



ESBL-E.coli-Ergebnisse aus Forschungsprojekten:
ESBL-bildende Bakterien –
eine Herausforderung für die Krankenhaushygiene

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Epidemiologie von ESBL-E.coli im Krankenhaus



ANTIBIOTIC RESISTANCE THREATS in the United States, 2013



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

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

EXTENDED SPECTRUM β-LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE

THREAT LEVEL
SERIOUS



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



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



CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

THREAT LEVEL
URGENT



This bacteria is an immediate public health threat that requires urgent and aggressive action.



9,000

DRUG-RESISTANT
INFECTIONS
PER YEAR



600

DEATHS

CARBAPENEM-
RESISTANT
KLEBSIELLA SPP.

7,900



1,400

CARBAPENEM-
RESISTANT
E. COLI



**CRE HAVE BECOME RESISTANT TO ALL
OR NEARLY ALL AVAILABLE ANTIBIOTICS**



Nosokomiale Infektionen und Antibiotika-Anwendung

Zweite nationale Prävalenzstudie in Deutschland

Michael Behnke, Sonja Hansen, Rasmus Leistner, Luis Alberto Peña Diaz, Alexander Gropmann, Dorit Sohr, Petra Gastmeier, Brar Piering

Behnke et al.
Dt. Ärztebl. 2013

TABELLE 1

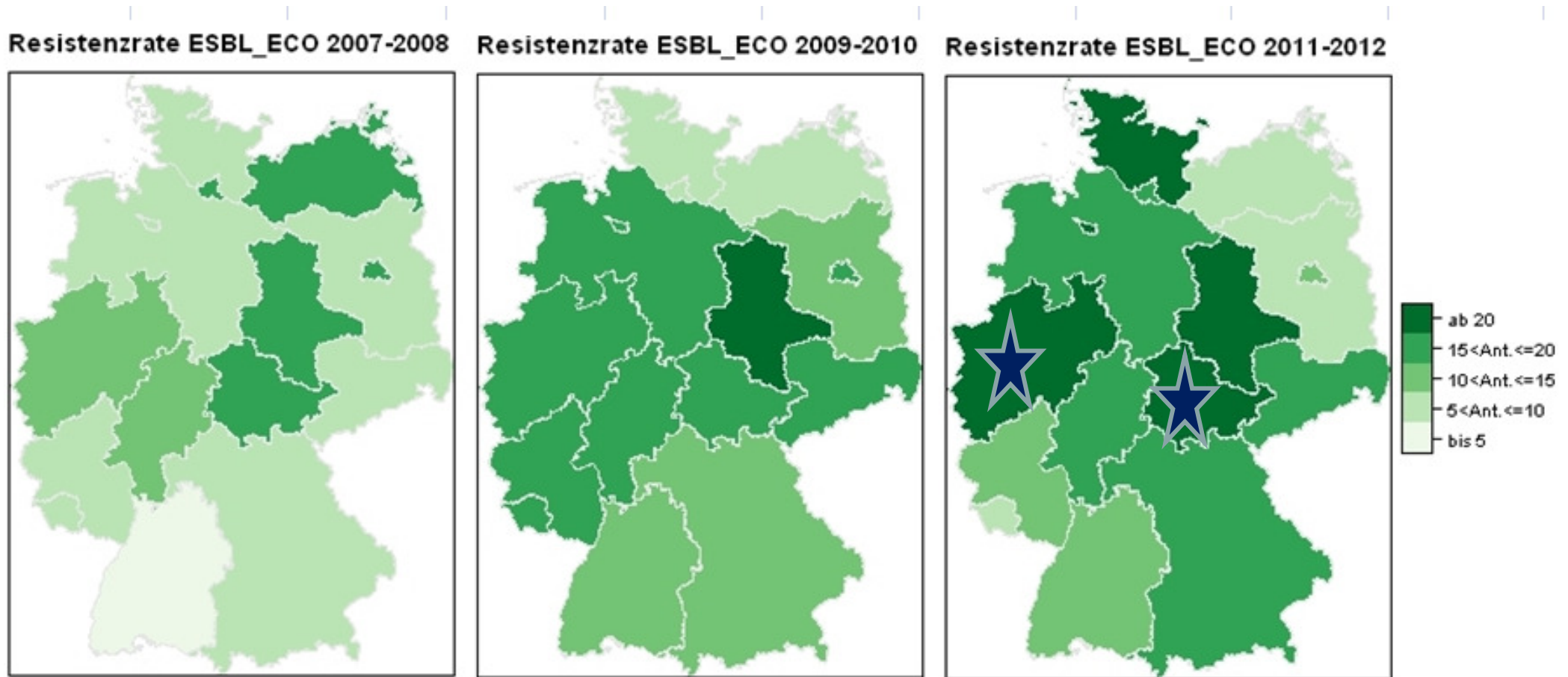
Prävalenz aller Patienten mit nosokomialen Infektionen und der Patienten mit während des aktuellen Krankenhausaufenthaltes erworbenen nosokomialen Infektionen*

Parameter	Gesamtmenge der teilnehmenden Krankenhäuser	repräsentative Stichprobe	NIDEP 1 1994
Anzahl Krankenhäuser	132	46	72
Median der Bettenzahl	359	216	< 400
Patienten	41 539	9 626	14 966
Prävalenz aller Patienten mit nosokomialen Infektionen	5,08 % 95-%-KI: 4,72–5,44	5,07 % 95-%-KI: 4,51–5,67	–
Prävalenz der Patienten mit während des aktuellen Krankenhausaufenthaltes erworbenen nosokomialen Infektionen	3,76 % 95-%-KI: 3,50–4,02	3,37 % 95-%-KI: 2,95–3,82	3,46 % 95-%-KI: 3,1–3,9
Prävalenz der Antibiotikaaanwendung	25,54 % 95-%-KI: 24,49–26,60	23,33 % 95-%-KI: 21,25–25,48	17,7 %

Schätzung zu den absoluten Anzahlen der nosokomialen Infektionen mit wichtigen MRE in Deutschland 2012

Erreger	Anzahl Infektionen	Key resistance	Anzahl Infektionen	Trend
<i>S.aureus</i>	65 000	MRSA	14 000	↓
<i>E.faecium</i>	30 000	VR <i>E.faecium</i>	5 500	↑
<i>E.coli</i>	90 000	ESBL <i>E.coli</i>	9 500	↑↑
<i>K.pneumoniae</i>	18 000	ESBL <i>K.pneumoniae</i>	2 000	↑
Summe	203 000		31 000	
				—

Percentage of ESBL E.coli/E.coli (%) 2007-2012 according to federal states

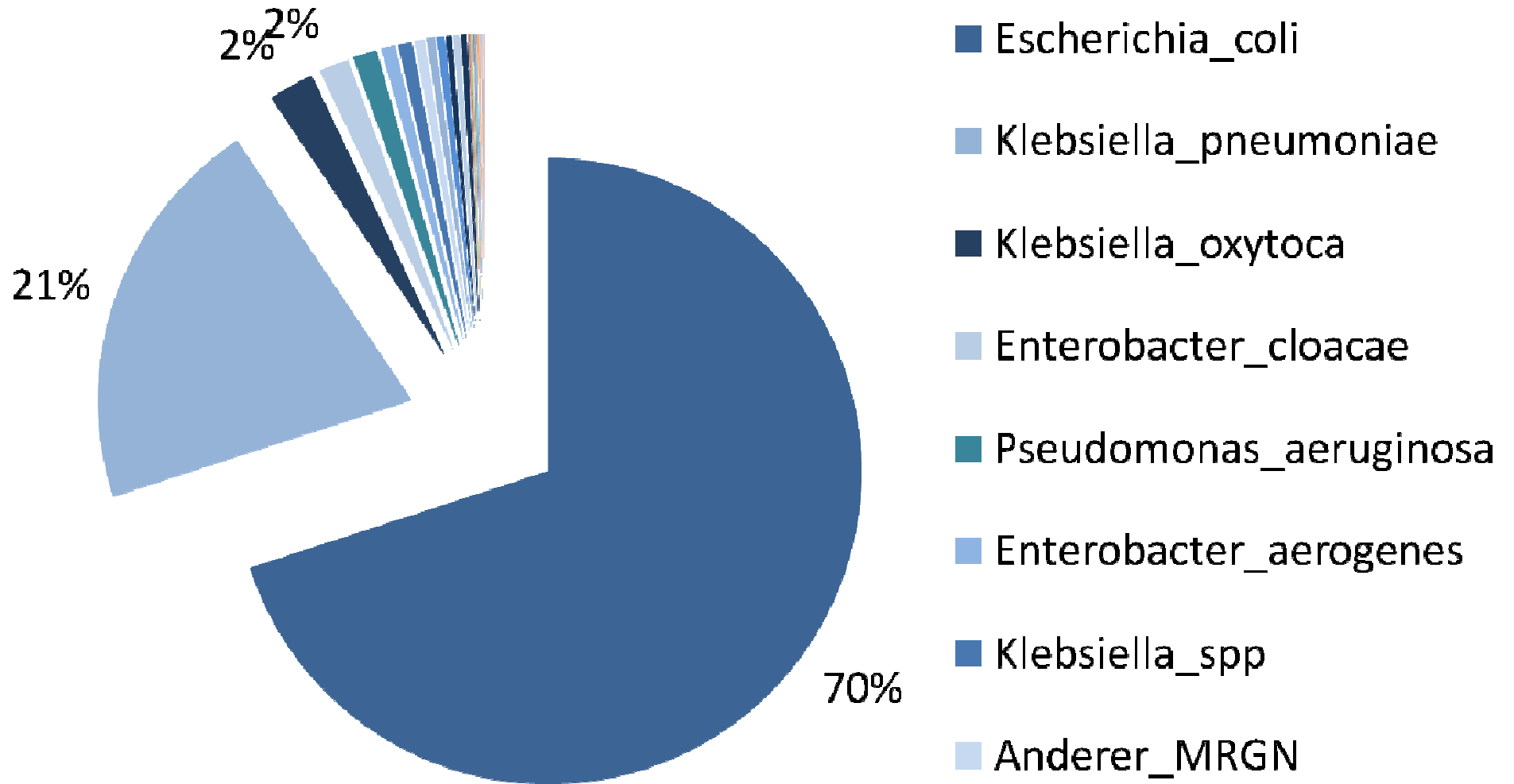


★ Significant higher percentage

ITS
KISS

OP
KISS

ESBL-Bildner



Die meisten Patienten bringen die ESBL bereits ins Krankenhaus mit ...

OPEN ACCESS Freely available online

 PLOS ONE

Risk Factors Associated with the Community-Acquired Colonization of Extended-Spectrum Beta-Lactamase (ESBL) Positive *Escherichia Coli*. An Exploratory Case-Control Study

Rasmus Leistner^{1,2*}, Elisabeth Meyer^{1,2}, Petra Gastmeier^{1,2}, Yvonne Pfeifer³, Christoph Eller³, Petra Dem^{1,2}, Frank Schwab^{1,2}

¹Institute of Hygiene and Environmental Medicine, Charité University Medicine Berlin, Berlin, Germany, ²German National Reference Center for the Surveillance of Nosocomial Infections, Berlin, Germany, ³Robert Koch Institute, Wernigerode, Germany

Leistner et al. PLOSone 2013; Sept. (Im Rahmen von RESET)

Recruitment diagram

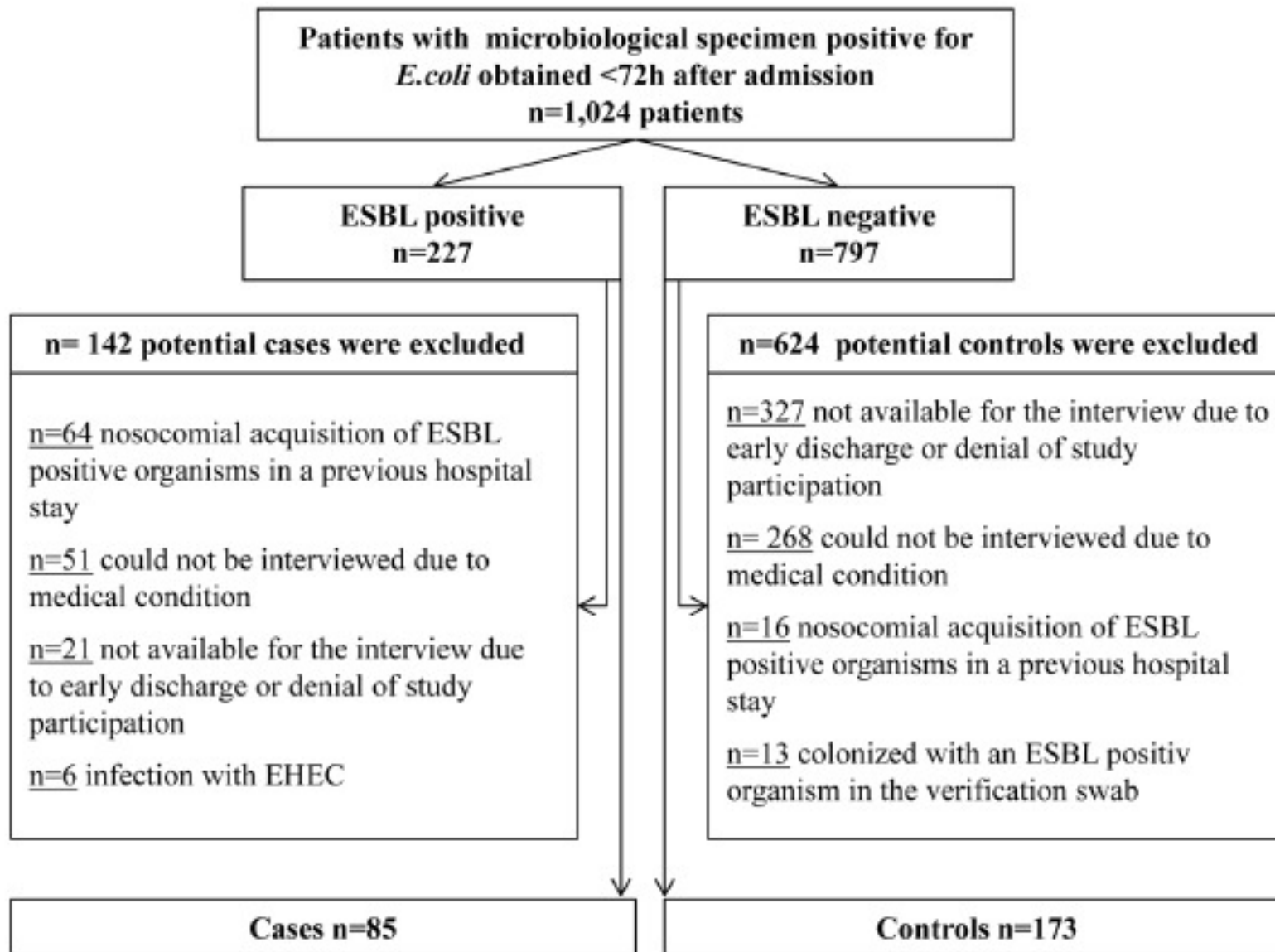


Figure 1. Recruitment diagram of cases and controls. EHEC, enterohemorrhagic *E. coli*. ESBL, extended-spectrum beta-lactamase. doi:10.1371/journal.pone.0074323.g001

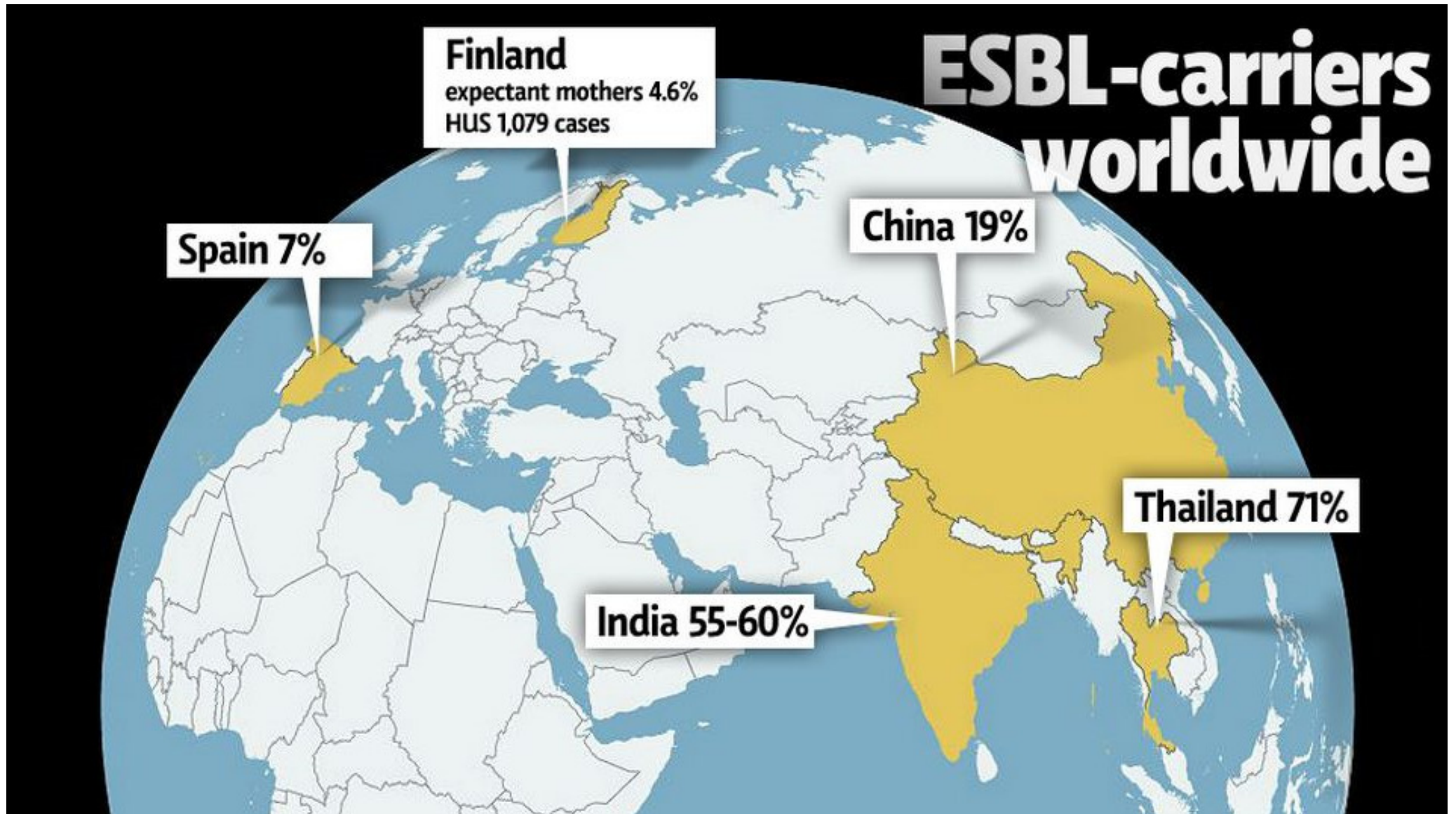
Table 4. Results of the multivariable conditional logistic regression analysis of risk factors for colonization with ESBL-positive *E. coli*.

Associated factor	Odds Ratio	95% CI	P-value
Asian mother tongue	13.4	3.3–53.8	<0.001
Frequent consumption of pork	3.5	1.8–6.6	<0.001

[doi:10.1371/journal.pone.0074323.t004](https://doi.org/10.1371/journal.pone.0074323.t004)

Leistner et al. PLOSone 2013; Sept.

RISK FACTOR TRAVELING



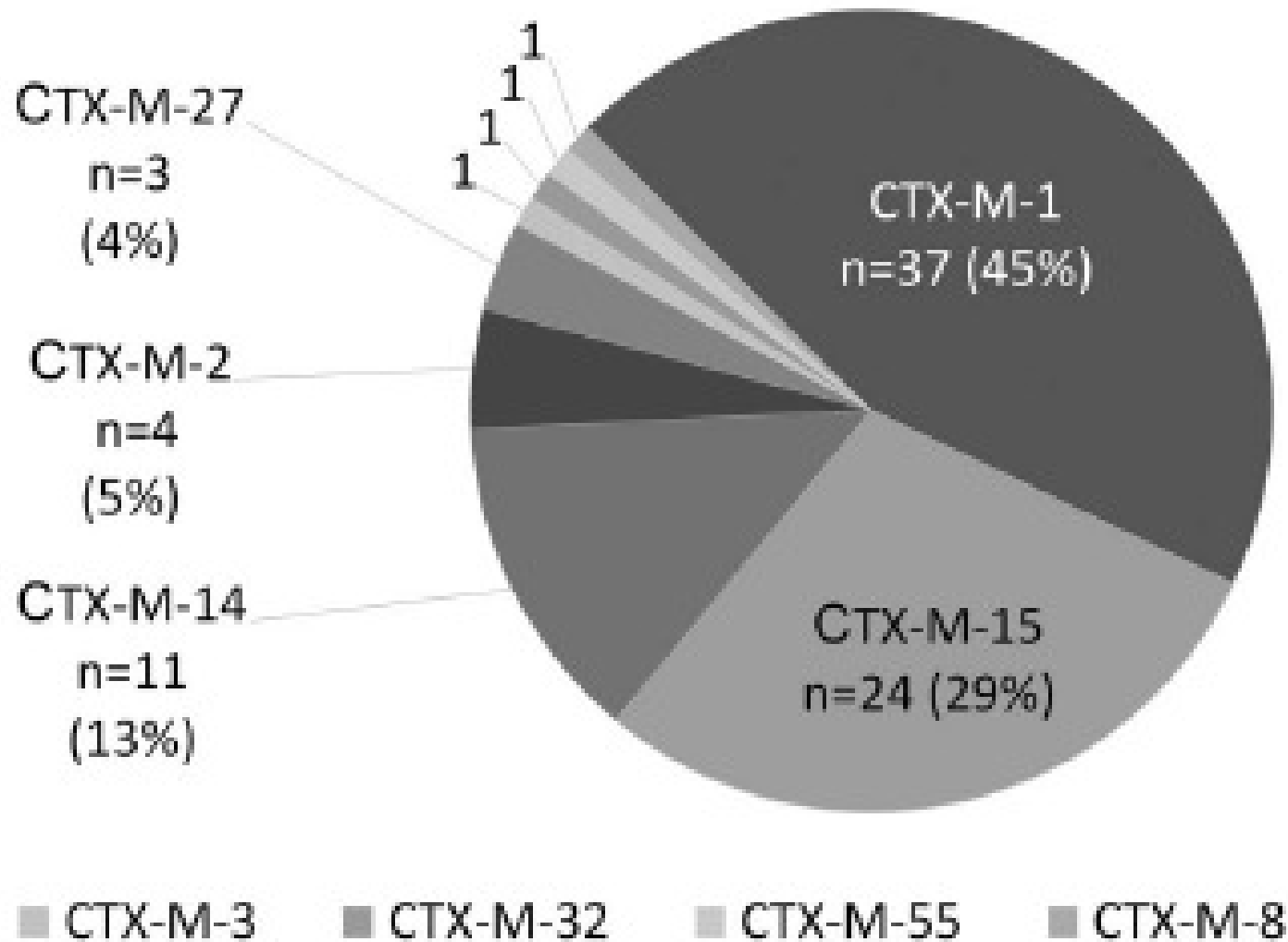


Figure 2. Distribution of CTX-M-genotypes in n = 83 CTX-M-positive community-acquired ESBL *E. coli* isolates.

doi:10.1371/journal.pone.0074323.g002

Risk Factors for Community-Acquired Urinary Tract Infections Caused by ESBL-Producing *Enterobacteriaceae* –A Case–Control Study in a Low Prevalence Country

Arne Søråas^{1*}, Arnfinn Sundsfjord^{2,3}, Irene Sandven⁴, Cathrine Brunborg⁴, Pål A. Jenum¹

¹ Department of Medical Microbiology, Vestre Viken Hospital Trust, Bærum, Norway, ² Department of Microbiology and Infection Control, Reference Centre for Detection of Antimicrobial Resistance, University Hospital of North Norway, Tromsø, Norway, ³ Department of Medical Biology, Research Group for Host-Microbe Interactions, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway, ⁴ Unit of Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway

Soraas et al. PLOSone 2013; July

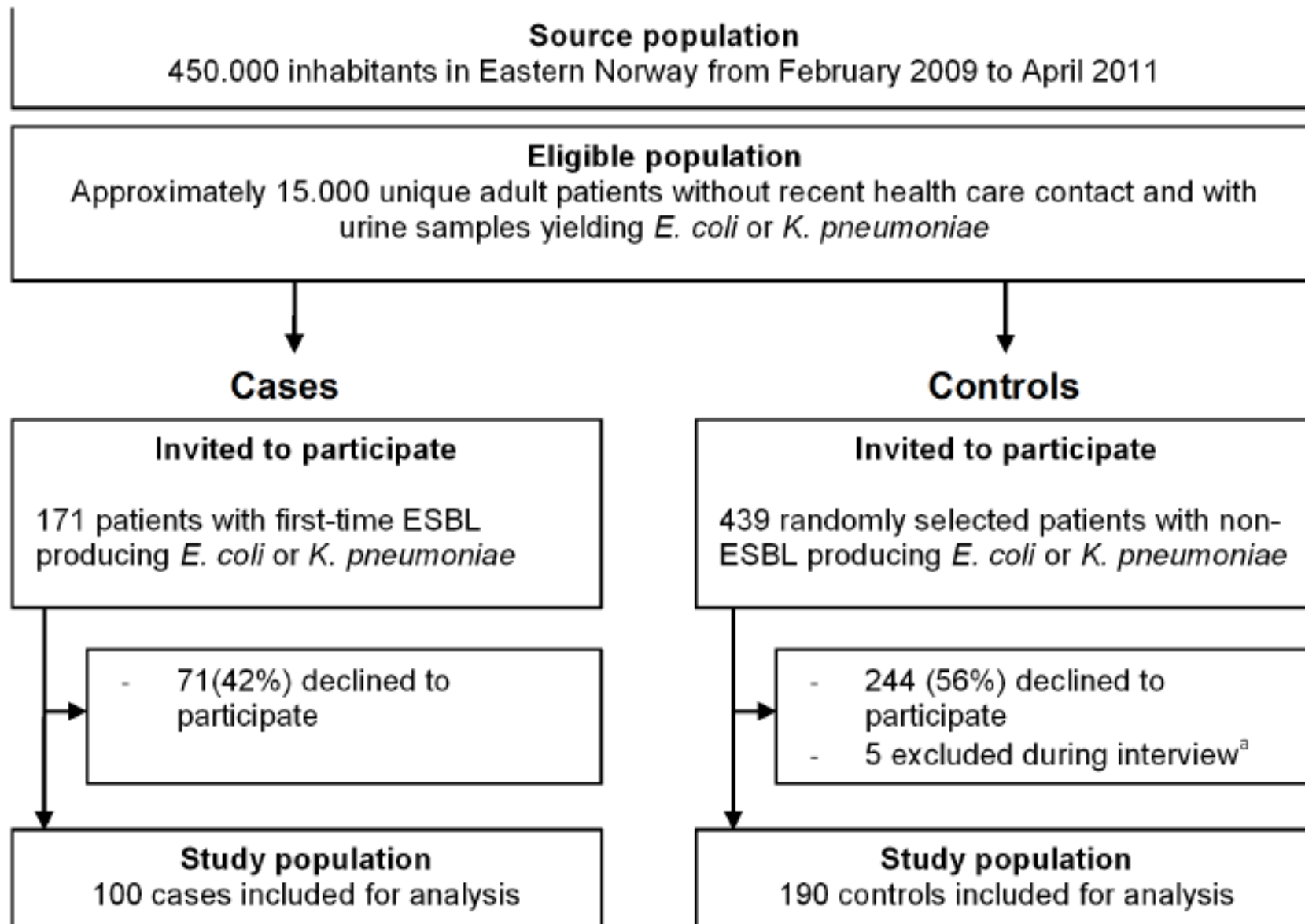


Figure 1. Selection of study population. ^aDementia (n=1), unable to reach by phone (n=2) and death (n=2).
doi:10.1371/journal.pone.0069581.g001

Table 4. Independent risk factors of ESBL positive community acquired urinary tract infection identified using multivariate logistic regression analysis.

Variable	Level	Adjusted OR	95% CI	P
Travelling to Asia, Middle East or Africa ^a				
- During the past 6 weeks	yes/no	21	4.5–97	<0.001
- Between the previous 6 weeks to 24 months	yes/no	2.3	1.2–4.4	0.017
Use of fluoroquinolones the past 90 days	yes/no	16	3.2–80	<0.001
Use of β -lactams except mecillinam in the past 90 days	yes/no	5.0	2.1–12	<0.001
Diabetes mellitus	yes/no	3.2	1.0–11	0.051
Recreational freshwater swim past year	yes/no	2.1	1.0–4.3	0.040
Age	5 year increase	0.89	0.82–0.97	0.014
Number of fish meals per week	1 meal increase	0.68	0.51–0.90	0.008

^aOnly trips lasting >24 hours are included.
doi:10.1371/journal.pone.0069581.t004

Soraas et al. PLOSone 2013; July

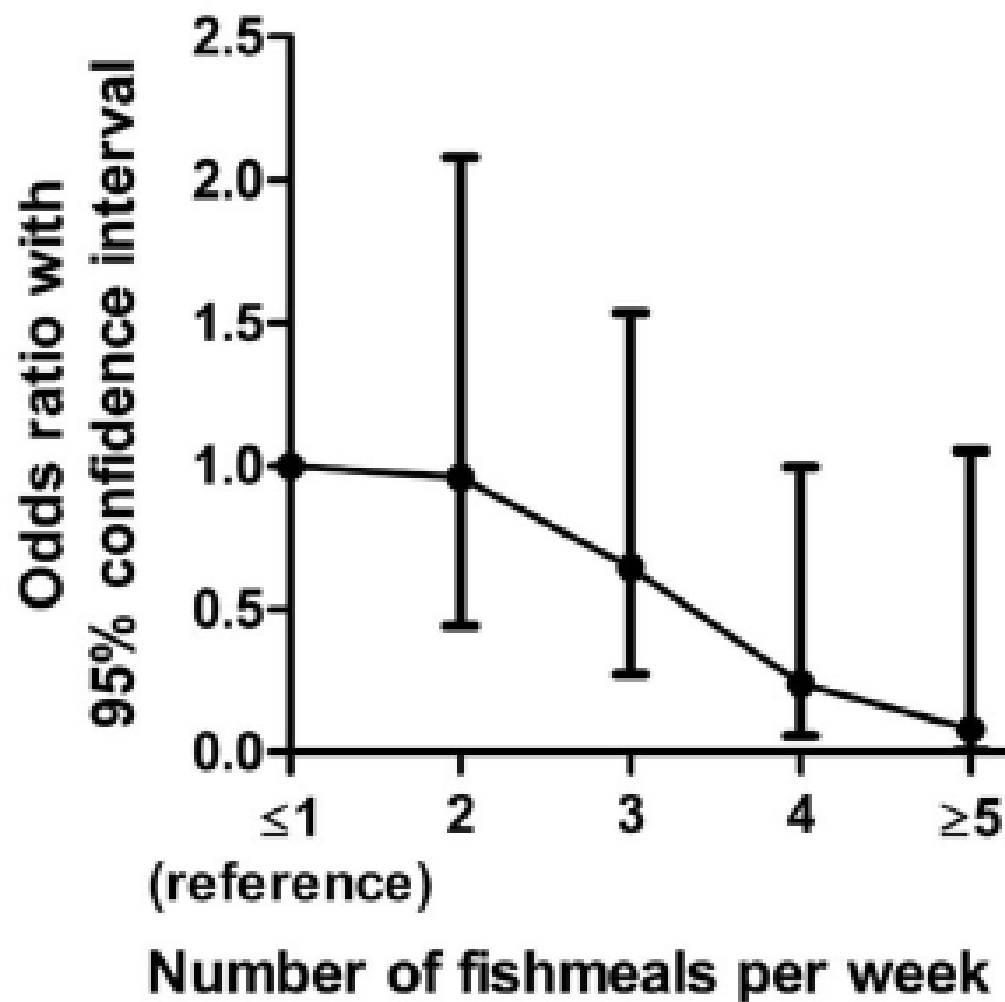


Figure 2. Decreasing risk^a of ESBL-positive urinary tract infection with increasing number of fishmeals per week^b.

^aControlling for the variables: Travelling to Asia, Middle east or Africa, Use of fluoroquinolones the past 90 days, Use of β -lactams except mecillinam the past 90 days, Diabetes mellitus, Recreational freshwater swim past year and age. ^bReference category: eating ≤ 1 fishmeal per week.

doi:10.1371/journal.pone.0069581.g002

Soraas et al.
PLOSone 2013;
July

ST 131 in Switzerland

- Fecal swabs were obtained from 291 primary care patients
- ESBL Enterobacteriaceae were detected in 15 (5.2%) of primary care patients.
- The pathogenic pandemic clone Escherichia coli ST131 was detected in 26.6% of the patients.

ST 131 in Denmark

- 115 ESBL -producing E.coli clinical isolates
- 38% of the ESBL isolates represented sequence type 131

Nüesch-Inderbinnen et al. Micro Drug Resist 2013; Epub
Olesen et al. J Clin Microbiol. 2013; 51:1779-85

Spezifische Problematik der ESBL- Enterobacteriaceae als Erreger von Krankenhausinfektionen



SHORT REPORT

Open Access

Carriage of extended-spectrum beta-lactamase-producing enterobacteriaceae among internal medicine patients in Switzerland

Janet Pasricha^{1,6}, Thibaud Koessler², Stephan Harbarth^{1*}, Jacques Schrenzel³, Véronique Camus¹, Gilles Cohen⁴, Arnaud Perrier², Didier Pittet^{1,5} and Anne Iten^{1,2}

	Patients screened	ESBL E.coli %
Admission screening	1072	51 (4.8%)
Admission and discharge screening	473	21 (4.4%)

Duration of colonization by ESBL-producing Enterobacteriaceae after hospital discharge



ELSEVIER

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org



Major article

Duration of colonization by extended-spectrum β -lactamase-producing *Enterobacteriaceae* after hospital discharge

Gabriel Birgand PharmD, MPH^{a,*}, Laurence Armand-Lefevre PharmD, PhD^{b,c}, Isabelle Lolom BS^a, Etienne Ruppe PharmD^{b,c}, Antoine Andreumont MD, PhD^{b,c}, Jean-Christophe Lucet MD, PhD^a

^a Infection Control Unit, Bichat-Claude Bernard Hospital, Paris, France

^b Bacteriology Laboratory, Bichat-Claude Bernard Hospital, Paris, France

^c EA 3964 University of Paris 7-Denis Diderot, Paris, France

Birgand G et al. Am J Infect Control. 2013 May;41(5):443-7.

Duration of colonization by ESBL-producing Enterobacteriaceae after hospital discharge.

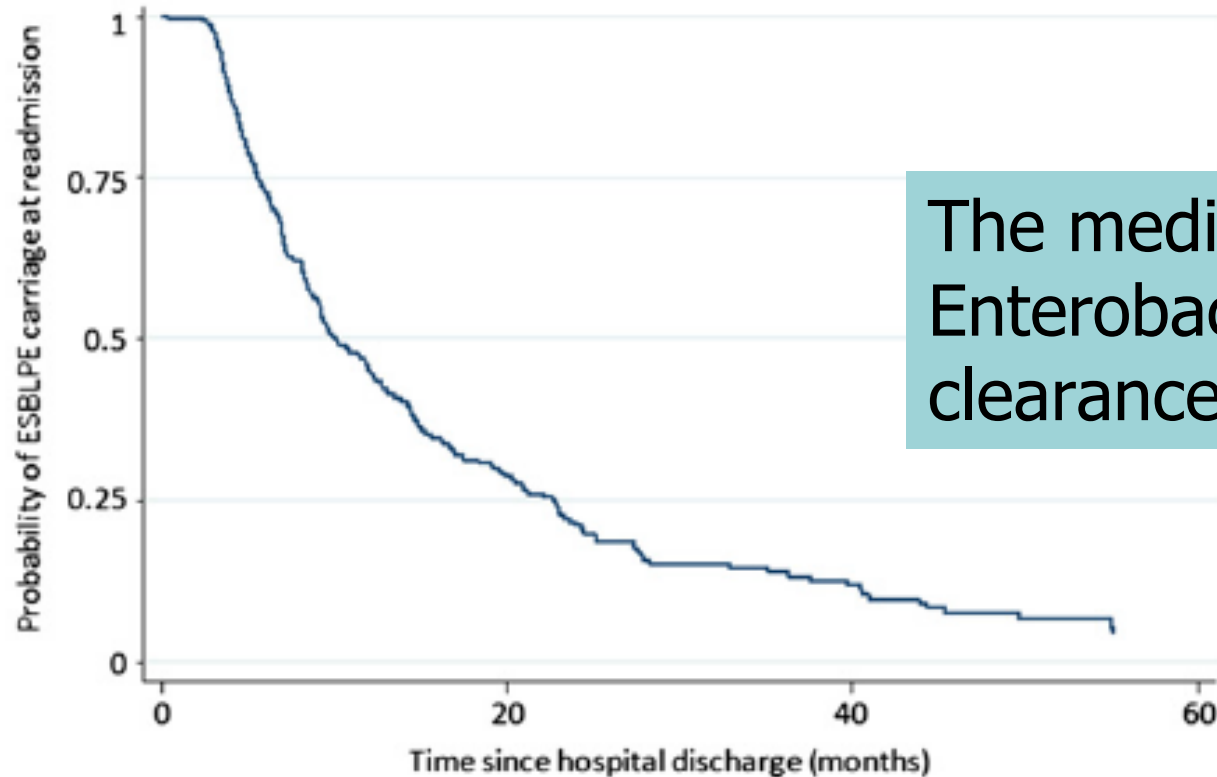


Fig 2. Kaplan-Meier estimate of time to clearance of extended-spectrum β -lactamase-producing *Enterobacteriaceae* (ESBLPE) in patients readmitted between January 1997 and December 2010 to the Bichat-Claude Bernard Hospital.

Birgand G et al. Am J Infect Control. 2013 May;41(5):443-7.

ESBL Decolonisation

Intervention: Colistin Sulfat (50mg 4x/d for 10 days) +
Neomycin Sulfat (250mg 4x/d for 10 days) +
Nitrofurantoin (100mg 3x/d for 5 days) for UTI

Design: RCT

Setting: Single centre

Endpoint: ESBL elimination

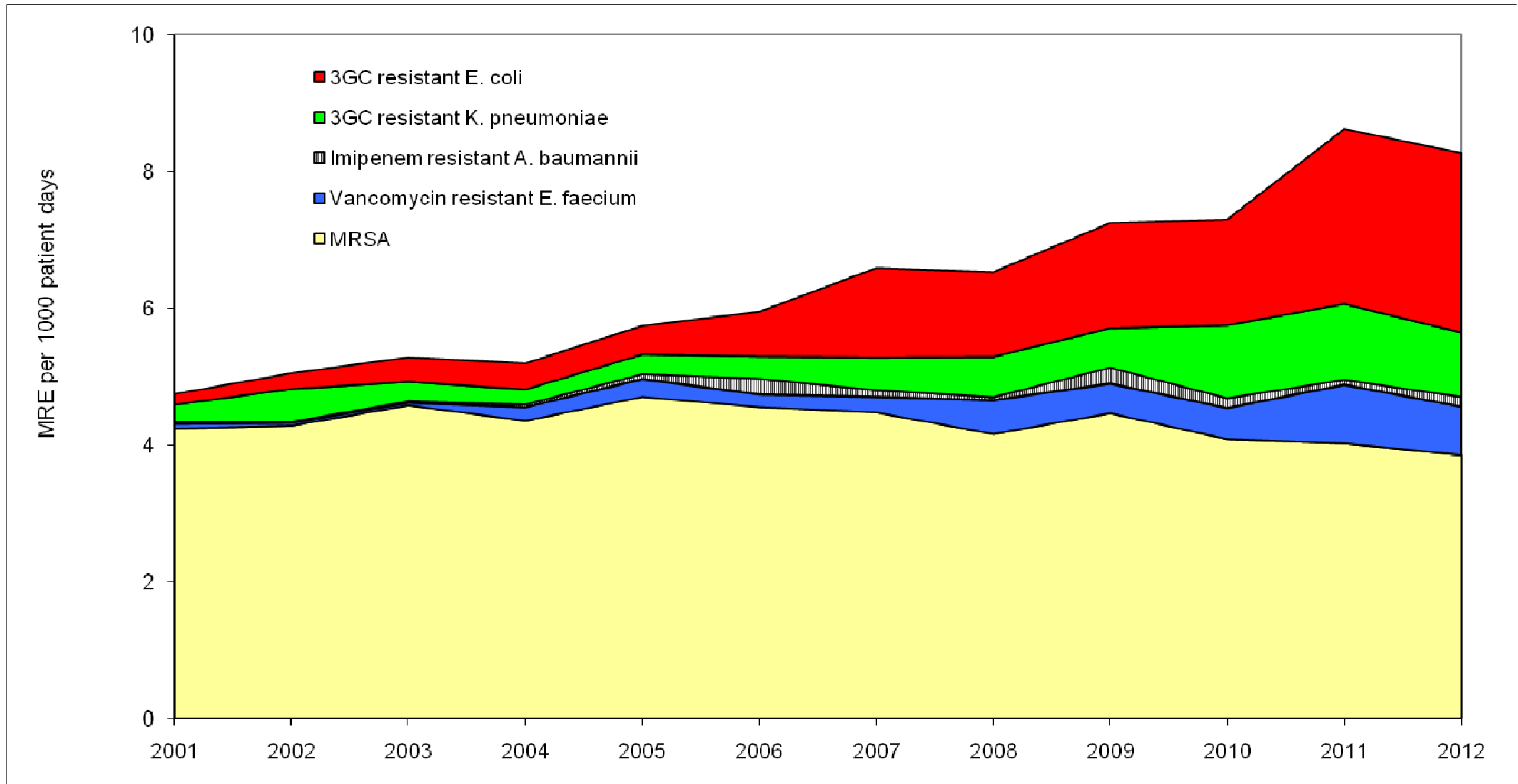
Outcome: ESBL carrierstatus	Intervention n=27	Placebo n=27	P value
Day 6 of therapy	9/26	19/22	<0,001
Day 1 after therapy	8/25	20/26	0,001
Day 7 after therapy	18/27	17/25	0,92
Day 28 after therapy	14/27	10/27	0,27

Schlechteres Outcome von ESBL-Patienten?

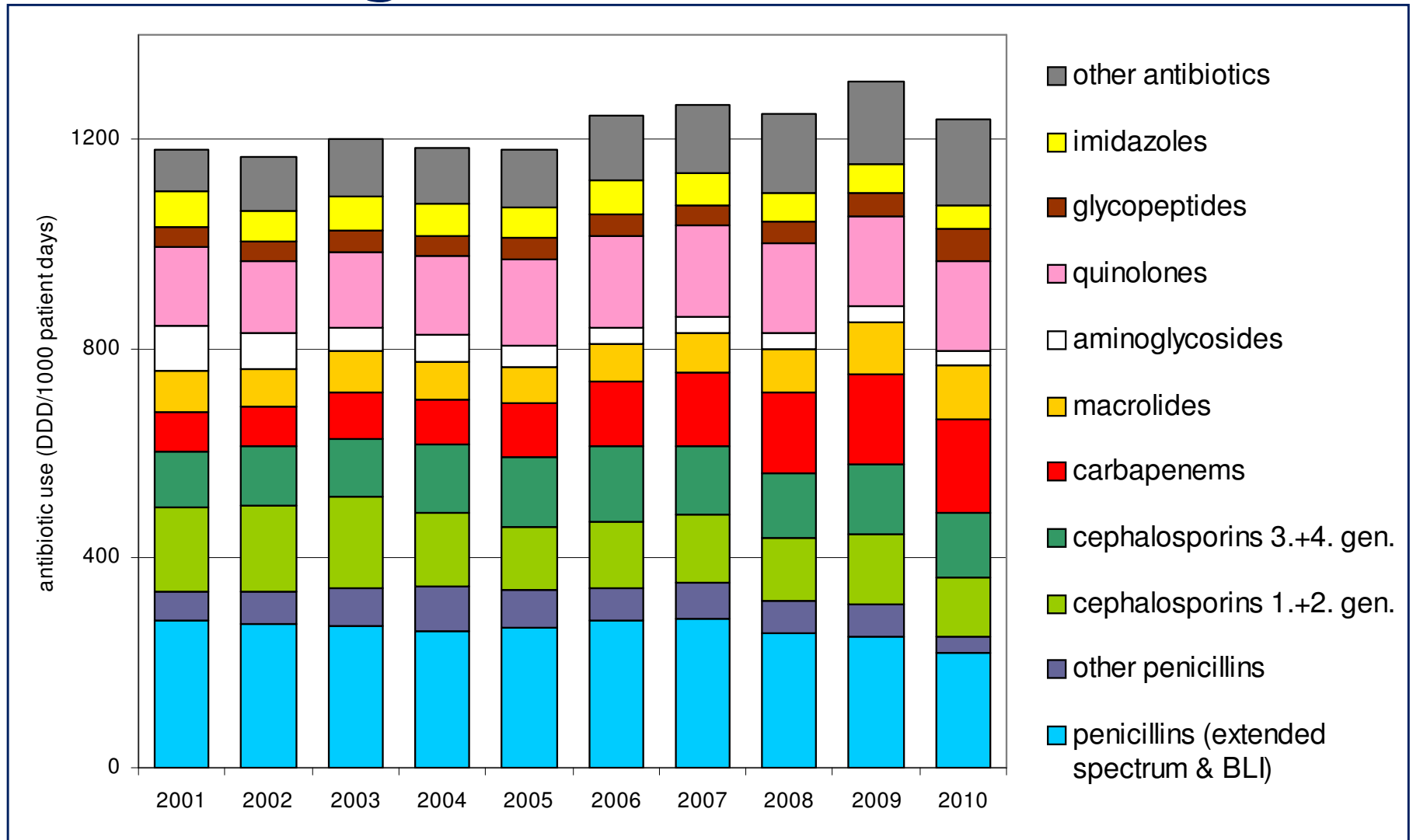
Author	Study Design	Study Country (study period)	Organism	Cases/ Controls	Mortality ESBL (+) vs. ESBL (-)
Leistner et al. 2013 Submitted*	Matched Case control study	Germany (2008-2010)	<i>E. coli</i>	92/92	20% vs. 20%, p=1.00
Stewardson et al. 2013	Multistate modeling	Switzerland (2009)	Enterobacteriaceae	30/96	20% vs. 10%, p=0.17

* Im Rahmen von RESET

Trend in Germany: SARI Intensive care units

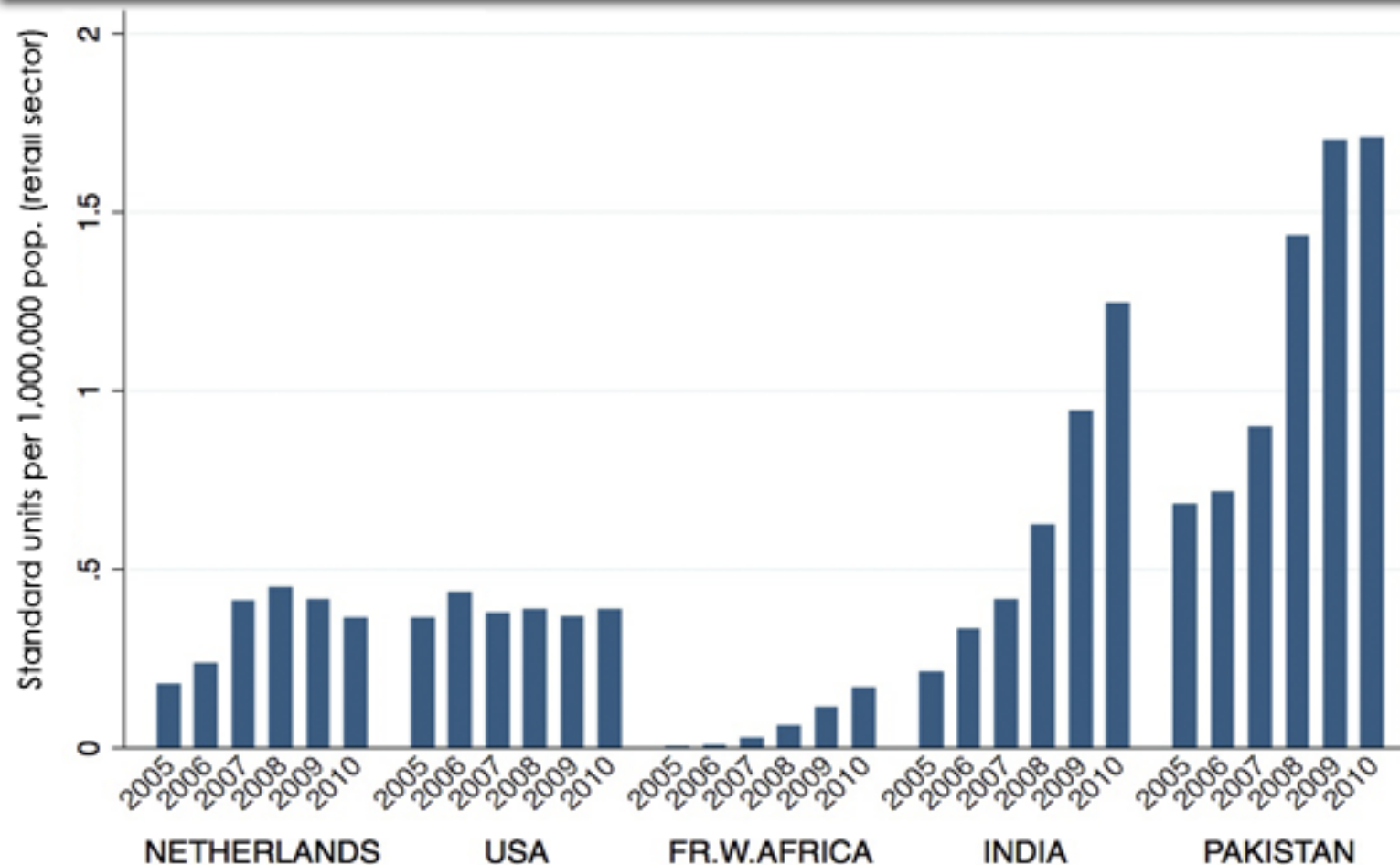


Entwicklung der Antibiotika- Anwendung in SARI-Intensivstationen



Courtesy: Meyer /Schwab

Retail sales of carbapenem antibiotics to treat Gram-negative bacteria are increasing rapidly in India and Pakistan



Source: Based on data obtained under license from IMS Health MIDASTM (January 2005 - December 2010). IMS Health Incorporated. All Rights Reserved.



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42

Mobile telephones more common than toilets in India, UN report finds



14 April 2010 – More people in India, the world's second most crowded country, have access to a mobile telephone than to a toilet, according to a set of recommendations released today by United Nations University (**UNU**) on how to cut the number of people with inadequate sanitation.

"It is a tragic irony to think that in India, a country now wealthy enough that roughly half of the people own phones, about half cannot afford the basic necessity and

KPC 3 outbreak in Berlin im February 2013

Wedding

Keim-Alarm auf Intensivstation der Charité

von Ingo Bach

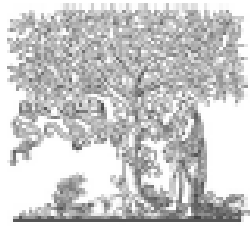


Erneut sorgen Keime für Aufregung bei der Charité. - FOTO: DPA

Auf einer Intensivstation des Virchow-Klinikums in Wedding haben sich in den vergangenen Monaten elf Patienten mit einem Keim namens Klebsiella Pneumoniae infiziert oder waren mit dem Bakterium besiedelt. Zwei Patienten sind inzwischen gestorben, jedoch an ihren Grunderkrankungen.



Erneut versetzt der Ausbruch von antibiotikaresistenten Krankheitserregern in der Charité die Ärzte in Unruhe. Auf einer Intensivstation des zur Charité gehörenden Virchow-Klinikums in Wedding haben sich in den vergangenen Monaten insgesamt elf Patienten mit einem Keim namens Klebsiella Pneumoniae (Klebsiellen) infiziert oder waren mit dem Bakterium symptomfrei besiedelt. Zwei Patienten sind inzwischen gestorben: einer bereits im vergangenen September, eine Frau vor gut zwei Wochen. Beide seien jedoch ihren schweren Grunderkrankungen erlegen, nicht der Klebsiellen-Infektion, sagte Ulrich Frei, der Ärztliche Direktor der Charité, am gestrigen Dienstag.



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: <http://www.elsevier.com/locate/ijantimicag>

Short Communication

Rapid emergence of secondary resistance to gentamicin and colistin following selective digestive decontamination in patients with KPC-2-producing *Klebsiella pneumoniae*: a single-centre experience

Christoph Lübbert^{a,*}, Sarah Fauchoux^b, Diana Becker-Rux^c, Sven Laudi^c, Axel Dürrbeck^d, Thilo Busch^c, Petra Gastmeier^e, Tim Eckmanns^f, Arne C. Rodloff^g, Udo X. Kaisers^c

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^b Hospital Hygiene Staff Unit, Leipzig University Hospital, Johannisallee 34, D-04103 Leipzig, Germany

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^d University Pharmacy, Leipzig University Hospital, Liebigstr. 20, D-04103 Leipzig, Germany

^e Institute of Hygiene and Environmental Medicine, Charité – University Medical Centre, Hindenburgdamm 27, D-12203 Berlin, Germany

^f Department for Infectious Disease Epidemiology, Robert Koch Institute, Nordufer 20, D-13353 Berlin, Germany

^g Institute for Medical Microbiology and Epidemiology of Infectious Diseases, Leipzig University Hospital, Liebigstr. 21, D-04103 Leipzig, Germany

The hospital mortality rate in patients receiving SDD was 36% (5/14).
Hospital mortality in KPC-2-positive patients without SDD was 45% (34/76).

Attributable mortality

Correa et al. *BMC Infectious Diseases* 2013, **13**:80
<http://www.biomedcentral.com/1471-2334/13/80>



RESEARCH ARTICLE

Open Access

A hospital-based matched case–control study to identify clinical outcome and risk factors associated with carbapenem-resistant *Klebsiella pneumoniae* infection

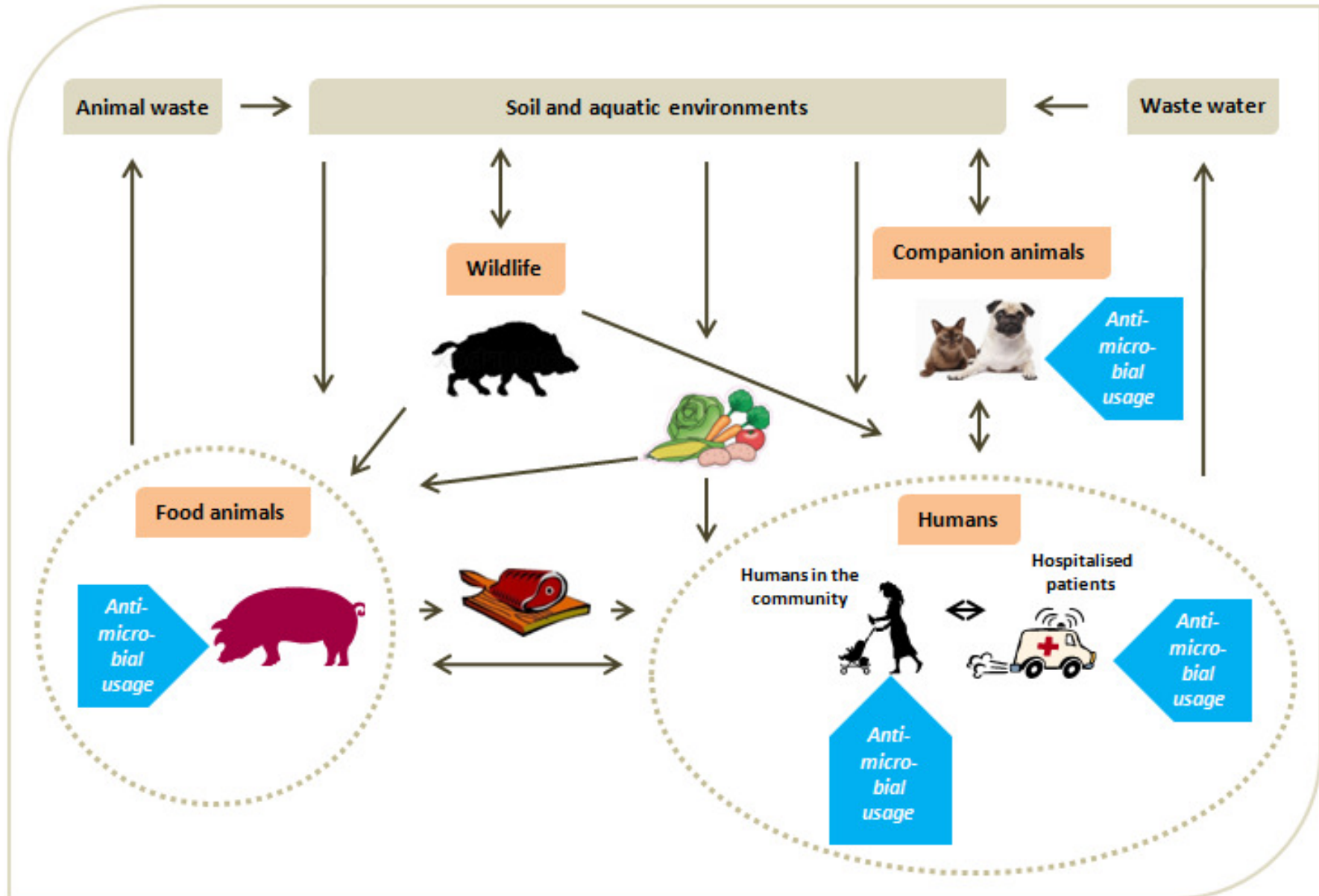
Luci Correa^{1,3*}, Marines Dalla Valle Martino², Itacy Siqueira², Jacyr Pasternak², Ana Cristina Gales³, Claudia Vallone Silva¹, Thiago Zinsly Sampaio Camargo⁴, Patricia Faria Scherer⁴ and Alexandre Rodrigues Marra⁴

20 cases:	mortality: 50,0 %
40 controls:	mortality: 25,7 %

Correa et al. *BMC Infectious Dis* 2013; 13:80

ONE HEALTH

Exchange of resistance genes and bacteria between different reservoirs



From: Yvonne Agersø, EFFORT-project

ONE WORLD



Die weltweite Reisetätigkeit gilt als ein wichtiger Risikofaktor zur Entstehung von Multiresistenzen.

Foto: Fotolia/Anton Balazh

Wir alle haben Anteil daran

Pharmaindustrie:

- Vorteil durch Antibiotikaverkauf für Mensch und Tier
- Vorteil durch den dringenden Bedarf an neuen Antibiotika

Bauern:

- Produktion von preiswertem Fleisch durch Antibiotikaaanwendung

Verbraucher:

- Wollen preiswertes Fleisch
- Wollen Antibiotika für schnelle Heilung bei Infektionen

Humanmediziner:

- Restriktiver Antibiotika-Gebrauch ist selten