New York State Partnership for Patients

The Impact of ASP on MDROs

Myths, Legends and Strategies Proven to Reduce MDRO

April 2018
3:00-4:00pm

Agenda

Topic	Speaker
Welcome and Introductions	NYSPFP Staff
The Impact of ASP on MDROs: Myths, Legends and Strategies Proven to Reduce MDROs	Keith S. Kaye, MD, MPH President of the Society for Health Epidemiology of America and Professor of Medicine in the Division of Infectious Diseases and Department of Medicine at University of Michigan Medical School
Hospital Questions and Discussion	Hospital Participants Facilitated by NYSPFP Staff
Next Steps	NYSPFP Staff

ASP/CDI/MDRO Initiative Overview

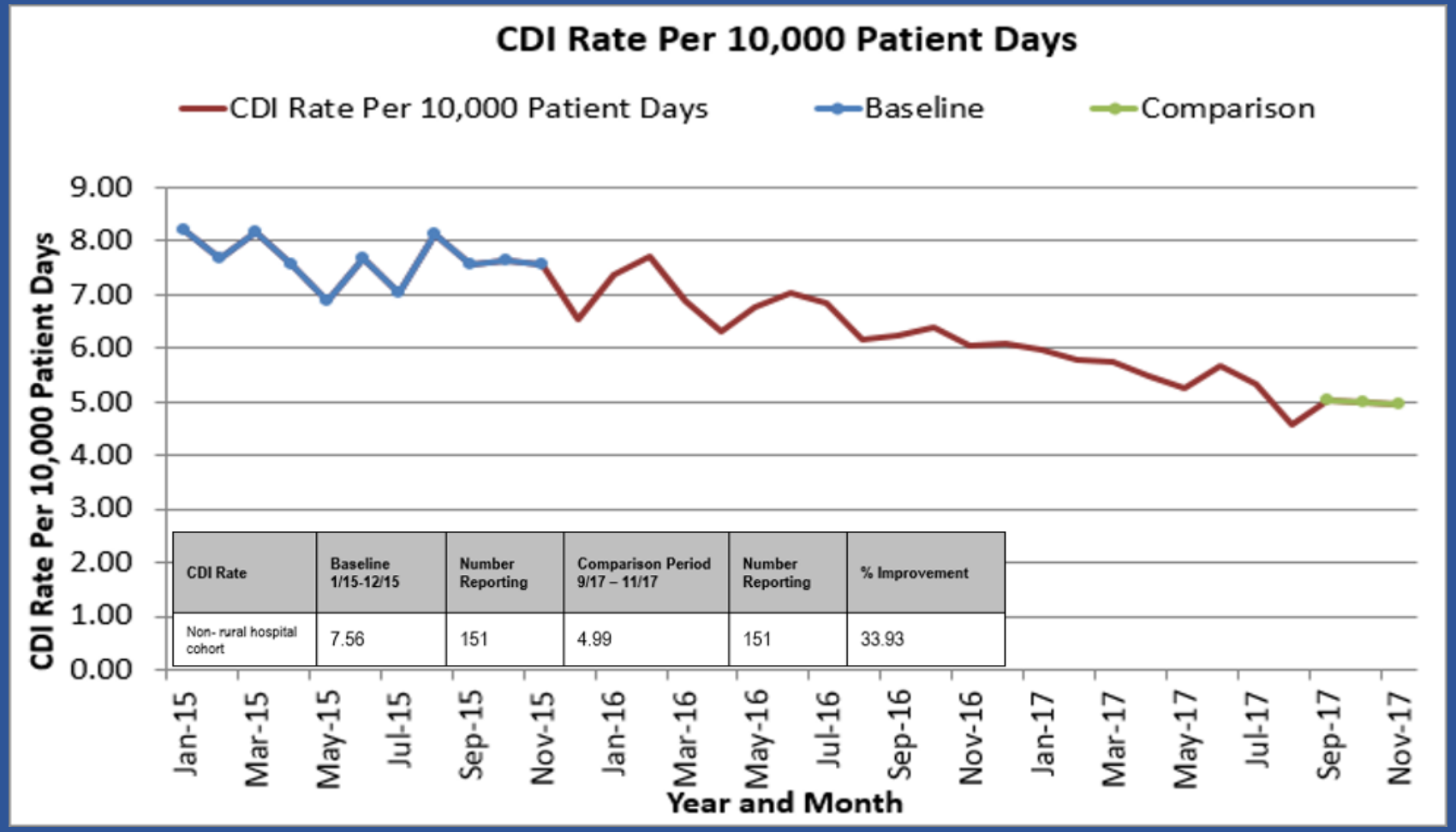
GOAL:

- Implement an antibiotic stewardship program (ASP)
- Reduce hospital multi-drug resistant organism (MDRO) infection and Clostridium difficile Infection (CDI) by 20%, from a 2015 baseline

OBJECTIVES

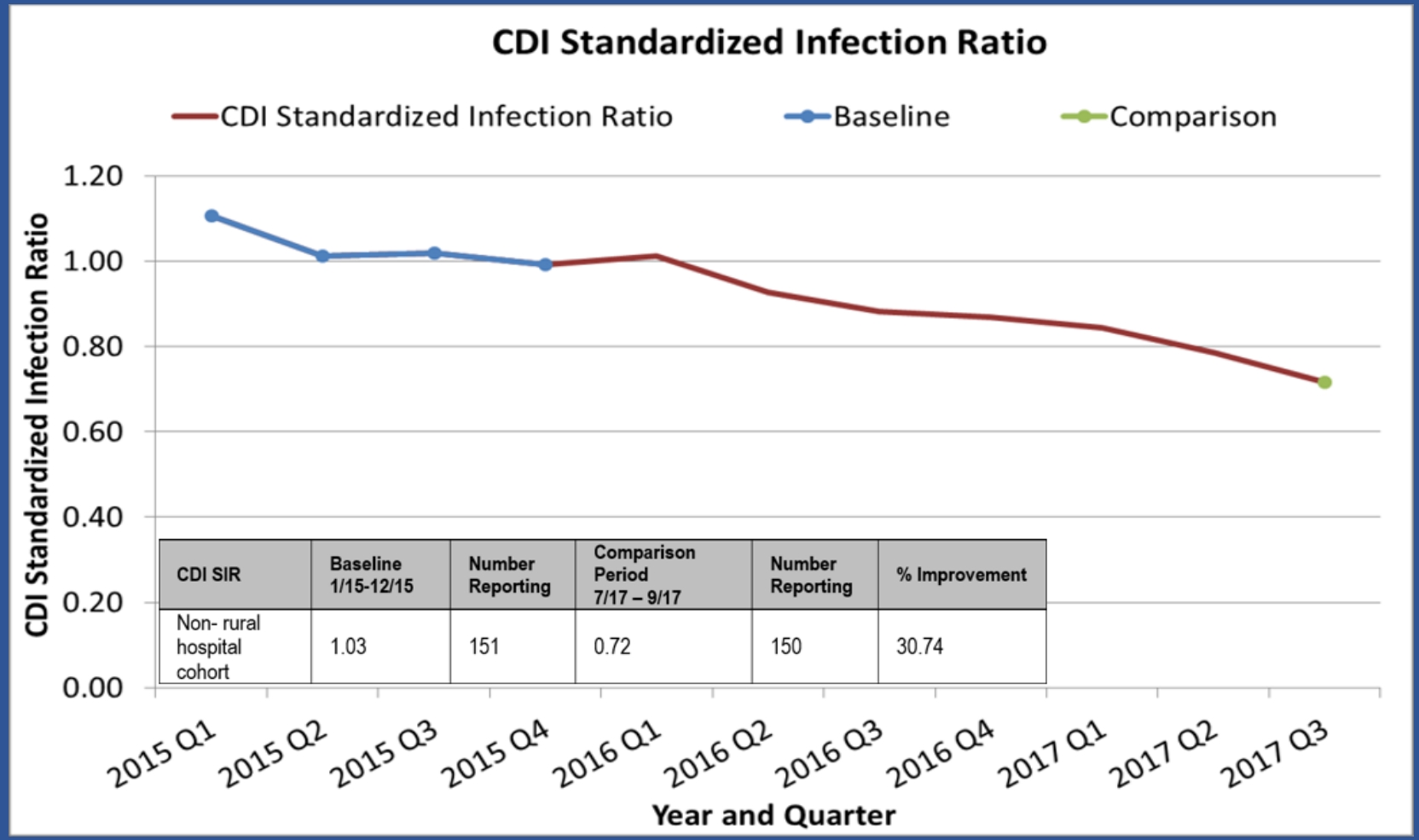
- Hospitals will implement all elements of the Centers for Disease Control's (CDC) "Core Elements of Antibiotic Stewardship Programs" as part of the hospital's ASP program by September 2018
- Reduce CDI by 20% by September 2018
- Reduce MDRO infections, particularly MRSA, by 20% by September 2018

C.difficile Rate



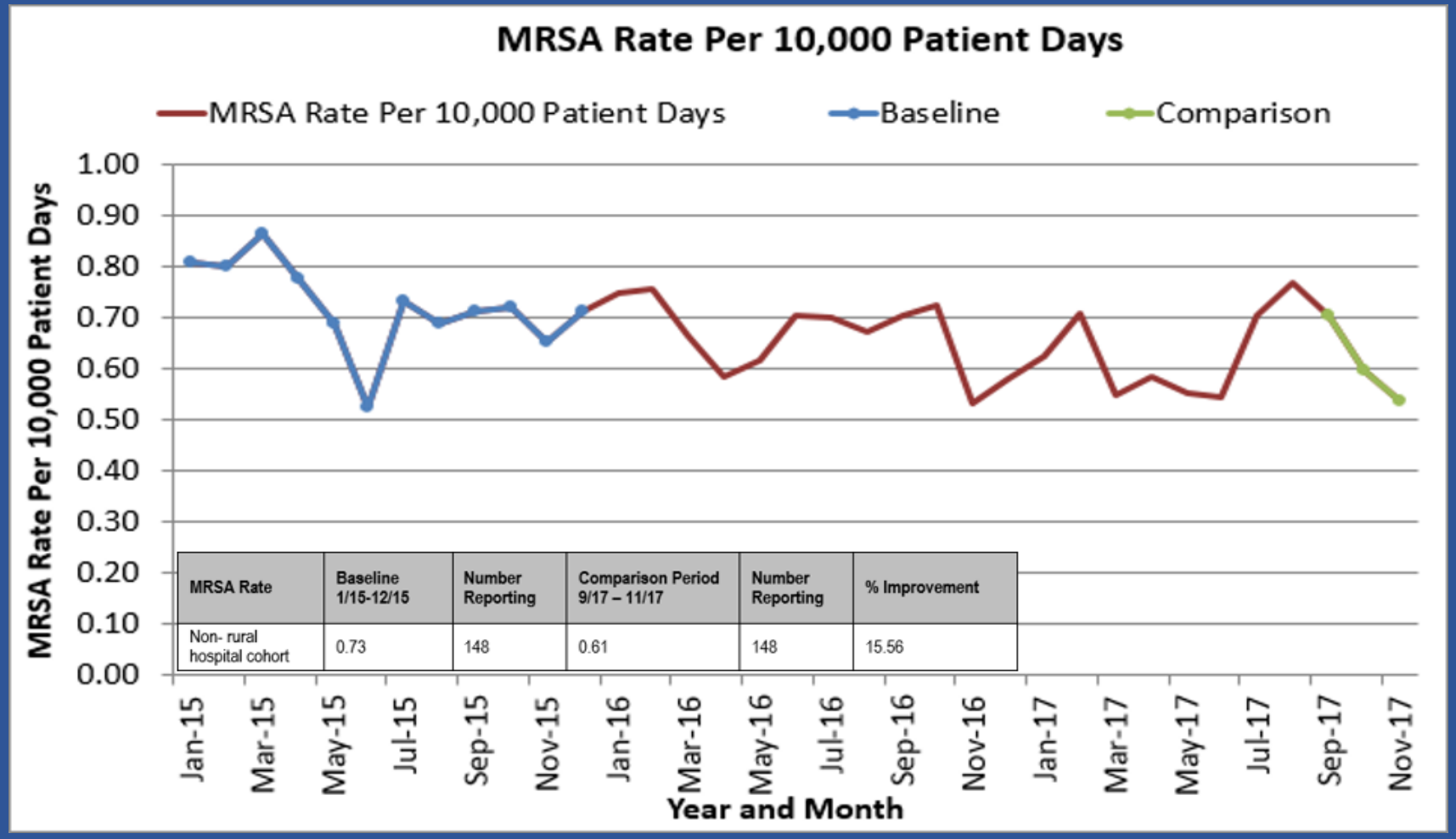
CDI Rate	Baseline 1/15-12/15	Number Reporting	Comparison Period 9/17 – 11/17	Number Reporting	% Improvement
Non- rural hospital cohort	7.56	151	4.99	151	33.93

C.difficile SIR



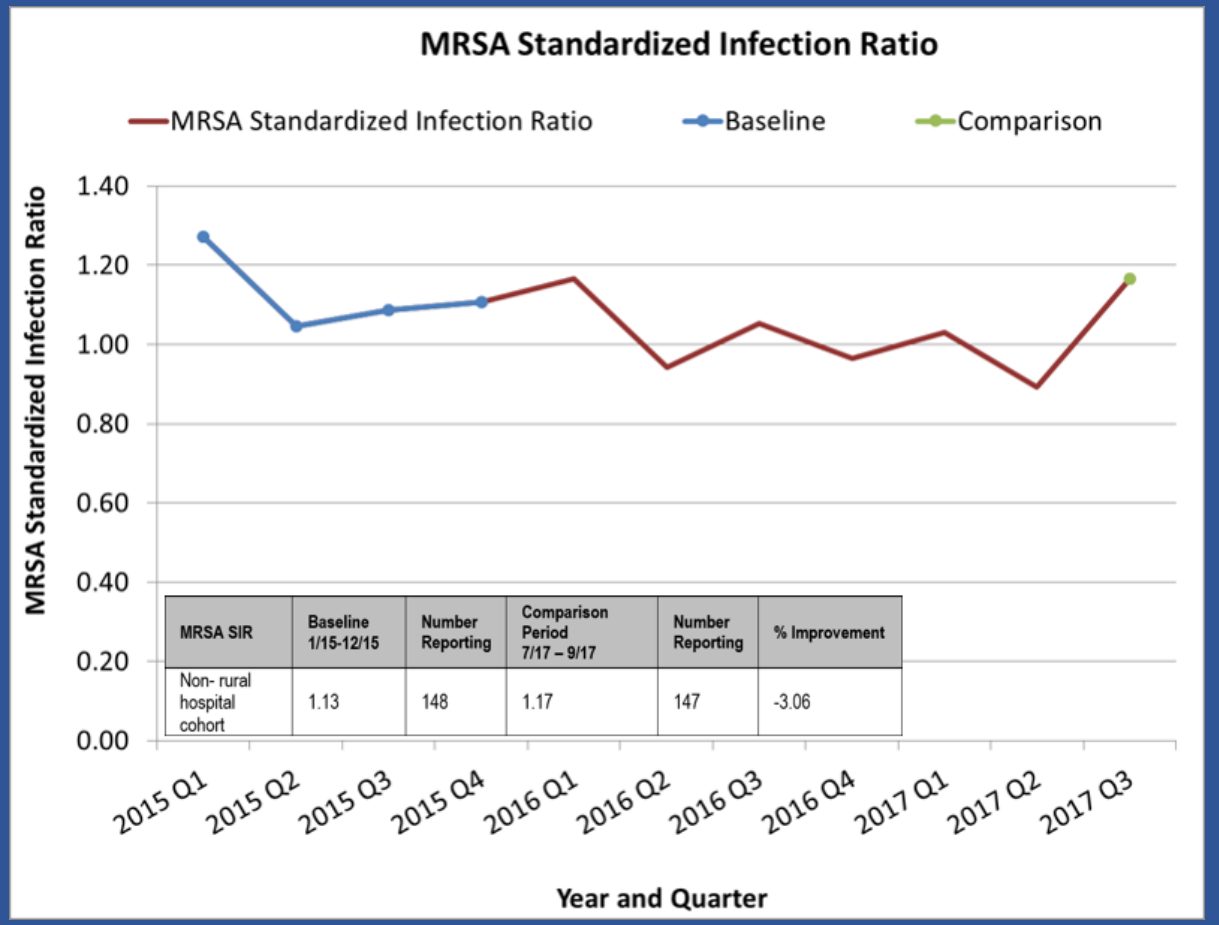
CDI SIR	Baseline 1/15-12/15	Number Reporting	Comparison Period 7/17 – 9/17	Number Reporting	% Improvement
Non- rural hospital cohort	1.03	151	0.72	150	30.74

MRSA Rate



MRSA Rate	Baseline 1/15-12/15	Number Reporting	Comparison Period 9/17 – 11/17	Number Reporting	% Improvement
Non- rural hospital cohort	0.73	148	0.61	148	15.56

MRSA SIR



MRSA SIR	Baseline 1/15-12/15	Number Reporting	Comparison Period 7/17 – 9/17	Number Reporting	% Improvement
Non- rural hospital cohort	1.13	148	1.17	147	-3.06

NYSPFP Programming

ASP

C.difficile and MDRO

April 2017

- Launch of ASP Rapid Cycle Improvement Project

May – Nov 2017

- Rapid Cycle Improvement Projects
- Coaching calls and on-site PM technical support

February 2018

- Successful strategies to reduce C.difficile

Apr – Nov 2018

- How ASP impacts MDROs and C.difficile
- Emerging topics in C.difficile

NYSPFP ASP in 2017

Antibiotic Stewardship Program : Rapid Cycle Improvement Projects (Based on CDC Core Elements of Hospital Antibiotic Stewardship programs)		
Phase 1 • Leadership commitment • Accountability • Drug expertise	**Phase 2** • Actions to support optimal antibiotic use	**Phase 3** • Tracking and monitoring antibiotic prescribing, use, and resistance • Reporting information on improving antibiotic use and resistance
Education of Clinicians and Patients and Families		

Materials for the ASP Rapid Cycle Improvement Project are available on www.nyspfp.org

CDC Core Elements of Antibiotic Stewardship in NYS

Core Elements	Percentage of Hospital's Reporting Yes (N = 91)
LEADERSHIP SUPPORT	
Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?	95%
Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?	74%
ACCOUNTABILITY	
Is there a physician leader responsible for program outcomes of stewardship activities at your facility?	92%
DRUG EXPERTISE	
Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?	99%

Data accurate as of 4/2/2018

CDC Core Elements of Antibiotic Stewardship in NYS (Cont).

Core Elements	Percentage of Hospital's Reporting Yes (N = 91)
ACTIONS TO SUPPORT OPTIMAL ANTIBIOTIC USE	
Does your facility have a policy that requires prescribers to document in the medical record or during order entry a dose, duration, and indication for all antibiotic prescriptions?	59%
Does your facility have facility-specific treatment recommendations, based on national guidelines and local susceptibility, to assist with antibiotic selection for common clinical conditions?	92%
Is there a formal procedure for all clinicians to review the appropriateness of all antibiotics 48 hours after the initial orders (e.g. antibiotic time out)?	41%
Do specified antibiotic agents need to be approved by a physician or pharmacist prior to dispensing (i.e., pre-authorization) at your facility?	88%

Data as of 4/2/2018

CDC Core Elements of Antibiotic Stewardship in NYS (Cont).

Core Elements	Percentage of Hospital's Reporting Yes (N = 91)
ACTIONS TO SUPPORT OPTIMAL ANTIBIOTIC USE	
Does your facility have Automatic changes from intravenous to oral antibiotic therapy in appropriate situations?	69%
Time-sensitive automatic stop orders for specified antibiotic prescriptions?	67%
Automatic alerts in situations where therapy might be unnecessarily duplicative?	75%

Data as of 4/2/2018

CDC Core Elements of Antibiotic Stewardship in NYS (Cont).

Core Elements	Percentage of Hospital's Reporting Yes (N = 91)
TRACKING: MONITORING ANTIBIOTIC PRESCRIBING, USE AND RESISTANCE	
Does your stewardship program monitor adherence to a documentation policy (dose, duration, and indication)?	63%
Does your stewardship program monitor adherence to facility-specific treatment recommendations?	64%
Does your stewardship program monitor compliance with one or more of the specific interventions in place?	85%

Data as of 4/2/2018

CDC Core Elements of Antibiotic Stewardship in NYS (Cont).

Core Elements	Percentage of Hospital's Reporting Yes (N = 91)
REPORTING INFORMATION TO STAFF	
Does your stewardship program monitor adherence to a documentation policy (dose, duration, and indication)?	69%
Does your stewardship program monitor adherence to facility-specific treatment recommendations?	88%
Does your stewardship program monitor compliance with one or more of the specific interventions in place?	81%

Data as of 4/2/2018

The Impact of ASP on MDROs: Myths, Legends and Strategies Proven to Reduce MDROs

Keith S. Kaye, MD, MPH
Professor of Medicine
University of Michigan Medial School

SHEA
The Society for Healthcare Epidemiology of America

UNIVERSITY OF MICHIGAN

Overview

- Antimicrobial overuse and limited pipeline
- Key MDROs of interest
- Basics of MDRO transmission in the hospital
- Impact of stewardship on MDRO acquisition in the hospital
- Review and evaluation of different stewardship strategies
- Unmet needs and research opportunities

Antimicrobial Overuse in the US

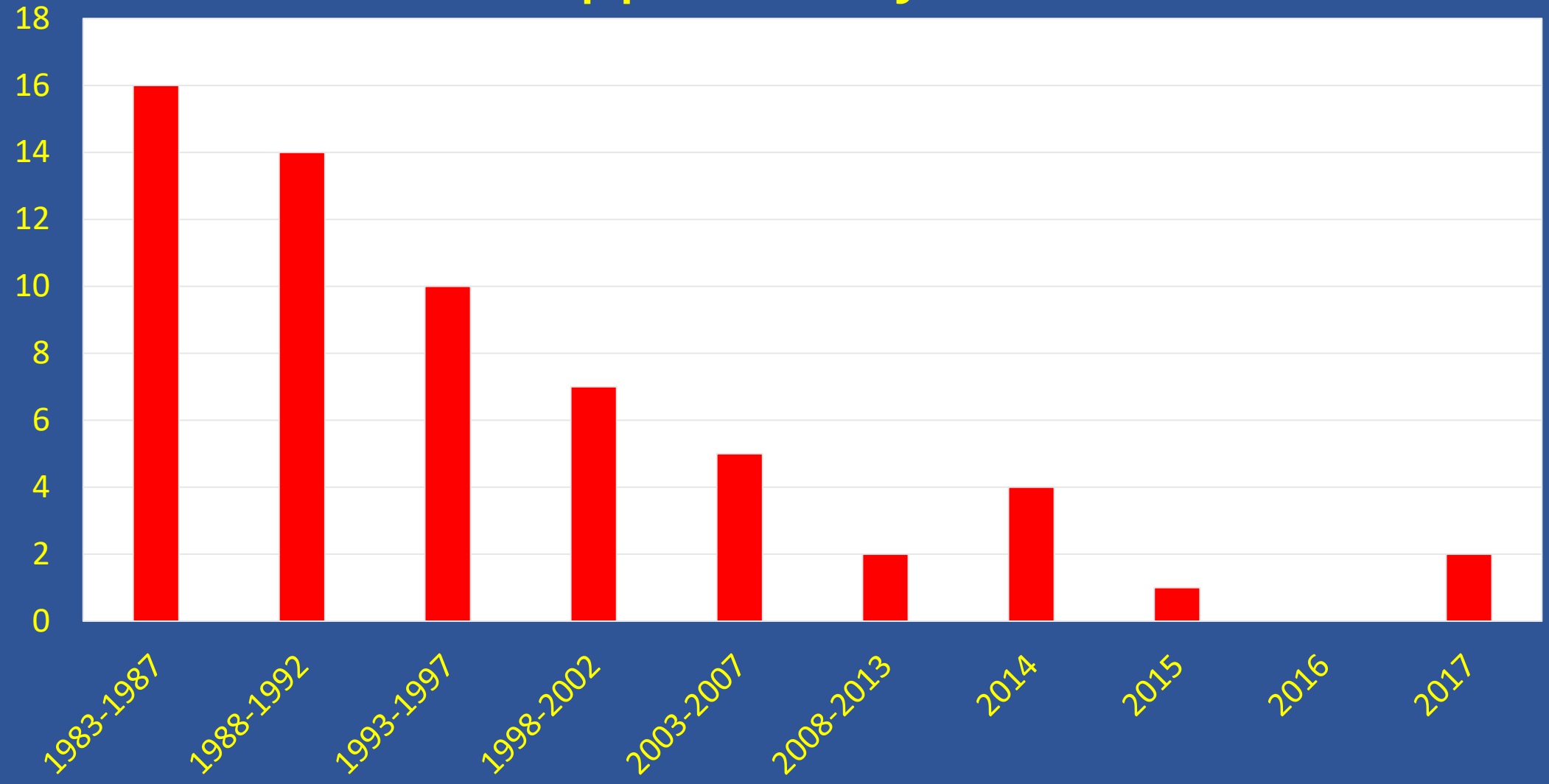
- 70% of all antimicrobials in the US fed to livestock

- 258 million courses of antibiotics prescribed to outpatients for human use in 2010,
  - Translates to 833 antibiotic prescriptions for every 1,000 people
  - 4/5 Americans prescribed an antibiotic annually

- Antibiotics prescribed in more than 12% of ambulatory care visits
  - More than 30% deemed to be inappropriate

N Engl J Med 2013; 368:1461-1462
JAMA, 2016; 315:1864-1873

Declining Number of New Systemic Antibiotic Agents Approved by US FDA

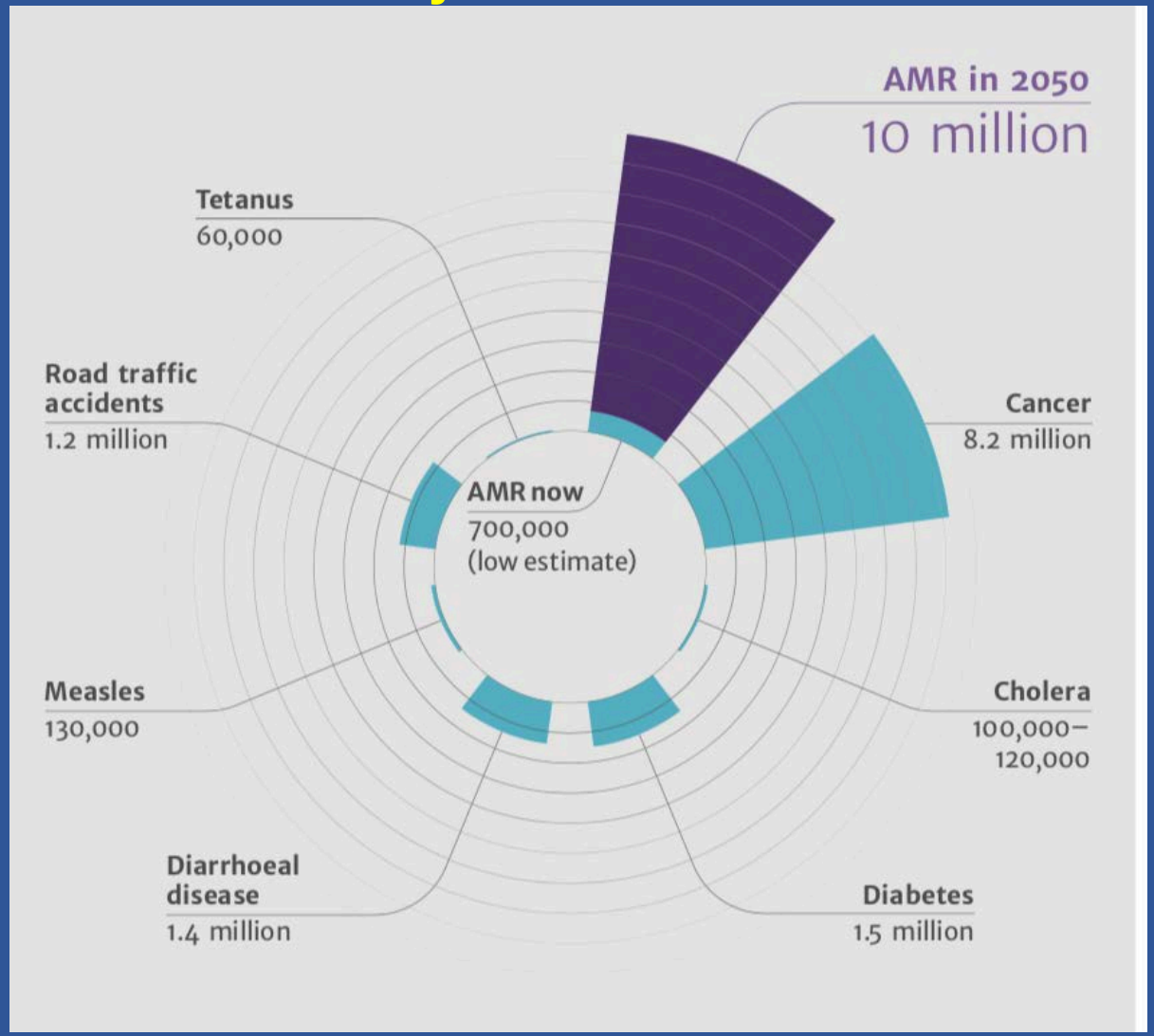


Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

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]

- Bad Bugs, No Drugs: No ESKAPE
  - *Enterococcus faecium* (E), *Staphylococcus aureus* (S), *Klebsiella pneumoniae* (K), *Acinetobacter baumannii* (A), *Pseudomonas aeruginosa* (P), and *Enterobacter* spp. (E)
- The late-stage clinical development pipeline remains unacceptably lean
  - Some important molecules for problematic pathogens such as MRSA
  - Few novel molecules for other ESKAPE pathogens
  - No new drugs for infection due to multidrug-resistant Gram-negative bacilli (eg, *A. baumannii* and *P. aeruginosa*)
  - None represent more than an incremental advance over currently available therapies

Deaths Attributable to AMR Every Year Compared to Other Major Causes of Death



The Review on Antimicrobial Resistance Chaired by Jim O'Neill, December 2014

Does Resistance Matter?

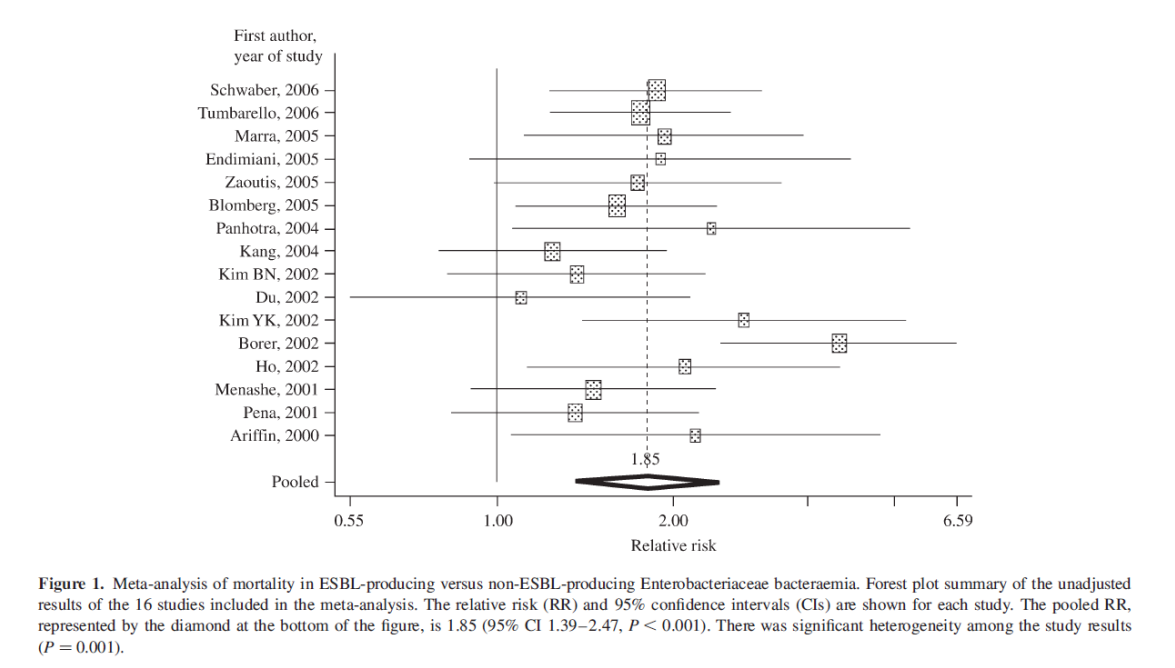


Figure 1. Meta-analysis of mortality in ESBL-producing versus non-ESBL-producing Enterobacteriaceae bacteraemia. Forest plot summary of the unadjusted results of the 16 studies included in the meta-analysis. The relative risk (RR) and 95% confidence intervals (CIs) are shown for each study. The pooled RR, represented by the diamond at the bottom of the figure, is 1.85 (95% CI 1.39–2.47, $P < 0.001$). There was significant heterogeneity among the study results ($P = 0.001$).

Schwaber et al, Journal of Antimicrobial Chemotherapy (2007) 913–920

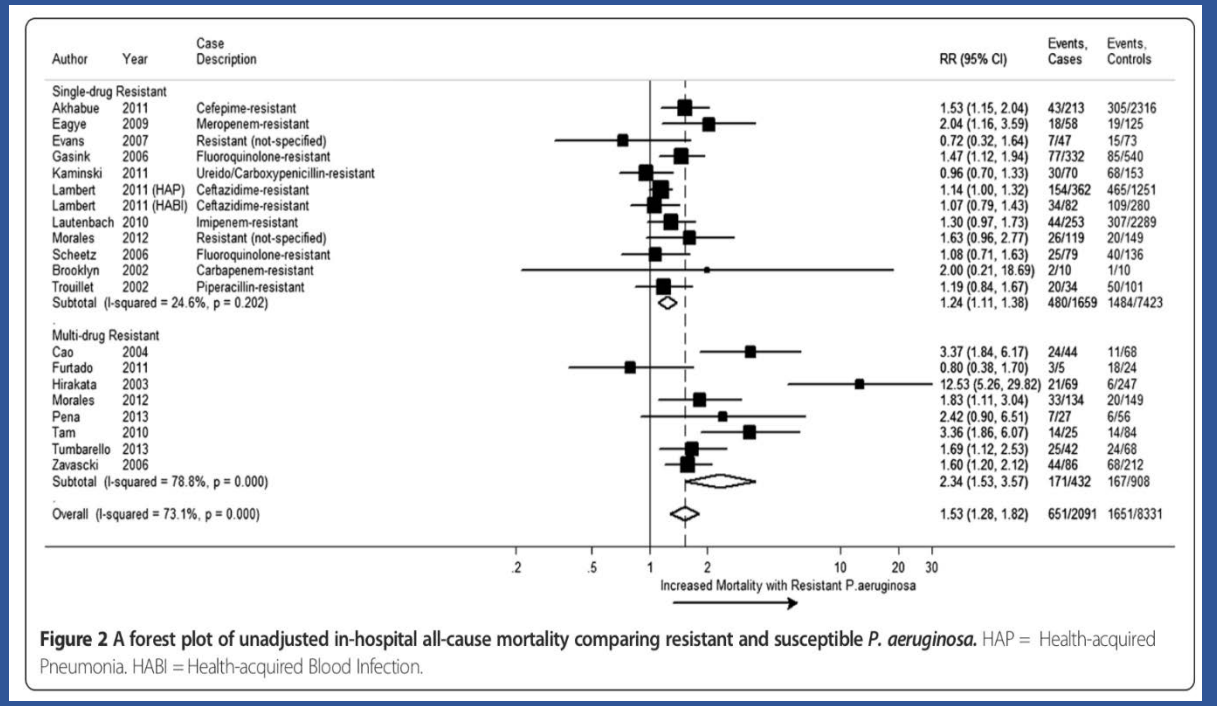
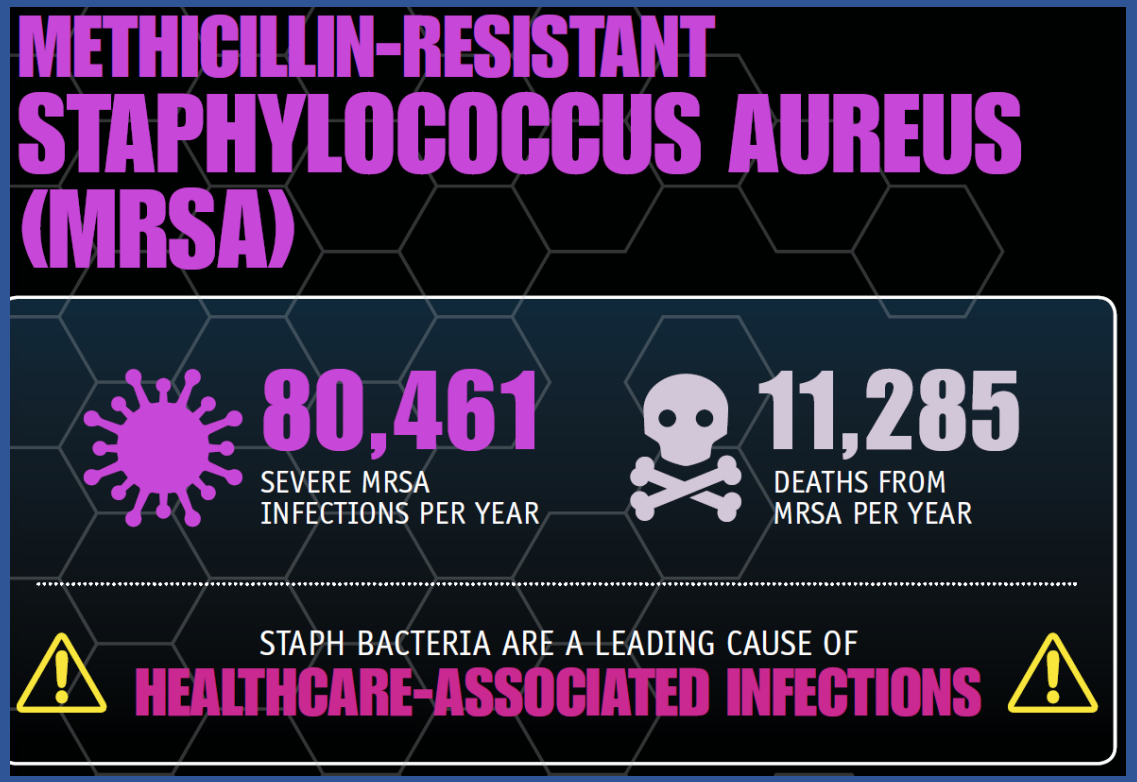


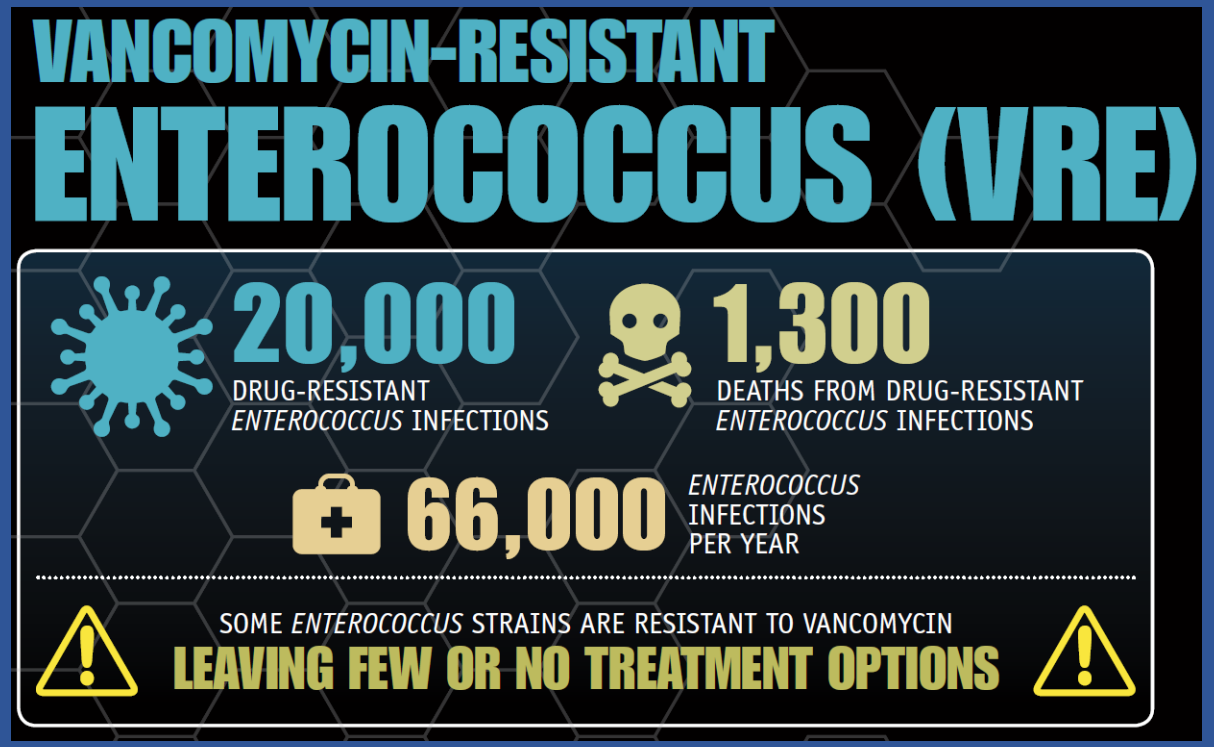
Figure 2 A forest plot of unadjusted in-hospital all-cause mortality comparing resistant and susceptible *P. aeruginosa.* HAP = Health-acquired Pneumonia. HABI = Health-acquired Blood Infection.

Nathwani et al. Antimicrobial Resistance and Infection Control (2014) 3:32

Poor outcomes driven by 1) patient population, 2) significant delays in time to appropriate therapy, 3) therapeutic options in patients with these infections

Resistance to Gram Positives





WHO Priority Pathogens List For R&D of New Antibiotics

Priority 2: Medium

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

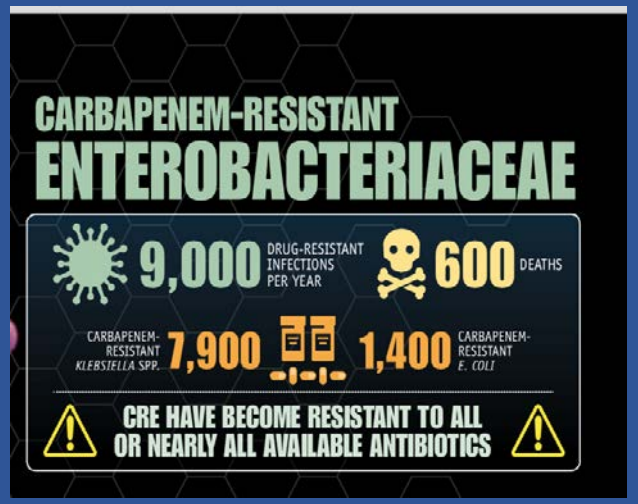
Helicobacter pylori, clarithromycin-resistant

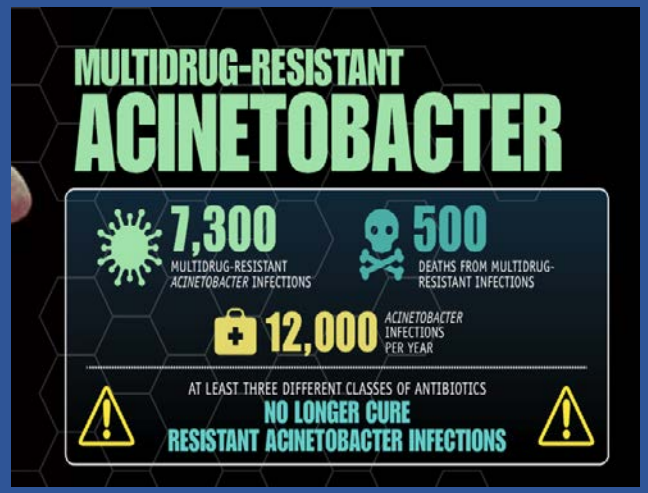
Campylobacter, fluoroquinolone-resistant

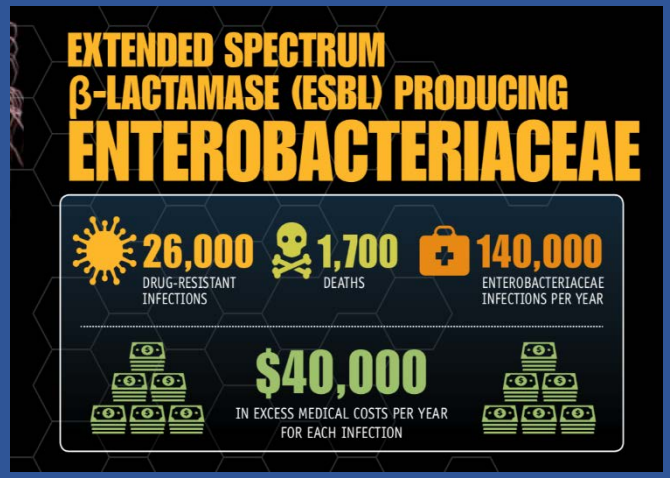
Salmonella *spp.*, fluoroquinolone-resistant

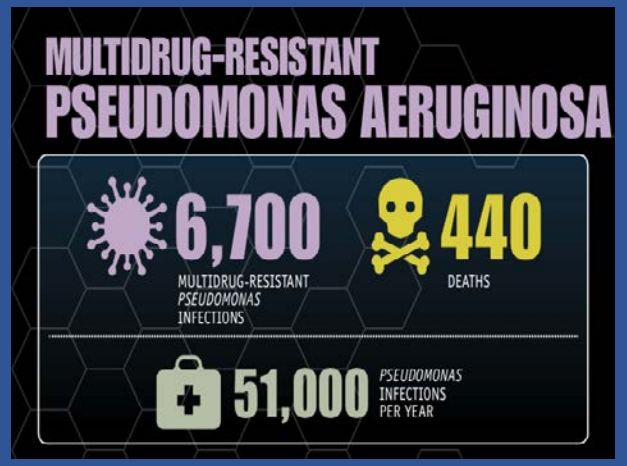
Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Resistance in Gram-negative pathogens: An International Threat









WHO Priority Pathogens List For R&D of New Antibiotics

Priority 1: Critical

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Infection Prevention and Multi-drug Resistant Organism (MDROs) in Healthcare Settings: What We Know

- Spread in healthcare settings[1]
  - Horizontal/cross-transmission: patient-patient via environment, healthcare workers hands/equipment
  - Vertical/endogenous – development of an MDRO from previously susceptible bacterial strain in the same patient
- Hand hygiene by healthcare workers critically important in preventing MDRO spread[2]
- The environment is an important reservoir for MDROs[3]
- Indwelling devices (eg central vascular catheters [CVCs]) are important risk factors
  - Use of care bundles for insertion and maintenance important in preventing infection
- Important MDRO reservoirs in longer-term care settings (particularly LTACs) [4]
  - A relatively high proportion of MDROs isolated in hospitals are imported by patients at time of admission (ie are present at time of admission or POA)

[1]http://www.who.int/water_sanitation_health/medicalwaste/148to158.pdf

[2]http://www.who.int/gpsc/5may/MDRO_literature-review.pdf

[3]Carling, Infect Dis Clin NA, Infect Dis Clin North Am. 2016 Sep;30(3):639-60

[4]Cassone et al, Curr Geriatr Rep, p 87-95, 2015

Antimicrobial Stewardship and Antimicrobial Resistance

- Antimicrobial stewardship has been associated with many positive outcomes
  - Reduced cost[1]
  - Improved clinical outcomes[2,3]
    - Including length of stay, mortality
  - Reduced *Clostridium difficile*[4]

- With growing focus on antimicrobial resistance there has been increased interest in using stewardship strategies to reduce resistance
  - Critical issues is lack of personnel trained in infectious diseases and stewardship – at physician and pharmacist level

- What is the evidence that antimicrobial stewardship reduces antimicrobial resistance? And which strategies are the most effective in doing so?
  - And how can strategies be implemented in settings lacking stewardship expertise

1– Macdougall, CMR, 2005, 638-56; 2- Pogue ICHE, 2014, 132-8; 3- Huang, CID, 2013, 1237-45; 4– Feazel, JAC, 2014, 1748-54

Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis

David Baur*, Beryl Primrose Gladstone*, Francesco Burkert, Elena Carrara, Federico Foschi, Stefanie Döbele, Evelina Tacconelli

- 32 studies in the meta-analysis, comprising 9,056,241 patient-days and 159 estimates of IRs

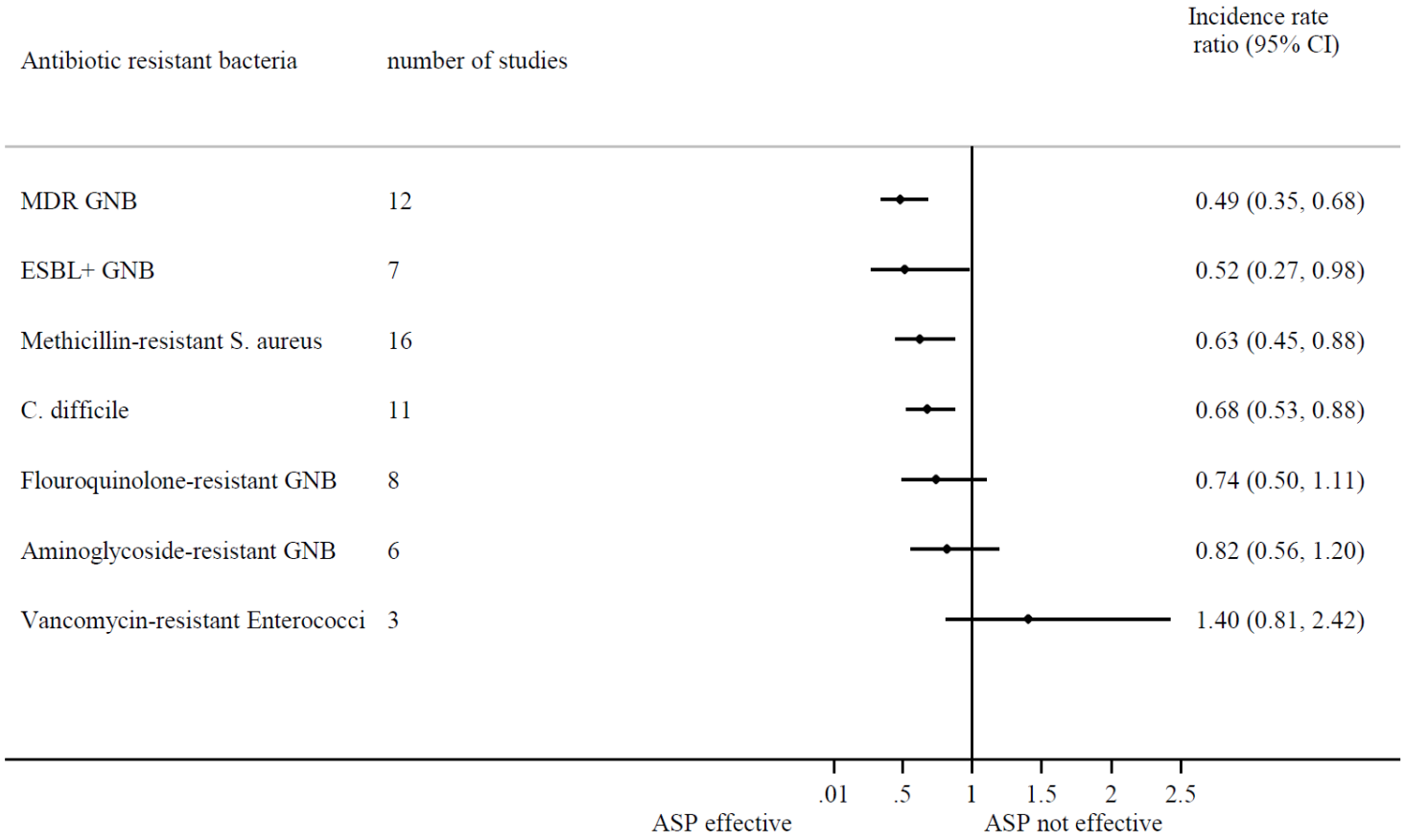
- ASPs reduced the incidence of infections and colonisation with
  - multidrug-resistant Gram-negative bacteria (51% reduction; IR 0·49, 95% CI 0·35–0·68)
  - ESBL-producing Gram-negative bacteria (48%; 0·52, 0·27–0·98)
  - MRSA (37%; 0·63, 0·45–0·88)
  - *C difficile* infections (32%; 0·68, 0·53–0·88).

- ASPs were more effective when implemented with IC measures (IR 0·69, 0·54–0·88), especially hand-hygiene interventions (0·34, 0·21–0·54)

- Antibiotic stewardship did not affect the IRs of vancomycin-resistant enterococci and quinolone-resistant and aminoglycoside-resistant Gram-negative bacteria

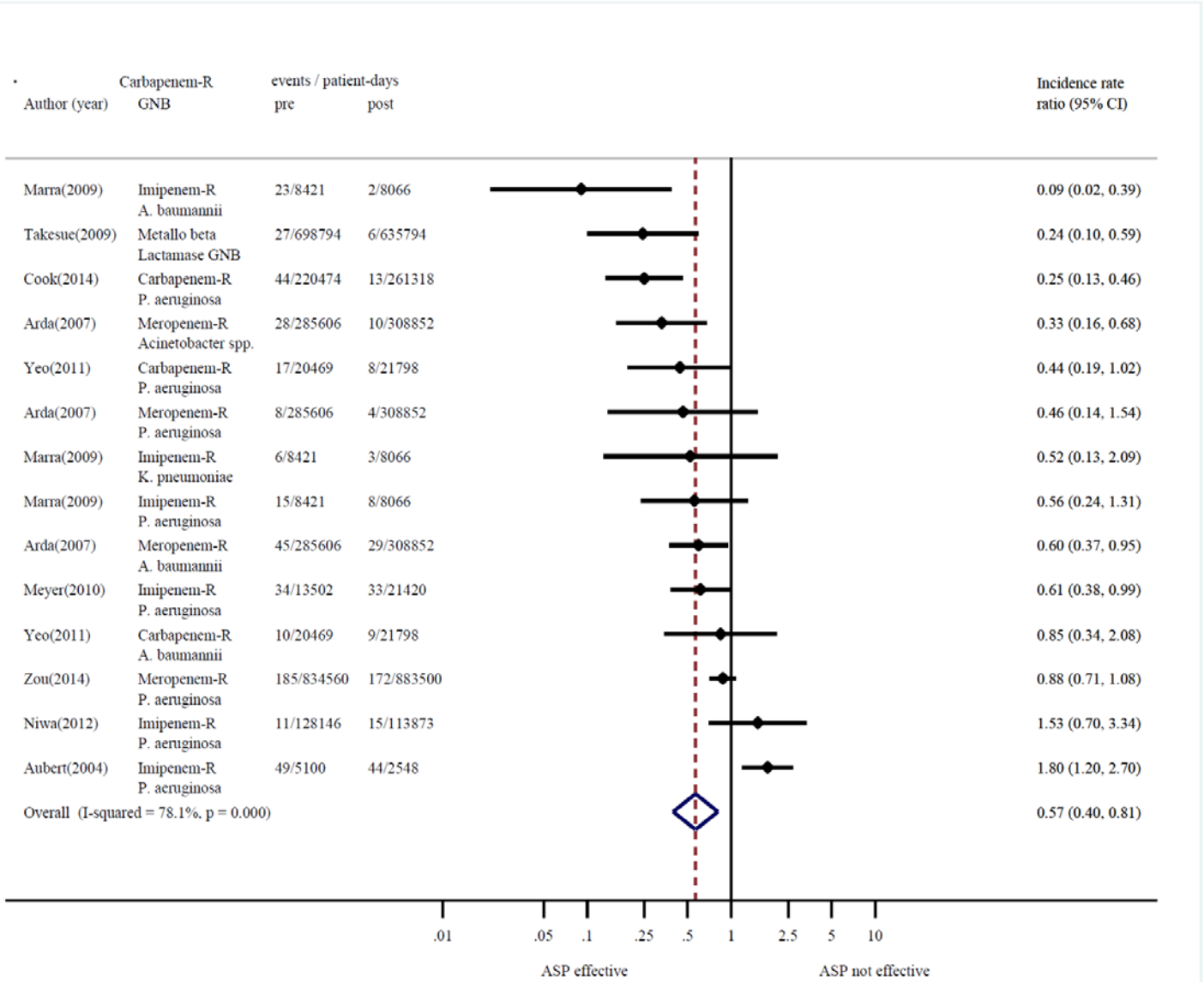
***Lancet Infect Dis* 2017; 17: 990–1001**

Figure 3: Summary Forest plot of incidence rate ratios for antibiotic-resistant bacteria targeted by the antibiotic stewardship intervention studies included in the meta-analysis (n=32)



CI = confidence interval; ESBL+ = extended spectrum ß-lactamase producer; GNB = gram-negative bacteria; MDR = multidrug-resistant; ASP = Antimicrobial stewardship programme.

Figure 4: Forest plot of the incidence rate ratios among studies targeting the effect of antibiotic stewardship on the incidence of carbapenem-resistant Gram negative bacteria



Significant reduction in studies focusing on carbapenem resistance (43%; 0.57, 95% CI 0.40–0.81)

- A. baumannii (56% reduction; IR 0.44, CI 0.17–1.13)
- P aeruginosa (29%; 0·71, CI 0.46–1.10)
- K pneumoniae 48% (IR 0·52, CI 0.13–2.09)

Bauer et al., Lancet Infect Dis, 2017, 990-1001

Stewardship and *C. difficile*

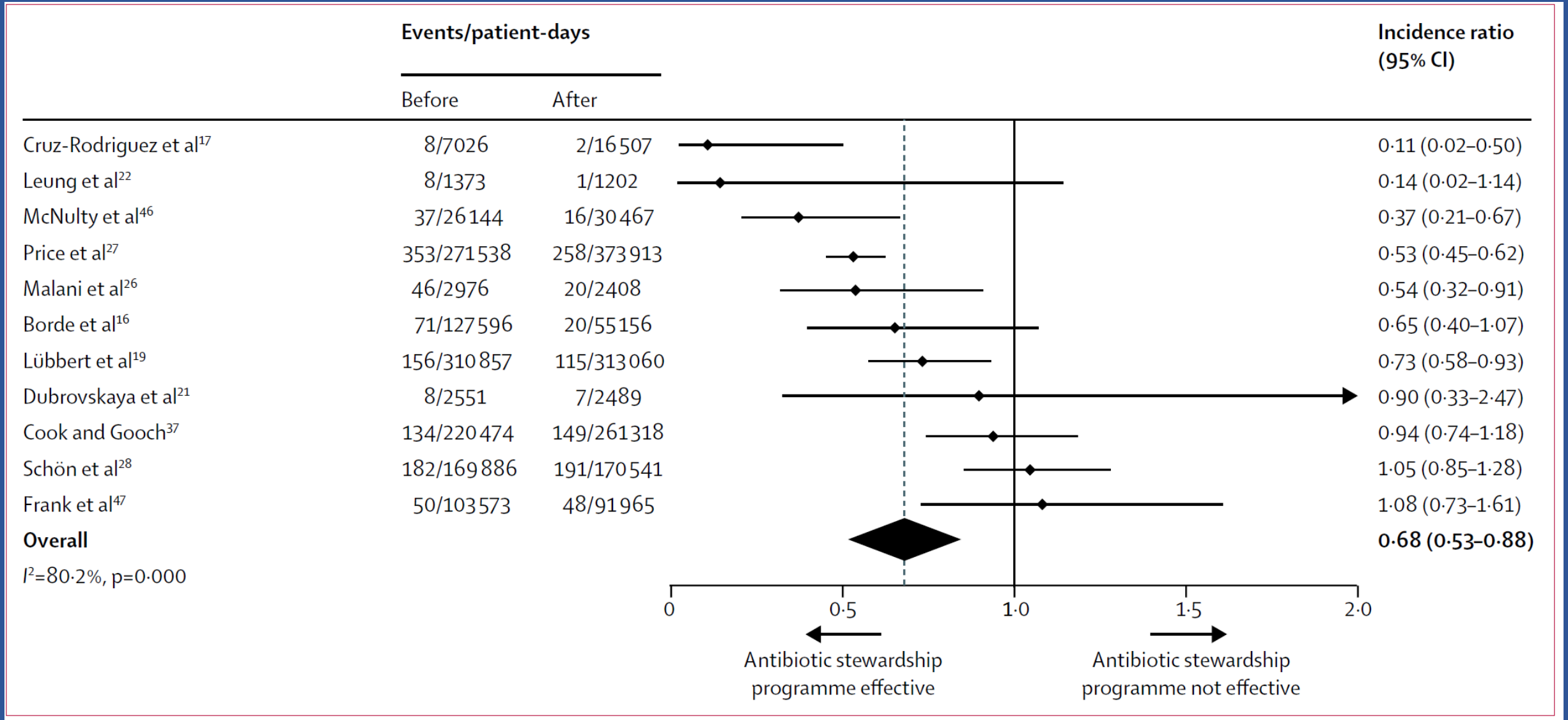


Figure 4: **Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of *Clostridium difficile* infections**

Stewardship Processes to Reduce Resistance

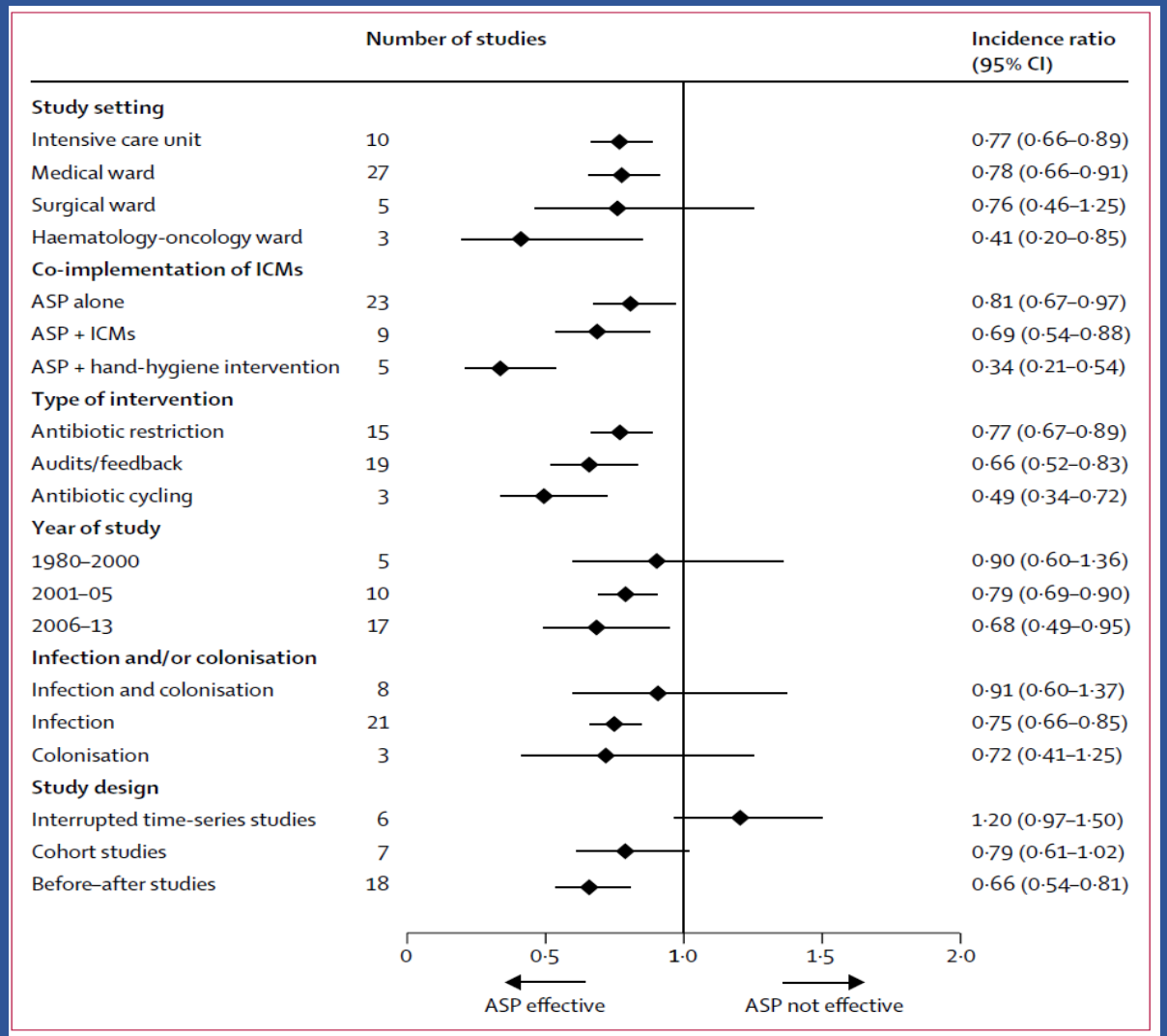


Figure 5: **Summary forest plot of the incidence ratios for studies investigating the effect of ASPs on antibiotic resistance, according to study characteristics**
ICM=infection control measure. ASP=antibiotic stewardship programme.

Characteristics of effective interventions

- Restriction
- Audits/feedback
- Cycling
- Co-implementation with IC measures

Bauer et al, Lancet ID, 2017

We Know Some ASP Processes That Work . . .

- But what is the mechanism by which ASP interventions decrease antimicrobial resistance?

- In studies we almost always don’t know the whole story about overall antibiotic utilization, utilization by class, changes in dosing and treatment strategies . . .

Bug-Drug Combinations

- Overuse of particular antimicrobials is notorious for promoting resistance to those antimicrobials among certain pathogens
  - Reducing their use is associated with reduced antimicrobial resistance

- Example – Group 2 carbapenems and carbapenem-resistant *Pseudomonas aeruginosa*[1-2]
  - Reduction in use of group 2; and using group 1 (ertapenem) instead, associated with decrease in carbapenem-resistant *P. aeruginosa*

1 – Goldstein, AAC, 53, 2009, 5122-26; 2 – Nicolau, Int J Antimicrob Agents, 39, 2012, 11-15

THE EFFECT OF CHANGES IN THE CONSUMPTION OF MACROLIDE ANTIBIOTICS ON ERYTHROMYCIN RESISTANCE IN GROUP A STREPTOCOCCI IN FINLAND

HELENA SEPPÄLÄ, M.D., TIMO KLAUKKA, M.D., JAANA VUOPIO-VARKILA, M.D., ANNA MUOTIALA, PH.D., HANS HELENIUS, M.SC., KATRINA LAGER, M.SC., PENTTI HUOVINEN, M.D., AND THE FINNISH STUDY GROUP FOR ANTIMICROBIAL RESISTANCE*

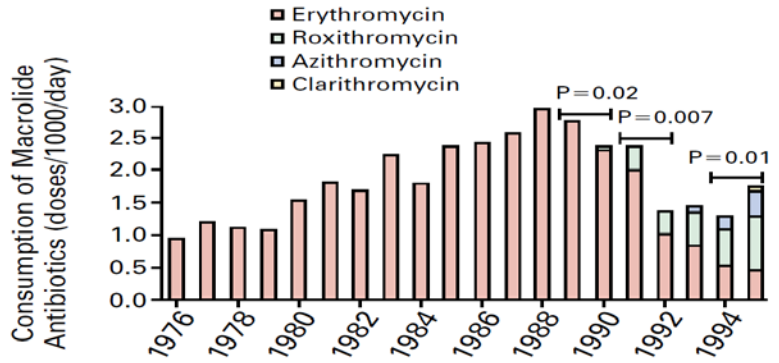


Figure 1. Total Consumption of Macrolide Antibiotics by Outpatients in Finland from 1976 through 1995.
Consumption is expressed in terms of defined daily doses per 1000 inhabitants per day.

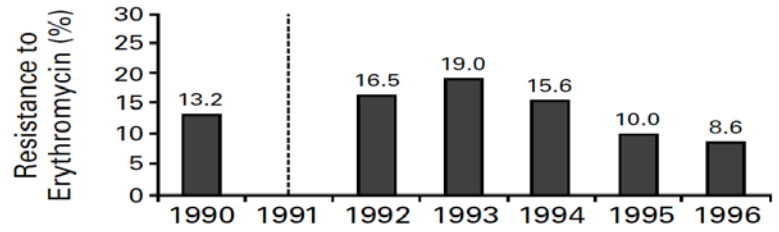


Figure 2. Frequency of Resistance to Erythromycin among Group A Streptococcal Isolates from Throat-Swab and Pus Samples in Finland in 1990 and in 1992 through 1996.
The data from 1990,[3] obtained from six regional microbiology laboratories, are shown here for comparison; the dashed line indicates that the 1990 data were not included in the statistical analyses reported in the text.

- Decreased macrolide use from 2.4 to 1.38 prescriptions per 1000 inhabitants per day
- Macrolide resistance decreased from 16.5% to 8.6%

Bug-Drug Combinations and Resistance - Limitations

- Studies measuring impact of stewardship interventions focused on avoiding certain antimicrobials on resistance have notable limitations
  - Often, increase in use of other antimicrobials and their impact on resistance not thoroughly evaluated
  - These types of “formulary level” interventions are generally performed at the hospital level
    - Impact at an individual patient level - which is where much of day to day activity of stewards is focused – has not been well documented

Different Stewardship Strategies to Combat Hospital-Based Resistance

- Beyond these types of “ bug-drug” examples, it is unclear which systemic stewardship processes are effective in reducing antimicrobial resistance
- Other stewardship strategies to reduce resistance
  - Dosing based
    - Optimize dose so as to reduce antimicrobial resistance
    - Combinations of antimicrobials
  - Reducing/minimizing the use of specific, targeted, broad-spectrum antimicrobial agents/classes
    - De-escalation
  - Reduction in overall antimicrobial use
    - Shortening duration of therapy

Dosing-Based Strategies and the Prevention of Resistance

- In vitro, aggressive dosing strategies can prevent the emergence of resistance
  - Example – quinolones and mutant prevention concentration
    - Concept is to provide high quinolone concentrations locally to overcome highest MIC conferred by first-order mutants, due to point mutations
      - Prevent growth of mutants and thus prevent resistance

- Major limitations
  - In clinical/hospital setting resistance often develops distant from site of infection (such as GI tract)
  - Amount of drug that can be safely administered; MICs of pathogens

Dosing-Based Strategies and the Prevention of Resistance (2)

- Combination therapy has been demonstrated in clinical settings to reduce emergence of resistance in certain pathogens such as HIV, tuberculosis
  - In vitro, combinations have been demonstrated to be effective in preventing the emergence of resistant bacterial subpopulations[1]
  - However, this has not been demonstrated to be effective in clinical studies

1 – Drusano, AAC, 2012, 231-242

De-escalation

- De-escalation is the narrowing of empiric antimicrobial therapy to an agent with a narrower spectrum but that still is effective

- Concept: narrower spectrum agents are less likely to promote antimicrobial resistance to the broader spectrum agents

  - Example: empiric carbapenem is started in the ICU. The patient subsequently has cultures that grow *Escherichia coli* that is susceptible. The patient is switched from meropenem to ceftriaxone.
  - Assumption: collateral damage due to meropenem is worse than due to ceftriaxone
  - Not clear that this is actually the case

De-escalation (cont)

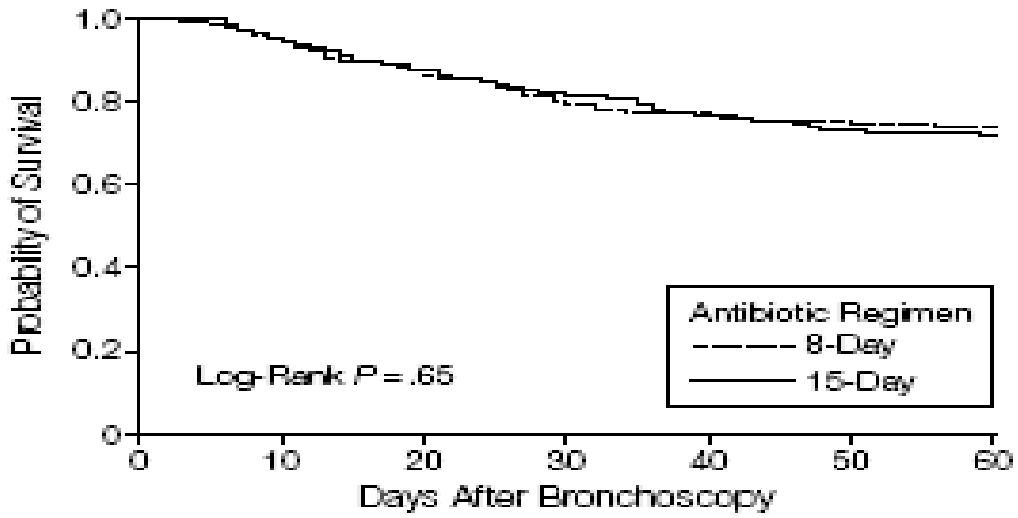
- No studies have demonstrated that this de-escalation reduces antimicrobial resistance
  - Observational/retrospective studies are/will be inherently flawed
    - Confounding by indication – who gets de-escalated and who doesn’t

- De-escalation has become extremely popular in the stewardship world, but its efficacy is not supported by good data

Reduction in Overall Antimicrobial Use

- Concept relatively simple: reduction in overall quantify of antimicrobials reduces amount of selective antimicrobial pressure and collateral damage
- Clinical trial data has supported this

Figure 2. Kaplan-Meier Estimates of the Probability of Survival



No. at Risk							
8-Day Antibiotic Regimen	197	187	172	158	151	148	147
15-Day Antibiotic Regimen	204	194	179	167	157	151	147

Probability of survival is for the 60 days after ventilator-assisted pneumonia onset as a function of the duration of antibiotic administration.

Chastre et al, JAMA, 2003, p 2588-98

Table 4. Primary Study Outcomes 28 Days After Bronchoscopy as a Function of Duration of Antibiotic Administration

Event	No./Total (%) 8-Day Regimen (n = 197)	No./Total (%) 15-Day Regimen (n = 204)	Between-Group Risk Difference (90% CI), %
Death from all causes*			
All patients	37/197 (18.8)	35/204 (17.2)	1.6 (–3.7 to 6.9)
Nonfermenting GNB†	15/64 (23.4)	19/63 (30.2)	–6.7 (–17.5 to 4.1)
MRSA	6/21 (28.6)	5/21 (23.8)	4.8 (–13.9 to 23.4)
Other bacteria	16/112 (14.3)	11/120 (9.2)	5.1 (–0.7 to 10.9)
Pulmonary infection recurrence*			
All patients	57/197 (28.9)	53/204 (26.0)	2.9 (–3.2 to 9.1)
Superinfection‡	39/197 (19.8)	38/204 (18.6)	1.2 (–4.3 to 6.6)
Relapse‡	33/197 (16.8)	23/204 (11.3)	5.5 (0.7 to 10.3)
Nonfermenting GNB†	26/64 (40.6)	16/63 (25.4)	15.2 (3.9 to 26.6)
Superinfection‡	13/64 (20.3)	8/63 (12.7)	7.6 (1.1 to 14.2)
Relapse‡	21/64 (32.8)	12/63 (19.0)	13.8 (7.8 to 19.7)
MRSA	7/21 (33.3)	9/21 (42.9)	–9.5 (–30.1 to 11.1)
Superinfection‡	6/21 (28.6)	5/21 (23.8)	4.8 (–8.8 to 18.3)
Relapse‡	3/21 (14.3)	4/21 (19.0)	–4.8 (–9.9 to 0.4)
Other bacteria	24/112 (21.4)	28/120 (23.3)	–1.9 (–9.5 to 5.6)
Superinfection‡	20/112 (17.9)	25/120 (20.8)	–3.0 (–8.2 to 2.2)
Relapse‡	9/112 (8.0)	7/120 (5.8)	2.2 (–1.3 to 5.7)
	Mean (SD)		Mean Difference (95% CI), %
No. of antibiotic-free days*			
All patients	13.1 (7.4)	8.7 (5.2)	4.4 (3.1 to 5.6)
Nonfermenting GNB†	12.0 (7.4)	7.5 (5.4)	4.5 (2.2 to 6.7)
MRSA	12.9 (7.0)	4.9 (5.7)	8.0 (4.6 to 12.1)
Other bacteria	13.7 (7.5)	10.0 (4.6)	3.7 (2.1 to 5.3)

Among patients with recurrent pulmonary infections, multi-drug resistant pathogens were significantly less common in the 8-day arm
(42.1% vs 62.3%, p=0.04)

Short-course Empiric Antibiotic Therapy for Patients with Pulmonary Infiltrates in the Intensive Care Unit

A Proposed Solution for Indiscriminate Antibiotic Prescription

NINA SINGH, PAUL ROGERS, CHARLES W. ATWOOD, MARILYN M. WAGENER, and VICTOR L. YU

- Clinical pulmonary infection score (CPIS) incorporates readily available data (eg temp, purulence, CXR findings) into a score predicting likelihood of pneumonia
- Patients with CPIS < 6 randomized to standard therapy (treatment per physician discretion) vs ciprofloxacin monotherapy with reevaluation at day 3
  - In Cipro arm, Cipro discontinued if CPIS remained < 6 at day 3 of therapy
  - Patients treated for pneumonia if CPIS ≥ 6 at day 3

TABLE 2

ANTIBIOTIC USAGE, DURATION, AND COST IN THE EXPERIMENTAL AND STANDARD THERAPY GROUPS

Variable	Experimental (*n* = 39)	Standard Therapy (*n* = 42)	p Value
Deaths at 3 d	0% (0/39)	7% (3/42)	NS*
CPIS > 6 at 3 d	21% (8/39)	23% (9/39)	NS
Extrapulmonary infections†	18% (7/39)	15% (6/39)	NS
Antibiotic continuation > 3 d	28% (11/39)	97% (38/39)	0.0001
Antibiotics in patients with CPIS ≤ 6 and no extrapulmonary infection			
Continuation < 3 d	0% (0/25)	96% (24/25)	0.0001
Duration of antibiotics, d, mean (range)	3 (3)	9.8 (4–20)	0.0001
Cost, mean	$259	$640	0.0001
Total	$6,482	$16,004	

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TABLE 5

ANTIMICROBIAL RESISTANCE AND SUPERINFECTIONS IN THE EXPERIMENTAL AND STANDARD THERAPY GROUPS

Variable	Experimental	Standard Therapy	p Value
Antimicrobial resistance and/or superinfections*	14% (5/37)	38% (14/37)	p = 0.017
Microorganisms†			
Pseudomonas aeruginosa	8% (3/37)	16% (6/37)	
Enterobacter cloacae	—	5% (2/37)	
MRSA	5% (2/37)	14% (5/37)	
Pseudomonas cepacia	3% (1/37)	—	
Citrobacter freundii	—	3% (1/37)	
Pseudomonas stutzeri	—	3% (1/37)	
Enterococcus species	3% (1/37)	11% (4/37)	
E. faecalis	1	3	
Vancomycin-resistant *E. faecium*	0	1	
Candida species	8% (3/37)	14% (5/37)	
C. albicans	3	3	
C. glabrata	0	2	

Shorter Durations are in Vogue

- In addition to HAP/VAP, other disease states are now being studied
- Intra-abdominal infection: Study comparing 4 vs 10 days of therapy showed no advantage of longer duration therapy[1]
- CAP in hospitalized patients: study comparing 5 vs. 10 days of therapy showed no advantage of longer duration therapy[2]
- Increasing focus on curtailing duration of therapy by antimicrobial stewardship programs
- Other diseases states that remain a challenge with regards to duration
  - Skin and soft tissue infection
  - Complicated urinary tract infection

1 – Sawyer et al, n engl j med 372;21, 2015 1996-2005; 2- Uranga, JAMA Internal Medicine 176,9, 2016, 1257-65

Different Stewardship Strategies to Combat Hospital-Based Resistance

- Other stewardship strategies to reduce resistance
  - Dosing based – in vitro data to support[1]
    - Optimize dose so as to reduce antimicrobial resistance
    - Combinations of antimicrobials
      - No good clinical data to support reduction in antimicrobial resistance
  - Reducing/minimizing the use of specific, targeted, broad-spectrum antimicrobial agents/classes
    - De-escalation
      - No good clinical data to support reduction in antimicrobial resistance (but commonly practiced)
  - Reduction in overall antimicrobial use
    - Shortening duration of therapy[2,3]
      - Data from randomized controlled trials supporting reduction in antimicrobial resistance
        - Pneumonia, intra-abdominal infection

[1] Drusano et al, AAC, 2012, 231-242; [2]Chastre et al, JAMA, 2003, p 2588-98; [3]Singh, AJRCC, 2000, p 505-11

Knowledge Gaps/Research Opportunities Related to Antimicrobial Stewardship and Antimicrobial Resistance

- De-escalation – impact of different algorithms in various settings/scenarios
  - Prospective, controlled studies utilizing patient-level resistance endpoints
- Duration of therapy – shorter durations for skin and skin structure infection, complicated UTI
  - Signs, symptoms, infection characteristics to guide duration
  - Establishing efficacy, safety of shorter therapies in prospective trials
- Dosing strategies, combination therapy
  - Is there a role for combination therapy in preventing emergence of resistance
- Implementation of effective stewardship processes in settings where there is little (if any) expertise
- Rapid diagnostics
  - Faster results
  - Utilization, implementation

Stewardship Strategies to Curtail Resistance: Conclusions

- Stewardship improves clinical outcomes and can reduce resistance
  - Except mechanism not clearly understood
- Best data available supports decreasing overall antimicrobial use to reduce resistance
  - Shorter durations of therapy in hospital-acquired pneumonia
  - More recent studies have evaluated shorter durations in intra-abdominal infection and community-acquired pneumonia
- No good clinical data supporting dosing strategies (including combination therapy)
- No good data supporting systematic de-escalation approaches to reduce antimicrobial resistance
  - This however doesn’t mean that this is not worth doing
- Clinical trials with antimicrobial resistance endpoints are needed

Facilitated by NYSPFP Staff

Next Steps

- Connect with your NYSPFP Project Manager to help you strengthen your ASP
- Watch for NYS Partnership for Patients announcements and upcoming events in your inbox