Nötropenik Ateşli Hastalarda Antibiyotik Direnci ve Enfeksiyon Kontrolü

Dr. Önder Ergönül
Koç Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Bölümü

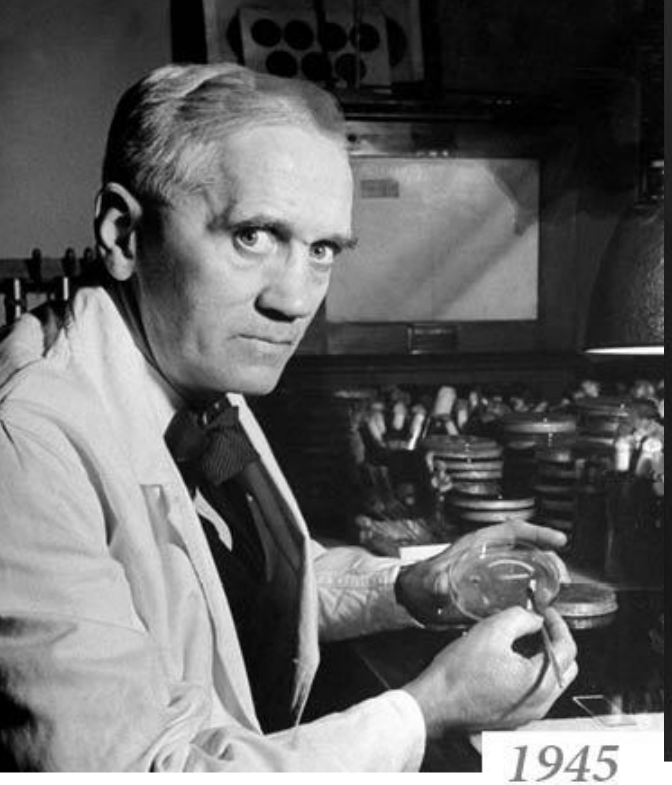
14 Aralık 2013

Sunum başlıkları

- Sorunun önemi: Antibiyotik direncinin sonuçları
  - CDC 2013 raporu
- Antibiyotik direnci ve antibiyotik kullanımı
- Ne yapılmalı? Antibiyotiklerin korunması
  - EHU, Türkiye örneği
  - Amerikan Hastanesi örneği

Hekimler,
çok az bildikleri ilaçları,
daha da az bildikleri hastalıklar için
hiç bilmedikleri “insanlara” reçeteleyen
kişilerdir.

Voltaire (1694-1778)



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

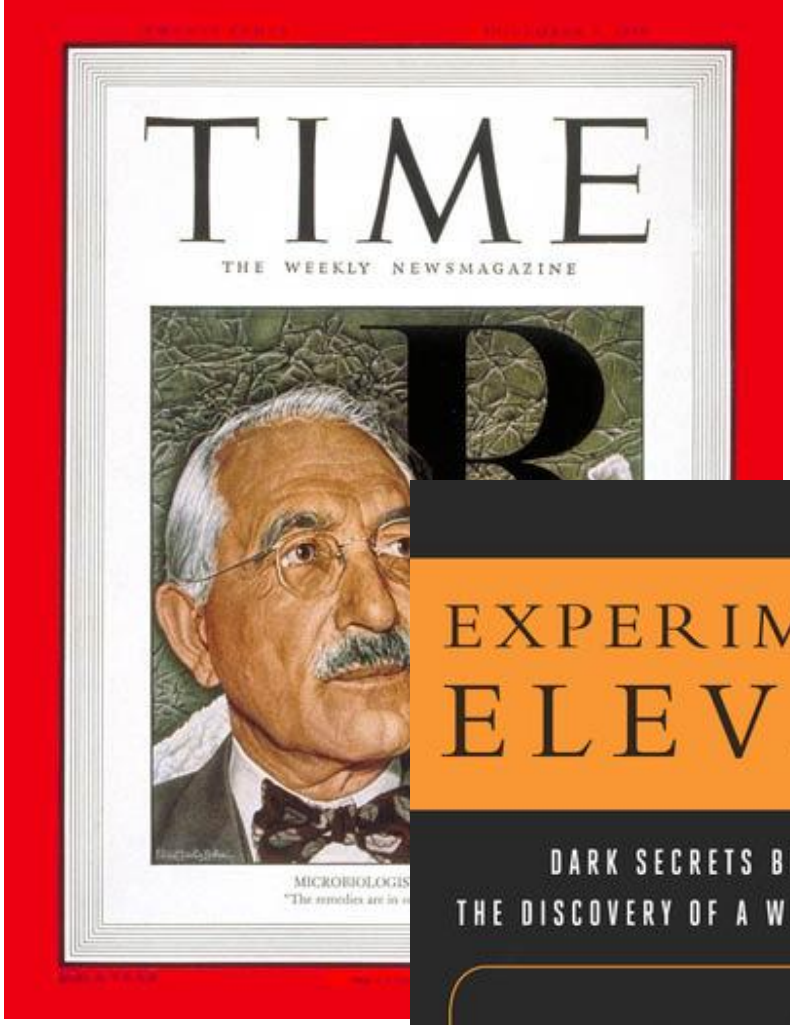
AND

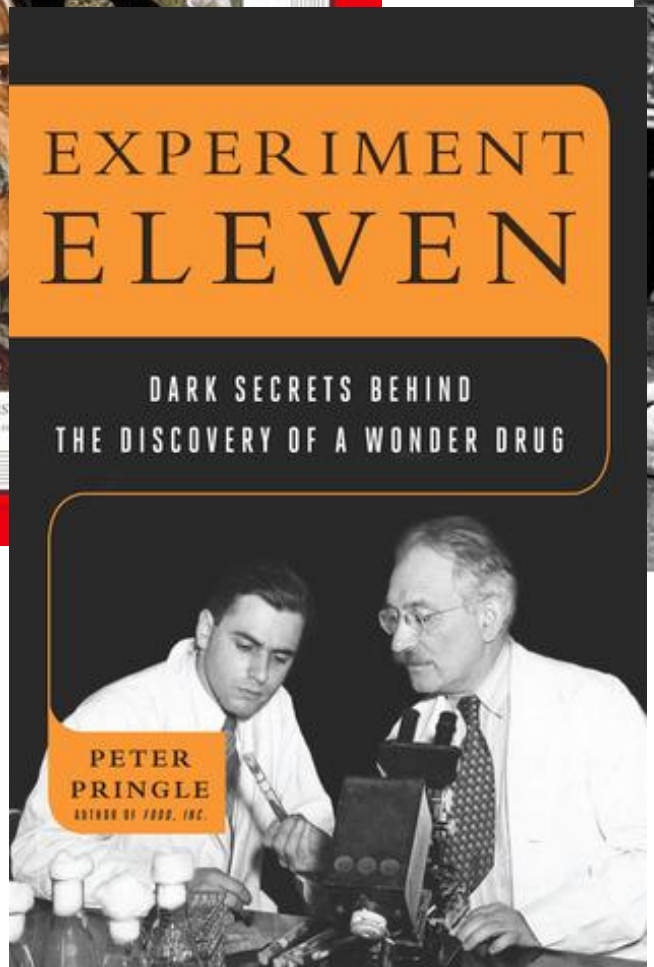
T. ANDERSON, M.B., Ch.B., M.R.C.P.Ed.
Deputy Superintendent, Rochill Hospital, Glasgow

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

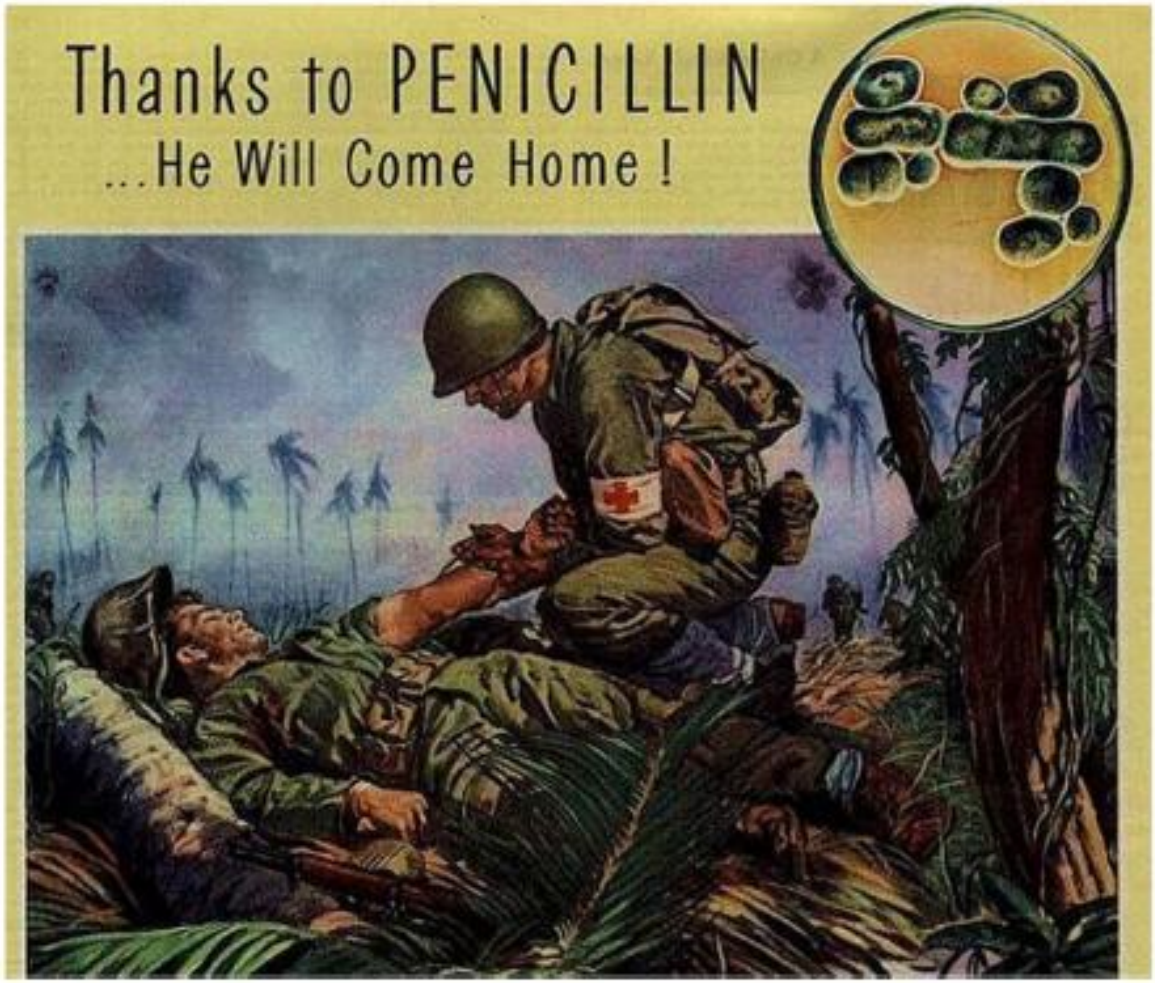
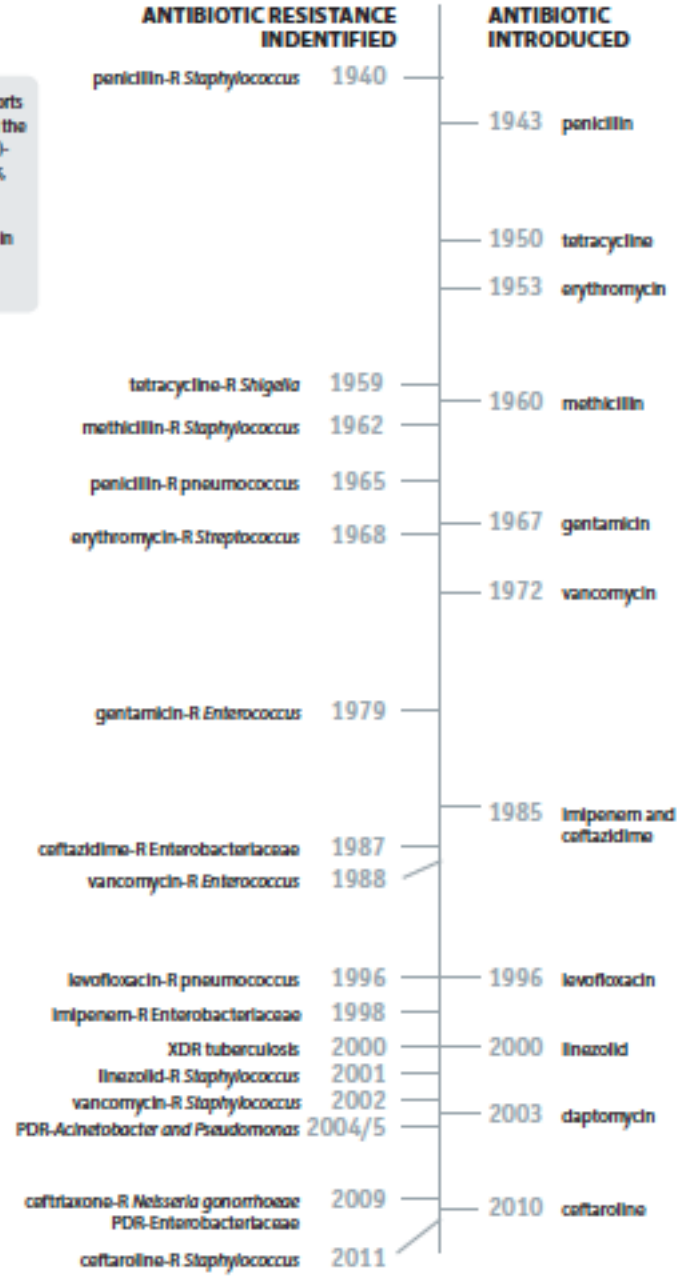


Figure 1 An advertisement by Schenley Laboratories Inc. By 1944, laboratories across the country were increasing penicillin production. Schenley's advertisement stated, "When the thunderous battles of this war have subsided to pages of silent print in a history book, the greatest news event of World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

Developing Resistance

Timeline of Key Antibiotic Resistance Events

Dates are based upon early reports of resistance in the literature. In the case of pan drug-resistant (PDR)-*Acinetobacter* and *Pseudomonas*, the date is based upon reports of healthcare transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.



“Antibiyotik direnci modern tıbbın sonunu getirebilir”

Dr. Margaret Chan

Dünya Sağlık Örgütü Direktörü

16 Mart 2012

NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least **2,049,442** illnesses,

23,000 deaths

**bacteria and fungus included in this report*

+

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least **250,000** illnesses,

14,000 deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.

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

CS230559

How Antibiotic Resistance Happens

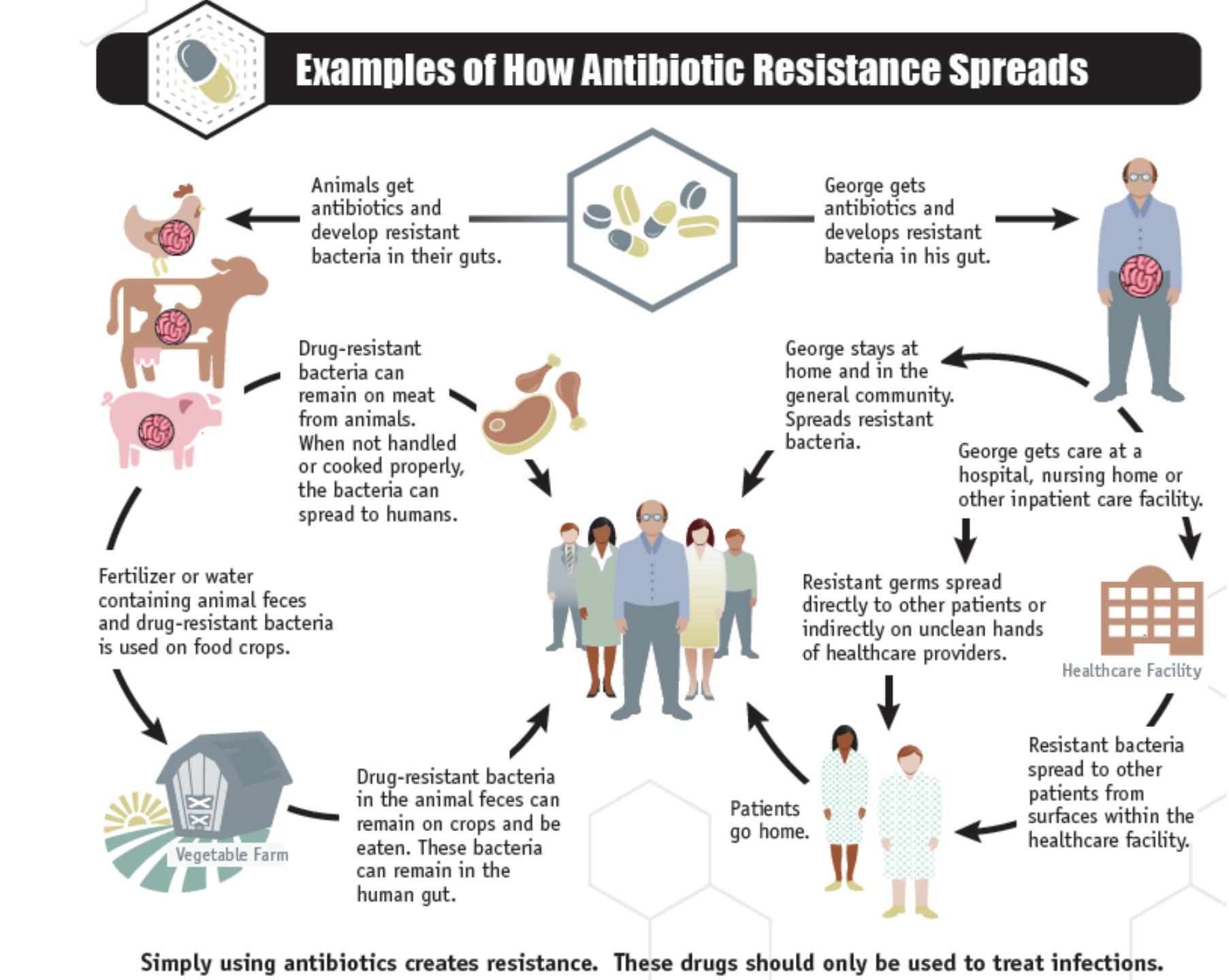
1.
Lots of germs.
A few are drug resistant.

2.
Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.

3.
The drug-resistant bacteria are now allowed to grow and take over.

4.
Some bacteria give their drug-resistance to other bacteria, causing more problems.

Examples of How Antibiotic Resistance Spreads



Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

Antibiotic Safety

ANTIBIOTICS ARE RESPONSIBLE FOR ALMOST

1 OUT OF 5

EMERGENCY DEPARTMENT VISITS FOR ADVERSE DRUG EVENTS

ANTIBIOTICS ARE THE **MOST COMMON CAUSE OF EMERGENCY DEPARTMENT VISITS** FOR ADVERSE DRUG EVENTS **IN CHILDREN UNDER 18 YEARS OF AGE.**

CANCER CHEMOTHERAPY

People receiving chemotherapy are often at risk for developing an infection when their white blood cell count is low. For these patients, any infection can quickly become serious and effective antibiotics are critical for protecting the patient from severe complications or death.

COMPLEX SURGERY

Patients who receive cardiac bypass, joint replacements, and other complex surgeries are at risk of a surgical site infection (SSI). These infections can make recovery from surgery more difficult because they can cause additional illness, stress, cost, and even death. For some, but not all surgeries, antibiotics are given before surgery to help prevent infections.

RHEUMATOID ARTHRITIS

Inflammatory arthritis affects the immune system, which controls how well the body fights off infections. People with certain types of arthritis have a higher risk of getting infections. Also, many medications given to treat inflammatory arthritis can weaken the immune system. Effective antibiotics help ensure that arthritis patients can continue to receive treatment.

DIALYSIS FOR END-STAGE RENAL DISEASE

Patients who undergo dialysis treatment have an increased risk for getting a bloodstream infection. In fact, bloodstream infections are the second leading cause of death in dialysis patients. Infections also complicate heart disease, the leading cause of death in diaysis patients. Infection risk is higher in these patients because they have weakened immune systems and often require catheters or needles to enter their bloodstream. Effective antibiotics help ensure that dialysis patients can continue to receive life-saving treatment.

ORGAN AND BONE MARROW TRANSPLANTS

Transplant recipients are more vulnerable to infections. Because a patient undergoes complex surgery and receives medicine to weaken the immune system for a year or more, the risk of infection is high. It is estimated that 1% of organs transplanted in the United States each year carry a disease that comes from the donor—either an infection or cancer. Effective antibiotics help ensure that organ transplants remain possible.

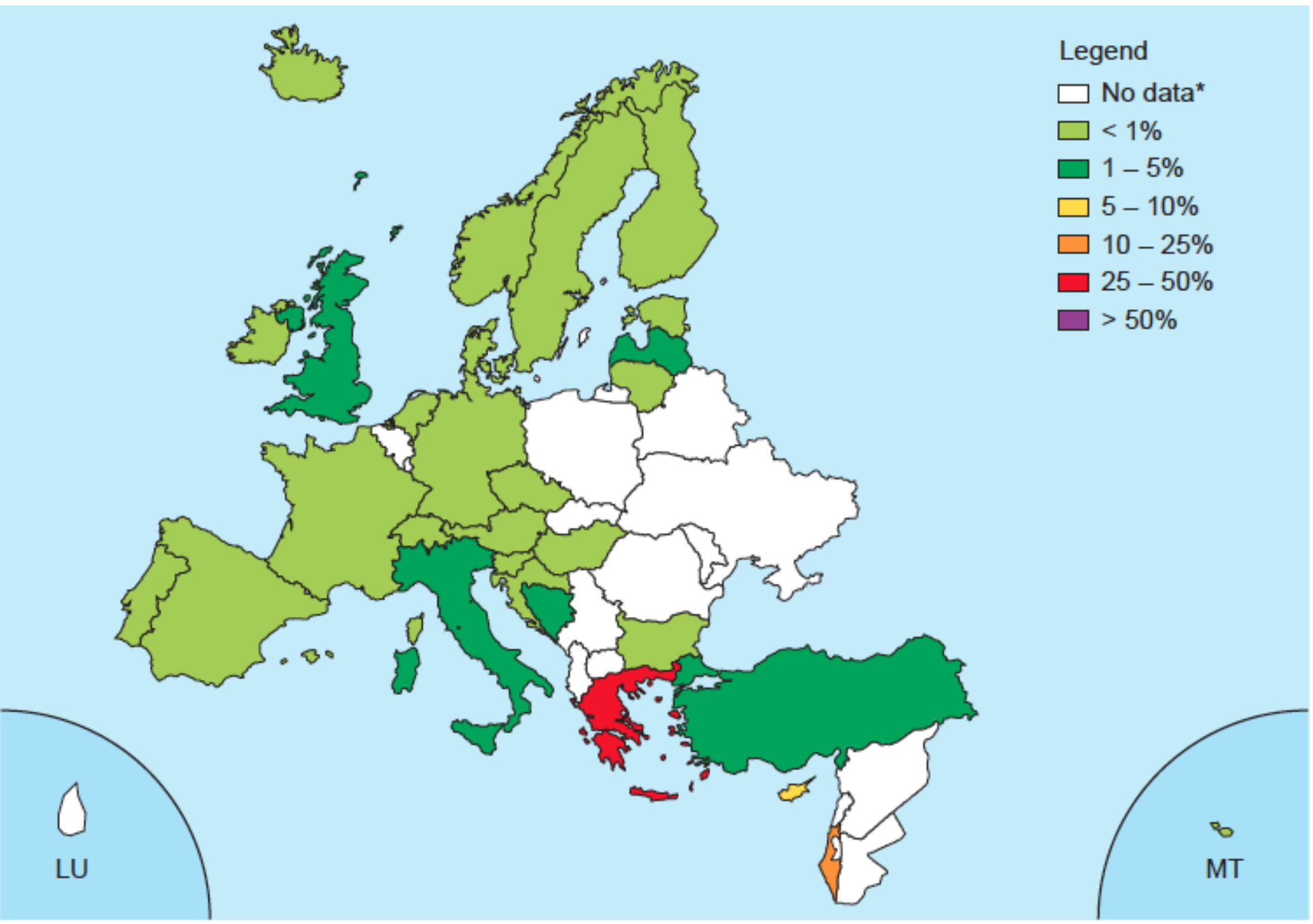
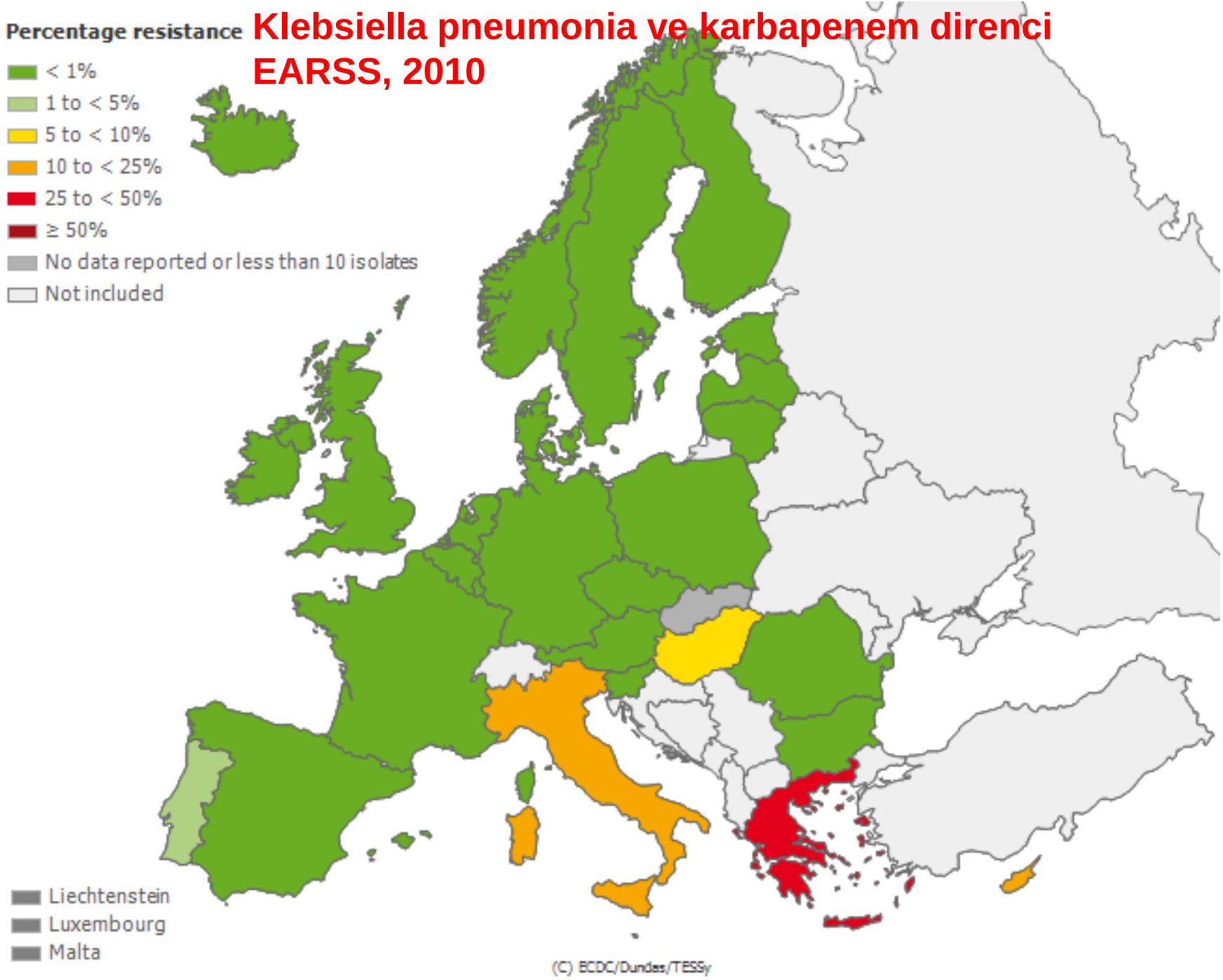


Figure 5.25. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2008.

Klebsiella pneumonia ve karbapenem direnci EARSS, 2010



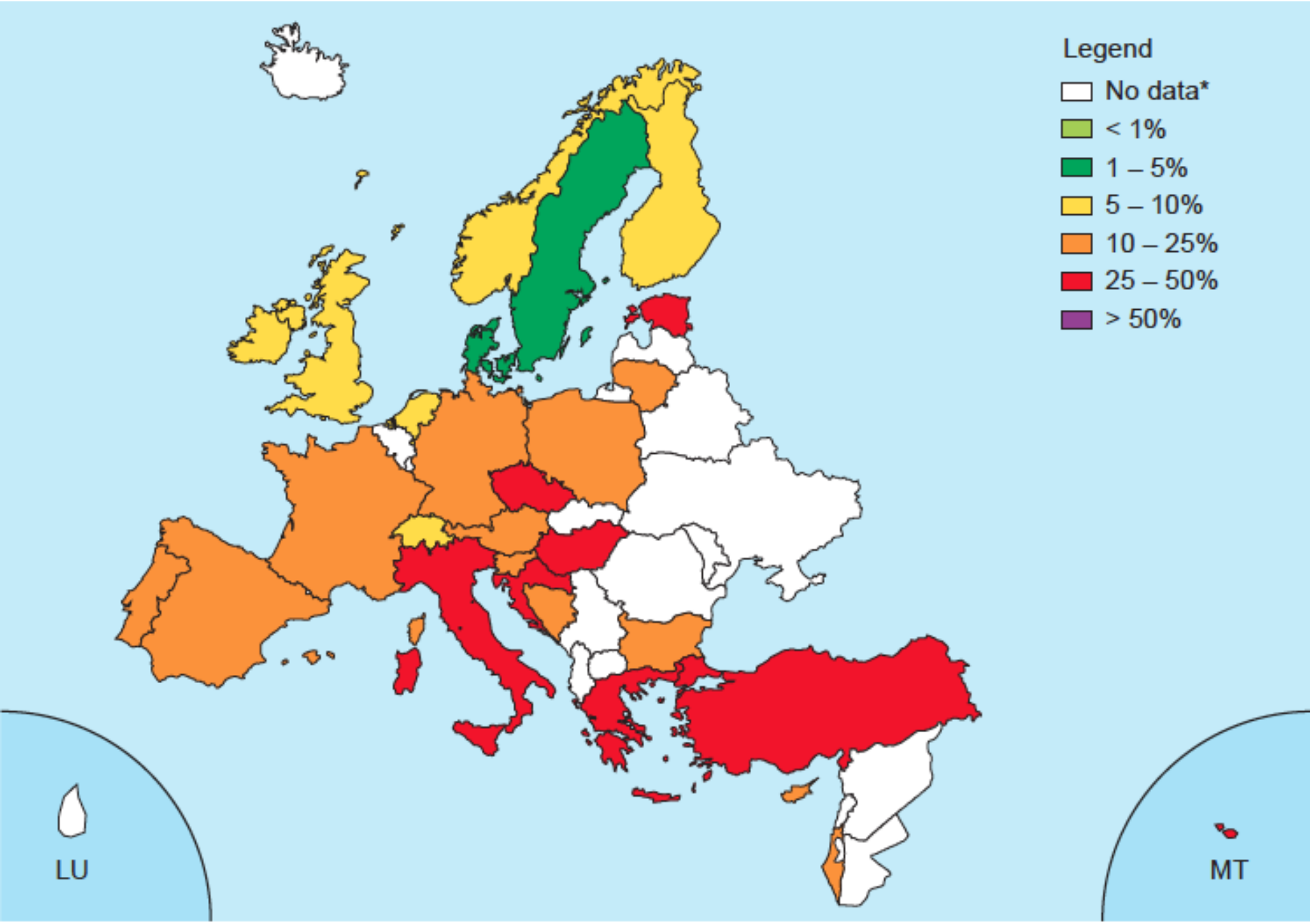
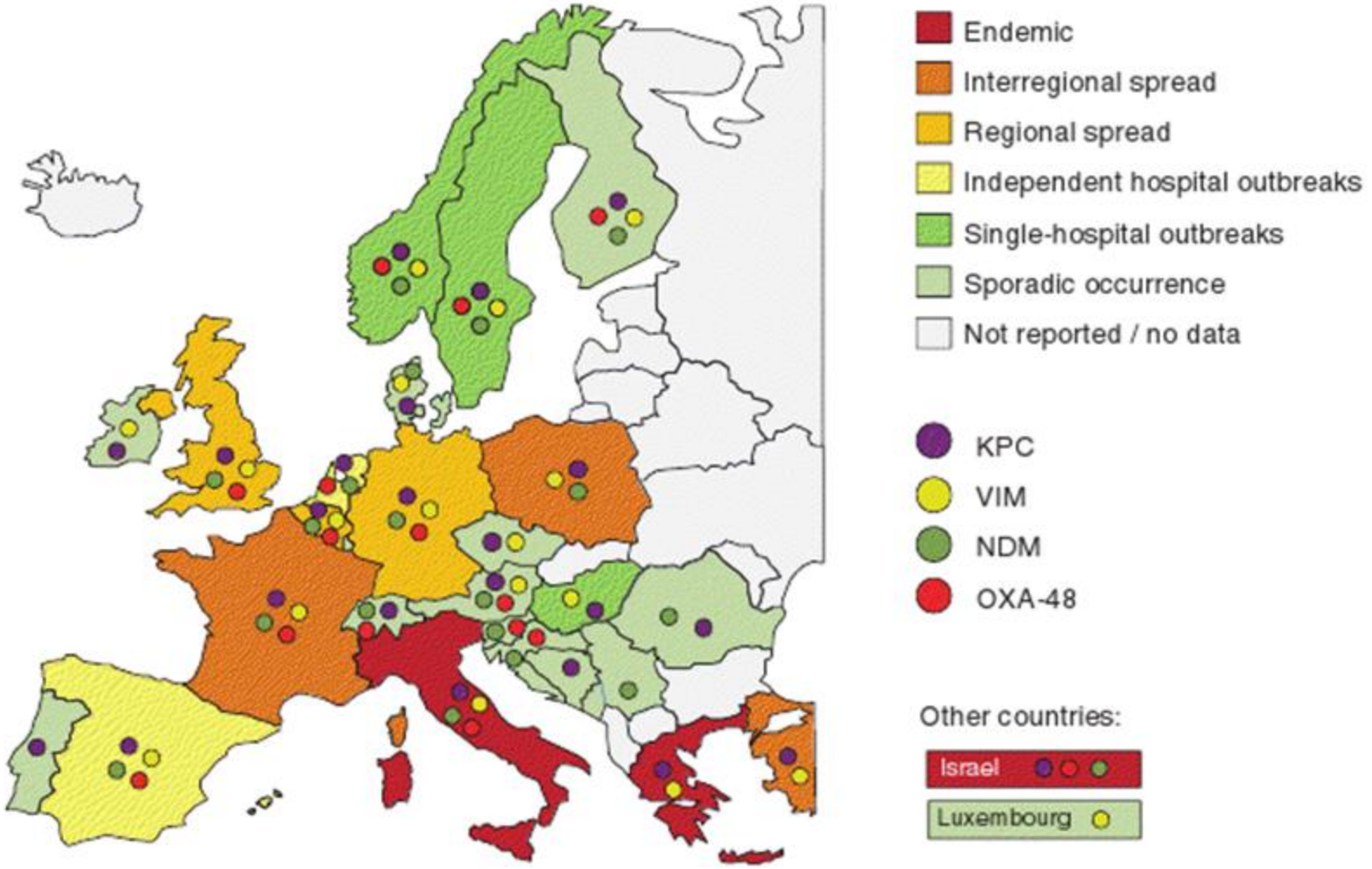


Figure 5.34. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to carbapenems in 2008.

Rapid Evolution and Spread of Carbapenemases



Canton Y, Akova M, Carmeli Y et al. Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe. Clin Microbiol Infect 2012

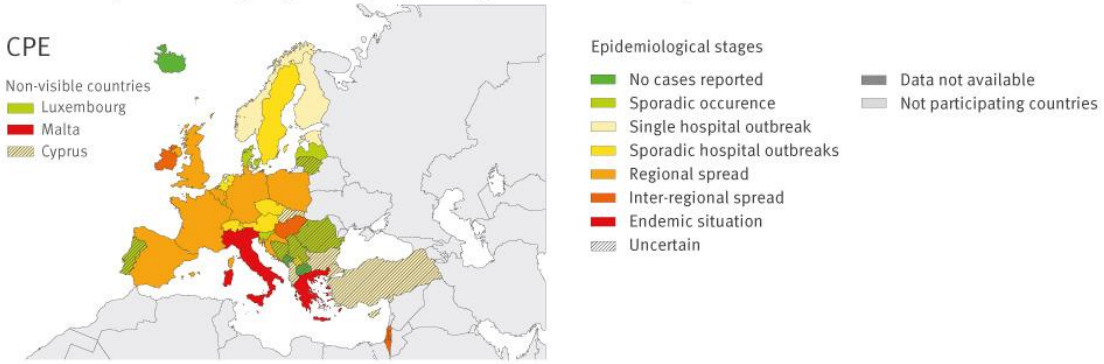
Carbapenemase producing Enterobacteriacea in Europe

Eurosurveillance, 2013

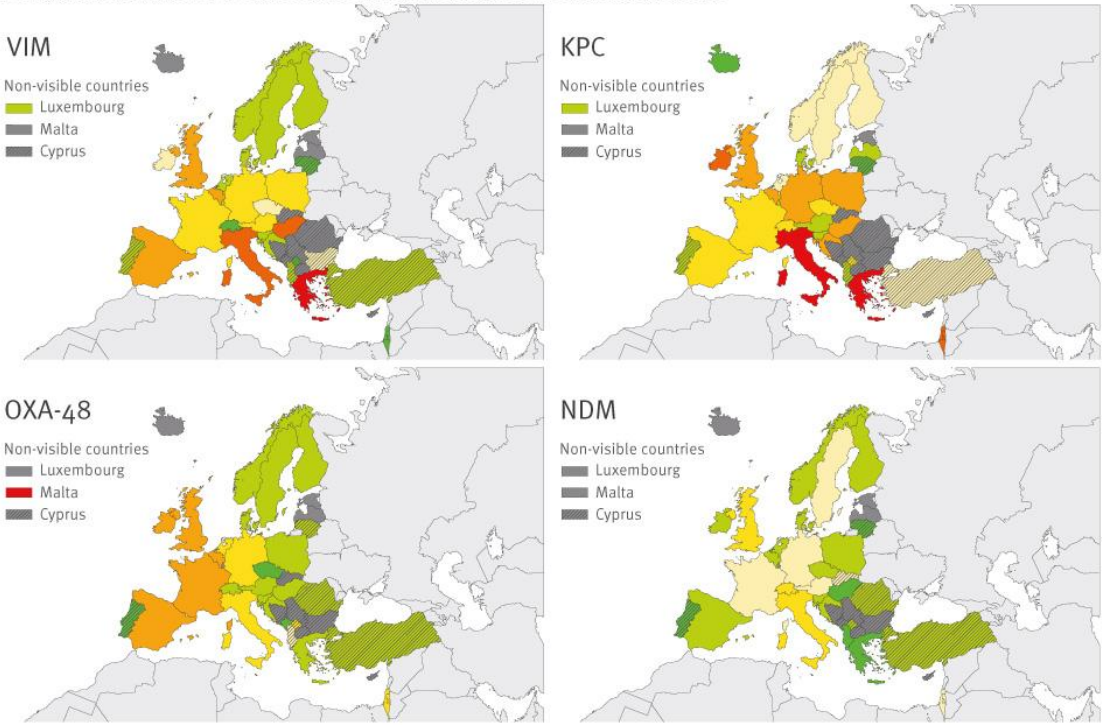
FIGURE

Occurrence of carbapenemase-producing *Enterobacteriaceae* (CPE) in 39 European countries based on self-assessment by respective national experts, 2013

A Overall European situation regarding CPE using an epidemiological scale of nationwide expansion



B Geographic distribution of CPE by resistance mechanism using the same epidemiological scale



KPC: *Klebsiella pneumoniae* carbapenemase-producing *Enterobacteriaceae*; NDM New Delhi metallo-beta-lactamase; OXA-48: carbapenem-hydrolysing oxacillinase-48; VIM: Verona integron-encoded metallo-beta-lactamase.

More details on the epidemiological stages are given in the manuscript Table 1.

In some countries, the epidemiological stage might not represent the true extent of the spread of CPE as it is a subjective judgment by national experts. Uncertainty about the epidemiological stage of a country is indicated by hatching. Results presented here reflect the uncertainty at the time of the survey. For Portugal, case notification and submission of isolates became mandatory on 21 February 2013.

MICROORGANISMS WITH A THREAT LEVEL OF SERIOUS

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***

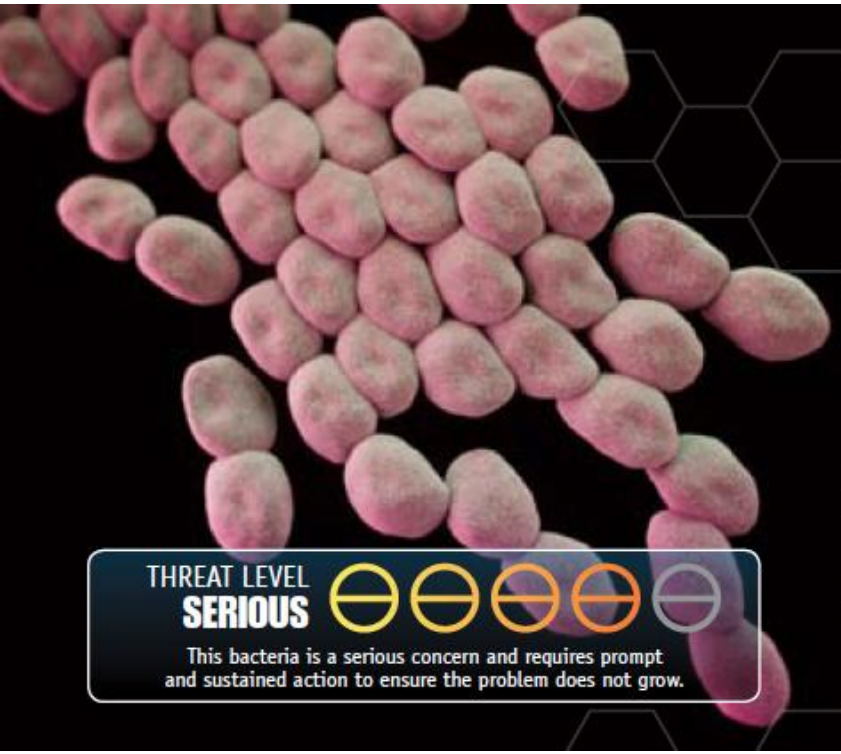
Drug-resistant ***Salmonella*** **Typhi**

Drug-resistant ***Shigella***

Methicillin-resistant ***Staphylococcus aureus*** **(MRSA)**

Drug-resistant ***Streptococcus pneumoniae***

Drug-resistant **tuberculosis**



THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

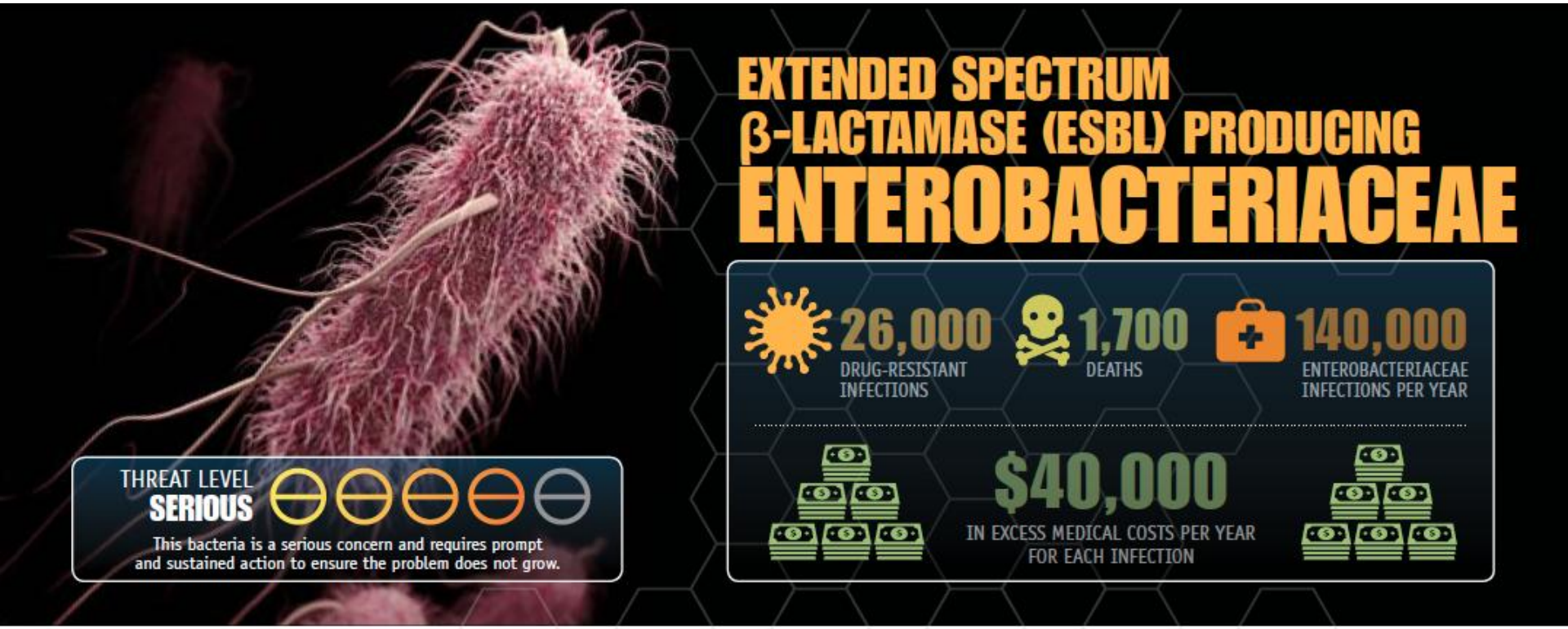
MULTIDRUG-RESISTANT ACINETOBACTER

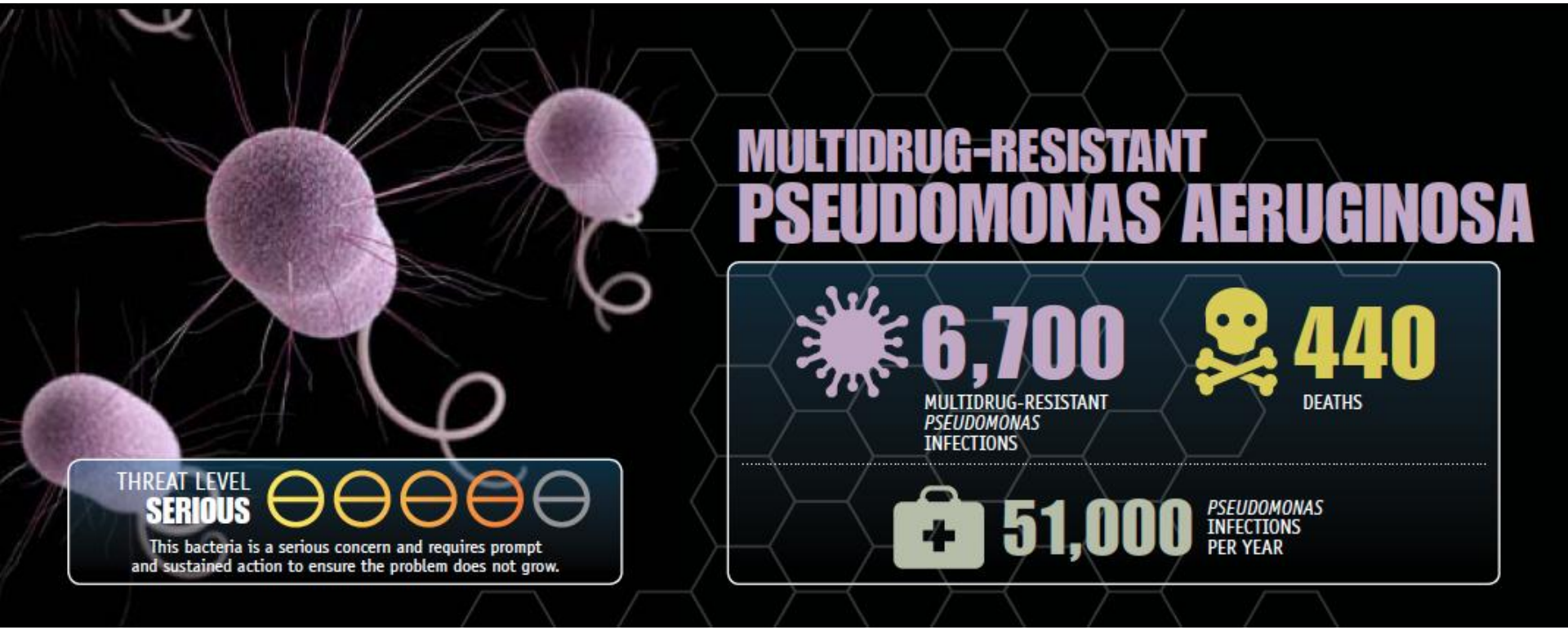
7,300
MULTIDRUG-RESISTANT *ACINETOBACTER* INFECTIONS

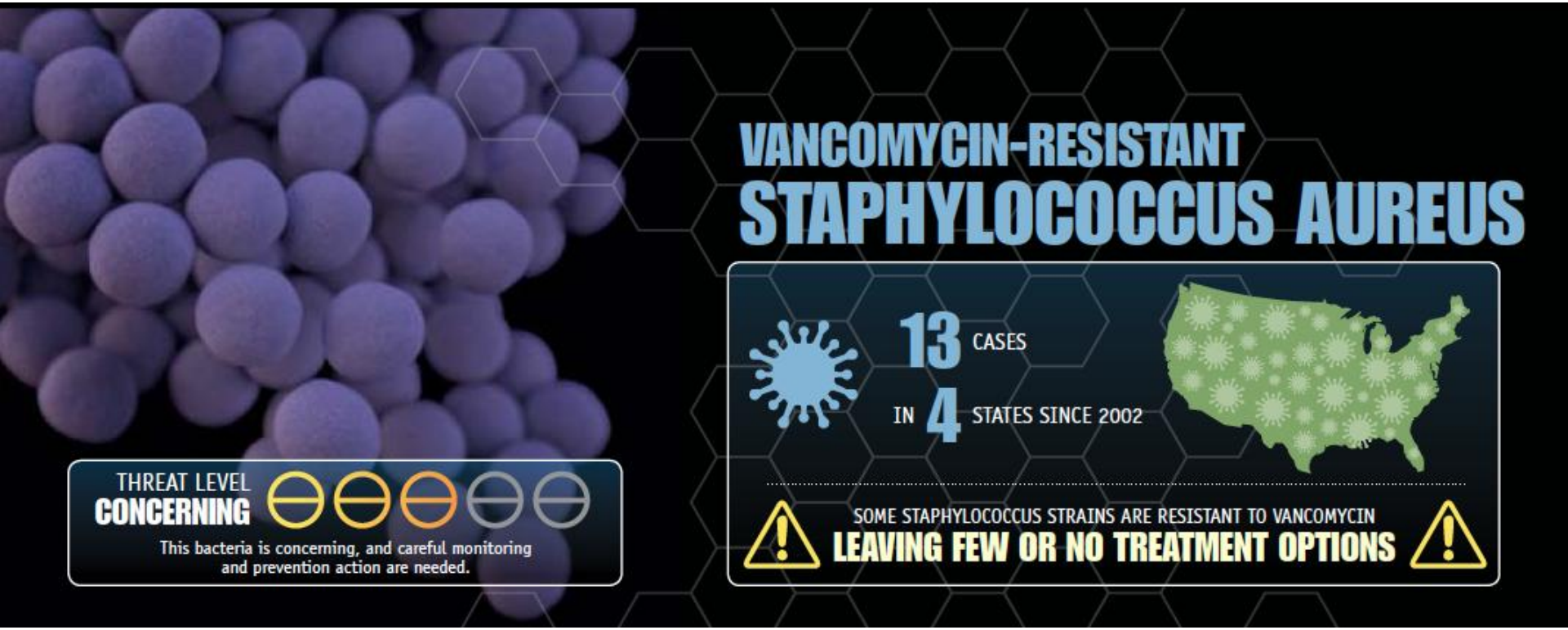
500
DEATHS FROM MULTIDRUG-RESISTANT INFECTIONS

12,000
ACINETOBACTER INFECTIONS PER YEAR

AT LEAST THREE DIFFERENT CLASSES OF ANTIBIOTICS
NO LONGER CURE
RESISTANT ACINETOBACTER INFECTIONS


EXTENDED SPECTRUM
β-LACTAMASE (ESBL) PRODUCING
ENTEROBACTERIACEAE
26,000
DRUG-RESISTANT INFECTIONS
1,700
DEATHS
140,000
ENTEROBACTERIACEAE INFECTIONS PER YEAR
$40,000
IN EXCESS MEDICAL COSTS PER YEAR FOR EACH INFECTION
THREAT LEVEL
SERIOUS
This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.


MULTIDRUG-RESISTANT
PSEUDOMONAS AERUGINOSA
6,700
MULTIDRUG-RESISTANT
PSEUDOMONAS
INFECTIONS
440
DEATHS
51,000
PSEUDOMONAS
INFECTIONS
PER YEAR
THREAT LEVEL
SERIOUS
This bacteria is a serious concern and requires prompt
and sustained action to ensure the problem does not grow.


VANCOMYCIN-RESISTANT
STAPHYLOCOCCUS AUREUS
13 CASES
IN 4 STATES SINCE 2002
SOME STAPHYLOCOCCUS STRAINS ARE RESISTANT TO VANCOMYCIN
LEAVING FEW OR NO TREATMENT OPTIONS
THREAT LEVEL
CONCERNING
This bacteria is concerning, and careful monitoring and prevention action are needed.

Hastane ve Toplum Kökenli MRSA Oranları

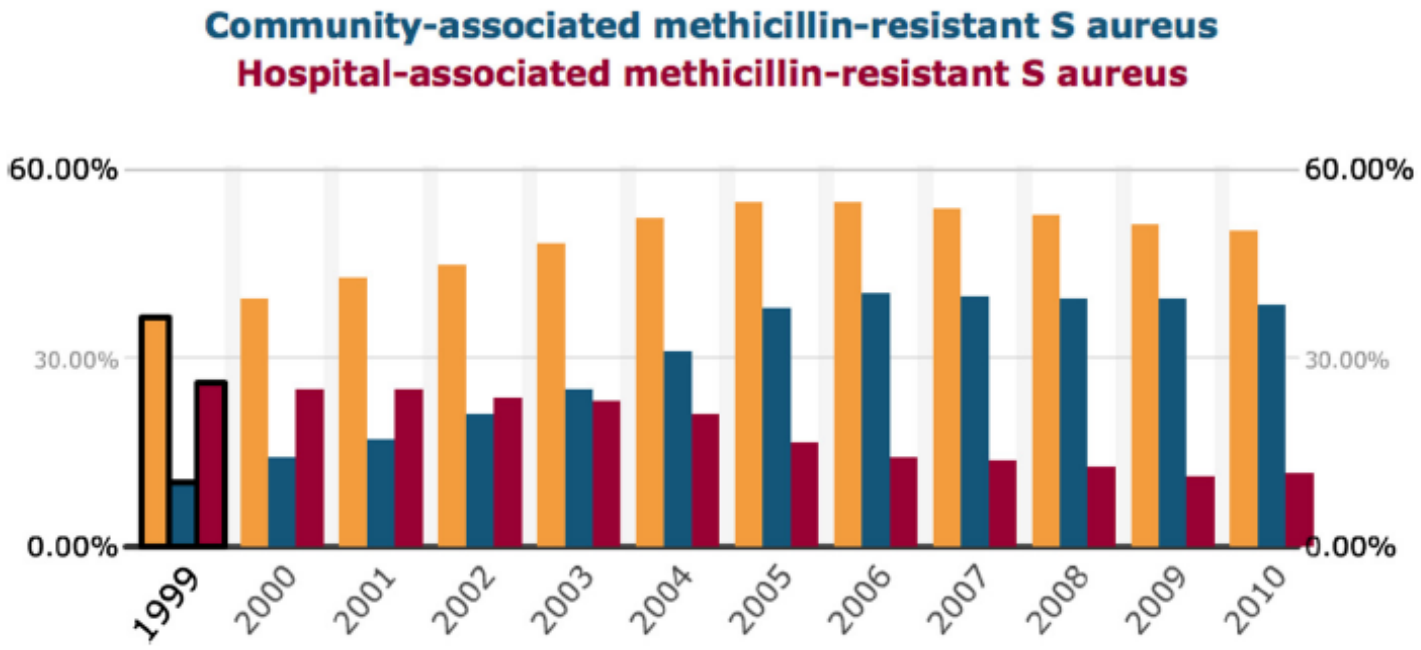


Figure 2 Community-associated, hospital-associated, and overall MRSA prevalences in the United States from 1999 through 2010. From the Center for Disease Dynamics, Economics and Policy (www.cddep.org).

Huttner A, et al. Antimicrob Resist Infect Control 2013

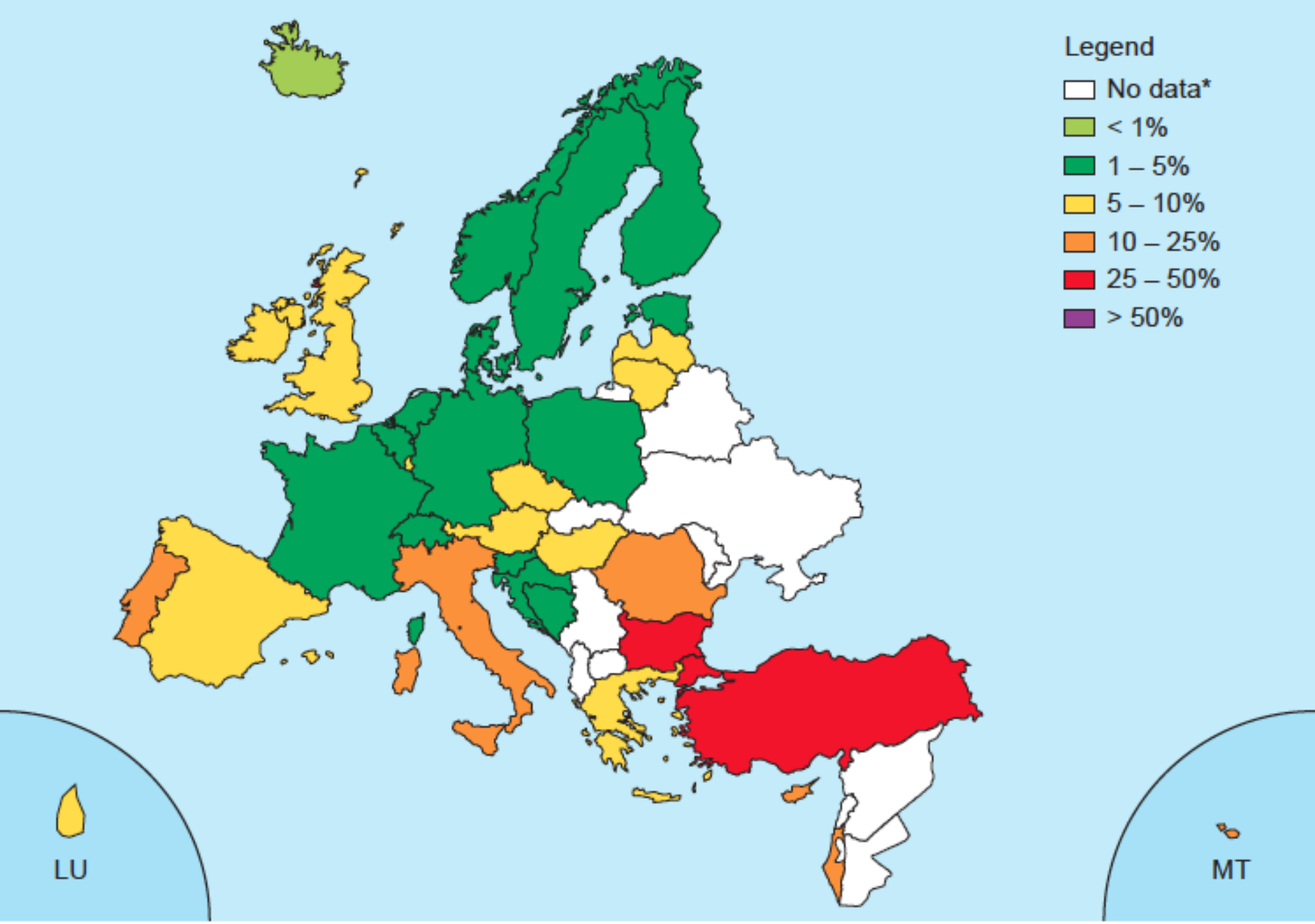


Figure 5.14. *Escherichia coli*: proportion of invasive isolates with resistance to third generation cephalosporins in 2008.

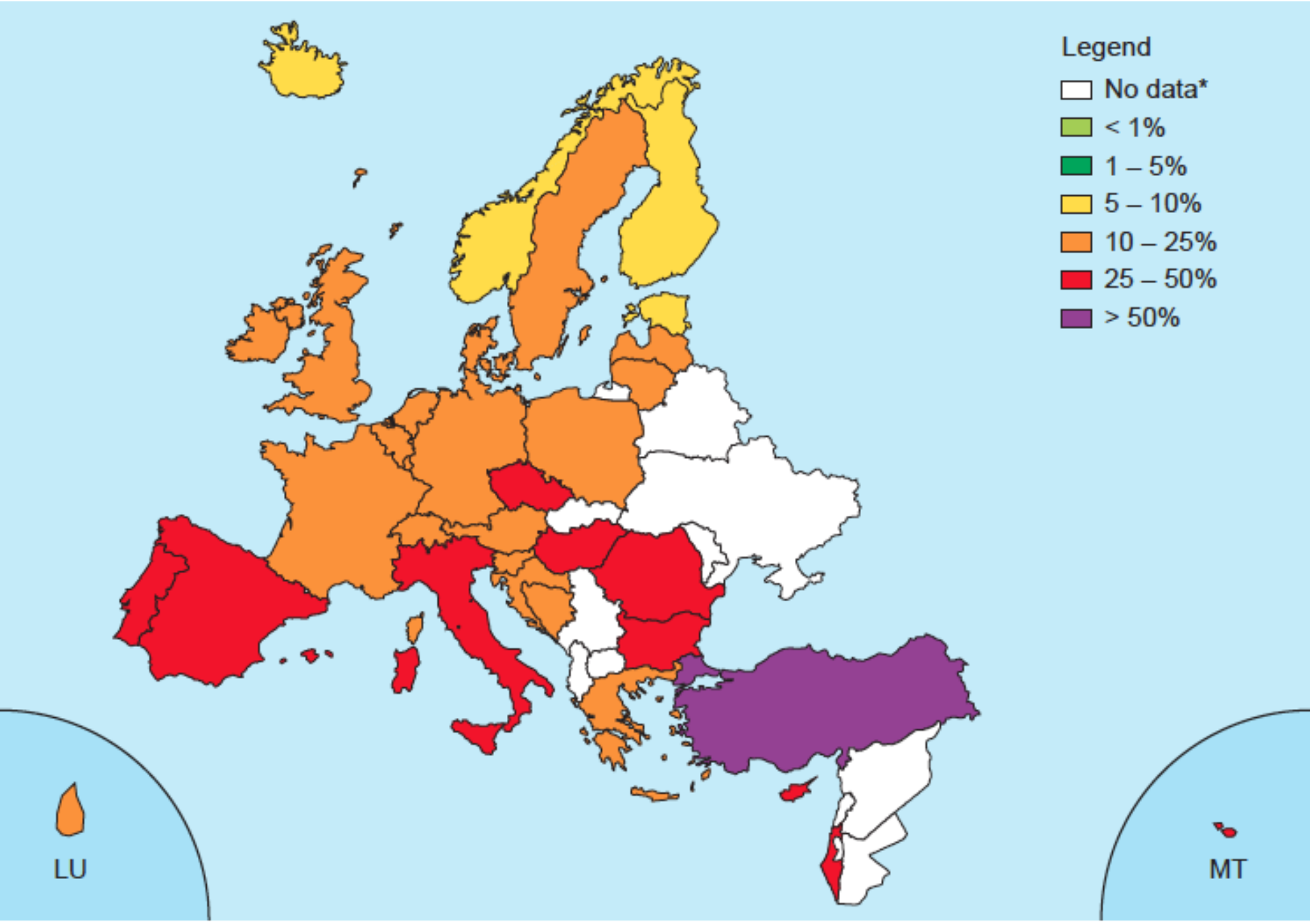


Figure 5.15. *Escherichia coli*: proportion of invasive isolates with resistance to fluoroquinolones in 2008.

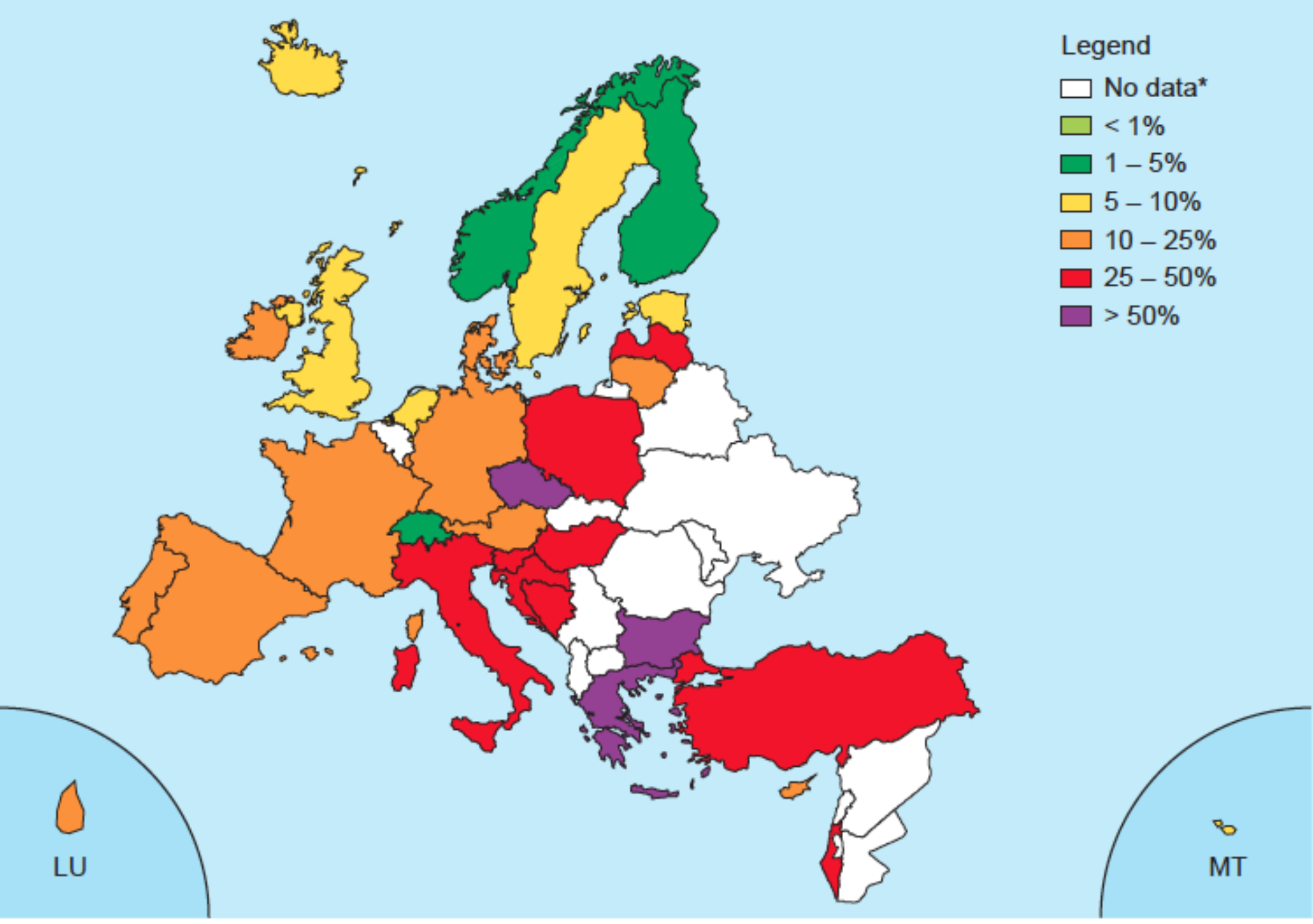


Figure 5.23. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to fluoroquinolones in 2008.

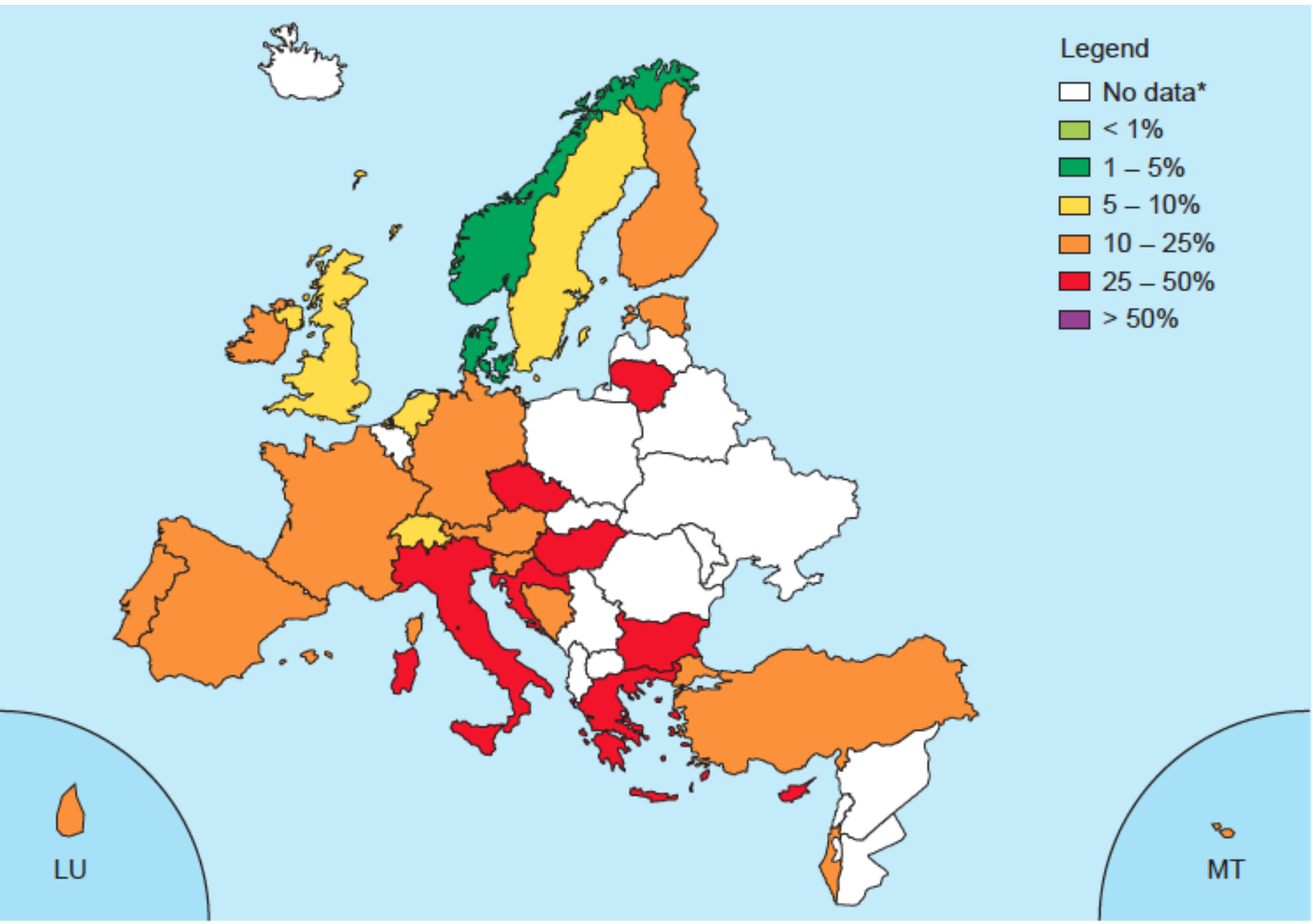
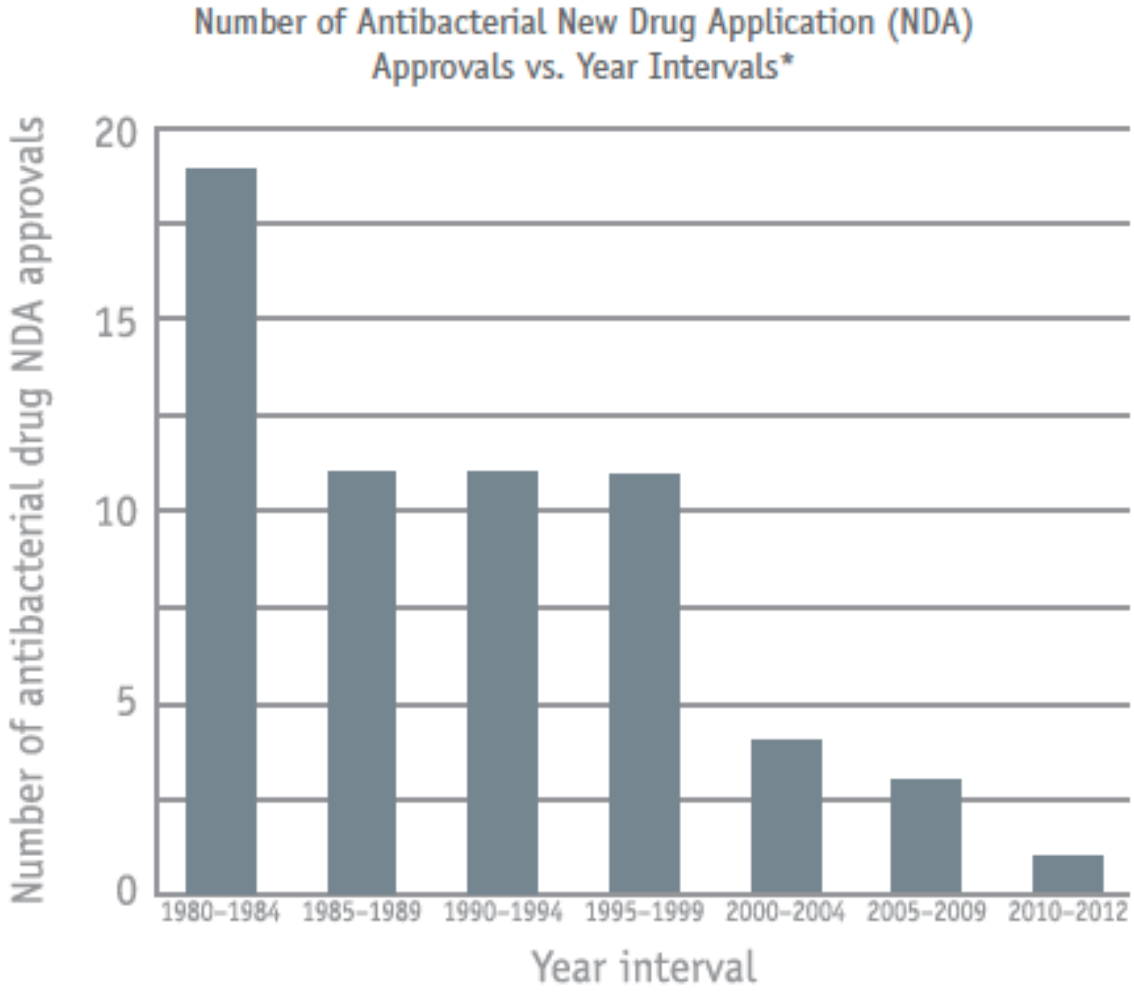


Figure 5.32. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to fluoroquinolones in 2008.

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.



*Intervals from 1980–2009 are 5-year intervals; 2010–2012 is a 3-year interval. Drugs are limited to systemic agents. Data courtesy of FDA' s Center for Drug Evaluation and Research (CDER).

FIGHTING BACK AGAINST ANTIBIOTIC RESISTANCE

Four Core Actions to Prevent Antibiotic Resistance

1 PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE

Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2 TRACKING

CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4 DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS

Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

Antibiyotikleri Koruma Programları

Antibiotic Stewardship

ANTIBIOTIC STEWARDSHIP

IN YOUR FACILITY WILL

DECREASE

- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE

- GOOD PATIENT OUTCOMES

PROMOTE ANTIBIOTIC BEST PRACTICES— A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- ENSURE ALL ORDERS HAVE DOSE, DURATION, AND INDICATIONS
- GET CULTURES BEFORE STARTING ANTIBIOTICS
- TAKE AN "ANTIBIOTIC TIMEOUT" REASSESSING ANTIBIOTICS AFTER 48–72 HOURS

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE A "WIN-WIN" FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED ONE ANTIBIOTIC STEWARDSHIP PROGRAM **SAVED A TOTAL OF $17 MILLION** OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS **IMPROVE PATIENT CARE AND SHORTEN HOSPTIAL STAYS,** THUS **BENEFITING PATIENTS AS WELL AS HOSPITALS**

Antibiyotik Rehberliği (Stewardship)

- Kanıta dayalı yaklaşım
- İnfeksiyon/kolonizasyon ayrımı
- Empirik başlama
  - Sonradan daraltma
  - modifikasyon
- Tedavi süresi
- Bazı ilaçların kanıt veya etki yoksa kesilmesi (örneğin vankomisin)

Başlangıç Tedavisinde Farklı Durumlar için Uyarılar

Epidemiyolojik veriler ve hastanın durumuna göre eklemeler:

i. MRSA: vankomisin, linezolid, veya daptomisin (B-III).

ii. VRE: linezolid veya daptomisin (B-III)

iii. ESBLs: karbapenem (B-III)

iv. KPCs: polimiksin-kolistin veya tigesiklin (C-III)

Ateş olmasa da semptom ve bulguları olan hastalar da yüksek risklidir (B-III).

Düşük riskli grupta siprofloksasin ve amoksisilin- klavulanat (A-I).

Febril Nötropenik Hastalarda Kan Dolaşımı Enfeksiyonlarının Epidemiyolojisi ve Sonuçları

Gram Negatif Enfeksiyonlar

Gram-negative bacteria (n=129)		
E.coli	66 (23)	7 (11)
Klebsiella pneumoniae	32 (11)	4 (6)
Pseudomonas aeruginosa	11 (4)	
Acinetobacter spp.	6 (2)	6 (10)
Enterobacter cloacae	5 (2)	6 (10)
Klebsiella oxytoca	2 (0.7)	1 (1.6)
Stenotrophomonas maltophilia	2 (0.7)	2 (3)
Other Enterobacteriacea	4(1)	1 (1.6)
Fungi (n=11)		
Candida tropicalis	5 (2)	
Candida albicans	2 (1)	2 (3)
Other fungi	4(1)	

V.Korten, H.Akan, E.Şenol, R.Öztürk, A.Özveren, P.Golabi, Ö.Ergönül, Ö.Akan, A.Çiftçioğlu, B.Mete, Ç.Erol, M. Akova· Epidemiology and Outcome of Bloodstream Infections in Febrile Neutropenic Hematologic Cancer Patients, ICAAC 2010

Febril Nötropenik Hastalarda Kan Dolaşımı Enfeksiyonlarının Epidemiyolojisi ve Sonuçları

	HR	Cl	p
ESBL production	7.5	1.81-31.33	0.005
Relaps	4.9	1.35-18.32	0.016
Previous hospitalization	0.8	0.14-5.21	0.871
Antibiotic use within last 3 months	1.5	0.28-8.24	0.618
Catheter use	1.6	0.19-14.27	0.651
Steroid use	4.3	0.9-20.63	0.066
Duration of febrile neutropenia > 10 days	0.3	0.09-1.31	0.122

V.Korten, H.Akan, E.Şenol, R.Öztürk, A.Özveren, P.Golabi, Ö.Ergönül, Ö.Akan, A.Çiftçioğlu, B.Mete, Ç.Erol, M. Akova· Epidemiology and Outcome of Bloodstream Infections in Febrile Neutropenic Hematologic Cancer Patients, ICAAC 2010

Febril Nötropenik Hastalarda Kan Dolaşımı Enfeksiyonlarının Epidemiyolojisi ve Sonuçları

Twenty-two of 95 (25%) initial and 5 of 11 (45%) breakthrough *E.coli* and *K.pneumoniae* isolates were extended spectrum beta lactamase (ESBL) producers.

Florokinolon direnci: %27 Gram negatif izolatlar, %35 E.coli

Pseudomonas infeksiyonunda seftazidim direnci %9

ESBL üreten *E.coli* and *K.pneumoniae* infeksiyonlarında başlangıçta in-vitro etkili karbapenem veya piperacillin/tazobactam alanların oranı %45

E.coli and *K.pneumoniae* bacteremisi olanlardan uygunsuz antibiyotik alanlarda fatalite belirgin olarak yüksek (14 vs. 7 days, p= 0.04).

V.Korten, H.Akan, E.Şenol, R.Öztürk, A.Özveren, P.Golabi, Ö.Ergönül, Ö.Akan, A.Çiftçioğlu, B.Mete, Ç.Erol, M. Akova. Epidemiology and Outcome of Bloodstream Infections in Febrile Neutropenic Hematologic Cancer Patients, ICAAC 2010

Febril Nötropenide İlaç Modifikasyonu Nasıl Yapılmalı

Genel durumu iyi olan ama açıklanamayan persistan ateşi olan hastalarda empirik değişiklik nadiren gerekir (A-I).

Vankomisin veya diğer gram pozitiflere karşı ajan başlandıysa ve 2 gün içinde gram pozitif infeksiyonu belirtisi yoksa kesilmelidir (A-II).

Düşük riskli hastaların durumu stabilse ilaçların basitleştirilmesi düşünülebilir (A-I).

Klinik durum stabilse iv formdan orale geçilebilir (A-I).

4-7 gün geniş spektrumlu antibakteriyel tedavi sonrası halen ateş yüksekse, empirik antifungal başlanabilir (A-II).

Empirik Antibiyotik Tedavi Süresi

Klinik veya laboratuvar olarak saptanana infeksiyona ve infeksiyon yerine göre değişir; nötropeniden çıkıncaya kadar devam etmelidir (B-III).

Etken saptanamamışsa, nötropeniden çıkıncaya kadar (B-II).

Alternatif olarak, tüm semptom ve bulgular gerilemesine rağmen, nötropeni devam ediyorsa, nötropeniden çıkıncaya kadar oral florokinolon profilaksisi sürdürülebilir (C-III).

Grip Benzeri Hastalarda Antibiyotik Kullanımı

	N=1220 (%)
Herhangibir antibiyotik	505 (40)
Kinolon	145 (12)
Makrolid	129 (10)
Amox-clav	118 (10)
Sefuroksim	87 (7)
3 jen. sefalosporin	39 (3)
oseltamivir	125 (10)

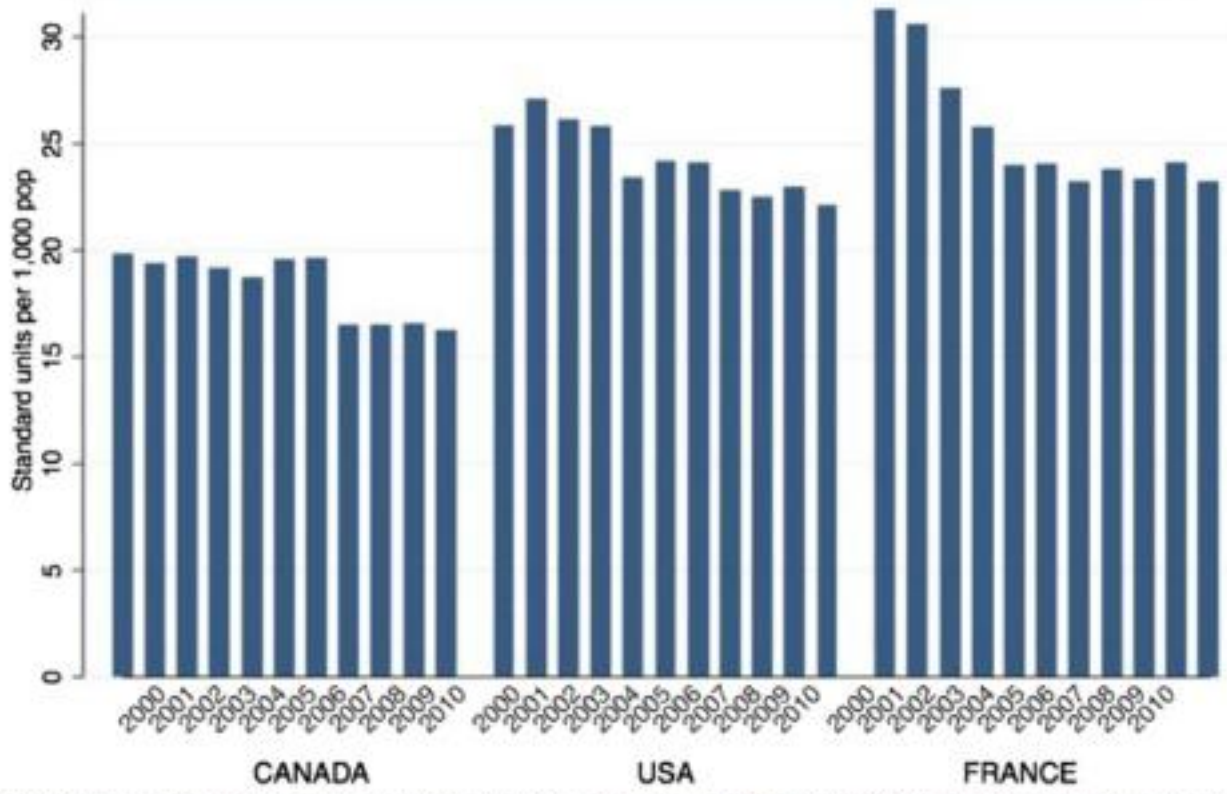
İnfluenza Bilinmesine Rağmen Antibiyotik

	Antibiyotik almayan	**Antibiyotik alan**	***p*=0.330**
Influenza test (--) pozitif	102 (%66)	53 (%34)	
İnfluenza test (+)	80 (%71)	32 (%29)	
	182 (%100)	85 (%100)	267

Hekimler Neden Antibiyotik Başlıyor?
(Tek değişkenli analiz)

	OR	GA	p
CRP >20	1.7	1.09-1.73	<0.001
PMNL >%80	2	1.41-2.93	<0.001
PA AC bulgusu	1.6	0.83-3.22	0.150
İnfluenza test pozitifliği	0.76	0.45-1.3	0.331

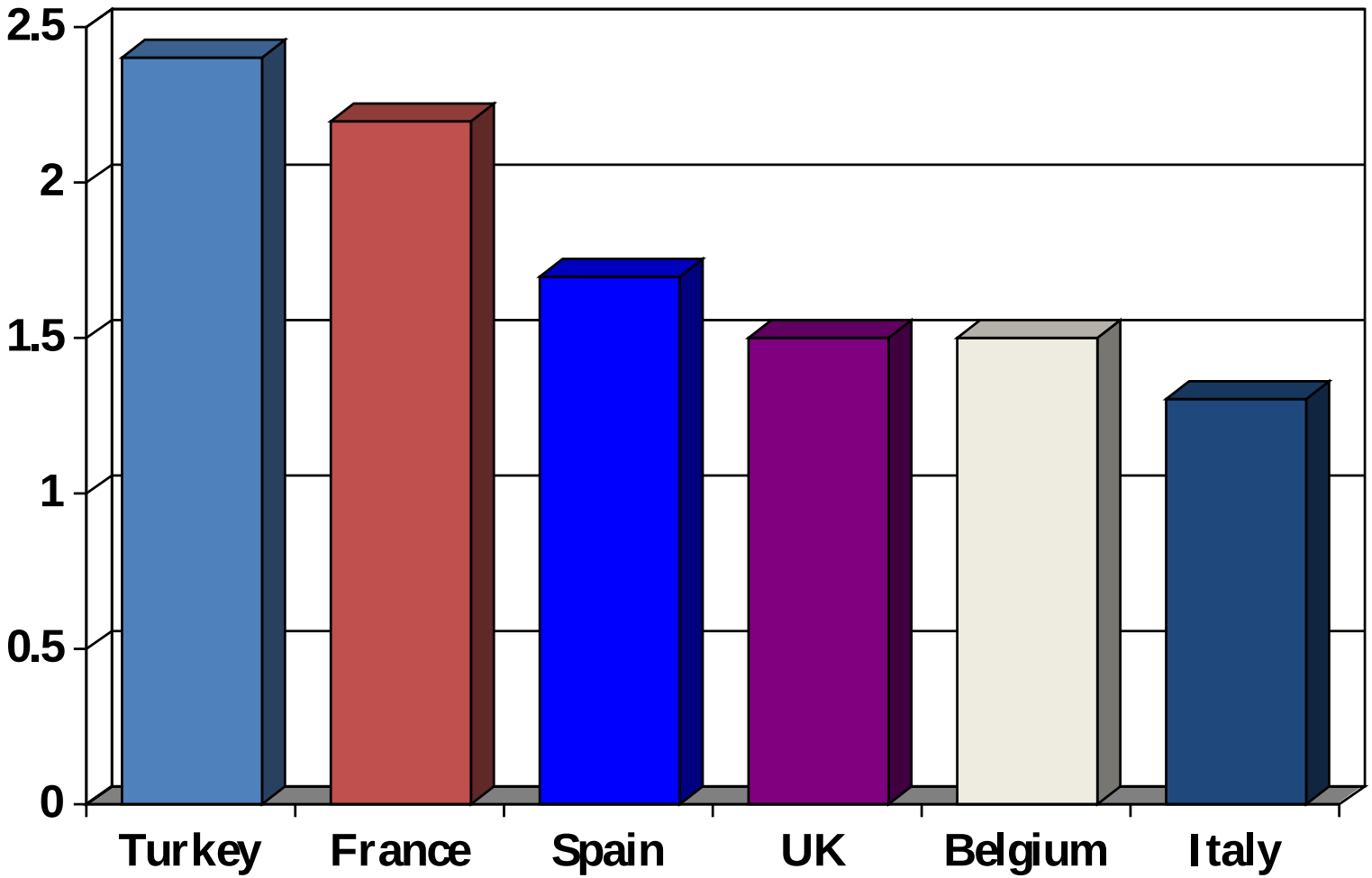
Per capita antibiotic use has decreased in Canada, the United States, and France, 2000-2010



CDDEP
THE CENTER FOR
Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Index of antibiotic demand --

Patients definitively expecting antibiotics for RTI



Branthwaite & Pechere; J Intern Med Research 1996; 24: 229-238

Journal of Antimicrobial Chemotherapy (2008) **62**, 830–836
doi:10.1093/jac/dkn260
Advance Access publication 30 June 2008

JAC

Antibiotic consumption in southern and eastern Mediterranean hospitals: results from the ARMed project

Michael A. Borg[1]*, Peter Zarb[1], Matus Ferech[2] and Herman Goossens[2]
on behalf of the ARMed Project Group

[1]*Infection Control Unit, Mater Dei Hospital, Msida, Malta;* [2]*Department of Medical Microbiology, Vaccine and Infectious Disease Institute, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk-Antwerp, Belgium*

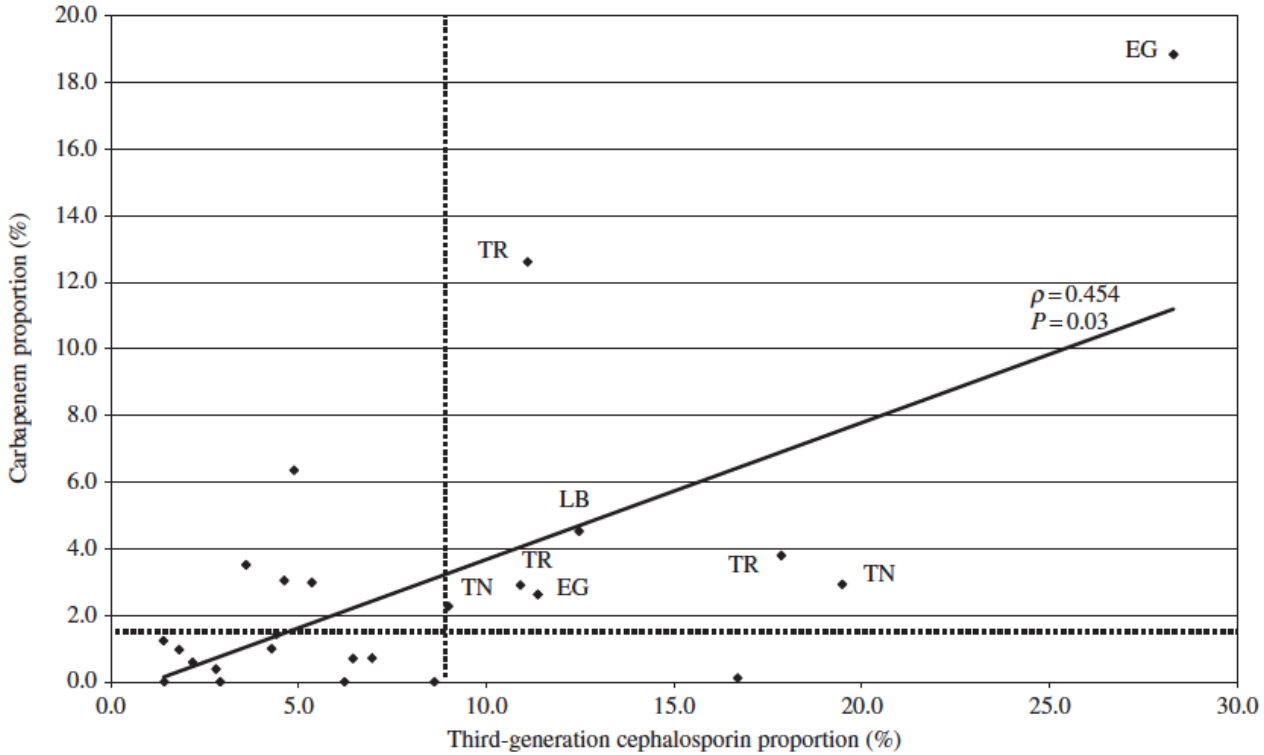


Figure 5. Correlation plot for proportional consumption of carbapenems and third-generation cephalosporins including median (dotted) lines as well as line of best fit and Spearman's ρ. EG, Egypt; LB, Lebanon; TN, Tunisia; TR, Turkey.

Journal of Antimicrobial Chemotherapy (2008) **61**, 1169–1171
doi:10.1093/jac/dkn055
Advance Access publication 13 February 2008

JAC

Increased antimicrobial consumption following reimbursement reform in Turkey

Oguz Karabay[1]* and Salih Hosoglu[2]

[1]*Department of Clinical Microbiology and Infectious Diseases, Abant Izzet Baysal University Hospital, Bolu, Turkey;* [2]*Department of Clinical Microbiology and Infectious Diseases, Dicle University Hospital, Diyarbakir, Turkey*

Table 2. Effects of SIR on antibiotic consumption in Turkey

Antibiotic class	Mean consumption (DDD)		Ratio (after/before SIR)	Difference in DDD
	before SIR (2001–04)	after SIR (2005–06)		
Aminoglycosides (J01G)	0.156	0.164	1.051	0.008
Amphenicols (J01B)	0.012	0.009	0.766	−0.003
Cephalosporins (J01DA)	2.530	5.927	2.343	3.397
Macrolides and lincosamides (J01F)	2.945	5.682	1.929	2.735
Penicillins (J01C)	8.160	14.065	1.724	5.905
Quinolones (J01M)	1.802	3.616	2.007	1.814
Tetracyclines (J01)	0.902	1.232	1.366	0.330
Antibacterials for systemic use (total) (J01)	16.598	30.960	1.865	14.363

IVYSPRING INTERNATIONAL PUBLISHER

International Journal of Medical Sciences

2011; 8(4):339-344

Research Paper

The Impact of a Nationwide Antibiotic Restriction Program on Antibiotic Usage and Resistance against Nosocomial Pathogens in Turkey

Adalet Altunsoy[1], Cenk Aypak[2]✉, Alpay Azap[1], Önder Ergönül[3], İsmail Balık[1]

Table 2: Comparison of antibiotic consumption two years before and after the initiation of NARP*

Restricted Antibiotics	Antibiotic consumption (grams)		% difference
	2001+2002	2003+2004	
Meropenem	113362	85236	-24.8
Imipenem	50532	45935.2	-9.1
Ceftazidim	60074	38129	-36.5
Ceftriaxone	300955	190281	-36.8
PIP-TAZO*	270594	417114	+54.1
Cefepime	100588	121799	+21.1
Vancomycin	113362	85236	-17.8
Teicoplanin	50532	45935.2	-1.4
Total	60074	38129	**-11.3**

*nationwide antibiotic restriction program, **piperacillin-tazobactam

Gelecekte Yapılması Gerekenler

Sağlık Otoritesi

1. Hayvanlarda kullanımının sınırlanması
2. Kontrolsüz (reçetesiz) satışların azaltılması
3. Diğer ülkelerin Sağlık Bakanlıklarıyla işbirliği içinde antibiyotik koruma programlarının geliştirilmesi
4. Farkındalık ve duyarlılık kampanyalarının düzenlenmesi
5. Sanitasyon sistemlerinin geliştirilmesi, el yıkama eğitimlerinin verilmesi
6. Yeni antibiyotiklerin gelişimi için destek olunması

ABD'DE ÇİFTLİK HAYVANLARINDA ANTİBİYOTİK KULLANIMI YASAKLANIYOR

New U.S. rules aim to cut antibiotic use in farm animals

KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Antibiyotikler Artık Reçetesiz Satılamayacak

Gelecekte Yapılması Gerekenler

İnsan ve Hayvan Sağlığı Alanında Çalışanlar

7. Direnç gelişimini izleme sistemlerinin oluşturulması

8. Tıp, veterinerlik ve hemşirelik eğitim programları ve mezuniyet sonrası eğitimlerde konunun gündemde tutulması

Toplum

9. Antibiyotik tüketenler için eylem planı geliştirilmesi

Endüstri

10. Hızlı tanı yöntemlerinin geliştirilmesi

Klinik Kararlarda Bilgisayar Desteği

4. Tanıda yardım

Öykü,
Fizik muayene,
Laboratuvar sonuçları
Olası tanı ve sorunları

Geniş bir veri tabanı üzerinde mümkündür.

Evans RS, Pestotnik SL, Classen DC, et al. A computer assisted management program for antibiotics and other antiinfective agents. N Engl J Med 1998; 338: 232-238.

Bilgisayarlı Antimikrobiyal Karar Desteği

- Yerel, klinisyen ürünü uzlaşı rehberleri bilgisayar destekli karar destek programlarına yerleştirilir (SLC/LDS hastanesi)
- 7 yılda antimikrobiyal alan 62 759 hasta

	1988	1994
Medicare case-mix endeksi	1.7481	2.0520
Hastane mortalitesi	3.65%	2.65%
Hasta başına antimikrobiyal maliyeti	$122.66	$51.90
Uygun zamanlı preoperatif antimikrobiyal	40%	99.1%

- Antimikrobiyal direnç kontrol altında
- Ters ilaç etkileri %30 azalmış

Pestotnik SL, Classen DC, Evans RS, et al. Implementing antibiotic practice guidelines through computer-assisted decision support. Clinical and financial outcomes. Ann Intern Med 1996; 124: 884-890.

En sık görülen yanlış antibiyotik kullanımı nedenleri

HEKİM İSTEMLERİ	
1. Gereksiz antibiyotik	83/306 (27%)
2. Mikrobiyoloji sonuçlarının yanlış yorumu	47/306 (15%)
3. Spektrum çakışması (overlapping)	36/306 (12%)
4. Fazla geniş spektrum	20/306 (7%)
BİLGİSAYAR	
1. Radyolojinin yanlış yorumu	58/254 (23%)
2. Mikrobiyoloji sonuçlarının yanlış yorumu	43/254 (17%)
3. Spektrum çakışması (overlapping)	20/254 (8%)
4. Yeterince geniş değil	18/254 (7%)

Ergonul O, Tettelbach W, et al. Preliminary evaluation of antiinfective agent orders supported by computer assistance. SHEA, April 2002, Salt Lake City.

Tettelbach W, Ergonul O, et al. Evaluation of antibiotic orders supported by computer assistance. ICAAC, September 2002, San Diego.

Logistic regression

Number of obs	= 300
LR chi2(5)	= 30.43
Prob > chi2	= 0.0000
Log likelihood = -192.06229	Pseudo R2 = 0.0734

uygundegil	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
notropeni	.1583027	.1740409	-1.68	0.094	.0183511	1.365572
ates	.6925483	.1940702	-1.31	0.190	.3998721	1.199441
preempt	.5513206	.3006638	-1.09	0.275	.1893214	1.605494
emp	.4380455	.1338906	-2.70	0.007	.2406277	.7974304
px	1.797085	.5314376	1.98	0.047	1.006583	3.208394

Hasta Kaydı

Komorbiditeler :

- [ ] Kalp Hastalığı
- [ ] DM
- [ ] Böbrek Yetmezliği
- [ ] SVO
- [ ] Pulmoner Yetmezlik
- [ ] Karaciğer Yemezliği
- [ ] KOAH
- [ ] Malinite

Alet Kullanımı :

- [ ] Damar İçi Kateter
- [ ] Mekanik Ventilatör
- [ ] İdrar Sondası
- [ ] SVK

Ameliyat Bilgileri

Ameliyat Adı	Bölüm	Cerrah	
İNSİZYONEL HERNİ ONARIMI	GENEL CERRAHİ POLİKLİNİĞİ	ALİ EMRE	○
RETROPERİTONEAL TÜMÖRDEN BİYOPSİ, BÖBREK VE ADRENAL BEZ DIŞI	GENEL CERRAHİ POLİKLİNİĞİ	ALİ EMRE	○

Toplam 2 adet kayıt mevcut. << 1 sayfanın 1. sayfası >>

Durum :

- ○ Temiz
- ○ Temiz-Kontamine
- ○ Kontamine
- ○ Kirli

Enfeksiyon Belirtisi :

- ○ Kızarıklık
- ○ Akıntı
- ○ Şişlik
- ○ Isı

Cerrahi Enfeksiyon :

- ○ Var
- ○ Yok

Enfeksiyon Varsa :

- ○ Yüzeysel
- ○ Derin

Tedavi Amaçlı Antibiyotik :

- ○ Evet

ABİS vs Antibiyografi

ABİS

- Hasta bazında
- Detaylı bilgi

- Otomatize değil
- Değerlendirmesi zor

- Ayrıntılı bilgi ile sorun saptanabilir.

Antibiyografi

- Genel bilgi ve genel gidiş

- Otomatize
- Değerlendirmesi kolay

- Sorun hakkınd kabaca fikir verebilir

Antibiyografi

Yatan hastalardan antibiyotik kullananların yatan hastaların toplamına oranı;

ab kullanan/yatan hasta

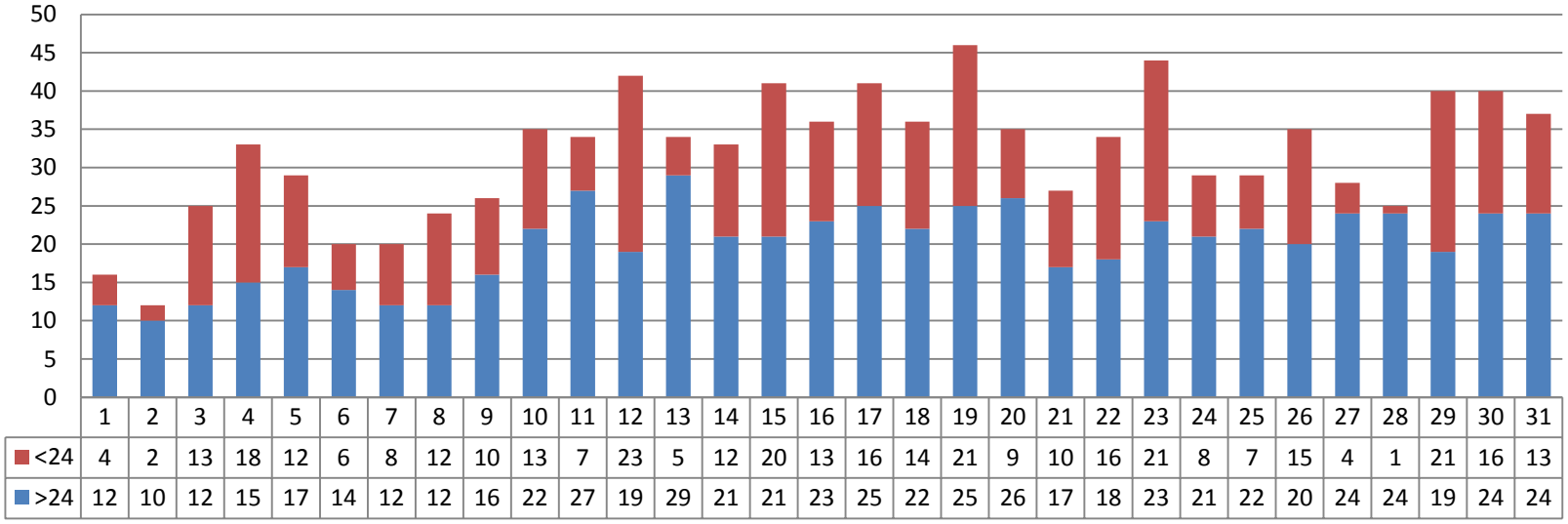
Antibiyotik kullanan yatan hastalardan kısıtlı antibiyotik kullananların antibiyotik kullananlara oranı;

KAK/ab kullanan

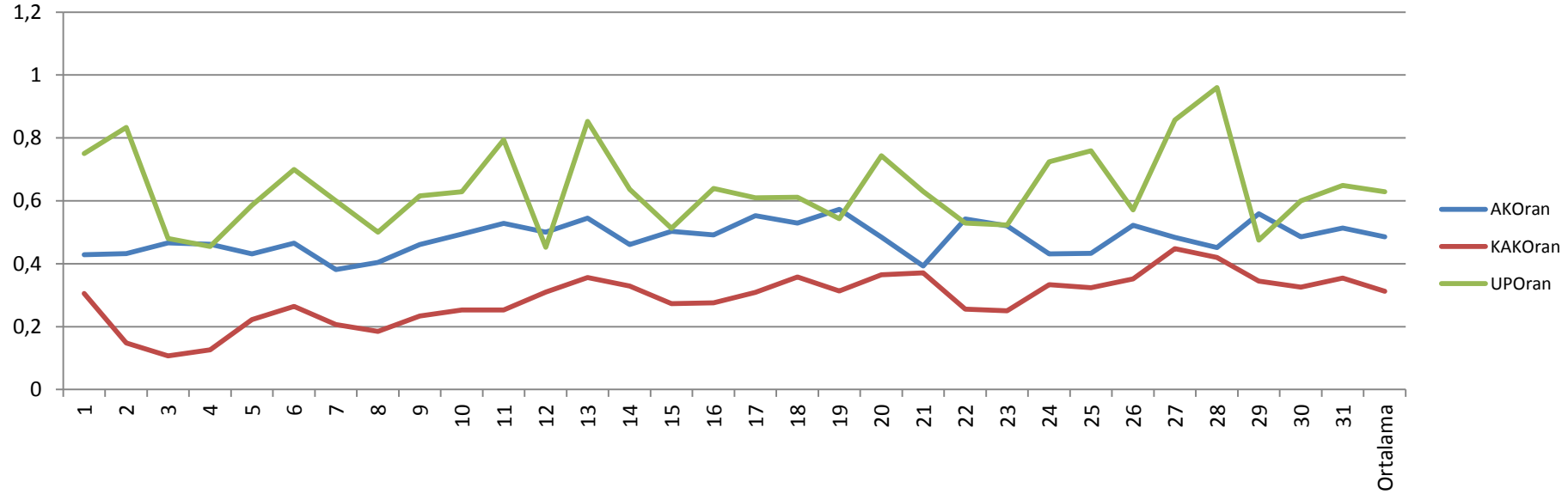
Cerrahi işlem sonrası >24 saattir profilaksi amaçlı antibiyotik uygulananların cerrahi işlem sonrası profilaksi uygulananlara oranını ifade eder.

px>24sa/ameliyat olanlar

Ocak 2013 Antibiyografi



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
<24	4	2	13	18	12	6	8	12	10	13	7	23	5	12	20	13	16	14	21	9	10	16	21	8	7	15	4	1	21	16	13
>24	12	10	12	15	17	14	12	12	16	22	27	19	29	21	21	23	25	22	25	26	17	18	23	21	22	20	24	24	19	24	24



Antibiyografi Sonuçlarına bir örnek:

ab kullanan/yatan hasta : %48

KAK/ab kullanan : %31

px>24sa/ameliyat olanlar : %63