

Antimicrobial Resistance Surveillance Systems and bias!



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AMR Surveillance

- **International official programmes**
 - none
- **European official programmes**
 - EARSS / EARS-NET
- **National official programmes**
 - Many initiatives
- **Many commercial initiatives**
 - Alexander project
 - SENTRY
 - MYSTIC
 - ECO-SENS
 - ...

Links to national and international programmes:
http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/external_sites/Pages/external_sites.aspx

Systems

- Commercial systems
 - often pointed toward a specific microorganism and/or class of drugs (Alexander project (URTI), ECO-SENS (E.coli))
 - Isolates sent to central laboratory (cash per isolate)
- Voluntary manual reporting of certain microorganisms, drugs and infections (EARS-NET)
- Voluntary computer-supported or fully automatic reporting of some/all microorganisms (NL, SE)
- Mandatory reporting systems for
 - defined bacteria (M.tb)
 - defined resistance geno/phenotypes (MRSA, VRE, NDM1, etc)

AMR surveillance is biased because it is based on routine "consecutive" isolates

- Bias
 - The Sick – "we do not culture the healthy"
 - The Failures – "we only culture when therapy fails"

How and where we collect our data will affect resistance levels

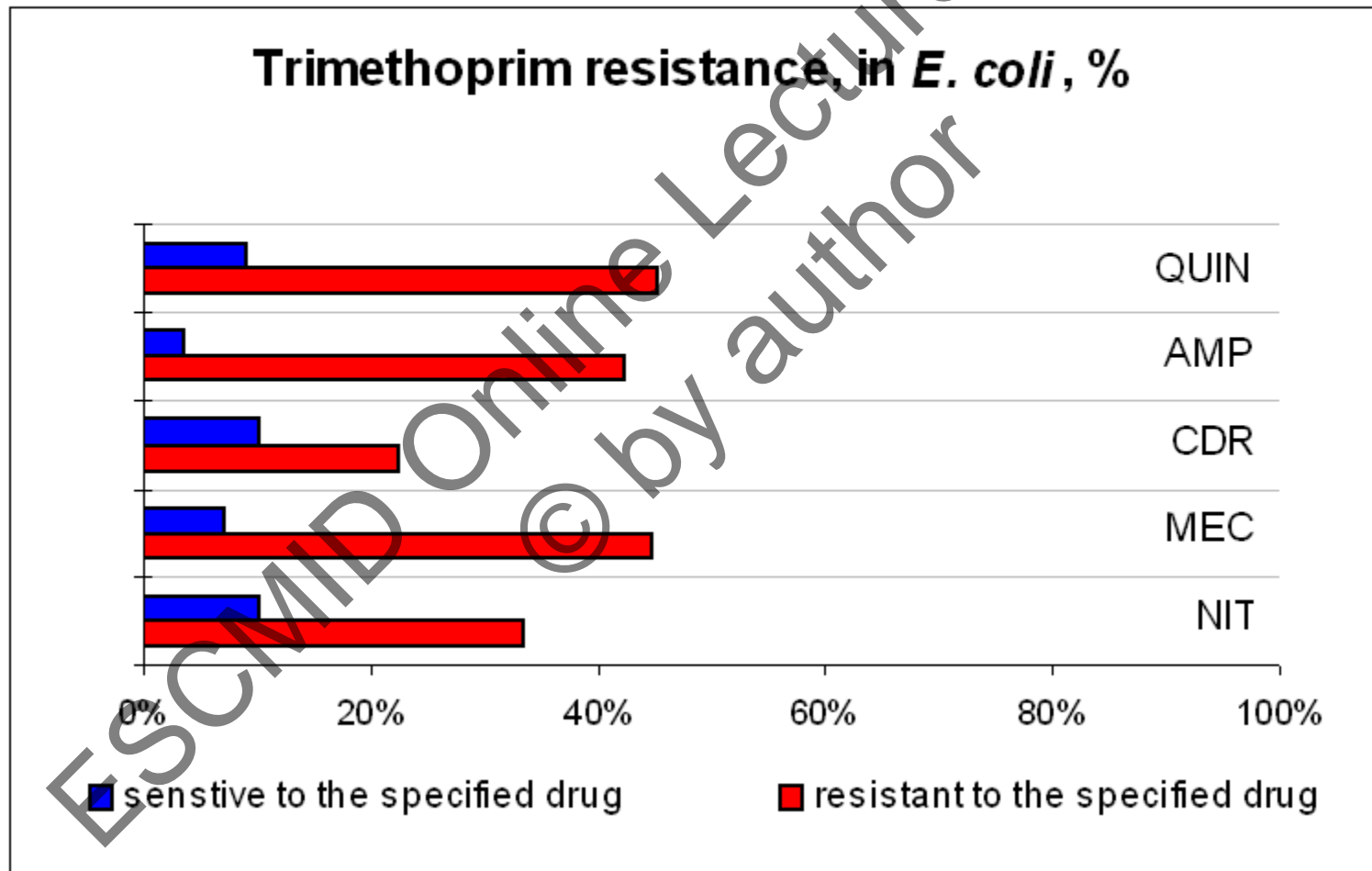
1. Breakpoints
2. Associated resistance
3. "Repeat isolates from a single patient" – rare resistance
4. "Repeat isolates from several patients" – clonal outbreak
5. Frequency of sampling
6. Origin of patients
 - i. International influence/local strains
 - ii. suburban/countryside,
 - iii. ICU/hospital/primary care
7. Age
8. Gender

Examples of bias:

ESCMID Online Lecture Library
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Associerad resistens

E. coli



Associated resistance: Resistance rates resulting from independent susceptibility tests are lower than those obtained through an algorithm (see cefotaxime; all tests 8.8%, independent tests 5.3%).

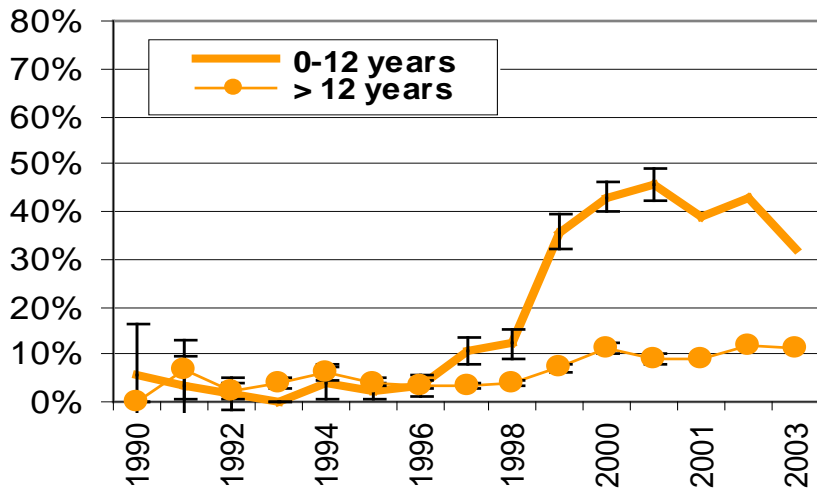
Summering

| Registreringar | |
|------------------------|--|
| Översikt | |
| Grunddata | |
| Laboratorier | |
| Antibiotikum | |
| Arter | |
| Personliga filter | |
| Ursprung | |
| Provtyp | |
| Analys | |
| EW-filter | |
| Synonym antibiotika | |
| Synonym art | |
| Synonym provtyp | |
| Synonym analys | |
| Ignorerade arter | |
| Ignorerade antibiotika | |
| Ignorerade provtyper | |
| Ignorerade analyser | |
| Administration | |

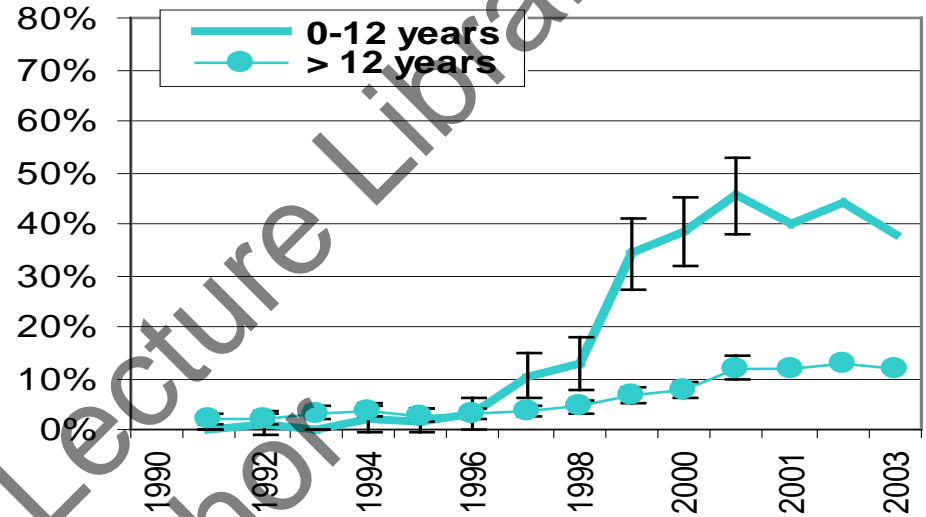
| | | | |
|--------------|------------------|----------------------|------|
| Art | ESCHERICHIA COLI | | |
| Lab | N/A | Regår Fr.o.m. | 2001 |
| Kön | N/A | Regår T.o.m | 2011 |
| | | Födår Fr.o.m. | N/A |
| Antal | 20542 | Födår T.o.m. | N/A |

| Antibiotikum | Totalt | S % | I % | R % | Prim=1 | S % | I % | R % |
|-------------------------|--------|------|------|------|--------|------|------|------|
| AMIKACIN | 5 | 100 | 0 | 0 | 0 | ? | ? | ? |
| AMOXICILLIN | 8 | 25 | 0 | 75 | 0 | ? | ? | ? |
| AMOXICILLINCLAVULANSYRA | 1 | 100 | 0 | 0 | 0 | ? | ? | ? |
| AMPICILLIN | 7 473 | 44,8 | 26,7 | 28,5 | 5 837 | 45,3 | 27,2 | 27,5 |
| AZTRÉONAM | 206 | 19,4 | 4,9 | 75,7 | 93 | 17,2 | 5,4 | 77,4 |
| CEFADROXIL | 20 688 | 66,7 | 29,9 | 3,4 | 13 882 | 70,3 | 26,8 | 2,9 |
| CEFEPIM | 206 | 36,4 | 2,4 | 61,2 | 93 | 33,3 | 1,1 | 65,6 |
| CEFOTAXIM | 7 055 | 90,6 | 0,6 | 8,8 | 5 119 | 94,5 | 0,3 | 5,3 |
| CEFOXITIN | 117 | 35,9 | 0 | 64,1 | 0 | ? | ? | ? |
| CEFPODOXIM | 137 | 7,3 | 0 | 92,7 | 8 | 12,5 | 0 | 87,5 |
| CEFTAZIDIM | 8 628 | 92,3 | 1,6 | 6,2 | 5 847 | 94,9 | 1 | 4,1 |
| CEFTIBUTEN | 12 547 | 98,5 | 0,1 | 1,4 | 9 449 | 98,7 | 0,1 | 1,2 |
| CEFUROXIM | 159 | 79,9 | 0 | 20,1 | 21 | 95,2 | 0 | 4,8 |
| CIPROFLOXACIN | 20 138 | 90 | 0,1 | 9,9 | 13 719 | 90,6 | 0,1 | 9,4 |
| COLISTIN | 1 | 100 | 0 | 0 | 0 | ? | ? | ? |
| DOXYCYKLIN | 1 | 0 | 0 | 100 | 0 | ? | ? | ? |
| ERTAPENEM | 108 | 98,1 | 0 | 1,9 | 3 | 100 | 0 | 0 |
| FOSFOMYCIN | 140 | 95 | 0 | 5 | 3 | 66,7 | 0 | 33,3 |
| FUSIDINSYRA | 1 | 0 | 0 | 100 | 0 | ? | ? | ? |
| GENTAMICIN | 1 854 | 91,2 | 0,4 | 8,5 | 179 | 91,6 | 1,1 | 7,3 |
| IMIPENEM | 587 | 99,8 | 0 | 0,2 | 57 | 100 | 0 | 0 |

Skåne county, Sweden

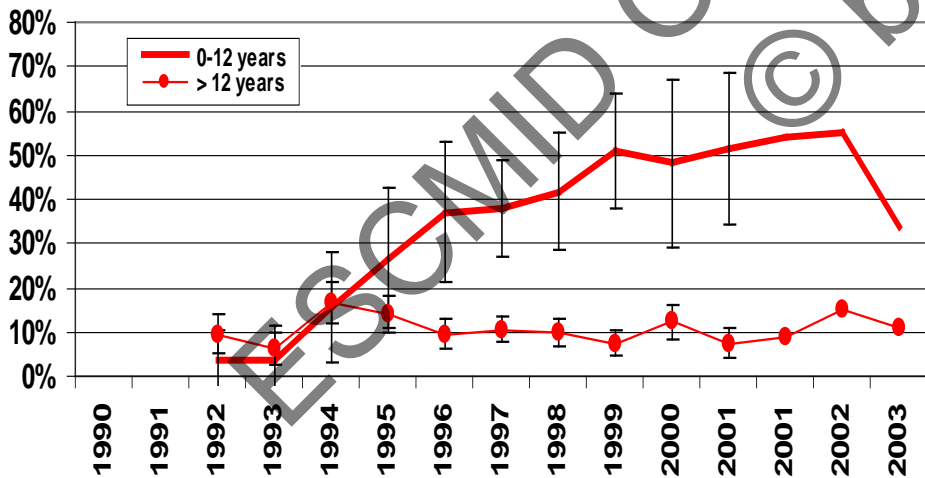


Västra Götaland county, Sweden

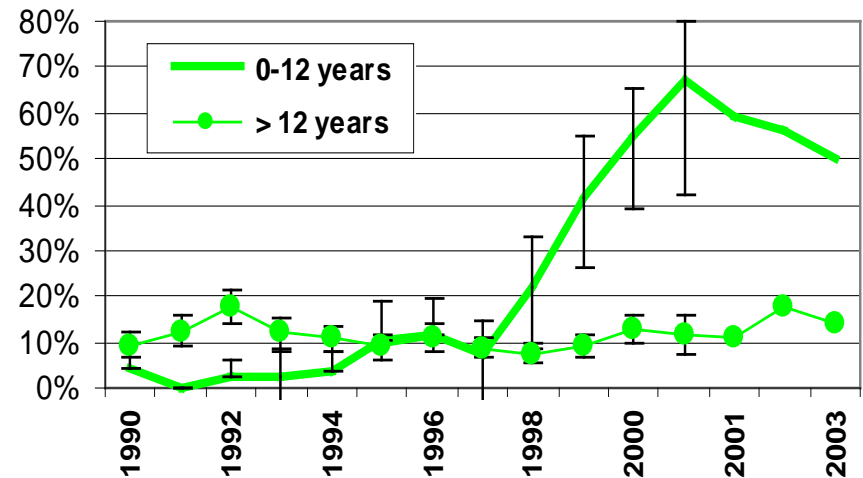


Fusidic acid resistance in S.aureus in children (0 – 12 yrs) and in adults (>12 yrs)

Blekinge county, Sweden



Kronoberg county, Sweden



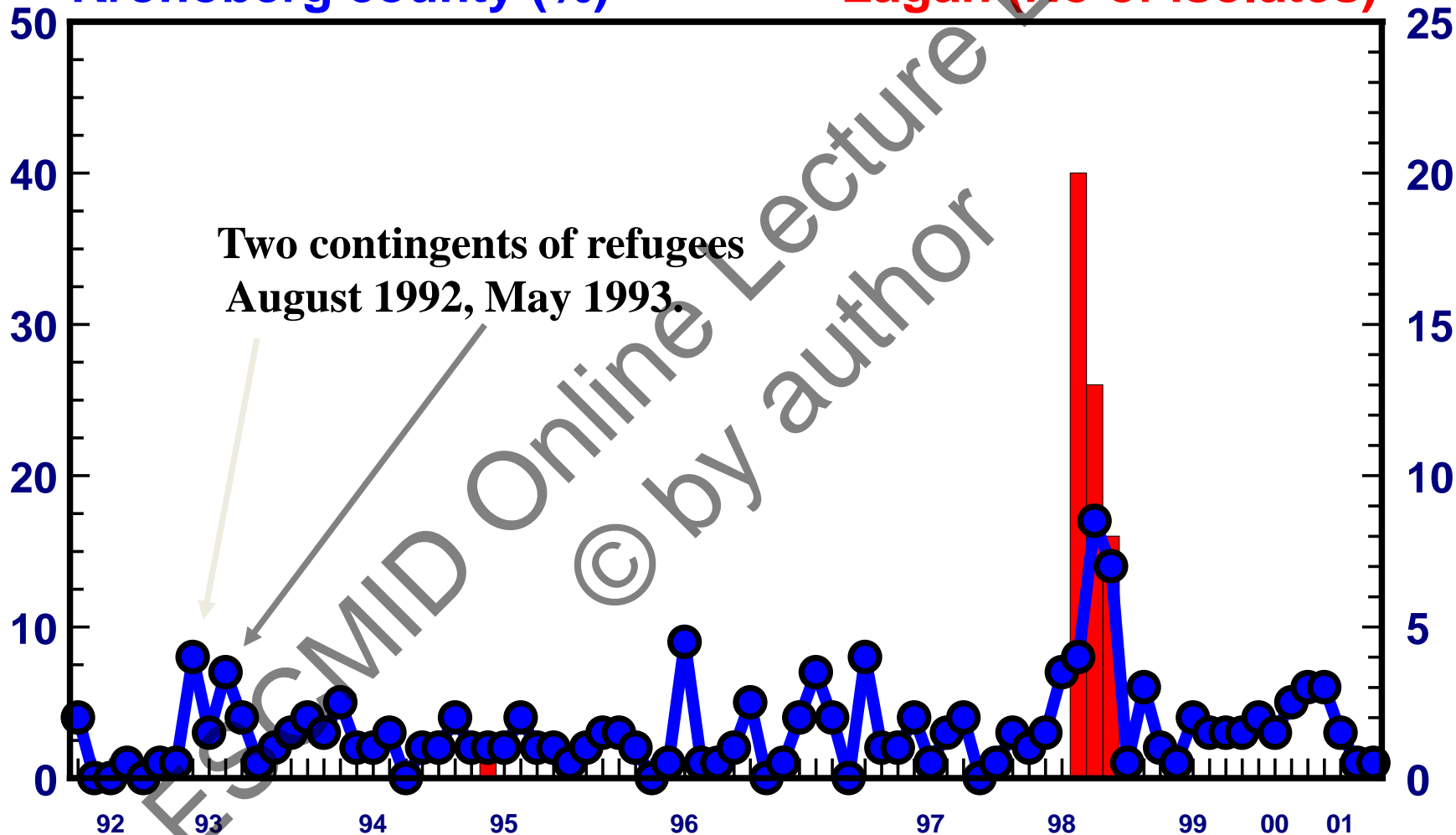
Penicillin non-susceptibility over time in a county in Sweden

Streptococcus pneumoniae

Penicillin MIC >0.125 mg/L

Kronoberg county (%)

Lagan (No of isolates)

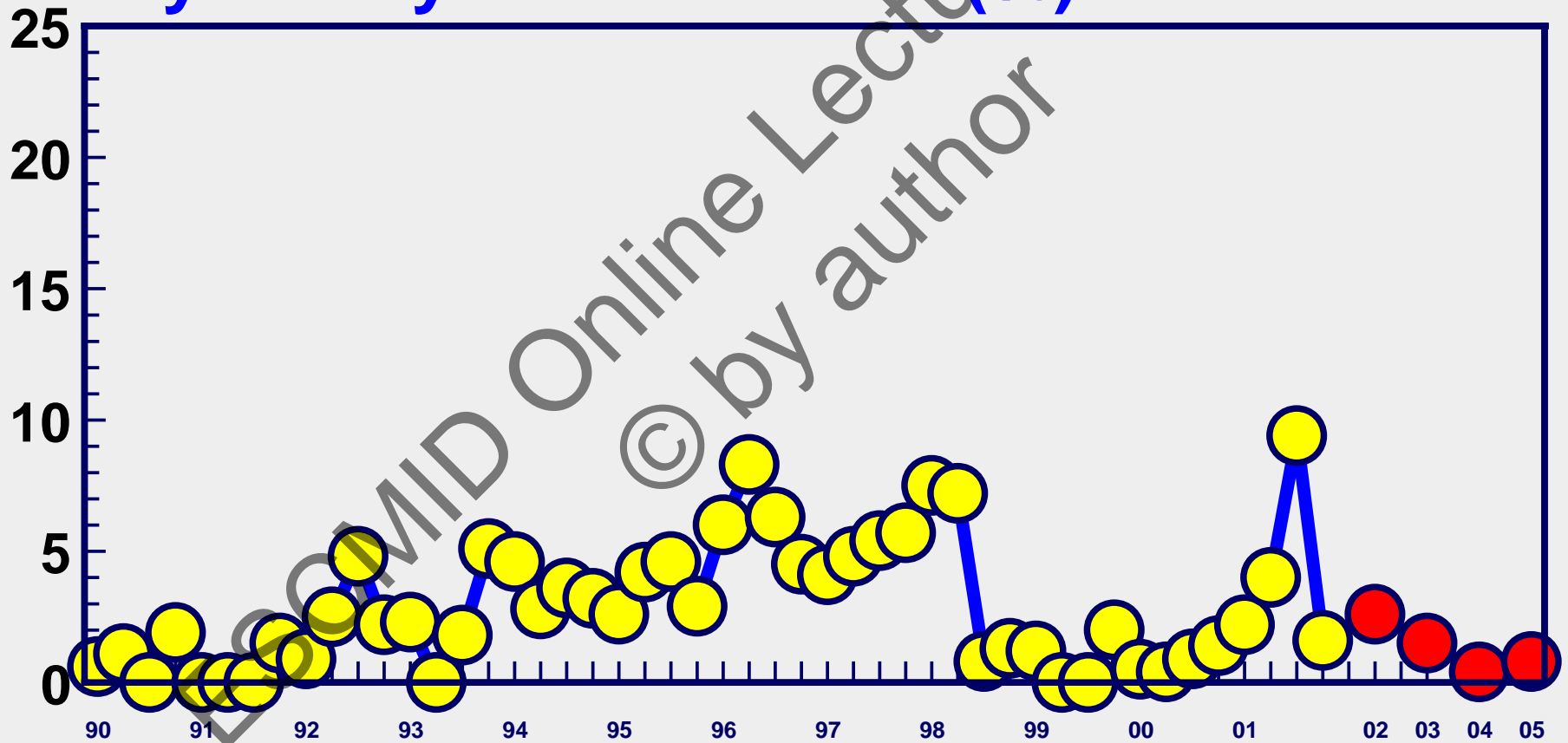


Streptococcus pyogenes

Quarterly and yearly (red) rates
Kronoberg county, Sweden

Events (unrelated to the use of the drug) may affect resistance

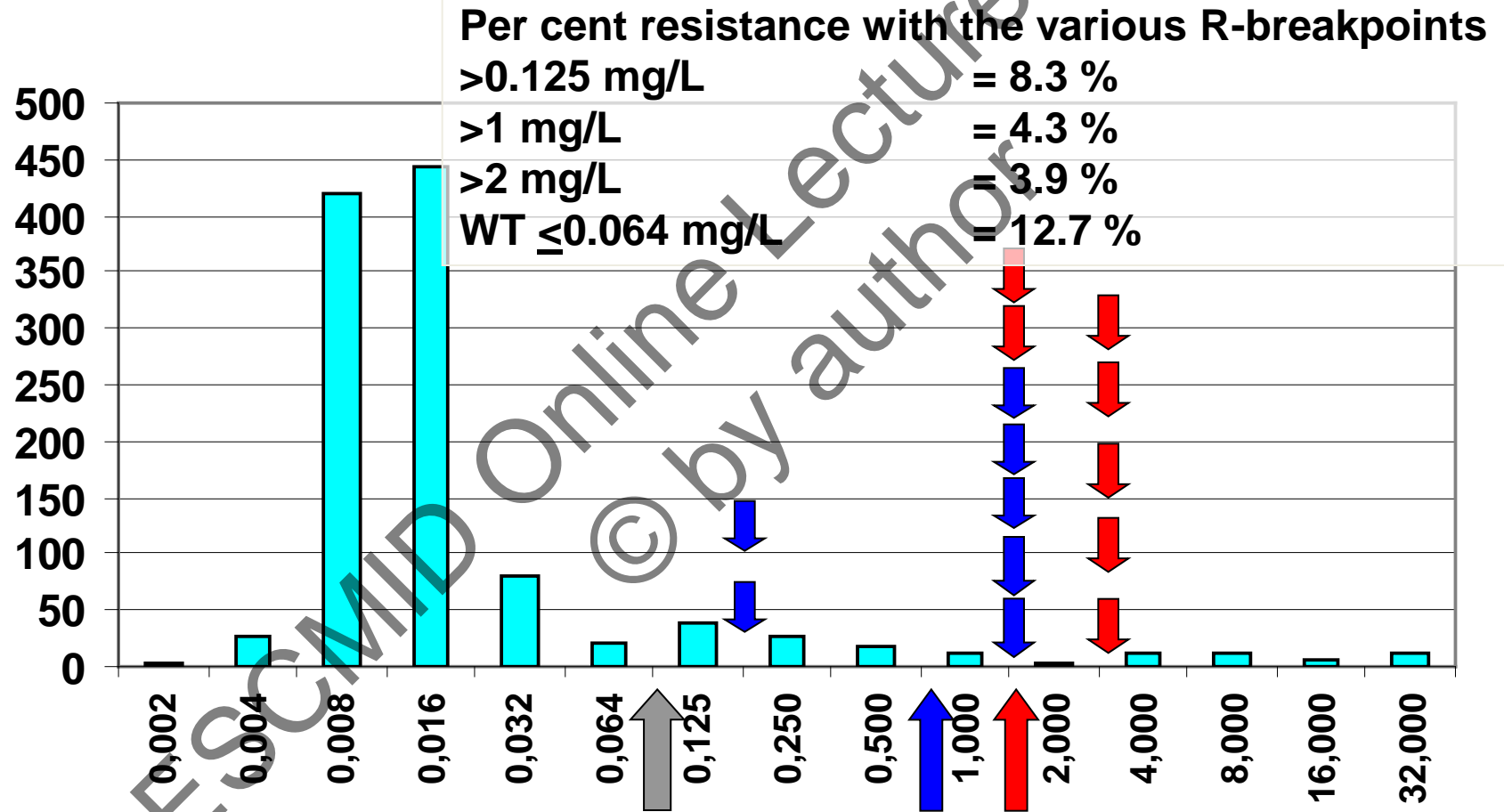
Erythromycin resistance (%)



Breakpoints obviously affect resistance levels

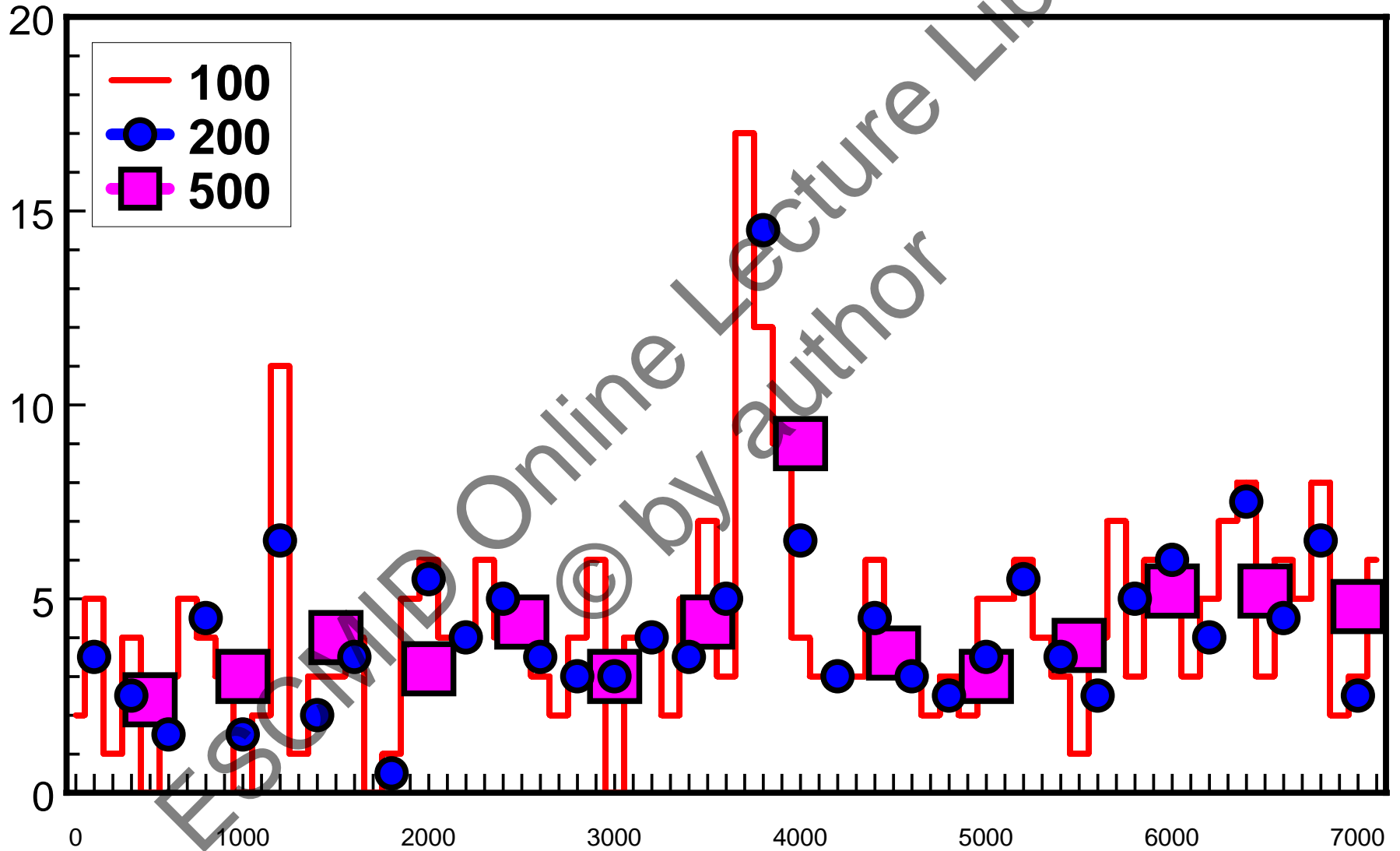
E.coli vs. Ciprofloxacin in EARSS 2002

EARSS data from Germany and Sweden

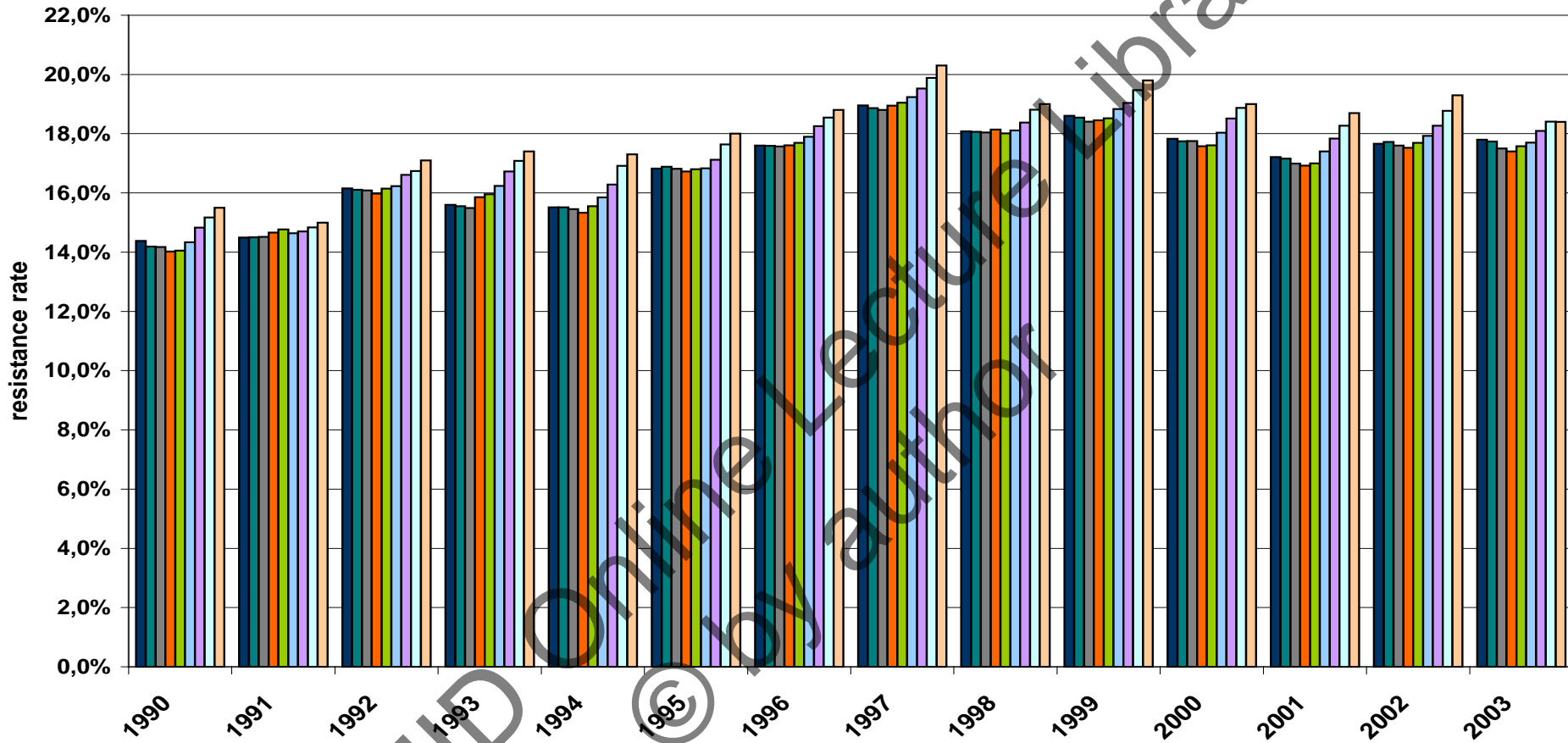


S.pneumoniae vs. penicillin 1995 - 2006

Resistance rates based on 100, 200 and 500 consecutive clinical isolates.



E. coli vs ampicillin



Effect on ampicillin resistance rate in community isolates of *E. coli* of different time cut-offs for the exclusion of duplicate isolates. Bars in the following order: No exclusion, Exclusion algorithm 7, 14, 30, 45, 90, 180, 270 and 365 days.

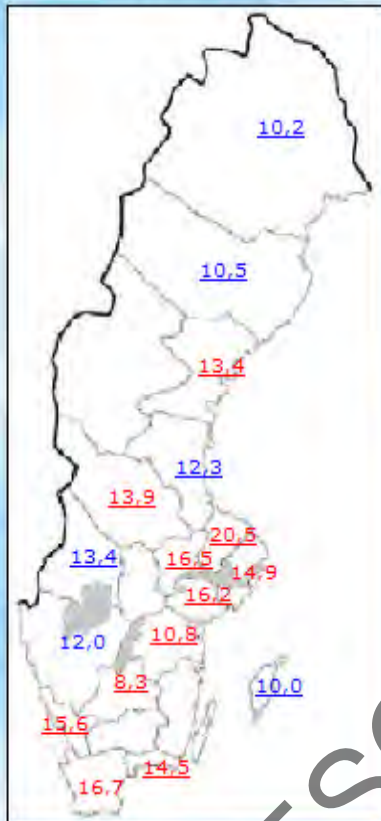
ResNet 2009; E.coli, Nalidixinsyra (090504)



[Meny](#) [Logga ut](#)

13,6% R

Andel resistenta - Sverige

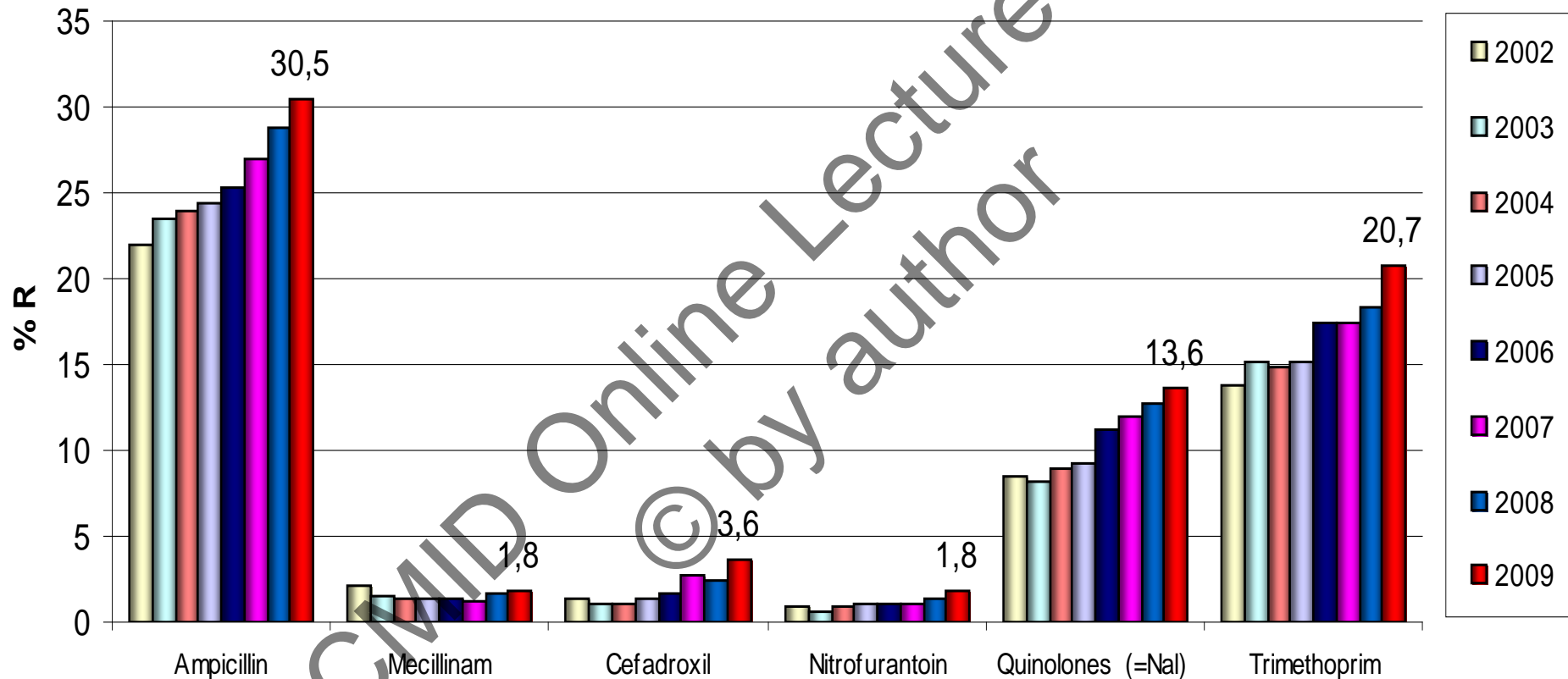


| Län | Andel resistenta | Län | Andel resistenta |
|------------------------|------------------|----------------------------|------------------|
| Blekinge | 14,5 (13,6) | - Medilab | 18,5 (13,6) |
| Dalarna | 13,9 (13,6) | - St Göran Nova Medical AB | - |
| Gotlands | 10,0 (13,6) | - Huddinge sjukhus | 11,8 (13,6) |
| Gävleborg | 12,3 (13,6) | Södermanland | 16,2 (13,6) |
| Halland | 15,6 (13,6) | Uppsala | 20,5 (13,6) |
| Jämtland | - | Värmland | 13,4 (13,6) |
| Jönköping | 8,3 (13,6) | Västerbotten | 10,5 (13,6) |
| Kalmar | - | Västernorrland | 13,4 (13,6) |
| Kronoberg | - | Västmanland | 16,5 (13,6) |
| Norrbottn | 10,2 (13,6) | Västra Götaland | 12,0 |
| Skåne | 16,7 (13,6) | - Borås | 10,5 (13,6) |
| - Lund | 20,1 (13,6) | - Göteborg | 16,5 (13,6) |
| - Kristianstad | - | - Skövde | 8,5 (13,6) |
| - Malmö | 13,3 (13,6) | - Uddevalla | 12,5 (13,6) |
| SMT | - | Örebro | - |
| Stockholm | 14,9 (13,6) | Östergötland | 10,8 (13,6) |
| - Karolinska sjukhuset | 14,4 (13,6) | | |
| Sverige: - | | | |

Art:

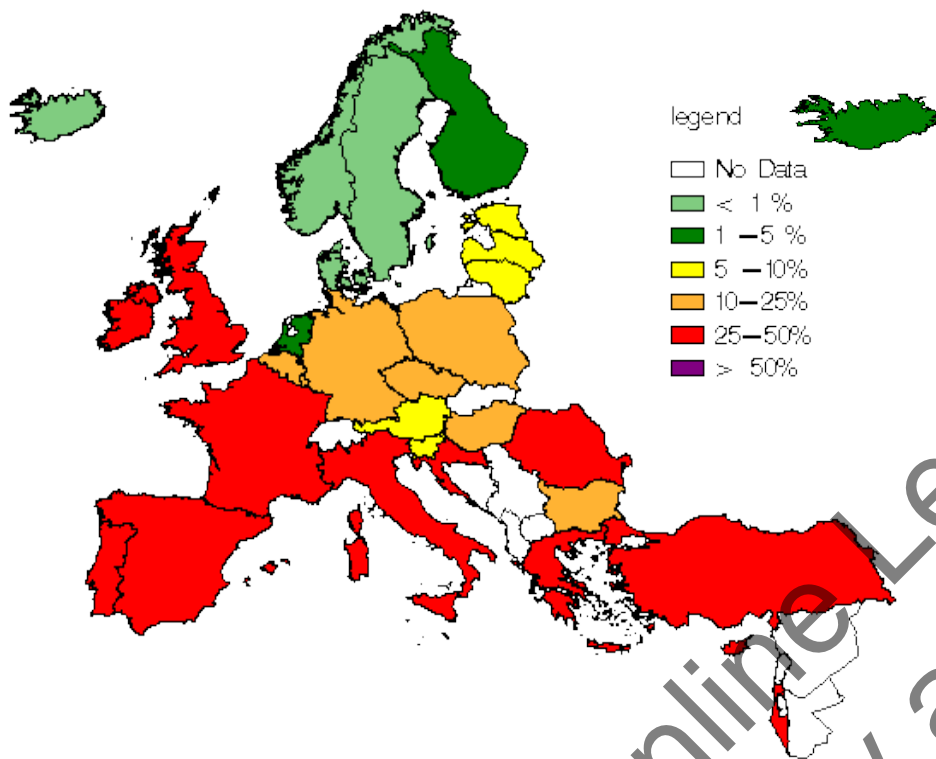
Antibiotikum:

ResNet 2009: E.coli från urin Sweden



Proportion of MRSA isolates in participating countries in 2007

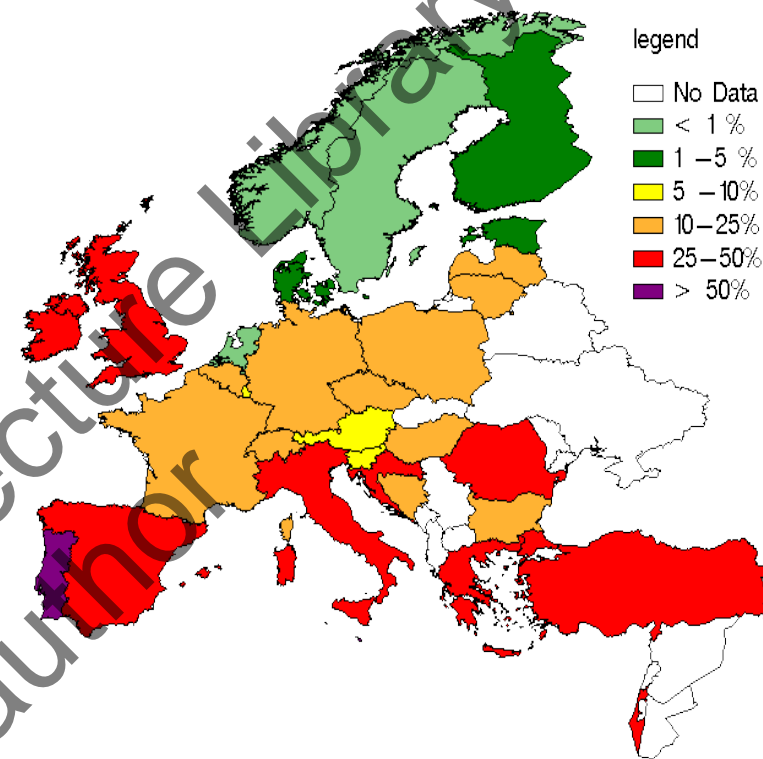
(c) EARSS



MRSA 2007

Proportion of MRSA isolates in participating countries in 2008

(c) EARSS



MRSA 2008

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Highlights of EARS-Net Annual Report 2009

Courtesy of Ole Heuer and the EARS-NET team

ECDC

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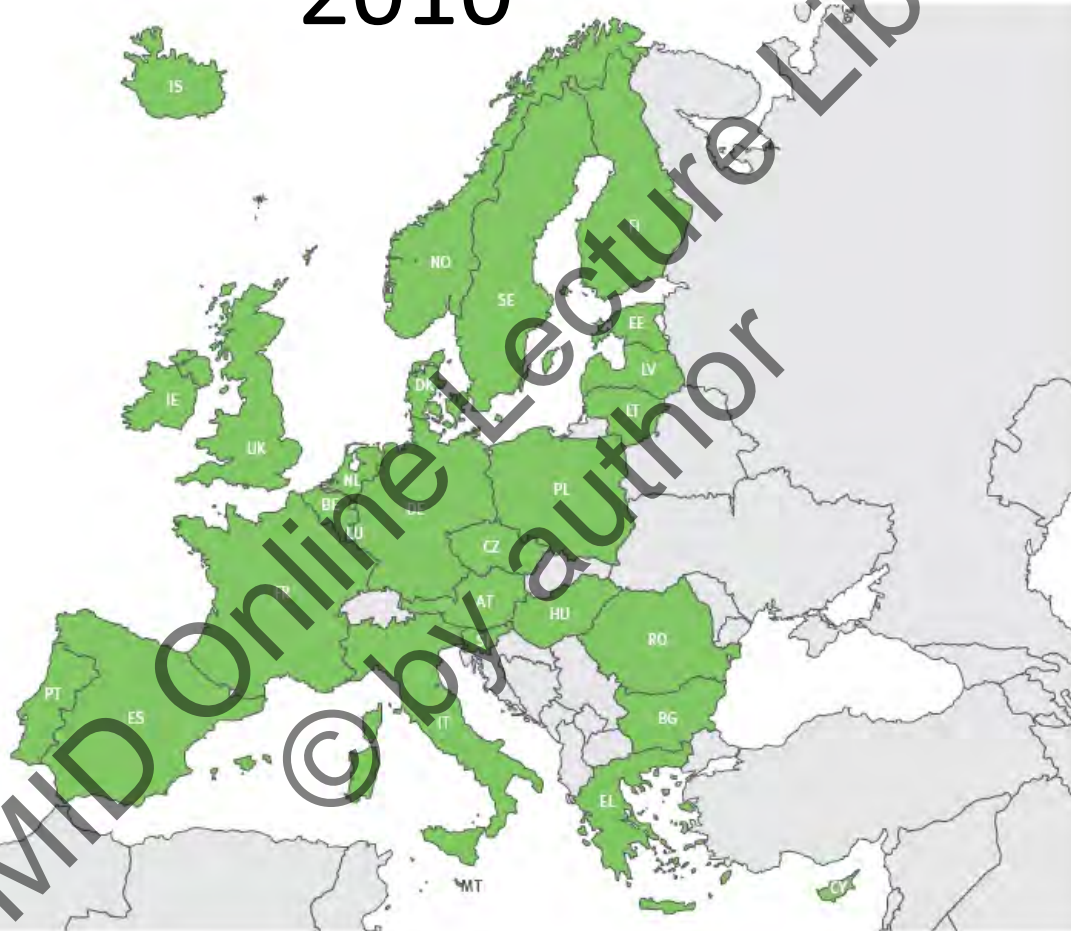
Pathogens in EARS-NET

- S. aureus
- E. coli
- K. pneumoniae
- P. aeruginosa
- E. faecalis and E. fecium
- S. pneumoniae

In blood and CSF

Countries participating in EARS-Net in 2010

■ Participating countries
■ Non participating countries



As of January 1st, 2010, five non-EU Member States previously participating in EARSS (Bosnia-Herzegovina, Croatia, Israel, Switzerland and Turkey) had to be detached from the network.

EARS-Net Annual Report 2009

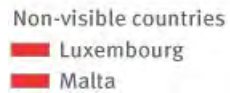
The EARS-Net Annual report 2009 (pdf) is available at the ECDC homepage: <http://ecdc.europa.eu/en/Pages/home.aspx>

The report can be found under “recent publications”.

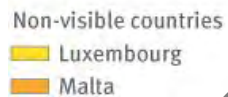


direct link:

http://www.ecdc.europa.eu/en/publications/Publications/1011_SUR_annual_EARSS_report.pdf



***Escherichia coli*: Proportion of invasive isolates with resistance to fluoroquinolones in 2009 (data: EARS-Net)**



***Escherichia coli*: Proportion of third generation cephalosporin resistance in 2009 (Data: EARS-Net)**

ESBL in *E. coli* and *K. pneumoniae*

Table 5.6: Number of invasive *E. coli* isolates resistant to third-generation cephalosporins (CREC) and proportion of ESBL positive among these isolates, as ascertained by the participating laboratories in 2009

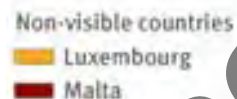
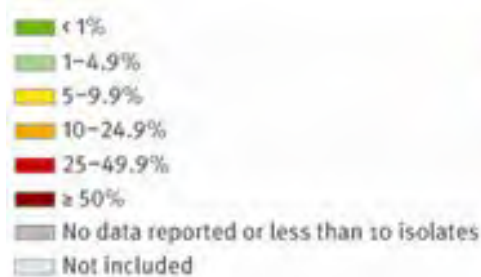
| Country | Number of laboratories | Number of CREC | %ESBL |
|----------------|------------------------|----------------|-------|
| Austria | 24 | 86 | 94.2 |
| Belgium | 4 | 14 | 92.9 |
| Bulgaria | 12 | 37 | 94.6 |
| Cyprus | 5 | 19 | 100 |
| Czech Republic | 42 | 270 | 85.6 |
| France | 38 | 316 | 64.9 |
| Ireland | 25 | 117 | 85.5 |
| Lithuania | 8 | 23 | 100 |
| Netherlands | 6 | 40 | 90 |
| Poland | 16 | 53 | 89 |
| Portugal | 15 | 122 | 91.8 |
| Slovenia | 7 | 52 | 92.3 |
| Spain | 33 | 432 | 90.7 |

Only data from laboratories consistently reporting the ESBL test results for all isolates identified as resistant to third-generation cephalosporins and from countries with at least 10 of such isolates were selected for the analysis.

Table 5.9: Number of invasive *K. pneumoniae* isolates resistant to third-generation cephalosporins (CRKP) and proportion of ESBL positive among these isolates, as ascertained by the participating laboratories in 2009

| Country | Number of laboratories | Number of CRKP | %ESBL |
|----------------|------------------------|----------------|-------|
| Austria | 16 | 40 | 87.5 |
| Bulgaria | 10 | 66 | 98.5 |
| Cyprus | 4 | 22 | 86.4 |
| Czech Republic | 44 | 737 | 79.9 |
| Estonia | 4 | 10 | 100 |
| Spain | 20 | 70 | 85.7 |
| France | 27 | 89 | 80.9 |
| Ireland | 12 | 32 | 78.1 |
| Italy | 7 | 47 | 91.5 |
| Lithuania | 9 | 38 | 97.4 |
| Latvia | 5 | 17 | 94.1 |
| Netherlands | 4 | 11 | 72.7 |
| Poland | 12 | 70 | 92.9 |
| Portugal | 11 | 92 | 90.2 |
| Romania | 3 | 10 | 100 |
| Slovenia | 7 | 57 | 96.5 |

Only data from laboratories consistently reporting ESBL test results for all isolates identified as resistant to third-generation cephalosporins and from countries with at least 10 of such isolates were selected for the analysis.



***Staphylococcus aureus*:**
 proportion of invasive isolates resistant to meticillin (MRSA) in 2009 (Data: EARS-Net)