ECDC initiatives on surveillance, prevention and control of antimicrobial resistance

Dominique L. Monnet, on behalf of ECDC Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) Programme
Madrid, 10 November 2015
Antimicrobial resistance (AMR): what does it mean?

Several, inter-related compartments of healthcare, i.e. patients in primary care, hospitals, nursing homes and long-term care facilities, food animals, food, environment)

Many types of infection, i.e. respiratory tract, urinary tract, skin and soft tissue, bloodstream, surgical site, related to medical devices, etc.)

Many bacteria/microorganisms

Many antimicrobials

Many different genes and mechanisms of resistance

Spread of clones...

... and of resistance genes between bacteria...
Patients with infections due to antimicrobial-resistant bacteria

ECDC PPS in European acute care hospitals, 2011-2012: comparing with other risks

Healthcare-associated infections: on a given day, 1 /18 patients (point prevalence survey, EU/EEA, 2011-2012)

An agency of the European Union, located in Stockholm, Sweden
Founded in 2005; nearly 300 employees in 2015
Mandate to ‘identify, assess and communicate current and emerging threats to human health from communicable diseases’
European Union (EU) (28) and European Economic Area (EEA) (3) = 31 countries with a total of more than 500 million people
Antimicrobial Resistance and Healthcare-associated Infections Programme

The programme on Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) covers two major public health issues:

- **Antimicrobial Resistance (AMR)**, i.e. the ability of microorganisms to become resistant to one or several antimicrobial agents used for therapy or prophylaxis;
- **Healthcare-Associated Infections (HAI)**, i.e. all infections associated with patient care, in particular hospitals and long-term care facilities.

The ARHAI programme focuses on 4 areas of public health: surveillance, response and scientific advice, training and communication to address the threat of antimicrobial resistance and healthcare-associated infections.

Read more about the programme

**IN FOCUS**

ECDC, EFSA and EMA publish the first integrated analysis of antimicrobial consumption and resistance data from humans and animals

For the first time, the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals in Europe were analysed in an integrated manner by three EU agencies: the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA).
Staphylococcus aureus: percentage of invasive isolates resistant to meticillin (MRSA); EU/EEA, 2013

Source: EARS-Net, 2014

The symbols \( \uparrow \) and \( \downarrow \) indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.
**Staphylococcus aureus**: percentage of invasive isolates resistant to meticillin (MRSA), selected EU/EEA countries, 2000-2013

Source: EARS-Net, 2014
**Escherichia coli:** percentage of invasive isolates resistant to third-generation cephalosporins; EU/EEA, 2013

The symbols ⬆️ and ⬇️ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.
Klebsiella pneumoniae: percentage of invasive isolates with combined resistance*; EU/EEA, 2013

*Combined resistance: resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides

Source: EARS-Net, 2014

The symbols † and ‡ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.
Klebsiella pneumoniae: percentage of invasive isolates resistant to carbapenems; EU/EEA, 2013

The symbols † and ‡ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.

Source: EARS-Net, 2014

The symbols `↑` and `↓` indicate a positive or negative change in stage between 2010 and 2013. This change could only be indicated for countries that reported for both years.


©Flickr - mardrom1

EuSCAPE post-survey: 12 Nov. 2015
ECDC risk assessment on the spread of carbapenemase-producing *Enterobacteriaceae*: risk factors for patient infection or colonisation

- **Prior use of antimicrobials**
  - Any antimicrobial
  - **Carbapenems** (associated with a high risk estimate)
  - Other antimicrobials (fluoroquinolones, cephalosporins, anti-pseudomonal penicillins, metronidazole)

- **Cross-border transfer of patients**
  - Strong evidence that it is associated with risk for transmission when:
    - Patients are transferred from countries with high rates of CPE to healthcare facilities in other countries
    - Patients had received medical care abroad in areas with high rates of CPE

- **Transfer of patients within units of same hospital**
  - Immunosuppression, severity of illness, invasive procedures

Antimicrobial use in EU/EEA hospitals

Prevalence of antimicrobial use in acute care hospitals (ECDC PPS)
On any given day in EU/EEA hospitals 33% patients [range: 21-55%]

Antibiotic consumption in the hospital sector
(DDD per 1,000 inhabitants per day, ESAC-Net)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, antibiotics (J01)</td>
<td><img src="image" alt="Graph" /></td>
<td>-0.02</td>
<td>n.s.</td>
</tr>
<tr>
<td>Carbapenems (J01DH)</td>
<td><img src="image" alt="Graph" /></td>
<td>0.003</td>
<td>significant</td>
</tr>
<tr>
<td>Polymyxins (J01XB)</td>
<td><img src="image" alt="Graph" /></td>
<td>0.002</td>
<td>significant</td>
</tr>
</tbody>
</table>

Klebsiella pneumoniae: % of invasive isolates with resistance to all antibiotic groups under surveillance*, EU/EEA, 2013

*Third-generation cephalosporins, fluoroquinolones, aminoglycosides, carbapenems and colistin).

Only among isolates that were tested for susceptibility to all these antibiotic groups were included.

EARS-Net 2014 report: 16 Nov. 2015

Source: EARS-Net, 2014
Outbreak of pandrug-resistant VIM-1
*Providencia stuartii*, Sept.-Nov. 2011

Modern medicine: not possible without effective antibiotics

- Hip / knee replacement
- Organ transplant
- Cancer chemotherapy
- Intensive care
- Care of preterm babies
Main actions to prevent and control antimicrobial resistance (AMR)

New antimicrobial agents
(with a novel mechanism of action, research, development)

Infection prevention and control
(hand hygiene, screening, isolation)

Prudent use of antimicrobial agents
(only when needed, correct dose, correct dose intervals, correct duration)
Hospitals
Availability of national guidance documents on CPE, 2011 & 2013

Infection control measures to prevent the spread of carbapenemase-producing *Enterobacteriaceae* (CPE) through cross-border transfer of patients

Scientific evidence for the effectiveness of:

- Hand hygiene, patient isolation, patient cohorting, nursing (or staff) cohorting (similar to dedicated nursing), environmental cleaning, staff education, case notification/flagging, contact tracing and antibiotic restriction

- Early implementation of active surveillance by rectal screening for CPE carriage upon admission to hospital, or specific wards/units, or during outbreaks

- Pre-emptive isolation on admission, dedicated nursing or other types of dedicated care by staff members, contact precautions (gloves and gowns)

CRE: Guidance on infection prevention and control

Directory of guidance on prevention and control of Carbapenem-resistant Enterobacteriaceae, published by ECDC, EU/EEA Member States, international and national agencies and professional societies

AGENCIES

EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL (ECDC)

- Systematic review of the effectiveness of infection control measures to prevent the transmission of carbapenem-producing Enterobacteriaceae through cross-border transfer of patients (2014)
- Review assessment of the spread of carbapenem-producing Enterobacteriaceae (CRE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer (2011)

US CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

- CDC 2012 CRE Toolkit: guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

US AGENCY FOR HEALTHCARE RESEARCH AND QUALITY (AHRQ)

- Carbapenem-resistant Enterobacteriaceae (CRE) Control and Prevention Toolkit

PROFESSIONAL SOCIETIES

EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIONS DISEASES (ESCMID)

- Supportive care and control of susceptible carbapenem-resistant Enterobacteriaceae (CPE) in healthcare settings (2014)
- ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalised patients

MEMBER STATES

AUSTRIA

Control of carbapenem-resistant-producing Enterobacteriaceae in Austria (Ministry of Health, 2015)

CZECH REPUBLIC

Control of carbapenem-resistant-producing Enterobacteriaceae in the Czech Republic (Ministry of Health, 2015)

FINLAND

Guidelines for the treatment of infections by multidrug-resistant bacteria. This document includes guidance for infection prevention and control of carbapenem-resistant Enterobacteriaceae (Finland, 2016)

FRANCE

Prevention of cross-transmission of emerging highly resistant bacteria. This document includes guidance targeting carbapenem-producing Enterobacteriaceae (Ministère de la Santé, France, 2015)

GERMANY

Infection control measures for infections or contamination by multidrug-resistant Gram-negative bacteria. This document applies to carbapenem-resistant Enterobacteriaceae (Robert Koch Institute, Commission for Hospital Hygiene and Infection Prevention, 2012)

Directory of online resources for prevention and control of antimicrobial resistance (AMR) and healthcare-associated infections (HAI)

The directory lists strategies, action plans and guidance documents on the prevention and control of antimicrobial resistance and healthcare-associated infections, which are available online.

These documents were published by ECDC, EU/EEA Member States, international and national agencies and professional societies to support healthcare professionals, hospital administrators and public health professionals.

In addition, the directory now also lists ongoing research projects and their corresponding websites.

**ECDC welcomes suggestions and further information on existing guidance. Comments can be provided to: arhai@ecdc.europa.eu.**

<table>
<thead>
<tr>
<th>Strategies, action plans and projects on AMR and HAI</th>
<th>Prevention and control of multidrug-resistant organisms and <em>Clostridium difficile</em></th>
<th>Prevention and control of healthcare-associated infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial resistance strategies and action plans</td>
<td>Carbapenem-resistant Enterobacteriaceae (CRE)</td>
<td>Organisation of infection prevention and control</td>
</tr>
<tr>
<td><strong>WHO “SAVE LIVES: Clean Your Hands”: 2015</strong></td>
<td>Meticillin-resistant <em>Staphylococcus aureus</em> (MRSA)</td>
<td>Hand hygiene in healthcare</td>
</tr>
<tr>
<td></td>
<td>Clostridium difficile (CDI)</td>
<td>Healthcare-associated and ventilator-associated pneumonia</td>
</tr>
</tbody>
</table>
Country visits to discuss antimicrobial resistance (AMR) issues, 2006-2015

- Based on Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC)
- Reports (observations, conclusions, suggestions, examples of best practice)
- 19 initial visits (see map)
- 5 follow-up visits (Czech Rep., Greece x 2 and Hungary x 2)
- **3 additional visits budgeted for 2016**
Core competencies for infection control and hospital hygiene professionals

- **2 levels**
  - Introductory (junior specialist)
  - Expert (senior specialist)

- **4 areas**
  - Programme management
  - Quality improvement
  - Surveillance of healthcare-associated infections and investigation of outbreaks
  - Infection control activities

- **16 domains**

ECDC PPS in European acute care hospitals, 2011-2012: structure and process indicators

- Alcohol hand rub consumption
- Beds in single rooms
- Infection prevention and control staff (nurses, doctors)

Alcohol hand rub consumption

Percentage of beds in single rooms

Hospital-wide indicators of infection prevention and control

Hospital organisation, management, and structure for prevention of health-care-associated infection: a systematic review and expert consensus

Walter Zingg, Alison Holmes, Markus Dettenkofer, Tim Goetting, Federica Secci, Lauren Clack, Benedetta Allegranzi, Anna-Pelagia Magiorakos, Didier Pittet, for the systematic review and evidence-based guidance on organization of hospital infection control programmes (SIGHT) study group*

Despite control efforts, the burden of health-care-associated infections in Europe is high and leads to around 37,000 deaths each year. We did a systematic review to identify crucial elements for the organisation of effective infection-prevention programmes in hospitals and key components for implementation of monitoring. 92 studies published from 1996 to 2012 were assessed and ten key components identified: organisation of infection control at the hospital level; bed occupancy, staffing, workload, and employment of pool or agency nurses; availability of and ease of access to materials and equipment and optimum ergonomics; appropriate use of guidelines; education and training; auditing; surveillance and feedback; multimodal and multidisciplinary prevention programmes that include behavioural change; engagement of champions; and positive organisational culture. These components comprise manageable and widely applicable ways to reduce health-care-associated infections and improve patients’ safety.

- Systematic review & expert opinion
  => 10 key components and proposed indicators

Indicators for hospital antimicrobial stewardship programmes

- **3 domains:**
  - infrastructure
  - policy and practice
  - monitoring and feedback

- **17 “core” indicators** essential to fully characterise all aspects of antimicrobial stewardship programmes

- **16 “supplemental” indicators**

---

<table>
<thead>
<tr>
<th>CORE Indicators for hospital antimicrobial stewardship programs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infrastructure</strong></td>
</tr>
<tr>
<td>1. Does your facility have a formal antimicrobial stewardship programme accountable for ensuring appropriate antimicrobial use?</td>
</tr>
<tr>
<td>2. Does your facility have a formal organizational structure responsible for antimicrobial stewardship (e.g., a multidisciplinary committee focused on appropriate antimicrobial use, pharmacy committee, patient safety committee or other relevant structure)?</td>
</tr>
<tr>
<td>3. Is an antimicrobial stewardship team available at your facility (e.g., greater than one staff member supporting clinical decisions to ensure appropriate antimicrobial use)?</td>
</tr>
<tr>
<td>4. Is there a physician identified as a leader for antimicrobial stewardship activities at your facility?</td>
</tr>
<tr>
<td>5. Is there a pharmacist responsible for ensuring appropriate antimicrobial use at your facility?</td>
</tr>
<tr>
<td>6. Does your facility provide any salary support for dedicated time for antimicrobial stewardship activities (e.g., percentage of full-time equivalent (FTE) for ensuring appropriate antimicrobial use)?</td>
</tr>
<tr>
<td>7. Does your facility have the IT capability to support the needs of the antimicrobial stewardship activities?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Policy and Practice</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Does your facility have facility-specific treatment recommendations based on local antimicrobial susceptibility to assist with antimicrobial selection for common clinical conditions?</td>
</tr>
<tr>
<td>9. Does your facility have a written policy that requires prescribers to document an indication in the medical record or during order entry for all antimicrobial prescriptions?</td>
</tr>
<tr>
<td>10. Is it routine practice for specified antimicrobial agents to be approved by a physician or pharmacist in your facility (e.g., pre-authorization)?</td>
</tr>
<tr>
<td>11. Is there a formal procedure for a physician, pharmacist, or other staff member to review the appropriateness of an antimicrobial at or after 48 hours from the initial order (post-prescription review)?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Monitoring and Feedback</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>12. Has your facility produced a cumulative antimicrobial susceptibility report in the past year?</td>
</tr>
<tr>
<td>13. Does your facility monitor if the indication is captured in the medical record for all antimicrobial prescriptions?</td>
</tr>
<tr>
<td>14. Does your facility audit or review surgical antimicrobial prophylaxis choice and duration?</td>
</tr>
<tr>
<td>15. Are results of antimicrobial audits or reviews communicated directly with prescribers?</td>
</tr>
<tr>
<td>16. Does your facility monitor antimicrobial use by grams (Defined Daily Dose [DDD]) or counts (Days of Therapy [DOT]) of antimicrobial(s) by patients per days?</td>
</tr>
<tr>
<td>17. Has an annual report focused on antimicrobial stewardship (summary antimicrobial use and/or practices improvement initiatives) been produced for your facility in the past year?</td>
</tr>
</tbody>
</table>

2nd ECDC point prevalence survey (PPS), 2016-2017 – an integrated approach for surveillance, prevention and control of HAI and AMR in European acute care hospitals

Outcome indicators (HAI, selected MDROs)

Guidance (directory of online resources)

Structure and process indicators (incl. antimicrobial consumption)

Source: ECDC, 2015.
Outpatients
Antibiotics are effective against cold and flu. True or false?

% respondents with correct answer (i.e., “false”): 52% (range: 24 – 77%)

Relationship between antibiotic use and resistance in the community

Carriers of macrolide-resistant streptococci (% volunteers)

Through month 6 (180 days)

Carriage of resistant bacteria following exposure to antibiotics

Streptococcus pneumoniae: percentage of invasive isolates not susceptible to macrolides; EU/EEA, 2013

The symbols $\uparrow$ and $\downarrow$ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.

Source: EARS-Net, 2014
Food animals

Photo: US Dept. of Agriculture
Comparison of biomass-corrected consumption of antimicrobials (milligrams per kilogram estimated biomass) in humans and animals by country in 26 EU/EEA countries in 2012

<table>
<thead>
<tr>
<th>Country</th>
<th>Total consumption in 2012 (expressed in mg/kg of estimated biomass)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In humans</td>
<td>116.4 mg/kg (range: 56.7 – 175.8 mg/kg)</td>
</tr>
<tr>
<td>In animals</td>
<td>144.0 mg/kg (range: 3.8 – 396.5 mg/kg)</td>
</tr>
</tbody>
</table>

Humans + Animals = One Health

Prudent use of antibiotics:
Everyone is responsible!
Uno de cada seis europeos no es consciente de que el mal uso de los antibióticos los hace menos eficaces.

¿Qué es la resistencia a los antibióticos y el uso prudente de los antibióticos? ¿Cómo se utilizan los antibióticos de forma responsable? Ver relatos de los pacientes, infografías y vídeos.

<table>
<thead>
<tr>
<th>Year</th>
<th>Toolkit for the general public</th>
<th>2008</th>
<th>32 countries participated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Toolkit for primary care prescribers</td>
<td>2009</td>
<td>32 countries participated</td>
</tr>
<tr>
<td>2010</td>
<td>Toolkit for hospital prescribers and hospitals</td>
<td>2010</td>
<td>32 countries participated</td>
</tr>
<tr>
<td></td>
<td>Matched Get Smart week in the U.S. and the campaign in Canada</td>
<td></td>
<td>2011 Patient stories and Euronews movie</td>
</tr>
<tr>
<td></td>
<td>Social media guidance</td>
<td></td>
<td>2011 37 countries participated</td>
</tr>
<tr>
<td>2011</td>
<td>Patient stories and Euronews movie</td>
<td>2011</td>
<td>37 countries participated</td>
</tr>
<tr>
<td></td>
<td>Social media guidance</td>
<td></td>
<td>2011 37 countries participated</td>
</tr>
<tr>
<td>2012</td>
<td>Collaboration with WHO/Europe: 43 countries participated</td>
<td>2012</td>
<td>43 countries participated</td>
</tr>
<tr>
<td></td>
<td>First EAAD Twitter chat</td>
<td></td>
<td>2012 First EAAD Twitter chat</td>
</tr>
<tr>
<td></td>
<td>Australia becomes a partner</td>
<td></td>
<td>2012 Australia becomes a partner</td>
</tr>
<tr>
<td>2013</td>
<td>Start work on self-medication with antibiotics, with PGEU and CPME</td>
<td>2013</td>
<td>43 countries participated</td>
</tr>
<tr>
<td></td>
<td>Training module and pilot course</td>
<td></td>
<td>2013 43 countries participated</td>
</tr>
<tr>
<td>2014</td>
<td>Revised toolkit for the general public on self-medication with antibiotics</td>
<td>2014</td>
<td>43 countries participated</td>
</tr>
<tr>
<td></td>
<td>New Zealand becomes a partner</td>
<td></td>
<td>2014 New Zealand becomes a partner</td>
</tr>
<tr>
<td></td>
<td>European Twitter chat</td>
<td></td>
<td>2014 New Zealand becomes a partner</td>
</tr>
<tr>
<td></td>
<td>Global Twitter conversation</td>
<td></td>
<td>2014 New Zealand becomes a partner</td>
</tr>
<tr>
<td>2015</td>
<td>Partner with the first World Antibiotic Awareness Week</td>
<td>2015</td>
<td>43 countries participated</td>
</tr>
</tbody>
</table>

Behaviour of European citizens, 2009-2013: oral antibiotics vs. smoking

Taking antibiotics
(orally, in the last 12 months)

Smoking
(cigarettes, cigars or a pipe)

Antimicrobial consumption drives antimicrobial resistance in hospitals

Implementation of control programme

European Antibiotic Awareness Day: translated materials for hospital prescribers

**Antibióticos: utilízense con precaución**
Prescripción de antibióticos: lista de verificación de cosas que debe recordar

- ¿Se han hecho los cultivos adecuados antes de instaurar el tratamiento antibiótico?
- ¿Exigen los resultados del cultivo iniciar un tratamiento con antibióticos o modificar el tratamiento en uso?
- ¿Cuál es la duración óptima de la antibioterapia para tratar este tipo de infección en este paciente?
- ¿Cuál es la dosis de antibiótico adecuada para tratar este tipo de infección en este paciente?
- ¿Se ajusta la elección del tratamiento antibiótico al perfil de resistencia a los antibióticos de su hospital (antibiograma)?
- ¿Ha consultado con algún especialista en enfermedades infecciosas, microbiólogo o farmacéutico?

**Check list**

**Web banner**

**Screen saver**

Prelevare campioni per le colture prima di iniziare la terapia antibiotica

European Antibiotic Awareness Day  http://antibiotic.ecdc.europa.eu