Rational use of antimicrobials: effective methods in hospitals and community

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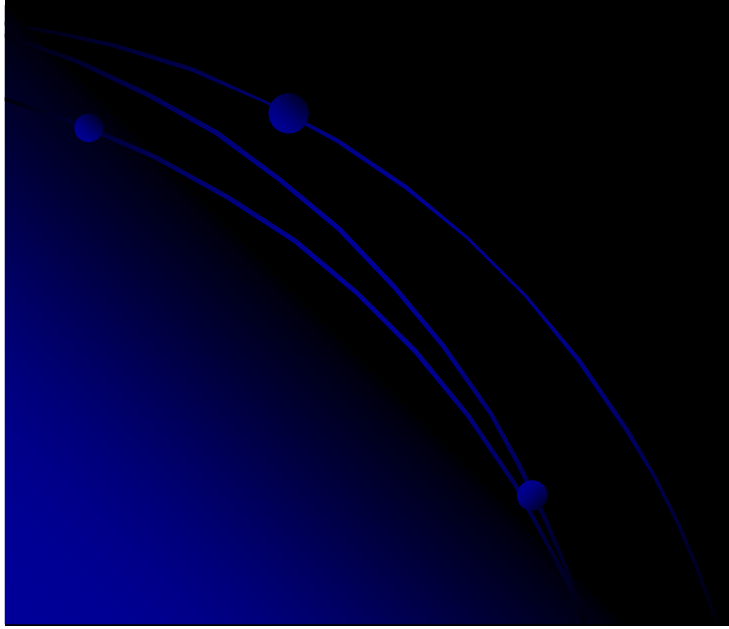
WHY?



…because resistant bacteria cause excessive morbidity, mortality and healthcare cost

- MRSA did not replace MSSA but aacounted for increasing rates of *S. aureus* bacteremia
- Inappropriate empirical treatment (mostly caused by infection with resistant bacteria) causes excessive death
- Increased length of stay, cost of new drugs…

Staphylococcus aureus bacteremia in two hospitals in Oxfordshire, UK, 1997 to 2003:

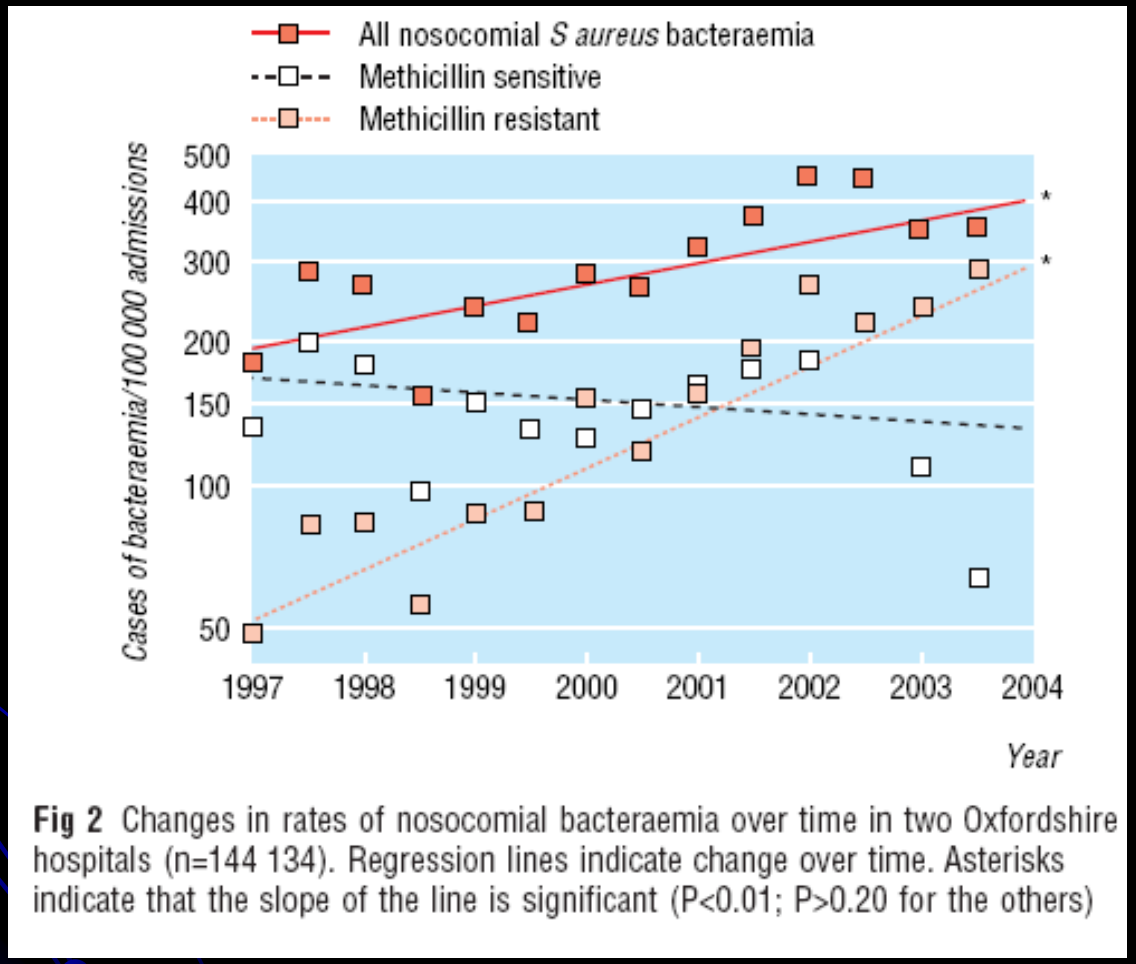


Fig 2 Changes in rates of nosocomial bacteraemia over time in two Oxfordshire hospitals (n=144 134). Regression lines indicate change over time. Asterisks indicate that the slope of the line is significant (P<0.01; P>0.20 for the others)

Wyllie DH, et al. BMJ 2006; 333: 281.

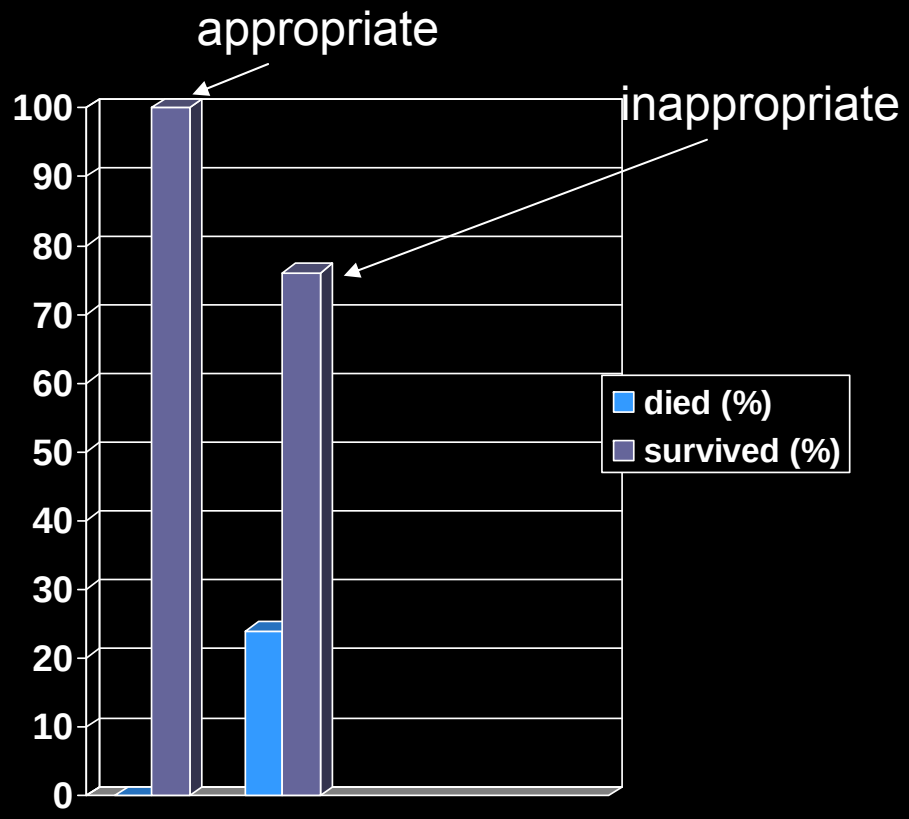
…resistance increases mortality: empirical treatment can not be appropriate.

Luna CM, 2006

Alvarez-Lerma F, 1996

Kollef MH, 1999

….



Luzar T. HAP in ICU. 2002, master thesis

…because we do not have new antibiotics against bacteria, becoming resistant to all effective treatment options

Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

Helen W. Boucher,[1] George H. Talbot,[2] John S. Bradley,[3,4] John E. Edwards, Jr,[5,6,7] David Gilbert,[8] Louis B. Rice,[9,10] Michael Scheld,[11] Brad Spellberg,[5,6,7] and John Bartlett[12]

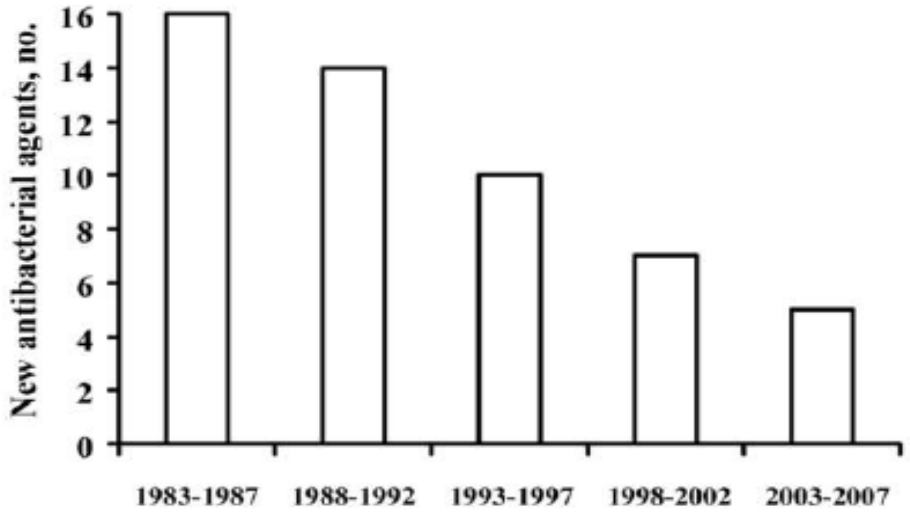


Figure 1. New antibacterial agents approved in the United States, 1983–2007, per 5-year period [2, 3].

Clinical Infectious Diseases 2009; 48:1–12

…because antibiotics cause/select resistance

	MRSA	VRE	ESBL	MDR PA	*C. difficile*
carbapenems	++	+++	+	+++	
piperacillin / tazobactam	++		+	+	
3rd generation cephalosporins	+++	+++	+++	+	+++
fluoroquinolones	+++	++	+++	+++	+++

+++, clear evidence of selection,

++, no clinical activity, potential to select,

+, borderline clinical activity and/or selection risk

Wilcox MH. Int J Antimicrob Agents 2009; 34:S3: S6-10.

European Antimicrobial Resistance Surveillance System: Gram positive microorganisms

(invasive isolates from 30 to 32 European countries)

% R (range)	Penicillin non-susceptible *S. pneumoniae*	Erythromycin and penicillin non-susceptible *S. pneumoniae*	MRSA	VRE
2004	9 (0-37)	NA	24 (0-73)	9 (0-42)
2005	10 (0-39)	10 (0-32)	25 (1-61)	14 (0-46)
2006	9 (0-38)	5 (0-26)	22 (0-67)	11 (0-42)
2007	10 (0-34)	6 (0-26)	22 (0-52)	10 (0-37)

www.earss.rivm.nl

European Antimicrobial Resistance Surveillance System: Gram-negative microorganisms

(invasive isolates from 30 to 32 European countries)

% R (range)	*E. coli*, resistant to f-quinolones	*K. pneumoniae* ESBL	*P. aeruginosa*, resistant to carbapenems
2004	14 (2-35)	-	-
2005	15 (3-30)	24 (0-66)	20 (4-61)
2006	18 (5-48)	22 (1-94)	20 (0-48)
2007	22 (7-53)	23 (0-80)	21 (0-47)

www.earss.rivm.nl

What is rational use of antimicrobials?

- To choose the most effective antibiotic therapy
- To minimize adverse events
- To minimize the development of antibiotic resistance
- At minimal cost

What is rational use of antimicrobials?

- To choose the most effective antibiotic therapy
- To minimize adverse events
- To minimize the
-

ANTIBIOTIC STEWARDSHIP

McGowan&Gerding, New Horiz 1996; 4: 370-6.

Interventions to improve antibiotic prescribing practices in ambulatory care

(Arnold SR, Straus SE. Cochrane Database Syst Rev 2005; 4. Art. No.: CD003539.)

- 39 studies: RC, QR, CBA, ITS
  - Printed educational material: no or only a small effect
  - Audit and feedback: no or only small effect
  - Interactive education better than didactic lectures
  - Outreach visits and reminders: mixed effect
  - Patient based intervention: no immediate effect
  - Multifacted interventions for physicians, patients and public: most effective in decreasing prescribing for inappropriate indications

Exeption: nationalwide recommendation in Finland decreased macrolide consumption from 2.4 TID to 1.38 TID.
Seppala H, et al. NEJM 1997; 337: 441-6.

Interventions to improve antibiotic prescribing practices in ambulatory care

(Arnold SR, Straus SE. Cochrane Database Syst Rev 2005; 4. Art. No.: CD003539.)

Authors' conclusion:

Effectivenes of the interventions depends to a large degree on particular prescribing behaviour and the barriers to change in the particular community.

Delayed prescribing strategies

- Studies showed reduction of antibiotic prescribing, but only in relation to near-universal antibiotic treatment in the control group.
- The proportion of patients using delayed antibiotics in these studies (37.5%) was similar to baseline prescribing rate (38.5%) in all other studies.

Ranji SR, et al. Med Care 2008; 46: 847-62.

Interventions in Outpatients in Slovenia

Čižman M, et al. JAC 2005; 55:758

- Restrictive measures for prescription of amoxicillin/clavulanate and fluoroquinolones were published in June 2000 by Health Insurance Institute of Slovenia because of steady increase of consumption.
- Respiratory FQ unrestricted use for severe CAP and COPB and infections with expected resistant bacteria (May 2004)
- No promotion for levofloxacin since June 2005
- Published articles with the key words “antibiotic drugs” and “bacterial resistance”
- Diagnostic tests: CRP, Streptococcal antigen tests

Antibiotic consumption (DDD/TID) in outpatients in Slovenia 1996-2005 (intervention June 2000)

Year	Total	AMOX/CA	FQ	Non-restricted
1996	15.21	3.25	1.08	10.88
1997	17.99	3.55	1.29	13.15
1998	19.66	4.92	1.53	13.21
1999	20.08	5.78	1.51	12.79
2000 ←	18.26	4.69	1.30	12.27
2001	17.55	4.35	1.26	11.94
2002	16.33	4.27	1.31	10.75
2003	16.98	4.11	1.15	11.72
2004	16.71	4.02	1.10	11.59
2005	16.1	4.12	1.1	10.9
2005 vs 1999	-19.8	- 27.2	- 28.8	- 14.8

Total antibiotic use, educational interventions in outpatients in Slovenia 1996-2003

Year	Total antibiotic use DDD/1000 inhabitants-day	Professional Communica-tions	Public communications	
			Lay articles	TV
1996	15.21	11	6	-
1997	17.99	8	11	-
1998	19.66	6	11	1
1999	20.08	2	13	1
2000	18.26	11	10	1
2001	17.55	30	8	12
2002	16.33	6	8	11
2003	16.98	10	7	9
Correlation	1	- 0.30	0.92	- 0.34

Rational antibiotic use in hospitals

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

Clinical Infectious Diseases 2007; 44:159–77

IDSA/SHEA guidelines

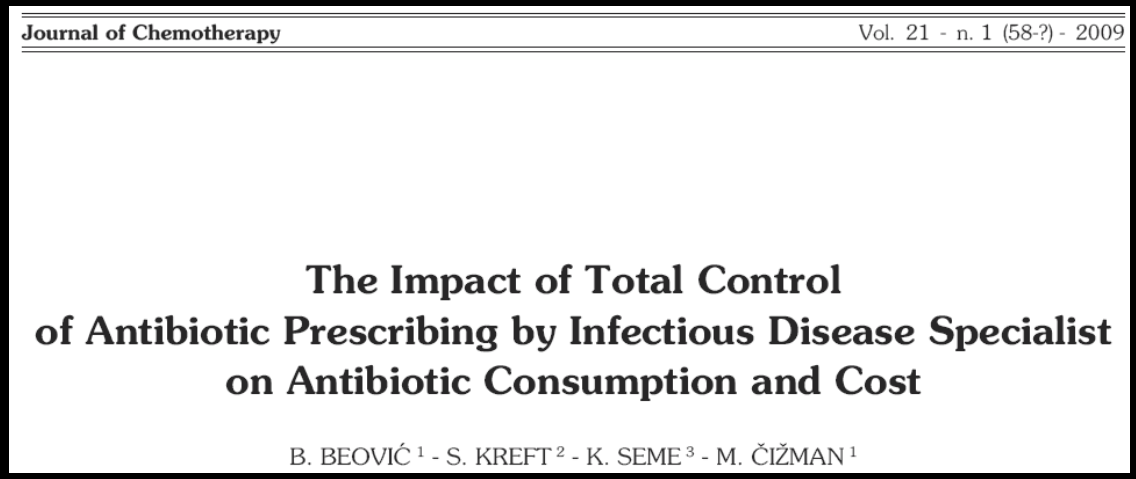
- Multidisciplinary antimicrobial stewardship team
- Good collaboration: multidisciplinary team – hospital hygiene – pharmacy
- Support and collaboration with hospital administration, medical staff leadership and local providers
- Authority, compensation, and outcomes
- Hospital administrative support for the infrastructure needed for antimicrobial consumption tracking on an on-going basis
- Two core proactive strategies
  - Prospective audit with intervention and feedback
  - Formulary restriction and preauthorization
- Supplemental elements: education, clinical guidelines and pathways, antibiotic forms, cycling, streamlining/deescalation, dose optimizing, parenteral to oral, combination therapy
- Health-care information technology: CPOE, medical records
- Computer-based surveillance
- Microbiology laboratory for the need of individual patient and the infection control efforts
- Outcome measures

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

Davey P, Brown E, Fenelon L, et al.

Cochrane Database of Systematic Reviews 2005; Issue 4. Art.No CD003543.

- 51/66 studies showed a significant improvement in at least one outcome.
- The results show that interventions to improve antibiotic prescribing to hospital inpatients are successful, and can reduce antimicrobial resistance or hospital acquired infections.



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The Impact of Total Control of Antibiotic Prescribing by Infectious Disease Specialist on Antibiotic Consumption and Cost

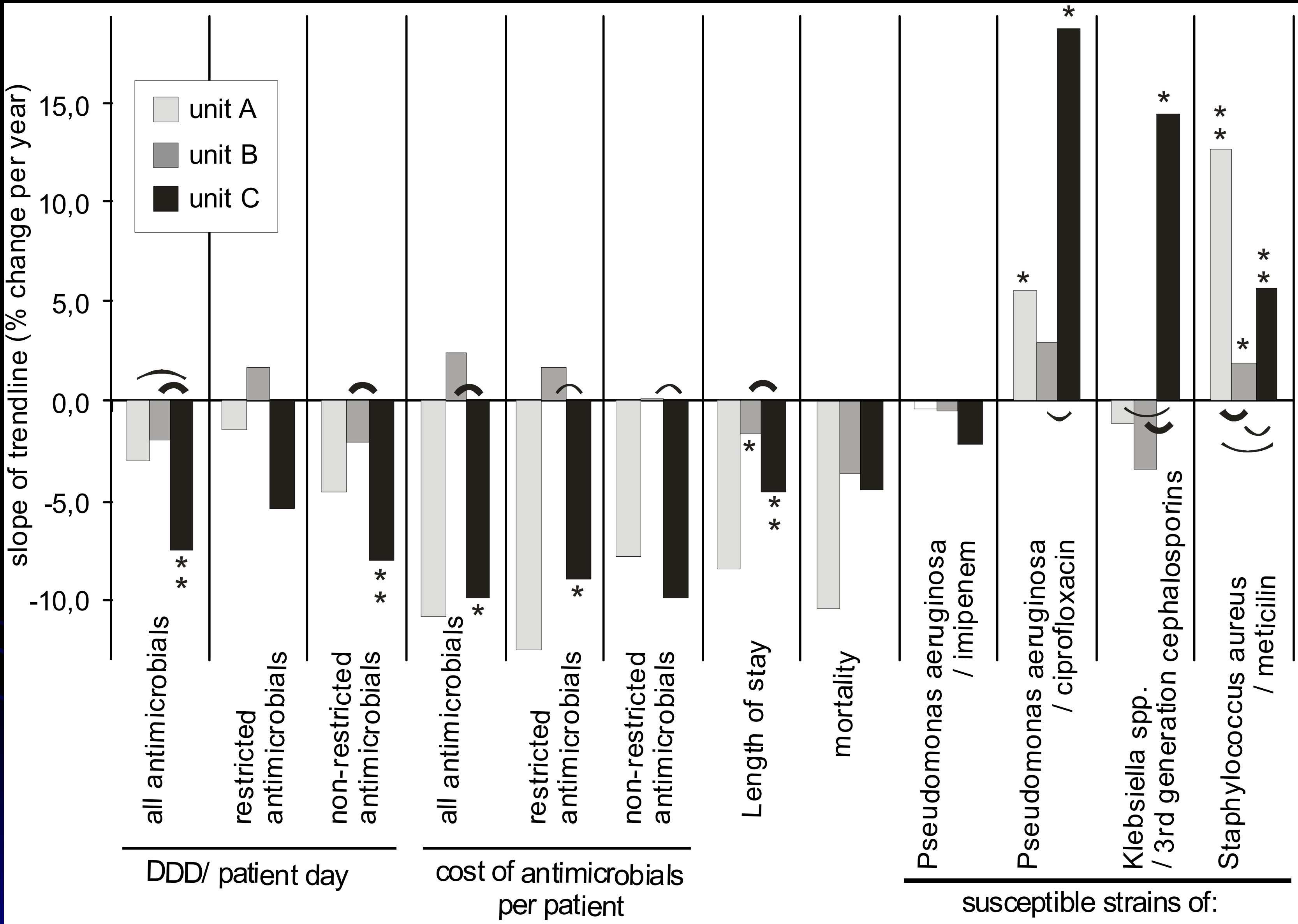
B. BEOVIĆ [1] - S. KREFT [2] - K. SEME [3] - M. ČIŽMAN [1]

Comparison of the approach in three units:

- A: restricted antimicrobials approved by ID
- B: restricted antimicrobials approved by the head of the department
- C: all antimicrobials prescribed by ID

Consumption of Antibiotics: DDD ATC 2005

Statistics: SPSS 15.0 (correlate : bivariate)



A, no restrictions

B, restrictions

C, total ID control

*, p<0.05

**, p<0.01

Beović B. J Chemother 2009

Thank you