Antibiotic Resistance in Greece Surveillance and Response

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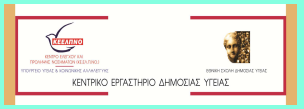
&
Central Public Health Laboratory
KEELPNO

23 Nov 2011



A. Surveillance

Surveillance of Antibiotic Resistance in Greece

1. The Greek System for the Surveillance of Antimicrobial Resistance (WHONET).
   - Resistance rates

2. The Early Warning System.
   - To trace the spread of resistance.

The Greek System for the Surveillance of Antimicrobial Resistance

- In Operation Since 1996
- Involves about 40 Hospitals all over Greece
  - Voluntary Basis
- Coordination Dept of Microbiology, National School of Public Health in Collaboration with KEELPNO (Greek ECDC)
- Based on the collection and analysis of Routine data
  - Uses the WHONET software.
- Collaborates with EARSS

The Greek System for the Surveillance of Antimicrobial Resistance

- Calculates resistance rates (proportions
- Collects ALL Routine Data
  - Analysis improves quality of Data

The Greek System for the Surveillance of Antimicrobial Resistance

- Mainly Automatic Download
- **All** lab records
- No added workload to the lab

- PASKO
- VITEK
- SENSITITRE
- MICROSCAN
- WIDER
- SCANNERS
  - OSIRIS
  - SIRSCAN

23 Nov 2011

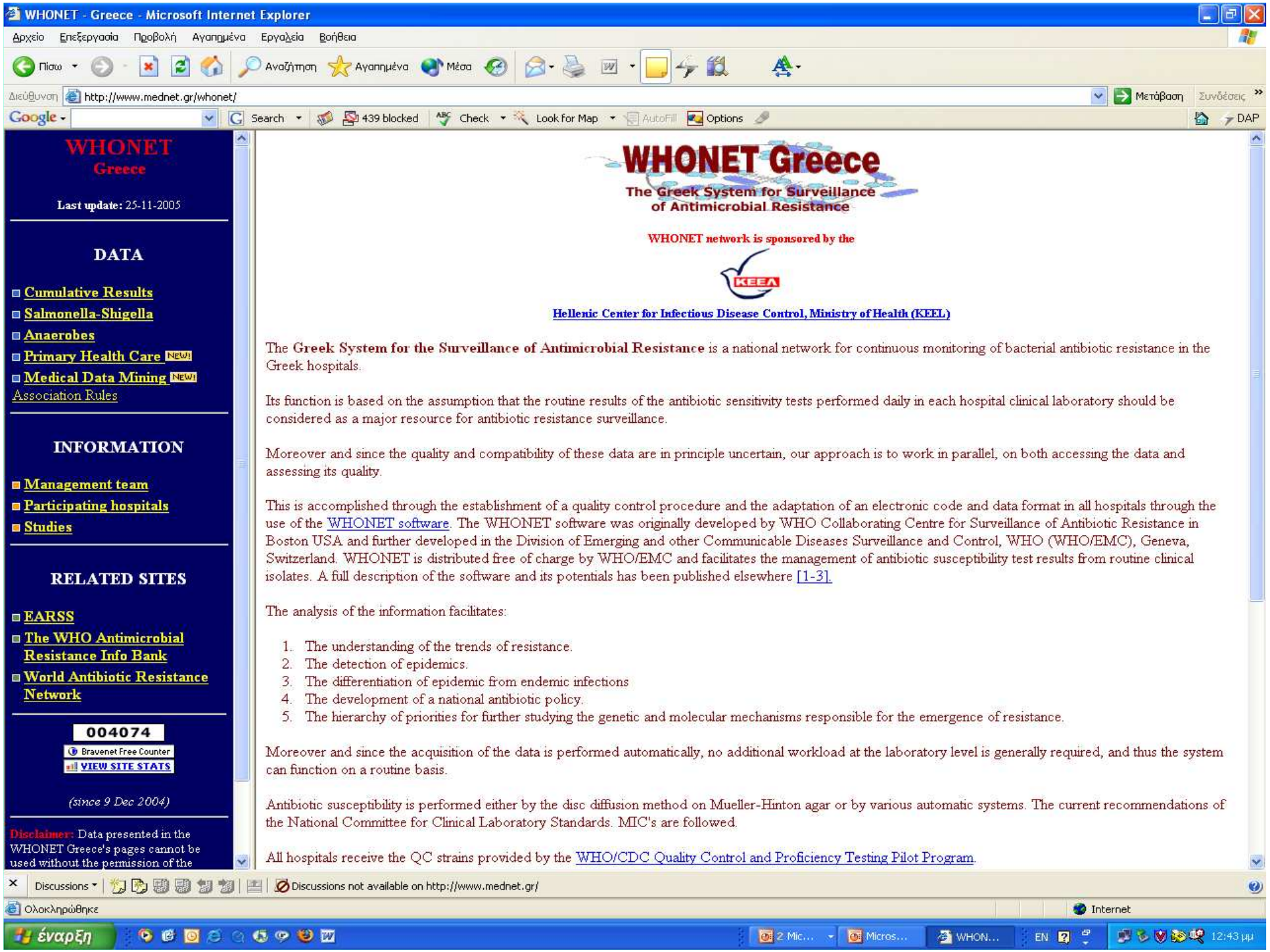
ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

The Greek System for the Surveillance of Antimicrobial Resistance

Deliverables (every 6 months)

1. Publishes statistics (In the internet)

2. Produces a feedback for each hospital


WHONET - Greece - Microsoft Internet Explorer
Αρχείο Επεξεργασία Προβολή Αγαπημένα Εργαλεία Βοήθεια
Πίσω Αναζήτηση Αγαπημένα Μέσα
Διεύθυνση http://www.mednet.gr/whonet/
Μετάβαση Συνδέσεις
Google Search 439 blocked Check Look for Map AutoFill Options DAP
WHONET
Greece
Last update: 25-11-2005
DATA
Cumulative Results
Salmonella-Shigella
Anaerobes
Primary Health Care NEW!
Medical Data Mining NEW!
Association Rules
INFORMATION
Management team
Participating hospitals
Studies
RELATED SITES
EARSS
The WHO Antimicrobial Resistance Info Bank
World Antibiotic Resistance Network
004074
Bravenet Free Counter
VIEW SITE STATS
(since 9 Dec 2004)
Disclaimer: Data presented in the WHONET Greece's pages cannot be used without the permission of the
WHONET Greece
The Greek System for Surveillance of Antimicrobial Resistance
WHONET network is sponsored by the
KEEL
Hellenic Center for Infectious Disease Control, Ministry of Health (KEEL)
The Greek System for the Surveillance of Antimicrobial Resistance is a national network for continuous monitoring of bacterial antibiotic resistance in the Greek hospitals.
Its function is based on the assumption that the routine results of the antibiotic sensitivity tests performed daily in each hospital clinical laboratory should be considered as a major resource for antibiotic resistance surveillance.
Moreover and since the quality and compatibility of these data are in principle uncertain, our approach is to work in parallel, on both accessing the data and assessing its quality.
This is accomplished through the establishment of a quality control procedure and the adaptation of an electronic code and data format in all hospitals through the use of the WHONET software. The WHONET software was originally developed by WHO Collaborating Centre for Surveillance of Antibiotic Resistance in Boston USA and further developed in the Division of Emerging and other Communicable Diseases Surveillance and Control, WHO (WHO/EMC), Geneva, Switzerland. WHONET is distributed free of charge by WHO/EMC and facilitates the management of antibiotic susceptibility test results from routine clinical isolates. A full description of the software and its potentials has been published elsewhere [1-3].
The analysis of the information facilitates:
1. The understanding of the trends of resistance.
2. The detection of epidemics.
3. The differentiation of epidemic from endemic infections
4. The development of a national antibiotic policy.
5. The hierarchy of priorities for further studying the genetic and molecular mechanisms responsible for the emergence of resistance.
Moreover and since the acquisition of the data is performed automatically, no additional workload at the laboratory level is generally required, and thus the system can function on a routine basis.
Antibiotic susceptibility is performed either by the disc diffusion method on Mueller-Hinton agar or by various automatic systems. The current recommendations of the National Committee for Clinical Laboratory Standards. MIC's are followed.
All hospitals receive the QC strains provided by the WHO/CDC Quality Control and Proficiency Testing Pilot Program.
Discussions Discussions not available on http://www.mednet.gr/
Ολοκληρώθηκε
Internet
έναρξη
2 Mic... Micros... WHON... EN 12:43 μμ


WHONET - Greece - Windows Internet Explorer
http://www.mednet.gr/whonet/
www.mednet.gr/whonet
WHONET - Greece
Last update: 17-6-2011
DATA
Cumulative Results
Salmonella-Shigella
Anaerobes
Mycobacterium tuberculosis
Primary Health Care
Medical Data Mining Association Rules
EDUCATIONAL RESOURCES (in Greek)
PowerPoint Presentations
INFORMATION
Management team
Participating hospitals
Studies
WHONET SOFTWARE
WhoNet Software 5.4
ΚΕΕΛΠΝΟ
ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ
CUMULATIVE RESULTS
July - December 2010
January - June 2010
July - December 2009
January-June 2009
July-December 2008
January-June 2008
July-December 2007
January-June 2007
July-December 2006
January-June 2006
July-December 2005
January-June 2005
July-December 2004
January-June 2004


WHONET - Greece - Windows Internet Explorer
http://www.mednet.gr/whonet/
Αρχείο Επεξεργασία Προβολή Αγαπημένα Εργαλεία Βοήθεια
Αγαπημένα
WHONET - Greece
Σελίδα Ασφάλεια Εργαλεία
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DATA
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(in Greek)
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WhoNet Software 5.4
CUMULATIVE RESULTS
Cumulative results from isolates from all hospitals of the network are presented.
Only the first isolate per patient and species is being processed.
(* List of Abbreviations and Acronyms Used in the Tables)
July - December 2010
PERCENT (%) RESISTANCE
TO SELECTED ANTIBIOTICS BY HOSPITAL
Acinetobacter baumanii
Amikacin (all clinical specimens)
Ceftazidime (all clinical specimens)
Ciprofloxacin (all clinical specimens)
Ampicillin/Sulbactam (all clinical specimens)
Cefepime (all clinical specimens)
Imipenem (all clinical specimens)
Piperacillin/Tazobactam (all clinical specimens)
Multiresistance (all clinical specimens)
Blood isolates (results from all hospitals)
Pseudomonas aeruginosa
Amikacin (all clinical specimens)
Ceftazidime (all clinical specimens)
Ciprofloxacin (all clinical specimens)
Imipenem (all clinical specimens)
Piperacillin/Tazobactam (all clinical specimens)
Multiresistance (all clinical specimens)
Ολοκληρώθηκε
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WHONET - Greece - ...
EN
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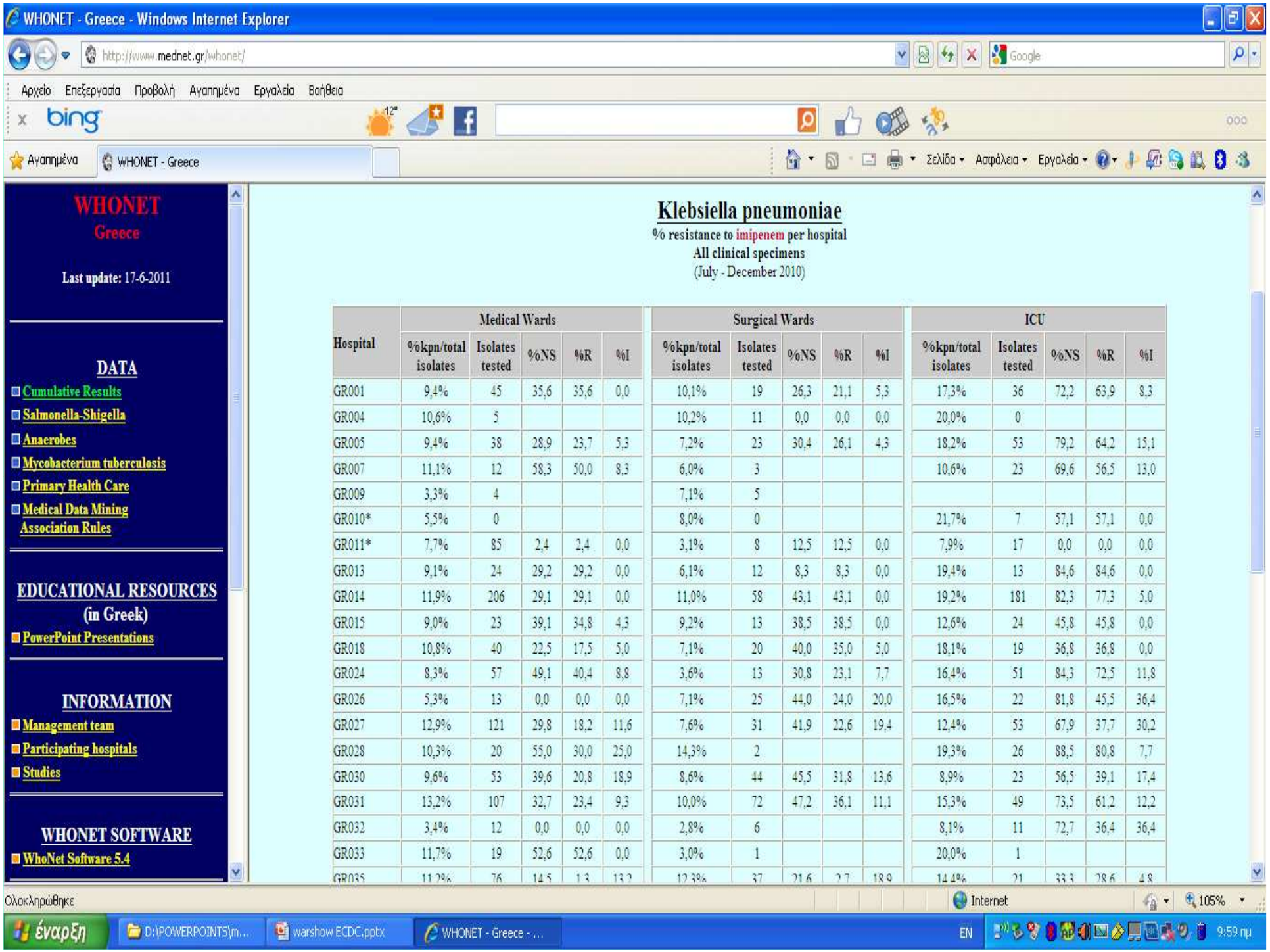
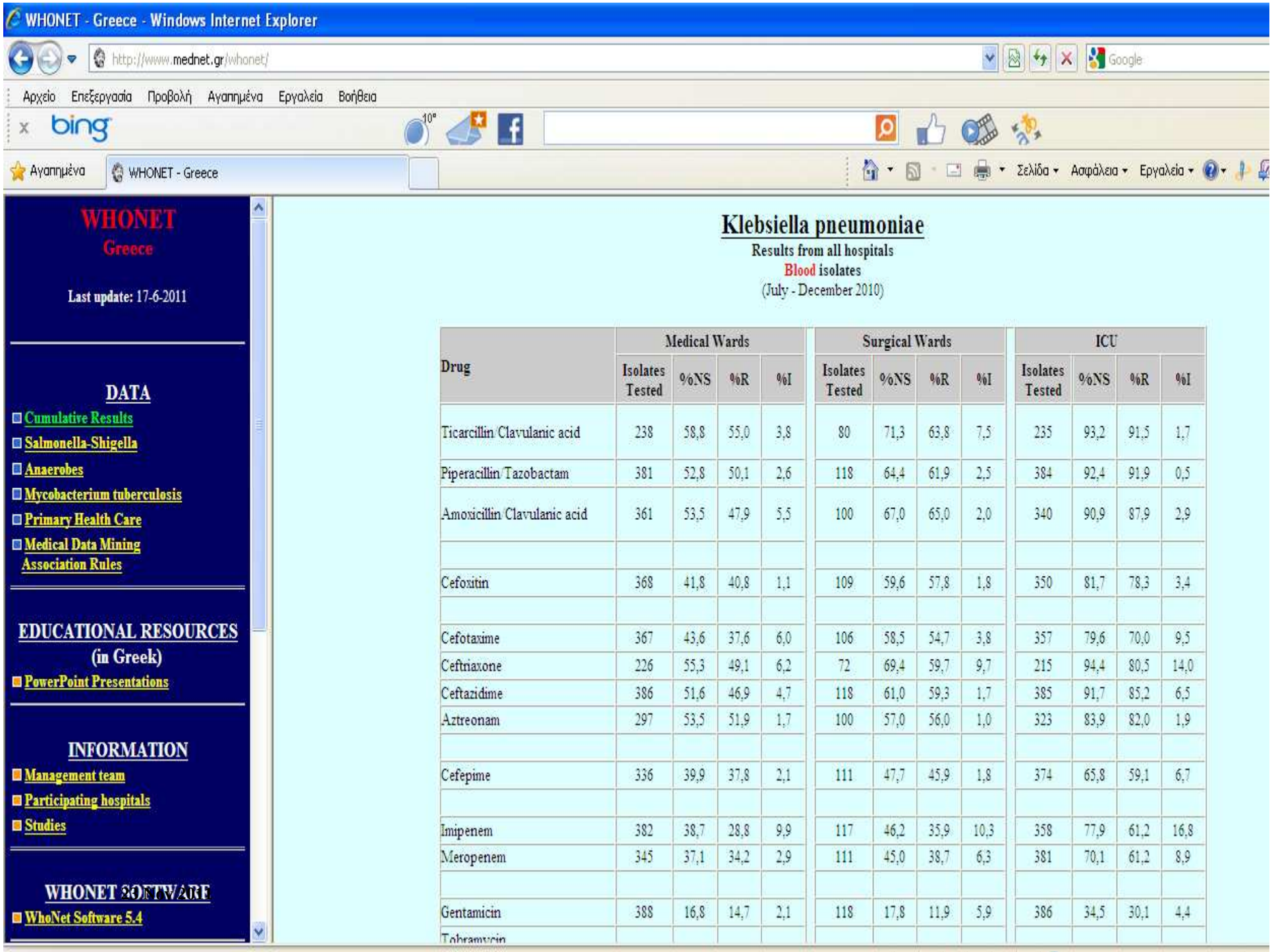


Klebsiella pneumoniae

% resistance to imipenem per hospital
All clinical specimens
(July - December 2010)

Hospital	Medical Wards					Surgical Wards					ICU				
	%kpn/total isolates	Isolates tested	%NS	%R	%I	%kpn/total isolates	Isolates tested	%NS	%R	%I	%kpn/total isolates	Isolates tested	%NS	%R	%I
GR001	9,4%	45	35,6	35,6	0,0	10,1%	19	26,3	21,1	5,3	17,3%	36	72,2	63,9	8,3
GR004	10,6%	5				10,2%	11	0,0	0,0	0,0	20,0%	0			
GR005	9,4%	38	28,9	23,7	5,3	7,2%	23	30,4	26,1	4,3	18,2%	53	79,2	64,2	15,1
GR007	11,1%	12	58,3	50,0	8,3	6,0%	3				10,6%	23	69,6	56,5	13,0
GR009	3,3%	4				7,1%	5								
GR010*	5,5%	0				8,0%	0				21,7%	7	57,1	57,1	0,0
GR011*	7,7%	85	2,4	2,4	0,0	3,1%	8	12,5	12,5	0,0	7,9%	17	0,0	0,0	0,0
GR013	9,1%	24	29,2	29,2	0,0	6,1%	12	8,3	8,3	0,0	19,4%	13	84,6	84,6	0,0
GR014	11,9%	206	29,1	29,1	0,0	11,0%	58	43,1	43,1	0,0	19,2%	181	82,3	77,3	5,0
GR015	9,0%	23	39,1	34,8	4,3	9,2%	13	38,5	38,5	0,0	12,6%	24	45,8	45,8	0,0
GR018	10,8%	40	22,5	17,5	5,0	7,1%	20	40,0	35,0	5,0	18,1%	19	36,8	36,8	0,0
GR024	8,3%	57	49,1	40,4	8,8	3,6%	13	30,8	23,1	7,7	16,4%	51	84,3	72,5	11,8
GR026	5,3%	13	0,0	0,0	0,0	7,1%	25	44,0	24,0	20,0	16,5%	22	81,8	45,5	36,4
GR027	12,9%	121	29,8	18,2	11,6	7,6%	31	41,9	22,6	19,4	12,4%	53	67,9	37,7	30,2
GR028	10,3%	20	55,0	30,0	25,0	14,3%	2				19,3%	26	88,5	80,8	7,7
GR030	9,6%	53	39,6	20,8	18,9	8,6%	44	45,5	31,8	13,6	8,9%	23	56,5	39,1	17,4
GR031	13,2%	107	32,7	23,4	9,3	10,0%	72	47,2	36,1	11,1	15,3%	49	73,5	61,2	12,2
GR032	3,4%	12	0,0	0,0	0,0	2,8%	6				8,1%	11	72,7	36,4	36,4
GR033	11,7%	19	52,6	52,6	0,0	3,0%	1				20,0%	1			
GR035	11,2%	76	14,5	1,3	13,2	12,3%	37	21,6	2,7	18,9	14,4%	21	33,3	28,6	4,8



Klebsiella pneumoniae

Results from all hospitals

Blood isolates

(July - December 2010)

Drug	Medical Wards				Surgical Wards				ICU			
	Isolates Tested	%NS	%R	%I	Isolates Tested	%NS	%R	%I	Isolates Tested	%NS	%R	%I
Ticarcillin/Clavulanic acid	238	58,8	55,0	3,8	80	71,3	63,8	7,5	235	93,2	91,5	1,7
Piperacillin/Tazobactam	381	52,8	50,1	2,6	118	64,4	61,9	2,5	384	92,4	91,9	0,5
Amoxicillin/Clavulanic acid	361	53,5	47,9	5,5	100	67,0	65,0	2,0	340	90,9	87,9	2,9
Cefoxitin	368	41,8	40,8	1,1	109	59,6	57,8	1,8	350	81,7	78,3	3,4
Cefotaxime	367	43,6	37,6	6,0	106	58,5	54,7	3,8	357	79,6	70,0	9,5
Ceftriaxone	226	55,3	49,1	6,2	72	69,4	59,7	9,7	215	94,4	80,5	14,0
Ceftazidime	386	51,6	46,9	4,7	118	61,0	59,3	1,7	385	91,7	85,2	6,5
Aztreonam	297	53,5	51,9	1,7	100	57,0	56,0	1,0	323	83,9	82,0	1,9
Cefepime	336	39,9	37,8	2,1	111	47,7	45,9	1,8	374	65,8	59,1	6,7
Imipenem	382	38,7	28,8	9,9	117	46,2	35,9	10,3	358	77,9	61,2	16,8
Meropenem	345	37,1	34,2	2,9	111	45,0	38,7	6,3	381	70,1	61,2	8,9
Gentamicin	388	16,8	14,7	2,1	118	17,8	11,9	5,9	386	34,5	30,1	4,4
Tobramycin												

High proportion of hospitals and isolates are represented

Table 2.1: Numbers of laboratories reporting continuously and average numbers of *K. pneumoniae* and *P. aeruginosa* isolates reported per country per year to EARSS/EARS-Net during 2005–2010

Country	*K. pneumoniae*		*P. aeruginosa*	
	Number of laboratories*	Average number of isolates per year	Number of laboratories*	Average number of isolates per year
Austria	7	336	8	396
Bulgaria	2	61	1	29
Cyprus	2	43	2	41
Czech Republic	1	654	30	485
Estonia	4	46	5	39
Finland	7	270	6	185
France	33	1 060	20	1 153
Greece	25	1 161	24	887
Hungary	15	351	16	530
Iceland	1	20	1	11
Ireland	8	189	9	154
Malta	1	35	1	44
Netherlands	5	392	4	288
Norway	7	292	9	125
Slovenia	7	75	8	82
Spain	10	569	9	456
Sweden	1	403	7	260
United Kingdom	4	396	9	355
Total	140		168	

* In some countries, data from several laboratories may be reported to EARS-Net from one central laboratory.

The Early Warning System

- Each hospital lab must report immediately certain “new” or “important resistant phenotypes.
  - To the Hospital Infection Control Committee
  - To KEELPNO
- The isolate must also be available for further testing.
  - Confirmation of the mechanism
  - Typing

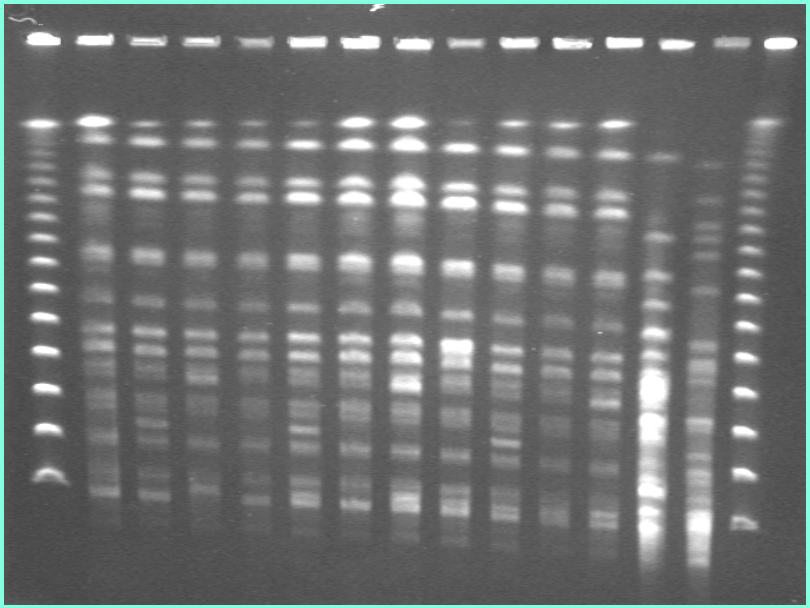
Early Warning System

- **2005**: 97 isolates from 22 Hospitals
- **2006**: 110 isolates from 19 Hospitals
- **2007**: 58 Isolates from 14 Hospitals.
- **2008**: 511 Isolates from 41 Hospitals
- **2009**: 602 Isolates from 45 Hospitals
- **2010**: 1250 Isolates from 58 Hospitals

- Carbapenem resistant gram negatives
- CA MRSA
- Multiresistant *Acinetobacter*

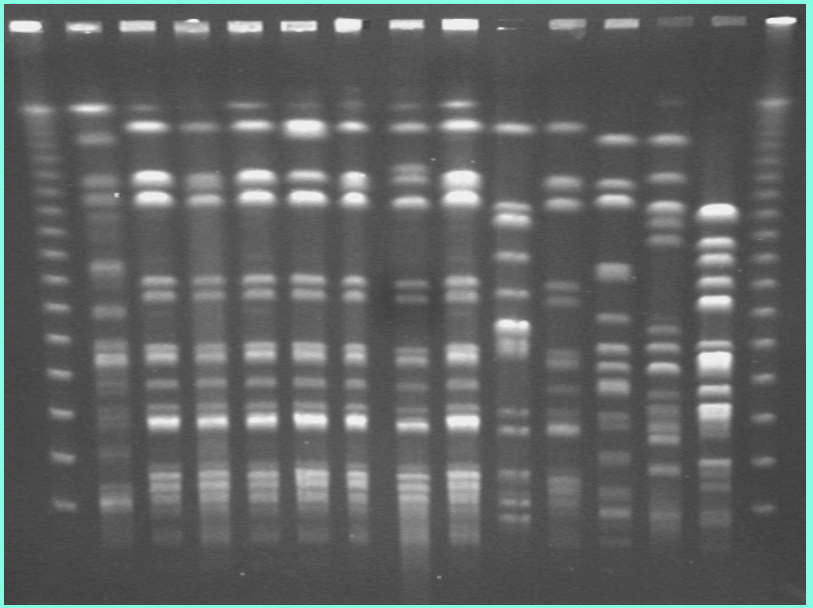
University Hospital

- Epidemic of VIM + ESBL producing *Klebsiella*
  - Proven clonal
  - Infection Control Measures established
  - Epidemic controlled



Hospital of Athens

- Epidemic of VIM + ESBL producing *Klebsiella*
  - ***Not*** *all strains clonal*
  - Infection Control Measures established
  - Epidemic controlled



Surveillance in Greece

The Good News

23 Nov 2011

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Euroroundups

UPDATE OF *CLOSTRIDIUM DIFFICILE* INFECTION DUE TO PCR RIBOTYPE 027 IN EUROPE, 2008

No C.dif 027 in Greece !

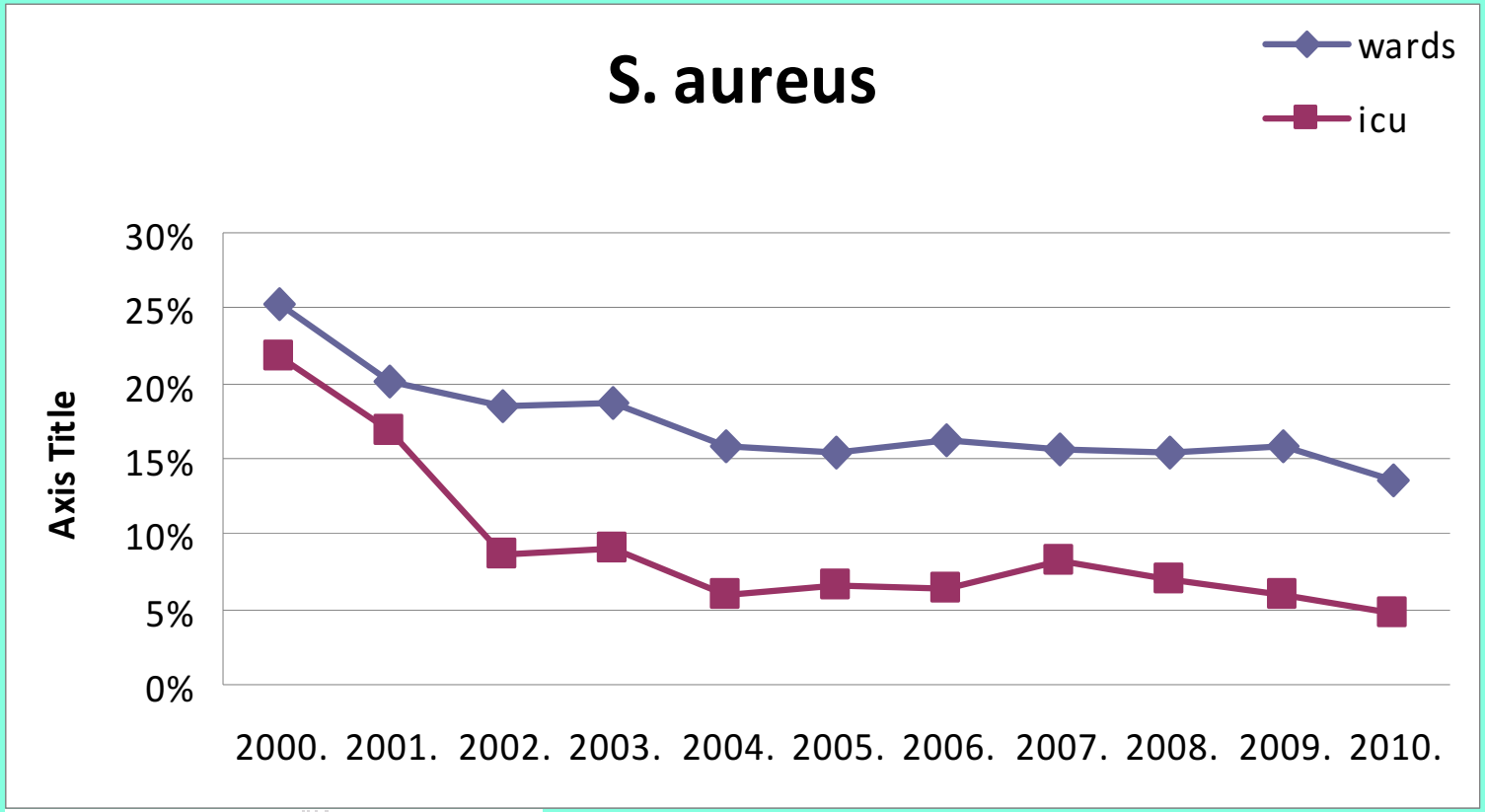
FIGURE

Distribution of *Clostridium difficile* Type 027 by country in Europe* as of June 2008

23 Nov 2011

Many rates are decreasing

Blood cultures
Trends 2000 -2010
21 Hospitals



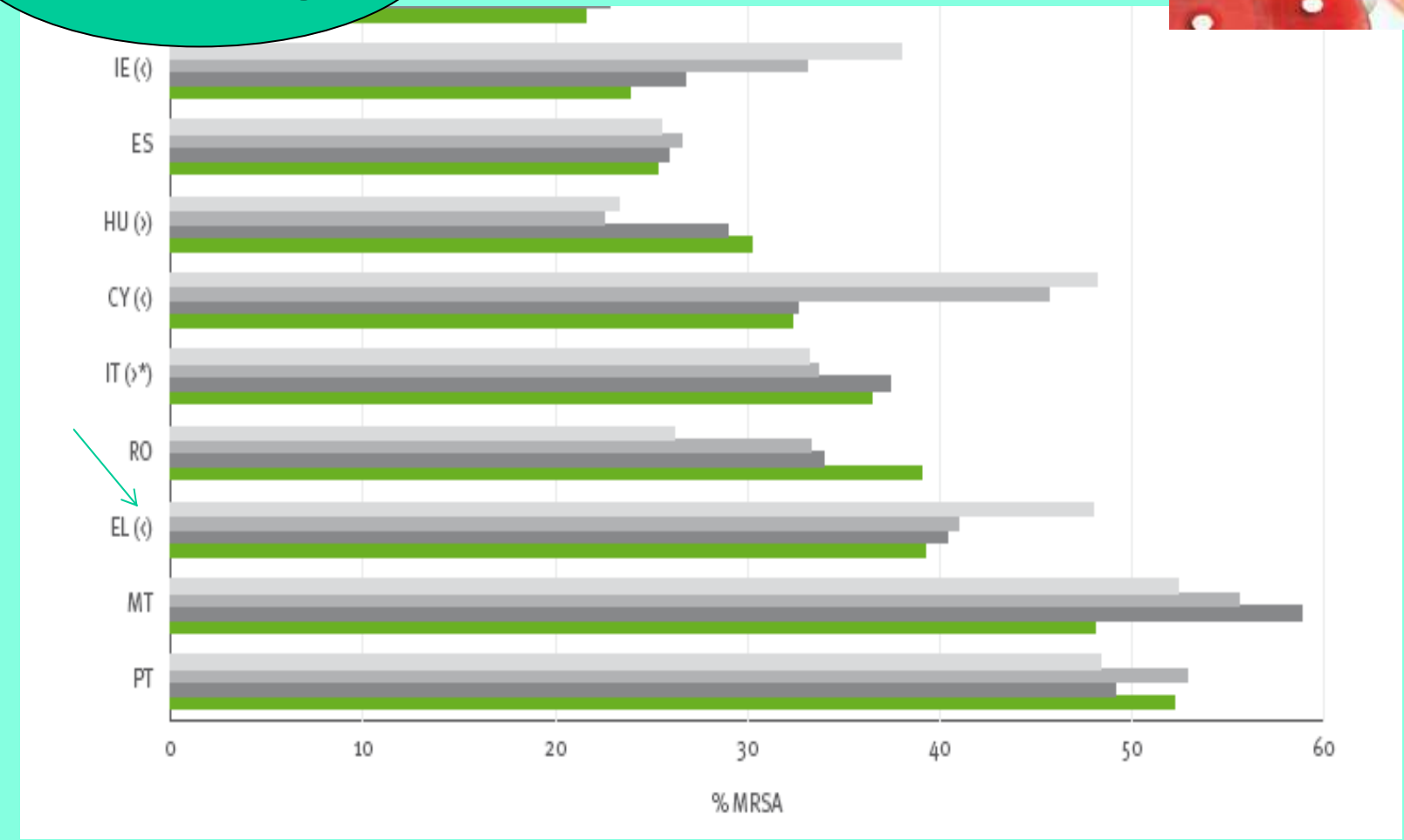
WHONET Greece
The Greek System for Surveillance of Antimicrobial Resistance

23 Nov 2011

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Many rates are decreasing

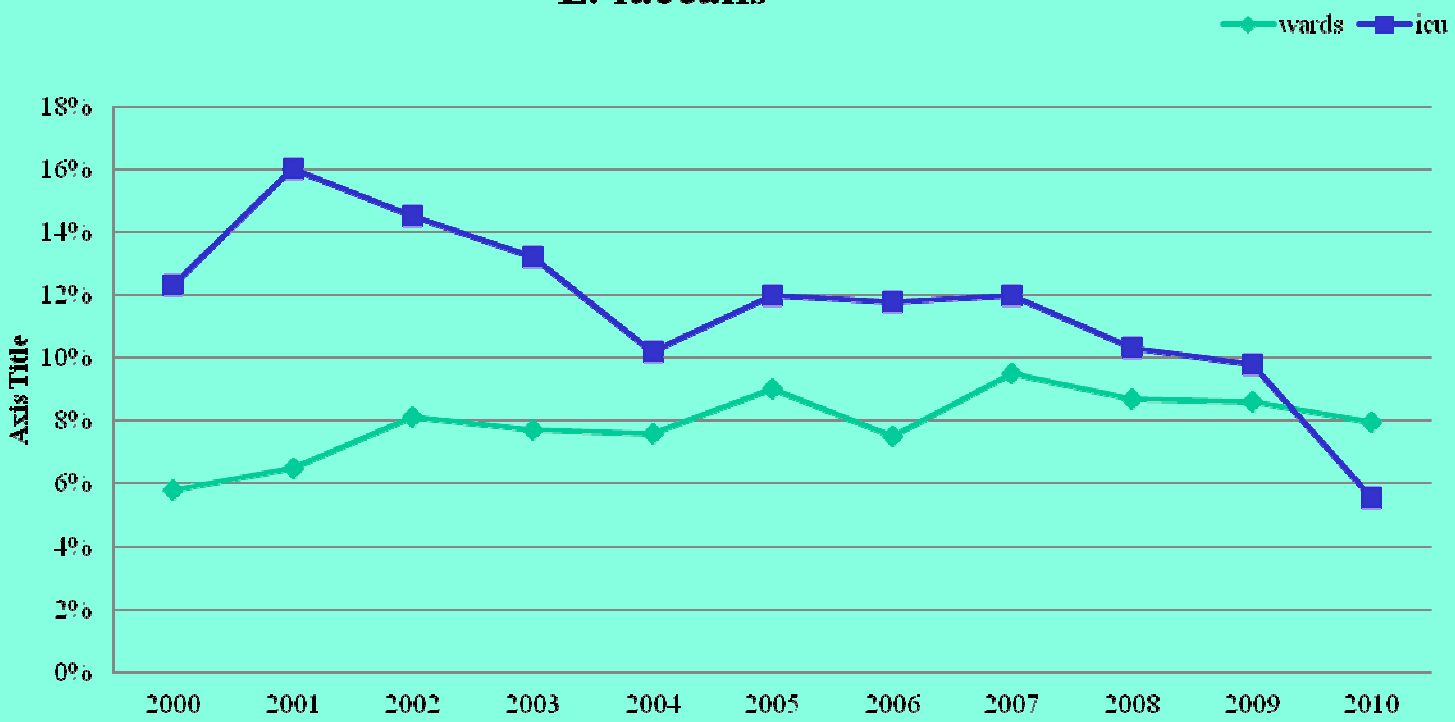
S aureus



Many rates are decreasing

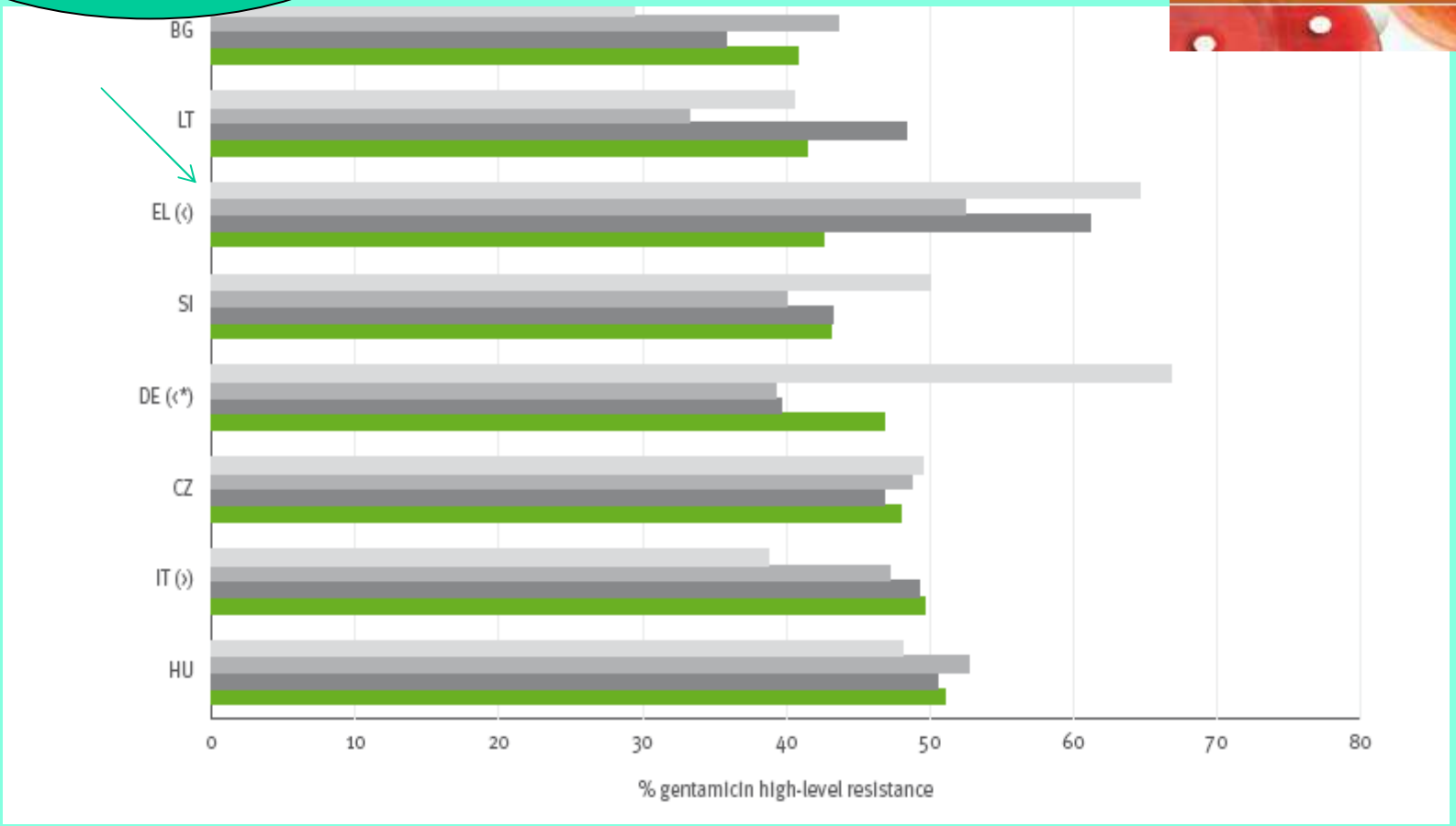
Blood cultures
Trends 2000 -2010
21 Hospitals

E. faecalis



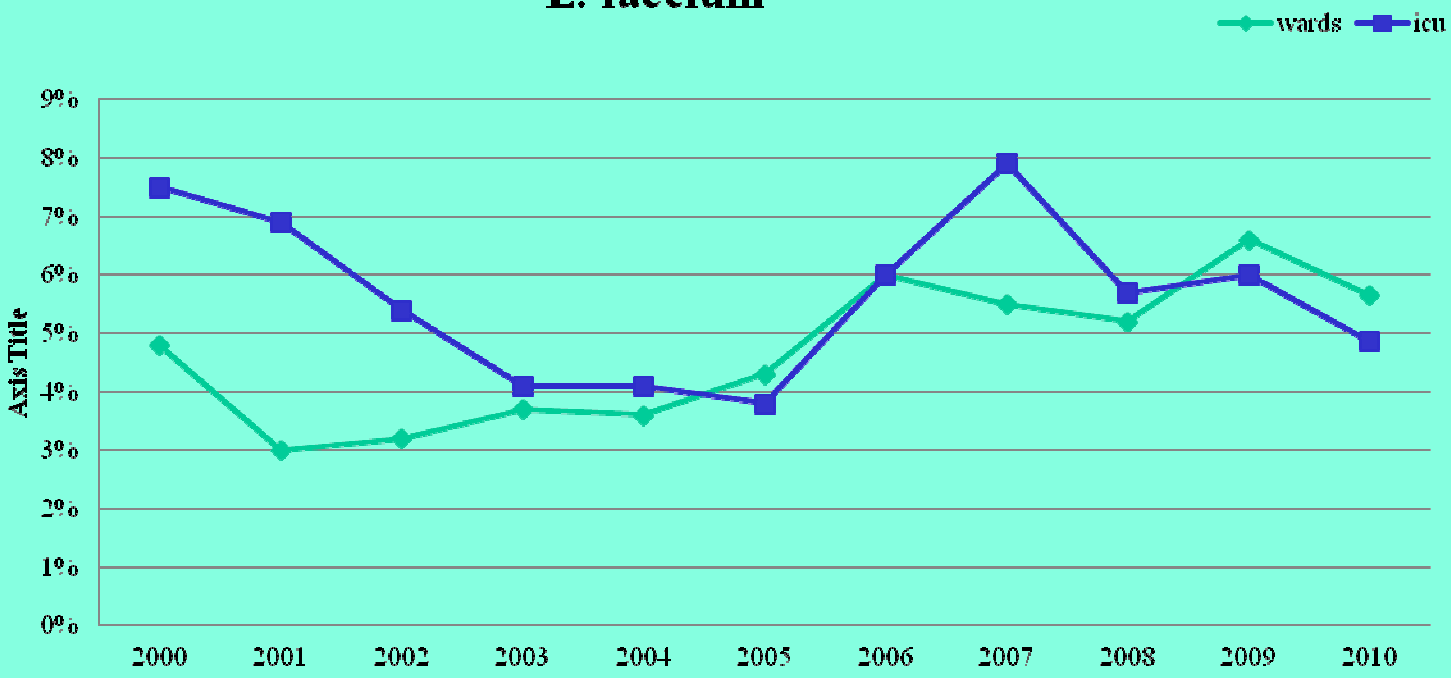
Many rates are decreasing

E faecalis



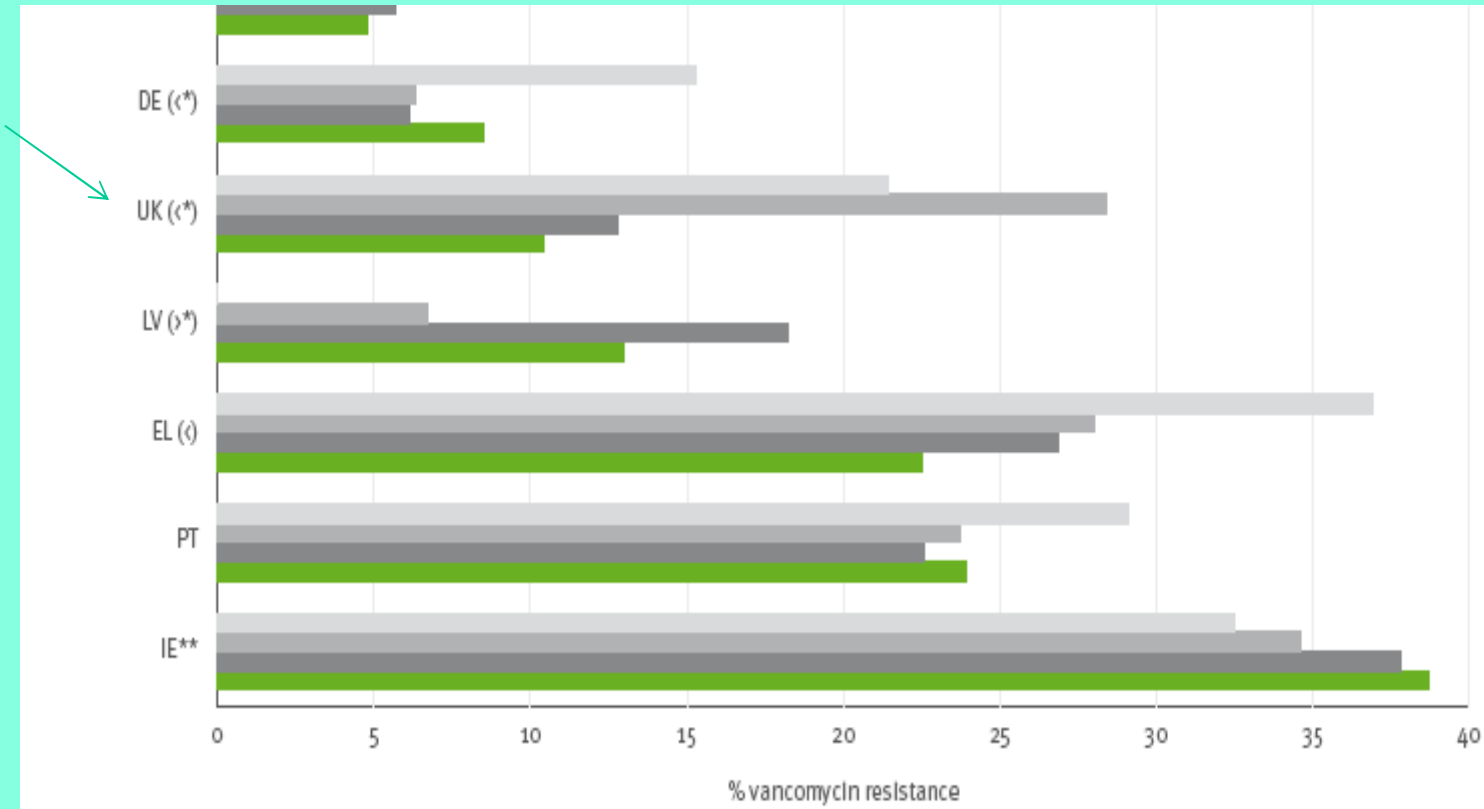
Blood cultures
Trends 2000 -2010
21 Hospitals

E. faecium



Many rates are decreasing

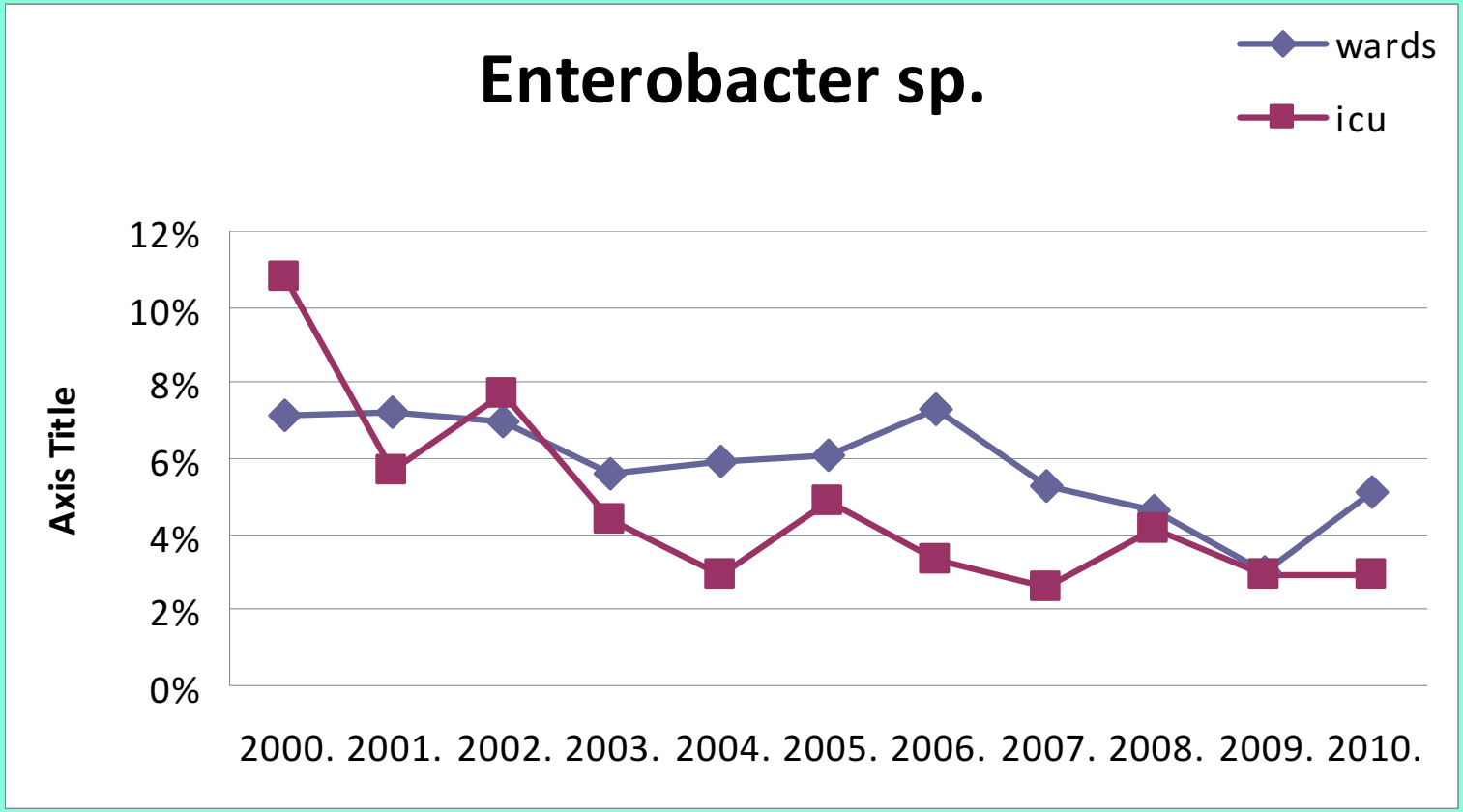
E faecium



Only countries that reported 20 isolates or more per year were included. The symbols › and ‹ indicate significant increasing and decreasing trends, respectively.
The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.
** Data for Ireland showed a significant increasing trend only for data from laboratories which reported continuously for the last four years.

Many rates are decreasing

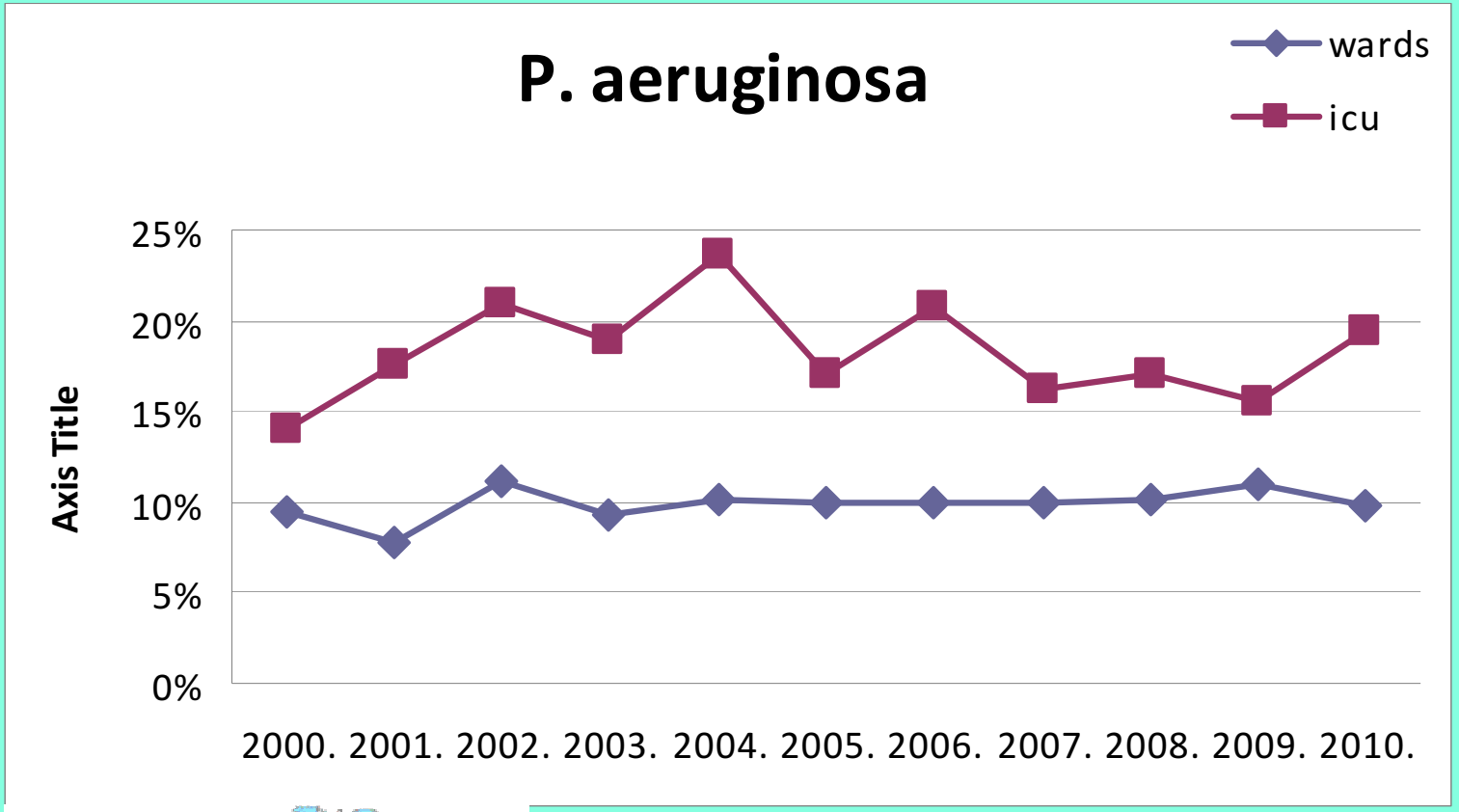
Blood cultures
Trends 2000 -2010
21 Hospitals



WHONET Greece
The Greek System for Surveillance of Antimicrobial Resistance

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Blood cultures
Trends 2000 -2010
21 Hospitals

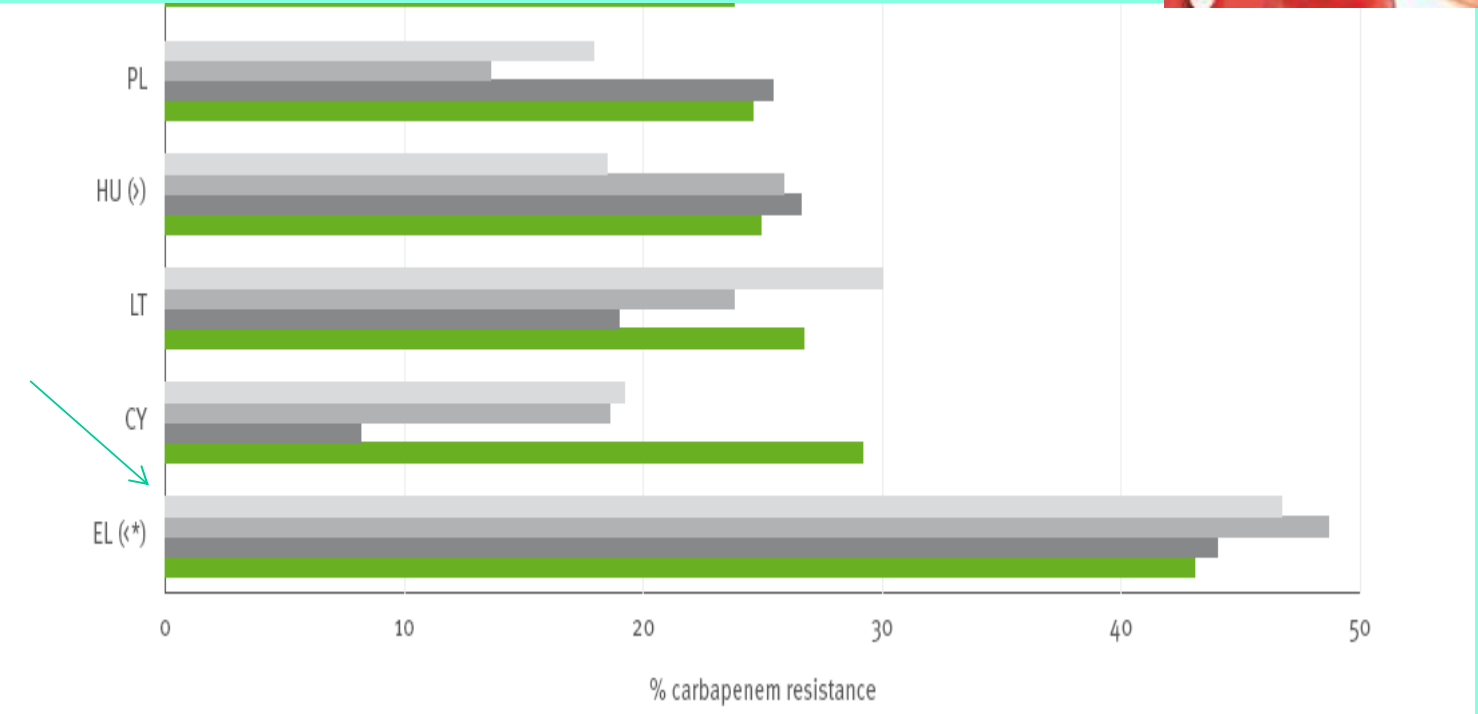


WHONET Greece
The Greek System for Surveillance of Antimicrobial Resistance

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Many rates are decreasing

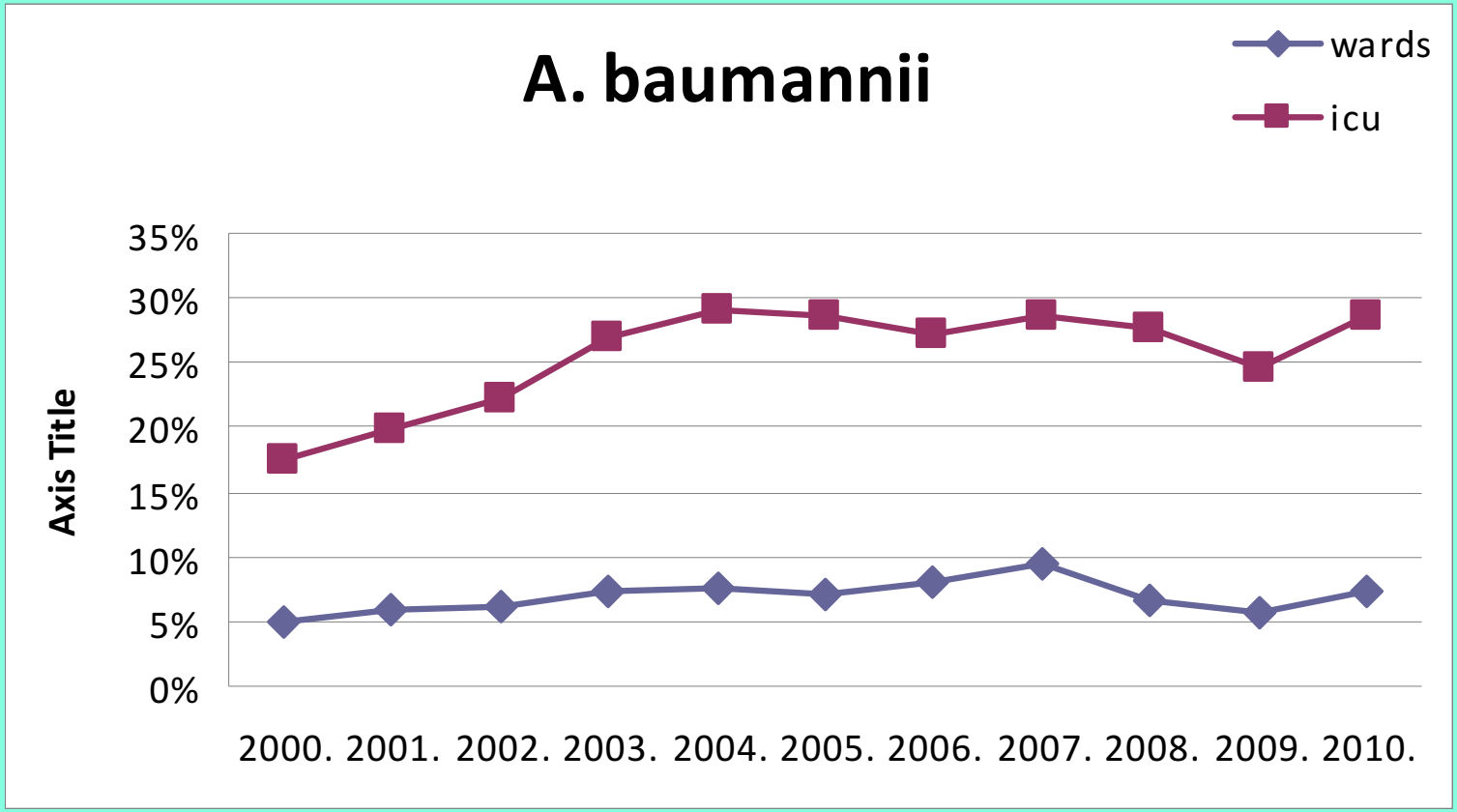
P aeruginosa



Trends

The bad News

Blood cultures
Trends 2000 -2010
21 Hospitals



WHONET Greece
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ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Blood cultures
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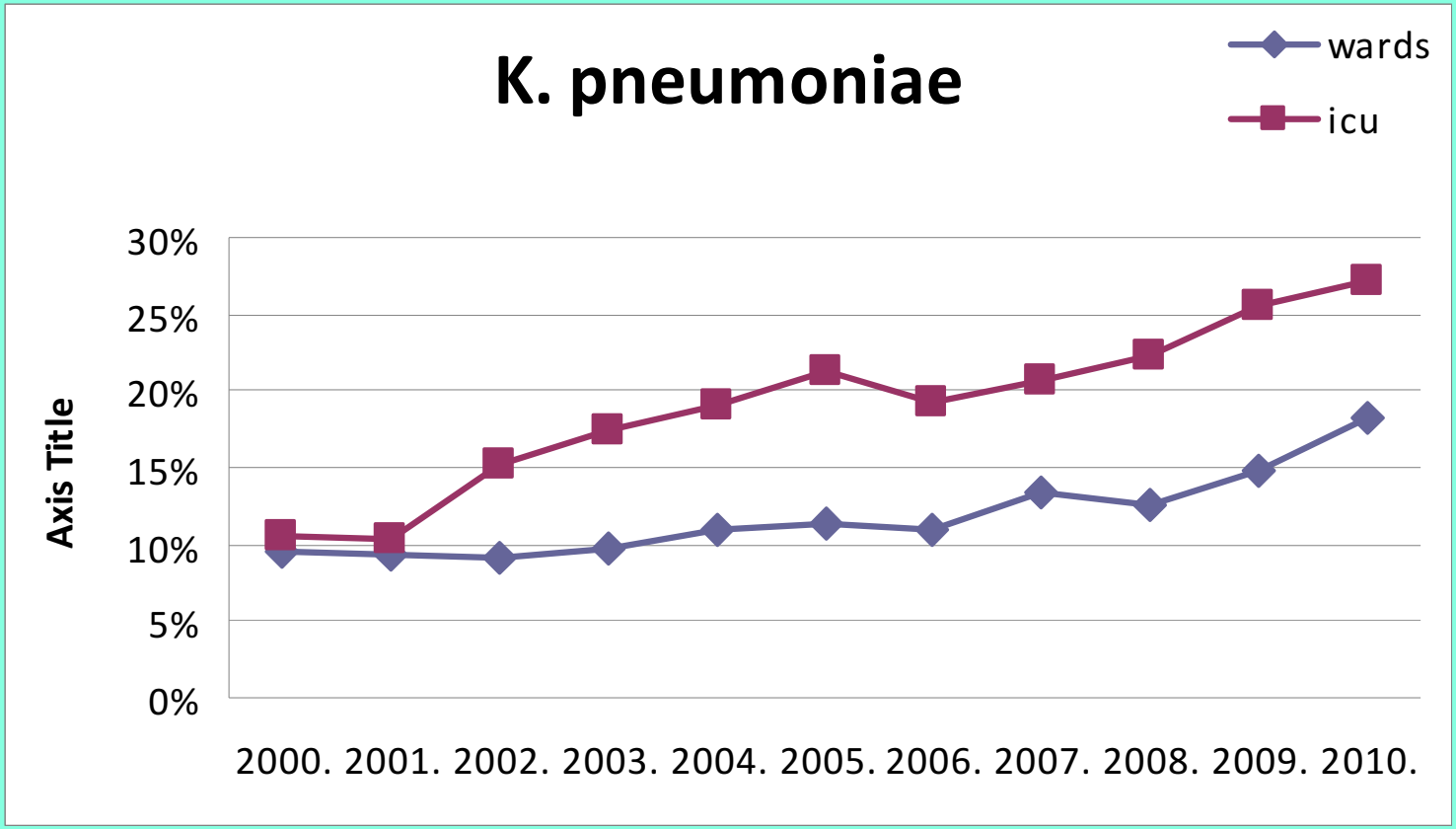
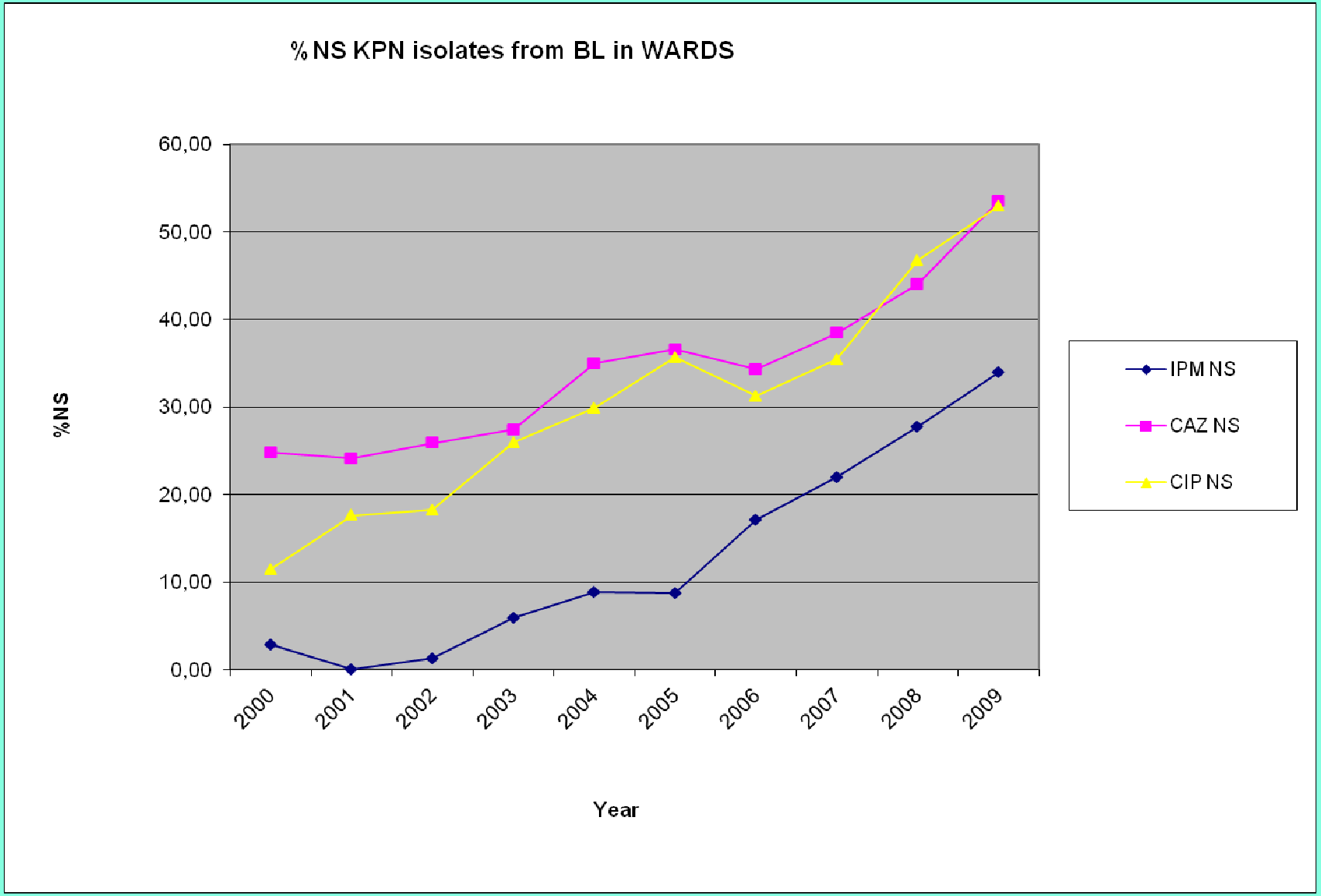


WHONET Greece
The Greek System for Surveillance of Antimicrobial Resistance

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ


% NS KPN isolates from BL in WARDS
60,00
50,00
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30,00
20,00
10,00
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%NS
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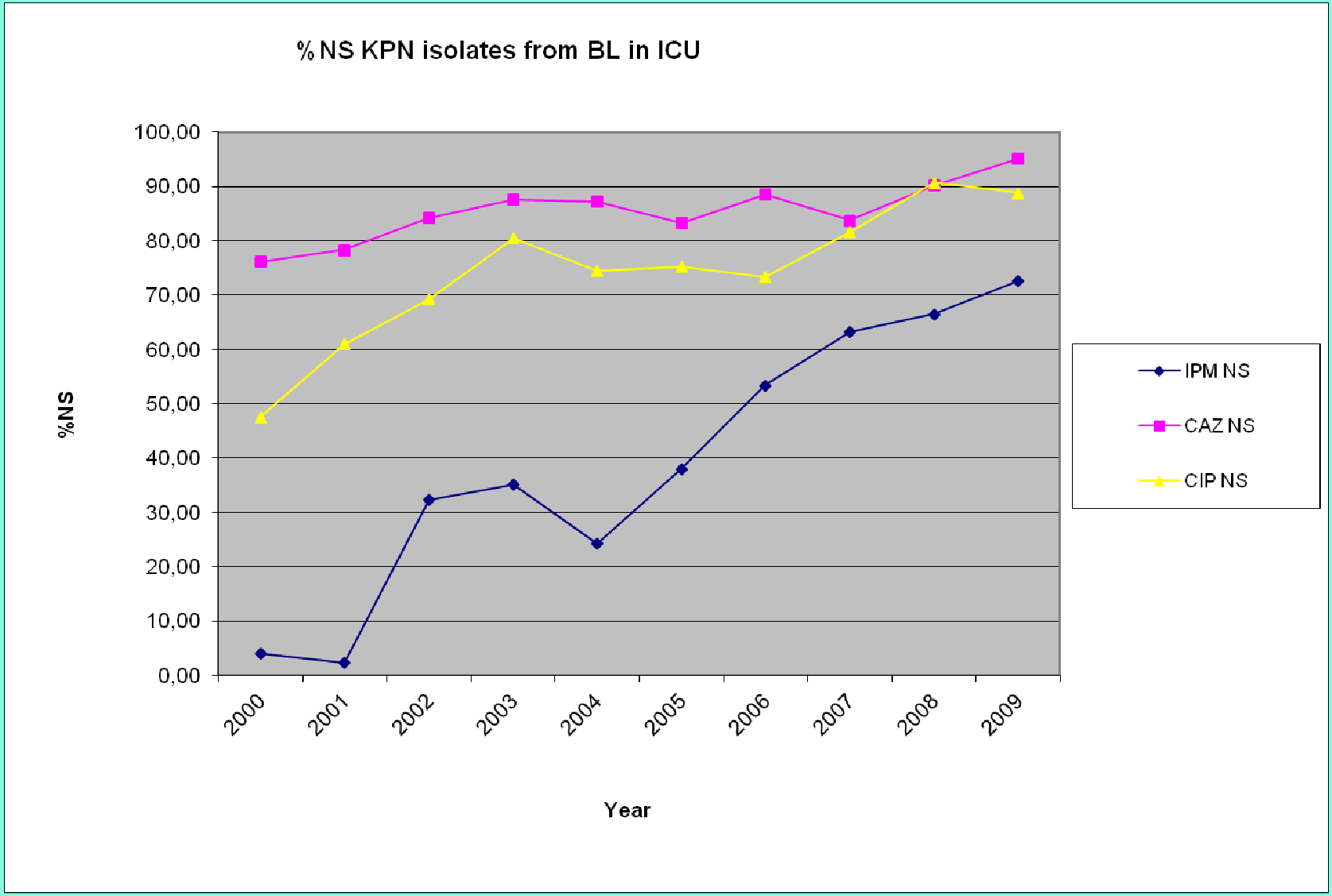
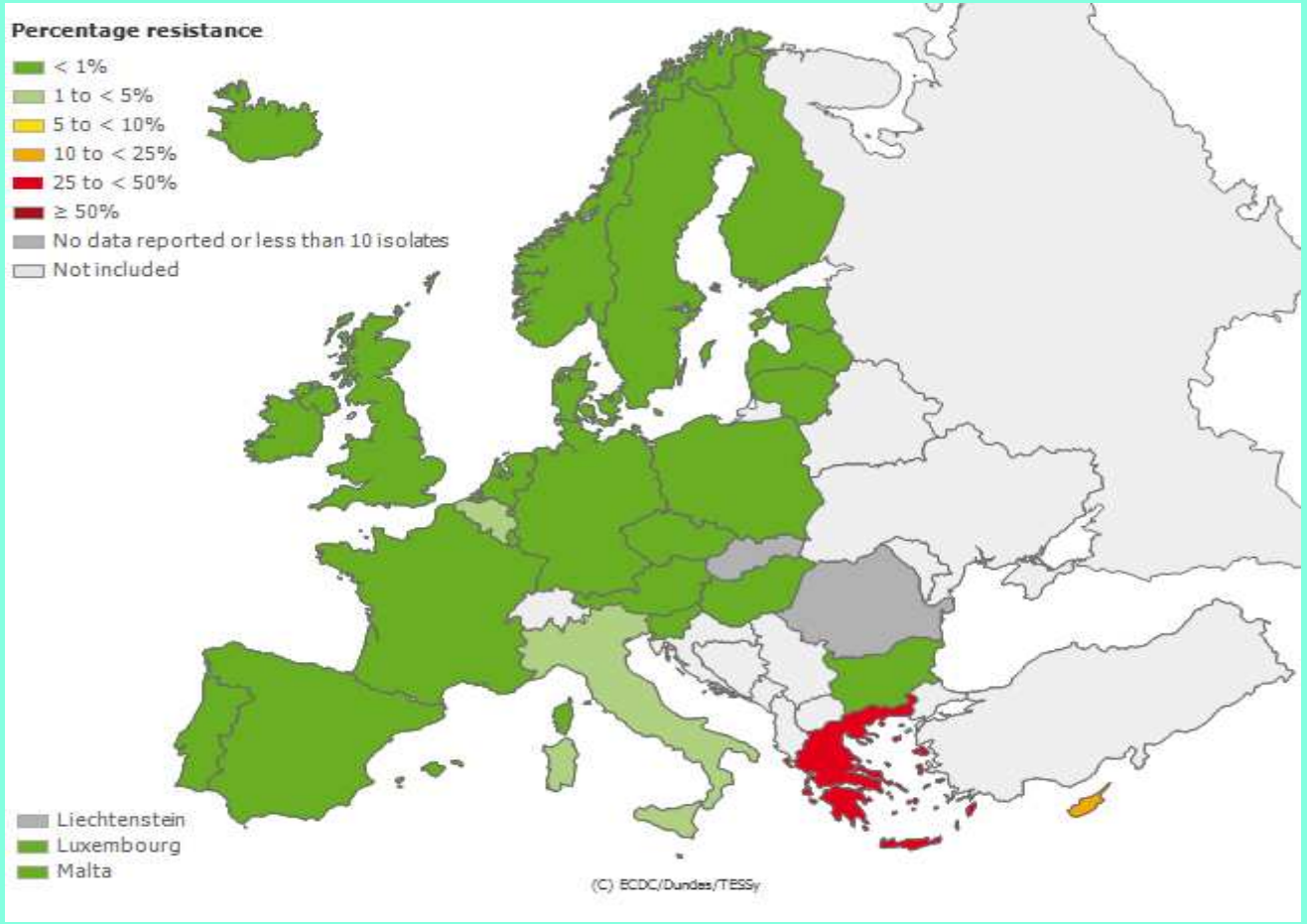

% NS KPN isolates from BL in ICU
%NS
100,00
90,00
80,00
70,00
60,00
50,00
40,00
30,00
20,00
10,00
0,00
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
Year
IPM NS
CAZ NS
CIP NS

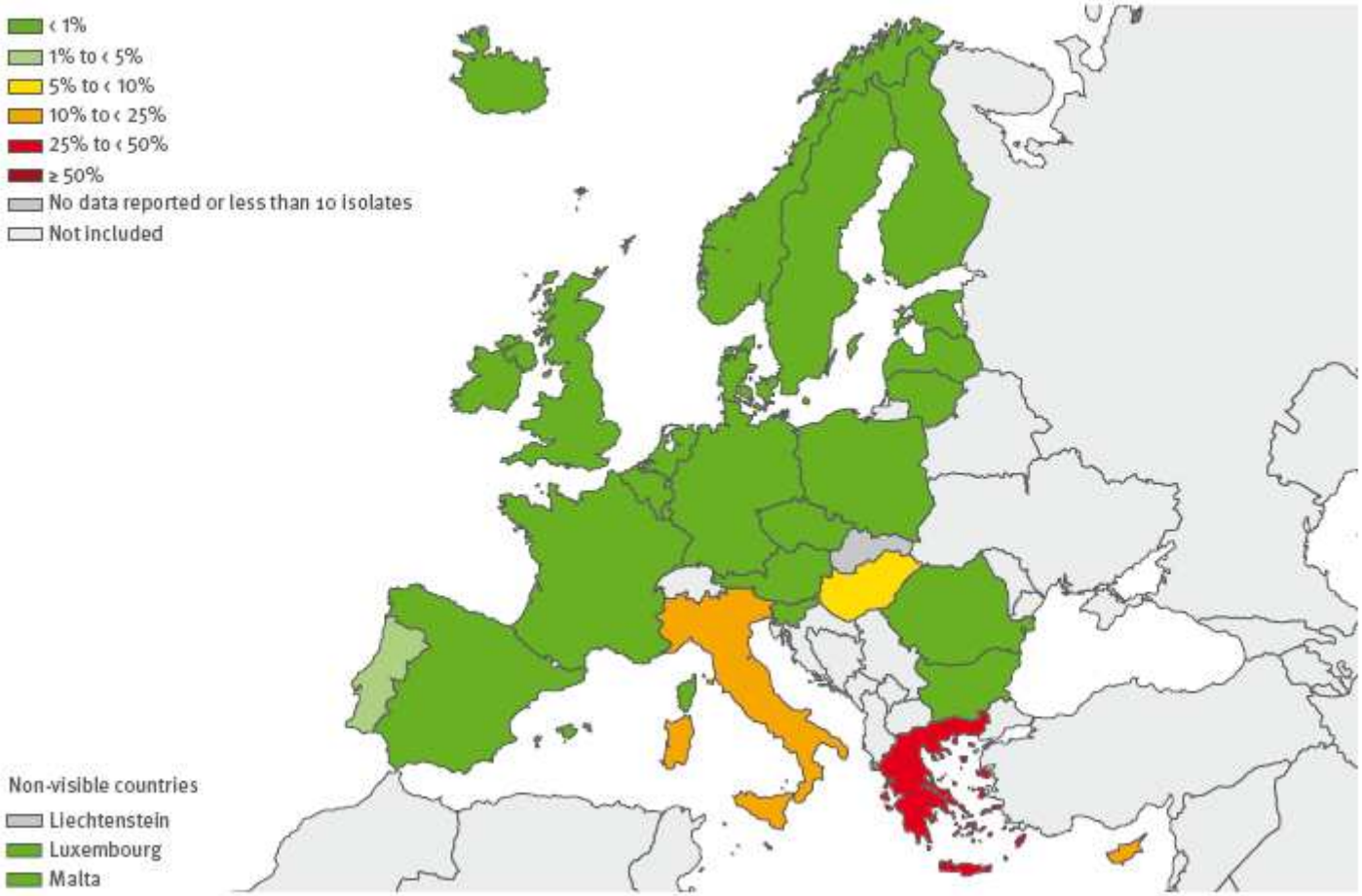
Carbapenem resistance
2009



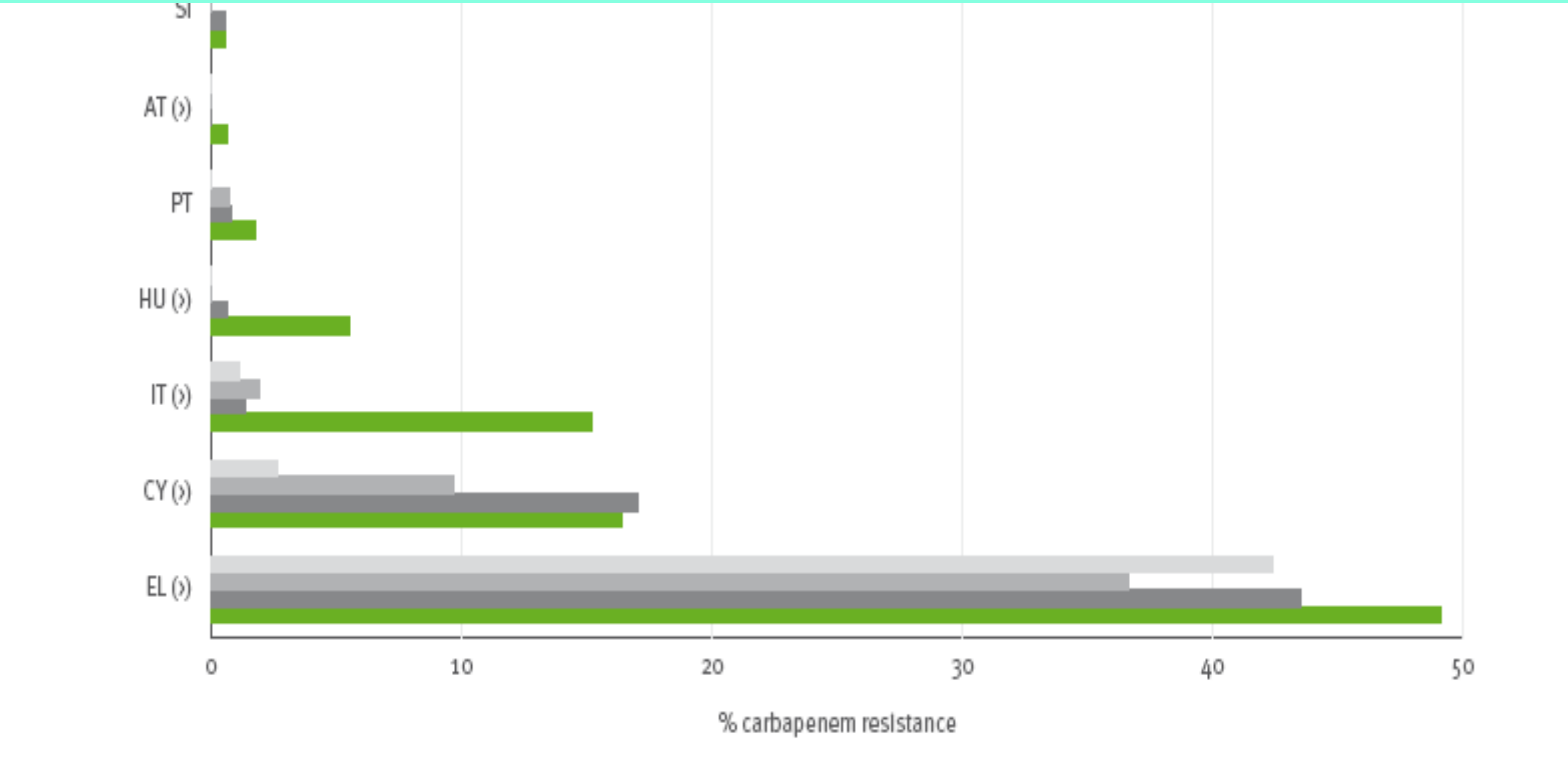
23 Nov 2011

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Figure 5.25: *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2010

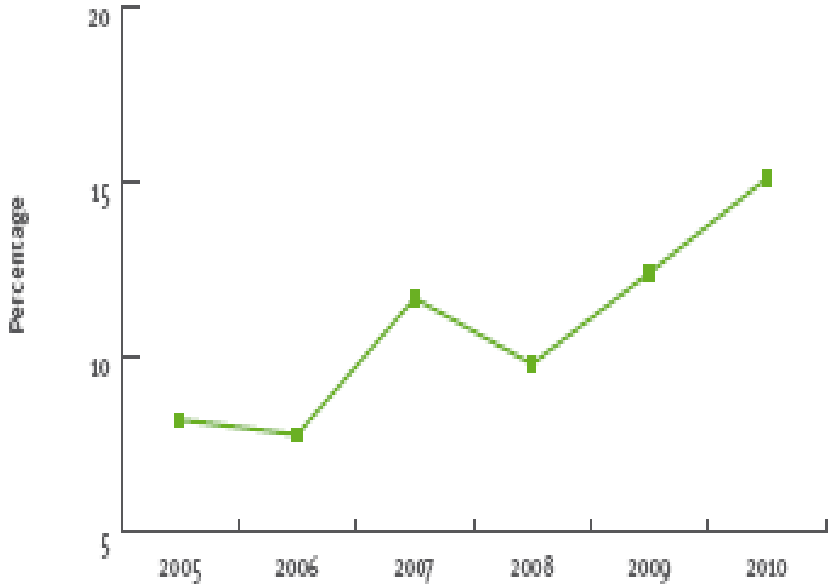


K pneumoniae



SURVEILLANCE REPORT

Figure 2.2: *Klebsiella pneumoniae*: Percentage of carbapenem-resistant invasive isolates reported to EARSS/EARS-Net by year, 2005–2010 (18 countries; 140 laboratories)



Only laboratories that continuously reported susceptibility results for carbapenems during the period 2005–2010 are included in the analysis.

TABLE 2

Epidemiological scale and stages of nationwide expansion of healthcare-associated carbapenem-non-susceptible *Enterobacteriaceae*

Epidemiological scale	Description	Stage
No cases reported	No cases reported	0
Sporadic occurrence	Single cases, epidemiologically unrelated	1
Single hospital outbreak	Outbreak defined as more than two epidemiologically related cases in a single institution	2a
Sporadic hospital outbreaks	Unrelated hospital outbreaks with independent, i.e. epidemiologically unrelated introduction or different strains, no autochthonous inter-institutional transmission reported	2b
Regional spread	More than one epidemiologically related outbreak confined to hospitals that are part of a regional referral network, suggestive of regional autochthonous inter-institutional transmission	3
Inter-regional spread	Multiple epidemiologically related outbreaks occurring in different health districts, suggesting inter-regional autochthonous inter-institutional transmission	4
Endemic situation	Most hospitals in a country are repeatedly seeing cases admitted from autochthonous sources	5

A new way of reporting

EUROROUNDUPS

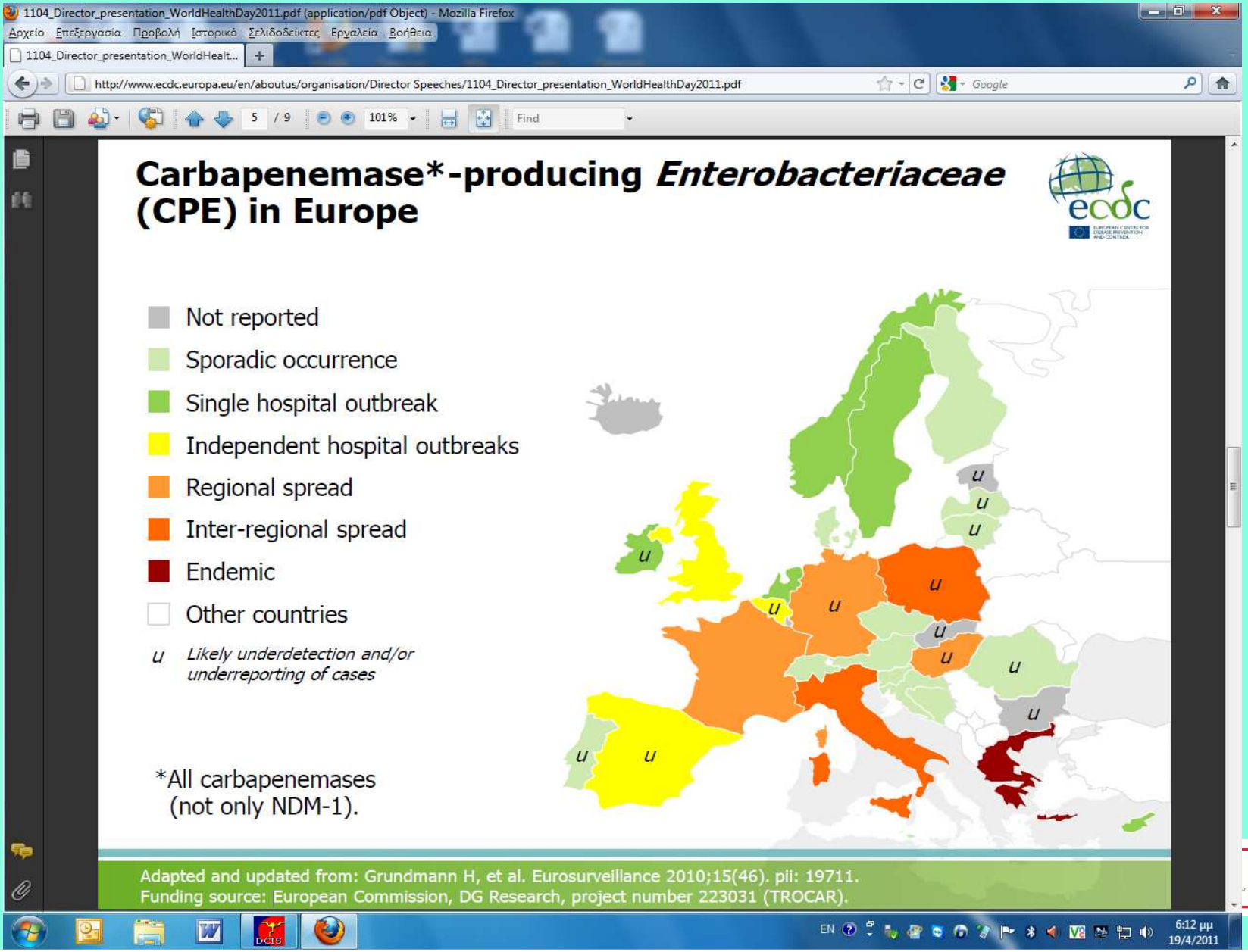
Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts

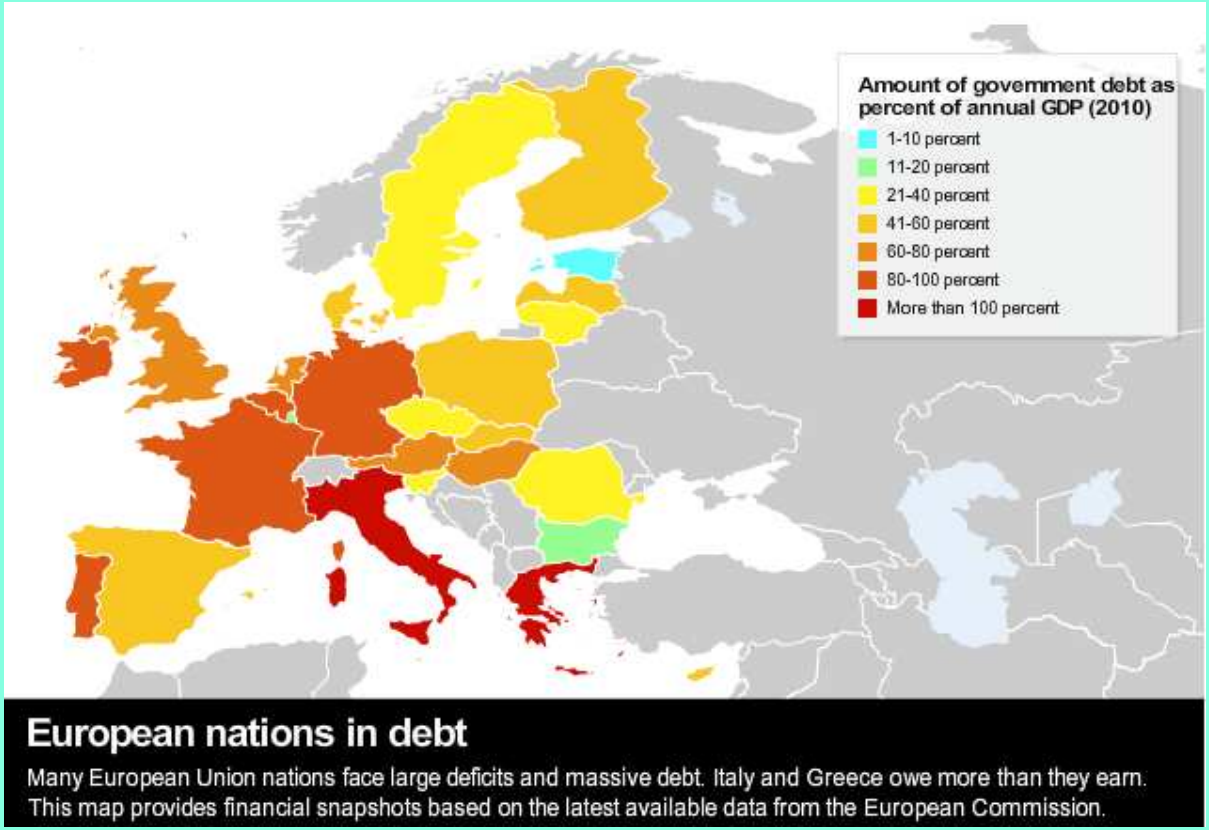
H Grundmann (Hajo.Grundmann@rivm.nl)[1,2], D M Livermore[3], C G Giske[4], R Canton[5,6], G M Rossolini[7], J Campos[8], A Vatopoulos[9], M Gniadkowski[10], A Toth[11], Y Pfeifer[12], V Jarlier[13], Y Carmeli[14], the CNSE Working Group[15]

1. Department of Medical Microbiology, University Medical Centre, Groningen, the Netherlands

23 Nov 2011
18/01/2012

Carbapenem resistance




Amount of government debt as percent of annual GDP (2010)
1-10 percent
11-20 percent
21-40 percent
41-60 percent
60-80 percent
80-100 percent
More than 100 percent
European nations in debt
Many European Union nations face large deficits and massive debt. Italy and Greece owe more than they earn. This map provides financial snapshots based on the latest available data from the European Commission.

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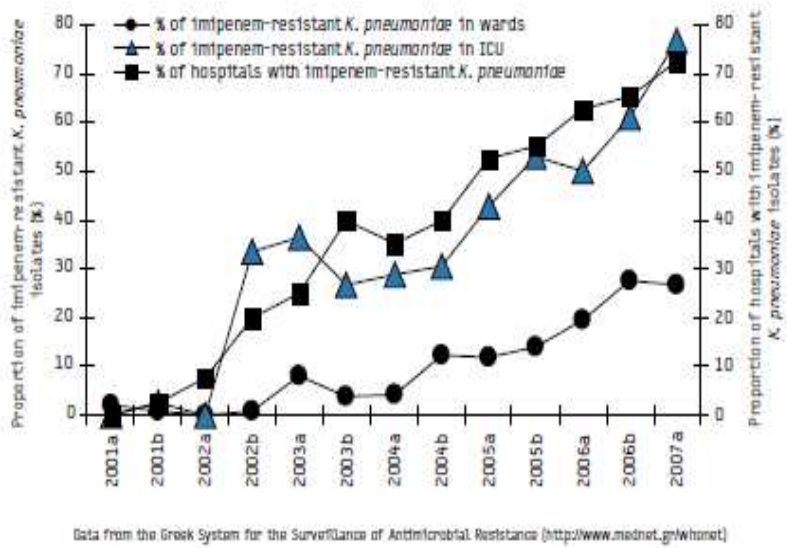
Carbapenem^{R} *Klebsiella* in Greece

TWO EPIDEMICS

- VIM (2003 – 2007)
- KPC (2007 - PRESENT)

FIGURE 2

Trends in proportion of imipenem-resistant *Klebsiella pneumoniae* isolates in hospitals in Greece, 2000-2006



Data from the Greek System for the Surveillance of Antimicrobial Resistance (http://www.mednet.gr/whonet)

•VIM Epidemic in *Klebsiella pneumoniae* in Greece

- Three outbreaks reported to us in ICU's in autumn 2002 involving 17 patients

(Giakkoupi et all 2003)

- Two more incidences in ICU's in early 2003

VIM Epidemic in Klebsiella pneumoniae in Greece in the three ICUs

- **VIM –1 .**
- Class I Integron
- MICs from 1 - >32 mg/L
- Harbored by (different) conjugative plasmids
- Co existence with ESBLs (in some instances)
- Few bacterial clones
  - even in the same hospital

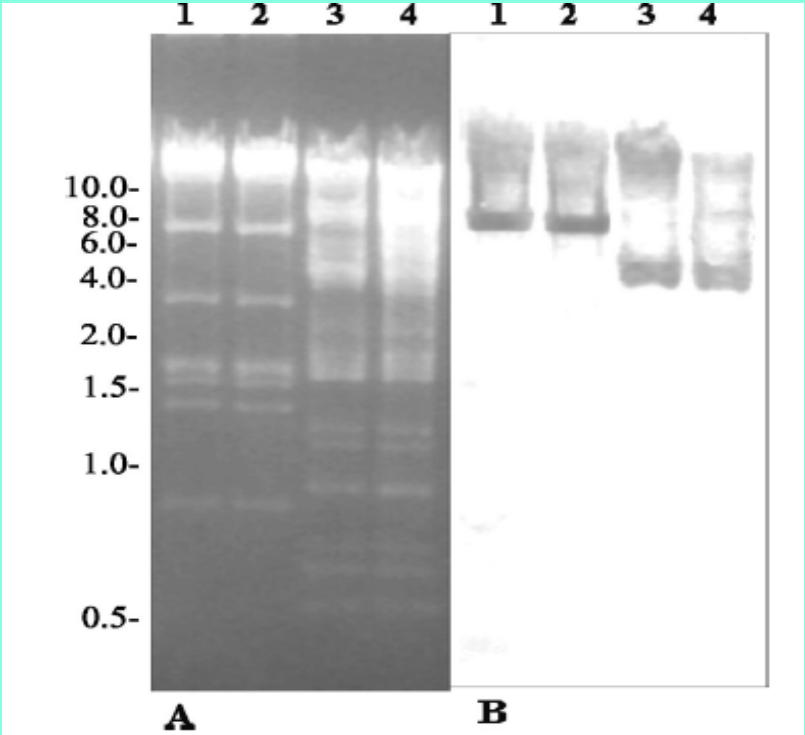
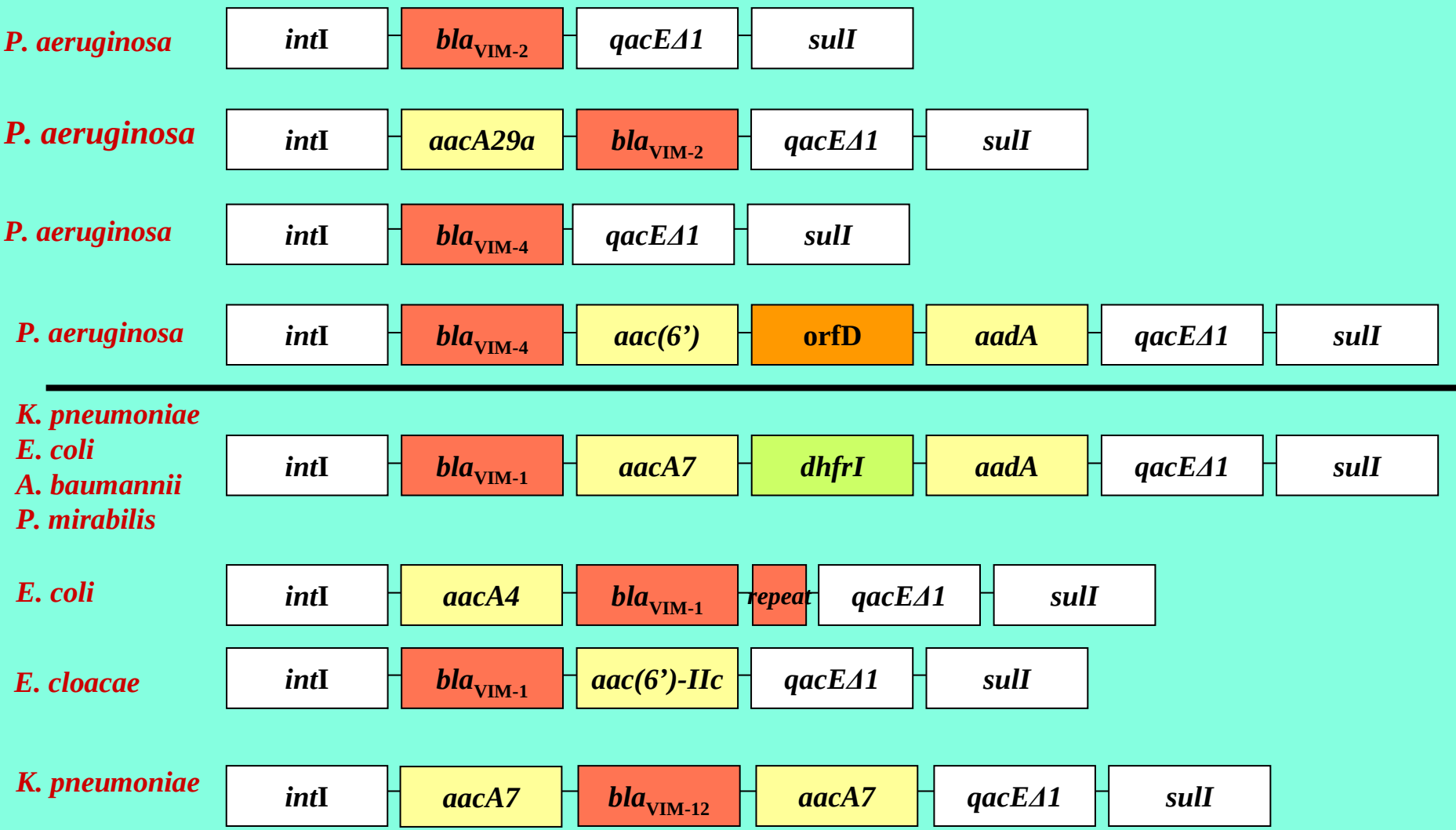


FIG. 2. (A) *Pst*I restriction profiles of the bla_{VIM-1}-carrying plasmids extracted from *E. coli* transconjugants trc-1, trc-2 (plasmid type 1), trc-8, and trc-13 (plasmid type 2) are presented in lanes 1 to 4, respectively. (B) Hybridization of the preparations shown in panel A with a bla_{VIM-1} probe.

(Giakkoupi et all 2003)

Integrons harboring *bla*$_{VIM}$ genes



Tsakris et al., 2000; Mavroidi et al., 2000; Pournaras et al., 2002; Pournaras et al., 2003; Miriagou et al., 2003; Giakkoupi et al., 2003a & 2003b; Scoulica et al., 2004; Galani et al., 2005; Ikonomidis et al., 2005; GenBank.

Journal of Antimicrobial Chemotherapy (2008) **61**, 59–63
doi:10.1093/jac/dkm443
Advance Access publication 13 November 2007

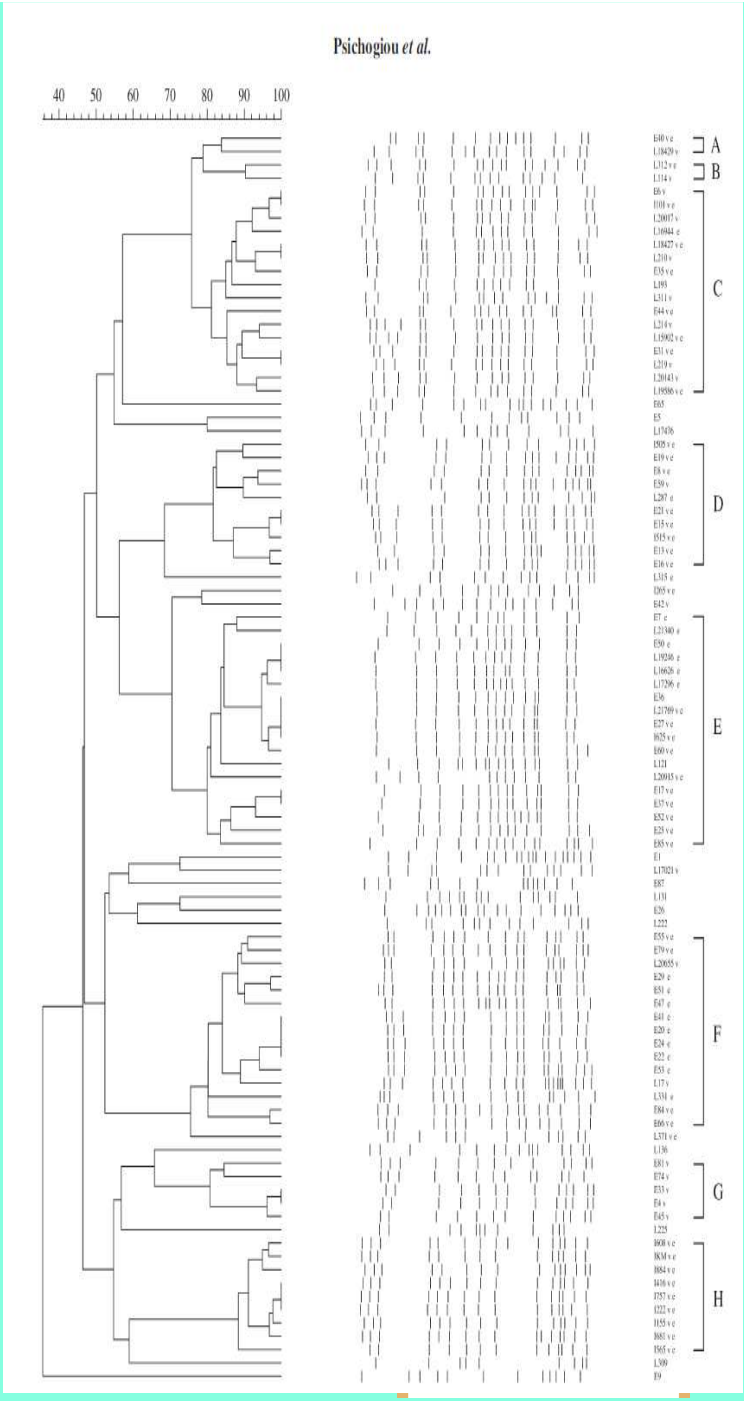
JAC

Ongoing epidemic of *bla*$_{VIM-1}$-positive *Klebsiella pneumoniae* in Athens, Greece: a prospective survey

M. Psichogiou[1], P. T. Tassios[2], A. Avlamis[3], I. Stefanou[3], C. Kosmidis[1], E. Platsouka[4], O. Paniara[4], A. Xanthaki[5], M. Toutouza[5], G. L. Daikos[1] and L. S. Tzouvelekis[2]*

Conclusions: A multiclonal epidemic of *bla*$_{VIM-1}$-carrying *K. pneumoniae* is under way in the major hospitals in Greece. Microorganisms producing both VIM-1 and SHV-5 constitute the prevalent multi-drug-resistant population of *K. pneumoniae* in this setting.

23 Nov 2011



Short report

Identification of Klebsiella pneumoniae carbapenemase (KPC) in Sweden

K Tegmark Wisell (karin.tegmark-wisell@smi.ki.se)[1], S Hæggman[1], L Gezelius[1], O Thompson[2], I Gustafsson[3], T Ripa[3], B Olsson-Liljequist[1]

1. Swedish Institute for Infectious Disease Control, Stockholm, Sweden
2. Department of Infectious Disease, County Hospital of Halmstad, Sweden
3. Department of Clinical Microbiology and Infectious Disease Control, County Hospital of Halmstad, Sweden

A *Klebsiella pneumoniae* expressing carbapenemase type 2 (KPC-2) enzyme has been identified in Sweden. The patient, who had a history of chronic obstructive lung disease, developed a respiratory tract infection while on holiday in Greece. After initial intensive care treatment in Greece, the patient was transferred to Sweden. Upon recovery, the central venous catheter was withdrawn and a multiresistant *Klebsiella pneumoniae* was isolated from the

KPC-producing *Enterobacteriaceae* have now been identified in at least four European countries, and we therefore encourage microbiological laboratories to be observant on abnormal carbapenem resistance phenotypes in order to detect KPC-producing isolates. Based on the New York experience, we stress the importance of early identification followed by intensified infection control measures to prevent the dissemination of Enterobacteriaceae with KPC enzymes

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ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Feb. 2008, p. 796–797 Vol. 52, No. 2
0066-4804/08/$08.00+0 doi:10.1128/AAC.01180-07

Plasmid-Mediated Carbapenem-Hydrolyzing β-Lactamase KPC-2 in *Klebsiella pneumoniae* Isolate from Greece[▽]

The emergence and dissemination of *Enterobacteriaceae* isolates harboring carbapenemases in various geographic regions

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23 Nov 2011

Phenotypic Detection and differentiation of the main types of carbapenemases

Hodge Test	EDTA TEST	Possible enzyme
+	+	Metalloenzyme (πχ VIM)
+	-	KPC type
-	-	Carbapenemase Negative*

* Possible due to AmpC production or reduced permeability etc

To be applied on strains
displaying reduced susceptibility to carbapenems

Summary of epidemiological, antibiotic susceptibility and transferability data by pulsotype of the KPC producing *Klebsiella pneumoniae* in Greece 2008

TABLE

Summary of epidemiological data and information on antibiotic susceptibility and transferability of the KPC-2-producing *Klebsiella pneumoniae* isolates described in this study

Pulsotype	Number of isolates	Number of hospitals	Resistance to other drug classes*	blaKPC gene transferred via conjugation	Other drug classes transferred
A	166	18	an, net, tb, spt, sxt, c, cip	No	
B	1	1	–	Yes	
C	2	1	an, net, tb, spt, sxt, cip	Yes	–
D	2	1	gm, an, net, tb, spt, sxt, c, cip	Yes	gm an net tb spt sxt c
E	2	2	net, tb, spt, sxt, c, cip	Yes	–

*Abbreviations:

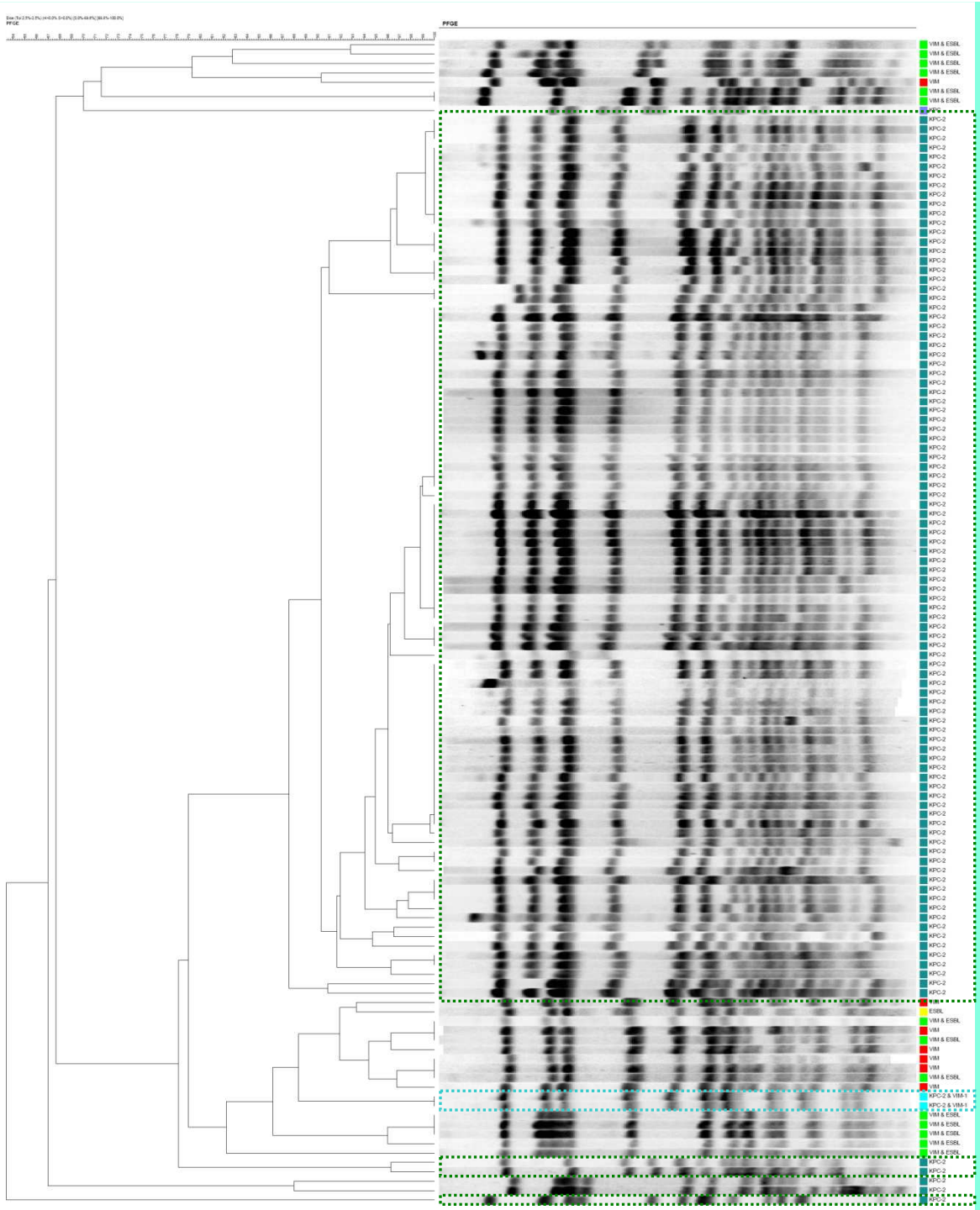
* an: Amikacin, net: metilmycin, tb: tobramycin, spt: streptomycon, sxt: cotrimixazole, c: n

Research articles

KPC-2-PRODUCING *KLEBSIELLA PNEUMONIAE* INFECTIONS IN GREEK HOSPITALS ARE MAINLY DUE TO A HYPEREPIDEMIC CLONE

P Giakoupi[1], H Maltezou[2], M Polemis[1], O Pappa[1], G Saroglou[3], A Vatopoulos (avatopou@nsph.gr)[1], the Greek System for the Surveillance of Antimicrobial Resistance[4]

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ



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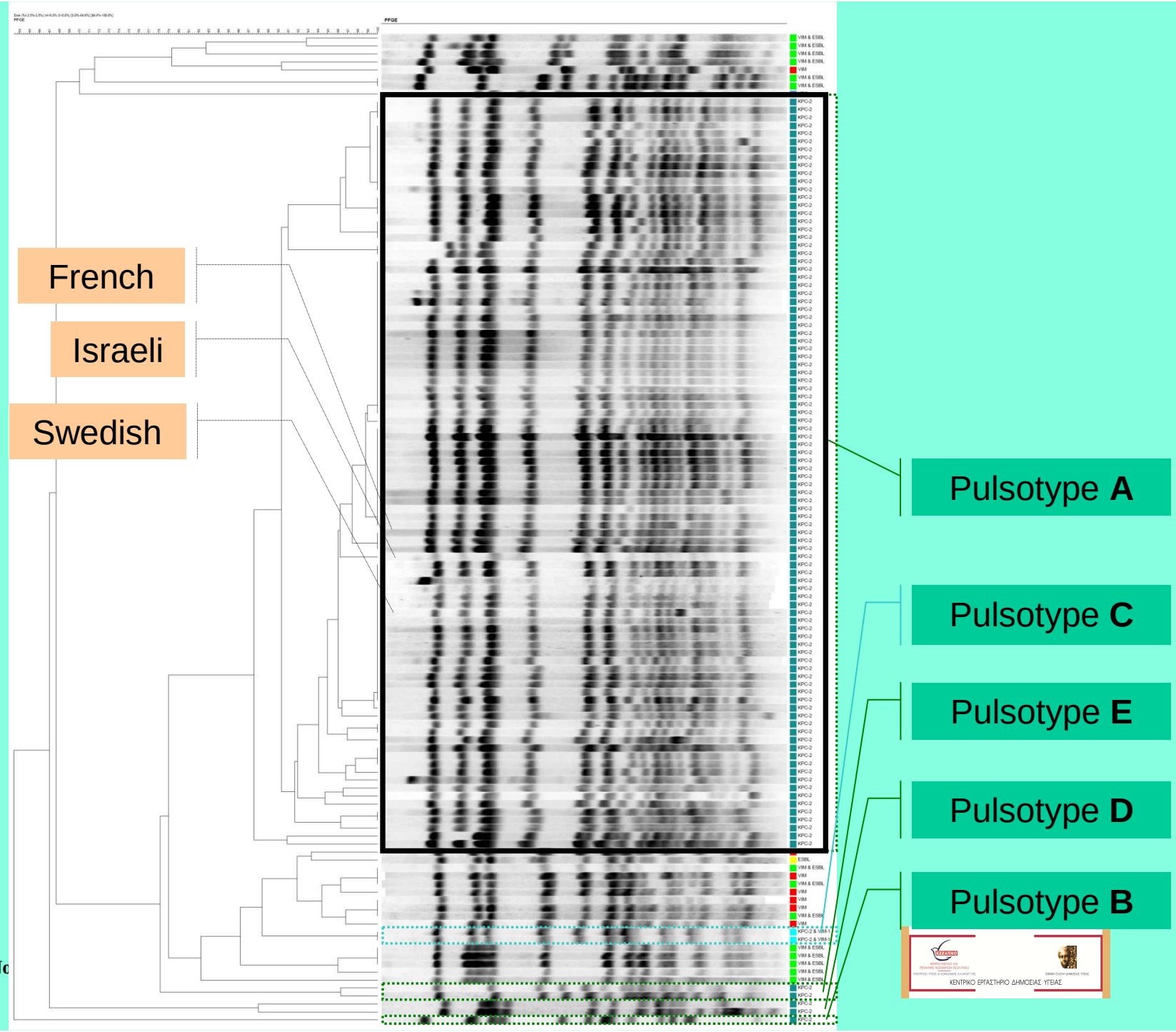
French
Israeli
Swedish
Pulsotype A
Pulsotype C
Pulsotype E
Pulsotype D
Pulsotype B
ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Journal of Antimicrobial Chemotherapy Advance Access published May 4, 2011

J Antimicrob Chemother
doi:10.1093/jac/dkr166

Journal of Antimicrobial Chemotherapy

An update of the evolving epidemic of *bla*$_{KPC-2}$-carrying *Klebsiella pneumoniae* in Greece (2009–10)

Panagiota Giakkoupi[1], Costas C. Papagiannitsis[1], Vivi Miriagou[2], Olga Pappa[3], Michalis Polemis[3], Kyriaki Tryfinopoulou[3], Leonidas S. Tzouvelekis[4] and Alkiviadis C. Vatopoulos[1]*

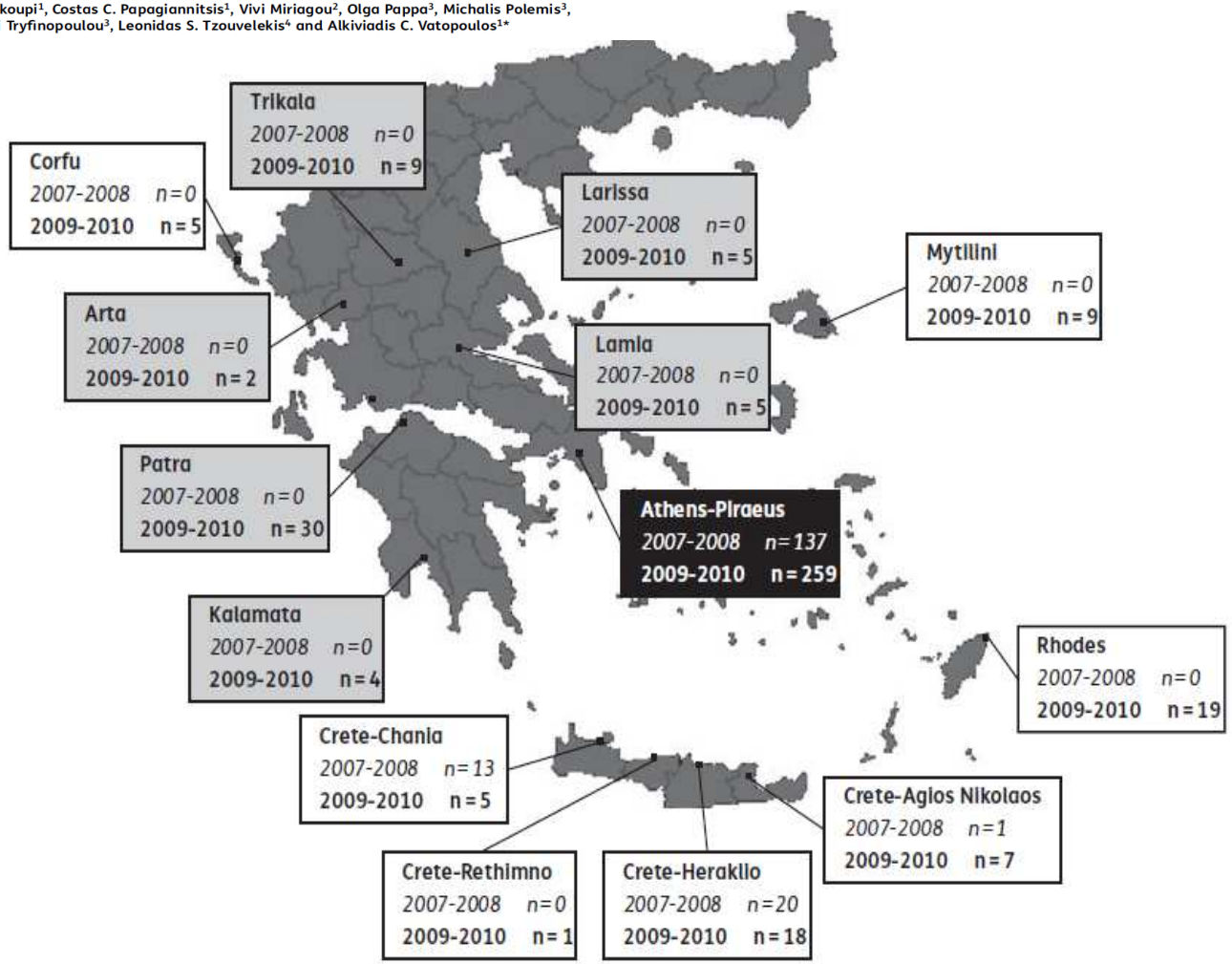

Figure 1. Geographical map showing the locations of the participating hospitals as well as the number of isolates collected during the initial survey (numbers in italics) and the update described in this study (numbers in bold). Black rectangle, Athens–Piraeus; grey rectangles, mainland cities; white rectangles, islands.

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Table 1. Regional distribution of 378 KPC-2-producing *K. pneumoniae* isolates and their classification by molecular typing

Geographical distribution (no. of hospitals)	PFGE types (STs)											
	A (258)	B (147)	C (340)	D (17)	E (383)	F (133)	G (274)	H (11)	I (323)	J (494)	K (495)	L (ND)	M (ND)
Athens (26)	216	12	2	—	9	6	4	—	3	2	1	3	1
Other mainland cities (6)	43	8	—	1	—	—	—	—	—	—	—	1	2
Crete and other islands (8)	63	—	—	—	—	—	—	1	—	—	—	—	—
Total no. of hospitals (40)	322	20	2	1	9	6	4	1	3	2	1	4	3

ND, not determined.

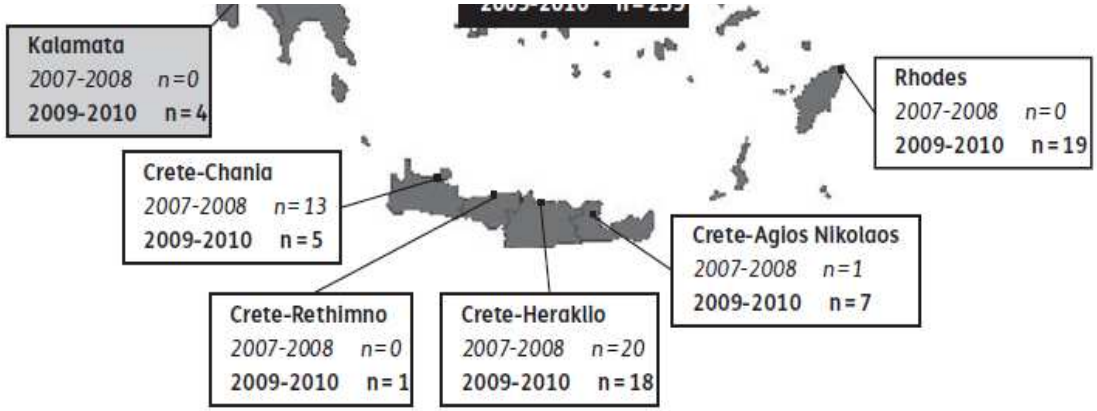

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Table 1. Characteristics of 256 *K. pneumoniae* isolates.

β-Lactamase content[a]	Total strains No (%)	PFGE types (No of strains typed)	No of strains isolated in each hospital							
			I (Athens)	II (Athens)	III (Athens)	IV (Athens)	V (Athens)	VI (Thess/niki)	VII (Thess/niki)	VIII (Creta)
CMY-4	3 (1.2)	E (1)		2	1					
CMY-4 + SHV-12	1 (0.4)	A (1)								1
CMY-4 + CTX-M-15	4 (1.2)	E (2)		1	1	2				
CMY-4 + CTX-M-15 + VEB-1	1 (0.4)	E (1)			1					
VEB-1	1 (0.4)	Nd[b]	1							
CTX-M-15	5 (2.0)	U (1)	1			1	1			2
SHV-12	11 (4.3)	A (2), E (1)		2		2	1	3	2	1
KPC-2	13 (5.1)	U (3)	5	2		3		3		
KPC-2 + VEB-1	1 (0.4)	U (1)				1				
KPC-2 + CMY-4	2 (0.8)	E (1)					2			
KPC-2 + CMY-4 + SHV-12	1 (0.4)	A (1)				0				1
KPC-2 + CMY-4 + CTX-M-15	1 (0.4)	E (1)				1				
KPC-2 + SHV-12	85 (33.2)	A (7), B (1)	22	19	5	15	7	8	3	6
KPC-2 + VIM-19 + CMY-4	1 (0.4)	E (1)		1						
KPC-2 + VIM-1 + SHV-12	2 (0.8)	U (1)	2							
KPC-2 + VIM-1	4 (1.6)	B (2)						4		
VIM-1	12 (4.7)	B (1)	9	1	1	1				
VIM-27	1 (0.4)	B (1)		1						
VIM-1 + SHV-12	3 (1.2)	B (1)	1	2						
VIM-27 + SHV-5	1 (0.4)	B (1)			1					
VIM-19 + CMY-4	2 (0.8)	E (1)		1	1					
VIM-19 + CMY-4 + CTX-M-15	3 (1.2)	E (1)		1			1	1		
no tested (susceptible isolates)	98 (38.3)	–	18	8	21	6	9	13	6	17
Totals (No of strains)	256		59	41	32	32	21	32	11	28

Diversity of acquired β-lactamases amongst *Klebsiella pneumoniae* in Greek hospitals

International Journal of Antimicrobial Agents

23 Nov 2011

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CMY-4										1
CMY-4 + SHV-12										
CMY-4 + CTX-M-15										
CMY-4 + CTX-M-15 + VEB-1										
VEB-1										2
CTX-M-15										1
SHV-12									2	
KPC-2										
KPC-2 + VEB-1										
KPC-2 + CMY-4										1
KPC-2 + CMY-4 + SHV-12										
KPC-2 + CMY-4 + CTX-M-15									3	6
KPC-2 + SHV-12										
KPC-2 + VIM-19 + CMY-4										
KPC-2 + VIM-1 + SHV-12										
KPC-2 + VIM-1										
VIM-1										
VIM-27										
VIM-1 + SHV-12										
VIM-27 + SHV-5	1 (0.4)	B (1)			1					
VIM-19 + CMY-4	2 (0.8)	E (1)		1	1					
VIM-19 + CMY-4 + CTX-M-15	3 (1.2)	E (1)		1			1	1		
no tested (susceptible isolates)	98 (38.3)	–	18	8	21	6	9	13	6	17
Totals (No of strains)	256		59	41	32	32	21	32	11	28

	No	%
VIM	22	16,7
KPC	103	78,0
VIM + KPC	7	5,3

Diversity of acquired β-lactamases amongst *Klebsiella pneumoniae* in Greek hospitals

International Journal of Antimicrobial Agents

23 Nov 2011

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

B. Response

National Action Plan to Combat Infections due to Multi-Drug Resistant, Gram-Negative Pathogens in Hospitals in Greece 2010 - 2015

"Procrustes "

23 Nov 2011

ΚΕΝΤΡΙΚΟ ΕΡΓΑΣΤΗΡΙΟ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

Principles of the Action Plan

- the estimation and follow-up of the **incidence and temporal trends** of MDR-GNB infections in hospitalized patients.

- the implementation of enhanced infection control measures in order to contain the spread of MDR-GNB within acute-care hospitals.

Principles of the Action Plan

- Establishment and operation at the Hellenic Center for Disease Control and Prevention (HCDCP), of a national surveillance system for MDR-GNB infections in hospitals in Greece.
- Systemic monitoring of the implementation of the appropriate infection control measures.
- Issue relevant legislations by the General Directorate – MoH ns.

Incidence VS resistance rates

- Describes burden of disease
- Is a more sensitive indicator of the results of the inervention

TARGET

- All cases of specific clinical infections caused by carbapenem-resistant *K. pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumanii* are **obligatory notifiable** to HCDCP, starting on November 1, 2010

METHODS

- Weekly notification to the HCDCP of all newly-detected cases of carbapenem-resistant *K. pneumoniae*, *P. aeruginosa*, and *A. baumanii* clinical infections.

- Immediate notification to the HCDCP, in case of onset of a MDR-GNB outbreak.

- Systemic communication to the hospital CEO regarding the burden and trends of MDR-GNB infections, the implementation of infection control measures, and possible deficits and problems that emerged during the daily implementation of the Action Plan within the hospital.

- Organization of educative activities in order to increase compliance of HCWs with infection control measures.

METHODS

Responsibility at the hospital level

- Hospital Task Force
  - Hospital CEO
  - Medical Director of the Committee for Nosocomial Infections
  - Director of the microbiology laboratory
  - Infection control nurse

Hospital Task Force

- Daily review of microbiology laboratory records in order to promptly identify all cases of MDR-GNB clinical infection or colonization.
- Daily communication with the physicians caring for known cases of MDR-GNB infections in order to follow:
  - the patients outcome
  - the strict and systemic implementation of infection control measures in order to contain the spread of MDR-GNB within the health-care facility
  - the compliance of health-care personnel with hand hygiene
  - the coordination of active surveillance cultures for colonization

Hospital Task Force

- Weekly notification to the HCDCP of all newly-detected cases of carbapenem-resistant *K. pneumoniae*, *P. aeruginosa*, and *A. baumanii* clinical infections.

- Immediate notification to the HCDCP, in case of onset of a MDR-GNB outbreak.

- Systemic communication to the hospital CEO regarding the burden and trends of MDR-GNB infections, the implementation of infection control measures, and possible deficits and problems that emerged during the daily implementation of the Action Plan within the hospital.

- Organization of educative activities in order to increase compliance of HCWs with infection control measures.

•

The role of the HCDCP

- ***Surveillance***
- Statistical analysis, interpretation, and follow-up of the burden and trends of infections due to MDR-GNB in acute-care hospitals in Greece.
- The incidence of MDR *K. pneumoniae*, *P. aeruginosa*, and *A. baumanii* clinical infections will be estimated per 1000 hospital days, based on data provided by hospitals.
- Monthly feedback to hospitals about the burden and trends of infections due to MDR-GNB

- ***Interventions***
- Communication with the Task Force of the hospital and the Director of the department
- When necessary, a HCDCP-based team intervenes in order to contain a nosocomial outbreak.
- Monthly communication to the General Directorate/ MoH of surveillance results and implemented measures.
- Issue and dissemination to all acute-care hospitals of guidelines about the management of patients with MDR-GNB infections,
- Organization of campaigns for the promotion of hand hygiene within health-care facilities and follow-up of HCW compliance.
- Organization of routine visits at hospitals
- Organization of training activities for the hospital Task Force teams.
- Communication to the general public about MDR nosocomial infections.
-

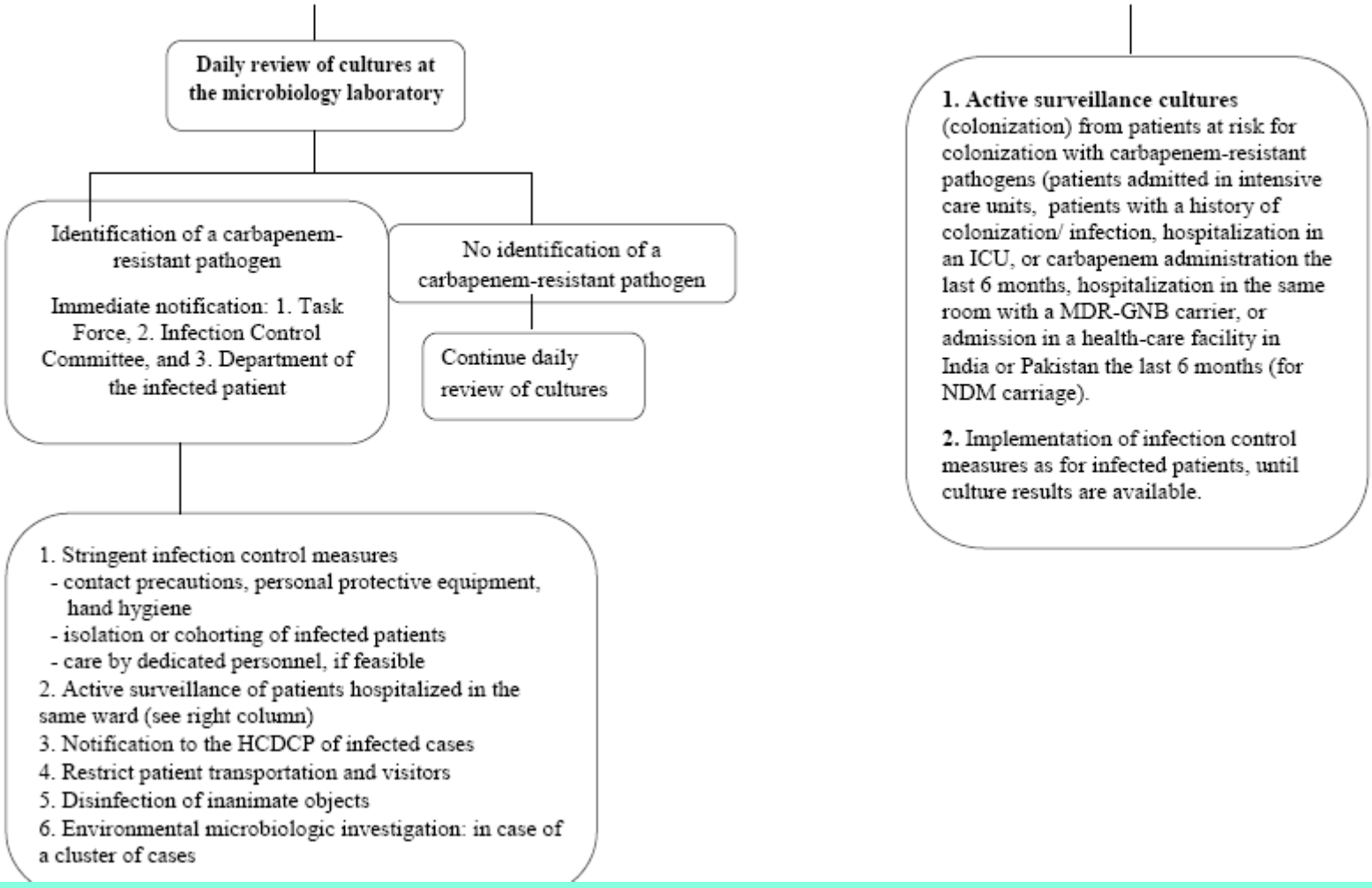
National Action Plan to Combat Infections due to Multi-Drug Resistant, Gram-Negative Pathogens in Hospitals in Greece 2010 - 2015

- Search and destroy strategy at the hospital level
- Close inspection of the hospitals

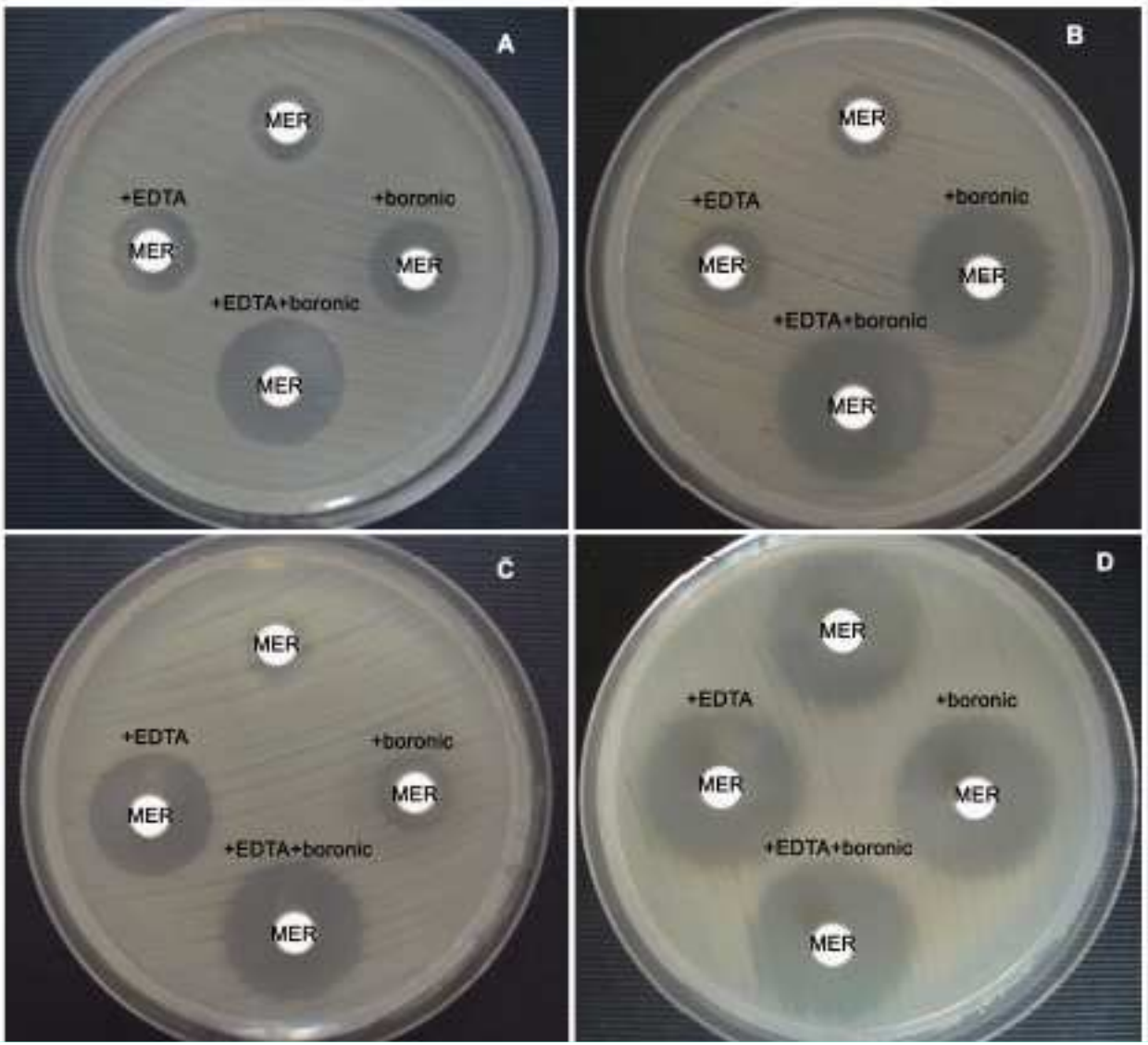
National Action Plan to Combat Infections due to Multi-Drug Resistant, Gram-Negative Pathogens in Hospitals in Greece 2010 - 2015

- Commitment at central level
- Commitment at peripheral level
- Commitment at hospital level

Figure 2. Algorithm of procedures following the detection of a carbapenem-resistant pathogen



Παραδείγματα φαινοτυπικού ελέγχου στο εργαστήρ για παραγωγή MBL (C), KPC (B) ή MBL/KPC (A)



Tsakris et all 2010

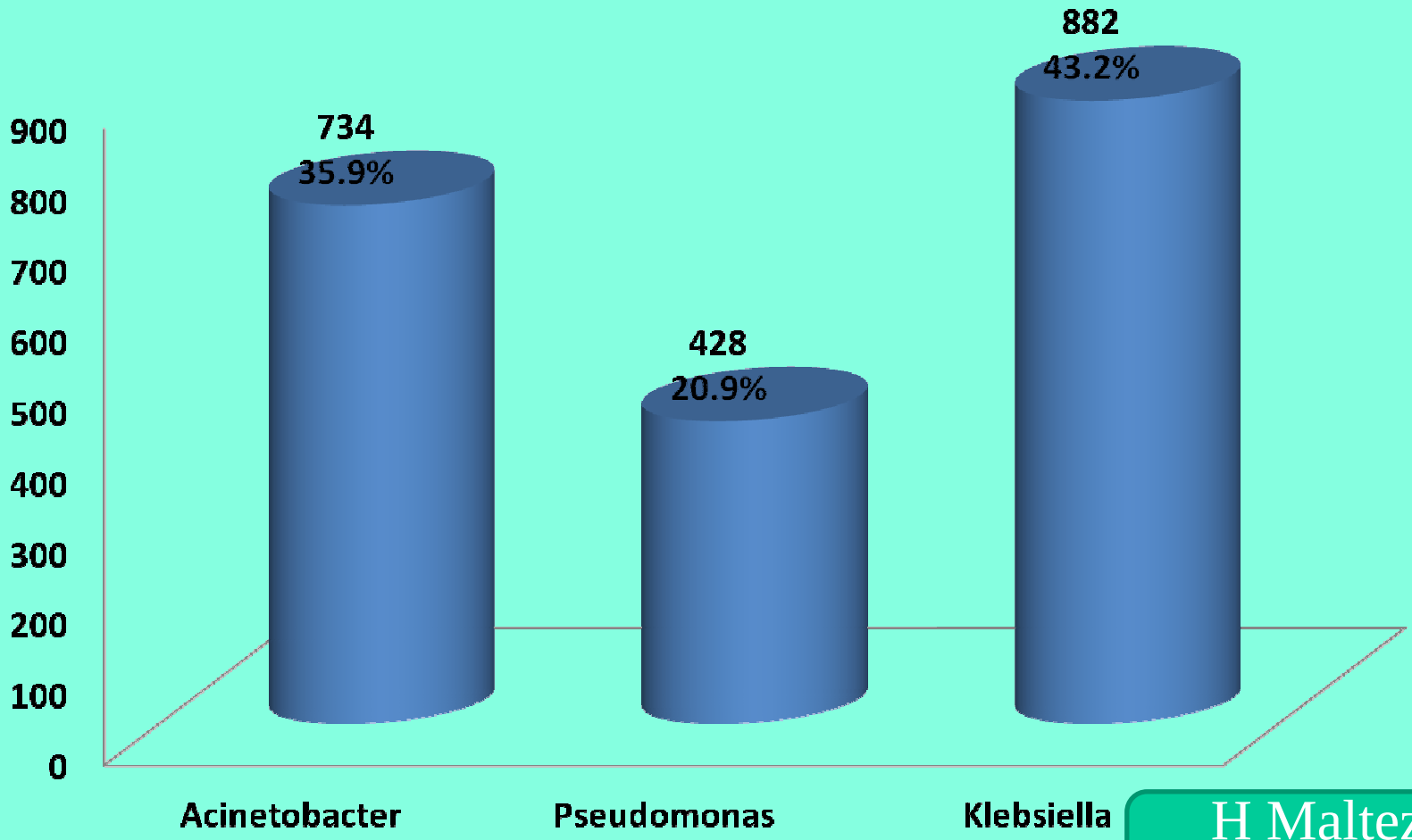
Preliminary Results, Jan – June 2011

Of 128 acute-care hospitals

- 99 hospitals participated in the surveillance system notifying a total of 2,060 cases
- 16 hospitals did not sent reports at all
- 13 hospitals were included in the surveillance system at a later stage

1,926 validated cases from 64 hospitals

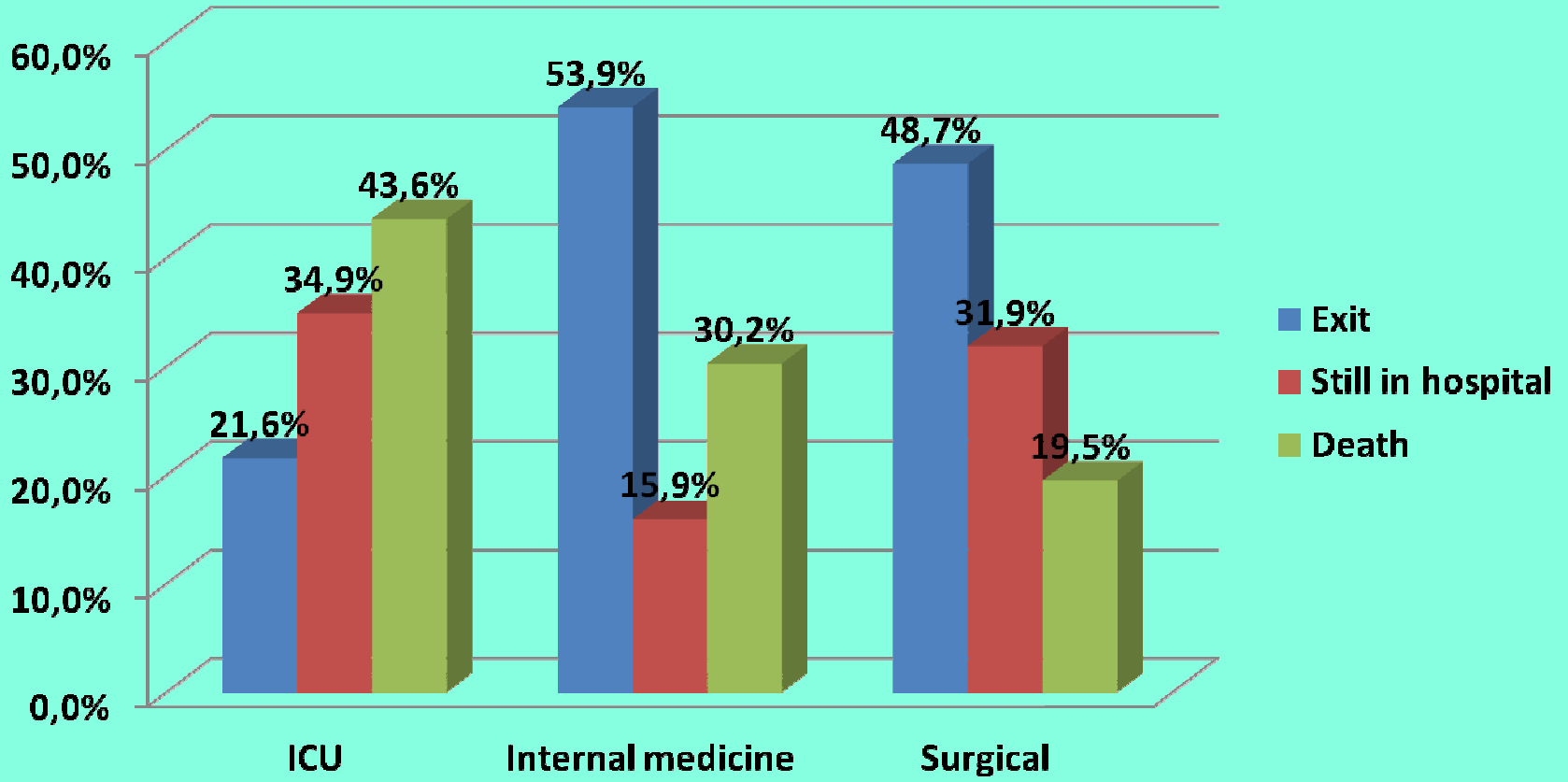
2,044 Isolates in 1,926 Notified Cases



23 Nov 2011

H Maltezou
HCDCP

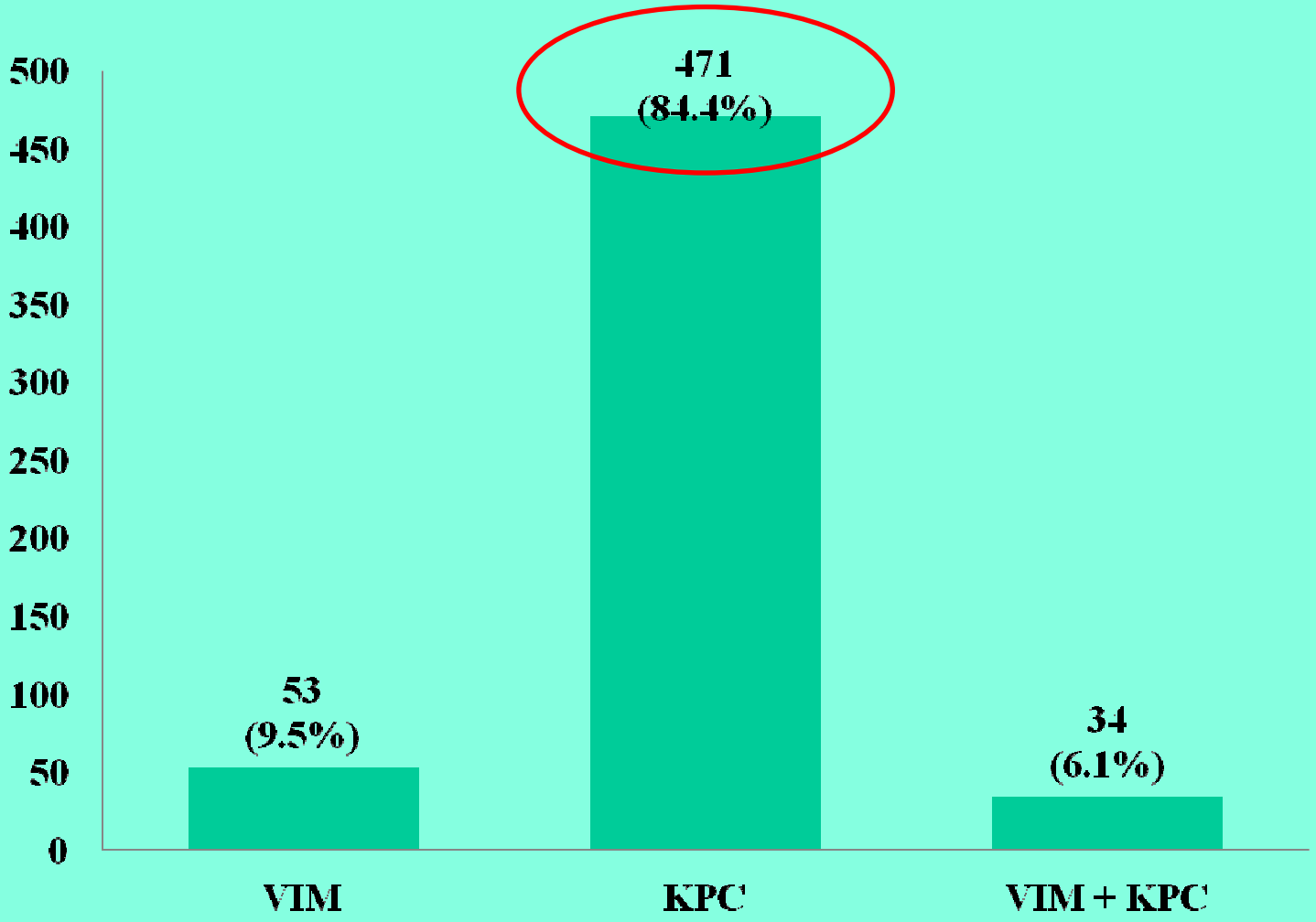
Outcome of Notified Cases by Department*



23 Nov 2011

H Maltezou
HCDCP

Mechanisms of Resistance in *Klebsiella* Isolates



Mean incidence of infections due to MDR-GNB pathogens in patients hospitalized in hospitals by number of beds

	Mean incidence /1000 hospital days
< 200 beds	0.356
201 – 500 beds	0.491
> 500 beds	0.506** p-value=0.03

Stepwise regression analysis to identify hospital characteristics associated with an increased prevalence of MDR-GNB infections

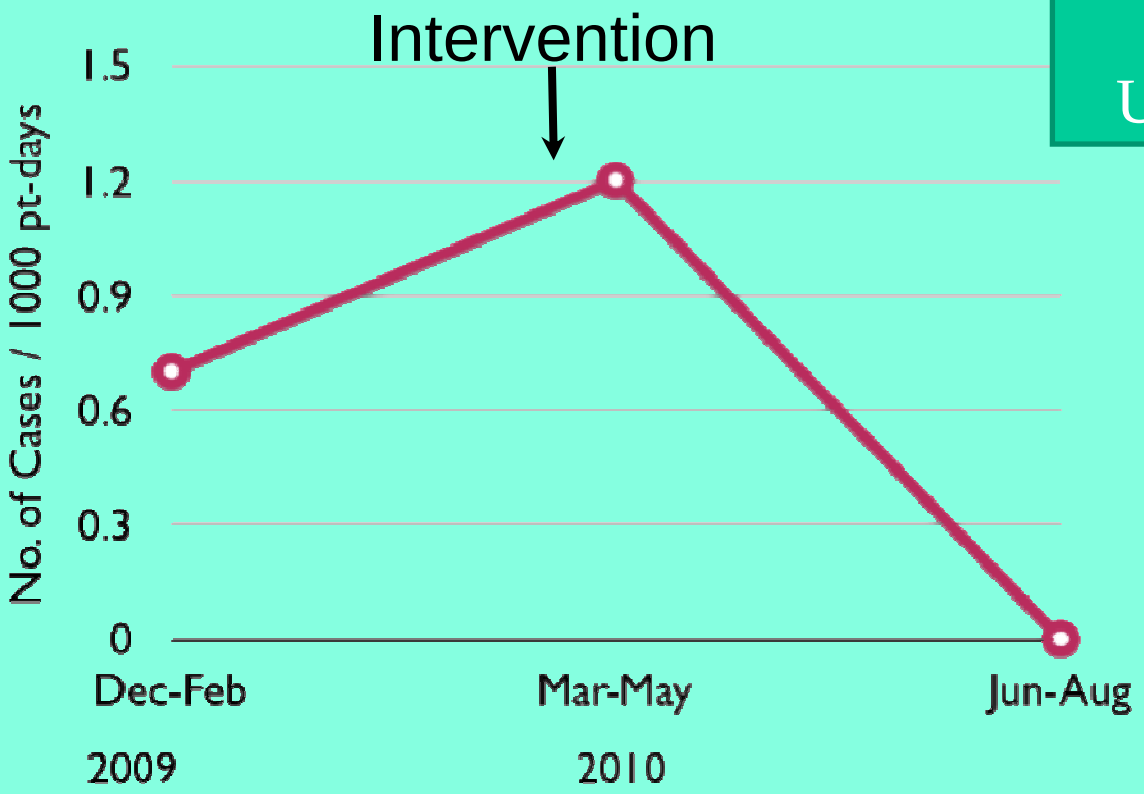
	Mean incidence /1000 hospital days
ICU in the hospital	**0.73**
no ICU in the hospital	**0.21**

p-value < 0.001

Response

The very early very good news!

Incidence of CPKP BSIs in Hematology Clinic



Daikos G
Unpublished

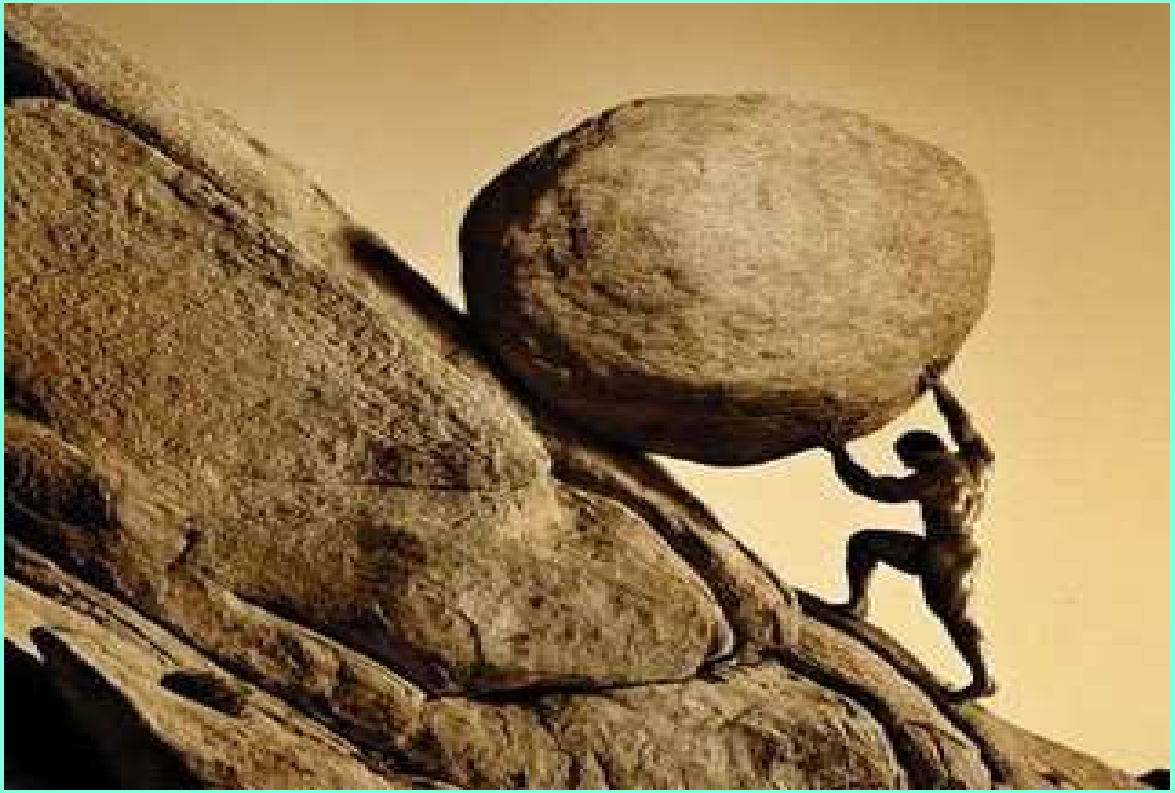
Response

- A public health problem to be confronted must be recognized.
  - By those involved
  - By the society in large
  - By all leaderships

- **Commitment**

With out commitment "*Procrustes* " will be..

With out commitment will be “sisyphus”



miracles **do** happen

Antibiotic resistance in Greece

- Commitment should the driving force
- Time (persistence and patience) is needed

13 November 2008