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SUPERBUGS
IL *COUNTDOWN* È INIZIATO

2050

Piano Nazionale di contrasto dell'Antimicrobico- Resistenza
dichiarazione di intenti o impegno concreto?

Lunedì, 29 gennaio 2018

Strategie future per un problema attuale

Nicola Petrosillo

Istituto Nazionale per le Malattie Infettive
«Lazzaro Spallanzani", IRCCS, Roma
Società Italiana Terapia Antinfettiva

Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study

Estimate of 2,609,911 new cases of HAI occurring every year in

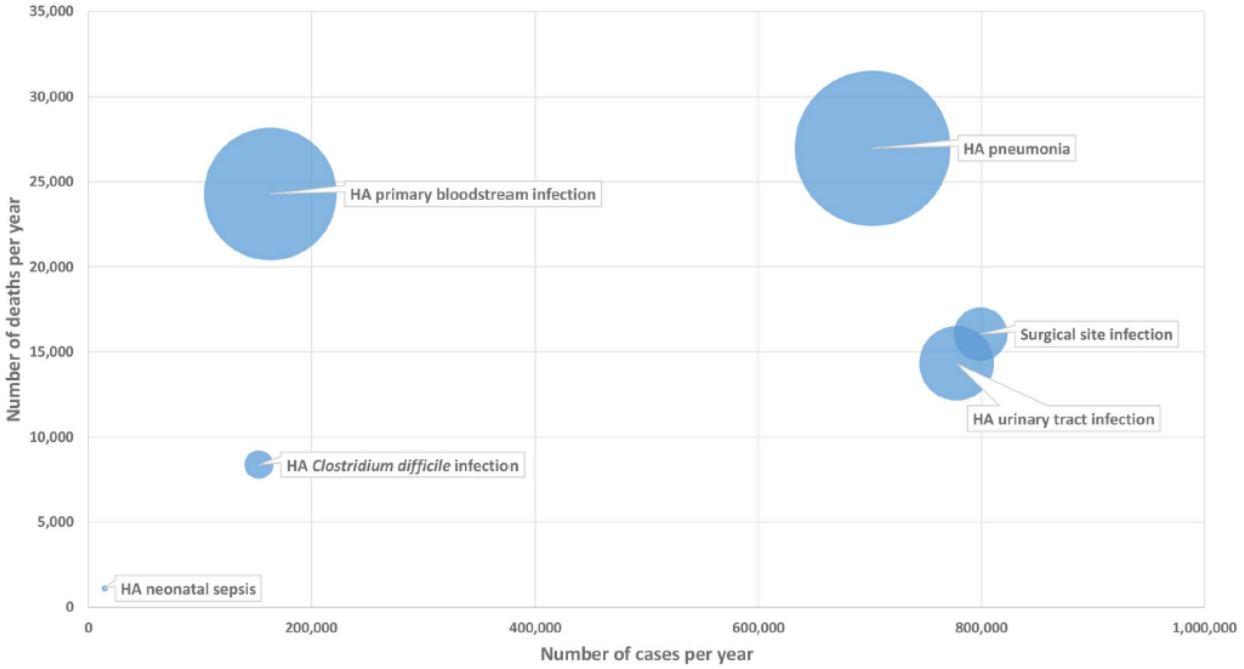


Fig 1. Six healthcare-associated infections according to their number of cases per year (*x*-axis), number of deaths per year (*y*-axis), and DALYs per year (width of bubble), EU/EEA, 2011–2012 (time discounting was not applied). DALY, disability-adjusted life year; HA, healthcare-associated.

91,130 deaths for the six HAIs

at least 1/2 of the deaths attributable to HAI due to the 7 most common MDRB

Cassini A et a PLoS Med 13(10): e1002150.

Background

- **Threats of MDR organisms and public health emergencies have exposed the need for more robust antimicrobial stewardship and for collaboration in the emergency preparedness.**

- **There is a need for coordinated efforts to effectively manage this «new deal».**

- **However, financial pressures are likely to compete with the expanding roles and expectations of physician-epidemiologists in IPC.**

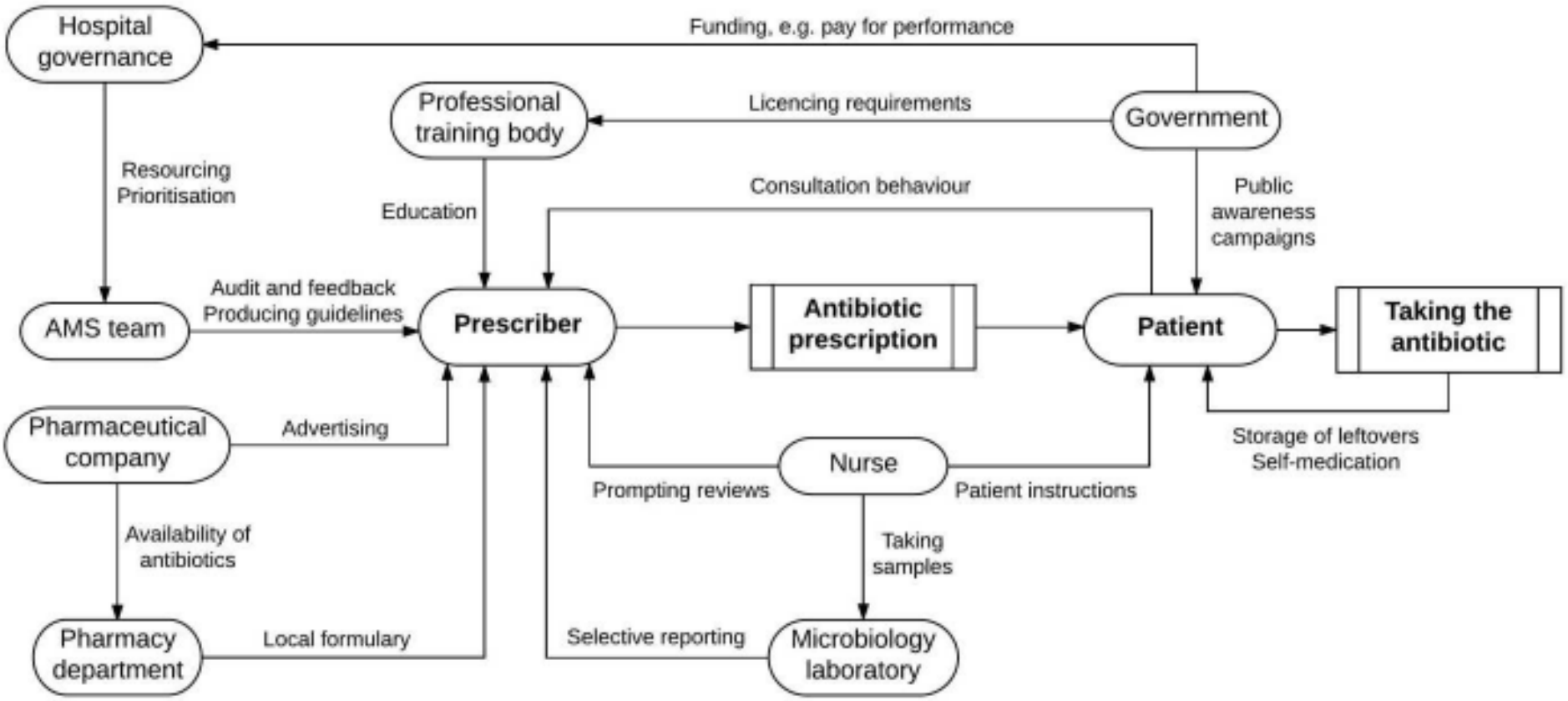
What is antimicrobial stewardship?

- **A strategy, a coherent set of actions designed to use antimicrobial responsibly.**
- **Responsible use: it should be defined and translated into context- and time-specific actions**



Dyar OJ et al. *Clin Microb Infection 2017 on press*

Figure 2. Examples of actors and actions within antimicrobial stewardship



Dyar OJ et al. *Clin Microb Infection 2017 on press*

Table 2: How we can be good antimicrobial stewards.

Actor	What it means to be good antimicrobial stewards	Example actions
Prescriber	I use antimicrobials responsibly by	• Making accurate diagnoses • Following local antimicrobial guidelines • Regularly reviewing the need for therapy
Nurse	I help ensure antimicrobials are used responsibly by	• Taking cultures at appropriate times • Ensuring patients understand how to take antimicrobials on discharge
Patient	I use antimicrobials responsibly by	• Taking antimicrobial courses as recommended by the prescriber • Not storing or using leftover antimicrobials
AMS team	We help others in our institution use antimicrobials responsibly by	• Developing guidelines for antimicrobial use • Supporting audit and feedback for prescribers • Educating prescribers
Hospital governance	Our institution uses antimicrobials responsibly by	• Ensuring sufficient sustainable and dedicated funding for AMS teams • Monitoring antimicrobial use and resistance • Investing in CDSS • Enabling formulary restrictions

ACCEPTED MANUSCRIPT

Dyar OJ et al. *Clin Microb Infection 2017 on press*

Producer/farmer	I use antimicrobials responsibly by	• Diagnosing selectivity
		• Not using antimicrobials as growth promoters
Pharmaceutical company	Our company ensures antimicrobials are used responsibly by	• Limiting advertising of antimicrobials, especially broad spectrum • Helping ensure there is a continuous supply of antimicrobials
National policy maker	Our country uses antimicrobials by	• Prioritising and funding AMS activities • Supporting the use of quality metrics and pay for performance

Table notes: CDSS = Clinical Decision Support System

MANUSCRIPT

Dyar OJ et al. *Clin Microb Infection 2017 on press*

Antibiotic stewardship: does it work in hospital practice?

Table 1 Examples of recommendations to guide the activities of the stewardship team [10]

Recommended appropriate antibiotic use	• Streamlining or de-escalation of therapy • Parenteral to oral conversion • Dose optimization
Recommended behavioural change interventions	• Prospective audit with intervention and feedback • Education • Antimicrobial order forms

RIPT

Marlies EJL et al. Clin Microb Infection 2017

Antibiotic stewardship: does it work in hospital practice?

Davey et al. 2017[45]	The authors conclude that they found evidence that interventions were effective and safe, probably reduced length of stay and might reduce *Clostridium difficile* infections. Both enablement and restriction independently increased effect size, and enablement enhanced the effect of restrictive interventions.
Karanika et al. 2016[46]	The authors conclude that ASPs significantly decrease antimicrobial consumption (overall use, use of restricted antimicrobial agents and broad-spectrum use), overall antimicrobial cost, and hospital length of stay among inpatients. Introduction of ASPs also decreases infections due to specific antimicrobial-resistant pathogens.

Marlies EJL et al. Clin Microb Infection 2017

ANTIBIOTIC STEWARDSHIP

IN YOUR FACILITY WILL



DECREASE

- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE

- GOOD PATIENT OUTCOMES



The marriage between ASP and IPC



A bundle that includes active surveillance, contact precaution for carriers, and cefazolin-based antimicrobial prophylaxis prevents methicillin-resistant *Staphylococcus aureus* infections in clean orthopedic surgery

- **Contact precautions and antimicrobial stewardship are effective in preventing nosocomial MRSA infections.**

- **Before-after study→ implementation of a bundle approach consisting of MRSA active surveillance, contact precautions for MRSA positive patients, and CFZ based AMP stewardship**

Kawamura H et al. Am J Infect Control 2016; 44: 210-4

A bundle that includes active surveillance, contact precaution for carriers, and cefazolin-based antimicrobial prophylaxis prevents methicillin-resistant *Staphylococcus aureus* infections in clean orthopedic surgery

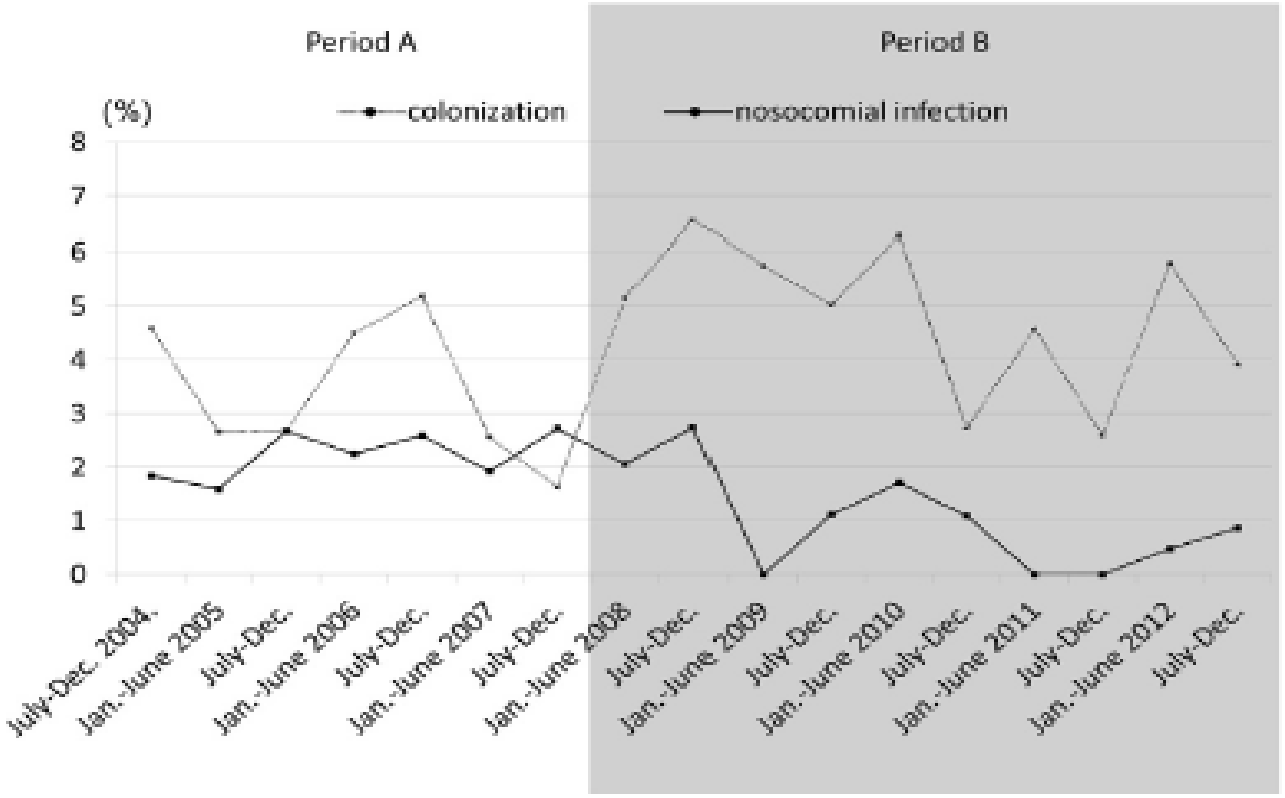


Fig 1. Incidence of methicillin-resistant *Staphylococcus aureus* colonization or nosocomial methicillin-resistant *S aureus* surgical site infection.

Kawamura H et al. Am J Infect Control 2016; 44: 210-4

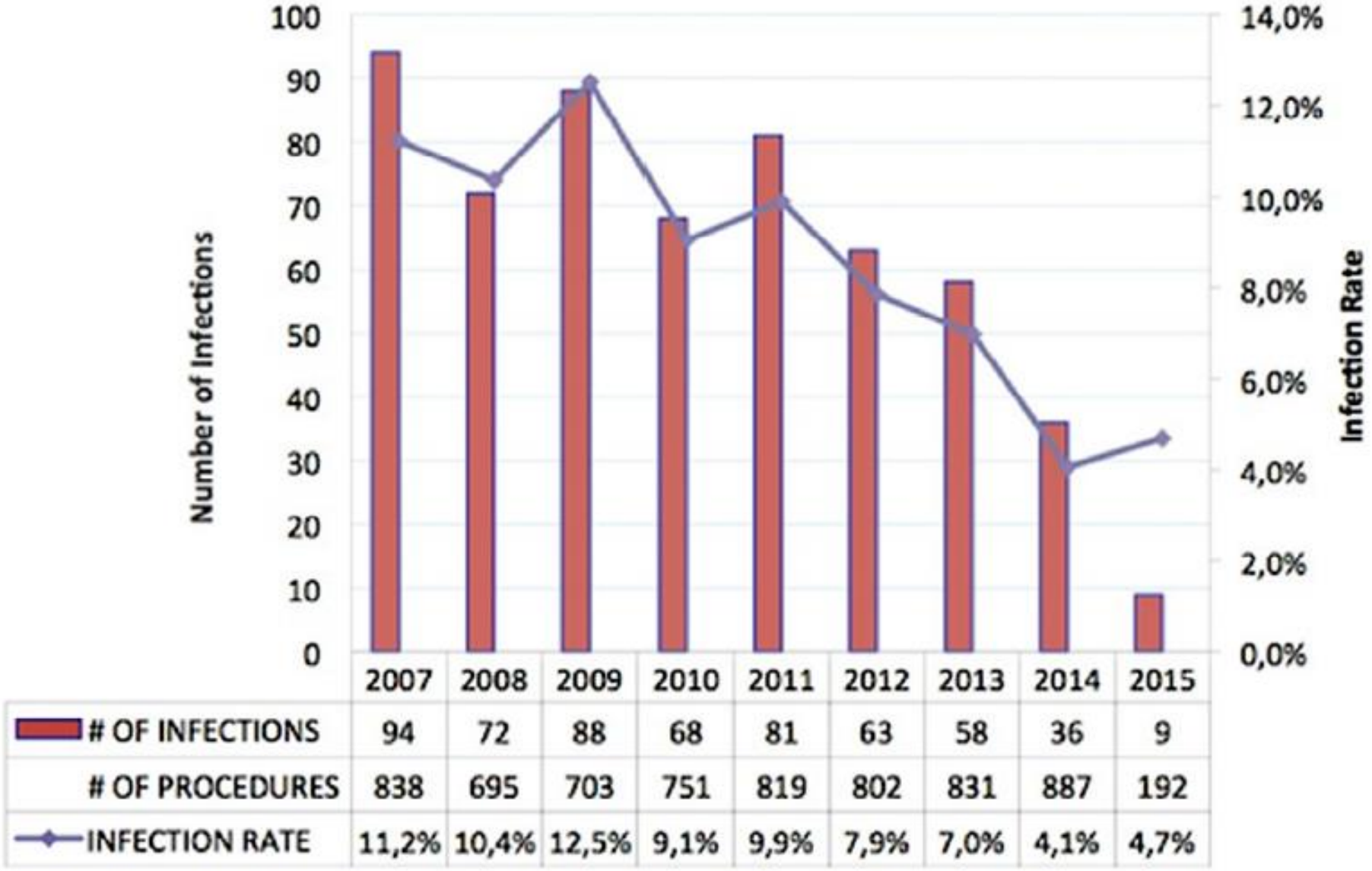
A bundle that includes active surveillance, contact precaution for carriers, and cefazolin-based antimicrobial prophylaxis prevents methicillin-resistant *Staphylococcus aureus* infections in clean orthopedic surgery

Correlations between the incidence of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) surgical site infections (SSIs) and antimicrobial use density (AUD), use of an alcohol-based hand hygiene solution, and the incidence of MRSA colonization

	Incidence of nosocomial MRSA SSI		
Variable	*R*	*P* value	95% Confidence interval
CEZ AUD	−0.76	<.001	−0.91 to −0.43
CTM AUD	0.54	.02	0.09-0.81
FMOX AUD	0.68	.002	0.29-0.87
PIPC AUD	−0.21	.43	−0.63 to 0.30
Carbapenems AUD	0.24	.35	−0.27 to 0.65
Glycopeptides AUD	0.58	.15	−0.36 to 0.59
Use of an alcohol-based hand hygiene solution	−0.68	.002	−0.87 to −0.29
Incidence of MRSA colonization	−0.12	.66	−0.57 to 0.39

CEZ, cefazolin; *CTM*, cefotiam; *FMOX*, flomoxef; *PIPC*, piperacillin.

Kawamura H et al. Am J Infect Control 2016; 44: 210-4



	2007	2008	2009	2010	2011	2012	2013	2014	2015
# OF INFECTIONS	94	72	88	68	81	63	58	36	9
# OF PROCEDURES	838	695	703	751	819	802	831	887	192
INFECTION RATE	11,2%	10,4%	12,5%	9,1%	9,9%	7,9%	7,0%	4,1%	4,7%

Fig 1. Annual surgical site infection rate.

Controlling endemic multidrug-resistant *Acinetobacter baumannii* in Intensive Care Units using antimicrobial stewardship and infection control

Shinhye Cheon[1,*], Mi-Ja Kim[2,*], Seon-Jin Yun[3], Jae Young Moon[4], and Yeon-Sook Kim[1,3]

The intervention consisted of

- **Antimicrobial stewardship**
- **Hospital staff education**
- **Active surveillance cultures**
- **Contact precautions**
- **Environmental cleaning**
- **Disinfection enforcement**
- **Hand hygiene promotion**

Korean J Intern Med 2016;31:367-374

Controlling endemic multidrug-resistant *Acinetobacter baumannii* in Intensive Care Units using antimicrobial stewardship and infection control

Shinhye Cheon[1,*], Mi-Ja Kim[2,*], Seon-Jin Yun[3], Jae Young Moon[4], and Yeon-Sook Kim[1,3]

KEY MESSAGE

1. Antimicrobial stewardship decreased the mean monthly use of carbapenem, from 134.99 ± 82.26 to 94.85 ± 50.98 defined daily doses/1,000 patient-days.
2. After implementing comprehensive infection control measures, adherence to hand hygiene practices increased from 71.4% to 86.5% and environmental cultures revealed no growth of multidrug-resistant *Acinetobacter baumannii*.
3. The year-long antimicrobial stewardship and comprehensive infection control measures resulted in a 10-fold decrease (from 22.82 to 2.68 cases/1,000 patient-days) in the incidence density rates of nosocomial multidrug-resistant *A. baumannii*.

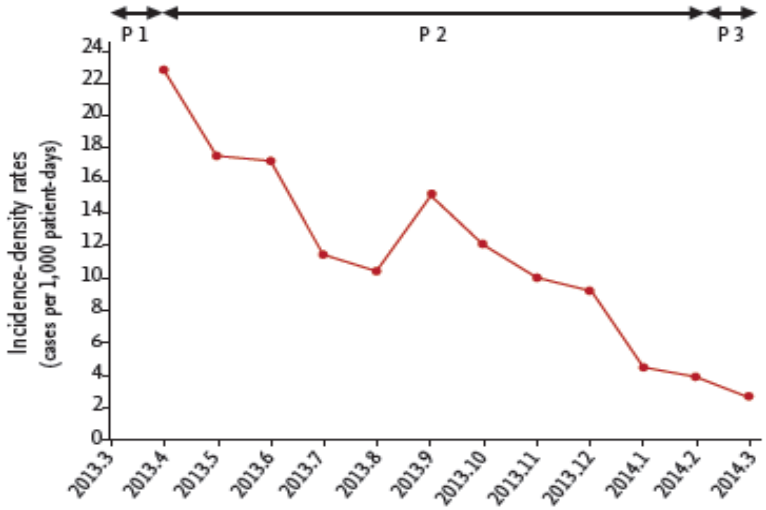


Figure 1. Incidence density rates of multidrug-resistant *Acinetobacter baumannii* during the study period. Data are recorded as the number of new nosocomial colonizations or infections per 1,000 patient-days. The infection control measures were implemented in May 2013.

Korean J Intern Med 2016;31:367-374

Impact of a hospital-wide multifaceted programme for reducing carbapenem-resistant *Enterobacteriaceae* infections in a large teaching hospital in northern Italy

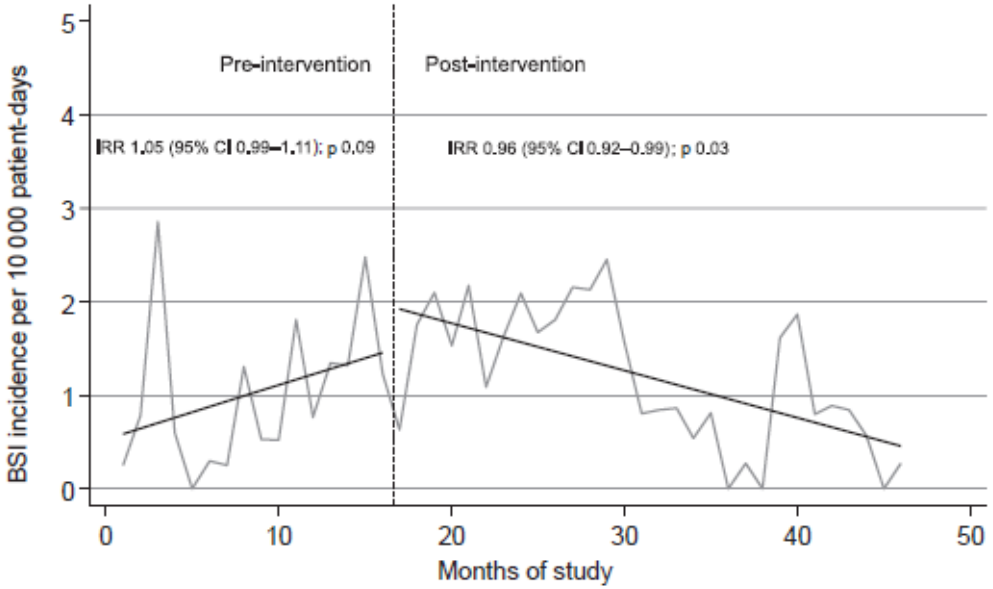


FIG. 1. Pre-intervention and post-intervention trends in the monthly incidence of carbapenem-resistant *Enterobacteriaceae* (CRE) bloodstream infection (BSI). A significant decline in the monthly incidence rate ratio (IRR) of CRE BSI during the 30-month post-intervention period was found by Poisson regression.

Viale P et al. Clin Microbiol Infect 2014

Association of Evidence-Based Care Processes With Mortality in *Staphylococcus aureus* Bacteremia at Veterans Health Administration Hospitals, 2003-2014

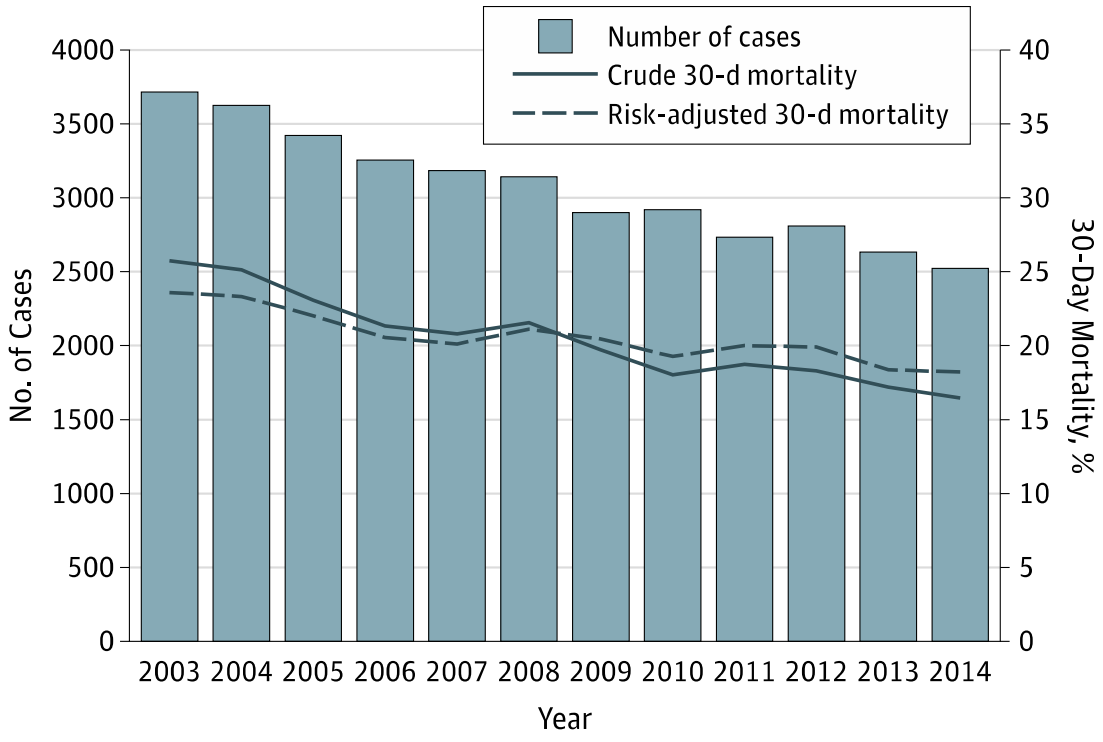
Findings In this cohort study of 36 868 patients with *S aureus* bacteremia at 124 Veterans Health Administration hospitals from January 1, 2003, through December 31, 2014, all-cause 30-day mortality decreased over time from 25.7% in 2003 to 16.5% in 2014, whereas use of appropriate antibiotic therapy, echocardiography, and infectious diseases consultation increased. An estimated 57.3% decrease in mortality could be attributed to increased use of evidence-based care processes.

Meaning Increasing application of evidence-based care may improve survival among patients with *S aureus* bacteremia in routine health care settings.

***Goto M et al. JAMA Intern Med* 2017; 177(10): 1489-1497**

Association of Evidence-Based Care Processes With Mortality in *Staphylococcus aureus* Bacteremia at Veterans Health Administration Hospitals, 2003-2014

Figure 1. Trends in the Incidence of *Staphylococcus aureus* Bacteremia and All-Cause 30-Day Mortality, 2003-2014



Goto M et al. JAMA Intern Med 2017; 177(10): 1489-1497

Association of Evidence-Based Care Processes With Mortality in *Staphylococcus aureus* Bacteremia at Veterans Health Administration Hospitals, 2003-2014

Figure 2. Trends in Rates of Use of Evidence-Based Care Process, 2003-2014

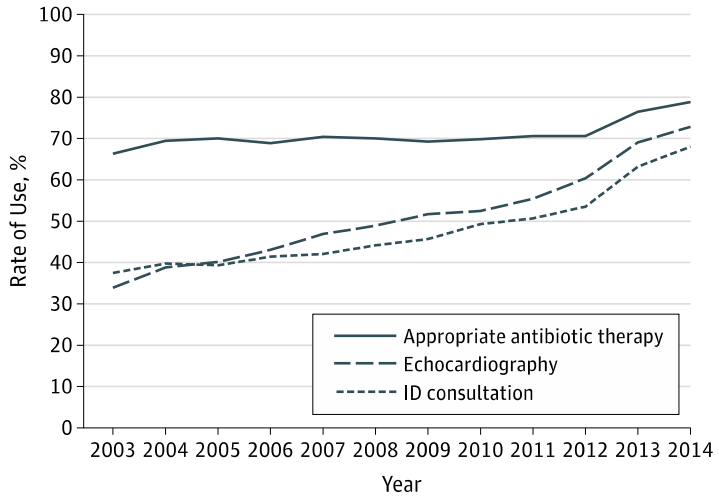
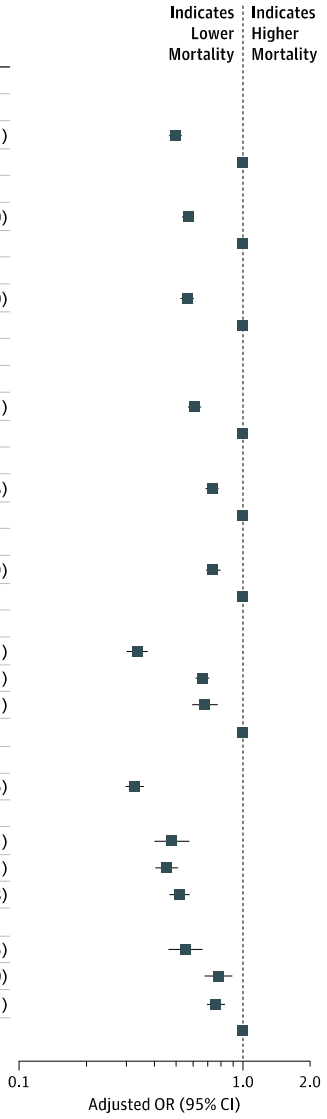


Figure 3. Associations Between Receipt of Evidence-Based Care Processes and 30-Day Mortality

Evidence-Based Care Processes	No. of Patients (%)	Adjusted OR (95% CI)
Process measures (not adjusted for other care processes)		
ID consultation during hospitalization		
ID consultation	17 289 (46.9)	0.50 (0.47-0.53)
No ID consultation	19 579 (53.1)	1 [Reference]
Echocardiography during hospitalization		
Echocardiography	18 345 (49.8)	0.57 (0.53-0.60)
No echocardiography	18 523 (50.2)	1 [Reference]
Appropriate therapy during hospitalization		
Appropriate therapy	26 037 (70.6)	0.56 (0.52-0.60)
Other therapy	10 831 (29.4)	1 [Reference]
Process measures (adjusted for other care processes)		
ID consultation during hospitalization		
ID consultation	17 289 (46.9)	0.61 (0.56-0.65)
No ID consultation	19 579 (53.1)	1 [Reference]
Echocardiography during hospitalization		
Echocardiography	18 345 (49.8)	0.73 (0.68-0.78)
No echocardiography	18 523 (50.2)	1 [Reference]
Appropriate therapy during hospitalization		
Appropriate therapy	26 037 (70.6)	0.74 (0.68-0.79)
Other therapy	10 831 (29.4)	1 [Reference]
Types of echocardiography		
TEE	5522 (15.0)	0.33 (0.30-0.37)
TTE	10 769 (29.2)	0.66 (0.61-0.71)
Undocumented type	2054 (5.6)	0.67 (0.59-0.77)
No echocardiography	18 523 (50.2)	1 [Reference]
Combination of care processes		
All 3 care processes	10 608 (28.8)	0.33 (0.30-0.36)
Two of 3 care processes		
ID consultation and echocardiography	1382 (3.7)	0.48 (0.40-0.57)
ID consultation and appropriate therapy	4012 (10.9)	0.45 (0.40-0.51)
Echocardiography and appropriate therapy	4692 (12.7)	0.52 (0.47-0.58)
One of 3 care processes		
ID consultation only	1258 (3.4)	0.55 (0.46-0.66)
Echocardiography only	1663 (4.5)	0.78 (0.67-0.90)
Appropriate therapy only	6725 (18.2)	0.76 (0.69-0.83)
No care process	6528 (17.7)	1 [Reference]



Goto M et al. JAMA Intern Med 2017; 177(10): 1489-1497

The impact of infectious disease specialists on antibiotic prescribing in hospitals

- **Review of 31 studies→ 7 RCTs, before/after controlled studies or before/after uncontrolled studies with interrupted-time-series analysis.**

- **IDS intervention was associated with a significant improvemente on the appropriateness of antibiotic prescribing as compared with prescriptions without any IDS input.**

Pulcini C et al. Clin Microbiol Infect 2014; 20: 963-72

The Value That Infectious Diseases Physicians Bring to the Healthcare System

ID PHYSICIANS IMPROVE OUTCOMES

Table 1. Roles of Infectious Diseases (ID) Physicians in the Healthcare System

Role	Comment(s)	Reference(s) or Source
Improve outcomes		
Patient care	More correct diagnoses, shorter lengths of stay, more-appropriate therapies, fewer complications, may use fewer antibiotics overall	[3–8]
S. aureus bacteremia	Reduced mortality	[9, 10]
Medicare recipients (272 327 stays)	Early ID physician intervention lowers costs, decreases length of stay and readmissions, decreases mortality	[12]

McQuillen DP et al. J Infect Dis 2017;216(suppl_5):S588-S593

The Value That Infectious Diseases Physicians Bring to the Healthcare System

ID PHYSICIANS IMPROVE OUTCOMES

Role	Comment(s)	Reference(s) or Source
Privately insured patients (29 050 stays)	Early ID physician intervention shortens length of stay, lowers cost, lowers mortality, lowers chance of readmissions, lowers total healthcare costs over 90 d	Unpublished data
Influence transitions of care		
Inpatient consultations (263) for community-based OPAT	Treatment optimized in 84%, significant change in assessment in 52%, additional medical care contribution in 71%, OPAT unnecessary in 27%, effective care transition to outpatient in 86%	[13]
Multicenter private practice OPAT (6120 patients)	57% started therapy in hospital, 94% successfully treated as outpatients, only 3% hospitalized after starting therapy, 19% had therapeutic complication	[14]
ID physician–staffed vs ED physician–staffed ED cellulitis clinic	40% in ID physician–staffed clinic given noncellulitis diagnosis vs 11% in ED physician–staffed clinic, recurrence and hospitalization rates lower in ID physician–staffed clinic, no difference in mortality	[15]
Lead infection prevention and antimicrobial stewardship programs		
CDC IP 2016 data	50% decrease in CLABSI, 17% decrease in SSI, 8% decrease in hospital-acquired CDI	[16]
ID physician–led AS program 70-bed rural hospital over 3 years	42% decrease in antiinfection expenditures, improved *P. aeruginosa* susceptibility	[17]
24-hospital network over 7 years	50% decrease in HAI rates, decreased costs, prevented 52–105 deaths from CLABSI or VAP	[18]
AS in LTAC hospital via remote EHR access	Decreased antibacterial use, decreased CDI rates	[19]

McQuillen DP et al. J Infect Dis 2017;216(suppl_5):S588-S593

The Value That Infectious Diseases Physicians Bring to the Healthcare System

Table 2. Risk-Adjusted Outcomes for Stays Receiving Early Versus Late Intervention by Infectious Diseases Physicians

Outcome	Early Intervention[a]	Late Intervention	*P*	Percentage Difference (95% CI)	OR (95% CI)
Index stay, length of stay, d	13.2	13.8	<.001	−3.8 (−4.8 to −2.9)	…
Index stay, length of ICU stay, d[b]	7.6	8.1	<.001	−5.1 (−7.7 to −2.4)	…
Index stay, mortality, %	7.1	7.5	.122	…	0.94 (.88–1.02)
30-d mortality, %[c]	8.6	9.6	<.001	…	0.87 (.82–.93)
30-d readmission rate, %[c]	24.6	26.1	<.001	…	0.92 (.89–.96)
ACH charge for index stay, $	95 135	98 015	<.001	−2.9 (−4.1 to −1.7)	…
Medicare payments to ACH for index stay, $	18 111	18 728	<.001	−3.3 (−4.3 to −2.3)	…
Medicare payments for index stay, $	21 453	22 207	<.001	−3.4 (−4.3 to −2.5)	…
Medicare payments for 30-d episode, $[c]	8739	9318	<.001	−6.2 (−8.8 to −3.5)	…

McQuillen DP et al. J Infect Dis 2017;216(suppl_5):S588-S593

An Antimicrobial Stewardship Program Based on Systematic Infectious Disease Consultation in a Rehabilitation Facility

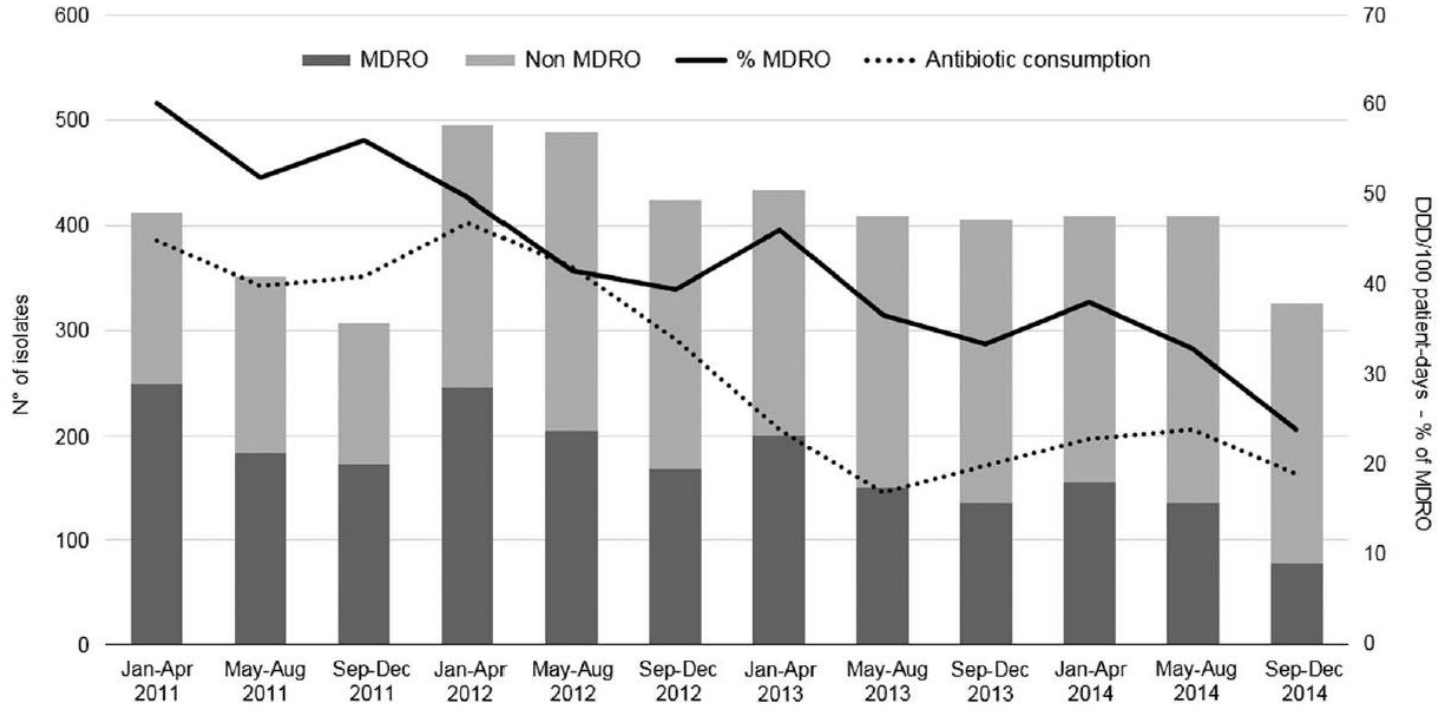


FIGURE 1. Secular trends of antibiotic consumption and overall resistance prevalence from January 2011 to December 2014. MDRO, multidrug-resistant organism; DDD, defined daily dose.

Tedeschi S et al. Infect Control Hosp Epidemiol 2017;38(1):76-82.

An Antimicrobial Stewardship Program Based on Systematic Infectious Disease Consultation in a Rehabilitation Facility

TABLE 1. Indicators of Activity and Outcome Measures During Study Period

Indicator	2011	2012	2013	2014
Admissions, No.	485	655	721	740
Patient days, No.	55,039	55,319	55,377	55,254
Mean length of stay, d	113.48	84.46	76.81	74.67
Bed occupancy, %	100.17	100.76	100.15	100.92
In-hospital mortality, No. (%)	16 (3.3)	11 (1.6)	14 (1.9)	12 (1.6)

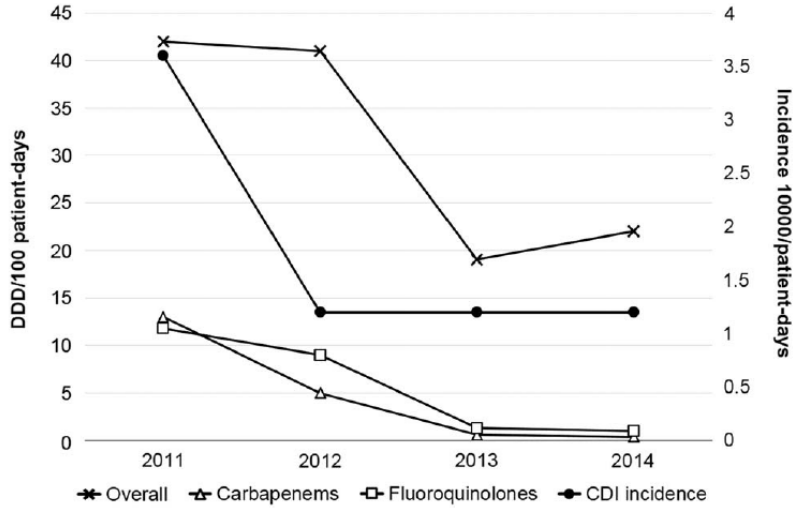
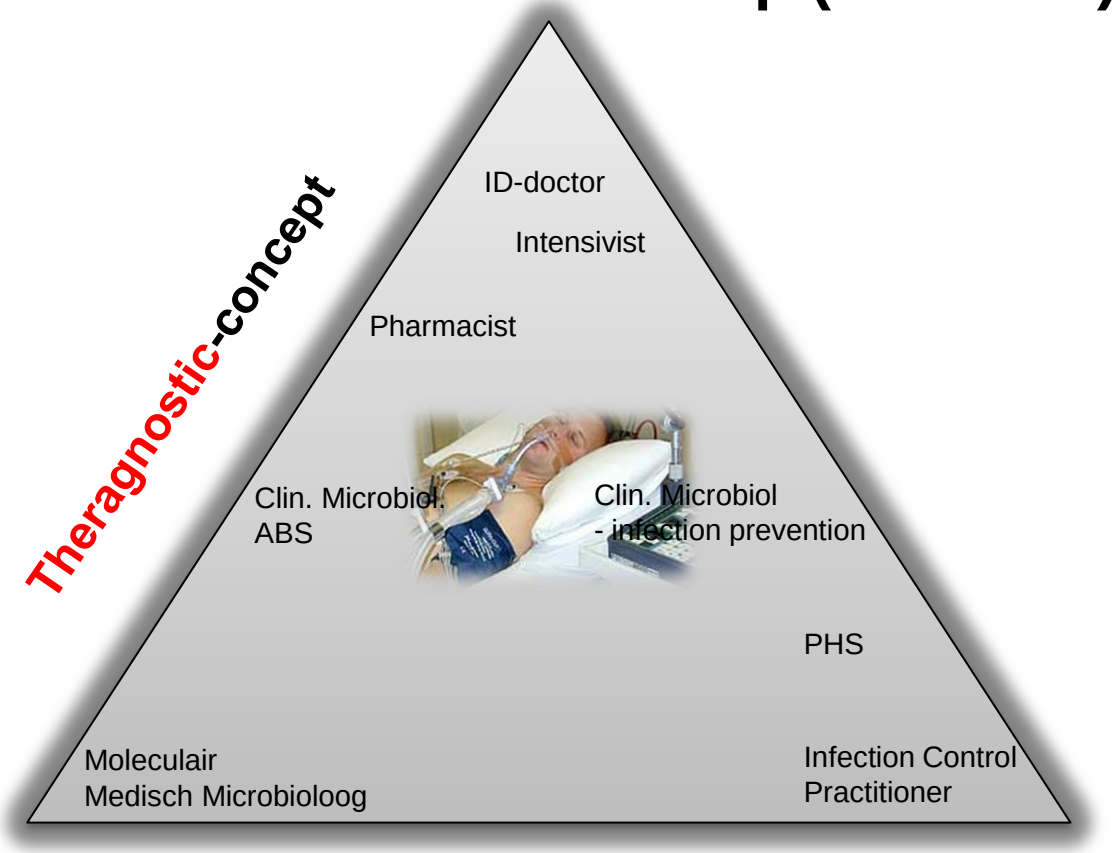


FIGURE 2. Decreasing consumption of overall antibiotics, carbapenems, and fluoroquinolons, and incidence of *Clostridium difficile* infection (CDI) from January 2011 to December 2014.

Tedeschi S et al. Infect Control Hosp Epidemiol 2017;38(1):76-82.

From competence to meta-competence

Thera-py
Antimicrobial Stewardship (A-Teams)



Dia-gnostic Stewardship

Infection Prevention Stewardship

Courtesy Prof. A Friedrich

Dik et al. 2015 Future Microbiology