Introduction to the identification and management of carbapenemase producing Enterobacteriaceae (CPE)

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and

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- Why the fuss?
- What are CRE?
- Who do we screen?
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- What happens if someone is positive?
- Key questions

THE END OF ANTIBIOTICS IS NIGH

Why the fuss?

“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, CMO

“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

Rising threat from MDR-GNR

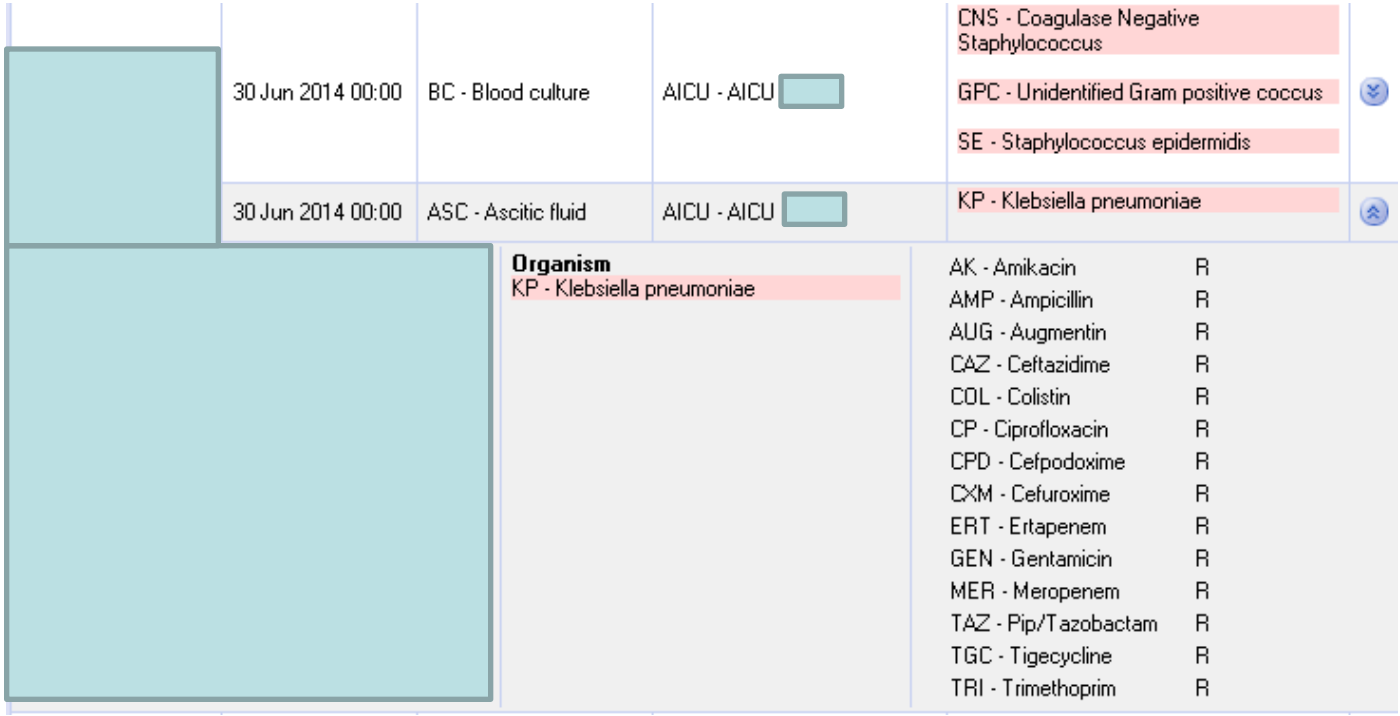
% of all HAI caused by GNRs.

% of ICU HAI caused by GNRs.

Non-fermenters	***Acinetobacter baumannii*** ***Pseudomonas aeruginosa*** ***Stenotrophomonas maltophilia***
Enterobacteriaceae	*Klebsiella pneumoniae* *Escherichia coli* *Enterobacter cloacae*

Hidron et al. *Infect Control Hosp Epidemiol* 2008;29:966-1011.
Peleg & Hooper. *N Engl J Med* 2010;362:1804-1813.

What's the fuss? Resistance



30 Jun 2014 00:00	BC - Blood culture	AICU - AICU	CNS - Coagulase Negative Staphylococcus GPC - Unidentified Gram positive coccus SE - Staphylococcus epidermidis
30 Jun 2014 00:00	ASC - Ascitic fluid	AICU - AICU	KP - Klebsiella pneumoniae

Organism
KP - Klebsiella pneumoniae

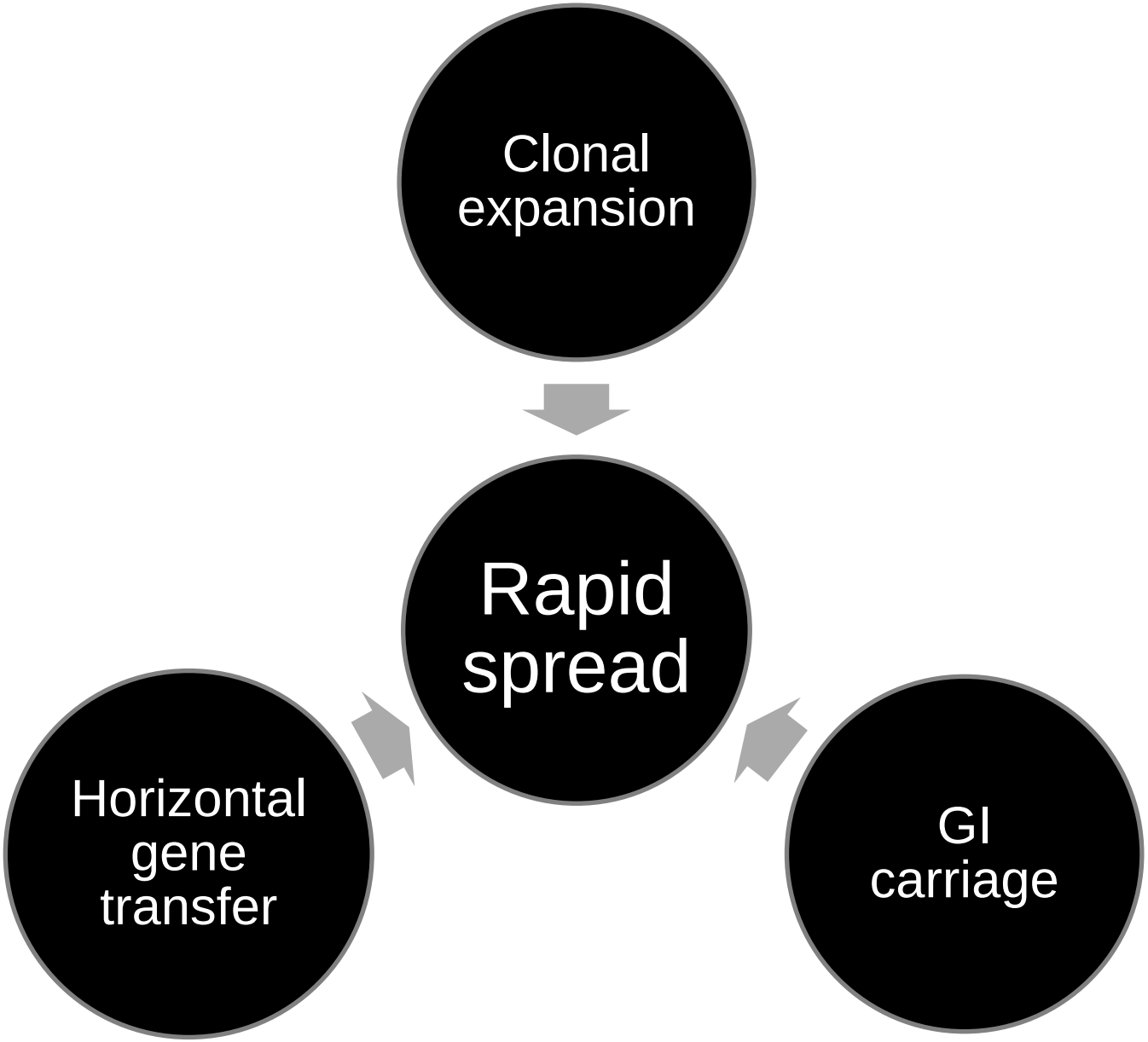
AK - Amikacin	R
AMP - Ampicillin	R
AUG - Augmentin	R
CAZ - Ceftazidime	R
COL - Colistin	R
CP - Ciprofloxacin	R
CPD - Cefpodoxime	R
CXM - Cefuroxime	R
ERT - Ertapenem	R
GEN - Gentamicin	R
MER - Meropenem	R
TAZ - Pip/Tazobactam	R
TGC - Tigecycline	R
TRI - Trimethoprim	R

Why the fuss? Mortality

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

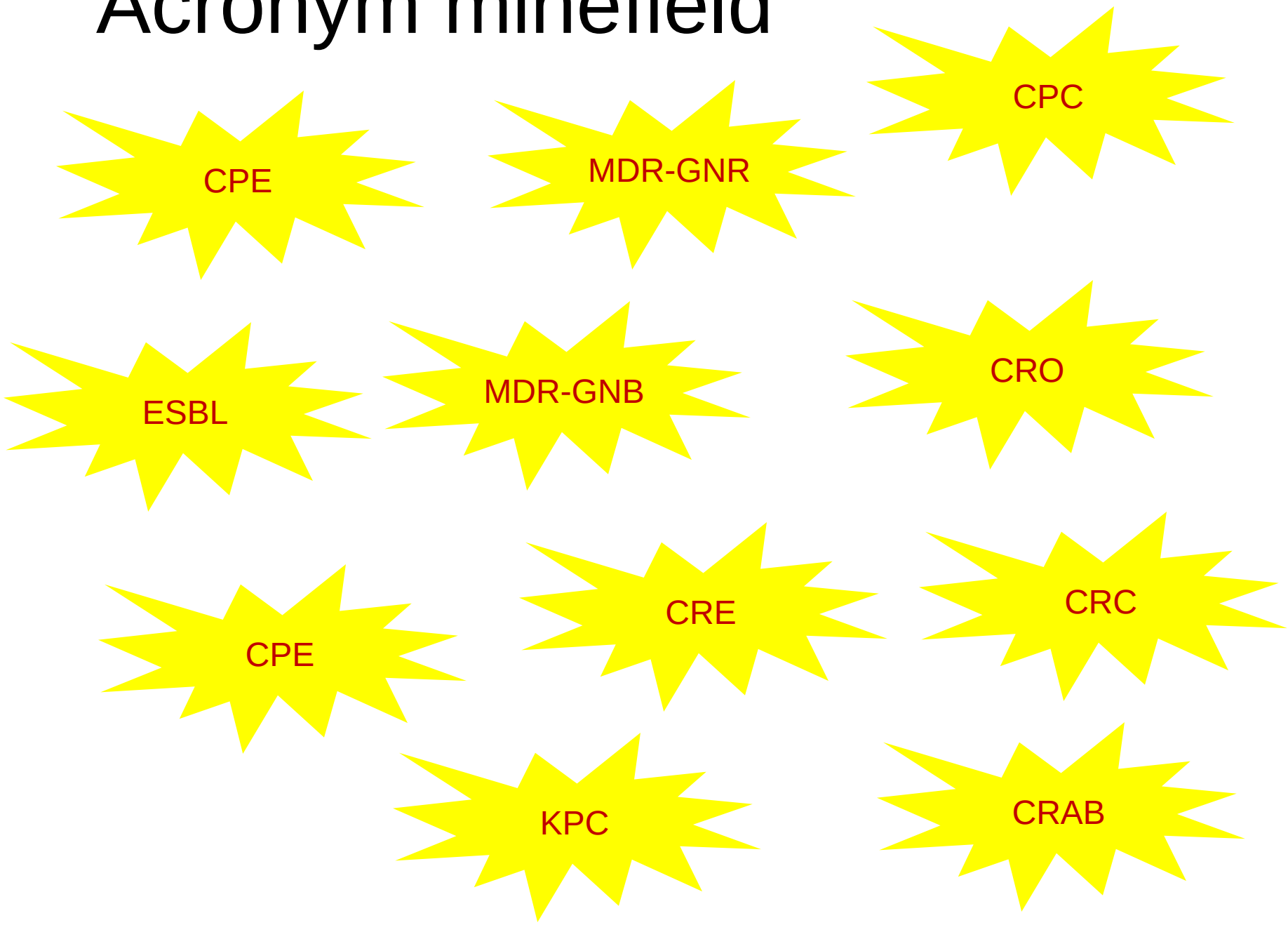
Shorr *et al. Crit Care Med* 2009;37:1463-1469.
Patel *et al. Iinfect Control Hosp Epidemiol* 2008;29:1099-1106.

Why the fuss? Rapid spread




DANGER
MINES

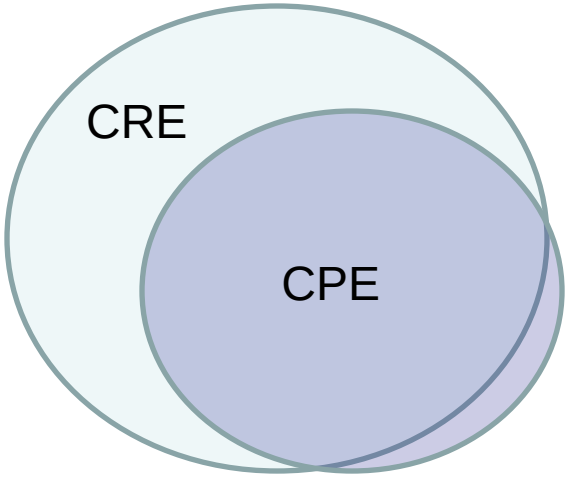
Acronym minefield



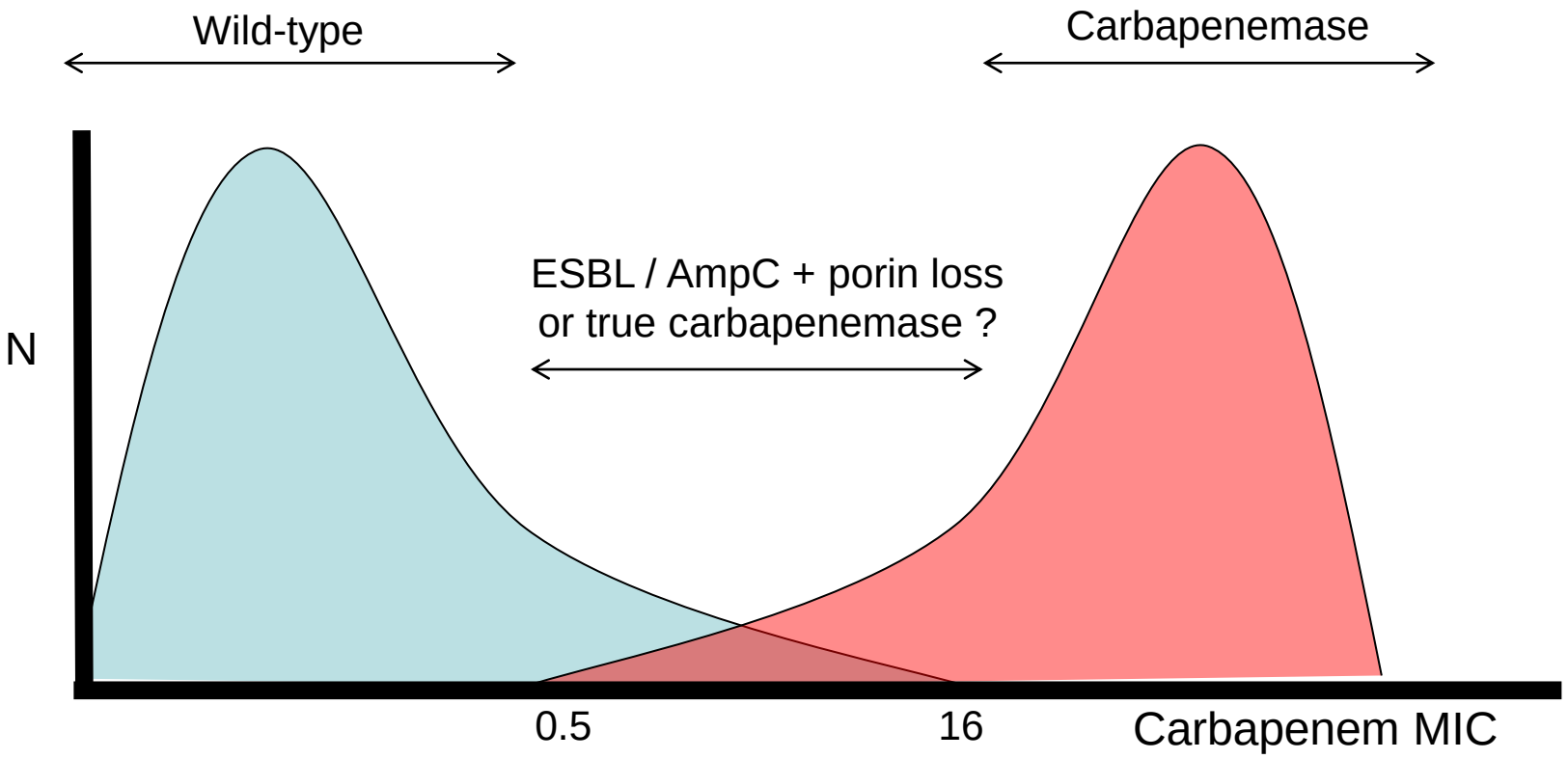
What are CRE?

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.

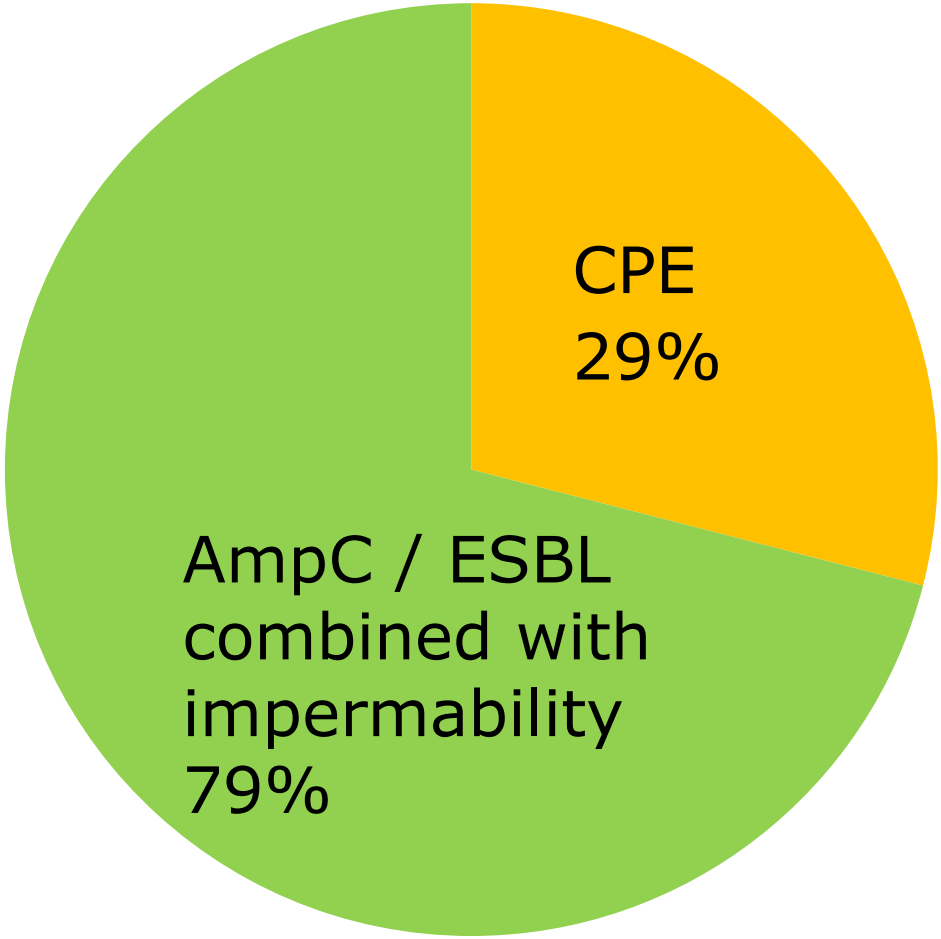


When CRE is not CPE



Courtesy of Dr Katie Hopkins, PHE.

Distinguishing CRE from CPE



Breakdown of 24 CRE isolates identified at Alder Hey, Sept 2011 – Aug 2012

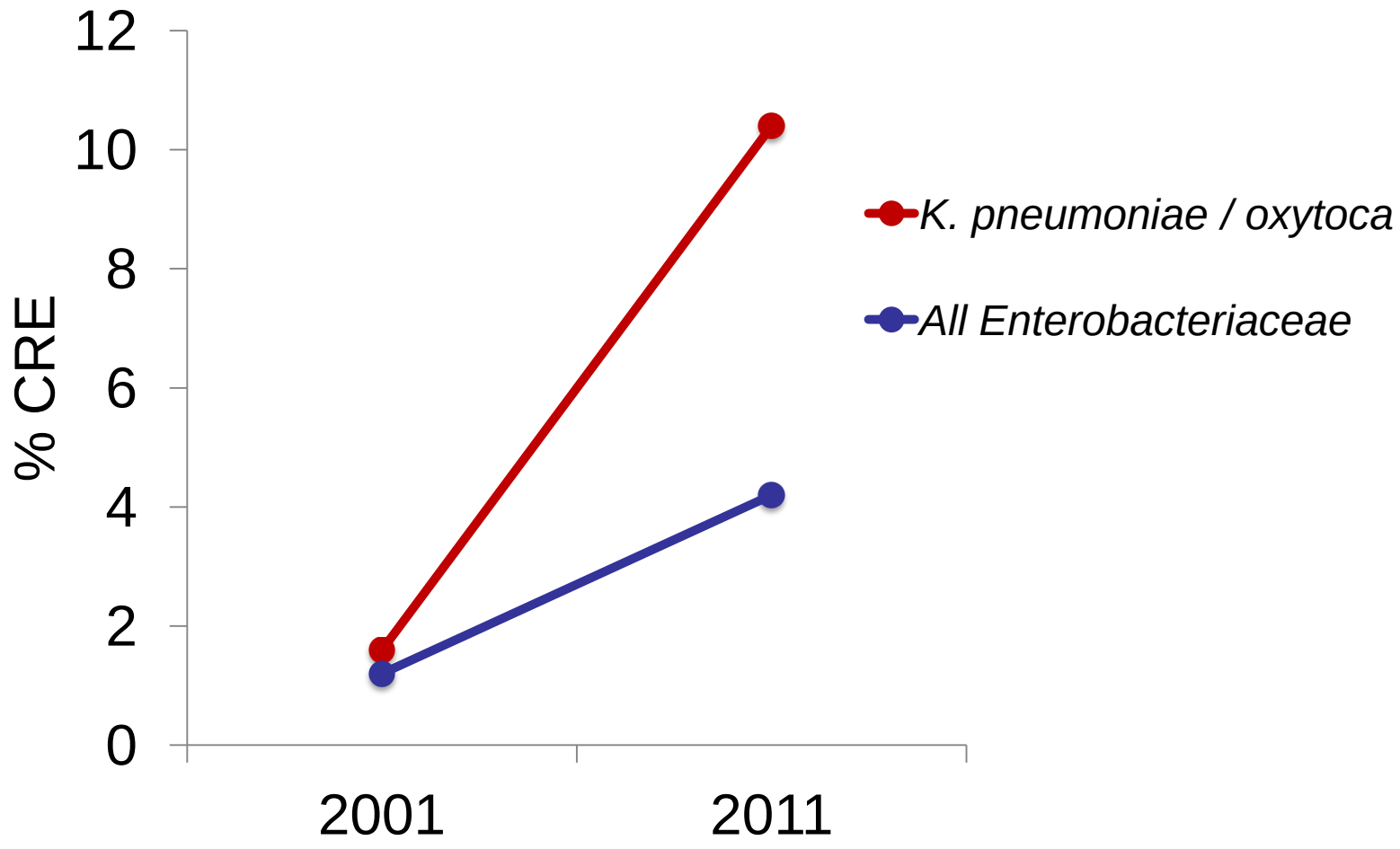
Drew *et al.* *J Hosp Infect* 2013;84:300-304.

Understanding the enemy

Pathogen	CPE[1]	MRSA	VRE	C. difficile
Resistance	+++	+	+	+/-
Resistance genes	Multiple	Single	Single	n/a
Species	Multiple	Single	Single	Single
HA vs CA	HA & CA	HA	HA	HA
At-risk pts	All	Unwell	Unwell	Old
Decolonisation	No	Yes	No	No
Virulence	+++	++	+/-	+
Environment	+/-	+	++	+++

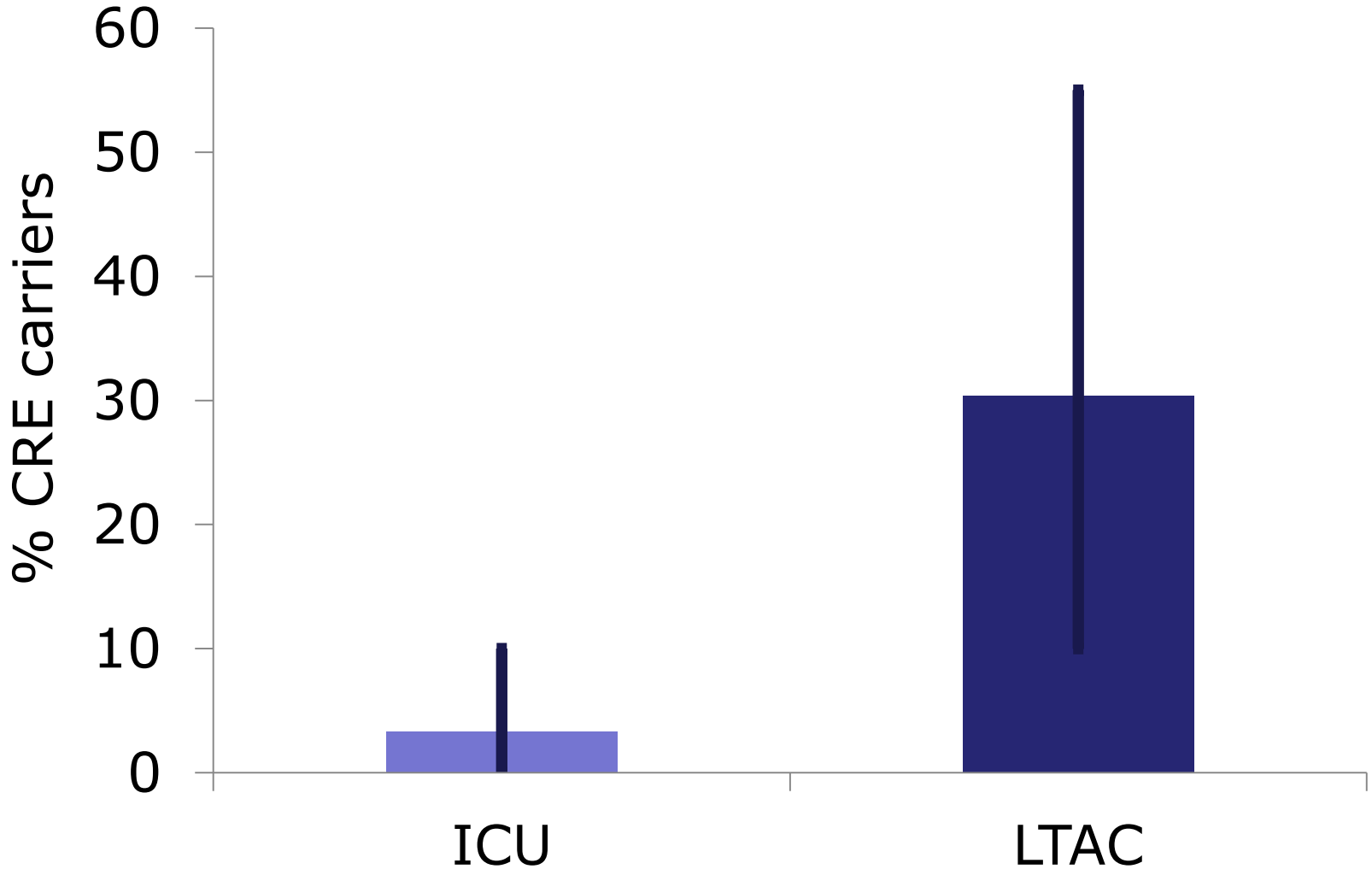
1. Carbapenem-resistant Enterobacteriaceae.

CRE in the USA



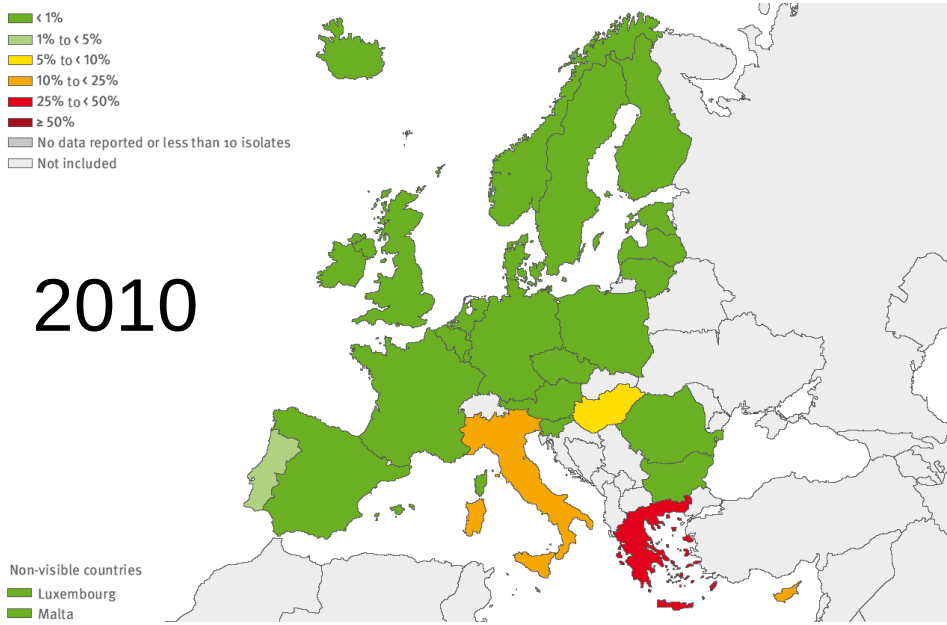
NHSN / NNIS data; *MMWR* 2013;62:165-170.

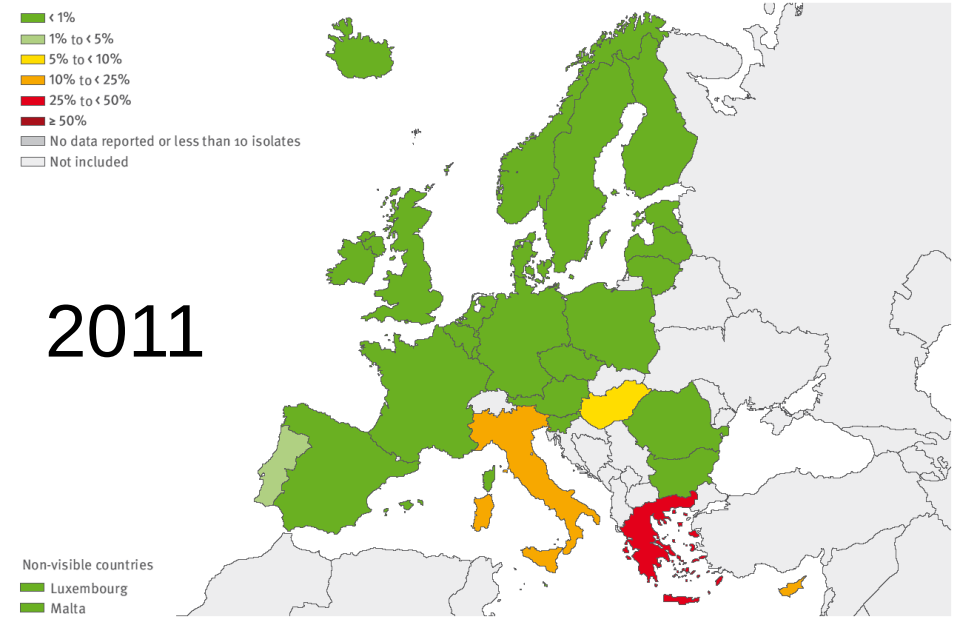
CRE in LTACs, USA



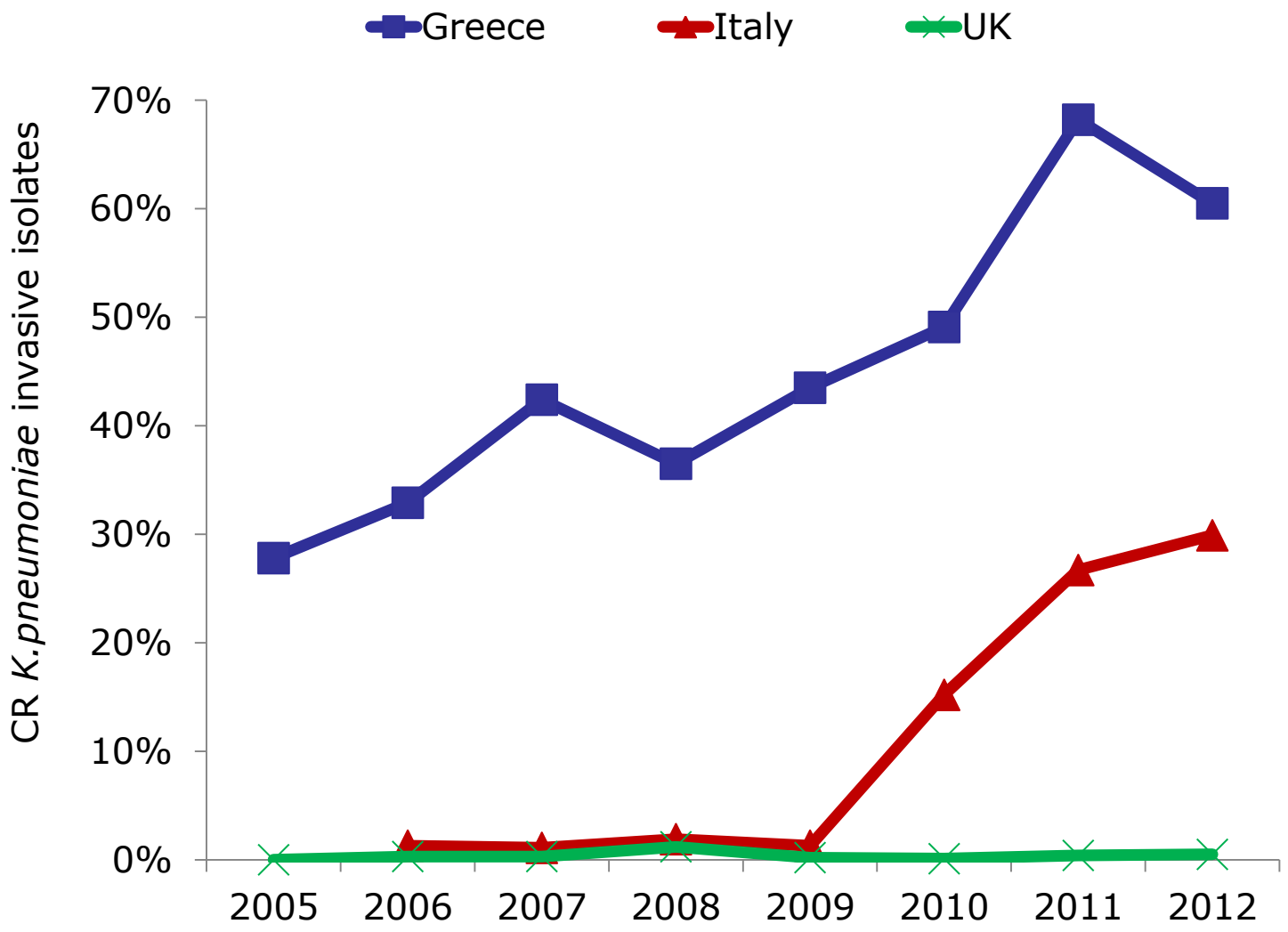
Lin *et al. Clin Infect Dis* 2013;57:1246-1252.

Invasive CRKP isolates (EARS-Net)



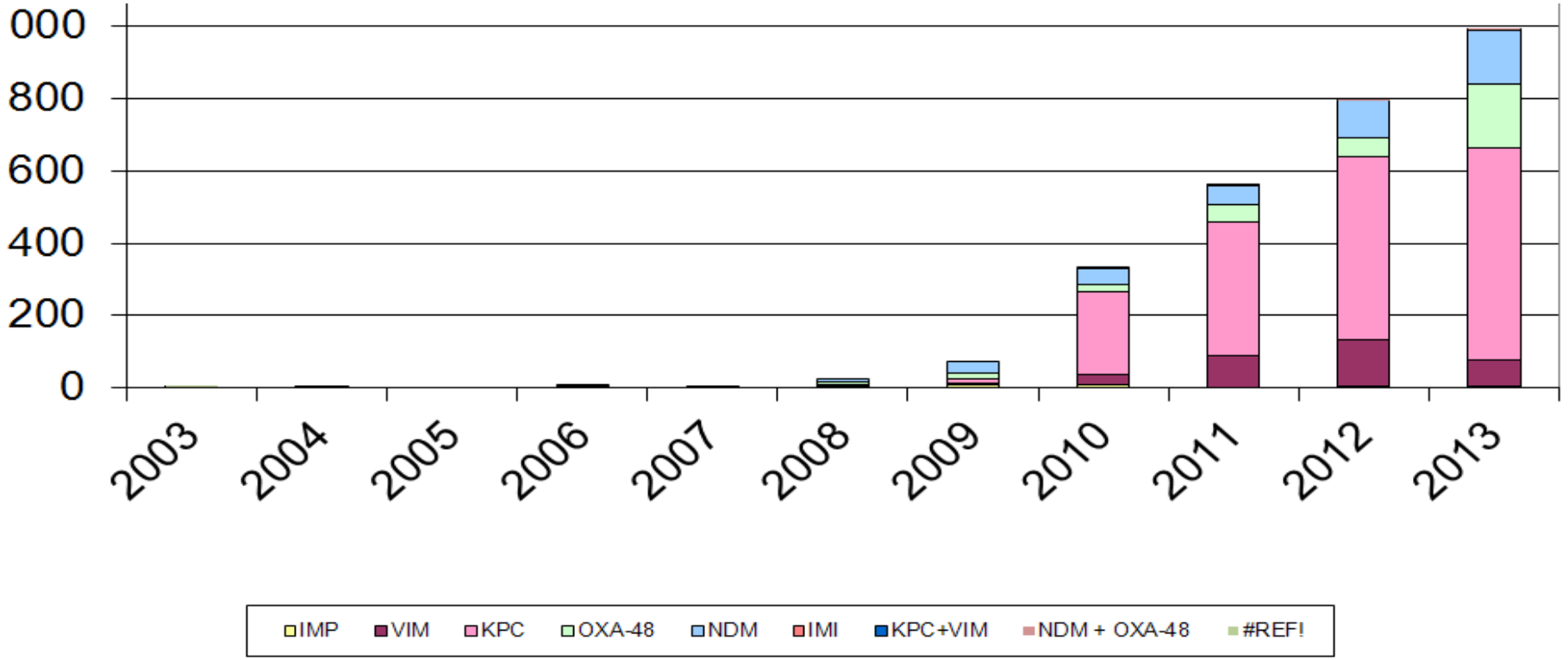


Invasive CRKP trends



ECDC EARS-Net

Emergence of CPE in the UK



PHE ARMRL, 24/01/14
Courtosy of Dr Neil Woodford

CPE in the UK

Public Health England

PHE Gateway number: 2013-499

To: Chief Executive Officer
CC: Director of Nursing
Medical Director

Health Protection and
Medical Directorate

Wellington House
133-155 Waterloo Ro
London SE1 8UG

Email: hcai@phe.gov.

27 February 2014

Dear Chief Executive Officer,

Re: Addressing the infection risk from carbapenemase-producing other carbapenem-resistant organisms

We are taking the unusual step of writing directly to you to ask for your es address the risk posed to trusts and other healthcare organisations by Enterobacteriaceae and other carbapenem-resistant organisms. Enterobacteriaceae represent one of the most serious emerging infectio currently face, and the failure to control their spread now, while we still have substantial human health and financial consequences. Infections c extremely difficult to treat as they are resistant to carbapenems, which antibiotics. Management of these infections is not only more difficult, aff also significantly more costly for the healthcare system.

In order to minimise the wide spread of these multidrug-resistant infectio be grateful if you could ensure, as a matter of highest priority and urgency national ***'Acute trust toolkit for the early detection, mana carbapenemase-producing Enterobacteriaceae***[1] is embedded into Trust.

Additionally, to ensure that trusts are fully informed about the need to ad the toolkit, next week NHS England will be circulating a Stage 2 P *'Addressing rising trends and outbreaks in carbapenemase-producing* resources and information that will support you in addressing the issue i included in the 'Key Information' appended to this letter.

These infections are already causing national concern due to the obs numbers of infections, outbreaks and clusters. Public Health Eng Resistance and Healthcare Associated Infection Reference Unit has w producing organisms since 2000 and is seeing year-on-year increases confirming up to 25 positive samples per week that have been submitte voluntary basis. PHE will continue to monitor the situation nationally an trusts available to professional colleagues and the public, including thr national efforts to address the public health threat.

[1] Acute trust toolkit for the early detection, management and control of car Enterobacteriaceae available at:
http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb

Public Health England

Acute trust toolkit for the early de management and control of carbapenemase-producing Enterobacteriaceae

Public Health England

NHS England

Patient Safety Alert

Stage Two: Resources

Addressing rising trends and outbreaks in carbapenemase-producing Enterobacteriaceae

6th March 2014

Alert reference number: NHS/PSA/Re/2014/004
Alert stage: Two - Resources

Enterobacteriaceae are a large family of bacteria that usually live harmlessly in the gut of all humans and animals, but, in the wrong place, can cause serious infections. Worldwide, a small but increasing number of strains of enterobacteriaceae have become resistant to carbapenem antibiotics, which have been defined by WHO as critically important antibiotics. Carbapenemases are enzymes made by some strains of these bacteria, which allow them to destroy carbapenem antibiotics and cause resistance. Increasing trends in sporadic infections, clusters and outbreaks of carbapenemase-producing Enterobacteriaceae (CPE) have been observed in a number of NHS trusts in England. There is a high risk of this problem becoming more widespread unless early and decisive action is taken by Trusts. These bacteria represent a significant challenge in terms of prevention, treatment and control. Inadequate measures to prevent and control transmission can have serious consequences for both patients, who may require more complex treatment to manage their infection, and hospitals in terms of ward closures and protracted patient stays. As a result of the escalating problem, Public Health England (PHE) is providing national support for ongoing efforts to control and reverse rising trends with the aim of minimising morbidity and preventing further outbreaks. Because the PHE resources are now available NHS England has been able to proceed to issuing a Stage 2 alert without a previous Stage 1 alert.

PHE have recently published a toolkit for acute trusts to assist them with the early detection, management and control of carbapenemase-producing Enterobacteriaceae. A key aspect of the control measures is to take special precautions for patients recently treated in countries known to have high levels of CPE or in UK hospitals with recent clusters or outbreaks of CPE.

This alert is to bring this significant infection prevention and control challenge to the attention of the NHS and to signpost the toolkit developed to support the NHS in both controlling existing transmission problems and preventing further spread.

The toolkit along with 'UK Standards for Microbiology Investigations: Laboratory Detection and Reporting of Bacteria with Carbapenem-Hydrolysing ß-lactamases (Carbapenemases)' can be found at:
www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1317140378529

BSAC antibiotic susceptibility testing guidance is available at:
www.bsac.org.uk/wp-content/uploads/2012/02/AST-testing-and-Reporting-guidance-v1-Final.pdf

Implementation advice on the tooklkit can be obtained from local PHE Centres: www.gov.uk/government/publications/phe-centre-addresses-and-phone-numbers/phe-local-and-regional-contact-details

Actions

Who: Chief Executives of NHS trusts and foundation trusts providing acute care and independent hospitals.

When: To commence immediately and completed by 30 June 2014

1. Bring this alert to the notice of the Director for Infection Prevention and Control (DIPC) and infection control staff to instigate the development of the board level CPE management plan.
2. In discussion with relevant clinical experts establish if there are / have been cases of CPE in the organisation and consider if immediate action is required locally to reduce the risk of such an incident / outbreak occurring.
3. In the light of the local situation the Infection Prevention and Control Committee to plan for local adoption and dissemination of the Acute Trust CPE toolkit to influence clinical practice. This will include advising front line staff of the issue and the Trust's plans for addressing CPE.

Note: This alert is being sent to GPs for information

Patient Safety | Domain 5
www.england.nhs.uk/patientsafety

Contact us: patientsafety.enquiries@nhs.net
Visit our website: www.england.nhs.uk/patientsafety
Report incidents: www.england.nhs.uk/reportingpsincidents

Publications Gateway Reference 01266 Page 1 of 2 © NHS England March 2014

How do we prevent a disaster

- We need to know who is a carrier of CRE
- We need to safely manage the carriers to prevent cross infection to others
- We need a coordinated approach for information between patients and other healthcare providers
- We need to educate healthcare staff about the dangers of CRE
- We need to educate the public, especially around antimicrobial use…

Identification and Screening

- All inpatients should be assessed for risk of CRE Carriage
- Initial assessment by admitting clinician using the questions on care pathway
- Nurse to screen patients identified as at risk
- No need to isolate pending results unless previously known positive or high index of suspicion.

Who do I screen?

PHE CPE Toolkit screening triggers:

a) an inpatient in a hospital abroad, or

b) an inpatient in a UK hospital which has problems with spread of CPE (if known), or

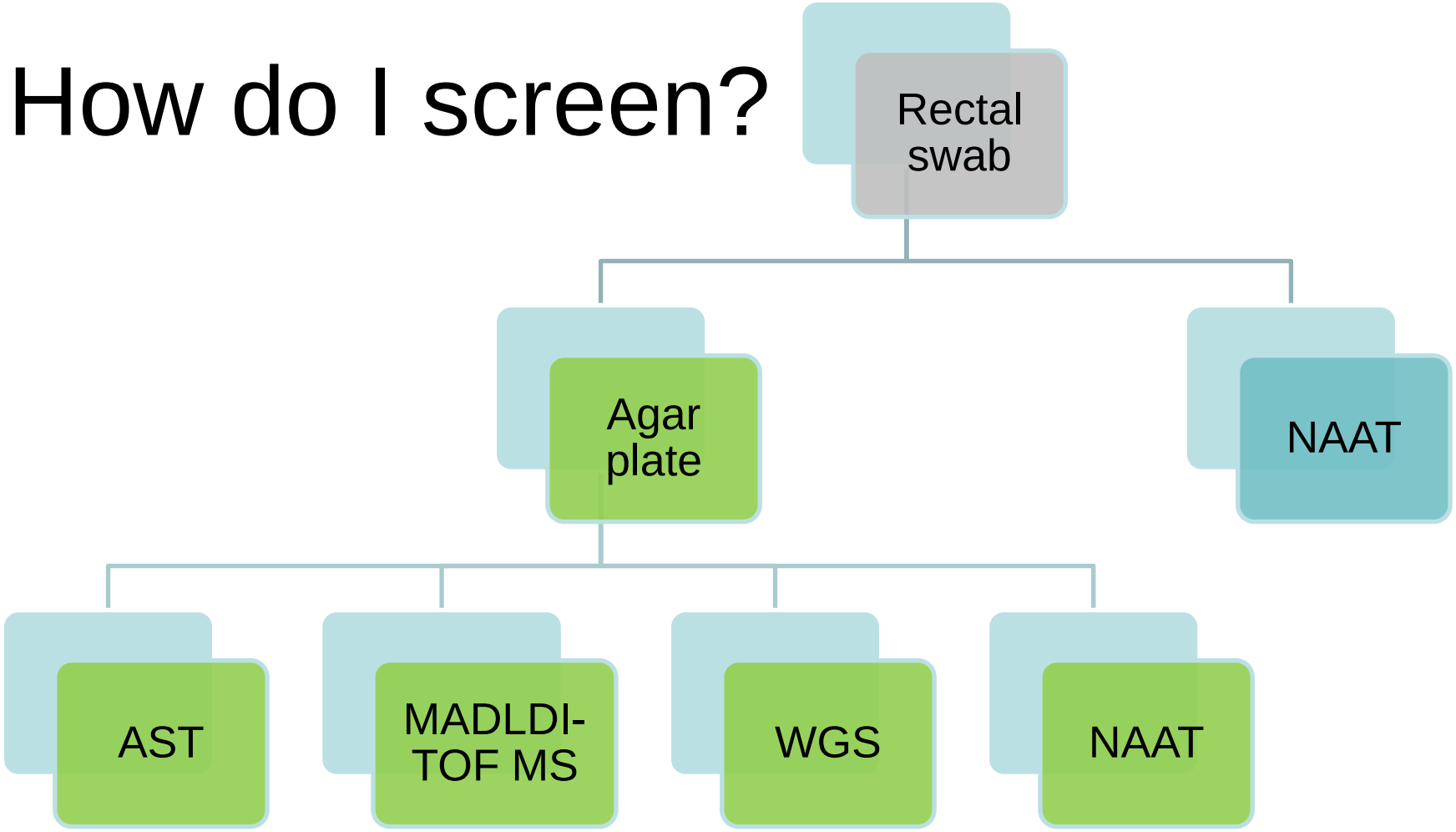
c) a ‘previously’ positive case.

Also consider screening admissions to high-risk units such as ICU, and patients who live overseas.

How do I screen?

- Rectal swab is the best sample
  - Insert no more than 2cm into rectum
  - Twist gently and withdraw
  - Want to see faeces on swab.
- Patient education as to why this is needed in order to overcome taboos
- Avoid rectal swabs in children and those with low platelets.
- Alternate specimen is faeces but have to wait for the patient to ‘go’

How do I screen?



NAAT = nucleic acid amplification techniques
AST = antimicrobial susceptibility testing
MALDI-TOF = Matrix-assisted laser desorption /ionization – time of flight mass spectrometry
WGS = whole genome sequencing

Before you throw away the agar plates…

Molecular diagnostics are great but:

- but do not deal with changing epidemiology; struggle with target variability;
- are expensive;
- rely on validation of carriage sites;
- do not tell you about phenotypic susceptibility;
- have a limit of detection often around a couple of logs;
- and need to manage shared resistance genes between species, especially for MDR-GNR

See further details in talk by Dr Dan Diekema

Initial Management when a patient is flagged as CRE positive

- Assess for increased cross infection risk
- Move to side room for isolation
- Screen all invasive sites as advised by IPCT
- Collect list of contacts for screening
- Ensure guidance sheet is available outside room for staff
- Give the patient an information sheet / leaflet

Risk Assessment for CRE carriage significance

- Do they have any invasive sites?
- Do they need intensive or high dependency care?
- Do they have loose stool?
- Do they have long term care needs?
- **If yes, the patient may present a higher risk for cross infection to others!**

Strict Source Isolation

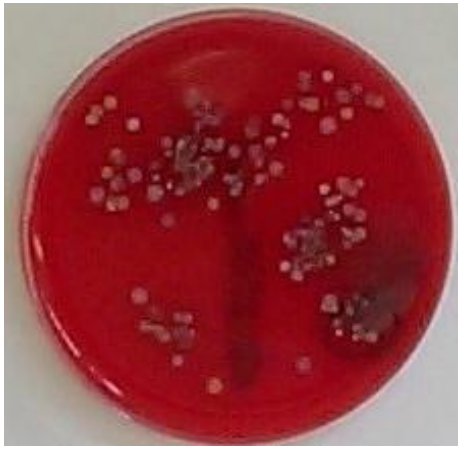
- Confirmed patients with a CRE take high priority for single room
- Patients with multiple risk factors for CRE spread MUST be isolated
- Isolation room should have an en suite toilet and shower
- If no room available discuss with IPCT
  - Own commode
- No unnecessary equipment in room (including your mobile phone!)
- Nothing out without thorough disinfection

Personal Protective Equipment

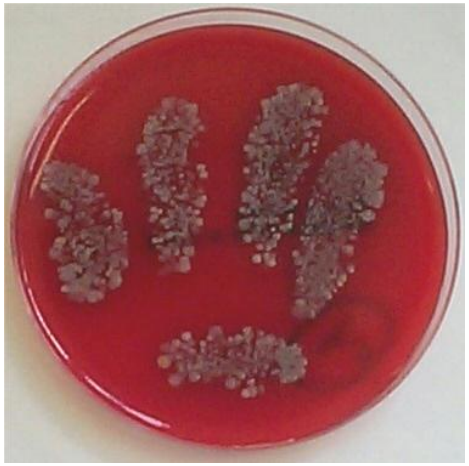
- Aim to reduce contamination from patient to others via the healthcare worker
- Scrub suits may be recommended for prolonged close care.
- Full length blue gowns with gloves
  - Masks not required
  - Use disposable apron over the top of the gown
  - Change apron and gloves as tasks require
- Clean hands and put gown and gloves on outside room
- Remove gown and gloves just before leaving room and wash hands
- Decontaminate hands with alcohol after leaving the room

Hand Hygiene

- Wash hands if physically soiled or after dealing with poo!
- If you wash – make sure you dry!
- Alcohol hand rub is recommended as a very effective means of killing Gram negative bacteria



Unwashed



Washed, not dried

Further Screening

- New positive patients should have a rectal screen and samples from sterile sites
- Known positives should be screen periodically
- Patient contacts of a known CRE patient should be screened weekly for 4 weeks or until discharged
- Other patients should be screened on advice of IPCT
- Patients with CRE are unlikely to clear the organism so repeated screening may be unhelpful.
- Screening should be determined by risk assessment on an individual basis as advised by the IPCT

Treatment for CRE

- Unlikely to clear the organism so any treatment should be based on clinical need
- Avoid antibiotics unless clinically indicated
- Always used under guidance from a microbiologist
- ‘Combination therapy’ may be used in pan-resistant infection
- Skin decolonisation with chlorhexidine based soaps are recommended to protect invasive devices
- Appropriate dressings should be used to contain exudating wounds or devices
- Closed systems for intubation or drainage should be used where possible
- Consider bowel management systems as appropriate

Environmental decontamination

- The room must be kept clean
- Minimise unnecessary clutter
- Clean room a minimum of twice a day using a chlorine based disinfectant
- All equipment must be cleaned before leaving the room
- Terminal clean should be completed with a hydrogen peroxide vapor process e.g. Bioquell arranged through the IPCT

Patient movement - inpatient

- Information is key
- Inform IPCT of any planned movements a.s.a.p.
- Ensure all relevant departments are notified in advance
- If going to another department
  - Wash patient with CHG soap
  - Clean the bed and change bed linen
  - Decontaminate the room whilst patient absent
- Ensure receiving department is cleaned when procedure is complete

Patient movement - discharge

- Communicate with:
  - Receiving institution
  - GP
  - PHE
  - Other healthcare providers
- Usually coordinated by IPCT
- Talk to the patient, and arm them with appropriate leaflets / info

Key questions

- Which interventions work?
- Are they different for Enterobacteriaceae and non-fermenters? (Probably, given their epidemiology.)
- What is the prevalence of CPE in the UK?
- How much do we believe a single negative screen?
- Do we need rapid molecular diagnostics?
- What is the duration of colonisation?
- Are there decolonisation strategies other than (virtually non) ‘selective decontamination’ using abx?

Conclusions

- This is a new an evolving problem
- Recognition of patient carriers is vital
- Appropriate management of identified carriers is crucial
- Information may change in time if we see more cases in the UK
- Important to try and stay up to date and carry on with safe infection prevention precautions…

Contributors

- Dr Jon Otter (employed part-time at Bioquell)
- Pat Cattini
- Image credit: ‘Danger! Mines!’ by Save the Wild UP.

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