

What is the evidence of Antibiotic Stewardship?

- Existing guidelines, existing framework -

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Disclosures

1. Position

→ Chief Pharmacist, Medical Center University of Freiburg

2. Participation in Advisory Boards

→ 2013-2016: Participation in AD Boards: BMS, Jazz, Pfizer and Roche

3. Shareholder

→ n/a

4. Honoraria

→ Honoraria / lecture fees from Astellas, B.Braun, Boehringer Ingelheim, Novartis, Pfizer, Roche, Sandoz, Sun Teva

5. Sponsorship for scientific research

→ none

6. Honoraria for Reviews

→ none

7. Other financial contributions

→ none

Questions for the ACASEM Survey

Which group is usually not a member of the ABS team

- a) Pharmacists
- b) Nurses
- c) Patients
- d) Department heads

How many recommendations can be found in the IDSA guideline?

- a) 12
- b) 20
- c) 27
- d) 28

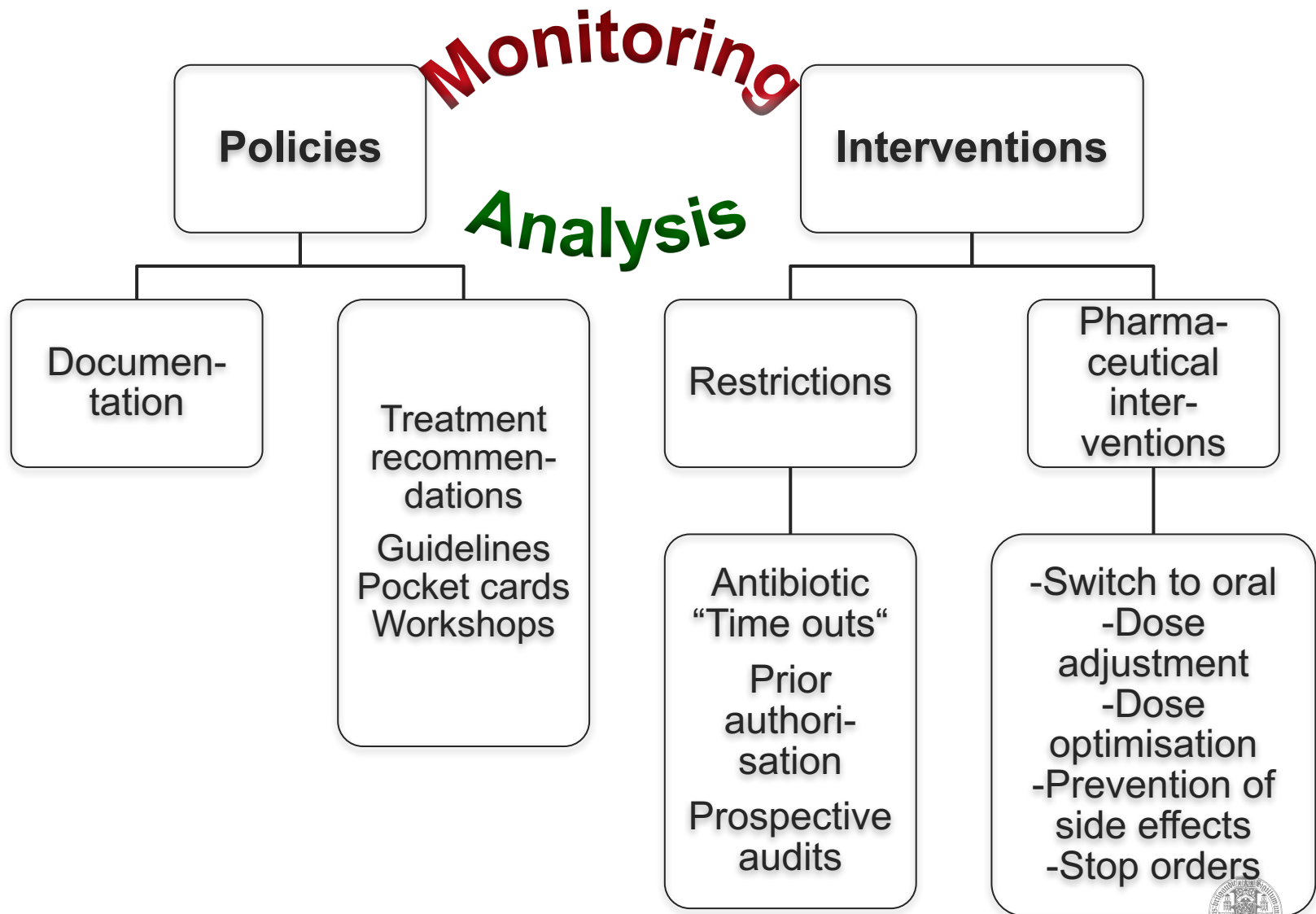
Which ABS intervention has the strongest impact on mortality?

- a) Switch from intravenous to oral therapy
- b) Prescribing empirical antimicrobial therapy according to guidelines
- c) Adjustment of therapy according to renal function
- d) Therapeutic drug monitoring

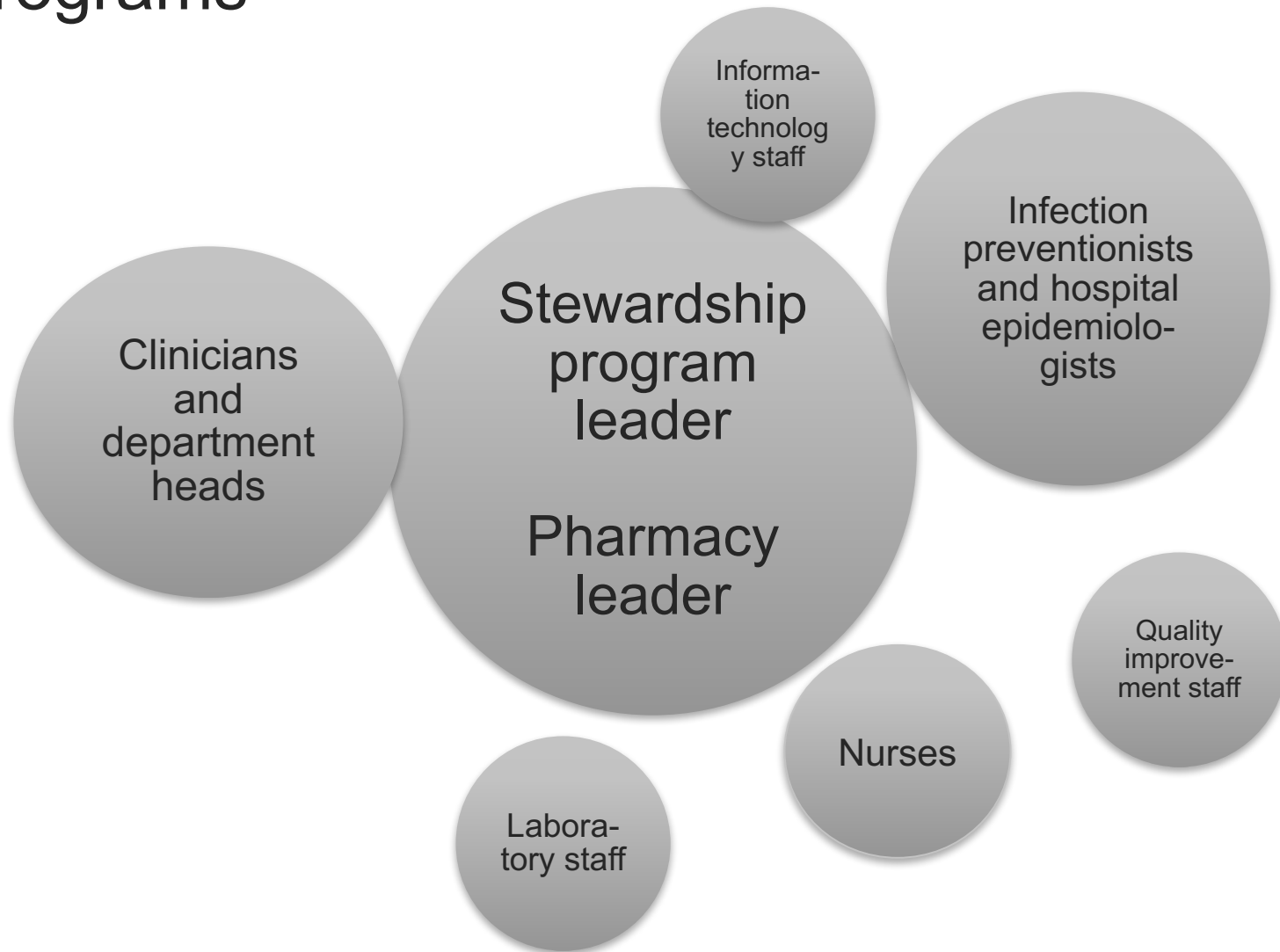
Antimicrobial resistance strategies and action plans



Key elements of anti(biotic)microbial stewardship

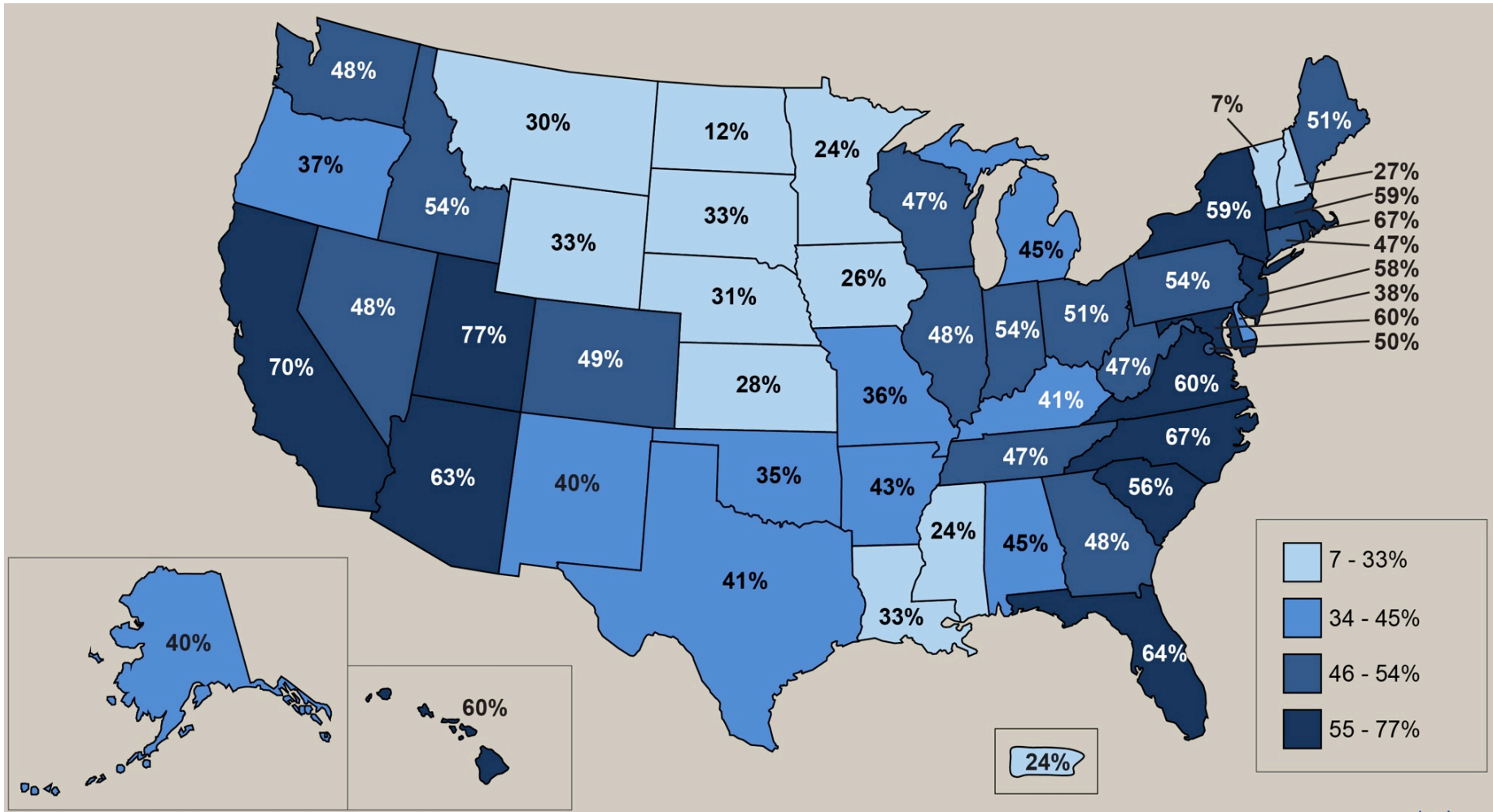


Core Members of Hospital Antibiotic Stewardship Programs



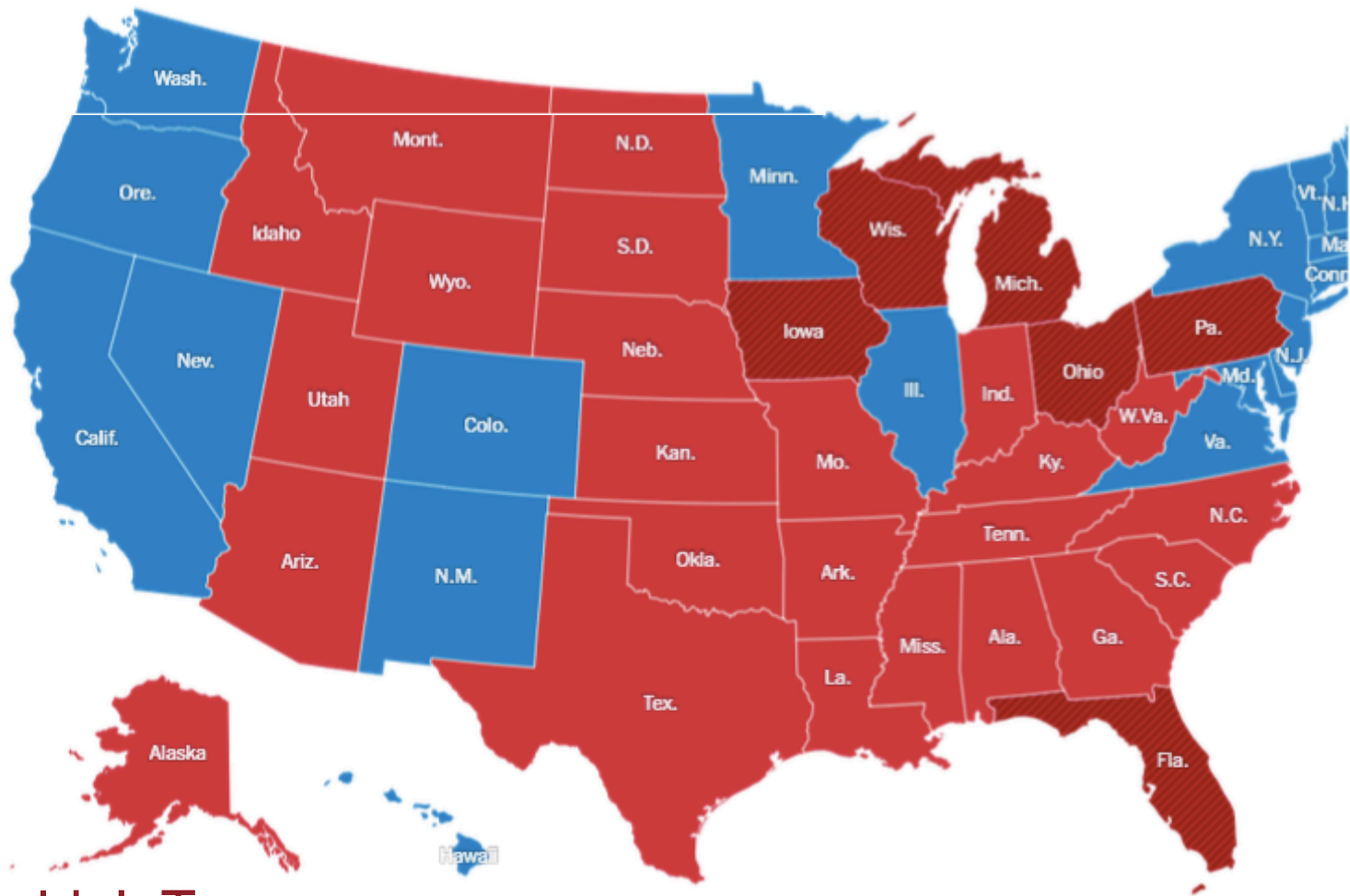
Percentage of Hospitals with ABS Programs by State

US data from 2015



Presidential election results

2016



Donald J. Trump
Hillary Clinton

Guidelines

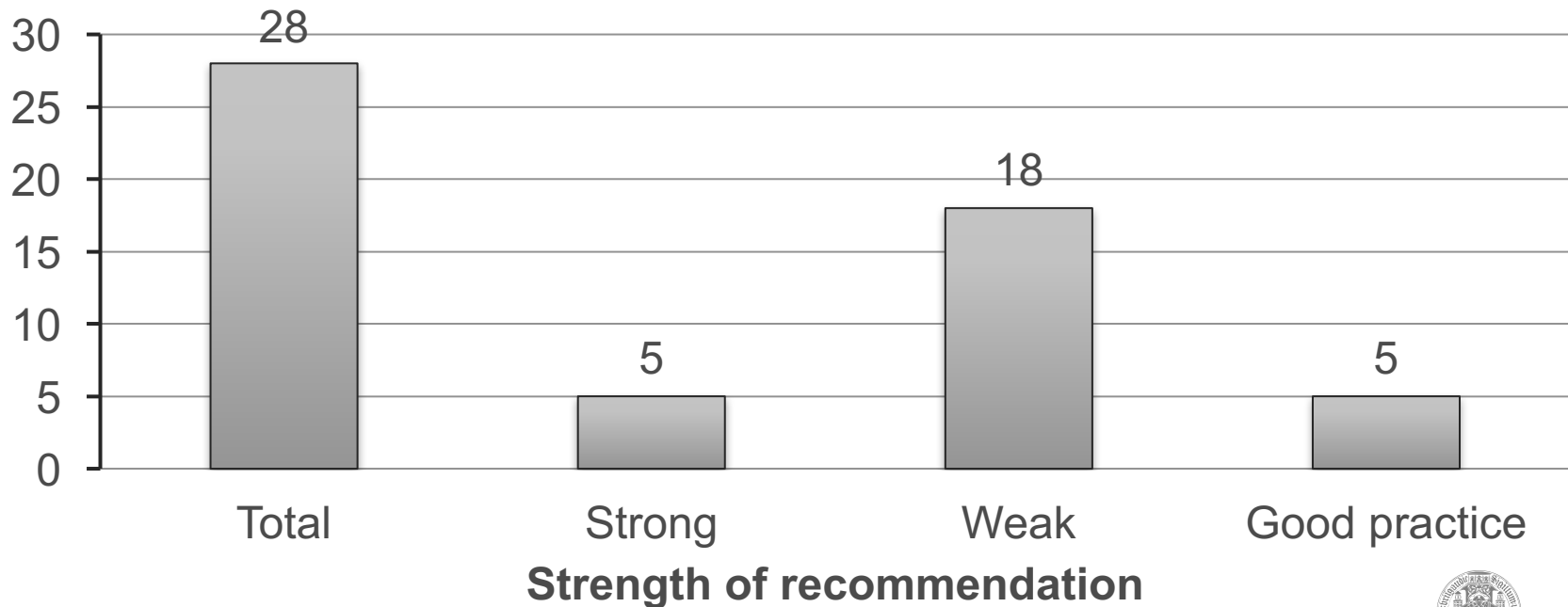
USA

Clinical Infectious Diseases

IDSA GUIDELINE



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



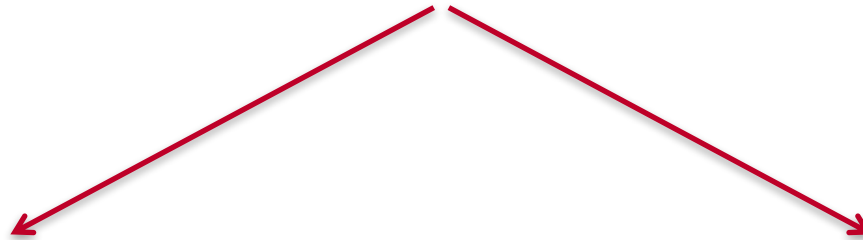
Strong recommendation – moderate evidence

Objective	Strength of recommendation	Level of evidence
Use of Preauthorization and/or Prospective Audit and Feedback	strong	moderate-quality
Reduce the Use of Antibiotics Associated With a High Risk of CDI	strong	moderate-quality
Pharmacokinetic (PK) Monitoring and Adjustment Program	strong	moderate-quality (aminoglycosides)
Interventions to Increase Use of Oral Antibiotics	strong	moderate-quality
Reduce Antibiotic Therapy to the Shortest Effective Duration	strong	moderate-quality

NICE Guideline on Antimicrobial stewardship

United Kingdom

- Recommendations for organisations (commissioners and providers)
- Recommendations for prescribers and other health and social care practitioners
- Recommendations for local decision-making groups
- Research recommendations



All antimicrobials

New antimicrobials

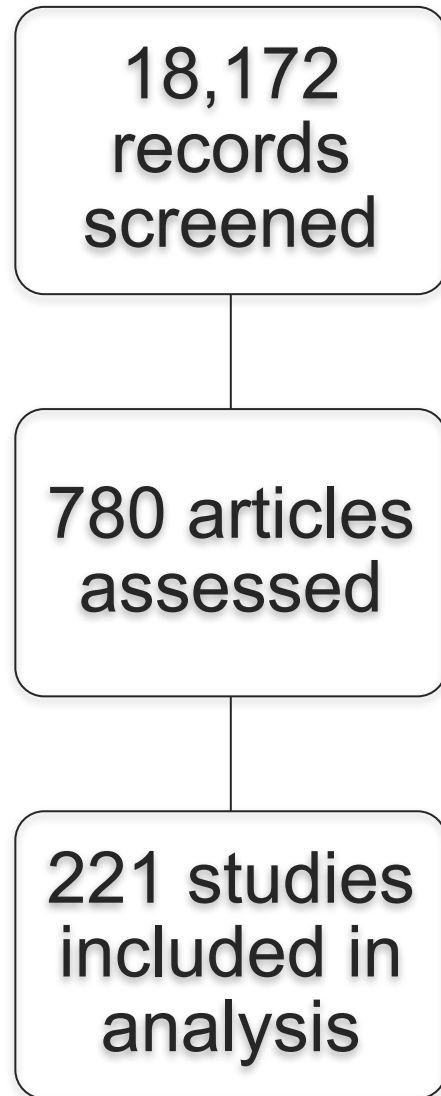
AWMF guideline on antibiotic stewardship

Austria + Germany

Requirements	ABS core strategies	Supplemental ABS strategies
Availability of a team of ABS experts	Application of local treatment guidelines	Special programmes for treatment optimisation
Availability of surveillance data on pathogens, resistance, and antimicrobial consumption	Design and implementation of education, training and information	Special rules for communication of microbiology results
	Conducting proactive audits of antiinfective use	Special rules for management of patients with multidrug-resistant microorganisms and <i>C. difficile</i>
	Quality indicators	Computerised information technology

Antibiotic Stewardship – searching for evidence I

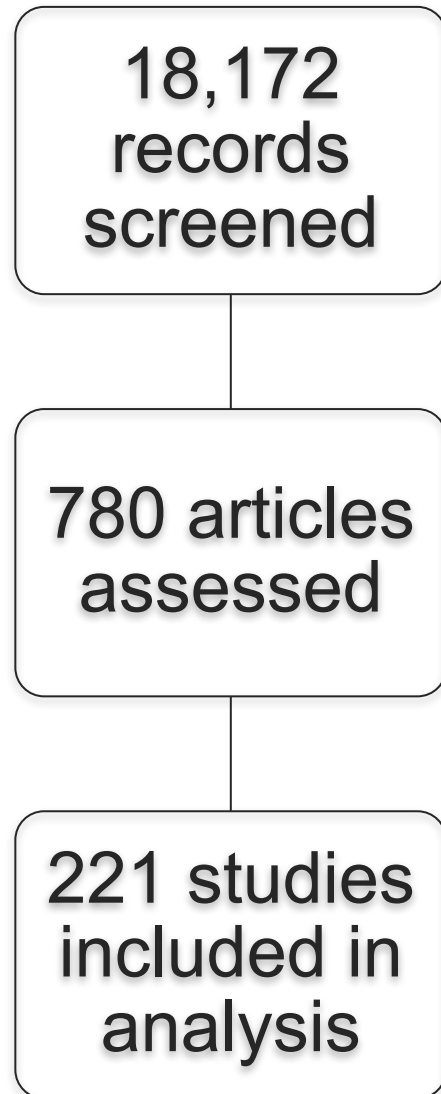
Data from Cochrane Database of Systematic Reviews



Region of origin	Number of studies
North America	96
Europe	87
Asia	19
South America	8
Australia	8
East Asia	3

Antibiotic Stewardship – searching for evidence I

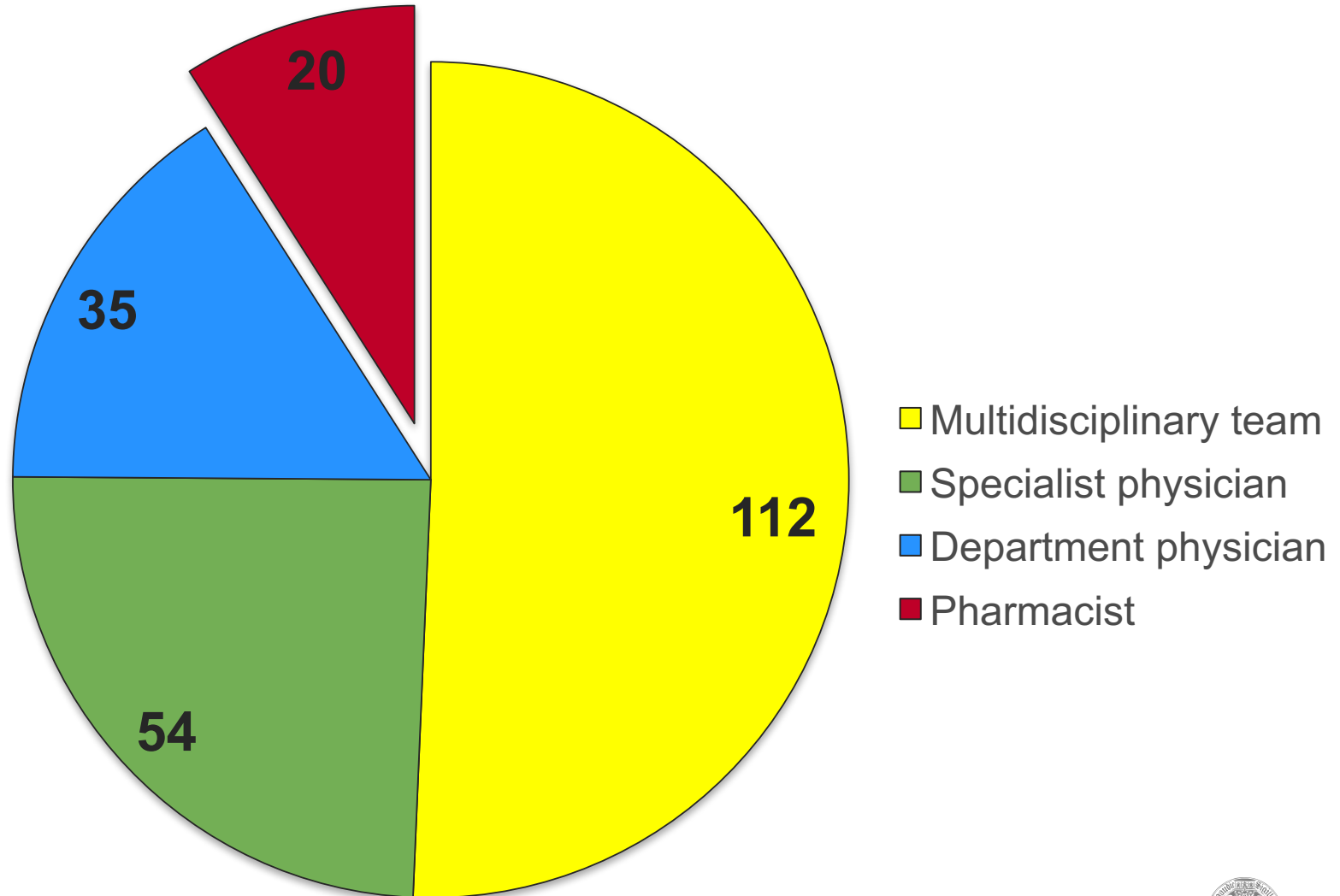
Data from Cochrane Database of Systematic Reviews



Country of origin	Number of studies
UK	22
Germany	12
France	11
Netherlands	11
Switzerland	11
Spain	5
Belgium	4
Denmark	3
Italy	3
Austria	2
Sweden	2
Croatia	1
Greece	1
Hungary	1
Israel	1
Norway	1
Serbia	1
Turkey	1

Persons that did the work by discipline

Interventions

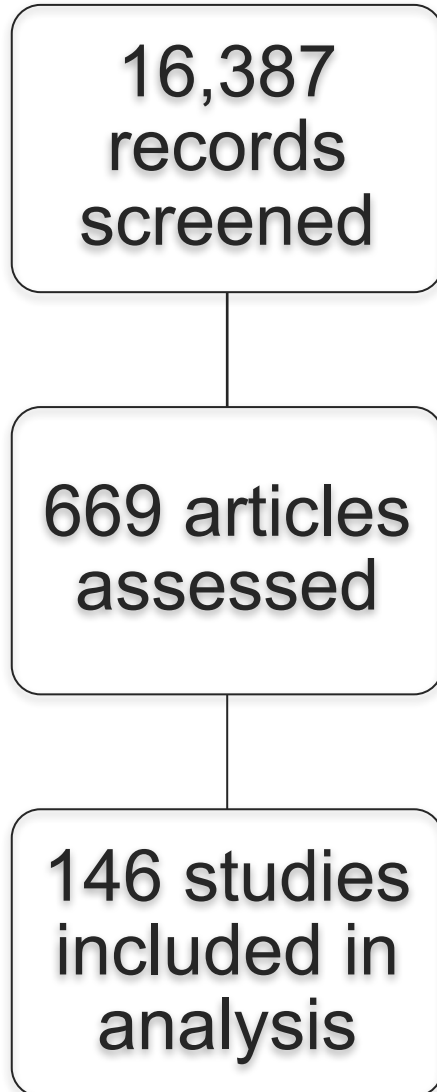


Summary of Findings

Objective	Parameter	Result
Treatment according to guidelines	Proportion of participants	Favours intervention (+ 15%)
Reduction of unnecessary prescribing	Risk difference	Favours intervention (0.15)
Duration of antibiotic treatment	Days of treatment	Favours intervention (-1.95 days)
Length of stay	Days	Favours intervention (-1.12 days)
Mortality	Risk difference	No difference (0.0)

Antibiotic Stewardship – searching for evidence II

Data from: Schuts EC et al. Lancet Infect Dis 2016; 16: 847–56



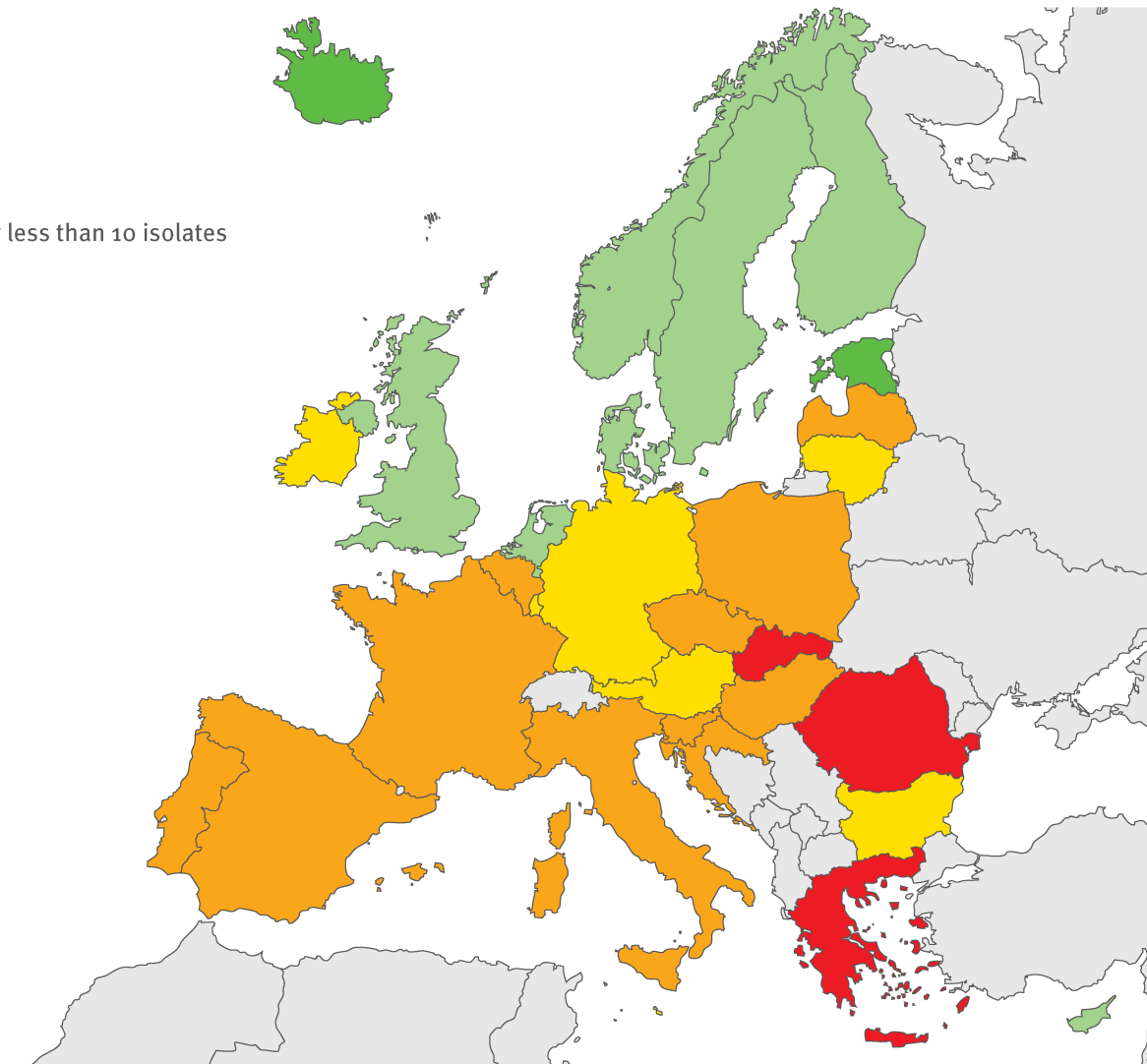
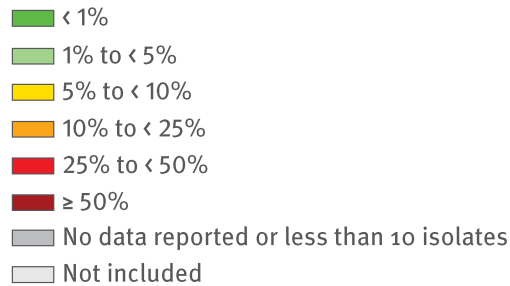
Objective	Number of studies
Empirical therapy according to the guidelines	40
De-escalation of therapy	25
Adjustment of therapy to renal function	5
Switch from intravenous to oral therapy	18
Therapeutic drug monitoring	17
Discontinuation of antibiotic therapy if infection not confirmed	3
Presence of a local antibiotic guide	1
List of restricted antibiotics	30
Bedside consultation	7

Summary of Findings

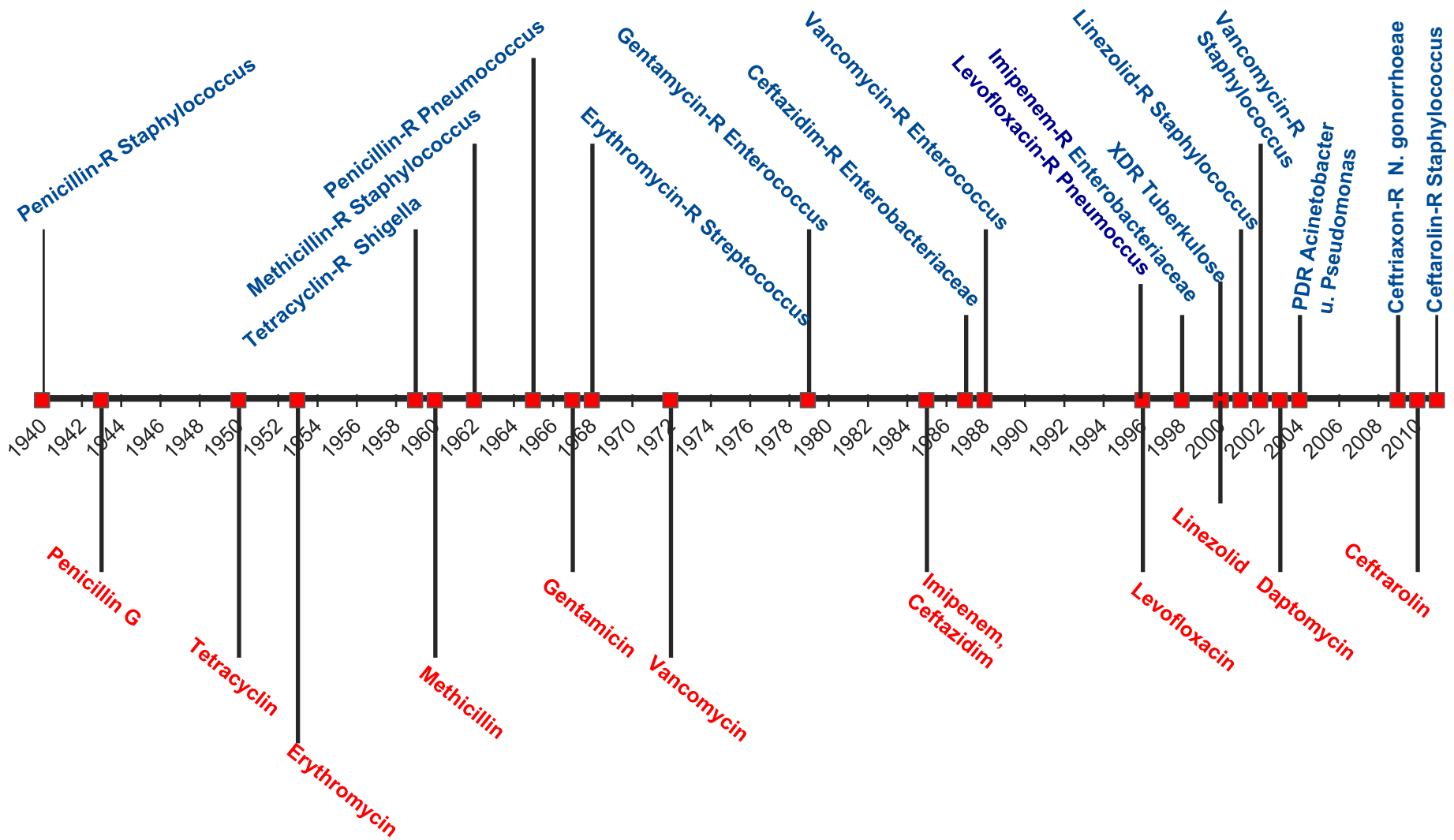
Objective	Parameter	Result
Prescribing empirical antimicrobial therapy according to guidelines	Mortality	Favours experimental (Odds ratio = 0.65)
De-escalation of therapy based on culture	Risk difference	Favours intervention (Risk reduction = 0.44)
Adjustment of therapy according to renal function	Adverse effects	Favours intervention
Switch from intravenous to oral therapy	Mortality	No significant difference
Therapeutic drug monitoring	Rate of nephrotoxicity	Favours intervention (Risk reduction = 0.50)

Emerging problem: multiresistant bugs

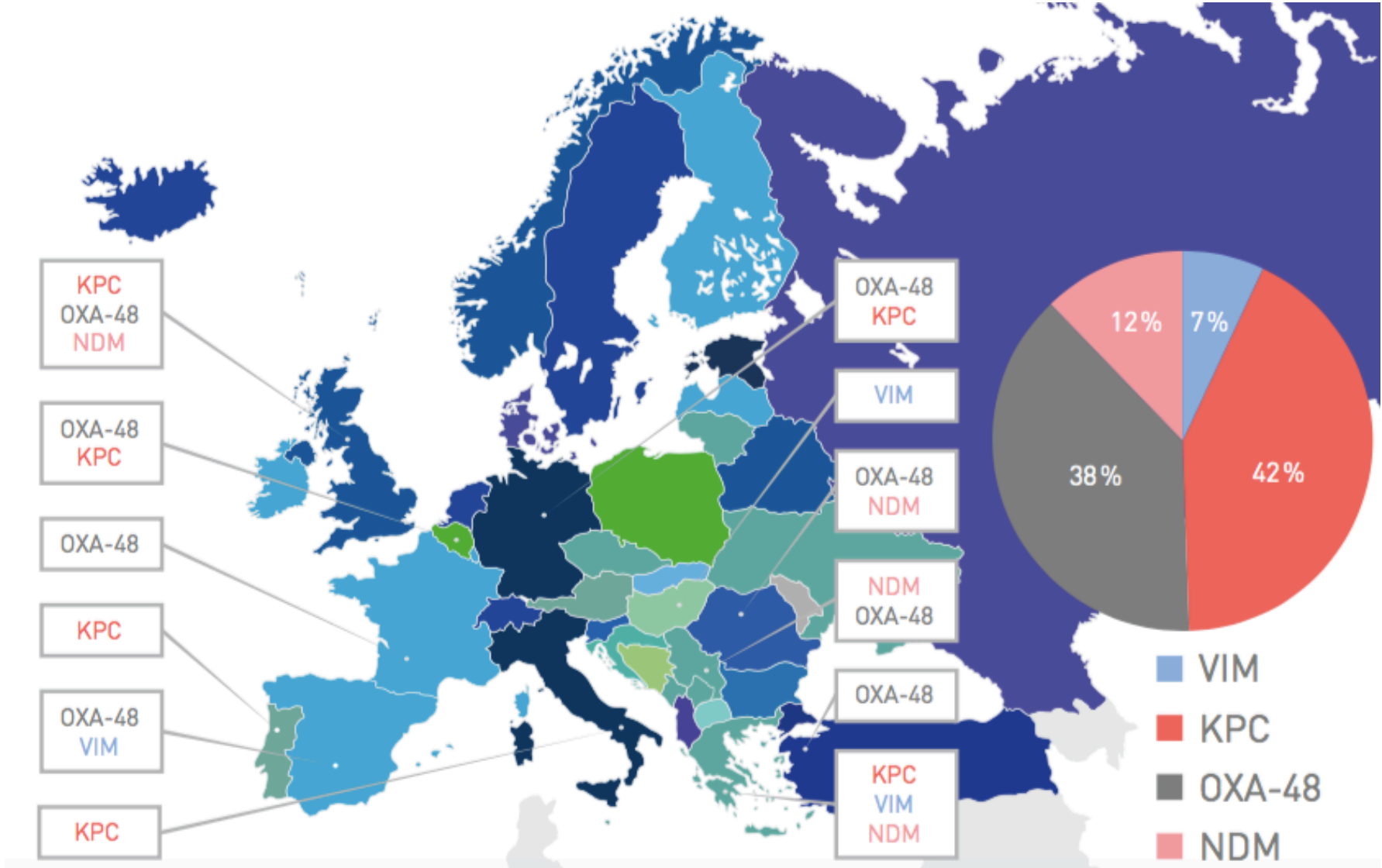
Clinical isolates of MRGN3-4 *Pseudomonas aeruginosa*



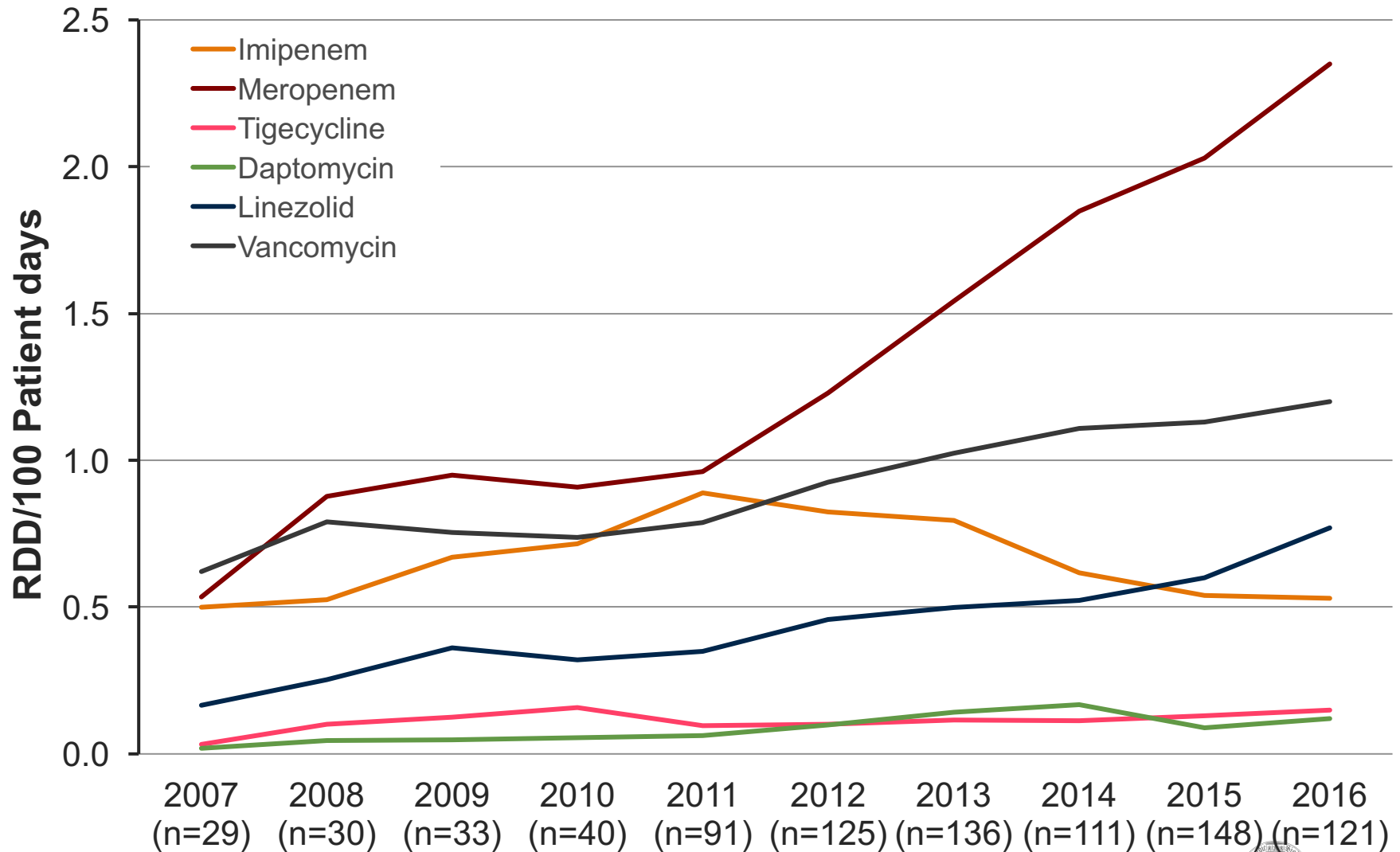
Antiinfectives and Resistance



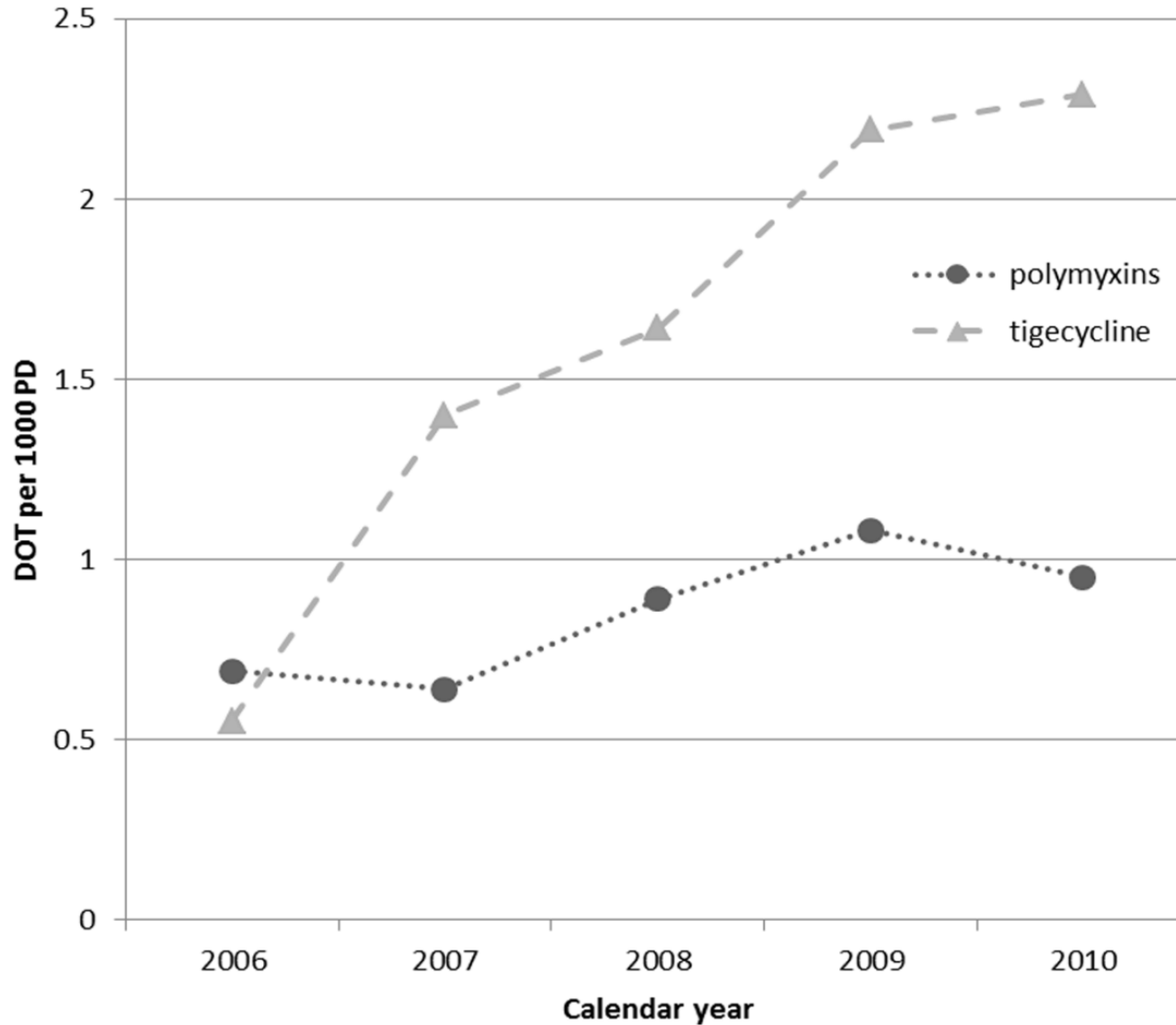
Distribution of ESBL producing Enterobacteriaceae



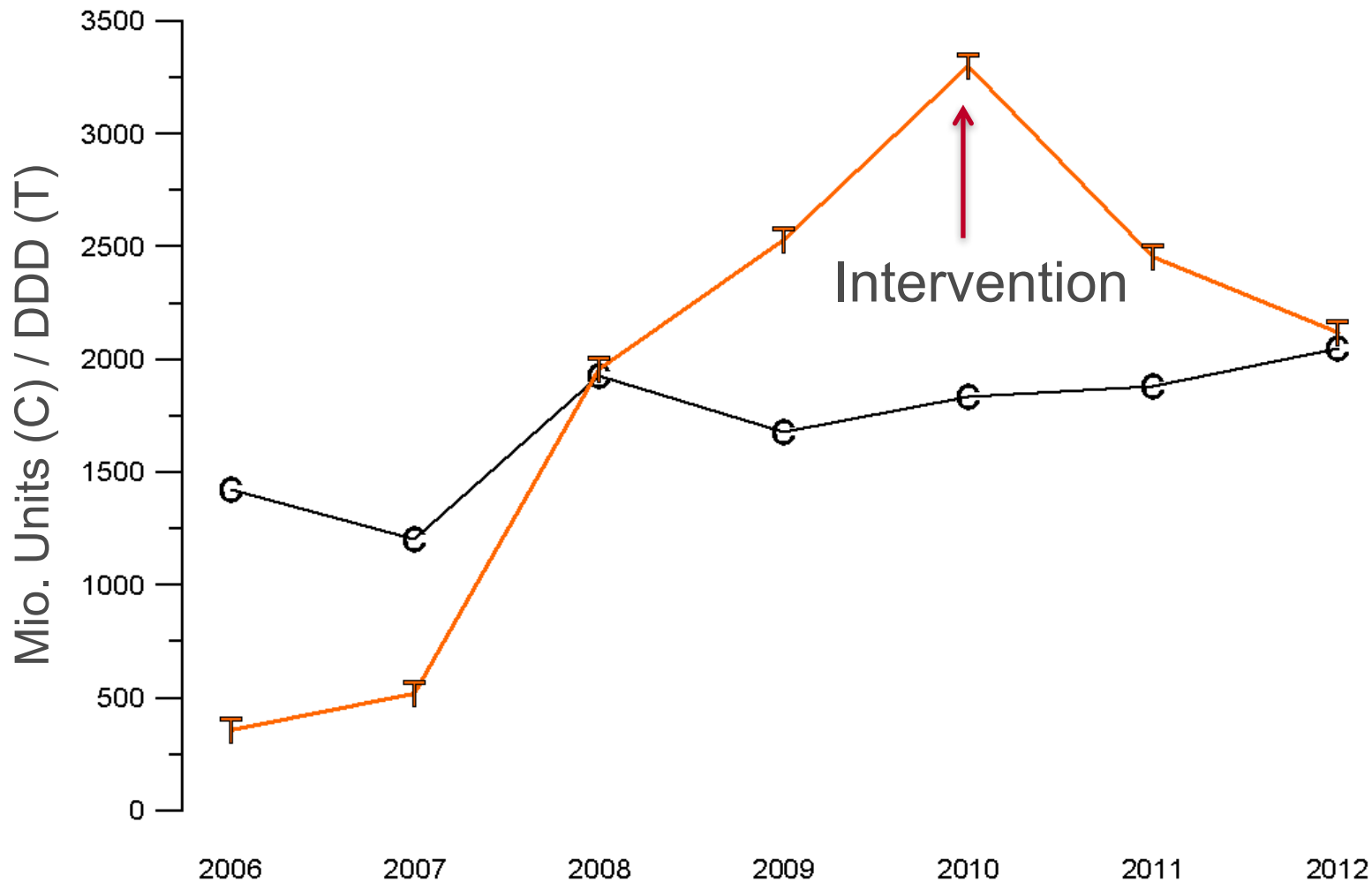
Use of *reserve* antibiotics among German hospitals



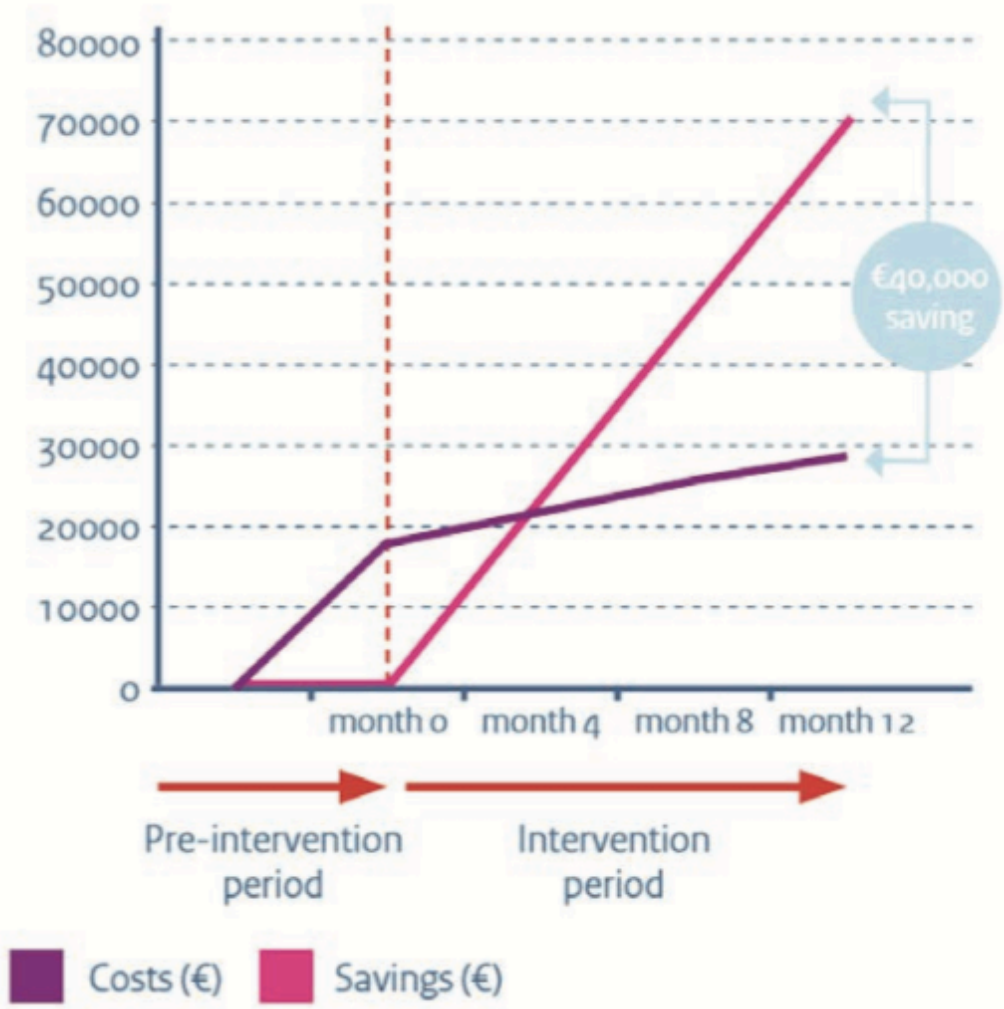
Consumption of polymyxins and tigecycline



Consumption of colistin (C) and tigecycline (T) at University Medical Center Freiburg

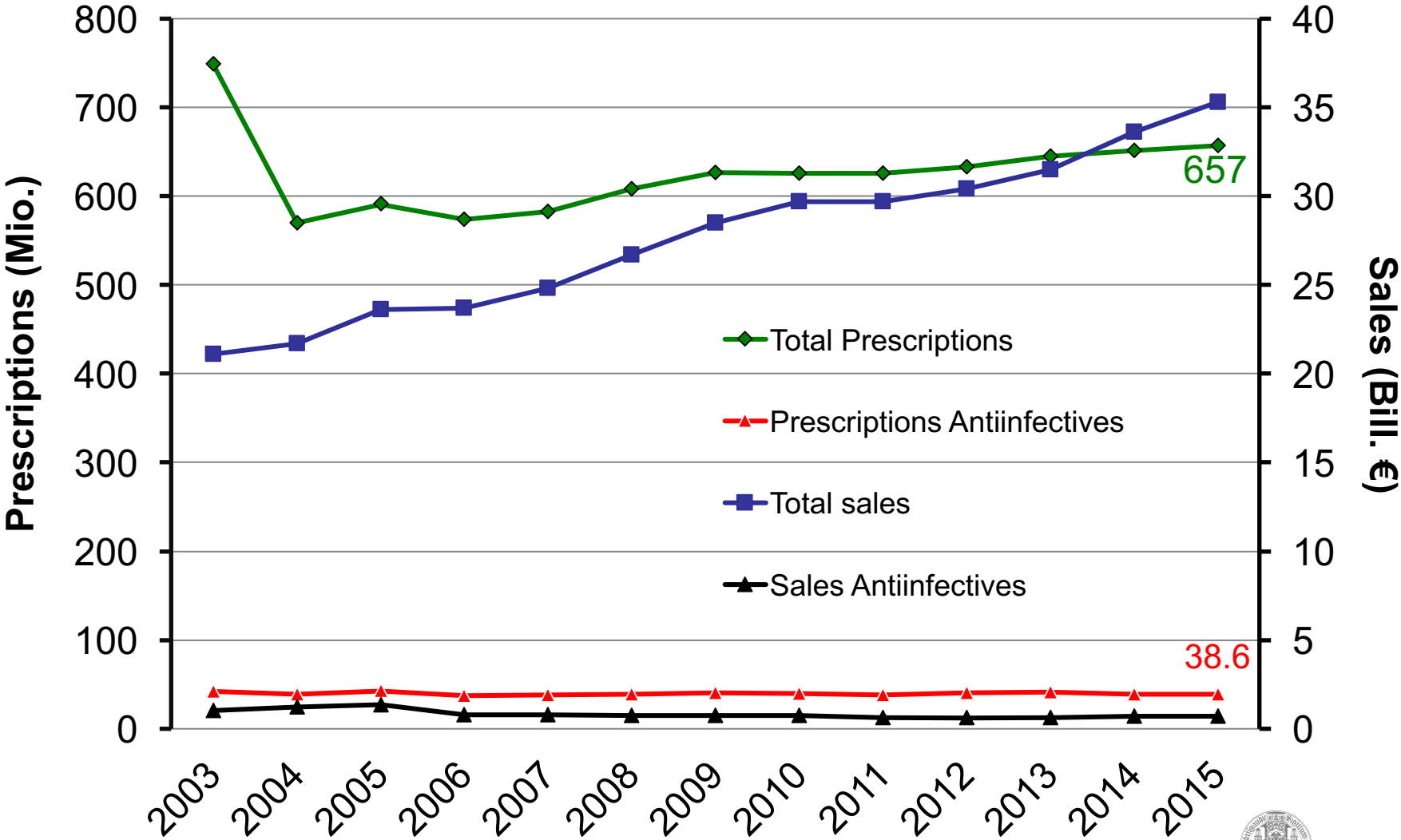


Evidence for cost savings



Prescriptions and sales of German retail pharmacies

Data: German sick funds

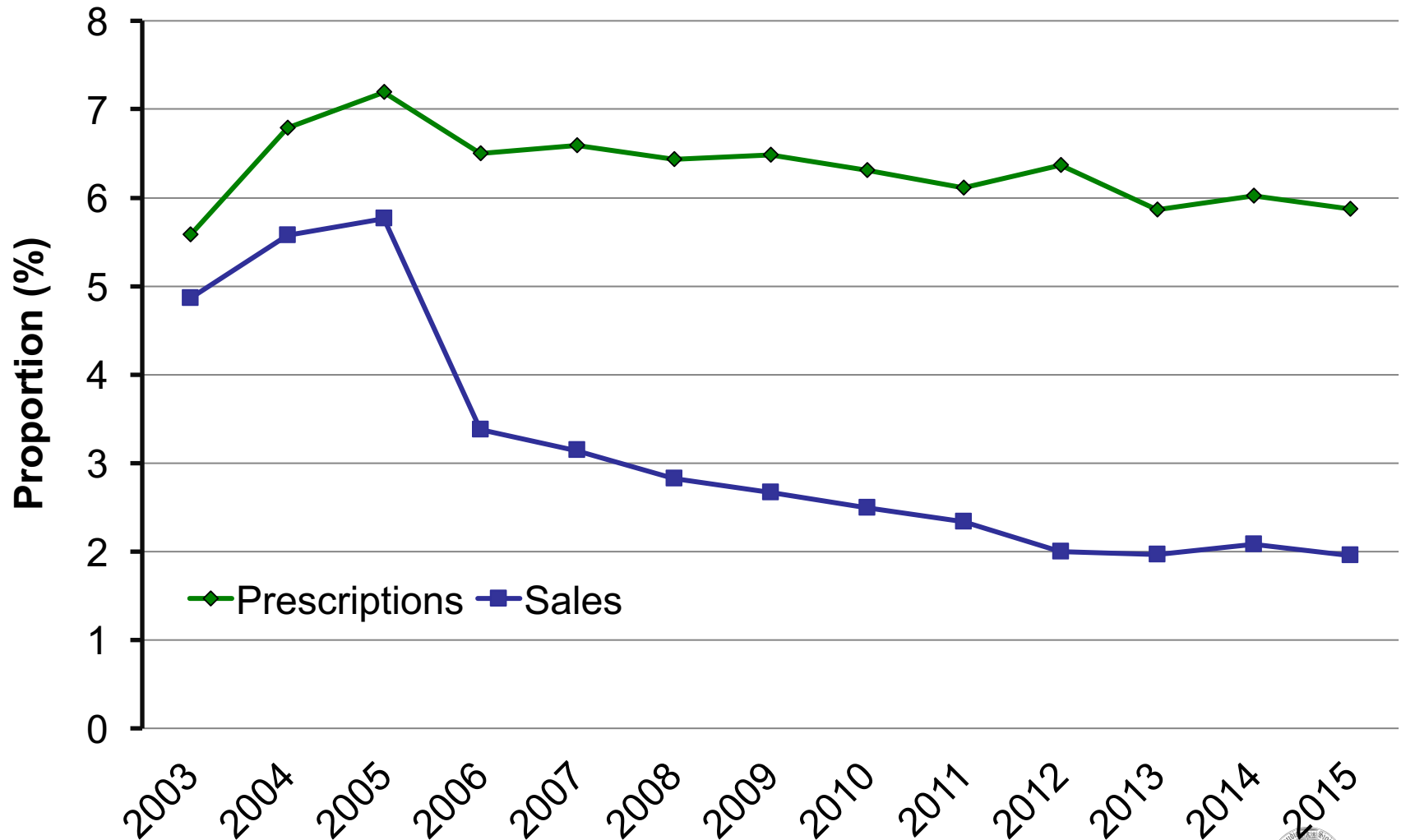


Data taken from: Schwabe, Paffrath (Hrsg.) Arzneiverordnungsreport 2003-2016

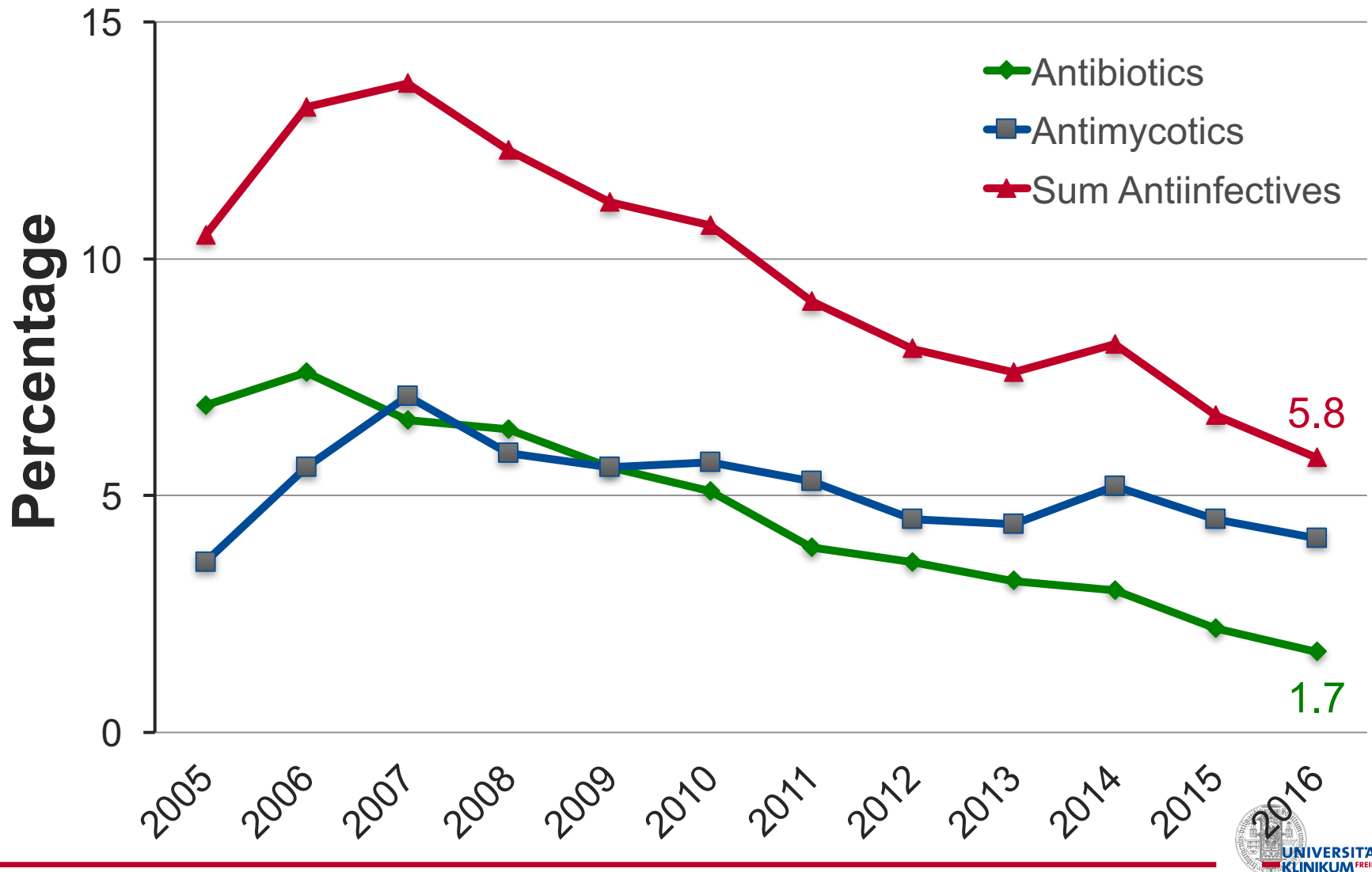


Prescriptions and sales of antiinfective drugs

Data: German sick funds

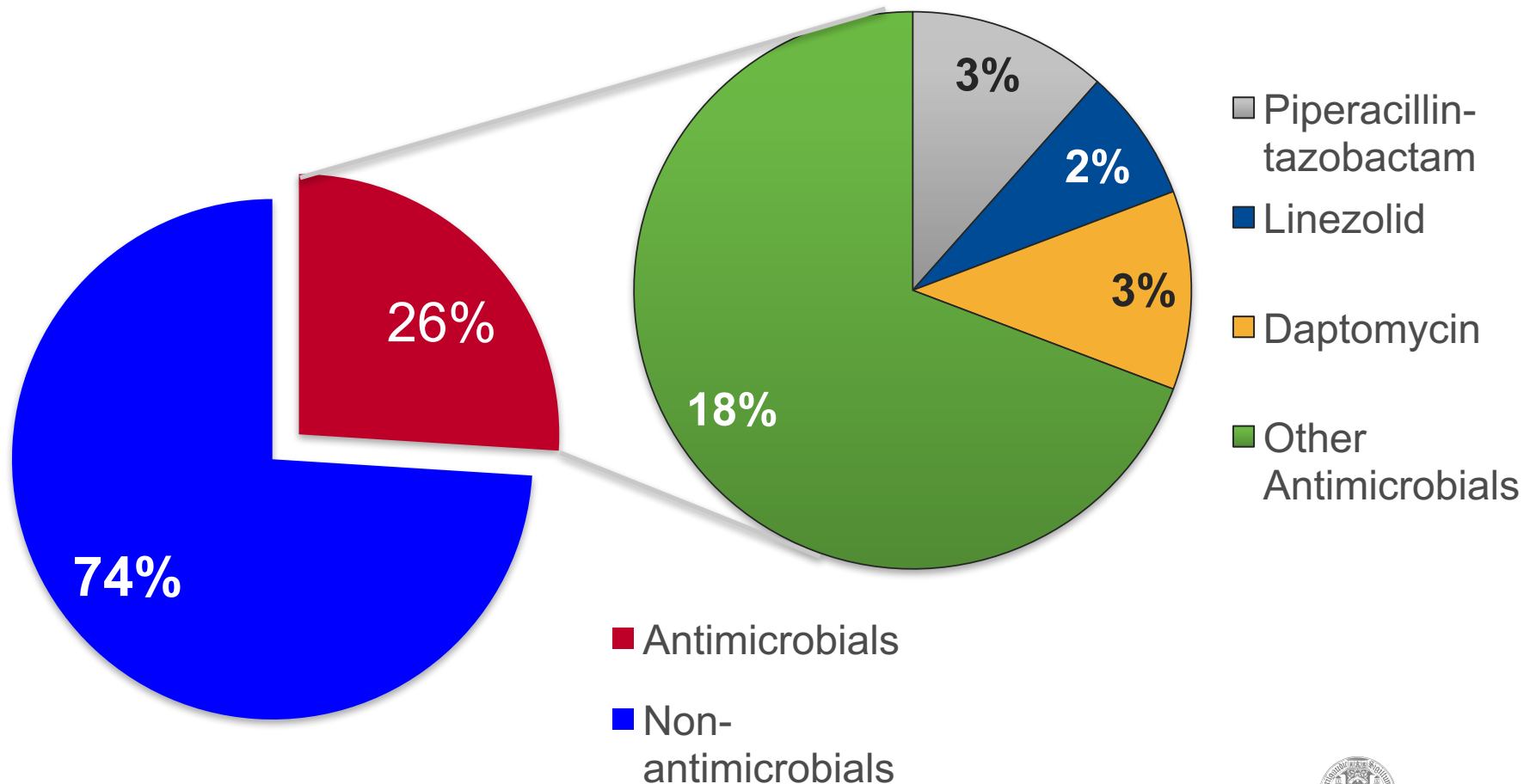


Costs of antiinfective drugs as percentage of total drug budget at University Medical Center Freiburg



Is there still evidence for cost effectiveness?

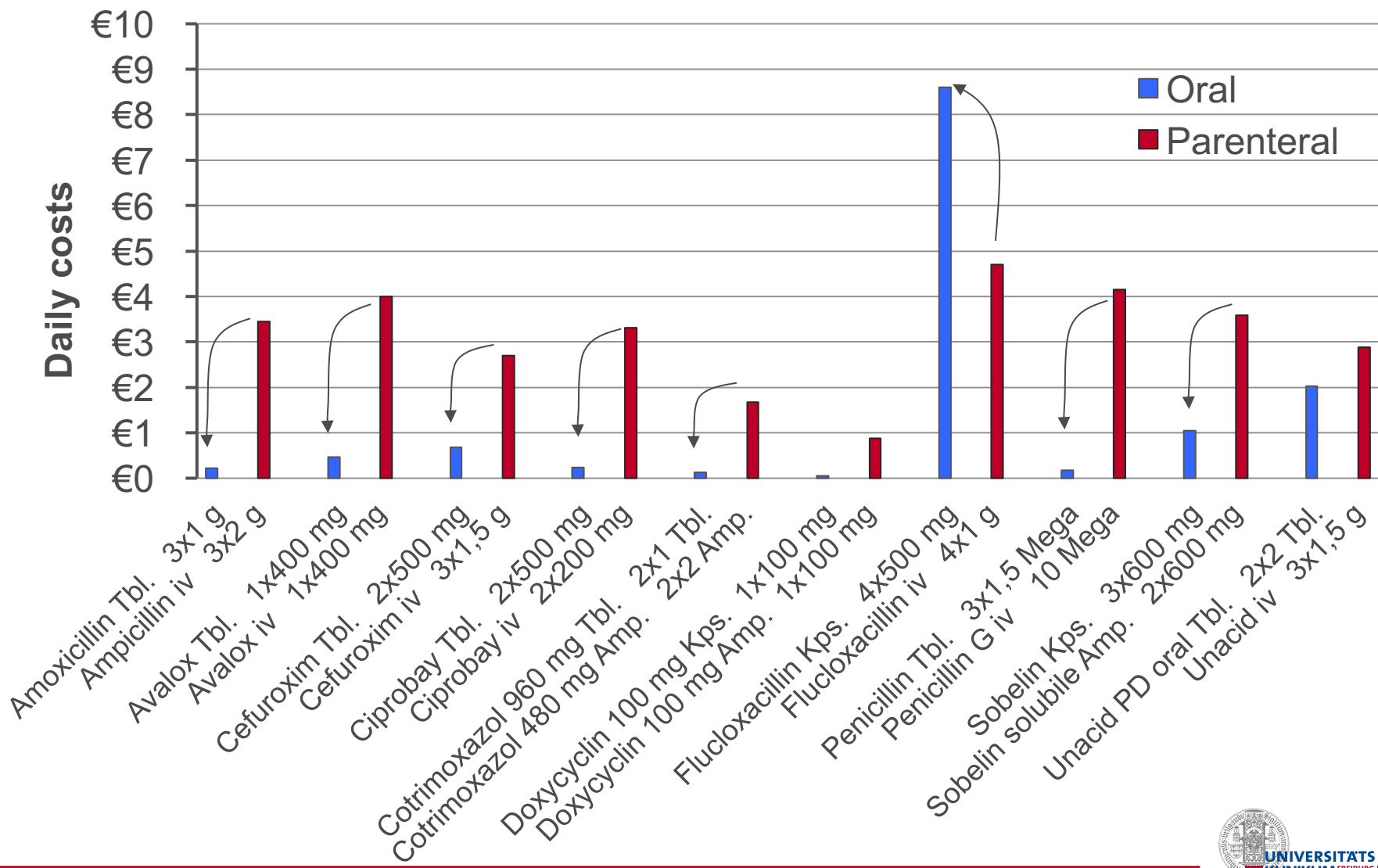
The Ohio State University Wexner Medical Center 2011 drug budget



Targeting costs

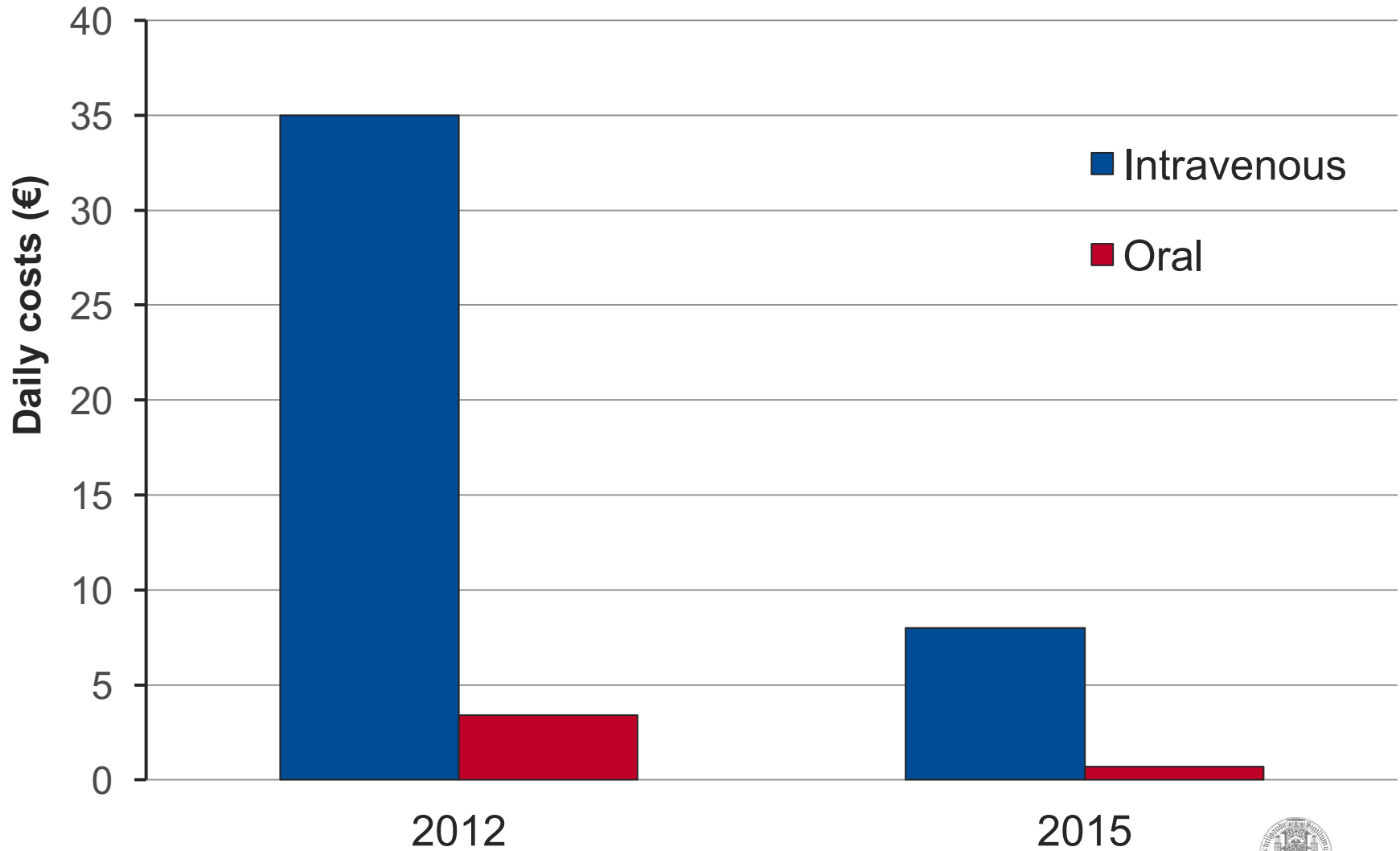
Objective	Number of references	Cost savings / Avoidance
Intravenous-to-oral conversion	7	\$46 - \$294 per patient \$242,713 – \$1,166,760 per year
Therapeutic substitution	1	\$ 218,877 per year
Batching iv antimicrobials	2	370 vials of daptomycin saved over 4 months 572 vials of caspofungin saved per year
Formulary restriction	3	Carbapenem cost savings: \$61,000 per year Total intravenous antimicrobial expenditures decreased by \$863,100

Cost effectiveness by switching from iv to oral



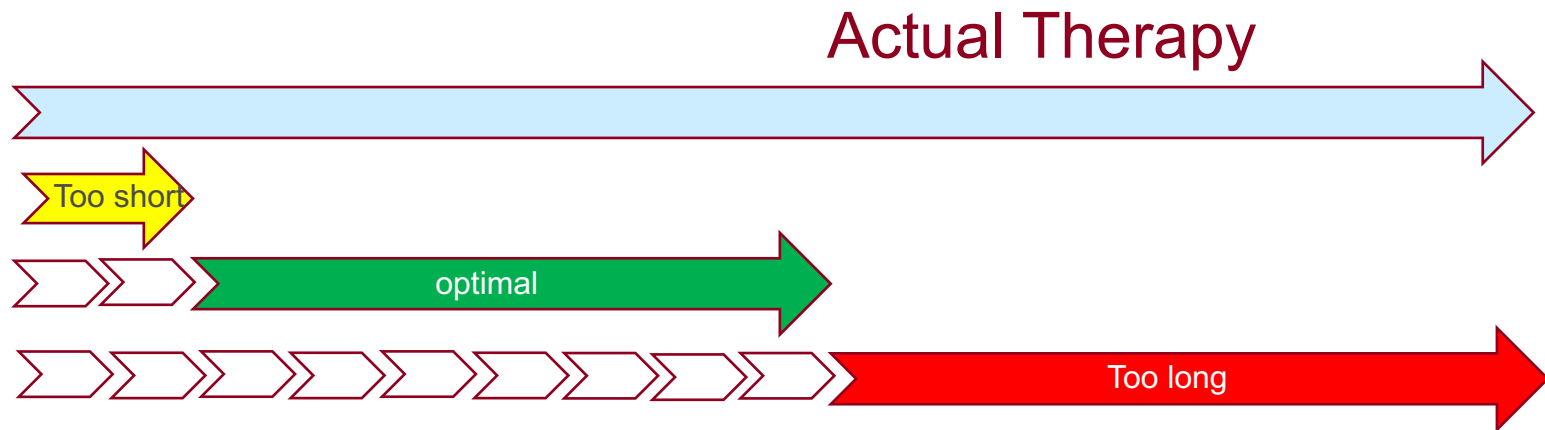
Problem: Effect of patent expiration

Moxifloxacin 400 mg



Any other ways to save costs ?

- Optimisation of drug therapy
- Increasing medication safety
 - Example: duration of therapy



Do we have a problem in that department?

Point prevalence studies
at University Medical Center Freiburg

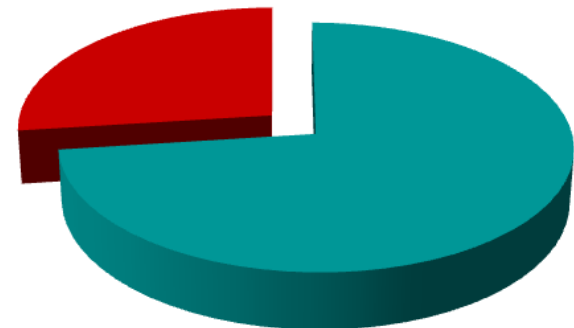
All wards at medical department
Selection of 18 different antibiotics

→ Adherence to recommended duration of treatment?

Welche Antinfektiva wurden in den letzten 2 Tagen vor dem aktuellen Erhebungstag verabreicht? Substanz-Nr.: 1		Welche Antinfektiva wurden in den letzten 2 Tagen vor dem aktuellen Erhebungstag verabreicht? Substanz-Nr.: 1	
Datum Vergabebeginn (TT.MM.JJJJ): Datum Vergebende: Intervall der Gabe: Einzeldosis (Angabe in Gramm): Tagesdosis (Angabe in Gramm):		Datum Vergabebeginn (TT.MM.JJJJ): Datum Vergebende: Intervall der Gabe: Einzeldosis (Angabe in Gramm): Tagesdosis (Angabe in Gramm):	
Wurde diese Dosis in eine eingeschränkte Nierenfunktion angepasst? <input type="checkbox"/> ja <input type="checkbox"/> nein		Wurde diese Dosis in eine eingeschränkte Nierenfunktion angepasst? <input type="checkbox"/> ja <input type="checkbox"/> nein <input type="checkbox"/> nicht notwendig	
iv-Gabe bei Substanzen mit guter Bioverfügbarkeit: Levofloxacin, Moxifloxacin, Ciprofloxacin, Ofloxacin, Moxonidazol, Clindamycin, Doxycyclin, Linezolid, Rifin, Clindamycin		iv-Gabe bei Substanzen mit guter Bioverfügbarkeit: Levofloxacin, Moxifloxacin, Ciprofloxacin, Ofloxacin, Moxonidazol, Clindamycin, Doxycyclin, Linezolid, Rifampicin, Rifamustin, Voriconazol, Caspofungin	
Bitte geben Sie den Hauptgrund der iv-Gabe bei folgenden Substanzen an: <input type="checkbox"/> schwere Sepsis / septischer Schock <input type="checkbox"/> E. faecium <input type="checkbox"/> Resistenzsituation		Bitte geben Sie den Hauptgrund der iv-Gabe bei folgenden Substanzen an: <input type="checkbox"/> schwere Sepsis / septischer Schock <input type="checkbox"/> keine medikationelle Indikation / sonstige <input type="checkbox"/> Resistenzsituation	
Die Beantwortung dieser Frage bezieht sich auf die Einschätzung des Darmtraktors: zu periperative Prophylaxe: Wurde die Antibiotikoprophylaxe innerhalb 1h vor Intubation verabreicht? <input type="checkbox"/> ja <input type="checkbox"/> nein		Die Beantwortung dieser Frage bezieht sich auf die Einschätzung des Darmtraktors: zu periperative Prophylaxe: Wurde die Antibiotikoprophylaxe innerhalb 1h vor Intubation verabreicht? <input type="checkbox"/> ja <input type="checkbox"/> nein <input type="checkbox"/> nicht dokumentiert	
Weiterer operativer / interventioneller Eingriff wurde durchgeführt? <input type="checkbox"/> ja <input type="checkbox"/> nein		Weiterer operativer / interventioneller Eingriff wurde durchgeführt? <input type="checkbox"/> ja <input type="checkbox"/> nein <input type="checkbox"/> nicht dokumentiert	
wenn ja, welche? <input type="checkbox"/> Kolorektalkirurgie <input type="checkbox"/> andere Abdominalchirurgie <input type="checkbox"/> Herzchirurgie		wenn ja, welche? <input type="checkbox"/> Kolorektalkirurgie <input type="checkbox"/> andere Abdominalchirurgie <input type="checkbox"/> Herzchirurgie <input type="checkbox"/> Knie- & Hüft-TEF-OP <input type="checkbox"/> andere	
Substanz-Nr.: 2		Substanz-Nr.: 2	

392 Therapies with selected antiinfectives
105 Therapies exceeded recommended duration of treatment

→ Potential for optimisation!

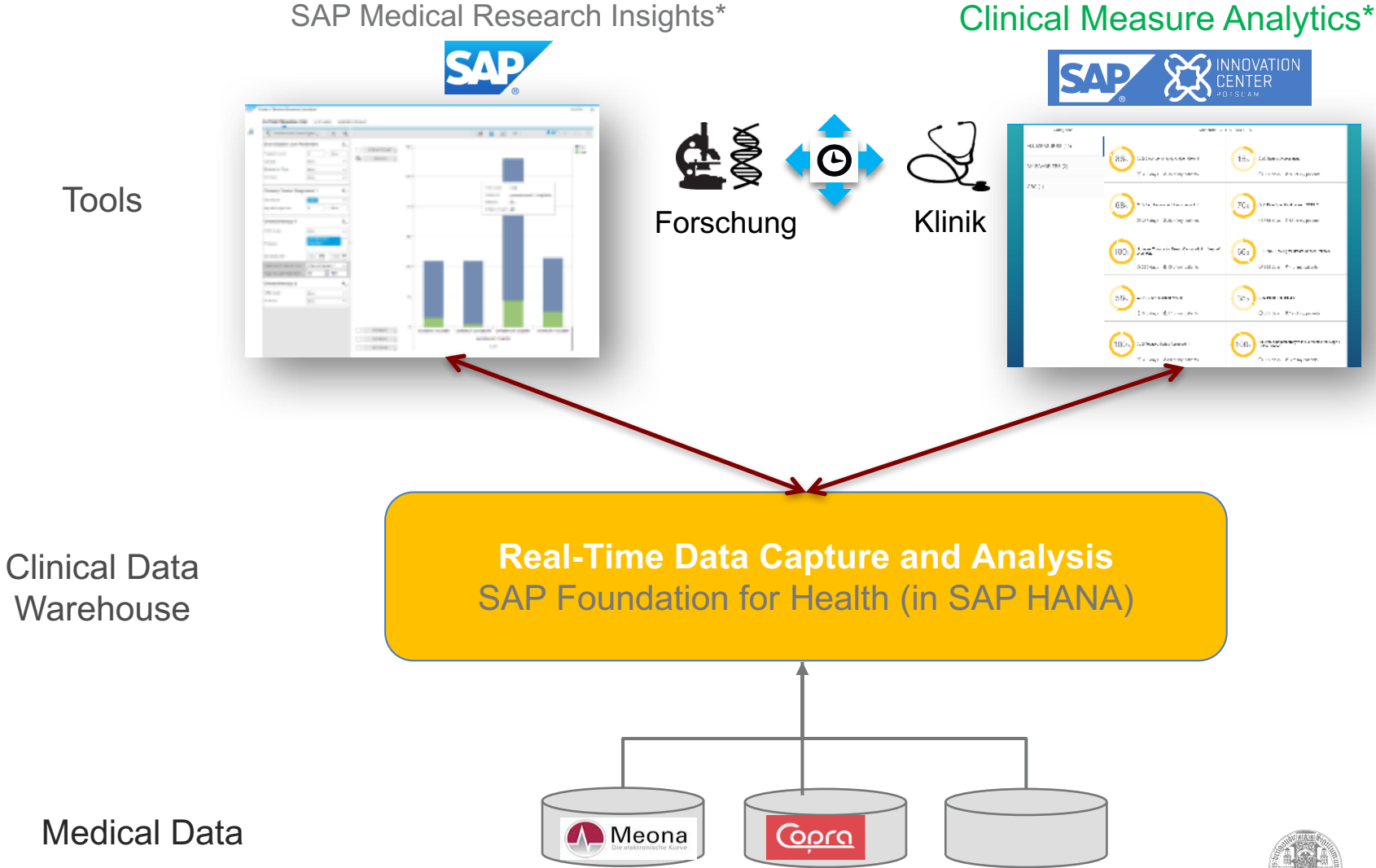


Within recommended duration of treatment

Exceeded recommended duration of treatment



Possible solution: SAP Foundation for Health



* SAP Standard Product

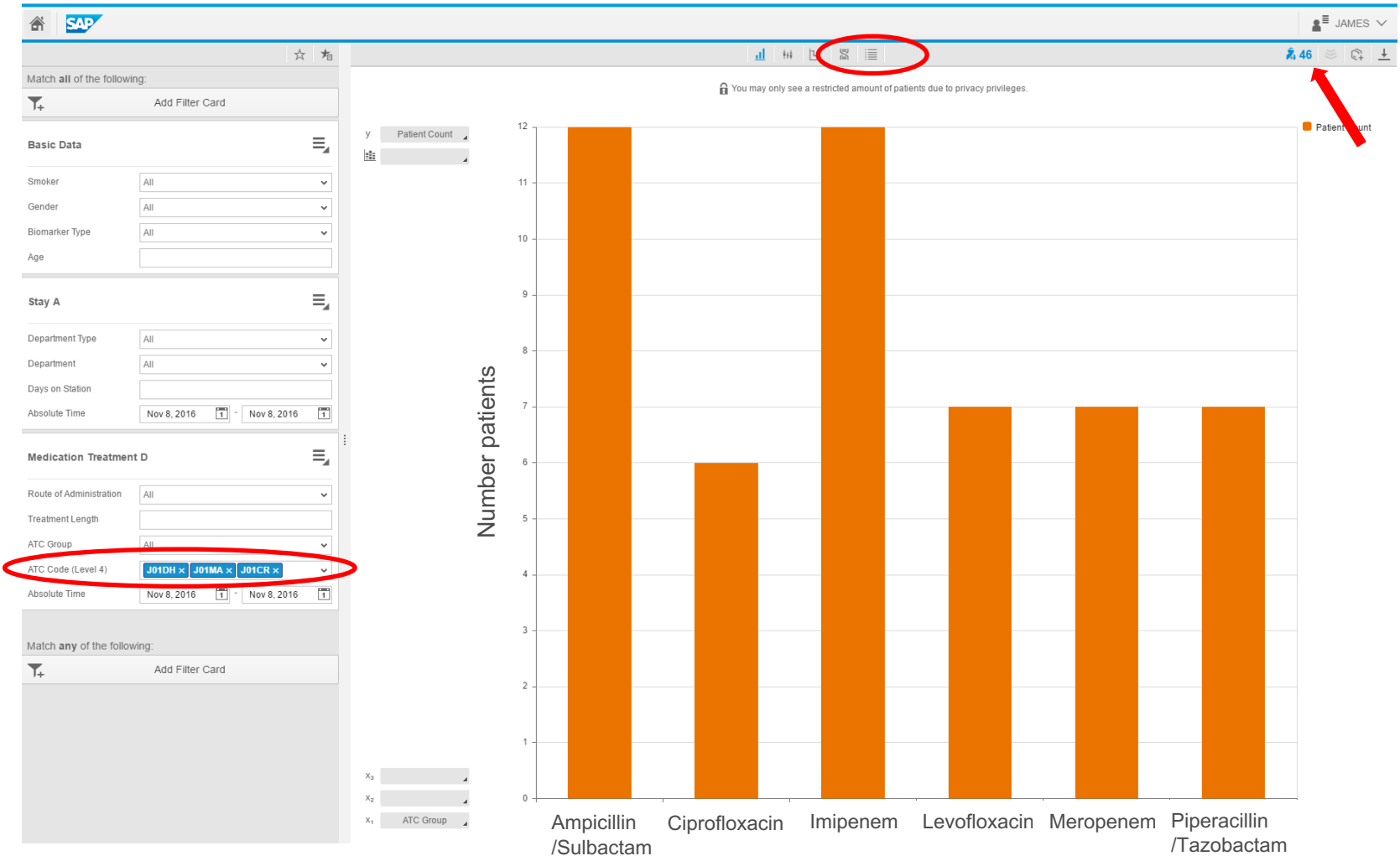
* Project Solution SAP Innovation Center Potsdam

Development of recommendations

- Data taken from SPC, guidelines, literature search
- Needs to be customised for each hospital / department
- Implementation in clinical software

Substance	Max. recommended duration of treatment [d]
Ampicillin/Sulbactam	7
Azithromycin	3
Ceftriaxon	7
Cefuroxim (po / iv)	5 / 7
Ciprofloxacin	7
Clarithromycin (po / iv)	7 / 5
Daptomycin	14
Imipenem	8
Levofloxacin	10
Linezolid	10
Meropenem	8
Moxifloxacin	7
Norfloxacin	3
Piperacillin/Tazobactam	10
Roxithromycin	7
Tigecyclin	10
Vancomycin (iv)	7

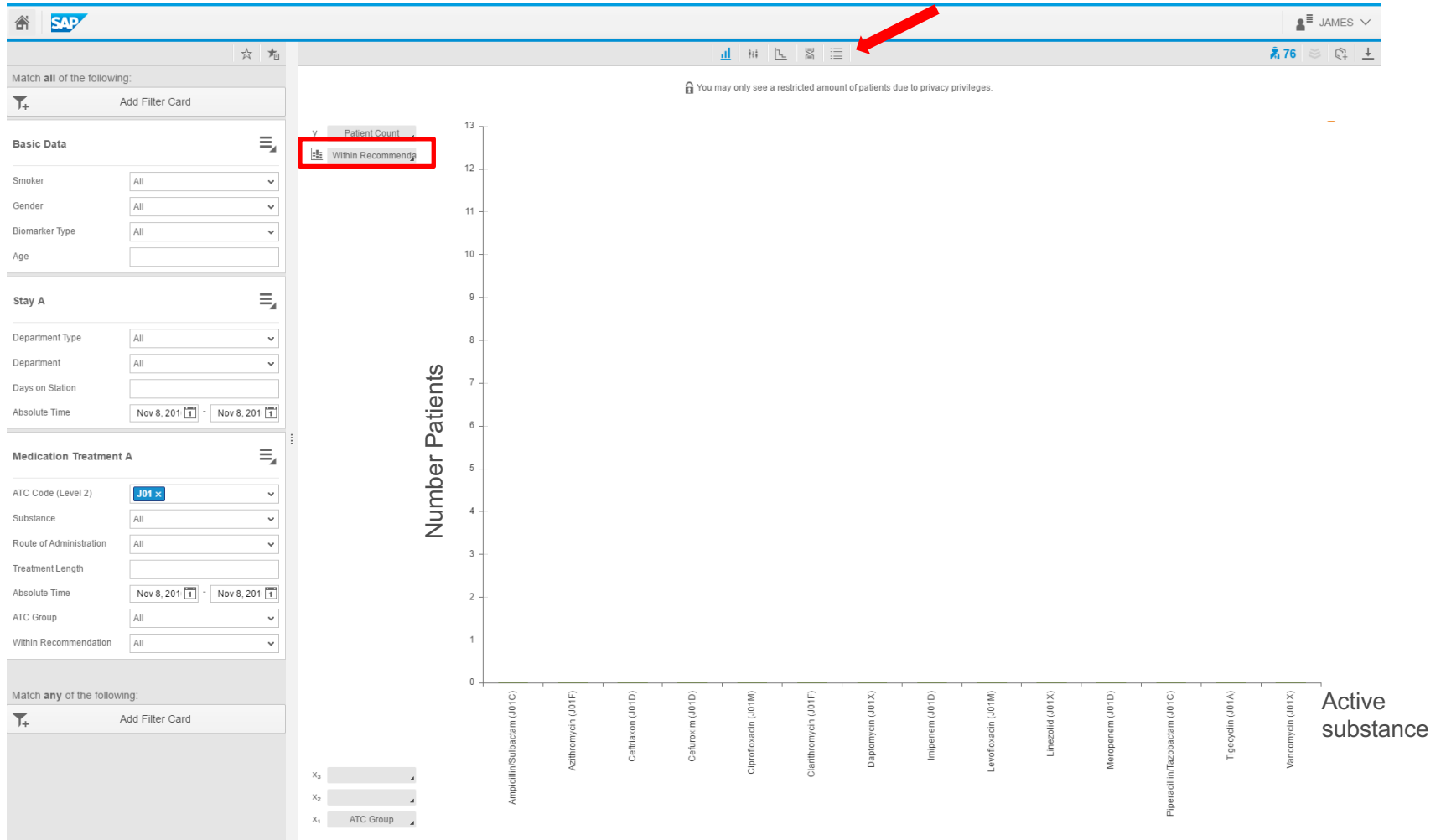
Analysis of the use of antiinfectives



- Patients currently treated with the respective antiinfectives

First results

Patients within (green) or above (orange) recommended duration of treatment



And the winner is...

**Gesundheits
Wirtschaft**
Das Entscheidermagazin

Das Journal für alle Entscheider der Gesundheitswirtschaft.
Das Forum für Deutschlands größte Wirtschaftsbranche.

12.02.2016 | pc

Uniklinik Freiburg und SAP belegen ersten Platz bei Entscheider-Event



Die Gewinner des Wettbewerbers um die fünf IT-Schlüsselthemen der diesjährigen Entscheiderfabrik stehen fest. Bei der Entscheiderfabrik treten jedes Jahr zwölf Teams von deutschen Kliniken und IT-Herstellern an, um zu einem der fünf von den Teilnehmern des Entscheider-Event gewählten finalen Hardwareprojekte zu werden, die in einer öffentlich begleiteten neun-monatigen Testphase an deutschen Krankenhäusern ausprobiert werden. Auf den ersten Platz stand gestern das Projektteam der Datenbankspezialisten von SAP Deutschland und der Leitung des Universitätsklinikums Freiburg. In ihrer

Präsentation stellten die Gruppe den über 270 Zuschauern im Industrie Club Düsseldorf die Idee einer Echtzeit-Analyse und Anpassung des Arzneimitteleinsatzes im klinischen Alltag vor.