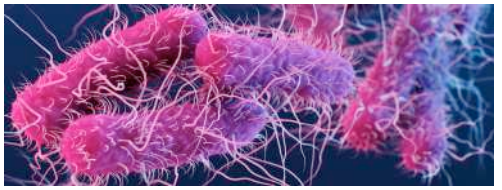




Direnç ve Bedeli: Hastaya

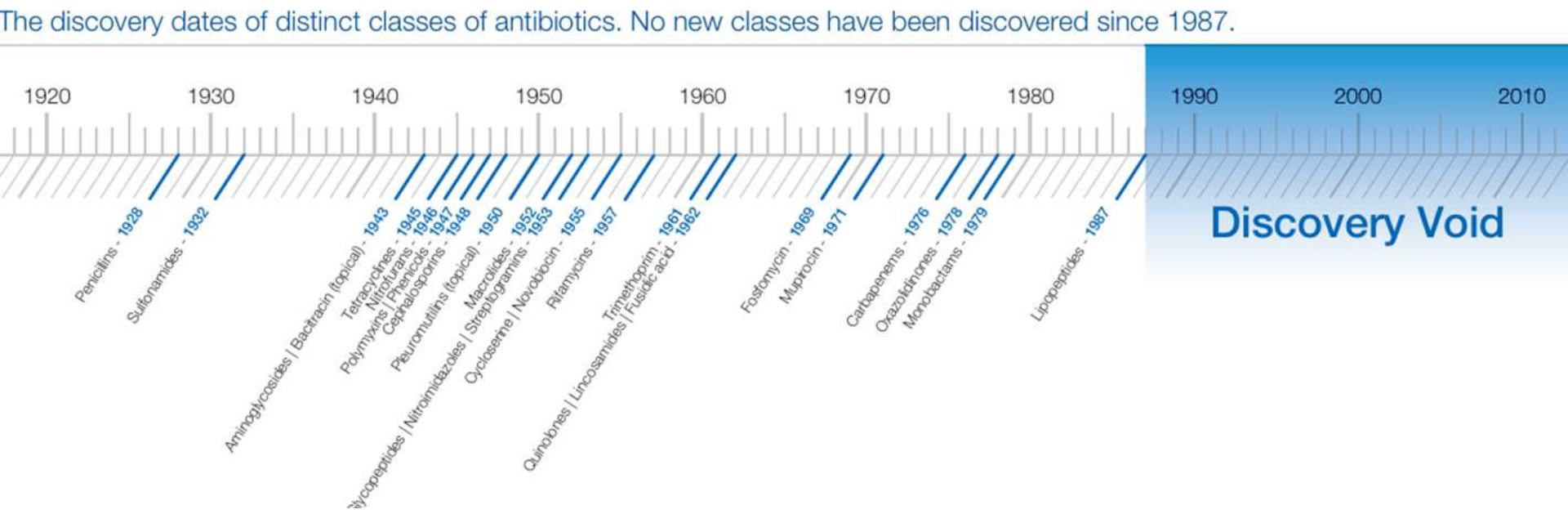
Prof. Dr. Meliha Meriç KOÇ
Bezmialem Vakıf Üniversitesi, Enfeksiyon Hastalıkları Ve Klinik Mikrobiyoloji AD

KLİMİK, İstanbul Bölge Toplantıları
28 Ocak 2020

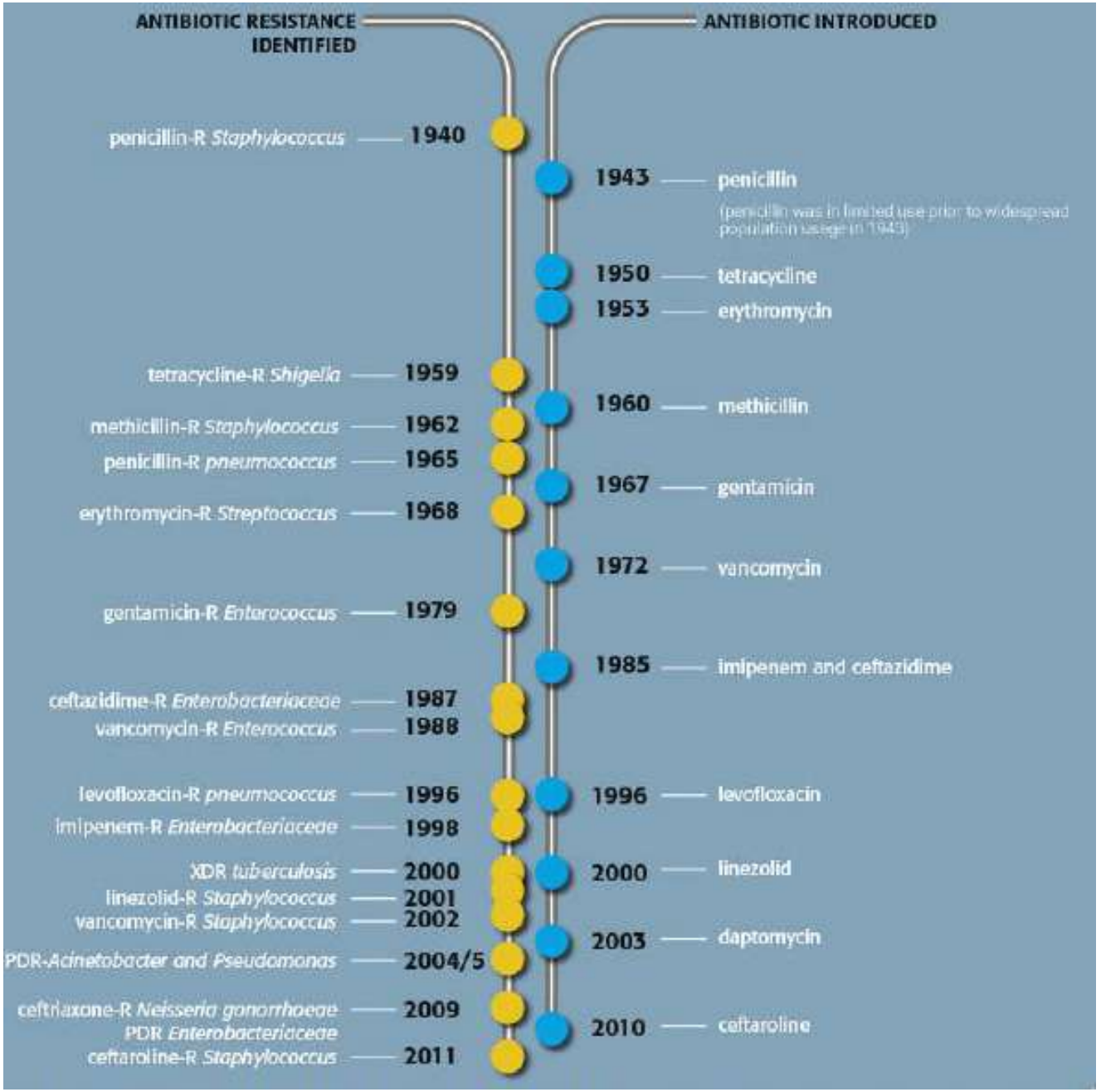
Sunum planı

- Direncin tarihçesi
- Gram negatif bakterilerdeki direnç durumu
- Direncin hastaya bedeli
  - Maddi
  - Manevi

Discovery of new antibiotics



World Economic Forum, Global risk report 2013



Antimicrobial resistance threats in United States, CDC report 2013

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Antibiotic Resistance Spreads Easily Across the Globe

Resistant bacteria and fungi can spread across countries and continents through people, animals, and goods.

Detect Resistant Threats

Prevent & Contain Resistant Germs

Improve Antibiotic Use

CDC-Antibiotic Resistance Threats in the United States, 2019

World Health Organization

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

GLOBAL PRIORITY LIST OF ANTIBIOTIC-RESISTANT BACTERIA TO GUIDE RESEARCH, DISCOVERY, AND DEVELOPMENT OF NEW ANTIBIOTICS,2017

ANTIBIOTIC RESISTANCE THREATS in the United States, 2013

HAZARD LEVEL URGENT

These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

Clostridium difficile (C. difficile), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

HAZARD LEVEL SERIOUS

These are significant antibiotic-resistant threats. For varying reasons (e.g., low or declining domestic incidence or reasonable availability of therapeutic agents), they are not considered urgent, but these threats will worsen and may become urgent without ongoing public health monitoring and prevention activities.

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 pneumonia*, Drug-resistant tuberculosis (MDR and XDR)

HAZARD LEVEL CONCERNING

These are bacteria for which the threat of antibiotic resistance is low, and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause severe illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.

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

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

New Antibiotic Resistance Threats List

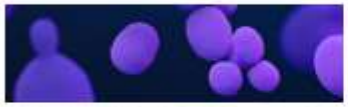
Updated urgent, serious, and concerning threats—totaling 18

5 urgent threats | **2** new threats | NEW: Watch List with **3** threats

Urgent Threats

These germs are public health threats that require urgent and aggressive action:

CARBAPENEM-RESISTANT ***ACINETOBACTER***



CANDIDA AURIS

CLOSTRIDIOIDES DIFFICILE

CARBAPENEM-RESISTANT **ENTEROBACTERIACEAE**

DRUG-RESISTANT ***NEISSERIA GONORRHOEAE***

Serious Threats

These germs are public health threats that require prompt and sustained action:

DRUG-RESISTANT ***CAMPYLOBACTER***

DRUG-RESISTANT ***CANDIDA***

ESBL-PRODUCING **ENTEROBACTERIACEAE**

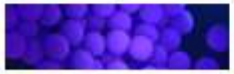
VANCOMYCIN-RESISTANT ***ENTEROCOCCI***

MULTIDRUG-RESISTANT ***PSEUDOMONAS AERUGINOSA***

DRUG-RESISTANT **NONTYPHOIDAL *SALMONELLA***

DRUG-RESISTANT ***SALMONELLA* SEROTYPE TYPHI**

DRUG-RESISTANT ***SHIGELLA***



METHICILLIN-RESISTANT ***STAPHYLOCOCCUS AUREUS***

DRUG-RESISTANT ***STREPTOCOCCUS PNEUMONIAE***

DRUG-RESISTANT **TUBERCULOSIS**

Urgent Threats

- Carbapenem-resistant *Acinetobac*
- *Candida auris*
- *Clostridioides difficile*
- Carbapenem-resistant Enterobacte
- Drug-resistant *Neisseria gonorrhoe*

Serious Threats

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- ESBL-producing Enterobacteriacea
- Vancomycin-resistant *Enterococci*
- Multidrug-resistant *Pseudomonas*
- Drug-resistant nontyphoidal *Salmo*
- Drug-resistant *Salmonella* serotype
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcu*
- Drug-resistant *Streptococcus pneu*
- Drug-resistant Tuberculosis

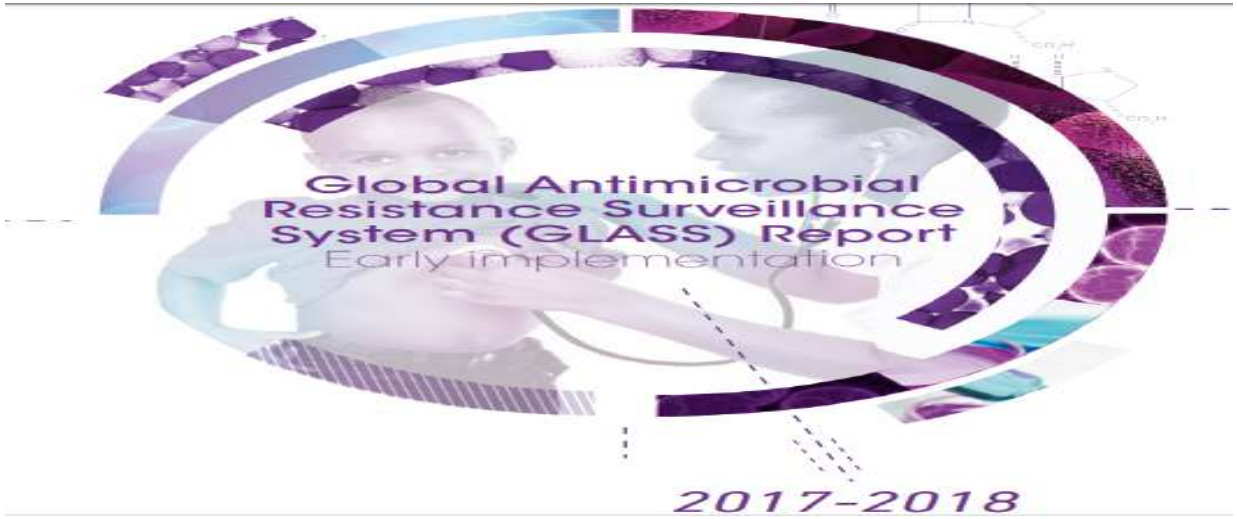
Concerning Threats

- Erythromycin-resistant group A *St*
- Clindamycin-resistant group B *Stre*

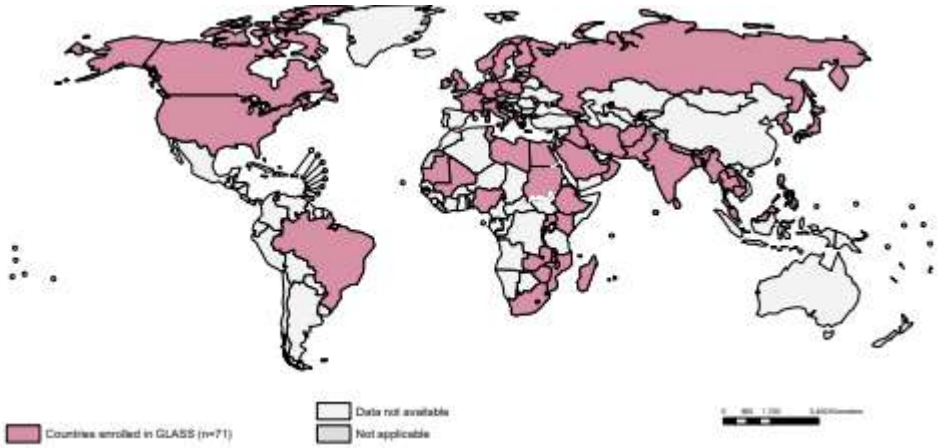
Watch List

- Azole-resistant *Aspergillus fumiga*
- Drug-resistant *Mycoplasma genita*
- Drug-resistant *Bordetella pertussis*

CDC-Antibiotic Resistance Threats in the United States, 2019



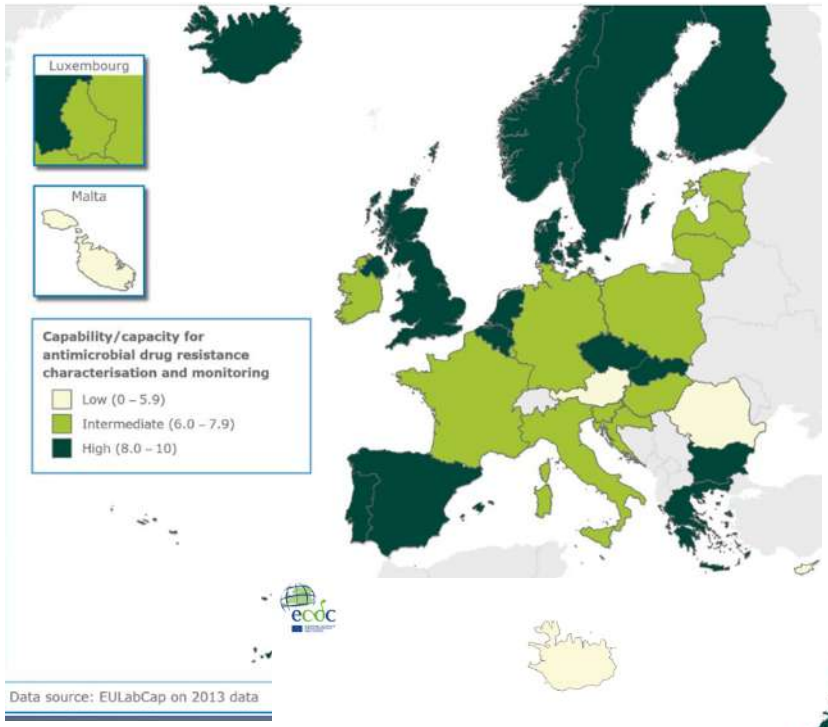
World Health Organization

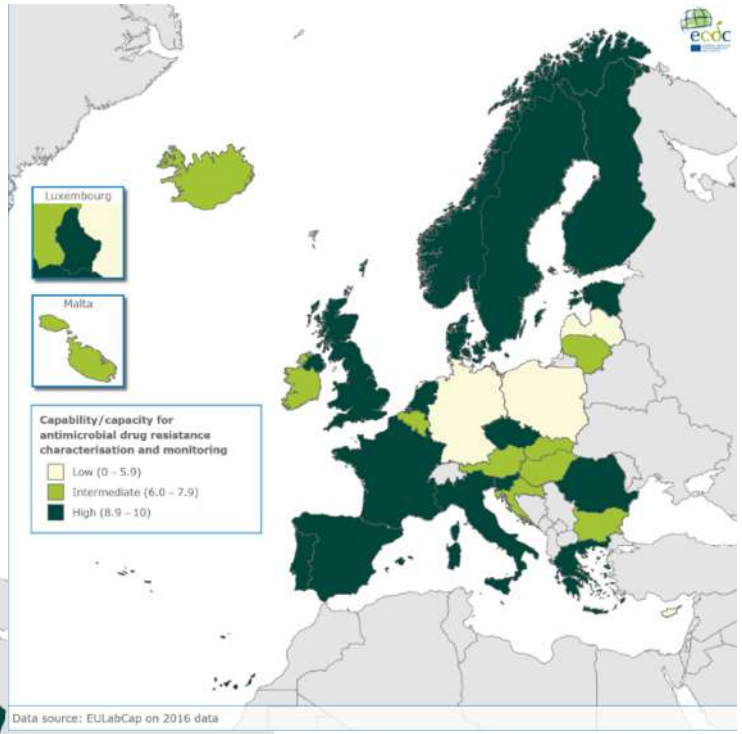


GLASS'a katılan ülkeler

Enterobacteriaceae (*E. coli*, *K. pneumoniae*, *Salmonella* spp., and *Shigella* spp.) were mainly tested for resistance to ciprofloxacin and imipenem, *Acinetobacter* spp. to imipenem, *S. pneumoniae* to penicillin and co-trimoxazole, and *N. gonorrhoea to* ceftriaxone. For *S. aureus*, GLASS collects only data on cefoxitin resistance, and, when not available, oxacillin resistance.

World Health Organization 2018


Luxembourg
Malta
Capability/capacity for antimicrobial drug resistance characterisation and monitoring
Low (0 – 5.9)
Intermediate (6.0 – 7.9)
High (8.0 – 10)
Data source: EULabCap on 2013 data


Luxembourg
Malta
Capability/capacity for antimicrobial drug resistance characterisation and monitoring
Low (0 – 5.9)
Intermediate (6.0 – 7.9)
High (8.0 – 10)
Data source: EULabCap on 2016 data

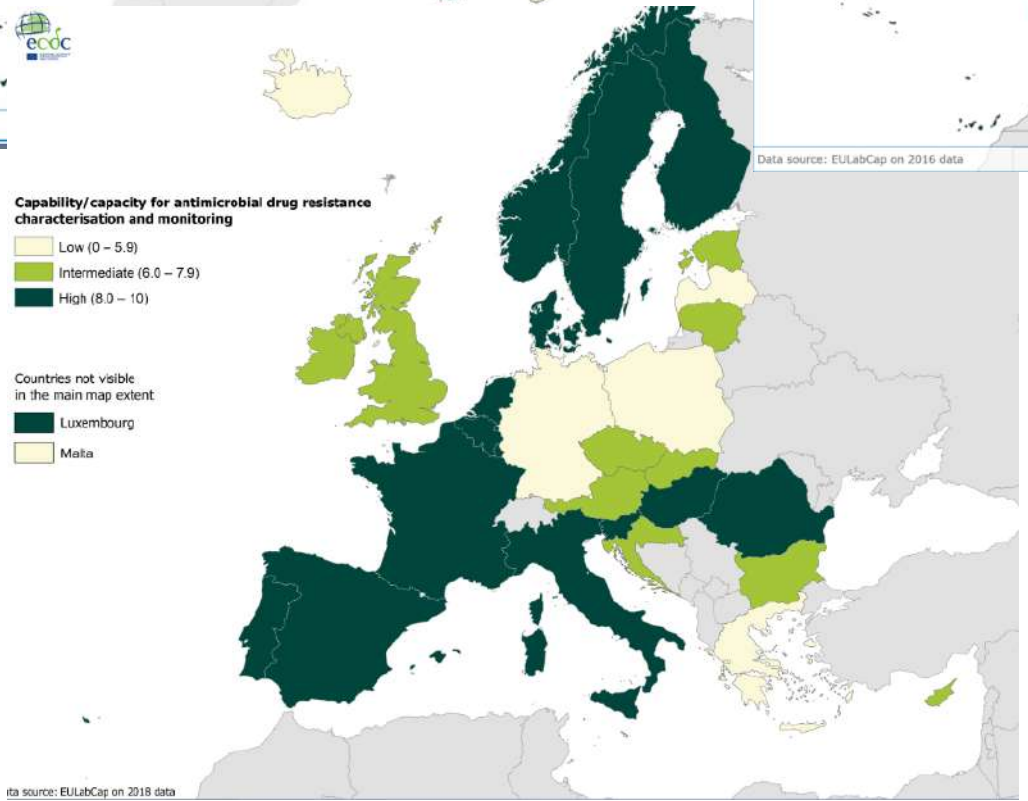

Capability/capacity for antimicrobial drug resistance characterisation and monitoring
Low (0 – 5.9)
Intermediate (6.0 – 7.9)
High (8.0 – 10)
Countries not visible in the main map extent
Luxembourg
Malta
ta source: EULabCap on 2018 data

Figure 3.5. ***Escherichia coli.*** **Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2018**

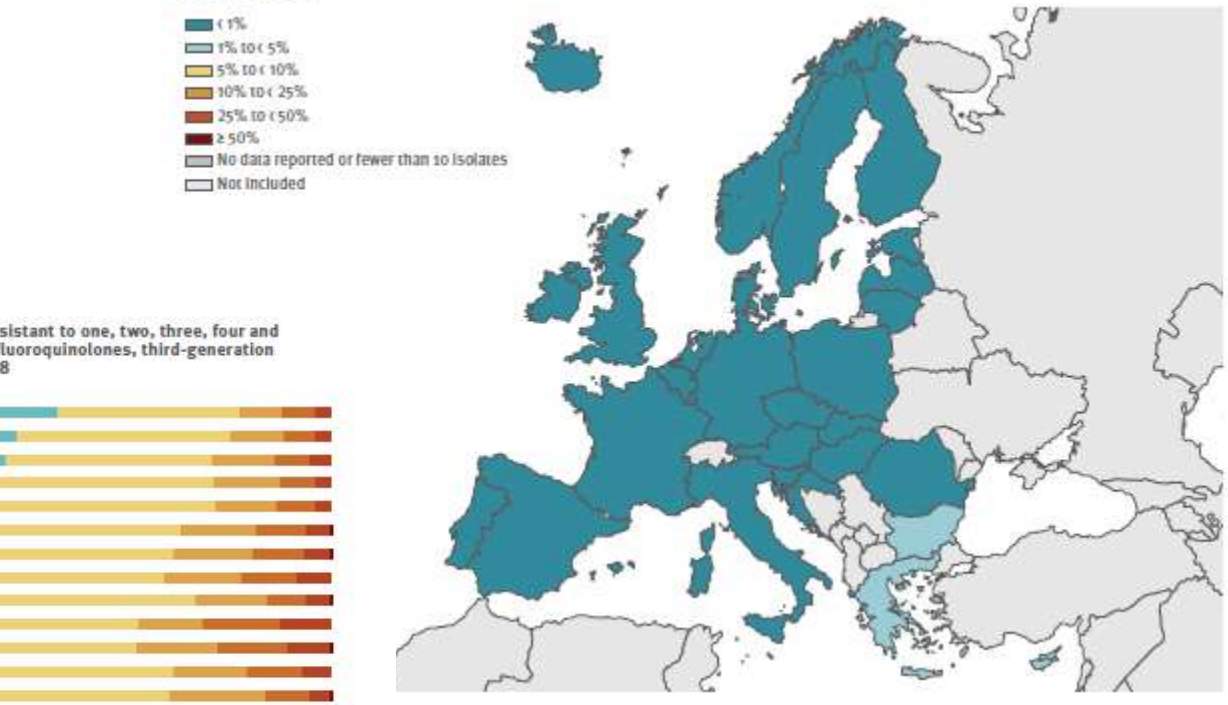
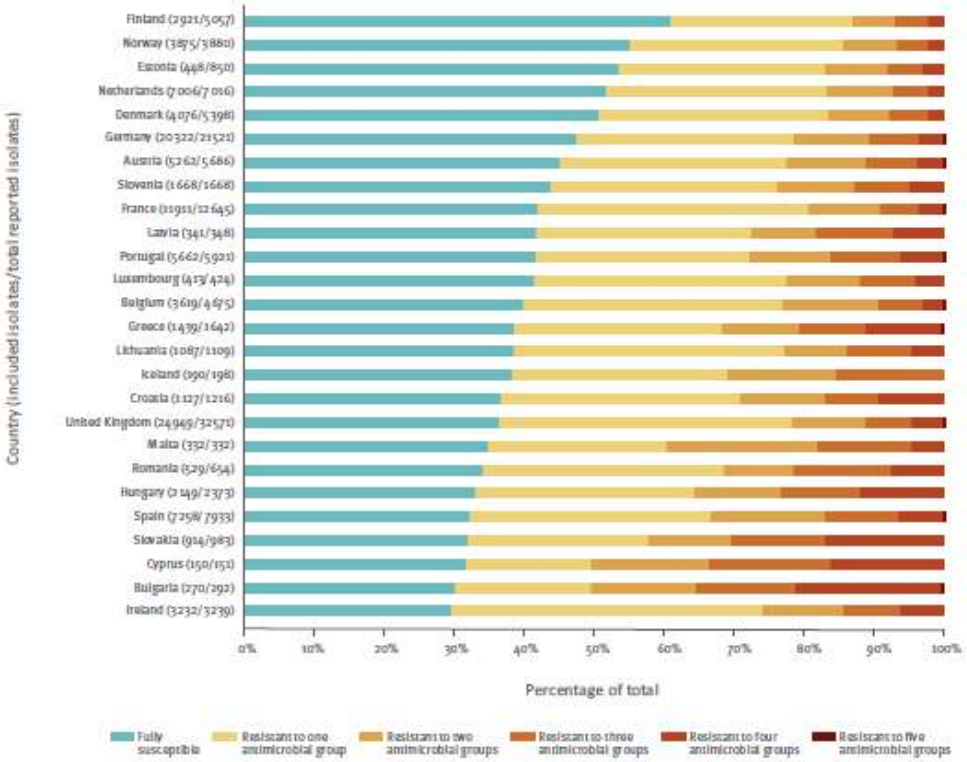


Figure 3.1. ***Escherichia coli.*** **Distribution of isolates: fully susceptible and resistant to one, two, three, four and five antimicrobial groups (among isolates tested against aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems), EU/EEA countries, 2018**



ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Figure 3.11. ***Klebsiella pneumoniae.*** **Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2018**

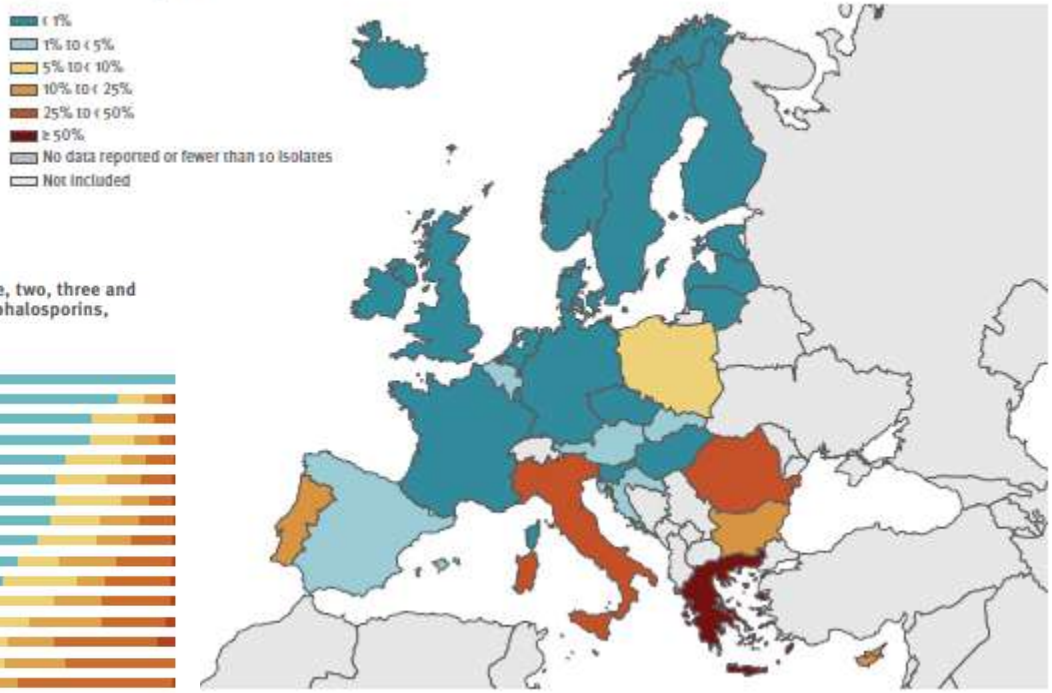
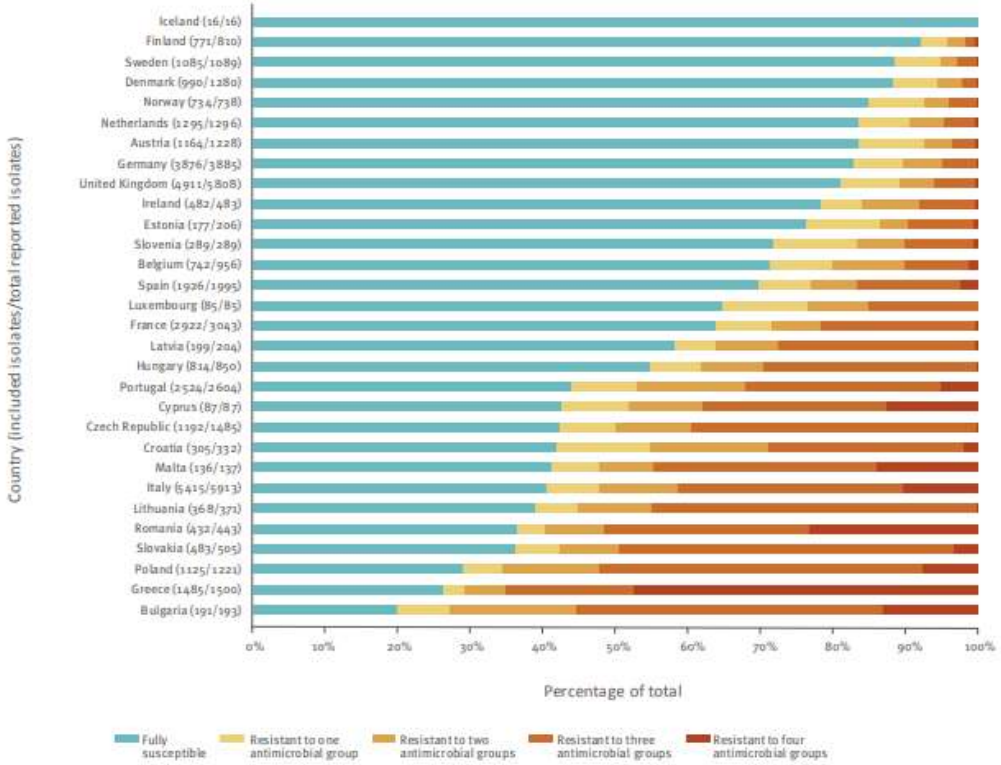


Figure 3.7. ***Klebsiella pneumoniae.*** **Distribution of isolates: fully susceptible and resistant to one, two, three and four antimicrobial groups (among isolates tested against fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems), EU/EEA countries, 2018**



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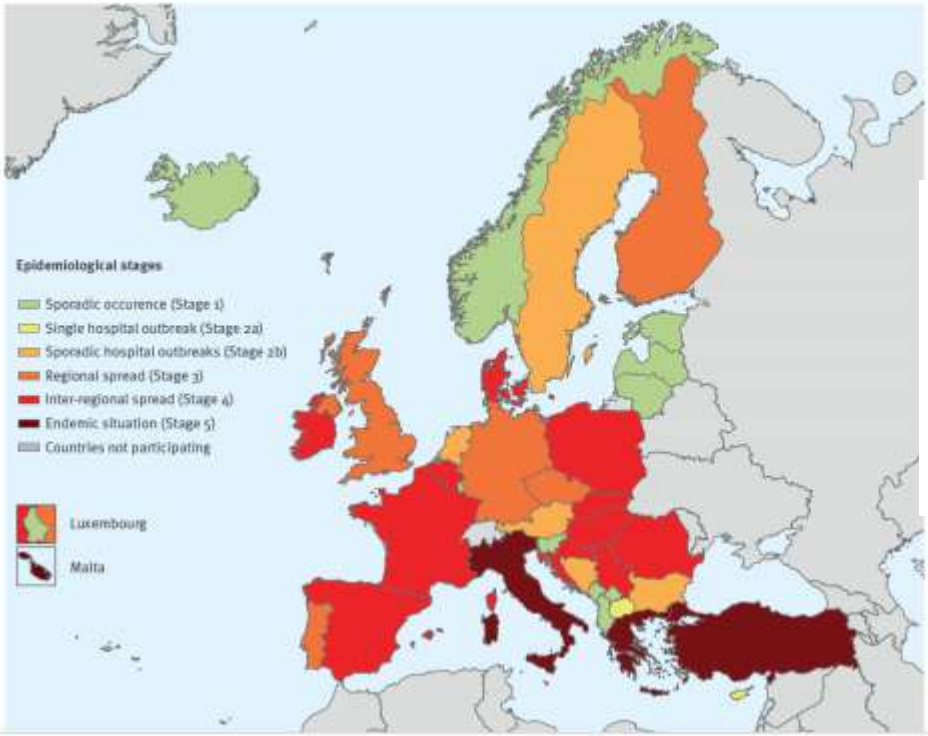
Carbapenem-resistant Enterobacteriaceae – second update

26 September 2019

Figure 2. Epidemiological situation of carbapenemase-producing Enterobacteriaceae, assessment by national experts in European countries, July 2018 (n=37) [2]



High mortality

High mortality rates, ranging from 30% to 75%, have been reported for patients with severe CRE infections [39]. Mortality above 50% has been reported in patients with CRE bloodstream infections [40], and a study has shown an excess mortality of 27% in patients with pneumonia or bloodstream infections caused by carbapenem-resistant *K. pneumoniae* [41]. The number of deaths attributable to infections with carbapenem-resistant *K. pneumoniae* and carbapenem-resistant *E. coli* has been estimated as 2 118 (range 1 795-2 473) and 141 (119-165) respectively in the EU/EEA for 2015 [3].

Hypervirulent *K. pneumoniae* strains with a hypermucoviscous phenotype are disseminating in the community causing severe infections in young healthy individuals without comorbidities [42]. Although antimicrobial resistance is rare in hypervirulent *K. pneumoniae* strains, strains combining carbapenem resistance, high transmissibility and hypervirulence have been described, so far mainly from Asia [42,43]. Extremely high overall mortality (84%) was associated with 86 *K. pneumoniae* bacteraemia isolates in India that exhibited hypervirulence (determined by a positive string test) and carbapenem resistance (determined by a meropenem minimum inhibitory (MIC) concentration of ≥16µg/ml) [44].

World Health Organization
REGIONAL OFFICE FOR Europe

Central Asian and Eastern European Surveillance of Antimicrobial Resistance

Annual report 2018

This report describes resistance data gathered through the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) network from 10 countries in the WHO European Region – Belarus, Bosnia and Herzegovina, Georgia, Montenegro, the Russian Federation, Serbia, Switzerland, the former Yugoslav Republic of Macedonia, Turkey and Ukraine – and Kosovo (in accordance with United Nations Security Council resolution 1244 (1999)). The fourth CAESAR report includes resistance data from Ukraine for the first time, provides a summary of the first five years of CAESAR external quality assessment (2013–2017) and presents preliminarily results of a proof-of-principle project in Armenia. It furthermore includes a reader's guide on how to interpret the surveillance data with caution, taking into account conditions which may reduce the reliability and representativeness of the data. The aim of this report is to

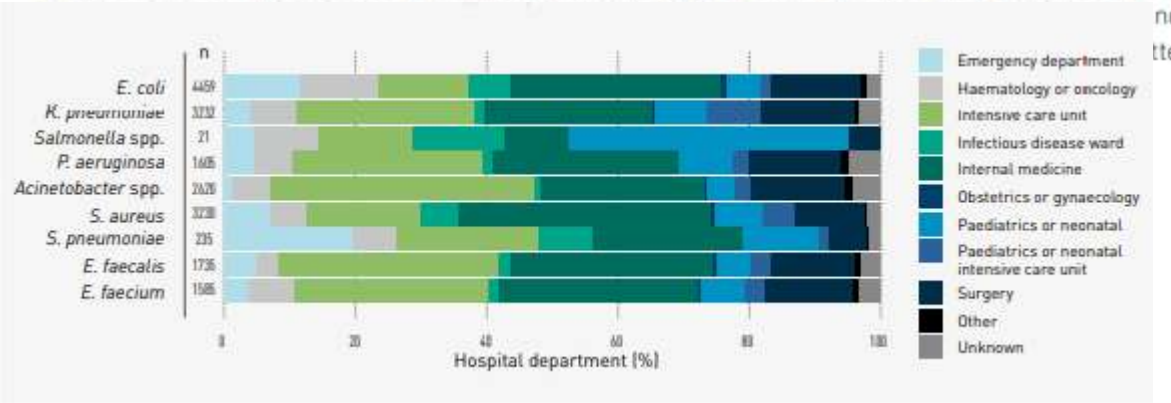
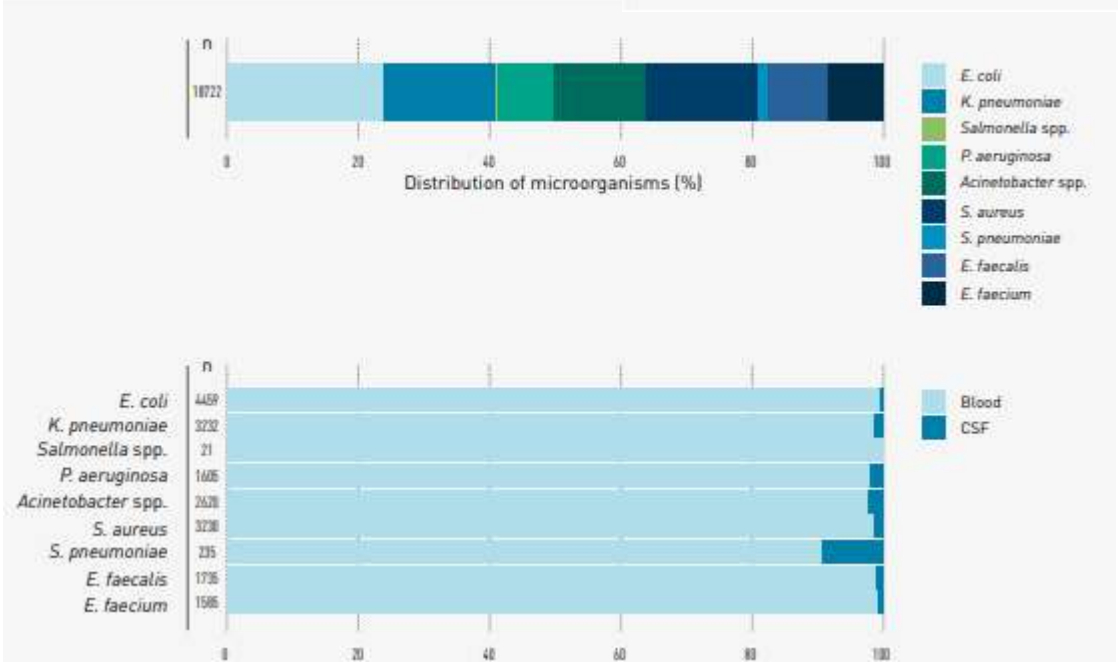


Fig. 5.9 Patient characteristics of isolates in Turkey in



18722 antibiyogram(kan ve BOS)

Toplum+Hastane kökenli

MDR

- *E.coli* %19
- *K. pneumoniae* %39
- *P.aeruginosa* %32
- *Acinetobacter spp.* %78

World Health Organization
Europe

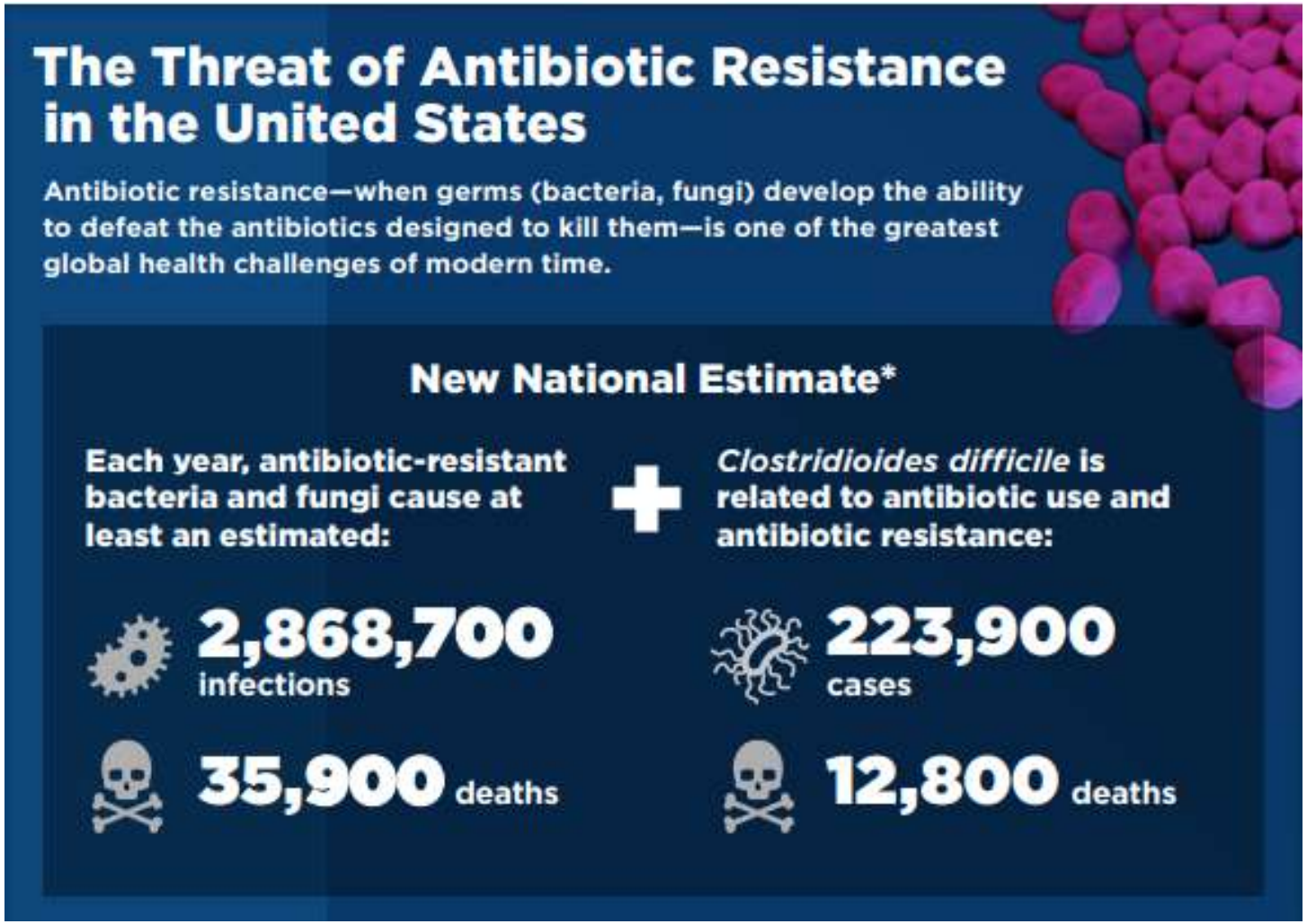
Central Asian and Eastern European Surveillance of Antimicrobial Resistance

Annual report 2018

ages of resistance for *E. coli* and *K. pneumoniae* among blood and CSF isolates in

Antibiotic (group)	*E. coli*		*K. pneumoniae*	
	N	Resistance (%)	N	Resistance (%)
Amoxicillin/ampicillin (R)[a]	3652	78	NA	NA
Amoxicillin-clavulanic acid (R)	3110	59	1980	72
Piperacillin-tazobactam (R)	4022	22	2998	58
Cefotaxime/ceftriaxone (R)[b]	4059	52	2880	71
Cefotaxime/ceftriaxone (I+R)[b]	4059	53	2880	72
Ceftazidime (R)	3701	44	2803	69
Ertapenem (R)	3818	6	2815	43
Imipenem/meropenem (R)[c]	4321	3	3165	32
Imipenem/meropenem (I+R)[c]	4321	4	3165	38
Gentamicin/tobramycin (R)[d]	4083	27	2991	45
Amikacin (R)	4218	2	3060	19
Ciprofloxacin/levofloxacin/ofloxacin (R)[e]	4022	52	3009	61
Ciprofloxacin/levofloxacin/ofloxacin (I+R)[e]	4022	60	3009	66
Multidrug resistance (R)[f]	3755	19	2821	39

Direncin Hastaya Bedeli



CDC-Antibiotic Resistance Threats in the United States, 2019

CDC-Antibiotic Resistance Threats in the United States, 2019

Literatürde –MDR Gr- Bakteri Enfeksiyonlarının Hastaya Bedeli

Association between infections caused by multidrug-resistant gram-negative bacteria and mortality in critically ill patients

World Journal of Critical Care Medicine

Elisabeth Paramythiotou, Christina Routsi

World J Crit Care Med 2016 May 4; 5(2): 111-120

- 24 çalışma (Pubmed, 2000-2015)
  - 10 çalışma antimikrobiyal direncin mortaliteyi arttırmadığı
  - 14 çalışma arttırdığını
- Çalışma metodları homojenize değil, confounder faktörler kontrol edilmemiş
- Gr- MDR enfeksiyonları ile mortalite ilişkisi doğrulanamamış

Abstract

The incidence of gram-negative multidrug-resistant (MDR) bacterial pathogens is increasing in hospitals and particularly in the intensive care unit (ICU) setting. The clinical consequences of infections caused by MDR pathogens remain controversial. The purpose of this review is to summarize the available data concerning the impact of these infections on mortality in ICU patients. Twenty-four studies, conducted exclusively in ICU patients, were identified through PubMed search over the years 2000-2015. Bloodstream infection was the only infection examined in eight studies, respiratory infections in four and variable infections in others. Comparative data on the appropriateness of empirical antibiotic treatment were provided by only seven studies. In ten studies the presence of antimicrobial resistance was not associated with increased mortality; on the contrary, in other studies a significant impact of antibiotic resistance on mortality was found, though, sometimes, mediated by inappropriate antimicrobial treatment. Therefore, a direct association between infections due to gram-negative MDR bacteria and mortality in ICU patients cannot be confirmed. Sample size, presence of multiple confounders and other methodological issues may influence the results. These data support the need for further studies to elucidate the real impact of infections caused by resistant bacteria in ICU patients.

Table 1 Studies describing mortality in intensive care unit patients with infections caused by multi-drug resistant bacteria *vs* susceptible

Ref.	Study design	No. of cases	Type of infection	Isolates/resistance definition	Results/comments
Blot *et al*[35]	Retrospective, cohort study	328	BSI	Variable/ceftazidime-resistance	Antibiotic resistance does not affect the outcome
Peres-Bota *et al*[36]	Prospective	186	Variable infections	Variable[2]/at least to ceftazidime, animoglycosides, carbapenems or quinolones	No difference in mortality
Ortega *et al*[37]	Single center prospective study	53	Colonization and infection	*P. aeruginosa*/resistant at least to two classes of antibiotics	No difference in mortality
Combes *et al*[38]	Secondary analysis of a large study	115	VAP	*P. aeruginosa*/resistance to piperacillin	28-d mortality not associated with piperacillin resistance
Mouloudi *et al*[43]	Double case -control study	59	BSI	*K. pneumoniae*/carbapenem resistance	Positive association between KPC producing *K. pneumoniae* and mortality
Michalopoulos *et al*[44]	Retrospective case-control study	84	Primary BSIs (78% ICU-acquired, 22% ward-acquired)	*K. pneumoniae, A. baumanni, P. aeruginosa*/resistance to at least 4 out of 7 antibiotic classes	Higher hospital mortality, compared to controls
Lambert *et al*[47]	Multicenter prospective cohort study	119699	Pneumonia,	*E.coli, A. baumannii, P. aeruginosa, S. aureus*/resistance to 3rd generation cephalosporins, ceftazidime, and oxacillin, respectively	The additional effect of the most common antimicrobial resistance patterns on mortality is comparatively low
Tabah *et al*[48]	Prospective multicentre cohort study	1156	BSI BSI	Multiple isolates[2]/according to the ESCMID	Resistance is associated with increased 28-d mortality
Patel *et al*[49]	Prospective cohort matched case-	298	Variable infections	*A. baumannii, K. pneumoniae, P. aeruginosa*/susceptible to ≤ 1	Resistance not associated with mortality
Papadimitriou-Olivgeris *et al*[53]	Single center study	273	Variable infections	*K. pneumoniae*/resistance to gentamicin, colistin and/or tigecycline	Positive association with mortality
Zilberberg *et al*[54]	Single center retrospective cohort study	1076	BSI	Variable gram-negative/*P.aeruginosa* resistant to at least 3 antimicrobials, ESBL, CPE	Impact of MDR on inappropriate therapy/indirect effect on increased hospital mortality
Shorr *et al*[55]	Retrospective cohort study	131	BSI	*A. baumannii*/carbapenem resistance	Impact of carbapenem resistance on inappropriate therapy/indirect effect on mortality
Dubar *et al*[56]	3-center, prospective cohort study	120	Variable infections	Variable pathogens/MDR *P. aeruginosa*: Resistance to at least 3 of the following: *Pseudomonas* acting beta-lactams, carbapenems, aminoglycosides, and quinolones	MDR *P. aeruginosa* infection was independent risk factor for mortality

PLoS One. 2020 Jan 10;15(1):e0227139. doi: 10.1371/journal.pone.0227139. eCollection 2020.

Impact of multi-drug resistant bacteria on economic and clinical outcomes of healthcare-associated infections in adults: Systematic review and meta-analysis.

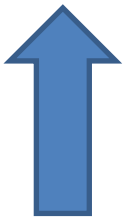
Serra-Burriel M[1], Keys M[1], Campillo-Artero C[1,2], Agodi A[3], Barchitta M[3], Gikas A[4,5], Palos C[6], López-Casasnovas G[1].

Abstract

BACKGROUND: Infections with multidrug resistant (MDR) bacteria in hospital settings have substantial implications in terms of clinical and economic outcomes. However, due to clinical and methodological heterogeneity, estimates about the attributable economic and clinical effects of healthcare-associated infections (HAI) due to MDR microorganisms (MDR HAI) remain unclear. The objective was to review and synthesize the evidence on the impact of MDR HAI in adults on hospital costs, length of stay, and mortality at discharge.

METHODS AND FINDINGS: Literature searches were conducted in PubMed/MEDLINE, and Google Scholar databases to select studies that evaluated the impact of MDR HAI on economic and clinical outcomes. Eligible studies were conducted in adults, in order to ensure homogeneity of populations, used propensity score matched cohorts or included explicit confounding control, and had confirmed

- Mart,Haziran ve 3 Eylül 2019 literatür taraması
- Homojenliği sağlayıcı metodlar kullanılmış, confounding faktör kontrolü yapılmış
- 16 makale (6122 MDR, 8326 non-MDR HAİ)
- MDR HAİ
  - Maliyeti (OR 1.33, %95 CI; 1.15-1.54)
  - Yatış süresini (OR 1.27, %95 CI; 1.1-1.37)
  - Mortaliteyi (OR 1.61, %95 CI; 1.36-1.90)



Literatürde –MDR *Enterobacteriaceae* Enfeksiyonlarının Hastaya Bedeli

Lancet Infect Dis. 2017 Jul;17(7):726-734. doi: 10.1016/S1473-3099(17)30228-1. Epub 2017 Apr 22.

Effect of appropriate combination therapy on mortality of patients with bloodstream infections due to carbapenemase-producing Enterobacteriaceae (INCREMENT): a retrospective cohort study.

- Çok merkezli retrospektif kohort (2004-2013)
  - 11 ülkeden 26 hastane
  - 437 CR-E bakteriyemi (%85'i Kp, %75CR)
  - Uygun mono/kombine tedavi…30 günlük mortalite
- Cox regresyon (mortalite) analizinde
  - Uygun tedavi başlanması (ilk 5 günde)
  - Mortalite açısından yüksek riskli (scor 8-15)

  hastalarda kombinasyon tedavisi mortaliteyi

Open Forum Infect Dis. 2018 Jul; 5(7): ofy150.

Open Forum Infectious Diseases

REVIEW ARTICLE

Association Between Carbapenem Resistance and Mortality Among Adult, Hospitalized Patients With Serious Infections Due to *Enterobacteriaceae*: Results of a Systematic Literature Review and Meta-analysis

Amber Martin,[1] Kyle Fahrbach,[1] Qi Zhao,[2,a] and Thomas Lodise[3]

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This study quantified mortality associated with serious infections caused by carbapenem-resistant (CRE) and carbapenem-susceptible *Enterobacteriaceae* (CSE). A systematic literature review was conducted, evaluating outcomes in hospitalized patients with CRE infections from a blood, urinary, pulmonary, or intra-abdominal source. A meta-analysis (MA) calculating odds ratios (ORs) for mortality was performed. Twenty-two studies met the criteria for inclusion in the MA: 12 included mortality data for CRE vs CSE populations. Compared with CSE, CRE was associated with a significantly higher risk of overall mortality (OR, 3.39; 95% confidence interval [CI], 2.35–4.89), as was monotherapy (vs combination therapy) treatment of patients with CRE infections (OR, 2.19; 95% CI, 1.00–4.80). These results document the increased mortality associated with serious CRE infections compared with CSE infections among hospitalized adults. It will be important to reevaluate the mortality in CRE and CSE populations, especially among patients who receive early appropriate therapy, as new antibiotics become available.

Keywords. bacterial drug resistance; carbapenems; *Klebsiella pneumoniae*; meta-analysis; mortality.

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RESEARCH ARTICLE
Clinical Science and Epidemiology

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A Cohort Study of the Impact of Carbapenem-Resistant *Enterobacteriaceae* Infections on Mortality of Patients Presenting with Sepsis

Sabrina Sabino,[a,b] Silvia Soares,[c] Fabiano Ramos,[a,b,c,d] Miriane Moretti,[e] Alexandre P. Zavascki,[d,f,g] Maria Helena Rigatto[a,b,g,h]

ABSTRACT The objective of this study is to evaluate the impact of carbapenem-resistant *Enterobacteriaceae* (CRE) infection on sepsis 30-day mortality. A retrospective cohort of patients >18 years old with sepsis and organ dysfunction or septic shock was conducted. Univariate analysis was done for variables potentially related to 30-day mortality, and the ones with *P* valu ward stepwise hierarchic Cox regression mode ues of <0.05 were retained in the model. A to lyzed. Gram-negative bacterial infections occu with positive cultures, of which 69 (17.7%) wer with CRE infections had significantly higher ($P < 0.01$). CRE infection was also associated wi cal therapy ($P < 0.01$) and with the presence of chic multivariate model, CRE remained significa variables, comorbidities, and infection site but septic shock and appropriate empirical therap status ($P < 0.01$), cirrhosis ($P < 0.01$), septic s related organ failure assessment (quick-SOFA) therapy ($P = 0.01$) remained in the final model. CRE infections were associated with higher crude mortality rates. A lower rate of appropriate empirical therapy and late diagnosis were more frequent in this group, and improvement of stewardship programs is needed.

TABLE 3 Stratified Cox regression analysis according to septic shock status[a]

	Septic shock			No septic shock		
Variable	HR	95% CI	*P* value	HR	95% CI	*P* value
CRE	0.87	0.57–1.33	0.52	2.36	1.46–3.83	<0.01
Age	1.01	1.00–1.102	<0.01	1.01	1.01–1.03	<0.01
HIV status	1.62	0.96–2.72	0.07	2.40	1.25–4.64	<0.01
Cirrhosis	1.77	1.04–3.00	0.04	3.13	1.37–7-19	<0.01
Quick SOFA	1.06	0.91–1.24	1.06	1.43	1.17–1.74	<0.01
Appropriate empirical therapy	0.69	0.51–0.92	0.01	0.89	0.59–1.37	0.60

[a]Abbreviations: HR, hazard ratio; CI, confidence interval; CRE, carbapenem-resistant *Enterobacteriaceae*.

Infect Control Hosp Epidemiol. 2017 Nov;38(11):1319-1328. doi: 10.1017/ice.2017.197. Epub 2017 Sep 27.

Carbapenem Resistance, Initial Antibiotic Therapy, and Mortality in Klebsiella pneumoniae Bacteremia: A Systematic Review and Meta-Analysis.

Kohler PP[1], Volling C[1], Green K[1], Uleryk EM[1], Shah PS[1], McGeer A[1].

Abstract

BACKGROUND Mortality associated with infections caused by carbapenem-resistant Enterobacteriaceae (CRE) is higher than mortality due to carbapenem-sensitive pathogens. OBJECTIVE To examine the association between mortality from bacteremia caused by carbapenem-resistant (CRKP) and carbapenem-sensitive Klebsiella pneumoniae (CSKP) and to assess the impact of appropriate initial antibiotic therapy (IAT) on mortality. DESIGN Systematic review and meta-analysis. METHODS We searched MEDLINE, EMBASE, CINAHL, and Wiley Cochrane databases through August 31, 2016, for observational studies reporting mortality among adult patients with CRKP and CSKP bacteremia. Search terms were related to Klebsiella, carbapenem resistance, and infection. Studies including fewer than 10 patients per group were excluded. A random-effects model and meta-regression were used
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- 31 Ağustos 2016'a kadar yayınlanan
  - CRKP ve CSKP bakteriyemi
  - Mortalite
- Random effect modeli ve meta regresyon (mortalite)
  - Karbepenem direnci mortaliteyi (OR 2.2;%95 Cl 1.8-2.6)
  - Uygun başlangıç tedavisi (OR 0.5 ;%95 Cl0.3-0.7)

International Journal of Antimicrobial Agents 55 (2020) 105833

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journal homepage: www.elsevier.com/locate/ijantimicag

Review

A systematic review and meta-analysis of treatment outcomes following antibiotic therapy among patients with carbapenem-resistant *Klebsiella pneumoniae* infections

Akosua A. Agyeman[a], Phillip J. Bergen[a], Gauri G. Rao[b], Roger L. Nation[c], Cornelia B. Landersdorfer[a,*]

A B S T R A C T

Introduction: Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) infections are a major global public health challenge. This study aimed to systematically review the evidence on treatment outcomes (mortality, clinical and microbiological response) following antibiotic therapy administered for CRKP infections.

Methods: Medline, EMBASE, the Cochrane Central Register of Controlled Trials, and the International Pharmaceutical Abstracts databases were searched from inception to 26 December 2018. Data were analysed

- Sistematik review ve meta analiz (26 Ekim 2018)
  - 1843 çalışma içinden
  - 54 gözlemsel çalışma, 3195 CRKp
- Mortalite %37.2
- Kombinasyon tedavisinin 14 ve 30günlük mortaliteyi
- Klinik / mikrobiyolojik cevabı etkilemediği

XDR-PDR Bakteri Enfeksiyonlarının Hastaya Bedeli

ORIGINAL ARTICLE

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-019-03784-9

Check for updates

Treatment pattern, prognostic factors, and outcome in patients with infection due to pan-drug-resistant gram-negative bacteria

Diamantis P. Kofteridis[1] · Angeliki M. Andrianaki[1] · Sofia Maraki[2] · Anna Mathioudaki[1] · Marina Plataki[1] · Christina Alexopoulou[3] · Petros Ioannou[1] · George Samonis[1] · Antonis Valachis[4]

- Yunanistan'da tek merkezli retrospektif Cohort (2010-2018)
- 64 PDR Gr- enfeksiyon
  - 31 Kp, 2 *Acinetobacter spp*, 6 *P.aeruginosa*
- Ölüm oranı %32

Variables	Odds ratio	95% confidence interval	*p* value
Charlson comorbidity index	1.5	1.0–2.3	0.030
Prior steroid use	4.1	1.0–17.0	0.049
Non-colistin, non-tigecycline empirical therapy	7.5	1.7–32.8	0.008

Table 3 Predictive factors for infection-related in-hospital mortality in patients with infection due to PDR pathogens

J Hosp Infect. 2018 Mar;98(3):260-263. doi: 10.1016/j.jhin.2017.11.014. Epub 2017 Dec 15.

Rapid emergence of colistin resistance and its impact on fatality among healthcare-associated infections.

Aydın M[1], Ergönül Ö[2], Azap A[3], Bilgin H[4], Aydın G[5], Çavuş SA[6], Demiroğlu YZ[7], Alışkan HE[8], Memikoğlu O[3], Menekşe Ş[9], Kaya Ş[10], Demir NA[11], Karaoğlan I[12], Başaran S[13], Hatipoğlu Ç[14], Erdinç Ş[14], Yılmaz E[15], Tümtürk A[16], Tezer Y[16], Demirkaya H[17], Çakar ŞE[18], Keske Ş[2], Tekin S[2], Yardımcı C[19], Karakoç Ç[20], Ergen P[21], Azap Ö[17], Mülazımoğlu L[4], Ural O[11], Can F[22], Akalın H[15]; Turkish Society of Clinical Microbiology and Infectious Diseases, Healthcare-related Infections Study Group, Turkey.

- Türkiye'de çok merkezli (2014-2015)
- 1556 Gr- HAİ-KDE
- Kp kolistin direnci %16.1
- Mortalite oranları;
  - En yüksek Acinetobacter bakteriyemilerinde (%58)
  - *P. aeruginosa (%45)*
  - *K. pneumonia (%41)*
  - *E. cloacea (%32)*
  - *E.coli (%28)*

- Mortaliteyi etkileyen faktörler;
  - Karbepenem MIC'i (OR 1.02, %95 CI 1.01-1.04)
  - Kolistin MIC'i (OR 1.1, %95 CI 1.03-1.17)

International Journal of Infectious Diseases 86 (2019) 208–211

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

The effect of colistin resistance and other predictors on fatality among patients with bloodstream infections due to *Klebsiella pneumoniae* in an OXA-48 dominant region

Şirin Menekşe[a,*], Yasemin Çağ[b], Mehmet Emirhan Işık[a], Suzan Şahin[c], Demet Hacıseyitoğlu[d], Fusun Can[e], Onder Ergonul[e]

Background: The aim of this study was to determine the effect of colistin resistance and other predictors on fatality among patients with *Klebsiella pneumoniae* bloodstream infections (Kp-BSI) and to describe the effect of amikacin and tigecycline on the outcome in an OXA-48 dominant country.

Method: This was a retrospective study performed among patients >16 years of age in a tertiary hospital with 4(

Results:

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- 210 hasta, Kp bağlı SBİ-KDE
- 30 günlük mortalite %58
- Ölen hastalarda
  - Karbapenem direnci
  - Kolistin MIC
- Mortaliteyi arttıran risk faktörleri
  - Karbapenem direnci (OR5.2,%95CI 2.47-10.9)
  - Yüksek APACHE II skoru(OR 1.19, %95CI 1.12-1.26)
- Mortaliteyi azaltan faktör
  - Kombinasyon rejiminde Amikasin (OR 0.05, %95 CI 0.01-0.23)

Risk Factors Affecting Patterns of Antibiotic Resistance and Treatment Efficacy in Extreme Drug Resistance in Intensive Care Unit-Acquired *Klebsiella Pneumoniae* Infections: A 5-Year Analysis

Durdu B[1], Meric Koc M[1], Hakyemez IN[1], Akkoyunlu Y[1], Daskaya H[2], Sumbul Gultepe B[3], Aslan T[1].

- 2012-2017 *K.pneumoniae* YBÜ enfeksiyonu
- Toplam 208 hasta (MDR olmayan 42, MDR 84, XDR-PDR 82)
- Direnç kategorisine göre kombinasyon tedavilerinin yaşam süresi ile ilişkisi

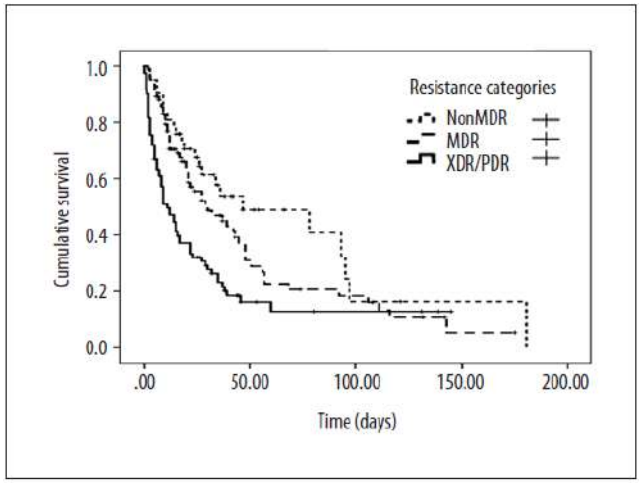

Figure 1. The relation between antibiotic resistance categories and cumulative survival.

Table 4. One-to-one effect of antibiotic groups on patient survival (Cox regression with enter method).

		HR	95.0% CI for HR	
	p		Lower	Upper
XDR-PDR	**<0.001**	1.481	1.238	1.772
Combinations with TMPS	**0.005**	0.460	0.267	0.794
Combinations with TGC	0.196	1.267	0.885	1.814
Combinations with CP/ single	0.370	1.171	0.829	1.655
Combinations with CS	0.432	1.148	0.814	1.618

Med Sci Monit, 2019; 25: 174-183
DOI: 10.12659/MSM.911338

Özet

- Ülkemizde dirençli E*nterobacteriaceae* enfeksiyonları ciddi bir sorun
- Literatürdeki çalışmalar direnç ile mortalitenin ilişkili olduğuna işaret ediyor
- Direnç aynı zamanda yatış süresi ve maliyeti de arttırmakta
- Başlanan uygun ampirik tedavi mortaliteyi azaltıyor
- Fakat PDR suşlarda uygun ve etkili antibiyotik yok
- Yeni antibiyotik üretimi ile ilgili sıkıntılar mevcut

Teşekkürler….