Carbapenemase Producing Enterobacteriaceae: Screening

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Aims

- Is CPE a problem?
- Does screening have the potential to help?
- What did we do? What do we do now?
- What approaches are there to screening?

Is CPE a problem?

- What do they cause?
- What is the epidemiology?

What are CPE?

Enzyme = -ase

- **KPC** Klebsiella pneumoniae carbapenemase
- **OXA** oxacillin-hydrolyzing

Metallobetalactamase

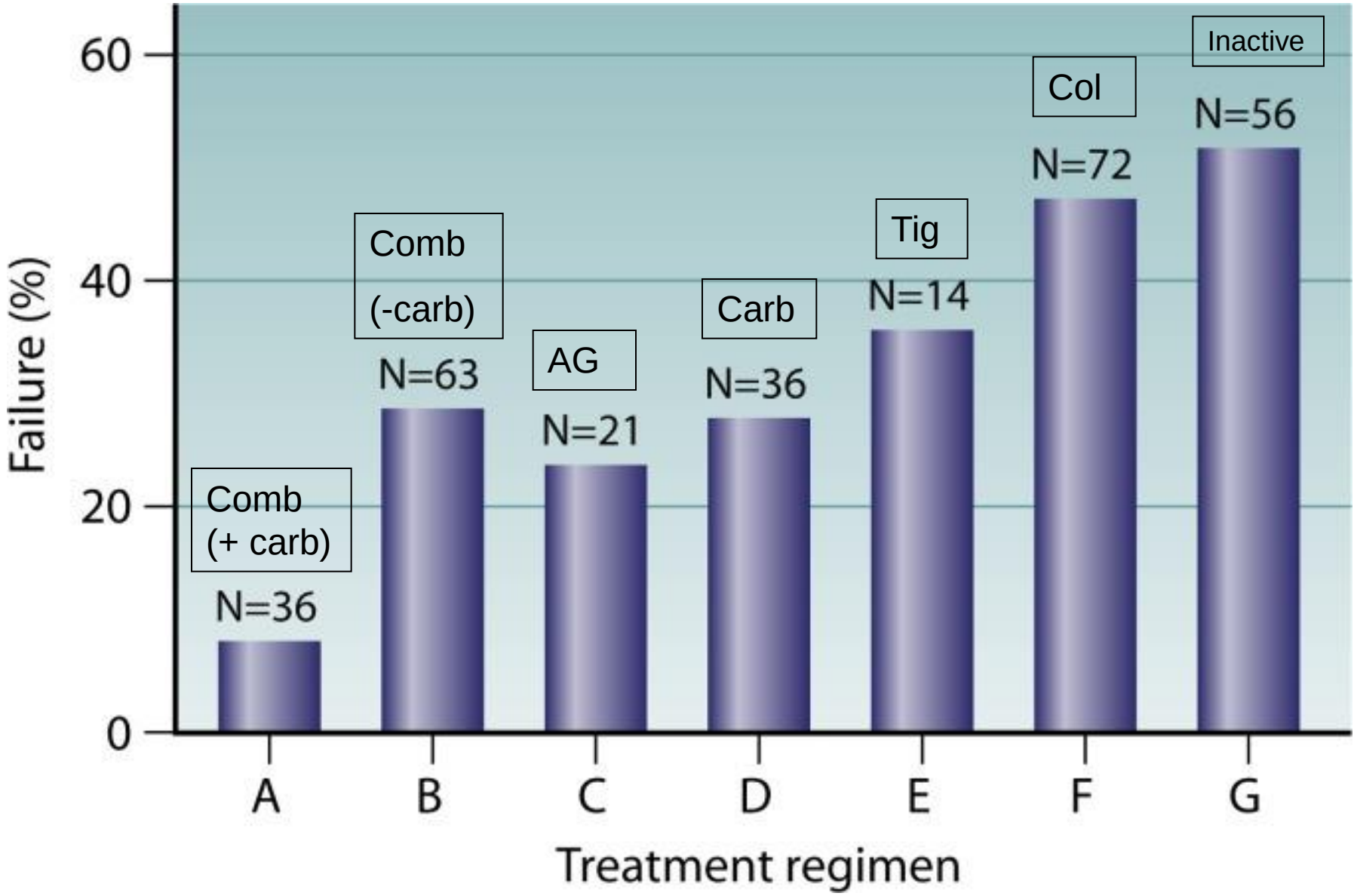
- **VIM** Verona integron-encoded metallo beta-lactamase
- **NDM** – New Delhi Metallobetalactamase
- **IMP** – active on Imipenem

- Successful Clones
  - KPC Klebsiella pneumoniae ST 258

What does it cause?

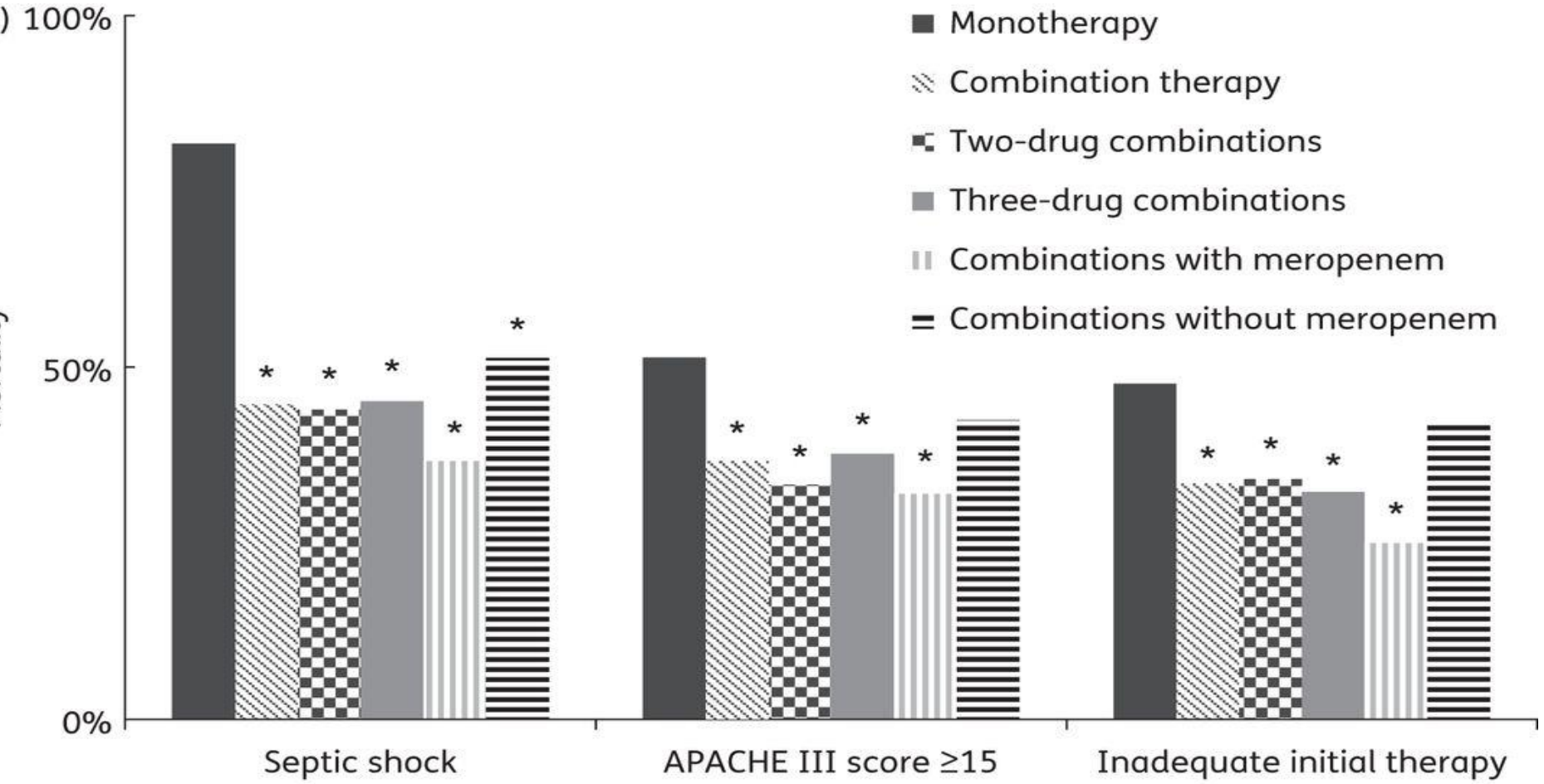
- Same infections as always

but…



Tzouvelelis LS et al. Clin Microbiol Rev. 2012 25:682-707

Mortality rates associated with different antimicrobial drug regimen categories in patients with different presenting features



Mario Tumbarello et al. J. Antimicrob. Chemother. 2015;70:2133-2143

Characteristics and clinical outcomes of cases of prosthetic joint infection caused by carbapenem-resistant *Klebsiella pneumoniae*

Variable	Case 1	Case 2	Case 3
Age (years), sex	58, male	72, male	70, female
Comorbidities	Osteoarthritis, diabetes	Osteoarthritis, coronary artery disease, congestive heart failure	RA on immunosuppression with methotrexate and hydroxychloroquine
Onset of first PJI (months from index surgery)	60	36	1
Primary organism PJI	MSSA	VSE, VRE, *Proteus mirabilis*	*Corynebacterium sp* and VSE
Onset of CRKP PJI (months from first PJI)	2	2	5
Number of procedures (*n*)	10	12	57
Antibiotics	Oxacillin; piperacillin–tazobactam; daptomycin and oral doxycycline; tigecycline and fluconazole; colistin, amikacin, and tigecycline	Ciprofloxacin, linezolid, and rifampin; daptomycin and ciprofloxacin; vancomycin and tigecycline → doxycycline; oxacillin, oxacillin and tigecycline → doxycycline	Vancomycin; tigecycline; colistin; tigecycline; tigecycline; tigecycline and vancomycin → oral ciprofloxacin and clindamycin; tigecycline; colistin; tigecycline, and amikacin; ciprofloxacin
WBC $\times 10^9$/l (median (IQR))	9.07 (0.63, 12.49)	8.45 (7.73, 9.75)	8.92 (7.40, 11.68)
Hospital LOS (days)	51	101	225
Hospitalization costs ($)	N/A	N/A	850 000
Functional status	Above-the-knee amputation	Full	Disarticulated
Outcomes	Died	Died	Alive with major disability

Case 1

Despite:

- left above-the-knee amputation
- maximum medical support
- Combined IV colistin, amikacin, and tigecycline,
- patient died on postoperative day 3

Case 3

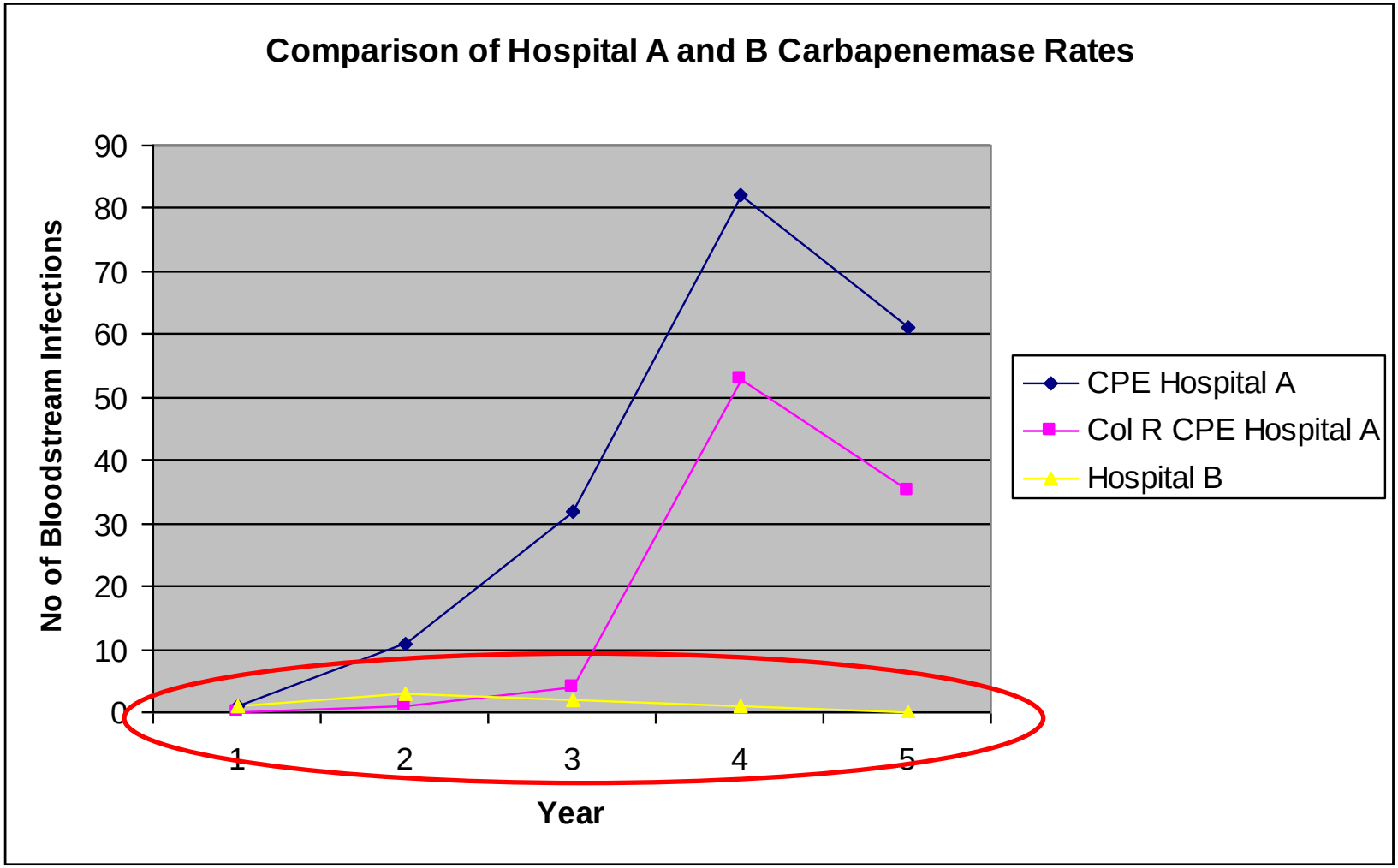
‘…. required five subsequent wound debridements

Culture of tissue …. grew CRKP, ….resistant to amikacin and colistin’

Consider extra measures for high risk areas

de Sanctis et al *Int J Infect Dis*. 2014; 25: 73–78

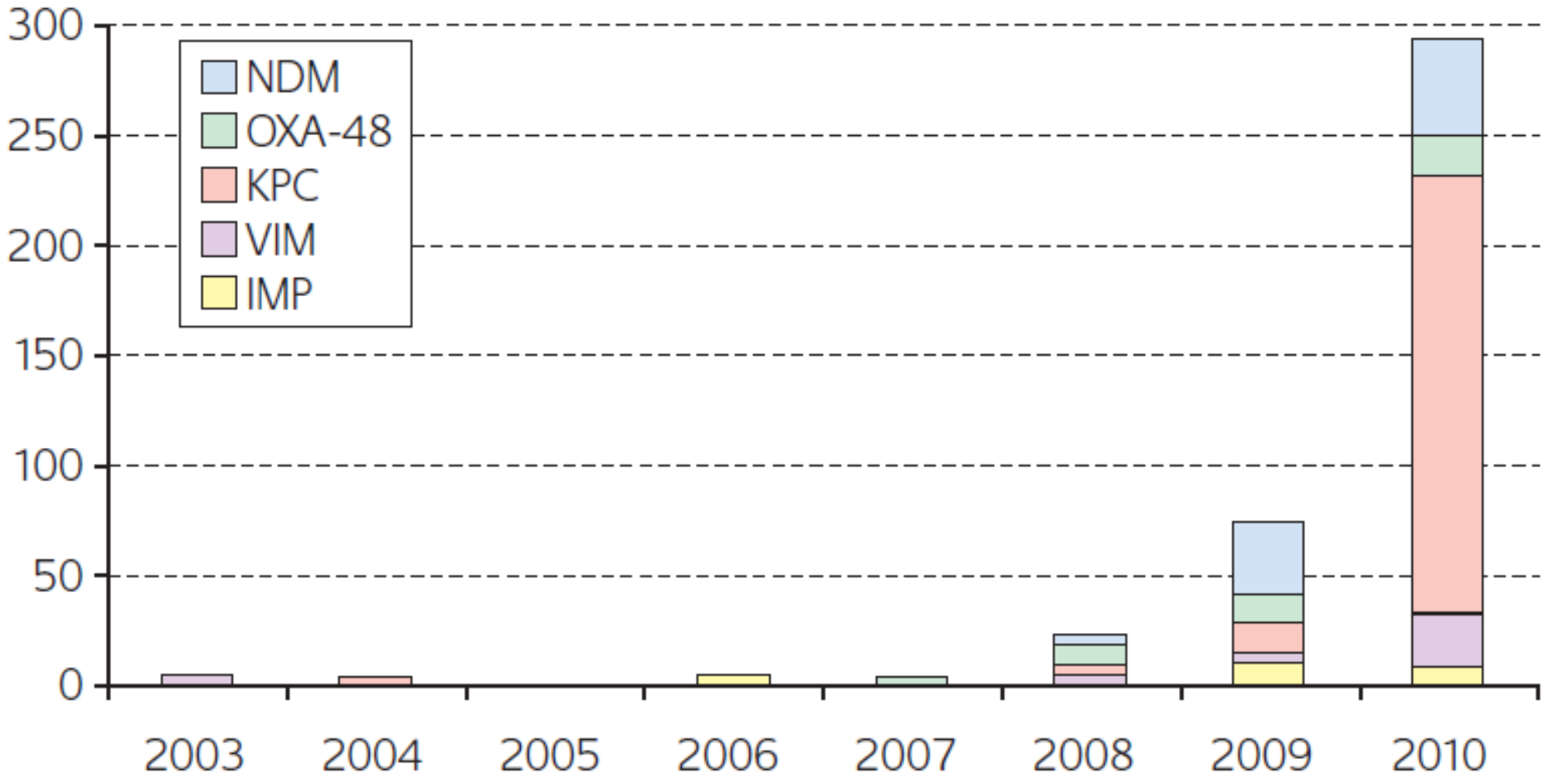
Spreading and Worsening?



Giani et al. Large Nosocomial Outbreak of Colistin-Resistant, Carbapenemase-Producing *Klebsiella pneumoniae* Traced to Clonal Expansion of an *mgrB* Deletion MutantJ Clin Microbiol 53:3341–3344

What Is The Epidemiology?

Carbapenemase-producing Enterobacteriaceae referred to ARMRL



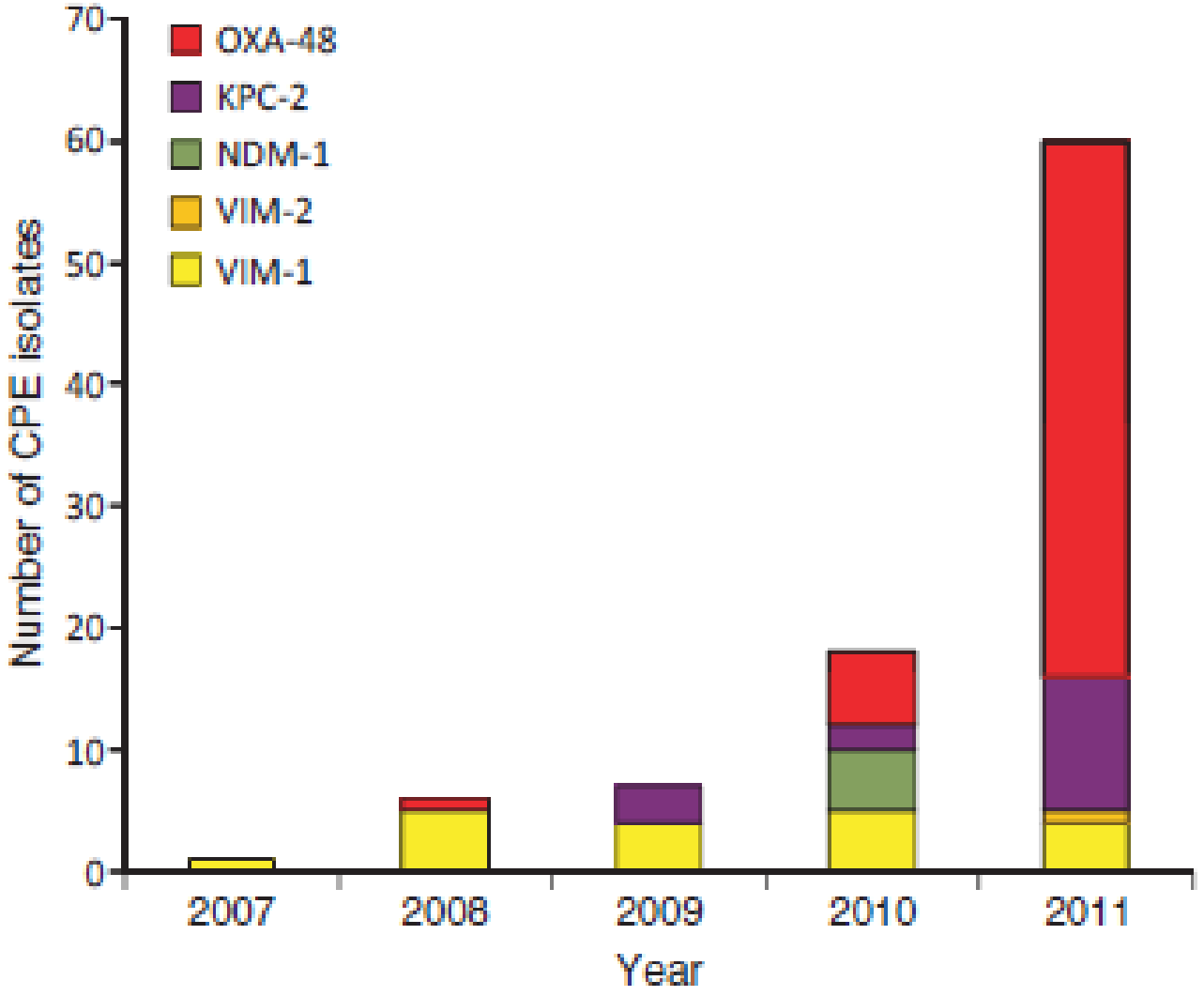
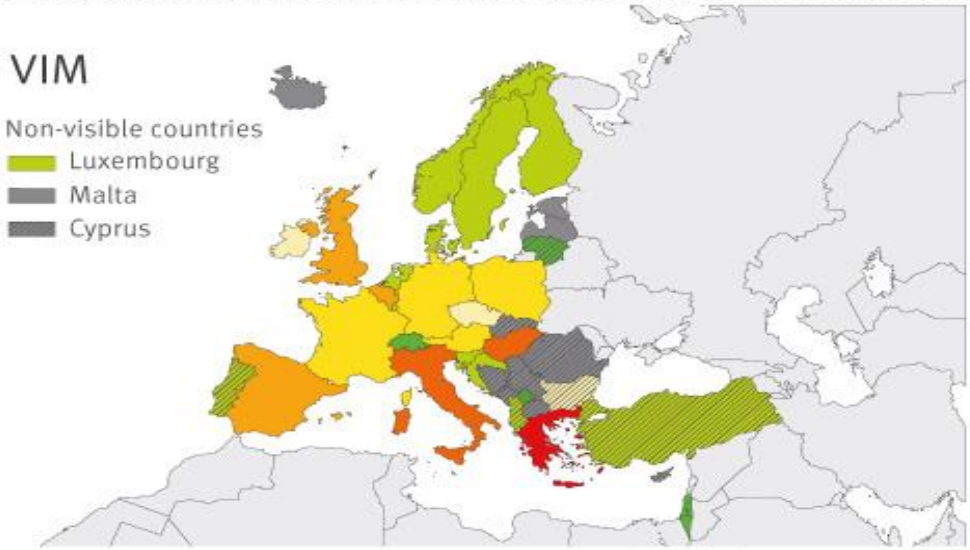


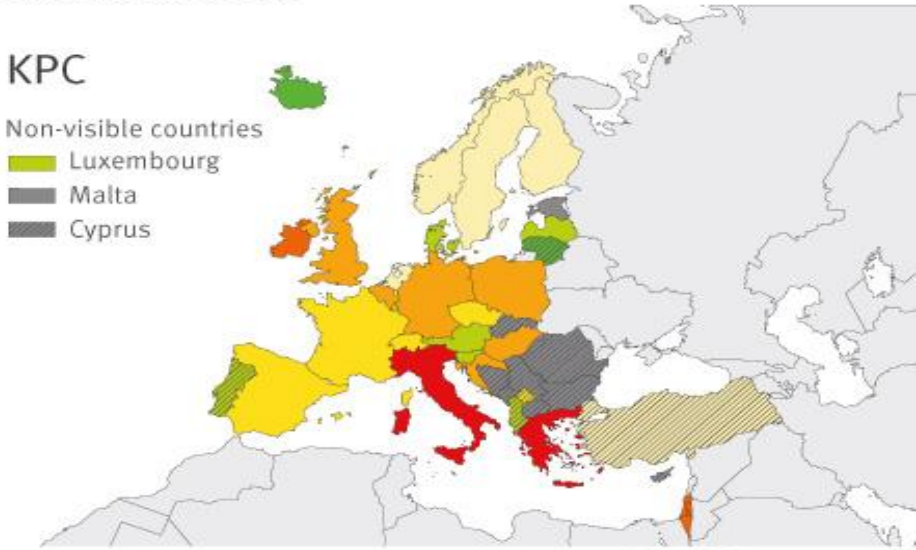
FIG. 3. Evolution of the carbapenemase-producing *Enterobacteriaceae* (CPE) isolates in Belgium (92 isolates referred to the National Reference Centre, Belgium, January 2007–December 2011) (data have been updated from reference 150).

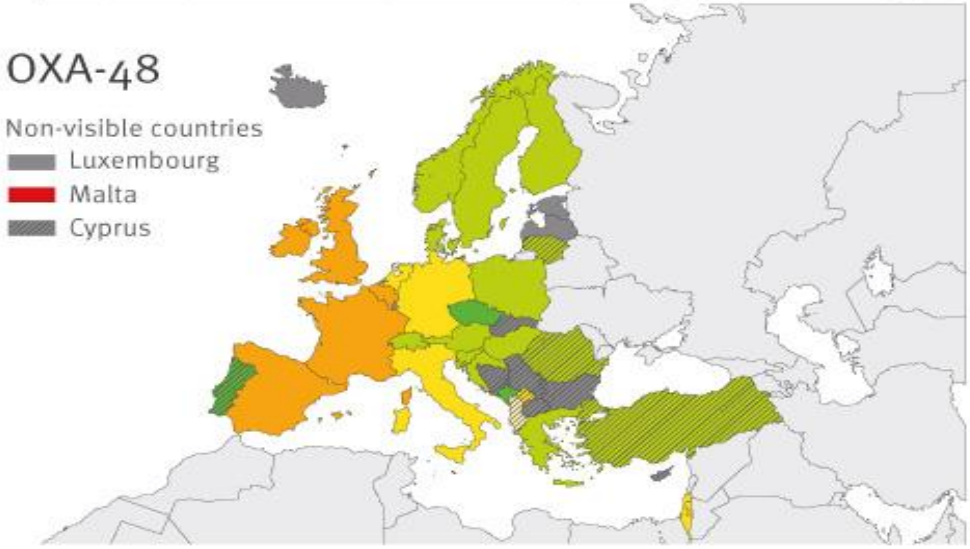
Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe
Canton Clin Microbiol Infect 2012; 18: 413–431

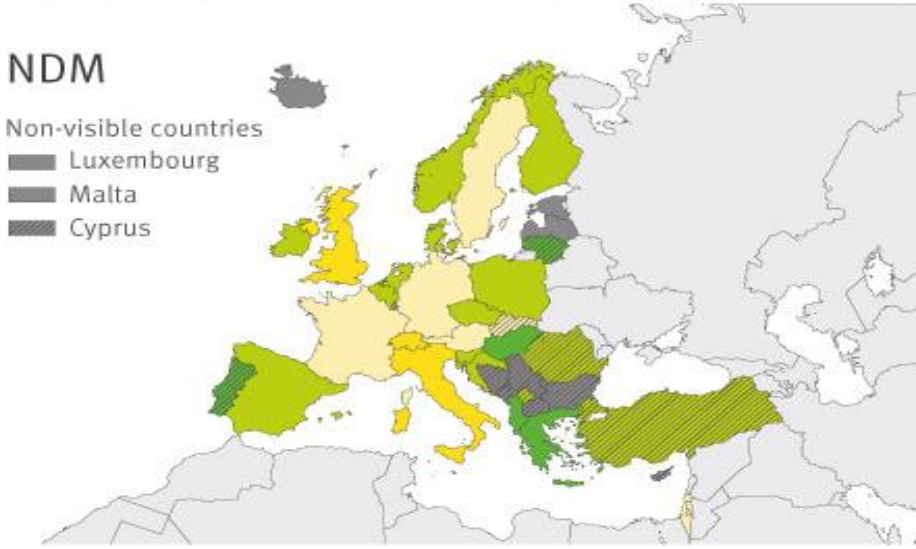
Eurosurveillance, Volume 18, Issue 28, 11 July **2013**

B Geographic distribution of CPE by resistance mechanism using the same epidemiological scale





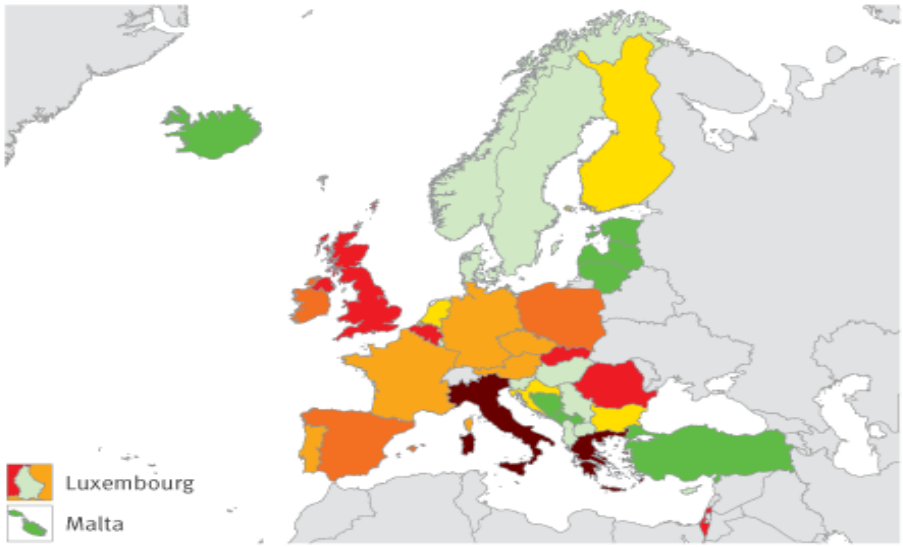




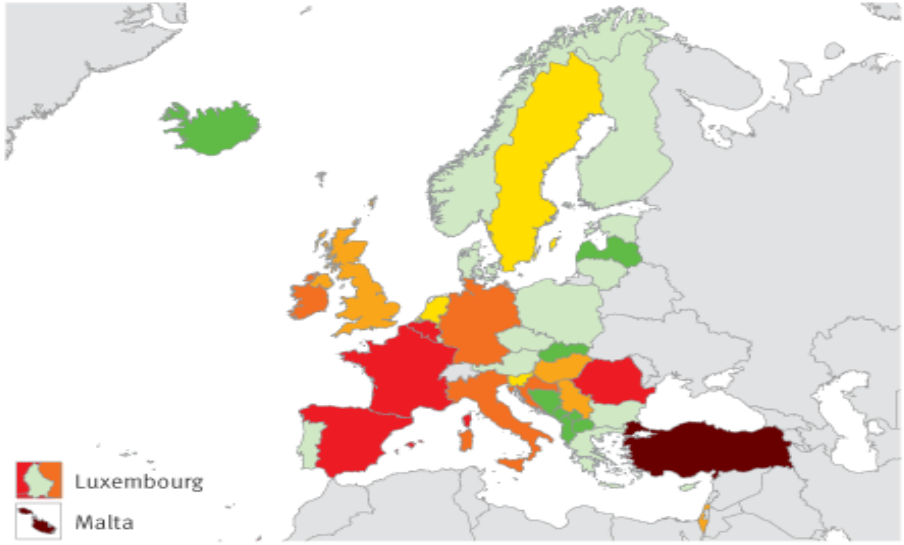
KPC: *Klebsiella pneumoniae* carbapenemase-producing *Enterobacteriaceae*; NDM New Delhi metallo-beta-lactamase; OXA-48: carbapenem-hydrolysing oxacillinase-48; VIM: Verona integron-encoded metallo-beta-lactamase.

Albiger et al May 2015. Euro Surveill. 2015

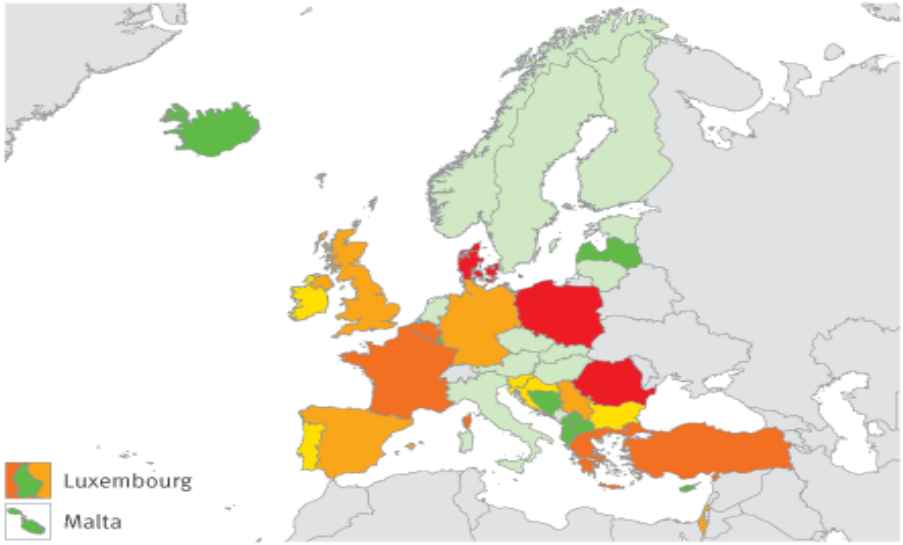
A. *Klebsiella pneumoniae* carbapenemase (KPC)



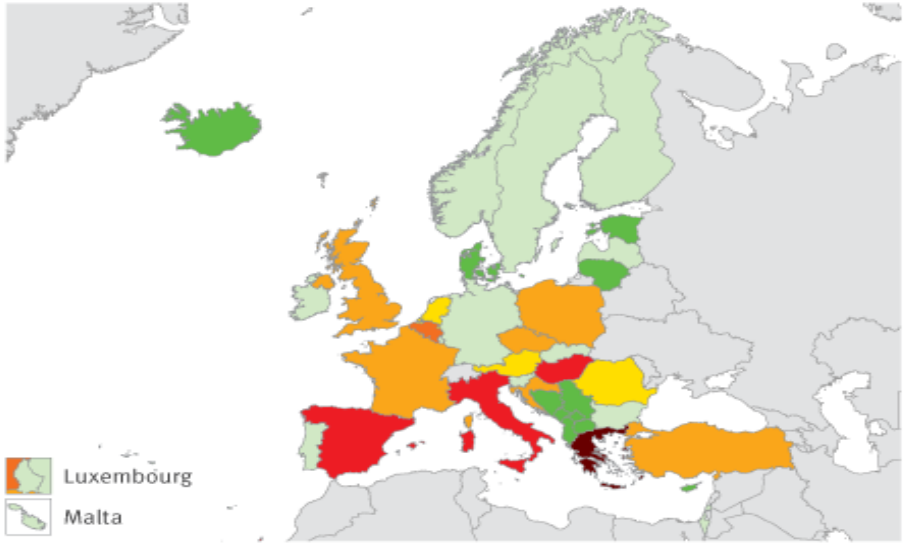
B. Oxacillinase-48 (OXA-48)



C. New Delhi metallo-beta-lactamase (NDM)



D. Verona integron-encoded metallo-beta-lactamase (VIM)



Epidemiological stages, 2014-2015

Who to screen? All hospital transfers: UK and Abroad

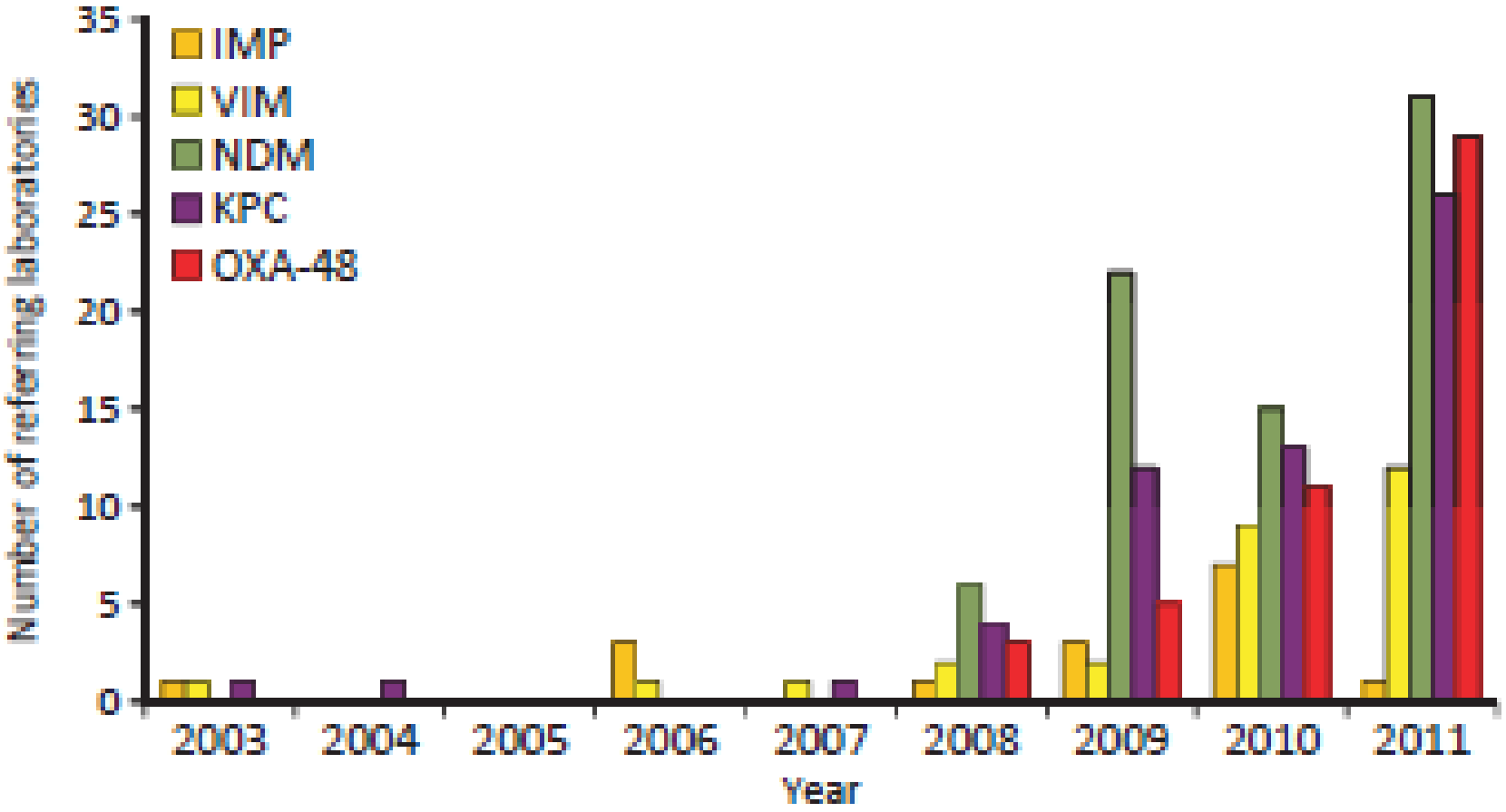
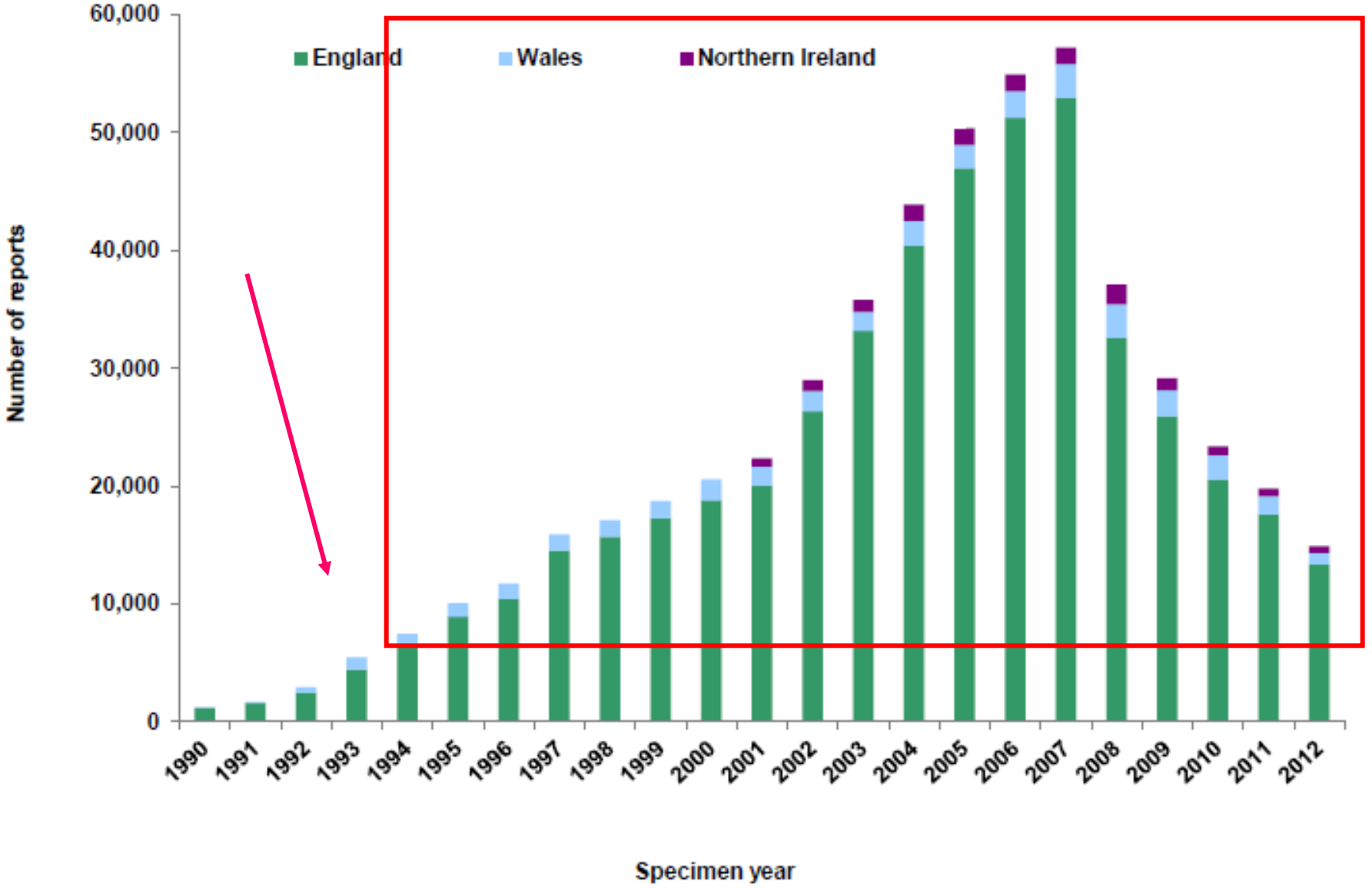


FIG. 4. Numbers of UK laboratories referring at least one carbapenemase-producing *Enterobacteriaceae* (CPE) isolate to the Antibiotic

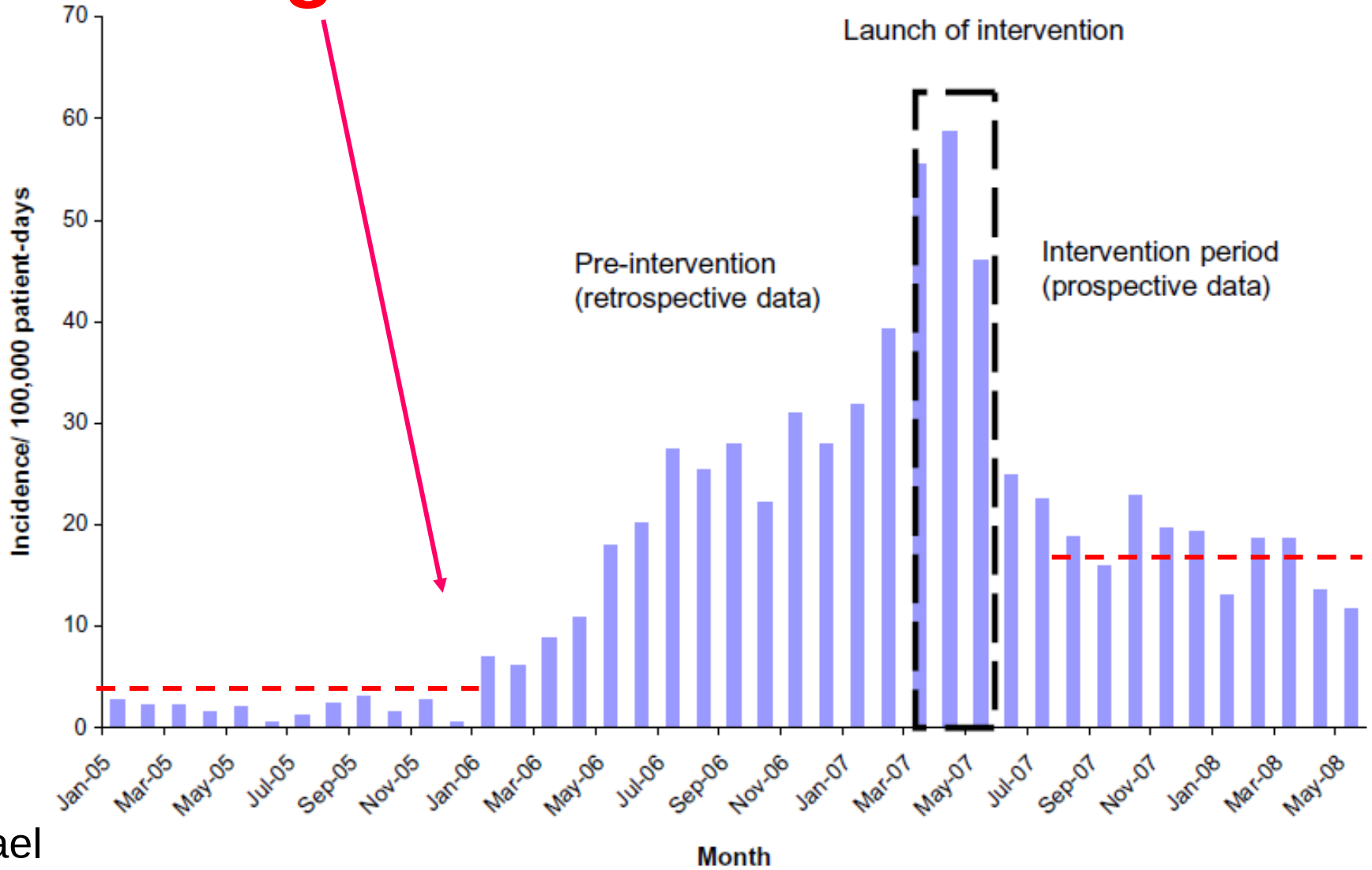
Canton Clin Microbiol Infect 2012; 18: 413–431



- National C.diff figures

CID 2011;52:848–855

Getting ahead of the curve??



Israel

Israel approach

Each hospital provides a daily census of :

- CRE carriers, including sample site
  - ADMISSION SCREENS
- Location of likely acquisition

Confirm
(1) labelled for contact isolation
(2) gowns/gloves required
(3) physical separation from non-carriers
(4) dedicated nursing staff

CID 2011;52:848–855

Our experience

- What did we do?
- What do we do now?
- What approaches are there to screening?

My Perspective: 700 yr old strategy

Effective separation = no transmission

Separate

- Isolate known positive cases
- ‘Quarantine’ suspect cases

Clean

- Hands/equipment/environment

Why screen?

1) Early isolation and IPC measures
   – Prevent further spread

   Cant effectively separate if you don't know who has it!

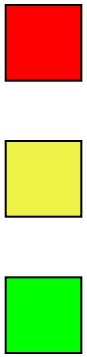
2) Early targetted treatment/prophylaxis
   – Reduce mortality/morbidity

First case May 2011

- Sputum with *Klebsiella pneumoniae*
  - Looks meropenem resistant
  - who to screen?

Who to screen?

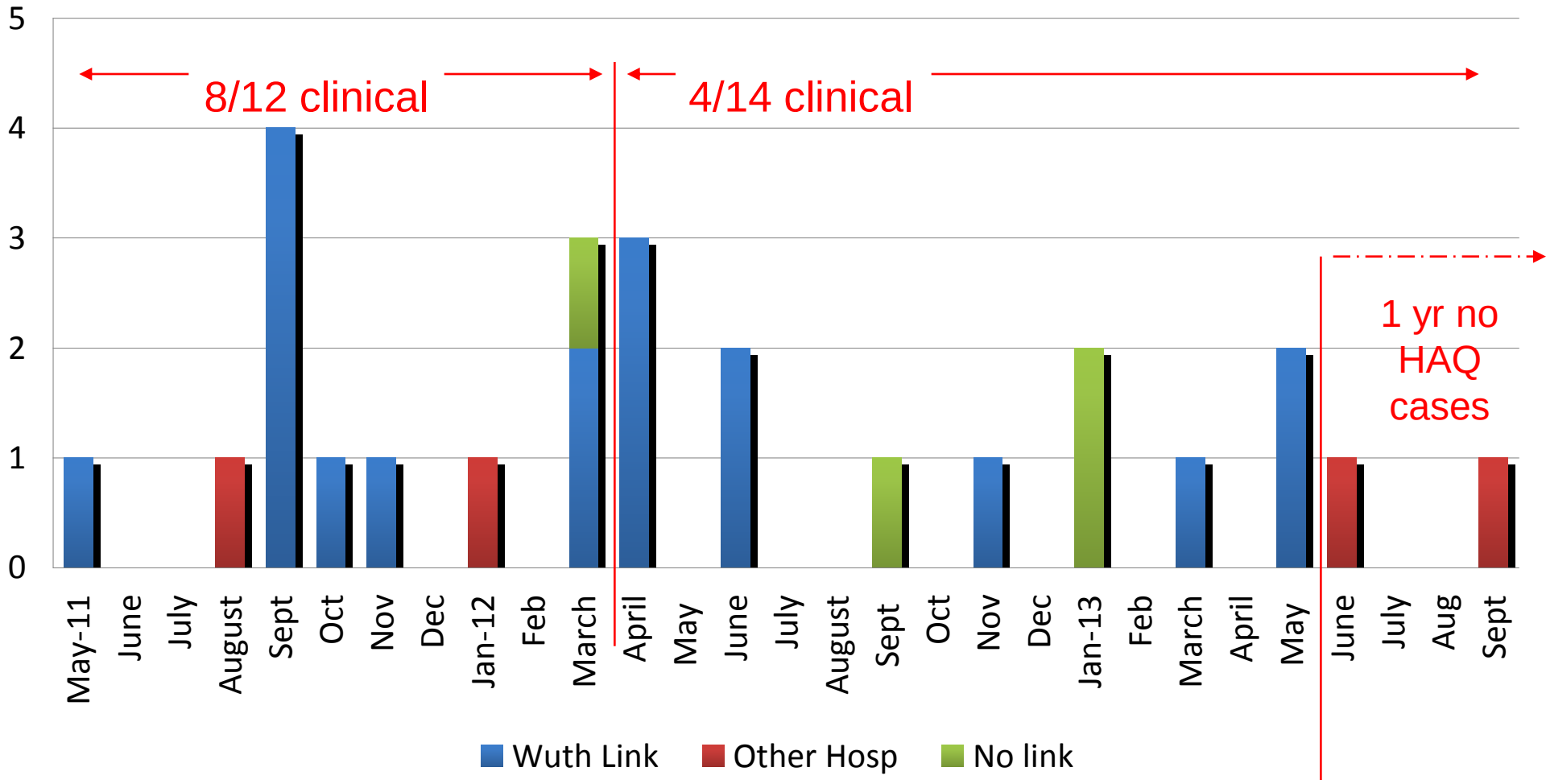
- Bay contacts?
- All current ward contacts?
- Other?

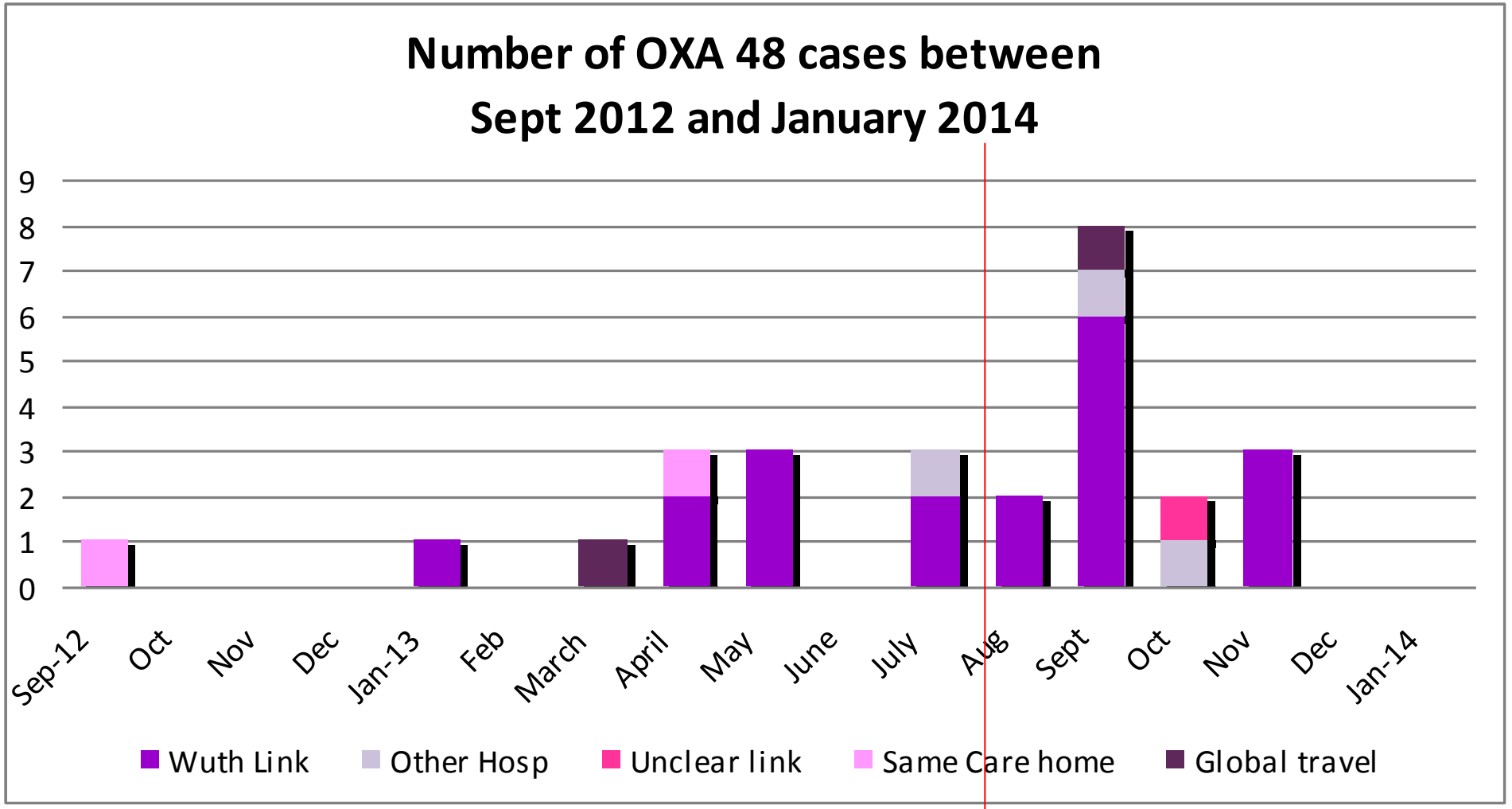


Previous ward contacts?

Previous bay contacts?

Number of VIMS
May 2011 to Sept 2013

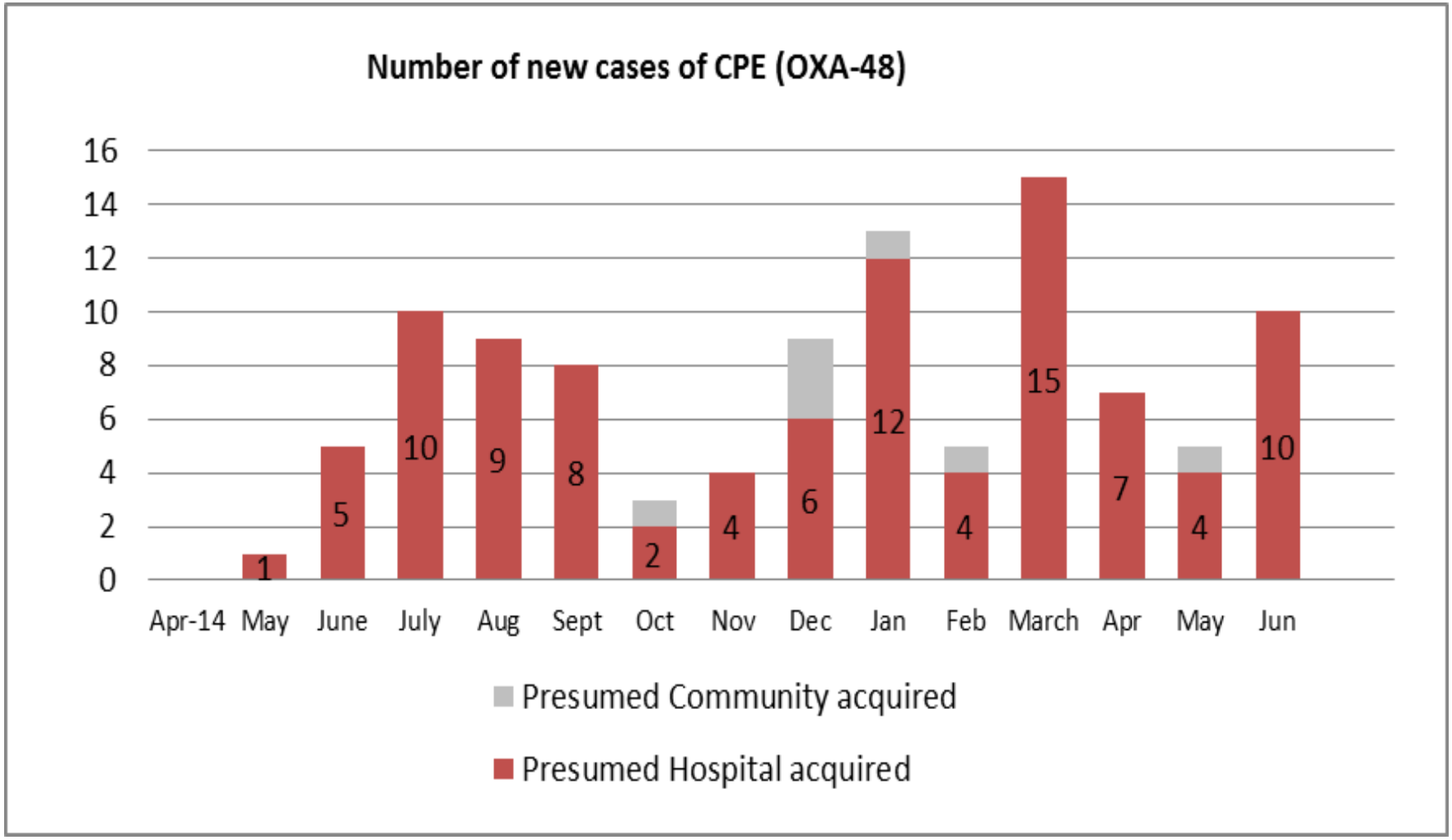




8/12 clinical

0/14 clinical

Then 6months of no cases


Number of new cases of CPE (OXA-48)
16
14
12
10
8
6
4
2
0
1
5
10
9
8
2
4
6
12
4
15
7
4
10
Apr-14
May
June
July
Aug
Sept
Oct
Nov
Dec
Jan
Feb
March
Apr
May
Jun
Presumed Community acquired
Presumed Hospital acquired

But also

- Transfers/admissions carrying:
  - IMP
  - KPC
  - NDM
- With no subsequent transmission
  - Early identification through screening allowed implementation of IPC measures

Back to First Case: Results

- Index patient
  - Rectal screen negative x 2
  - Bay contacts negative
  - Ward contacts negative
- Interpretation??

Should I stop/start screening?

Patient is in side room

4 weeks of full ward screening is complete

No new positives

STOP screening?

Patient isolated on admission,

START screen contacts?

Should I stop screening as soon as last patient discharged?

What we did:

- 4 wks of ward screening AFTER last carrier discharged

- C.F. French guidelines

2013 *Acute trust toolkit* (PHE)

Advises

- 4 weeks of contact screening after identifying a case

- screening of patients in the same setting is NOT normally required if the case was identified on admission and isolated immediately

Our approach identified 13 (25%) additional cases compared with the PHE toolkit

Should discharged contacts be screened?

- Yes 
- No 
- Ridiculous! 

Netherlands

Patients in the high-risk group were

- screened on readmission when hospitalised
- if not hospitalised through post-discharge screening
  - received information and material for sampling to returned by mail (POO in the POST…!)

Successful control of a hospital-wide outbreak of OXA-48 producing Enterobacteriaceae in the Netherlands, 2009 to 2011

Eurosurveillance, Volume 19, Issue 9, 06 March 2014

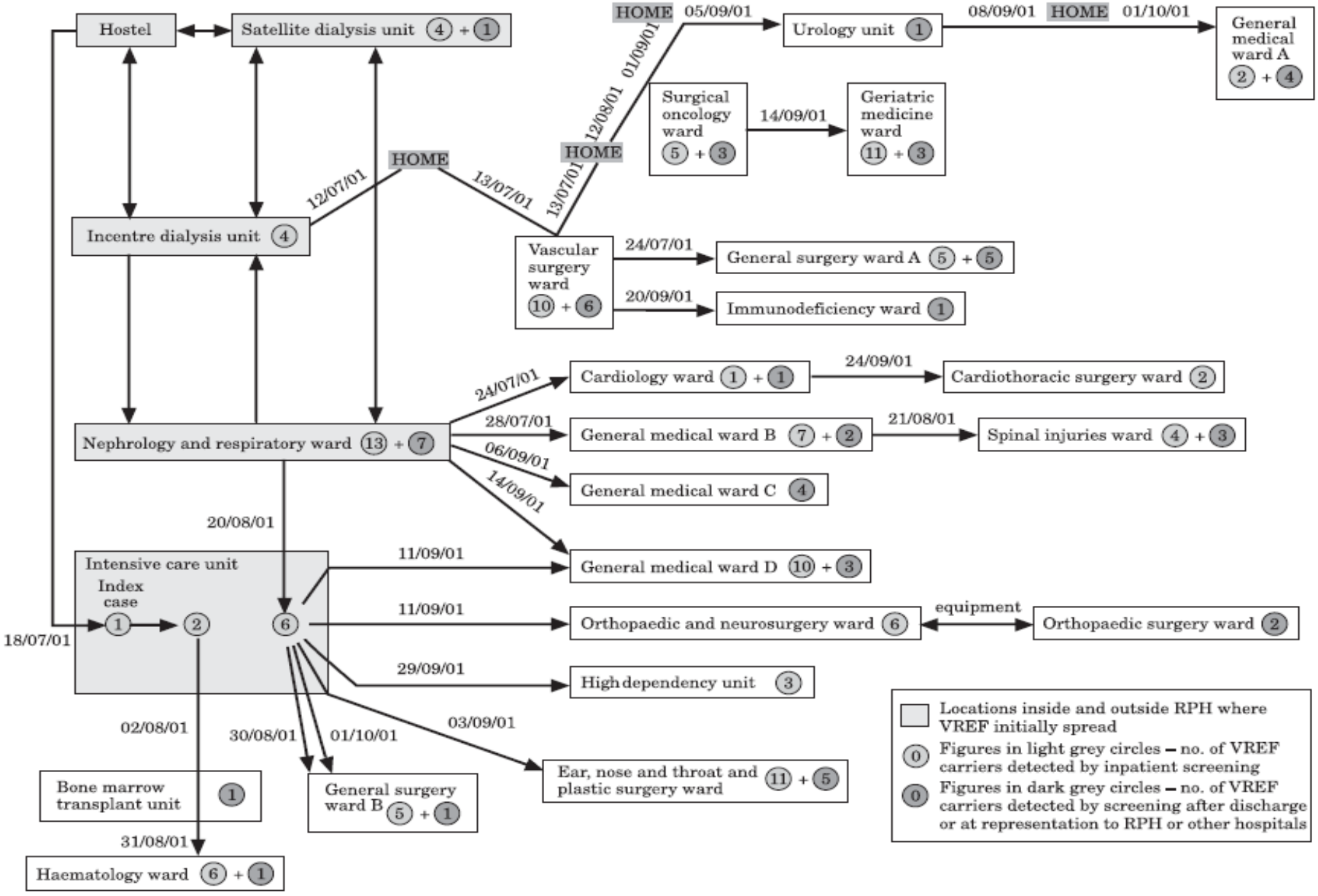


Figure 1 Single-strain outbreak of vancomycin-resistant *Enterococcus faecium* (VREF) of *vanB* genotype in the Royal Perth Hospital (RPH), July—December 2001, and VREF carriers detected after discharge from hospital, 28 September 2001—30 April 2002. Source: Pearman JW, *et al. Aust Infect Control* 2003;8:77—87. Copyright Australian Infection Control Association, reproduced with permission.

Pearman. JHI(2006) 63, 14-26

Does anyone have it right?

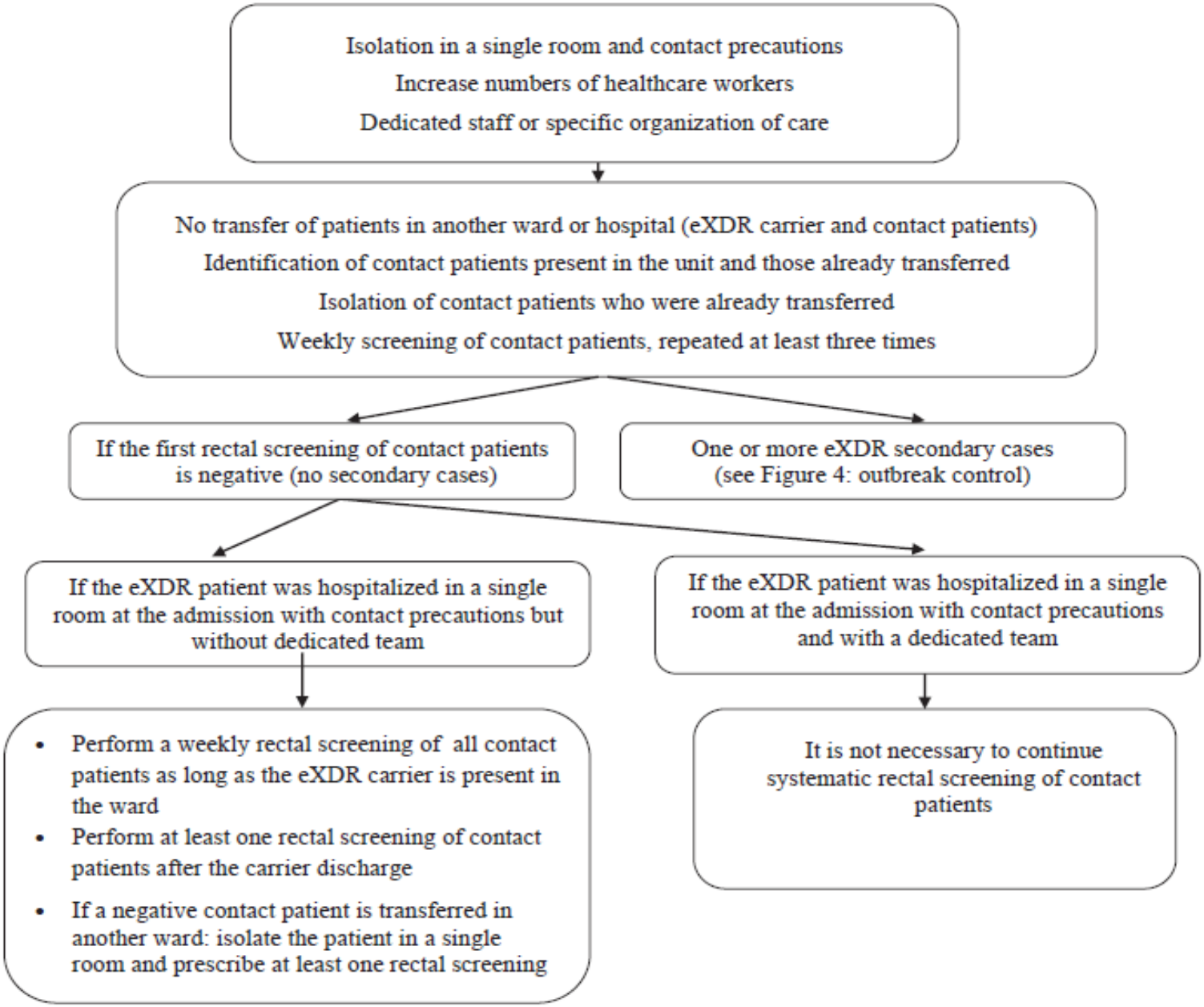


Figure 3. Recommendations to control the spread of emerging extensively resistant (eXDR) bacteria when detected from a clinical sample during hospitalization.

D. Lepelletier et al. / Journal of Hospital Infection 90 (2015) 186-195

Low risk

Isolated at admission

- Weekly rectal screening on all contacts with the carrier
- screening all contacts before transfer to another ward or hospital
- Screening repeated at least once after they have been transferred
- at least one post-exposure rectal screen on all contacts who are still hospitalized after carrier discharged
- Screen readmitted contacts

Intermediate risk

Detected after admission with no isolation

- Line list
- Rectal screening on hospitalized contacts
- letter to inform discharged patients and the need to declare that they have been in contact with a carrier
- No transfers of contacts (except emergency)
  - If happens, a single room and three-weekly rectal screening
- If 3 weeks screening of all contacts negative, the risk of cross-transmission becomes low

High risk of transmission

Several secondary cases have been identified (outbreak)

Recommendations:

- 3 rectal screens of all contact patients
- Do not transfer contact patients
- Vigilance for conversion in contacts exposed to antibiotic treatment
- Dedicate nurse and medical staff in three different cohorts
  - to separate clean/exposed/carrier

D. Lepelletier et al. / Journal of Hospital Infection 90 (2015) 186-195

TABLE 2

Occurrence of outbreak and number of secondary cases according to measures implemented around a carbapenemase-producing Enterobacteriaceae (CPE) index case at Assistance Publique–Hôpitaux de Paris, France, 2004–2012

Event[a] and related cases	Measures implemented within two days following admission of the index case		Delayed measures of control[b]	P value
	Dedicated nursing staff	Barrier precautions		
Number of events	18	55	67	–
Number of outbreaks (proportion of outbreaks among events)	0 (0%)	6 (11%)	11 (16%)	0.17
Number of cases	18	74	108	–
Number of secondary cases (proportion of secondary cases among cases)	0 (0%)	19 (26%)	41 (38%)	0.001

[a] An event was defined as one index case, followed or not by secondary case(s).

[b] Control measures were implemented but occurred later than two days after admission of the index case, because the patient was not identified as infected/colonised with CPE within the first days of admission.

- rapidly isolating index patients with barrier precautions was not always sufficient to avoid secondary cases and these occurred in six of 55 events
- Dedicated nursing staff is probably one of the most relevant measure to avoid cross transmission

Eurosurveillance, Volume 19, Issue 19, 15 May 2014
Long-term control of carbapenemase-producing Enterobacteriaceae at the scale of a large French multihospital institution: a nine-year experience, France, 2004 to 2012

Sensitivity of one swab?

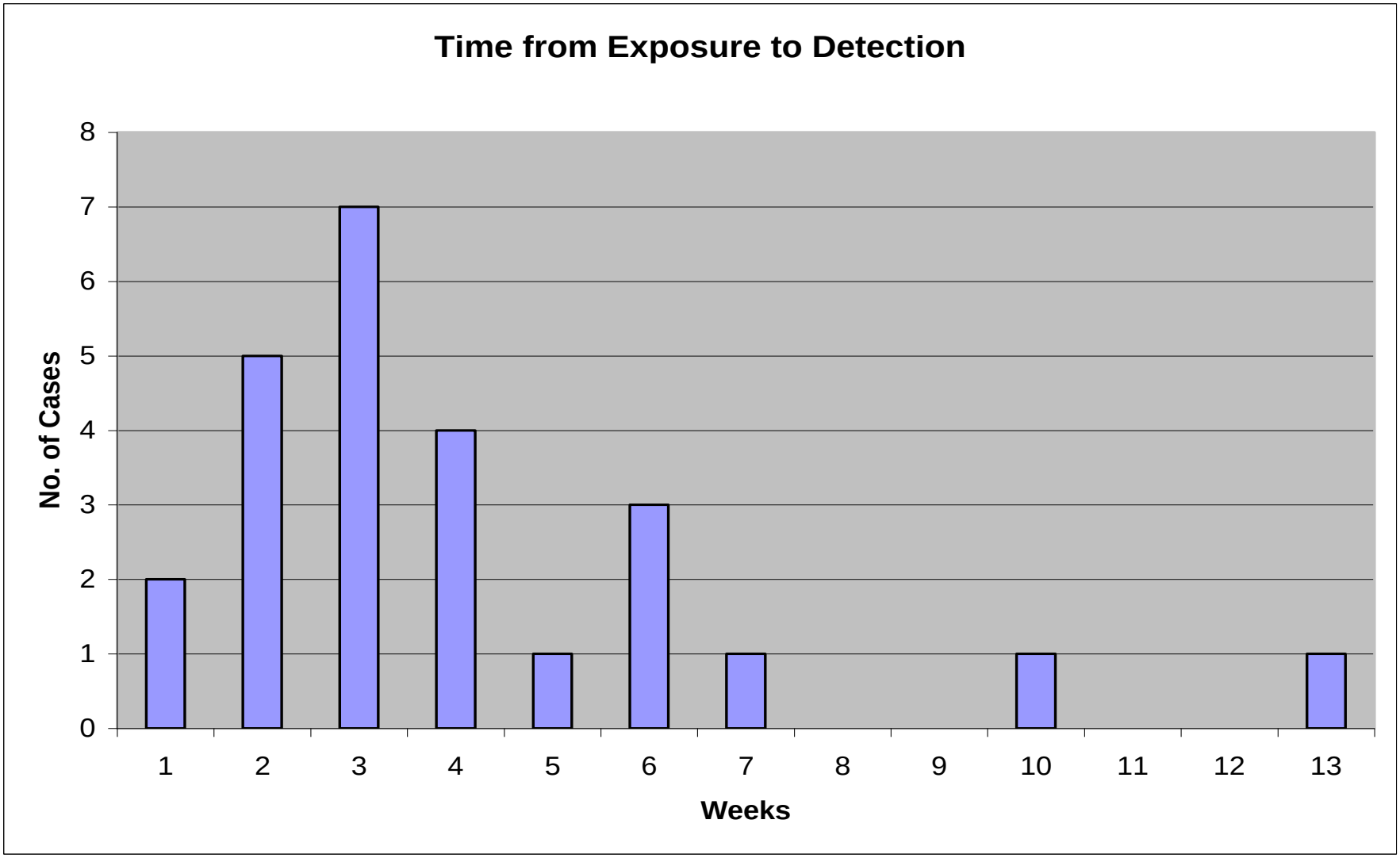
2004 Lowbury Lecture: the Western Australian experience with vancomycin-resistant enterococci from disaster to ongoing control

Pearman. JHI(2006) 63, 14-26

Table II Sensitivity of single and multiple rectal swabs for detecting vancomycin-resistant *Enterococcus faecium* (VREF) carriers

	Number of carriers						
Number of rectal swabs	1	2	3	4	5	6	7 or more
VREF carriers detected for first time	96	31	17	15	4	2	7
Cumulative number of carriers detected	96	127	144	159	163	165	172
Cumulative percentage of carriers detected (sensitivity)	56	74	84	92	95	96	100

Source: Pearman JW, *et al*. *Commun Dis Intell* 2003;27(Suppl):S97–S102. Copyright Commonwealth of Australia, reproduced with permission.



Results

25 patients were identified (14 VIM-4, 11 OXA-48).

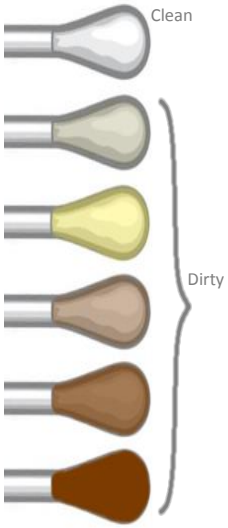
The mean conversion time was 26 days

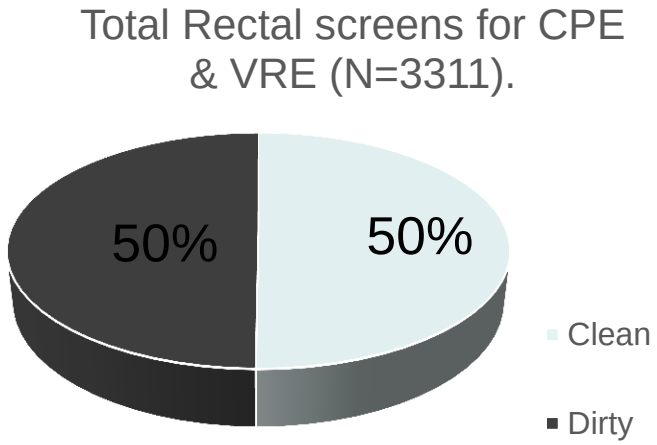
Range of 4 to 85 days

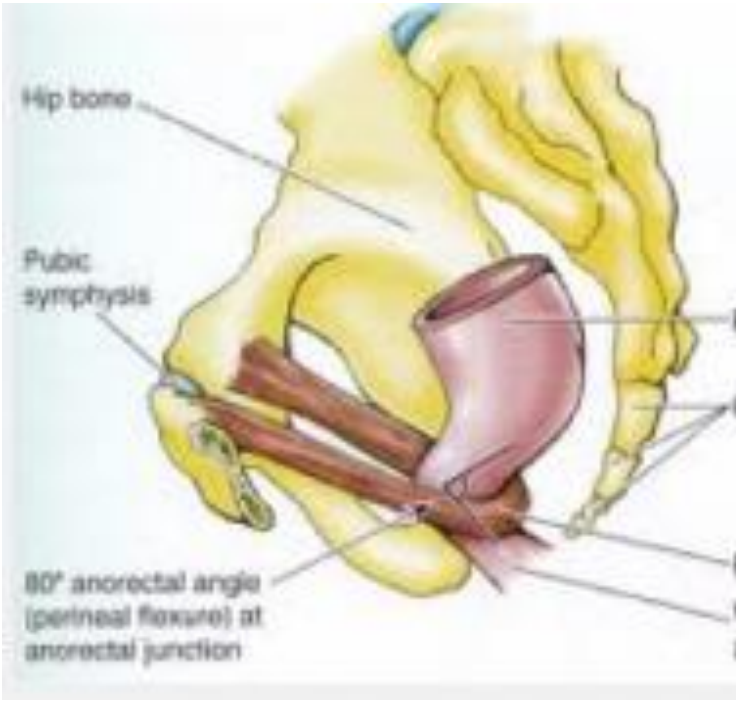
Comparing VIM-4 with OXA-48, the mean was 23 days vs 31 days.

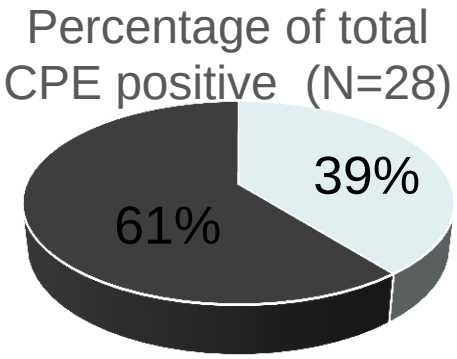
72% of cases were identified by 4 weeks, 88% by 6 weeks, 100% by 13 weeks

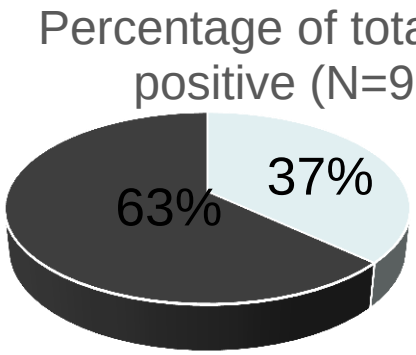
Are “dirty” rectal swabs better than “clean” rectal swabs for the detection of Carbapenemase Producing Enterobacteriaceae and Vancomycin Resistant Enterococci?











Is all this screening really worth it?

2013 fiscal year

- 102000 universal MRSA vs 7100 targetted CPE

33 new cases found

- ~1% of unique patient screens

Compare with VRE

Ostrowsky et al. screening and isolation

→ prevalence 2.2% in 1997 → 0.5% in 1999.

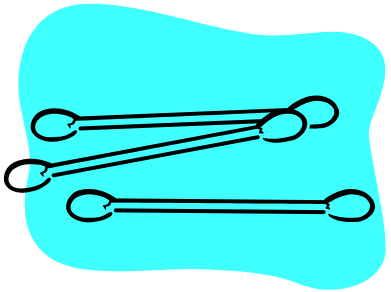
HICPAC: Management of Multidrug-Resistant Organisms In Healthcare Settings, 2006

Ostrowsky, B. E., et al. (2001) *N Engl J Med* **344,** 1427-1433

PCR vs conventional

- PCR
  - Increased sensitivity
  - Can be delivered Near/Point of Care
    - Direct from rectal swab
    - Immediate IPC decisions
  - Rapid confirmation of clinical isolates

Summary



ACTIVE SURVEILLANCE TESTING

- Screen: all transfers PCR
- Screen: high risk areas admission (PCR), weekly

EPIDEMIOLOGICALLY TRIGGERED TESTING

- Screen: weekly if carrier is inpatient
- Screen: even if rapidly isolated
- Track back to find all linked patients

- Screen: 4 weeks after last carrier discharged (3 weeks if PCR)
- Screen: minimum 6 weeks from exposure

- Screen: discharged high risk contacts in community

- Screen all readmitted contacts PCR
- Screen all hospital readmissions once once a threshold of cases reached

- Screen all admissions??

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