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ARS – Antibiotikaresistenz-Surveillance in der Humanmedizin

Tim Eckmanns, Robert-Koch-Institut

BfR-Symposium
Antibiotikaresistenz
in der Lebensmittelkette
Berlin, 2. – 3. November 2015

International

COMMENT

ISSOUF SANOGO/AFP/GETTY

Unregulated sales of medicines in developing countries contribute to the rise in antimicrobial resistance.

An intergovernmental panel on antimicrobial resistance

Drug-resistant microbes are spreading. A coordinated, global effort is needed to keep drugs working and develop alternatives, say **Mark Woolhouse** and **Jeremy Farrar**.

Better surveillance is essential. But it will not provide solutions; many calls to action on antimicrobial resistance have been made over the past 20 years, but there has been too little progress. The WHO missed the opportunity to provide leadership on what is urgently needed to really make a difference.

We call for the creation of an organization similar to the Intergovernmental Panel on Climate Change (IPCC) to marshal evidence and catalyse policy across governments and stakeholders.

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The £10m Longitude Prize 2014

offered by the independent innovation charity Nesta and the government funded formerly Technology Strategy Board, now Innovate UK

6 categories for the world's most pressing scientific issue

- How people with dementia can live independently for longer
- How to ensure that everyone has access to safe and clean water
- How to ensure universal access to nutritious, sustainable food
- Whether air travel is possible without damage to the environment
- **How to overcome resistance to antibiotics**
- How to restore movement to people with paralysis

BMJ 2014; 348 doi: http://dx.doi.org/10.1136/bmj.g3417 (Published 20 May 2014)
BMJ 2014; 349 doi: http://dx.doi.org/10.1136/bmj.g4418 (Published 03 July 2014)

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G7 GERMANY
2015 | Schloss Elmau

Think Ahead. Act Together.
An morgen denken. Gemeinsam handeln.

Abschlusserklärung
G7-Gipfel, 7.–8. Juni 2015

Antibiotikaresistenzen

Antibiotika spielen für die heutigen und zukünftigen Erfolge in der Human- und Veterinärmedizin eine entscheidende Rolle. Wir unterstützen uneingeschränkt den kürzlich beschlossenen globalen Aktionsplan der WHO zu Antibiotikaresistenzen. Wir werden unsere eigenen nationalen Aktionspläne erstellen oder überarbeiten und wirksam umsetzen und andere Staaten bei der Entwicklung ihrer jeweiligen nationalen Aktionspläne unterstützen.

Wir bekennen uns nachdrücklich zu dem „One Health"-Ansatz, der alle Bereiche – die Gesundheit von Mensch und Tier sowie Landwirtschaft und Umwelt – einbezieht. Wir werden eine fachgerechte Verwendung von Antibiotika fördern und uns daran beteiligen, die Grundlagenforschung, die Forschung zu Epidemiologie, Infektionsprävention und -bekämpfung und die Entwicklung von neuen Antibiotika, alternativen Therapien, Impfstoffen und Schnelltests zu stärken. Wir sind entschlossen, bei der Erstellung oder Überarbeitung und der Bereitstellung unserer nationalen Aktionspläne den Annex (Gemeinsame Anstrengungen zur Bekämpfung von Antibiotikaresistenzen) zu berücksichtigen.

World Health Organization

SIXTY-EIGHTH WORLD HEALTH ASSEMBLY
Agenda item 15.1

A68/A/CONF./1 Rev.1
25 May 2015

Global action plan on antimicrobial resistance

Draft resolution with amendments resulting from informal consultations

The plan sets out 5 objectives:

- improve awareness and understanding of antimicrobial resistance
- **strengthen surveillance and research**
- reduce the incidence of infection
- optimize the use of antimicrobial medicines
- ensure sustainable investment in countering antimicrobial resistance

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Datenquellen zu Erreger und Resistenz in Deutschland

- **Surveillance-Systeme**
  - **ARS (Antibiotika-Resistenz-Surveillance) /EARS-Net**
  - **ARMIN (Antibiotika-Resistenz-Monitoring in Niedersachsen)**
  - **KISS (Krankenhaus-Infektions-Surveillance-System)**
    - **MRSA-KISS**
    - **Stations-KISS/Erreger (MRE-Surveillance)**
    - **CDAD-KISS**
  - **SARI (Surveillance der Antibiotika-Anwendung und der bakteriellen Resistenz auf Intensivstationen)**

Datenquellen zu Erreger und Resistenz in Deutschland

- **Meldepflicht (bundesweit)**
  - **MRSA**
  - **Schwere Verläufe CDI**
- **Meldepflicht (Länderverordnungen)**
  - **Carbapenem-Resistenz bzw. verminderte Carabapenem-Empfindlichkeit bei gramnegativen Erregern**
- **Nationale Referenzzentren**
- **Studien**
  - **PEG-Resistenzstudie /PEG-Blutkulturstudie**

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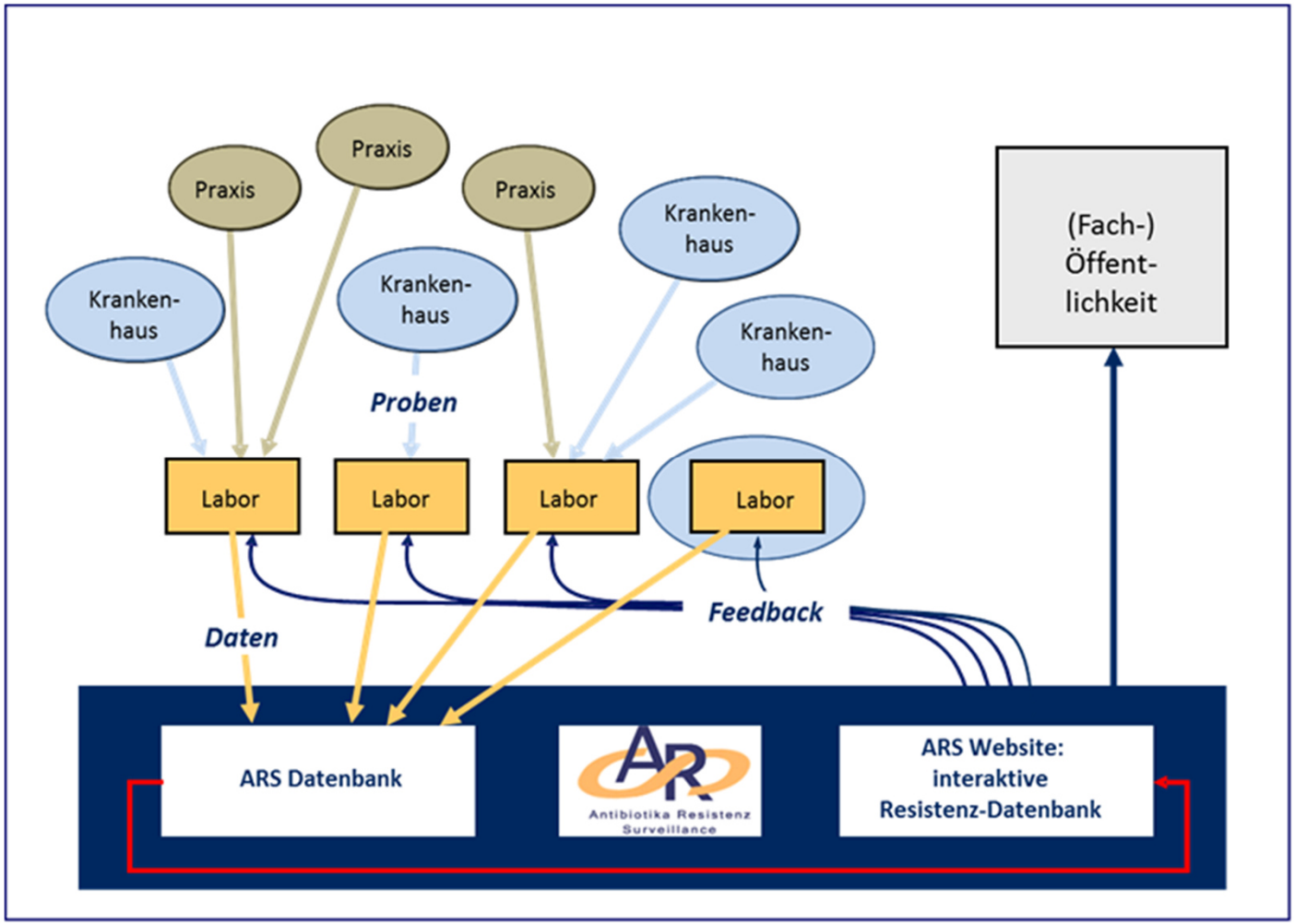
ARS

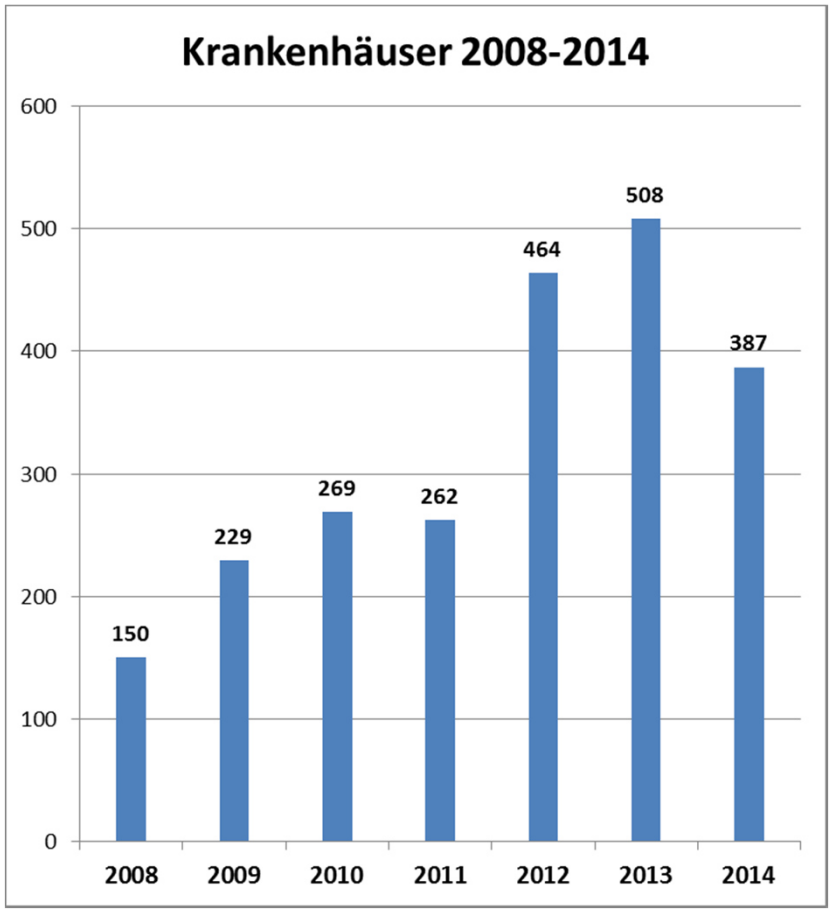
Antibiotika-Resistenz-Surveillance in Deutschlar

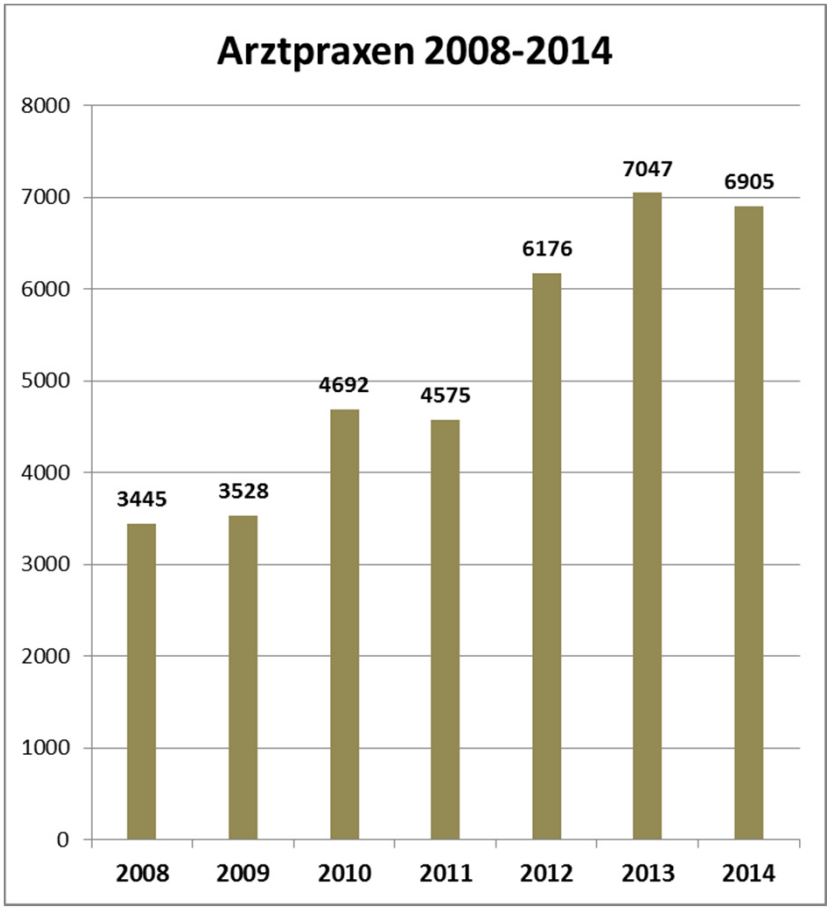
- Basis: Deutsche Antibiotika-Resistenzstrategie DART 2008
  "Stärkung der Surveillance-Systeme zur Antibiotika-Resistenz
  und zum Antibiotika-Verbrauch "
- Konzeption & Koordination: RKI seit 2008
- Teilnahme: mikrobiologische Labore, auf freiwilliger Basis
- Erhebungsumfang:
  Resistenzdaten aus der Routine
  für alle klinisch relevanten bakteriellen Erreger aus allen Materialien
- Ziel: Bereitstellung von Referenzdaten zur Resistenzlage
  - in der stationären Versorgung
  - in der ambulanten Versorgung
- Kooperation:
  Teilnahme am European Antimicrobial Resistance Surveillance Network (EARS-Net)

ARS - Netzwerk



ARS – Daten repräsentieren





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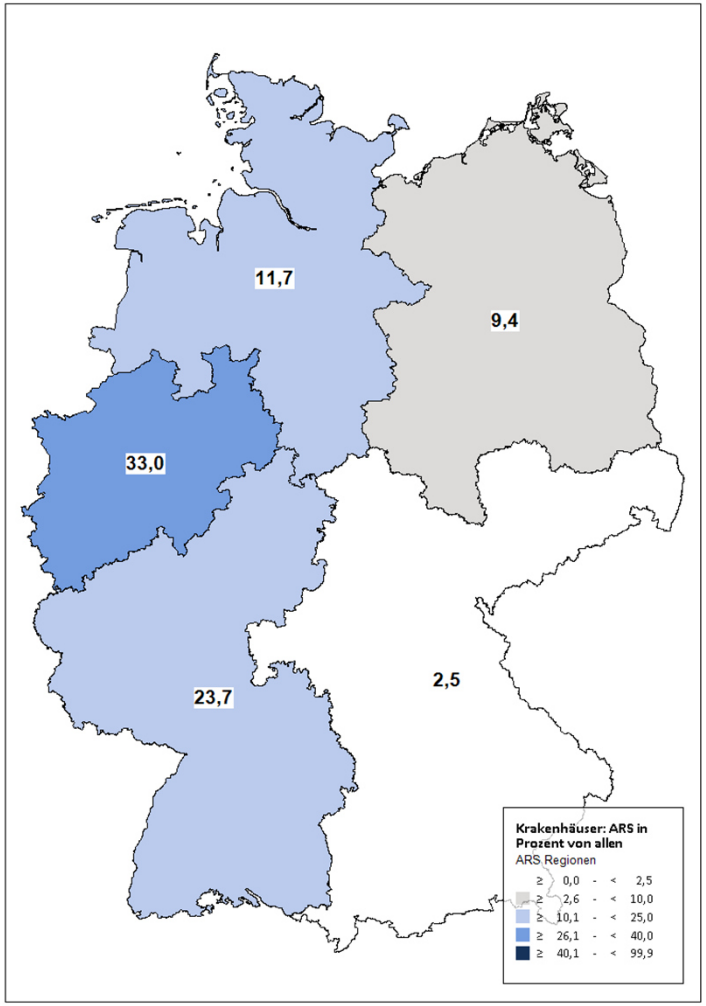
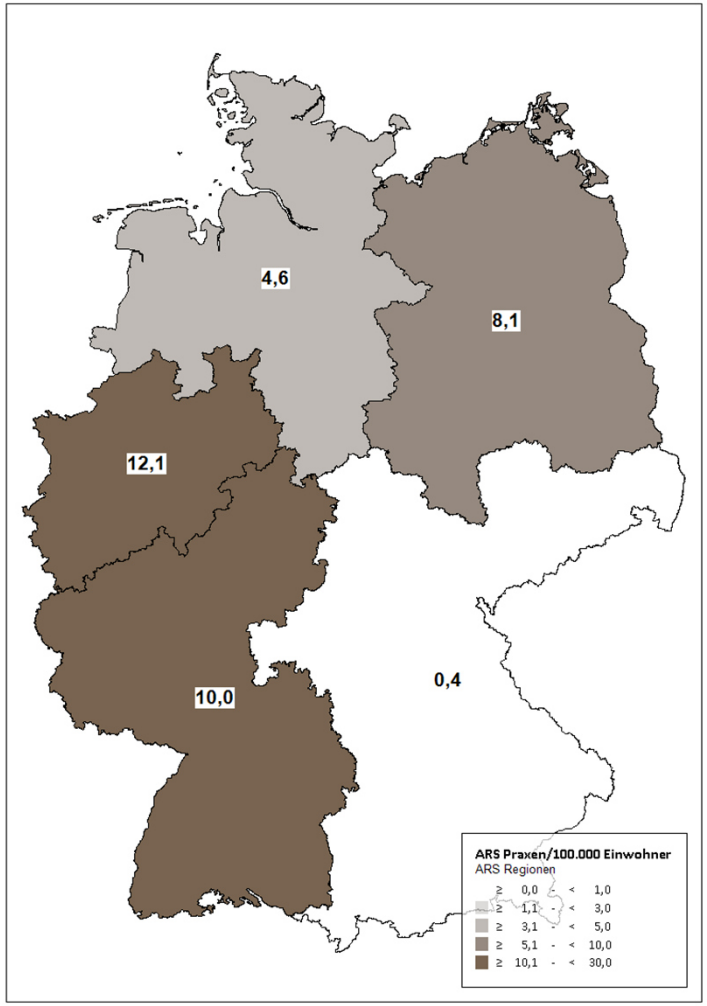
ARS - Teilnahme

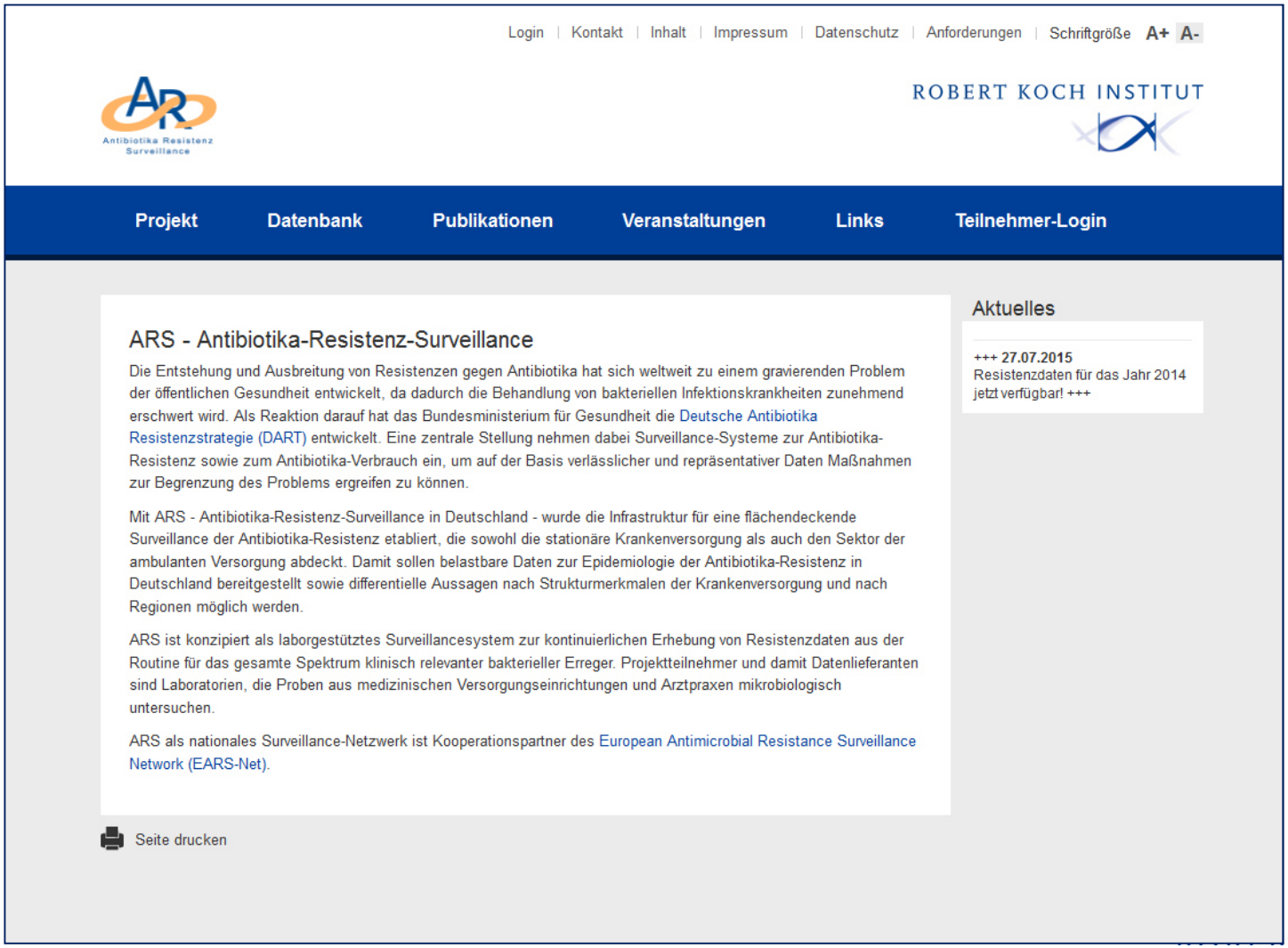
regionale Verteilung von Krankenhäusern und Arztpraxen 2014





INSTITUT

ARS – Homepage



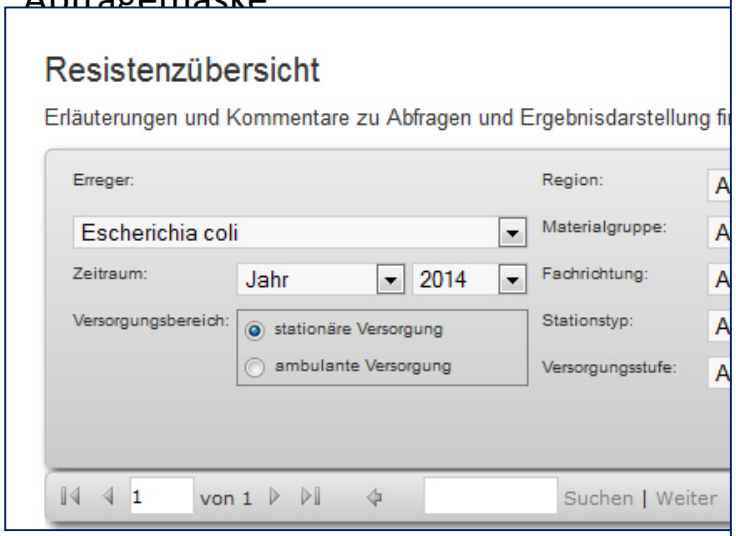
https://ars.rki.de

ARS – interaktive Datenbank

Resistenzübersicht & Resistenz

für die häufigsten & klinisch bedeutsamst

Abfragemaske:



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Parameter:

Erreger:	Escherichia coli	Region:	Alle
Zeitraum:	Jahr 2014	Materialgruppe:	Alle
Versorgungsbereich:	stationäre Versorgung	Fachrichtung:	Alle
		Stationstyp:	Alle
		Versorgungsstufe:	Alle

Datenstand: 01.07.2015

abgerufen am: 21.09.2015

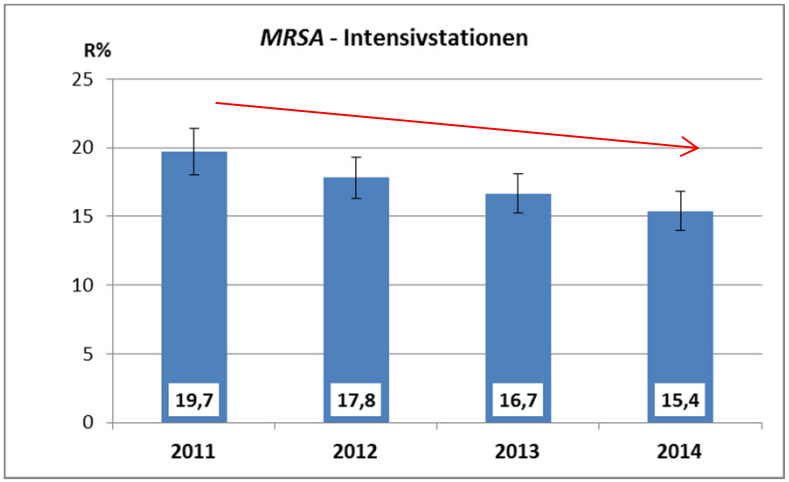
Antibiotikum	R		I		S		Total
	n	%	n	%	n	%	n
Amoxicillin	10006	48.4	2	0.0	10675	51.6	20683
Amoxicillin/Clavulansäure	14649	40.5	117	0.3	21384	59.2	36150
Ampicillin	39482	50.3	434	0.6	38647	49.2	78563
Ampicillin/Sulbactam	41666	41.1	968	1.0	58849	58.0	101483
Piperacillin	39157	49.0	67	0.1	40706	50.9	79930
Piperacillin/Tazobactam	8925	9.0	6591	6.6	83704	84.4	99220
Cefepim	225	12.4	3	0.2	1586	87.4	1814
Cefotaxim	11157	12.6	113	0.1	77618	87.3	88888
Ceftazidim	7913	8.9	5063	5.7	75778	85.4	88754
Cefuroxim	18359	17.7	338	0.3	85068	82.0	103765
Ertapenem	23	0.1	5	0.0	22224	99.9	22252
Imipenem	18	0.0	20	0.0	102731	100.0	102769
Meropenem	12	0.0	13	0.0	103620	100.0	103645

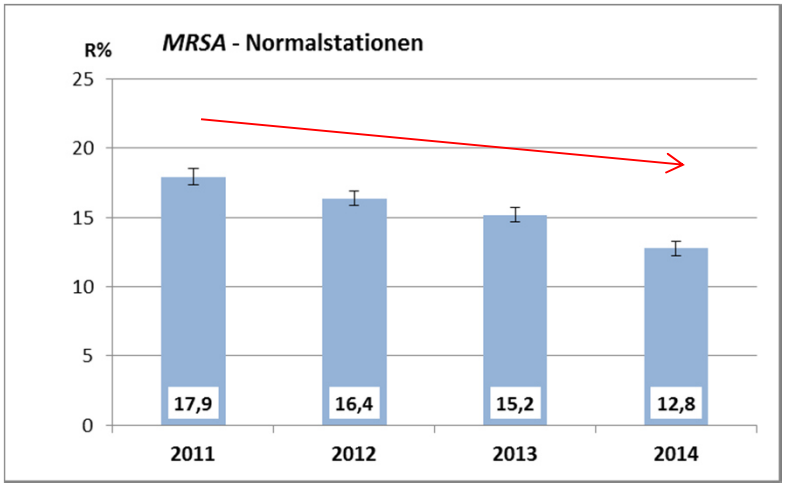
Ergebnisse

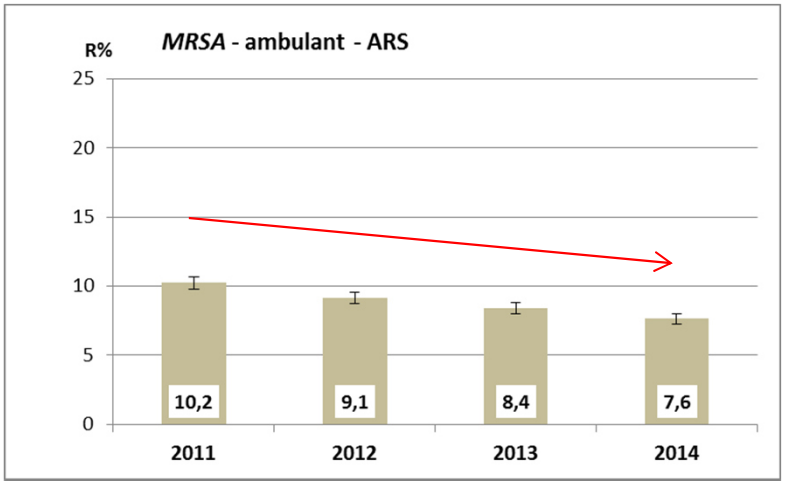
- zeitliche Entwicklung 2010 – 2014
  - *MRSA*
  - *E. coli - Cefotaxim-Resistenz (als Marker für ESBL)*
  - *K. pneumoniae - Cefotaxim-Resistenz (als Marker für ESBL)*
- in verschiedenen Versorgungsbereichen
  - Intensivstationen | Normalstationen | ambulante Versorgung
- im europäischen Vergleich
- Berechnung von Resistenzraten
  - *alle Probenmaterialien (ohne Screening-Proben)*
  - *Erstisolate = 1. Isolat pro Patient-Erreger-Jahr*
  - *Bewertungen RIS der Resistenztestergebnisse*
- Berechnung für Trends

  Beschränkung auf Proben von Krankenhäusern / Arztpraxen, die im untersuchten Zeitraum kontinuierlich Daten an ARS geliefert haben

Ergebnisse 1: *MRSA*







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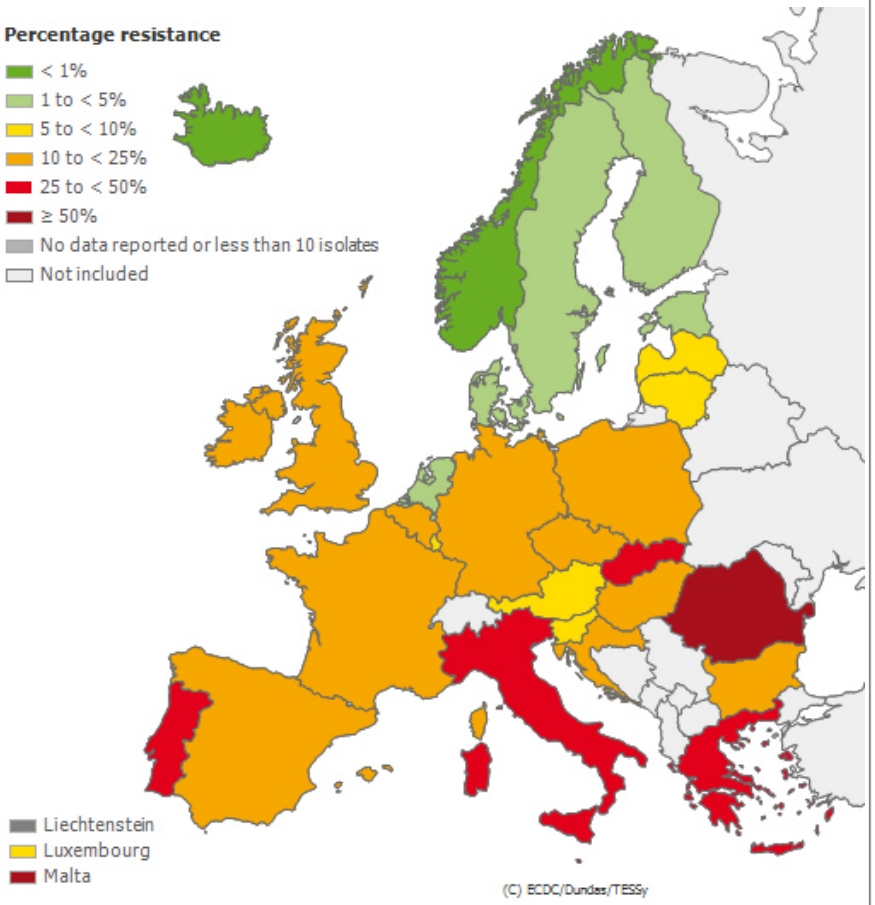
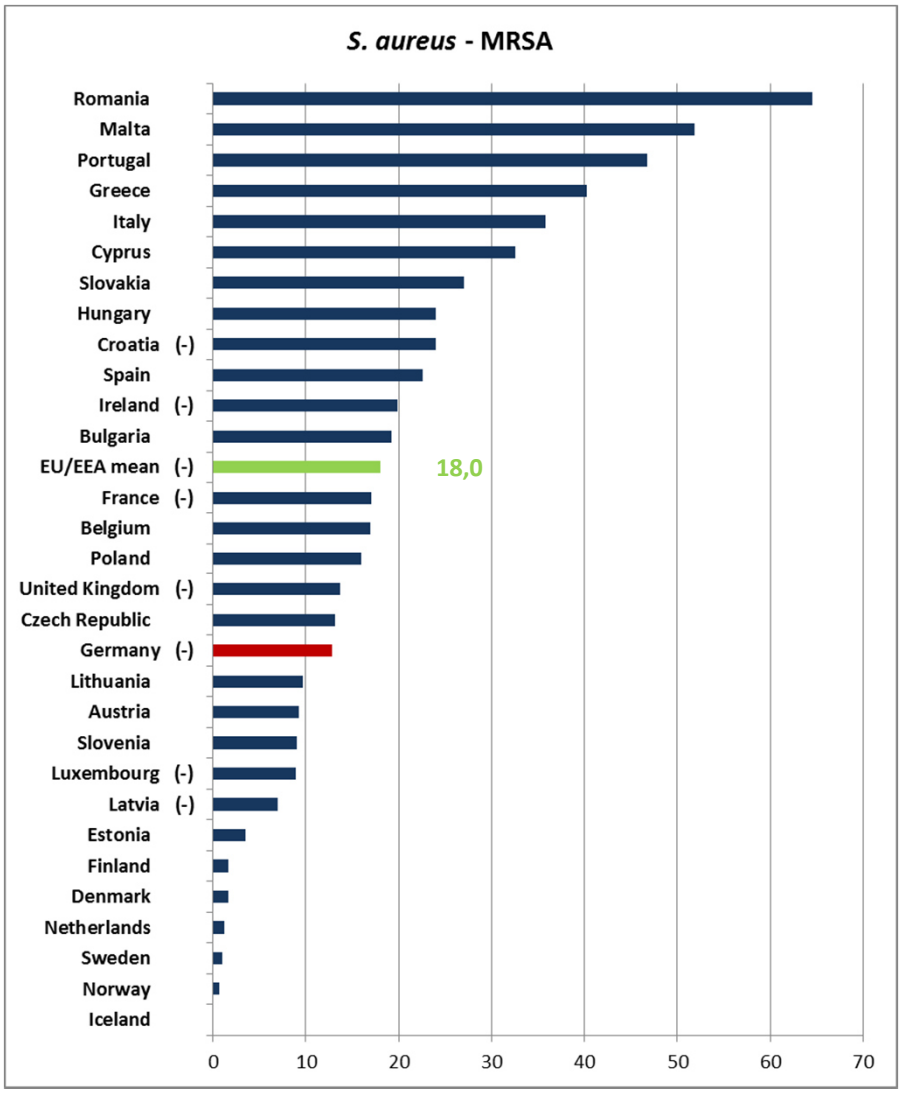
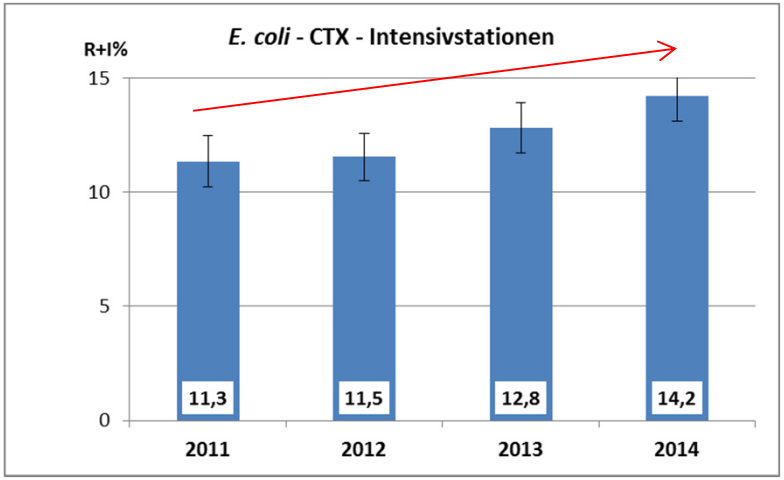
Ergebnisse 1: *MRSA*

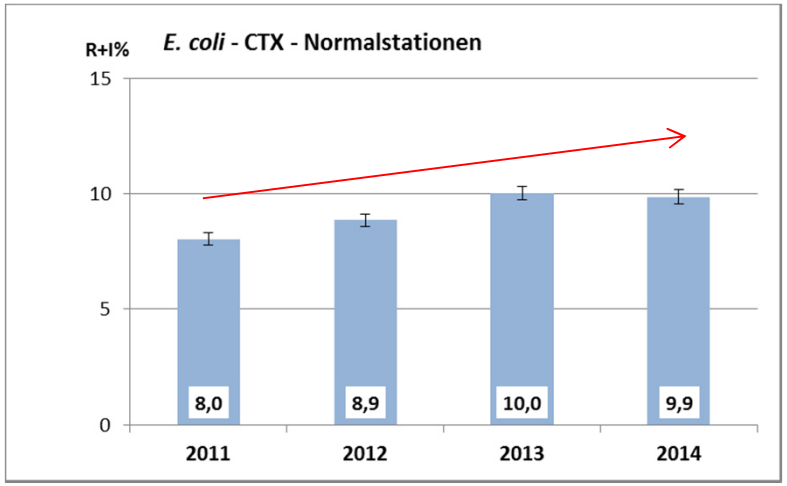
EARS-Net:
D im europäischen Kontext 2013

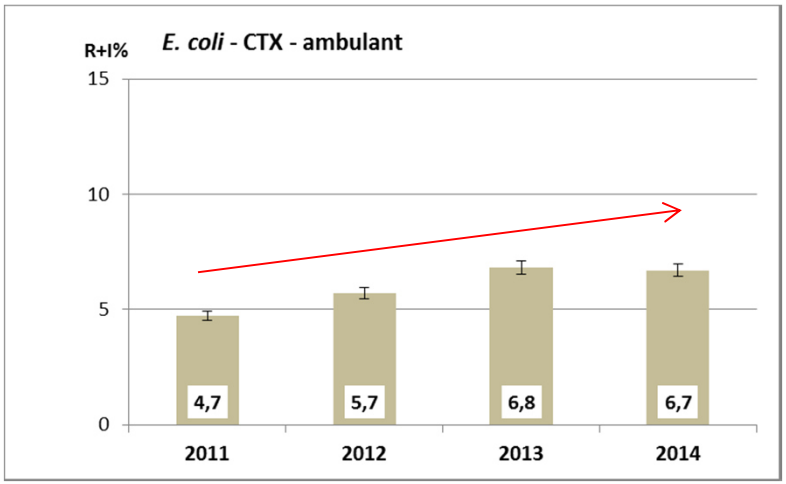




Ergebnisse 2: *E. coli*







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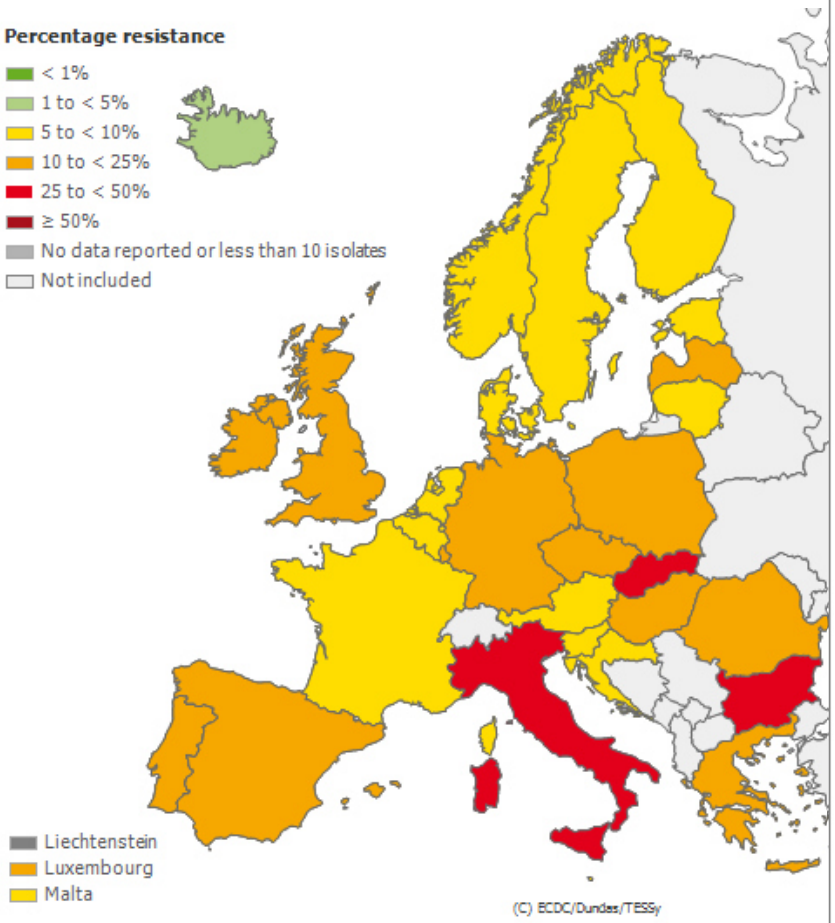
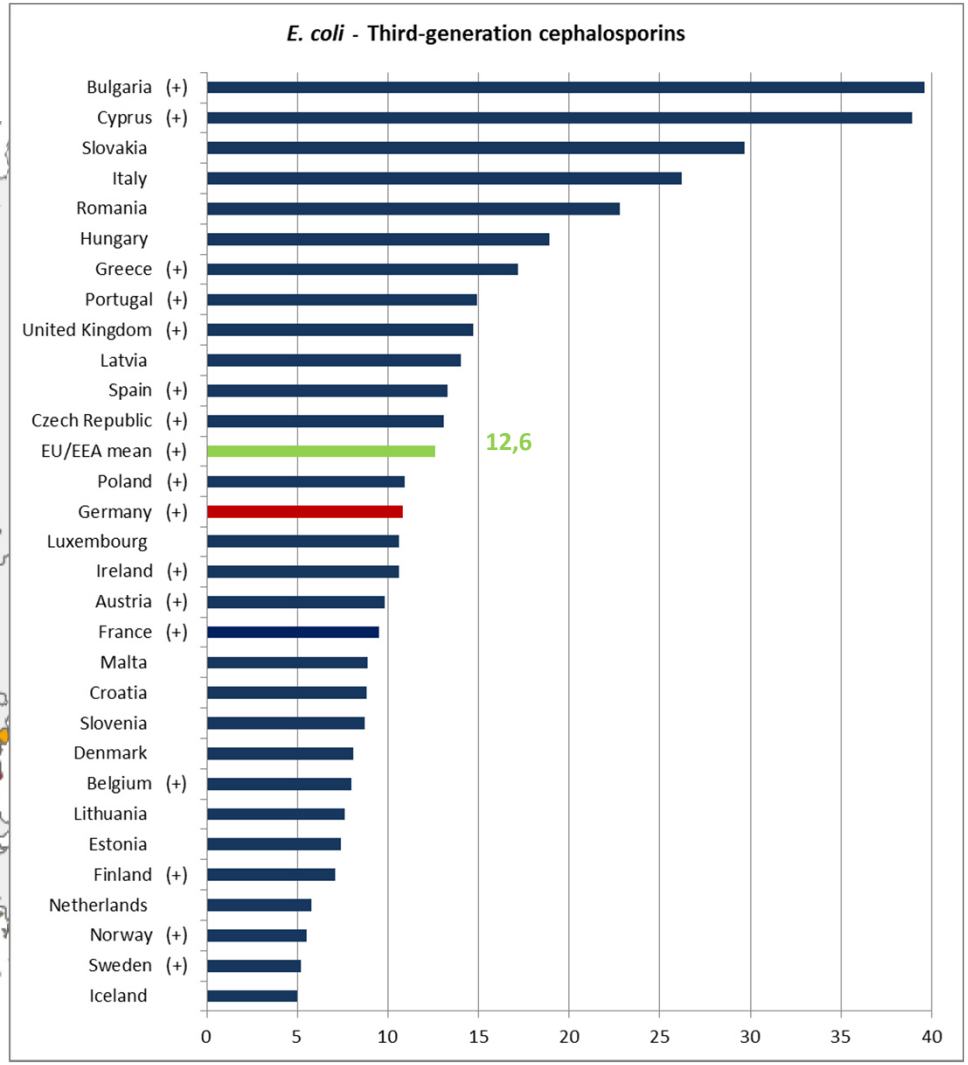
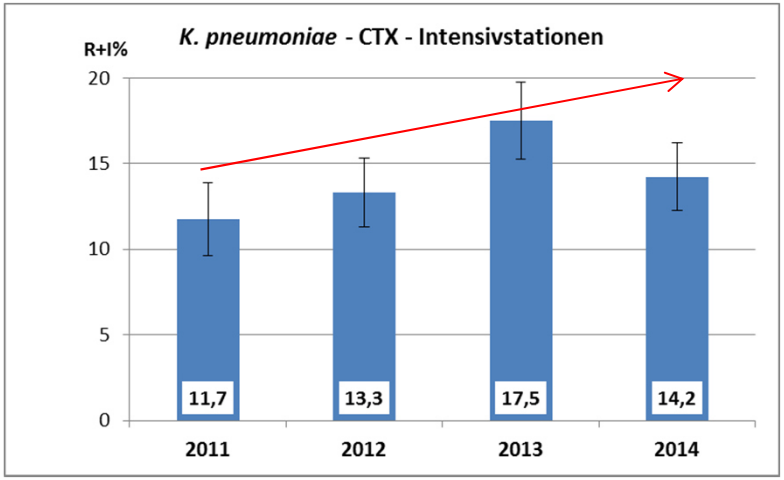
Ergebnisse 2: *E. coli*

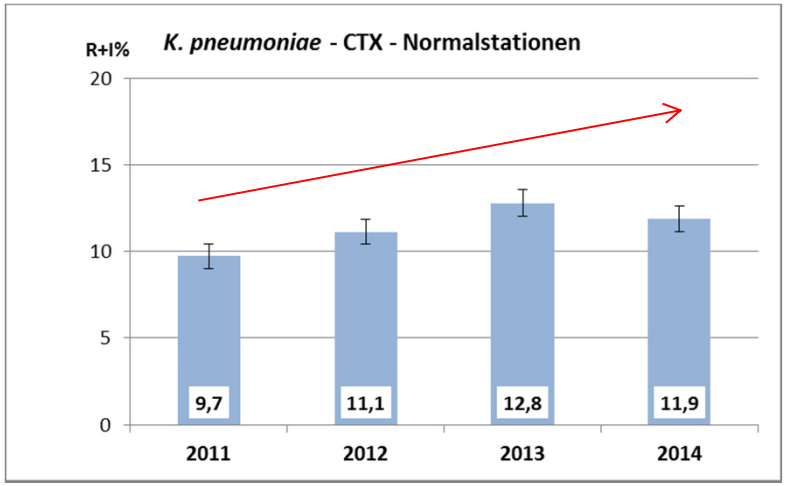
EARS-Net:
D im europäischen Kontext 2013

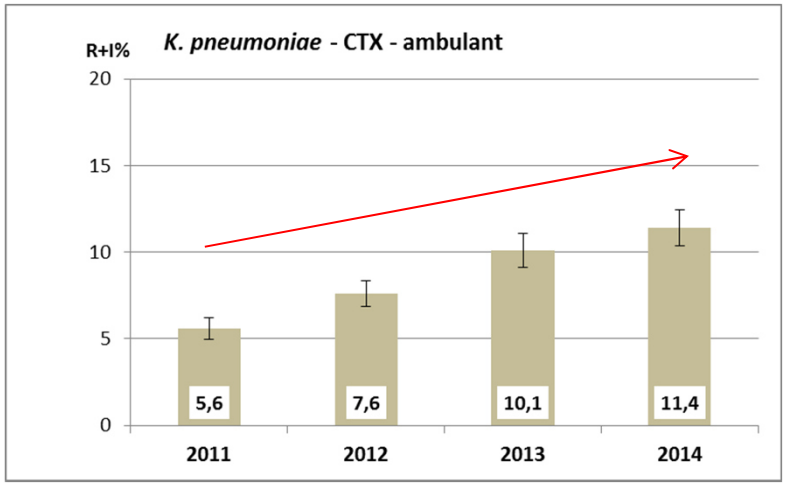




Ergebnisse 3: *K. pneumoniae*

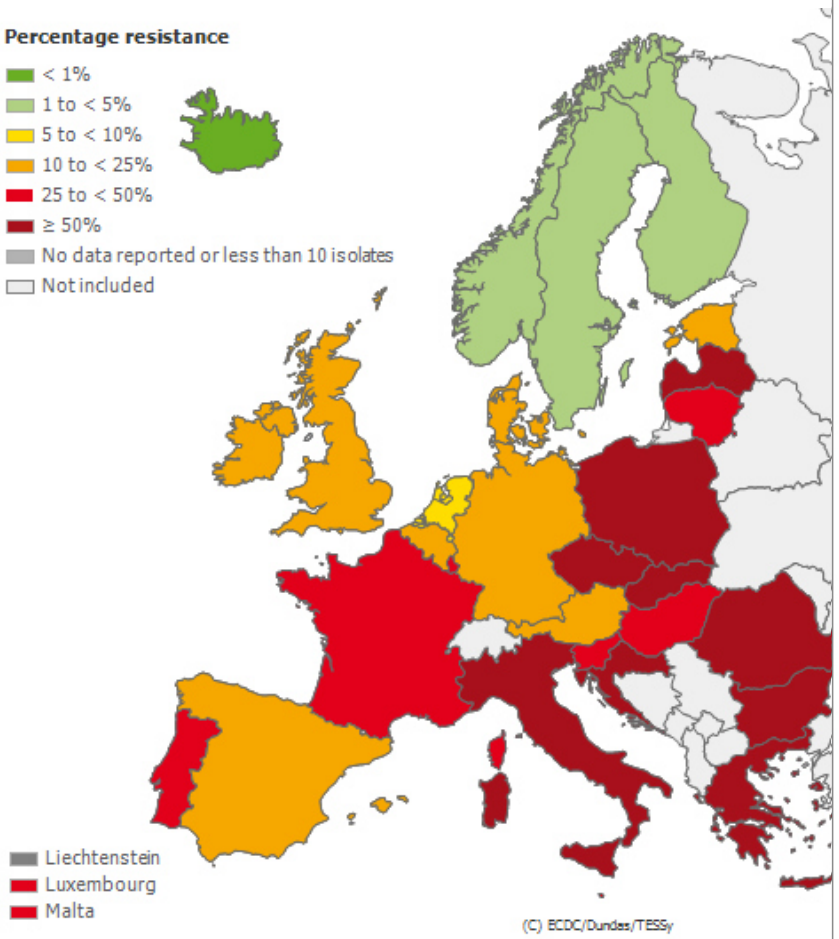


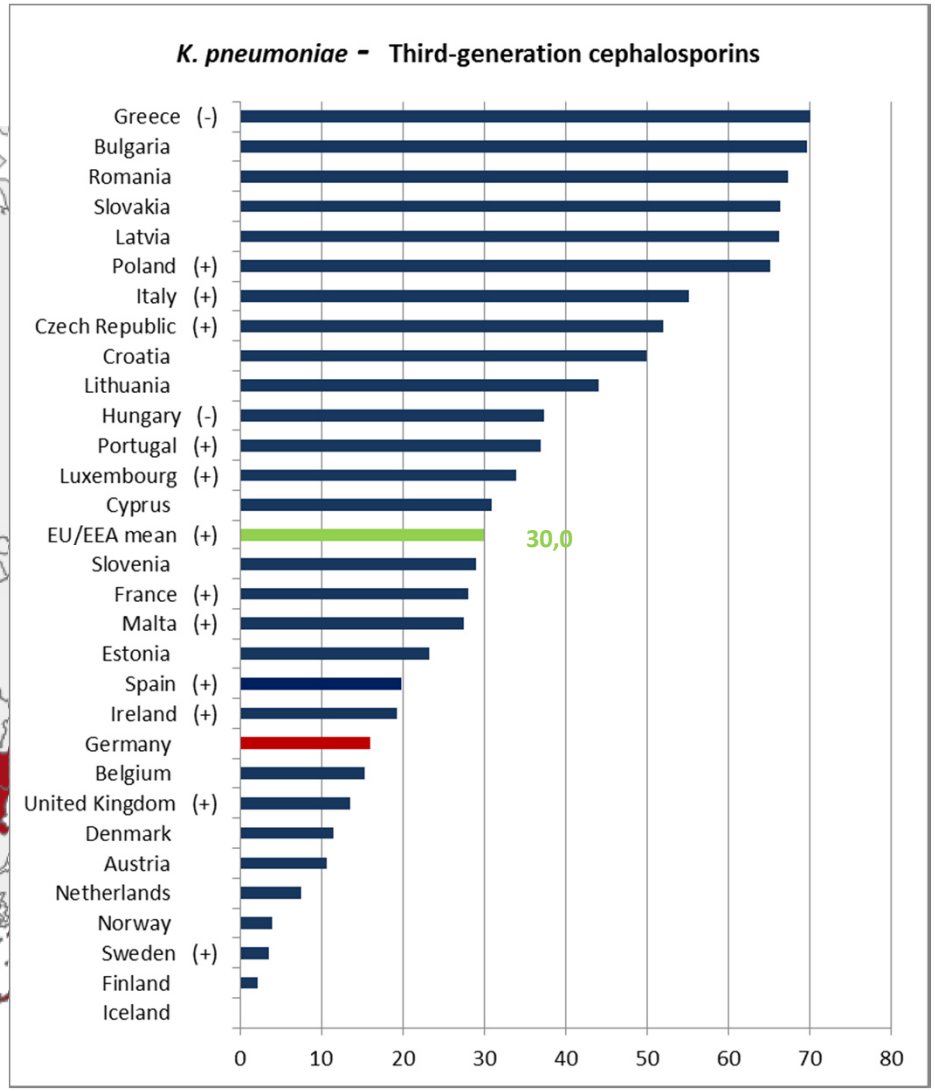




Ergebnisse 3: *K. pneumoniae*

EARS-Net:
D im europäischen Kontext 2013





Demographische Stratifizierung

Verteilung der Resistenzanteile von *S. aureus* und *E. coli* aus dem <u>stationären</u> Bereich in den Jahren 2011 und 2012, alle Materialien

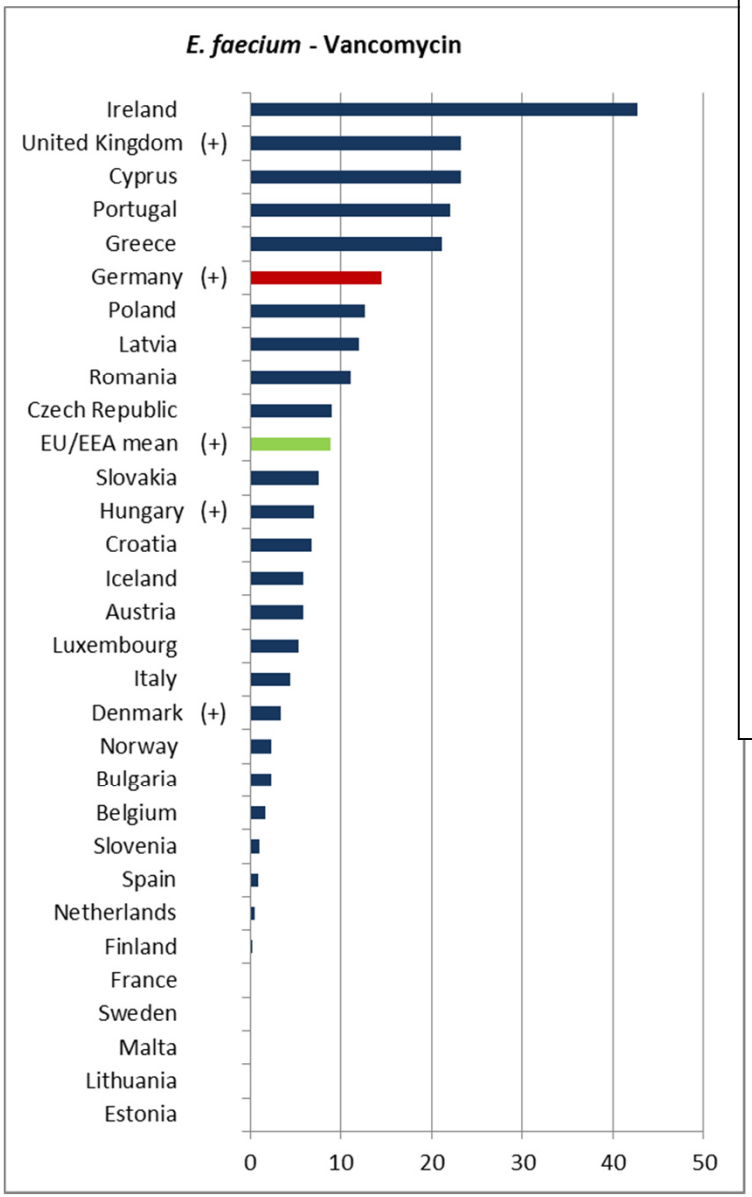
Geschlecht	Alters-gruppe Jahre	*S. aureus* – Oxacillin R %	KI 95%	n	*E. coli* – Cefotaxim R+I %	KI 95%	n
männlich	< = 18	3,4	2,4–4,3	1490	6,9	5,5–8,3	1251
	19–60	14,9	13,8–16,1	3619	10,4	9,4–11,3	3853
	> = 61	22,5	21,6–23,4	7867	12,9	12,2–13,5	10 921
weiblich	< = 18	3,1	2,1–4	1270	5,5	4,6–6,5	2164
	19–60	11,2	10–12,5	2573	6,5	6–7	8262
	> = 61	20,2	19,2–21,2	6020	9,0	8,7–9,3	26 621

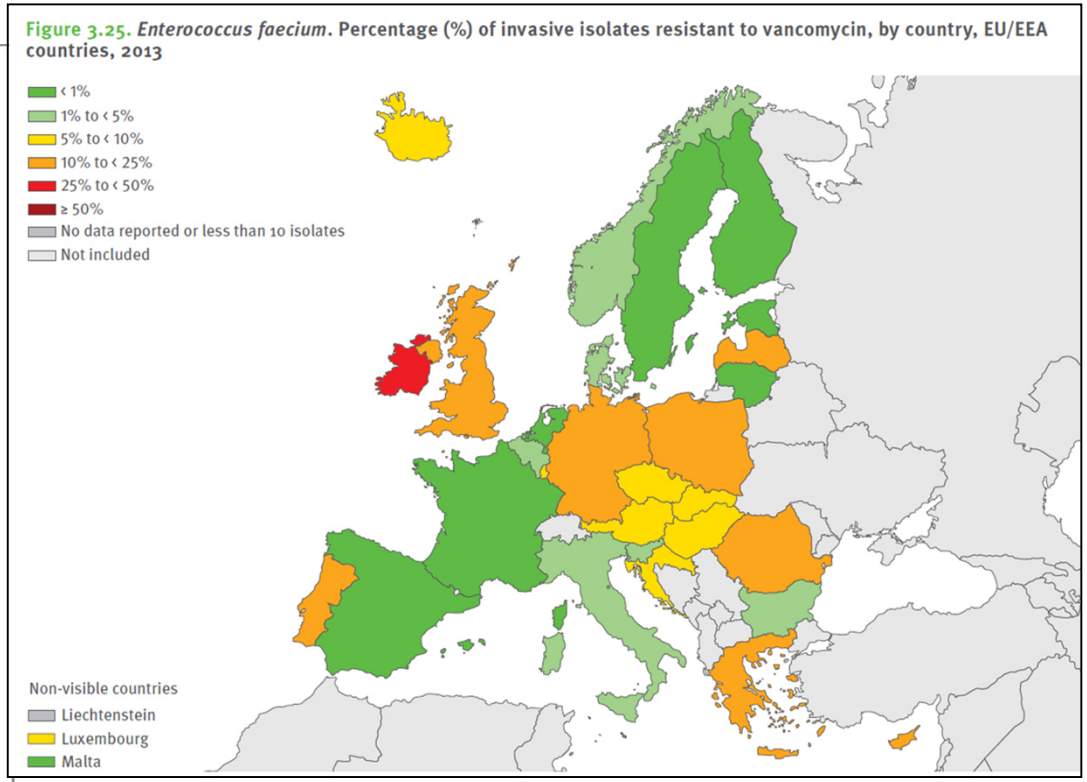
Verteilung der Resistenzanteile von *S. aureus* und *E. coli* aus dem <u>ambulanten</u> Bereich in den Jahren 2011 und 2012, alle Materialien

Geschlecht	Alters-gruppe Jahre	*S. aureus* – Oxacillin R %	KI 95%	n	*E. coli* – Cefotaxim R+I %	KI 95%	N
männlich	< = 18 (1)	3,3	2,3–4,2	1341	5,4	3,7–7,2	663
	19–60 (2)	7,0	6,1–7,8	3333	5,6	4,7–6,5	2509
	> = 61 (3)	19,0	17,7–20,2	3859	9,3	8,4–10,1	4207
weiblich	< = 18 (1)	2,9	2,1–3,8	1474	2,3	1,9–2,7	4849
	19–60 (2)	5,2	4,5–5,9	3814	3,3	3–3,6	16 381
	> = 61 (3)	16,1	14,9–17,2	3927	5,5	5,2–5,8	19 546

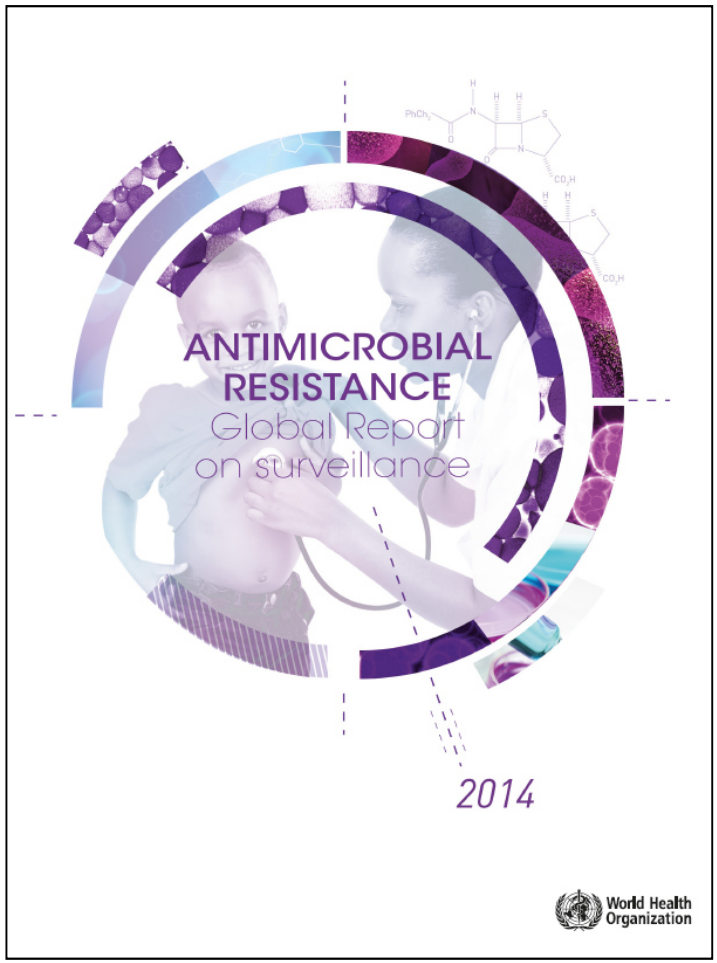
Modifiziert aus Eckmanns et al. Berl Münch Tierärztl Wochenschr 127, 10–13, 2014

EARS-Net





Enterococcus faecium	2011	2012	2013	2014
Vancomycin R	11,4	16,2	14,5	9,1



First published April 2014, reprinted with changes June 2014

Bacteria commonly causing infections in hospitals and in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data
Escherichia coli/	Urinary tract infections, blood stream infections	
- vs 3rd gen. cephalosporins		86
- vs fluoroquinolones		92
Klebsiella pneumoniae/	Pneumonia, blood stream infections, urinary tract infections	
- vs 3rd gen. cephalosporins		87
- vs 3rd carbapenems		71
Staphylococcus aureus/	Wound infections, blood stream infections	
- vs methicillin "MRSA"		85

Bacteria mainly causing infections in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data
Streptococcus pneumoniae/ - non-susceptible or resistant to penicillin	Pneumonia, meningitis, otitis	67
Nontyphoidal Salmonella/	Foodborne diarrhoea, blood stream infections	
- vs fluoroquinolones		68
Shigella species/	Diarrhoea ("bacillary dysenteria")	
- vs fluoroquinolones		35
Neisseria gonorrhoeae/ - vs 3rd gen. cephalosporins	Gonorrhoea	42

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AMR Global Report on surveillance
Escherichia coli

Table 3 *Escherichia coli:* Resistance to third-generation cephalosporins[a] (summary of reported or published proportions of resistance, by WHO region)

Data sources based on at least 30 tested isolates[b]	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in invasive isolates[c] (no. of reports)
African Region		
– National data (n=13 countries)	2–70	28–36 (n=4)
– Publications (n=17) from 7 additional countries	0–87	0–17 (n=5)
Region of the Americas		
– National data or report to ReLAVRA (n=14 countries)	0–48	
– Publications (n=10) from 5 additional countries	0–68	
Eastern Mediterranean Region		
– National data (n=4 countries)	22–63	41 (n=1)
– Surveillance network in 1 country[d]	39 (caz)–50 (cro)	
– Publications (n=44) from 11 additional countries	2–94	11–33 (n=6)
European Region		
– National data or report to EARS-Net (n=35 countries)	3–82	3–43 (n=32)
– Publications (n=5) from 2 additional countries	0–8	0-8 (n=2)
South-East Asia Region		
– National data (n=5 countries)	16–68	
– Publications (n=26) from 2 additional countries	19–95	20–61 (n=2)
Western Pacific Region		
– National data (n=13 countries)	0–77	
– Institute surveillance (data from 3 hospitals in one country)	4–14	
– Publications (n=4) from 2 additional countries	8–71	

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AMR Global Report on surveillance
Klebsiella pneumonia

Table 5 *Klebsiella pneumoniae:* Resistance to third-generation cephalosporins[a] (summary of reported or published proportions of resistance, by WHO region)

Data sources based on at least 30 tested isolates[b]	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in invasive isolates[c] (no. of reports)
African Region		
– National data (n=13 countries)	8–77	41–62 (n=3)
– Publications (n=4) from 1 additional country	9–69	
Region of the Americas		
– National data or report to ReLAVRA (n=17 countries)	4–71	
– Publications (n=3) from 3 additional countries	15–56	56 (n=1)
Eastern Mediterranean Region		
– National data (n=4 countries)	22–50	48 (n=1)
– Surveillance network[d] (n=1) in 1 additional country	72 (caz)–82 (cro)	
– Publications (n=16) from 7 additional countries	6–75	17 (ctx); 43 (caz); 50 (cro) (n=1)
European Region		
– National data or report to EARS-Net (n=33 countries)	2–82	2–82 (n=31)
– Publications (n=2) from 2 additional countries	4–61	11 (cro); 16 (ctx); 18 (caz) (n=1)
South-East Asia Region		
– National data (n=4 countries)	34–81	
– Publications (n=23) from 4 additional countries	5–100	53.3–100 (n=4)
Western Pacific Region		
– National data (n=14 countries)	1–72	72 (n=1)
– Institute surveillance (data from 3 hospitals in 1 country)	17–30	
– Publications (n=3) from 2 additional countries	27–35	27 (n=1)

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Table A2.22 *Klebsiella pneumoniae*: Resistance to carbapenems[a] European Region

Countries, territories and other areas or groupings	Data source[b, c, d]	Resistance (%)	No. tested isolates	Type of surveillance, population or samples[c]	Period for data collection	Year of publication or report
Albania	National data not available					2013
Andorra	No information obtained for this report					
Armenia	National data not available					2013
Austria	National data	0.2	610	Invasive isolates	2011	2013
Azerbaijan	National data not available					2013
Belarus	No information obtained for this report[e]					
Belgium	National data	0.3	646	Invasive isolates	2011	2013
Bulgaria	National data	0	116	Invasive isolates	2011	2013
Croatia	National data	0	4945	Comprehensive	2012	2013
Cyprus	National data	15.7	83	Invasive isolates	2011	2013
Czech Republic	National data	0.1	1193	Invasive isolates	2011	2013
Denmark	National data	0	589	Invasive isolates	2011	2013
Estonia	National data	0	73	Invasive isolates	2011	2013
Finland	National data	0	318	Invasive isolates	2011	2013
France	National data	0	1640	Invasive isolates	2011	2013
Georgia	National data	57.1	7	Comprehensive	2012	2013
Georgia	Publication (*67*)	2	45	Blood isolates (neonates)	2003–2004	2009
Germany	National data	0	512	Invasive isolates	2011	2013
Greece	National data	68.2	1636	Invasive isolates	2011	2013
Hungary	National data	1.9	413	Invasive isolates	2011	2013
Iceland	National data not available					2013
Ireland	National data	0.3	302	Invasive isolates	2011	2013
Israel	Publication (*145*)	7	299	Patient screening	2007–2008	2012
Israel	Publication (*146*)	5.4	298	Carrier screening		2010
Italy	National data	26.7	615	Invasive isolates	2011	2013
Kazakhstan	No information obtained for this report[e]					
Kyrgyzstan	National data not available					2013
Latvia	National data	0	65	Invasive isolates	2011	2013
Lithuania	National data	0	19	Invasive isolates	2011	2013
Luxembourg	National data	0	48	Invasive isolates	2011	2013
Malta	National data	3.8	52	Invasive isolates	2011	2013

CID, 2011

Massive Increase, Spread, and Exchange of Extended Spectrum β-Lactamase–Encoding Genes Among Intestinal *Enterobacteriaceae* in Hospitalized Children With Severe Acute Malnutrition in Niger

Paul-Louis Woerther,[1,2] Cécile Angebault,[1,2] Hervé Jacquier,[3,5] Henri-Charles Hugede,[1] Ann-Carole Janssens,[4] Sani Sayadi,[4] Assiya El Mniai,[1] Laurence Armand-Lefèvre,[1,2] Etienne Ruppé,[1,2] François Barbier,[1,2] Laurent Raskine,[5] Anne-Laure Page,[4] Nathalie de Rekeneire,[4] and Antoine Andremont[1,2]

[1]French National Reference Center for Bacterial Resistance in Commensal Flora, Laboratory of Bacteriology, Bichat–Claude Bernard Hospital, Assistance Publique–Hôpitaux de Paris; [2]EA3964, [3]INSERM, UMR-S 722, and Université Paris Diderot, Sorbonne Paris Cité, Medical School, and [4]Epicentre, Médecins Sans Frontières, Paris; and [5]Laboratory of Bacteriology, Lariboisière Hospital, Assistance Publique–Hôpitaux de Paris, France

Background. From the time of CTX-M emergence, extended-spectrum β-lactamase–producing enterobacteria (ESBL-E) have spread worldwide in community settings as well as in hospitals, particularly in developing countries. Although their dissemination appears linked to *Escherichia coli* intestinal carriage, precise paths of this dynamic are largely unknown.

Methods. Children from a pediatric renutrition center were prospectively enrolled in a fecal carriage study. Antibiotic exposure was recorded. ESBL-E strains were isolated using selective media from fecal samples obtained at admission and, when negative, also at discharge. ESBL-encoding genes were identified, their environments and plasmids were characterized, and clonality was assessed with polymerase chain reaction–based methods and pulsed-field gel electrophoresis for *E. coli* and *Klebsiella pneumoniae*. *E. coli* strains were subjected to multilocus sequence typing.

Results. The ESBL-E carriage rate was 31% at admission in the 55 children enrolled. All children enrolled received antibiotics during hospitalization. Among the ESBL-E–negative children, 16 were resampled at discharge, and the acquisition rate was 94%. The $bla_{\text{CTX-M-15}}$ gene was found in >90% of the carriers. Genetic environments and plasmid characterization evidenced the roles of a worldwide, previously described, multidrug-resistant region and of IncF plasmids in CTX-M-15 *E. coli* dissemination. Diversity of CTX-M-15–carrying genetic structures and clonality of acquired ESBL *E. coli* suggested horizontal genetic transfer and underlined the potential of some ST types for nosocomial cross-transmission.

Conclusions. Cross-transmission and high selective pressure lead to very high acquisition of ESBL-E carriage, contributing to dissemination in the community. Strict hygiene measures as well as careful balancing of benefit–risk ratio of current antibiotic policies need to be reevaluated.

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RESEARCH ARTICLE Open Access

The risk to import ESBL-producing Enterobacteriaceae and *Staphylococcus aureus* through chicken meat trade in Gabon

Frieder Schaumburg[1,2*], Abraham S Alabi[2,3], Lisa Frielinghaus[1,2], Martin P Grobusch[2,3,4], Robin Köck[5], Karsten Becker[1], Saadou Issifou[2,3], Peter G Kremsner[2,3], Georg Peters[1] and Alexander Mellmann[5]

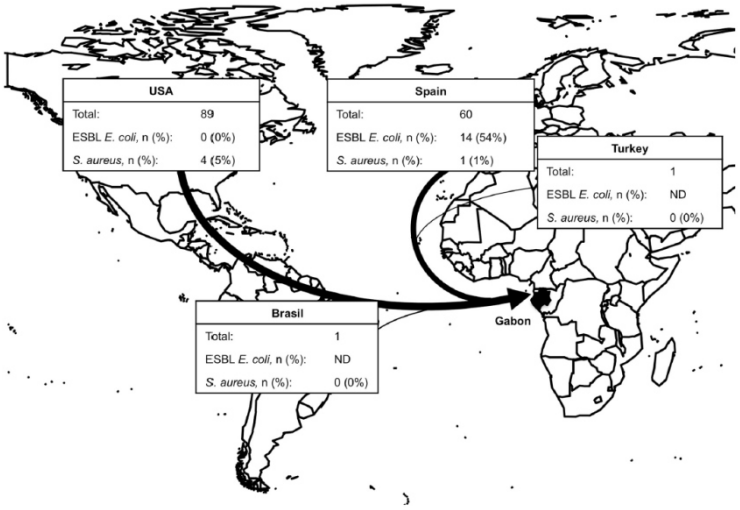

Figure 1 Origin of imported poultry meat in Gabon. The total number of samples and the proportion of ESBL *E. coli* and *S. aureus* in each country are shown. Screening for ESBL-producing Enterobacteriaceae was only done for a subset of samples from the USA (n = 34) and Spain (n = 26). Width of arrows represents the amount of imported poultry. The map was created with "R" (package "maps").

	No. (%)
Imported chicken meat samples	151 (100%)
Samples screened for *S. aureus*	151 (100%)
Samples screened for ESBL *E. coli*[a]	60 (39.7%)
ESBL *E. coli*	14 (23.3%)[b]
S. aureus	5 (3.3%)

Kapazität und Ressourcen

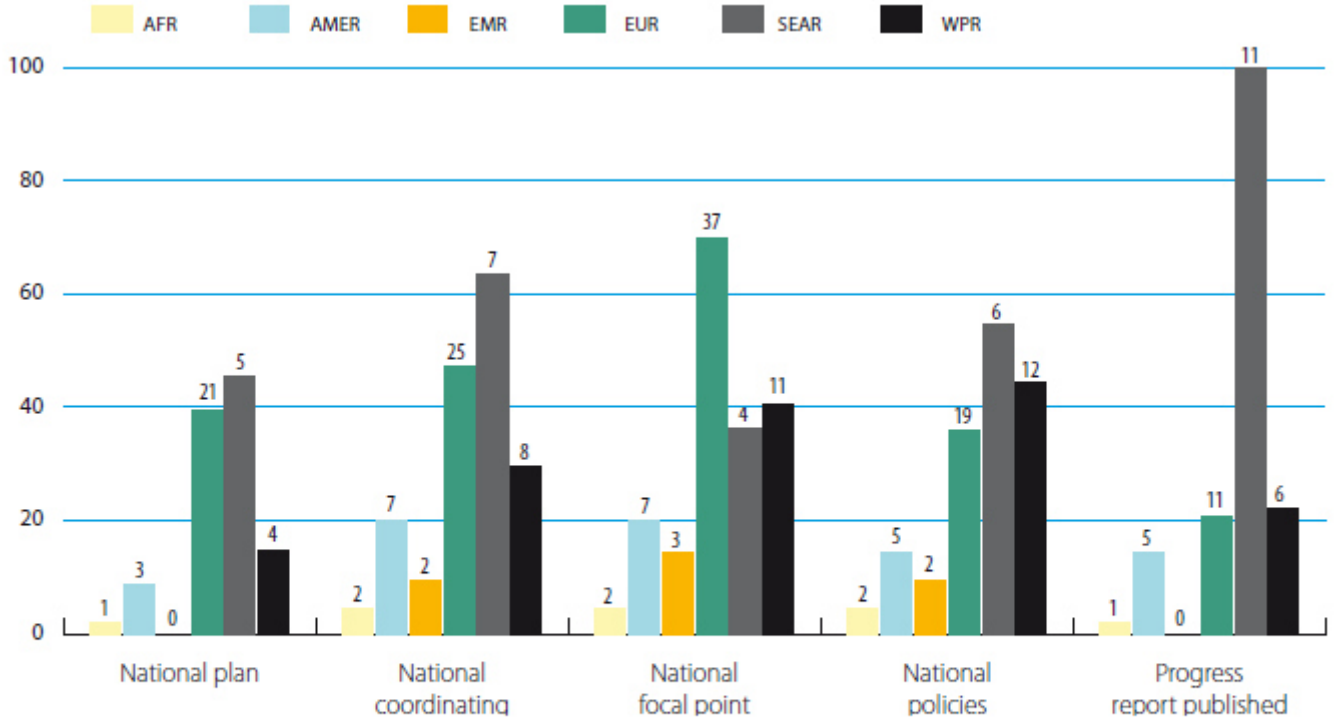

Figure 1.2 – **Percentages of Member States that had a national plan for antimicrobial resistance, a coordinating mechanism, a focal point, a policy or a strategy and had prepared a report in the previous 5 years, by region**
(Note: numbers above the bars represent the numbers of participating Member States that answered "yes")

http://apps.who.int/iris/bitstream/10665/163468/1/9789241564946_eng.pdf?ua=1&ua=1

ROBERT KOCH INSTITUT

- Afrika ist unvorbereitet: Nachvollziehbar, da andere Probleme → keine Gesundheitsinfrastruktur, aber es gibt schon besorgniserregende Ausbrüche

Zusammenfassung

- One Health und Global Health
- Deutschland
  - Grampositive insbesondere MRSA gute Entwicklung
  - Gramnegative Anstieg

  Keine dramatische Situation
- Global teilweise besorgniserregend
  - Positive Entwicklung der Medizin wird erschwert oder unmöglich gemacht

Dank

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  Ines Noll, Britta Schweickert, Marcel Feig
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