GRAM NEGATİF BAKTERİLERDE ANTİBİYOTİK DUYARLILIĞI : EPİDEMİYOLOJİ

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Epidemiyolojik Çalışmalar

- ✓ Alexander projesi
- ✓ MYSTIC
  - o OPTAMA
- ✓ EARSS
- ✓ SENTRY
- ✓ HITIT
- ✓ PROTEKT
- ✓ LIBRA

- ✓ Escherichia coli
- ✓ Klebsiella pneumoniae
- ✓ Pseudomonas aeruginosa
- ✓ Acinetobacter baumannii
- ✓ Haemophilus influenzae
- ✓ Moraxella catarrhalis

Alexander Projesi - I

- ✓1992
- ✓Uluslar arası, çok merkezli, boylamsal çalışma
- ✓Solunum sistemi patojenleri
  - o S. pneumoniae
  - o H. İnfluenzae
  - o M. Catarrhalis
- ✓10 merkez

Journal of Antimicrobial Chemotherapy (2003) **52**, 229–246
DOI: 10.1093/jac/dkg321
Advance Access publication 15 July 2003

JAC

The Alexander Project 1998–2000: susceptibility of pathogens isolated from community-acquired respiratory tract infection to commonly used antimicrobial agents

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Received 24 May 2002; returned 1 July 2002; revised 30 April 2003; accepted 7 May 2003

***Objectives*: The Alexander Project is a continuing surveillance study, begun in 1992, examining the susceptibility of pathogens involved in adult community-acquired respiratory tract infections (CARTI) to a range of antimicrobial agents.**

***Materials and methods*: This study tested the susceptibility of isolates of *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* collected between 1998 and 2000 to 23 antimicrobials. Minimum inhibitory concentrations of agents were determined using the broth microdilution method and interpreted according to NCCLS and pharmacokinetic/pharmacodynamic (PK/PD) breakpoints.**

***Results*: In total, 8882 isolates of *S. pneumoniae*, 8523 isolates of *H. influenzae* and 874 isolates of *M. catarrhalis* were collected during 1998–2000 from centres in 26 countries. The world-wide prevalence of penicillin resistance (penicillin MICs ≥ 2 mg/L) in isolates of *S. pneumoniae* was 18.2% over the study period, and the prevalence of macrolide resistance (erythromycin MICs ≥ 1 mg/L) in this pathogen was 24.6%. Over the study period, macrolide resistance exceeded penicillin resistance in 19 of the 26 countries included in the study. Of the non-fluoroquinolone agents, the only oral agents to which over 90% of *S. pneumoniae* isolates were susceptible at both NCCLS and PK/PD breakpoints were amoxicillin (95.1%) and co-amoxiclav (95.5–97.9%). The prevalence of fluoroquinolone-resistant *S. pneumoniae* (ofloxacin MICs ≥ 8 mg/L) was 1.1%. Gemifloxacin was the most potent fluoroquinolone tested against *S. pneumoniae* (99.9% susceptible). In isolates of *H. influenzae*, β-lactamase production was 16.9%, whereas the prevalence of β-lactamase-negative, ampicillin-resistant strains was low (0.2%). β-Lactamase production in *M. catarrhalis* world-wide remained high over the period studied (92.1%). Using PK/PD breakpoints, the most active non-fluoroquinolone agents against *H. influenzae* were ceftriaxone (100% susceptible), cefixime (99.8%) and co-amoxiclav (98.1–99.6%). Co-amoxiclav, cefdinir and cefixime (100%) were the most active β-lactams against *M. catarrhalis*. Both *H. influenzae* and *M. catarrhalis* were highly susceptible to the fluoroquinolones.**

***Conclusions*: These data demonstrate the continued evolution of and geographical variation in bacterial resistance and highlight the need for appropriate prescribing of antimicrobials in CARTI, using agents with adequate activity, based on local susceptibility profiles and PK/PD parameters.**

Keywords: surveillance, antimicrobial resistance, community-acquired respiratory tract infection, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*

Introduction

Streptococcus pneumoniae, *Haemophilus influenzae* and *Moraxella catarrhalis* are the major bacterial pathogens involved in community-acquired respiratory tract infections (CARTI).[1–3] Choice of antimicrobial therapy in CARTI is usually empirical. However, this choice is complicated by the increasing prevalence of resistance amongst these three major bacterial pathogens. In *Haemophilus* and

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†The Alexander Study group participants are listed in the Acknowledgements.

Alexander Projesi - I

- ✓ M. catarrhalis
  - o Fransa
    İngiltere
    Hong Kong
    } % 100 ß-laktamaz (+)
- ✓ H. İnfluenzae
  - o ß – laktamaz İngiltere, Fransa ↑
  - o ABD' de % 24.5
  - o Azitromisin duyarlılığı % 99
  - o Ko-trimaksazol ve doksisiklin duyarlılığı ↓

MYSTIC - I

- ✓ The Meropenem Yearly Susceptibility Test Information Collection
- ✓ Uluslar arası, çok merkezli
- ✓ 1997
- ✓ 46 merkez katılımlı
  - o 29 Avrupa
  - o 14 Amerika
  - o 3 Orta Doğu ve Asya

MYSTIC - II

- ✓1999 – 2008
- ✓27289 izolat
  - o P. aeruginosa (n=439) % 85.4
  - o Enterobacteriaceae (n=1537) %97.3
  - o Acinetobacter (n=127) %45.7
- ✓En fazla antimikrobiyal direnç oranları FLOROKİNOLONLAR !!

Rhomberg PR et al,Diag.Microbiol. Infect. Dis. 2009 Dec;65(4):414-26

OPTAMA

- The Optimising Pharmacodynamic Target Attainment using MYSTIC Antibiogram
- *E.coli, K. pneumoniae, P. aeruginosa, A. baumannii*
- Meropenem, imipenem, seftazidim, sefepim, piperasilin/tazobaktam, siprofloksasin
- Farmakodinamik hedef (Monte Carlo simulasyonu)

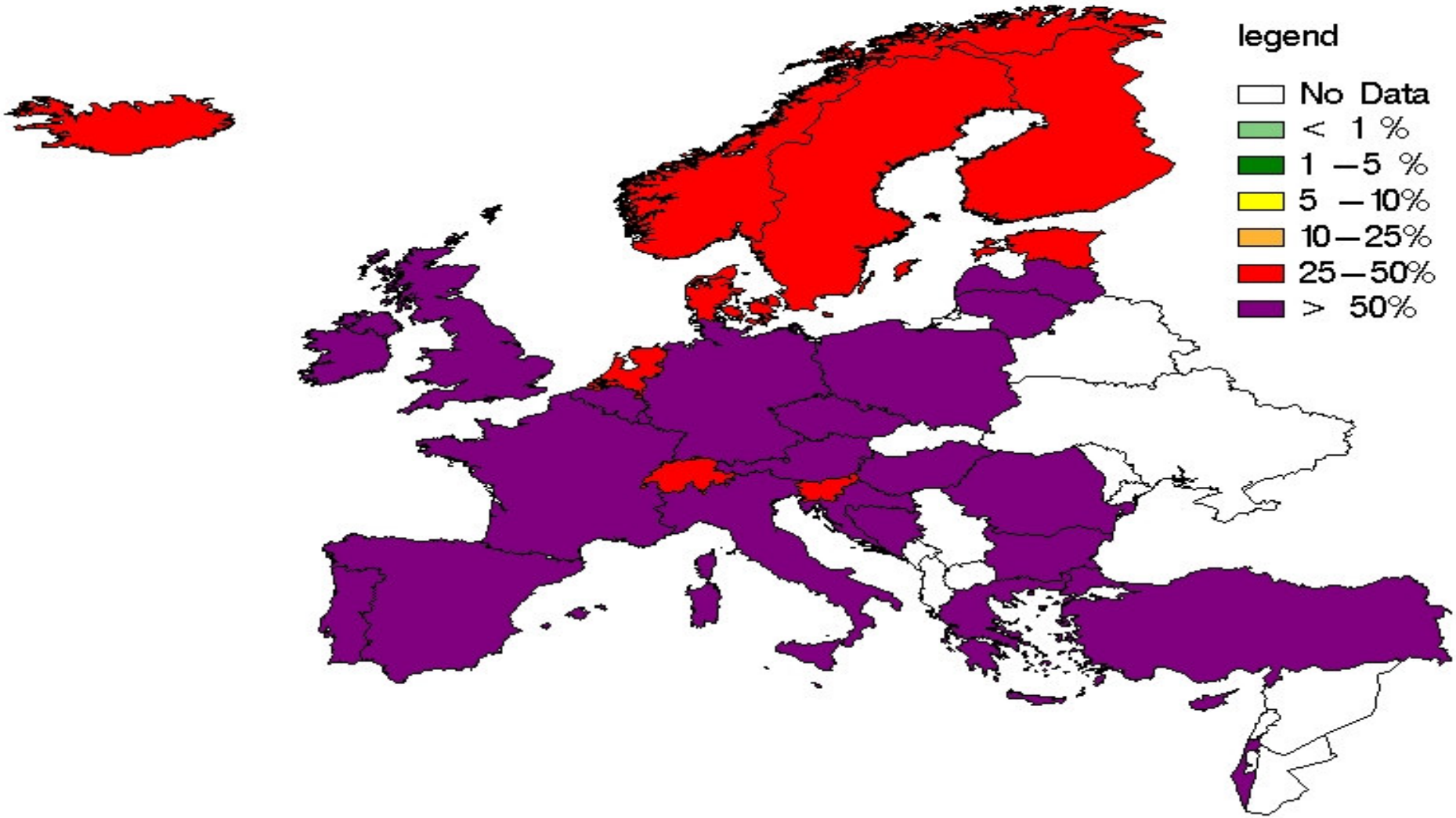
EARSS

- ✓ European Antimicrobial Resistance Surveillance System
- ✓ 1999
- ✓ 33 ülke
- ✓ 1500 hastane
- ✓ 900 laboratuvar
- ✓ 2001 -2008 arası 51341 izolat

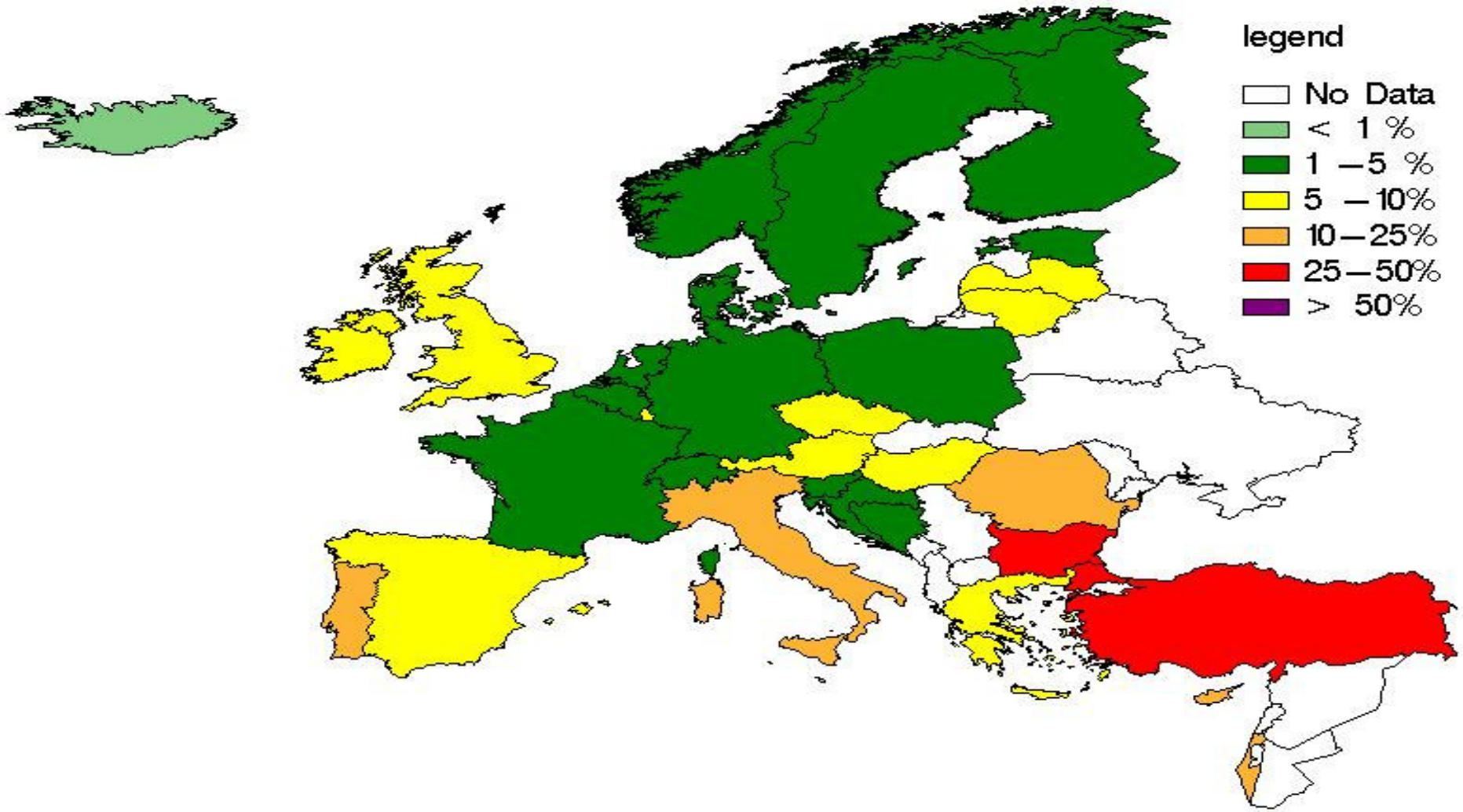
Ocak 2008 – Ağustos 2009 EARSS Bilgi Ağı

Austria	AT	Italy	IT
Belgium	BE	Latvia	LV
Bosnia Herzegovina	BA	Lithuania	LT
Bulgaria	BG	Luxembourg	LU
Croatia	HR	Malta	MT
Cyprus	CY	Netherlands	NL
Czech Republic	CZ	Norway	NO
Denmark	DK	Poland	PL
Estonia	EE	Portugal	PT
Finland	FI	Romania	RO
France	FR	Slovenia	SI
Germany	DE	Spain	ES
Greece	GR	Sweden	SE
Hungary	HU	Switzerland	CH
Iceland	IS	Turkey	TR
Ireland	IE	United Kingdom	UK
Israel	IL		

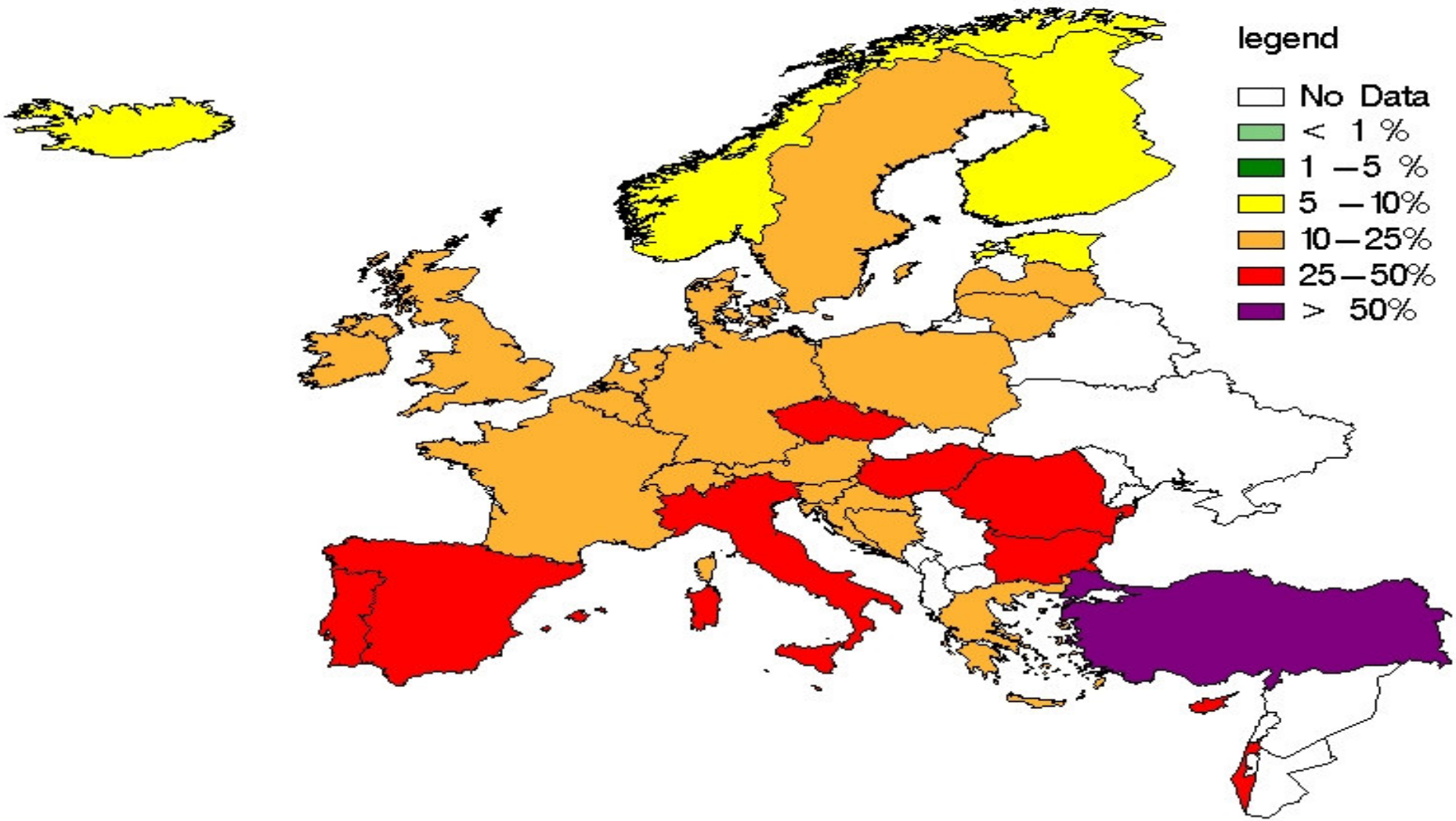
Escherichia coli İzolatlarında 2008 Yılı Aminopenisilin Direnç Oranları



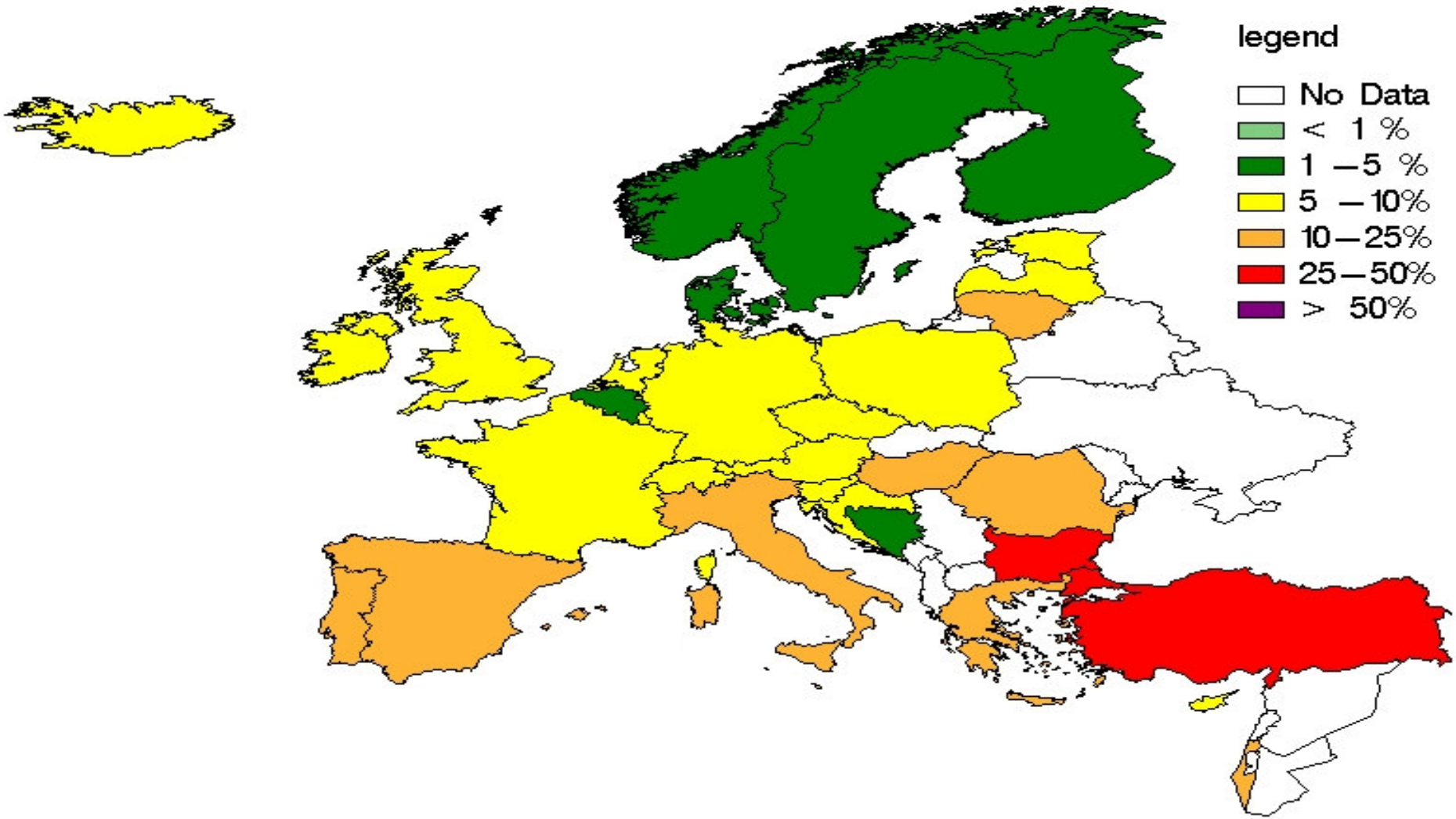
Escherichia coli İzolatlarında 2008 Yılı 3. Kuşak Sefalosporin Direnç Oranları



Escherichia coli İzolatlarında 2008 Yılı Florokinolon Direnç Oranları



Escherichia coli İzolatlarında 2008 Yılı Aminoglikozid Direnç Oranları



İnvaziv *E. coli* İnfeksiyonlarında 2002 – 2009* Direnç Oranları

Time period	Number of labs	Number of isolates	%AMP-R*	%3GC-R*	%CIP-R*	%GEN-R*	%GEN/TOB/ AMK-R*
2002	21	741	62.2	3.0	5.4	2.7	2.9
2003	27	991	61.9	2.5	9.5	3.9	4.3
2004	40	1256	65.0	2.6	12.6	5.7	6.1
2005	42	1445	67.6	4.1	17.3	8.5	8.6
2006	42	1656	70.7	4.2	21.5	7.7	8.6
2007	44	1784	68.3	6.7	22.1	9.9	10.6
2008	42	1924	70.3	7.6	23.3	10.2	11.0
2009**	44	1545	68.3	7.3	22.2	8.5	9.3
2009Q1	44	444	67.8	7.2	20.2	7.2	8.1
2009Q2	44	526	70.5	6.1	21.7	8.2	9.7
2009Q3	44	575	66.8	8.6	24.2	9.8	9.8

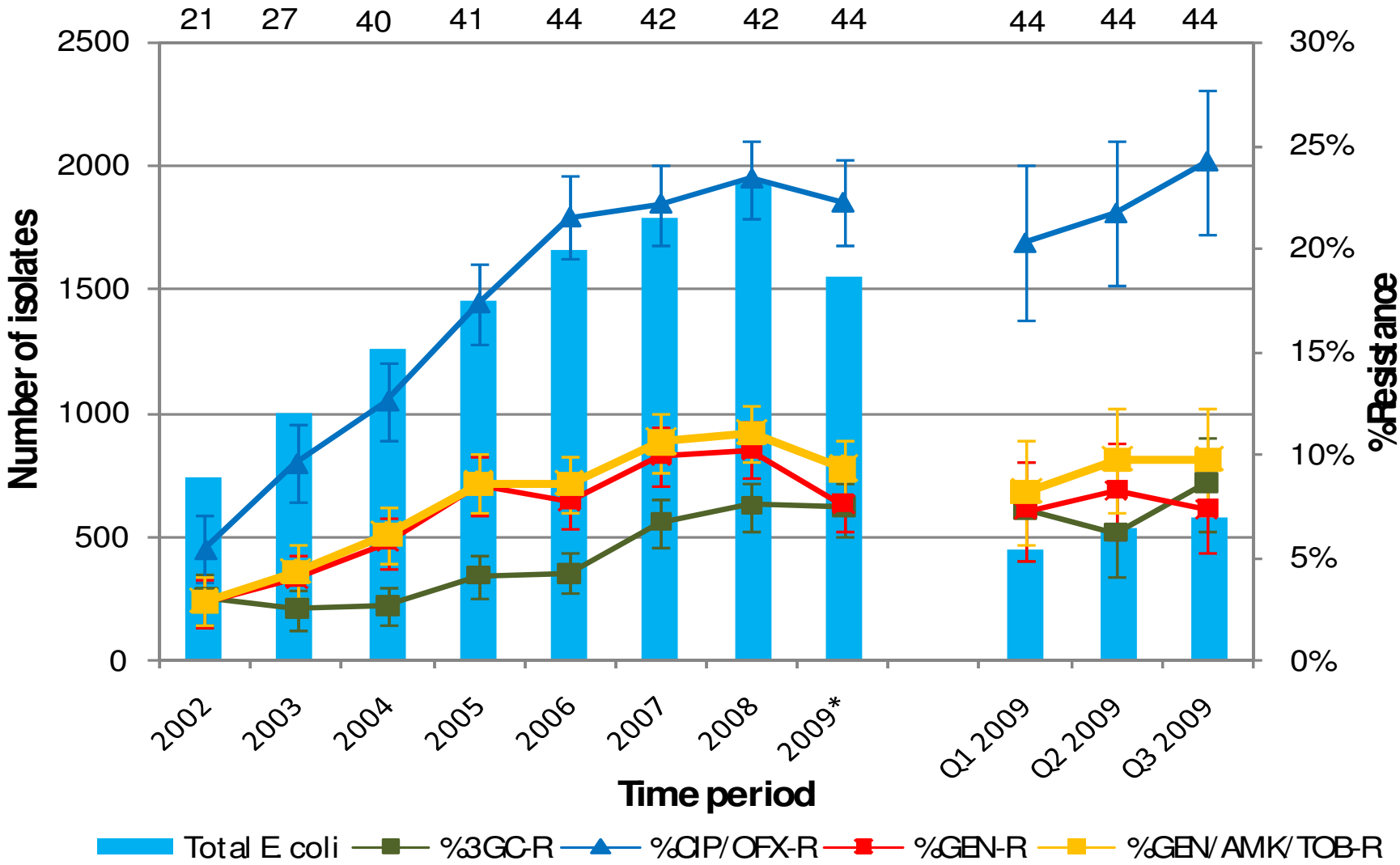
* Tüm suşlar test edilmemiştir;
** Kesin olmayan 2009 son çeyrek verileri

İnvaziv *E. coli* İnfeksiyonlarında 2002 – 2009* ESBL ve ÇİD Oranları

Time period	Number of labs	Number of isolates	%3GC-R*	%ESBL+*	%MDR*
2002	21	741	3.0	1.2	2.4
2003	27	991	2.5	1.3	3.8
2004	40	1256	2.6	1.1	5.6
2005	42	1445	4.1	2.4	7.7
2006	42	1656	4.2	2.5	9.0
2007	44	1784	6.7	4.1	11.4
2008	42	1924	7.6	5.0	12.1
2009**	44	954	7.3	5.5	9.9
2009Q1	44	444	7.2	4.7	8.4
2009Q2	44	526	6.1	4.9	9.8
2009Q3	44	575	8.6	6.7	11.0

* Tüm suşlar test edilmemiştir;
** Kesin olmayan 2009 son çeyrek verileri

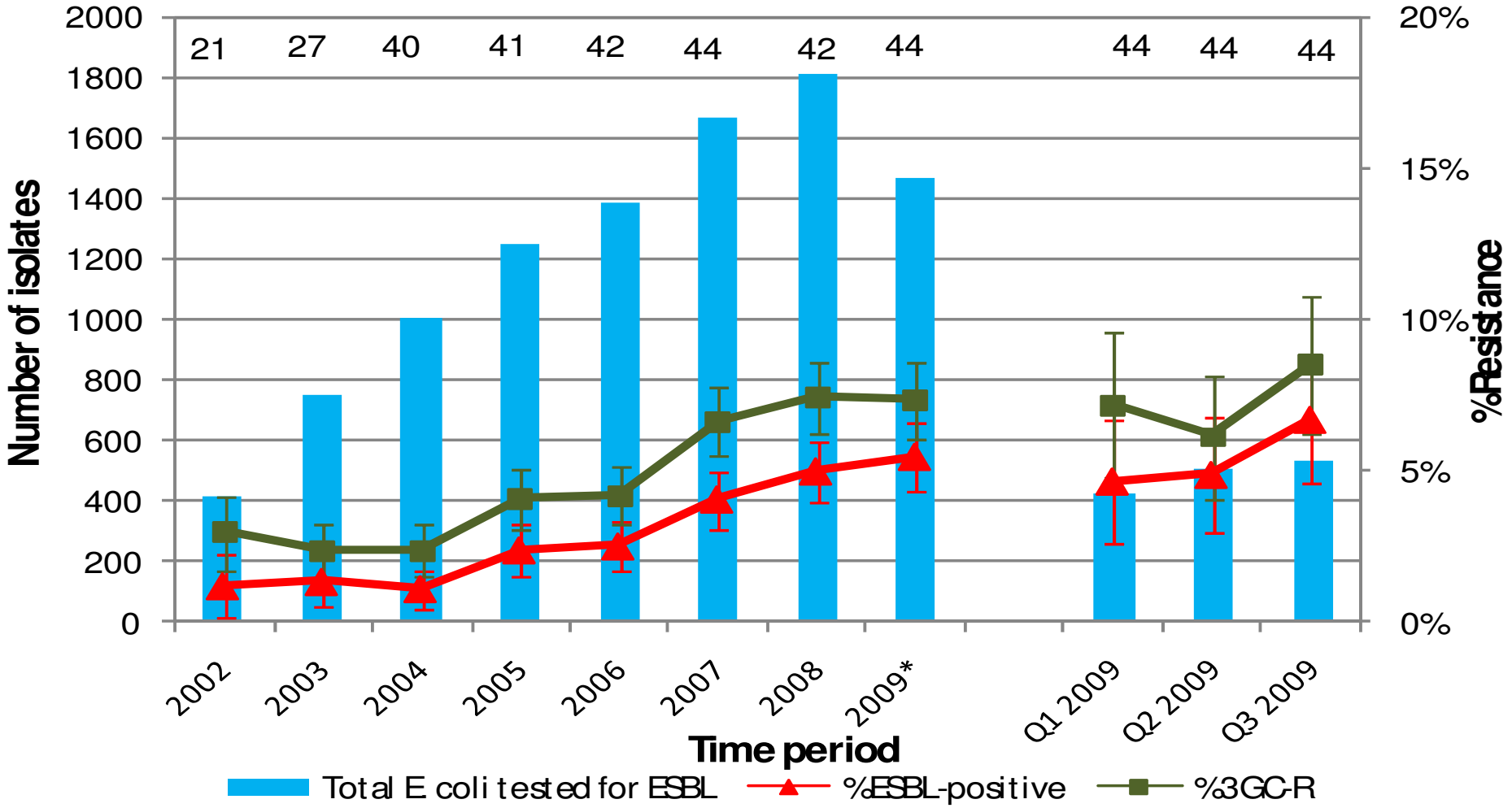
İnvaziv *E. coli* İnfeksiyonlarında 2002 – 2009* Direnç Eğilimleri



* Kesin olmayan 2009 son çeyrek verileri

Yıl ya da çeyreğin sonunda katılan laboratuvar sayıları barlarla gösterilmiştir

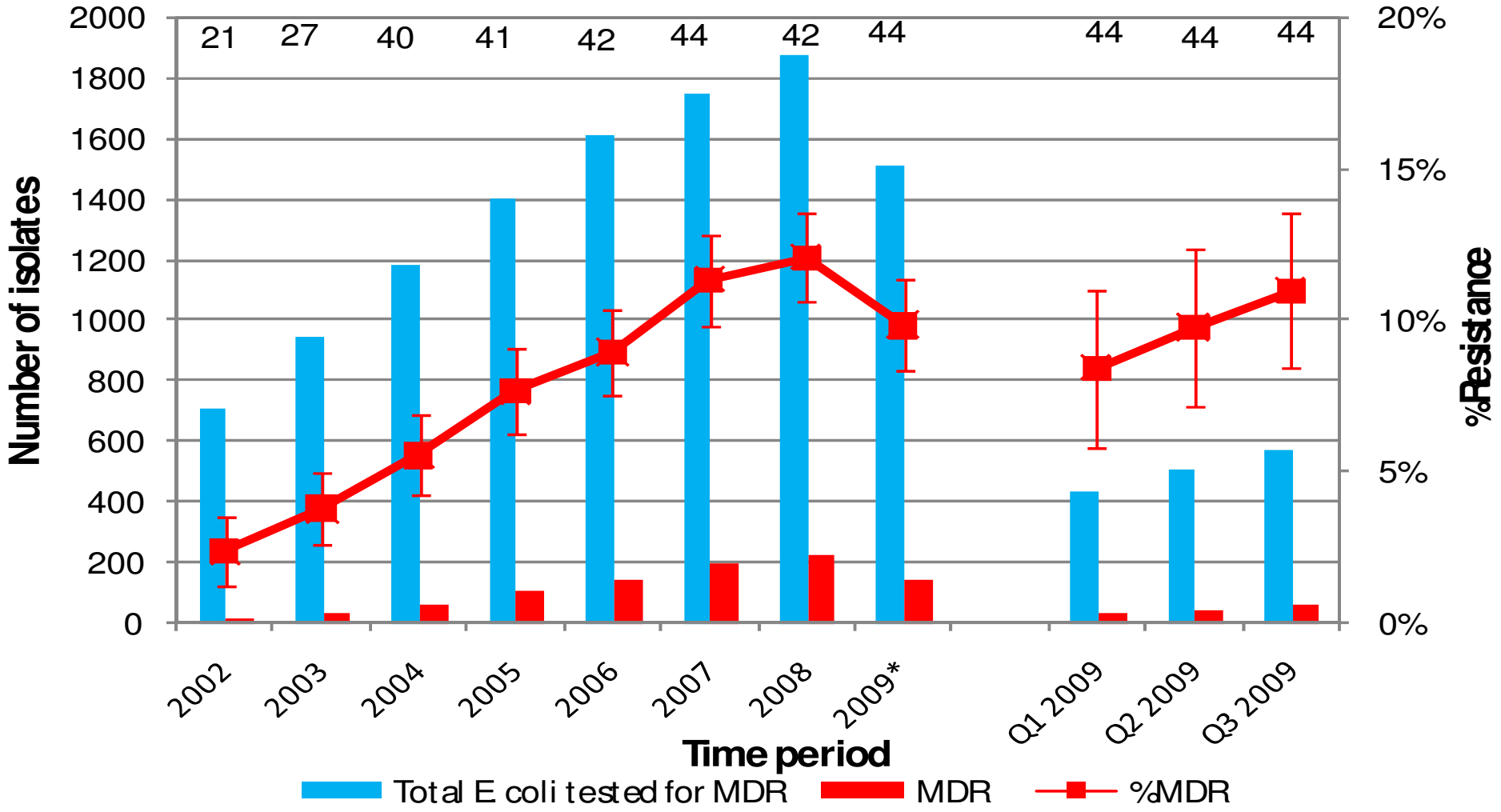
İnvaziv *E. coli* İnfeksiyonlarında 2002 – 2009* Direnç Eğilimleri: 3. Kuşak Sefalosporinler ve ESBL



* Kesin olmayan 2009 son çeyrek verileri

Yıl ya da çeyreğin sonunda katılan laboratuvar sayıları barlarla gösterilmiştir

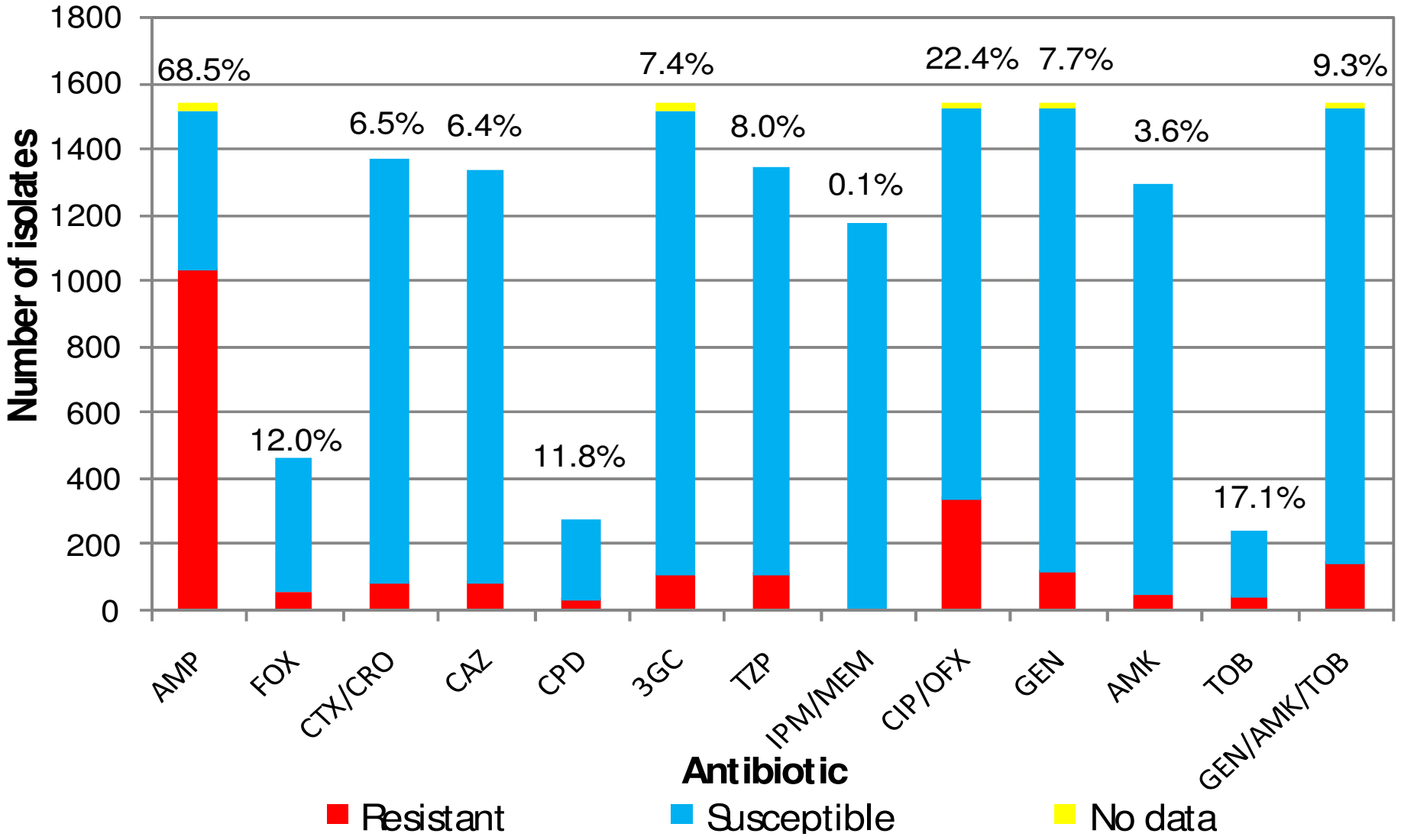
İnvaziv ÇİD *E. coli* eğilimleri, 1999-2009*



* Kesin olmayan 2009 son çeyrek verileri

Yıl ya da çeyreğin sonunda katılan laboratuvar sayıları barlarla gösterilmiştir

İnvaziv *E. coli* izolatlarında, 2009 1.-3. Çeyrek Duyarlılık Verileri (n=1545)



İnvaziv K. Pneumoniae 2006 -2009 * Direnç Oranları

Time period	Number of labs	Number of isolates	%AMP-R*	%3GC-R*	%CIP/ OFX-R*	%GEN-R*	%IPM/ MEM-R*
2006	36	217	97.7	10.2	15.3	7.8	0.0
2007	39	244	99.2	9.9	18.1	9.9	0.6
2008	41	310	99.7	11.0	12.8	10.4	0.0
2009**	42	132	98.5	6.9	9.8	9.1	0.0
2009Q1	42	56	100.0	10.9	10.7	12.5	0.0
2009Q2	42	76	97.3	3.9	9.2	6.6	0.0

* Not all isolates tested;

** Data for 2009 provisional up to the end of Q2

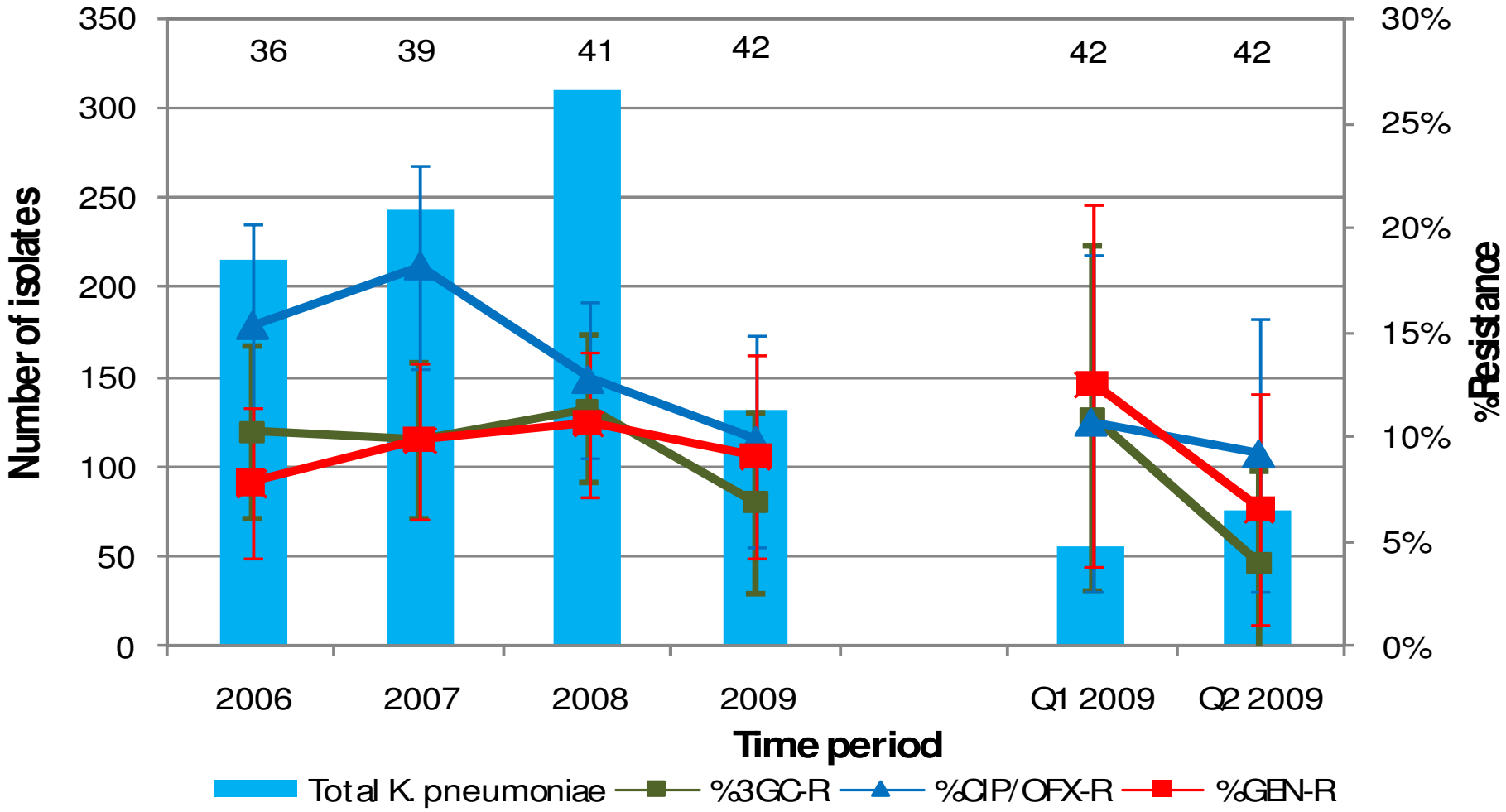
*** *K. pneumoniae* are inherently resistant to ampicillin: such isolates usually represent either an error in the identification of the organism or the susceptibility result****

İnvaziv K. Pneumoniae İnfeksiyonlarında ESBL ve ÇİD Oranları 2006 -2009 *

Year	Number of labs	Number of isolates	%3GC-R*	%ESBL+*	%MDR*
2006	36	217	10.2	8.6	11.2
2007	39	244	9.9	3.7	11.9
2008	41	310	11.0	7.4	10.0
2009**	42	132	6.9	6.3	7.8
2009Q1	42	56	10.9	9.4	10.9
2009Q2	42	76	3.9	4.1	5.4

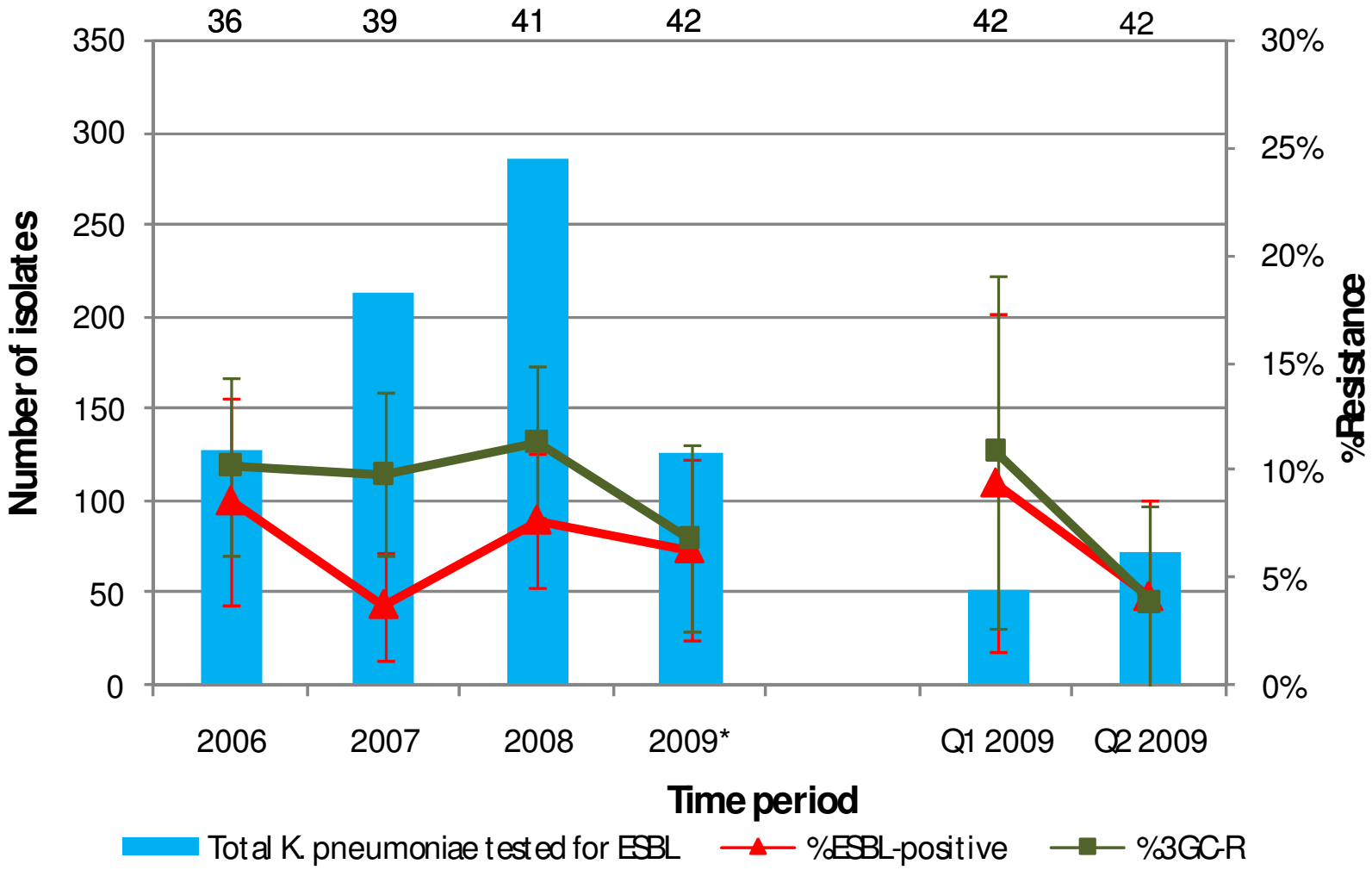
* Not all isolates tested;
** Data for 2009 provisional up to the end of Q2

İnvaziv K. Pneumoniae Direnç Eğilimi, 2006-2009*



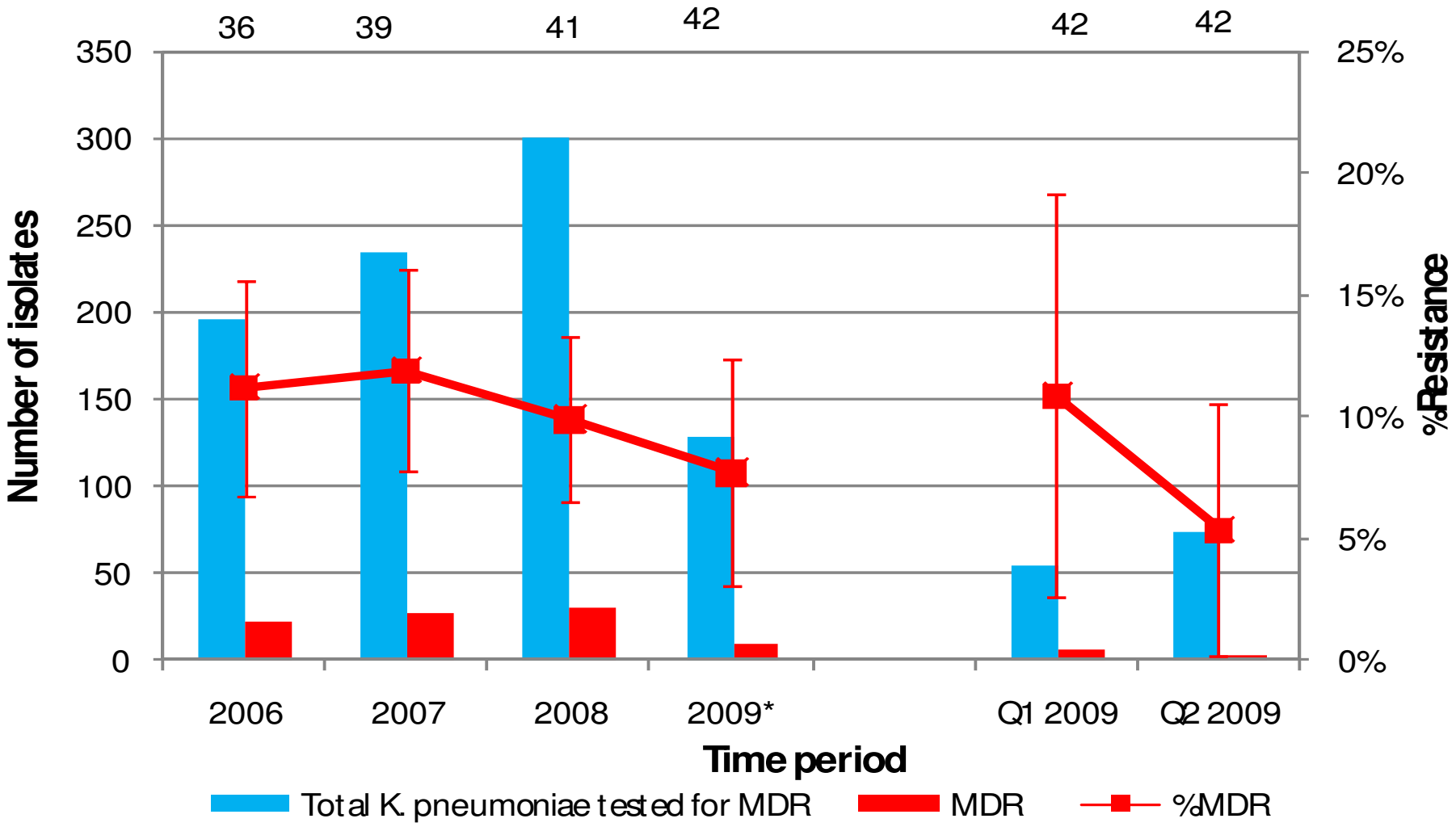
* Data for 2009 provisional up to the end of Q2;
Number of laboratories participating by year-end and quarter are indicated above the bars

İnvaziv K. Pneumoniae Direnç Eğilimi, 2006-2009*: 3.kuşak sefalosporinler ve ESBL



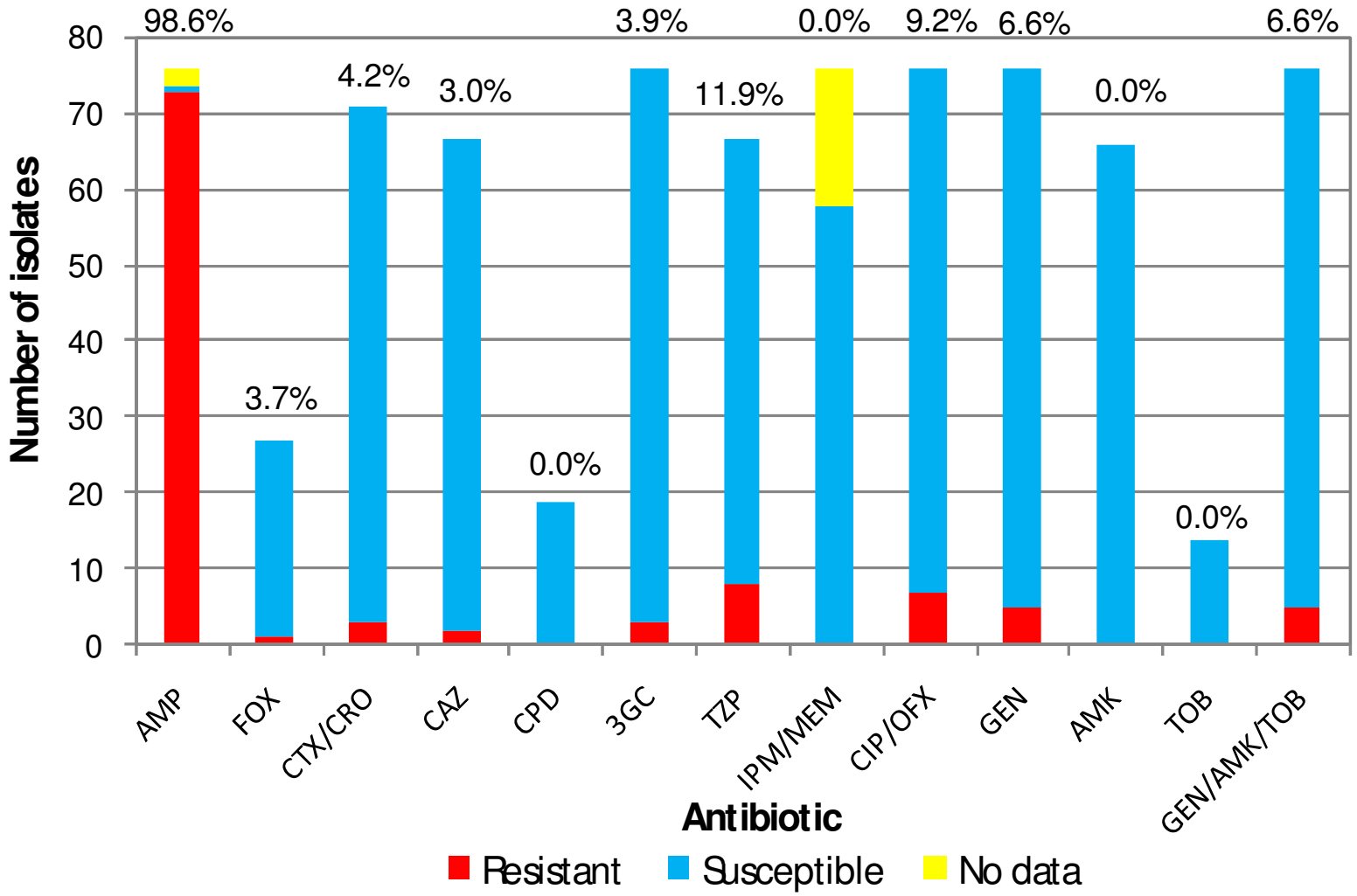
* Data for 2009 provisional up to the end of Q2;
Number of laboratories participating by year-end and quarter are indicated above the bars

İnvaziv ÇİD *K. pneumoniae* eğilimleri, 2006-2009*



* Data for 2009 provisional up to the end of Q2;
Number of laboratories participating by year-end and quarter are indicated above the bars

İnvasive *K. pneumoniae* izolatlarında duyarlılık verileri Q2 2009 (n=76)

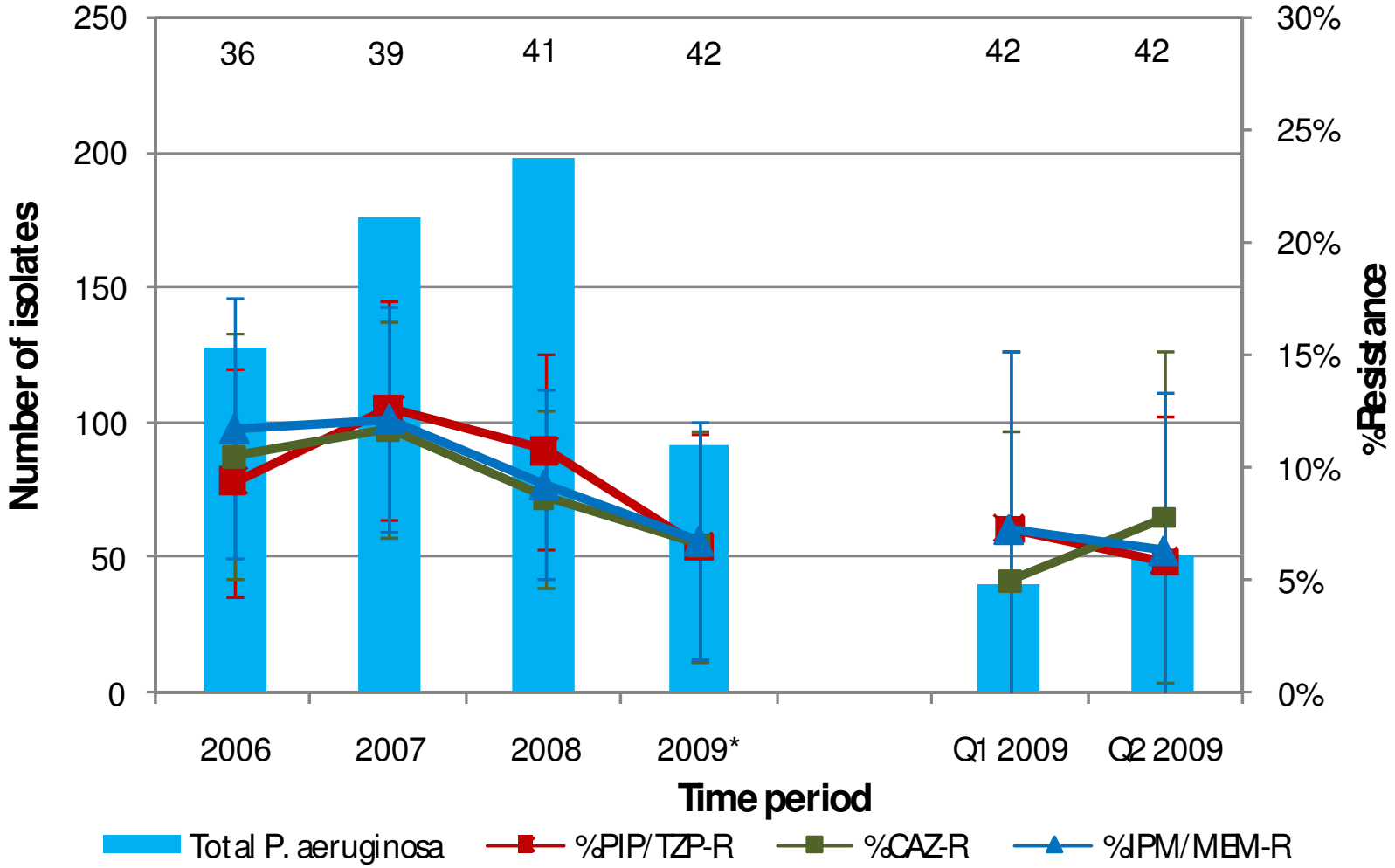


P. aeruginosa invaziv infeksiyonu direnç oranları, 2006-2009*

Time period	Number of labs	Number of isolates	%PIP/ TZP-R*	%CAZ-R*	%IPM/ MEM-R*	%CIP/ OFX-R*	%GEN-R*	%MDR
2006	36	128	9.4	10.6	11.8	18.0	9.5	9.5
2007	39	177	12.6	11.8	12.2	22.9	13.3	12.5
2008	41	199	10.8	8.7	9.3	21.8	9.0	11.1
2009**	42	41	6.5	6.6	6.8	13.0	7.7	5.7
2009Q1	42	41	7.3	5.0	7.3	17.1	10.0	5.0
2009Q2	42	51	5.9	7.8	6.4	9.8	5.9	6.4

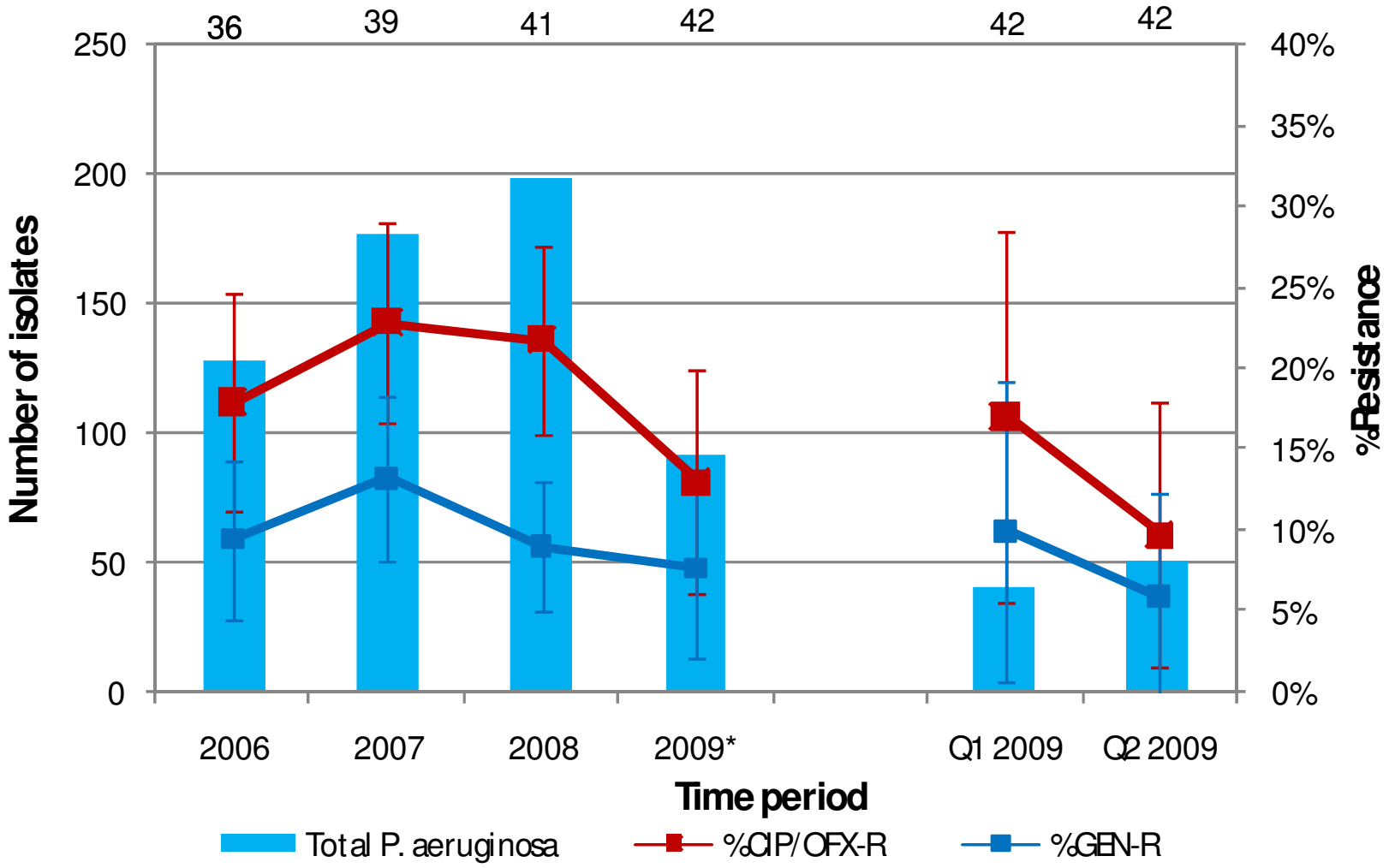
* Not all isolates tested;
** Data for 2009 provisional up to the end of Q2

Invaziv *P. aeruginosa* direnç eğilimi (1), 2006-2009*



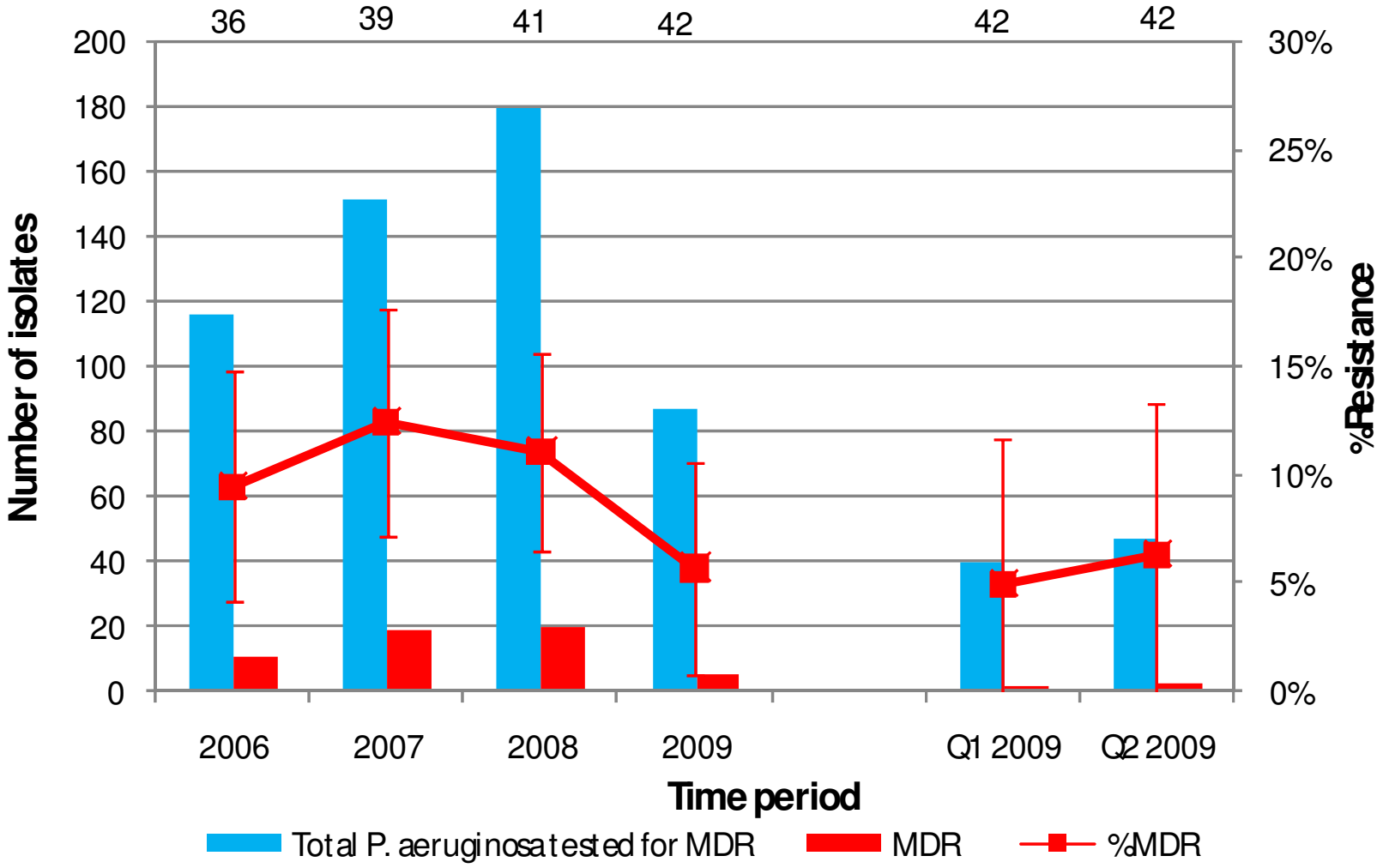
* Data for 2009 provisional up to the end of Q2;
Number of laboratories participating by year-end and quarter are indicated above the bars

Invaziv *P. aeruginosa* direnç eğilimi (2), 2006-2009*



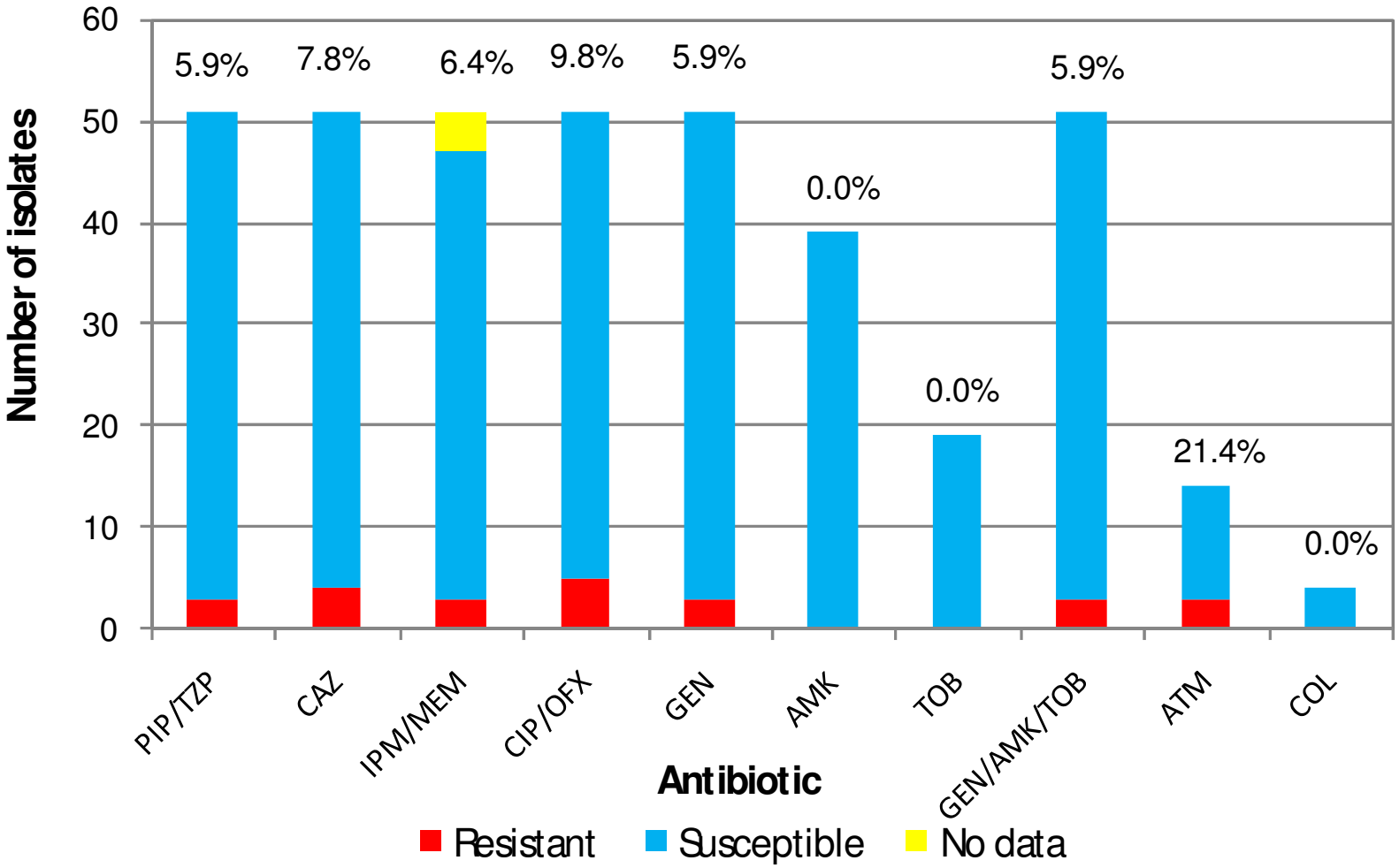
* Data for 2009 provisional up to the end of Q2;
Number of laboratories participating by year-end and quarter are indicated above the bars

Invaziv ÇİD *P. aeruginosa* eğilimi, 2006-2009*



* Data for 2009 provisional up to the end of Q2;
Number of laboratories participating by year-end and quarter are indicated above the bars

invasive *P. aeruginosa* izolatları duyarlılık verileri Q2 2009 (n=51)



P. aeruginosa izolatları direnç profili, Q2 2009

Resistance Profile	Number of isolates
Fully susceptible	38
M	2
C	3
P3	1
3CG*	1
P3MG*	1
P3CG*	1
Not tested against all	4
Total	**51**

P, Piperacillins; **3**, Ceftazidime; **M**, Meropenem; **C**, Ciprofloxacin; **G**, Gentamicin

* Multi-drug resistant (defined as resistance to 3 or more classes)

Table 1. Summary of EARS data by pathogen and year

Pathogen	Year									
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Number laboratories by year-end	**12**	**19**	**20**	**23**	**28**	**41**	**42**	**42**	**44**	**42**
S. aureus										
Number of isolates	510	639	815	1042	1140	1323	1424	1412	1393	1289
Number Meticillin-R (or MRSA)	198	249	337	445	480	553	592	592	536	435
Meticillin-R (or MRSA)	38.8%	39.0%	41.3%	42.7%	42.1%	41.8%	41.6%	41.9%	38.5%	33.7%
Number VISA	0	0	0	0	0	0	0	2	1	0
VISA*	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.1%	0.0%
S. pneumoniae										
Number of isolates	157	201	245	278	364	400	401	407	438	447
Penicillin-NS*	19.1%	13.4%	12.2%	11.5%	11.8%	10.3%	11.7%	15.7%	17.4%	23.1%
of which: HLR	0.0%	3.5%	1.6%	1.4%	2.2%	1.8%	3.0%	2.9%	5.7%	6.1%
Int	16.6%	8.5%	10.6%	9.7%	8.8%	7.0%	8.7%	12.5%	11.0%	16.9%
Erythromycin-R*	14.0%	12.0%	12.5%	12.7%	11.6%	14.4%	12.1%	16.1%	16.4%	16.7%
Number laboratories by year-end				**21**	**27**	**40**	**41**	**42**	**44**	**42**
E. faecalis										
Number of isolates	No data	No data	No data	168	218	242	290	294	281	301
Ampicillin-R*				8.1%	5.1%	0.8%	3.5%	4.5%	2.2%	0.7%
Vancomycin-R				2.4%	1.4%	1.3%	2.5%	3.7%	2.8%	3.7%
HLG-R*				38.5%	33.9%	41.3%	43.1%	42.4%	37.2%	30.5%
E. faecium										
Number of isolates	No data	No data	No data	85	135	187	224	265	332	406
Ampicillin-R*				88.9%	91.0%	95.7%	92.3%	93.9%	93.1%	95.1%
Vancomycin-R				11.1%	19.4%	23.2%	31.7%	37.1%	33.5%	35.7%
HLG-R*				16.7%	53.8%	58.0%	51.4%	44.3%	34.9%	28.1%
MDR*				3.7%	11.4%	18.5%	25.6%	25.6%	22.3%	16.2%
E. coli										
Number of isolates	No data	No data	No data	741	991	1256	1445	1656	1784	1923
Ampicillin-R*				62.2%	61.9%	65.0%	67.6%	70.7%	68.3%	70.3%
3GC-R*				3.0%	2.4%	2.4%	4.1%	4.1%	6.7%	7.5%
Ciprofloxacin-R*				5.4%	9.5%	12.6%	17.3%	21.5%	22.1%	23.4%
Gentamicin-R*				2.7%	3.9%	5.7%	8.5%	7.7%	9.9%	10.2%
ESBL-producers*				1.2%	1.3%	1.1%	2.4%	2.5%	4.1%	5.0%
MDR*				2.4%	3.8%	5.6%	7.7%	9.0%	11.4%	12.1%
Number laboratories by year-end								**36**	**39**	**41**
K. pneumoniae										
Number of isolates	No data	No data	No data	No data	No data	No data	No data	217	244	311
Ampicillin-R*								97.7%	99.2%	99.7%
3GC-R*								10.2%	9.9%	11.3%
Ciprofloxacin-R*								15.3%	18.1%	12.7%
Gentamicin-R*								7.8%	9.9%	10.6%
Imipenem/meropenam-R*								0.0%	0.6%	0.0%
ESBL-producers*								8.6%	3.7%	7.7%
MDR*								11.2%	11.9%	9.9%
P. aeruginosa										
Number of isolates	No data	No data	No data	No data	No data	No data	No data	128	177	199
Pipericillin/tazobactam-R*								10.2%	13.2%	10.8%
Ceftazidime-R*								10.6%	11.8%	8.7%
Imipenem/meropenam-R*								11.8%	12.2%	9.3%
Ciprofloxacin-R*								18.0%	22.9%	21.8%
Gentamicin-R*								10.2%	13.3%	9.0%
MDR*								9.5%	12.5%	11.1%

R, Resistant; NS, Non-Susceptible [includes isolates with intermediate (Int) and high-level resistance (HLR)]
MRSA, Meticillin-Resistant *S. aureus*; VISA, Vancomycin-Intermediate *S. aureus*
HLG, High-Level Gentamicin; 3GC, 3rd-Generation Cephalosporin (includes cefotaxime, ceftriaxone, ceftazidime and cefpodoxime); ESBL, Extended-Spectrum Beta-Lactamase; MDR, Multi-Drug Resistant
* Not all isolates tested