Antimicrobial Stewardship: How to Implement and How to Deal with Barriers

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Faculty/Presenter Disclosure

• **Faculty:** Jan DE WAELE

• **Relationships with commercial interests:**
  - **Grants/Research Support:** Sr. Clinical Researcher Fund Scientific Research
  - **Speakers Bureau/Honoraria***: Accelerate, Bayer Healthcare, Grifols, MSD, Pfizer
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  - **Other:** Surviving Sepsis Campaign Panel Member, ESICM Research Committee Chair

* Fees and honoraria paid to institution
Antibiotic stewardship in ICU

Why?
- Reduce resistance
- Improve patient outcome
- Reduce AB side effects
- Control costs

How?
- Identify barriers
- Choose interventions
- Plan and implement
- Use tools (e.g. PCT)

What?
- Focus on rapid and accurate diagnosis
- Decrease AB exposure
- Optimize PK

Who?
- Intensivist
- Microbiologist / ID
- Clinical pharmacist
- Infection control unit

De Waele, JJ. Intensive Care Med 2015
Antibiotic stewardship in ICU

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Biomarker-guided antibiotic stewardship in suspected ventilator-associated pneumonia (VAPrapid2): a randomised controlled trial and process evaluation


Summary
Background Ventilator-associated pneumonia is the most common intensive care unit (ICU)-acquired infection, yet accurate diagnosis remains difficult, leading to overuse of antibiotics. Low concentrations of IL-1β and IL-8 in bronchoalveolar lavage fluid have been validated as effective markers for exclusion of ventilator-associated pneumonia. The VAPrapid2 trial aimed to determine whether measurement of bronchoalveolar lavage fluid IL-1β and IL-8 could...
Why Don’t Physicians Follow Clinical Practice Guidelines?
A Framework for Improvement

Michael D. Cabana, MD, MPH
Cynthia S. Rand, PhD

Context Despite wide promulgation, clinical practice guidelines have had limited effect on changing physician behavior. Little is known about the process and factors involved in changing physicians' practice patterns.
Figure. Barriers to Physician Adherence to Practice Guidelines in Relation to Behavior Change

Sequence of Behavior Change

Knowledge

- Lack of Familiarity
  - Volume of Information
  - Time Needed to Stay Informed
  - Guideline Accessibility

- Lack of Awareness
  - Volume of Information
  - Time Needed to Stay Informed
  - Guideline Accessibility

Attitudes

- Lack of Agreement With Specific Guidelines
  - Interpretation of Evidence
  - Applicability to Patient
  - Not Cost-Beneficial
  - Lack of Confidence in Guideline Developer

- Lack of Agreement With Guidelines in General
  - "Too Cookbook"
  - Too Rigid to Apply
  - Biased Synthesis
  - Challenge to Autonomy
  - Not Practical

- Lack of Outcome Expectancy
  - Physician Believes That Performance of Guideline Recommendation Will Not Lead to Desired Outcome

- Lack of Self Efficacy
  - Physician Believes that He/She Cannot Perform Guideline Recommendation

- Lack of Motivation/
  - Inertia of Previous Practice
  - Habit
  - Routines

Behavior

- External Barriers
  - Patient Factors
    - Inability to Reconcile Patient Preferences With Guideline Recommendations
  - Guideline Factors
    - Guideline Characteristics
    - Presence of Contradictory Guidelines
  - Environmental Factors
    - Lack of Time
    - Lack of Resources
    - Organizational Constraints
    - Lack of Reimbursement
    - Perceived Increase in Malpractice Liability
Choose your intervention!

- **Structural interventions**
  - Guidelines
  - Stewardship team
  - Clinical pharmacy support
  - Infection Prevention and Control
  - Local epidemiology details

- **Persuasive interventions**
  - Audit and feedback
  - Education
  - Decision support
  - Campaigns

- **Restrictive interventions**
  - Restricted formulary
  - Selective reporting of microbiology
  - Pre-authorization
  - Restricted provision of antibiotics
WHO WANTS CHANGE?

WHO WANTS TO CHANGE?
How to approach this?

1. Define good quality care
2. Analyse current performance
3. Analyse barriers
4. Develop strategy
5. Plan, execute and evaluate this strategy
Determinants of practice

57 determinants in 7 domains

• Guideline factors
• Individual health professional factors
• Patient factors
• Professional interactions
• Incentives and resources
• Capacity for organizational change
• Social, political and legal factors
<table>
<thead>
<tr>
<th>Determinants</th>
<th>Definitions</th>
<th>Questions</th>
<th>Examples of specific factors</th>
<th>Examples of related implementation strategies</th>
<th>Methods for identifying the determinants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. GUIDELINE FACTORS</td>
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</tr>
<tr>
<td>• Recommendation</td>
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<tr>
<td>• Quality of evidence</td>
<td>How confident we are in the estimates of effects</td>
<td>What is the quality of the evidence supporting the recommendation and has it been assessed appropriately?</td>
<td>The quality of the evidence that supports the recommendation may not be clear or may not be judged appropriately</td>
<td>Clearly and accurately communicate the quality of the evidence; Don’t invest resources in implementing recommendations for which there is low quality evidence</td>
<td>Critical review of the guideline using GRADE&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>supporting the</td>
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<tr>
<td>recommendation</td>
<td></td>
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<tr>
<td>• Strength of recommendation</td>
<td>How confident we are that the desirable effects of adherence to the</td>
<td>What is the strength of the recommendation, has it been assessed</td>
<td>The strength of the recommendation may not be clear or appropriate, or the implications of a weak recommendation may not be clearly communicated&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Clearly communicate the implications of the strength of the recommendation</td>
<td>Critical review of the guideline using GRADE&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>recommendation</td>
<td>the recommendation outweigh the undesirable effects</td>
<td>appropriately, and are the implications of the strength of the recommendation clearly communicated?</td>
<td></td>
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<tr>
<td>• Clarity</td>
<td>The clearness of the target population, the settings in which the</td>
<td>Is the recommended action (what to do) stated specifically and unambiguously?</td>
<td>The recommendation may be ambiguous, lack sufficient detail or be longwinded</td>
<td>Clearly communicate a specific and unambiguous action with sufficient detail about how to do it to allow the targeted healthcare professionals to perform the recommended action</td>
<td>Critical review of the guideline using the Guideline Implementability Appraisal (GLIA)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Cultural appropriateness</td>
<td>The extent to which the recommendation is suitable in the social context</td>
<td>Is the recommendation culturally appropriate?</td>
<td>The recommendation may not be congruous with customs or norms in the context where they are being implemented</td>
<td>Adapt the recommendation so that it is congruous; Communicate the recommendation in a way that is more congruous</td>
<td>Reflection; Interviews or focus group discussion with targeted healthcare professionals and with patients</td>
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<tr>
<td>Cognitions (including attitudes)</td>
<td>Agreement with the recommendation</td>
<td>The extent to which the targeted healthcare professionals agree with the recommendation</td>
<td>Do the targeted healthcare professionals agree with the recommendation? If not, why?</td>
<td>The targeted healthcare professionals may interpret the quality of the evidence or its applicability differently, may not think the recommended intervention is cost-effective, or may lack confidence in the guideline developer</td>
<td>Educational strategies that address the reasons for disagreement; A local consensus process</td>
</tr>
<tr>
<td></td>
<td>Attitudes towards guidelines in general</td>
<td>The perceptions that the targeted healthcare professionals have regarding guidelines in general</td>
<td>How do the targeted healthcare professionals view guidelines in general?</td>
<td>The targeted healthcare professionals may perceive guidelines as being oversimplified or cookbook, lacking sufficient flexibility or adaptability, restricting their autonomy, or not practical</td>
<td>Use strategies that do not depend on the targeted healthcare professionals’ attitudes towards guidelines; Educational strategies that address negative attitudes towards guidelines; Design guidelines to address legitimate concerns</td>
</tr>
<tr>
<td>Expected outcome</td>
<td>The extent to which the targeted healthcare professionals believe that adherence with the recommendation will lead to desired outcomes</td>
<td>Do the targeted healthcare professionals believe that adherence with the recommendation will lead to desired outcomes?</td>
<td>The targeted healthcare professionals may not believe that adherence with the recommendation will lead to desired outcomes</td>
<td>Information or educational strategies that provide compelling evidence; Audit and feedback</td>
<td>Survey, interviews or focus group discussion with targeted healthcare professionals</td>
</tr>
<tr>
<td>Intention and motivation</td>
<td>The extent to which the targeted healthcare professionals intend to adhere and are motivated to do so</td>
<td>Do the targeted healthcare professionals intend to adhere? Are they motivated to adhere? What concerns do they have about adhering to the recommendation?</td>
<td>The targeted healthcare professionals may not intend to adhere; They may not be persuaded to change their behaviour due to inertia or their stage of change</td>
<td>Local discussion and consensus; Discuss resistance; Provide good arguments why adherence is important; Involve opinion leaders; Strategies that are tailored to the stage of change of individuals in the targeted healthcare professionals</td>
<td>Survey, interviews or focus group discussion with targeted healthcare professionals</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>The targeted healthcare professionals’ self-perceived competence or confidence in their abilities</td>
<td>Do the targeted healthcare professionals believe that they are capable of adhering to the recommendation? If not, why?</td>
<td>The targeted healthcare professionals may lack confidence in their ability to adhere</td>
<td>Skills training; Feedback; Education or counselling to change the targeted healthcare professionals’ self-assessment of their competency</td>
<td>Interviews or focus group discussion with targeted healthcare professionals</td>
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<tr>
<td><strong>Patient beliefs and knowledge</strong></td>
<td>Patients’ beliefs or knowledge or ability to learn, or the targeted healthcare professionals’ ability or perceived ability to inform or teach patients necessary knowledge and skills</td>
<td>What are the targeted healthcare professionals’ perceptions of patients’ knowledge or ability to learn, or the targeted healthcare professionals’ ability or perceived ability to inform or teach patients necessary knowledge and skills? How do those perceptions correspond with actual patient knowledge and ability to learn?</td>
<td>Patients may have beliefs that hinder implementation of the recommendation; Patients may lack necessary knowledge or skills; The targeted healthcare professionals may lack confidence in their ability to adequately educate patients: The targeted healthcare professionals may have misperceptions of patients’ beliefs, knowledge, skills or ability to learn</td>
<td>Patient education materials; Train the targeted healthcare professionals to provide patient education; Shift responsibility for patient education; Provide the targeted healthcare professionals with accurate information about patients’ knowledge, skills or ability to learn</td>
<td>Interviews or focus group discussion with targeted healthcare professionals and with patients</td>
</tr>
<tr>
<td><strong>Patient preferences</strong></td>
<td>Patients’ values in relationship to professional values or those in the recommendation</td>
<td>Do the targeted healthcare professionals perceive patients to have values that are different than their own or those in the recommendation? How do those perceptions correspond with actual patient values?</td>
<td>Patients may have values that are different than those of the targeted healthcare professionals or those in the recommendation; The targeted healthcare professionals may have misperceptions of patient values</td>
<td>Change the recommendation if it is based on values that are different from those of the targeted patients; A decision aid for patients to help them clarify their values; Provide the targeted healthcare professionals with accurate information about patient values</td>
<td>Interviews or focus group discussion with targeted healthcare professionals and with patients</td>
</tr>
<tr>
<td><strong>Patient motivation</strong></td>
<td>The targeted healthcare professionals’ ability or perceived ability to motivate patients to adhere</td>
<td>Do the targeted healthcare professionals perceive difficulties motivating patients to adhere? How do those perceptions correspond with actual patient motivation?</td>
<td>Patients may not be motivated to adhere; The targeted healthcare professionals may have misperceptions of patients’ motivation</td>
<td>Provide the targeted healthcare professionals with aids or strategies to motivate patients; Shift responsibility for motivating patients; Provide the targeted healthcare professionals with accurate information about patients’ motivation</td>
<td>Interviews or focus group discussion with targeted healthcare professionals and with patients</td>
</tr>
<tr>
<td><strong>Patient behaviour</strong></td>
<td>Patient behaviours that motivate or demotivate adherence with the recommendation</td>
<td>Do the targeted healthcare professionals experience patients behaving in ways that discourage them from adhering?</td>
<td>Patients may behave in ways that hinder adherence (e.g. they may not adhere to recommended treatment or they may under or overuse health services)</td>
<td>Provide targeted healthcare professionals with strategies for coping with patient behaviours that are demotivating</td>
<td>Interviews or focus group discussion targeted healthcare professionals and with patients</td>
</tr>
</tbody>
</table>
Step 1: Identify your priorities

• Inventory of biggest challenges or greatest potential for benefit
• Suggested criteria
  • Consequences of non-adherence
  • Evidence of non-adherence
  • Feasibility of recommended practice

• Examples
  • Unnecessary antibiotics
  • Overuse of antifungals
  • Time to antibiotics
  • Guideline adherence
Step 2: assess determinants (AKA barriers)

For each priority – identify determinants

E.g. delay in antibiotic therapy in the ER
   ➔ Quality of evidence not judged appropriately, lack of knowledge among junior staff, limited stock of antibiotics in ER

E.g. use of antibiotics in primary care
   ➔ Patient expectations, incentives from industry
<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Internal barriers</th>
<th></th>
<th>Internal barriers</th>
<th></th>
<th>External barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribing an empirical antibiotic regimen</td>
<td>Knowledge</td>
<td>Lack of familiarity (R/S)</td>
<td>Lack of outcome expectancy (R/M)</td>
<td>Guideline factors (R/S)</td>
<td></td>
</tr>
<tr>
<td>adherent to the guidelines</td>
<td></td>
<td>“I do not know what the exact content of the guideline is.”</td>
<td>“I think we are afraid of missing things, afraid to take risks with our own patients by prescribing narrow-spectrum therapy even when the guidelines recommend it.”</td>
<td>“The antibiotic booklet is unclear, confusing, poorly presented.”</td>
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<td></td>
<td></td>
<td>Lack of insight in one’s own behaviour (R/S)</td>
<td>Lack of agreement with the guideline</td>
<td>Social context</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>“I realize now that I actually never follow our hospital guideline recommendations.”</td>
<td>-Interpretation of evidence (R/S)</td>
<td>-Social pressure (R/S)</td>
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<td></td>
<td>“…recent studies show that enterobacteriaceae should be covered by aspiration pneumonia…so penicillin is just not enough…”</td>
<td>“Everyone feels safe with cefuroxime (broad-spectrum betalactam antibiotic)...colleagues will not quickly criticize you for this choice.”</td>
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<td></td>
<td></td>
<td></td>
<td>-Applicability to patient (R/S)</td>
<td>-Internists and pulmonologists make different antibiotic choices.</td>
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<td></td>
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<td></td>
<td>“I will deliberately deviate from this guideline for a patient with co-morbidities or one who is severely ill on admission.”</td>
<td>Organizational context (S)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>-Lack of confidence in guideline developer (S)</td>
<td>“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...”</td>
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<td></td>
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<td>“Microbiologists (who drew up the antibiotic guidelines) have a fundamentally different view than clinicians…”</td>
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<td></td>
<td></td>
<td></td>
<td>Inertia of current practice, lack of motivation (S)</td>
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<td></td>
<td></td>
<td></td>
<td>“I have been treating patients with this non-guideline-adherent antibiotic since medical school and it is always successful…”</td>
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</tbody>
</table>
Step 3: Prioritize barriers

- Consider potential impact on recommendation adherence
- List potential implementation strategies
- Identify targets for implementation strategy
Step 4: Develop implementation strategy

Linking a barrier to an intervention

Consider

- Likely impact of the intervention
- Feasibility of the intervention
- Targeted or not?
Our reviews

Our Reviews

By subtopic:

- Delivery of healthcare services (87)
- Financial arrangements (21)
- Governance arrangements (20)
- Implementation strategies (89)
- Interventions targeted at healthcare organizations (3)
- Interventions targeted at healthcare recipients (3)
- Interventions targeted at healthcare workers (31)
What works and what not?

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

What works and what not?

221 studies on 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
Step 5: Plan, execute and evaluate this strategy
Stepwise approach

1. Define good quality care
2. Analyse current performance
3. Analyse barriers
4. Develop strategy
5. Plan, execute and evaluate this strategy
Behavioral Approach to Appropriate Antimicrobial Prescribing in Hospitals
The Dutch Unique Method for Antimicrobial Stewardship (DUMAS) Participatory Intervention Study

Jonne J. Sikkens, MD, MSc; Michel A. van Agtmael, MD, PhD; Edgar J. G. Peters, MD, PhD; Kamilla D. Lettinga, MD, PhD; Martijn van der Kuip, MD, PhD; Christina M. J. E. Vandenbroucke-Grauls, MD, PhD; Cordula Wagner, PhD; Mark H. H. Kramer, MD, PhD

IMPORTANCE Inappropriate antimicrobial prescribing leads to antimicrobial resistance and suboptimal clinical outcomes. Changing antimicrobial prescribing is a complex behavioral process that is not often taken into account in antimicrobial stewardship programs.

OBJECTIVE To examine whether an antimicrobial stewardship approach grounded in behavioral theory and focusing on preserving prescriber autonomy and participation is effective in improving appropriateness of antimicrobial prescribing in hospitals.

DESIGN, SETTING, AND PARTICIPANTS The Dutch Unique Method for Antimicrobial Stewardship (DUMAS) study was a prospective, stepped-wedge, participatory intervention study performed from October 1, 2011, through December 31, 2015. Outcomes were measured during a baseline period of 16 months and an intervention period of 12 months. The study was performed at 7 clinical departments (2 medical, 3 surgical, and 2 pediatric) in a tertiary care medical center and a general teaching hospital in the Netherlands. Physicians
Problem
Hospital department with relatively low antimicrobial appropriateness and/or high rate of antimicrobial consumption

Cause
Root cause analysis of the problem, based on interviews of nurses and physicians and appropriateness measurements

Participatory action

Start-up
(equal for each department)
Presentation of root cause analysis to department members
Appointment of antibiotic ambassador(s)
Choice of interventions by department

Implementation
(different interventions for each department)
Development and implementation of ≥1 chosen intervention
Department members participate actively

Evaluation
Repeated measurement of antimicrobial appropriateness
Monitoring of intervention process
Reflection with antibiotic ambassador(s)
Adjust interventions if necessary
<table>
<thead>
<tr>
<th>Identified causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(No. of 7 departments at which each cause was identified)</td>
</tr>
</tbody>
</table>

**Physicians**
- 7 Lack knowledge
- 5 Are inexperienced
- 3 Fear infectious complications
- 3 Prefer one-size-fits-all solutions

**Culture**
- 2 Prudent antimicrobial prescribing and resistance development unimportant
- 2 Reject uninvited interference

**Organization**
- 4 Microbiologists or infectious diseases specialists set wrong example
- 3 Heavy workload and poor supervisory support
- 2 Pediatric infectious diseases receive less attention

**Guidelines**
- 6 Hard to find or use
- 4 Conflicting or incorrect
- 3 Unknown on work floor
A  Antimicrobial appropriateness

Start of intervention

Period
- Baseline
- Intervention

Antimicrobial Appropriateness, %

Time Relative to Intervention Period Start, mo

RR (95% CI)
- Period 1.17 (1.04 to 1.27)*
- Time 1.00 (0.99 to 1.01)
- Period × time 0.99 (0.98 to 1.01)

B  Antimicrobial consumption

Start of intervention

Period
- Baseline
- Intervention

Length of Therapy per Admission, d

Time Relative to Intervention Period Start, mo

RR (95% CI)
- Period -8.8 (-27.1 to +9.8)
- Time +0.6 (-0.6 to +1.9)
- Period × time +0.1 (-1.5 to +2.4)
In conclusion

• Implementation severely underappreciated
• Avoid jumping in unprepared
• Focus on small number of recommendations
• Don’t forget baseline measurement
• Identify barriers
• Link barriers to interventions
• Keep it real!
“Evidence based medicine should be complemented by evidence based implementation”

Richard Grol
Useful references

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