

Antimikrobiyal Dirente Son Durum

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KLİMİK AYLIK TOPLANTISI
19 KASIM 2015, İSTANBUL

ANTİBİYOTİK DİRENCİ (ABR)

- ▶ ABR antimikrobiyal ilaçların kullanımı ile artan doğal bir süreçtir
- ▶ Dirençli kökenler yayılarak varlıklarını sürdürür
- ▶ Günlük kullanımdaki antibiyotiklere yüksek orandaki direnç gelişimi
 - Hem hastanede
 - Hem de toplumda

hasta prognozunu olumsuz etkiler

ANTİBİYOTİK DİRENCİNİN OLUMSUZ ETKİLERİ

- ▶ Sık görülen enfeksiyonlarda tedavi seçenekleri azalır;
 - Morbiditede artış
 - Mortalitede artış
 - Yatış süresinde uzama
 - İş gücü kaybı
- ▶ Sağlık giderlerinde artış (ekonomik yük)

Estimates of Burden of Antibacterial Resistance

European Union *population 500m*

25,000 deaths per year

2.5m extra hospital days

Overall societal costs
(€ 900 million, hosp. days)
Approx. €1.5 billion per year



Source: ECDC 2007

Thailand *population 70m*

>38,000 deaths

>3.2m hospital days

Overall societal costs
US\$ 84.6–202.8 mill. direct
>US\$1.3 billion indirect



Source: Pumart et al 2012

United States *population 300m*

>23,000 deaths

>2.0m illnesses

Overall societal costs
Up to \$20 billion direct
Up to \$35 billion indirect



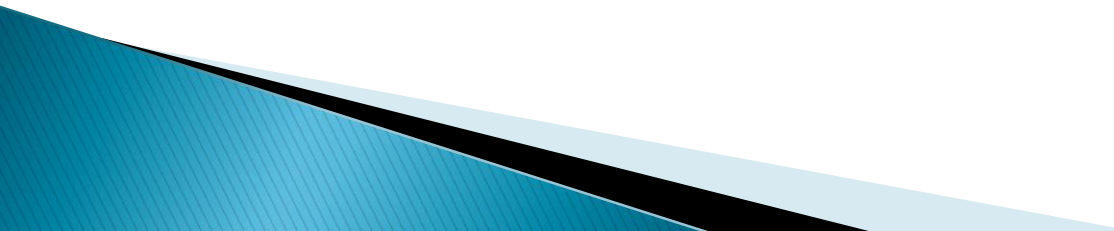
Source: US CDC 2013

Global information is insufficient to show complete disease burden impact and costs

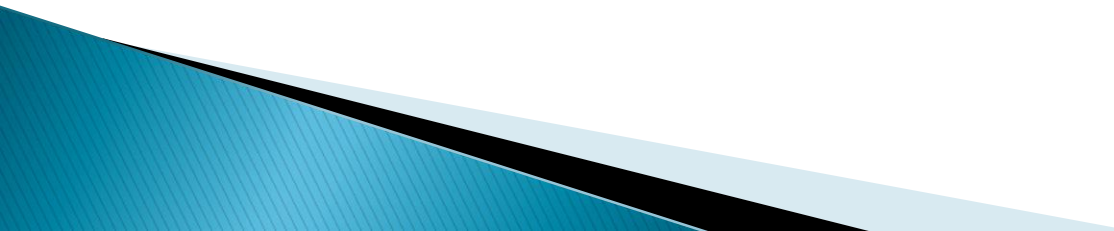


CDC'nin antibiyotik direnci raporu 2013 (ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES, 2013)

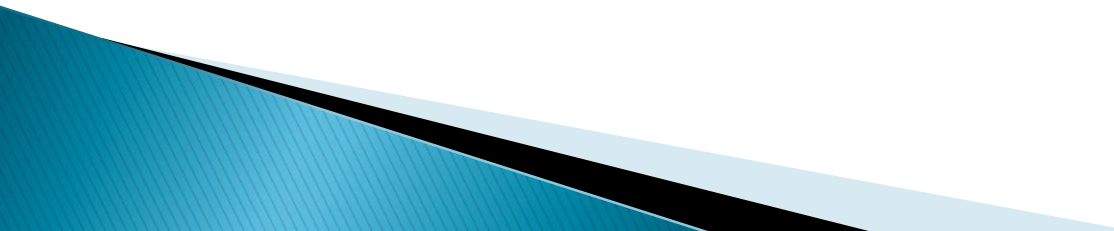
Antibiyotiklere dirençli bakteriler

- ▶ Acil tehlike oluşturanlar
 - ▶ Ciddi tehlike oluşturanlar
 - ▶ Muhtemel tehlike oluşturanlar
- 

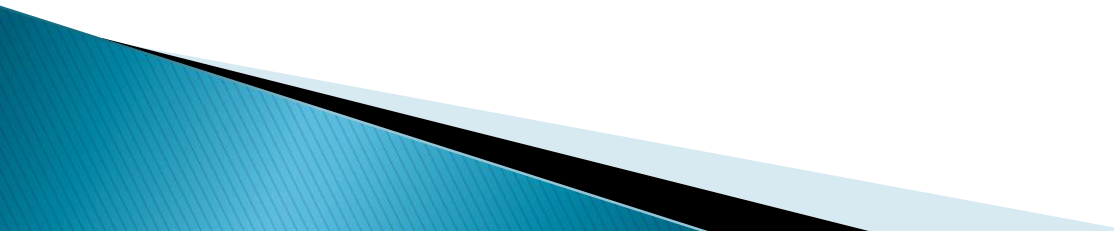
ACİL tehlike oluşturanlar

- Clostridium difficile
 - Carbapenem-resistant Enterobacteriaceae (CRE)
 - Drug-resistant Neisseria gonorrhoeae
- 

Ciddi tehlike oluşturanlar

- **Multidrug-resistant Acinetobacter**
 - **Drug-resistant Campylobacter**
 - **Fluconazole-resistant Candida (a fungus)**
 - **Extended spectrum β -lactamase producing Enterobacteriaceae (ESBLs)**
 - **Vancomycin-resistant Enterococcus (VRE)**
 - **Multidrug-resistant Pseudomonas aeruginosa**
 - **Drug-resistant Non-typhoidal Salmonella**
 - **Drug-resistant Salmonella Typhi**
 - **Drug-resistant Shigella**
 - **Methicillin-resistant Staphylococcus aureus (MRSA)**
 - **Drug-resistant Streptococcus pneumoniae**
 - **Drug-resistant tuberculosis**
- 

Muhtemel tehlike oluşturanlar

- Vancomycin-resistant *Staphylococcus aureus* (VRSA)
 - Erythromycin-resistant Group A *Streptococcus*
 - Clindamycin-resistant Group B *Streptococcus*
- 

Erdem H et al. Surveillance, control and management of infections in intensive care units in Southern Europe, Turkey and Iran. A prospective multicenter point prevalence study. Journal of Infection (2014) 68, 131–140

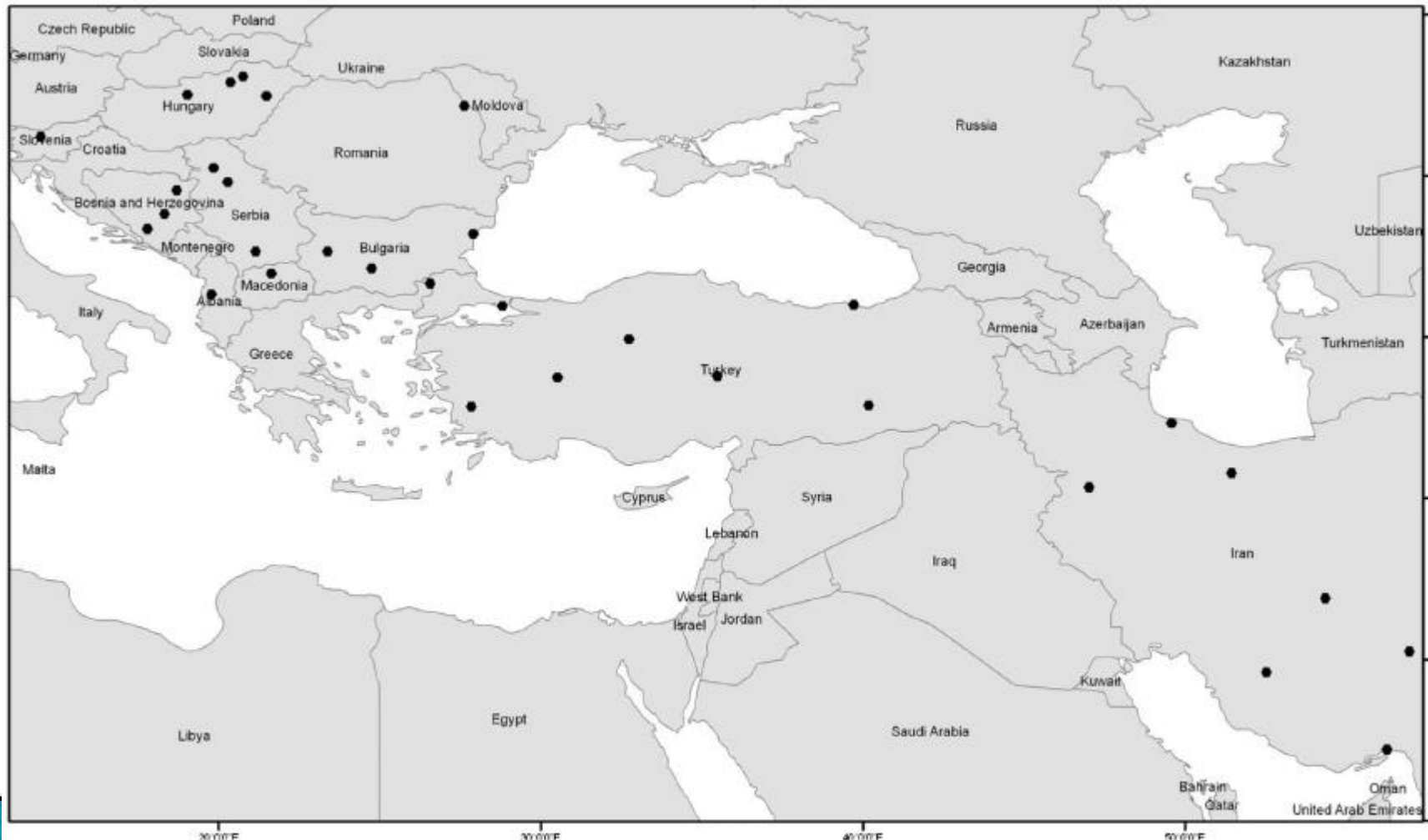


Figure 1 The cities in which the participating centers were located.

Table 5 The distribution of resistance patterns of isolated microorganisms from clinical specimens, according to country groups.^a

Microorganism	Overall	Southeast Europe	Turkey	p Value ^b	Iran
Enteric Gram-negative bacilli (n = 62)					
Multidrug resistant	39 (63%)	20/34 (58.8)	18/26 (69.2)	0.43	1/2 (50)
Extensively drug resistant	5 (8%)	4/34 (11.8)	1/26 (3.8)	0.38	0
Pandrug resistant	0	0	0	ND	0
<i>Acinetobacter spp.</i> (n = 47)					
Multidrug resistant	31 (66%)	19/25 (80)	11/19 (57.9)	0.33	0
Extensively drug resistant	13 (28%)	4/25 (20)	8/19 (42.1)	0.09	0
Pandrug resistant	5 (11%)	2/25 (4)	0	ND	3/3 (100)
<i>Pseudomonas aeruginosa</i> (n = 29)					
Multidrug resistant	16 (55%)	7/13 (53.8)	7/14 (50)	1.0	1/2 (50)
Extensively drug resistant	7 (14%)	4/13 (30.8)	3/14 (21.4)	0.82	0
Pandrug resistant	2 (7%)	2/13 (15.4)	0	ND	0
<i>Staphylococcus aureus</i> (n = 17)					
Multidrug resistant	8 (47%)	7/16 (43.8)	0	ND	1/1 (100)
Extensively drug resistant	0	0	0	ND	0
Pandrug resistant	0	0	0	ND	0
<i>Enterococcus spp.</i> (n = 17)					
Multidrug resistant	10 (59%)	6/9 (66.7)	3/7 (42.9)	1.0	1/1 (100)
Extensively drug resistant	1 (6%)	0	1/7 (14.3)	ND	0
Pandrug resistant	0	0	0	ND	0

^a Data expressed as n/N (%), ND: Not determined.

^b Comparisons were performed between Southeast Europe and Turkey.

Erdem et al. Surveillance, control and management of infections in intensive care units in Southern Europe, Turkey and Iran. A prospective multicenter point prevalence study. Journal of Infection (2014), 68, 131–140

Alterations in resistance rates (%) of isolated microorganisms from device-associated infections in an intensive care unit of a teaching hospital in Istanbul (2004–2010)

Years/MDR bacteria	2004	2010	P value
MDR Acinetobacter spp.	5.8	76.6	<0.0001
MDR P.auruginosa	6.8	53.1	<0.0001
ESBL+ Enterobacteriaceae	23.1	54.2	0.01
VRE	0.0	12.5	0.0003

Inan A et al Japanese J Inf Dis. 2012;65:2:146–151

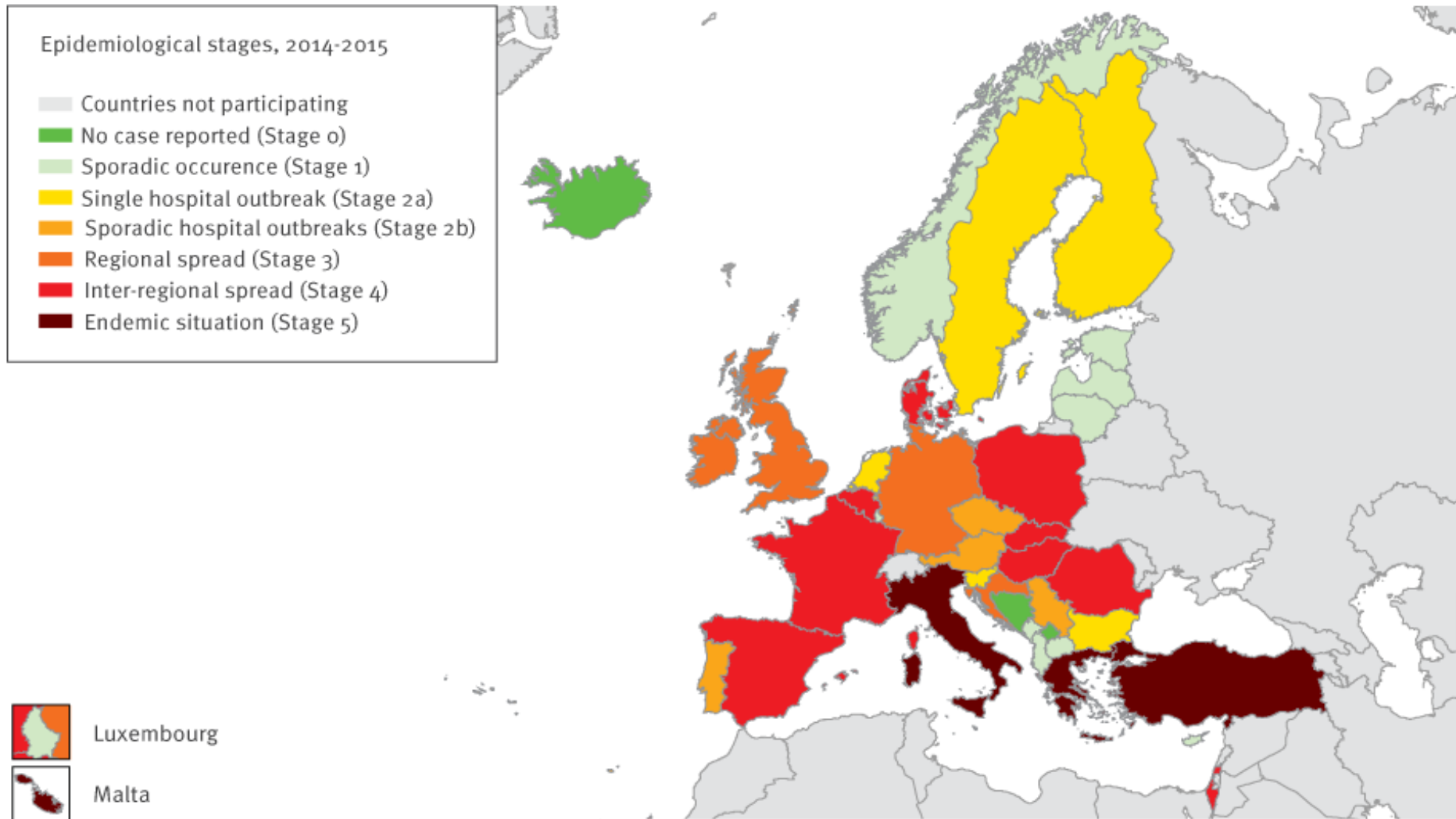
ANTİMİKROBİYAL DİRENÇ ORANLARI

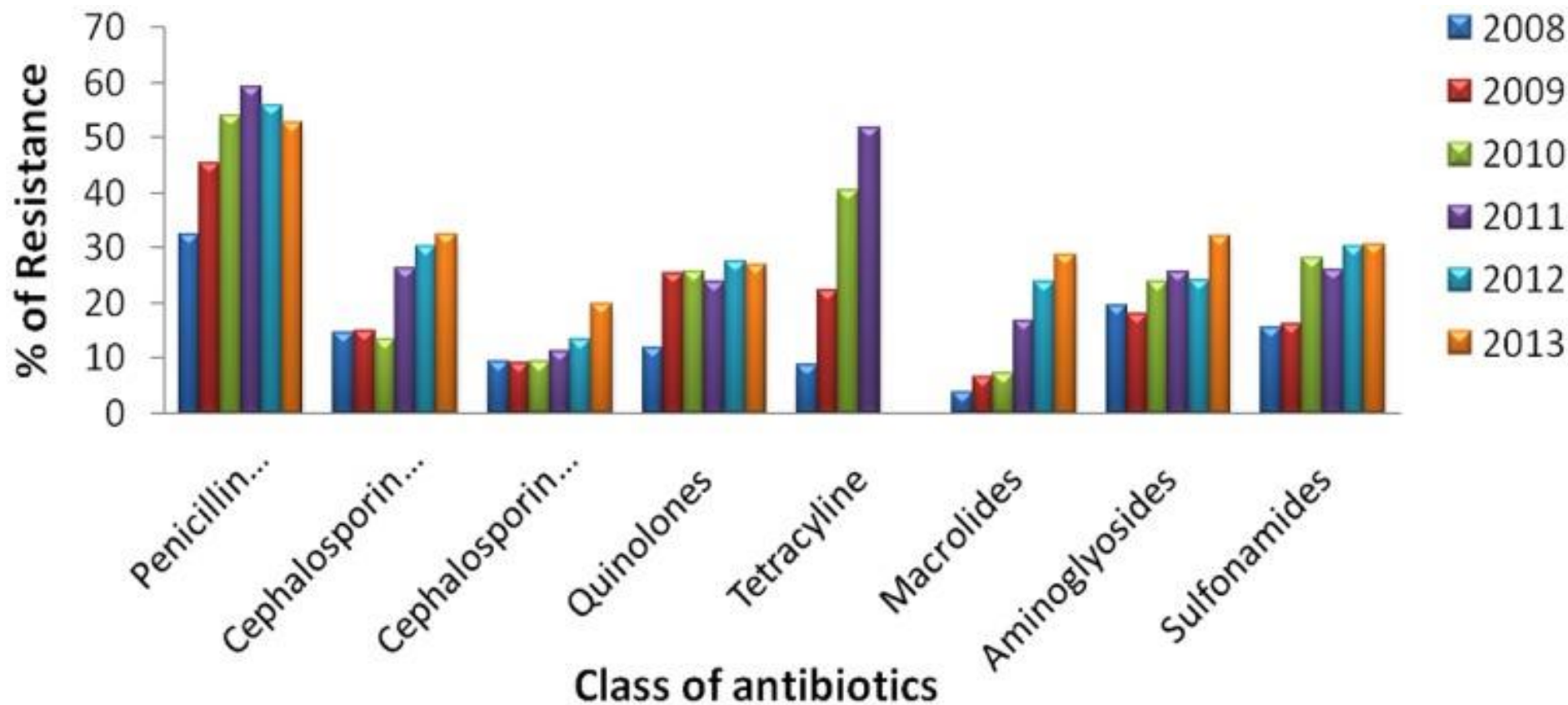
Tablo 20 . Antimikrobiyal Direnç Oranları* ve Dağılımları,2014.

UHESA Verileri

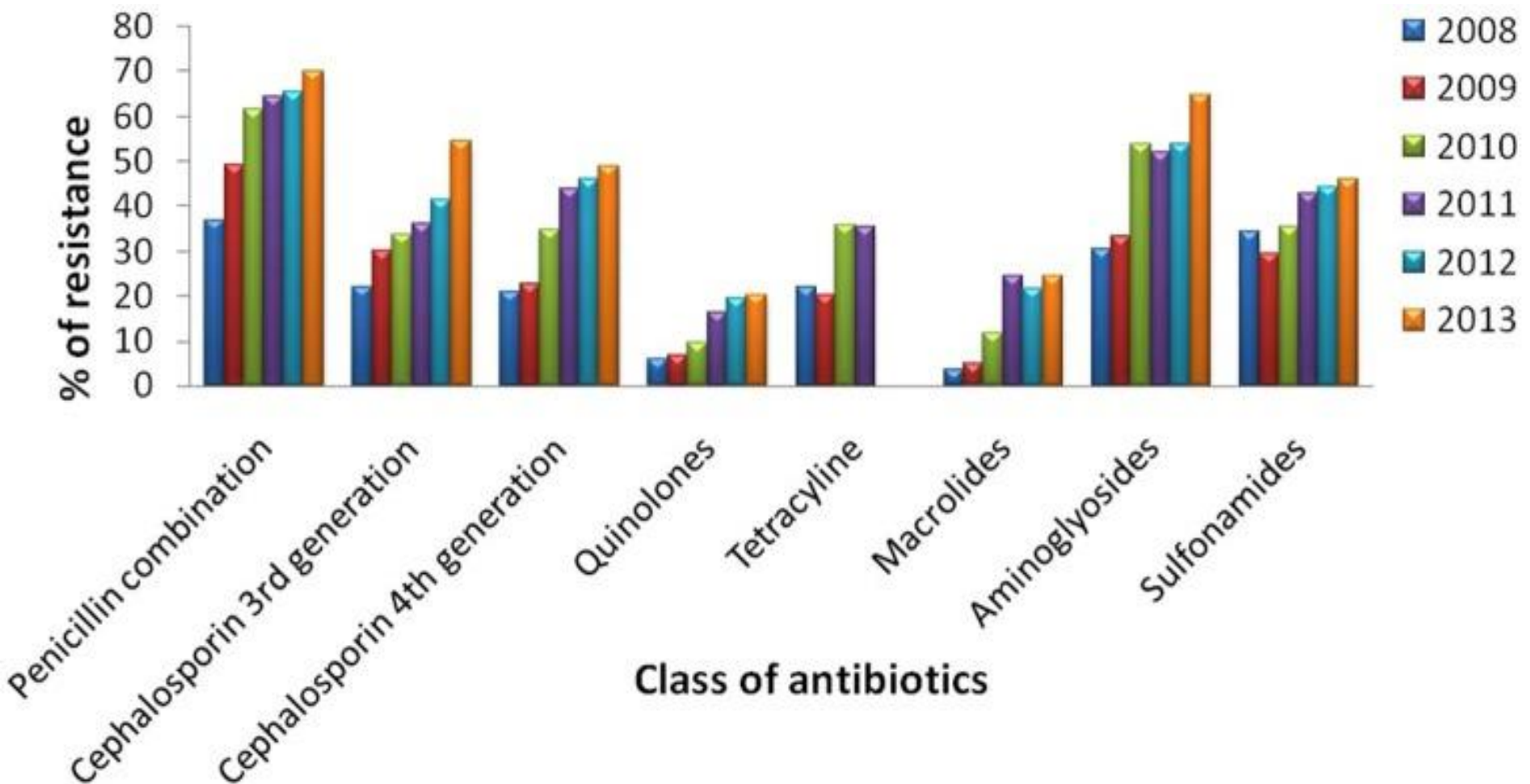
Antimikrobiyal Direnç Hızları					PERSENTİL				
ANTİMİKROBİYAL DİRENÇLİ PATOJEN	Birim sayısı	Etken sayısı (toplam)	Dirençli etken sayısı	Ağırlıklı genel ortalama	10%	25%	50% (Ortanca)	75%	90%
TÜRKİYE GENELİ									
VRE	607(81)	1798	371	20.63	0.00	0.00	14.29	33.33	50.00
MRSA	400(73)	1731	840	48.53	14.49	28.29	51.85	70.54	85.66
MRKNS	301(86)	2429	2141	88.14	63.94	80.00	90.91	97.81	100.00
E.Coli suşlarında ESBL	457(126)	4688	2755	58.77	34.32	50.00	61.90	80.00	90.20
<i>Klebsiella Pneumoniae</i> suşlarında ESBL	351(114)	3875	2436	62.86	29.66	50.00	69.23	81.56	93.54
Karbapenem dirençli <i>Acinetobacter baumannii</i>	338(146)	7197	6589	91.55	80.00	89.72	94.31	98.01	100.00
Karbapenem dirençli <i>Pseudomonas aeruginosa</i>	425(113)	3468	1491	42.99	17.75	30.38	41.67	56.31	70.00
Kolistin dirençli <i>Acinetobacter baumannii</i>	603(174)	7714	428	5.55	0.00	0.00	2.24	5.88	12.33
SAĞLIK BAKANLIĞI DEVLET HASTANELERİ									
VRE	216(7)	90	7	7.78	-	-	-	-	-
MRSA	155(11)	220	144	65.45	-	-	-	-	-
MRKNS	127(16)	241	208	86.31	-	-	-	-	-
E.Coli suşlarında ESBL	187(43)	989	646	65.32	38.66	50	67.24	81.25	91.15
<i>Klebsiella Pneumoniae</i> suşlarında ESBL	133(33)	571	418	73.20	45.00	60.36	75.00	91.83	98.79
Karbapenem dirençli <i>Acinetobacter baumannii</i>	135(52)	1333	1222	91.67	80.55	89.97	94.44	100.00	100.00
Karbapenem dirençli <i>Pseudomonas aeruginosa</i>	169(36)	587	250	42.59	10.51	20.43	40.00	57.21	78.59
Kolistin dirençli <i>Acinetobacter baumannii</i>	233(58)	1400	54	3.86	0.00	0.00	0.00	6.20	10.18
SAĞLIK BAKANLIĞI EĞİTİM VE ARAŞTIRMA HASTANELERİ									
VRE	139(27)	584	85	14.55	0.00	0.00	10.00	19.23	45.55
MRSA	59(31)	619	290	46.85	10.60	28.00	45.45	64.70	84.35
MRKNS	55(30)	921	826	89.69	77.82	84.88	93.01	100.00	100.00
E.Coli suşlarında ESBL	61(35)	1469	850	57.86	23.48	47.82	61.11	78.76	86.78

Occurrence of carbapenemase-producing *Enterobacteriaceae* based on self-assessment by national experts, 38 European countries, May 2015





Antibiotic resistance pattern of *E. coli*. Change of resistance pattern of different antimicrobials in *E. coli* over the last 6 years (from 2008 to 2013).



Antibiotic resistance pattern of *Klebsiella* spp. Change of resistance pattern of different antimicrobials in *Klebsiella* spp. over the last 6 years (from 2008 to 2013).

Resistance rates (%) of E.coli strains isolated from urine cultures against several antibiotics

Antibiotics	1996-2001 ^a	2002-2007 ^b	2008-2012 ^c
AMP	70.20	67.44	62.06
AMC	33.40	38.73	37.48
CZ	31.43	29.82	32.15
CXM	27.93	24.21	25.56
CRO	14.71	13.59	19.22
IMP	4.16	2.30	2.85
TMP-SMX	50.51	48.91	47.83
NIT	23.90	10.49	8.55
GN	14.75	17.40	17.46
CIP	12.27	23.16	30.98
AK	7.02	6.58	5.85
FEP	2.73	14.17	18.43
SXT	26.01	51.36	52.29
TZP	11.30	11.13	17.53
PIP	43.44	56.98	39.95
GSBL	8.09	10.61	28.17

Antibiotic susceptibility rates of pneumococci to several antibiotics

Antibiotic	Susceptible %	Intermediate %	Resistant %
Penicillin, oral	23 (37.8)	33 (54)	5 (8.2)
Penicillin, parenteral*	60 (98.4)	1 (1.6)	0
Ceftriaxone	57 (93.4)	4 (6.6)	0
Erythromycin	27 (44.2)	2 (3.3)	32 (52.5)
Clindamycin	33 (54)	0	28 (46)
Tetracycline	35 (52.5)	0	26 (47.5)
Vancomycin	61 (100)	0	0
Levofloxacin	61 (100)	0	0
Trimethoprim-sulfamethoxazole	19 (31.2)	1 (1.6)	41 (67.2)

*Evaluated according to the non-meningitis isolates criteria suggested by CLSI.

Gelmez G A. Serotype Distribution and Antibiotic Susceptibilities of Streptococcus pneumoniae Causing Acute Exacerbations and Pneumonia in Children with Chronic Respiratory Diseases. Mikrobiyol Bul 2013; 47(4): 684-692

Antibiyotik direncinin artmasının nedenleri

- ▶ ABR nin gelişmesi aslında doğal bir olaydır
- ▶ Antibiyotiklerin uygunsuz ve yaygın kullanılması
- ▶ Hayvancılıkta aby kullanılması dirençli kökenlerin gelişmesi ve seçilmesine yol açar
- ▶ Enfeksiyonların önlenmesine ve kontrolüne yönelik uygulamaların yetersizliği ABR kökenlerin artmasına ve yayılmasına yol açar

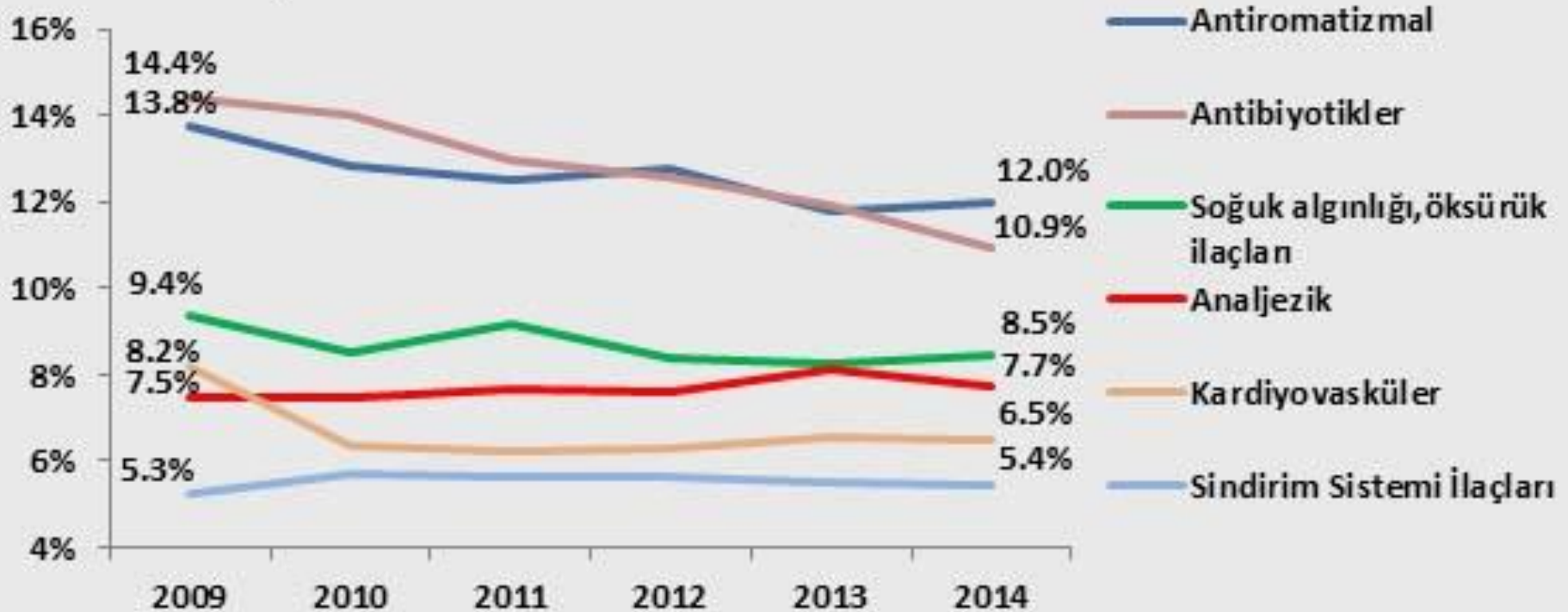
Türkiyede en fazla satılan 20 ilaç

BELOC ZOK 50 MG KONTR. SAL. 20 FILM TAB.
CORASPIN 100 MG 30 TAB.
DOLOREX 50 MG 20 DRAJE
PAROL 500 MG 20 TAB.
ARVELES 25 MG 20 FILM TAB.
MAJEZIK 100 MG 15 FILM TAB.
DOLVEN PEDIYATRİK 100 ML SURUP
OKSAMEN-L 20 MG 1 FLAKON
VOLTAREN SR 75 MG 10 TAB.
GAVISCON 500 MG 200 ML LİKİT
LANSOR 30 MG 28 KAPSUL
RENNIE DUO 100 ML SUSPANSİYON
NOOTROPİL 800 MG 30 FILM TAB.
MULTISEF 750 MG İM ENJ. TOZ İC. 1 FLAKON
NUROFEN COLD FLU 24 TAB.
MINOSET 500 MG 20 TAB.
NEXIUM 40 MG ENTERİK KAPLI 28 PEL. TAB.
TRAVAZOL 15 GR KREM
IESPOR İM 1 GR 1 FLAKON
PEDİFEN 100 MG 100 ML SURUP

ITS data

Kutu bazında en çok satan ilaçlar

Kutu Pazar Payı



Kaynak:IMS,iEİS

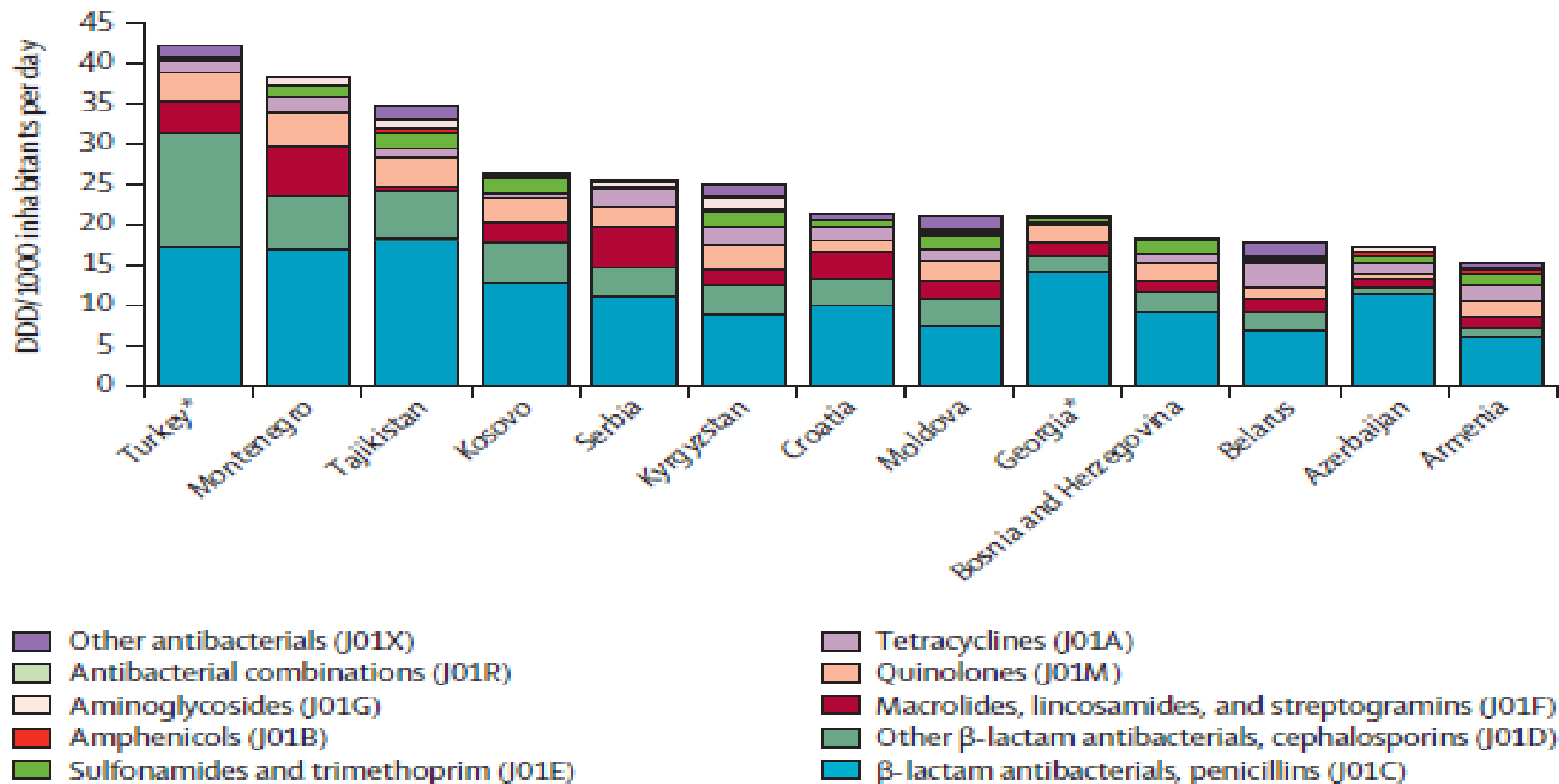


Figure 1: Total antibiotic use in 12 European countries and Kosovo, 2011

The category (WHO anatomical therapeutic chemical subgroup) "Other β-lactam antibacterials, cephalosporins" includes carbapenems and monobactams. "Other antibacterials" includes glycopeptide antibacterials, polymyxins, fusidic acid, imidazole derivatives, nitrofurantoin derivatives, and other antibacterials. DDD=defined daily doses.

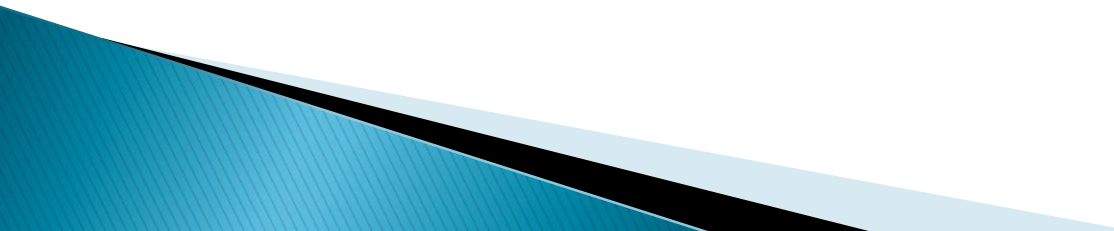
*Reported only outpatient antibiotic use.

Versporten A et al. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis 2014; 14: 381-87

- ▶ **“European Surveillance of Antimicrobial–Network” (ESAC–Net) ülkeleriyle karşılaştırıldığında, Türkiye Avrupa’da en fazla aby kullanılan ülkedir**

Versporten A et al. Antibiotic use in eastern Europe: a cross–national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis 2014; 14: 381–87

Antiyotik direncinde en sorunlu bakteriler: Güncel durum

- ▶ **Karbapenem dirençli
K.pneumoniae**
 - ▶ **MDR Acinetobacter spp.**
 - ▶ **MDR P.aeruginosa**
 - ▶ **ESBL+ Enterobacteriaceae**
 - ▶ **VRE**
 - ▶ **MRSA**
- 

Avrupa Antibiyotik Farkındalık Günü 2013: Basın Toplantısı (KLİMİK)



Avrupa Antibiyotik Farkındalık Günü 2014: Basın Toplantısı (KLİMİK)



*Avrupa Antibiyotik Farkındalık
Gününde Dernek Merkezinde
Basın Toplantısı Yapıldı*

(18 Kasım 2014)

Avrupa Antibiyotik Farkındalık Haftası 2015

WORLD ANTIBIOTIC AWARENESS WEEK

16-22 NOVEMBER 2015





TABLE 6. Definitions for multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR) bacteria

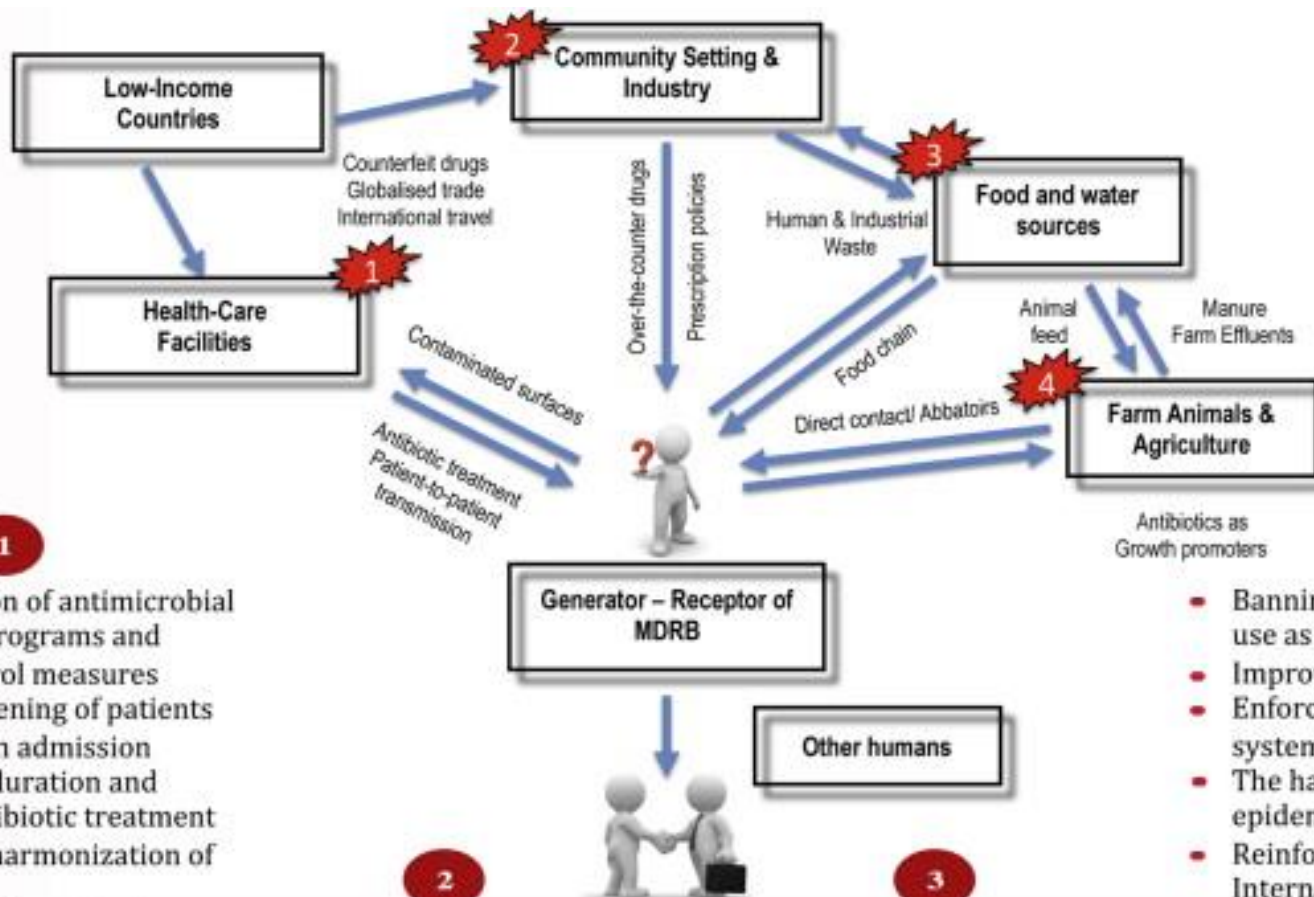
Bacterium	MDR	XDR	PDR
<i>Staphylococcus aureus</i>	The isolate is non-susceptible to at least 1 agent in Table 1 ^a	The isolate is non-susceptible to at least 1 agent in Table 1 ^a and 1 agent in Table 2	The isolate is non-susceptible to all antimicrobial categories in Table 1 ^a
<i>Enterobacteriaceae</i>	The isolate is non-susceptible to at least 1 agent in Table 3	The isolate is non-susceptible to at least 1 agent in Table 3 or fewer antimicrobial categories in Table 4	The isolate is non-susceptible to all antimicrobial categories in Table 4
<i>Pseudomonas aeruginosa</i>	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories in Table 5	The isolate is non-susceptible to at least 1 agent in all antimicrobial categories in Table 5	The isolate is non-susceptible to all antimicrobial categories in Table 5
<i>Acinetobacter spp.</i>	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories in Table 5	The isolate is non-susceptible to at least 1 agent in all antimicrobial categories in Table 5	The isolate is non-susceptible to all antimicrobial categories in Table 5

^aAll MRSA isolates are defined as MDR because of their resistance to all antimicrobials except β -lactams, glycopeptides, fusidic acid, rifamycins, β -lactamase inhibitors and carbapenems currently approved up until 25 January 2011).

http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/AMR/AMR/Pages/AMR_consensus_definition_of_clinical_microbiology_infection_article.aspx

Causes of inappropriate and widespread use of antimicrobial drugs in Turkey

- ▶ Relation between antimicrobial consumption and government's reimbursement policy
- ▶ Attitudes and behaviors of Family Physicians regarding use of antibiotics
- ▶ Over the counter selling by pharmacists (High rates of self-medication)
- ▶ Patient or family request



1

- Implementation of antimicrobial stewardship programs and infection control measures
- Universal screening of patients for MDRB upon admission
- Evaluation of duration and regimes of antibiotic treatment
- International harmonization of breakpoints
- Development of rapid and affordable diagnostic technologies
- Active surveillance
- Re-launching discovery and development of new antimicrobial drugs
- Reinforce International/National regulations

2

- Educational programs for prescribers and users
- Assessing antibiotic consumption
- Assessing prevalence of MDR strains
- Update local antibiotic prescribing guidelines
- Active surveillance
- Improved sanitation
- Reinforce International/National

3

- Assessment of antibiotic concentrations of sewages and wastewater treatment plants
- Improved sanitation of industrial systems
- Decontamination of hospital sewage water
- Reinforce International/National regulations

4

- Banning/regulating antibiotic use as growth promoters
- Improving Farm Biosecurity
- Enforcing joint surveillance systems in humans and animals
- The harmonisation of epidemiological cut-off values
- Reinforce International/National regulations