

Do you know your CRE from your CRAB?

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Disclosures

- I have research funding from the Guy's and St. Thomas' Charity
- I have given paid lectures for 3M, BD and Society for Applied Microbiology

THE END OF
ANTIBIOTICS IS NIGH

What's the problem?



“CRE are nightmare bacteria.”

Dr Tom Frieden, CDC Director



“If we don't take action, then we may all be back in an almost 19th Century environment where infections kill us as a result of routine operations.”

Dame Sally Davies, Chief Medical Officer



“If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine where treatable infections and injuries will kill once again.”

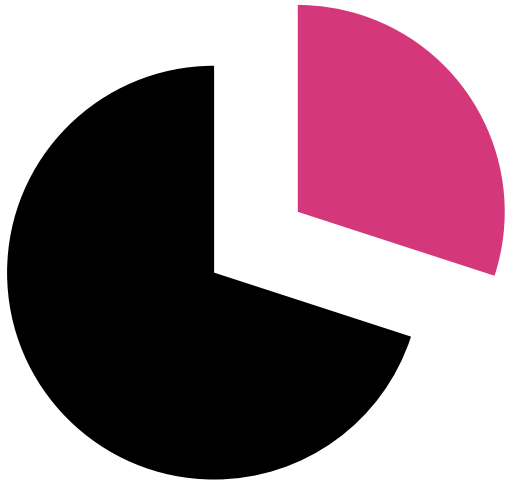
David Cameron, Prime Minister, UK



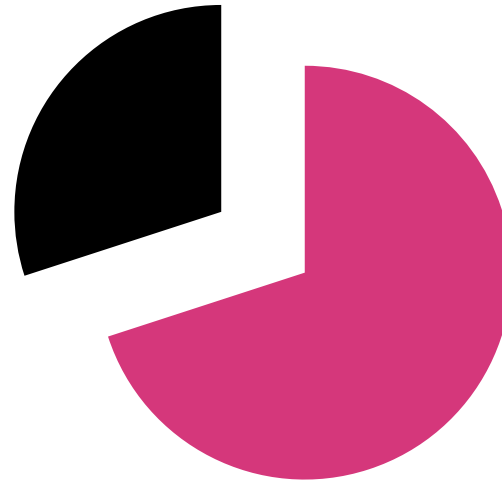
“The rise of antibiotic-resistant bacteria, however, represents a serious threat to public health and the economy.”

Barack Obama, President USA

Rising threat from MDR-GNR



% of all HAI caused by GNRs.



% of ICU HAI caused by GNRs.

Non-fermenters	<i>Acinetobacter baumannii</i> <i>Pseudomonas aeruginosa</i> <i>Stenotrophomonas maltophilia</i>
Enterobacteriaceae	<i>Klebsiella pneumoniae</i> <i>Escherichia coli</i> <i>Enterobacter cloacae</i>

DANGER



MINES

Acronym minefield

CPE

MDR-GNR

CPC

ESBL

MDR-GNB

CRO

CPE

CRE

CRC

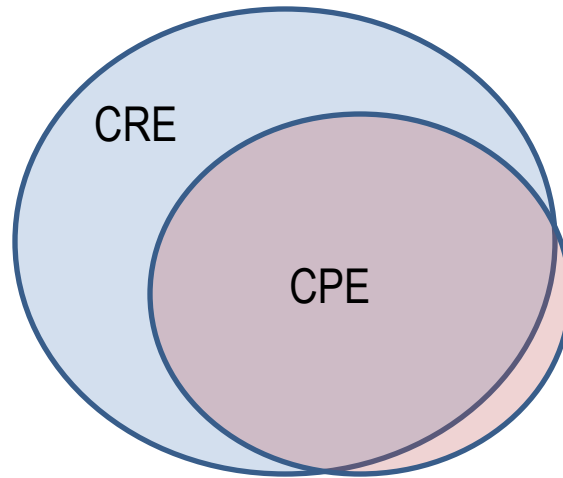
KPC

CRAB

What are CRE?

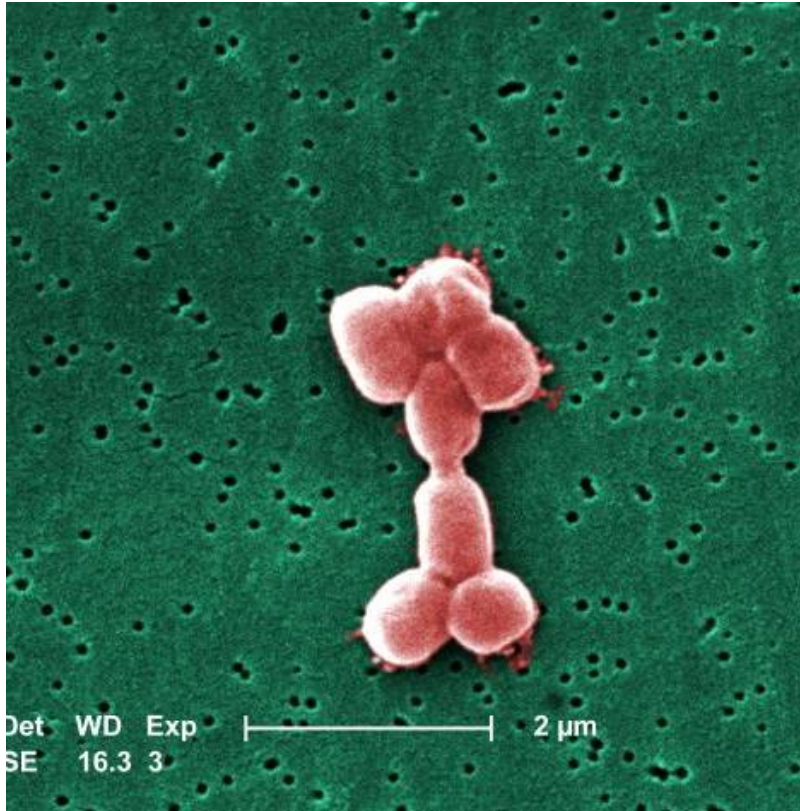
Carbapenem-resistant Enterobacteriaceae (CRE) –
Enterobacteriaceae that are resistant to carbapenems by any
mechanism.

Carbapenemase-producing Enterobacteriaceae (CPE) –
Enterobacteriaceae that are resistant to carbapenems by means of an
acquired carbapenemase.

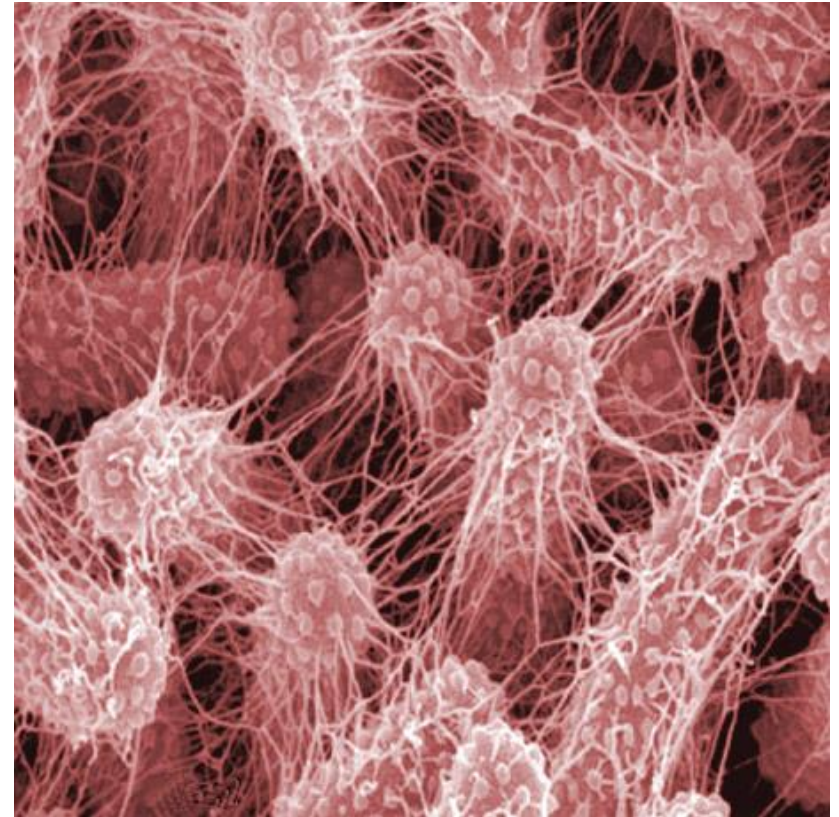


Resistant Enterobacteriaceae v non-fermenters

	Enterobacteriaceae (<i>K. pneumoniae</i>)	Non-fermenters (<i>A. baumannii</i>)
Microbiology	Rods	Coccobacilli
At-risk population	Primarily acute pts	ICU, burns
Risk factors	Travel	Trauma, ICU stay
Epidemic potential	High	Low
Clinical manifestation	UTI	VAP
Attributable mortality	Stark increase (CPE)	Minimal increase
Prevalence	Emerging (rapidly)	Patchy but stable
Sites of colonisation	GI tract	Resp, GI, skin
Colonization duration	Months to >1 year	Days to weeks
Transmission routes	Hands ++, Env +/-	Hands +, Env ++
Resistance	Mainly acquired	Intrinsic & acquired
Common clones	KPC-producing ST258	Intl clones I-III



Acinetobacter baumannii



Klebsiella pneumoniae

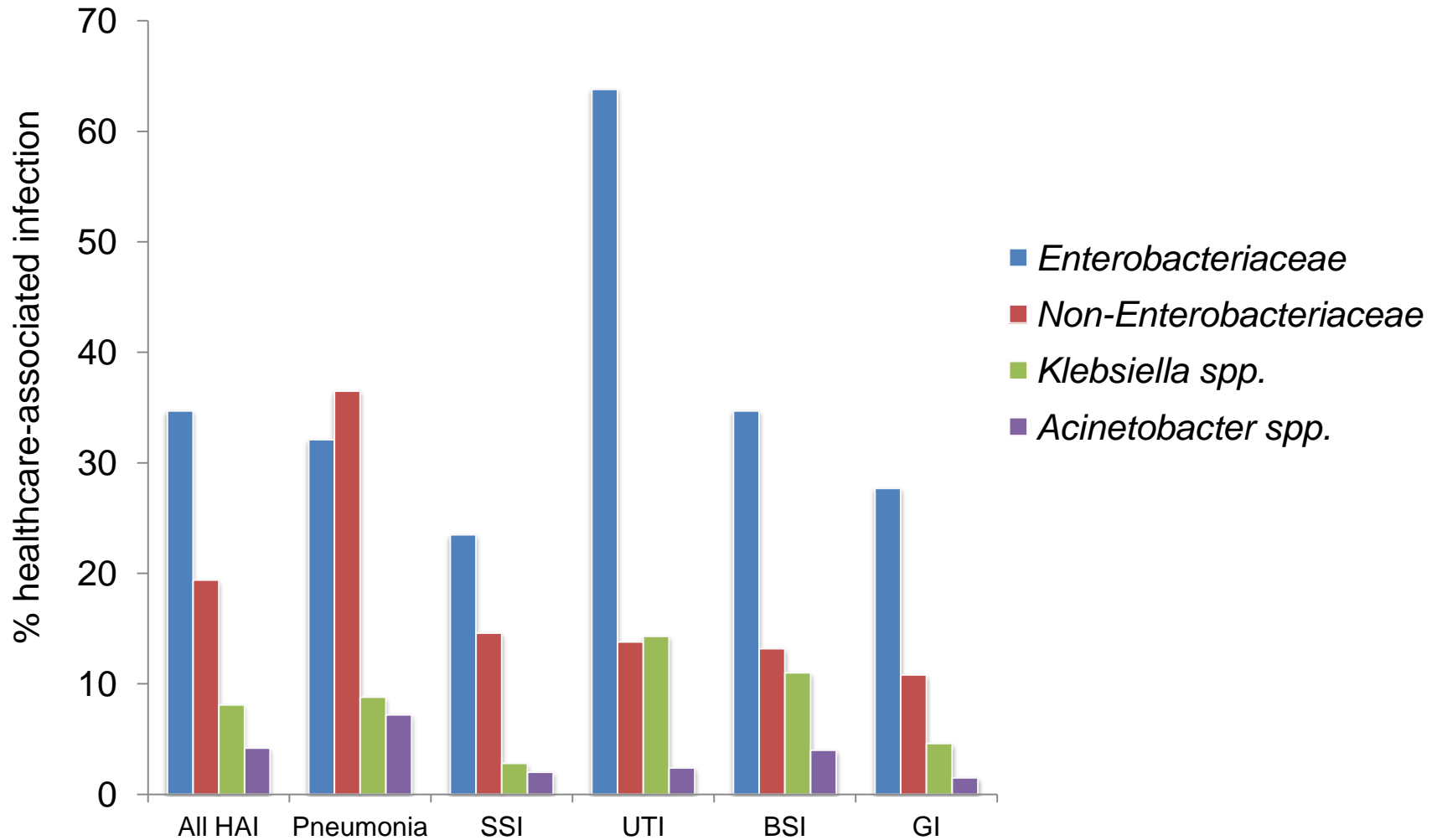
Risk factors & at-risk population

	Enterobacteriaceae	Non-fermenters
Risk factors	LOS ICU stay Catheters / devices Ventilation Prior antibiotics Travel	LOS ICU stay Catheters / devices Ventilation Prior antibiotics Trauma (esp. burns)
At-risk population	Patients in acute settings, particularly those with recent travel to areas of high prevalence. Potential for community spread.	High-risk patients in the ICU and burns units; rare cause of community-acquired infection.

ECDC CPE risk assessment, 2011.

Peleg *et al. Clin Microbiol Rev* 2008;21:538-582

Clinical manifestation



Attributable mortality

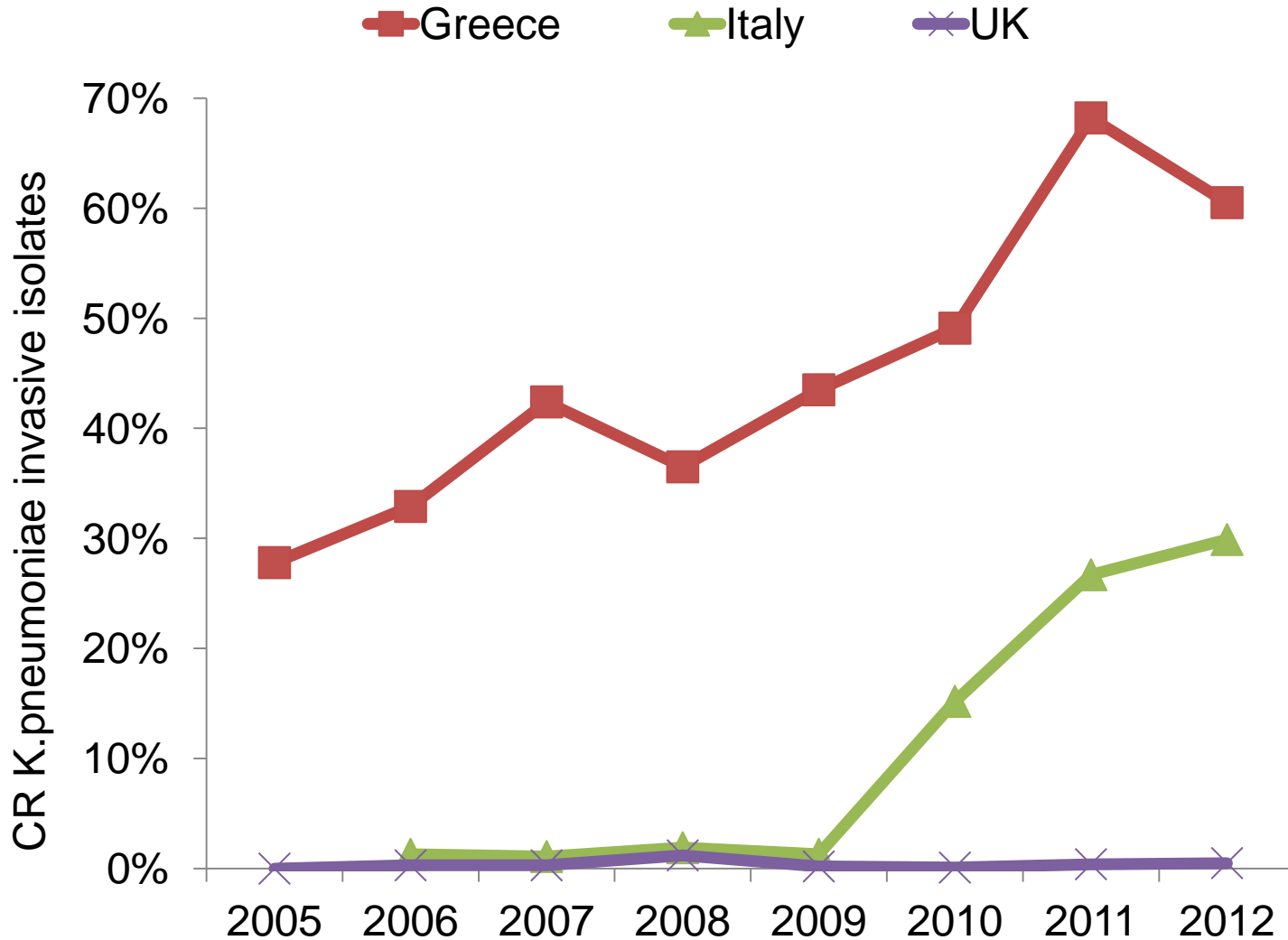
	Enterobacteriaceae		Non fermenters
Organism	AmpC / ESBL	CPE	<i>A. baumannii</i>
Attributable mortality	Moderate	Massive (>50%)	Minimal

Shorr *et al. Crit Care Med* 2009;37:1463-1469.

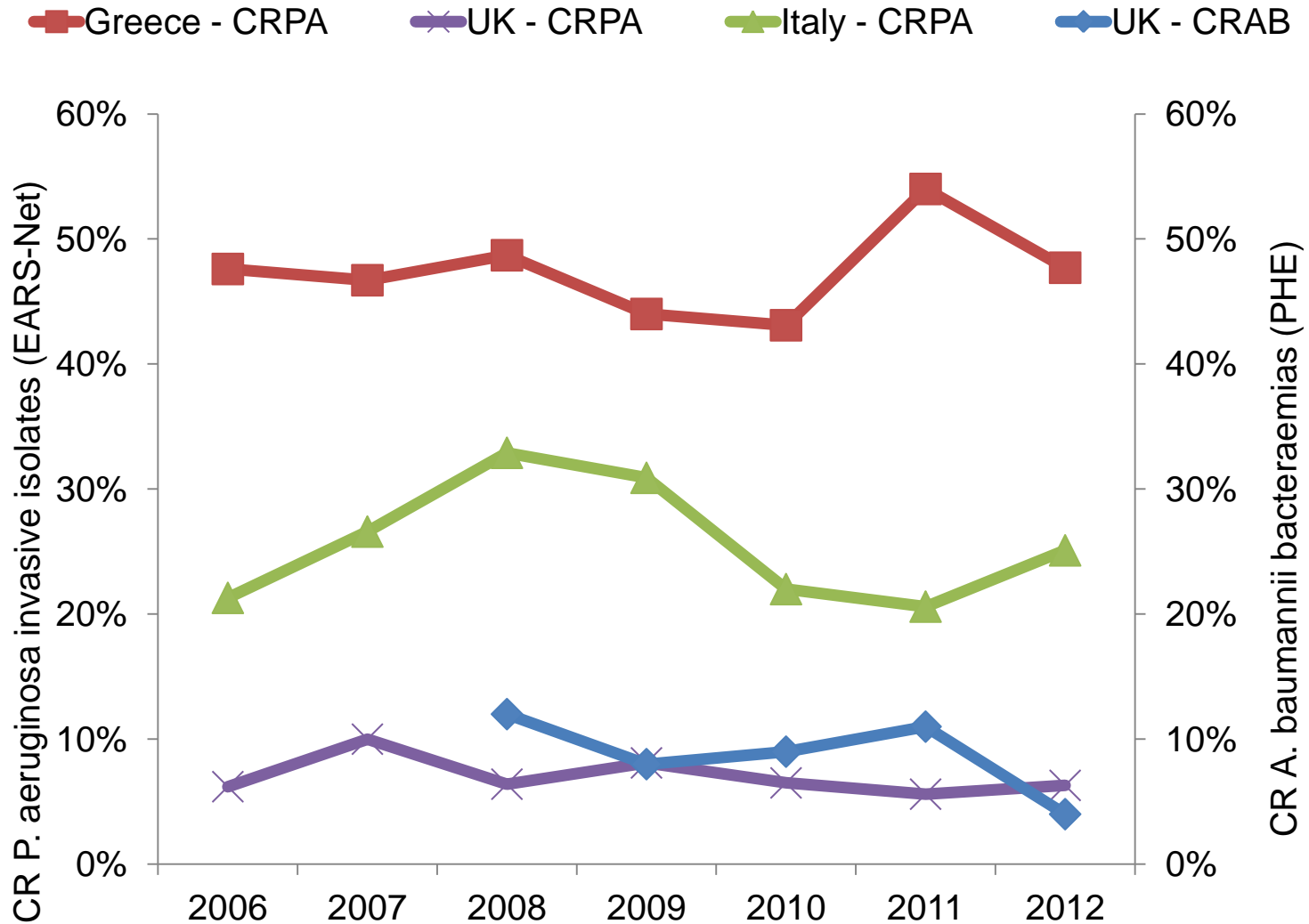
Patel *et al. ICHE* 2008;29:1099-1106.

Falagas *et al. Emerg Infect Dis* 2014;20:1170-1175.

Invasive CR *K. pneumoniae* trends



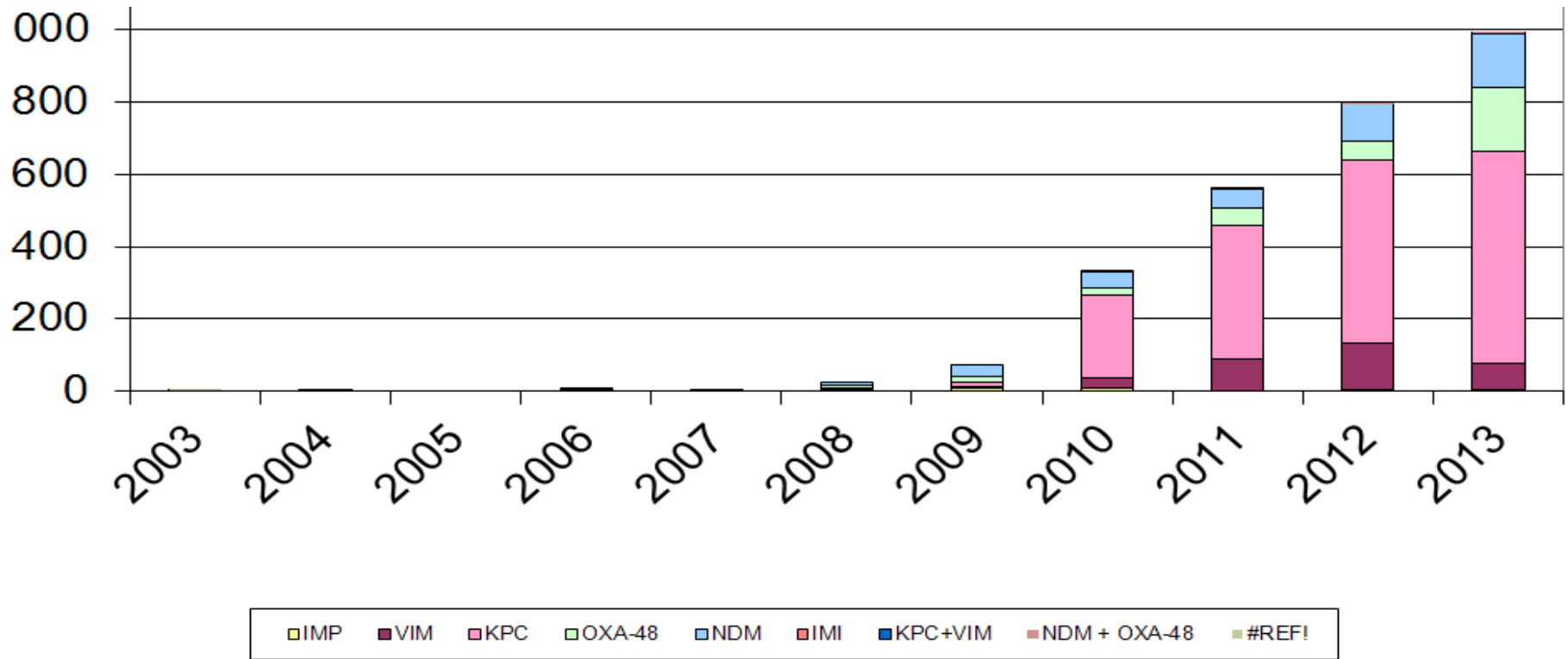
Invasive CR non-fermenters trends



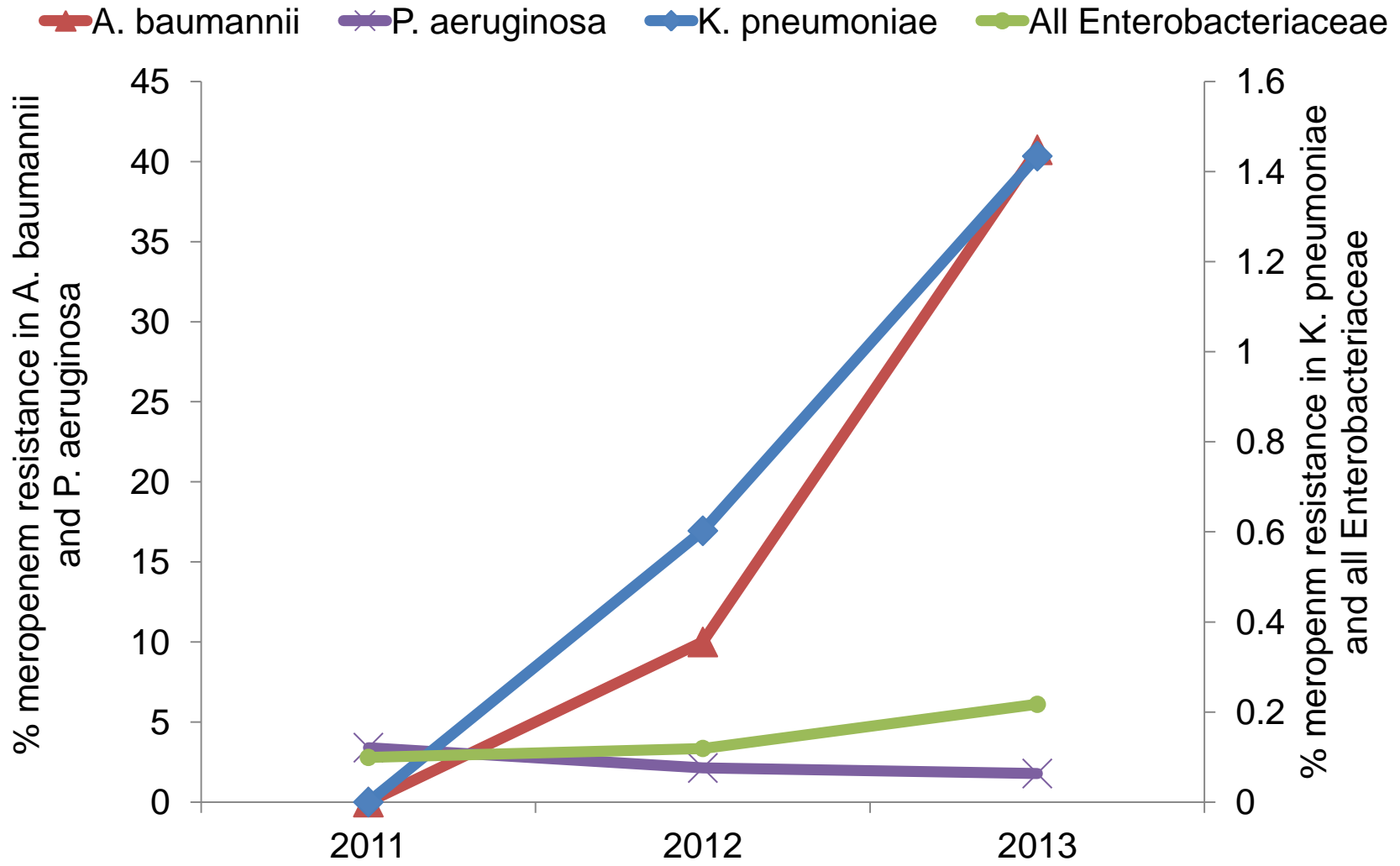
P. aeruginosa: ECDC EARS-Net

A. baumannii: PHE Health Protection Report 2013;7.

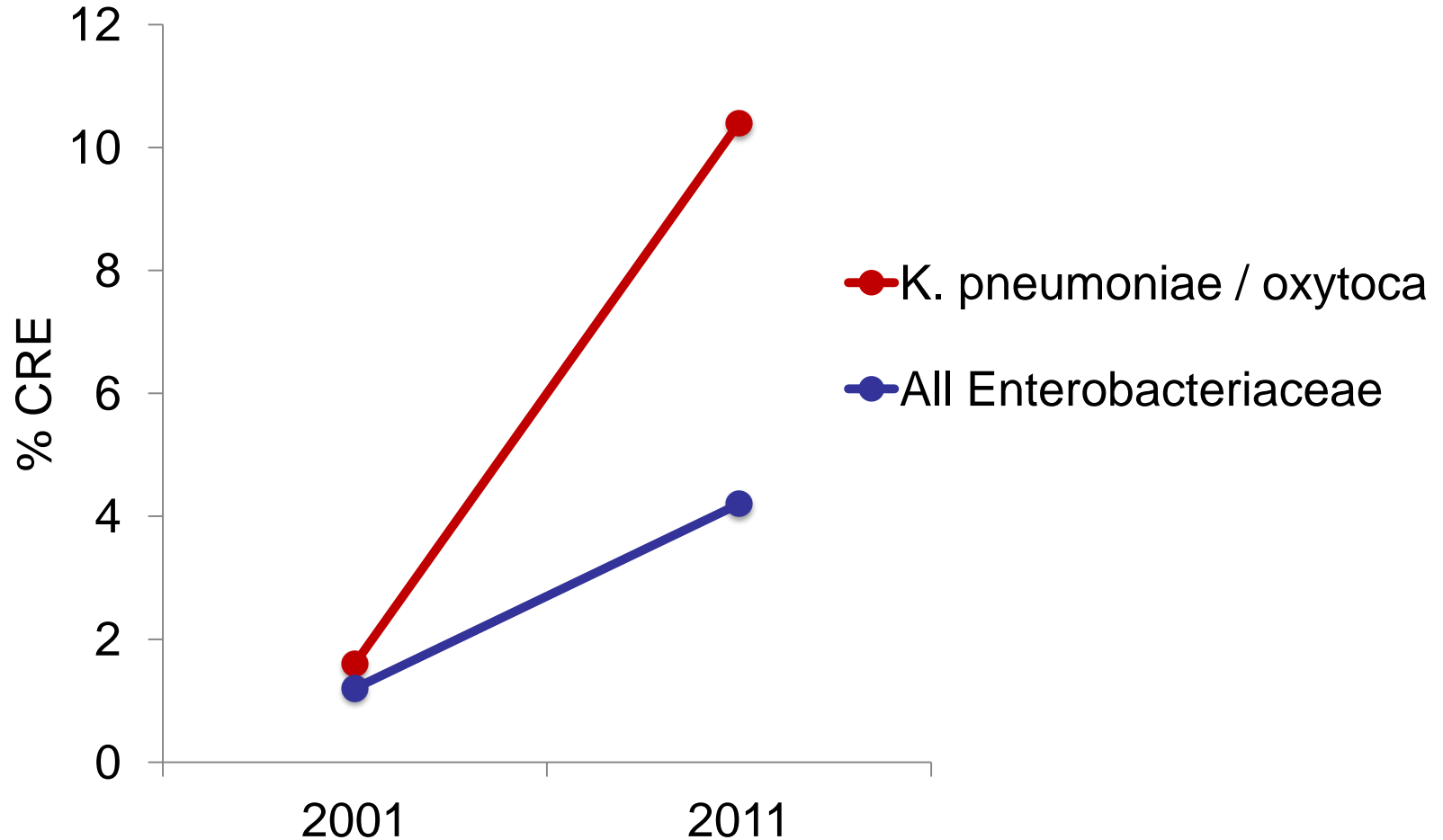
Emergence of CPE in the UK



Prevalence at Guy's and St. Thomas', London

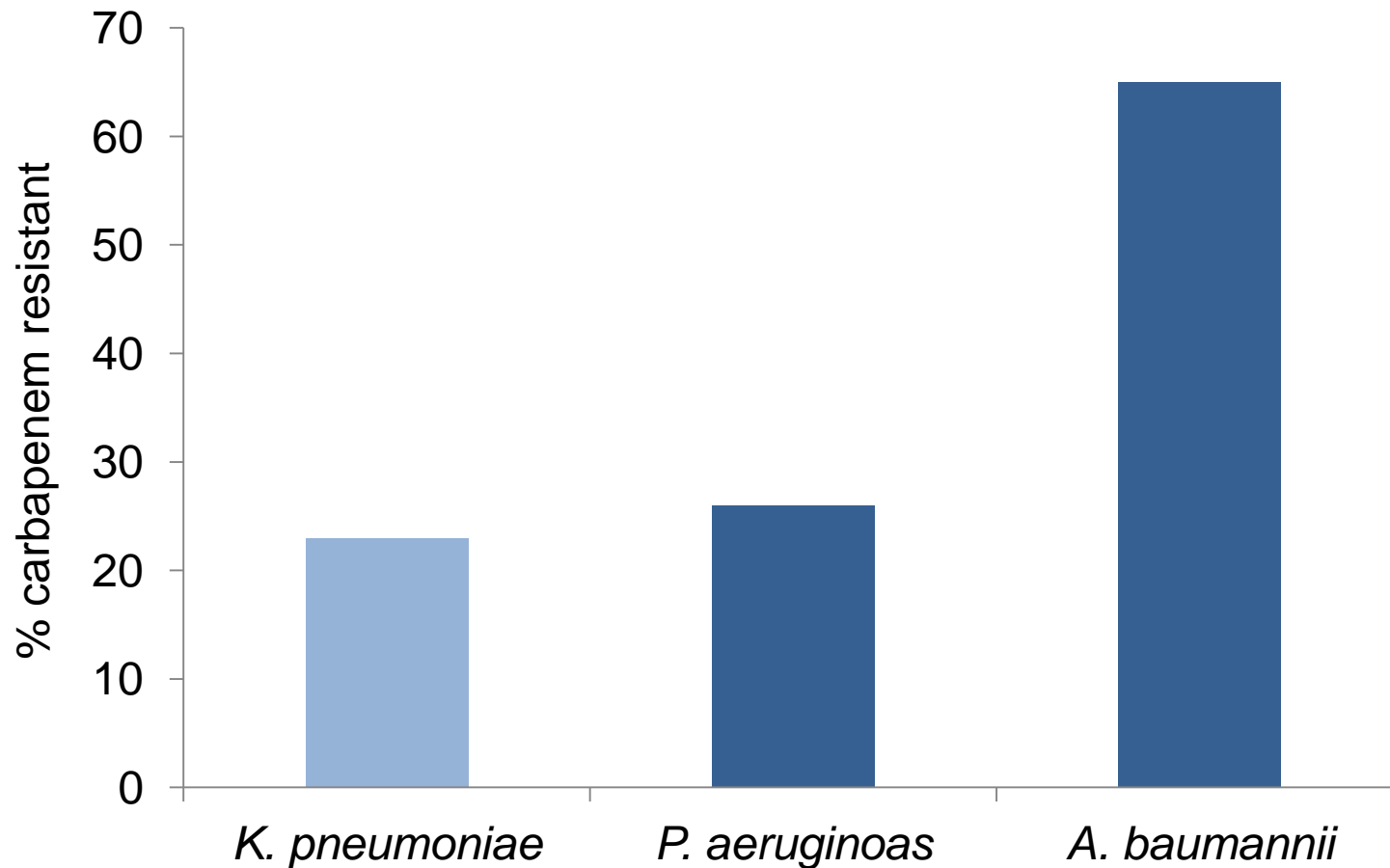


CRE in the USA

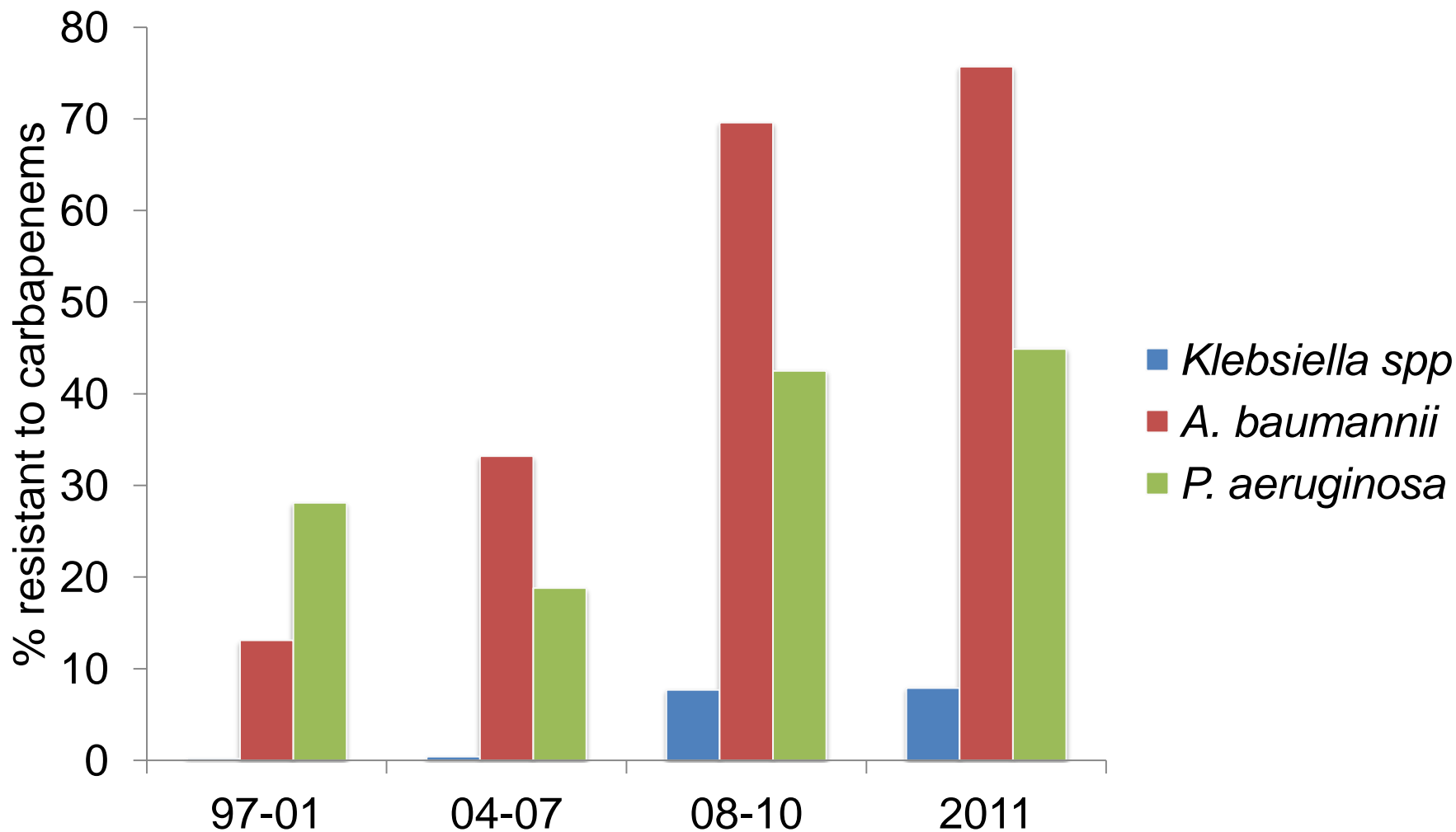


CRE and CRNF in the USA

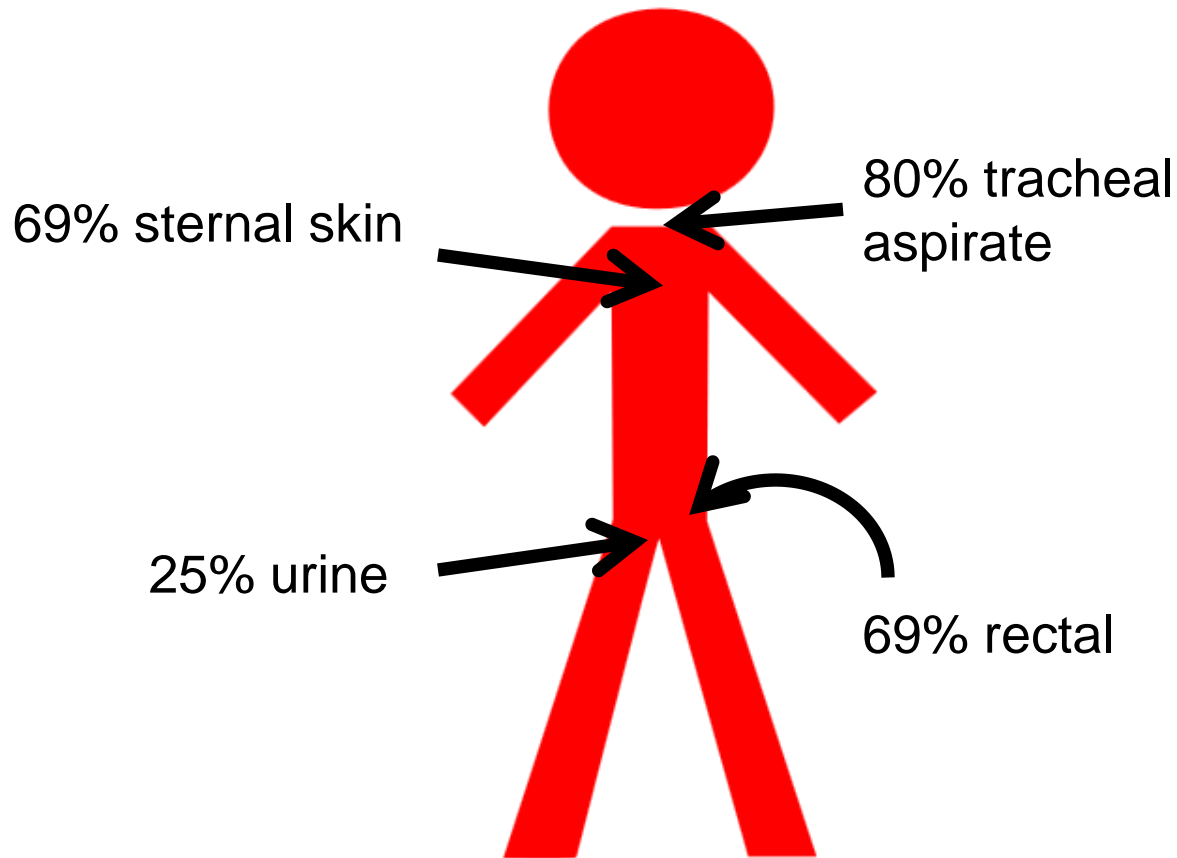
Central line-associated bloodstream infection (CLABSI) resistant to carbapenems in the national NHSN network.¹



Latin America – carbapenem resistance

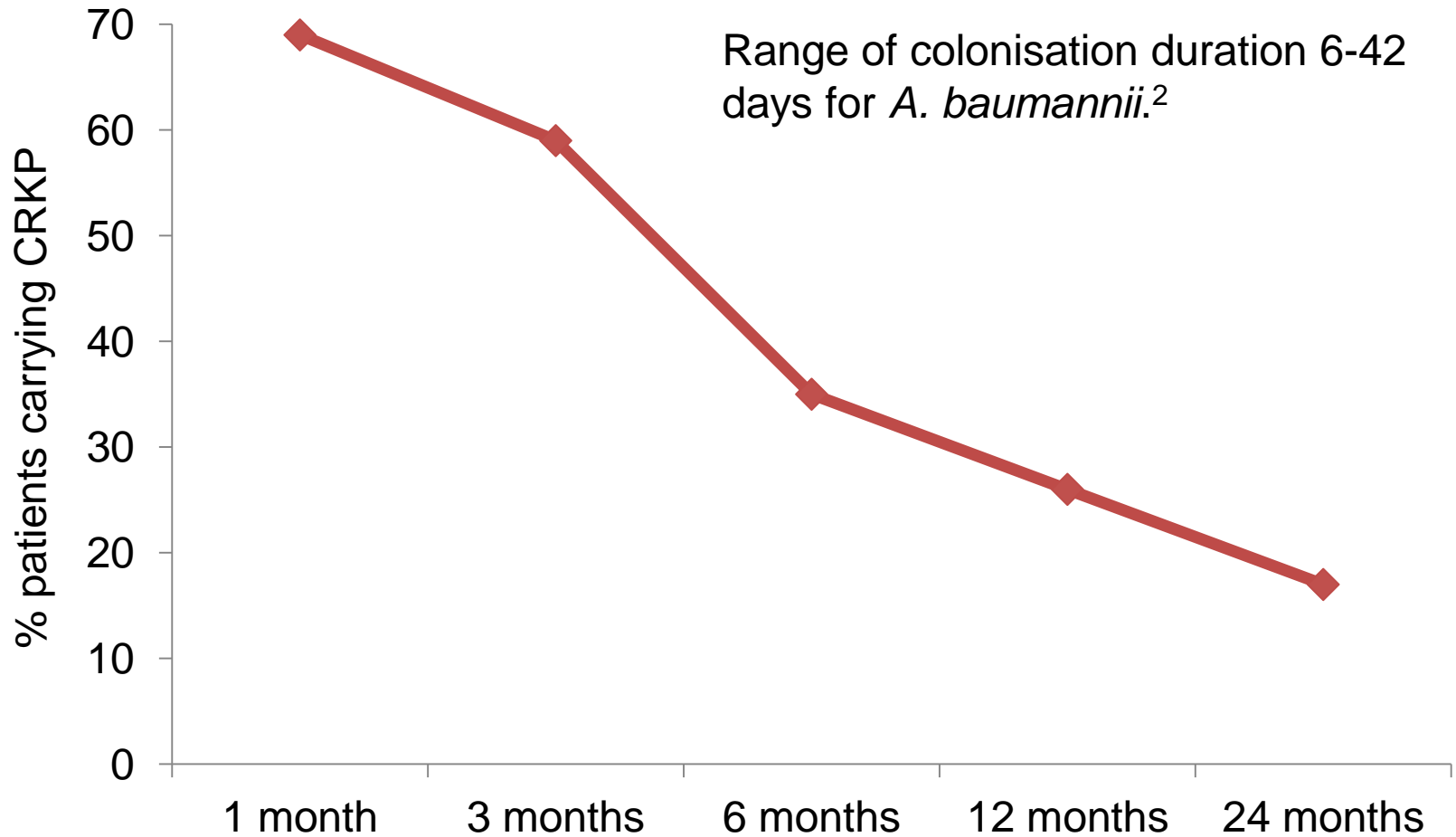


Sites of colonisation – 103 CRAB patients



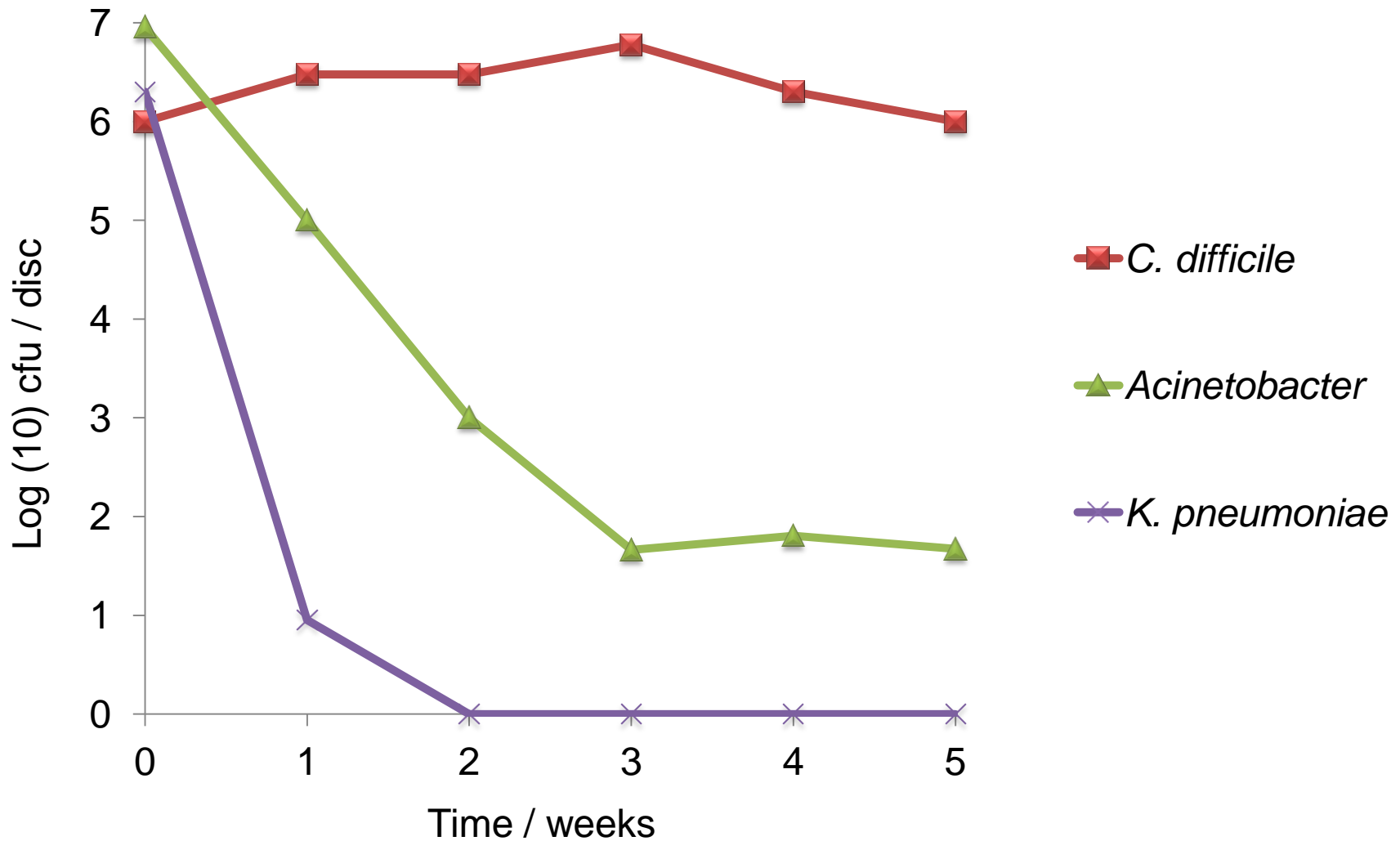
Duration of colonisation - CRKP

Rectal or stool specimens from 103 CRKP patients over 24 months.¹

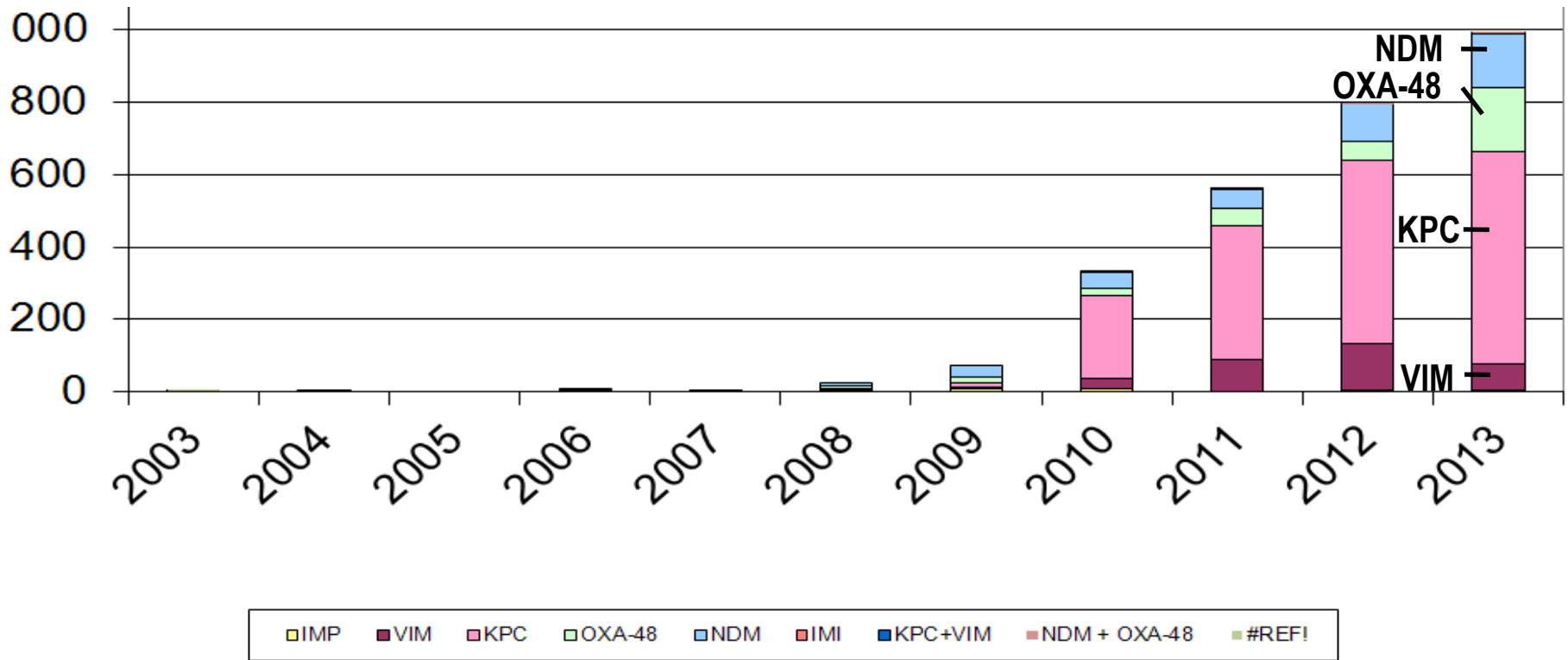


1. Lubert *et al.* *Am J Infect Control* 2014;42:376-380.
2. Dijkshoorn *et al.* *Epidemiol Infect* 1987;99:659-667.

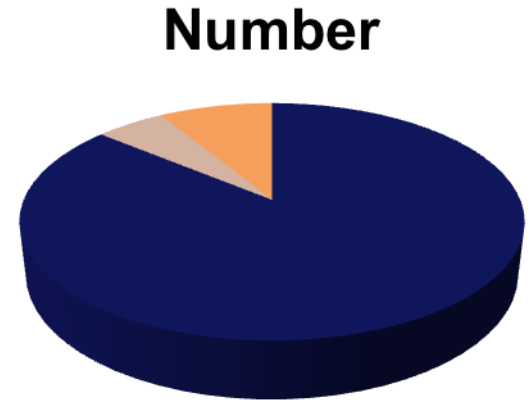
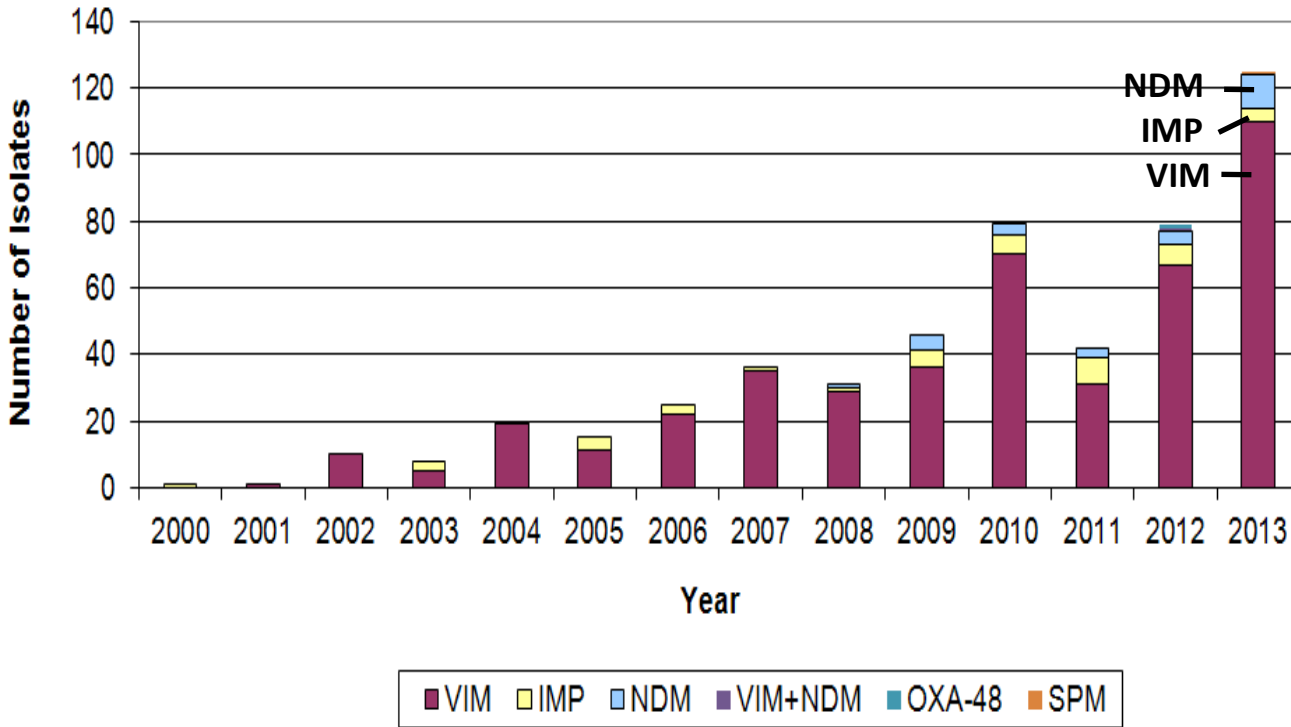
Surface survival



CPE in the UK: mainly KPC, OXA-48 and NDM



Non-fermenters in the UK: mainly VIM



- *P. aeruginosa*
- *Acinetobacter* spp.
- *Pseudomonas* spp.

Common clones – CC258 KPC

K. pneumoniae

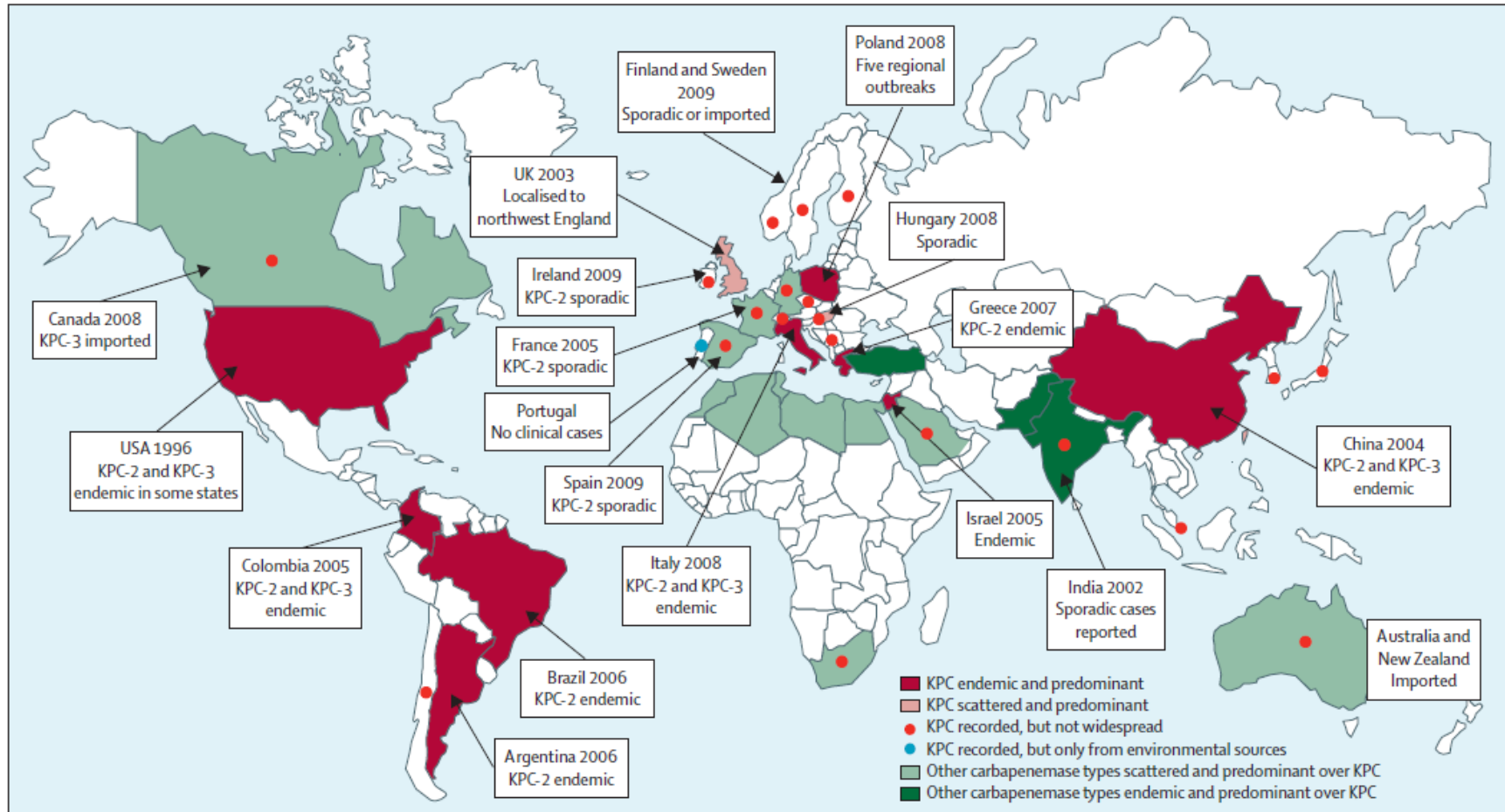
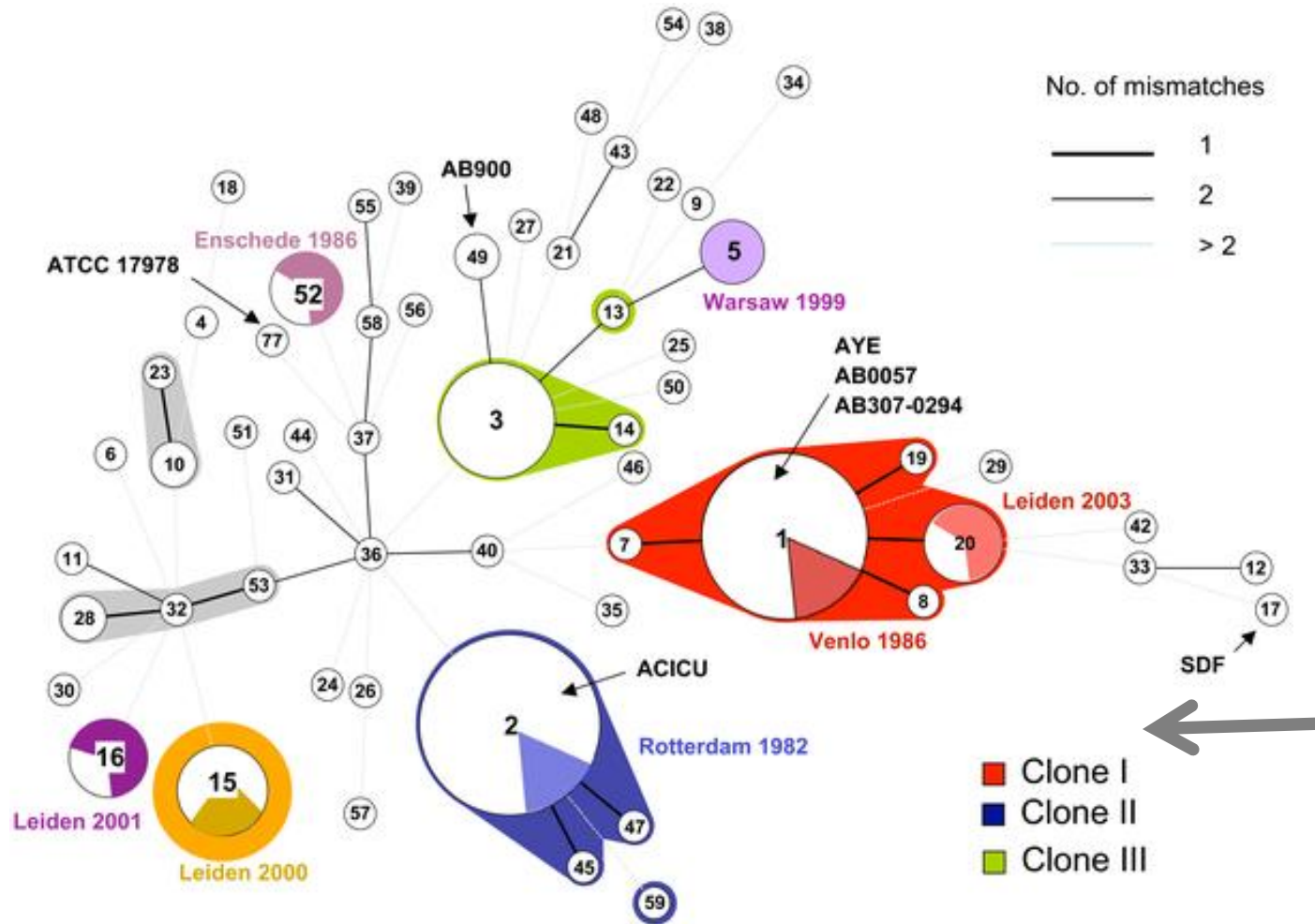


Figure: Epidemiological features of producers of *Klebsiella pneumoniae* carbapenemases by country of origin
Other carbapenemase types include VIM, OXA-48, or NDM. KPC=*Klebsiella pneumoniae* carbapenemase.

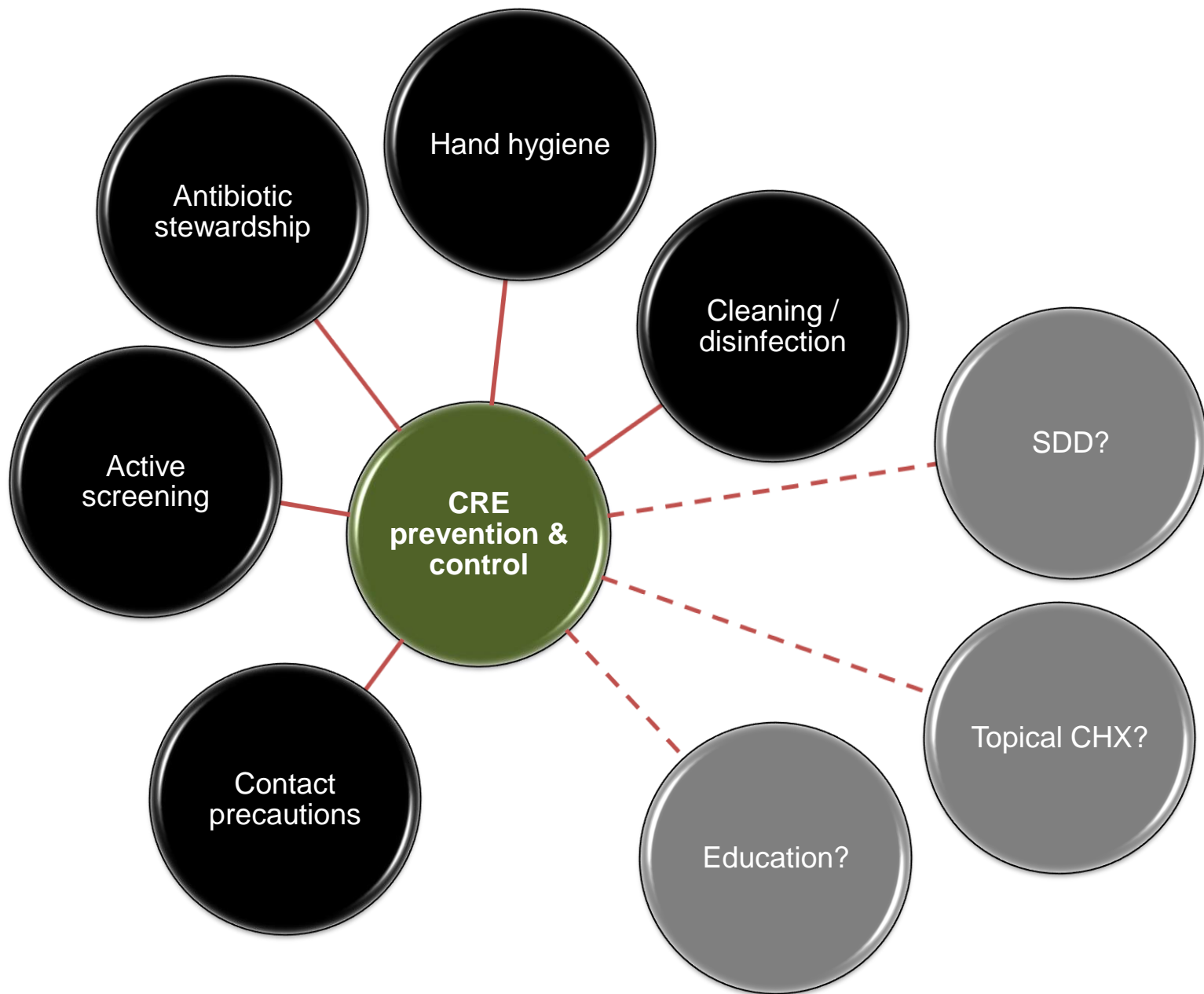
Common clones – *A. baumannii* clones I, II, III

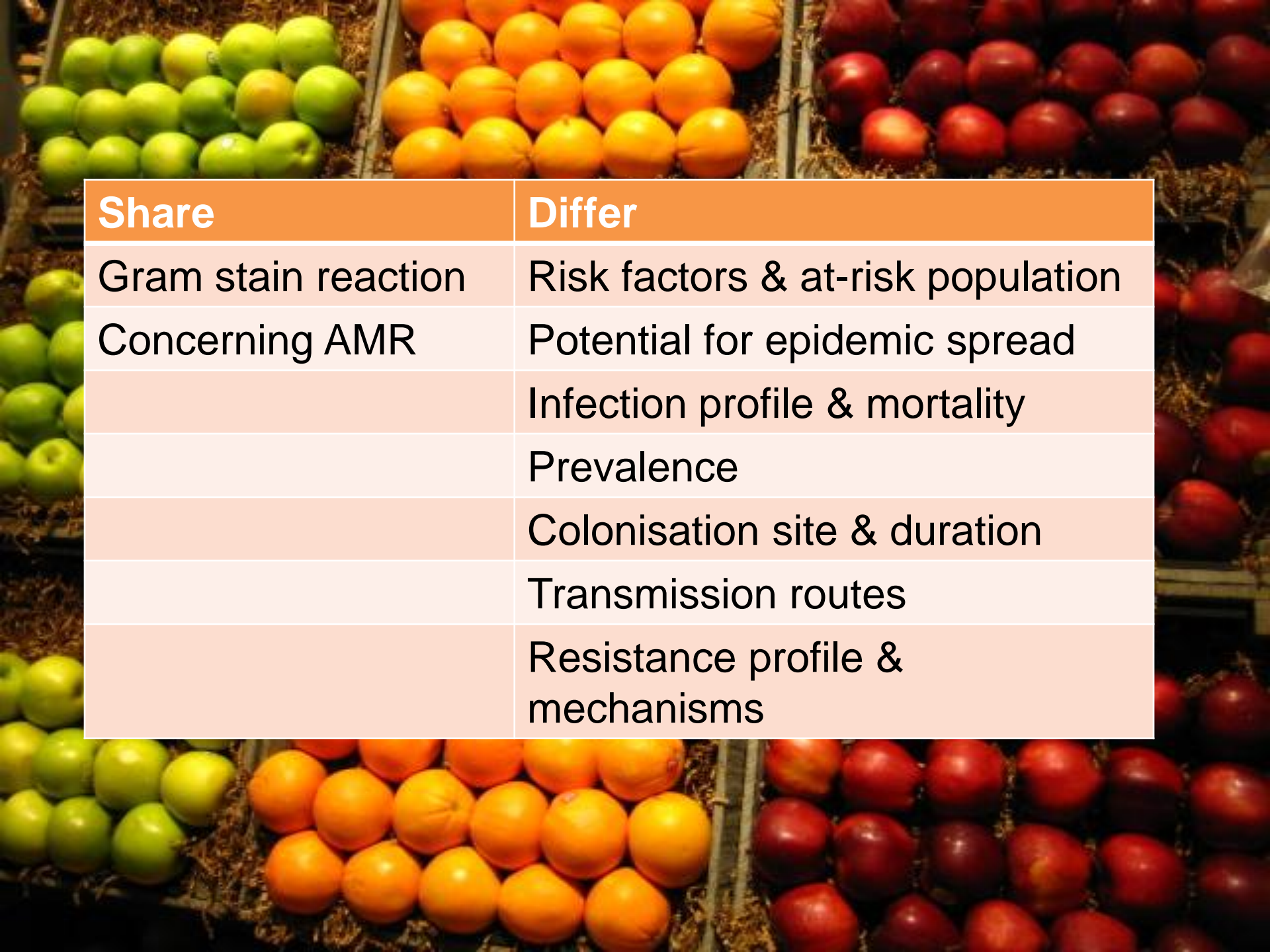


Infection prevention and control challenges

Pathogen	CRE ¹	CRAB ²	MRSA	VRE	<i>C. difficile</i>
Resistance	+++	+++	+	+	+/-
Resistance genes	Multiple	Multiple	Single	Single	n/a
Species	Multiple	Single	Single	Single	Single
HA vs CA	HA & CA	HA (ICU)	HA	HA	HA
At-risk pts	All	ICU	Unwell	Unwell	Old
Virulence	+++	+/-	++	+/-	+
Environment	+/-	+++	+	++	+++

1. Carbapenem-resistant Enterobacteriaceae.
2. Carbapenem-resistant *Acinetobacter baumannii*.





Share	Differ
Gram stain reaction	Risk factors & at-risk population
Concerning AMR	Potential for epidemic spread
	Infection profile & mortality
	Prevalence
	Colonisation site & duration
	Transmission routes
	Resistance profile & mechanisms

Summary

1. Resistant Gram-negative rods represent a more serious threat than the 'usual suspects', mainly due to the threat of pan-drug resistance.
2. Enterobacteriaceae (mainly *K. pneumoniae*) and non-fermenters (mainly *A. baumannii*) have fundamental differences in their epidemiology.
3. CRE and CRNF are both emerging problems, but they are not the same problem. ~~CRD~~
4. The prevention and control strategy will look different for Enterobacteriaceae vs. non-fermenters.