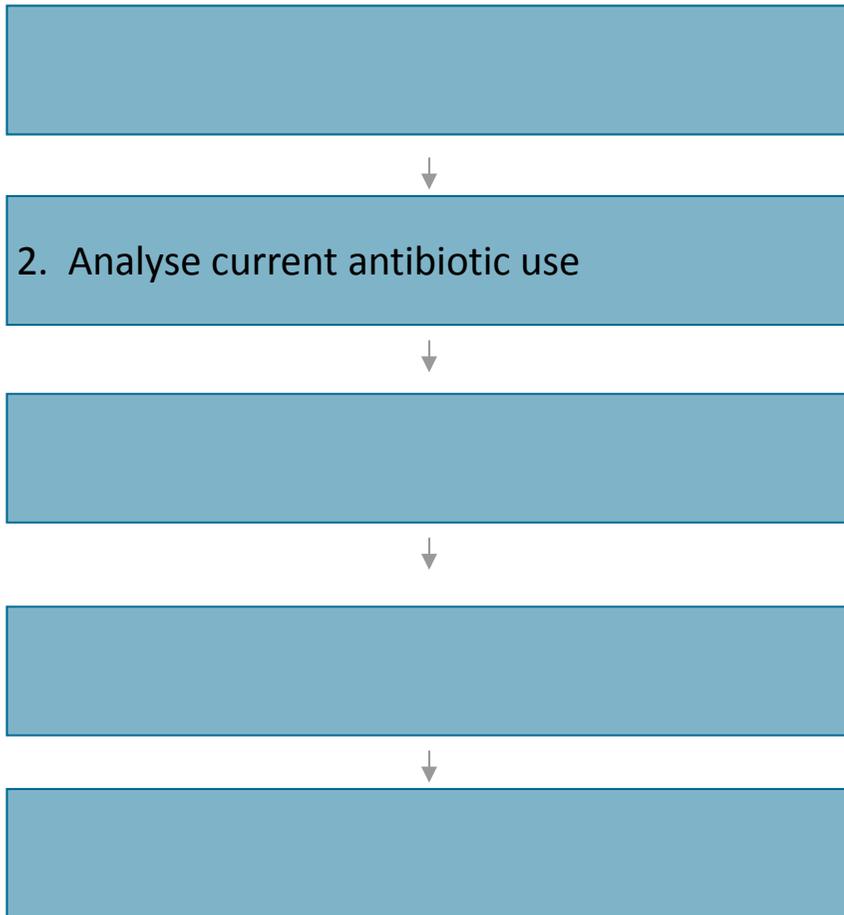
**Conclusions:** Five out of 11 stewardship objectives were actively monitored by A-teams. Without extra effort, 4 A-teams could report on the quality of use of restricted antibiotics. Therefore, this aspect of antibiotic use should be the starting point of the national antimicrobial stewardship registry. Our registry is expected to become a powerful tool to evaluate progress and impact of antimicrobial stewardship programs in hospitals.

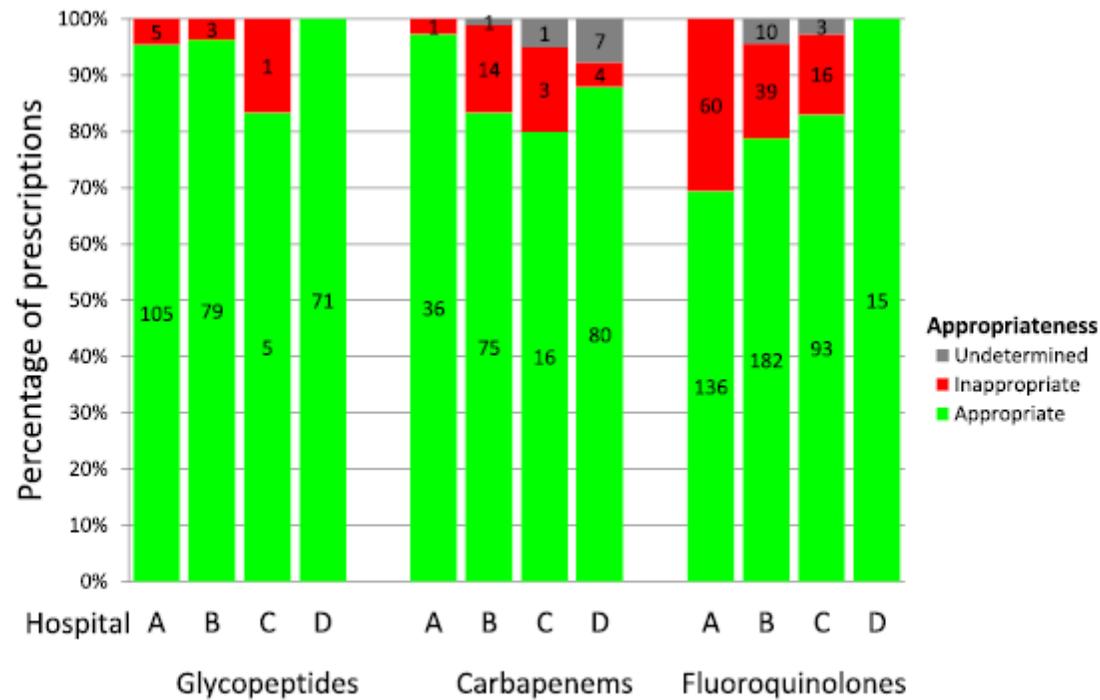
**Keywords:** Antibiotic stewardship, Quality indicator, Benchmarking, Antimicrobial stewardship team, Antimicrobial stewardship program, Quality of care

## Quality of Use indicators National level

Antimicrobial stewardship programs and the quality of antibiotic use are monitored in a national stewardship registry. In this study, we established a national registry.

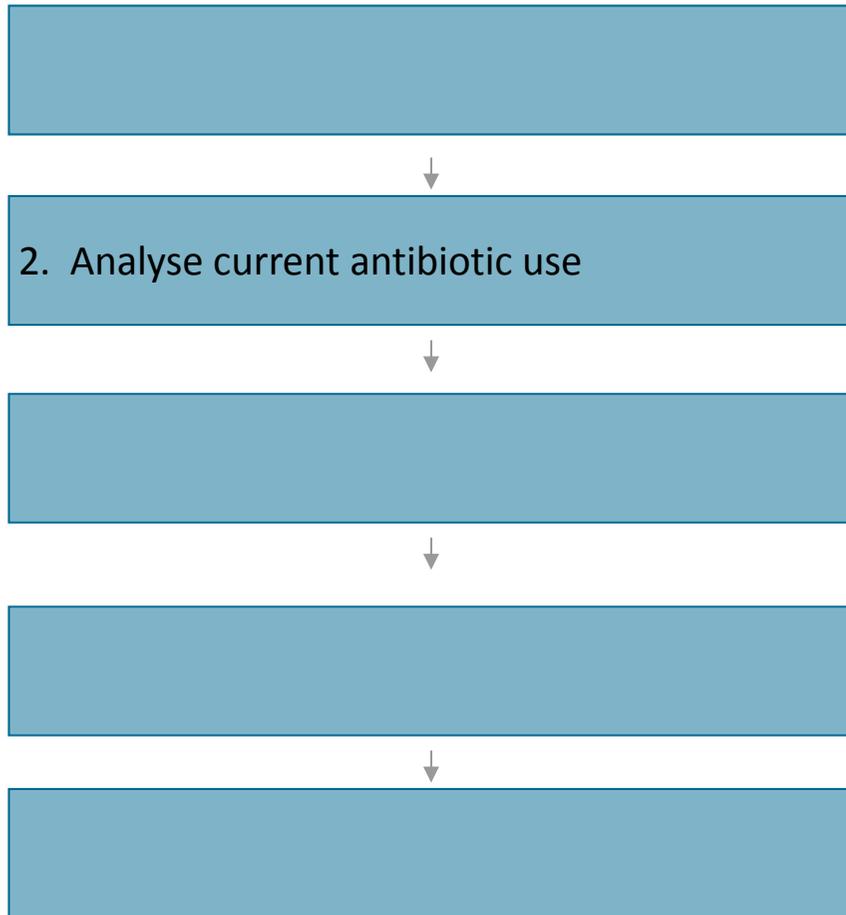
We performed a pilot study in which 14 hospitals participated. The quality of antibiotic use was monitored and reported in a national registry.





**Fig. 1** Appropriateness of antibiotic prescriptions. Number in the bars represents the numbers of prescriptions reviewed per category. In hospital "D" pre-authorization for the use of glycopeptides resulted in an appropriateness of 100%

# Framework for implementation of AMS



JAC Antimicrob Resist  
doi:10.1093/jacamr/dlaa086

JAC-  
Antimicrobial  
Resistance

## Proxy indicators to estimate the appropriateness of medications prescribed by paediatricians in infectious diseases: a cross-sectional observational study based on reimbursement data

N. Thilly<sup>1,2</sup>, O. Pereira<sup>3</sup>, J. Schouten<sup>4</sup>, M. E. J. L. Hulscher<sup>5</sup> and C. Pulcini<sup>1,6\*</sup>

<sup>1</sup>Université de Lorraine, APEMAC, Nancy, France; <sup>2</sup>Université de Lorraine, CHRU-Nancy, Département Méthodologie, Promotion, Investigation, Nancy, France; <sup>3</sup>Direction Régionale du Service Médical Grand Est, Nancy, France; <sup>4</sup>Radboud University Medical Centre, Radboud Institute for Health Sciences, Department of Intensive Care Medicine, Nijmegen, The Netherlands; <sup>5</sup>Radboud University Medical Centre, Radboud Institute for Health Sciences, Scientific Center for Quality of Healthcare (IQ healthcare), Nijmegen, The Netherlands; <sup>6</sup>Université de Lorraine, CHRU-Nancy, Infectious Diseases Department, Nancy, France

\*Corresponding author. E-mail: celine.pulcini@univ-lorraine.fr

Received 4 May 2020; accepted 8 September 2020

**Background:** We previously developed proxy indicators (PIs) that can be used to estimate the appropriateness of medications used for infectious diseases (in particular antibiotics) in primary care, based on routine reimbursement data that do not include clinical indications.

**Objectives:** To: (i) select the PIs that are relevant for children and estimate current appropriateness of medications used for infectious diseases by French paediatricians and its variability while using these PIs; (ii) assess the clinimetric properties of these PIs using a large regional reimbursement database; and (iii) compare performance scores for each PI between paediatricians and GPs in the paediatric population.

**Methods:** For all individuals living in north-eastern France, a cross-sectional observational study was performed analysing National Health Insurance data (available at prescriber and patient levels) regarding antibiotics prescribed by their paediatricians in 2017. We measured performance scores of the PIs, and we tested their clinimetric properties, i.e. measurability, applicability and room for improvement.

**Results:** We included 116 paediatricians who prescribed a total of 44 146 antibiotic treatments in 2017. For all four selected PIs (seasonal variation of total antibiotic use, amoxicillin/second-line antibiotics ratio, co-prescription of anti-inflammatory drugs and antibiotics), we found large variations between paediatricians. Regarding clinimetric properties, all PIs were measurable and applicable, and showed high improvement potential. Performance scores did not differ between these 116 paediatricians and 3087 GPs.

**Conclusions:** This set of four proxy indicators might be used to estimate appropriateness of prescribing in children in an automated way within antibiotic stewardship programmes.

### Introduction

Antimicrobial resistance, in particular antibiotic resistance, is a global threat. To address this public health issue, two main strategies must be implemented: infection prevention and control as well as antimicrobial stewardship programmes.<sup>1</sup> Metrics or indicators reflecting the appropriateness of antibiotic prescriptions are needed, initially to assess whether current antibiotic use is appropriate or whether improvement is necessary, and then, if this assessment shows targets for improvement, to optimize antibiotic

use relying upon a multifaceted strategy that includes audit and feedback, for which, again, such metrics are crucial.<sup>2</sup>

A recent literature review identified quality indicators that could be used to assess the appropriateness of antibiotics prescribed in the outpatient setting.<sup>3</sup> However, all these quality indicators need data on the clinical indication to be calculated. Since data on clinical indication are rarely available in electronic medical records or in routine reimbursement databases,<sup>4</sup> quality indicators usually rely on manual collection of data, which is time-consuming. Finding a

© The Author(s) 2020. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

1 of 6

# Framework for implementation of AMS

# JAR

Indicators to estimate paediatric antibiotic appropriateness

**Table 1.** List of PIs to estimate the appropriateness of medications prescribed for infectious diseases by paediatricians

| PI  | Numerator description   | Denominator description  | Unit                                 | Target value | Target patients |
|---|---|--|--------------------------------------|--------------|-----------------|
| PI 1: Seasonal variation of total antibiotic use (%)            | [number of prescriptions of antibiotics (J01) during the cold-weather season (January–March and October–December)/number of prescriptions of antibiotics (J01) during the hot-weather season (April–September) – 1] × 100 |  | percentage of prescriptions per year | <20%         | all patients    |
| PI 2: Amoxicillin/second-line antibiotics (ratio)               | number of prescriptions of amoxicillin (J01CA04)  | number of prescriptions of amoxicillin/clavulanic acid (J01CR02) + quinolones (J01M) + cephalosporins (J01D) + MLSK (J01F) | number of prescriptions per year     | >1           | all patients    |
| PI 3: Co-prescription antibiotic + systemic NSAIDs (%)          | number of antibiotic(s) (J01) + systemic NSAID(s) (M01A) co-prescribed on the same day  | total number of antibiotic prescriptions   | percentage of prescriptions per year | <5%          | all patients    |
| PI 4: Co-prescription antibiotic + systemic corticosteroids (%) | number of antibiotic(s) (J01) + systemic corticosteroid(s) (H02AB) co-prescribed on the same day  | total number of antibiotic prescriptions   | percentage of prescriptions per year | <5%          | all patients    |

MLSK, macrolides, lincosamides, streptogramins and ketolides; NSAIDs, non-steroidal anti-inflammatory drugs.

---

# Framework for implementation of AMS

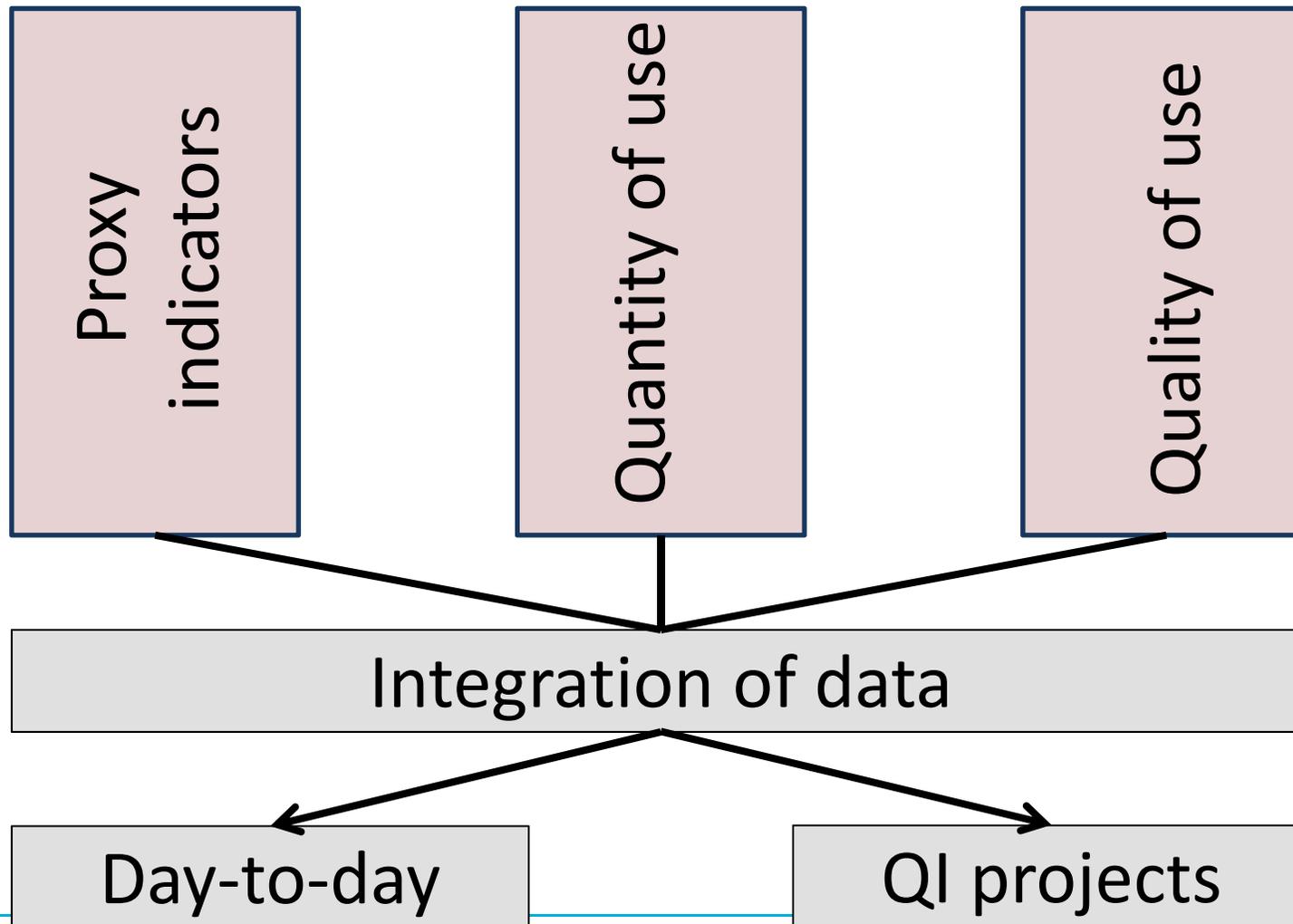
**Table 2.** Results for the four proxy indicators, calculated at paediatrician level

| PI   | Target value | Median (IQR)      | Percentage of paediatricians who reached the target (performance) |
|--|--------------|-------------------|---|
| PI 1: Seasonal variation of total antibiotic use (%)   | <20%         | 88.7 (59.2–126.7) | 6.9   |
| PI 2: Amoxicillin/second-line antibiotics (ratio)      | >1           | 1.9 (1.0–3.2)     | 74.1  |
| PI 3: Co-prescription antibiotic + NSAIDs (%)          | <5%          | 9.1 (4.3–16.6)    | 25.9  |
| PI 4: Co-prescription antibiotic + corticosteroids (%) | <5%          | 9.4 (4.1–19.2)    | 29.3  |

NSAIDs, non-steroidal anti-inflammatory drugs.

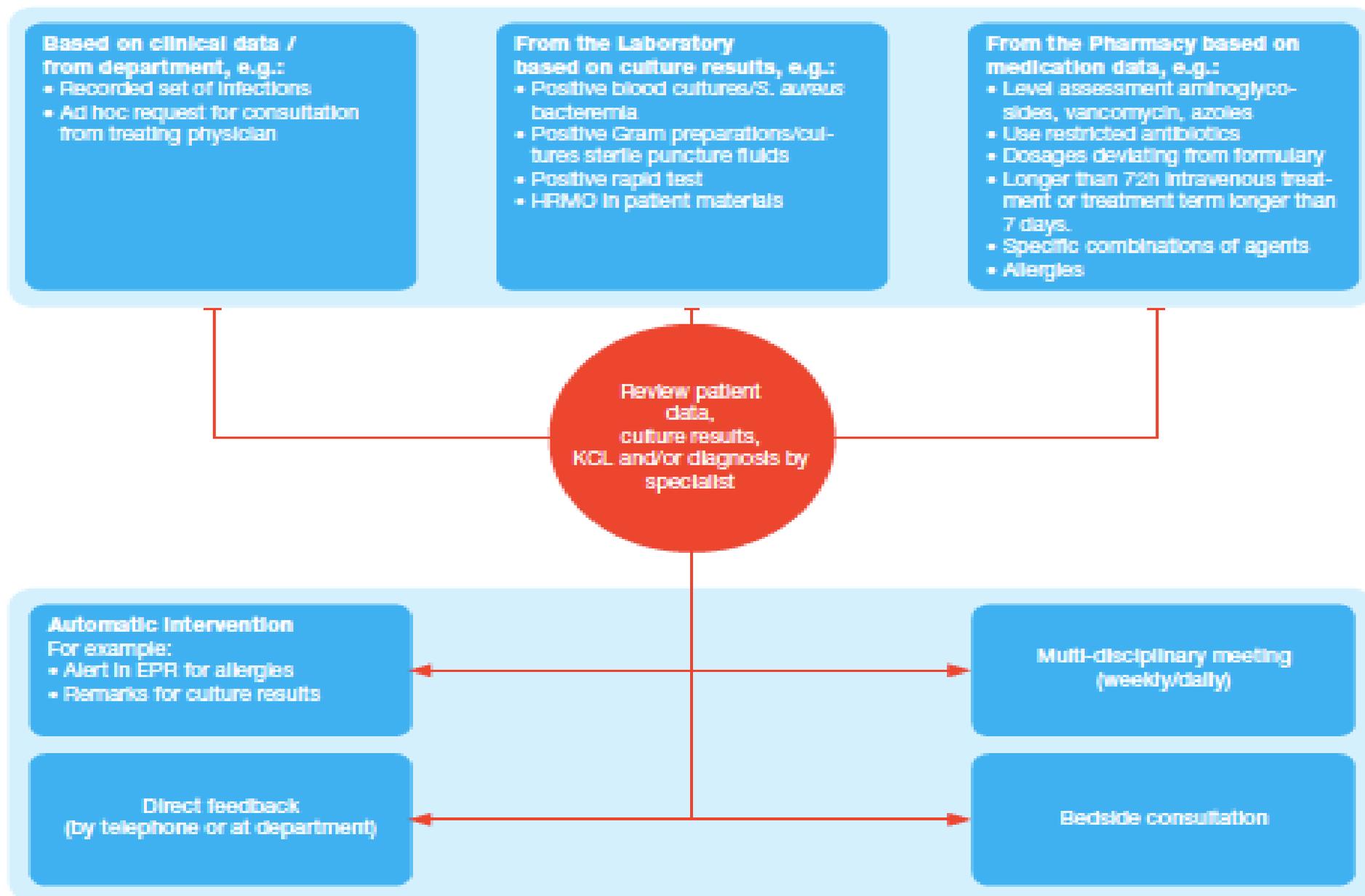
---

## Three pillars of tracking data

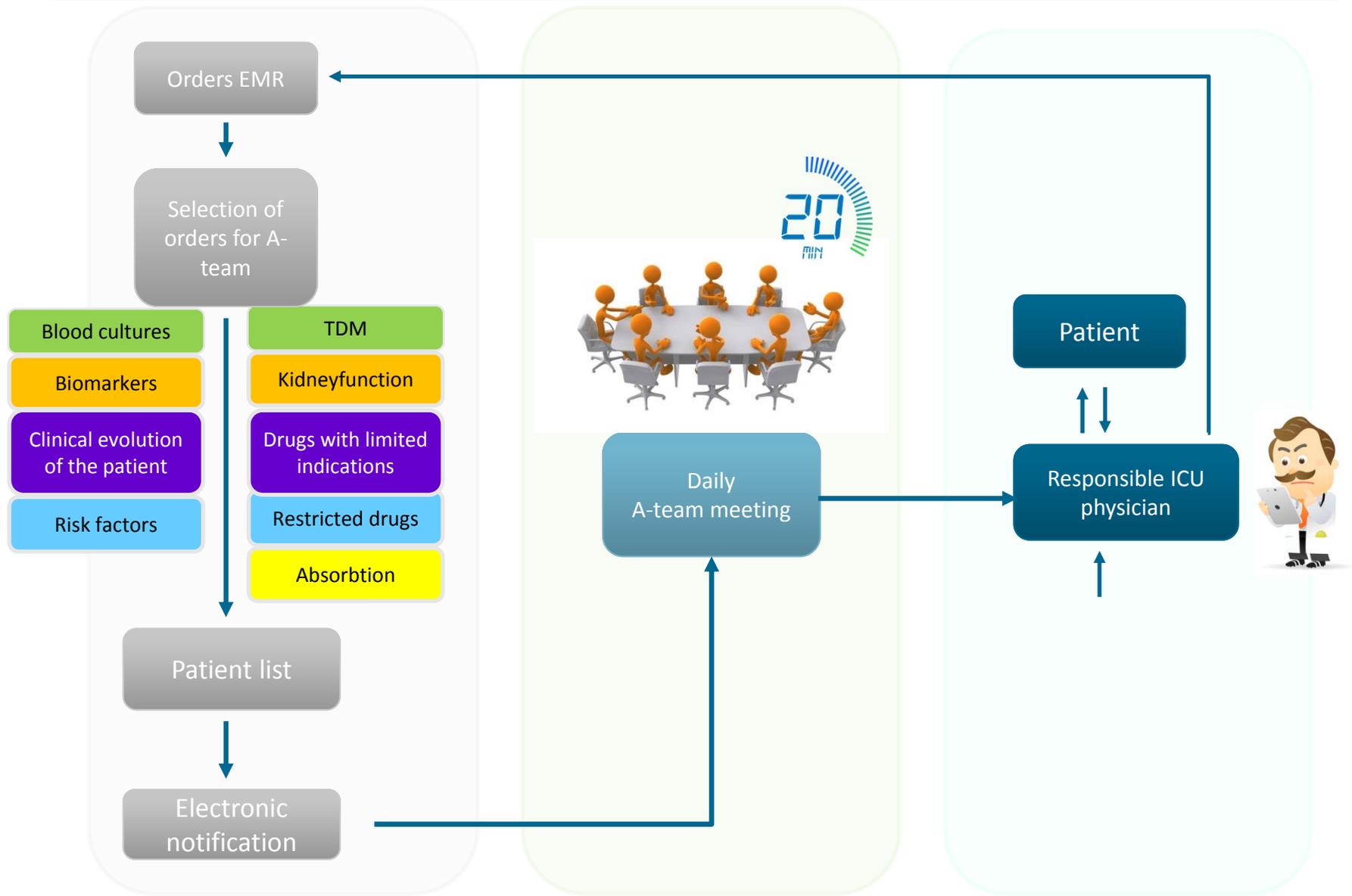


A schematic overview of the set-up of this day to day practice of monitoring and advice is provided in figure 1.

## Day to day monitoring



# Day-to-day tracking



# Day-to-day tracking

**Specifiek rapport infectie**

Naar nu gaan | 27-10-2015 | 27-10-15 - Vandaag

24u: | 27-10 00:01 | 28-10 00:01 | 29-10 00:01 | 30-10 00:01 | 31-10 00:01 | 01-11 00:01 | 02-11 00:01 | 03-11 00:01 | 04-11 00:01 | 05-11 00:01 | 06-11 00:01 | 07-11 00:01 | 08-11 00:01 | 09-11 00:01 | 10-11 00:01

▼ **Temperatuur**

▼ **Temperatuur**

| Temperatuur [°C] | 27-10 00:01 | 28-10 00:01 | 29-10 00:01 | 30-10 00:01 | 31-10 00:01 | 01-11 00:01 | 02-11 00:01 | 03-11 00:01 | 04-11 00:01 | 05-11 00:01 | 06-11 00:01 | 07-11 00:01 | 08-11 00:01 | 09-11 00:01 | 10-11 00:01 |
|------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Temperatuur      | 36,5        | 36,7        | 37          | 36,8        | 36,5        | 36,4        | 36,7        | 36,8        | 36,5        | 37          | 36,7        | 36,3        | 36,8        | 36,6        | 36,5        |

▼ **Medicatie**

|                                | 27-10 00:01 | 28-10 00:01 | 29-10 00:01 | 30-10 00:01 | 31-10 00:01 | 01-11 00:01 | 02-11 00:01 | 03-11 00:01 | 04-11 00:01 | 05-11 00:01 | 06-11 00:01 | 07-11 00:01 | 08-11 00:01 | 09-11 00:01 | 10-11 00:01 |
|--------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| aciclovir Infopli conc(mg)     | 500         | 500         | 500         |             |             |             |             |             |             |             |             |             |             |             |             |
| amfotericine b (liposomaal)... | 300         |             |             | 300         |             |             |             |             |             |             |             |             |             |             |             |
| ceftazidim Pdr v injvls(mg)    | 3.000       | 3.000       | 3.000       | 3.000       | 3.000       |             |             |             |             |             |             |             |             |             |             |
| posaconazol Tablet msr(mg)     |             |             |             |             |             |             | 300         | 300         | 300         | 300         | 300         | 300         | 300         | 300         | 400         |
| trimethoprim/sulfamethoxaz...  | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           | 1           |
| valaciclovir Tablet(mg)        |             |             |             | 500         | 500         | 500         | 500         | 500         | 500         | 500         | 500         | 500         | 500         | 500         | 500         |

▼ **Immunomodulatie**

|                               | 27-10 00:01 | 28-10 00:01 | 29-10 00:01 | 30-10 00:01 | 31-10 00:01 | 01-11 00:01 | 02-11 00:01 | 03-11 00:01 | 04-11 00:01 | 05-11 00:01 | 06-11 00:01 | 07-11 00:01 | 08-11 00:01 | 09-11 00:01 | 10-11 00:01 |
|-------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| ciclosporine Drank(mg)        |             |             |             |             |             |             | 100         | 200         | 200         | 100         |             |             |             | 125         | 250         |
| ciclosporine Infopli conc(mg) | 70          | 70          | 70          | 70          | 70          | 70          | 35          | 35          | 35          | 70          | 70          | 35          | 35          | 35          |             |
| prednisolon Pdr v injvls(mg)  | 60          | 60          | 60          | 60          | 45          | 60          | 45          | 60          | 45          | 60          | 45          | 60          | 45          | 60          | 45          |

▼ **Lab**

|             | 27-10 00:01 | 28-10 00:01 | 29-10 00:01 | 30-10 00:01 | 31-10 00:01 | 01-11 00:01 | 02-11 00:01 | 03-11 00:01 | 04-11 00:01 | 05-11 00:01 | 06-11 00:01 | 07-11 00:01 | 08-11 00:01 | 09-11 00:01 | 10-11 00:01 |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Leucocyten  |             | 8.4         | 7.7         | 8.0         | 8.4         | 6.6         | 9.1         | 9.0         |             |             | 8.0         |             | 7.0         | 9.4         |             |
| Trombocyten |             | 85          | 85          | 98          | 108         | 115         | 127         | 145         |             |             | 151         |             | 186         | 201         |             |
| Kreatinine  | 62          | 76          | 75          | 73          | 78          | 74          | 70          | 74          |             |             | 69          |             | 75          | 79          |             |
| MDRD-GFR    | >90         | 74          | 75          | 77          | 72          | 76          | 81          | 76          |             |             | 82          |             | 74          | 70          |             |

▼ **[VERWIJDERD] Centraal veneuze katheter 4 lumen 15-10-15 4 Lumen 8.5F 20cm Subclavia rechts**

verwijdering Datum/Tijd: 29-10-15 14:12 Plaatsing Datum/Tijd: 15-10-15 15:00 Soort katheter: 4 Lumen 8.5F 20cm Locatie CVK: Subclavia rechts Op afdeling: E00 Indicatie: Voeding;Antibiotica

|                                 | 27-10 00:01 | 28-10 00:01 | 29-10 00:01 | 30-10 00:01 | 31-10 00:01 | 01-11 00:01 | 02-11 00:01 | 03-11 00:01 | 04-11 00:01 | 05-11 00:01 | 06-11 00:01 | 07-11 00:01 | 08-11 00:01 | 09-11 00:01 | 10-11 00:01 |
|---------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Ontstekingsverschijnselen v...  |             |             | Nee         |             |             |             |             |             |             |             |             |             |             |             |             |
| Klinische verdenking lijnsep... |             |             | Nee         |             |             |             |             |             |             |             |             |             |             |             |             |
| Insteekopening                  |             |             | Norm..      |             |             |             |             |             |             |             |             |             |             |             |             |

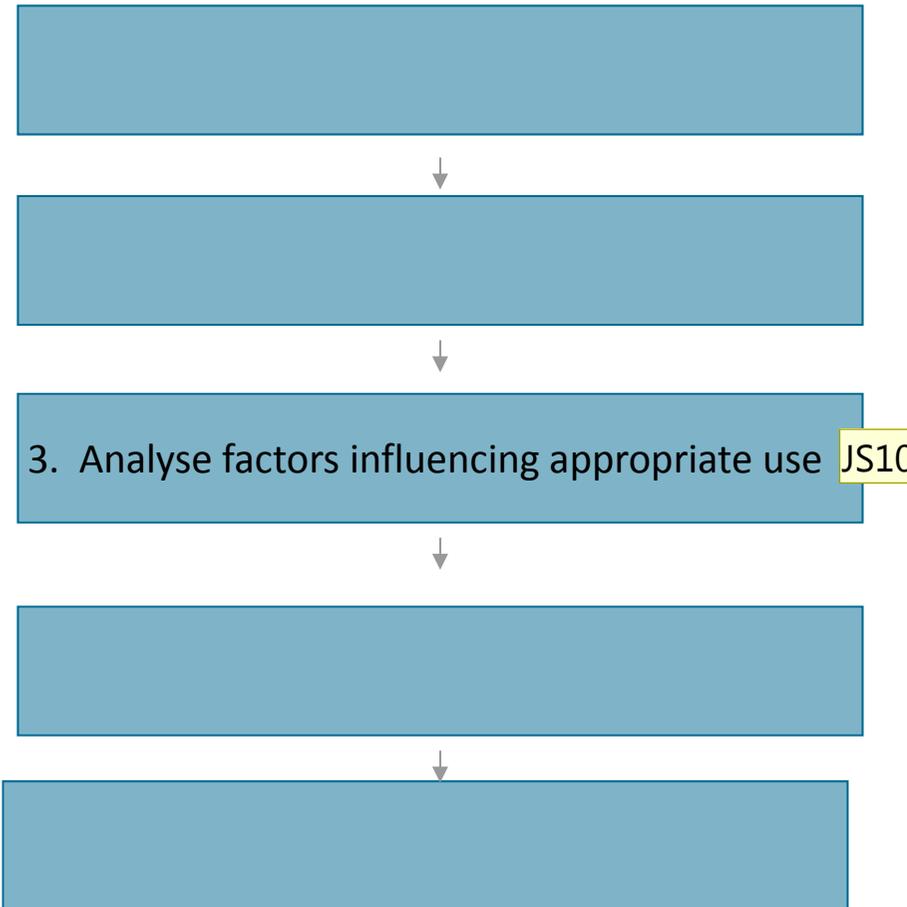
▼ **Samenvatting interventie voor**

**Open interventies**

| Soort | Subtype | Status | Geopend door | Geopend op | Reactie | Uitkomst |
|-------|---------|--------|--------------|------------|---------|----------|
| Geen  |         |        |              |            |         |          |

**Specifiek rapport infectie**

# Framework for implementation of AMS



## DEVELOPING RESEARCH AND PRACTICE

### Barriers to optimal antibiotic use for community-acquired pneumonia at hospitals: a qualitative study

Jeroen A Schouten, Marlies E J L Hulscher, Stephanie Natsch, Bart-Jan Kullberg, Jos W M van der Meer, Richard P T M Grol

Qual Saf Health Care 2007;16:143-149. doi: 10.1136/qshc.2005.017327

See end of article for authors' affiliations

Correspondence to: Dr J A Schouten, Centre for Quality of Care Research (117), Radboud University Medical Centre, PO Box 9101, Nijmegen, The Netherlands; j.schouten@isg.umcn.nl

Accepted 22 October 2006

Community-acquired pneumonia (CAP) is a common, potentially life-threatening disease that is associated with much morbidity, mortality and use of healthcare resources. Recognition of the consequences of CAP and unexplained variation in quality of care has resulted in the development of clinical practice guidelines in various countries.<sup>1,2</sup> Several papers have reported underperformance with respect to key recommendations of these guidelines and have shown that poor physician adherence may be associated with poorer patient outcome.<sup>3,4</sup> However, implementation of such guidelines has not consistently resulted in improved antibiotic use in CAP.<sup>5-8</sup>

The limited ability of strategies to change physician prescribing behaviour may be due to a lack of understanding about specific factors impeding and facilitating optimal performance in CAP. Studies have shown that implementation strategies are more likely to be effective if they focus directly on problems in care provision and factors that influence change.<sup>11</sup> Surveys of internists' attitudes toward clinical guidelines in general report barriers such as a lack of familiarity with or confidence in the guideline. Internists said they were worried about effects of guidelines on their clinical autonomy, on healthcare costs and on satisfaction with daily clinical practice.<sup>12-15</sup> For CAP guidelines, a questionnaire has clarified that physicians' low awareness may account for poor compliance.<sup>16</sup> In another study, professionals reported that a large variety of barriers inhibited successful implementation of a critical-care pathway for CAP.<sup>17,18</sup> These studies all focussed mainly on professional knowledge and attitudes.

**Background:** Physician adherence to key recommendations of guidelines for community-acquired pneumonia (CAP) is often not optimal. A better understanding of factors influencing optimal performance is needed to plan effective change.

**Methods:** The authors used semistructured interviews with care providers in three Dutch medium-sized hospitals to qualitatively study and understand barriers to appropriate antibiotic use in patients with CAP. They discussed recommendations about the prescription of empirical antibiotic therapy that adheres to the guidelines, timely administration of antibiotics, adjusting antibiotic dosage to accommodate decreased renal function, switching and streamlining therapy, and blood and sputum culturing. The authors then classified the barriers each recommendation faced into categories using a conceptual framework (Cabana).

**Results:** Eighteen interviews were performed with residents and specialists in pulmonology and internal medicine, with medical microbiologists and a clinical pharmacist. Two additional multidisciplinary small group interviews which included nurses were performed. Each guideline recommendation elicited a different type of barrier. Regarding the choice of guideline-adherent empirical therapy, treating physicians said that they worried about patient outcome when prescribing narrow-spectrum antibiotic therapy. Regarding the timeliness of antibiotic administration, barriers such as conflicting guidelines and organisational factors (for example, delayed laboratory results, antibiotics not directly available, lack of time) were reported. Not streamlining therapy after culture results became available was thought to be due to the physicians' attitude of "never change a winning team".

**Conclusions:** Efforts to improve the use of antibiotics for patients with CAP should consider the range of barriers that care providers face. Each recommendation meets its own barriers. Interventions to improve adherence should be tailored to these factors.

We used in-depth interviews and small group sessions to qualitatively study the whole spectrum of patient, care-provider, system and guideline barriers that impede judicious antibiotic treatment for CAP. We discussed six key recommendations from guidelines on antibiotic treatment for CAP and used a validated framework to standardise the reporting of barriers.<sup>19,20</sup> This model suggests that physicians fail to adhere to guidelines in the presence of an internal barrier that has a cognitive (awareness or knowledge) or affective (attitude or motivation) component, or in the presence of an external barrier (patient, guideline and environmental factors) that restricts the professionals' ability.

Data obtained with these qualitative techniques will help us to better understand which barriers we should overcome and will enable us to generate hypotheses for potentially effective strategies to improve physician adherence.

#### METHODS

##### Study design

We conducted semistructured interviews to understand the barriers to optimal performance with respect to six key recommendations of antibiotic treatment for CAP (table 1).

##### Participants

We selected care providers with all levels of experience from various professional backgrounds and hospital settings (purpose sampling<sup>21</sup>). To do so, we asked medical directors of three

Abbreviation: CAP, community-acquired pneumonia

**Dia 38**

---

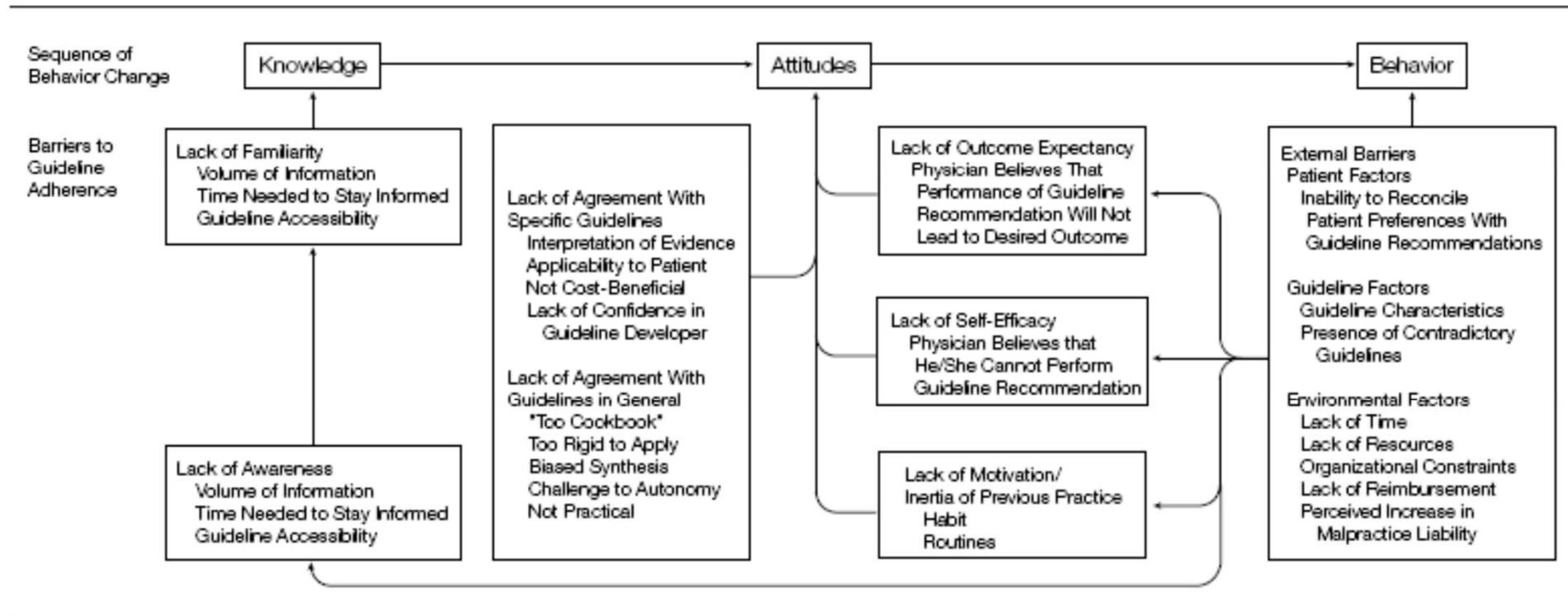
**JS10**

mixed methods qualitative research

Jeroen Schouten; 5-4-2018

# Framework for implementation of AMS

**Figure.** Barriers to Physician Adherence to Practice Guidelines in Relation to Behavior Change



Cabana JAMA 1999

---

# Flottorp et al. Implementation Science 2013: 57 barriers within 7 domains

- Guideline factors
- Individual health professional factors
- Patient factors
- Professional interactions
- Incentives and resources
- Capacity for organisational change
- Social, political and legal factors



# Mixed methods qualitative approach

| Recommendation   | Internal barriers<br>Knowledge  | Internal barriers<br>Attitude  | External barriers   |
|--|---|--|---|
| Prescribing an empirical antibiotic regimen adherent to the guidelines | <p>Lack of familiarity (R/S)<br/>"I do not know what the exact content of the guideline is."</p> <p>Lack of insight in one's own behaviour (R/S)<br/>"I realize now that I actually never follow our hospital guideline recommendations."</p> | <p>Lack of outcome expectancy (R/M)<br/>"I think we are afraid of missing things, afraid to <u>take risks with our own patients by prescribing narrow-spectrum therapy even when the guidelines recommend it.</u>"</p> <p>Lack of agreement with the guideline<br/>-<i>Interpretation of evidence</i> (R/S)<br/>"...recent studies show that enterobacteriaceae should be covered by aspiration pneumonia... so penicillin is just not enough..."<br/>-<i>Applicability to patient</i> (R/S)<br/>"I will deliberately deviate from this guideline for a patient with co-morbidities or one who is severely ill on admission."<br/>-<i>Lack of confidence in guideline developer</i> (S)<br/>"Microbiologists (who drew up the antibiotic guidelines) have a fundamentally different view than clinicians..."</p> <p>Inertia of current practice, lack of motivation (S)<br/>"<u>I have been treating patients with this non-guideline-adherent antibiotic since medical school and it is always successful...</u>"</p> | <p>Guideline factors (R/S)<br/>"The antibiotic booklet is unclear, confusing, poorly presented."</p> <p>Social context<br/>-<i>Social pressure</i> (R/S)<br/>"<u>Everyone feels safe with cefuroxime (broad-spectrum betalactam antibiotic)...colleagues will not quickly criticize you for this choice.</u>"</p> <p>"Internists and pulmonologists make different antibiotic choices."</p> <p>Organizational context (S)<br/>"You know, you don't see the patient yourself at night; it is often difficult to assess from your bed whether a patient needs broad-spectrum antibiotic therapy..."</p> |
| Timely initiation of antibiotic therapy                                | <p>Lack of awareness or insight (S/M)<br/>"I assume that antibiotics are always administered immediately, but I am not sure."<br/>"Doctors and nurses do not realize how important timely administration of antibiotics is for outcome."</p>  | <p>Lack of agreement with guideline<br/>-<i>Applicability to patient</i> (R/S)<br/>"This rule only applies to a patient with CAP who is severely ill."</p> <p>Lack of control of circumstances (R)<br/>"Once a patient is admitted to the ward, I am afraid I cannot control the schedule, I cannot guarantee timely administration."</p>  | <p>Guideline factors<br/>-<i>Presence of conflicting guidelines</i> (M/S/N)<br/>"<u>Nurses take recommendations of getting blood and sputum cultures before first administration of antibiotics very literally, which may cause several hours of delay.</u>"</p> <p>-<i>Guideline characteristics</i> (R/S/M/N)<br/>"There is no clear recommendation on this subject in our guideline."</p>  |

R resident S specialist M microbiologist N nurse

|   | Odds Ratio (95% CI)           | P        |
|---|-------------------------------|----------|
| <b>Timely initiation of antibiotic therapy (within 4 hours)</b> |                               |          |
| → Low oxygen saturation on admission                            | 1.11 (1.04-1.19) <sup>b</sup> | 0.004    |
| → Chronic Obstructive Pulmonary Disease (COPD)                  | 0.51 (0.27-0.96)              | 0.026    |
| → Initiation of antibiotic therapy at the Emergency Department  | 3.9 (1.96-8.73)               | 0.001    |
| <b>Explained variance (%)</b>                                   | <b>31.3</b>                   |          |
| <b>Empirical antibiotics according to national guidelines</b>   | <b>Odds Ratio (95% CI)</b>    | <b>P</b> |
| Pleural effusion present on admission                           | 0.27 (0.12-0.65)              | 0.004    |
| Chronic Obstructive Pulmonary Disease (COPD)                    | 2.40 (1.40-4.08)              | 0.002    |
| → Recent antibiotic therapy in outpatient setting (< 30 days)   | 0.46 (0.26-0.80)              | 0.007    |
| Presence of an antibiotic committee                             | 0.27 (0.08-0.90)              | 0.034    |
| <b>Explained variance (%)</b>                                   | <b>14.4</b>                   |          |
| <b>Adapting dose of antibiotic to renal function</b>            | <b>Odds Ratio (95% CI)</b>    | <b>P</b> |
| Age (patient)   | 0.55 (0.39-0.68) <sup>c</sup> | <0.0001  |
| Heart failure   | 0.52 (0.28-0.96)              | 0.038    |
| Admission to a respiratory care ward                            | 5.13 (2.56-10.23)             | <0.0001  |
| Presence of an antibiotic committee                             | 8.82 (1.03-75.88)             | 0.048    |
| <b>Explained variance (%)</b>                                   | <b>37.4</b>                   |          |
| <b>Switching from iv to oral therapy</b>                        | <b>Odds Ratio (95% CI)</b>    | <b>P</b> |
| → Clinical experience of treating physician (no. of years)      | 0.95 (0.92-0.99)              | 0.042    |
| <b>Explained variance (%)</b>                                   | <b>34.1</b>                   |          |
| <b>Streamlining therapy</b>                                     | <b>Odds Ratio (95% CI)</b>    | <b>P</b> |
| Presence of a clinical pharmacist at ward meetings              | 0.24 (0.08-0.72)              | 0.012    |
| Teaching Hospital   | 4.14 (1.44-11.96)             | 0.010    |
| <b>Explained variance (%)</b>                                   | <b>27.9</b>                   |          |
| <b>Taking 2 blood samples for culture</b>                       | <b>Odds Ratio (95% CI)</b>    | <b>P</b> |
| Temperature on admission (> 37.5°C or < 36.0°C)                 | 7.75 (4.53-13.23)             | <0.0001  |
| Low sodium concentration on admission                           | 1.10 (1.03-1.16) <sup>d</sup> | 0.003    |
| → Treating physician other than pulmonologist                   | 2.82 (1.30-6.13)              | 0.009    |
| <b>Explained variance (%)</b>                                   | <b>27.6</b>                   |          |
| <b>Obtaining sputum samples for Gram stain &amp; culture</b>    | <b>Odds Ratio (95% CI)</b>    | <b>P</b> |
| Male sex (patient)  | 2.15 (1.29-3.56)              | .003     |
| Chronic Obstructive Pulmonary Disease (COPD)                    | 1.95 (1.16-3.26)              | .012     |
| Recent antibiotic therapy in outpatient setting (< 30 days)     | 2.16 (1.28-3.64)              | .004     |
| Admission to a respiratory care ward                            | 2.35 (1.18-4.59)              | .017     |
| <b>Explained variance (%)</b>                                   | <b>13.9</b>                   |          |

Center for Infectious Diseases

# Framework for implementation of AMS

Looijmans-van den Akker et al. *Implementation Science* 2011, 6:47  
<http://www.implementationscience.com/content/6/1/47>



## RESEARCH

## Open Access

### How to develop a program to increase influenza vaccine uptake among workers in health care settings?

Ingrid Looijmans-van den Akker<sup>1</sup>, Marlies E Hulscher<sup>2</sup>, Theo JM Verheij<sup>1</sup>, Josien Riphagen-Dalhuisen<sup>3</sup>, Johan JM van Delden<sup>1</sup> and Eelko Hak<sup>2\*</sup>

#### Abstract

**Background:** Apart from direct protection and reduced productivity loss during epidemics, the main reason to immunize healthcare workers (HCWs) against influenza is to provide indirect protection of frail patients through reduced transmission in healthcare settings. Because the vaccine uptake among HCWs remains far below the health objectives, systematic programs are needed to take full advantage of such vaccination. In an earlier report, we showed a mean 9% increase of vaccine uptake among HCWs in nursing homes that implemented a systematic program compared with control homes, with higher rates in those homes that implemented more program elements. Here, we report in detail the process of the development of the implementation program to enable researchers and practitioners to develop intervention programs tailored to their setting.

**Methods:** We applied the intervention mapping (IM) method to develop a theory- and evidence-based intervention program to change vaccination behaviour among HCWs in nursing homes.

**Results:** After a comprehensive needs assessment, we were able to specify proximal program objectives and selected methods and strategies for inducing behavioural change. By consensus, we decided on planning of three main program components, *i.e.*, an outreach visit to all nursing homes, plenary information meetings, and the appointment of a program coordinator – preferably a physician – in each home. Finally, we planned program adoption, implementation, and evaluation.

**Conclusion:** The IM methodology resulted in a systematic, comprehensive, and transparent procedure of program development. A potentially effective intervention program to change influenza vaccination behaviour among HCWs was developed, and its impact was assessed in a clustered randomised controlled trial.

#### Introduction

Following 2004 guidelines by the World Health Organization, the Dutch association of nursing home physicians (Verenso) has been recommending influenza vaccination of healthcare workers (HCWs) [1]. In nursing homes, higher uptake of influenza vaccines has been associated with reduced morbidity and mortality among their frail patient population [2]. In a recent Cochrane review, an overall reduction in all-cause mortality of 32% (95% confidence interval 16 to 45%) was

found in long-term care facilities in which part of the HCWs were vaccinated versus control homes. One of the studies from that review [3] revealed that in the control homes in a sample of 30 deaths 20% was caused by influenza. In the intervention homes none of the sampled deaths had evidence of influenza infection, which corresponds with a 100% reduction in deaths caused by influenza. In addition, Thomas *et al.* obtained an estimate of 29% reduction (95% confidence interval between 10 and 45%) in influenza-like illness in intervention homes as compared with control homes. It has been well established that during influenza epidemics, the etiological fraction of culture or PCR-confirmed influenza virus in elderly patients is high – between 55%

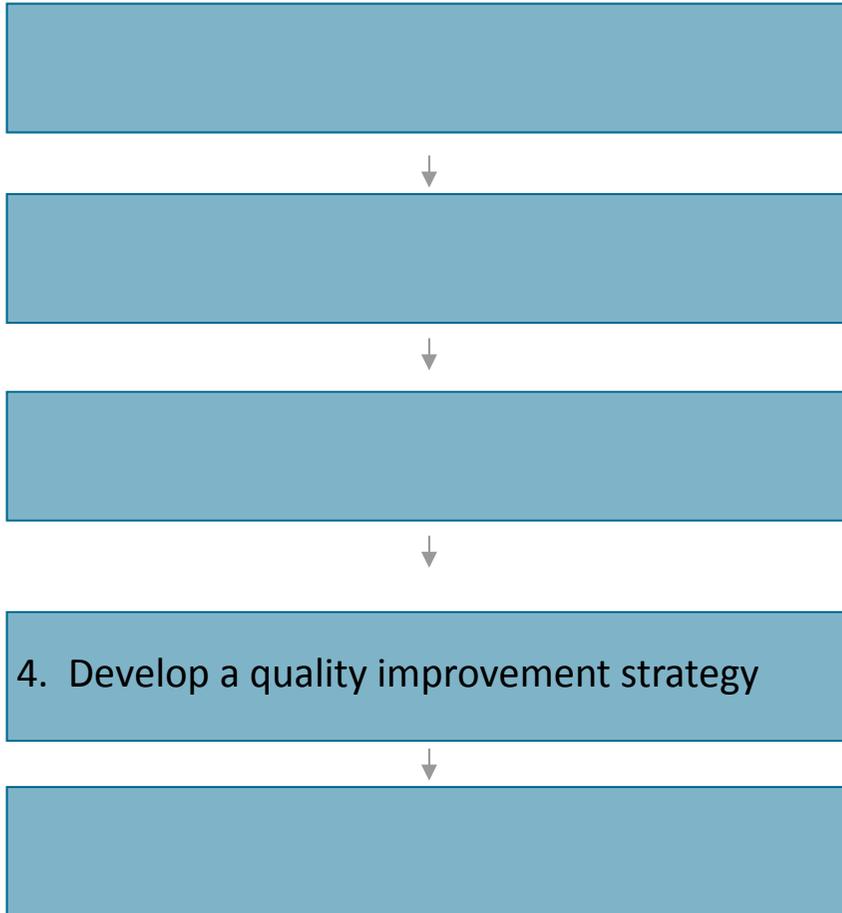
\* Correspondence: e.hak@rug.nl

<sup>1</sup>University of Groningen, Department of Pharmacy, Pharmacoepidemiology and Pharmacoeconomics, A. Deusinglaan 1, 9713 AV, Groningen, The Netherlands

Full list of author information is available at the end of the article



© 2011 Looijmans-van den Akker et al.; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



# Addressing the determinants systematically



## TYPES OF CHANGE STRATEGIES

Basic methods at individual level

Methods to increase knowledge

Methods to change awareness & risk perception

Methods to change habits, automatic and impulsive behaviors

Methods to change attitudes, beliefs, outcome expectations

Methods to change social influence

Methods to skills, capability, self-efficacy and overcoming barriers

Methods to reduce public stigma

Methods to change environmental conditions

Methods to change social norms

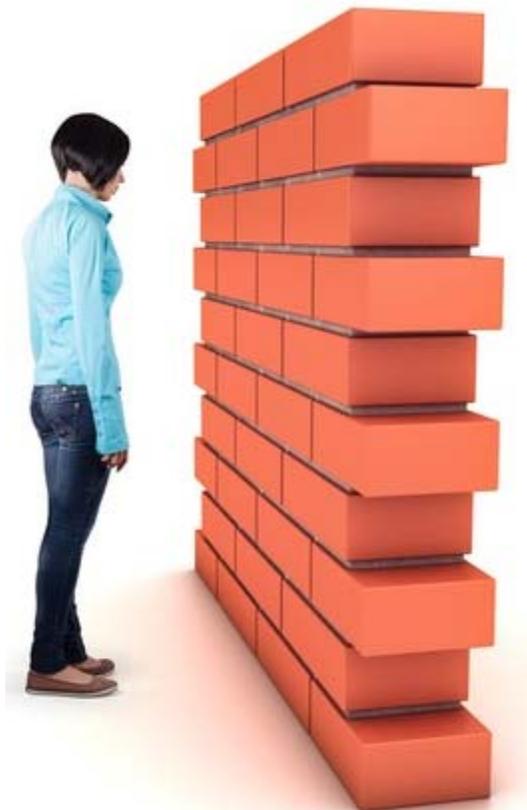
Methods to change social support and social networks

Methods to change organizations

Methods to change communities

Methods to change policy

# Addressing the determinants systematically: EPOC taxonomy



Cochrane Library | Cochrane.org | Follow us on Twitter | Admin

 **Cochrane**  
Effective Practice and  
Organisation of Care

Trusted evidence.  
Informed decisions.  
Better health.

News | About us | **Our evidence** | Resources | Get involved | Satellites

### Our reviews

- Our reviews
  - Supplementary material
- Our priority topics
  - Australian satellite
  - Norwegian satellite
  - UK editorial base
- EPOC projects

#### Our Reviews

| Full list | By Subtopic | New - Updated |
|-----------|-------------|---------------|
|-----------|-------------|---------------|

(Stage filter not available for Subtopic view)

**By subtopic:**

- ▶ Delivery of healthcare services (76)
- ▶ Financial arrangements (22)
- ▶ Governance arrangements (21)
- ▼ Implementation strategies (94)
  - ▶ Interventions targeted at healthcare organizations (3)
  - ▶ Interventions targeted at healthcare recipients (2)
  - ▶ Interventions targeted at healthcare workers (30)
  - ▶ Interventions targeted at specific types of practice, conditions or settings (59)

 **Cochrane**

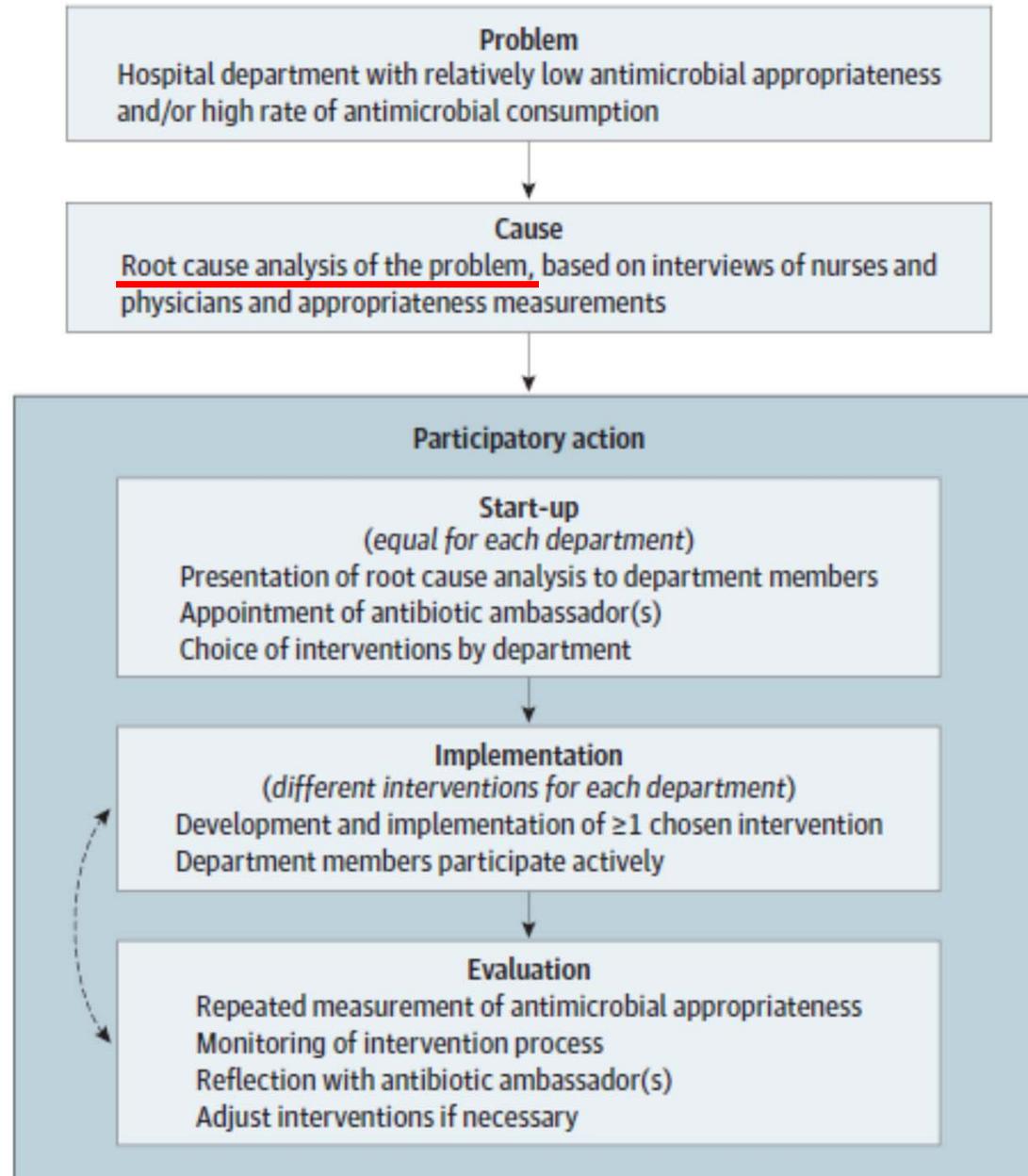
About Cochrane | Publications | Community | Contact us

Copyright © 2017 The Cochrane Collaboration Disclaimer | Privacy | Cookie policy

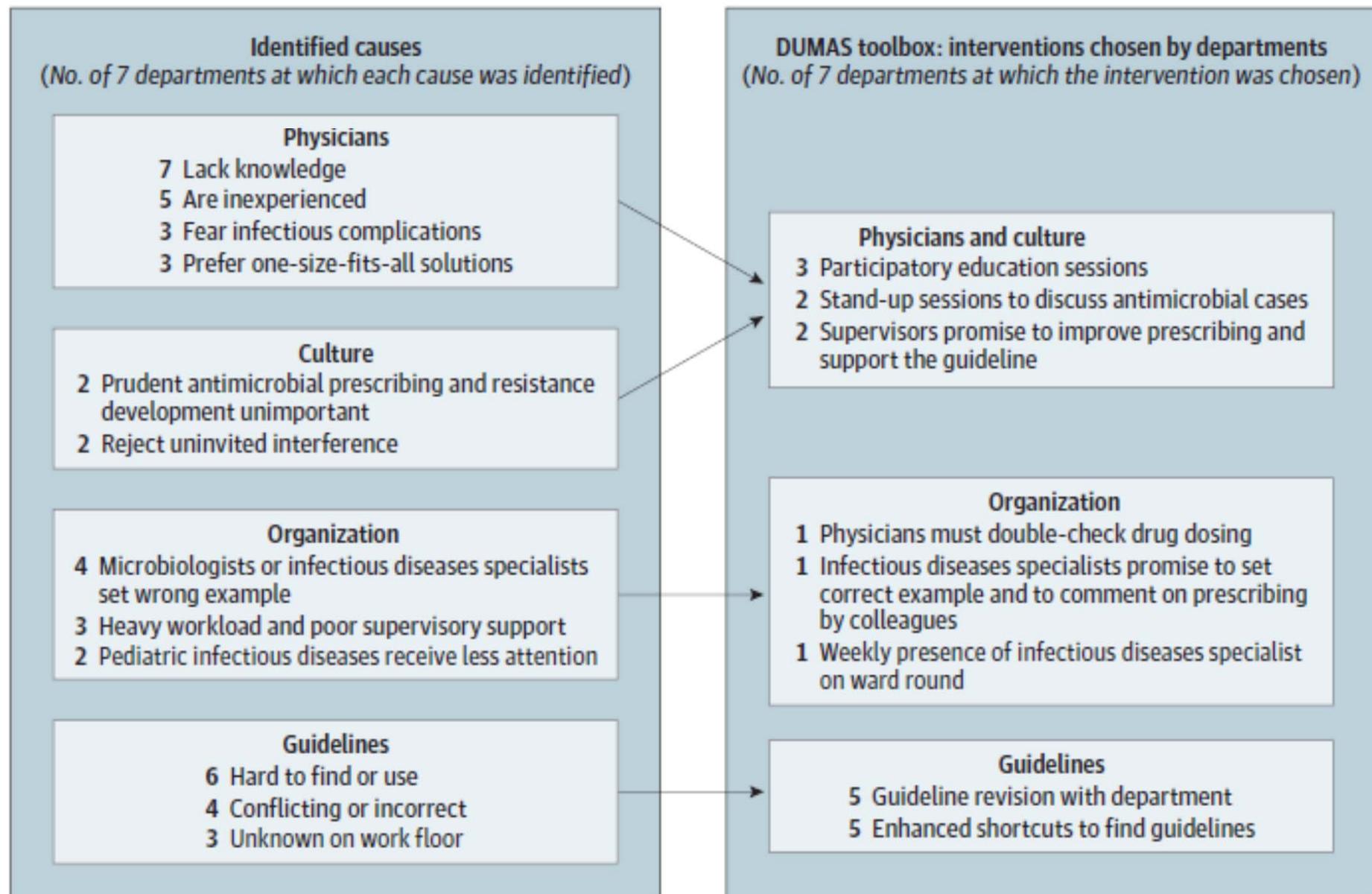
<http://epoc.cochrane.org/our-reviews>

---

# DUMAS study

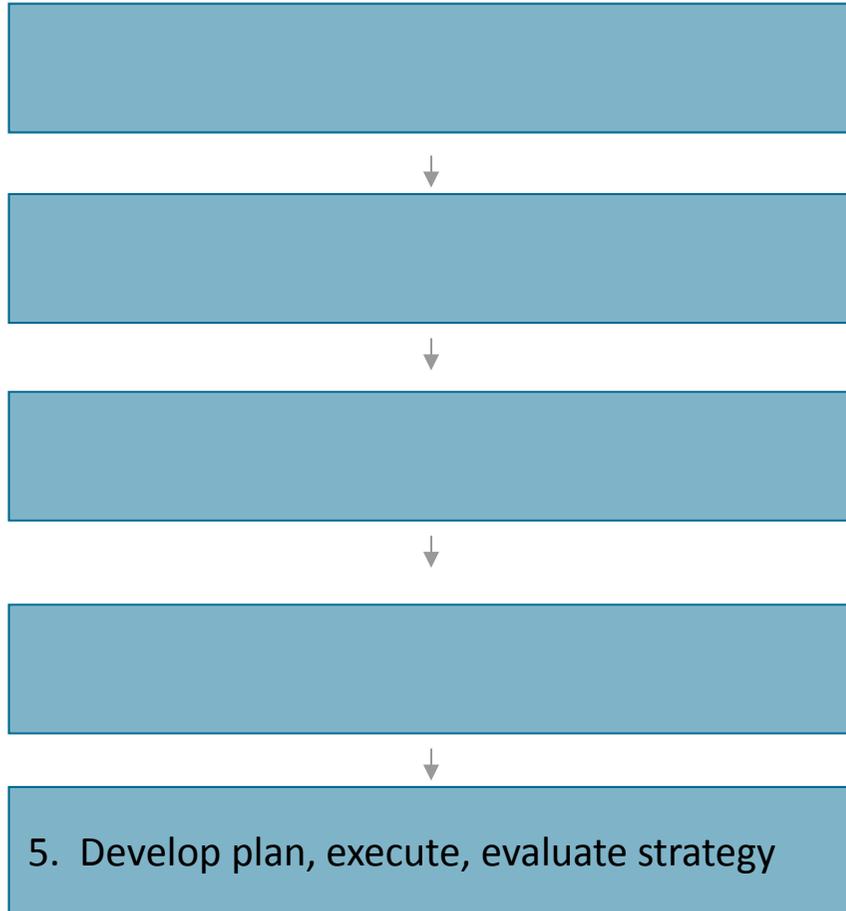


**Figure 2. Summary of the Root Cause Analyses and Interventions Chosen by the Departments to Improve Their Prescribing**



# Framework for implementation of AMS

MAJOR ARTICLE



## Tailored Interventions to Improve Antibiotic Use for Lower Respiratory Tract Infections in Hospitals: A Cluster-Randomized, Controlled Trial

Jeroen A. Schouten,<sup>1,2,3</sup> Marlies E. J. L. Hulscher,<sup>1</sup> Janine Trap-Liefers,<sup>1</sup> Reinier P. Akkermans,<sup>1</sup> Bart-Jan Kullberg,<sup>2,3</sup> Richard P. T. M. Grol,<sup>1</sup> and Jos W. M. van der Meer<sup>2,3</sup>

<sup>1</sup>Centre for Quality of Care Research and <sup>2</sup>Department of General Internal Medicine, Radboud University Nijmegen Medical Centre, and <sup>3</sup>Nijmegen University Centre for Infectious Diseases, Nijmegen, The Netherlands

(See the editorial commentary by File and Gross on pages 942–4)

**Background.** Limited data exist on the most effective approach to increase the quality of antibiotic use for lower respiratory tract infections at hospitals.

**Methods.** One thousand nine hundred six patients with community-acquired pneumonia or an exacerbation of chronic obstructive pulmonary disease (acute exacerbation of chronic bronchitis) were included in a cluster-randomized, controlled trial at 6 medium-to-large Dutch hospitals. A multifaceted guideline-implementation strategy that was tailored to baseline performance and considered the barriers in the target group was used. Principal outcome measures were (1) guideline-adherent antibiotic prescription, (2) adaptation of dose and dose interval of antibiotics according to renal function, (3) switches in therapy, (4) streamlining of therapy, and (5) Gram staining and culture of sputum samples. Secondary process outcomes were applicable to community-acquired pneumonia (e.g., timely administration of antibiotics) or acute exacerbation of chronic bronchitis (e.g., not prescribing macrolides).

**Results.** The rate of guideline-adherent antibiotic prescription increased from 50.3% to 64.3% in the intervention hospitals (odds ratio [OR], 2.63; 95% confidence interval [CI], 1.57–4.42;  $P = .0008$ ). The rate of adaptation of antibiotic dose according to renal function increased from 79.4% to 95.1% in the intervention hospitals (OR, 7.32; 95% CI, 2.09–25.7;  $P = .02$ ). The switch from intravenous to oral therapy improved more in the control hospitals (from 53.3% to 71.9%) than in the intervention hospitals (from 74% to 83.6%). The change from broad-spectrum empirical therapy to pathogen-directed therapy improved by 5.7% in the intervention hospitals ( $P =$  not significant). Fewer sputum samples were obtained from both the intervention group (rate of sputum samples obtained decreased from 55.8% to 53.1%) and the control group (rate of sputum samples obtained decreased from 49.6% to 42.7%). Timely administration of antibiotics for community-acquired pneumonia increased significantly in the intervention group (from 55.2% to 62.9%; OR, 2.49; 95% CI, 1.11–5.57;  $P = .026$ ).

**Conclusions.** With regard to some important aspects, tailoring interventions to change antibiotic use improved the quality of treatment for patients hospitalized with lower respiratory tract infection.

Improvement of the quality of antibiotic use for hospitalized patients with lower respiratory tract infection (LRTI)—for example, by means of the timely administration of antibiotics and ensuring the appropriate

selection of the initial antibiotic regimen—is related to better patient outcomes [1, 2]. Inappropriate use of antibiotics contributes to the emergence and spread of drug-resistant microorganisms, as well as to increased treatment costs [3]. International guidelines provide recommendations for the initial evaluation and treatment of LRTI and include advice about judicious antibiotic therapy [4–7]. However, studies have shown a wide variation of adherence to these guidelines in daily practice [8].

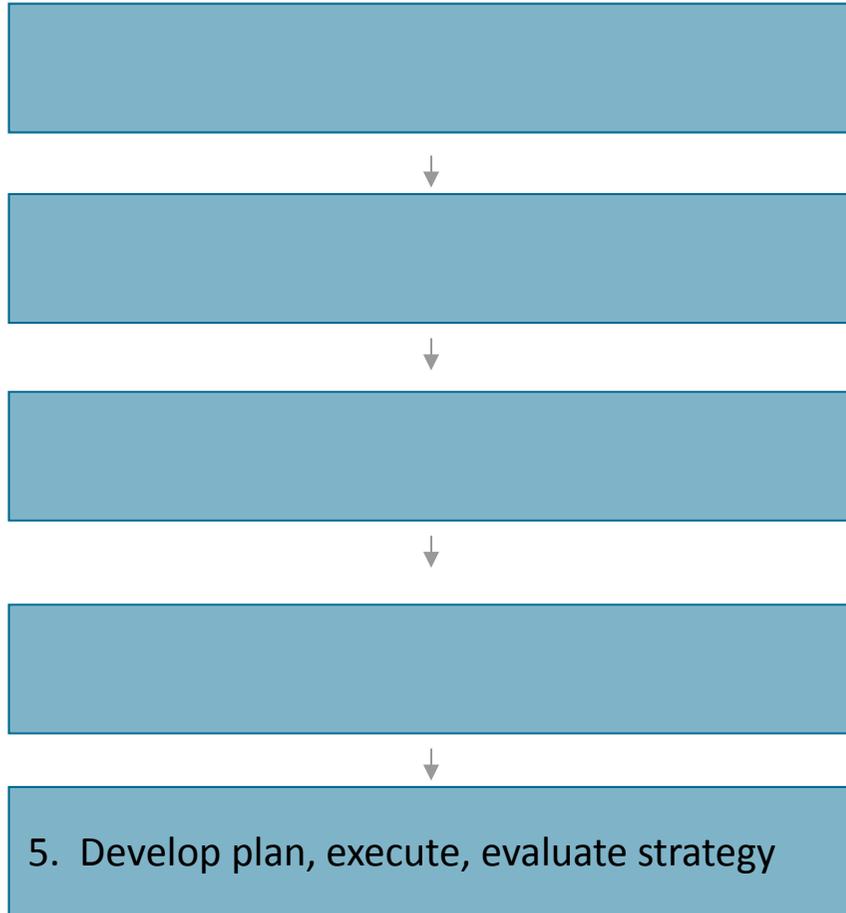
A systematic review of studies of the improvement of management of community-acquired pneumonia (CAP) reported various strategies that can improve ad-

Received 5 July 2006; accepted 25 November 2006; electronically published 20 February 2007.

Reprints or correspondence: Dr. Jeroen A. Schouten, Centre for Quality of Care Research (KNAZ) 117, Radboud University Medical Centre, P.O. Box 9101, Nijmegen, The Netherlands (J.Schouten@isg.umcn.nl).

**Clinical Infectious Diseases** 2007;44:931–41  
© 2007 by the Infectious Diseases Society of America. All rights reserved.  
1093-4038/2007/4407-931\$15.00  
DOI: 10.1093/cid/cil193

# Framework for implementation of AMS



van Daalen et al. *BMC Infectious Diseases* (2015) 15:134  
DOI 10.1186/s12879-015-0867-2



## STUDY PROTOCOL

Open Access

### A cluster randomized trial for the implementation of an antibiotic checklist based on validated quality indicators: the AB-checklist

Frederike V van Daalen<sup>1\*</sup>, Jan M Prins<sup>3</sup>, Brent C Opmeer<sup>2</sup>, Marja A Boermeester<sup>3</sup>, Caroline E Visser<sup>4</sup>, Reinier M van Hest<sup>5</sup>, Marlies E J L Hulscher<sup>6</sup> and Suzanne E Geerlings<sup>1</sup>

#### Abstract

**Background:** Recently we developed and validated generic quality indicators that define 'appropriate antibiotic use' in hospitalized adults treated for a (suspected) bacterial infection. Previous studies have shown that with appropriate antibiotic use a reduction of 13% of length of hospital stay can be achieved. Our main objective in this project is to provide hospitals with an antibiotic checklist based on these quality indicators, and to evaluate the introduction of this checklist in terms of (cost-) effectiveness.

**Methods/Design:** The checklist applies to hospitalized adults with a suspected bacterial infection for whom antibiotic therapy is initiated, at first via the intravenous route. A stepped wedge study design will be used, comparing outcomes before and after introduction of the checklist in nine hospitals in the Netherlands. At least 810 patients will be included in both the control and the intervention group. The primary endpoint is length of hospital stay. Secondary endpoints are appropriate antibiotic use measured by the quality indicators, admission to and duration of intensive care unit stay, readmission within 30 days, mortality, total antibiotic use, and costs associated with implementation and hospital stay. Differences in numerical endpoints between the two periods will be evaluated with mixed linear models; for dichotomous outcomes generalized estimating equation models will be used. A process evaluation will be performed to evaluate the professionals' compliance with use of the checklist. The key question for the economic evaluation is whether the benefits of the checklist, which include reduced antibiotic use, reduced length of stay and associated costs, justify the costs associated with implementation activities as well as daily use of the checklist.

**Discussion:** If (cost-) effective, the AB-checklist will provide physicians with a tool to support appropriate antibiotic use in adult hospitalized patients who start with intravenous antibiotics.

**Trial registration:** Dutch trial registry: NTR4872

**Keywords:** Checklist, Antibiotics, Implementation, Quality indicators, Stepped-wedge design

#### Background

##### The need to improve antibiotic use

The increasing antimicrobial resistance rate is one of the most important health care problems at this moment. The total consumption of antibiotics is the main driving force [1,2]. The World Health Organization signalled the emergence of antimicrobial resistance (AMR), along with the

steady decline in the discovery of new antimicrobials, as a major health threat for the coming decade. To help control AMR, a better use of the current agents is necessary [3]. Recent studies have shown considerable room for improvement in the two most common bacterial infections: respiratory and urinary tract infections [4,5]. An important question is how to achieve such an improvement.

Previous studies have shown that appropriate antibiotic use is not only of great importance to curb antimicrobial resistance, but also has a short-term consequence. The

\* Correspondence: [F.vandaalen@mc.uva.nl](mailto:F.vandaalen@mc.uva.nl)

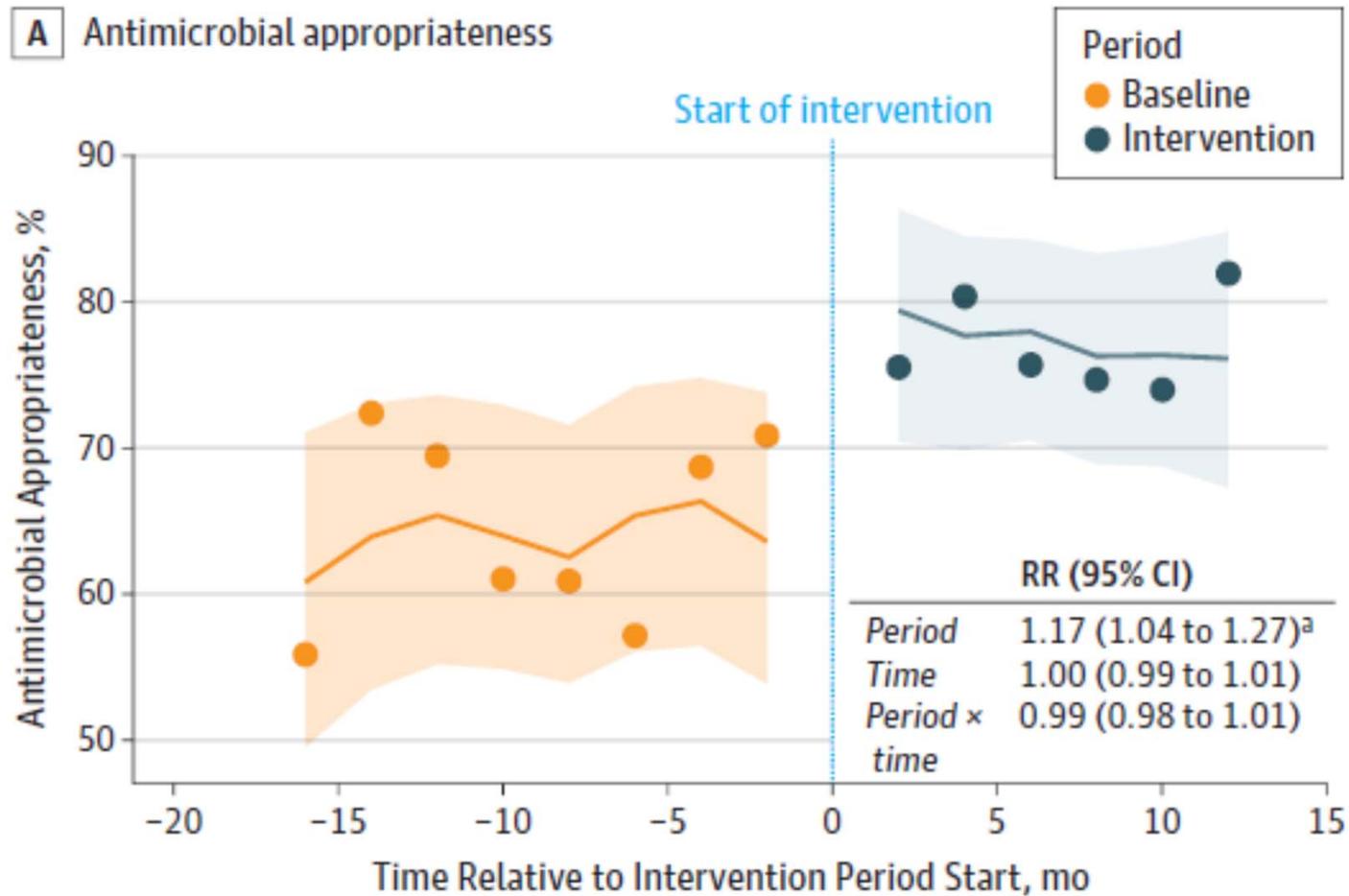
<sup>1</sup>Department of Internal Medicine, Division of Infectious Diseases, Academic Medical Centre, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands

Full list of author information is available at the end of the article



© 2015 van Daalen et al.; licensee BioMed Central. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

# Evaluation strategy in Interrupt Time Interval



Sikkens, *JAMA Internal medicine*, 2017

---

## This is research, what about daily practice?

- Start small
- Choose limited amount of QI's
- Use PPS or small audits for baseline and follow-up measurement
- Invest time in talking to professionals for barrier analysis
- Adapt interventions to barriers using common sense

---

# Masterclass Dutch Antimicrobial Stewardship

## **How to improve antibiotic use?**

A practical introduction to the development and implementation of Antimicrobial Stewardship Programs

**19-23rd May 2021, Nijmegen  
The Netherlands**



