Implementing Science to Reduce MDR-GNB

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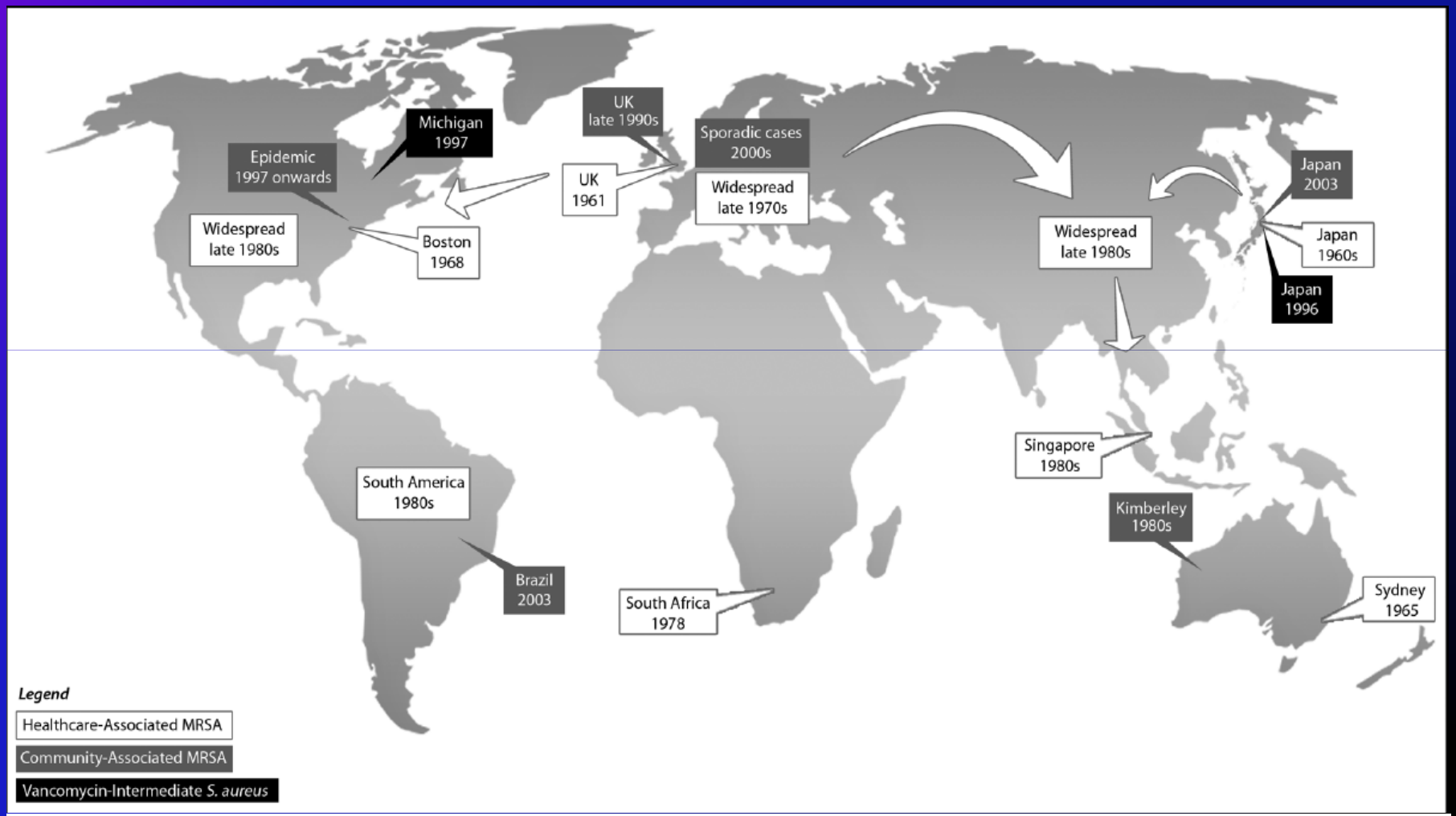
Objectives

- What are Implementation Barriers?
- Can we Overcome It?
- Example of Implementation Science

It is Clear that MDR-GNB Have Been Spread Throughout the World

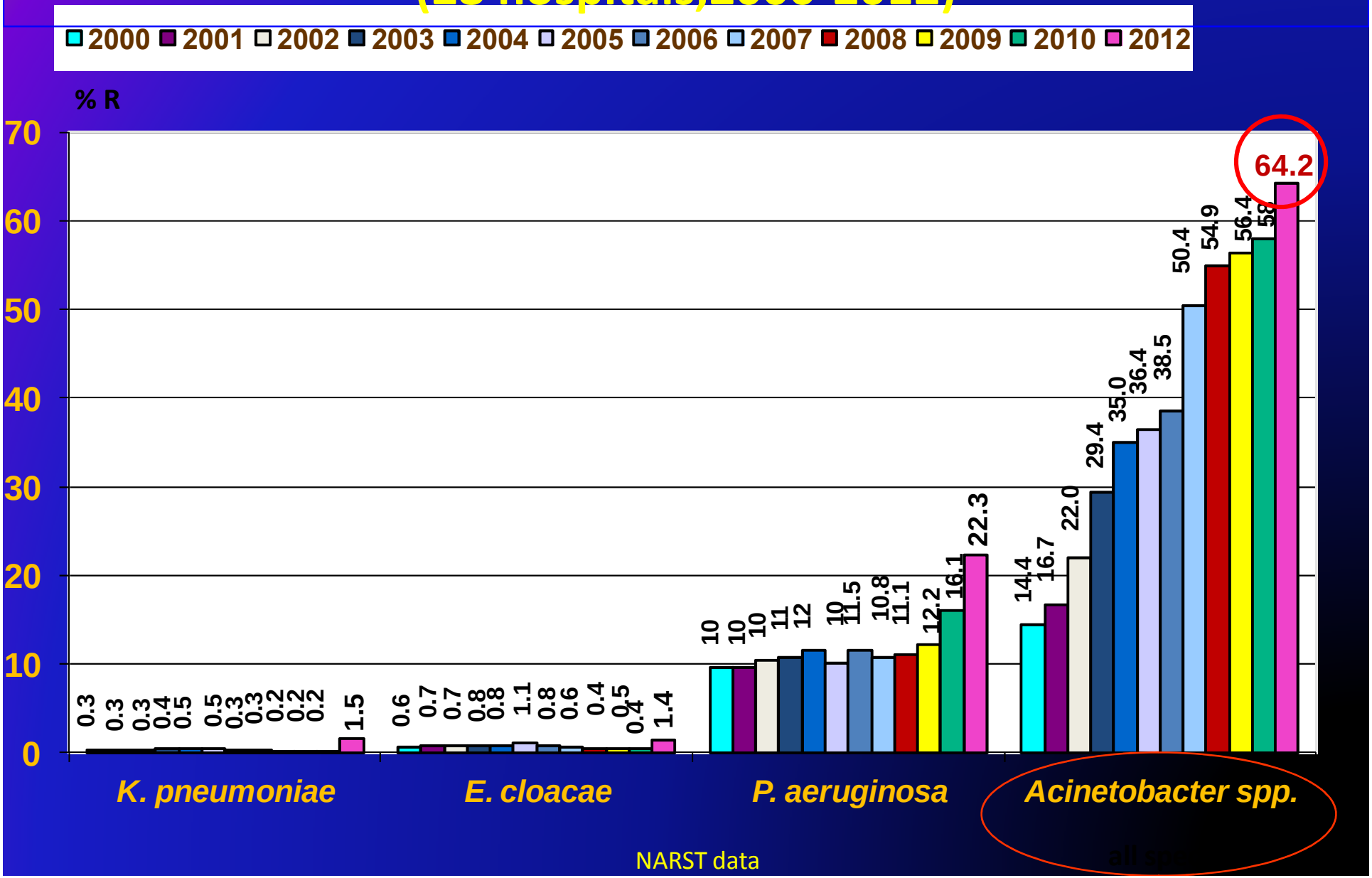


James S. Molton,[1,2] Paul A. Tambyah,[1,2] Brenda S. P. Ang,[3] Moi Lin Ling,[4] and Dale A. Fisher[1,2]

Clinical Infectious Diseases 2013;56(9):1310–8

Rate of Imipenem Resistant Acinetobacter spp.

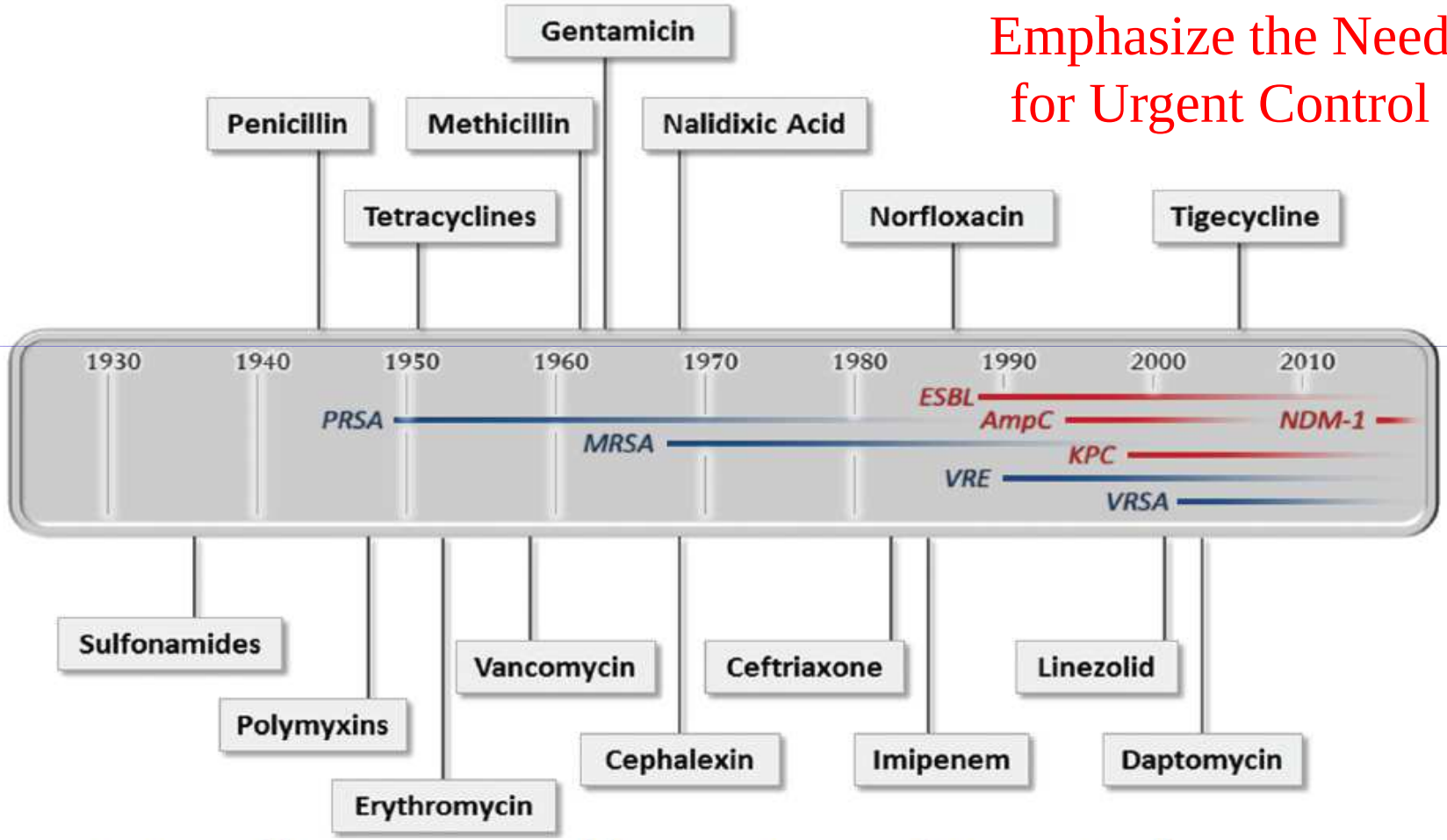
(28 hospitals,2000-2012)



NARST data

It is Also Obvious That No New Antibiotics Target MDR-GNB will Come Out Any Time Soon

Emphasize the Need for Urgent Control



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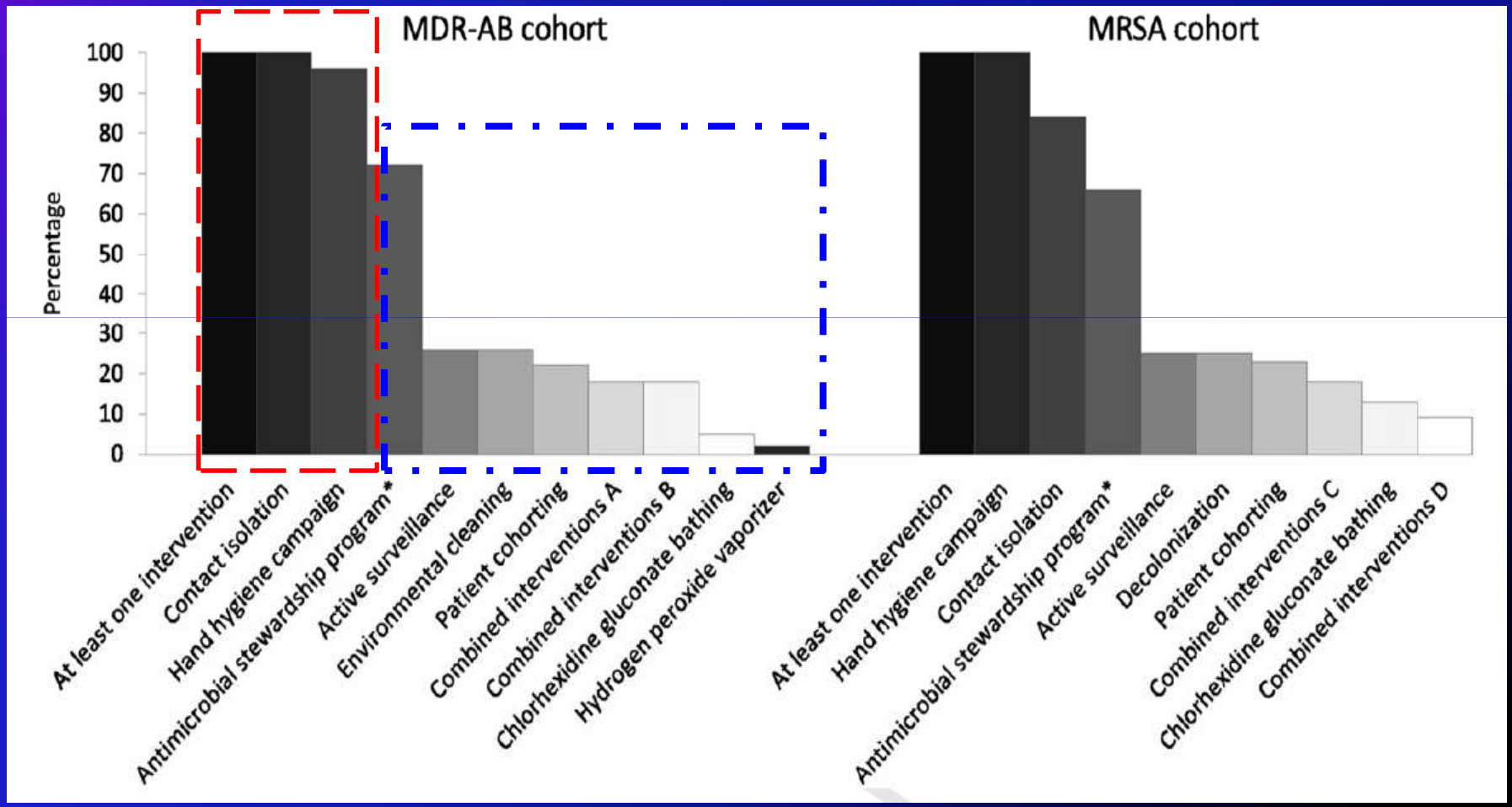
Despite these facts, few hospitals implementing evidence-based practices to control MDR-GNB



A. Apisarnthanarak et al. / American Journal of Infection Control xxx (2012) 1-6

"Nothing is more difficult to plan nor more perilous to conduct than the introduction of change. The innovator has for enemies all those who have prospered under the old, and only lukewarm defenders in those who may prosper under the new…. When his enemies have the opportunity to attack they do so with the zeal of partisans, while supporters defend him feebly, endangering both the innovator and the cause."

– Niccolo Machiavelli. The Prince, 1513 AD

A True Story…

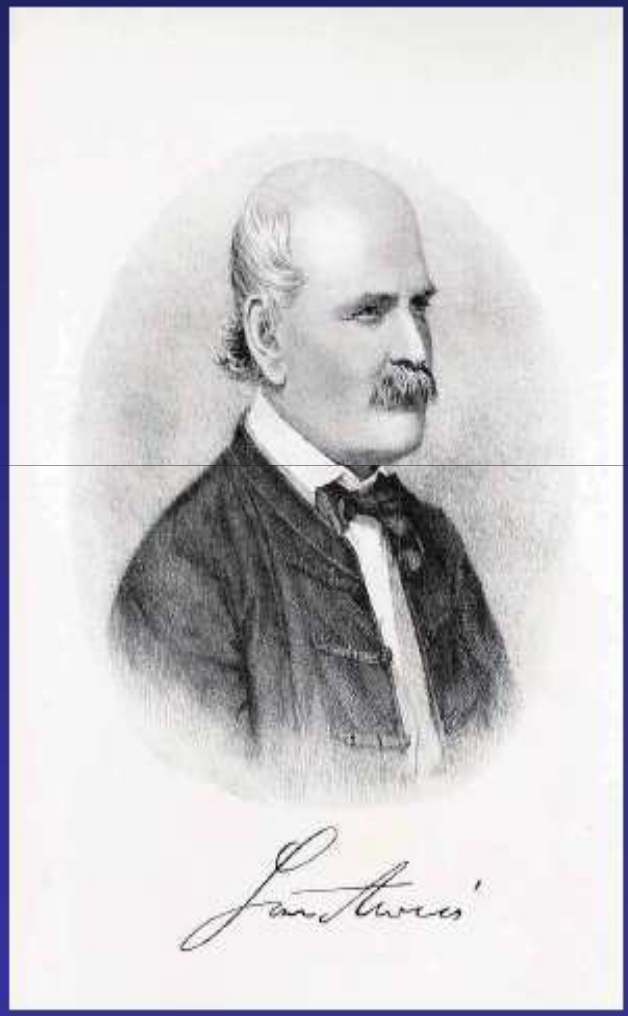
- Smart (and brash) physician begins a new job at a hospital in a famous city
- Watches people dying needlessly on a unit
- Comes up with a simple solution to prevent deaths
- Implements the solution on a small scale and observes a dramatic benefit

A True Story, continued…

- Attempts to spread his ideas and implement his simple solution elsewhere
- (Mostly) ignored, ridiculed, rejected…out of a job
- Goes to a different hospital; confirms his findings
- (Mostly) ignored, ridiculed, rejected…dies at the age of 47…

in an insane asylum.

Ignaz Semmelweis (1818 – 1865)



(Pittet & Boyce. Hand Hygiene: Pursuing the Semmelweis Legacy. Lancet Infect Dis 2001)

Possible Causes for the Non-Adoption of Semmelweis's Findings

(Joel D. Howell, MD, PhD, Professor of Medicine & History)

- Did not publish his data in a timely manner (delay of ~14 years)

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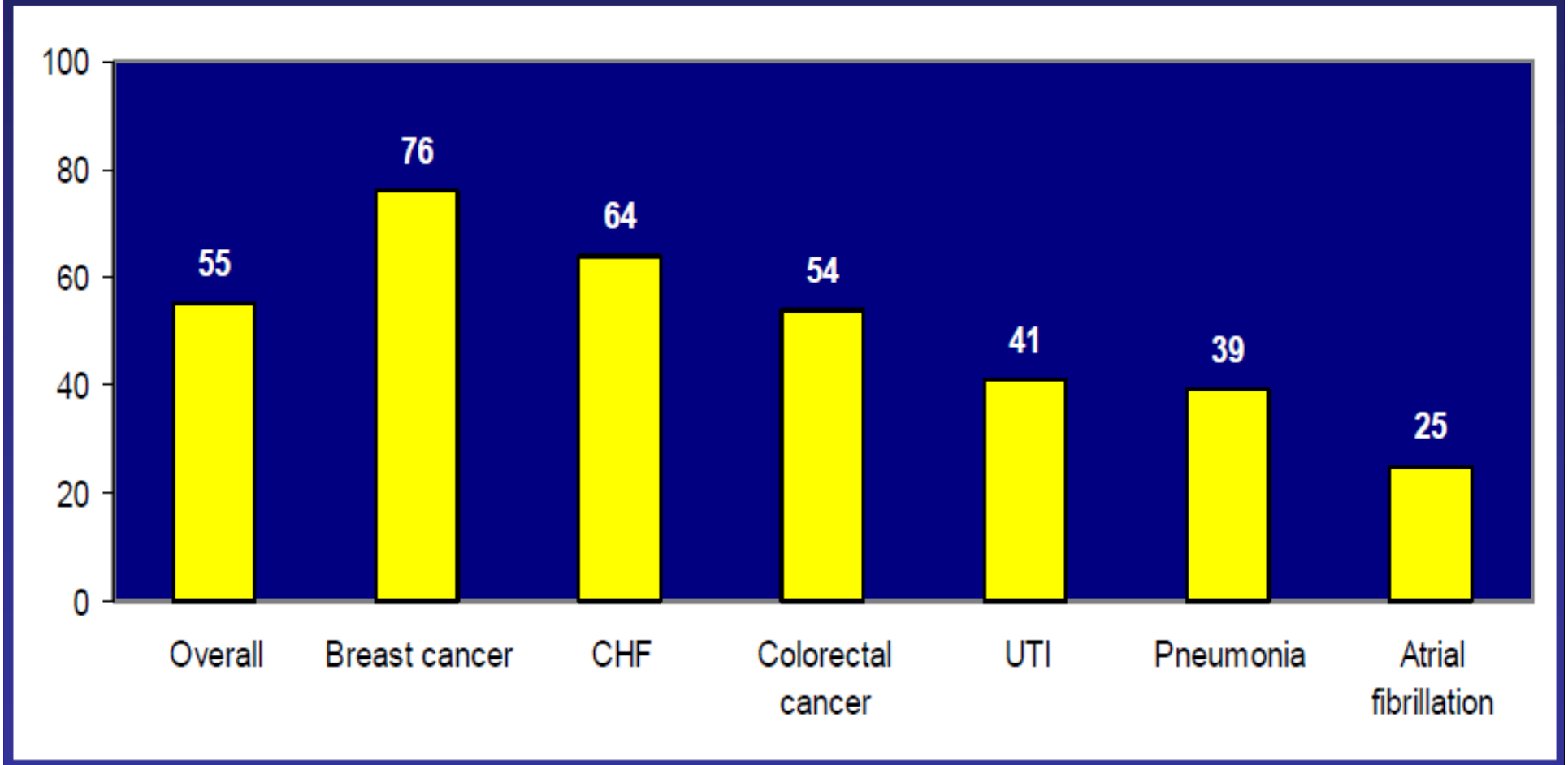
- His approach was superbly offensive
- Did not have a conceptual model to explain his striking findings

Consistently Using Evidence-Based Practices Remains a Challenge…

U.S. Adults Receive Only About Half of Recommended Care – Quality Varies by Condition



(McGlynn. "The Quality of Health Care Delivered to Adults in the U.S." N Engl J Med 2003)

Given this Gap of What should Be Done and What is Done…

- Focus Should be On Implementation Science
- The Scientific Study of Method to Promote the Systematic Uptake of Research Findings into Routine Practice

Implementation Science: Conceptual Model

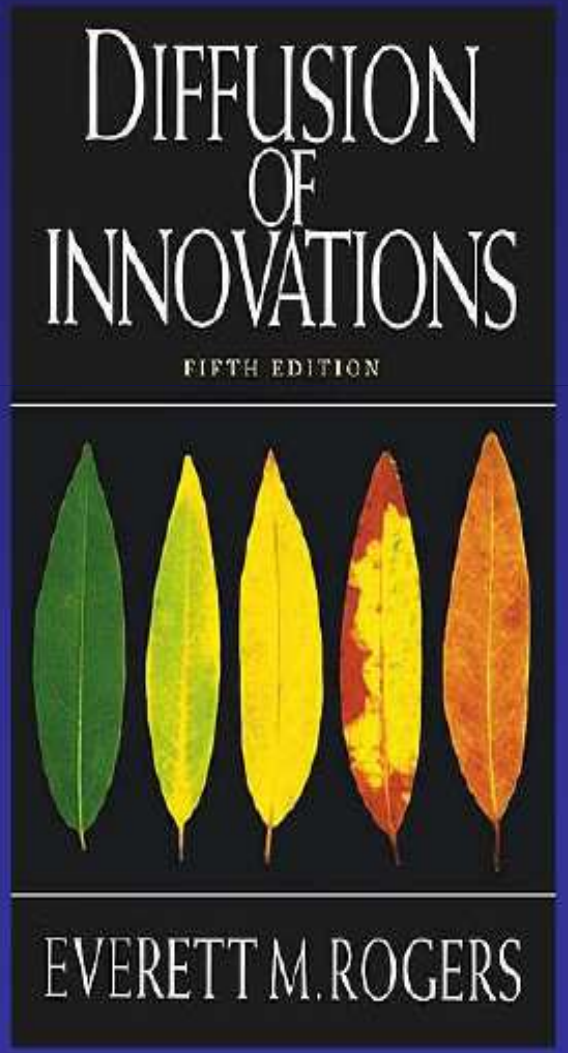
- In the last 6 decades, "knowledge utilization" field dominated by one person: Everett Rogers, PhD

(Estabrooks et al. Implementation Science. Nov 2008)

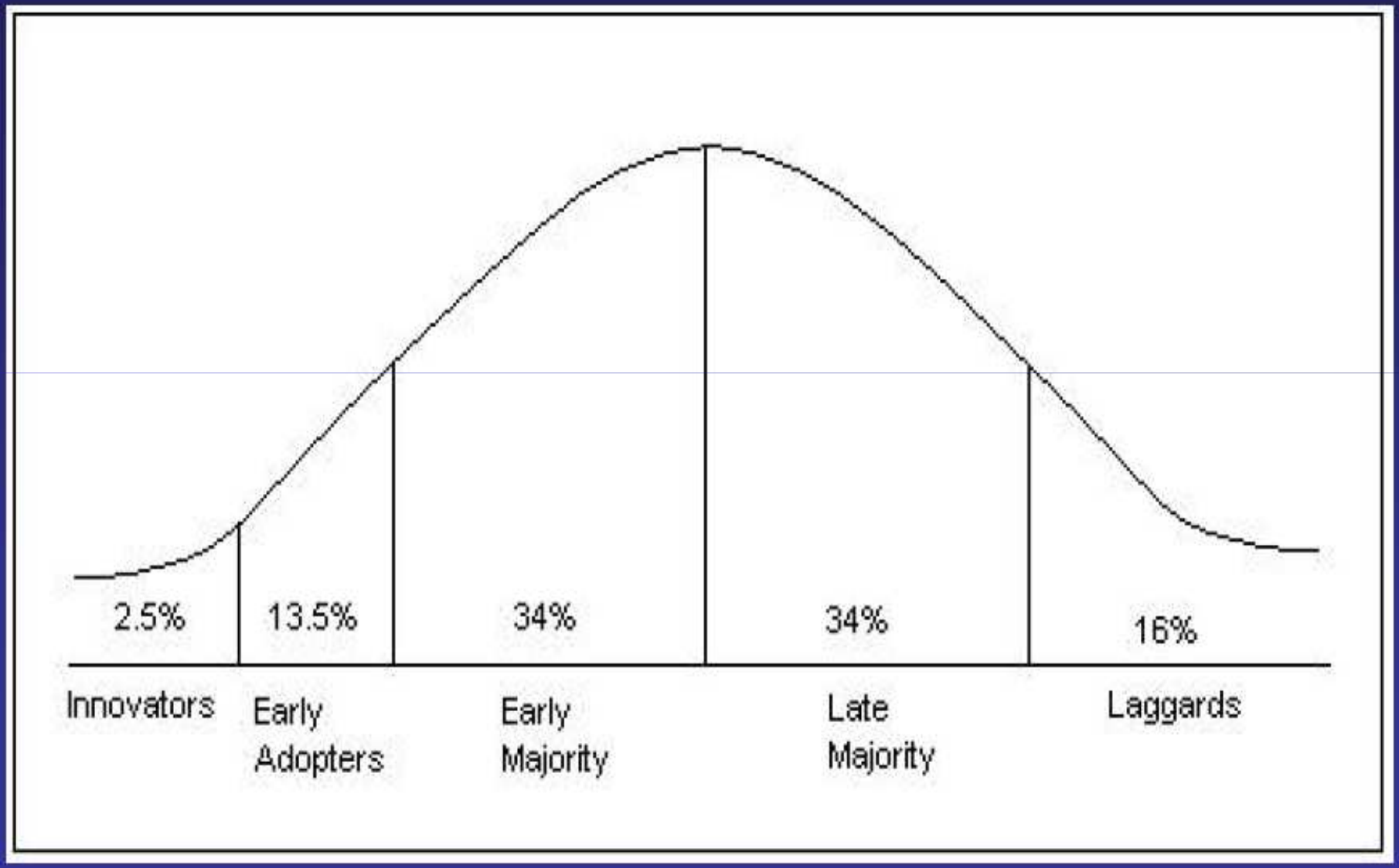
- Rogers' "Diffusion of Innovation" Model is the canonical model since World War 2
- A descriptive model that helps explain why innovations diffuse slowly

"Diffusion of Innovation" Model of Everett Rogers, PhD

- Definitions:
  - Diffusion = spread
  - Innovation = a new practice
- Originally developed for the study of agriculture



Adopter Categories



Hospital Epidemiology and Infection Preventionist are Well Aware of the Evidence-Based to Control MDROs

Table 3. Key tiered recommendations from the Healthcare Infection Control Practices Advisory Committee to Contain Multidrug-Resistant Gram-Negative Bacteria.

Tier 1 recommendation	Example	Examples of Tier 2 recommendations [†]	Example
Administrative control and adherence monitoring	Obtain and document administration support	Obtain expert consultation	Use of real-time feedback to enhance adherence
Education	Focus on best prevention and practices for HCWs	Intensified educational program	Increase frequency of education and provide timely feedback
Antibiotic control program	Monitor susceptibility patterns	Target key antibiotic restrictions	Increase frequency of feedback susceptibility to clinicians
Surveillance for MDR-GNB	Estimate MDR-GNB burden stratified by units at risk	Implement ASC	ASC and track patients with MDR-GNB (e.g., use of line listing)
Infection control (e.g., contact isolation and hand hygiene)	Monitor adherence to basic infection control measures	Intensified program with monitoring and feedback	Use of cohort section together with real-time feedback
Environmental measure (e.g., environmental cleaning)	Implement policy and monitor cleaning practices	Monitor cleaning performance using checklist or special approaches[‡]	Use of nontouch technology (e.g., ultraviolet light, hydrogen peroxide vapor)

[†]Intensified program.
[‡]For example, glow germ and ATP bioluminescence assays.
ASC: Active surveillance culture; HCW: Healthcare worker.
Data taken from [90].

Apisanthanarak A, et al. Exp Rev Antimicrob Ther 2013

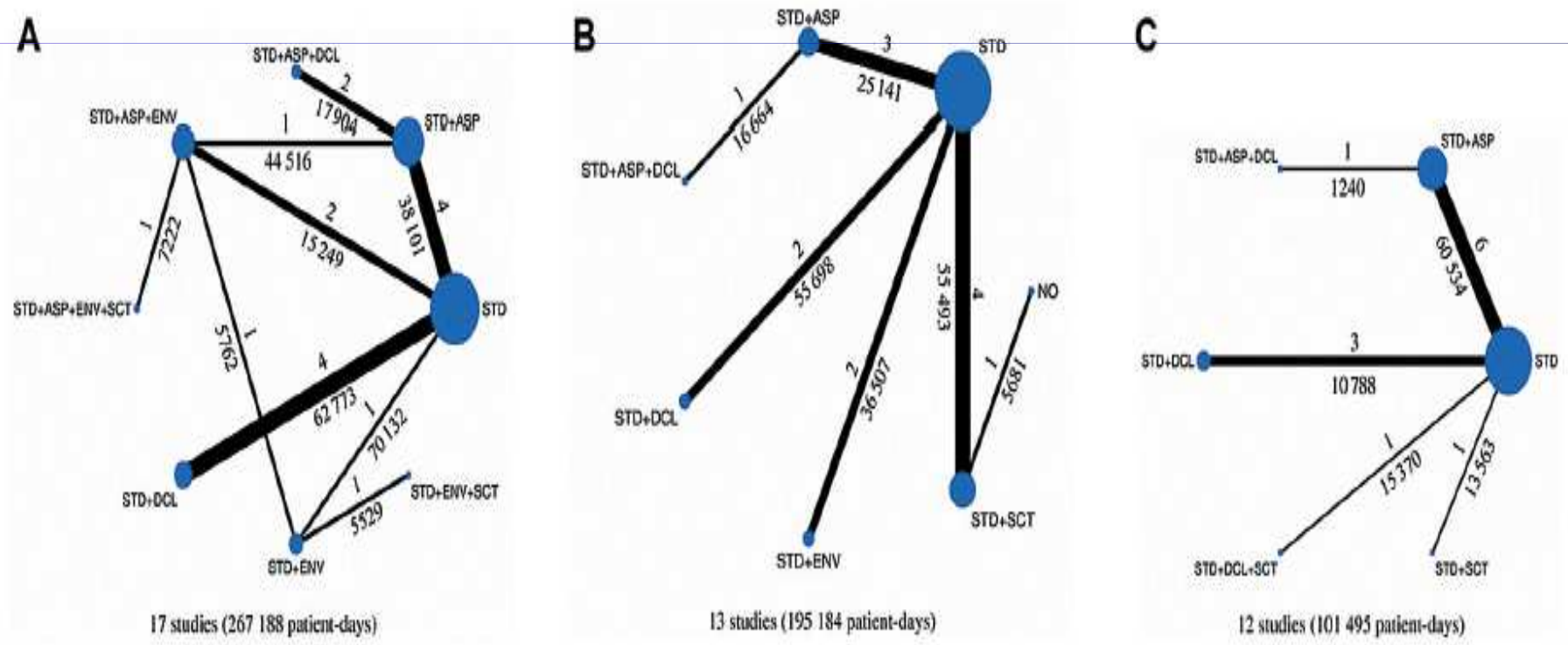
Clinical Infectious Diseases

SUPPLEMENT ARTICLE

Prevention and Control of Multidrug-Resistant Gram-Negative Bacteria in Adult Intensive Care Units: A Systematic Review and Network Meta-analysis

Nattawat Teerawattanapong,[1] Kirati Kengkla,[2] Piyameth Dilokthornsakul,[3] Surasak Saokaew,[2,3,4] Anucha Apisarnthanarak,[5] and Nathorn Chaiyakunapruk[3,4,6,7]

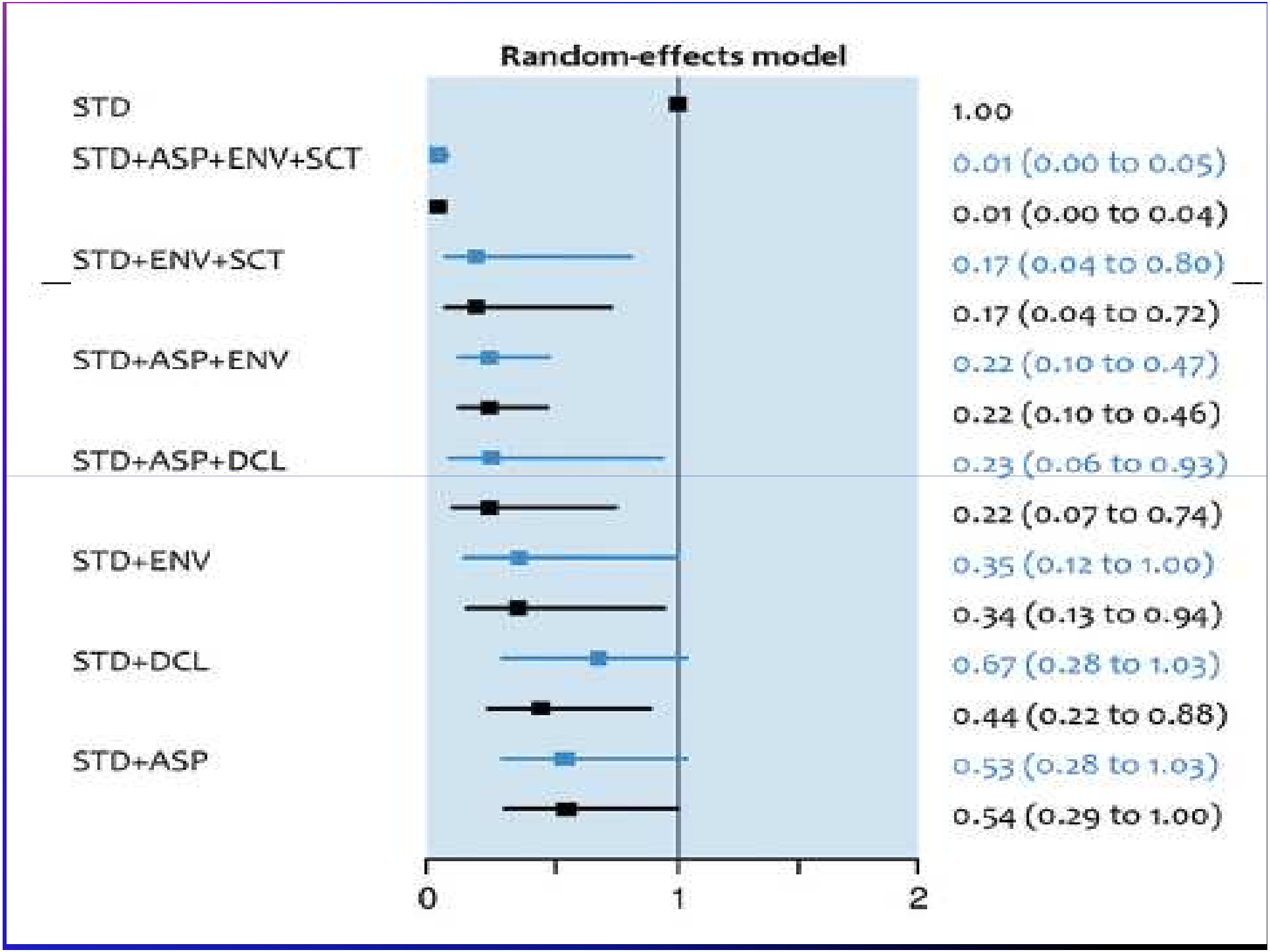
[1]Division of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Ubon Ratchathani University, [2]Center of Health Outcomes Research and Therapeutic Safety, School of Pharmaceutical Sciences, University of Phayao, and [3]Center of Pharmaceutical Outcomes Research, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, Thailand; [4]School of Pharmacy, Monash University Malaysia, Selangor; [5]Division of Infectious Diseases, Faculty of Medicine, Thammasat University Hospital, Pathumthani, Thailand; [6]School of Pharmacy, University of Wisconsin–Madison; and [7]School of Population Health, University of Queensland, Brisbane, Australia



17 studies (267 188 patient-days)

13 studies (195 184 patient-days)

12 studies (101 495 patient-days)


Random-effects model
STD
1.00
STD+ASP+ENV+SCT
0.01 (0.00 to 0.05)
0.01 (0.00 to 0.04)
STD+ENV+SCT
0.17 (0.04 to 0.80)
0.17 (0.04 to 0.72)
STD+ASP+ENV
0.22 (0.10 to 0.47)
0.22 (0.10 to 0.46)
STD+ASP+DCL
0.23 (0.06 to 0.93)
0.22 (0.07 to 0.74)
STD+ENV
0.35 (0.12 to 1.00)
0.34 (0.13 to 0.94)
STD+DCL
0.67 (0.28 to 1.03)
0.44 (0.22 to 0.88)
STD+ASP
0.53 (0.28 to 1.03)
0.54 (0.29 to 1.00)
0
1
2

STD+ASP+ ENV+SCT							
0.05 (.01, 0.38)	STD+ENV +SCT						
0.04 (.01, 0.16)	0.76 (.19, 3.13)	STD+ASP+ ENV					
0.04 (.01, 0.27)	0.75 (.12, 4.87)	0.99 (.27, 3.66)	STD+ASP+ DCL				
0.02 (.00, 0.13)	0.48 (.17, 1.41)	0.63 (.25, 1.58)	0.64 (.14, 2.96)	STD+ENV			
0.02 (.00, 0.11)	0.38 (.07, 1.93)	0.50 (.18, 1.37)	0.50 (.13, 2.02)	0.79 (.23, 2.68)	STD+DCL		
0.02 (.00, 0.08)	0.31 (.07, 1.45)	**0.40 (.18, 0.90)**	0.41 (.15, 1.15)	0.64 (.21, 1.95)	0.81 (.32, 2.04)	STD+ASP	
0.01 (.00, 0.04)	**0.17 (.04, 0.72)**	**0.22 (.10, 0.46)**	**0.22 (.07, 0.74)**	**0.34 (.13, 0.94)**	**0.44 (.22, 0.88)**	0.54 (.29, 1.00)	STD

CONCLUSIONS

In conclusion, our network meta-analysis suggests that a 4-component IPC strategy is the most effective intervention to prevent MDR-GNB acquisition in adult ICU patients. We suggest that infection preventionists adopt effective interventions per the assessment of infrastructure and resource availability. Well-designed RCTs to determine the efficacy of different types of IPC strategies for different MDR-GNB will further inform the findings of this network meta-analysis.

How can We Implement Change to Reduce MDR-GNB?

Implementation

Technical

Socio-adaptive

Key Pre-Requisite Must Be in Place

Table 2
Multivariate analysis of factors associated with organism-specific infection prevention control interventions among hospitals with endemicity of multidrug-resistant *Acinetobacter baumannii* and methicillin-resistant *Staphylococcus aureus* in multivariate analyses

Cohort	Infection control interventions	Factors	Adjusted odds ratio (95% confidence interval)	*P* value
MDR-AB*	Patient cohorting	Lead ICP is a physician	2.55 (1.21-5.37)	.01
		Good to excellent administrative support	3.09 (1.01-9.50)	.04
	Hand hygiene campaign	Participation in a collaborative prevention effort	27.99 (0.47-373.03)	.09
	Active surveillance	Participation in a collaborative prevention effort	4.69 (2.05-10.72)	<.001
		Lead ICP is a physician	1.99 (0.96-4.12)	.06
	Environmental cleaning	Participation in a collaborative prevention effort	4.69 (2.05-10.72)	<.001
		Lead ICP is a physician	1.99 (0.96-4.12)	.06
	Antimicrobial stewardship program†	Medical school affiliation	40.05 (11.04-145.33)	<.001
		Participation in a collaborative prevention effort	38.93 (4.73-320.46)	.001
	Chlorhexidine gluconate bathing	Safety score‡	3.90 (0.77-19.85)	.10
		Lead ICP is a physician	1.80 (0.89-3.65)	.10
	Hydrogen peroxide vaporizer	None	— — —	— — —
	Combined interventions A	Lead ICP is a physician	2.54 (0.87-7.44)	.08
	Combined interventions B	Lead ICP is a physician	2.54 (0.87-7.44)	.08
MRSA§	Contact isolation	None	— — —	— — —
	Patient cohorting	None	— — —	— — —
	Active surveillance	None	— — —	— — —
	Decolonization	None	— — —	— — —
	Chlorhexidine gluconate bathing	Medical school affiliation	7.59 (1.46-39.34)	.02
	Antimicrobial stewardship program†	Medical school affiliation	30.53 (6.47-144.07)	<.001
		Participation in a collaborative prevention effort	21.05 (2.79-437.80)	<.001
	Combined interventions C	Medical school affiliation	2.43 (0.83-7.11)	.09
	Combined interventions D	Medical school affiliation	12.68 (1.56-275.66)	.004

Infection Prevention Control Bundle of Multidrug-Resistant *Acinetobacter baumannii and* Methicillin-Resistant *Staphylococcus aureus*: Which One Is More Important?

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY FEBRUARY 2014,

TABLE 1. Infection Prevention Control (IPC) Interventions Associated with Reduction in Multidrug-Resistant (MDR) *Acinetobacter baumannii* and Methicillin-Resistant *Staphylococcus aureus* (MRSA) Incidence as Reported by Representatives from 204 Thai Hospitals

Pathogen, compliance, %	aOR (95% CI), by intervention
MDR *A. baumannii*	
40–60	...
60–80	IPC bundle A: 1.55 (1.05–3.45); IPC bundle B: 1.69 (1.19–4.96)
80–100	Hand hygiene: 1.59 (1.12–5.46); antimicrobial stewardship program: 1.24 (1.09–6.45); IPC bundle A: 2.45 (1.41–6.93); IPC bundle B: 2.93 (1.56–5.69)
MRSA	
40–60	...
60–80	IPC bundle D: 1.45 (1.08–5.45)
80–100	Hand hygiene: 1.55 (1.06–4.93); contact isolation: 1.05 (1.01–5.46); IPC bundle D: 3.36 (2.12–5.69)

Anucha Apisarnthanarak, MD;[1]
Linda M. Mundy, MD, PhD[2]

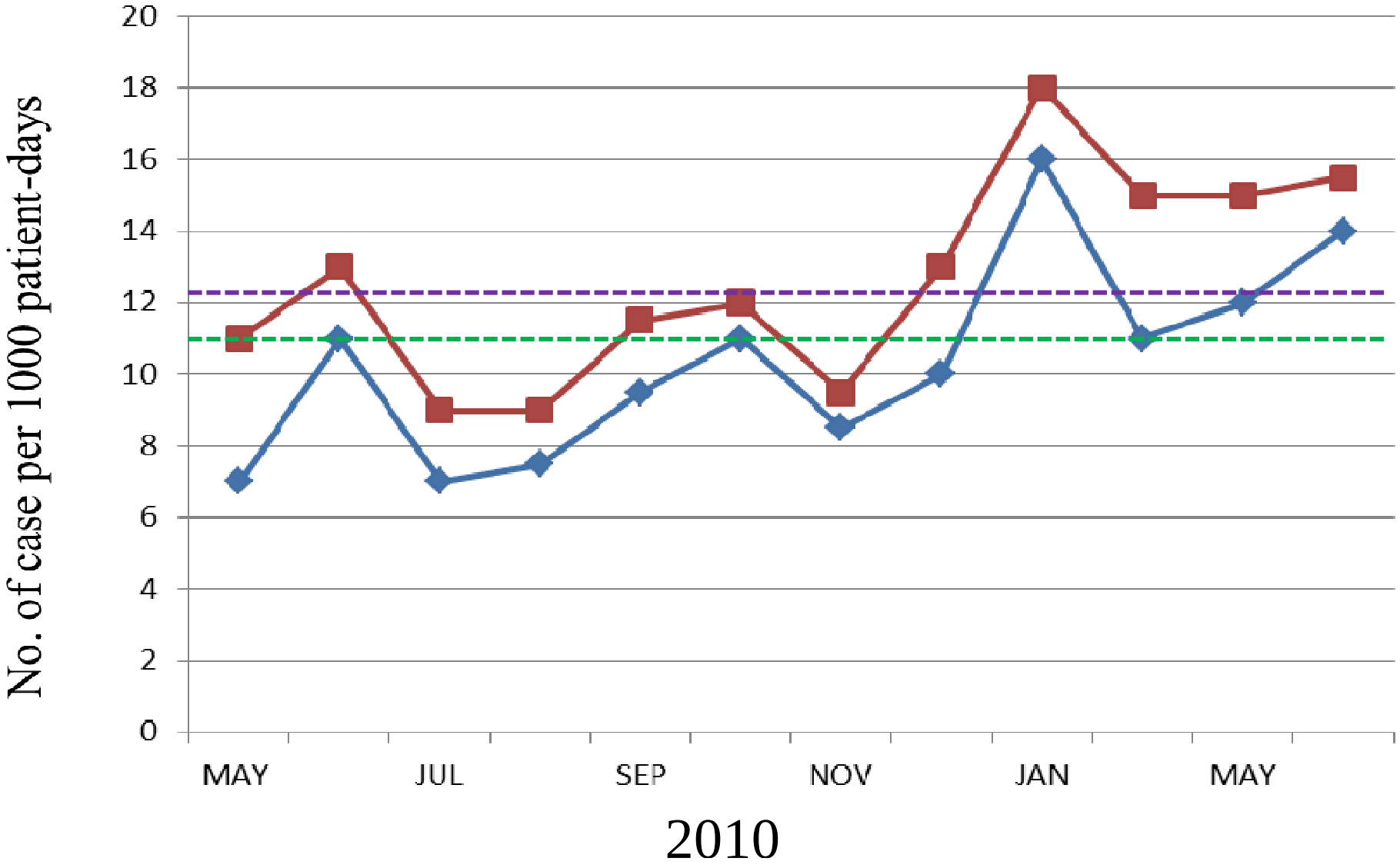
Need To Know Barrier:
National Survey of Thai IPs in the Era of Patient Safety

Top 5 most important barriers for infection control work

Lack of a physician champion who will advocate for change	46(23)
Difficulty staying current with new recommendations	34(17)
Cost of recommended practices	29(14)
Ineffective hospital leadership	29(14)
Other	28(14)

A. Apisarnthanarak et al. / American Journal of Infection Control xxx (2012) 1-6

Example: Carbapenem Resistant *Acinetobacter baumannii* in MICU



Molecular Epidemiology Suggested a Clonal Spread of *CR-Acinetobacter baumannii*

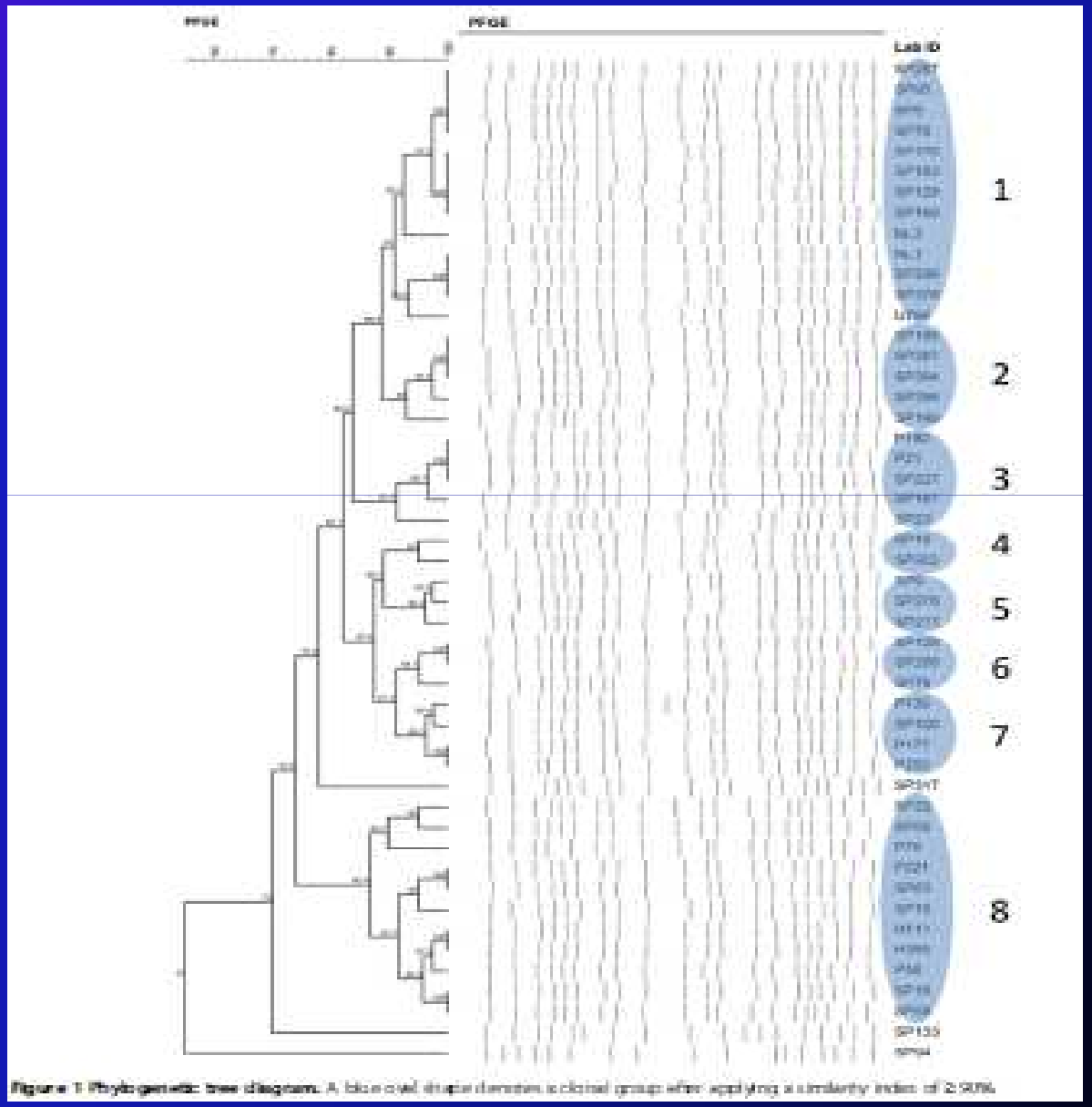
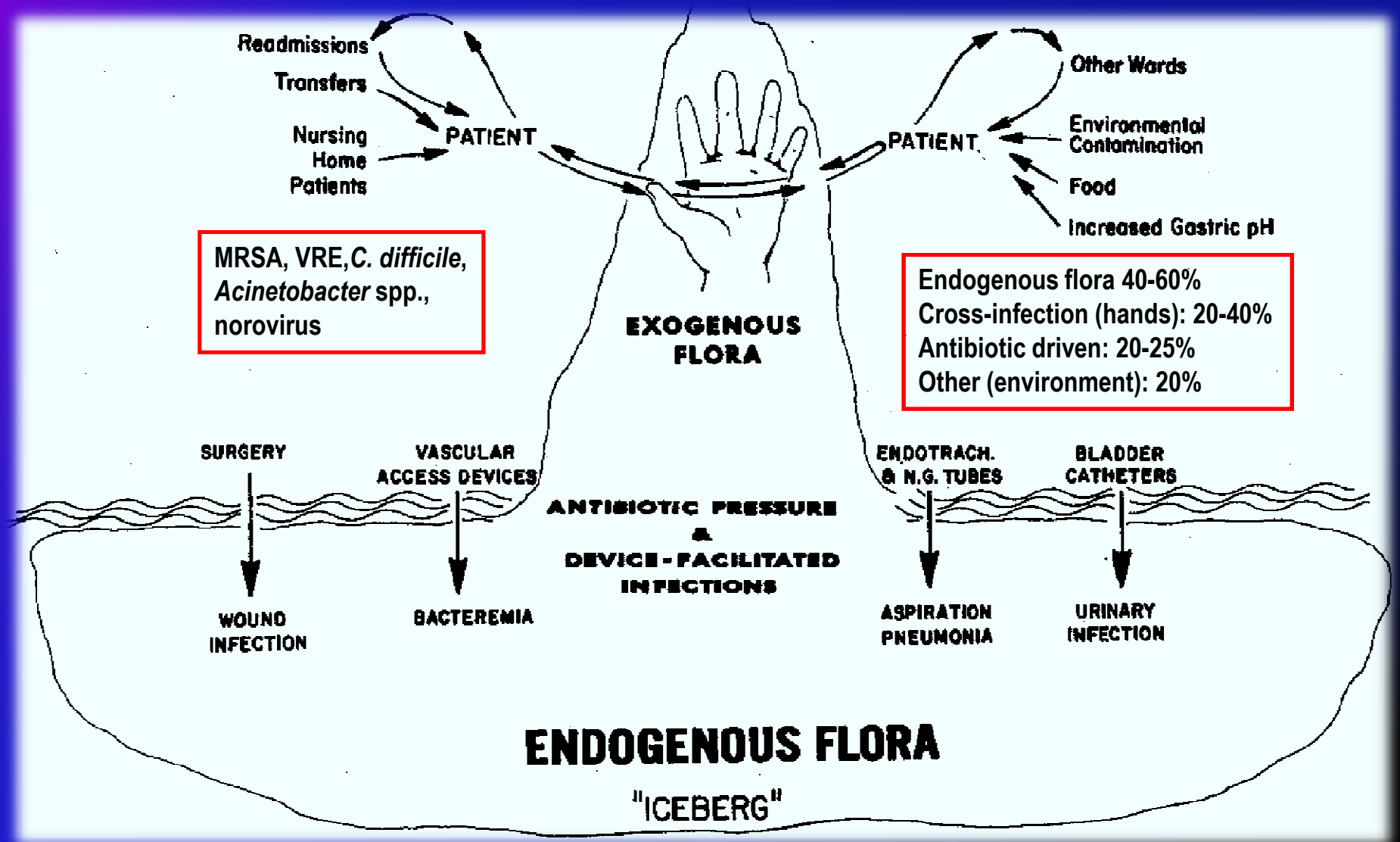


Figure 1 Phylogenetic tree diagram. A blue oval shape denotes a clonal group after applying a similarity index of ≥ 80%.

Teo *et al. Antimicrobial Resistance and Infection Control* (2015) 4:2

MDROs Transmission



Weinstein RA. Am J Med 1991;91(suppl 3B):179S

Why is Source Control Important?

Decrease burden of patient skin contamination

Prevent infections due to potential pathogens on patient skin

Decrease contamination of healthcare worker hands and the environment

Decrease spread of potential pathogens to other patients

Key Roles and Responsibilities to Prevent MDROs

Role or Responsibility	Example of Personnel to Consider
Project coordinator	ID and Hospital Epidemiologist
Nurse champion (engage nursing personnel)	ICU charge nurse
Physician champion (engage medical personnel)	MICU director, intensivist, hospital epidemiologist, ID fellow and residents
Data collection, monitoring, reporting	Infection Preventionist

Implement the Bundles together with Chlorhexidine bathing

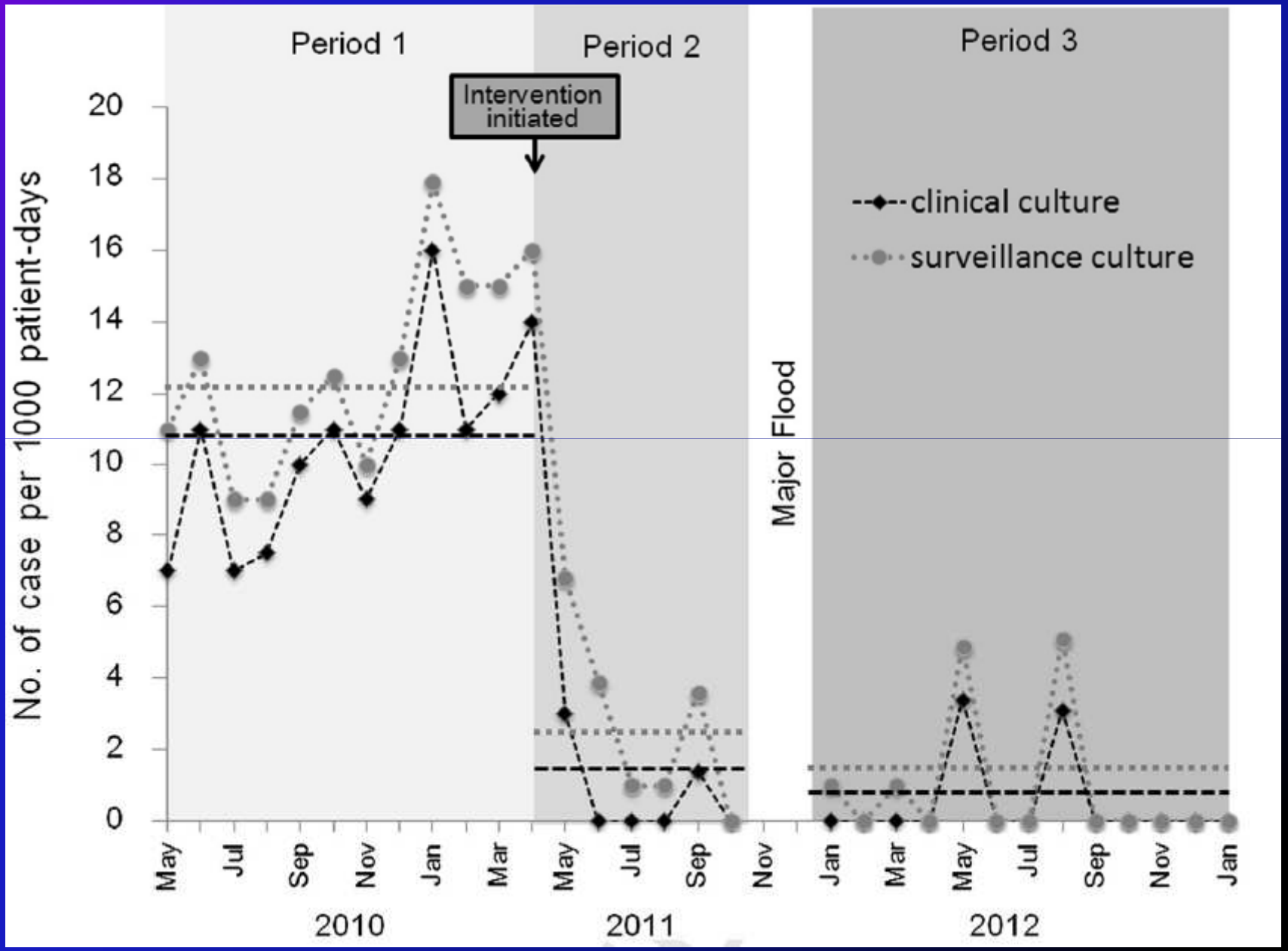
How to Engage Nurses and Doctors?

1. Develop a common purpose (patient safety)
2. View nurses/doctors as partners (not barriers)
3. Identify nurse champions early
4. Standardize evidence-based processes (and make the right thing to do, the easy thing to do)
5. Provide support from leadership for the efforts of the nurse champion

Using Chlorhexidine Bath

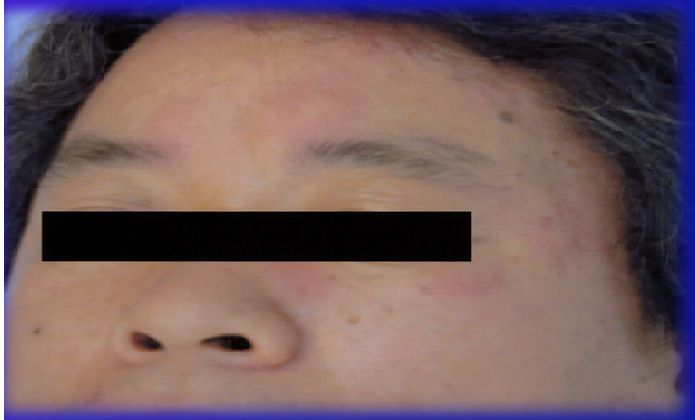
- Nursing workload can be an issue
- A Nurse: "…the workload will be increased if you have increasing number of MDROs…."
- Nurse buy-in is key to success
- A physician administrator: "Because the nurses on the MICU wanted to have their patients discharge from ICU as soon as they are ready…they viewed MDROs as the most important enemy.."
- A nurse champion is critically important!

Implement, Data monitoring and Feedback



Apisarnthanarak A, et al. AJIC 2013

Watch Out for Unique Side Effect of CHG in Asia Pacific Regions



- **CHG-induced rashes was found in 5% (5/92) among Thai HCWs in one study.**
- **The rash occurred after exposure to 4% and later 2%.**
- **Majority of HCWs had underlying diseases of dermatitis or allergy.**
- **Several reports in Asia Pacific regions (e.g., Japan, Korea) also suggested high incidence of rash and anaphylactic reactions to CHG.**
- **This may be related to genetic factors and increase proportion of IgE or IgG antibodies to CHG.**

- Apisarnthanarak A, et al. High incidence of CHG-induced rash among Thai HCWs. CID 2011.
- Bugelski PJ, et al. Genetic effects of immune-mediated adverse drug effects. Nat Rev Drug Dis 2005.
- Layton GT, et al. The incidence of IgE and IgG antibodies to CHG. Clin Exp Allergy 1989.
- Bae YJ, et al. A case of anaphylaxis to CHG. Korean J Med Sci 2008.

Increase in Chlorhexidine Minimal Inhibitory Concentration of *Acinetobacter baumannii* Clinical Isolates after Implementation of Advanced Source Control

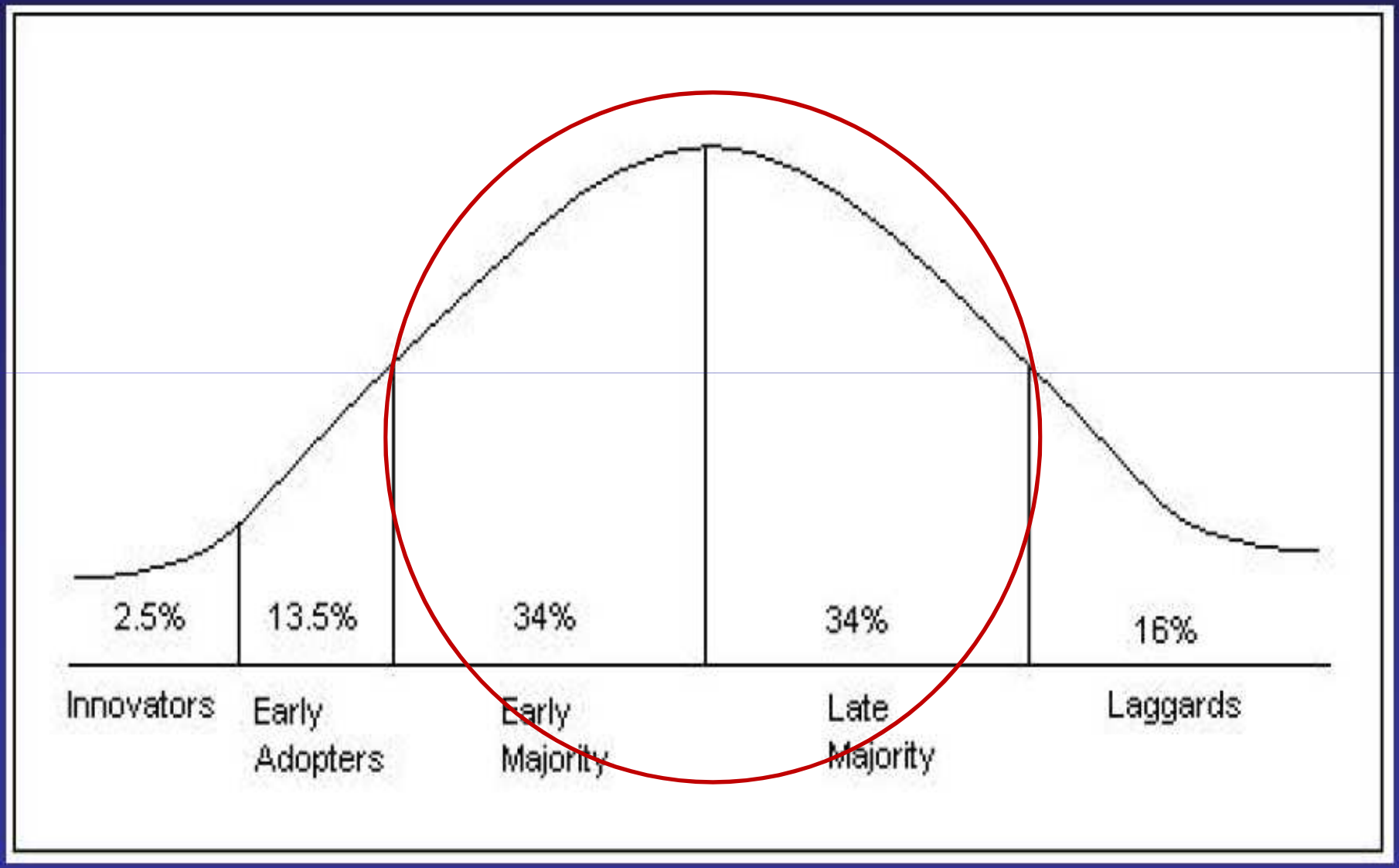
INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY JANUARY 2014, VOL. 35, NO. 1

TABLE 1. Comparison of the Epidemiology of Chlorhexidine Minimum Inhibitory Concentrations (MICs) among Extensively Drug-Resistant (XDR) *Acinetobacter baumannii* Clinical Isolates before and after Implementation of Advanced Source Control

		Prechlorhexidine (n = 50)			Postchlorhexidine (n = 50)		
Hospital unit	n	Chlorhexidine consumption (L/unit/month)	Chlorhexidine MIC 50/90	Incidence of XDR *A. baumannii* per 1,000 patient-days	Chlorhexidine consumption (L/unit/month)	Chlorhexidine MIC 50/90	Incidence of XDR *A. baumannii* per 1,000 patient-days
Intensive care	70	2.4	32/32	12.5	15.5	64/128	2.9
General medicine	15	0.9	32/32	11.4	9.8	64/128	6.3
General surgical	10	0.5	16/32	9.6	4.5	64/128	4.6
Other[a]	5	0.1	16/32	1.2	2.5	64/128	0.6

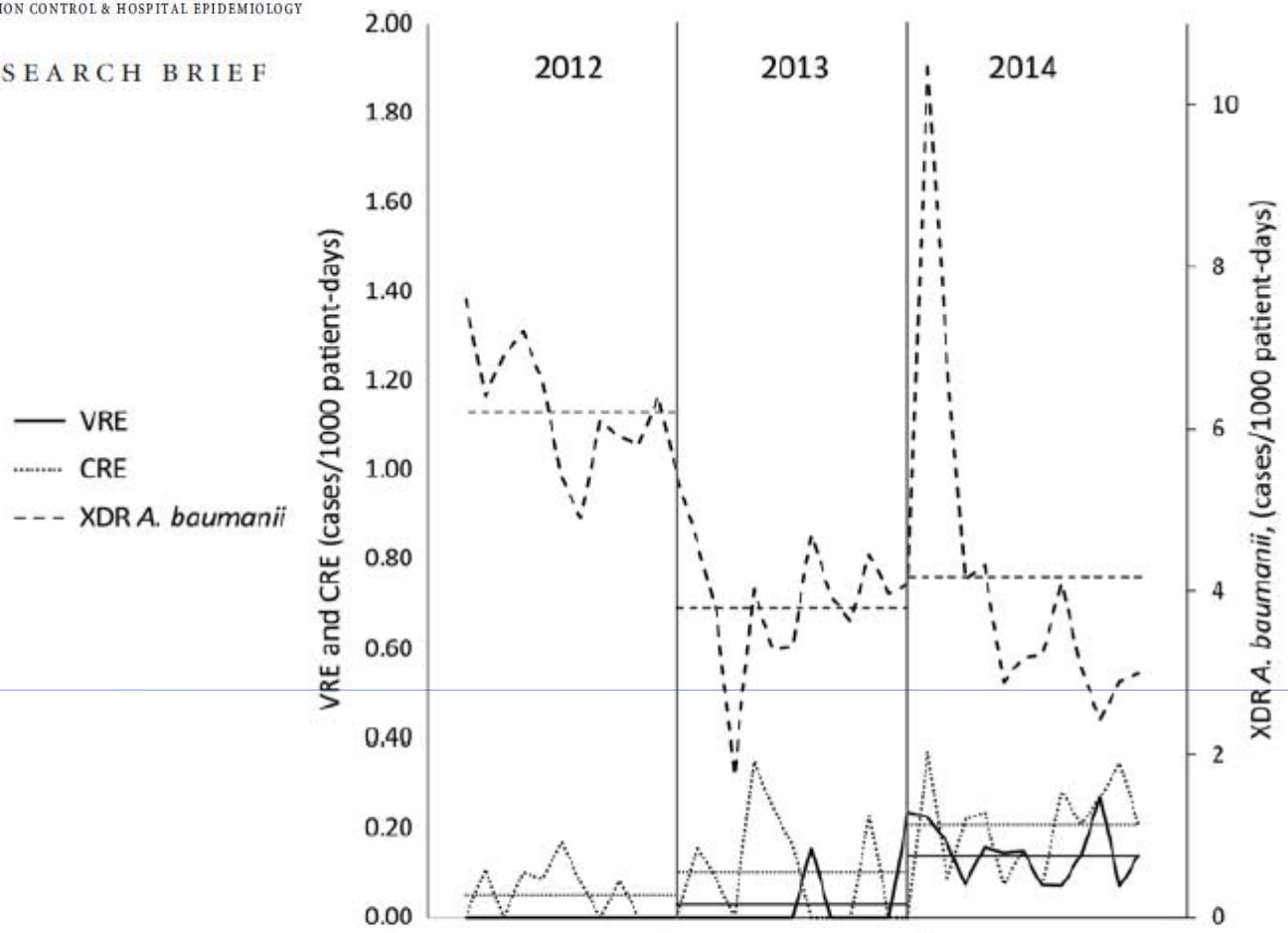
Anucha Apisarnthanarak, MD;[1] Li Yang Hsu, MD;[2] Tze-Peng Lim, MSc;[2,3] Linda M. Mundy, MD, PhD[4]

Adopter Categories



INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY

RESEARCH BRIEF



Compliance (%)	2012				2013				2014			
Hand Hygiene	66	74	74	76	90	90	88	90	88	88	73	82
Contact Precautions	40	36	38	40	66	59	56	56	43	61	58	54
Environmental Cleaning	36	37	37	37	67	63	60	58	45	61	59	58
Antibiotic Use (DDD/1000 patient-days)												
Cephalosporins, 3rd Generation	51				54				55			
Quinolones	8.9				8.2				9.1			
Carbapenems	37				38				42			

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Nattapol Pruetpongpun, MD;[2]
Aubonphan Buppajarntham, MD;[2]
Anucha Apisarnthanarak, MD[2]

Controlling Nosocomial Transmission of Drug-Resistant Pathogens at Different Endemic Stages in a Resource-Limited Setting

Conclusions

- MDR-GNB increasing dramatically in several Asia countries.
- There is still a clear gap between the knowledge and practice to control MDR-GNB.
- Integration of science to control MDR-GNB MUST include the implementation science to make it happen in reality.

Thank you very much for your attention!