7ο Πανελλήνιο Συνέδριο
Ελληνικής Εταιρείας Ελέγχου Λοιμώξεων
«Έλεγχος Λοιμώξεων - Ασφάλεια ασθενών: γεφυρώνοντας το χάσμα»
Ξενοδοχείο «Royal Olympic» Αθήνα
6-7 Νοεμβρίου 2014

Τι νεώτερο στη μικροβιακή αντοχή;

Δεδομένα από το σύστημα επιτήρησης της αντοχής WHONET-GREECE (MEDNET)

Παναγιώτα Γιακκούπη
Επιστημονική Συνεργάτης
Τομέας Μικροβιολογίας Δημόσιας Υγείας
Εθνική Σχολή Δημόσιας Υγείας

ΕΘΝΙΚΗ ΣΧΟΛΗ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ
ΥΓΕΙΟΝΟΜΙΚΗ ΣΧΟΛΗ ΑΘΗΝΩΝ 1929-1994
NATIONAL SCHOOL OF PUBLIC HEALTH
ATHENS SCHOOL OF HYGIENE 1929-1994

ΔΕΝ ΕΧΩ ΚΑΝΕΝΑ ΣΥΜΦΕΡΟΝ ΑΠΟ ΤΙΣ ΕΤΑΙΡΕΙΕΣ ΧΟΡΗΓΟΥΣ ΤΗΣ ΕΠΙΣΤΗΜΟΝΙΚΗΣ ΣΥΝΑΝΤΗΣΗΣ

Συστήματα Επιτήρησης Αντοχής στην Ελλάδα

- WHONET (σύνδεση με EARS-NET) 1996 – σήμερα
  - Καταγραφή επιπολασμού (ποσοστά αντοχής)

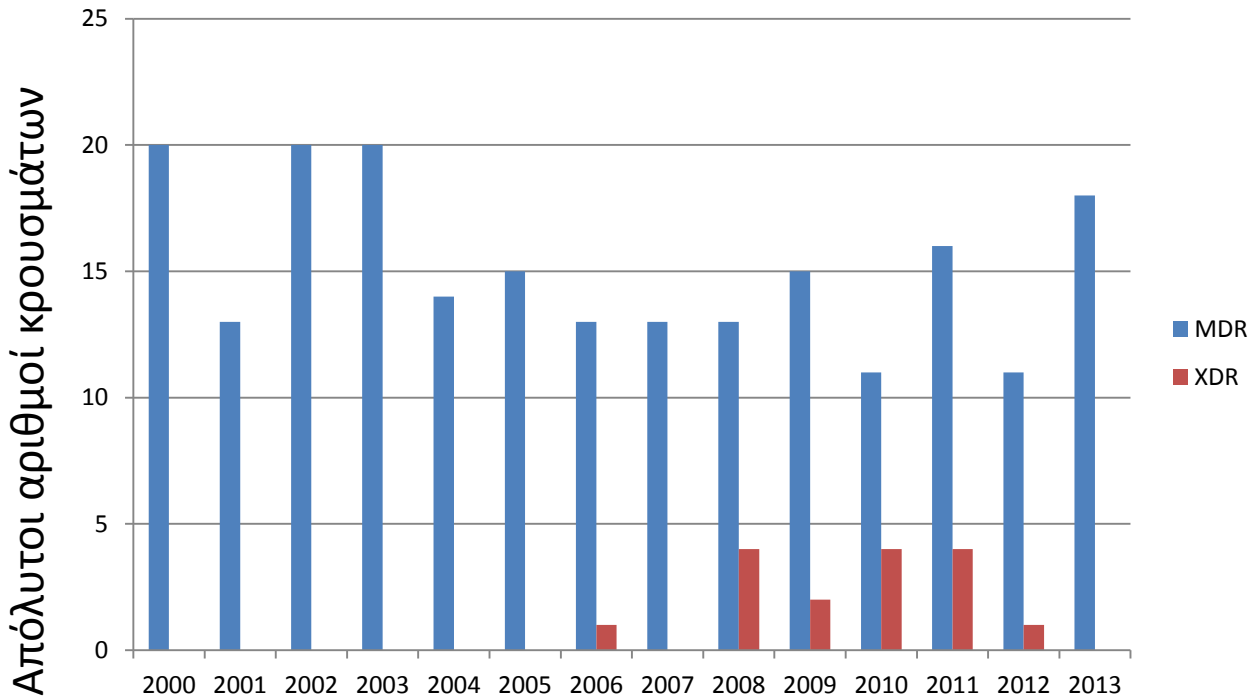
- «Προκρούστης» 2010 – σήμερα
  - Καταγραφή επίπτωσης πολυανθεκτικών
    - *Acinetobacter baumanii*
    - *Pseudomonas aeruginosa*
    - *Klebsiella pneunoniae*

Mycobacterium tuberculosis (Μικροβιολογικά τεκμηριωμένα περιστατικά)

***National Reference Laboratory for Mycobacteria*, NRLM_GR**

Sotiria Chest Diseases Hospital,
152 Mesogion Avenue, Athens 115 27, Greece

Coordinating Director: Dr E.D. Vogiatzakis, MD, PhD



MDR: Resistance to isoniazid and rifampicin

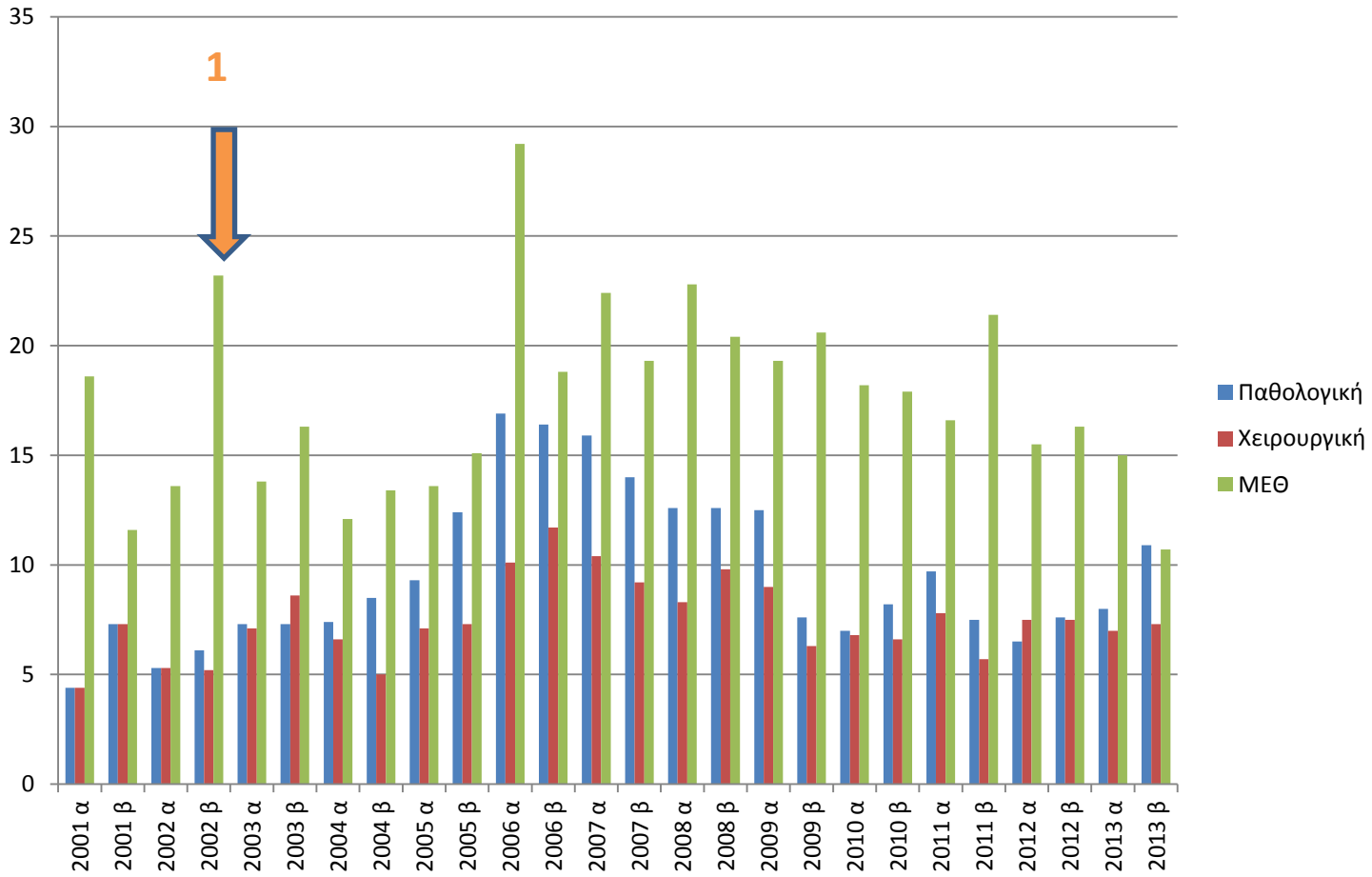
XDR: Resistance to isoniazid, rifampicin, quinolones PLUS amikacin OR kanamycin OR capreomycin

ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

Enterococcus spp

% resistance to vancomycin

All clinical specimens



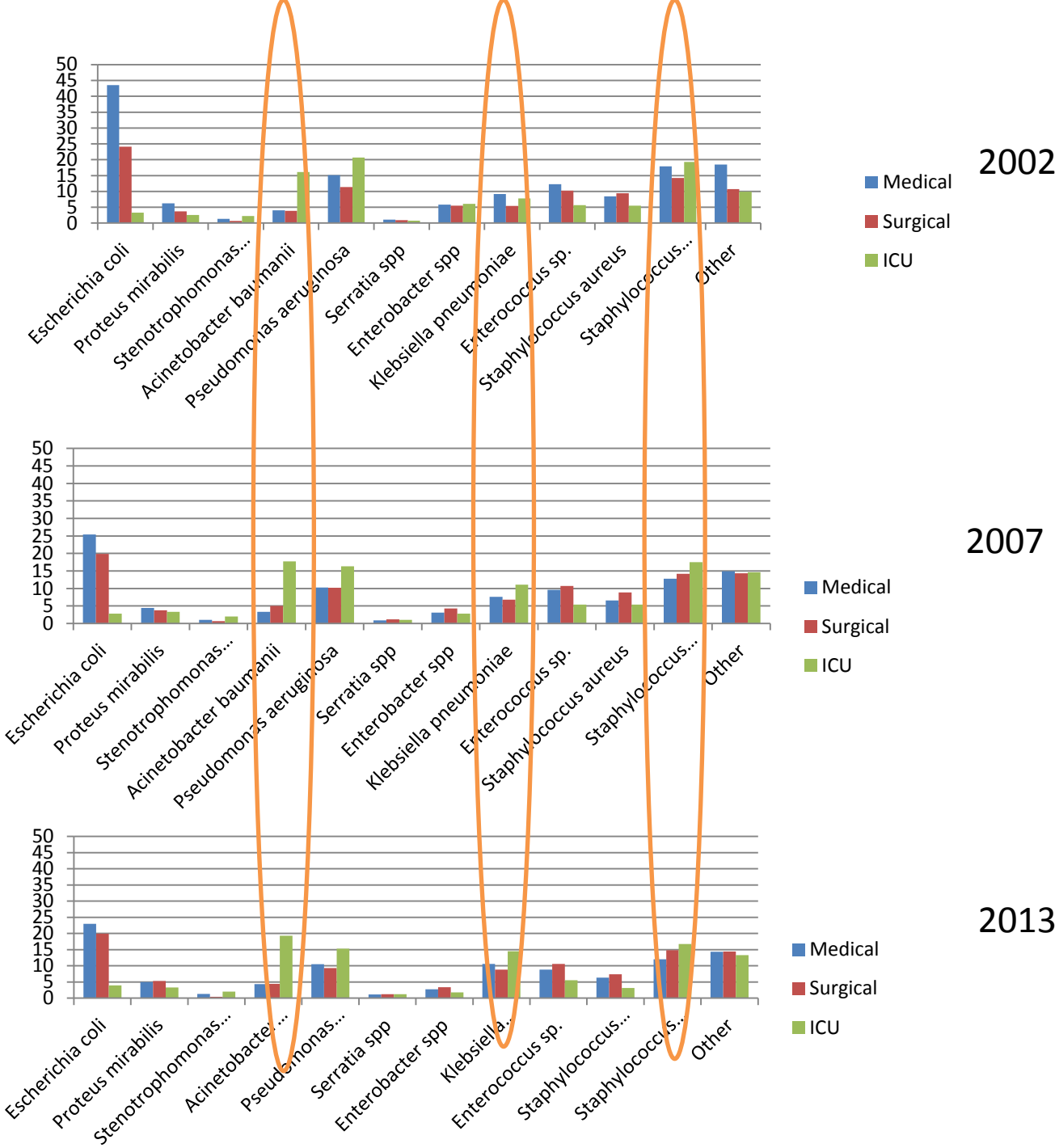
ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

1. J Clin Microbiol. 2005 Nov;43(11):5796-9.

Epidemiology and molecular analysis of intestinal colonization by vancomycin-resistant enterococci in greek hospitals. (ποσοστό 20%)

Gikas A, Christidou A, Scoulica E, Nikolaidis P, Skoutelis A, Levidiotou S, Kartali S, Maltezos E, Metalidis S, Kioumis J, Haliotis G, Dima S, Roumbelaki M, Papageorgiou N, Kritsotakis EI, Tselentis Y.

Αλλαγή της σχετικής συχνότητας απομόνωσης κάθε βακτηριακού είδους σε όλα τα δείγματα ανά κλινική

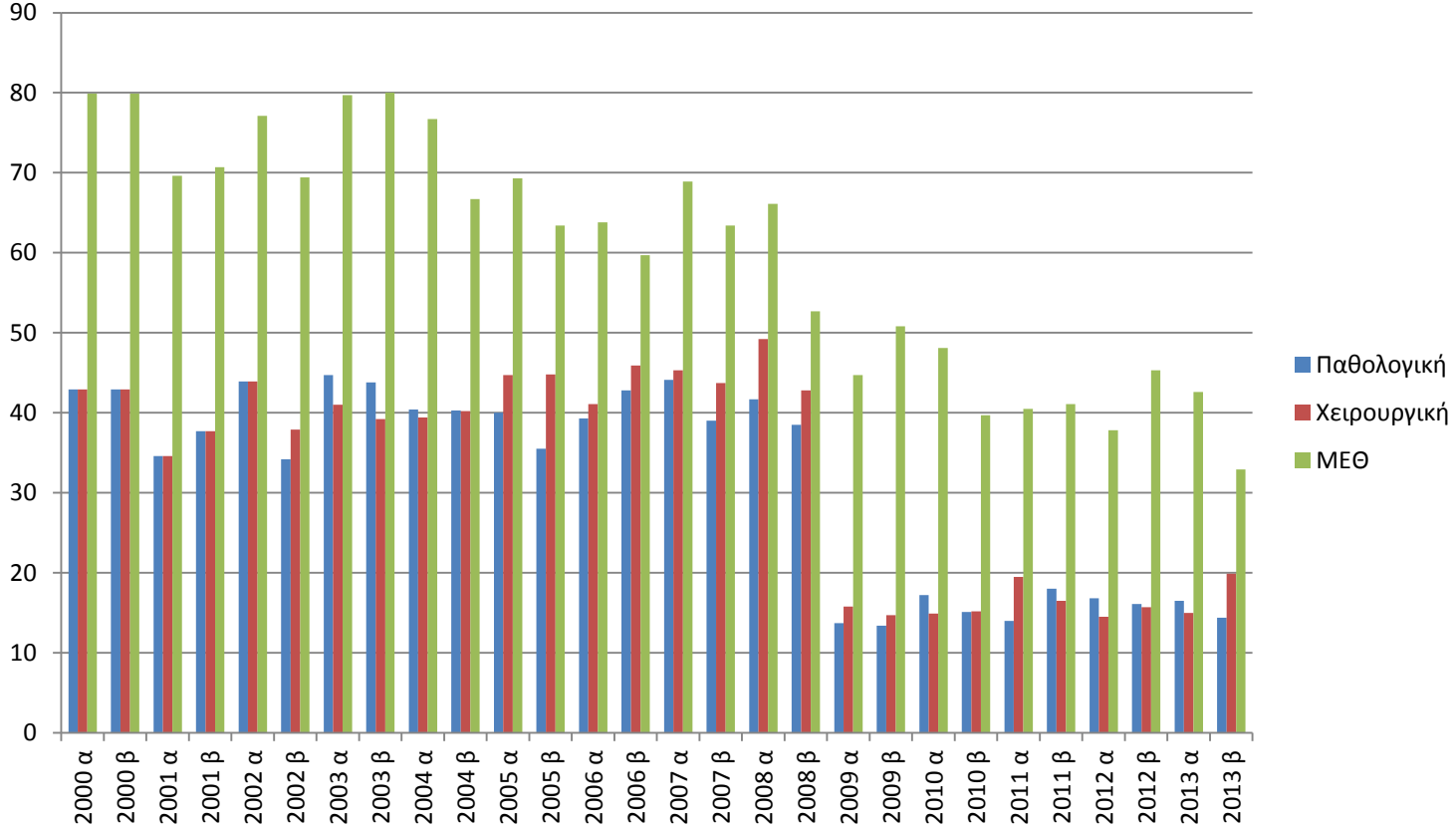


ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

S. aureus

% MRSA

All clinical specimens



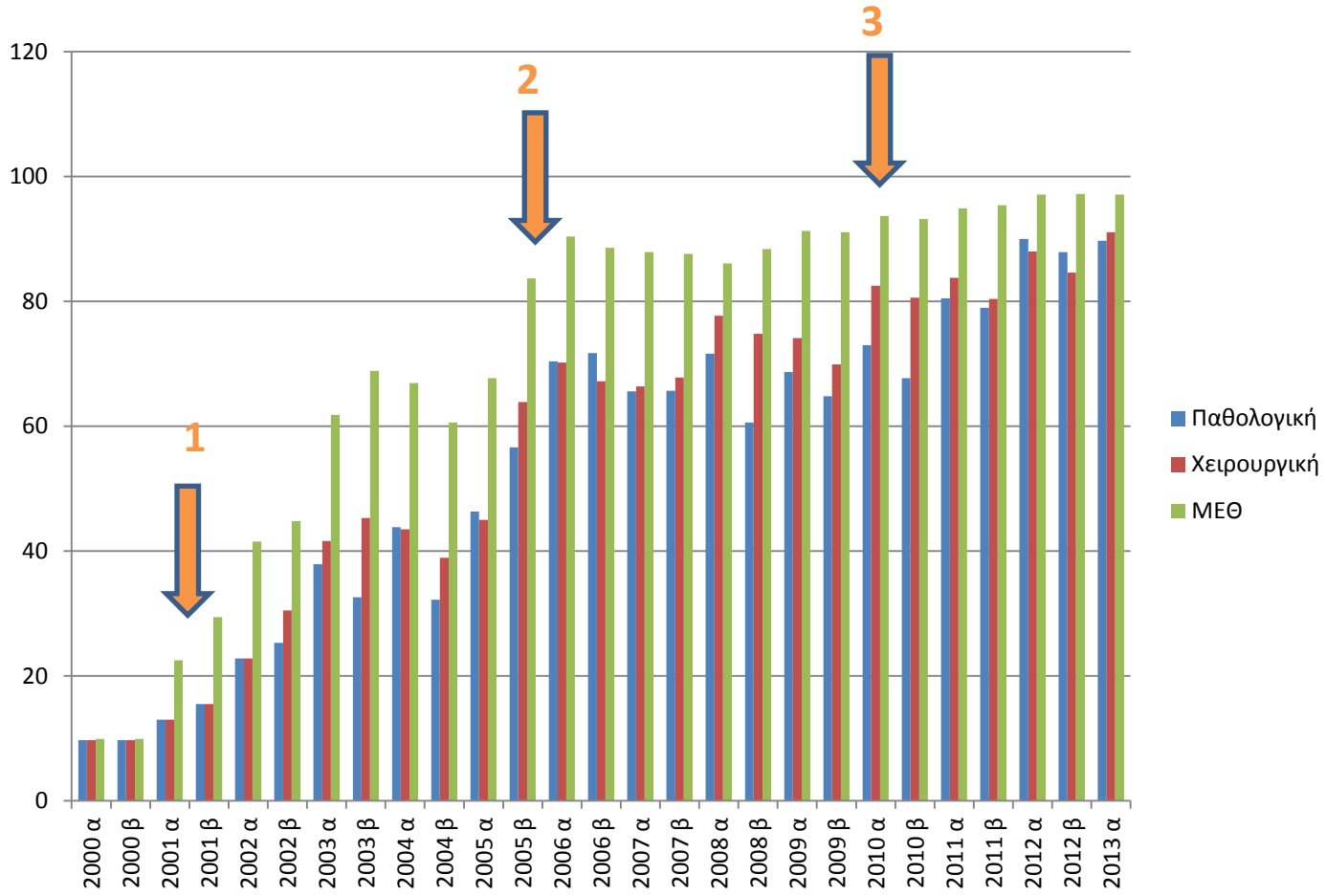
Η μείωση του ποσοστού ΔΕΝ οφείλεται στη μείωση του απόλυτου αριθμού απομονώσεων άλλα στην αύξηση των απομονώσεων των Gram (-) βακτηρίων

ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

Acinetobacter baumanii

Resistant to imipenem (to all β-lactams)

All clinical specimens



ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

Epidemiol. Infect. (2007), **135**, 877–881. © 2006 Cambridge University Press
doi:10.1017/S0950268806007527 Printed in the United Kingdom

1

Αναδρομική μελέτη 2000-2005

SHORT REPORT

Low genetic diversity of the intrinsic OXA-51-like class D carbapenemases among *Acinetobacter baumannii* clinical isolates in Greece

A. IKONOMIDIS[1], S. POURNARAS[1], A. MARKOGIANNAKIS[2], A. N. MANIATIS[1], E. N. MANOLIS[2] AND A. TSAKRIS[3]*

2

Journal of Antimicrobial Chemotherapy (2006) **57**, 557–561
doi:10.1093/jac/dkl004
Advance Access publication 23 January 2006

JAC

Outbreak of multiple clones of imipenem-resistant *Acinetobacter baumannii* isolates expressing OXA-58 carbapenemase in an intensive care unit

S. Pournaras[1], A. Markogiannakis[2], A. Ikonomidis[1], L. Kondyli[3], K. Bethimouti[3], A. N. Maniatis[1], N. J. Legakis[2] and A. Tsakris[2]*

3

RAPID COMMUNICATIONS

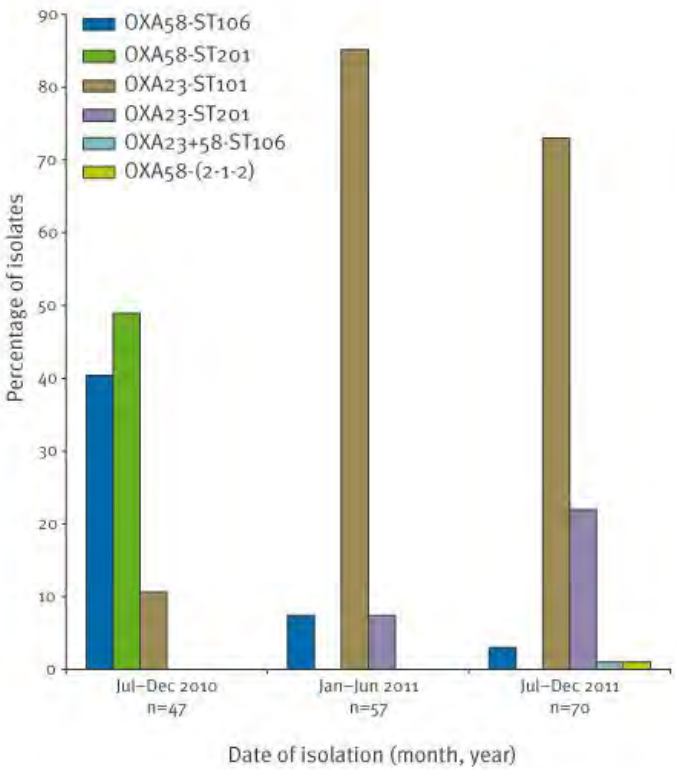
Identification of OXA-23-producing *Acinetobacter baumannii* in Greece, 2010 to 2011

A Liakopoulos[1], V Miriagou[2], E A Katsifas[3], A D Karagouni[3], G L Daikos[4], L S Tzouvelekis[5], E Petinaki (petinaki@med.uth.gr)[1]
1. Department of Microbiology, University Hospital of Larissa, Larissa, Greece
2. Laboratory of Bacteriology, Hellenic Pasteur Institute, Athens, Greece
3. Faculty of Biology, Department of Botany, Microbiology Group, University of Athens, Athens, Greece
4. 1st Department of Propaedeutic Medicine, Medical School, University of Athens, Athens, Greece
5. Department of Microbiology, Medical School, University of Athens, Athens, Greece

Citation style for this article:
Liakopoulos A, Miriagou V, Katsifas EA, Karagouni AD, Daikos GL, Tzouvelekis LS, Petinaki E. Identification of OXA-23-producing Acinetobacter baumannii in Greece, 2010 to 2011.
Euro Surveill. 2012;17(11):pii=20117. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20117

FIGURE

Isolation frequencies of carbapenem-resistant *Acinetobacter baumannii* strains, University Hospital of Larissa, Thessaly, Greece, July 2010–December 2011 (n=174)

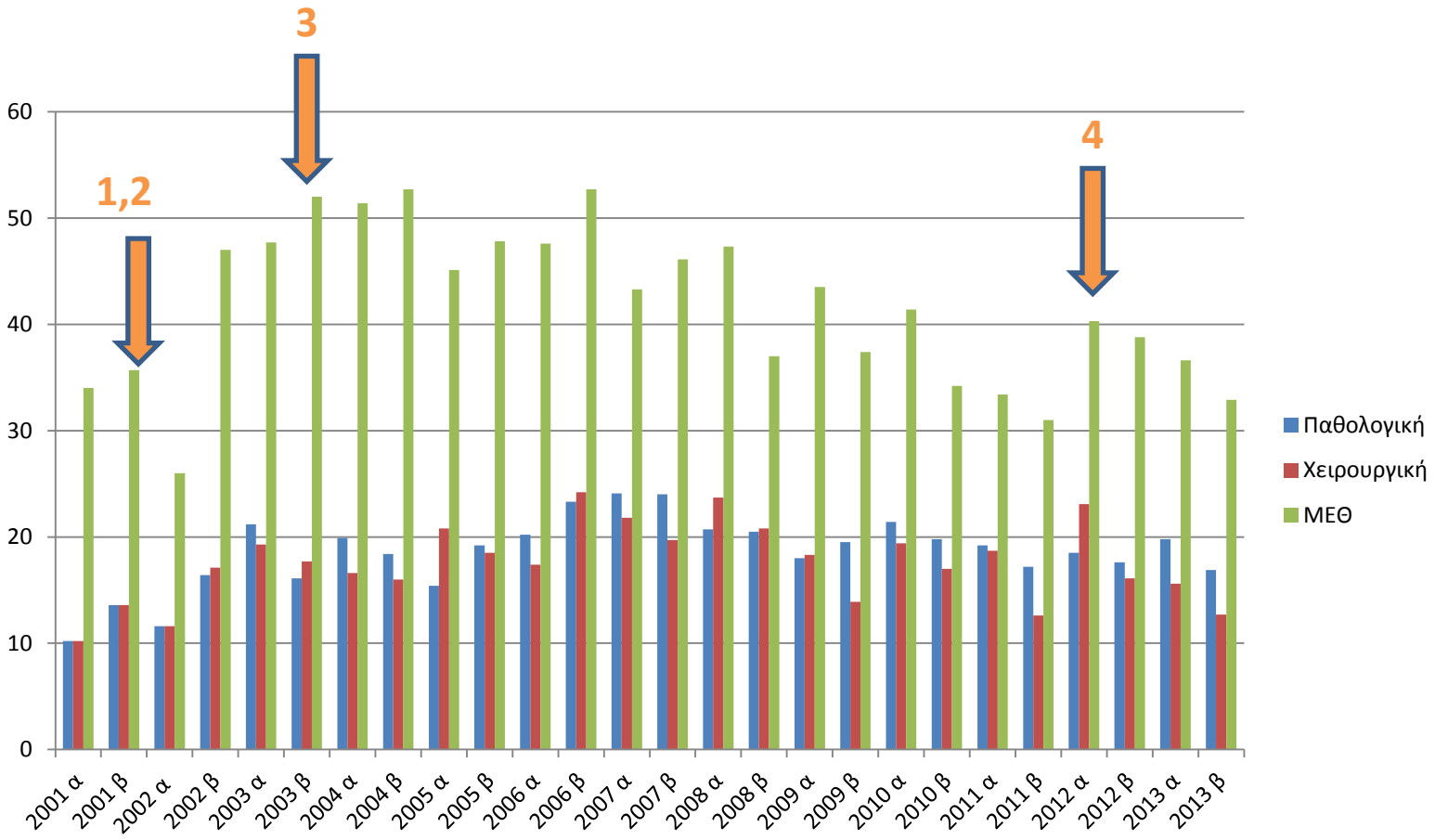


ST: sequence type.

Pseudomonas aeruginosa

ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

% Multiresistance
(resistance to ceftazidime, amikacin and ciprofloxacin)
All clinical specimens



ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

1. J Clin Microbiol. 2000 Mar;38(3):1290-2.
Outbreak of infections caused by Pseudomonas aeruginosa producing VIM-1 carbapenemase in Greece.
Tsakris A, Pournaras S, Woodford N, Palepou MF, Babini GS, Douboyas J, Livermore DM.

1996-1998 : 6 VIM producers /211 isolates IPM-NS

2. JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2003, p. 822–825 Vol. 41, No. 2
Spread of Integron-Associated VIM-Type Metallo-β-Lactamase Genes among Imipenem-Nonsusceptible *Pseudomonas aeruginosa Strains* in Greek Hospitals
P. Giakkoupi, G. Petrikkos, L. S. Tzouvelekis, S. Tsonas, The WHONET GREECE Study Group, N. J. Legakis, and A. C. Vatopoulos
May 2001 : 36 VIM producers /58 isolates IPM-NS

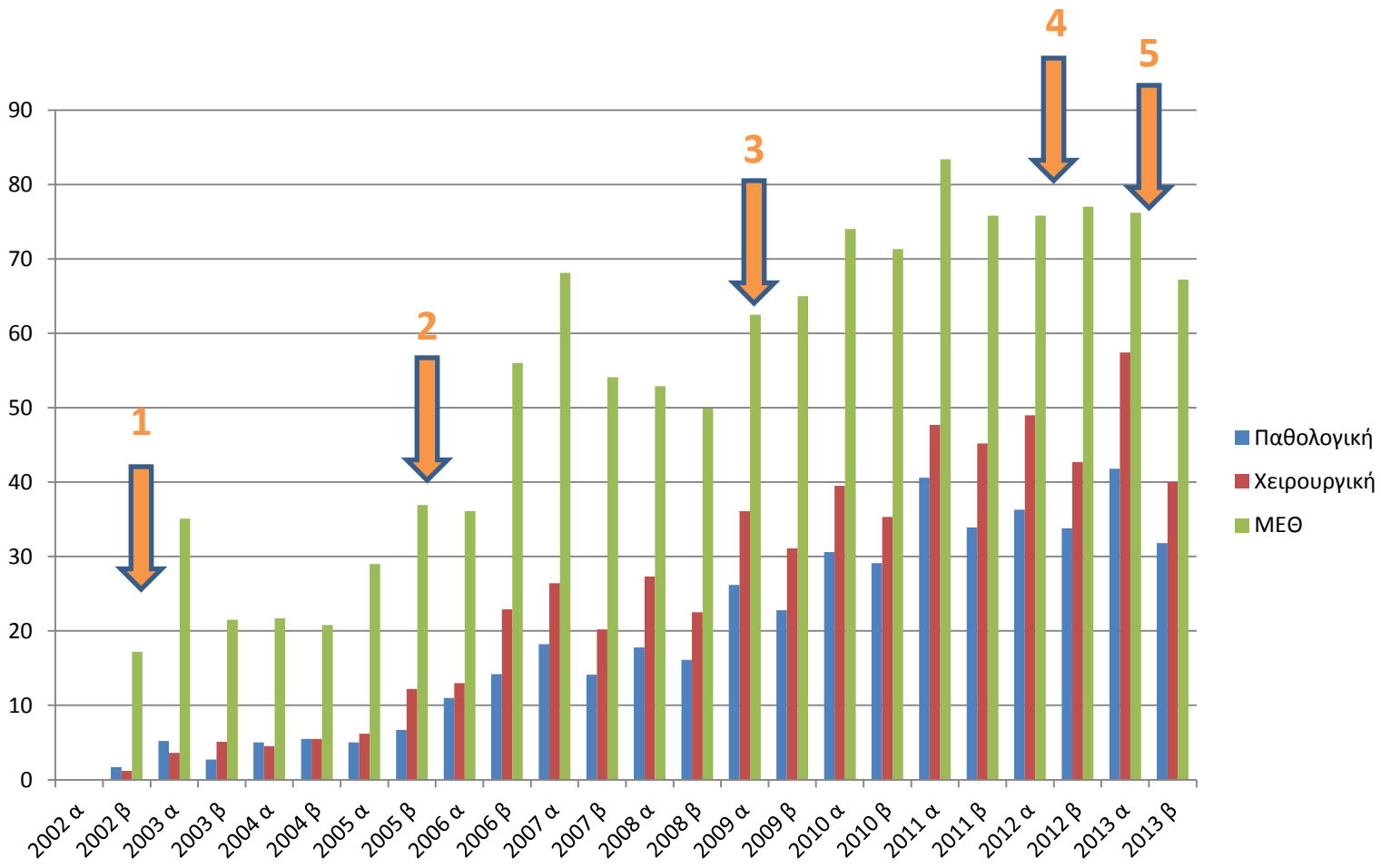
3. J Chemother. 2008 Jun;20(3):307-11.
Epidemiology of metalloenzyme-producing Pseudomonas aeruginosa in a tertiary hospital in Greece.
Zappas S, Giakkoupi P, Vourli S, Hadjichristodoulou C, Polemis M, Tzouvelekis LS, Avlami A, Vatopoulos A, Daikos GL, Petrikkos G.
Jun 2002-Jun 2003: 32 VIM producers /112 isolates IPM-NS

4. J Clin Microbiol. 2013 Feb;51(2):665-8. **2010-2011: 49 VIM producers/148 IPM-NS**
Spread of multidrug-resistant Pseudomonas aeruginosa clones in a university hospital.
Koutsogiannou M, Drougka E, Liakopoulos A, Jelastopulu E, Petinaki E, Anastassiou ED, Spiliopoulou I, Christofidou M.
Τα ανθεκτικά isolates επιλέγονται ΜΕΣΑ στη ΜΕΘ και μέσω του αποικισμού των ασθενών διασπείρονται στις υπόλοιπες κλινικές.

Klebsiella pneumoniae

% resistance to imipenem

All clinical specimens



ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

1. J Clin Microbiol. 2003 Aug;41(8):3893-6.

VIM-1 Metallo-beta-lactamase-producing Klebsiella pneumoniae strains in Greek hospitals.

Giakkoupi P, Xanthaki A, Kanelopoulou M, Vlahaki A, Miriagou V, Kontou S, Papafraggas E, Malamou-Lada H, Tzouvelekis LS, Legakis NJ, Vatopoulos AC.

Antimicrob Agents Chemother. 2003 Jan;47(1):395-7.

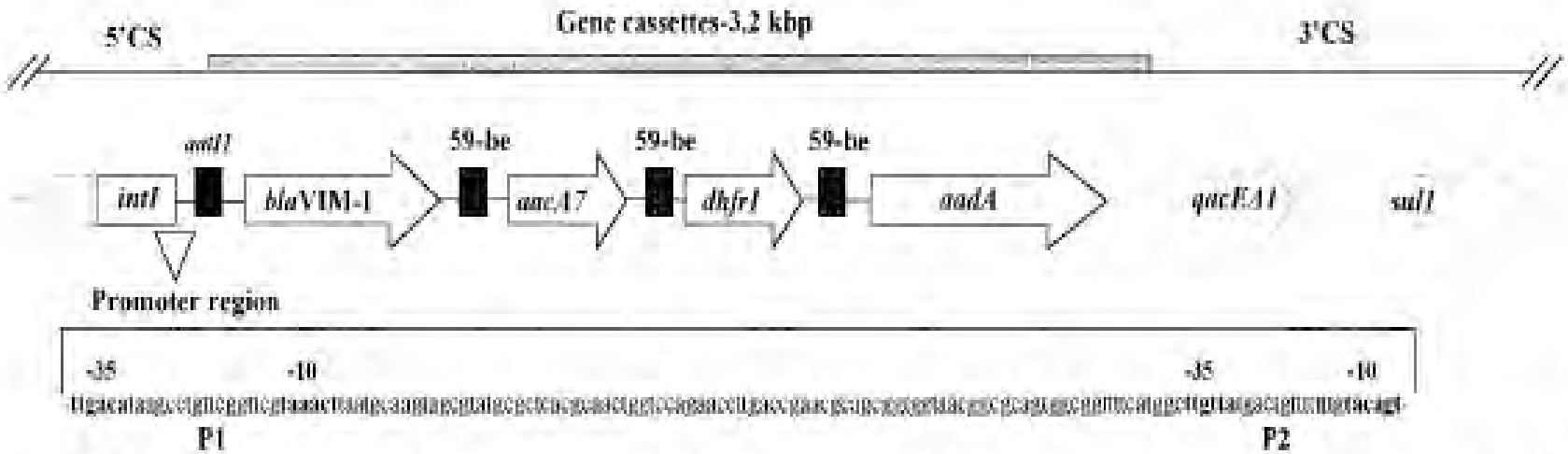


FIG. 1. Schematic presentation of the bla_{VIM-1}-containing class 1 integron carried by plasmid p541. Part of the variable region and the 3' conserved sequence (dashed lines) were postulated on the basis of PCR assays. The sequence of the promoter region is also shown. CS, conserved segment.

1. J Clin Microbiol. 2003 Aug;41(8):3893-6.

VIM-1 Metallo-beta-lactamase-producing Klebsiella pneumoniae strains in Greek hospitals.

Giakkoupi P, Xanthaki A, Kanelopoulou M, Vlahaki A, Miriagou V, Kontou S, Papafraggas E, Malamou-Lada H, Tzouvelekis LS, Legakis NJ, Vatopoulos AC.

2. J Antimicrob Chemother. 2006 Sep;58(3):669-72.

Sources of diversity of carbapenem resistance levels in Klebsiella pneumoniae carrying blaVIM-1.

Loli A, Tzouvelekis LS, Tzelepi E, Carattoli A, Vatopoulos AC, Tassios PT, Miriagou V.

***Conclusions*: A VIM-1-producing strain of *K. pneumoniae* has evolved through OMP alterations and rearrangements in the bla_{VIM-1}-carrying plasmid probably mediated by IS*26*, generating isolates with imipenem MICs ranging from susceptibility to resistance.**

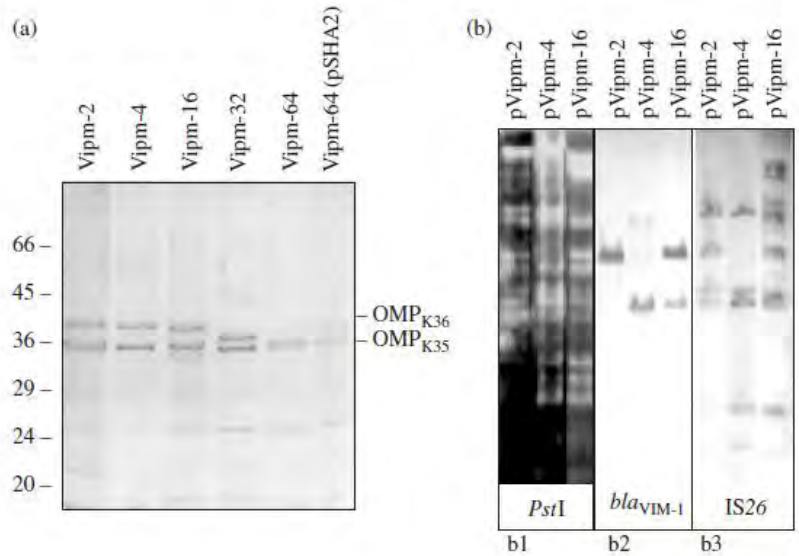


Figure 1. (a) OMP profiles of Vipm-2, Vipm-4, Vipm-16, Vipm-32, Vipm-64 and Vipm-64 (pSHA2). (b) Restriction fragments of pVipm-2, pVipm-4 and pVipm-16 derived after digestion with *Pst*I (b1) and hybridization with bla_{VIM-} (b2) and IS*26*-specific DNA probes (b3).

1. J Clin Microbiol. 2003 Aug;41(8):3893-6.
VIM-1 Metallo-beta-lactamase-producing Klebsiella pneumoniae strains in Greek hospitals.
Giakkoupi P, Xanthaki A, Kanelopoulou M, Vlahaki A, Miriagou V, Kontou S, Papafraggas E, Malamou-Lada H, Tzouvelekis LS, Legakis NJ, Vatopoulos AC.

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Loli A, Tzouvelekis LS, Tzelepi E, Carattoli A, Vatopoulos AC, Tassios PT, Miriagou V.

3. J Infect. 2009 Mar;58(3):213-9.
Outbreak of infections due to KPC-2-producing Klebsiella pneumoniae in a hospital in Crete (Greece).
Maltezou HC, Giakkoupi P, Maragos A, Bolikas M, Raftopoulos V, Papahatzaki H, Vrouhos G, Liakou V, Vatopoulos AC.

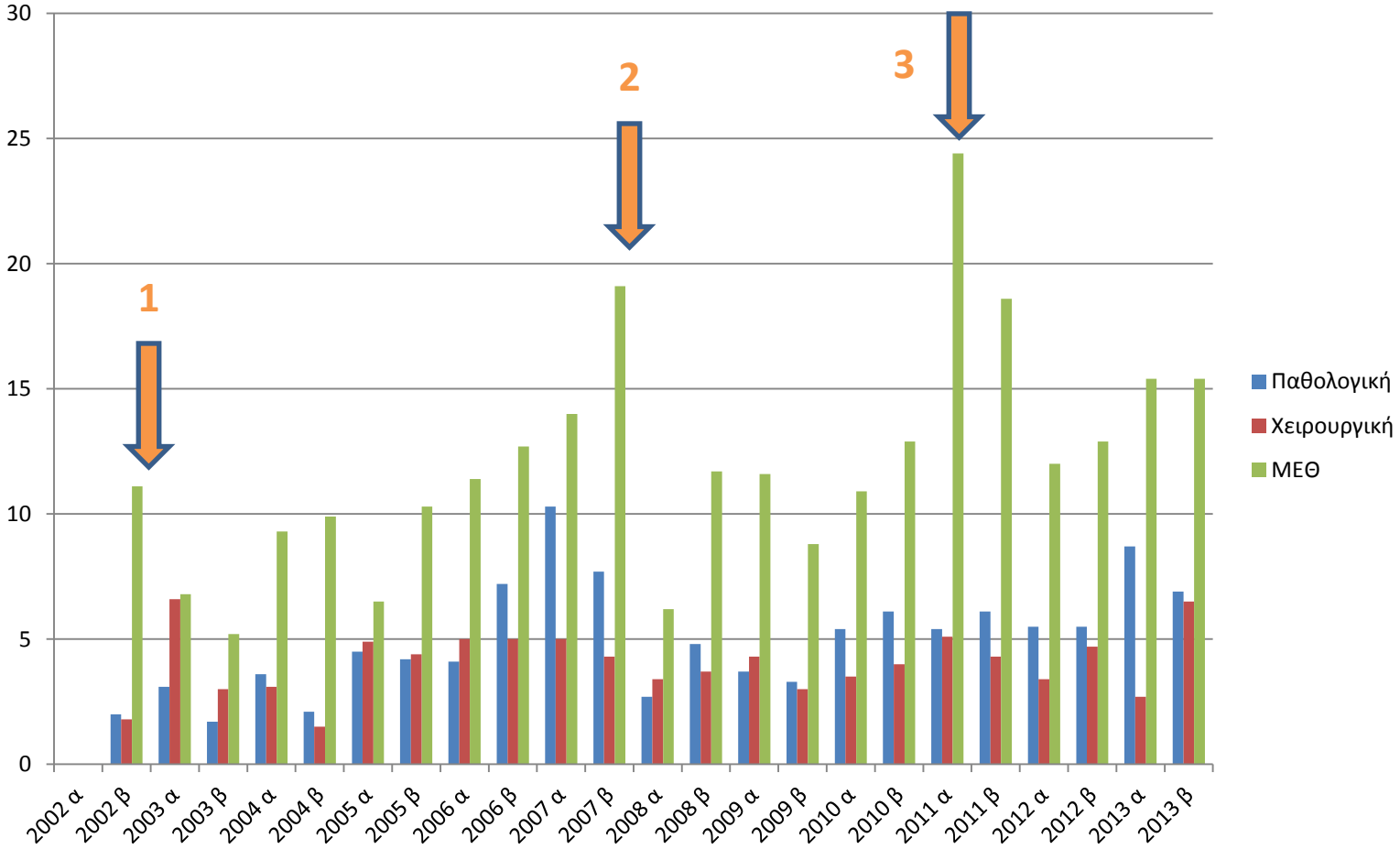
4. J Antimicrob Chemother. 2013 Jan;68(1):84-8.
Outbreak of OXA-48 carbapenemase-producing Klebsiella pneumoniae in Greece involving an ST11 clone.
Voulgari E, Zarkotou O, Ranellou K, Karageorgopoulos DE, Vrioni G, Mamali V, Themeli-Digalaki K, Tsakris A.

5. Diagn Microbiol Infect Dis. 2013 Dec;77(4):382-4.
Emergence of NDM-producing Klebsiella pneumoniae in Greece.
Giakkoupi P, Tryfinopoulou K, Kontopidou F, Tsonou P, Golegou T, Souki H, Tzouvelekis L, Miriagou V, Vatopoulos A.

Enterobacter spp

% resistance to imipenem

All clinical specimens



ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

1. Antimicrob Agents Chemother. 2002 May;46(5):1577-80.
Outbreak of infections caused by Enterobacter cloacae producing the integron-associated beta-lactamase IBC-1 in a neonatal intensive care unit of a Greek hospital.
Kartali G, Tzelepi E, Pournaras S, Kontopoulou C, Kontos F, Sofianou D, Maniatis AN, Tsakris A.

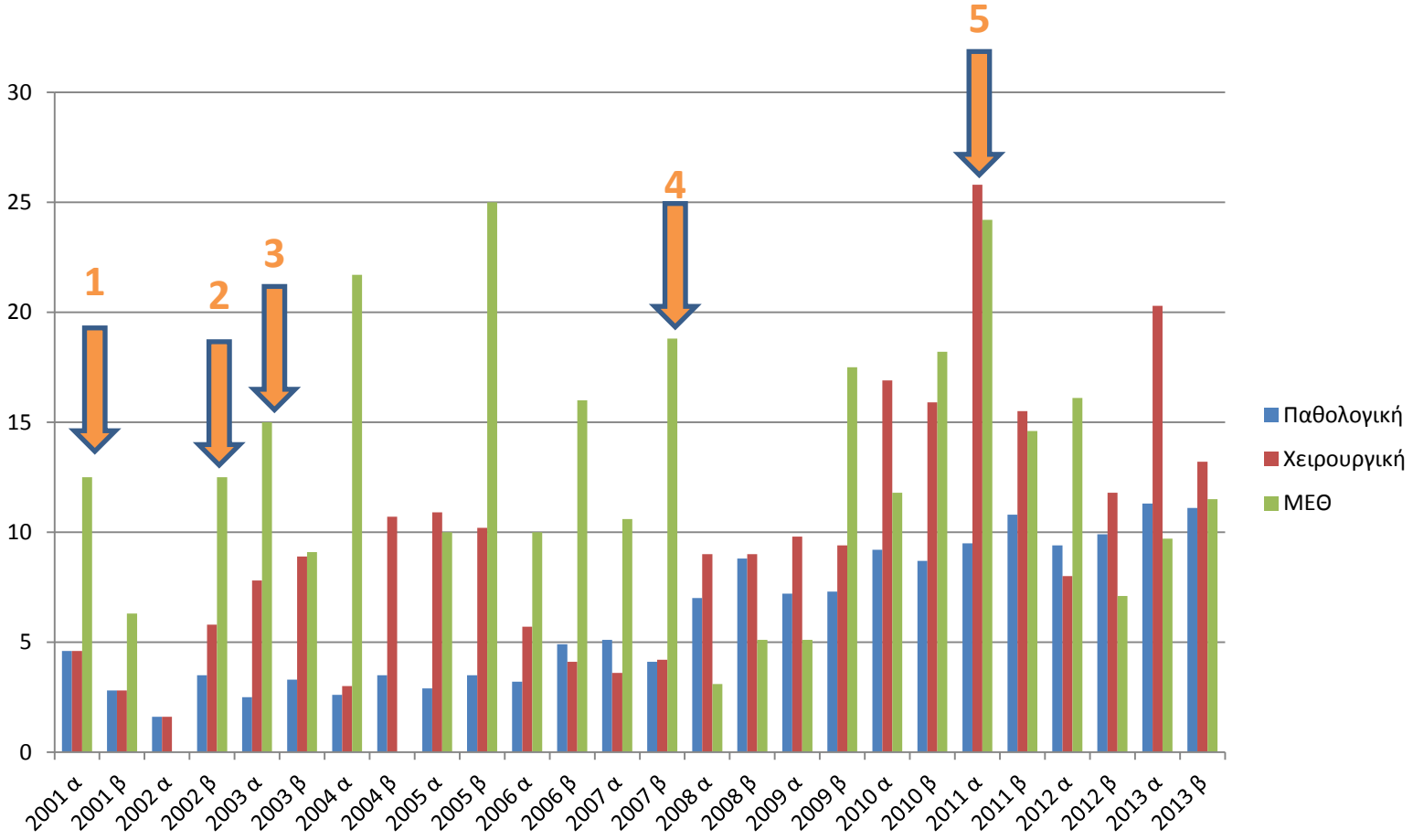
2. Clin Infect Dis. 2008 Mar 15;46(6):847-54.
Clinical experience of serious infections caused by Enterobacteriaceae producing VIM-1 metallo-beta-lactamase in a Greek University Hospital. (αναδρομική για 3 έτη)
Souli M, Kontopidou FV, Papadomichelakis E, Galani I, Armaganidis A, Giamarellou H.

3. J Clin Microbiol. 2012 Jun;50(6):1841-6.
Comparative evaluation of a prototype chromogenic medium (ChromID CARBA) for detecting carbapenemase-producing Enterobacteriaceae in surveillance rectal swabs.
Vrioni G, Daniil I, Voulgari E, Ranellou K, Koumaki V, Ghirardi S, Kimouli M, Zambardi G, Tsakris A. (6 KPC(+) E.cloacae)

Escherichia coli

Results from all hospitals

Blood isolates – Ceftazidime NS



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1. J Antimicrob Chemother. 1990 Nov;26(5):635-48.
Prevalence of a transferable SHV-5 type beta-lactamase in clinical isolates of Klebsiella pneumoniae and Escherichia coli in Greece.
Vatopoulos AC, Philippon A, Tzouvelekis LS, Komninou Z, Legakis NJ.

1. J Antimicrob Chemother. 1998 Oct;42(4):419-25.
Transferable class C beta-lactamases in Escherichia coli strains isolated in Greek hospitals and characterization of two enzyme variants (LAT-3 and LAT-4) closely related to Citrobacter freundii AmpC beta-lactamase.
Gazouli M, Tzouvelekis LS, Vatopoulos AC, Tzelepi E.

2. Microb Drug Resist. 2002 Spring;8(1):35-7.
CTX-M-3 beta-lactamase-producing Escherichia coli from Greece.
Mavroidi A, Tzelepi E, Miriagou V, Gianneli D, Legakis NJ, Tzouvelekis LS.

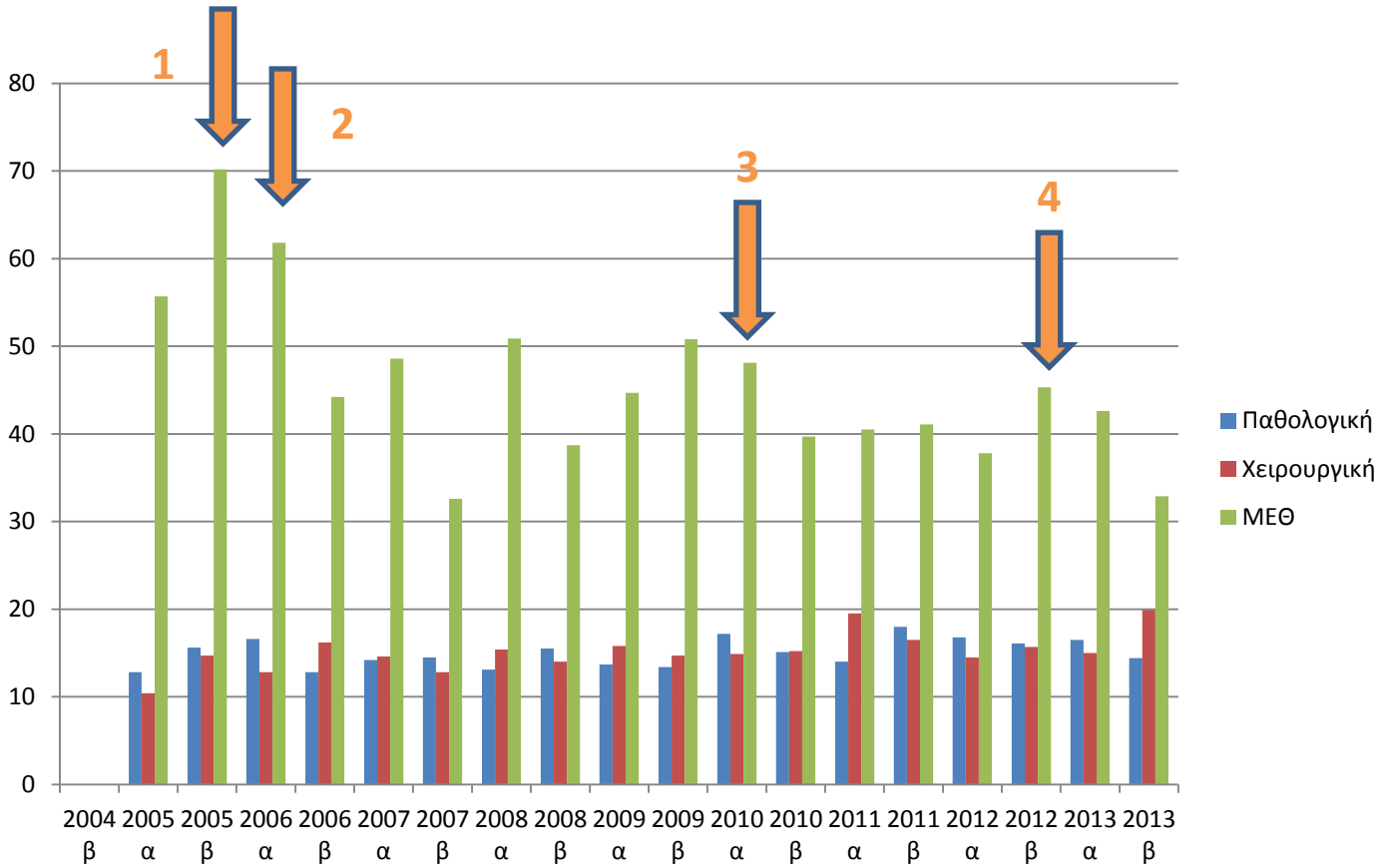
3. Antimicrob Agents Chemother. 2003 Jan;47(1):395-7.
Escherichia coli with a self-transferable, multiresistant plasmid coding for metallo-beta-lactamase VIM-1.
Miriagou V, Tzelepi E, Gianneli D, Tzouvelekis LS.

4. Int J Antimicrob Agents. 2007 May;29(5):598-600.
Detection of CTX-M-15 and CTX-M-33, a novel variant of CTX-M-15, in clinical Escherichia coli isolates in Greece.
Galani I, Souli M, Chryssouli Z, Giamarellou H.

5. Int J Antimicrob Agents. 2012 Mar;39(3):247-50
Emergence of Escherichia coli sequence type 410 (ST410) with KPC-2 β-lactamase.
Mavroidi A, Miriagou V, Malli E, Stefos A, Dalekos GN, Tzouvelekis LS, Petinaki E.

Proteus mirabilis

% Multiresistance
(resistance to ceftazidime, tobramycin and ciprofloxacin)
All clinical specimens



ΔΕΔΟΜΕΝΑ ΑΠΟ http://www.mednet.gr/whonet/

1. Clin Microbiol Infect. 2006 Jul;12(7):691-4.
Emergence of Proteus mirabilis carrying the bla metallo-beta-lactamase gene.
Vourli S, Tsorlini H, Katsifa H, Polemis M, Tzouvelekis LS, Kontodimou A, Vatopoulos AC.

2. Journal of Antimicrobial Chemotherapy, 2007, doi:10.1093/jac/dkl508
Emerging bacterial pathogens: Escherichia coli, Enterobacter aerogenes and Proteus mirabilis clinical isolates harbouring the same transferable plasmid coding for metallo-b-lactamase VIM-1 in Greece
Irene Galani, Maria Souli, Evangelos Koratzanis, George Koratzanis, Zoi Chryssouli and Helen Giamarellou

3. Antimicrob Agents Chemother. 2012 Jul;56(7):4024-5.
Characterization of a transmissible plasmid encoding VEB-1 and VIM-1 in Proteus mirabilis.
Papagiannitsis CC, Miriagou V, Kotsakis SD, Tzelepi E, Vatopoulos AC, Petinaki E, Tzouvelekis LS.

4. J Antimicrob Chemother. 2013 Jan;68(1):97-100.
Complete nucleotide sequence of the large conjugative pTC2 multireplicon plasmid encoding the VIM-1 metallo-β-lactamase.
Drieux L, Decré D, Frangeul L, Arlet G, Jarlier V, Sougakoff W.

ΕΛΛΗΝΙΚΟ ISOLATE

- Η μέτρηση του επιπολασμού δε μπορεί να ανιχνεύσει σε πραγματικό χρόνο την είσοδο ενός νέου μηχανισμού αντοχής στο βακτηριακό πληθυσμό

- Η μέτρηση του επιπολασμού μπορεί να αξιολογήσει την πορεία και την επιτυχία ενός νέου μηχανισμού αντοχής μέσα στο βακτηριακό πληθυσμό και μέσα στο χρόνο

- Η μέτρηση της επίπτωσης είναι ΑΠΑΡΑΙΤΗΤΗ για την κατανόηση της σημαντικότητας της αντοχής των μικροβίων για τη Δημόσια Υγεία

ΣΥΝΕΡΓΕΙΑ ΤΩΝ ΣΥΣΤΗΜΑΤΩΝ ΕΠΙΤΗΡΗΣΗΣ