Control of Carbapemenase-producing *Enterobacteriaceae* (CPE) in France

Vincent Jarlier
Bactériologie-Hygiène
Pitié-Salpêtrière – Charles Foix Hospital, Paris
Infection control team, Medical Direction
Assistance Publique – Hôpitaux de Paris (APHP)

Bruno Coignard
Healthcare-associated Infections & Antimicrobial Resistance
Institut de Veille Sanitaire (InVS)

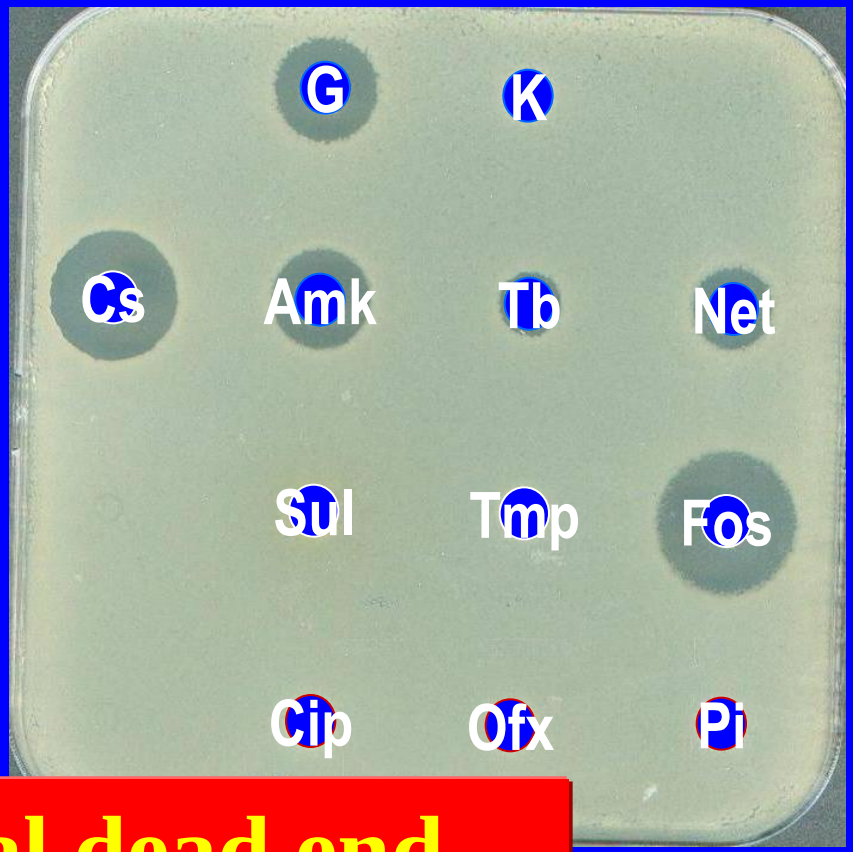
1st Outbreak of CPE in France :

Winter 2003-Summer 2004

Paul Brousse hospital (Paris) 2004

Klebsiella pneumoniae **VIM-1** + SHV-5

(index case : transfer from Athens)



~Therapeutical dead end

MIC: imipenem 32 mg/l ; gentamicin 8 mg/l

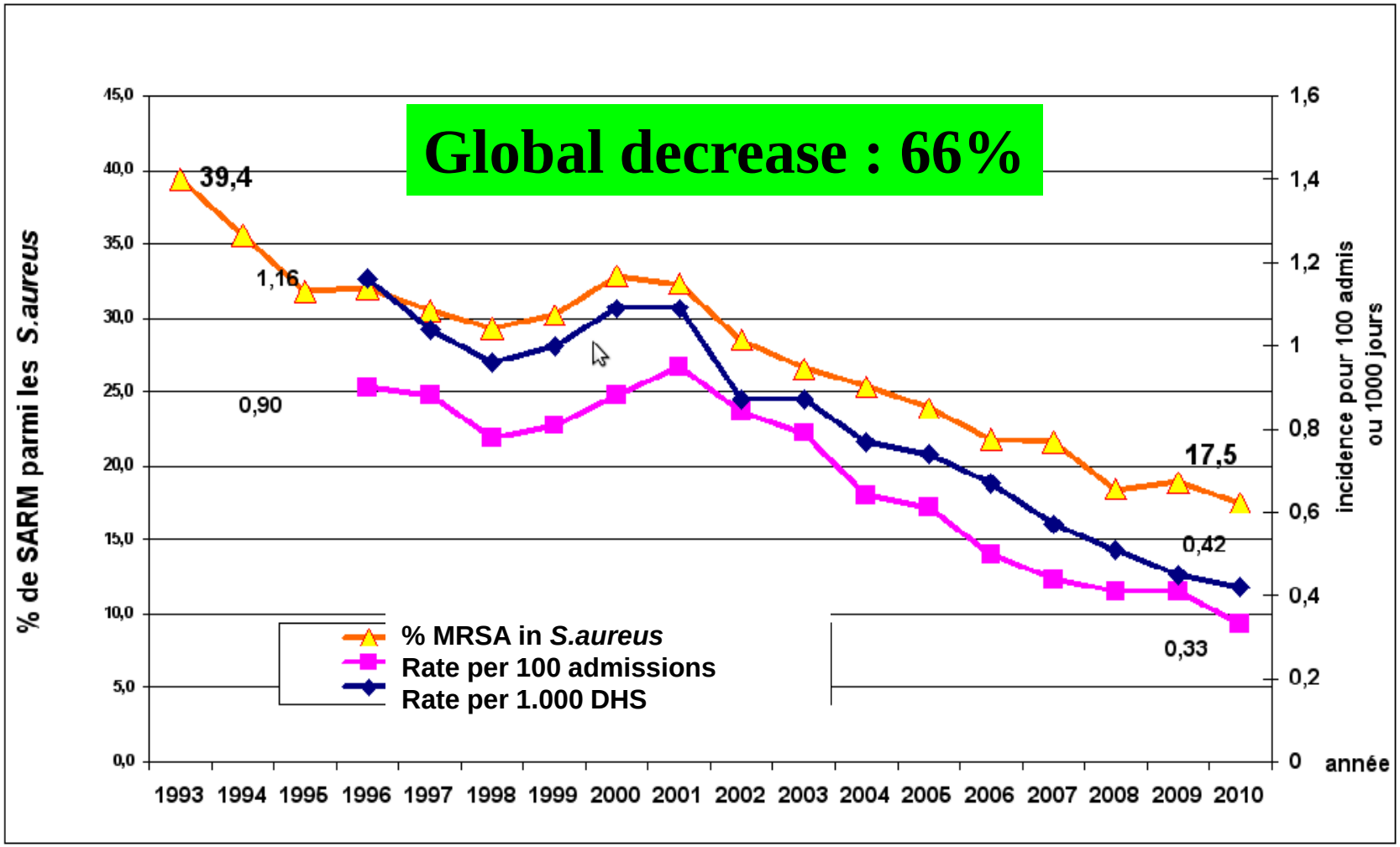
Courtesy: N. Kassis-Chikhani

Initial control measures from December 2003 to June 2004 (model = MRSA programme launched in 1993)

- IR-Kp carriers isolation in 1-bed rooms
- Promotion of alcohol-based handrubs
- Staff training
- Screening ICU patients at admission and 1/week (rectal swabs, 4 mg/l imipenem containing agar)

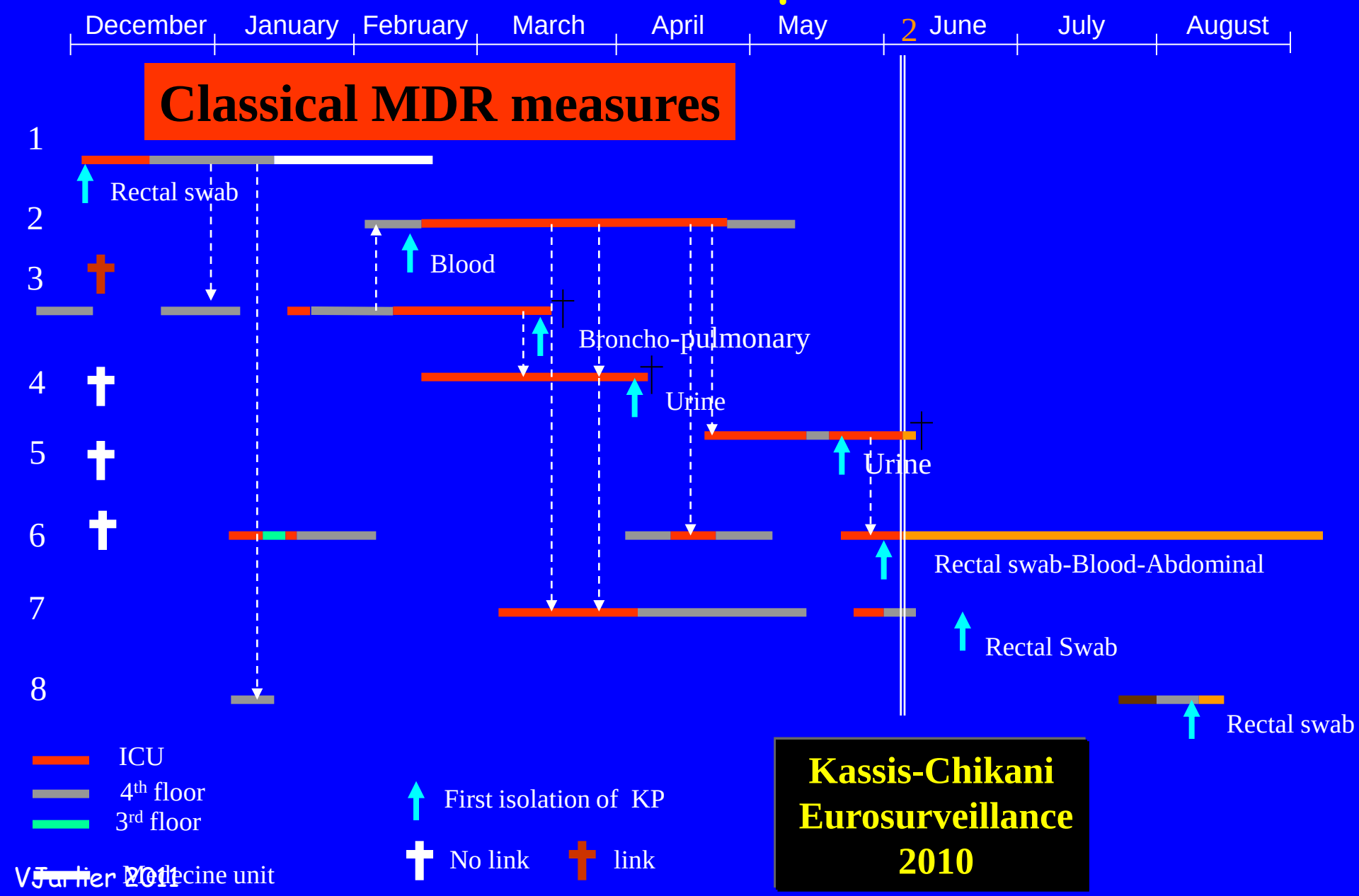
Kassis-Chikani Eurosurveillance 2010

% MRSA in *S.aureus* and MRSA incidence in acute care, APHP hospitals (n=38), Paris area 1993-2010



Jarlier Arch Int Med 2009

Paul Brousse Hospital, 2004



Extended control measures implemented in June 2004 (1)

- **ICU divided in 3 separate sections**
  - 1 for cohorting IR-Kp carriers ("**IR-Kp ICU**")
  - 2 for the IR-Kp-free patients ("**IR-Kp free ICU**")
    - for expected stay >> 2days of "heavy" ICU (""**long**")
    - for expected stay ≤2days and "ligth" ICU ("**short**")
- **Acute care divided in two sections** :
  - 1 for contact patients (at risk to be carrier : "**contact patients**")
  - 1 for new patients (not at risk : "**IR-KP free ACF**")

Kassis-Chikani Eurosurveillance 2010

Extended control measures implemented in June 2004 (2)

- nurse staff dedicated to “IR-Kp ICU”
- nurse staff dedicated to “IR-Kp free ICU”

“cohorting”

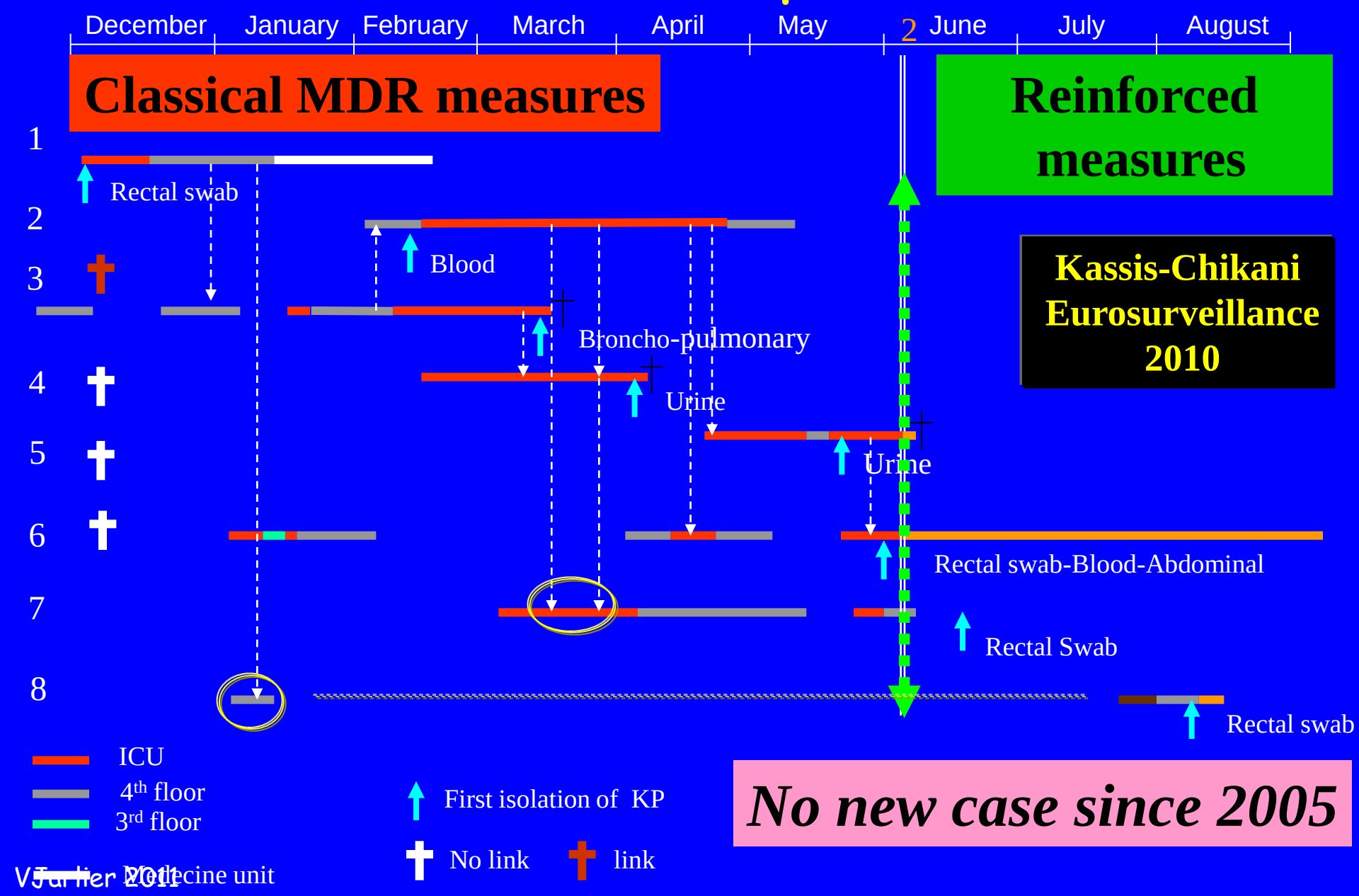
Kassis-Chikani Eurosurveillance 2010

Extended control measures implemented in June 2004 (3)

- Limitation of patient transfer to other wards or other care centers
- Screening all contact patients till discharge (+ if readmitted)
- Limitation of broad spectrum antibiotics
- IR-Kp carriers informed on their status + instructions at discharge
- Systematic efforts to inform contact patients who have been discharged at the beginning of the outbreak without being screened : letter to GPs, help line with 2 MDs during 2 weeks

Kassis-Chikani Eurosurveillance 2010

Paul Brousse hospital 2004

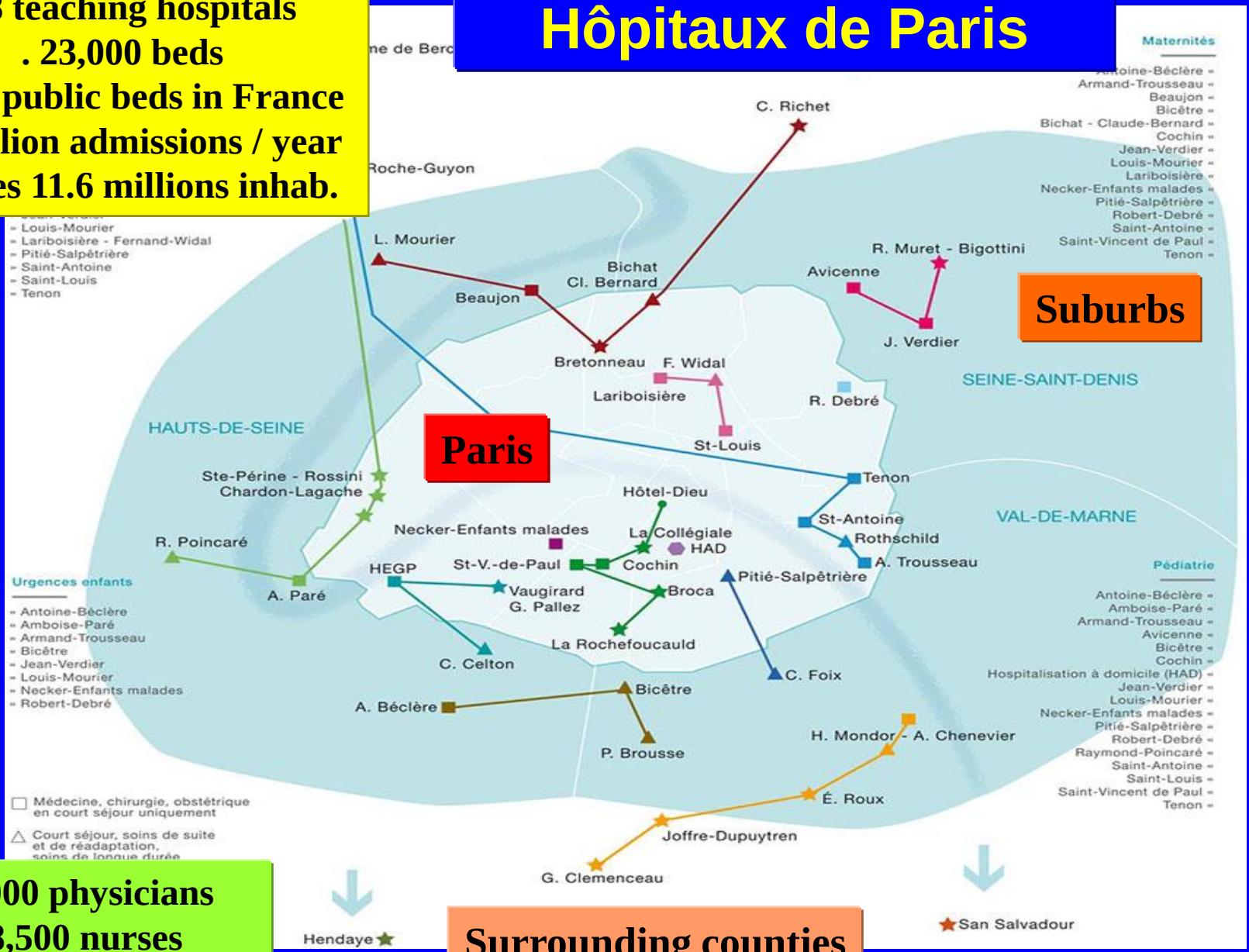


"Practicing" the reinforced measures for emerging MDROs control in France

The VRE period
2004-2007

. Single institution
. 38 teaching hospitals
. 23,000 beds
. 10% public beds in France
. 1 million admissions / year
. serves 11.6 millions inhab.

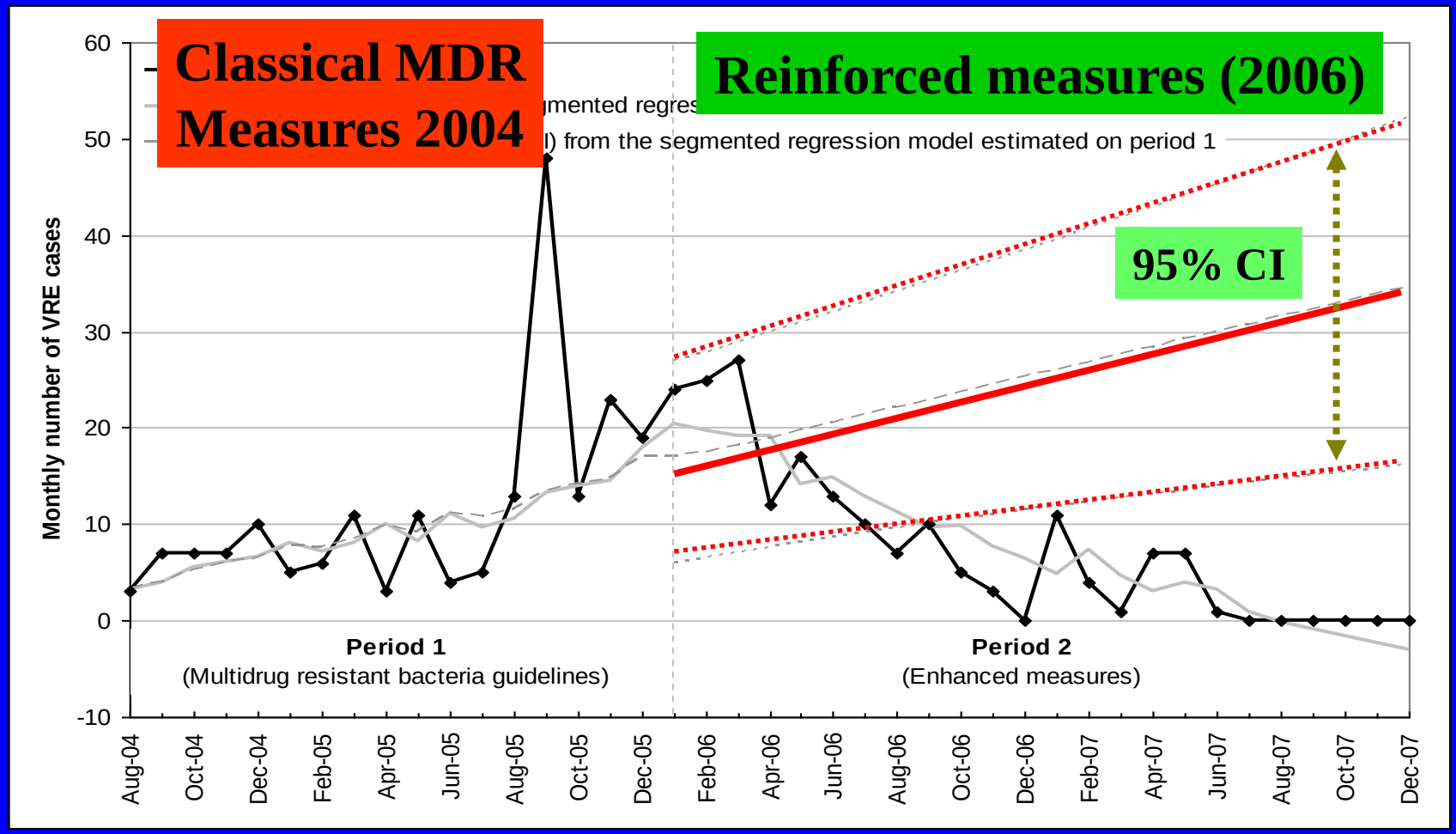
Assistance publique – Hôpitaux de Paris



. 19,000 physicians
. 18,500 nurses
. 29,800 assistant nurses

Surrounding counties

VRE cases per month
observed and predicted by time series analysis
38 AP-HP hospitals, 2004-2007



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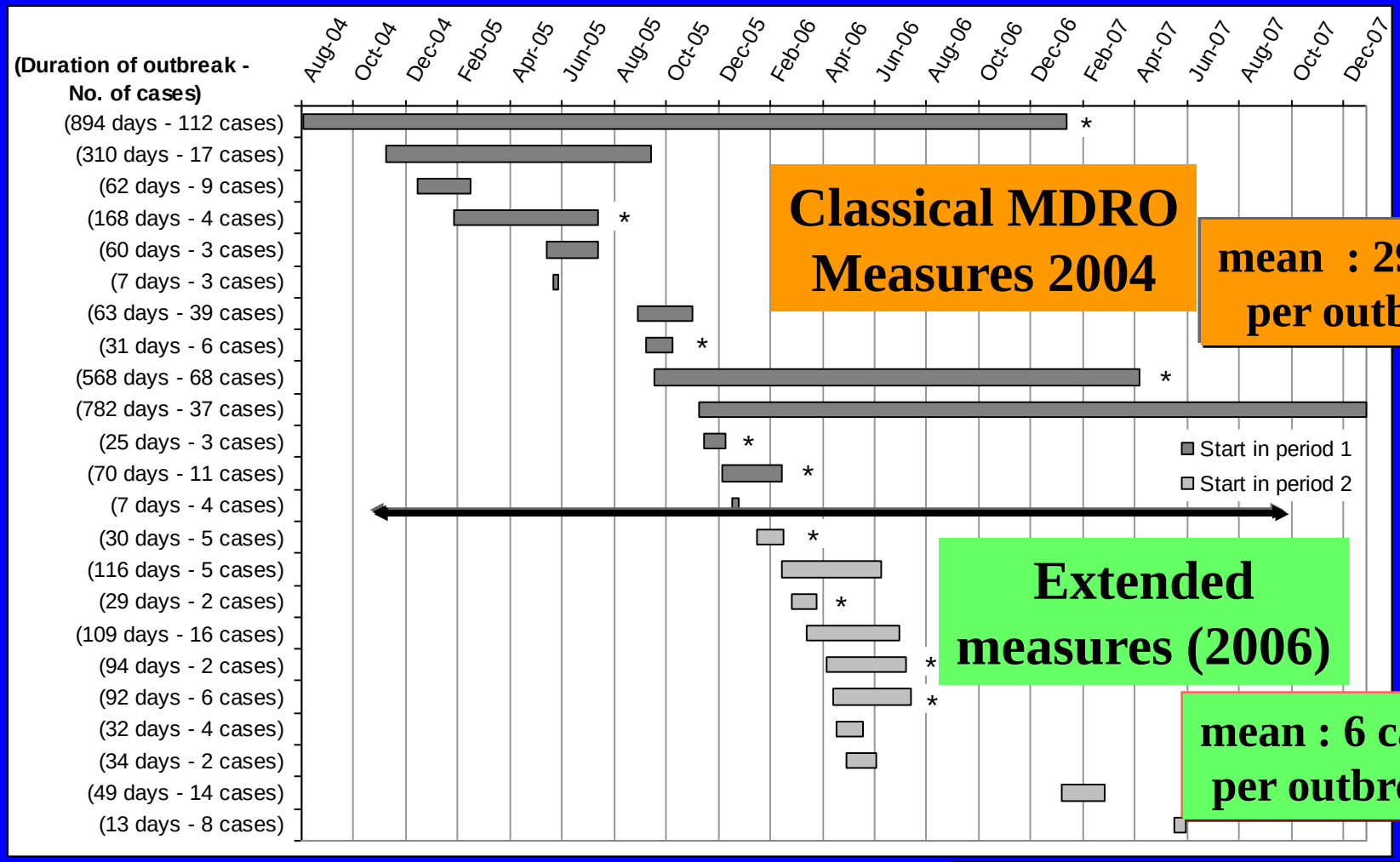
Length of the VRE outbreaks in the 38 AP-HP hospitals 2004-2007



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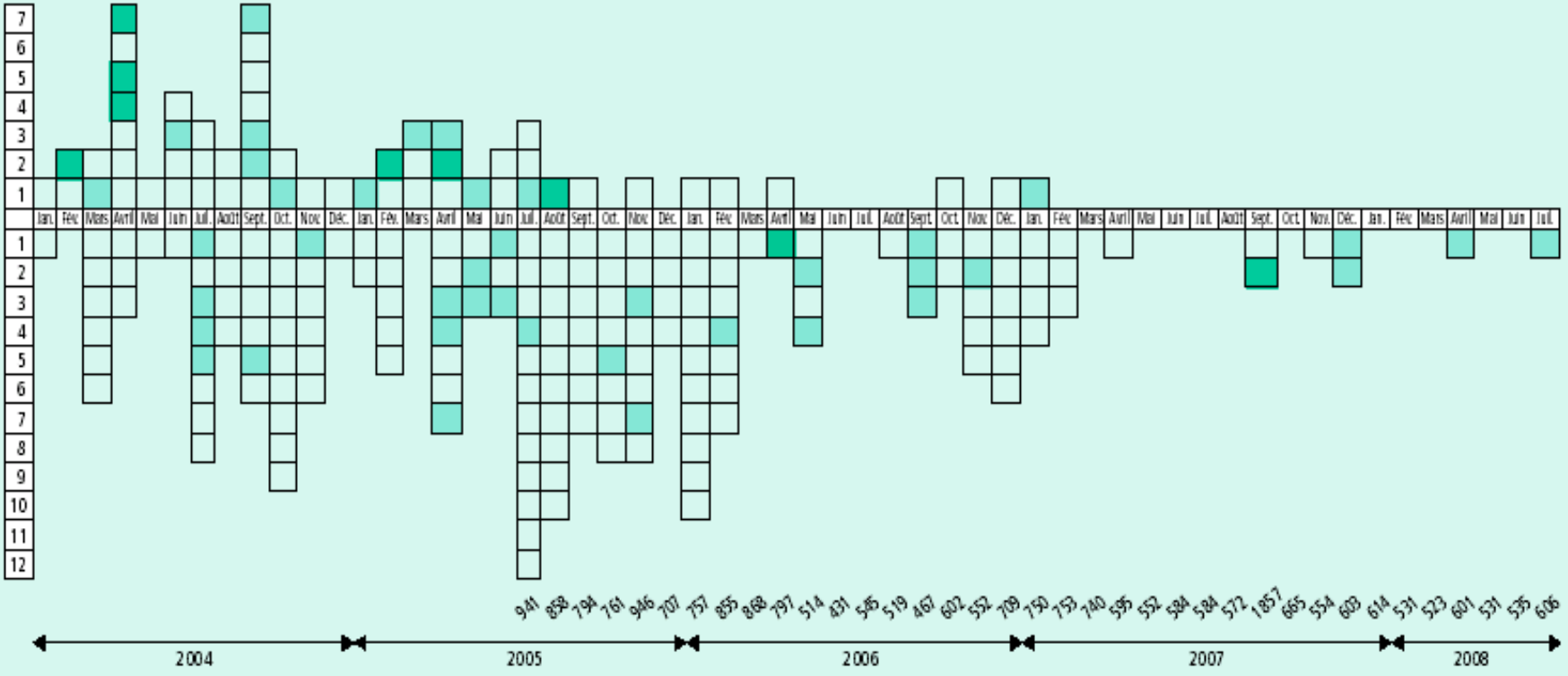
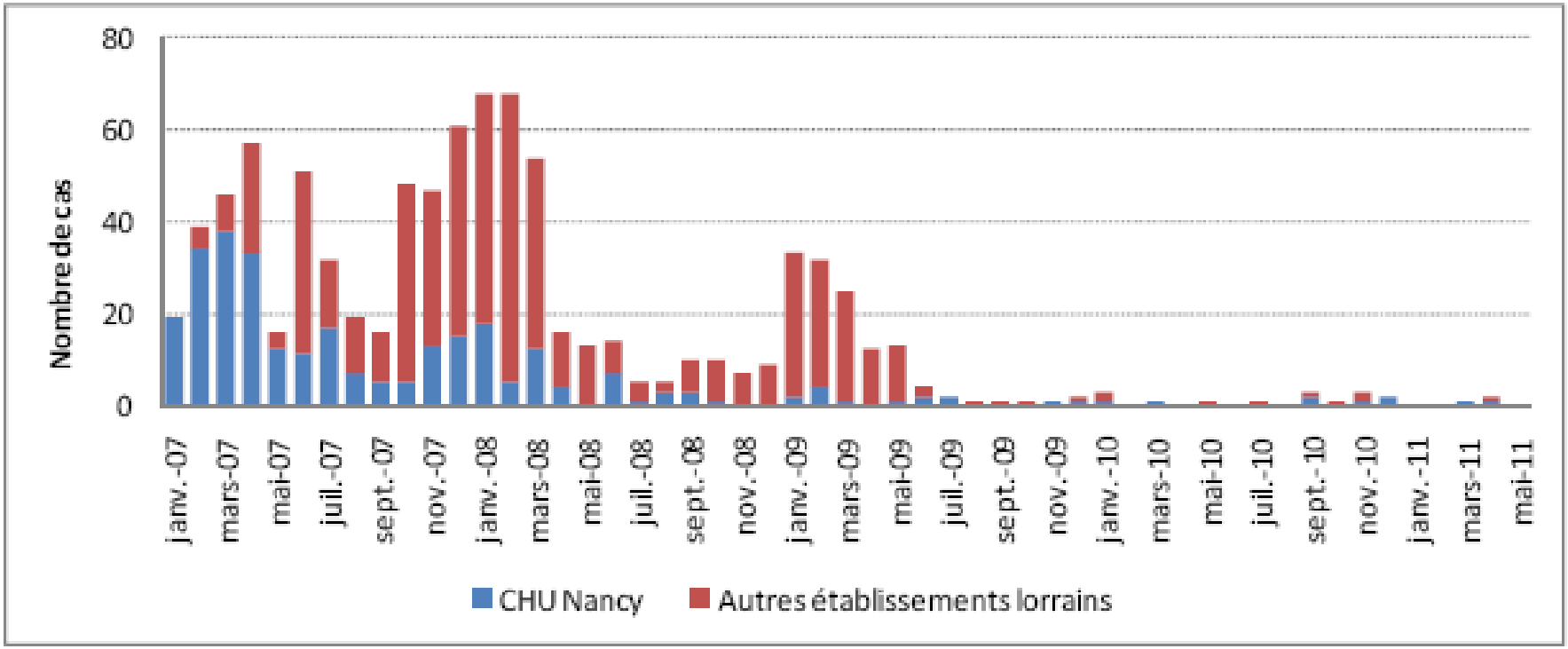
Control of VRE in Clermont Ferrand hospitals (Auvergne) 2004-2008

Figure Patients colonisés par *Enterococcus faecium* résistant aux glycopeptides (ERG) et patients porteurs d'ERG de janvier 2004 à août 2007, France
Figure Patients colonised by glycopeptides-resistant Enterococcus faecium (GRE) and patients carriers of GRE from January 2004 to August 2007, France



Lesens BEH 2008

Control of VRE in Lorraine hospitals (Nancy area) 2007-2010



French national guidelines (MOH) for emerging MDROs control (VRE, CPE) based on APHP experience

2006 (new edition 2010)

As soon as identification of the 1st case

- Isolate the patient in a single bedroom
- Alert hospital administrator and Inf. Control team
- **Stop transfer** to other units or hospitals of case and contact patients
- Limit admissions in the unit as much as possible
- **Screen contact patients till discharge**

French emerging MDRO control guidelines 2006, 2010

The two days following the identification

- **Identify other contact patients**: e.g. those already transferred at time of detection of the index case
- **Screen them**
- **Re-enforce hand hygiene** (ABHRS)
- Identify antibiotics that could be used in case of serious infection with the strain

French emerging MDRO control guidelines 2006, 2010

During the entire period of the outbreak

- **Cohort patients in distinct sections**, with dedicated staff:
  - case patients (« **case section**")
  - contact patients ("**contact patient section** ")
  - newly admitted patients ("**free section** ")
- **Screen once weekly all contact patients till discharge**
- after 3 neg. screenings, contact patients can be transferred but **continue to isolate and screen** them
- Strengthen survey of contact patients if receiving antibiotic
- Restrict antibiotics use
- Update the list of cases and contact discharged patients
- Set up an **information system allowing to identify cases and contact patients if re-admitted**

French emerging MDRO control guidelines 2006, 2010

CPE episodes in France : a programme for exhaustive survey at national level (2004)

Programme for exhaustive CPE survey

- notification by healthcare facilities using the French national HAI Early Warning / Response System (HAI-EWRS) :
  - to the regional health care authorities
  - transmitted and analyzed at the national level by InVS
- each event followed up at the regional level by teams specialized in infection control and epidemiology
- additional "not-notified" events systematically searched by InVS with the help of French hospital micro-labs that have expertise in beta-lactamases (n=12)

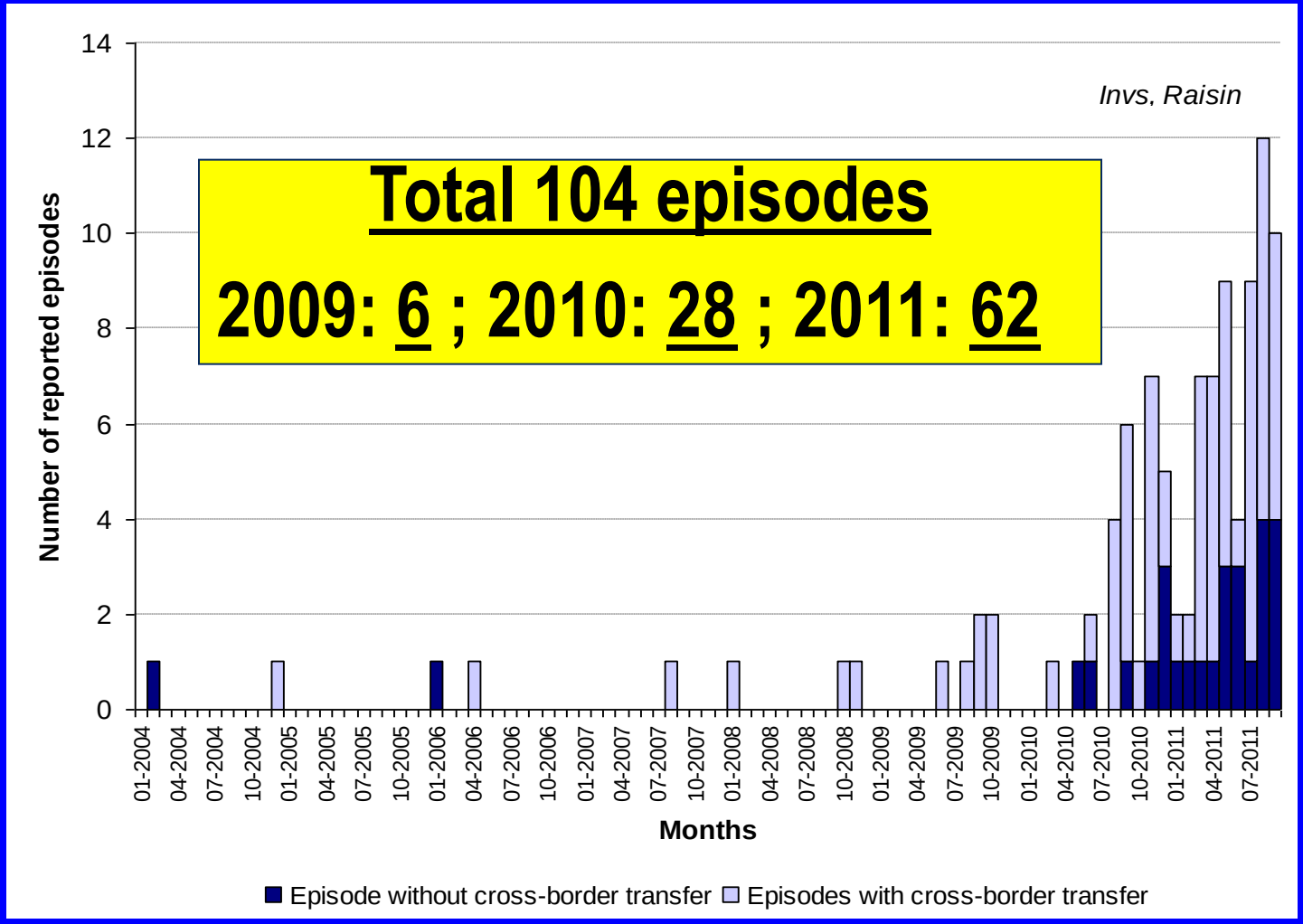
Courtesy Sophie Vaux , InVS

Definitions for CPE survey programme

- case = patient infected or colonized by a CPE bacteriologically confirmed by a reference or expert laboratory
- episode = sporadic case or several related cases (same chain of transmission)
- **Data updated on 27 September 2011**

Courtesy Sophie Vaux , InVS

Episodes of CPE infections or colonisations, by month, France, January 2004 – 27 September 2011 (N=104)



Courtesy Sophie Vaux , InVS

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Species/enzymes in French CPE episodes (n=104)

Species	N episodes	%
K.pneumoniae	**67**	**59 %**
E. coli	**25**	**22 %**
E. cloacae	14	12 %
E. aerogenes	3	3 %
C. freundii	3	3 %
P. mirabilis	1	<1 %
S.marcescens	1	<1 %
P. stuartii	1	<1 %
TOTAL	**115***	**100 %**

Enzyme	N episodes	%
OXA-48	**54**	**43 %**
KPC	**28**	**30 %**
NDM-1	14	13 %
VIM	10	11 %
IMI	1	
IMP	1	2 %
TOTAL	108*	100 %

** few episodes with >1 species and/or enzymes*

Courtesy Sophie Vaux , InVS

FRENCH INSTITUTE FOR PUBLIC HEALTH SURVEILLANCE

RAISIN HEALTHCARE-ASSOCIATED INFECTION EARLY WARNING, INVESTIGATION AND SURVEILLANCE NETWORK

Episodes associated with cross-border transfer within one year (N=76)

Overall : 73 % of all episodes

Context	N episodes	%
Direct transfer from a foreign hospital	50	66 %
Previous hospitalisation in a foreign hospital	13	17 %
Travel abroad without hopitalisation	7	9 %
Living abroad without hospitalisation	6	8 %
TOTAL	76	100 %

Courtesy Sophie Vaux , InVS

Enzymes in episodes of **foreign origin** (index case hospitalised or stayed abroad) (n = 76)

Country	KPC	OXA-48	VIM	NDM-1	Total
Greece	16 2007		4 2004		19*
Morocco	2 2011	15 2010			17
India	2 2011			9 2010	9*
Italy	3 2010		2 2008		5
Algeria	1 2010	2 2010	1 2008		4
Egypt	1 2011	2 2009	1 2010		4
Turkey		4 2010			4
Tunisia		3 2011			3
Senegal		3 2011			3
Koweit		2 2011			2
Israël	1 2011	1 2011			2
Iraq				1 2010	1
USA	1 2006				1
Spain		1 2011			1
Serbia				1 2011	1
Total	27	33	8	11	76

N Year of 1st report

* 2 enzymes in 1 episode

Enzymes in episodes in episodes without cross-border transfer (n = 28)

KPC	OXA-48	VIM	NDM-1	IMI	IMP	Total
1 2010	21 2010	2 2004	3 2010	1 2011	1 2004	28*

* 2 enzymes in 1 episode

- 27% of all episodes with no identified cross-border transfer (or stay abroad) of the index case
  - 1/28 for KPC, 3/14 for NDM-1, 2/10 for VIM
  - 21/54 (39 %) for OXA-48, occurred in 12 counties of 4 regions
- Suggesting the beginning of an autochthonous circulation of OXA-48 CPE in France

Courtesy Sophie Vaux , InVS

Characteristics of CPE episodes in France 2004-2011

- 249 cases for 104 episodes
  - infected: 29%
  - colonized: 71%
- 82 episodes with 1 sporadic case (79% of episodes)
- 22 outbreaks (21 % of episodes)
- 2 to 43 2ary cases per outbreak:
  - mean number 2ary cases per outbreak: 6.6
  - mean number 2ary cases per episode: 1.4
- Crude lethality: 20%

CPE in bacteremias due to *Klebsiella pneumoniae* (%) EARS-net-France 2007-2010 (56 hospitals)

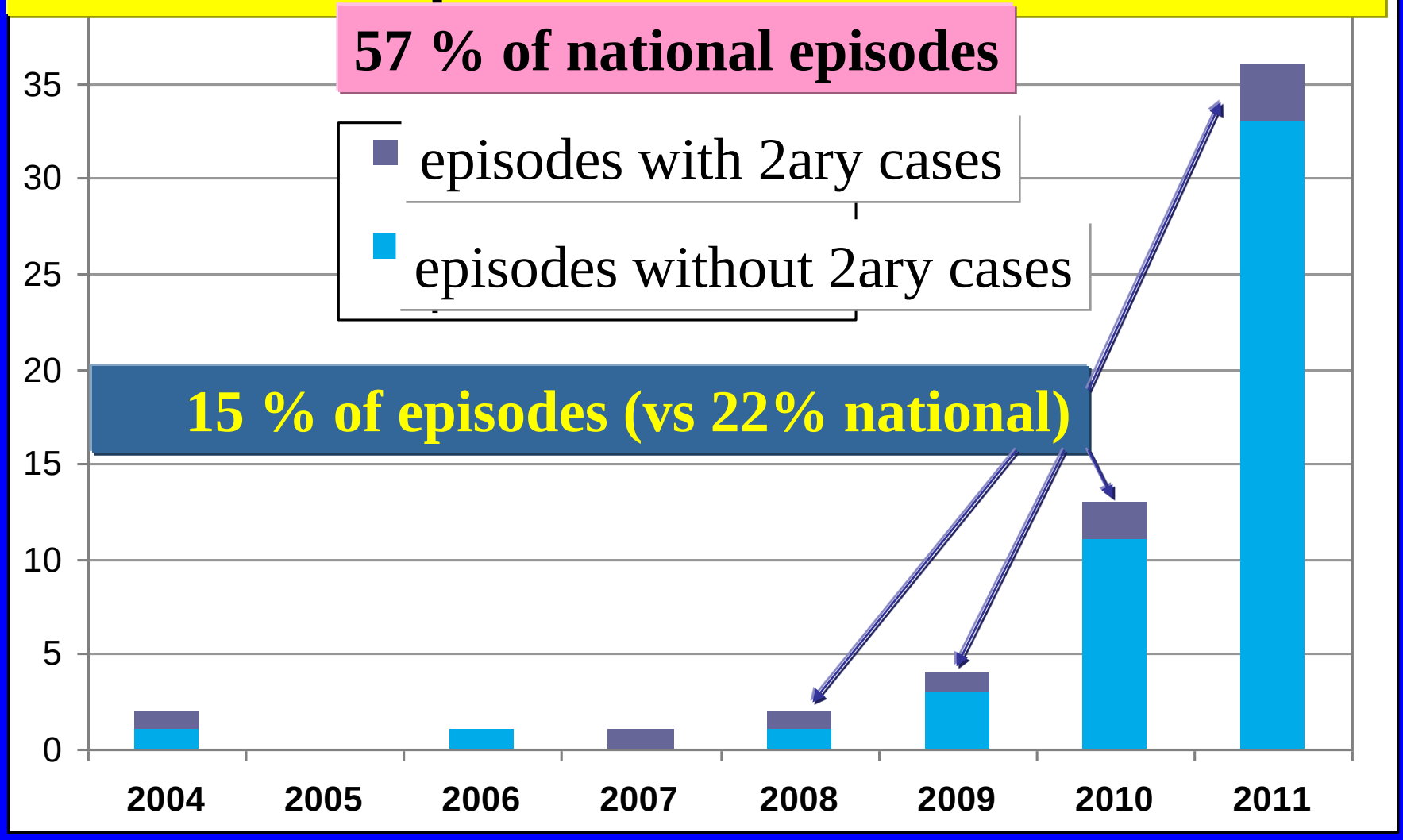
	N bacteremias	N CPE	% CPE
2007	1187	1	0.1
2008	1138	0	0
2009	1378	2	0.2
2010	1542	1	0.1

Controlling further CPE in the 38 APHP hospitals, applying the "Emerging MDRO control national guidelines"

. 23.000 beds, Paris and surrounding counties
. Institution infection control and antibiotic stewardship programme
. Central infection control team (4 persons) following up all CPE (and VRE) episodes and helping local infection control teams to implement guidelines

2006-2011

CPE episodes (n = 59) in the 38 hospitals of APHP 2004 – Oct 2011



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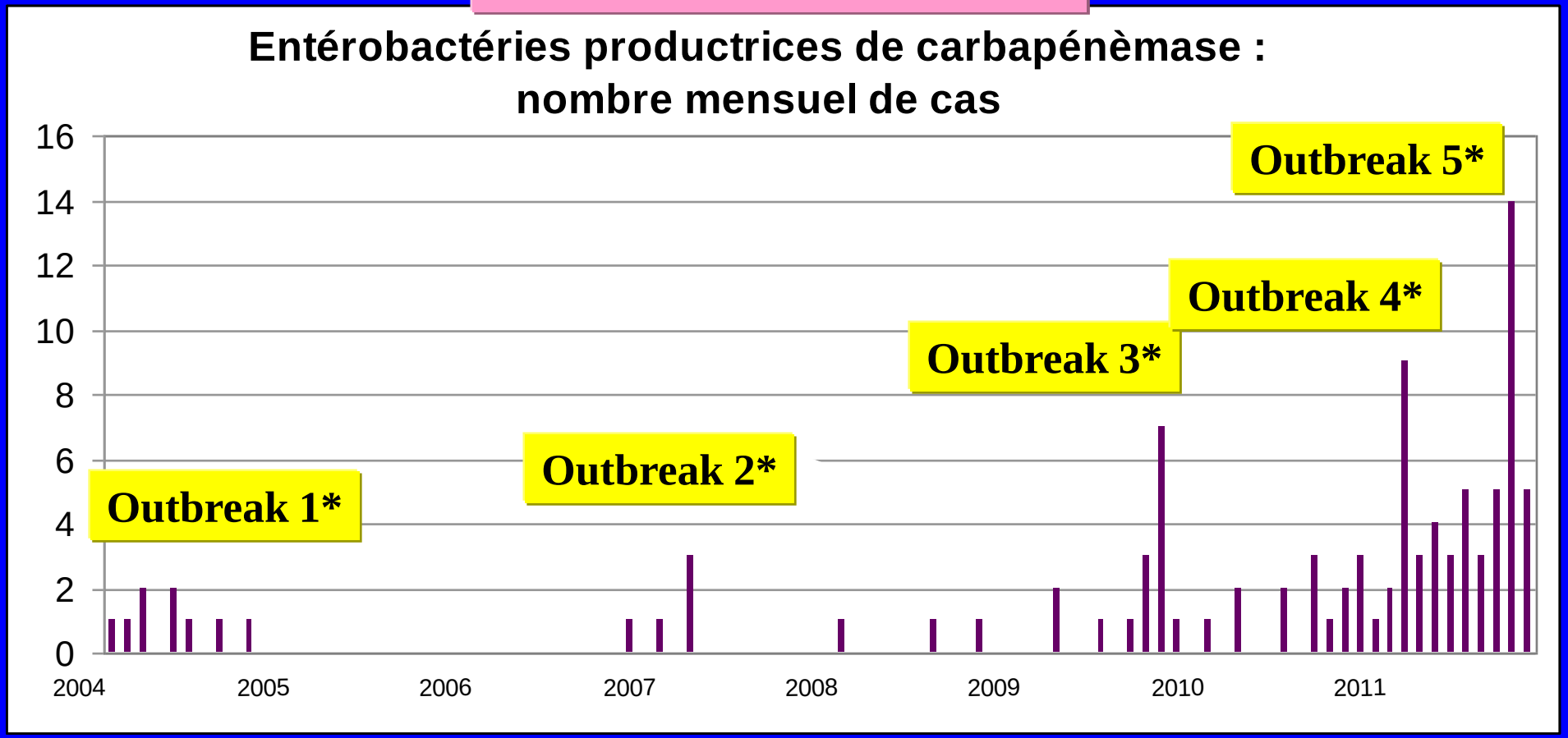
CPE cases (n = 100) in the 38 hospitals of APHP 2004 – Oct 2011

40 % of national cases



> 2 cases, definition based on epidemiological and microbiological data (fingerprint, enzyme)

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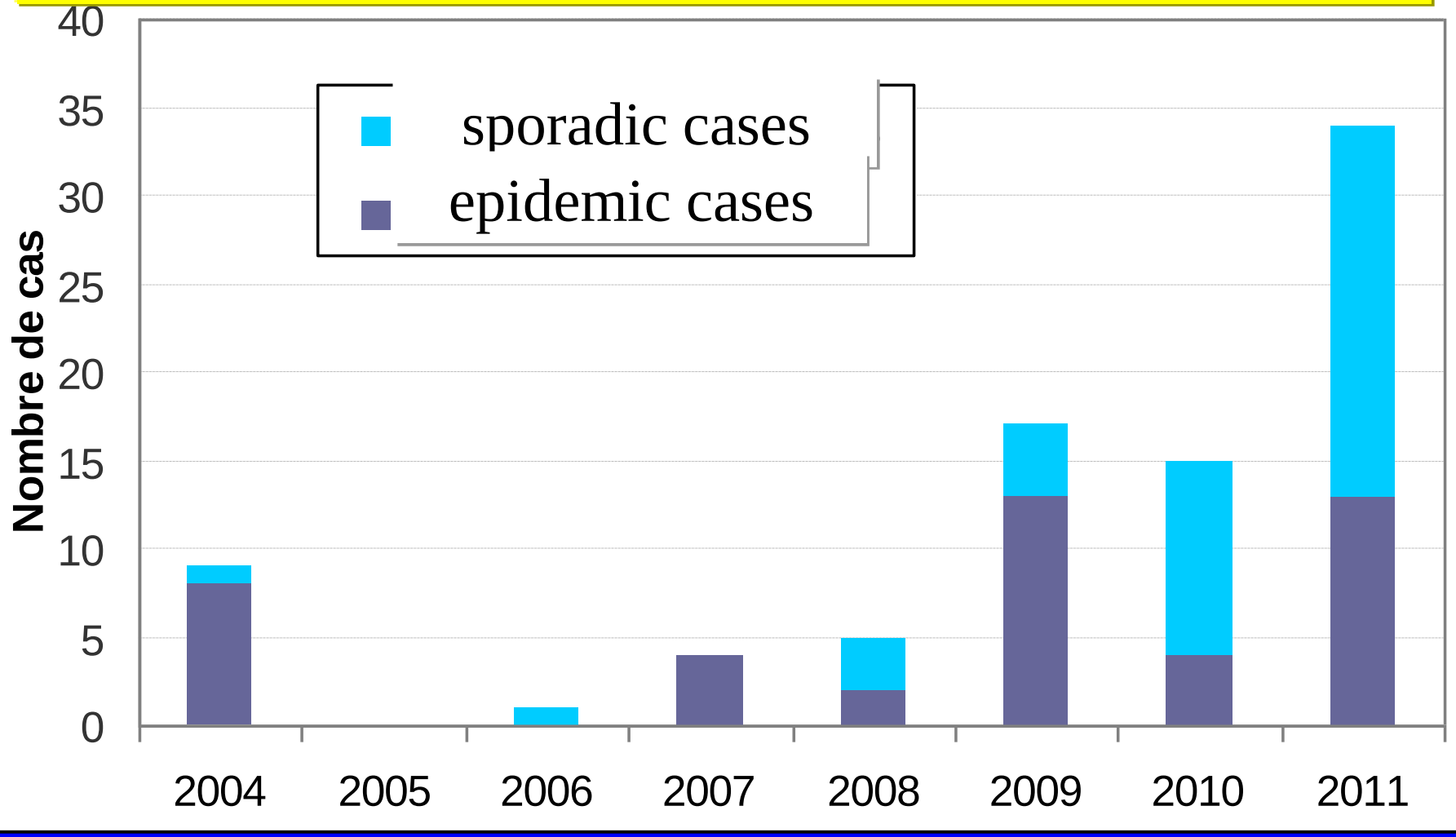
CPE cases (n = 100)
in the 38 hospitals of APHP 2004 – Oct 2011



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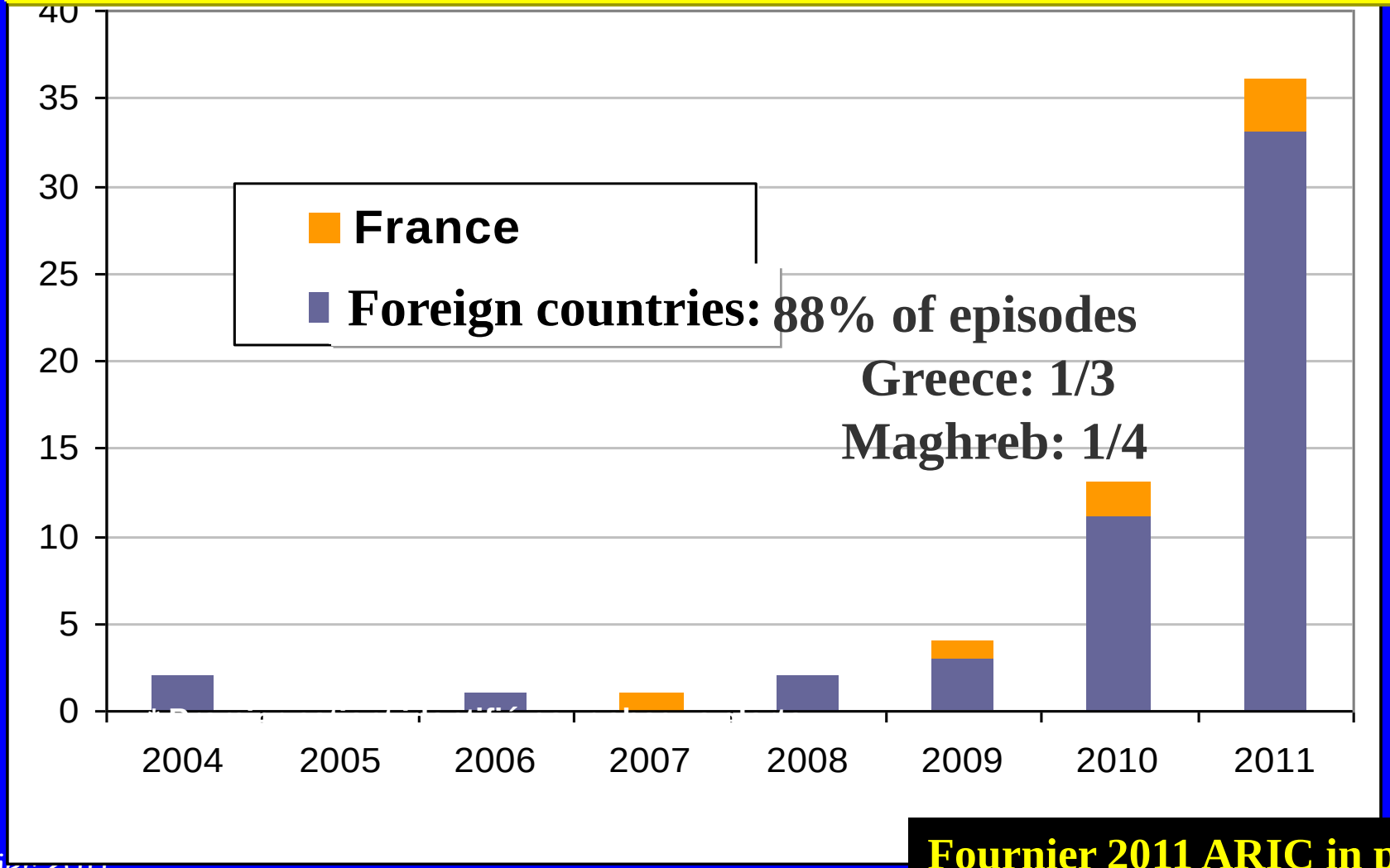
Origin of CPE episodes in the 38 hospitals of APHP 2004 – Oct 2011



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AP-HP recommendations to isolate and screen for emerging MDROs (VRE, CPE) patients transferred from hospitals of foreign countries : October 2008

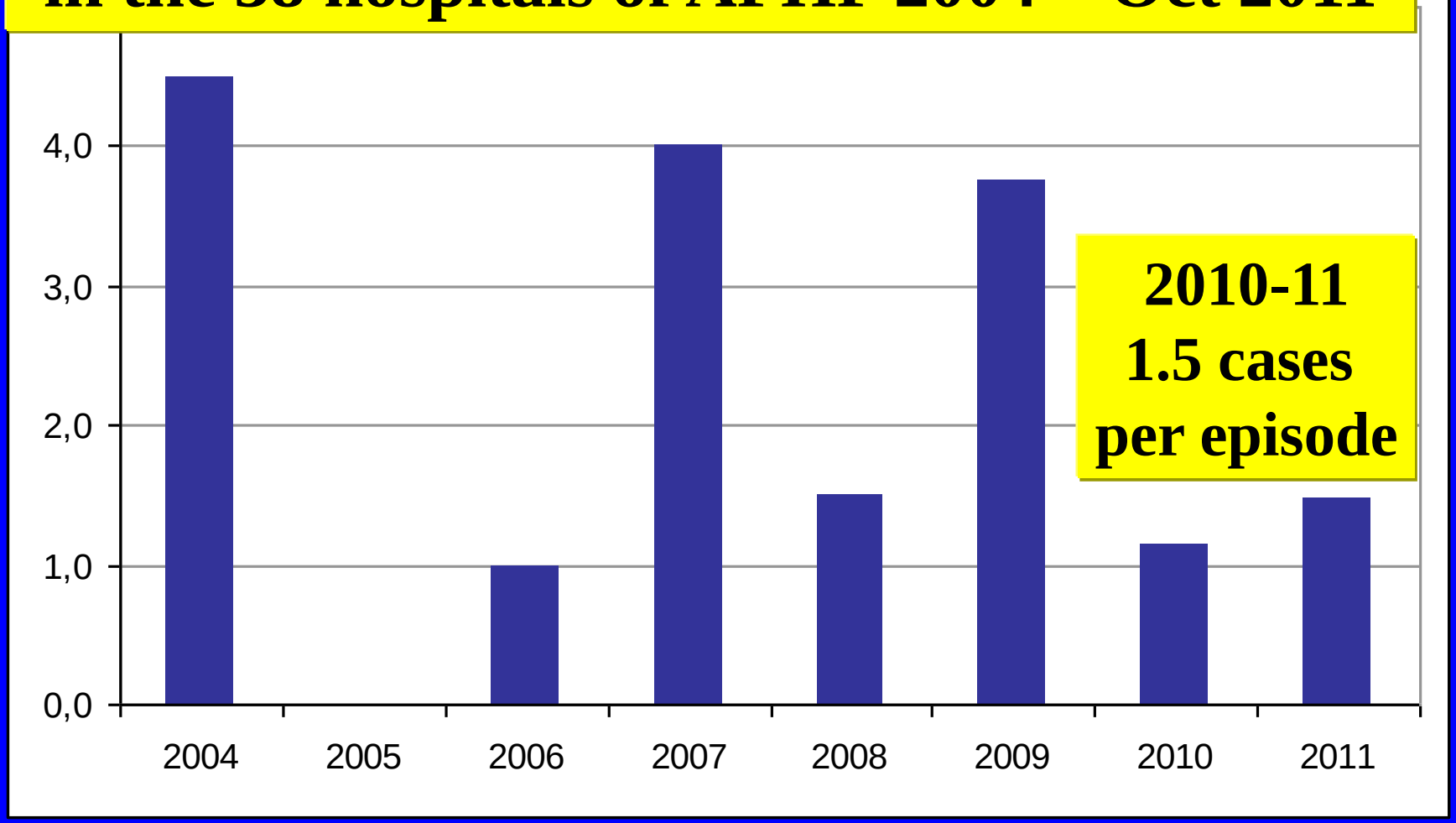
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS
CLIN CENTRAL

Patient en provenance d'un hôpital d'un pays à prévalence élevée de BMR émergentes

Recommandations du 20/10/2008

Generalized at national level November 2010

Mean number of cases per CPE episode in the 38 hospitals of APHP 2004 – Oct 2011



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EPC episodes in the 38 hospitals AP-HP 2004 till October 2011

- Total 100 cases
- 42 secondary cases :
  - mean 4.7 per outbreak (vs. 6.6 national)
  - mean 0.7 per episode (vs. 1.4 national)

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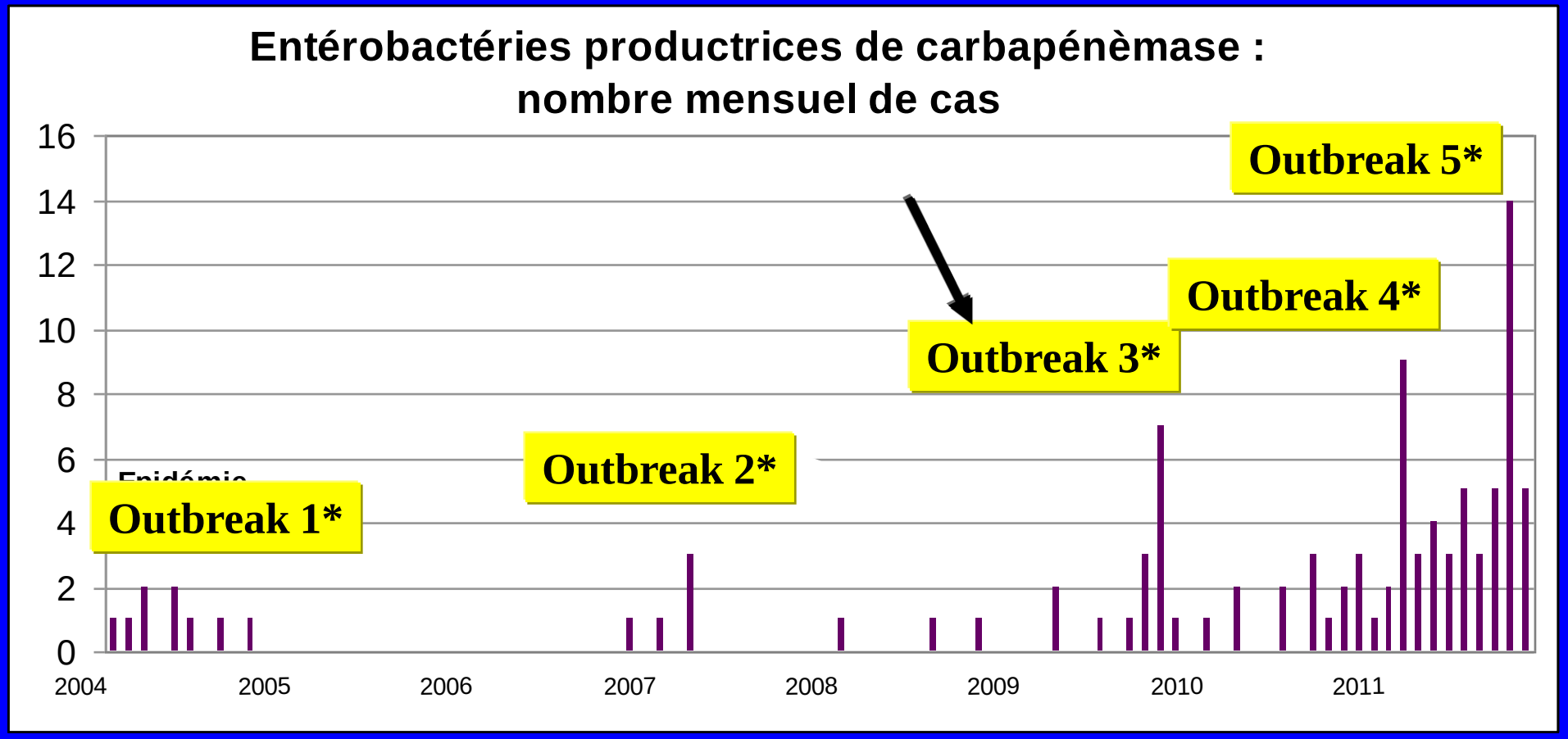
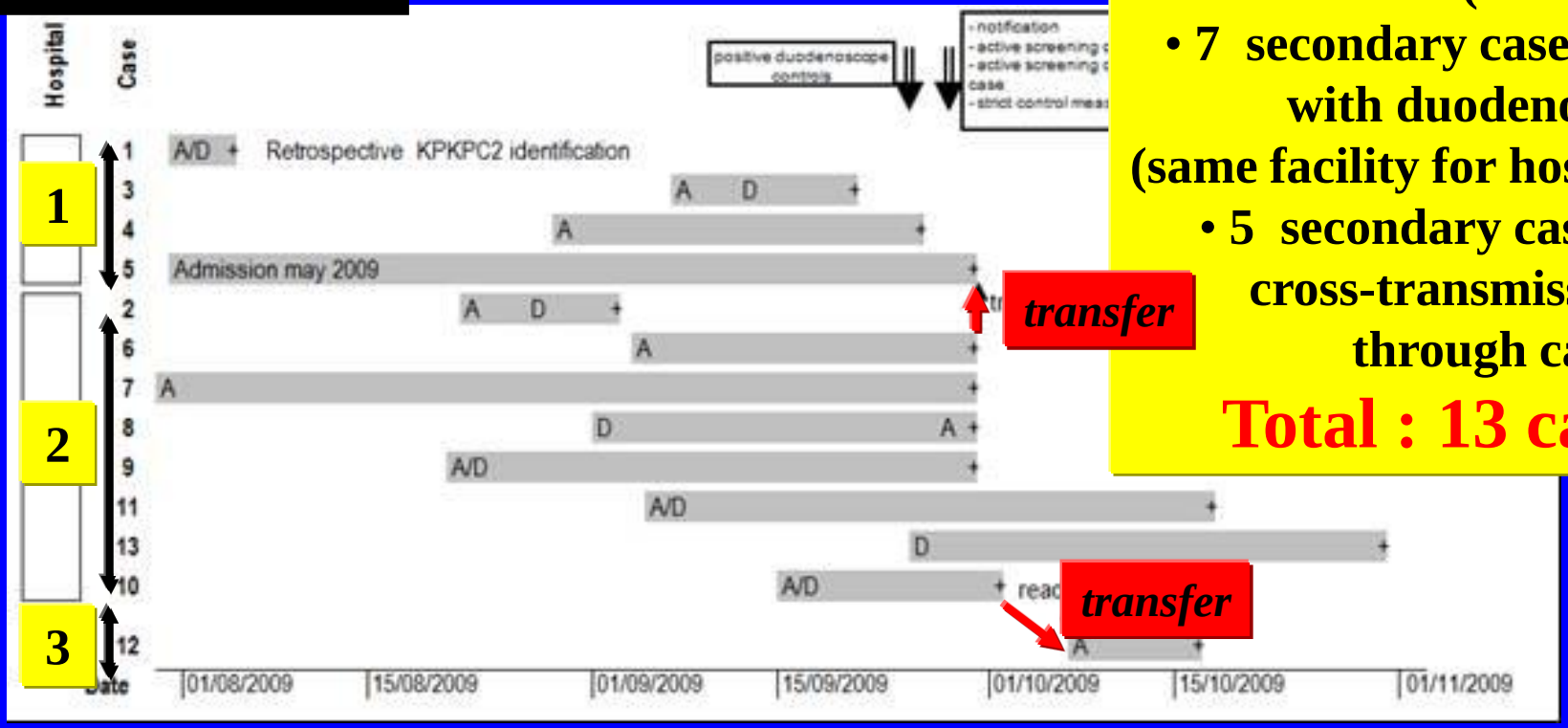
Number of CPE cases in the 38 hospitals of APHP 2004 – Oct 2011



> 2 cases, definition based on epidemiological and microbiological data (fingerprint, enzyme)

KP-KPC2 outbreak in 2 APHP hospitals September-December 2009

Carbonne Eurosurveillance 2010



- 1 source case (from Greece)
- 7 secondary cases linked with duodenoscopy (same facility for hosp. 1 & 2)
- 5 secondary cases by cross-transmission through cares

Total : 13 cases

A : date of admission ; D : date of duodenoscopy ; + : date of 1st positive specimen

<u>Gaps</u> in implementation of control programme :

- **<u>delayed CPE identification</u> in hospitals 1 and 2**
- **2 contact patients <u>transferred</u> to other hospitals <u>before</u> 3 neg. screening**

ESBL and Carbapenemases : break « the infernal circle »

EARS-net : *E.coli* resistant to 3rd gen. cephalosporins (%) in bacteremias

2%

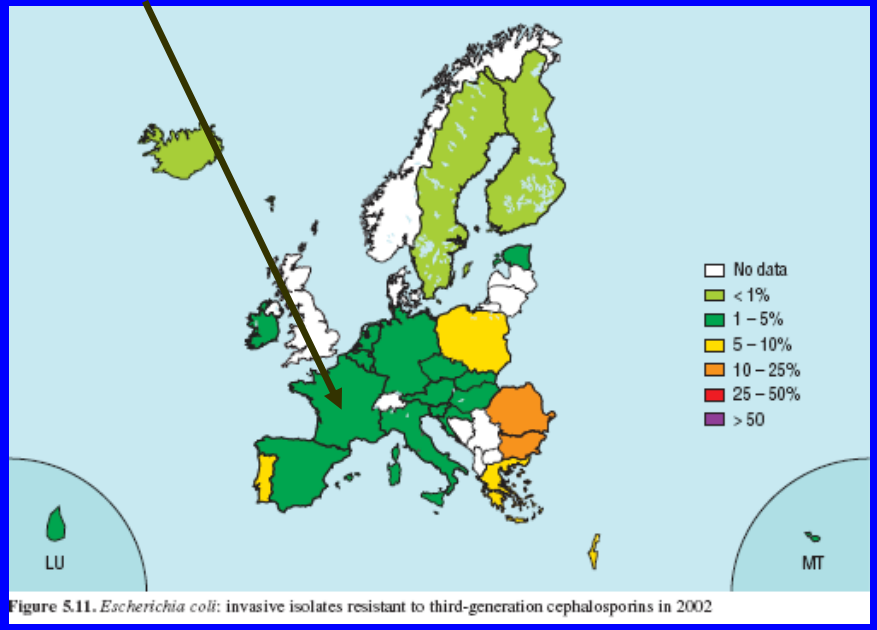
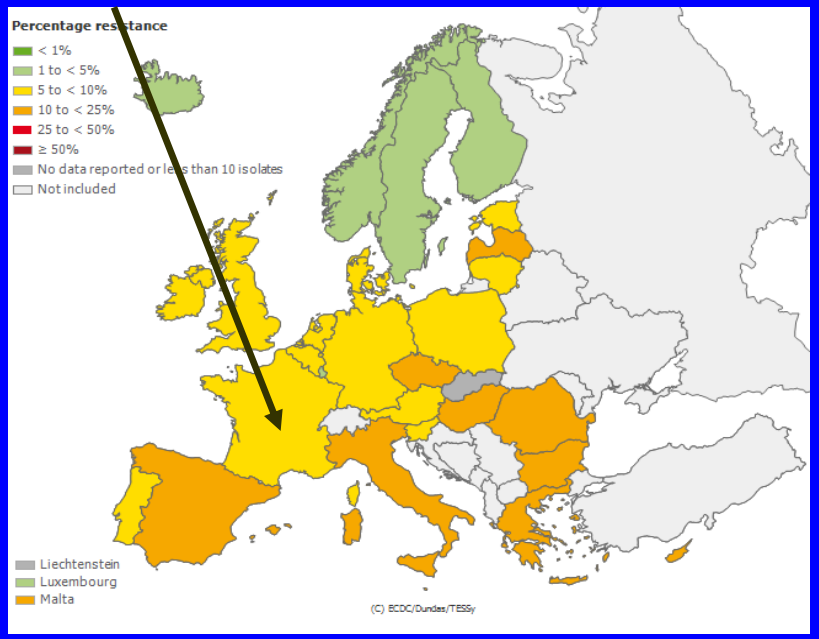


Figure 5.11. *Escherichia coli*: invasive isolates resistant to third-generation cephalosporins in 2002

2002

7% (5% ESBL)



2010

Extrapolation : ~2,000 ESBLcases /year in France in 2010

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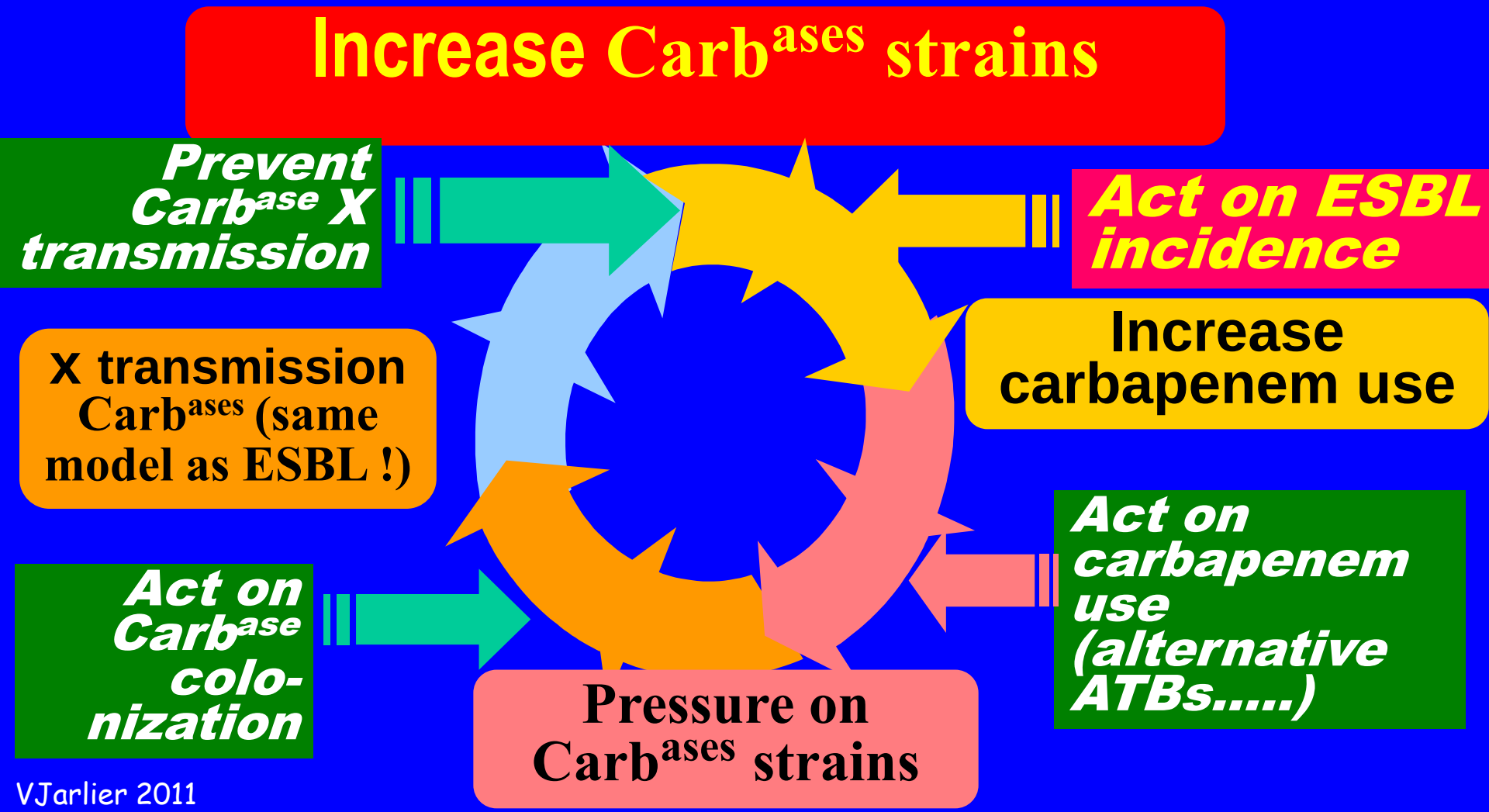
ESBLs and carbapemenases : let's break the infernal circle



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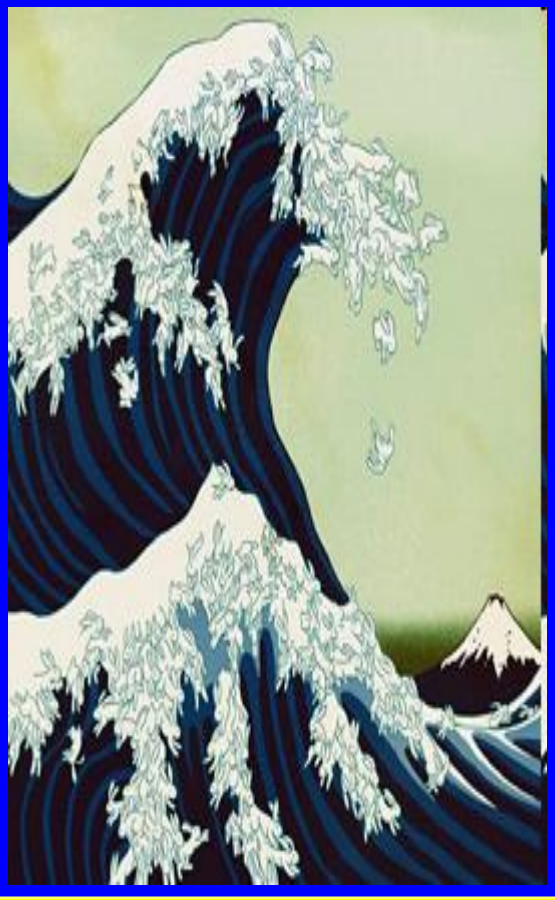
The 3 waves of plasmid-born B-lactamase mediated resistance in enterobacteria (Hokusai's vision of resistance)



Same ways of cross-transmission :
strains and/or mobile elements (plasmids…)
between humans, animals, environment
(water wastes → agriculture → food…)
"new fecal threat"

Control : centrifuge successive barriers like for firefighting and flood control

Penicillinases (TEM-1…)
Amox-R

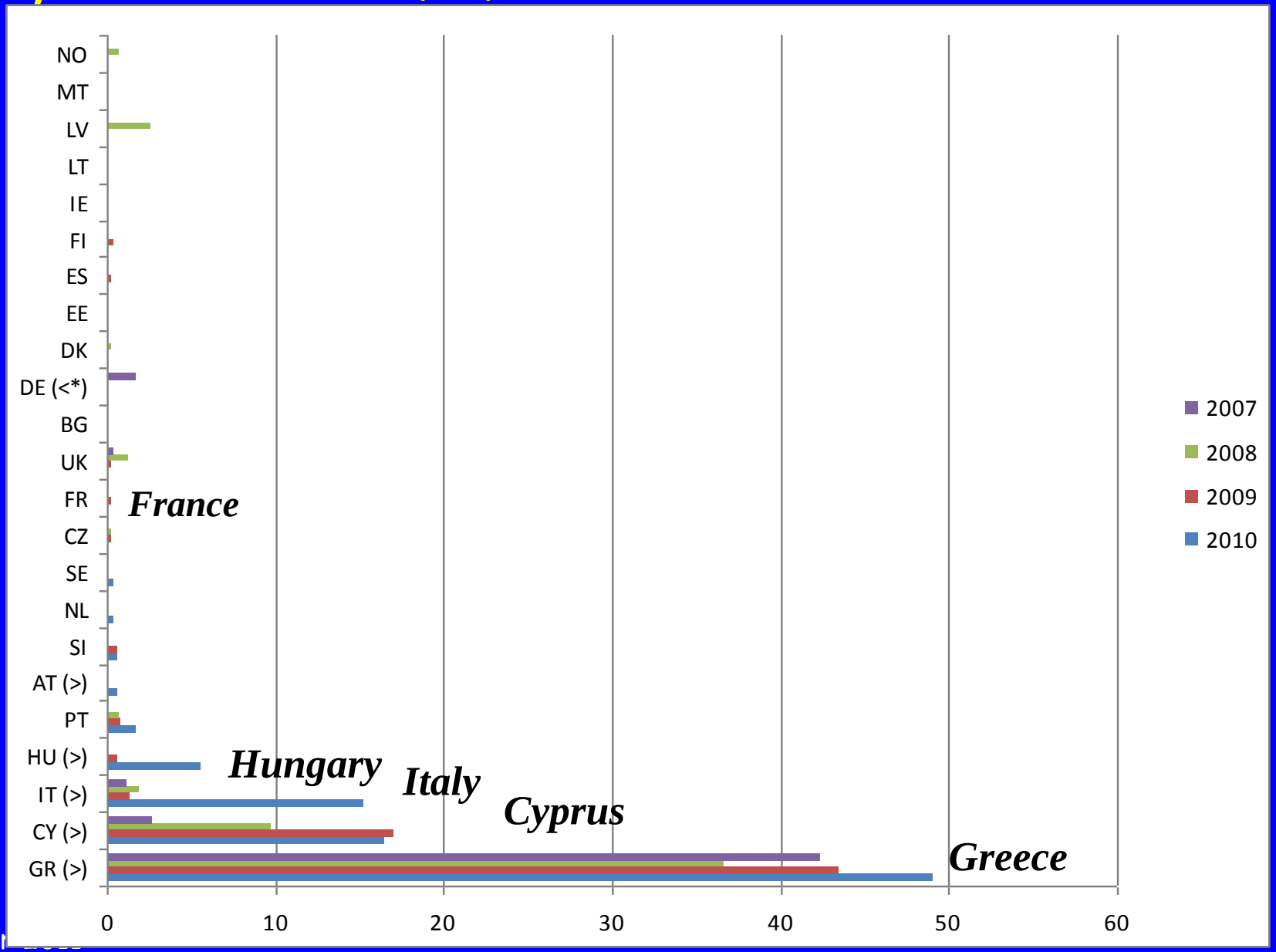
ESBLs
Amox-C3G-R

Carbapemenases
Amox-C3G-Carb-R

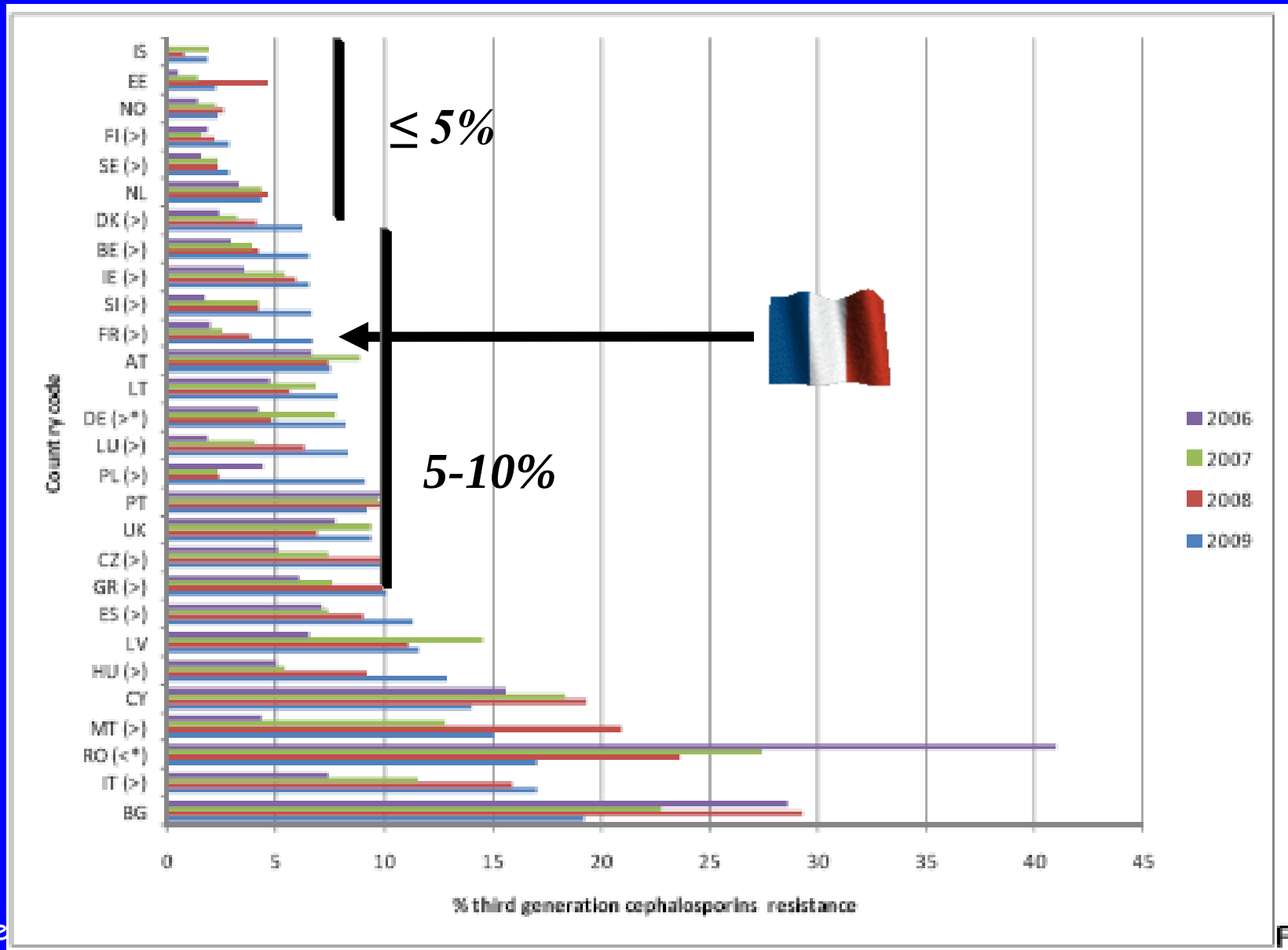
→ C3G use

→ Carb use

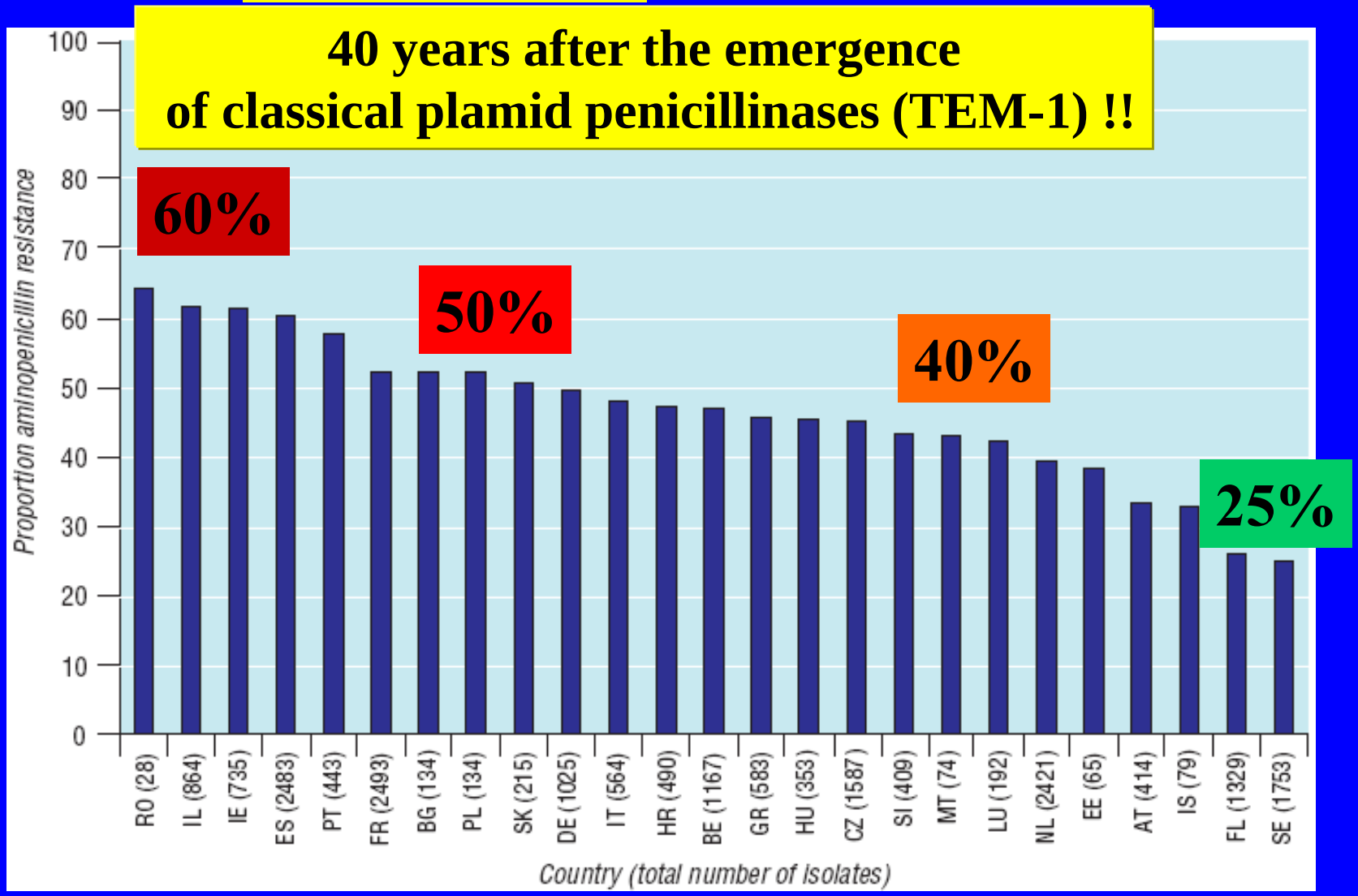
Bacteremias due to CPE *Klebsiella pneumoniae* (%) EARS-net 2007-2010

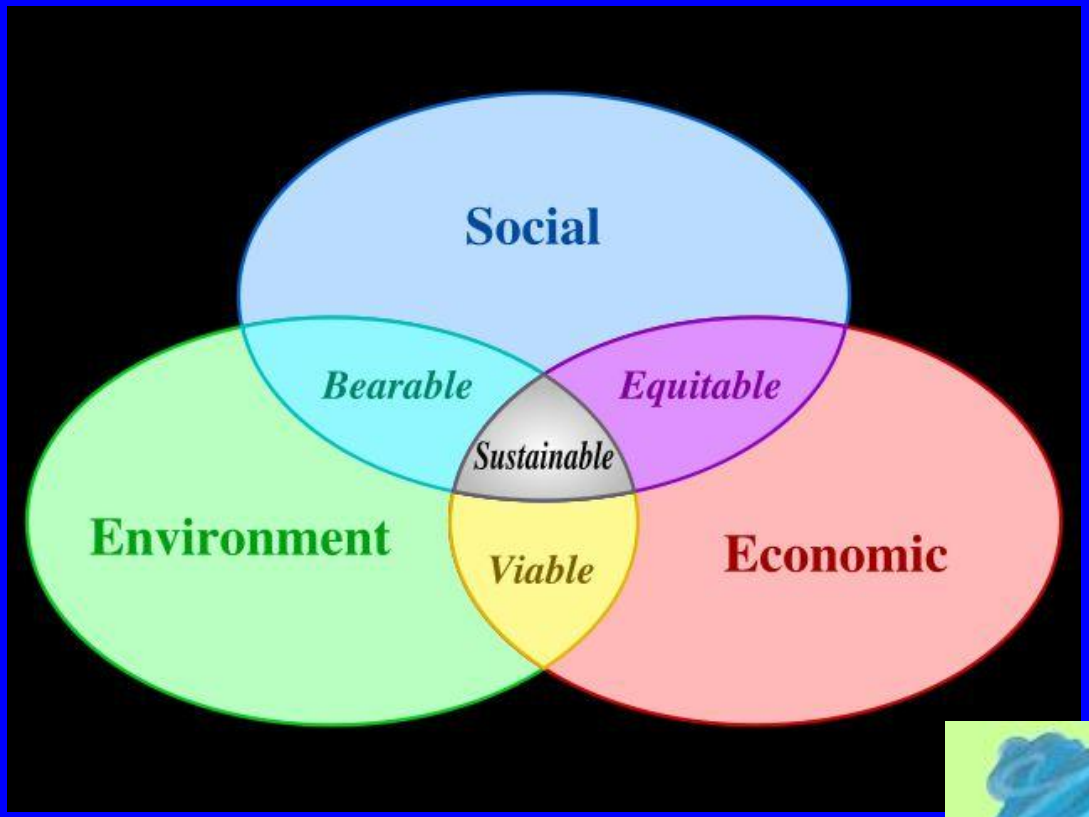


% R 3rd gener. Cephalosporins in *E.coli* Bacteremias in Europe, EARSS 2006-09



E.coli resistant to ampicillin (%) in bacteremias, EARSS 2002





Sustainable development

- Water & forests
- Nuclear energy
- Global warming
- Antibiotic susceptibility