Prevention of Multidrug Resistant Organism Spread in the Hospital – Strategies Targeting the Patient

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Overview

- The patient as reservoir for multidrug-resistant organisms (MDROs)
- Preventing MDRO spread – strategies focused on the patient
  - Contact precautions
  - Active surveillance
  - Cohorting
  - Topical decolonization
  - Antimicrobial stewardship
- Importance of bundled approaches to controlling MDRO spread

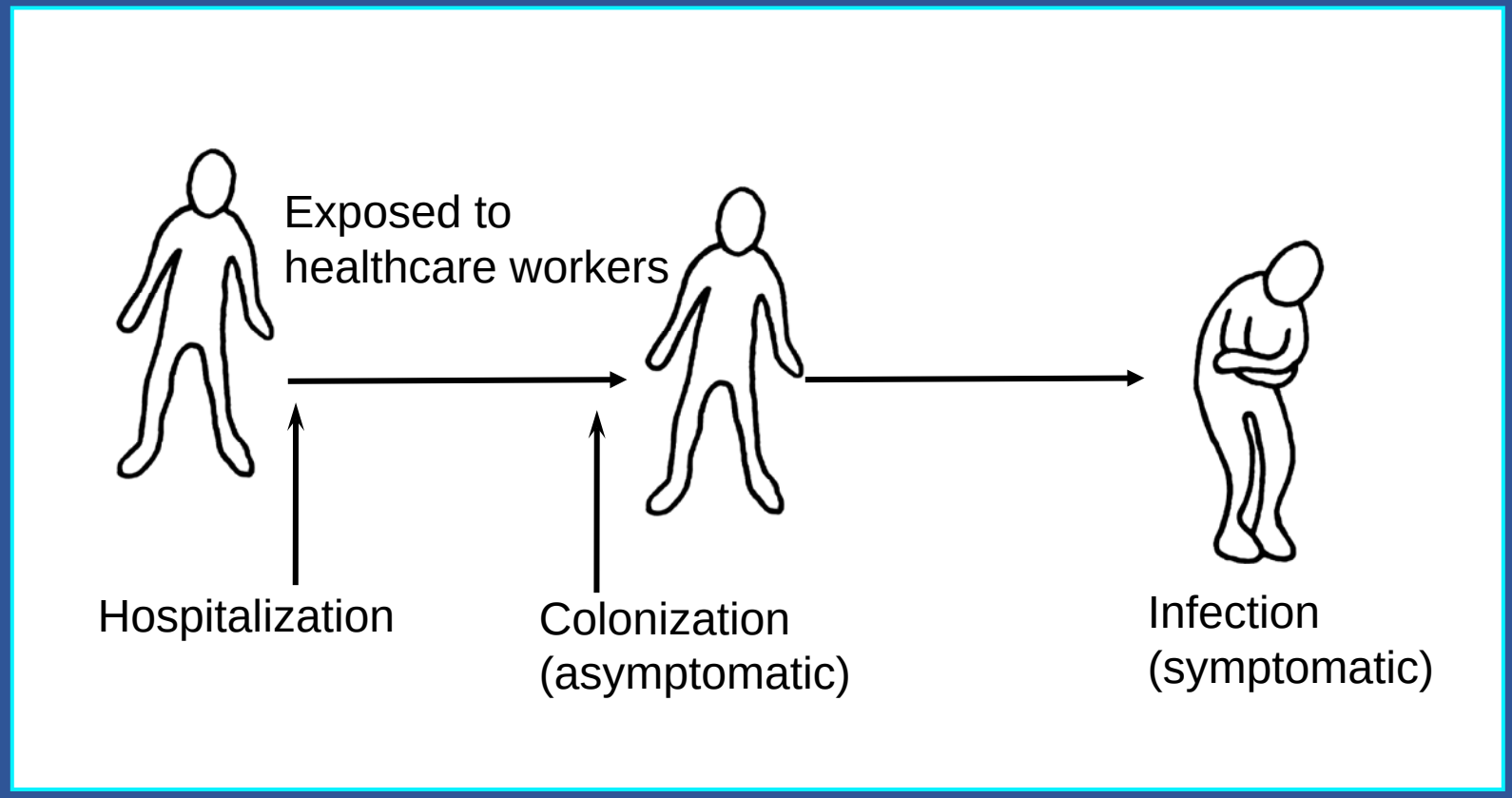
Modes of Transmission for Pathogens (Including MDROs) in the Hospital

- Contact Transmission (bacteria, most common)
- Droplet Transmission (influenza, meningococcus)
- Airborne/aerosol transmission (TB)
- Blood and Body Fluids (needlesticks: HIV, HCV)
- Food and Water
- Vector -borne

Pathogenesis of HAI

- Usually bacterial infection
- Colonization usually precedes infection
  - Both colonized and infected patients are contagious
- Bugs are spread among patients, environment
  - Healthcare workers (HCWs) - hands, equipment (eg stethoscope)
    - Transient colonization most common
  - Environment
- Major risks: indwelling devices, debilitated state
  - More frequent contact with HCW, higher risk
- Prevention: hand hygiene, contact precautions, patient isolation, cohorting

Pathogenesis of HAI



Reservoirs for MDROs in the Hospital

- Patient
- Healthcare worker
- Environment

Horizontal Interventions Aimed at Reducing Transmission of All Pathogens

- Standard precautions (hand hygiene, barrier precautions when required)
- Environmental cleaning and disinfection
- Minimizing unnecessary medical devices
- Universal gowning and gloving
- Universal decolonization of all patients (CHG bath)

Vertical Interventions Aimed at Reducing Transmission of a Particular Pathogen

- Active surveillance for a particular pathogen
- Targeted decolonization for a particular pathogen
  - Search and destroy
- Contact precautions for specific pathogens
- Isolation and/or cohorting for specific pathogens

Contact Precautions

- Involves use of gown and gloves for contact with patient and/or patient's environment

- CDC recommends "for all patients infected with target multidrugresistant organisms(MDROs) and for patients that have been previously identified as being colonized with target MDROs"
  - Single patient room, dedicated equipment (stethoscope)

- In the US, primarily used for MRSA, VRE (and *C. difficile*)
  - When clinical cultures are used, ~ 5-10% of patients isolated; with active surveillance, ~ 20-25% isolated

Morgan et al, JAMA October 8, 2014 Volume 312, Number 14, 1395-6

Contact Precautions (cont)

- Limitations of contact precautions include
  - Gown and glove use (expense and time)
  - ? Fewer room visits by providers
  - ? Associated adverse events
  - Efficacy has not been demonstrated in endemic settings for MRSA, VRE
  - In some studies, MRSA acquisition rates relatively uncommon in the hospital
  -
- Until fairly recently, no prospective studies evaluating contact precautions and impact on prevention of MRSA, VRE acquisition in endemic hospital settings until . . .

Morgan et al, JAMA October 8, 2014 Volume 312, Number 14, 1395-6

Original Investigation

Universal Glove and Gown Use and Acquisition of Antibiotic-Resistant Bacteria in the ICU

A Randomized Trial

Anthony D. Harris, MD, MPH; Lisa Pineles, MA; Beverly Belton, RN, MSN; J. Kristie Johnson, PhD; Michelle Shardell, PhD; Mark Loeb, MD, MSc; Robin Newhouse, RN, PhD; Louise Dembry, MD, MS, MBA; Barbara Braun, PhD; Eli N. Perencevich, MD, MS; Kendall K. Hall, MD, MS; Daniel J. Morgan, MD, MS; and the Benefits of Universal Glove and Gown (BUGG) Investigators

- Cluster-randomized trial in 20 medical and surgical ICUs in 20 US hospitals from January 4, 2012, to October 4, 2012
- In the intervention ICUs, all health care workers were required to wear gloves and gowns for all patient contact and when entering any patient room
- The primary outcome was acquisition of MRSA or VRE based on surveillance cultures collected on admission and discharge from the ICU
- Secondary outcomes included individual VRE acquisition, MRSA acquisition, frequency of health care worker visits, hand hygiene compliance, health care–associated infections, and adverse events

JAMA, 2013

Table 2. Rates at Risk of Acquisition of Antibiotic-Resistant Bacteria per 1000 Patient-Days

	Intensive Care Units							
	Intervention			Control				
	No. of Acquisitions	Patient-Days at Risk	Mean Rate (95% CI)[a]	No. of Acquisitions	Patient-Days at Risk	Mean Rate (95% CI)[a]	Difference (95% CI)[b]	*P* Value[c]
Drug-Resistant Bacteria								
VRE or MRSA								
Study period	577	32 693.0	16.91 (14.09 to 20.28)	517	31 765.0	16.29 (13.48 to 19.68)		
Baseline	178	8684.0	21.35 (17.57 to 25.94)	176	9804.5	19.02 (14.20 to 25.49)		
Change[d]			−4.47 (−9.34 to 0.45)			−2.74 (−6.98 to 1.51)	−1.71 (−6.15 to 2.73)	.57
VRE								
Study period	411	27 765.5	13.59 (10.26 to 17.99)	337	28 340.5	11.88 (8.65 to 16.33)		
Baseline	108	7691.5	15.18 (10.50 to 21.95)	122	8818.0	14.37 (10.31 to 20.02)		
Change[d]			−1.60 (−7.18 to 3.98)			−2.48 (−5.53 to 0.56)	0.89 (−4.27 to 6.04)	.70
MRSA								
Study period	199	30 454.5	6.00 (4.63 to 7.78)	191	30 024.0	5.94 (4.59 to 7.67)		
Baseline	77	7841.0	10.03 (8.05 to 12.50)	59	9182.0	6.98 (4.50 to 10.83)		
Change[d]			−4.03 (−6.50 to −1.56)			−1.04 (−3.37 to 1.28)	−2.98 (−5.58 to −0.38)	.046

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus;* VRE, vancomycin-resistant *Enterococcus*.

[a] Per 1000 patient-days at risk.

[b] Absolute difference in absolute changes $(\text{study period} - \text{baseline})_{\text{intervention ICUs}} - (\text{study period} - \text{baseline})_{\text{control ICUs}}$.

[c] From weighted paired *t* test on the log scale with 9 degrees of freedom.

[d] Absolute change, study period −baseline.

Table 3. Average Hand-Hygiene Compliance and Health Care Worker Visits per Hour

	Intensive Care Units							
	Intervention			Control				
	No. of Events	No. of Observations[a]	Mean (95% CI), %[b]	No. of Events	No. of Observations[a]	Mean (95% CI), %[b]	Mean Difference (95% CI), %[c]	*P* Value[d]
Hand-hygiene compliance, %								
Room entry	1563	2828	56.1 (47.2 to 66.7)	1644	3231	50.2 (41.4 to 60.9)	5.91 (−6.91 to 18.7)	.42
Room exit	2027	2649	78.3 (72.1 to 85.0)	2080	3266	62.9 (54.4 to 72.8)	15.4 (8.99 to 21.8)	.02
Health care-worker visits	3213	756.5	4.28 (3.95 to 4.64)	3775	716.5	5.24 (4.46 to 6.16)[e]	−0.96 (−1.71 to −0.21)	.02

[a] Observed entries and observed exits for hand-hygiene compliance, number of hours of observation for health care worker visits.

[b] Percent for hand-hygiene compliance, per hour of observation for health care worker visits.

[c] Absolute difference (intervention intensive care units [ICUs] −control ICUs).

[d] From weighted paired *t* test on the log scale with 9 degrees of freedom.

[e] In control ICUs, those patients on contact precautions had 4.78 mean visits per hour from health care workers.

The Effect of Universal Glove and Gown Use on Adverse Events in Intensive Care Unit Patients

Lindsay D. Croft,[1] Anthony D. Harris,[1,2] Lisa Pineles,[1] Patricia Langenberg,[1] Michelle Shardell,[1] Jeffrey C. Fink,[1,2,3] Linda Simoni-Wastila,[4] and Daniel J. Morgan[1,2]; for the Benefits of Universal Glove and Gown (BUGG) Primary Investigators

[1]Department of Epidemiology and Public Health, University of Maryland School of Medicine, [2]VA Maryland Healthcare System, [3]Department of Medicine, Division of General Internal Medicine, University of Maryland School of Medicine, and [4]Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore

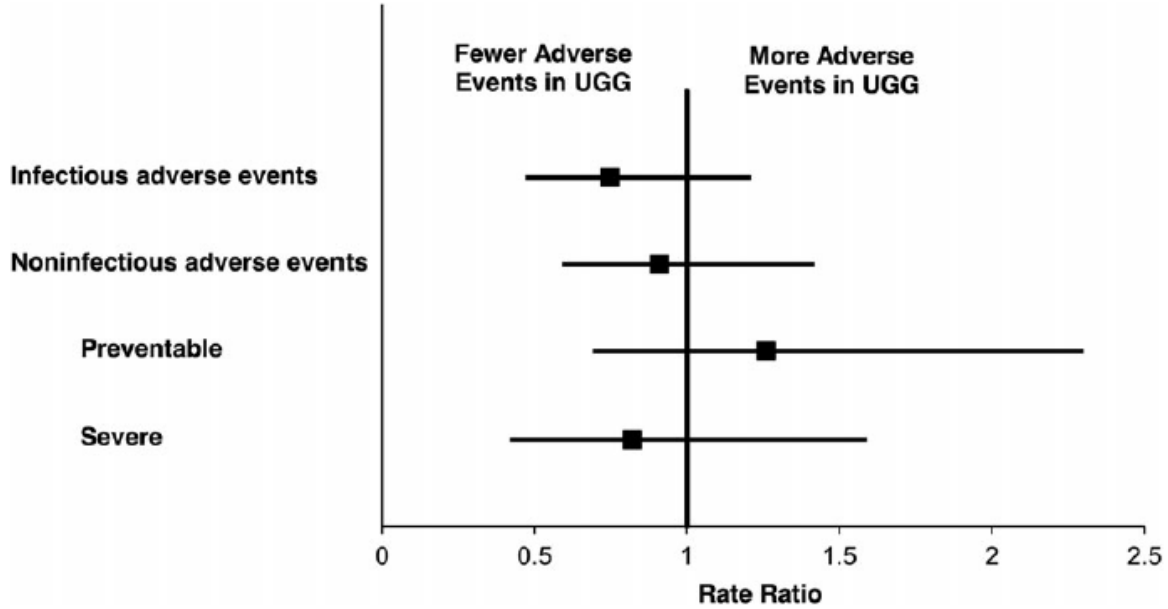


Figure 1. Adjusted rate of adverse events among 900 patients in universal glove and gown (UGG) use intensive care units (ICUs) compared with 900 patients in control ICUs by subtype of adverse event.Each adverse event model is adjusted for ICU type (combined medical-surgical ICU [MICU-SICU], SICU only [reference: MICU only]), case mix index ≤1.83, nonacademic hospital setting, and ICU bed size. Boxes represent rate ratio point estimate and lines represent 95% confidence intervals.

Reconsidering Contact Precautions for Endemic Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant *Enterococcus*

Daniel J. Morgan, MD, MS;[1] Rekha Murthy, MD;[2] L. Silvia Munoz-Price, MD, PhD;[3] Marsha Barnden, RNC, MSN, CIC;[4] Bernard C. Camins, MD, MSc;[5] B. Lynn Johnston, MD, MSc;[6] Zachary Rubin, MD;[7] Kaede V. Sullivan, MD;[8] Andi L. Shane, MD, MPH, MSc;[9] E. Patchen Dellinger, MD;[10] Mark E. Rupp, MD;[11] Gonzalo Bearman, MD, MPH[12]

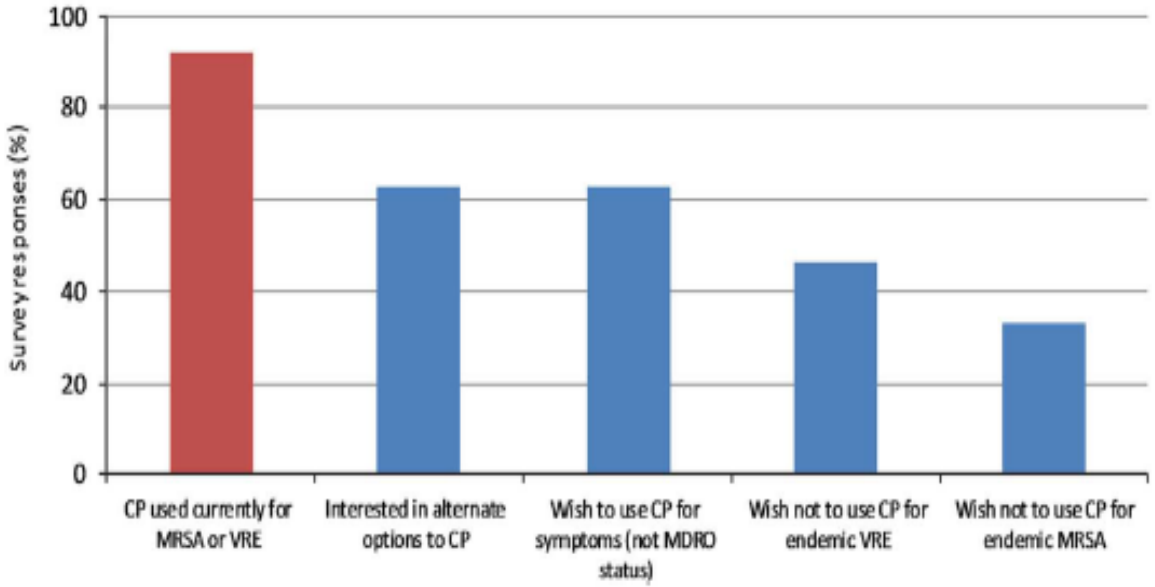


FIGURE 1. Results from Society for Healthcare Epidemiology of America Research Network survey respondents regarding opinions for use of contact precautions (CP). MDRO, multidrug-resistant organisms; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus*.

- Literature review - No high quality data support or reject use of CP for endemic MRSA or VRE
- Survey of 87 member hospitals of SHEA Research Network

Infection Control & Hospital Epidemiology, 2015, pp 1163 - 1172

Infection Control Successes for CRE Prevention: A Nationwide Intervention

- Israeli experience
  - Nationwide intervention
  - Ministry of Health mandated reporting of CRE, isolation of patients with CRE, and other contact measures to decrease transmission
  - Self-contained nursing units for patients (ie cohorting of patients and nurses)

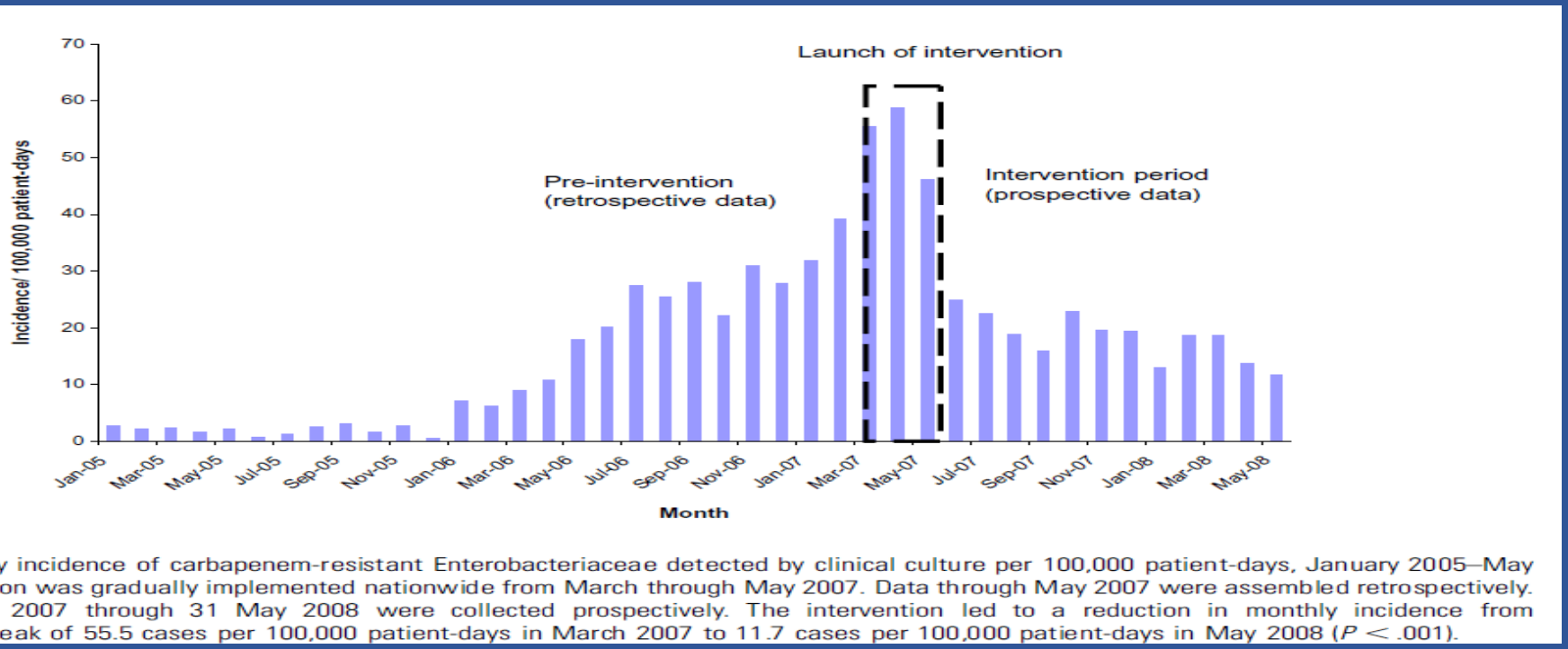


Figure 1. Monthly incidence of carbapenem-resistant Enterobacteriaceae detected by clinical culture per 100,000 patient-days, January 2005–May 2008. The intervention was gradually implemented nationwide from March through May 2007. Data through May 2007 were assembled retrospectively. Data from 1 June 2007 through 31 May 2008 were collected prospectively. The intervention led to a reduction in monthly incidence from a pre-intervention peak of 55.5 cases per 100,000 patient-days in March 2007 to 11.7 cases per 100,000 patient-days in May 2008 ($P < .001$).

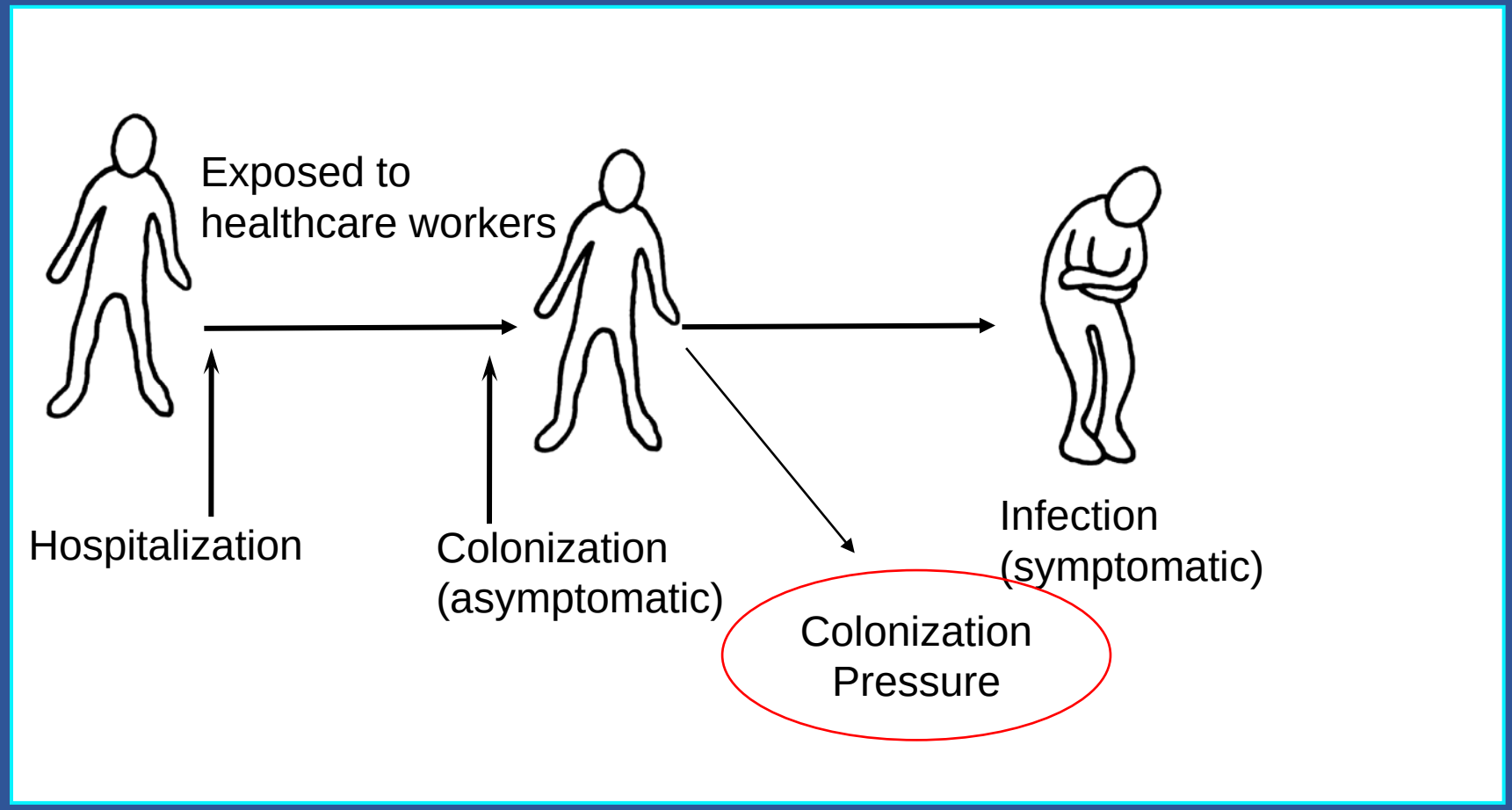
\Scwaber MJ et.al. Clin Infect Dis. 2011;52(7):848-55

Conclusion:
Contact Precautions for MRSA, VRE

- Most hospitals in US use contact precautions for MRSA, VRE
  - Many hospitals are reconsidering
- Recent data suggests more effect on decreasing MRSA than VRE
- Contact precautions often used for CRE, XDR-GNB
- Adverse events do not appear to be more common among patients in contact isolation
- Healthcare workers enter the room less frequently when a patient is on contact isolation

Active Surveillance Testing

- Based on the observation that active surveillance reflects colonization pressure better than clinical specimens (passive surveillance)



Active Surveillance and Contact Precautions To Prevent CRE

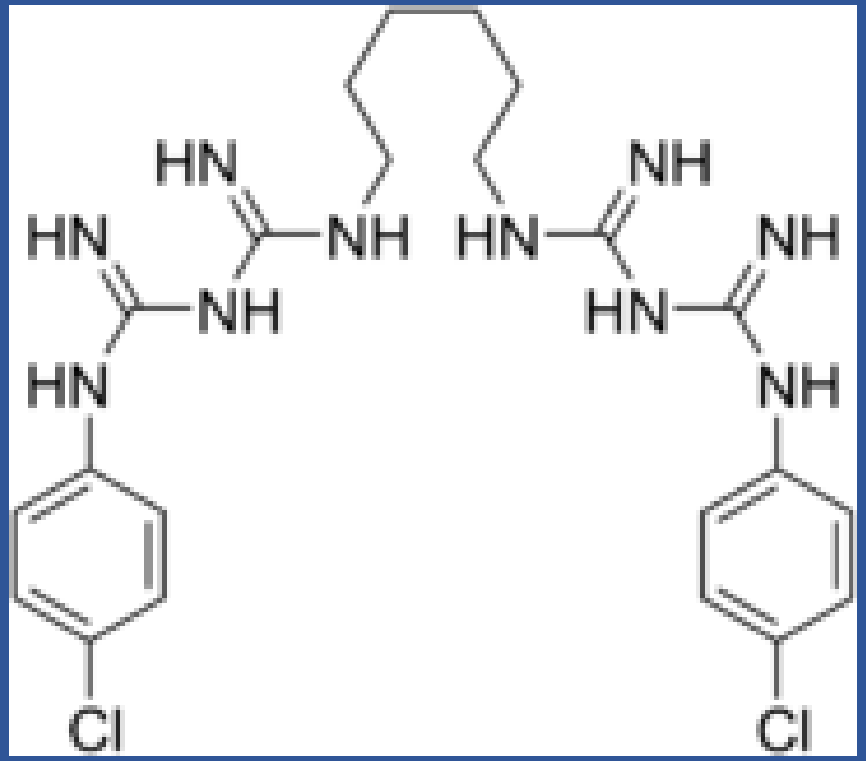
- Montefiore Medical Center
- ICU based initiative
- Active surveillance for detection of CRE coupled with contact precautions for all colonized patients
- Led to 53% reduction in prevalence of CRE colonization in the unit

MMWR. June 22,2012 61(24)

Active Surveillance and Contact Precautions for MDROs - Summary

- Primarily used for MRSA, VRE
- CRE - often used in conjunction with other modalities
- Other MDROs less experience
  - ESBL producing *Enterobacteriaceae*
    - Mostly evaluated in outbreak settings.
    - May not be effective when prevalence is very low or very high
  - Carbapenem resistant *P. Aeruginosa*
    - No evidence to support or refute
  - *A. baumannii*
    - Effective in outbreak settings, might be effective in endemic settings as well

Chlorhexidine



- In healthcare, Chlorhexidine Digluconate (CHG) is one of the common forms of Chlorhexidine
- Soluble in water - - enhances delivery of CHG
- Chlorhexidine Diacetate (DHA) has been bonded with polyurethane for use in medical devices

Mechanism of Action

- Broad spectrum (Gram-positive, Gram-negative bacteria, fungi)
- Bactericidal and/or bacteriostatic depending on concentration
- Works rapidly (can kill 100% of bacteria within 30 seconds)
- Can kill all categories of microbes

Role of CHG Bathing With Regards to Hospital Infection and MDRO

- Protect the patient
  - Decrease the degree of colonization/burden of pathogens on skin of individual patient
  - By doing so, decrease risk for device-related infection (ie CLABSI)

- Protect other patients
  - By decreasing the burden of pathogens on an individual patient, the likelihood of spread to other patients (via contaminated healthcare workers and/or environment) is decreased

Daily bathing strategies and cross-transmission of multidrug-resistant organisms: Impact of chlorhexidine-impregnated wipes in a multidrug-resistant gram-negative bacteria endemic intensive care unit

Jesus Ruiz MD [a], Paula Ramirez PhD [b,*], Esther Villarreal MD [a], Monica Gordon PhD [b], Inmaculada Saez NP [b], Alfonso Rodríguez MD [b], María Jesús Castañeda NP [b], Álvaro Castellanos-Ortega PhD [b]

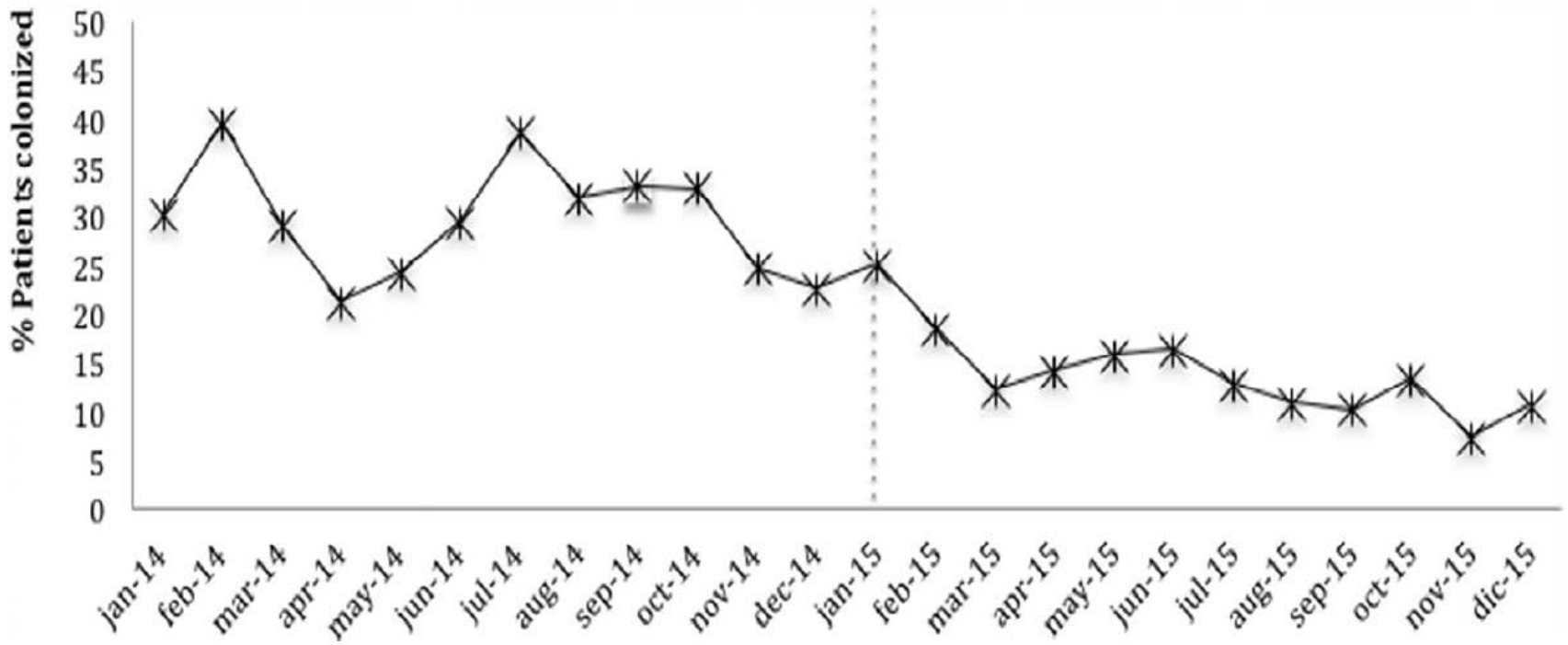
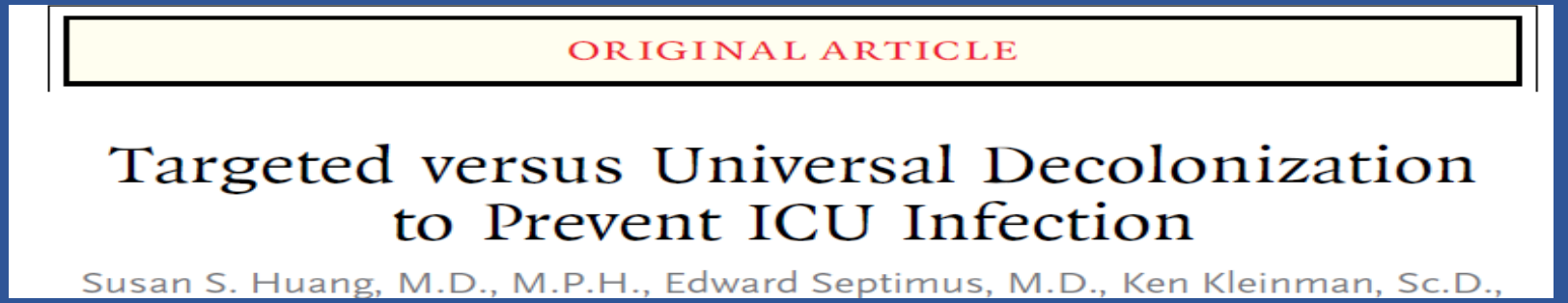


Fig 1. Trends in the colonization incidence during the pre- and postintervention periods.

- CHG bathing of all patients on mechanical ventilation or colonized with MDRO
- Significant reduction in MDRO acquistion

American Journal of Infection Control 45 (2017) 1069-73


ORIGINAL ARTICLE

Targeted versus Universal Decolonization to Prevent ICU Infection

Susan S. Huang, M.D., M.P.H., Edward Septimus, M.D., Ken Kleinman, Sc.D.,

- Three group, cluster randomized multicenter prospective trial in ICU (n=74,000)
  - Group 1- Screening and isolation for MRSA if positive test or previous H/O MRSA colonization
  - Group 2- Screening + targeted decolonization - +ve patients underwent 5 day regimen of mupirocin to bilateral nares and CHG cloth bathing
  - Group 3- Universal decolonization- No screening and every patient admitted to ICU received decolonization as did +ve patients in group 2

N Engl J Med 2013;368:2255-65

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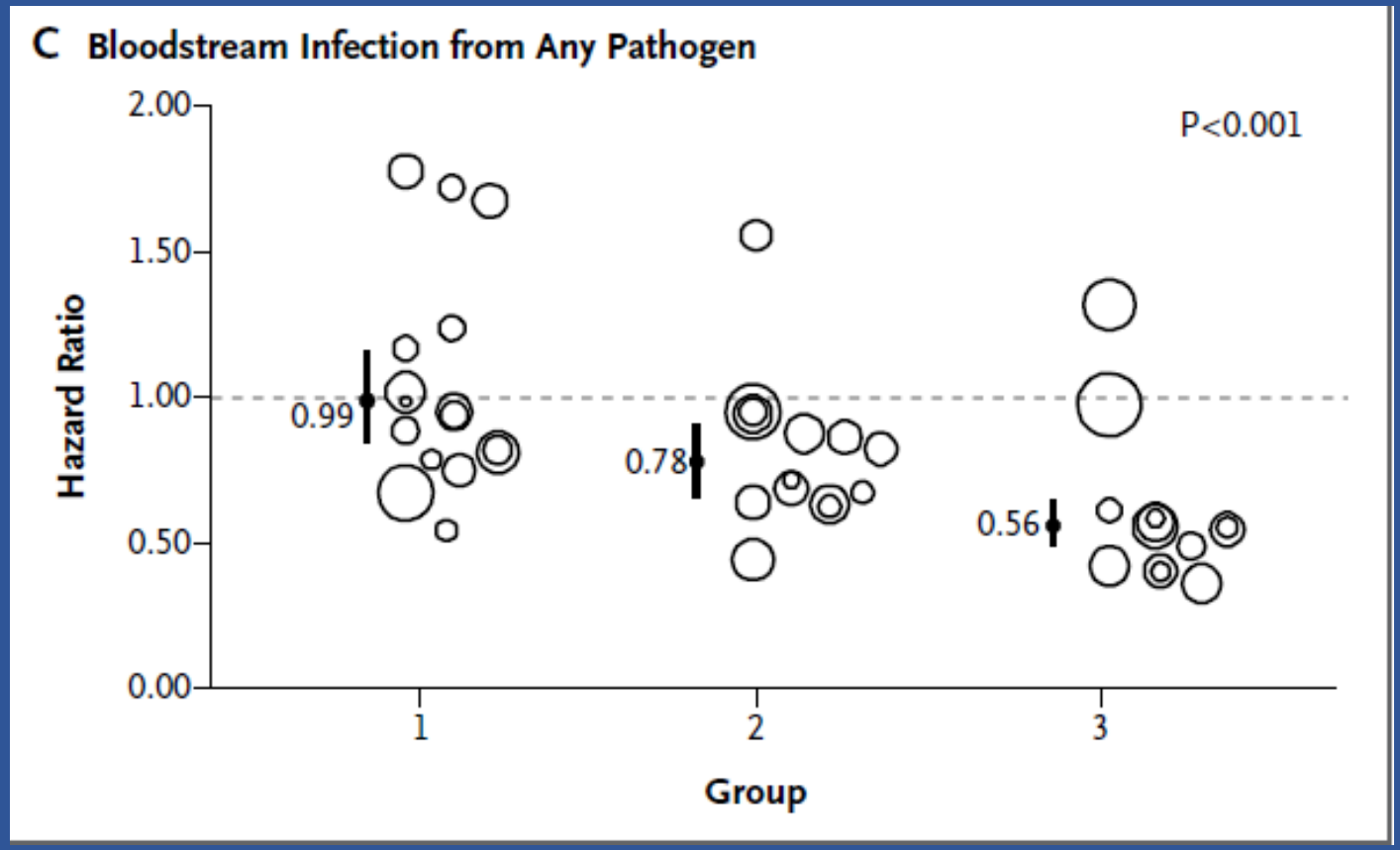
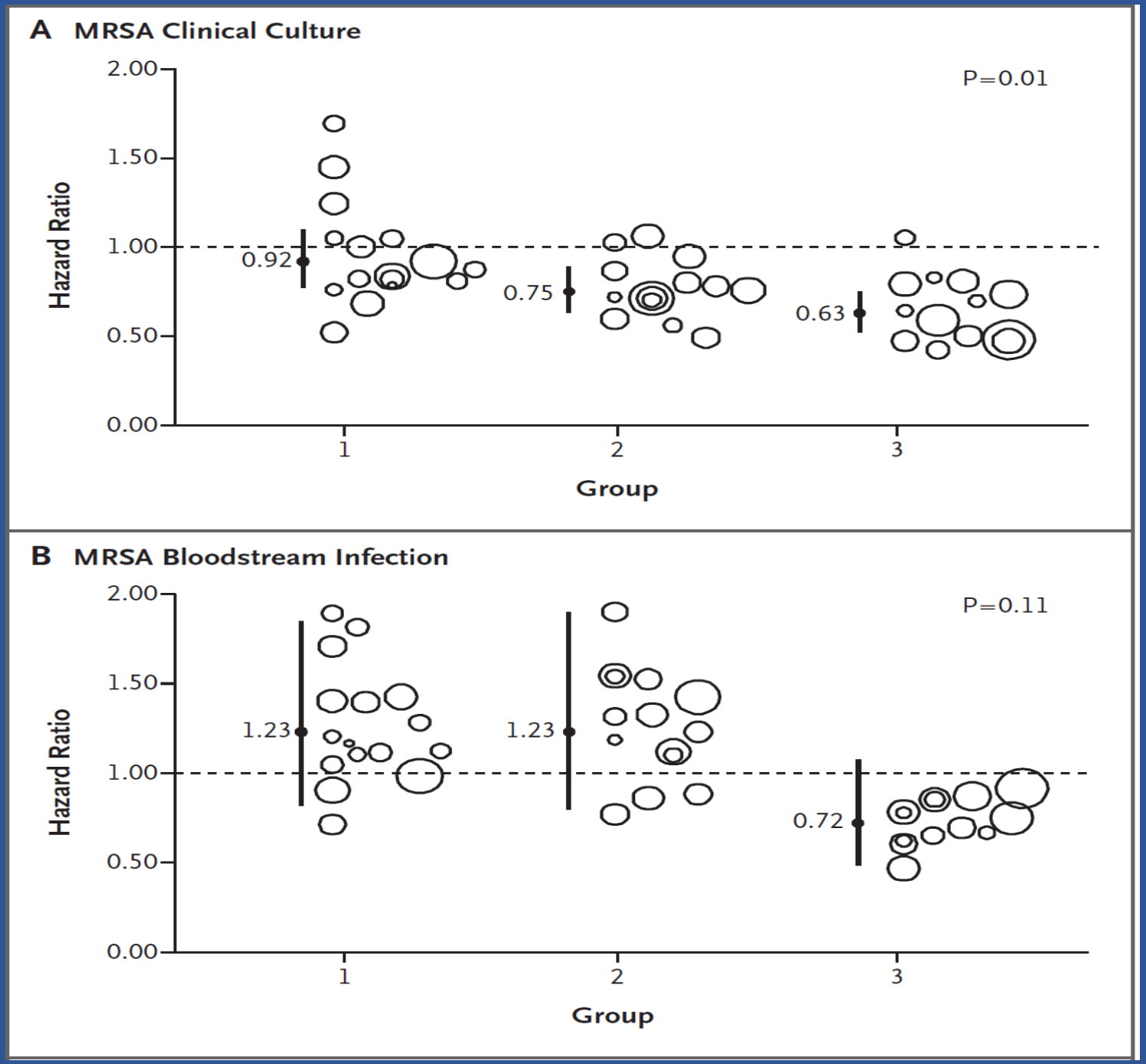


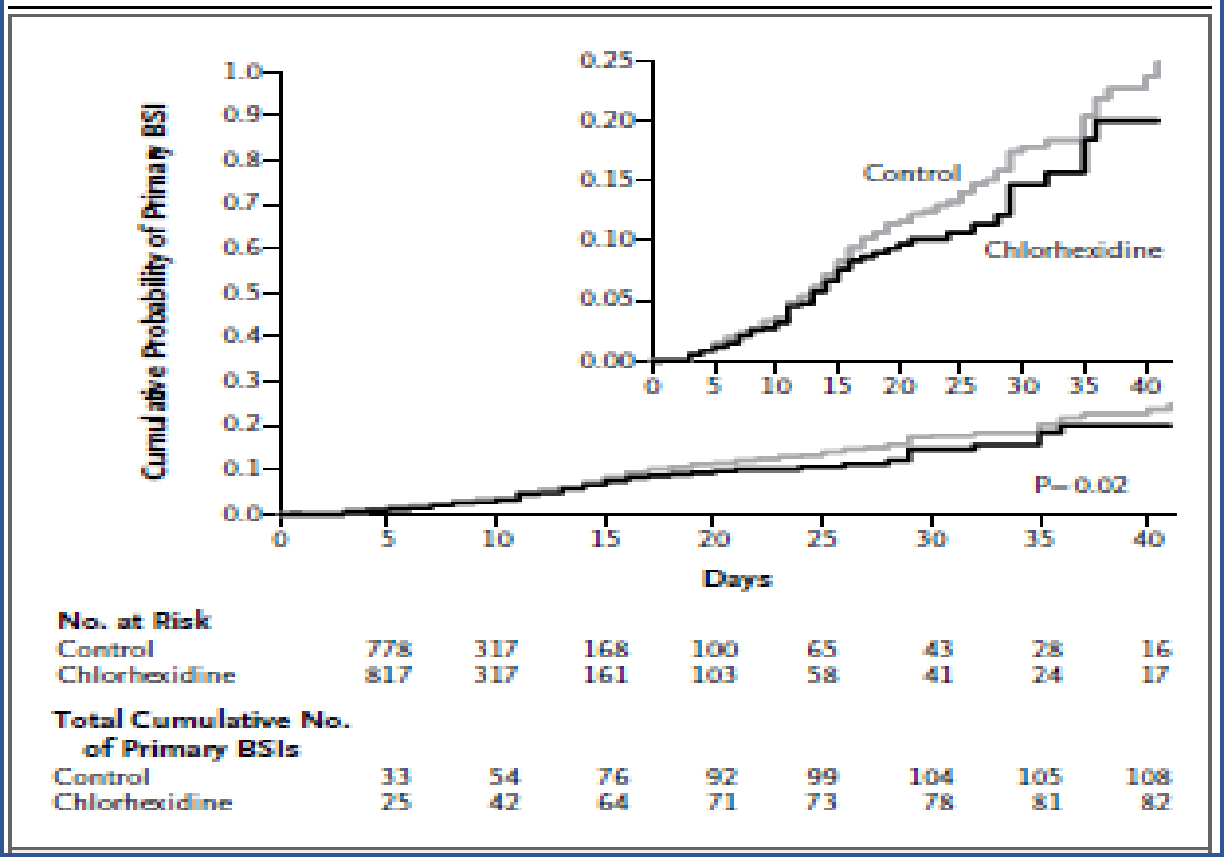

A MRSA Clinical Culture
P=0.01
Hazard Ratio
2.00
1.50
1.00
0.50
0.00
0.92
0.75
0.63
1
2
3
Group
B MRSA Bloodstream Infection
P=0.11
Hazard Ratio
2.00
1.50
1.00
0.50
0.00
1.23
1.23
0.72
1
2
3
Group

Effect of Daily Chlorhexidine Bathing on Hospital-Acquired Infection

Michael W. Climo, M.D., Deborah S. Yokoe, M.D., M.P.H., David K. Warren, M.D.,

N Engl J Med 2013;368:533-42.

Multicenter, cluster-randomized, nonblinded crossover trial to evaluate the effect of daily bathing with chlorhexidine-impregnated washcloths on the acquisition of MDROs and the incidence of hospital-acquired bloodstream infections



No. at Risk								
Control	778	317	168	100	65	43	28	16
Chlorhexidine	817	317	161	103	58	41	24	17
Total Cumulative No. of Primary BSIs								
Control	33	54	76	92	99	104	105	108
Chlorhexidine	25	42	64	71	73	78	81	82

- Decrease in hospital acquired bloodstream infections by 28% (p=0.007)
- Decrease in acquisition of MDRO (MRSA and VRE) by 23% (p=0.03) (5.1 vs 6.6 per 1000 patient days)

CHG Bathing – Summary

- Wealth of evidence suggests that routine, daily CHG bathing of ICU patients
  - Decreases CLABSI and primary BSI
  - Decreases MDRO acquisition
  - Seems to be most effective in populations with relatively high BSI, MDRO rates
- Unanswered questions
  - Non-ICU populations
  - Cloths vs solution
  - Resistance concerns – has occurred, but relatively “low-level”

Bundles for MDROs

- Process bundles effective in reducing device-associated infections
- Increasingly apparent that in many cases, no single process can optimally prevent MDRO acquisition
- Antimicrobial resistance bundles have been effective in preventing MDRO acquisition

Prevention of Colonization and Infection by *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae in Long-term Acute-Care Hospitals

Mary K. Hayden,[1,2] Michael Y. Lin,[1] Karen Lolans,[2] Shayna Weiner,[1] Donald Blom,[1] Nicholas M. Moore,[3] Louis Fogg,[4] David Henry,[5] Rosie Lyles,[6] Caroline Thurlow,[1] Monica Sikka,[1] David Hines,[7] and Robert A. Weinstein[1,6]; for the Centers for Disease Control and Prevention Epicenters Program

- Stepped-wedge design
- Bundled intervention in 4 LTACs
  - Screening patients for KPC rectal colonization upon admission and every other week
  - Contact isolation and geographic separation of KPC positive patients in ward cohorts or single rooms
  - Daily CHG bathing
  - HCW education and monitoring
- Outcome: colonization and infection due to KPC

Clinical Infectious Diseases, 2015; p 1153–61

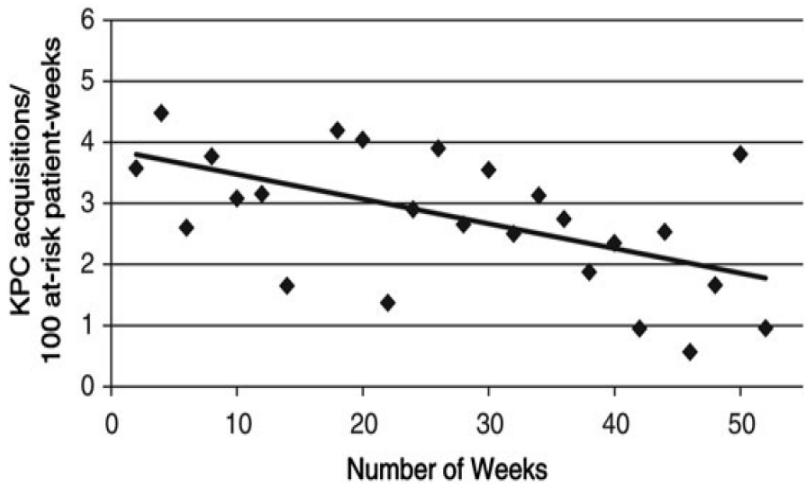


Figure 3. Incidence rate of *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae (KPC) rectal colonization during the intervention period. Each data point represents the number of patients who acquired KPC per 100 patient-weeks, averaged over the preceding 2 weeks. Definite incident cases and data for the first 52 weeks during which each of the 4 long-term acute-care hospitals participating in the study are shown. $P = .004$ for linear decline.

Table 3. Effect of Intervention Bundle on Clinical Cultures and Blood Culture Contamination

	Preintervention[a]			Intervention[a]				
Outcome	No. of Events	Events/1000 Patient-days	95% CI	No. of Events	Events/1000 Patient-days	95% CI	Change in Event Rate	*P* Value
KPC in any clinical culture	656	3.7	3.4–4.0	285	2.5	2.2–2.8	−1.2	.001
KPC bloodstream infection	165	0.9	.8–1.1	48	0.4	.3–.5	−0.5	.008
Bloodstream infection due to any pathogen	2004	11.2	10.7–11.7	870	7.6	7.1–8.1	−3.6	.006
Contaminated blood culture	865	4.9	4.5–5.2	261	2.3	2.0–2.6	−2.6	.03

Abbreviations: CI, confidence interval; KPC, *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae.

[a] There were 178 516 patient-days in the preintervention period and 114 070 patient-days in the intervention period.

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

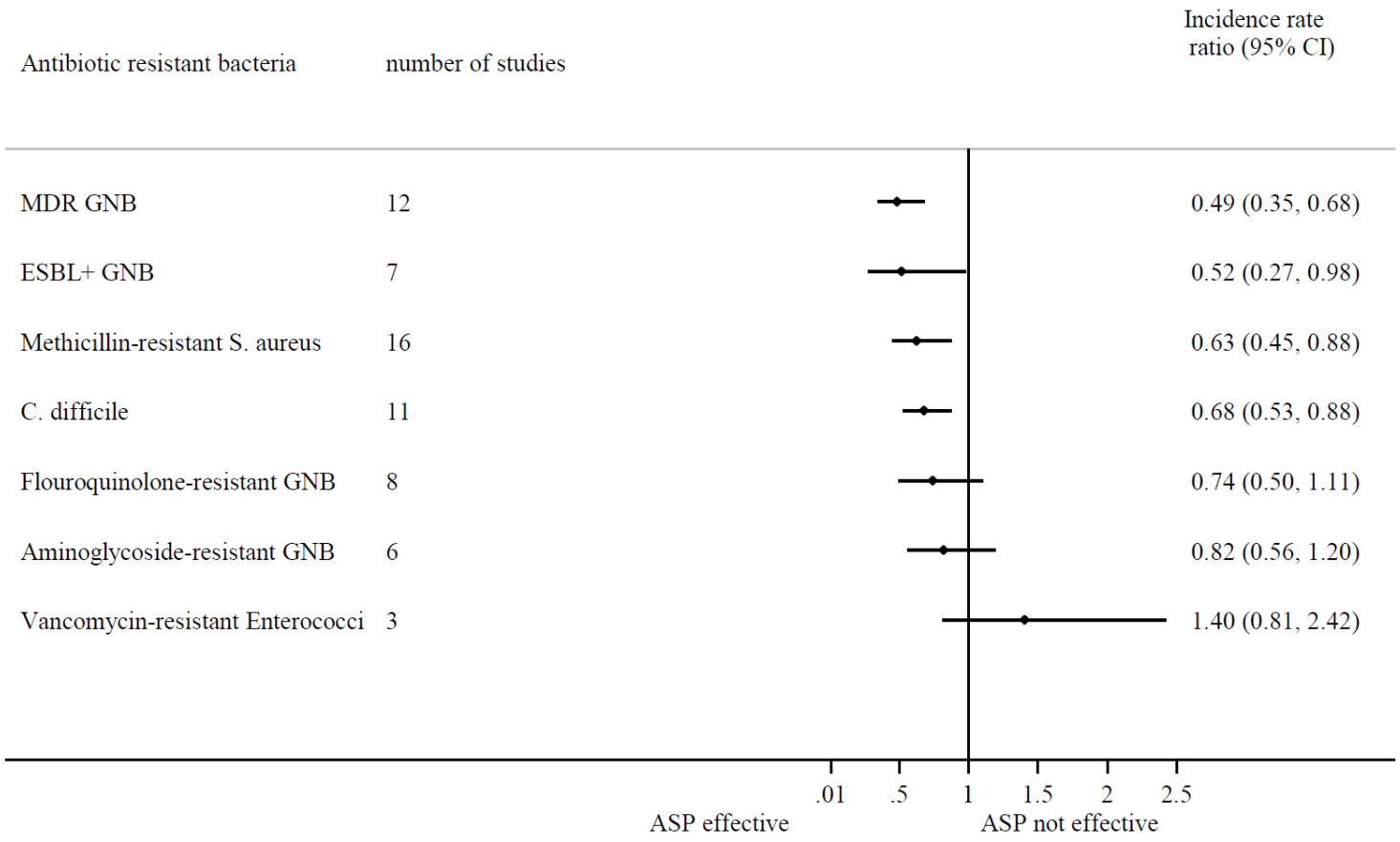
- ASPs reduced the incidence of infections and colonisation with
  - multidrug-resistant Gram-negative bacteria (51% reduction; IR 0·49, 95% CI 0·35–0·68)
  - ESBL-producing Gram-negative bacteria (48%; 0·52, 0·27–0·98)
  - MRSA (37%; 0·63, 0·45–0·88)
  - *C difficile* infections (32%; 0·68, 0·53–0·88).

- 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

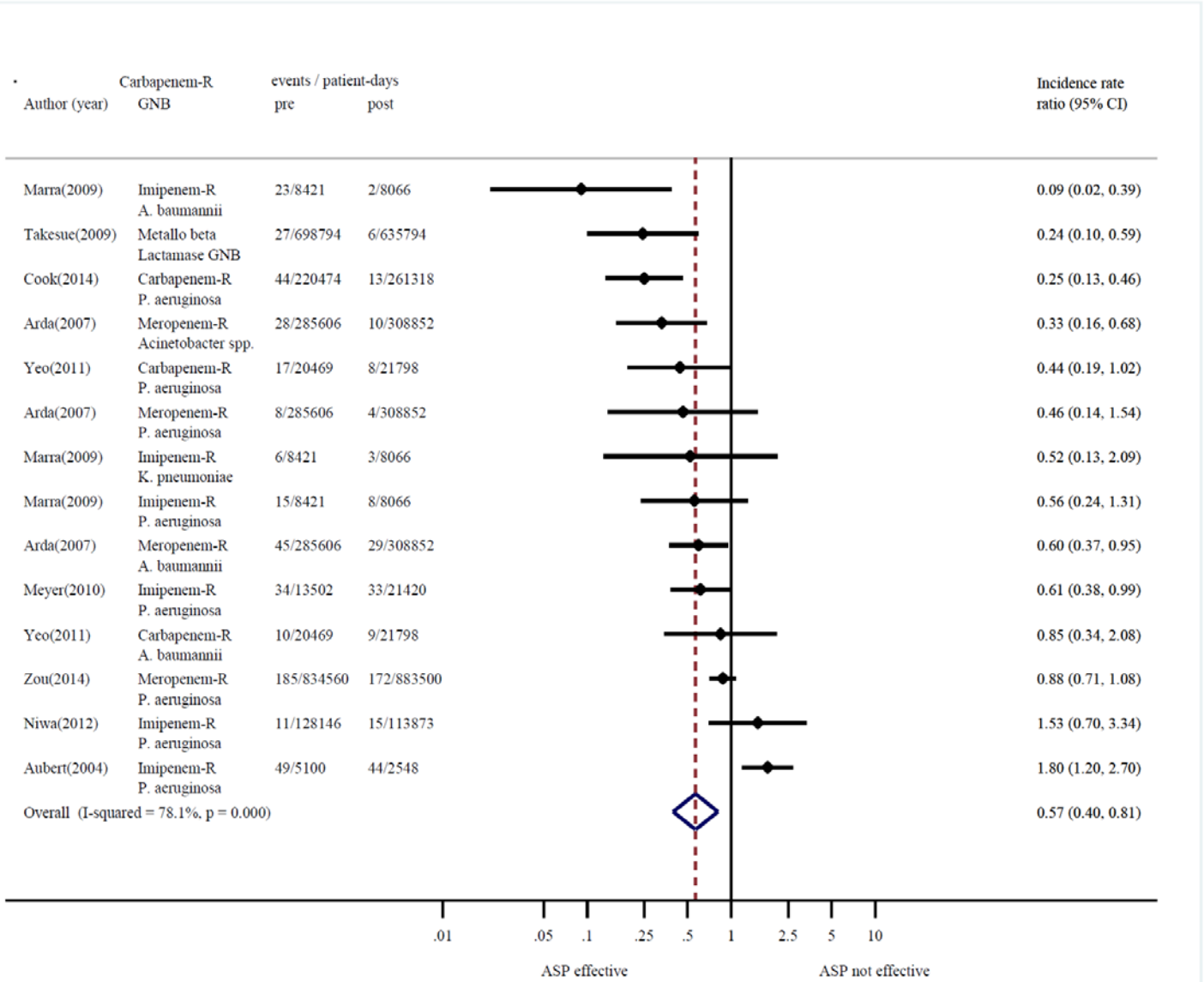
***Lancet Infect Dis* 2017; 17: 990–1001**

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

Targeting the Patient for MDRO Prevetnion: Conclusions

- Contact precautions remain important for C. difficile and in outbreak scenarios
  - Role for endemic spread of pathogens uncertain
  - Often used for MRSA, VRE, CRE, XDR-Gram negatives
- Active surveillance has a role in controlling MDROs, particularly CRE
  - It's role as an isolated process remains questionable
- CHG bathing is effective in reducing CLABSI and MDRO risk including MRSA, CRE
  - Experience primarily in ICU, vulnerable patients
  - Role outside the ICU remains unclear
- Bundling of processes effective in limiting MRSA and CRE spread
  - Hand hygiene, contact precautions, CHG bathing
  - Cohorting of patients and staff in outbreak, hyperendemic scenarios
- Antimicrobial stewardship is an important component of MDRO prevention and should be incorporated into prevention bundles

Questions?