

# Epidemiology and Burden of Multidrug-resistant Bacterial Infection in Thailand

Cherry Lim

Wellcome Trust Training Fellowship



# ACKNOWLEDGEMENT

## Co-authors

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- Vanaporn Wuthiekanaun
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- Saowapak Hinjoy
- Nick PJ Day
- Sharon J Peacock
- Direk Limmathurotsakul

Lim C, Takahashi E, Hongsuwan M, et al. *Elife*. 2016 Sep 6;5.

## Contributors

- Bacterial Infection in Northeast Thailand (BINET) network
- Ministry of Interior, Thailand

## Administrative supports

- Mayura Malasit
- Jittana Suwannapruk
- Directors of all participated hospitals

## IT supports

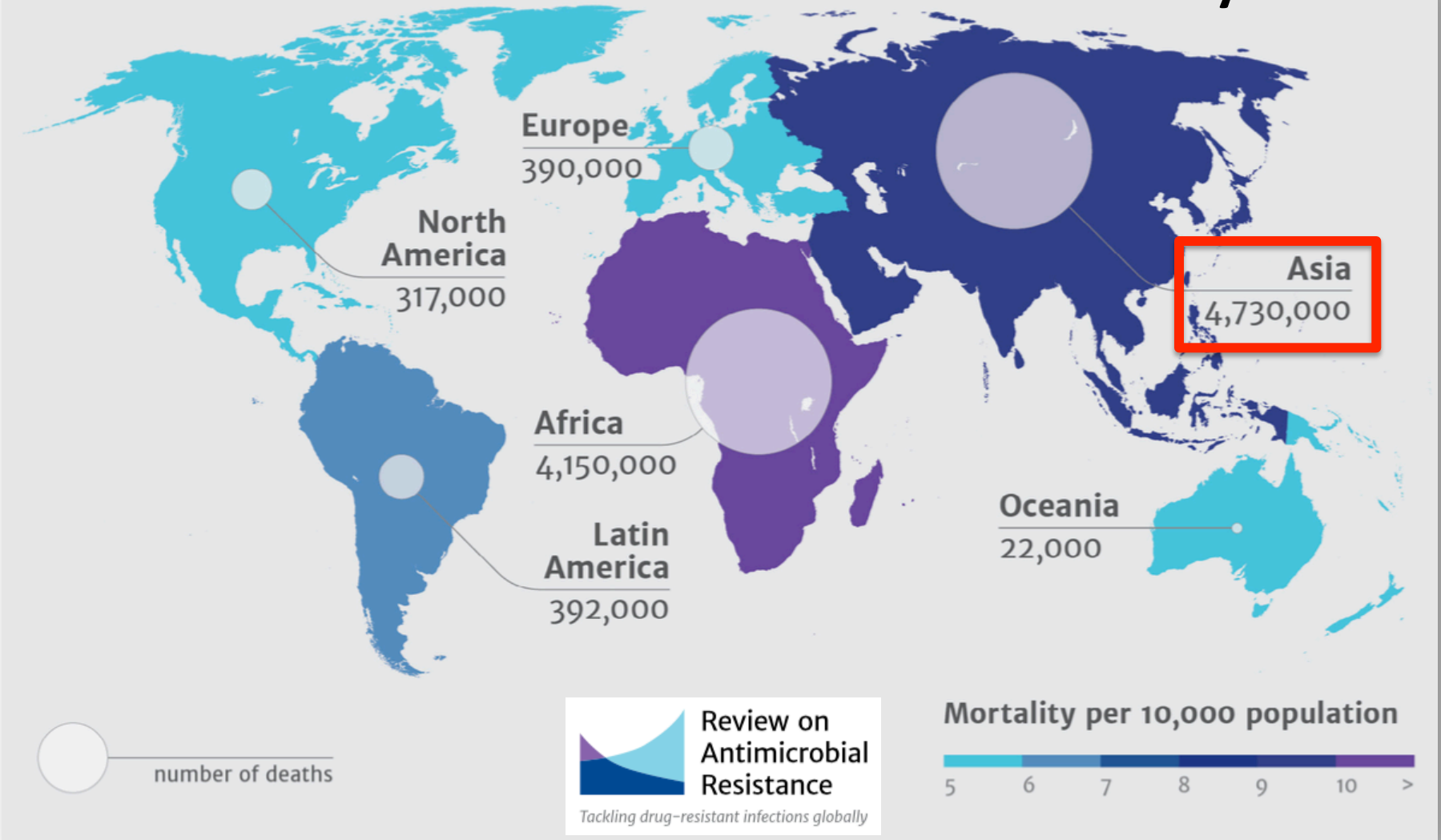
- Prapass Wanapinij
- Mongkol Fungprasertkul
- Dean Sherwood

## Special Thank you to

- Nick J. White
- Ben Cooper

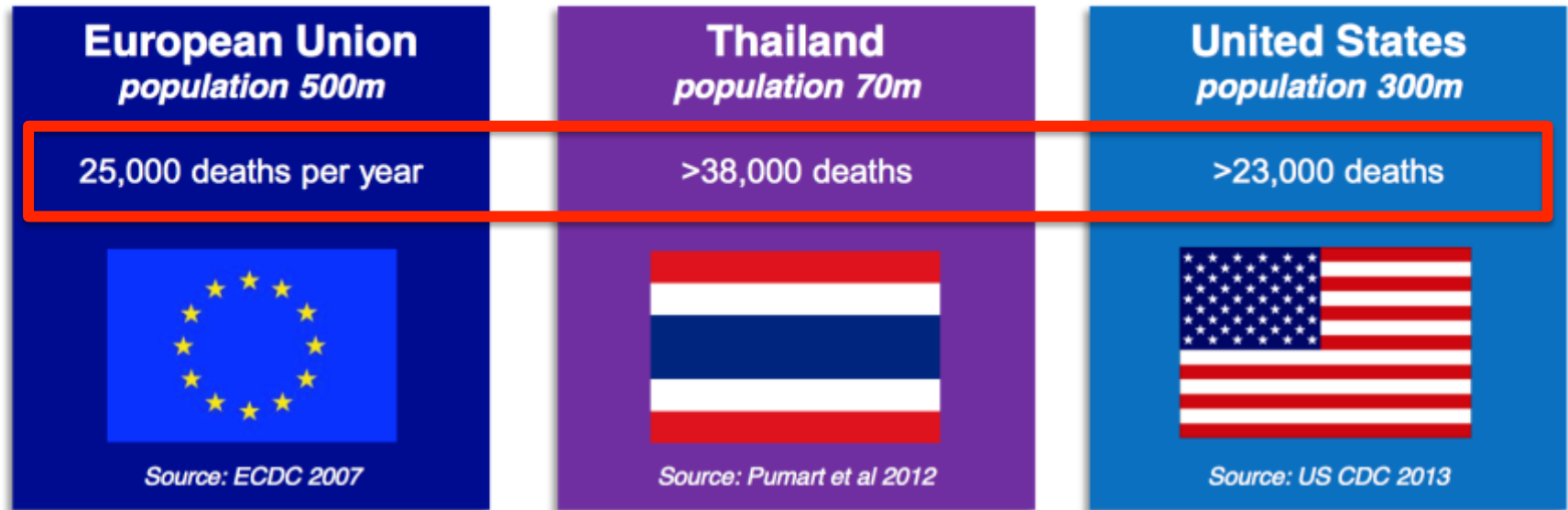


**10 million** deaths by 2050



Currently **700,000** deaths (low estimate) due to antimicrobial resistant infection

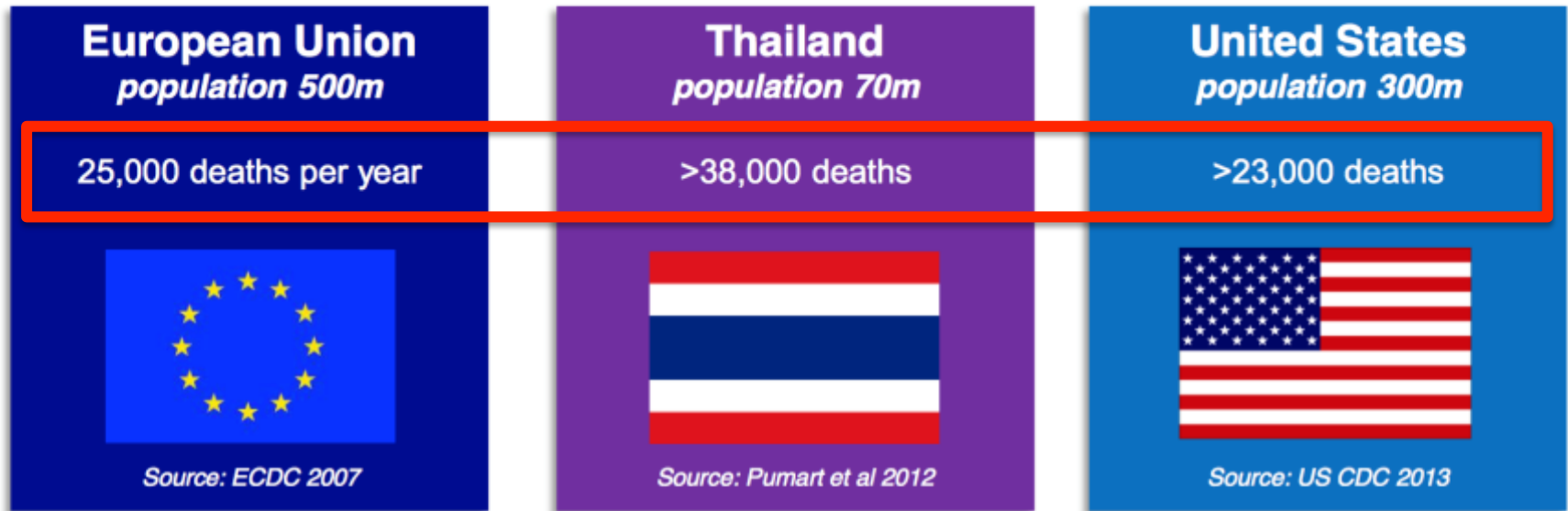
# Estimates of Burden of Antibacterial Resistance



Global information is insufficient to show complete disease burden impact and costs



# Estimates of Burden of Antibacterial Resistance



Global information is insufficient to show complete disease burden impact and costs

**38,000 in Thailand is “total mortality”**  
**However, it’s not comparable**  
**“attributable mortality” should be used**

# Epidemiology and burden of multidrug-resistant bacterial infection in a developing country

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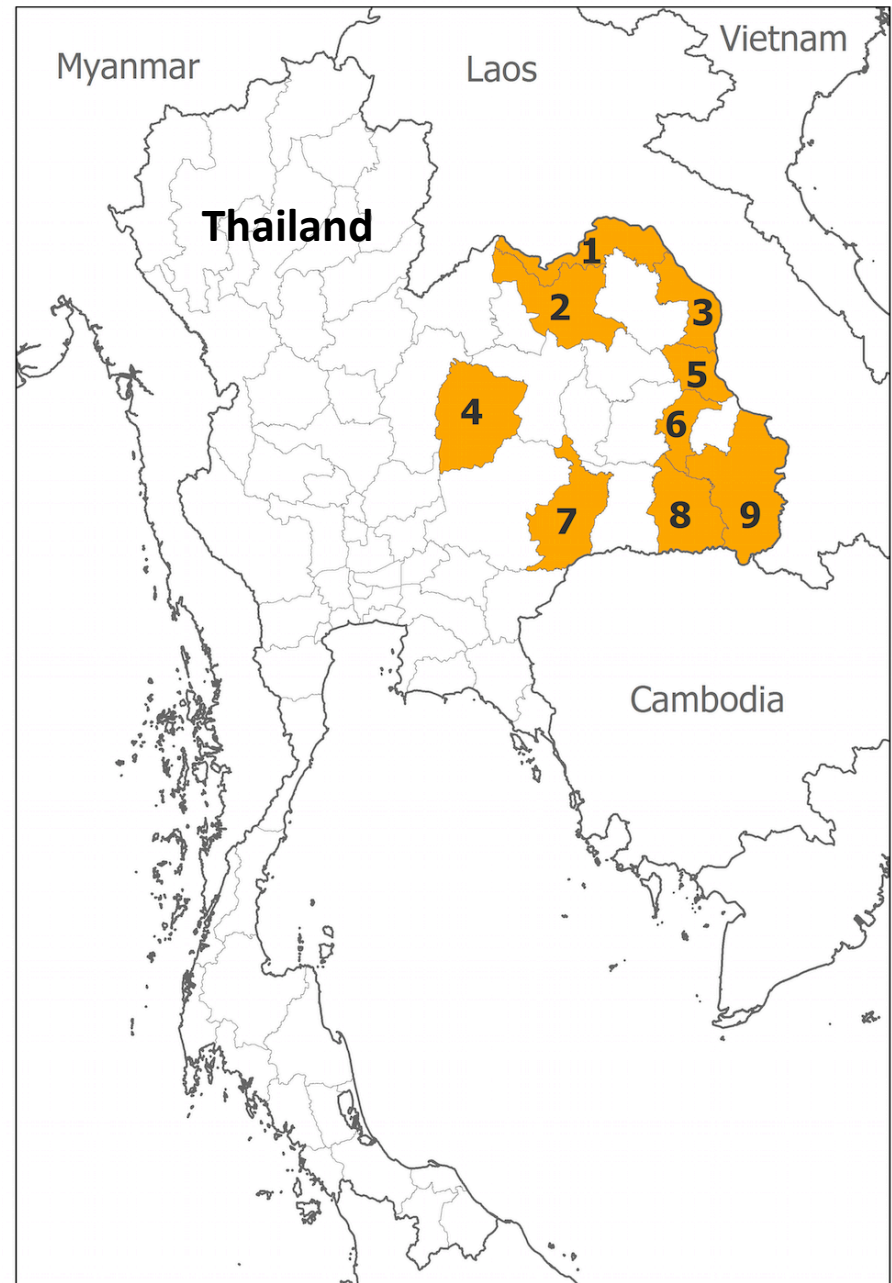
## Contributors

- Bacterial Infection in Northeast Thailand (BINET) network
- Ministry of Interior, Thailand

1. Nong Khai 2. Udon Thani 3. Nakhon Phanom 4. Chaiyaphum 5. Mukdahan  
6. Yasothon 7. Buriram 8. Sisaket 9. Ubon Ratchathani

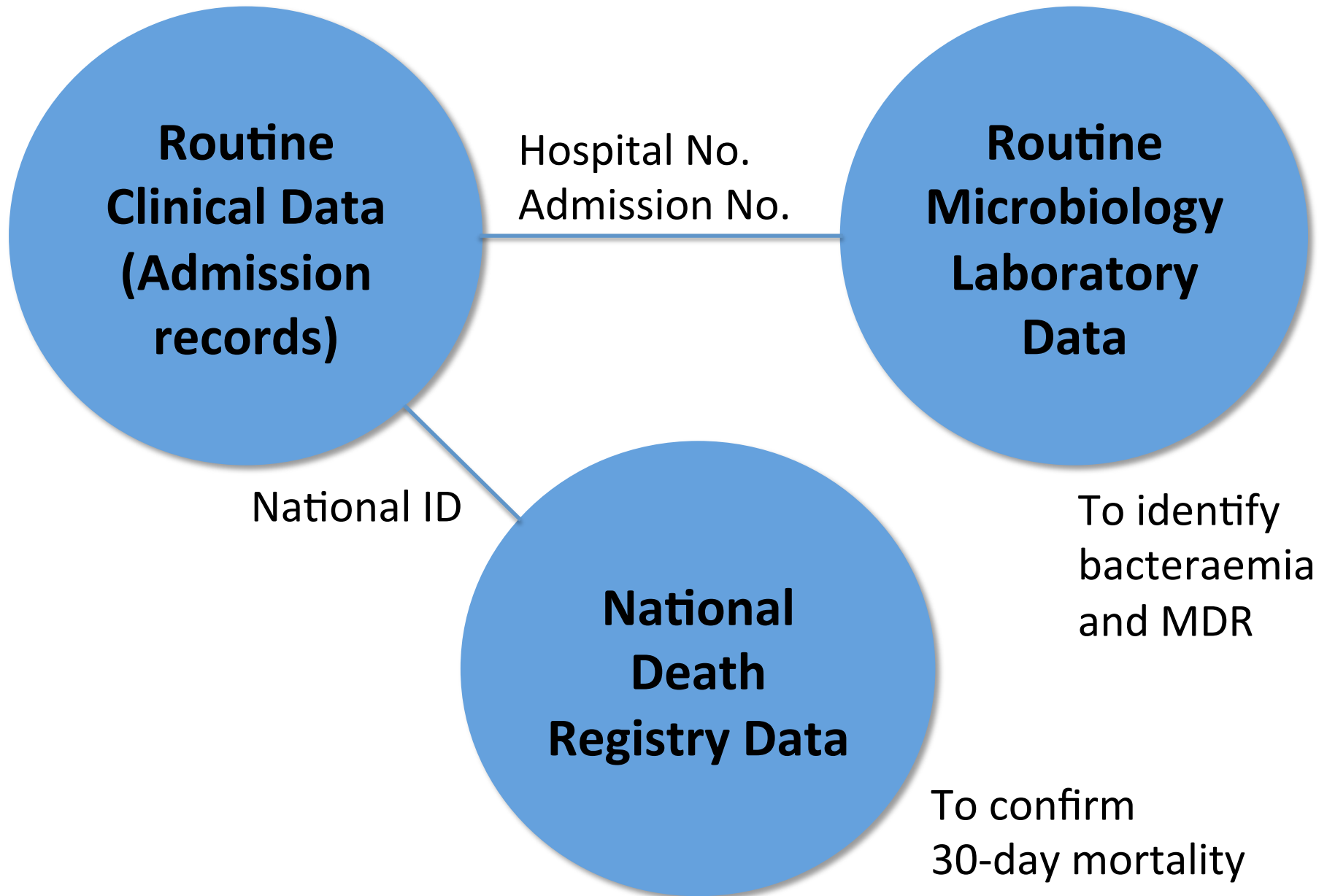
# Study Design

- Retrospective, multicentre surveillance study
- Bacteraemia cases
- Jan 2004 - Dec 2010
- 9 provincial hospitals in Northeast Thailand





# Methods - Data sources





# Methods

## Multidrug-resistant (MDR)

- Non-susceptible to  $\geq 1$  agents in  $\geq 3$  categories of antibiotics
- All MRSA are considered MDR

Margiorakos AP., et al. *Clin Microbiol Infect.* 2012.

## Multivariable logistic regression

- Stratified by hospitals
- Adjusted for gender, age, time to infection (for HAB only) and year of admission

# Methods

Mortality attributable to MDR  
in hospital-acquired bacteraemia (our study)



← Correction factors

Martone WJ., et al. 1998.



Mortality attributable to MDR  
in hospital-acquired infections (all sites)

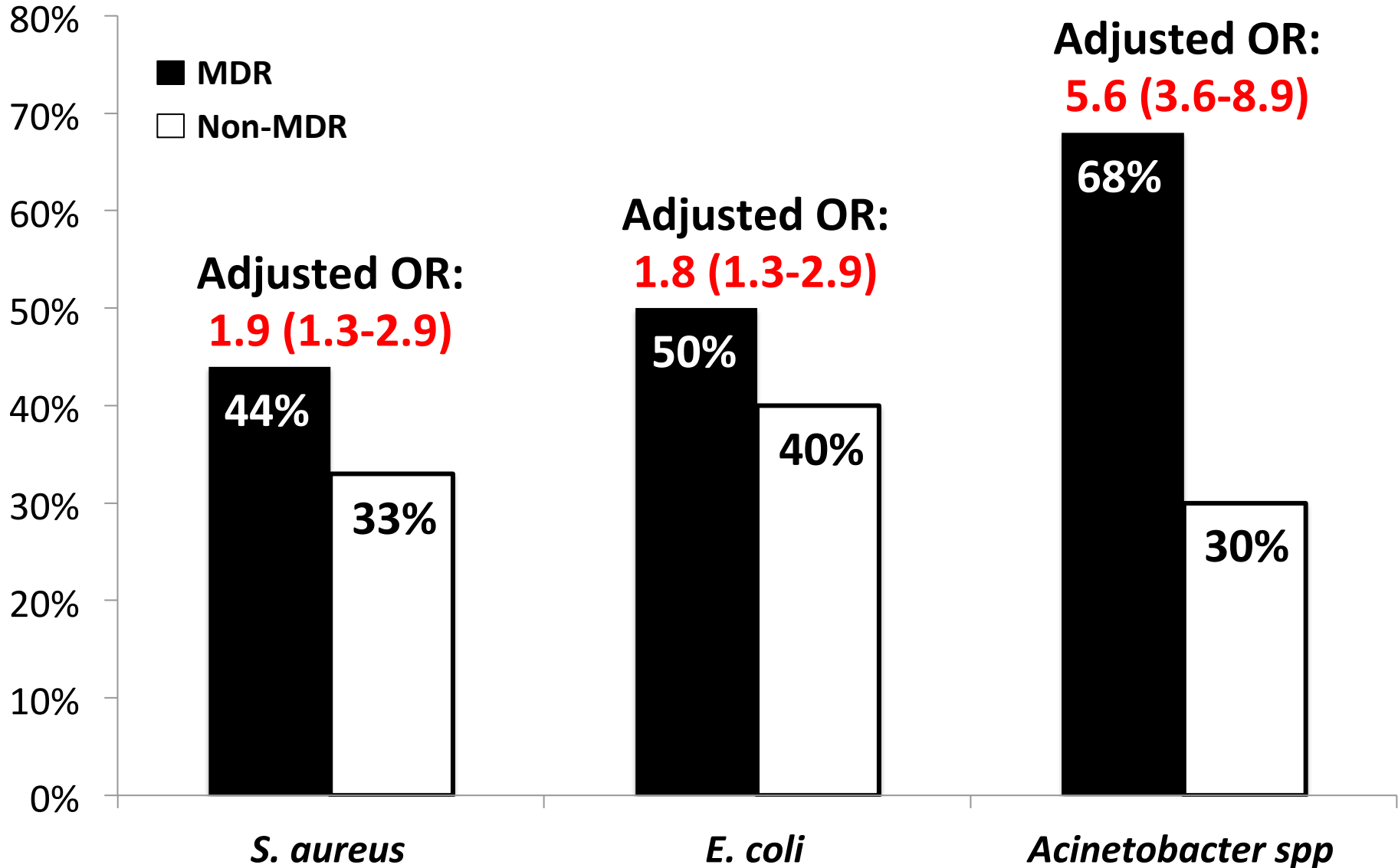


← National statistics of  
nosocomial MDR infections

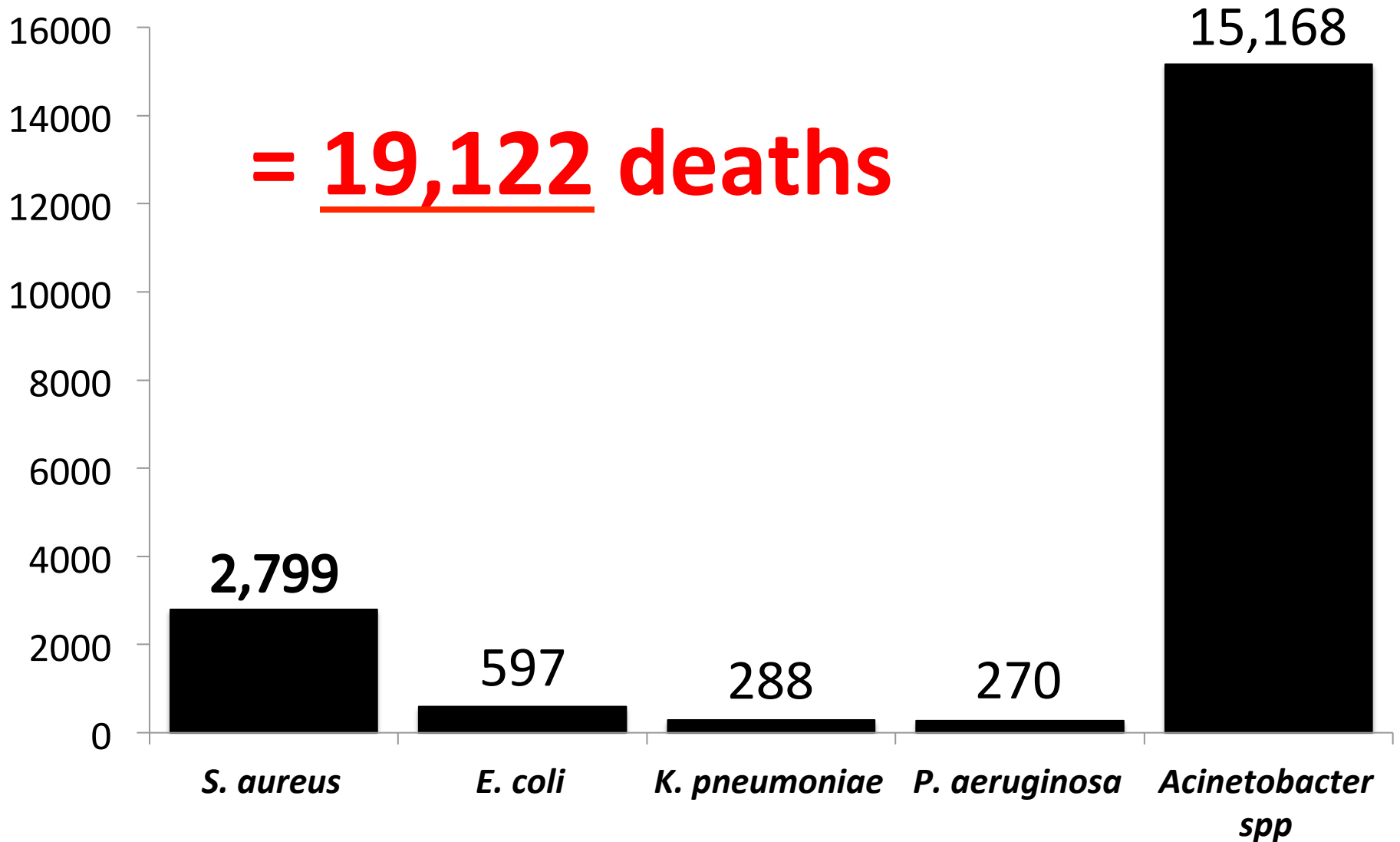
Pumart P., et al.  
2012.

Mortality attributable to MDR  
in hospital-acquired infections in Thailand

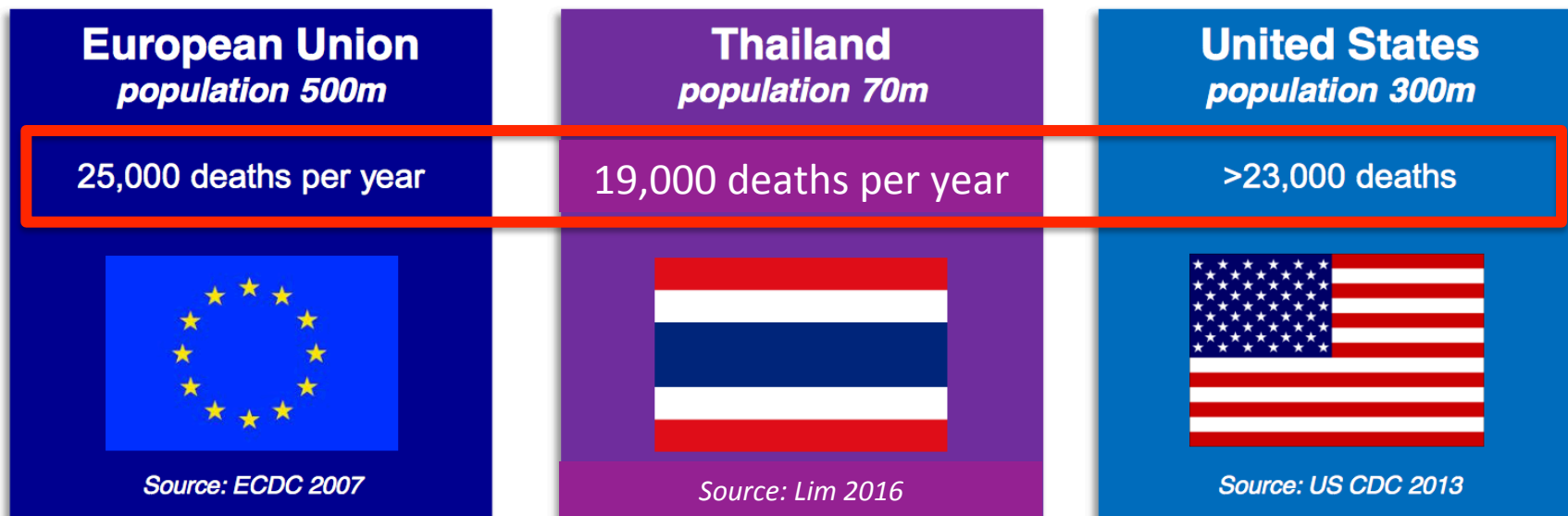
# Results – 30 day mortality in patients with hospital-acquired bacteraemia



# Excess deaths due to MDR in hospital-acquired infections in Thailand



# Estimates of Burden of Antibacterial Resistance



Global information is insufficient to show complete disease burden impact and costs

**THANK YOU**



vs

**Our study**

~3,000 deaths due to  
*S. aureus* + *E. coli* + *K. pneumoniae* AMR infection

~3,600 deaths due to  
*S. aureus* + *E. coli* + *K. pneumoniae* AMR infection

**PLUS**

~15,000 deaths due to  
*Acinetobacter* spp AMR  
infection



- $X_{\text{MDR}}$  = observed mortality in MDR infected patients
- aOR = adjusted odds ratio from multivariable logistic regression model
- $O_{\text{non-MDR}}$  = estimated odds of mortality if infected with non-MDR pathogens

$$O_{\text{non-MDR}} = (1/\text{aOR}) * (X_{\text{MDR}} / (1 - X_{\text{MDR}}))$$

$$\text{Attributable mortality} = X_{\text{MDR}} - (O_{\text{non-MDR}} / (1 + O_{\text{non-MDR}}))$$

# Methods - Categories of bacteraemia

Culture-positive from blood taken  
after **2 days** of admission?

**No**

**Yes**

Hospital stay within 30 days  
prior to the admission?

**Hospital-acquired  
bacteraemia (HAB)**

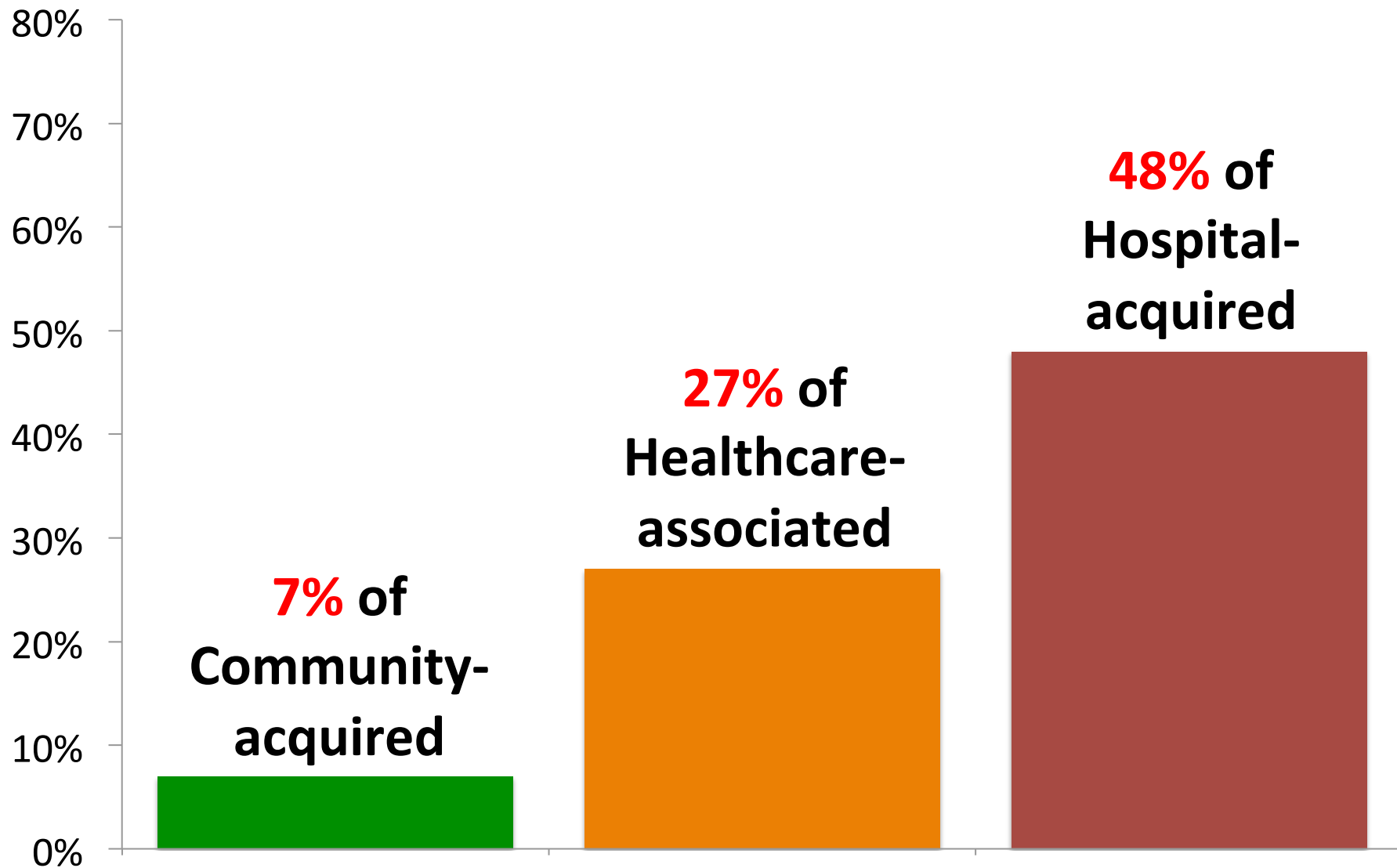
**No**

**Yes**

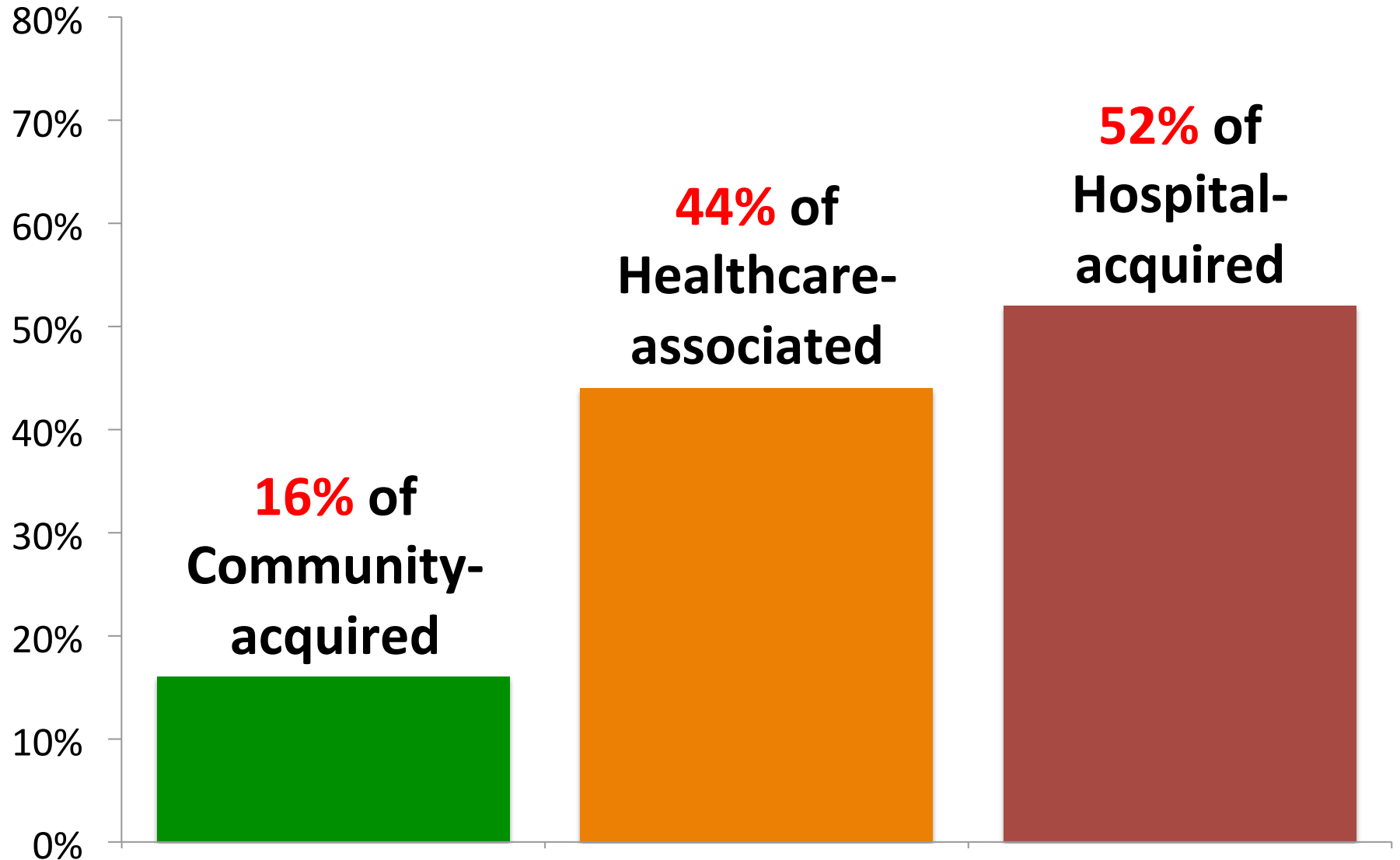
**Community-acquired  
bacteraemia (CAB)**

**Healthcare-associated  
bacteraemia (HCAB)**

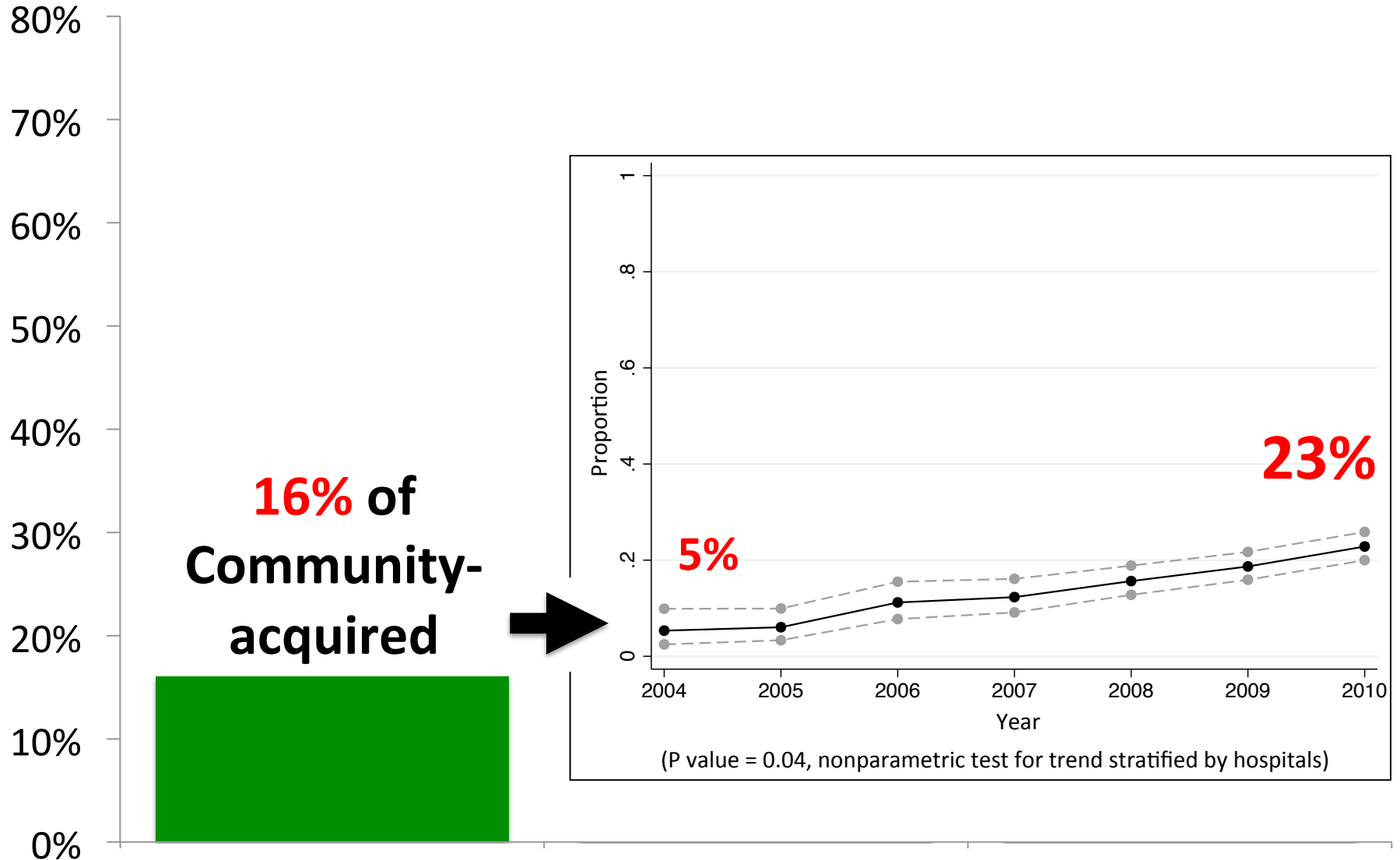
# Results - Proportion of *S. aureus* bacteraemia being MRSA



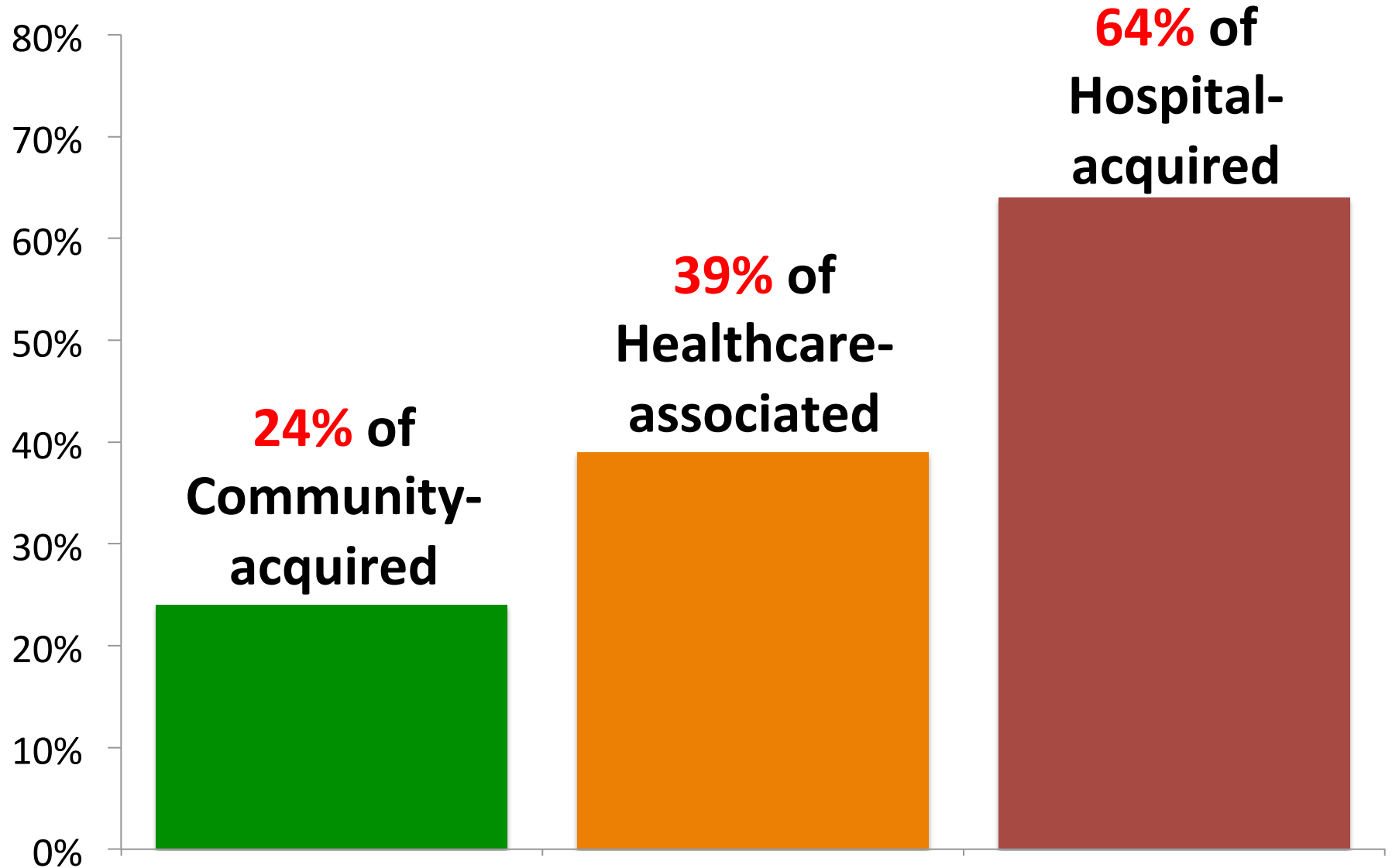
# Results - Proportion of *E. coli* bacteraemia being ESBL



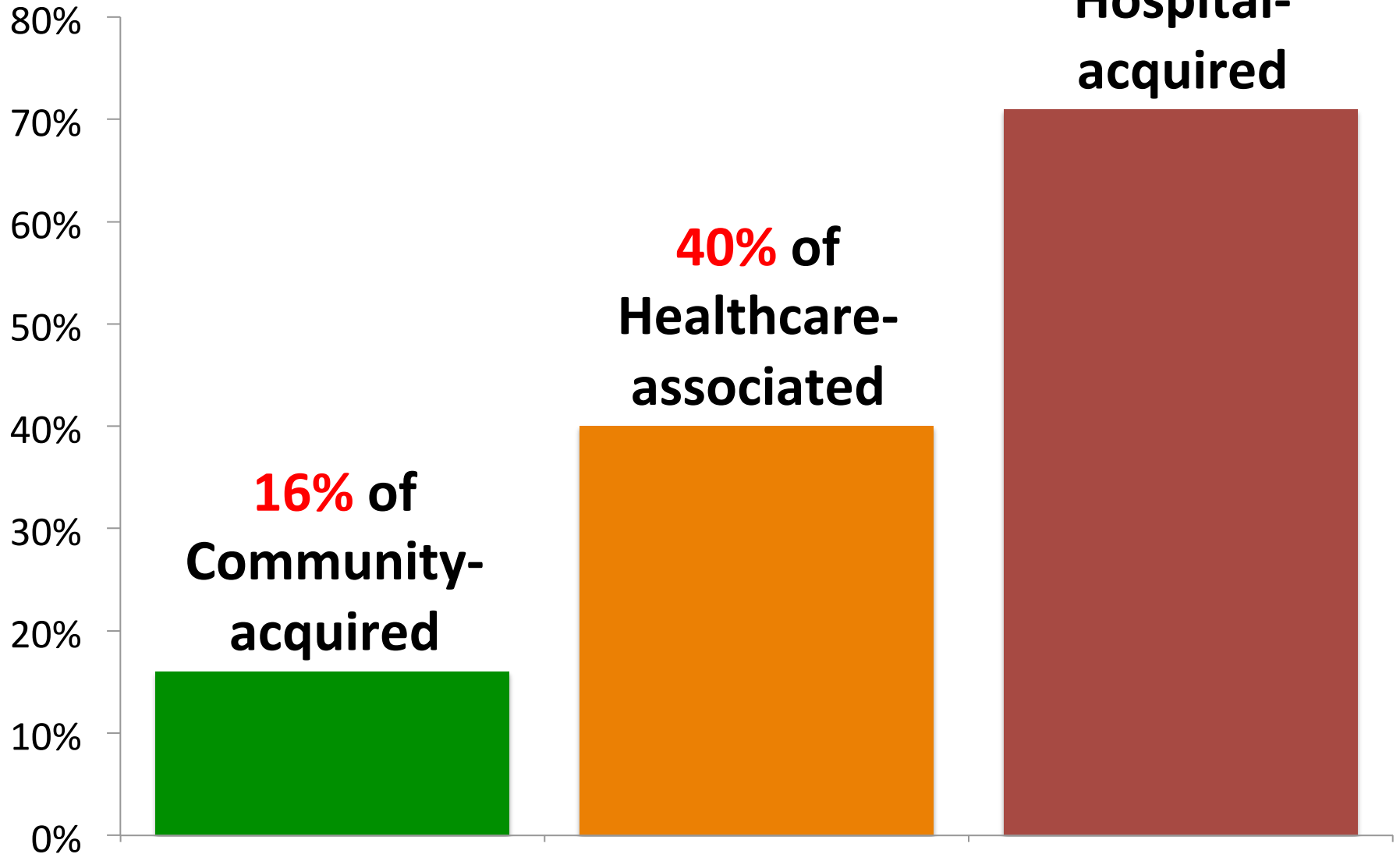
# Results - Proportion of *E. coli* bacteraemia being ESBL



# Results - Proportion of *Acinetobacter* spp bacteraemia being carbapenem-resistance

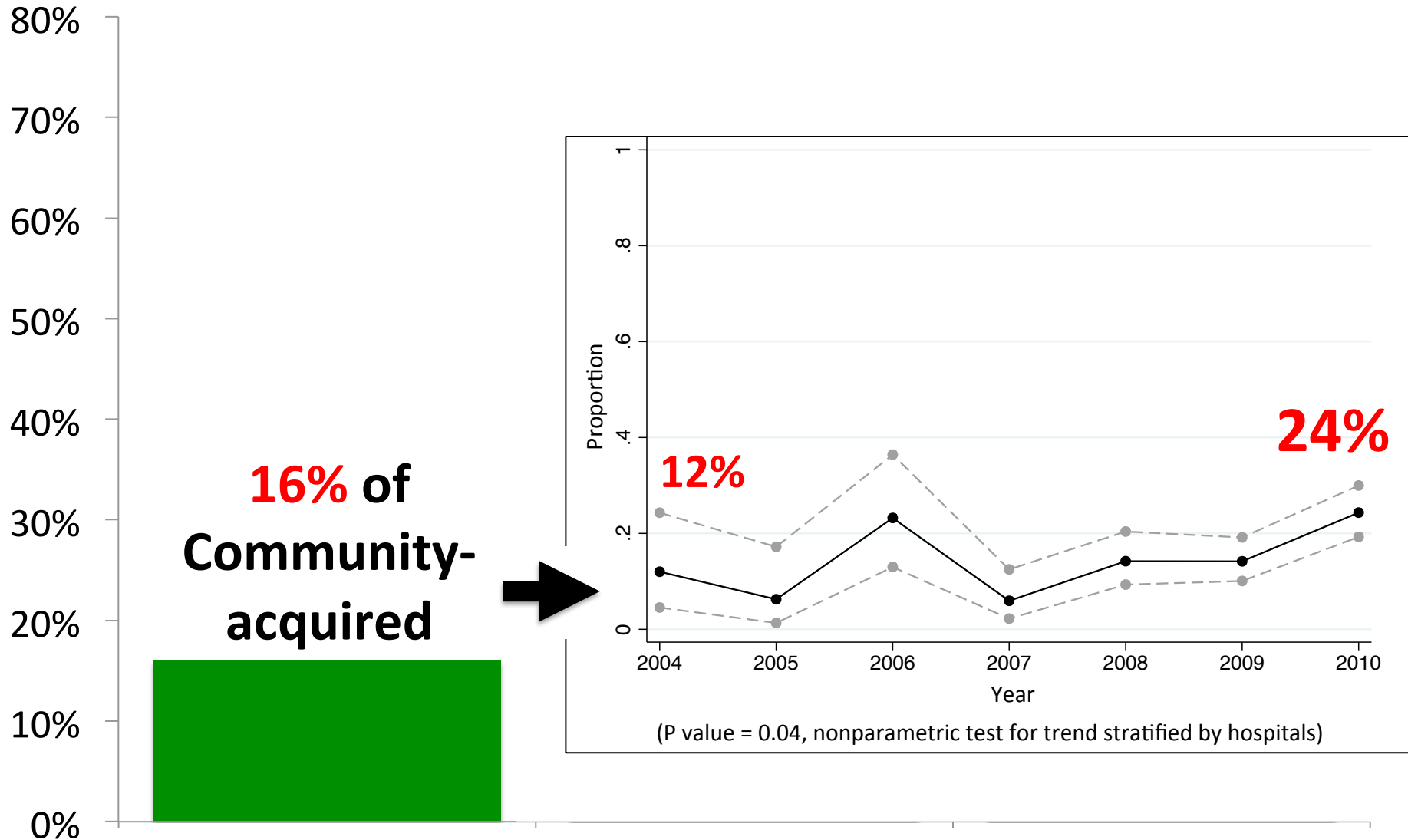


# Proportion of *K. pneumoniae* bacteraemia being ESBL

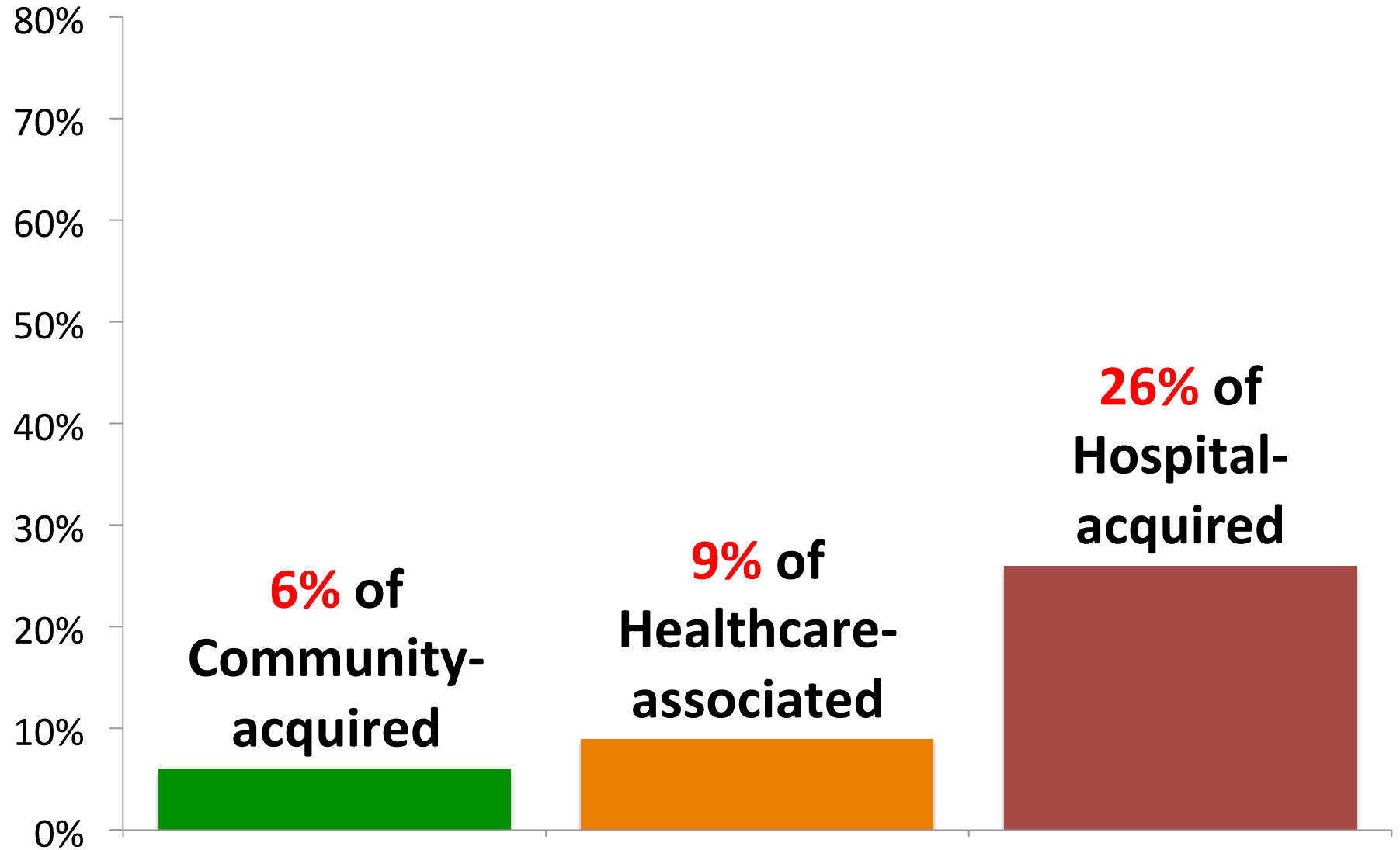




# Proportion of *K. pneumoniae* bacteraemia being ESBL



# Proportion of *P. aeruginosa* bacteraemia being carbapenem-resistance



## RESULTS – ASSOCIATION BETWEEN MDR AND MORTALITY

- Mortality in community-acquired bacteraemia

Causative Pathogen	30 day mortality (%)		aOR (95% CI)
	MDR	Non-MDR	
<i>S. aureus</i>	43% (40/94)	32% (348/1082)	1.4 (0.9-2.2)
<i>Enterococcus</i> spp	NA	31% (55/176)	NA
<i>E. coli</i>	33% (388/117)	26% (566/2205)	<b>1.5 (1.2-1.7)</b>
<i>K. pneumonia</i>	41% (60/146)	43% (373/864)	1.0 (0.7-1.4)
<i>P. aeruginosa</i>	54% (7/13)	51% (138/273)	1.2 (0.4-3.6)
<i>Acinetobacter</i> spp	43% (54/125)	35% (115/324)	<b>1.5 (1.0-2.3)</b>
Subtotal (I-sq=0%, p=0.42)	35% (549/1555)	32% (1595/4924)	1.4 (1.2-1.6)

I-sq= I-squared

## RESULTS – ASSOCIATION BETWEEN MDR AND MORTALITY

- Mortality in healthcare-associated bacteraemia

Causative Pathogen	30 day mortality (%)		aOR (95% CI)
	MDR	Non-MDR	
<i>S. aureus</i>	41% (30/73)	30% (56/186)	1.5 (0.9-2.7)
<i>Enterococcus</i> spp	NA	45% (22/49)	NA
<i>E. coli</i>	45% (131/288)	34% (71/206)	<b>1.7 (1.1-2.5)</b>
<i>K. pneumonia</i>	52% (37/71)	40% (50/125)	1.5 (0.9-2.8)
<i>P. aeruginosa</i>	50% (5/10)	48% (45/93)	1.0 (0.3-3.7)
<i>Acinetobacter</i> spp	76% (44/58)	35% (20/57)	<b>5.3 (2.3-12.1)</b>
Subtotal (I-sq=51%, p=0.09)	49% (247/500)	37% (264/716)	1.9 (1.2-2.8)

I-sq= I-squared

## RESULTS – ASSOCIATION BETWEEN MDR AND MORTALITY

- Mortality in hospital-acquired bacteraemia

Causative Pathogen	30 day mortality (%)		aOR (95% CI)
	MDR	Non-MDR	
<i>S. aureus</i>	44% (97/222)	33% (74/224)	<b>1.9 (1.3-2.9)</b>
<i>Enterococcus</i> spp	50% (2/4)	50% (56/113)	1.1 (0.1-8.4)
<i>E. coli</i>	50% (126/252)	40% (60/151)	<b>1.8 (1.1-2.7)</b>
<i>K. pneumonia</i>	43% (130/301)	48% (74/154)	1.1 (0.7-1.7)
<i>P. aeruginosa</i>	64% (29/45)	60% (81/134)	1.2 (0.6-2.5)
<i>Acinetobacter</i> spp	68% (256/374)	30% (38/127)	<b>5.6 (3.6-8.9)</b>
Subtotal (I-sq=83%, p<0.01)	53% (640/1198)	42% (383/903)	1.9 (1.2-3.2)

I-sq= I-squared