ESCMID Postgraduate Education Course

Antimicrobial Stewardship: Principles and Practice

Istanbul, Turkey
5 – 6 October 2017

AMS Guidelines:
USA
Germany-Austria

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Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

Tamar F. Barlam,[1,a] Sara E. Cosgrove,[2,a] Lilian M. Abbo,[3] Conan MacDougall,[4] Audrey N. Schuetz,[5] Edward J. Septimus,[6] Arjun Srinivasan,[7] Timothy H. Dellit,[8] Yngve T. Falck-Ytter,[9] Neil O. Fishman,[10] Cindy W. Hamilton,[11] Timothy C. Jenkins,[12] Pamela A. Lipsett,[13] Preeti N. Malani,[14] Larissa S. May,[15] Gregory J. Moran,[16] Melinda M. Neuhauser,[17] Jason G. Newland,[18] Christopher A. Ohl,[19] Matthew H. Samore,[20] Susan K. Seo,[21] and Kavita K. Trivedi[22]

Clinical Infectious Diseases™ 2016;62(10):e51–e77

Infection (2016) 44:395–439
DOI 10.1007/s15010-016-0885-z

dgi DEUTSCHE GESELLSCHAFT FÜR INFEKTIOLOGIE e.V.

CrossMark

GUIDELINE

Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious Diseases

K. de With[1] · F. Allerberger[2] · S. Amann[3] · P. Apfalter[4] · H.-R. Brodt[5] · T. Eckmanns[6] · M. Fellhauer[7] · H. K. Geiss[8] · O. Janata[9] · R. Krause[10] · S. Lemmen[11] · E. Meyer[12] · H. Mittermayer[4] · U. Porsche[13] · E. Presterl[14] · S. Reuter[15] · B. Sinha[16] · R. Strauß[17] · A. Wechsler-Fördös[18] · C. Wenisch[19] · W. V. Kern[20]

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Clinical Infectious Diseases™ 2016;62(10):e51–e77

In USA…

- **2007**, IDSA, Antimicrobial stewardship guideline
- **2014**, CDC, Core elements of hospital antimicrobial stewardship programs
- **2015**, White House, National Action Plan for Combating Antibiotic Resistant Bacteria
- **2016**

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NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

By 2020, implementation of the *National Action Plan* will lead to major reductions in the incidence of urgent and serious threats, including carbapenem-resistant *Enterobacteriaceae* (CRE), methicillin-resistant *Staphylococcus aureus* (MRSA), and *Clostridium difficile* (see Table 1). The *National Action Plan* will also result in improved antibiotic stewardship in healthcare settings, prevention of the spread of drug-resistant threats, elimination of the use of medically-important antibiotics for growth promotion in food animals, and expanded surveillance for drug-resistant bacteria in humans and animals. Other significant outcomes include creation of a regional public health laboratory network, establishment of a specimen repository and sequence database that can be accessed by industrial and academic researchers, development of new diagnostic tests through a national challenge, and development of two or more

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- Total # recommendations: **28**
  - # strong recommendations: **5**
  - # weak recommendations: **18**
  - # good practice recommendations: **5**

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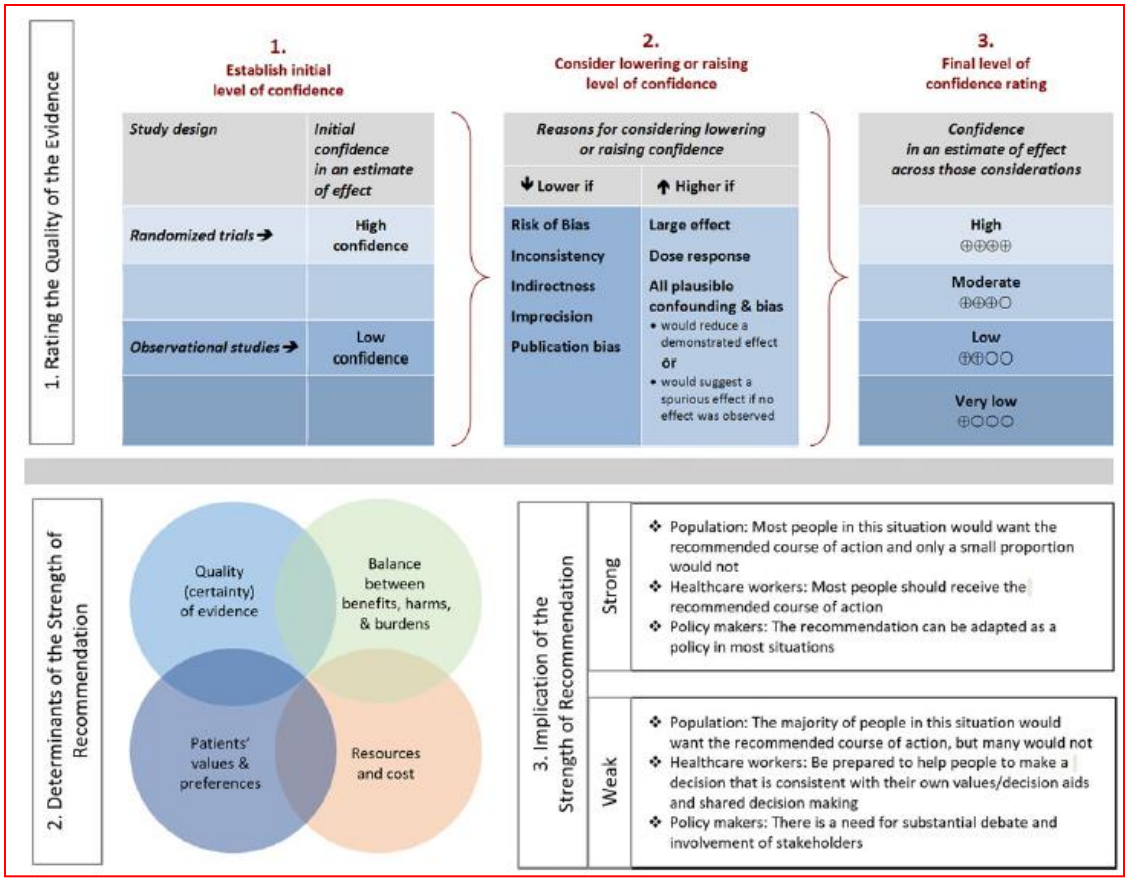
GRADE

The Grading of Recommendations Assessment, Development and Evaluation (short GRADE)



STRONG

I. Does the Use of Preauthorization and/or Prospective Audit and Feedback Interventions by ASPs Improve Antibiotic Utilization and Patient Outcomes?

Recommendation

1. We recommend preauthorization and/or prospective audit and feedback over no such interventions *(strong recommendation, moderate-quality evidence)*.

- Population: Most people in this situation would want the recommended course of action and only a small proportion would not
- Healthcare workers: Most people should receive the recommended course of action
- Policy makers: The recommendation can be adapted as a policy in most situations

- Total # recommendations: **28**
  - # strong recommendations: **5**
  - # weak recommendations: **18**
  - # good practice recommendations: **5**

WEAK

- Population: The majority of people in this situation would want the recommended course of action, but many would not
- Healthcare workers: Be prepared to help people to make a decision that is consistent with their own values/decision aids and shared decision making
- Policy makers: There is a need for substantial debate and involvement of stakeholders

7. We suggest incorporation of computerized clinical decision support at the time of prescribing into ASPs *(weak recommendation, moderate-quality evidence)*.

News

IDSA/SHEA Guidelines on Antibiotic Stewardship Released

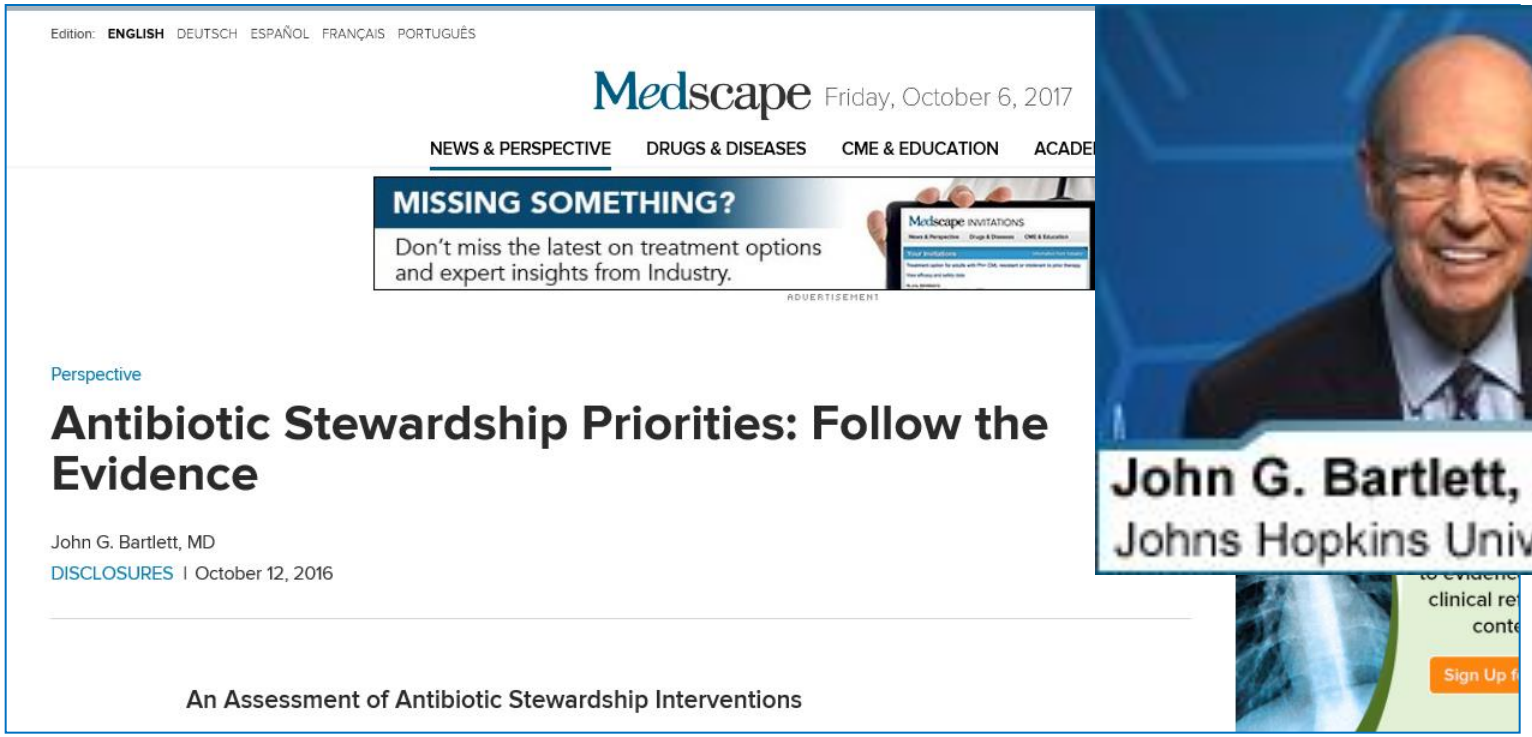
Susan London
April 14, 2016

5 Comments

New national guidelines on antibiotic stewardship take a more practical approach to the issue, offering pragmatic advice and endorsing programs tailored to each institution's unique situation.

"I hope that these guidelines will set a foundation for programs, both in existence and just being implemented, to really look through this menu and see what works for them," lead author Tamar Barlam, MD, told *Medscape Medical News*. "And ultimately, what we all hope is that they improve antibiotic use, so that patients have better outcomes and less resistance."

The panel gave most of the recommendations a "weak" rating, even though some of the underpinning interventions had positive results in randomized trials, Dr Barlam noted. "We were looking to see if an intervention had proven effective as a stewardship intervention," she explained. "When you looked at it from that lens, we really had very few recommendations that were strong recommendations."



visits for URIs, sinusitis, or bronchitis.[12] Data to evaluate antibiotic stewardship activities are evolving rapidly. The 2016 guidelines have 225 references, but only nine citations are dated after 2014, calling attention to the need for timely recommendation updates.

GOOD PRACTICE recommendation

27. We suggest implementation of antibiotic stewardship interventions to reduce inappropriate antibiotic use and/or resistance in the NICU *(good practice recommendation)*.

COMMENTARY

Guideline panels should seldom make good practice statements: guidance from the GRADE Working Group

Guideline panels may present what we would interpret as good practice statements as strong recommendations based on low-quality evidence, or do so formally and

Journal of Clinical Epidemiology 80 (2016) 3–7

Strong recommendations

I. Does the Use of Preauthorization and/or Prospective Audit and Feedback Interventions by ASPs Improve Antibiotic Utilization and Patient Outcomes?
Recommendation

1. We recommend preauthorization and/or prospective audit and feedback over no such interventions *(strong recommendation, moderate-quality evidence).*

V. Should ASPs Implement Interventions Designed to Reduce the Use of Antibiotics Associated With a High Risk of CDI?
Recommendation

5. We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics associated with a high risk of CDI compared with no such intervention *(strong recommendation, moderate-quality evidence).*

XI. Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?
Recommendation

12. We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics *(strong recommendation, moderate-quality evidence).*

IX. In Hospitalized Patients Requiring Intravenous (IV) Antibiotics, Does a Dedicated Pharmacokinetic (PK) Monitoring and Adjustment Program Lead to Improved Clinical Outcomes and Reduced Costs?
Recommendations

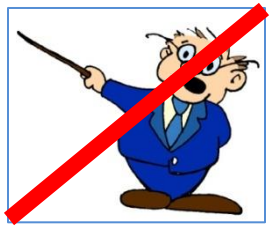
9. We recommend that hospitals implement PK monitoring and adjustment programs for aminoglycosides *(strong recommendation, moderate-quality evidence).*

XIII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy to the Shortest Effective Duration?
Recommendation

14. We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration *(strong recommendation, moderate-quality evidence).*

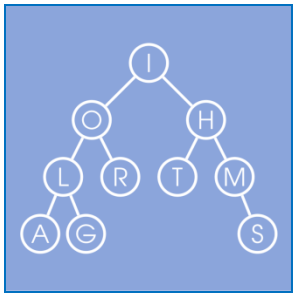
Weak recommendations

2. We suggest against relying solely on didactic educational materials for stewardship *(weak recommendation, low-quality evidence)*.



3. We suggest ASPs develop facility-specific clinical practice guidelines coupled with a dissemination and implementation strategy *(weak recommendation, low-quality evidence)*.

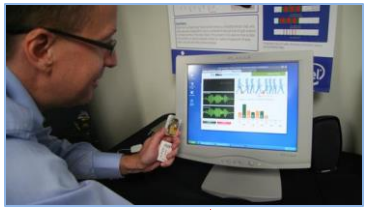
4. We suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes *(weak recommendation, low-quality evidence)*.



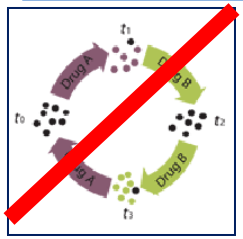
6. We suggest the use of strategies (eg, antibiotic time-outs, stop orders) to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing *(weak recommendation, low-quality evidence)*.

Weak recommendations

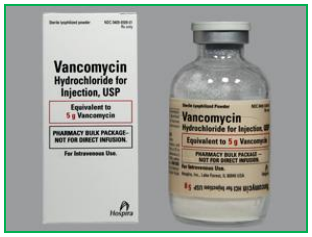
7. We suggest incorporation of computerized clinical decision support at the time of prescribing into ASPs *(weak recommendation, moderate-quality evidence)*.



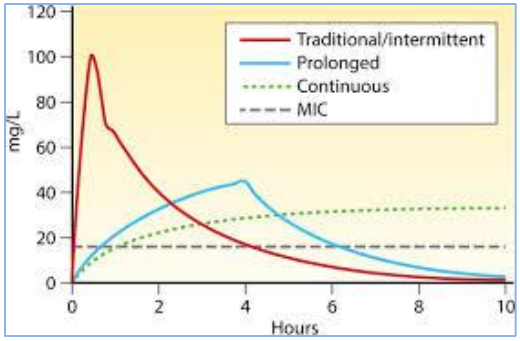
8. We suggest against the use of antibiotic cycling as a stewardship strategy *(weak recommendation, low-quality evidence)*.



10. We suggest that hospitals implement PK monitoring and adjustment programs for vancomycin *(weak recommendation, low-quality evidence)*.

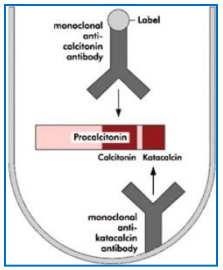


11. In hospitalized patients, we suggest ASPs advocate for the use of alternative dosing strategies vs standard dosing for broad-spectrum β-lactams to decrease costs *(weak recommendation, low-quality evidence)*.

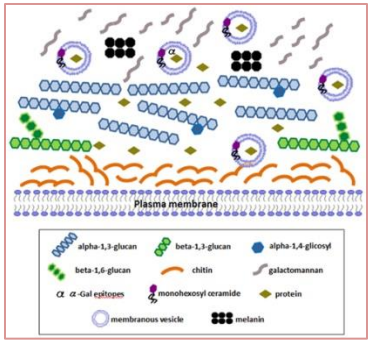


Weak recommendations

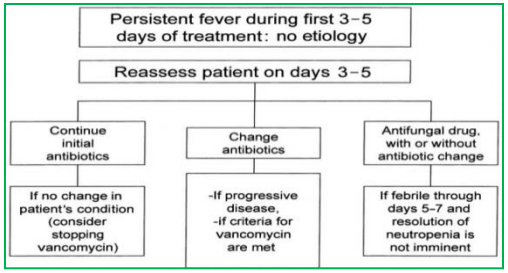
19. In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use *(weak recommendation, moderate-quality evidence)*.



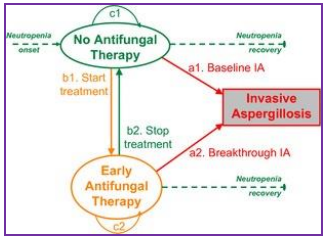
20. In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), we suggest incorporating nonculture-based fungal markers in ASP interventions to optimize antifungal use *(weak recommendation, low-quality evidence)*.



24. We suggest ASPs develop facility-specific guidelines for F&N management in hematology-oncology patients over no such approach *(weak recommendation, low-quality evidence)*.

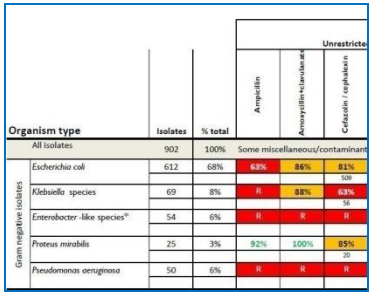


25. We suggest implementation of ASP interventions to improve the appropriate prescribing of antifungal treatment in immunocompromised patients *(weak recommendation, low-quality evidence)*.



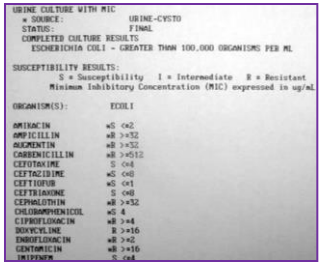
Weak recommendations

15. We suggest development of stratified antibiograms over solely relying on nonstratified antibiograms to assist ASPs in developing guidelines for empiric therapy *(weak recommendation, low-quality evidence)*.



Organism type	Isolates	% total	Ampicillin	Amoxycillin-clavulanate	Cefazolin / cephalexin
	All isolates	902	100%	Some miscellaneous/contaminant	
Gram negative isolates	*Escherichia coli*	612	68%	63%	86%	81%
	Klebsiella species	69	8%	R	88%	63%
	*Enterobacter -like species**	54	6%	R	R	R
	Proteus mirabilis	25	3%	92%	100%	85%
	Pseudomonas aeruginosa	50	6%	R	R	R

16. We suggest selective and cascade reporting of antibiotics over reporting of all tested antibiotics *(weak recommendation, low-quality evidence)*.



URINE CULTURE WITH MIC
SOURCE: URINE-CYSTO
STATUS: FINAL
COMPLETED CULTURE RESULTS
ESCHERICHIA COLI - GREATER THAN 100,000 ORGANISMS PER ML

SUSCEPTIBILITY RESULTS:
S = Susceptibility I = Intermediate R = Resistant
Minimum Inhibitory Concentration (MIC) expressed in ug/mL

ORGANISM(S): ECOLI

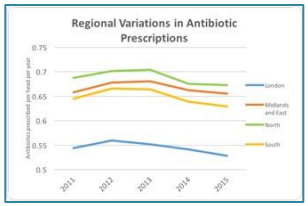
AMIKACIN	≤S	≤2
AMPICILLIN	≥R	>=32
AUGMENTIN	≥R	>=32
CARBENICILLIN	≥R	>=512
CEFOTAXIME	S	<=1
CEFTAZIDIME	≤S	<=0
CEFTIOFUR	≤S	<=1
CEFTRIAXONE	S	<=0
CEPHALOTHIN	≥R	>=32
CHLORAMPHENICOL	≤S	4
CIPROFLOXACIN	≥R	>=4
DOXYCYCLINE	R	>=16
ENROFLOXACIN	≥R	>=2
GENTAMICIN	≥R	>=16
IMIPENEM	S	<=1

18. We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation *(weak recommendation, moderate-quality evidence)*.

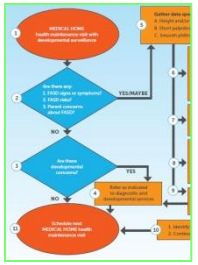
21. We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD) *(weak recommendation, low-quality evidence)*.

Good practice recommendations

22. We recommend measuring antibiotic costs based on prescriptions or administrations instead of purchasing data *(good practice recommendation)*.



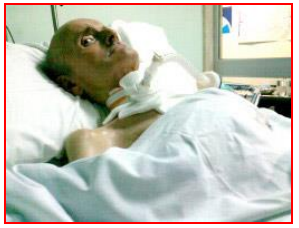
23. Measures that consider the goals and size of the syndrome-specific intervention should be used *(good practice recommendation)*.



26. In nursing homes and skilled nursing facilities, we suggest implementation of antibiotic stewardship strategies to decrease unnecessary use of antibiotics *(good practice recommendation)*.

27. We suggest implementation of antibiotic stewardship interventions to reduce inappropriate antibiotic use and/or resistance in the NICU *(good practice recommendation)*.

28. In terminally ill patients, we suggest ASPs provide support to clinical care providers in decisions related to antibiotic treatment *(good practice recommendation)*.



Strong recommendations

Which method?

Preauthorization?

Prospective audit and feedback?

I. Does the Use of Preauthorization and/or Prospective Audit and Feedback Interventions by ASPs Improve Antibiotic Utilization and Patient Outcomes?

Recommendation

1. We recommend preauthorization and/or prospective audit and feedback over no such interventions *(strong recommendation, moderate-quality evidence)*.

- Implementing one of them is better than doing nothing!

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Advantages…. Disadvantages….

Table 1. Comparison of Preauthorization and Prospective Audit and Feedback Strategies for Antibiotic Stewardship

Preauthorization	Prospective Audit and Feedback
Advantages	
• Reduces initiation of unnecessary/ inappropriate antibiotics • Optimizes empiric choices and influences downstream use • Prompts review of clinical data/ prior cultures at the time of initiation of therapy • Decreases antibiotic costs, including those due to high-cost agents • Provides mechanism for rapid response to antibiotic shortages • Direct control over antibiotic use	• Can increase visibility of antimicrobial stewardship program and build collegial relationships • More clinical data available for recommendations, enhancing uptake by prescribers • Greater flexibility in timing of recommendations • Can be done on less than daily basis if resources are limited • Provides educational benefit to clinicians • Prescriber autonomy maintained • Can address de-escalation of antibiotics and duration of therapy
Disadvantages	
• Impacts use of restricted agents only • Addresses empiric use to a much greater degree than downstream use • Loss of prescriber autonomy • May delay therapy • Effectiveness depends on skill of approver • Real-time resource intensive • Potential for manipulation of system (eg, presenting request in a biased manner to gain approval) • May simply shift to other antibiotic agents and select for different antibiotic-resistance patterns	• Compliance voluntary • Typically labor-intensive • Success depends on delivery method of feedback to prescribers • Prescribers may be reluctant to change therapy if patient is doing well • Identification of interventions may require information technology support and/or purchase of computerized surveillance systems • May take longer to achieve reductions in targeted antibiotic use

Advantages

Preauthorization

- Faster reductions in inappropriate antibiotic use
- Optimized empirical choices
- Culture results are more commonly encountered while prescribing antibiotics
- The cost of antibiotics are decreased
- The direct "control" of antibiotics are obtained

Prospective audit and feedback

- ASP becomes more visible, helps building collegial relationships
- Prescribers face more clinical data
- Flexibility in timing of recommendations
- Can be done less than daily
- Educational benefit
- Prescriber autonomy

Disadvantages

Preauthorization

- Only restricted agents
- Loss of prescriber autonomy
- Delay in treatment
- Potential for manipulation
- Shift to other antibiotics
- …

Prospective audit and feedback

- Compliance voluntary
- Labour intensive
- Method of feedback is important
- Reluctance to change therapy
- It takes longer to achieve reductions in antibiotic use
- …

Treatment durations

XIII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy to the Shortest Effective Duration?

Recommendation

14. We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration *(strong recommendation, moderate-quality evidence)*.

➢The shortest effective duration is the best!

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Shorter **vs** Longer duration of antibiotics

Table 2. Meta-analyses and Examples of Randomized Clinical Studies Comparing Shorter Versus Longer Duration of Antibiotics

Reference	Clinical Condition/Population	Treatment Duration, d	Clinical Outcome[a]
Meta-analyses			
Dimopoulos et al, 2008 [123]	Adults and children with CAP	3–7 vs 5–10	Clinical success, relapse, mortality, adverse events
Pugh et al, 2011 [124]	Adults with VAP	7–8 vs 10–15	Antibiotic-free days[b], recurrence[b]
Dimopoulos et al, 2013 [125]	Adults with VAP	7–8 vs 10–15	Relapse, mortality, antibiotic-free days[c]
Randomized clinical trials			
Chastre et al, 2003 [127]	Adults with VAP	8 vs 15	Mortality, recurrent infections[d]
El Moussaoui et al, 2006 [128]	Adults with CAP	3 vs 5	Clinical and radiological success
Greenberg et al, 2014 [129]	Children with CAP	5 vs 10	Treatment failure[e]
Hepburn et al, 2004 [130]	Adults with cellulitis	5 vs 10	Clinical success
Sandberg et al, 2012 [131]	Adult females with acute pyelonephritis	7 vs 14	Clinical efficacy, adverse events
Talan et al, 2000 [132]	Women with acute uncomplicated pyelonephritis	7 vs 14	Bacteriologic and clinical cure[f]
Runyon et al, 1991 [133]	Adults with spontaneous bacterial peritonitis	5 vs 10	Mortality, bacteriologic cure, recurrence
Saini et al, 2011 [134]	Neonatal septicemia	2–4 vs 7 (with sterile culture)	Treatment failure
Sawyer et al, 2015 [135]	Adults with intra-abdominal infection	4 vs ≤10	Composite of surgical site infection, recurrent intra-abdominal infection, or death
Bernard et al, 2015 [136]	Adults with vertebral osteomyelitis	42 vs 84	Cure at 1 y by independent committee and secondary outcomes

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Oral treatment

XI. Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?

Recommendation

12. We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics *(strong recommendation, moderate-quality evidence)*.

Oral treatment

- Initial therapy
- Sequential therapy after iv usage

Advantages

- Lower cost
- Shorter hospital stay

PK monitoring and adjustment program

IX. In Hospitalized Patients Requiring Intravenous (IV) Antibiotics, Does a Dedicated Pharmacokinetic (PK) Monitoring and Adjustment Program Lead to Improved Clinical Outcomes and Reduced Costs?

Recommendations

9. We recommend that hospitals implement PK monitoring and adjustment programs for aminoglycosides *(strong recommendation, moderate-quality evidence)*.

PK monitoring programs for **aminoglycosides**

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C.difficile

V. Should ASPs Implement Interventions Designed to Reduce the Use of Antibiotics Associated With a High Risk of CDI?

Recommendation

5. We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics associated with a high risk of CDI compared with no such intervention *(strong recommendation, moderate-quality evidence)*.

Comment: The goal of reducing CDI is a high priority for all ASPs and should be taken into consideration when crafting stewardship interventions.

- Avoidance of antibiotics with high risk for *C.difficile*
- Infection control measures

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Weak recommendations

Implementing AMS for spesific infectious diesases syndromes

IV. Should ASPs Implement Interventions to Improve Antibiotic Use and Clinical Outcomes That Target Patients With Specific Infectious Diseases Syndromes?

Recommendation

4. We suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes *(weak recommendation, low-quality evidence).*

- Community acquired pneumonia
- Hospital acquired pneumonia
- Cellulitis
- Asymptomatic bacteriuria
- ……

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Which measures?

Table 3. Possible Metrics for Evaluation of Interventions to Improve Antibiotic Use and Clinical Outcomes in Patients With Specific Infectious Diseases Syndromes

Process Measures	Outcome Measures
Excess days of therapy (ie, unnecessary days of therapy avoided based on accepted targets and benchmarks)[a]	Hospital length of stay
Duration of therapy	30-day mortality
Proportion of patients compliant with facility-based guideline or treatment algorithm[a]	Unplanned hospital readmission within 30 d
Proportion of patients with revision of antibiotics based on microbiology data	Proportion of patients diagnosed with hospital-acquired *Clostridium difficile* infection or other adverse event(s) related to antibiotic treatment[a]
Proportion of patients converted to oral therapy	Proportion of patients with clinical failure (eg, need to broaden therapy, recurrence of infection)

Process measures

- *Excess* days of therapy
- Duration of therapy
- Compliance with algorithms
- Treatment revision based on microbiological data
- Switch to oral therapy

Outcome measures

- Length of hospital stay
- 30 day mortality
- Adverse events due to atbs: *C.difficile inf* ..etc
- Clinical failure, recurrent infection

Clinical Infectious Diseases™ 2016;62(10):e51–e77

Stratified antibiograms

XIV. Should ASPs Work With the Microbiology Laboratory to Develop Stratified Antibiograms, Compared With Nonstratified Antibiograms?

Recommendation

15. We suggest development of stratified antibiograms over solely relying on nonstratified antibiograms to assist ASPs in developing guidelines for empiric therapy *(weak recommendation, low-quality evidence)*.

➢Antimicrobial susceptibility data based on departments, samples….etc

Clinical Infectious Diseases™ 2016;62(10):e51–e77

Antibiotic cycling

VIII. Should ASPs Implement Strategies That Promote Cycling or Mixing in Antibiotic Selection to Reduce Antibiotic Resistance?

Recommendation

8. We suggest against the use of antibiotic cycling as a stewardship strategy *(weak recommendation, low-quality evidence)*.

- Antibiotic cycling is NOT RECOMMENDED!

Clinical Infectious Diseases™ 2016;62(10):e51–e77

Rapid diagnosis:
Procalcitonin, viral antigen tests, fungal biomarkers, molecular methods

XVI. Should ASPs Advocate for Use of Rapid Viral Testing for Respiratory Pathogens to Reduce the Use of Inappropriate Antibiotics?

Recommendation

17. We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics *(weak recommendation, low-quality evidence).*

Comment: Although rapid viral testing has the potential to reduce inappropriate use of antibiotics, results have been inconsistent. Few studies have been performed to assess whether active ASP intervention would improve those results.

XVII. Should ASPs Advocate for Rapid Diagnostic Testing on Blood Specimens to Optimize Antibiotic Therapy and Improve Clinical Outcomes?

Recommendation

18. We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation *(weak recommendation, moderate-quality evidence).*

XVIII. In Adults in Intensive Care Units (ICUs) With Suspected Infection, Should ASPs Advocate Procalcitonin (PCT) Testing as an Intervention to Decrease Antibiotic Use?

Recommendation

19. In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use *(weak recommendation, moderate-quality evidence).*

XIX. In Patients With Hematologic Malignancy, Should ASPs Advocate for Incorporation of Nonculture-Based Fungal Markers in Interventions to Optimize Antifungal Use?

Recommendation

20. In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), we suggest incorporating nonculture-based fungal markers in ASP interventions to optimize antifungal use *(weak recommendation, low-quality evidence).*

Clinical Infectious Diseases™ 2016;62(10):e51–e77

Monitoring antibiotic use: DDD or DOT ?

XX. Which Overall Measures Best Reflect the Impact of ASPs and Their Interventions?

Recommendation

21. We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD) *(weak recommendation, low-quality evidence).*

DDD: Daily Defined Dose

- Recommended by WHO
- Easier than DOT
- Widely used and offers comparability
- Limited use in pediatrics

DOT: Days of Therapy

- Not impacted by dose adjustments; can be used both for adults and pediatric patients
- CDC requires DOT
- Patient-level antibiotic data is required; not feasible at every facility

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Stop orders

VI. Do Strategies to Encourage Prescriber-Led Review of Appropriateness of Antibiotic Regimens, in the Absence of Direct Input From an Antibiotic Stewardship Team, Improve Antibiotic Prescribing?

Recommendation

6. We suggest the use of strategies (eg, antibiotic time-outs, stop orders) to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing *(weak recommendation, low-quality evidence).*

Good practice recommendations

‘End of life antibiotic treatment’

XXVII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy in Terminally Ill Patients?

Recommendation

28. In terminally ill patients, we suggest ASPs provide support to clinical care providers in decisions related to antibiotic treatment *(good practice recommendation)*.

- In terminally ill patients, ASPs should support clinicians in the decision of antibiotic treatment

Clinical Infectious Diseases™ 2016;62(10):e51–e77

In Europe…

- 2001, European Comission
- 2010, European Community, Antimicrobial resistance surveillance and monitoring antibiotic consumption

In Europe…

Antimicrobial resistance

- News
- Events
- **About AMR**
- Policy
- Surveillance
- Multimedia
- Publications
- Personal stories
- Contact us

AMR in the WHO European Region

Antimicrobial resistance (AMR), and resistance to antibiotics in particular, is a serious threat to public health in the Region.

The resistance of some pathogens now reaches over 50% in some countries of the Region, and new resistance mechanisms are emerging and spreading rapidly. The situation is especially worrying for gram-negative bacteria, such as Klebsiella pneumoniae and Escherichia coli.

The Region also displays great variation on AMR data depending on the bacterium, antimicrobial group and geographical region. These variations are most likely related to differences in antimicrobial use, infection control and health care utilization practices in countries.

WHO

Consumption of antibiotics decreased by 6% overall in the European Union (EU) over the last 7 years, but there are large differences between countries: since 2013, Denmark, Latvia, the Netherlands and Romania decreased consumption by up to 9%, while Italy and Spain increased consumption by up to 9%.

Every year in the EU alone, an estimated 25 000 patients die as a result of infections that cannot be treated with antimicrobial drugs. Infections due to these selected multidrug-resistant bacteria in the EU result in extra health care costs and productivity losses of at least €1.5 billion each year.

Infection (2016) 44:395–439
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dgi DEUTSCHE GESELLSCHAFT FÜR INFEKTIOLOGIE e.V.

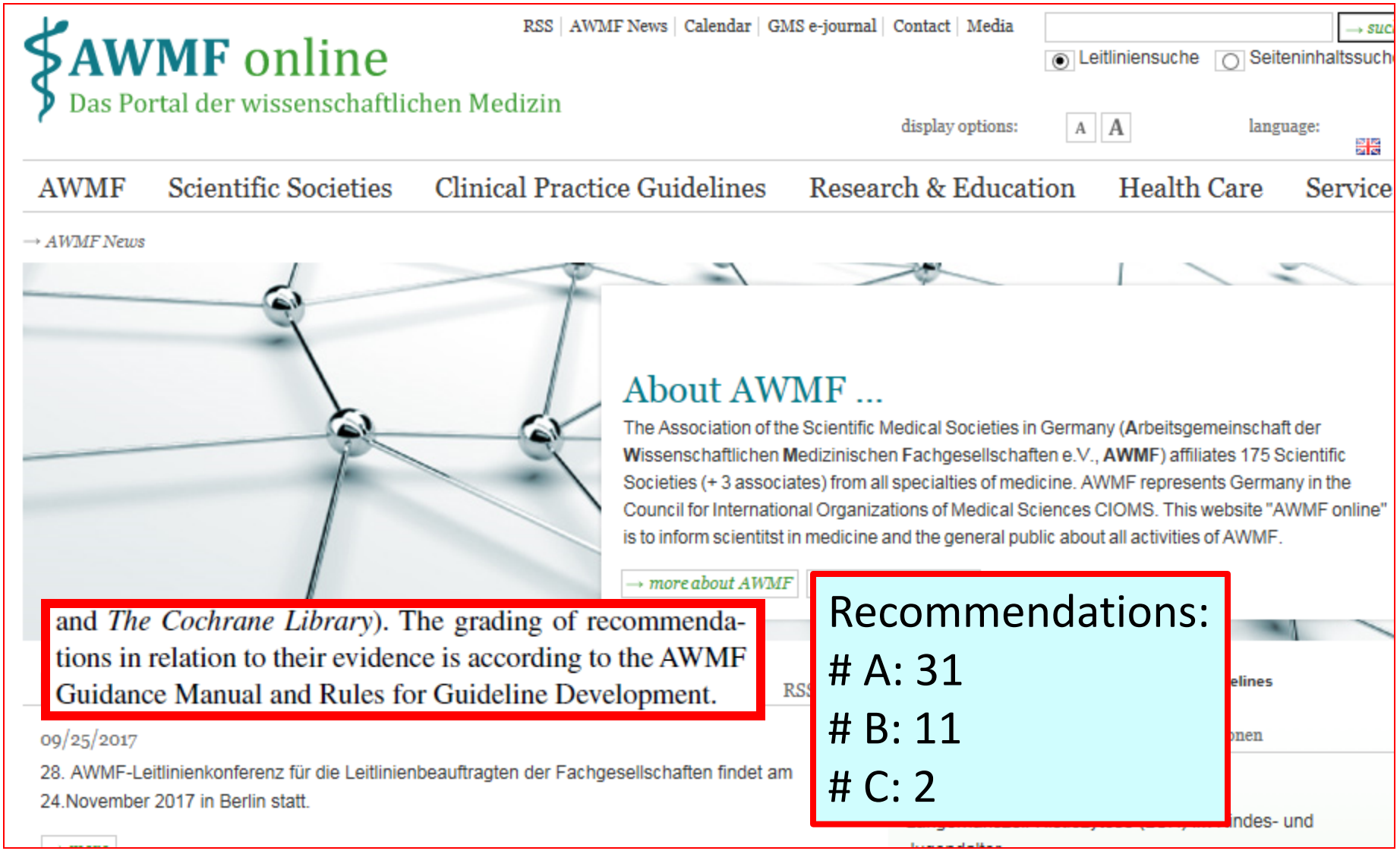
CrossMark

GUIDELINE

Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious Diseases

K. de With[1] · F. Allerberger[2] · S. Amann[3] · P. Apfalter[4] · H.-R. Brodt[5] · T. Eckmanns[6] · M. Fellhauer[7] · H. K. Geiss[8] · O. Janata[9] · R. Krause[10] · S. Lemmen[11] · E. Meyer[12] · H. Mittermayer[4] · U. Porsche[13] · E. Presterl[14] · S. Reuter[15] · B. Sinha[16] · R. Strauß[17] · A. Wechsler-Fördös[18] · C. Wenisch[19] · W. V. Kern[20]

Infection (2016) 44:395–439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The Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., AWMF) affiliates 175 Scientific Societies (+ 3 associates) from all specialties of medicine. AWMF represents Germany in the Council for International Organizations of Medical Sciences CIOMS. This website "AWMF online" is to inform scientitst in medicine and the general public about all activities of AWMF.
more about AWMF
and The Cochrane Library). The grading of recommendations in relation to their evidence is according to the AWMF Guidance Manual and Rules for Guideline Development.
Recommendations:
A: 31
B: 11
C: 2
09/25/2017
28. AWMF-Leitlinienkonferenz für die Leitlinienbeauftragten der Fachgesellschaften findet am 24.November 2017 in Berlin statt.

The team should consist of…

1 Requirements

1.1 Availability of a team of ABS experts

The team should consist of at least one infectious diseases physician (or clinician with infectious diseases training) and an experienced clinical pharmacist/hospital pharmacist, as well as a specialist in microbiology, virology and infection epidemiology being responsible for laboratory diagnostic and microbiological consultation; furthermore, the physician

Various ABS programmes describe an FTE of 0.5 per 250 beds as being the minimum staff resources necessary to cost-effectively conduct an ABS programme.

- 0.5 FTE for 250 beds
- FTE: Full time equivalent

- **Infectious diseases specialist**
- **Clinical pharmacist**
- Microbiology specialist
- Epidemiyologist
- Infection control consultant

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Surveillance

1.2 Availability of surveillance data on pathogens, resistance, and antimicrobial consumption

Conducting an additional material analysis (e.g. number of blood culture sets per patient or 1000 patient-days, number of urine cultures per patient, number of catheter-associated urine cultures, etc.) also with regard to

Use density should be presented by antibiotic class and not only by individual agent.
Reporting consumption data and antiinfective costs ranked by individual agent or class (e.g. top 5 or 10) is also reasonable.
Point prevalence surveys are a simple tool to examine process quality.

- Number of cultures per 1000 patient days: Blood, urine..

- Resistance data should be accessible at least on yearly basis
- Resistance data should be reported on department basis, sample basis..etc
- Surveilance culture results should be reported seperately
- Point prevelance surveys
- Antibiotic consumption data: by AB class, top 5 or 10

Quarterly use density (RDD/100patient days)

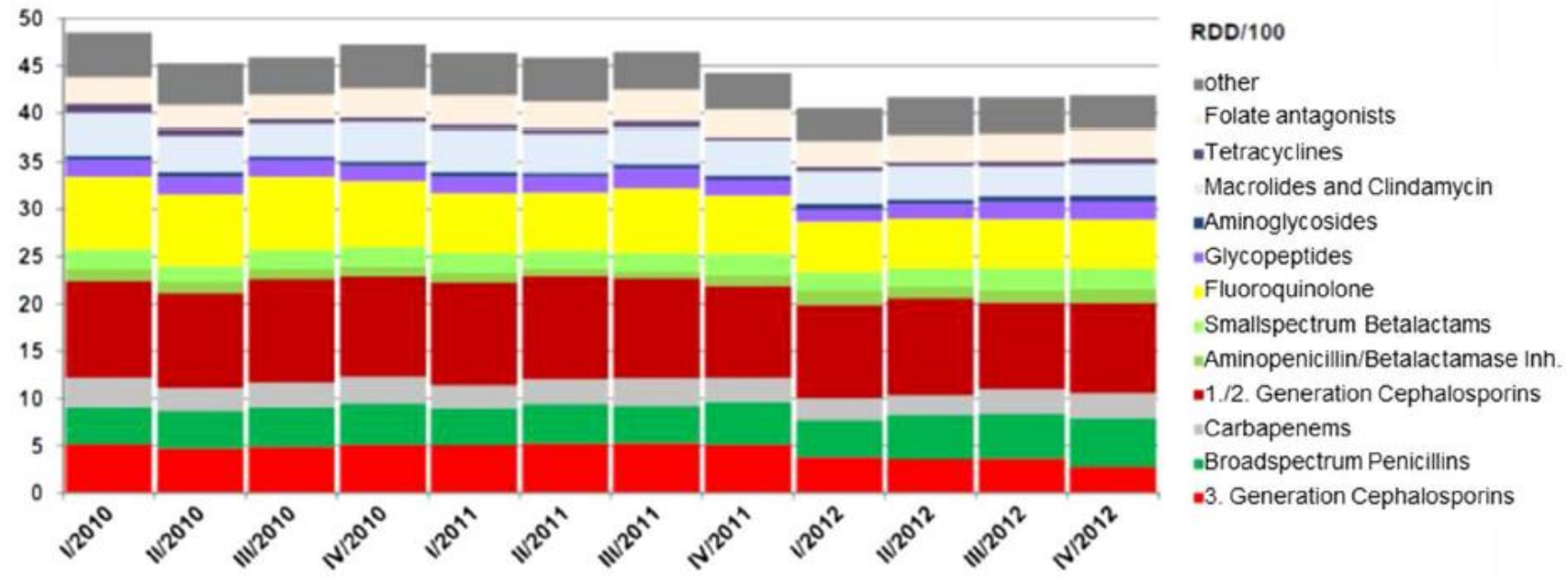

Fig. 1 Graphical presentation of quarterly use density (RDD/100 patient-days) for different antibiotic classes

Targeted proactive audits of antiinfective use

Table 4 Examples for performing targeted proactive audits of antiinfective use

- Perioperative antibiotic prophylaxis in selected surgical fields
- Targeted therapy of bacteremic patients hospital-wide
- Community-acquired pneumonia in the emergency department
- Sequential therapy on general wards with antibiotics of high bioavailability

Point prevalance surveys

Antibiotic use for

- Surgical prophylaxis
- Bacteremia
- Pneumonia at the Emergency Department
- Sequential therapy; PE to oral

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Hospital formulary is important!

Antibiotic (AB)- Group	Appl.	Trade Name	Active agent	Recommended daily dose RDD		DTC
				Normal renal function CrCl > 80 ml/min	Impaired renal function CrCl 80-50 ml/min	
Penicillins	i.v. **oral**	Infectocillin **Penicillin V 1 Mega**	Benzylpenicillin **Phenoxymethyl penicillin**	3 x 10 million IU or 4 x 5 million IU **3 x 1 million IE**	2 x 10 million IU **3 x 1 million IU**	€€ **€**
Aminopenicillins	i.v. **oral**	Ampicillin **AmoxiHexal**	Ampicillin **Amoxicillin**	3 x 2 g **3 x 1 g**	2 x 2 g **3 x 1 g**	€€ **€**
Aminopenicillins + beta-lactamase inhibitors	i.v. **oral**	Ampicillin+ Sulbactam **Amoclav 500 plus**	Ampicillin/ Sulbactam **Amoxicillin/ Clavulanic acid**	3 x 2000/1000 mg **3 x 500/125 mg**	2 x 2000/1000mg **3 x 500/125 mg**	€€ **€**
Acylaminopenicillins	i.v.	Piperacillin	Piperacillin	3 x 4 g	2 x 4 g	€€
Acylaminopenicillins + beta-lactamase inhibitors	i.v.	Piperacillin+ Tazobactam	Piperacillin/ Tazobactam	3 x 4g/0,5 g	2 x 4g/0,5 g	€€
Carbapenems	i.v.	Meropenem	Meropenem	3 x 1 g for meningitis: 3 x2 g	4 x 500 mg	€€€€
Tetracycline	i.v. **oral**	DoxyHexal SF **DoxyHexal Tabs**	Doxycycline **Doxycycline**	**1 x 200 mg, then 100-200 mg/day**	no dose adjustment necessary	€ **€**
Aminoglycosides	i.v. i.v.	TobraCell Gentamicin	Tobramycin Gentamicin	1 x 5-6 mg/kg KG 1 x4,5 mg/kg KG	Confer with Senior physician	€€ €€
Nitroimidazoles	i.v. **oral**	Metronidazol **Metronidazol**	Metronidazole **Metronidazole**	3 x 500 mg **3 x 400 mg**	3 x 500 mg **3 x 400 mg**	€ **€**
Oxazolidinons	i.v. **oral**	Zyvoxid **Zyvoxid**	Linezolid **Linezolid**	2 x 600 mg **2 x 600 mg**	2 x 600 mg **2 x 600 mg**	€€€€ **€€€€**
Green: Recommended Antibiotic	As a matter of principle preference should be given to oral drugs, provided that the patient's condition allows					
Yellow: Reserve Antibiotic	The recommended daily dose refers to an adult patient (~ 70 kg)					
Red: Special Antibiotic, Confer with senior physician	DTC: Daily Therapeutic Cost DTC: €: 0 to €2; €€: 2 to €10; €€€: 10 to €25; €€€€: 25 to €50; €€€€€: more than 50 € to €150					
Bold	Available oral antibiotics					

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Treatment optimisation

3.1 Special programmes for treatment optimisation

De-escalation includes conversion from an empirical combination therapy to targeted monotherapy based on knowledge of the microorganism isolated, susceptibility and infectious disease.

De-escalation should be initiated early on (after 48–72 h), which also includes discontinuation of initial therapy if diagnosis is not secured. Observational studies show that this strategy is not adopted in 20–60 % of cases.
De-escalation programmes should point out that depending on the exact diagnosis in some cases instead of de-escalation, escalation may in fact be necessary.

Prolonged infusion of beta-lactams (taking into account physico-chemical stability) is reasonable and recommended particularly in critically ill patients.
TDM can avoid under-/over-dosing and minimise organ toxicity.
Programmes for doses optimisation are cost-effective.

- Optimisation of treatment does not necessarily mean de-escalation; sometimes requires escalation
- Evaluation at 48-72 hours of therapy
- Prolonged infusion of beta lactams…etc
- TDM of antibiotics

Computerised information technology

3.4 Computerised information technology

The local treatment guideline and the antiinfective formulary should be readily electronically accessible from every clinical computer workstation.
For ABS activities or for surveillance and analysis of antimicrobial usage, computer physician order entry (CPOE) systems should be designed in such a way as to allow automated generation of exact lists of the antiinfectives used.
Surgical software should be utilisable in such a manner as to ensure that antibiotic prophylaxis is compliant with guidelines.
Computer-based expert systems cannot replace a physician's clinical judgement.

- Treatment guidelines
- Hospital formulary
- Surveillance results
- ….

should be readily electronically accessible

KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 31 .Yıl

Gram negatif bakteriler için

ANTİMİKROBİYAL YÖNETİM REHBERİ

Hazırlayan: KLİMİK DERNEĞİ