Antimikrobiyal Yönetimde Güncel Durum

Önder Ergönül, MD, MPH

Koç Üniversitesi Tıp Fakültesi

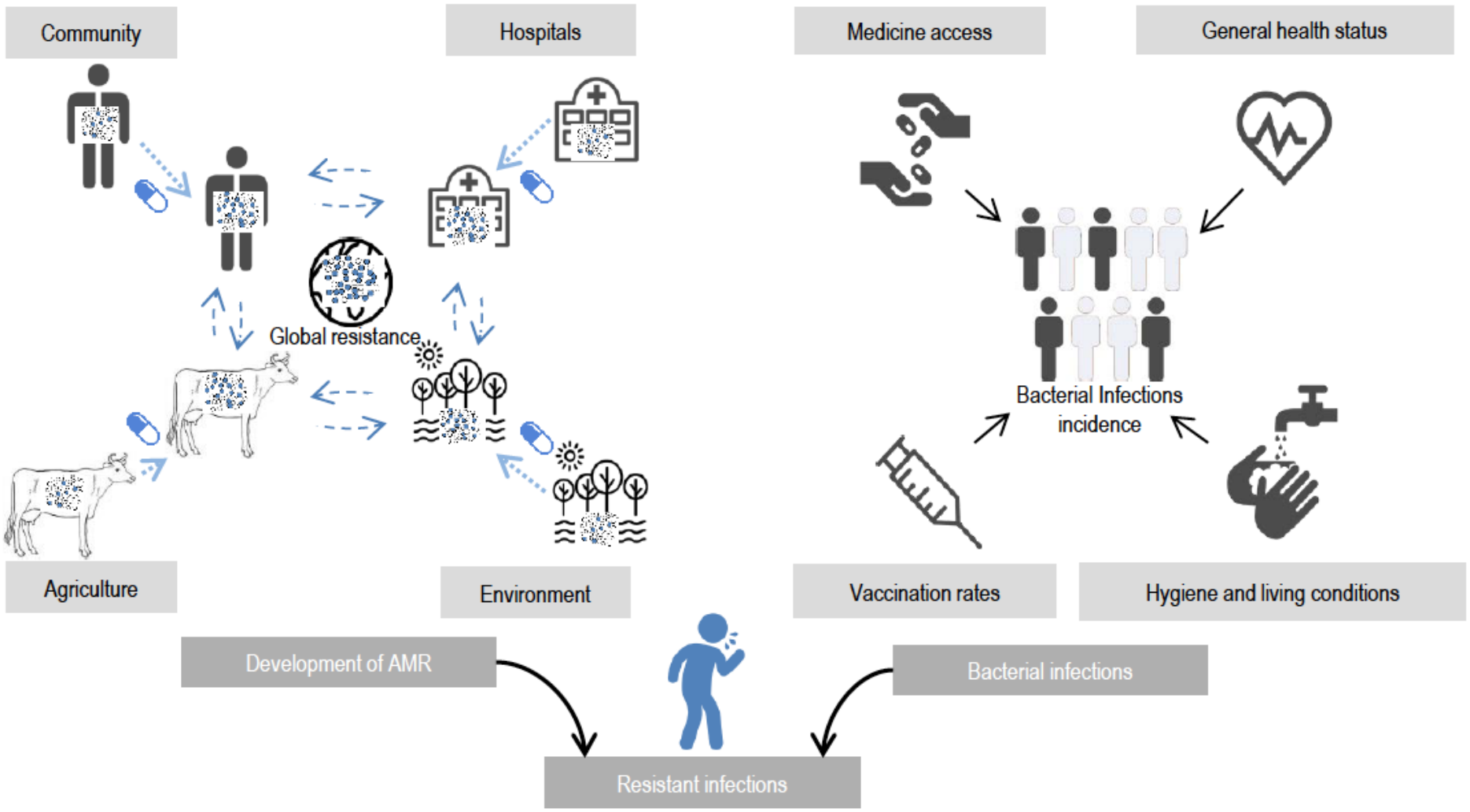
16 Mart 2019, KLİMİK

Sunum

- Dünyada Antibiyotik Direnci
  - CESAR
  - OECD

- Türkiye Çalışması
  - Ne yapmalı?

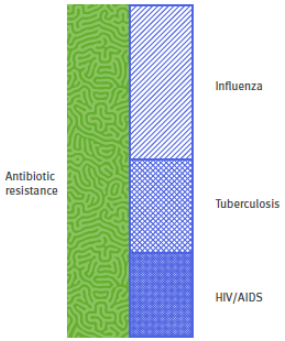
Figure 2.5. Factors influencing bacterial resistance, bacterial infections, and resistant infections



Antibiotic resistance – an increasing threat to human health

Antibiotic resistance is the ability of bacteria to combat the action of one or antibiotics. Humans and animals do not become resistant to antibiotics, but bacteria carried by humans and animals can.

The burden of infections with bacteria resistant to antibiotics on the European population is comparable to that of influenza, tuberculosis and HIV/AIDS combined.



Last-line antibiotics

39% of the burden is caused by infections with bacteria resistant to last-line antibiotics such as carbapenems and colistin - the last treatment option available.

33000 deaths

Each year, 33000 people die from an infection due to bacteria resistant to antibiotics. This is comparable to the total number of passengers of more than 100 medium-sized airplanes.

75 % healthcare-associated infections

75% of the burden of bacteria resistant to antibiotics in Europe is due to healthcare-associated infections. This could be minimised through adequate infection prevention and control measures, as well as antibiotic stewardship in healthcare settings.

Solutions

There is still time to turn the tide of antibiotic resistance and ensure that antibiotics remain effective in the future by:

Using antibiotics prudently and only when they are necessary.

Implementing good infection prevention and control practices, including hand hygiene as well as screening for carriage of/infection with multidrug-resistant bacteria and isolation of carriers/infected patients.

Promoting research and development of new antibiotics with novel mechanisms of action.

Increasing burden

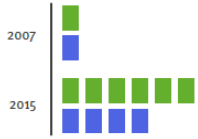
Between 2007 and 2015, the burden of each of the 16 antibiotic-resistant bacteria under study has increased in particular for *Klebsiella pneumoniae* and *Escherichia coli*:

Klebsiella pneumoniae

The number of deaths attributable to infections with *Klebsiella pneumoniae* resistant to carbapenems – a group of last-line antibiotics – increased six-fold.

Escherichia coli

The number of deaths attributable to infections with third-generation cephalosporin-resistant *Escherichia coli* increased four-fold.



Everyone is responsible

Everyone is responsible for addressing this threat to human health: patients, doctors, nurses, pharmacists, veterinarians, farmers, policy makers.

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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

EUROPEAN ANTIBIOTIC AWARENESS DAY
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antibiotic.ecdc.europa.eu

#KeepAntibioticsWorking
#EAAD

Quantifying drivers of antibiotic resistance in humans: a systematic review

Anuja Chatterjee, Maryam Modarai, Nichola R Naylor, Sara E Boyd, Rifat Atun, James Barlow, Alison H Holmes, Alan Johnson, Julie V Robotham

Mitigating the risks of antibiotic resistance requires a horizon scan linking the quality with the quantity of data reported on drivers of antibiotic resistance in humans, arising from the human, animal, and environmental reservoirs. We did a systematic review using a One Health approach to survey the key drivers of antibiotic resistance in humans. Two sets of reviewers selected 565 studies from a total of 2819 titles and abstracts identified in Embase, MEDLINE, and Scopus (2005–18), and the European Centre for Disease Prevention and Control, the US Centers for Disease Control and Prevention, and WHO (One Health data). Study quality was assessed in accordance with Cochrane recommendations. Previous antibiotic exposure, underlying disease, and invasive procedures were the risk factors with most supporting evidence identified from the 88 risk factors retrieved. The odds ratios of antibiotic resistance were primarily reported to be between 2 and 4 for these risk factors when compared with their respective controls or baseline risk groups. Food-related transmission from the animal reservoir and water-related transmission from the environmental reservoir were frequently quantified. Uniformly quantifying relationships between risk factors will help researchers to better understand the process by which antibiotic resistance arises in human infections.

Lancet Infect Dis 2018; 18: e368–78

Published Online August 29, 2018 http://dx.doi.org/10.1016/S1473-3099(18)30296-2

National Institute for Health Research, Health Protection Research Unit in Healthcare Associated Infection and Antimicrobial Resistance, Imperial College London, London, UK (A Chatterjee MSc, M Modarai PhD, N R Naylor MSc, S E Boyd MRCP,

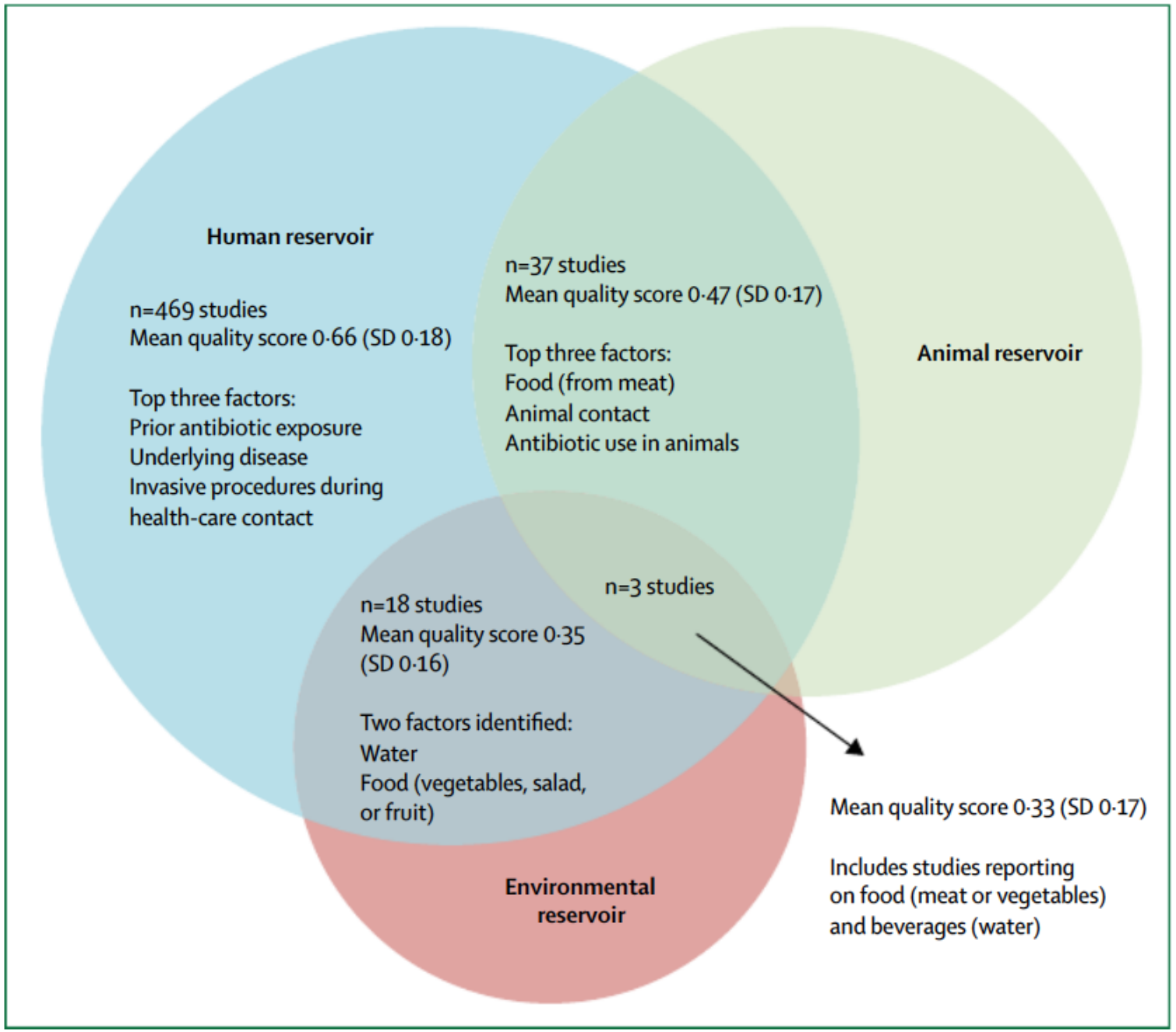


Figure 2: **Specific number of studies, quality, and top risk factors in each reservoir**
Studies within the scope of the blue circle were reviewed. Additional details are shown in the appendix.

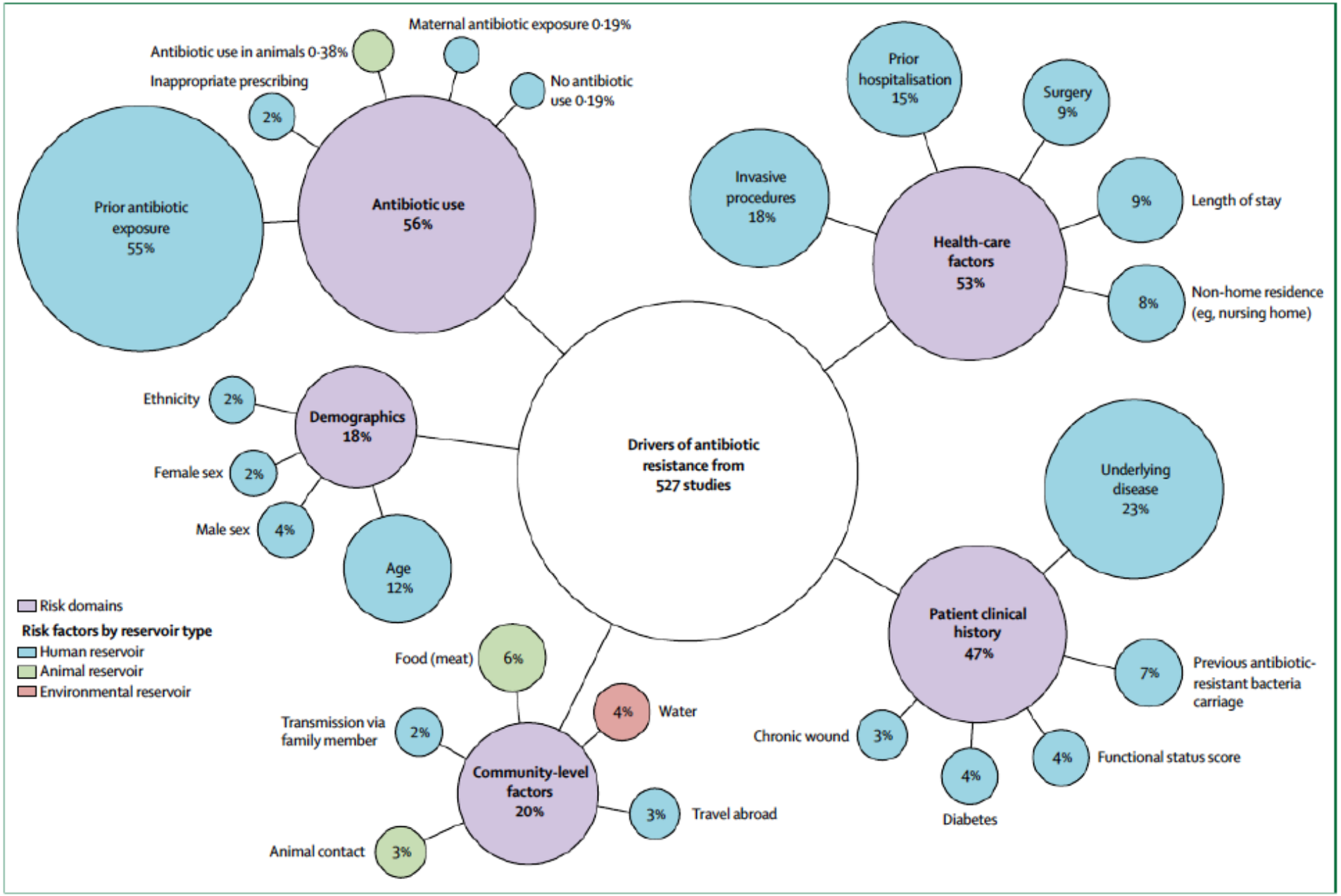
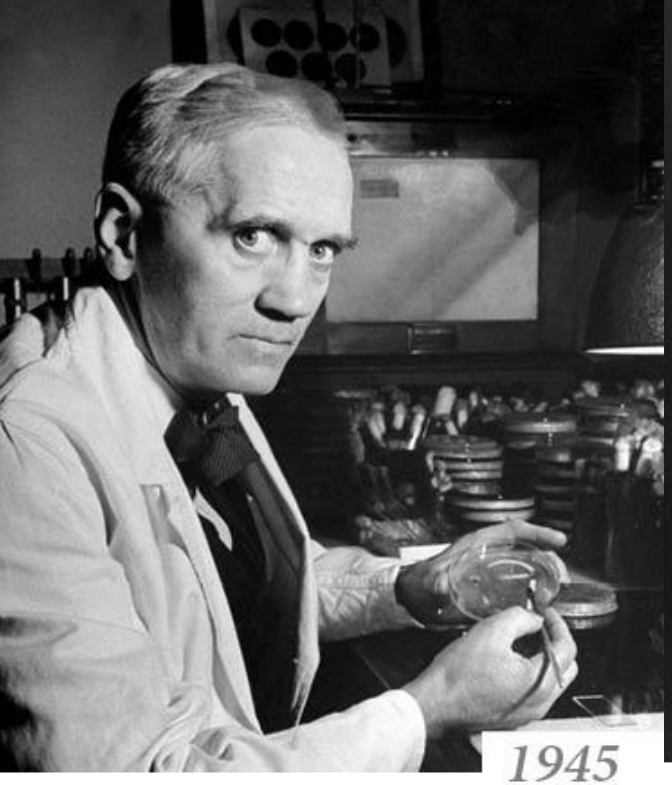


***Figure 3*: Percentage of studies quantifying drivers of antibiotic resistance in humans**

Bubble size represents the percentage of studies out of the total number of primary studies (n=527) for both the risk domains and their individual risk factors. For ease of presentation and clarity, only the top five risk factors from the individual risk domains are shown; therefore, these percentages might not add up to the total risk domain percentage. Because a single study could report a variety of risk factors across all the domains, the domains include duplicate studies and thus these percentages add up to more than 100%. Distances between bubbles are arbitrary.

Doktor, Sir Samuel Luke Fildes, 1891



1945

Sir Alexander FLEMING

Ödül nedeni: "Penisilinin ve çeşitli infeksiyon hastalıkları üzerindeki tedavi edici etkisinin keşfi"

Doğum: 6 Ağustos 1881, Lochfield, İskoçya
Ölüm: 11 Mart 1955, Londra, Birleşik Krallık (İngiltere)
Ödüllü aldığında çalıştığı kurum: Londra Üniversitesi, Londra, Birleşik Krallık (İngiltere)

Famous observation

1945

Ernst Boris CHAIN

Ödül nedeni: "Penisilinin ve çeşitli infeksiyon hastalıkları üzerindeki tedavi edici etkisinin keşfi"

Doğum: 19 Haziran 1906, Berlin, Almanya
Ölüm: 12 Ağustos 1979, Mulrany, İrlanda
Ödüllü aldığında çalıştığı kurum: Oxford Üniversitesi, Oxford, Birleşik Krallık (İngiltere)

Stable extraction of molecule

1945

ir Howard Walter FLOREY

ül nedeni: "Penisilinin ve çeşitli infeksiyon hastalıkları üzerindeki tedavi ci etkisinin keşfi

ğum: 24 Eylül 1898, Adelaide, Avustralya
im: 21 Şubat 1968, Oxford, Birleşik Krallık (İngiltere)
ülü aldığında çalıştığı kurum: Oxford Üniversitesi, Oxford, leşik Krallık (İngiltere)

Production in US

1939

BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 17 1937

PRONTOSIL IN THE TREATMENT OF ERYSIPELAS

A CONTROLLED SERIES OF 312 CASES*

BY

W. R. SNODGRASS, M.A., B.Sc., M.D., F.R.F.P.S.G.,

Assistant Physician, Western Infirmary, Glasgow

AND

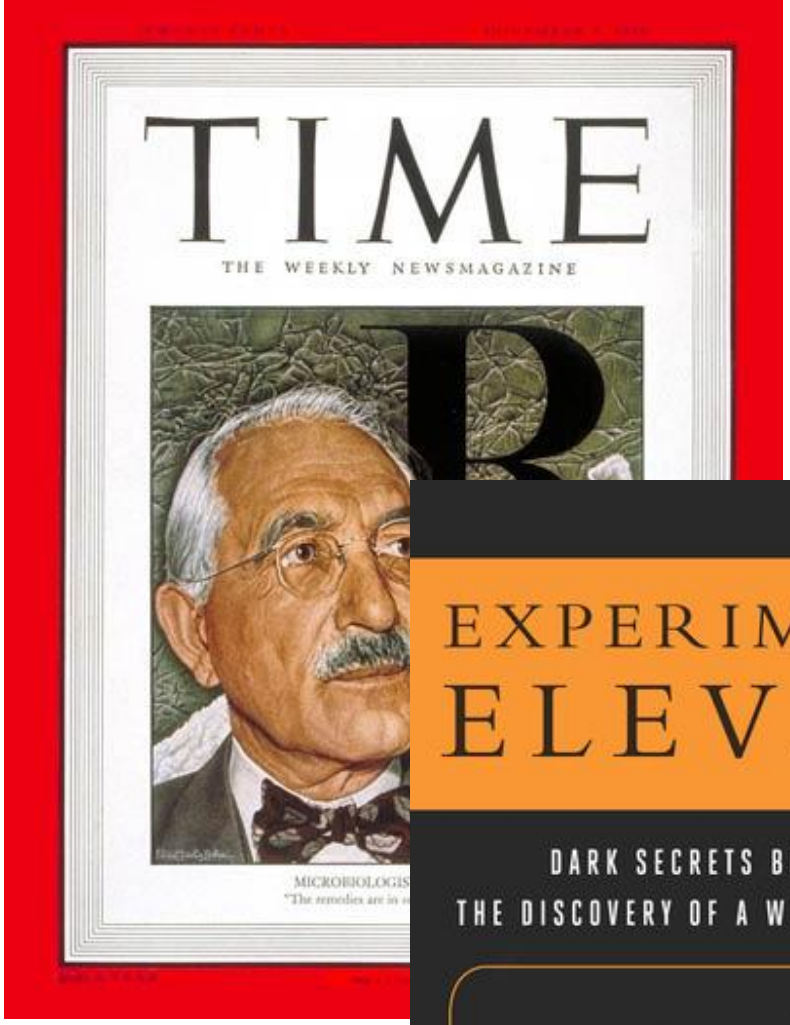
T. ANDERSON, M.B., Ch.B., M.R.C.P.Ed.

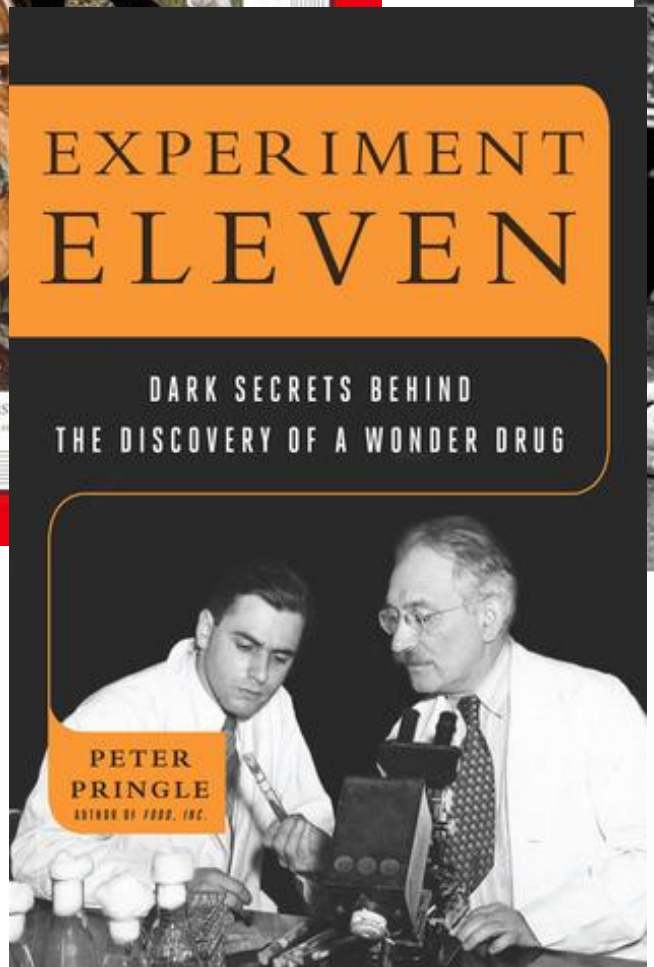
Deputy Superintendent, Rochill Hospital, Glasgow

Gerhard DOMAGK

Ödül nedeni: "Prontosilin antibakteriyel etkisinin keşfi"

Doğum: 30 Ekim 1895, Lagow, Almanya
Ölüm: 24 Nisan 1964, Burgberg, Batı Almanya
Ödülü aldığında çalıştığı kurum: Munster Üniversitesi, Munster, Almanya





1952

Selman Abraham WAKSMAN

Ödül nedeni: "Tüberküloza karşı etkili ilk antibiyotik olan streptomisinin keşfi"

Doğum: 22 Temmuz 1888, Priluka, Çarlık Rusyası (Ukrayna)
Ölüm: 16 Ağustos 1973, Hyannis, MA, ABD
Ödüllü aldığında çalıştığı kurum: Rutgers Üniversitesi, New Brunswick, NJ, ABD

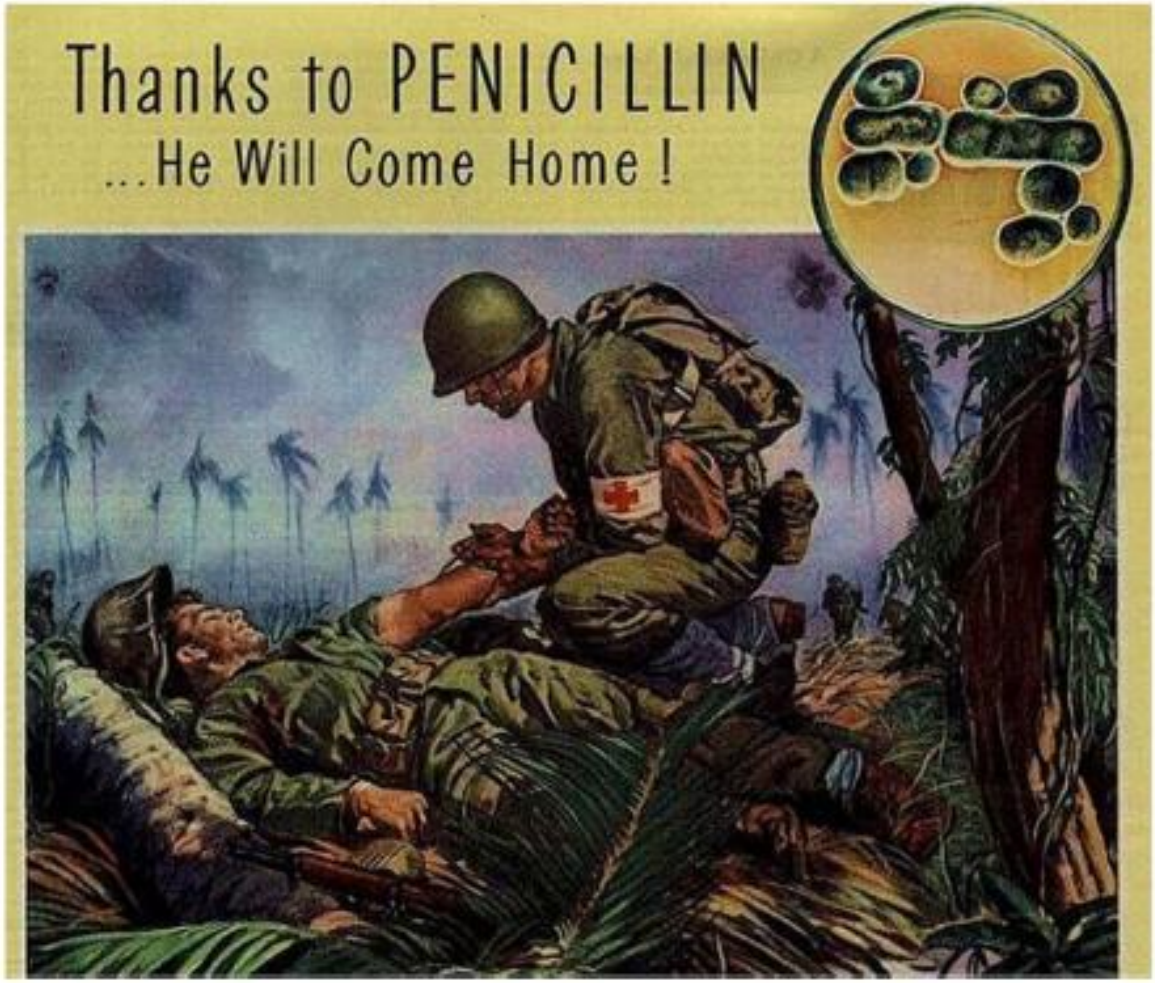


Figure 1 An advertisement by Schenley Laboratories Inc.
By 1944, laboratories across the country were increasing penicillin production. Schenley's advertisement stated, "When the thunderous battles of this war have subsided to pages of silent print in a history book, the greatest news event of World War II may well be the discovery and development of penicillin." Credit: Research and Development Division, Schenley Laboratories Inc., Lawrenceburg, Indiana, USA.

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- Comprehensive review of scientific research
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- 200 tincture ratios

STEPHEN HARROD BUHNER

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— from the Foreword by James A. Duke, PhD, author of *The Green Pharmacy*

World Health Organization
REGIONAL OFFICE FOR Europe

Central Asian and Eastern European Surveillance of Antimicrobial Resistance

Annual report 2017

Box 2.4. Priority pathogens

In 2017 WHO published a list of priority pathogens (Tacconelli et al., 2018[37]) for which urgent action is needed. This list divided pathogens into critical, high, and medium priority groups according to the threat level each poses to human health. Bacteria and specific antibiotic resistances, according to priority category, are:

Critical priority pathogens:

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, third-generation cephalosporin-resistant

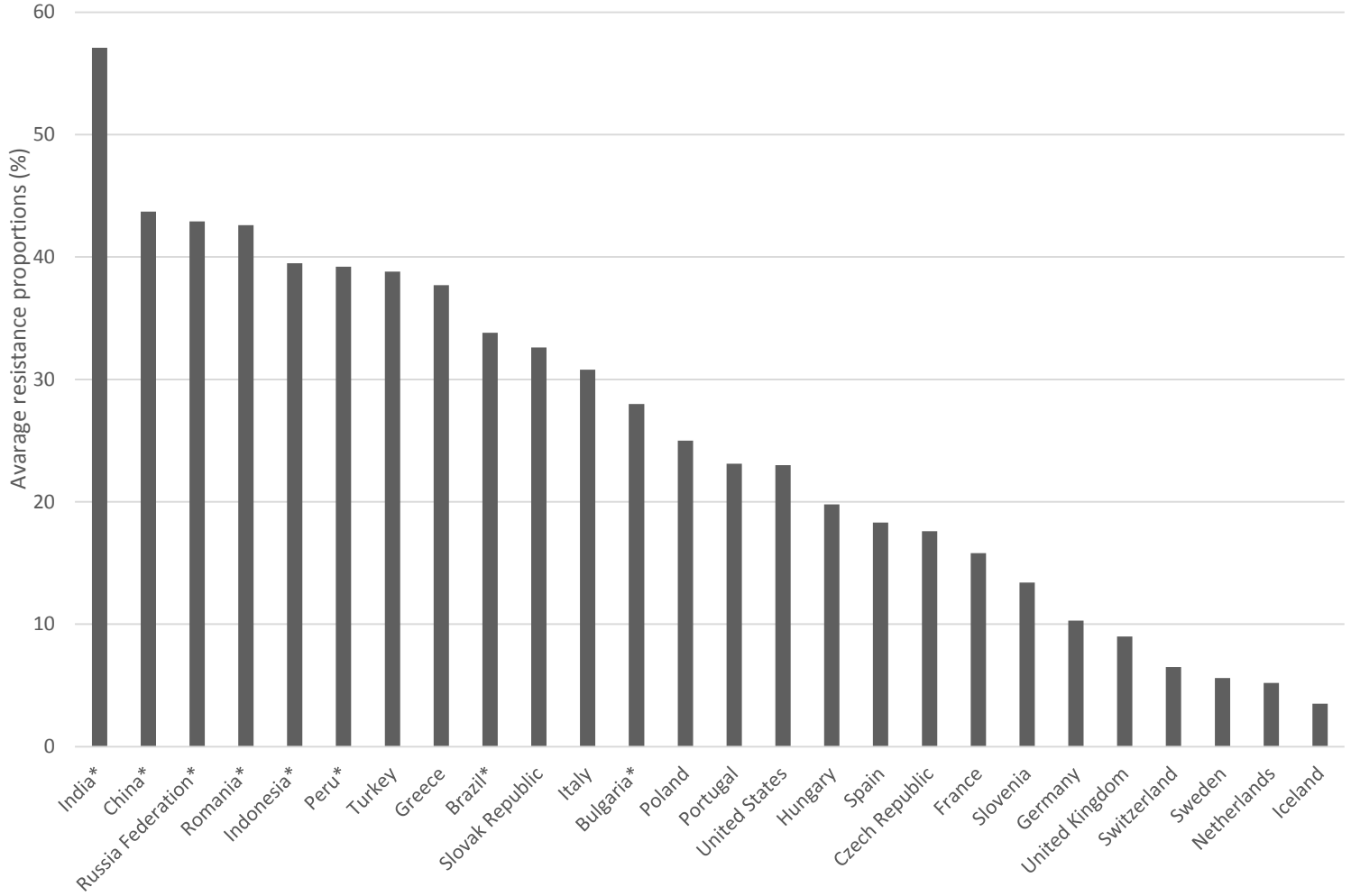
High priority pathogens:

- *Enterococcus faecium*, vancomycin-resistant
- *Staphylococcus aureus*, methicillin-resistant, vancomycin intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter spp.*, fluoroquinolone-resistant
- *Salmonella spp.*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, third generation cephalosporin-resistant, fluoroquinolone-resistant

Medium priority pathogens:

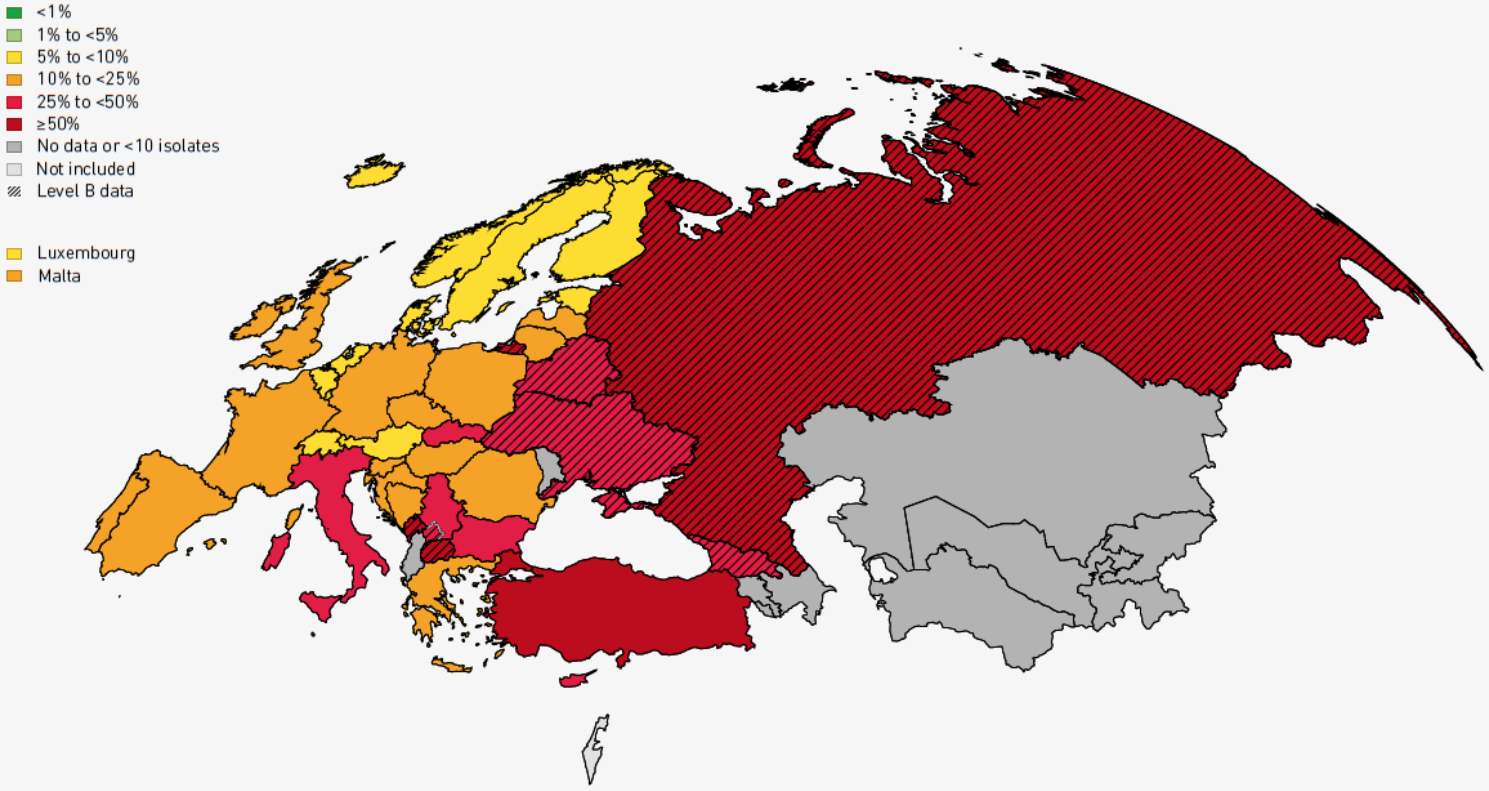
- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant
- *Shigella spp.*, fluoroquinolone-resistant

Antibiyotik Direnci Ortalaması, 2015



8 önemli sorun; (FREC: fluoroquinolone-resistant *E. coli*, VRE: vancomycin-resistant *E. faecium and E.faecalis*, 3GCREC: third-generation cephalosporin-resistant *E. coli*, CRKP: carbapenem-resistant *K. pneumoniae*, 3GCRKP: third-generation cephalosporin-resistant *K. pneumoniae*, CRPA: carbapenem-resistant *P. aeruginosa*, MRSA: methicillin-resistant *S. aureus*, PRSP: penicillin-resistant *S. pneumoniae*, CRAB: carbapenem-resistant *A. baumannii*)

E. coli: 3. Kuşak Sefalosporin Direnci



Level B data: the data provide an indication of the resistance patterns present in clinical settings in the country or area, but the proportion of resistance should be interpreted with care. Improvements are needed to attain a more valid assessment of the magnitude and trends of AMR in the country or area. See section 4.2 for more information about levels of evidence, which are only provided for CAESAR countries and areas.

EARS–Net countries: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.
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Data sources: 2017 data from the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2018) and 2017 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net, ©ECDC 2018).

Fig. 7.1 Third-generation cephalosporin-resistant *E. coli* in the European Region (EARS-Net and CAESAR), 2017

E. coli: Karbapenem Direnci

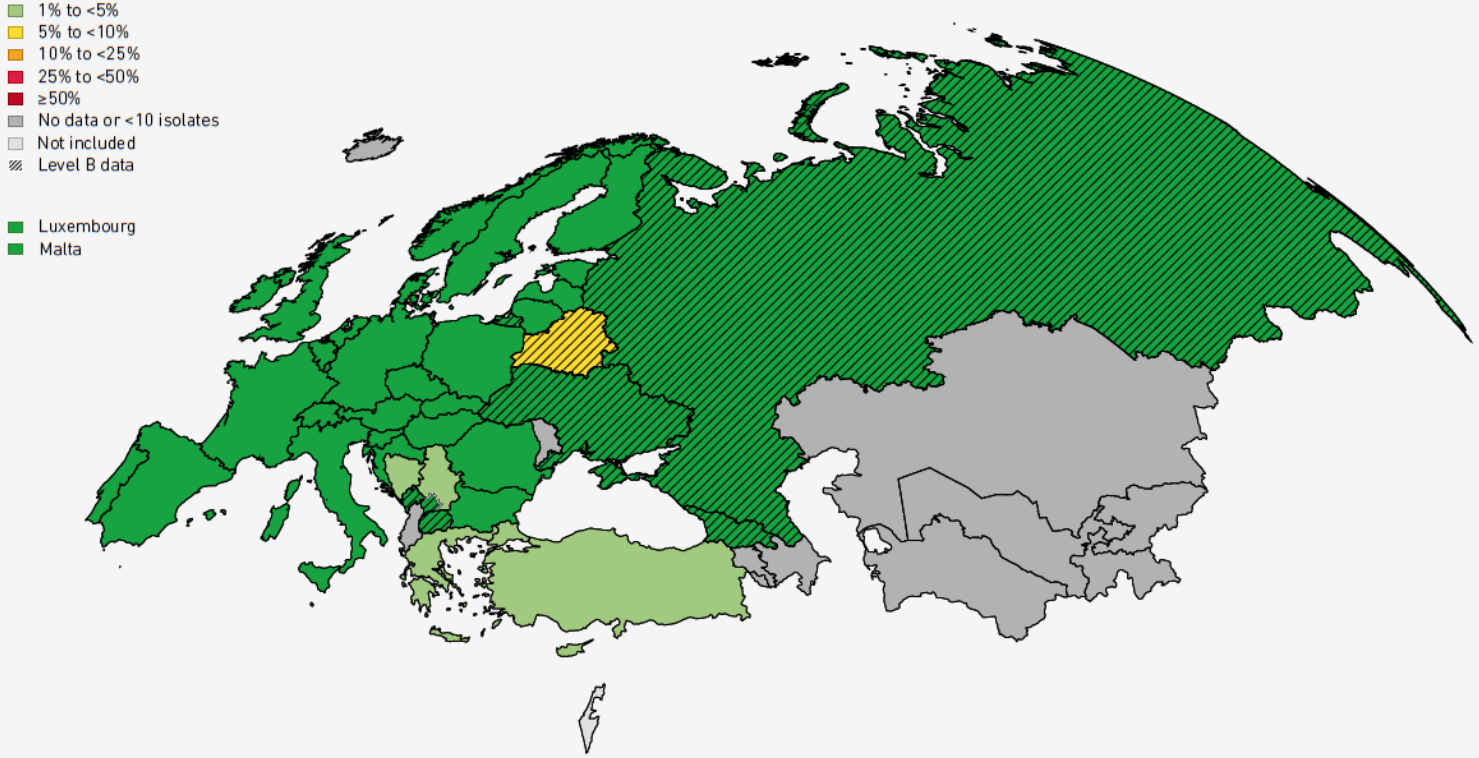

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Fig. 7.2 Carbapenem-resistant *E. coli* in the European Region (EARS-Net and CAESAR), 2017

K.pneumonia: MDR (3. Kuşak Sef, FQ, AG)

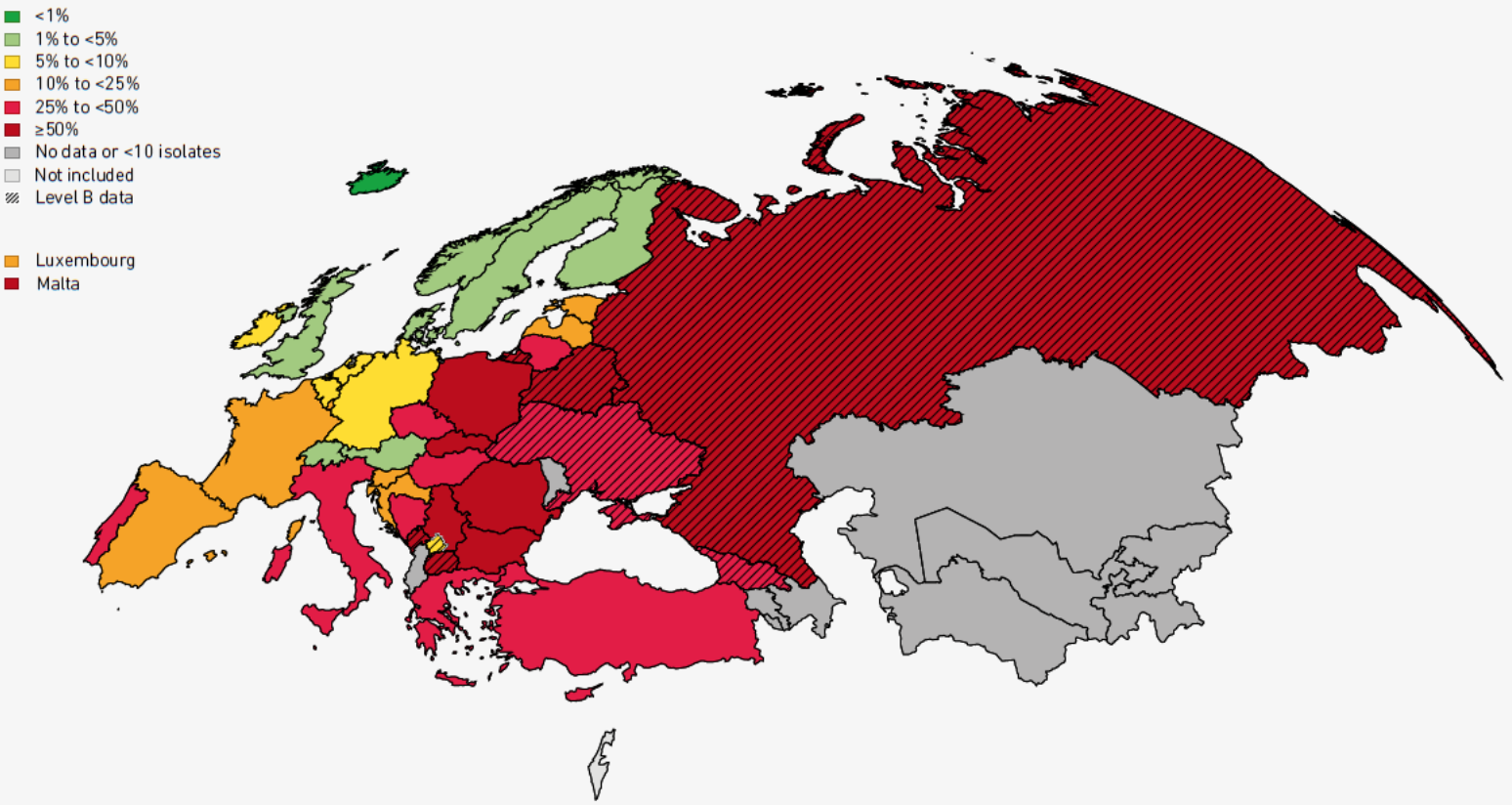

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Fig. 7.3 Multidrug-resistant (combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides) *K. pneumoniae* in the European Region (EARS-Net and CAESAR), 2017

K.pneumonia: Karbapenem Direnci

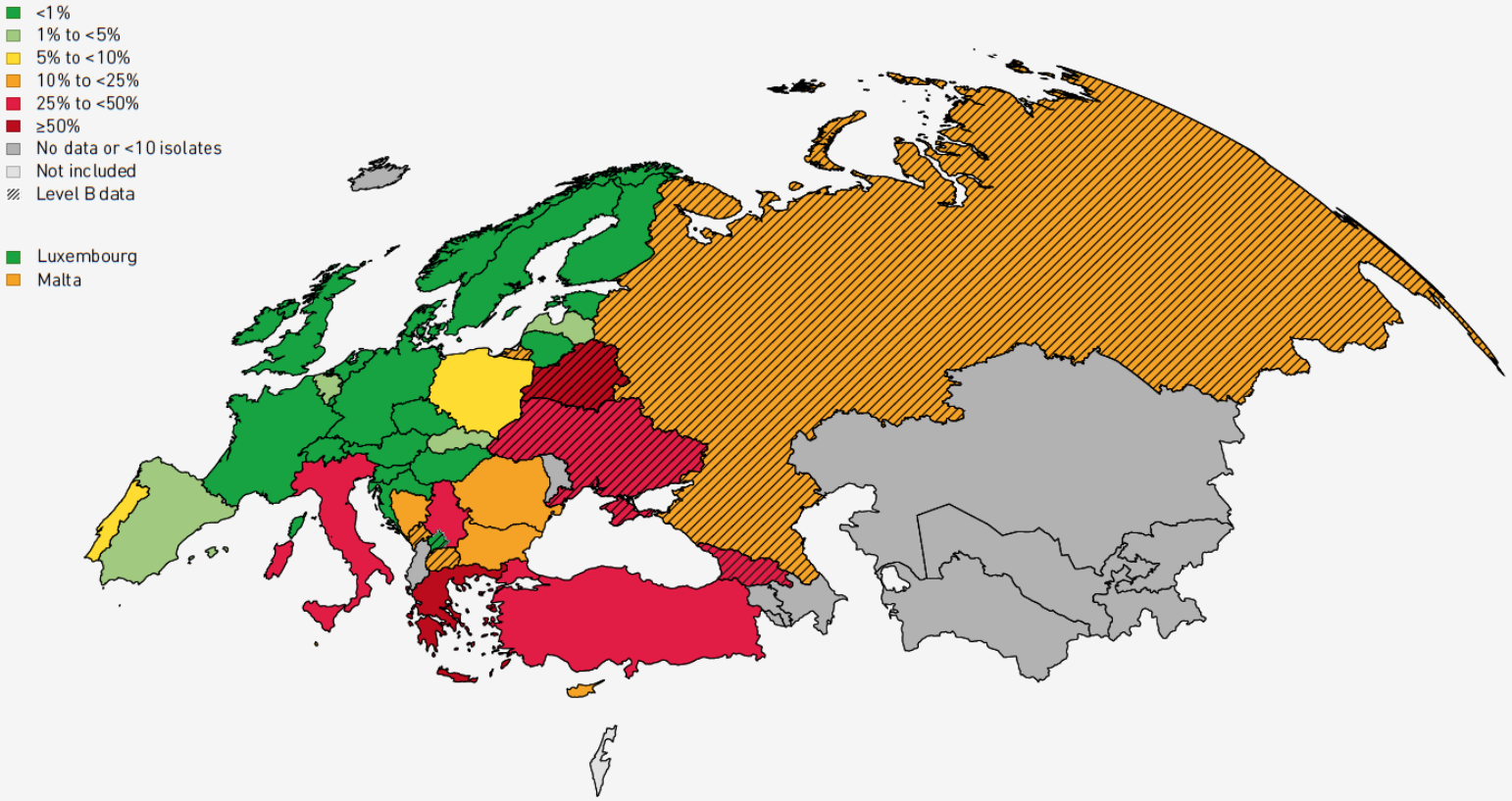

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Fig. 7.4 Carbapenem-resistant *K. pneumoniae* in the European Region (EARS-Net and CAESAR), 2017

Acinetobacter: MDR (3. Kuşak Sef, FQ, AG)

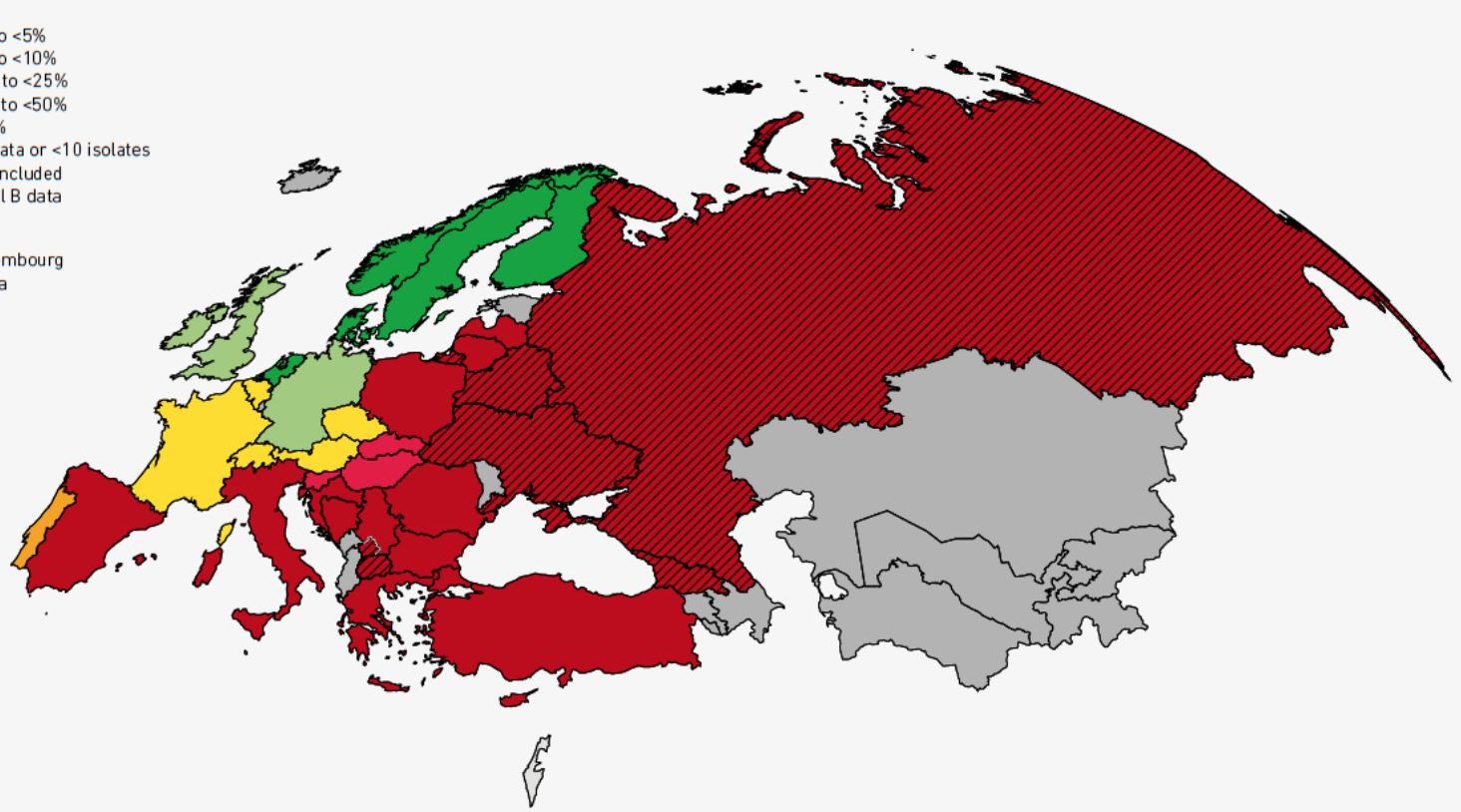

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Fig. 7.5 Multidrug-resistant (combined resistance to fluoroquinolones, aminoglycosides and carbapenems) *Acinetobacter* spp. in the European Region (EARS-Net and CAESAR), 2017

MRSA: 2017

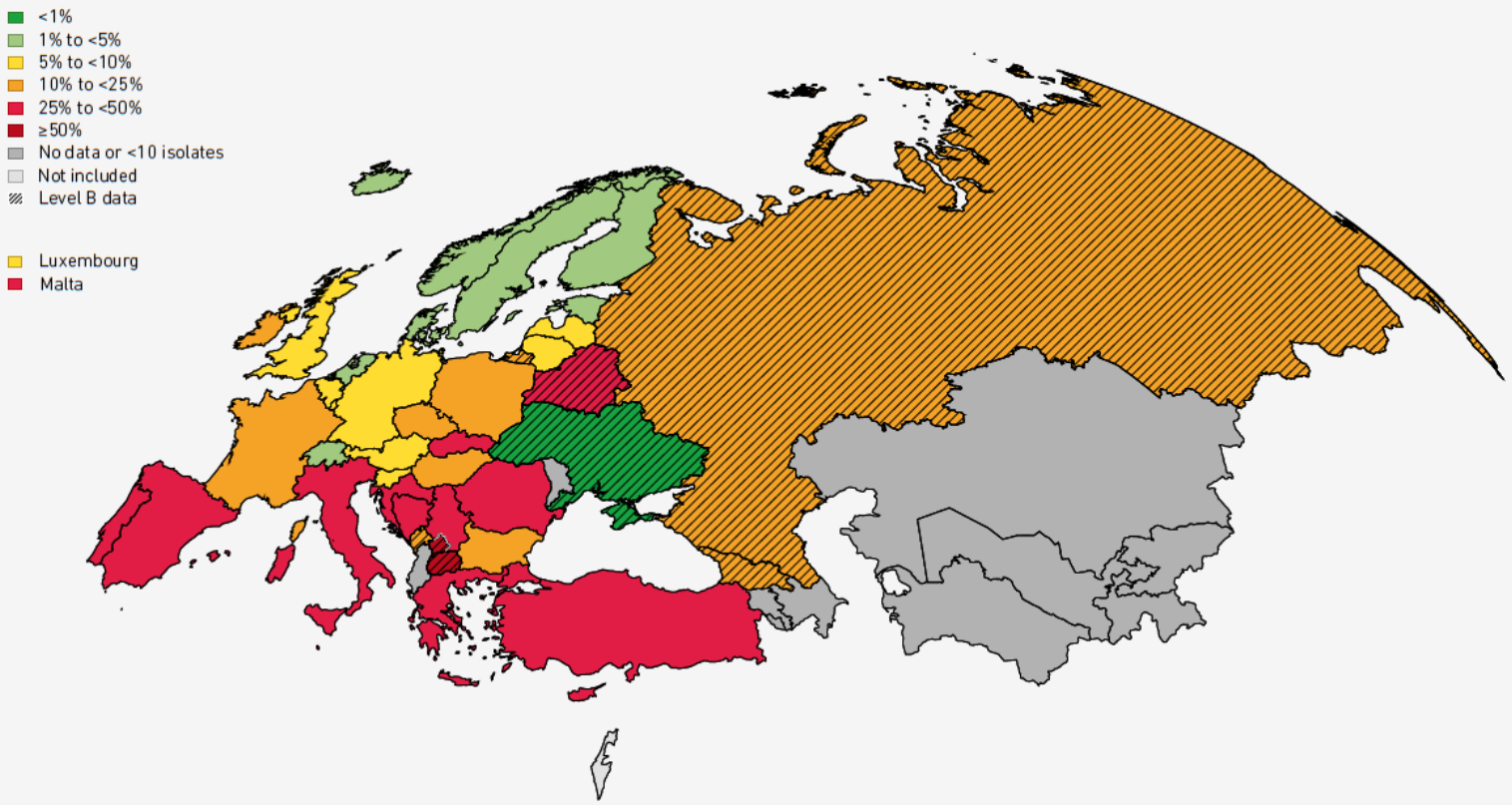

Fig. 7.6 MRSA in the European Region (EARS-Net and CAESAR), 2017

Level B data: the data provide an indication of the resistance patterns present in clinical settings in the country or area, but the proportion of resistance should be interpreted with care. Improvements are needed to attain a more valid assessment of the magnitude and trends of AMR in the country or area. See section 4.2 for more information about levels of evidence, which are only provided for CAESAR countries and areas.

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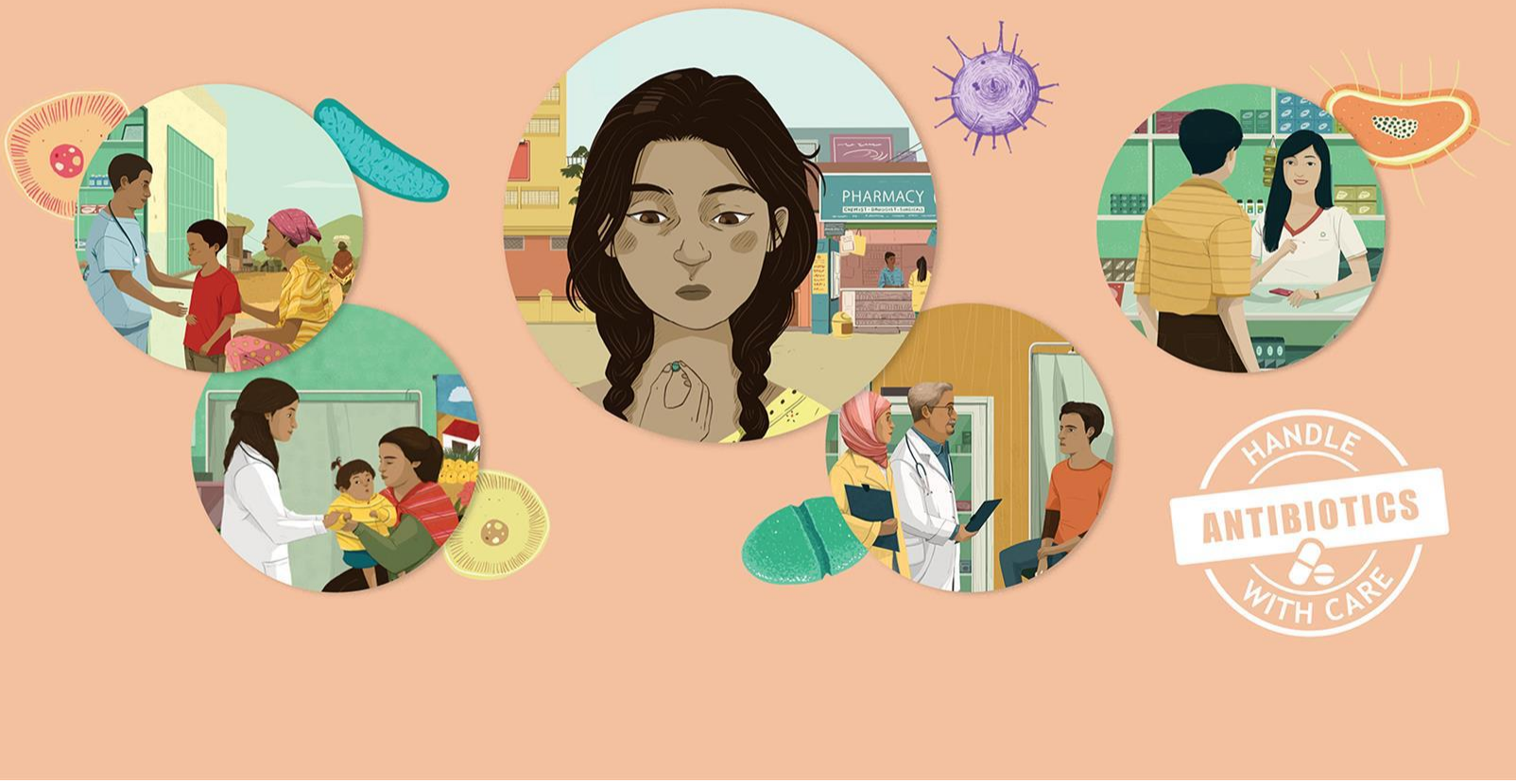
Dünya Antibiyotik Farkındalık Haftası
12-18 Kasım 2018



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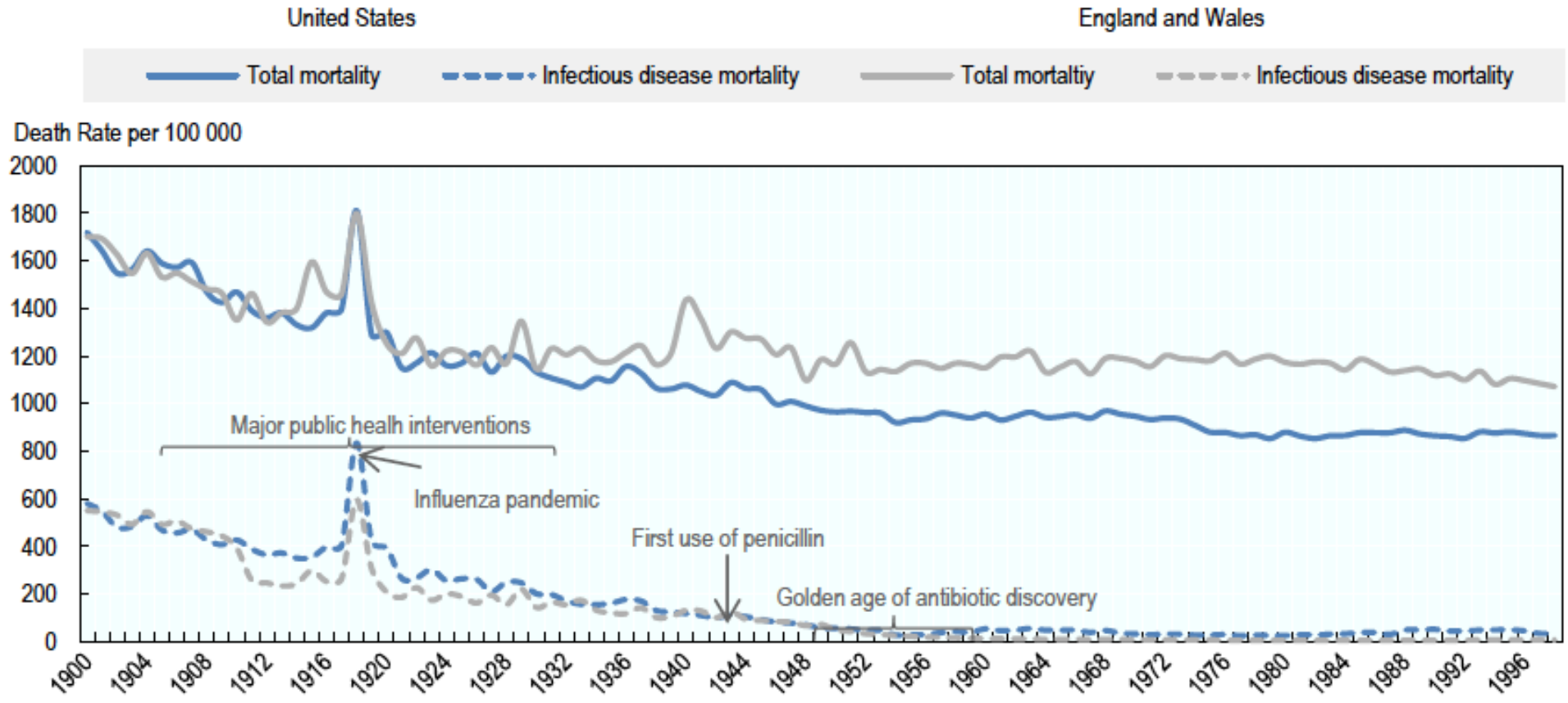
United States
England and Wales
Total mortality
Infectious disease mortality
Total mortaltiy
Infectious disease mortality
Death Rate per 100 000
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Major public health interventions
Influenza pandemic
First use of penicillin
Golden age of antibiotic discovery
1900
1904
1908
1912
1916
1920
1924
1928
1932
1936
1940
1944
1948
1952
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1976
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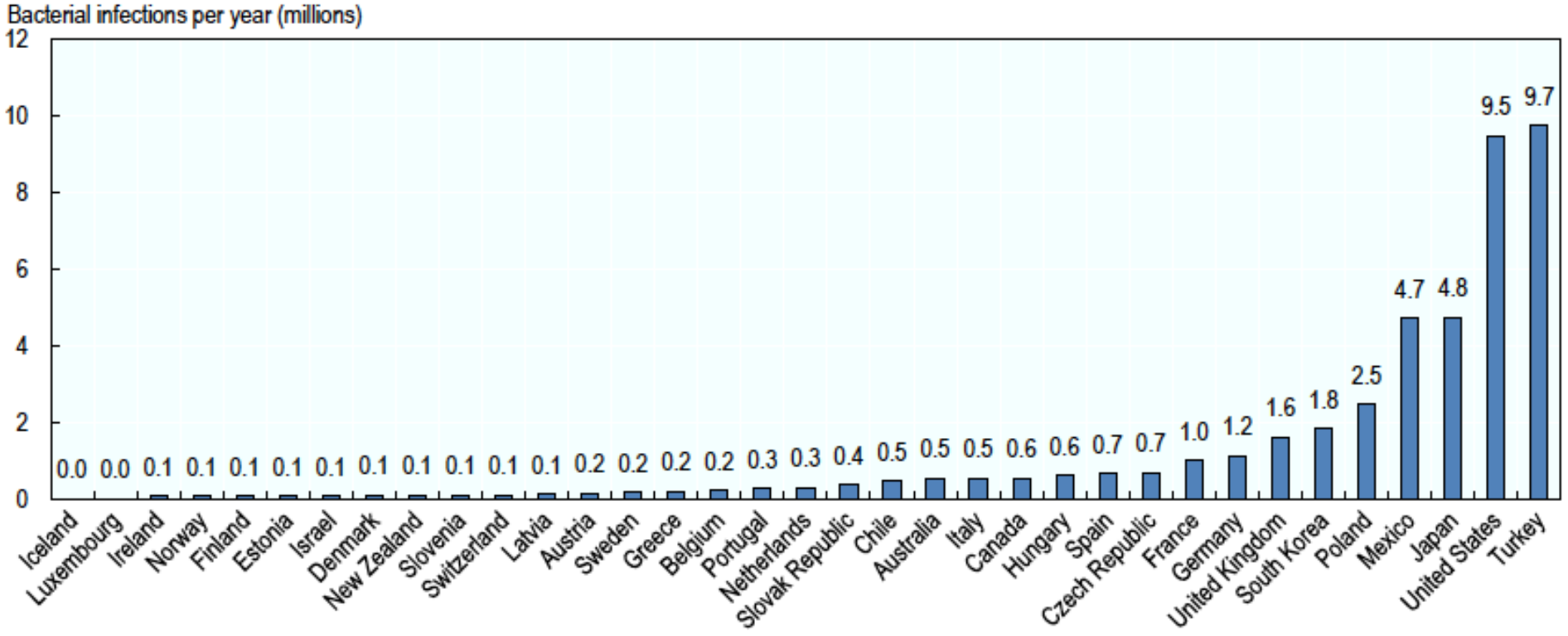
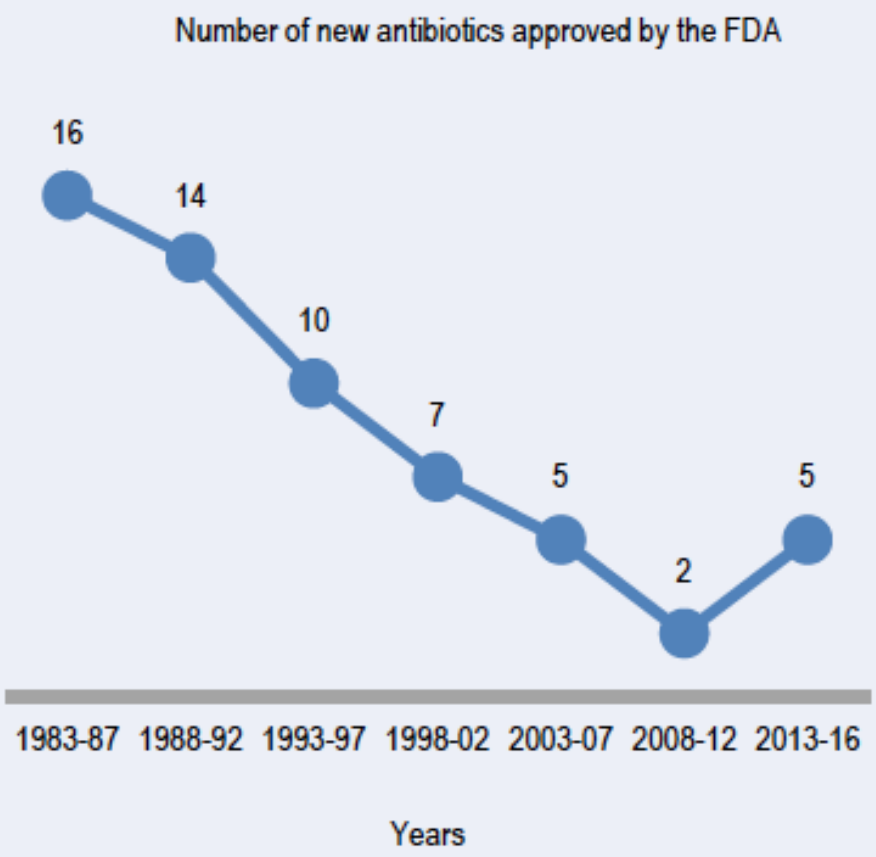
1992
1996

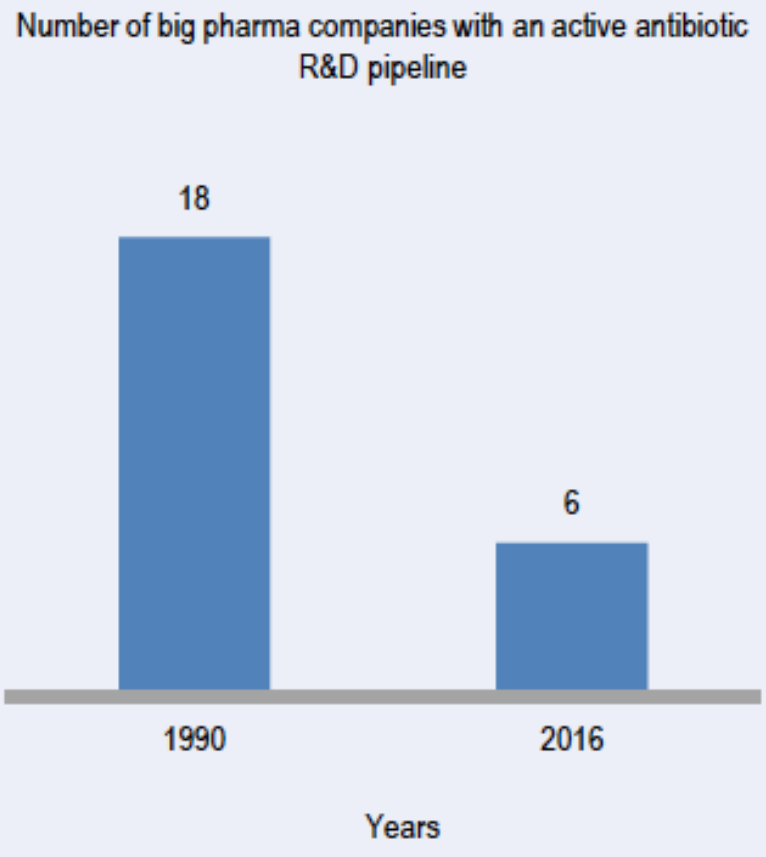
Figure 2.2. Infections by microbes susceptible to the development of resistance in OECD countries



Note: The graph includes the following infections: gonococcal, chlamydial, lower respiratory, syphilis, tuberculosis, whooping cough, paratyphoid fever, typhoid fever, and meningitis.
Source: IHME (2018[8]).

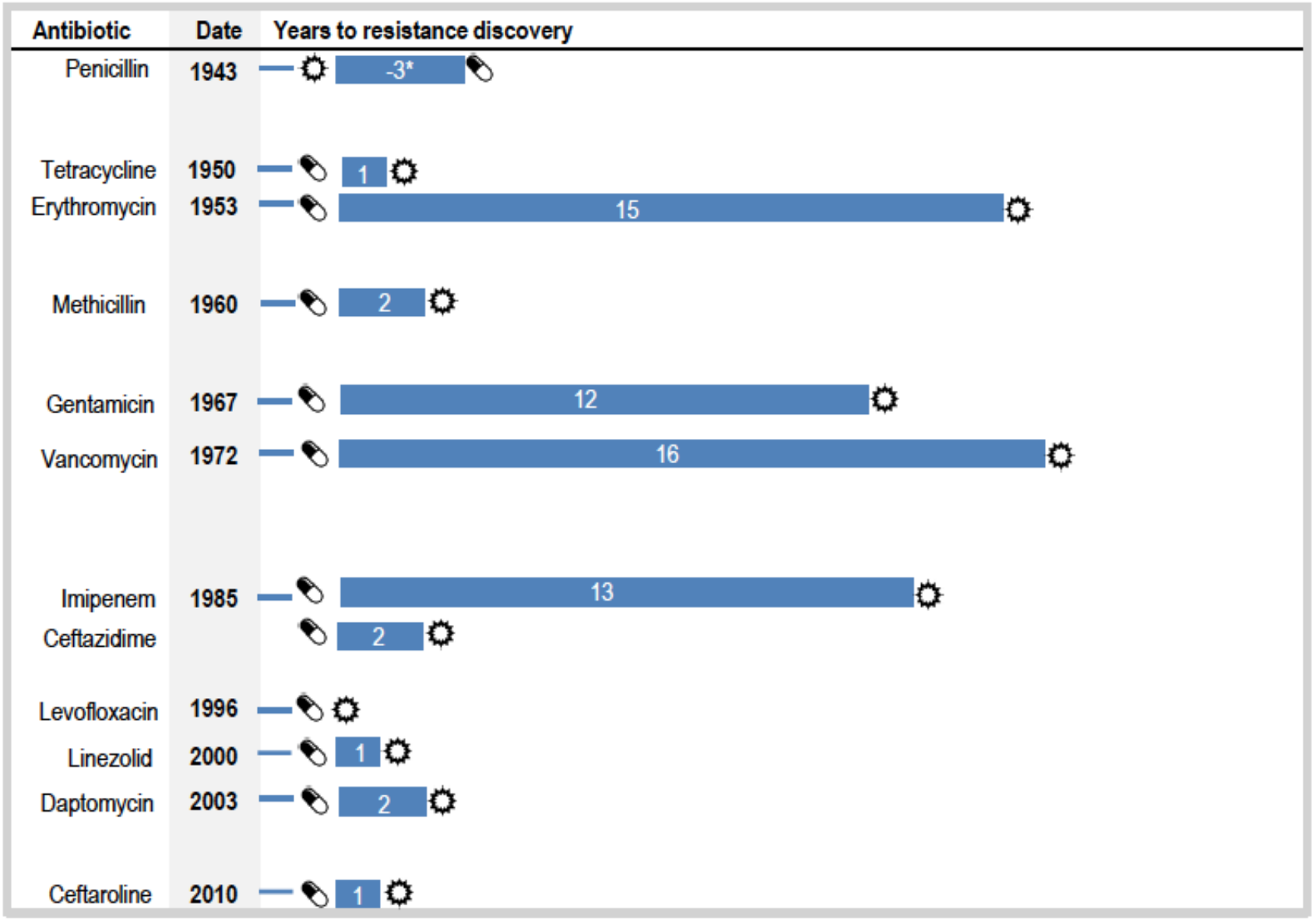
Figure 2.3. The decline in antibiotic R&D





Source: OECD, WHO, FAO and OIE (2017[19]).

Figure 2.4. Timeline of antibiotic discovery and detection of antibiotic resistance



* Resistance identified before antibiotic introduction

“Antibiyotik direnci modern tıbbın sonunu getirebilir”

Dr. Margaret Chan

Dünya Sağlık Örgütü Direktörü

16 Mart 2012

Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis

*Alessandro Cassini, Liselotte Diaz Högberg, Diamantis Plachouras, Annalisa Quattrocchi, Ana Hoxha, Gunnar Skov Simonsen, Mélanie Colomb-Cotinat, Mirjam E Kretzschmar, Brecht Devleesschauwer, Michele Cecchini, Driss Ait Ouakrim, Tiago Cravo Oliveira, Marc J Struelens, Carl Suetens, Dominique L Monnet, and the Burden of AMR Collaborative Group**

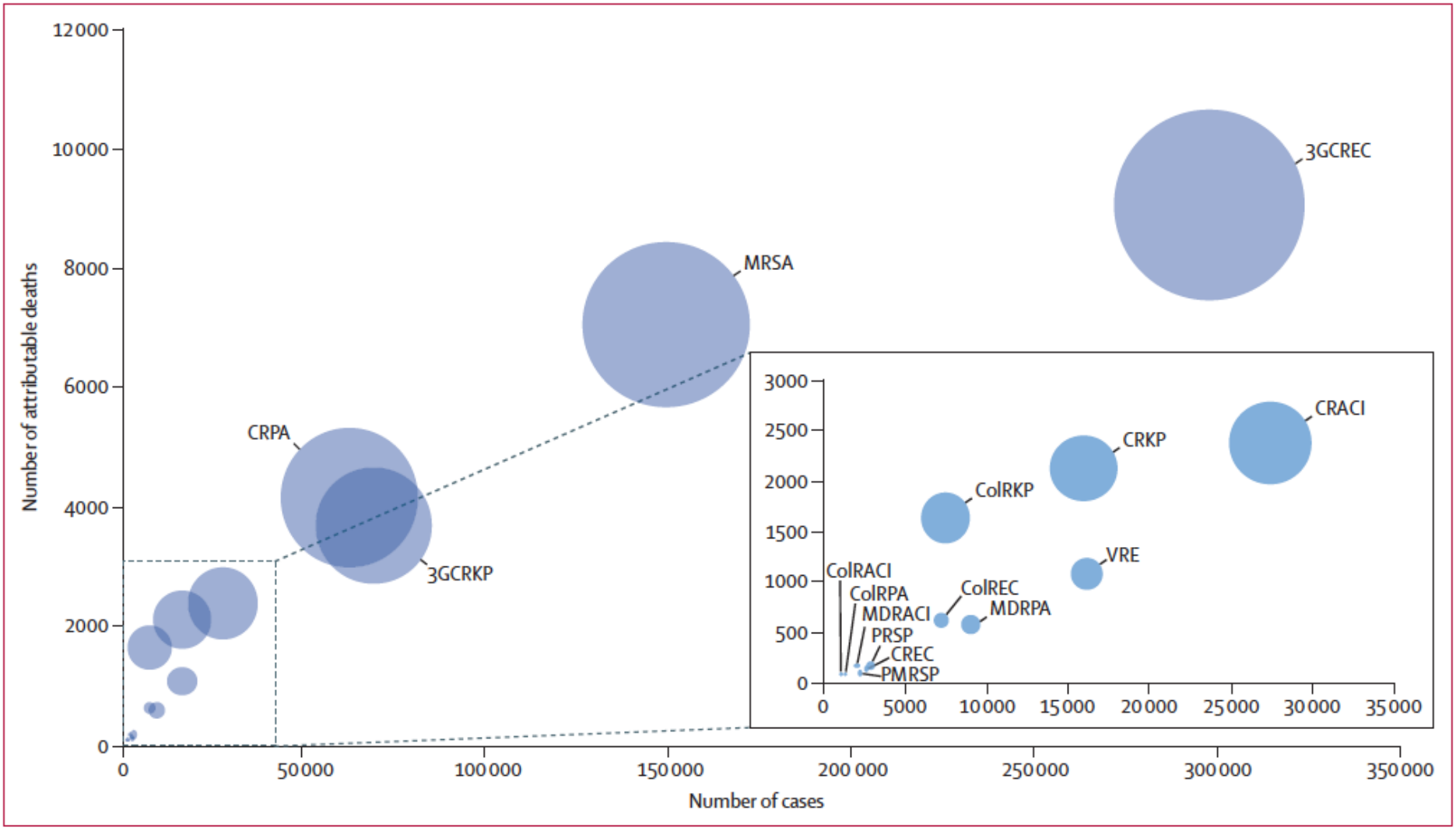


Figure 1: **Infections with antibiotic-resistant bacteria, EU and European Economic Area, 2015**

Diameter of bubbles represents the number of disability-adjusted life-years. ColRACI=colistin-resistant *Acinetobacter* spp. CRACI=carbapenem-resistant *Acinetobacter* spp. MDRACI=multidrug-resistant *Acinetobacter* spp. VRE=vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium*. ColREC=colistin-resistant *Escherichia coli*. CREC=carbapenem-resistant *E coli*. 3GCREC=third-generation cephalosporin-resistant *E coli*. ColRKP=colistin-resistant *Klebsiella pneumoniae*. CRKP=carbapenem-resistant *K pneumoniae*. 3GCRKP=third-generation cephalosporin-resistant *K pneumoniae*. ColRPA=colistin-resistant *Pseudomonas aeruginosa*. CRPA=carbapenem-resistant *P aeruginosa*. MDRPA=multidrug-resistant *P aeruginosa*. MRSA=meticillin-resistant *Staphylococcus aureus*. PRSP=penicillin-resistant *Streptococcus pneumoniae*. PMRSP=penicillin-resistant and macrolide-resistant *S pneumoniae*.

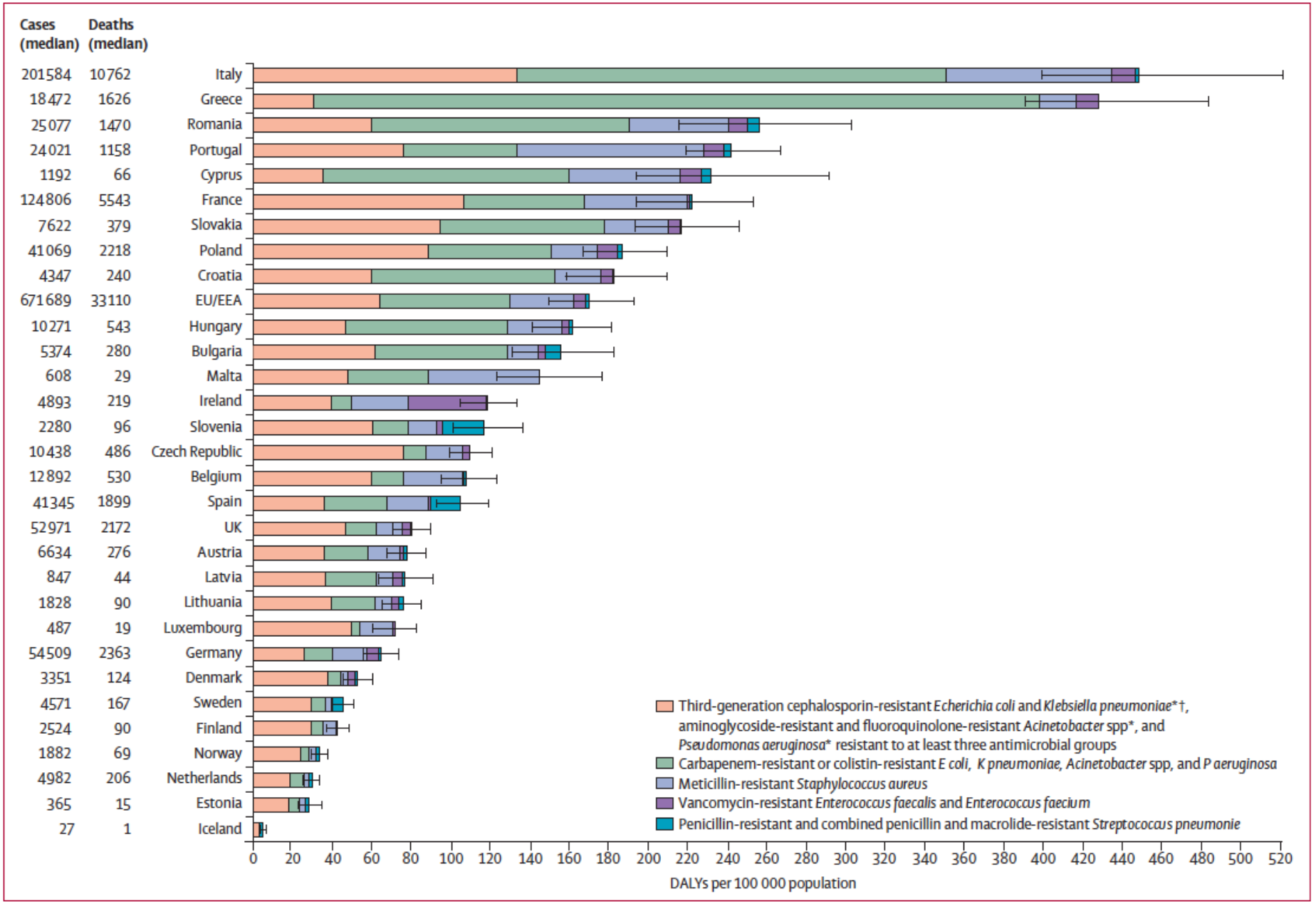


***Figure 3*: Burden of infections with antibiotic-resistant bacteria in DALYs, EU and European Economic Area, 2015**

Error bars are 95% uncertainty intervals. Greece did not report data on *S pneumoniae* isolates to the European Antimicrobial Resistance Surveillance Network in 2015. DALY rates are age-standardised to limit the effect of demographic differences across countries; numbers of cases and deaths are not age-standardised. DALYs=disability-adjusted life-years. *Excludes those resistant to carbapenem or colistin. †In 2015, most of the third-generation cephalosporin-resistant *E coli* (88·6%) and *K pneumoniae* (85·3%) isolates reported to the European Antimicrobial Resistance Surveillance Network produced an extended-spectrum β-lactamase.[9]

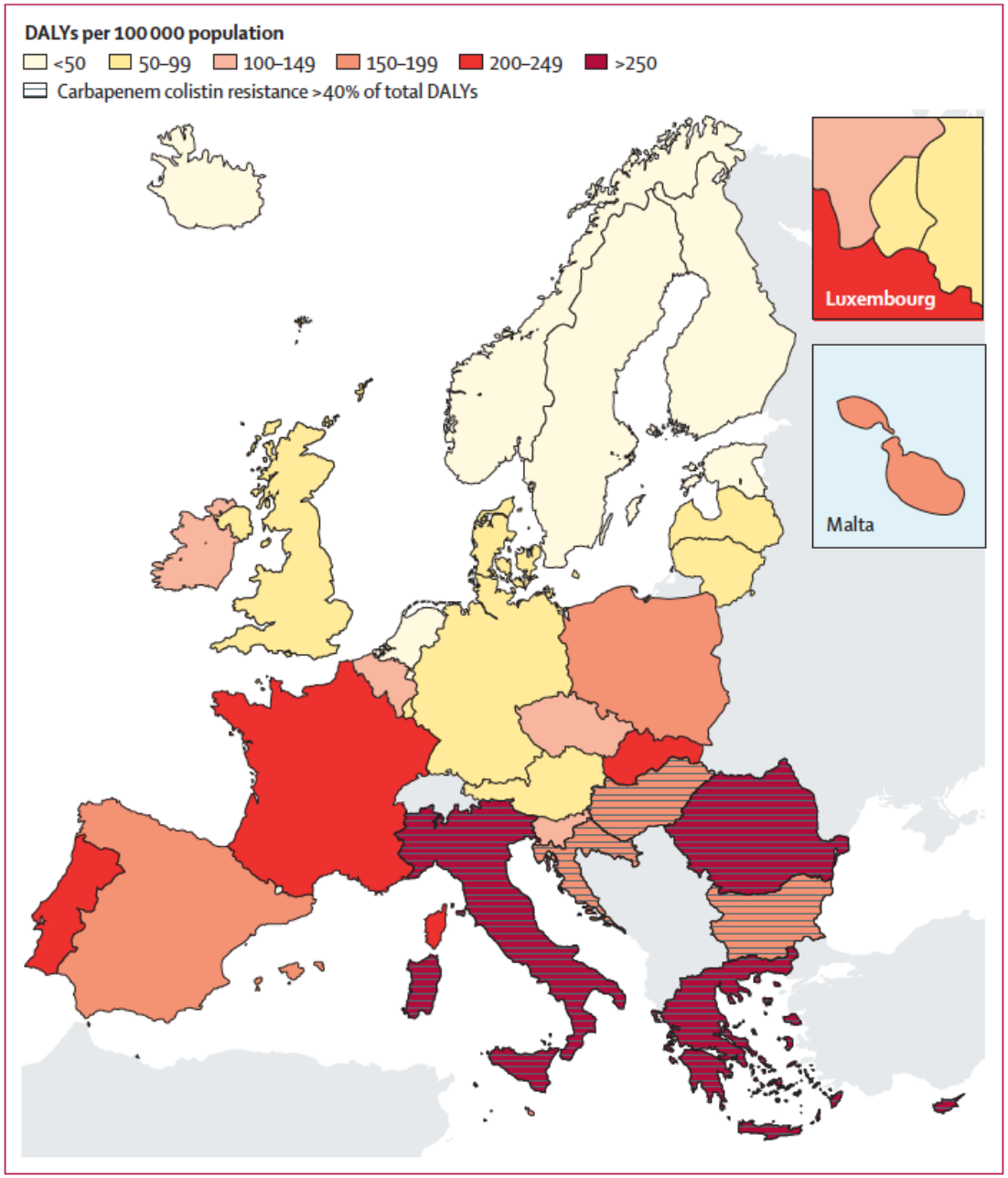
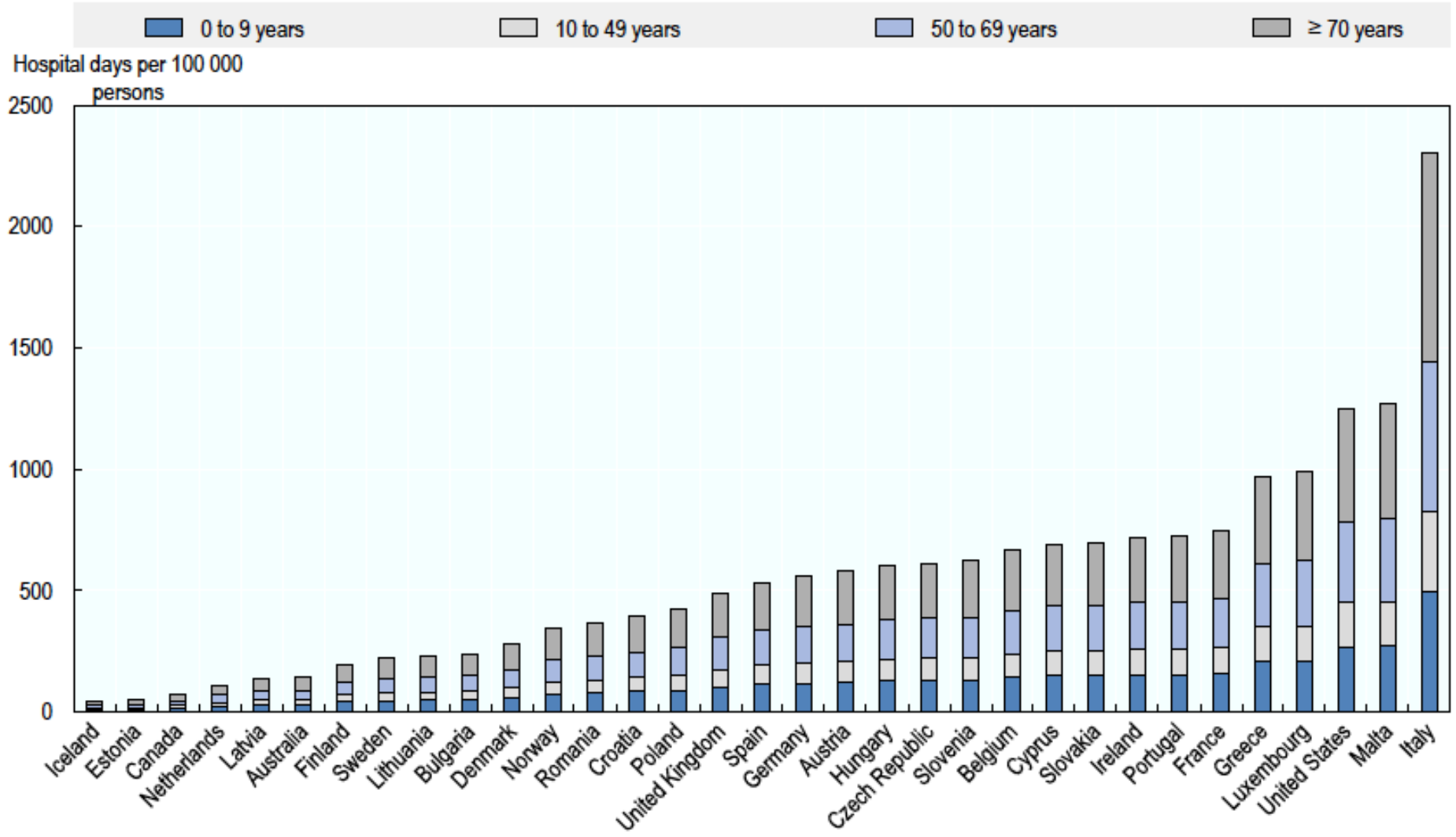


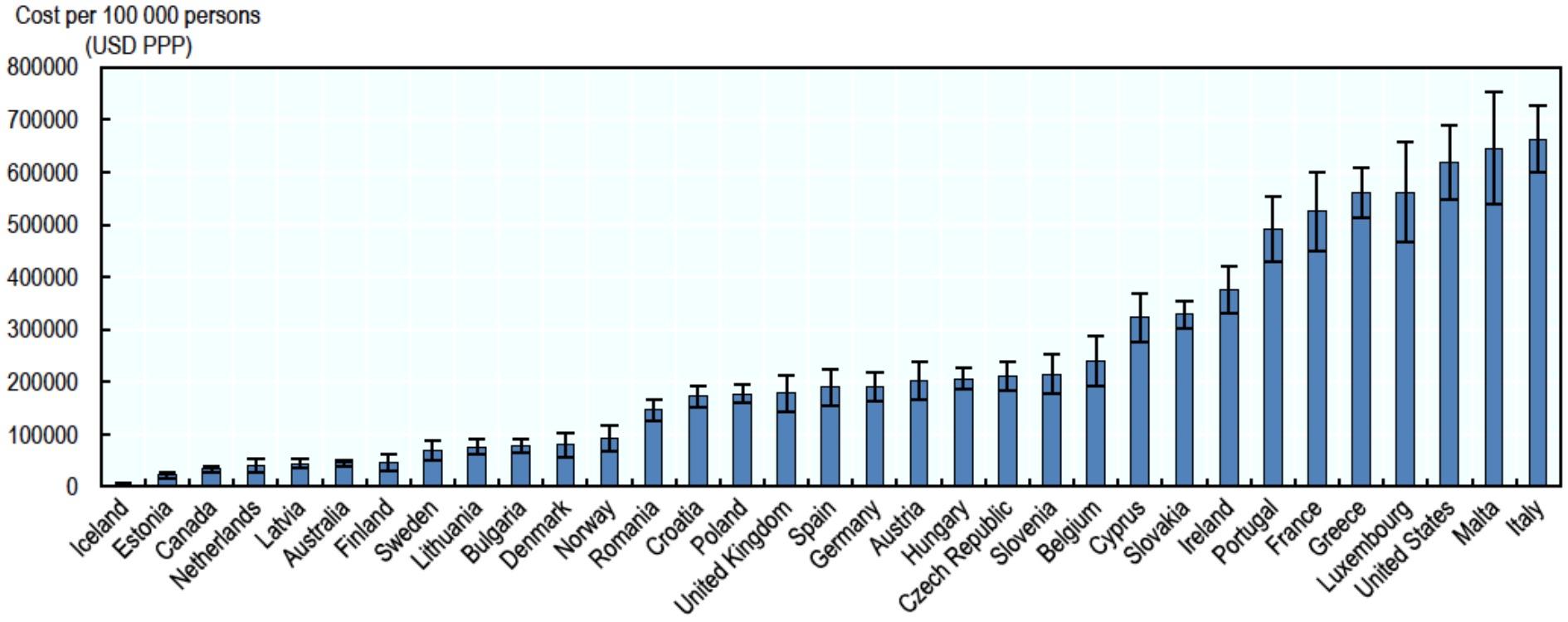
Figure 4: **Model estimates of the burden of infections with selected antibiotic-resistant bacteria of public health importance in DALYs per 100 000 population, EU and European Economic Area, 2015**
Greece did not report data on *S pneumoniae* isolates to the European Antimicrobial Resistance Surveillance Network in 2015. DALYs=disability-adjusted life-years.

Figure 4.5. Average annual number of extra hospital days associated AMR – 2015-2050

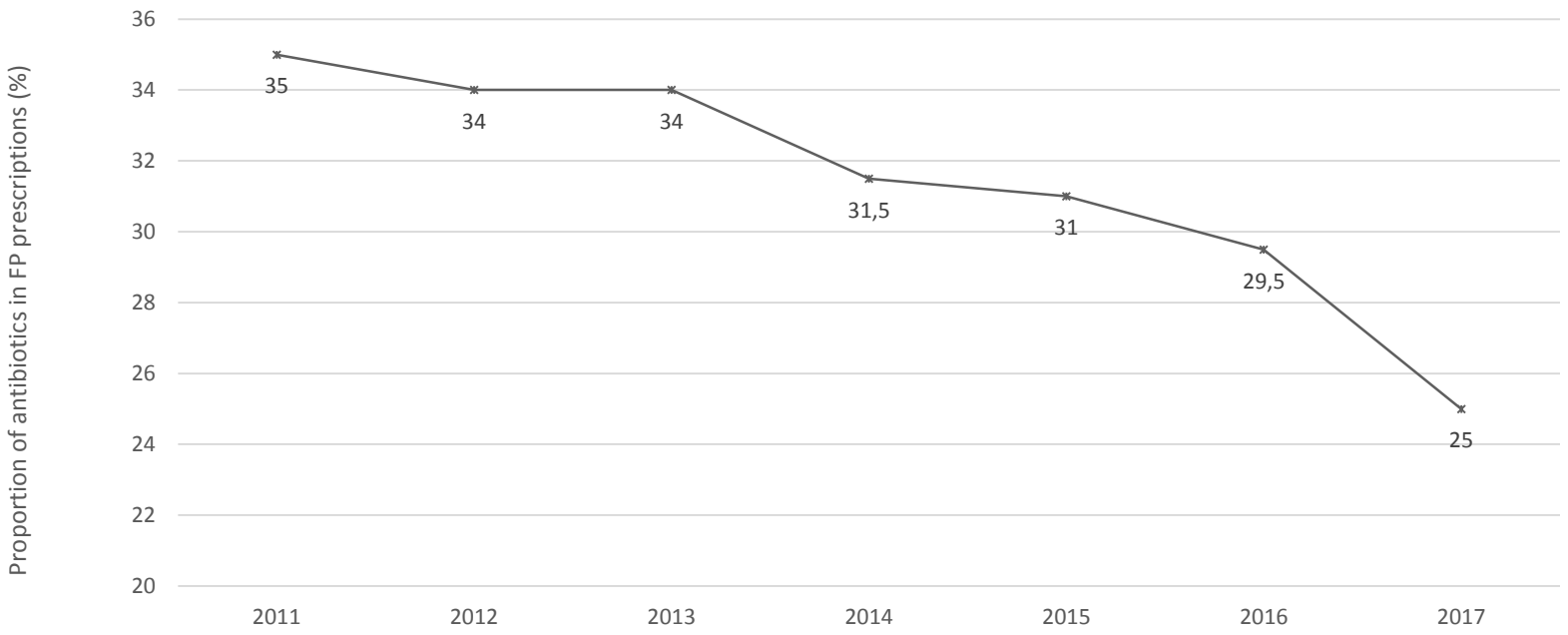


OECD, 2018

Figure 4.6. Annual health care expenditure associated with AMR – 2015-2050



Aile Hekimliği Reçetelerinde Antibiyotik Oranı



İşler B, CMI 2019

ELSEVIER

International Journal of Antimicrobial Agents 21 (2003) 308–312

INTERNATIONAL JOURNAL OF Antimicrobial Agents

www.ischemo.org

Evaluation of antibiotic use in a hospital with an antibiotic restriction policy

Ayşe Erbay [a,*], Aylin Çolpan [a], Hürrem Bodur [a], Mustafa A. Çevik [a], Matthew H. Samore [b], Önder Ergönül [b]

[a] *Ankara Numune Education and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey*
[b] *University of Utah, School of Medicine, Department of Internal Medicine, Division of Clinical Epidemiology, Salt Lake, UT, USA*

1) Agree with choice of antibiotic, but dosage was inappropriate per literature
2) Disagree with choice of antibiotics because the spectrum of the antibiotics were overlapped
3) Disagree with choice of antibiotic because the spectrum was not broad enough
4) Disagree with choice of antibiotic because the spectrum was overly broad
5) Disagree with choice of antibiotic because an equally effective drug was available at a lower cost
6) Disagree with need for an antibiotic.

Table 1
Resistance rates of some Gram-negative microorganisms in ANERH in 2000

	Klebsiella spp. (%)	*E. coli* (%)	*Pseudomonas* spp. (%)	*Acinetobacter* spp. (%)
Cefotaxime	80.0	56.0	93.4	100
Ceftazidime	76.3	49.3	62.6	96.3
Cefoperazone–sulbactam	59.4	50.0	50.0	50.0
Ticarcillin–clavulanate	84.8	81.4	76.7	85.7
Piperacillin–tazobactam	57.1	25.7	42.6	82.8
Cefepime	56.9	39.5	57.1	71.9
Imipenem	6.9	2.4	31.4	39.2
Gentamicin	66.6	58.0	65.2	88.0
Amikacin	45.7	20.0	36.9	70.3
Ciprofloxacin	56.6	57.6	46.5	80.0

Erbay A, Colpan A, Bodur H, Cevik MA, Samore MA, Ergonul O. IJAA 2003

Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dki344

JAC

10 YIL ÖNCE (2005)

Risk factors for ciprofloxacin resistance among *Escherichia coli* strains isolated from community-acquired urinary tract infections in Turkey

Hande Arslan[1], Özlem Kurt Azap[1]*, Önder Ergönül[2] and Funda Timurkaynak[1] on behalf of the Urinary Tract Infection Study Group[†]

E. coli (komplike olmayan) **cipro R: %20**

E. coli (komplike) **cipro R: %38**

Clinical Infectious Diseases Advance Access published December 3, 2014

MAJOR ARTICLE

10 YIL SONRA (2015)

Emerging *Escherichia coli* O25b/ST131 Clone Predicts Treatment Failure in Urinary Tract Infections

E. coli (komplike olmayan) **cipro R: %39**

Fusun Can,[1] Ozlem Kurt Azap,[2] Ceren Seref,[1] Pelin Ispir,[1] Hande Arslan,[2] and Onder Ergonul[3]

[1]Department of Medical Microbiology, Koç University, School of Medicine, Istanbul, [2]Department of Infectious Diseases, Baskent University, School of Medicine, Ankara, and [3]Department of Infectious Diseases, Koç University, School of Medicine, Istanbul, Turkey

Journal of Hospital Infection xxx (2016) 1–5

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Short report

Healthcare-associated Gram-negative bloodstream infections: antibiotic resistance and predictors of mortality

Ö. Ergönül [a,*], M. Aydin [b], A. Azap [c], S. Başaran [d], S. Tekin [a], Ş. Kaya [e], S. Gülsün [e], G. Yörük [f], E. Kurşun [g], A. Yeşilkaya [h], F. Şimşek [i], E. Yılmaz [j], H. Bilgin [k], Ç. Hatipoğlu [l], H. Cabadak [m], Y. Tezer [m], T. Togan [n], İ. Karaoğlan [o], A. İnan [p], A. Engin [q], H.E. Alışkan [g], S.Ş. Yavuz [d], Ş. Erdinç [l], L. Mulazimoglu [k], Ö. Azap [h], F. Can [a], H. Akalın [j], F. Timurkaynak [b], Turkish Society of Clinical Microbiology and Infectious Diseases, Healthcare-Related Infections Study Group

Antibiotic resistance rates in healthcare-associated Gram-negative bloodstream infections

Bacteria	Carbapenem *N* (%)	Fluoroquinolones *N* (%)	Third-generation cephalosporins *N* (%)	Aminoglycosides *N* (%)	Colistin *N* (%)
Acinetobacter baumannii	239 (94)	240 (94)	247 (97)	187 (73)	15 (6)
Klebsiella pneumoniae	88 (40)	130 (60)	159 (72)	56 (25)	14 (6)
Escherichia coli	13 (6.4)	128 (63)	143 (71)	47 (23)	0
Pseudomonas aeruginosa	32 (43)	36 (49)	37 (51)	19 (26)	1 (1)
Enterobacter cloacae	5 (16)	6 (19)	16 (53)	5 (16)	0

Journal of Hospital Infection 98 (2018) 260–263

Available online at www.sciencedirect.com

Journal of Hospital Infection

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

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

M. Aydın [a,*], Ö. Ergönül [b], A. Azap [c], H. Bilgin [d], G. Aydın [c,e], S.A. Çavuş [f], Y.Z. Demiroğlu [g], H.E. Alışkan [h], O. Memikoğlu [c], Ş. Menekşe [i], Ş. Kaya [j], N.A. Demir [k], İ. Karaoğlan [l], S. Başaran [m], Ç. Hatipoğlu [n], Ş. Erdinç [n], E. Yılmaz [o], A. Tümtürk [p], Y. Tezer [p], H. Demirkaya [q], Ş.E. Çakar [r], Ş. Keske [b], S. Tekin [b], C. Yardımcı [s], Ç. Karakoç [t], P. Ergen [u], Ö. Azap [q], L. Mülazımoğlu [d], O. Ural [k], F. Can [v], H. Akalın [o], Turkish Society of Clinical Microbiology and Infectious Diseases, Healthcare-related Infections Study Group, Turkey

Table I
Antibiotic resistance rates in 1556 episodes of healthcare-associated Gram-negative bacteraemia

Species	*N* (%) of isolates that were resistant to:				
	Carbapenems	Fluoroquinolones	Third-generation cephalosporins	Aminoglycosides	Colistin
Acinetobacter baumannii N = 437	401 (91.8)	389 (89.0)	410 (93.8)	310 (70.9)	9 (2.1)
Klebsiella pneumoniae N = 416	216 (51.9)	266 (63.9)	320 (76.9)	200 (48.1)	67 (16.1)
Escherichia coli N = 339	34 (10.0)	189 (55.8)	203 (59.9)	103 (30.4)	3 (0.9)
Pseudomonas aeruginosa N = 205	88 (42.9)	102 (49.8)	103 (50.2)	65 (31.7)	18 (8.8)
Enterobacter cloacae N = 159	37 (23.3)	46 (28.9)	59 (37.1)	51 (32.1)	9 (5.7)

SnapShot: Antibiotic Resistance

Idan Yelin and Roy Kishony
Department of Biology, Technion - Israel Institute of Technology, Haifa 3200003, Israel

Cell

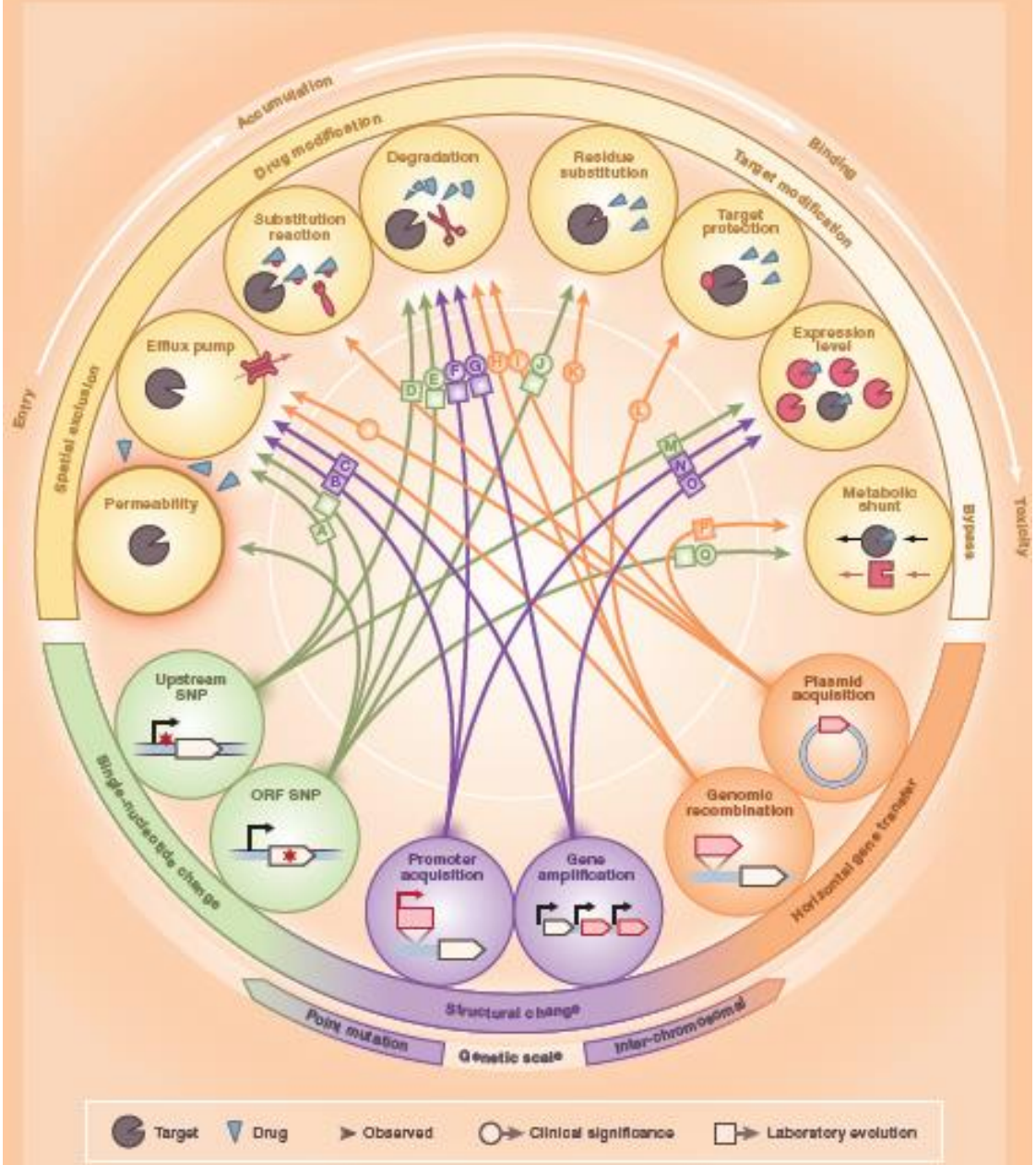


Table 2.1. Antibiotic targets and resistance mechanisms

Resistance mechanism	Action	Effective against
Efflux pumps	Pumps antibiotic out of cell before it reaches target	Fluoroquinolones Aminoglycosides Tetracyclines Beta-lactams Macrolides
Immunity and Bypass	Antibiotics or antibiotic targets bound by proteins preventing antibiotic binding	Tetracyclines Trimethroprim Sulfonamides Vancymycin
Target modification	Antibiotic targets are modified to prevent antibiotic binding	Fluoroquinolones Rifamycins Vancymycin Penicillins Macrolides Aminoglycosides
Inactivating enzymes	Destroys antibiotic through catalysation	Beta-lactams Aminoglycosides Macrolides Rifamycins

Source: Adapted from Wright (2010[35]).

J Antimicrob Chemother
doi:10.1093/jac/dkx532

Journal of Antimicrobial Chemotherapy

Impact of the ST101 clone on fatality among patients with colistin-resistant *Klebsiella pneumoniae* infection

Fusun Can[1]*, Sirin Menekse[2], Pelin Ispir[1], Nazlı Atac[1], Ozgur Albayrak[1], Tuana Demir[3], Doruk Can Karaaslan[3], Salih Nafiz Karahan[3], Mahir Kapmaz[4], Ozlem Kurt Azap[5], Funda Timurkaynak[6], Serap Simsek Yavuz[7], Seniha Basaran[7], Fugen Yoruk[8], Alpay Azap[8], Safiye Koculu[9], Nur Benzonana[10], Nathan A. Lack[11,12], Mehmet Gönen[3,13] and Onder Ergonul[14]

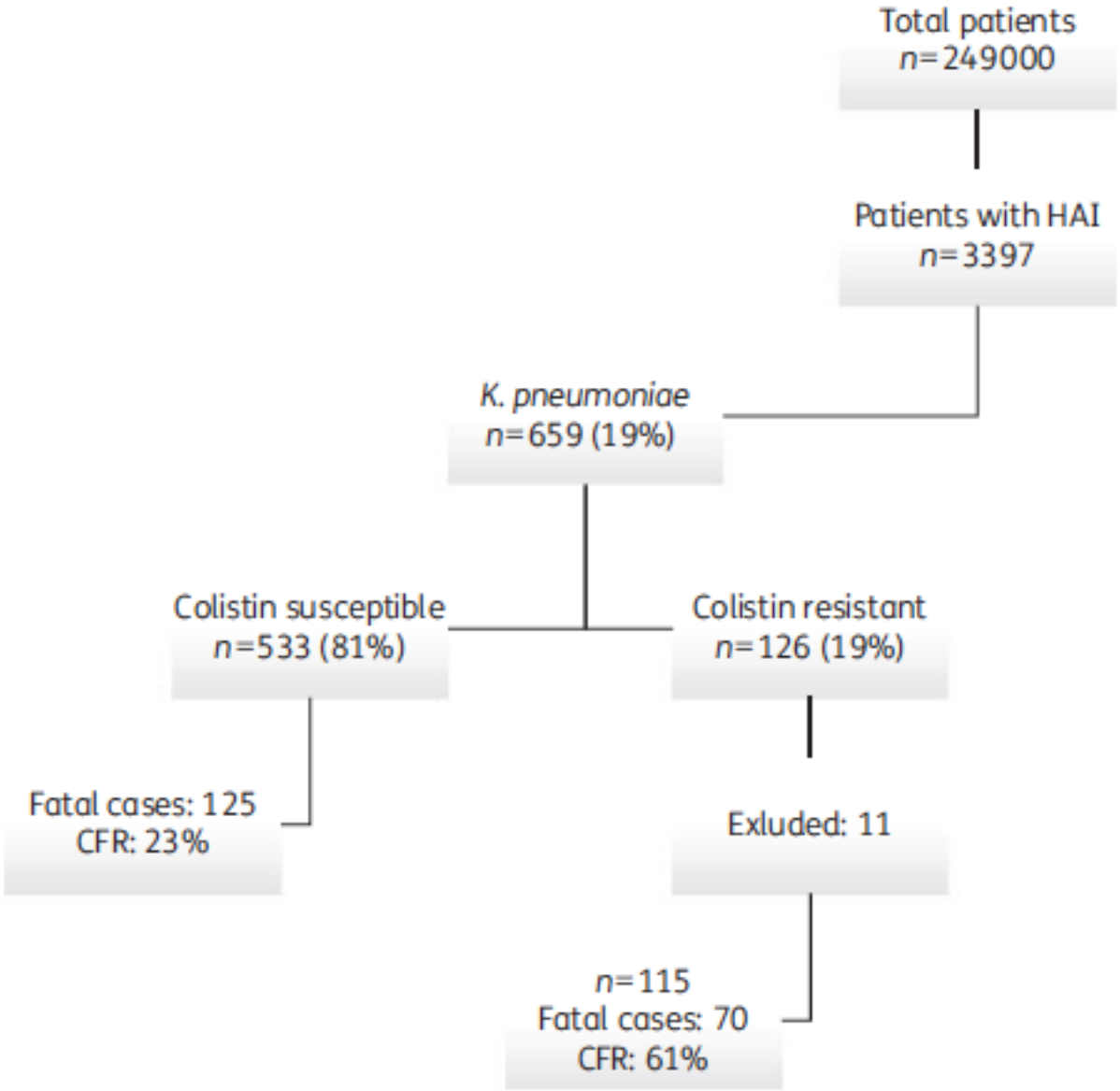


Figure 1. Flow chart for included ColR-Kp cases. CFR, case fatality rate.

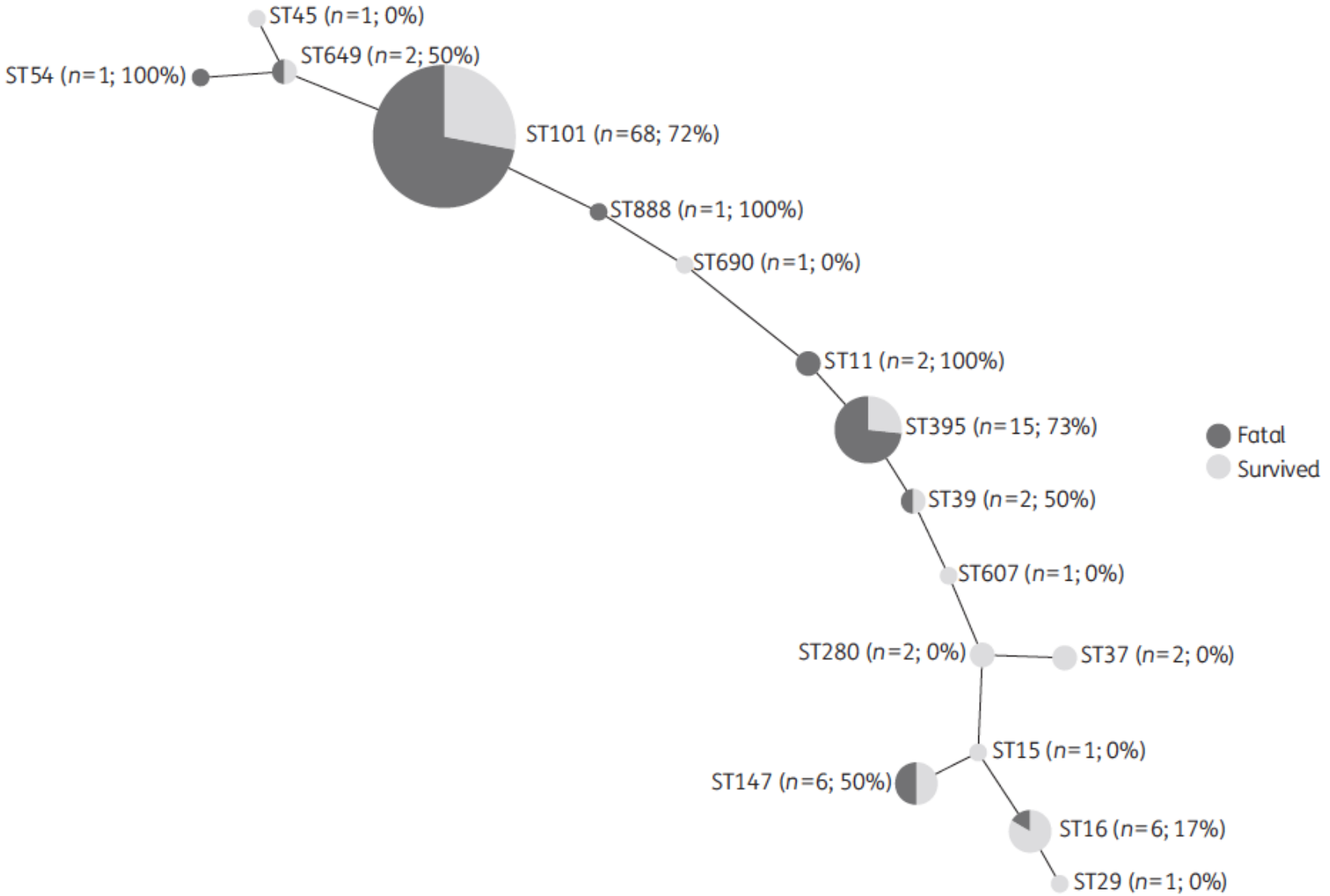


Figure 2. Minimum spanning tree of ColR-Kp by MLST ST and gene allele profiles. Each node within the tree represents a single ST. The area of the nodes is proportional to the number of isolates within each node; the proportions of fatal and survived cases are depicted as pie charts. The edge lengths between the node pairs are proportional to the number of different alleles out of seven MLST genes between two connected STs. Each node is labelled with the corresponding ST; the number of isolates and the 30 day mortality rate are given in parentheses.

Table 4. Predictors of ST101 presence in patients infected with ColR-Kp

	Univariate analysis			Adjusted analysis[a]		
	OR	CI	*P*	OR	CI	*P*
Female	1.2	0.53–2.72	0.705	–	–	–
ICU stay	1	0.3–3.25	>0.999	–	–	–
Bacteraemia	0.8	0.34–1.75	0.564	–	–	–
Comorbidity	0.8	0.34–2.03	0.681	–	–	–
VAP	2.2	0.98–5.17	0.057	2.0	0.67–6.14	0.216
Prior colistin use within the last 3 months	0.6	0.27–1.39	0.254	–	–	–
Carbapenem resistance	3.9	0.6–42.49	0.12	–	–	–
Empirical carbapenem	0.7	0.29–1.48	0.342	–	–	–
NDM-1	0.0	0.00–0.08	<0.001	0.0	0.00–infinity	0.992
OXA-48	14.3	3.79–81.64	<0.001	6.0	1.09-36.60	0.038
mgrB alteration	22.8	6.82–100.59	<0.001	12.9	3.66–54.37	<0.001

[a]We included variables with a univariate *P* value of <0.1 for ST101 presence in the multivariate analysis.

Developments in Emerging and Existing Infectious Diseases
Series Editors: Önder Ergönül and Füsun Can
2

ANTIMICROBIAL STEWARDSHIP

Edited by

Céline Pulcini, Bojana Beović, Önder Ergönül, Füsun Can

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MANAGING INFECTIONS PROMOTING SCIENCE

ESGAP
ESCMID STUDY GROUP FOR ANTIBIOTIC POLICIES
European Society of Clinical Microbiology and Infectious Diseases

TÜRKİYE'NİN ALTI BÖLGESİNDEN 16 HASTANEDEKİ ANTİMİKROBİYAL YÖNETİMİN DEĞERLENDİRİLMESİ

Hızlı ITanı Testleri

	Kamu dışı hastane	Kamuya bağlı hastane	p
Clostridium difficile	3/5 (%60)	3/10 (%30)	0.264
Solunum paneli	2/5 (%40)	%20	0.409
İshal paneli	1/5 (%20)	0	0.143

Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.

Yoğun Bakım Ünitesi'nde Prokalsitonin ve Hastanede C-Reaktif Protein Bakılma Sıklığı

	Haftada en az 5 gün n (%)	Haftada 3-4 gün n (%)	Haftada 1-2 gün n (%)	Bakılmıyor n (%)
Prokalsitonin	4 (26.7)	2 (13.3)	6 (40)	3 (20)
C-Reaktif Protein	6 (40)	4 (26.7)	5 (33.3)	0

Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.

2015 Yılında Sağlık Bakımıyla İlişkili İnfeksiyonlarda Bakteriyemi Etkenleri Arasında Direnç Oranları

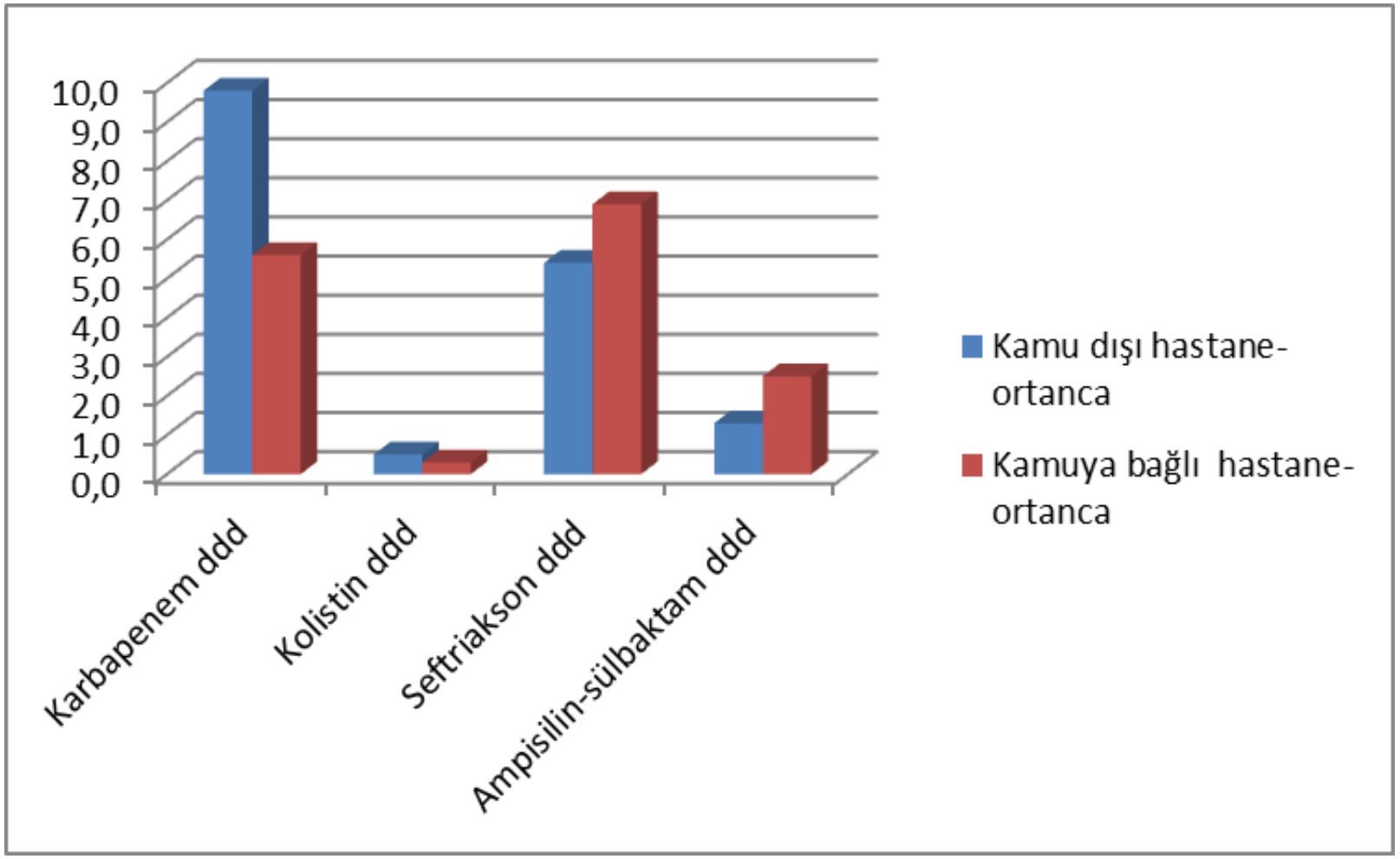
Etkenler ve Suş Sayısı	Karbapenem Direnci	Kolistin Direnci	Kinolon Direnci
Klebsiella spp (190)	75 (%39.5)	46 (%24.2)	101 (%53.2)
E.coli (165)	13 (%7.9)	0	63 (%38.2)
Acinetobacter spp (179)	157 (%87.7)	19 (%10.6)	153 (%85.5)
Pseudomonas spp (97)	56 (%57.7)	8 (%8.3)	49 (%50.5)

Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.

Antibiyotik Kullanım Oranları

	Kamu dışı hastane ortanca	Kamuya bağlı hastane ortanca	p
Karbapenem ddd	9.8	5.6	0.007
Kolistin ddd	0.5	0.3	0.610
Seftriakson ddd	5.4	6.9	0.861
Ampisilin-sülbaktam ddd	1.3	2.5	0.335

Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.



Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.

Gram Negatif Bakterilerde Karbapenem Direnç Oranları

	Kamu Dışı Hastane	Kamuya Bağlı Hastane	p
Klebsiella spp- Karbapenem direnci	19/84 (%37)	56/106 (%50)	0.535
Pseudomonas spp- Karbapenem direnci	26/44 (%39)	30/53 (%48)	0.644
Acinetobacter spp- Karbapenem direnci	56/70 (%87)	101/109 (%92)	0.447

Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.

Ankete Katılan Hekimlerin Hastaneleri ile İlgili Antimikrobiyal Yönetimiyle İlgili Değerlendirmeleri

Olumlu	Olumsuz
Yoğun bakım ünitesi ve kritik birimlerde aktif sürveyans uygulanması	İnfeksiyon kontrollerine uyumsuzluk
Hastanede antimikrobiyal seçiminde İHKMU'na danışılması	Eğitim çalışmalarının sürekliliğinin sağlanamaması
Tedaviye erken başlanması	Cerrahi profilaksi süresini uzatma eğilimi-uyumsuzluk
De-Eskalasyonun kısmi de olsa uygulanabilmesi	Klinik eczacı/farmakoloğun bulunmaması
Cerrahi profilaksi doğru başlanması	MİK bakılamaması
Mikrobiyoloji laboratuvarının kısıtlı antibiyogram bildirmesi	Biyobelirteçlerin yeterince istenmemesi

Taşdelen-Fışgın N, Keske S, İsler B, Azap O, Şimşek F, Azap A, Aydın GÇ, Demiroğlu YZ, Menekşe S, Karakoç ZÇ, Fincancı M, Aydın M, Erbay A, Ural O, Kaya Ş, Arslan E, Alıravcı ID, Ergönül O.

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Int J Infect Dis. 2019 Mar 4. pii: S1201-9712(19)30109-2. doi: 10.1016/j.ijid.2019.02.044. [Epub ahead of print]

The Need for Antibiotic Stewardship Program in a Hospital Using a Computerized Preauthorization System.

Ertürk Şengel B[1], Bilgin H[1], Ören Bilgin B[2], Gidener T[3], Saydam S[3], Pekmezci A[3], Ergönül Ö[4], Korten V[1].

Author information

Abstract

OBJECTIVES: Antimicrobial stewardship programs (ASPs) have an important role in the appropriate utilization of antibiotics. Some of the core strategies recommended for ASPs are preauthorization, prospective audit and feedback. In Turkey, a unique nationwide antibiotic restriction program (NARP) is in use since 2003. We aimed to measure the effect of a prospective audit and feedback strategy system along with NARP.

METHODS: We designed a prospective quasi-experimental study between March and June of 2017. To approve the antibiotics a computerized preauthorization system was used as an ASP strategy. During baseline period patients with intravenous (IV) antibiotic use ≥72hours were monitored without intervention. In the second period, feedback and treatment recommendations were given to attending physician with an IV antibiotic use ≥72hours. The modified Kunin et al. and Gyssens et al. criteria were followed for appropriateness of prescribing. Days of therapy (DOT) and lenght of stay (LOS) were calculated compared between two study periods.

RESULTS: Among 519 patients, 866 antibiotic episodes were observed. A significant systemic antibiotic consumption reduction was observed in the intervention period (575 vs 349 DOT per 1000 patient days; p <0.001). In multivariate analysis prospective audit and feedback (OR, 1.5; 95% CI, 1.09-2.04; p=0.011) and preauthorization of restricted antibiotics (OR, 1.7; 95% CI, 1.2-2.31; p=0.002) were the predictors for appropriate antimicrobial use. Mean LOS was decreased 2.9days (p=0 .095).

CONCLUSION: This study shows that the antimicrobial restriction program alone is effective, but the system should be supported by a tailored ASP such as prospective audit and feedback.

Yerleştirme (kurumsallaştırma) Bilimi

Flottorp et al. Implementation Science 2013:

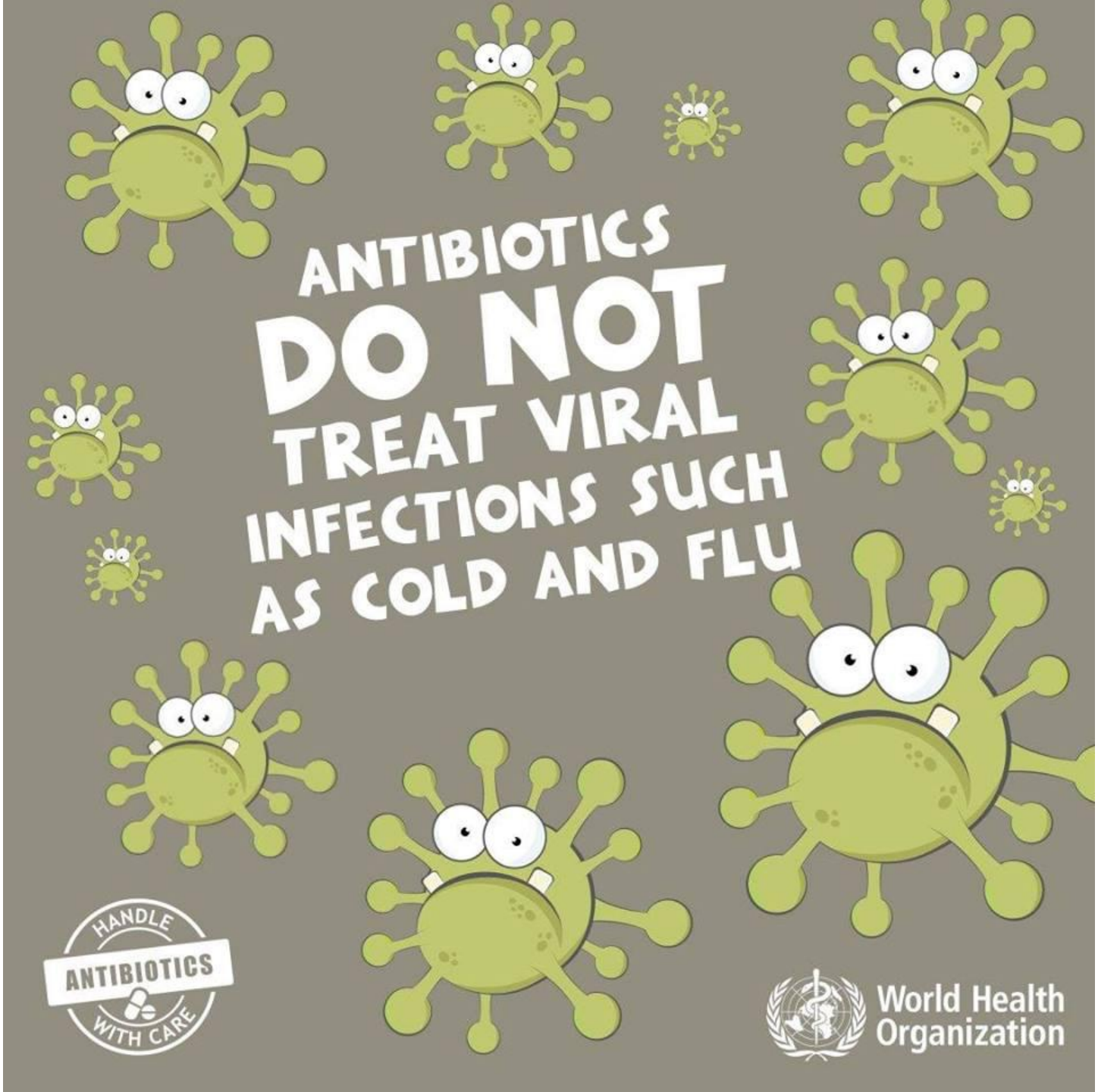
7 ana başlıkta 57 engel

1. *Rehberlere ait faktörler*
2. *Bireysel mesleksel faktörler*
3. *Hasta faktörü*
4. *Profesyonel etkileşim*
5. *Teşvik ve kaynaklar*
6. *Kurumsal değişim kapasitesi*
7. *Sosyal, politik ve hukuksal faktörler*

What's got you sick?

Common Condition	Common Cause			Are Antibiotics Needed?
	Bacteria	Bacteria or Virus	Virus	
Strep throat	✓			Yes
Whooping cough	✓			Yes
Urinary tract infection	✓			Yes
Sinus infection		✓		Maybe
Middle ear infection		✓		Maybe
Bronchitis/chest cold (in otherwise healthy children and adults)*		✓		No*
Common cold/runny nose			✓	No
Sore throat (except strep)			✓	No
Flu			✓	No

* Studies show that in otherwise healthy children and adults, antibiotics for bronchitis won't help you feel better.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