What is Antimicrobial Resistance (AMR)?

Medicines for treating infections lose effect because the microbes change;
1. mutate
2. acquire genetic information from other microbes to develop resistance

Types of AMR

1. Antibacterial resistance (e.g. to antibiotics and other antibacterial drugs)
2. Antiviral resistance (e.g. to anti-HIV medicines)
3. Antiparasitic resistance (e.g. to anti-malaria medicines)
4. Antifungal resistance (e.g. to medicines used to treat Candidiasis)

AMR is a natural phenomenon accelerated by use of antimicrobial medicines. Resistant strains survive and aggregate.
Antimicrobial Resistance Global Report on Surveillance 2014 (I)

- Focuses on antibacterial resistance (ABR)

- Information gathered include:

  - Surveillance of ABR according to WHO regions
  - National and published data on 7 bacteria
  - Systematic reviews of evidence of health and economic burden in 5 bacteria/resistance combinations
  - Identification of gaps
Antimicrobial Resistance Global Report on Surveillance 2014 (II)

Summaries of surveillance and current resistance situation:

Disease-specific programs
- Tuberculosis
- Malaria
- HIV
- Influenza

Other related areas
- ABR in food-producing animals and food chain
- Antifungal resistance

WHO tools facilitating surveillance of ABR
## Selected Bacteria/Resistance Combinations

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>Resistance/ decreased susceptibility to:</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>3rd generation cephalosporins, fluoroquinolones</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>3rd generation cephalosporins, carbapenems</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Methicillin (beta-lactam antibiotics) i.e. MRSA</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>Penicillin</td>
</tr>
<tr>
<td>Nontyphoidal <em>Salmonella</em> (NTS)</td>
<td>Fluoroquinolones</td>
</tr>
<tr>
<td><em>Shigella</em> species</td>
<td>Fluoroquinolones</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>3rd generation cephalosporins</td>
</tr>
</tbody>
</table>
Data Collection
Resistance Proportions and Surveillance

National official sources > National and international networks of ABR surveillance > Scientific literature

Published from 2008 when no data could be obtained
Available National Data* on Resistance for Nine Selected Bacteria/Antibacterial Drug Combinations, 2013

*National data means data obtained from official sources, but not that data necessarily are representative for the population or country as a whole.
# Bacteria Commonly Causing Infections in Hospitals and Communities

<table>
<thead>
<tr>
<th>Name of bacterium/resistance</th>
<th>Examples of typical diseases</th>
<th>No. of 194 MS providing national data</th>
<th>No. of WHO regions with national reports of 50 % resistance or more</th>
<th>Range of reported proportion of resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>Urinary tract infections, blood stream infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-vs 3rd gen. cephalosporins</td>
<td></td>
<td>84</td>
<td>5/6</td>
<td>0-82</td>
</tr>
<tr>
<td>-vs fluoroquinolones</td>
<td></td>
<td>90</td>
<td>5/6</td>
<td>3-96</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>Pneumonia, blood stream infections, urinary tract infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-vs 3rd gen. cephalosporins</td>
<td></td>
<td>85</td>
<td>6/6</td>
<td>2-82</td>
</tr>
<tr>
<td>-vs carbapenems</td>
<td></td>
<td>69</td>
<td>2/6</td>
<td>0-68</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Wound infections, blood stream infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-vs methicillin “MRSA”</td>
<td></td>
<td>83</td>
<td>5/6</td>
<td>0.3-90</td>
</tr>
</tbody>
</table>
# Bacteria Mainly Causing Infections in the Community

<table>
<thead>
<tr>
<th>Name of bacterium/resistance</th>
<th>Examples of typical diseases</th>
<th>No. of 194 MS providing national data</th>
<th>No. of WHO regions with national reports of 25% resistance or more</th>
<th>Range of reported proportion of resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td>Pneumonia, meningitis, otitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-non-susceptible to penicillin</td>
<td></td>
<td>66</td>
<td>6/6</td>
<td>0-73</td>
</tr>
<tr>
<td><strong>Nontyphoidal Salmonella</strong></td>
<td>Foodborne diarrhoea, blood stream infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-vs fluoroquinolones</td>
<td></td>
<td>66</td>
<td>3/6</td>
<td>0-96</td>
</tr>
<tr>
<td><strong>Shigella species</strong></td>
<td>Diarrhoea (“bacillary dysentery”)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- vs fluoroquinolones</td>
<td></td>
<td>34</td>
<td>2/6</td>
<td>0-47</td>
</tr>
<tr>
<td><strong>Neisseria gonorrhoeae</strong></td>
<td>Gonorrhoea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-vs 3rd gen. cephalosporins</td>
<td></td>
<td>42</td>
<td>3/6</td>
<td>0-36</td>
</tr>
</tbody>
</table>
Neisseria Gonorrhoeae

Detection of decreased susceptibility to 3rd generation cephalosporin and treatment failures up to 2010

*Note: cefixime >0.25μg/L or ceftriaxone >0.125μg/L. The definition of decreased susceptibility to third-generation cephalosporins differs across AMR testing methods. Countries are shaded where there has been any report of decreased susceptibility within their jurisdiction.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization
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Is there any difference in outcome from infections caused by resistant vs sensitive bacteria?
## Risk of Death is Higher in Patients Infected with Resistant Strains

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>Resistance</th>
<th>Outcome (number of studies included)</th>
<th>Deaths (%)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em> resistant to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd gen. cephalosporins</td>
<td></td>
<td>Bacterium attributable mortality (n=4)</td>
<td>23.6</td>
<td>12.6</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
<td>Bacterium attributable mortality (n=1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> resistant to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd gen. cephalosporins</td>
<td></td>
<td>Bacterium attributable mortality (n=4)</td>
<td>20</td>
<td>10.1</td>
</tr>
<tr>
<td>Carbapenems</td>
<td></td>
<td>Bacterium attributable mortality (n=1)</td>
<td>27</td>
<td>13.6</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> resistant to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin (MRSA)</td>
<td></td>
<td>Bacterium attributable mortality (n=46)</td>
<td>26.3</td>
<td>16.9</td>
</tr>
</tbody>
</table>
## Does Published Literature Indicate Additional Costs Due to ABR?

<table>
<thead>
<tr>
<th>Antibacterial resistance</th>
<th>Studies included in SR (n)</th>
<th>Studies reporting cost data (n)</th>
<th>Excess cost (n = studies reporting costs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hospitalization</td>
</tr>
<tr>
<td><strong>Escherichia coli</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>resistant to:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>3rd gen. cephalosporins</td>
<td>25</td>
<td>2</td>
<td>Yes (n=2)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>12</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>resistant to:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd gen. cephalosporins</td>
<td>24</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>13</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>resistant to:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin</td>
<td>147</td>
<td>19</td>
<td>-</td>
</tr>
</tbody>
</table>
Estimates of Burden of Antibacterial Resistance

**European Union**
- Population 500m
- 25,000 deaths per year
- 2.5m extra hospital days
- Overall societal costs (€ 900 million, hosp. days)
  - Approx. €1.5 billion per year

**Thailand**
- Population 70m
- >38,000 deaths
- >3.2m hospital days
- Overall societal costs
  - US$ 84.6–202.8 mill. direct
  - >US$1.3 billion indirect

**United States**
- Population 300m
- >23,000 deaths
- >2.0m illnesses
- Overall societal costs
  - Up to $20 billion direct
  - Up to $35 billion indirect

Source: ECDC 2007
Source: Pumart et al 2012
Source: US CDC 2013

Global information is insufficient to show complete disease burden impact and costs
Overall Economic Impact Much Higher

- Reduced consumer income, employment, savings
- Increased national investment, spending, healthcare delivery
- Reduced gross domestic product (GDP): 1.4% to 1.6%

1. High proportions of resistance were reported in all regions to common treatments for bacteria causing infections in both healthcare settings and in the community.

2. Antibacterial resistance has a negative effect on patient outcomes and health expenditures.

3. Treatment options for common infections are running out.

4. Despite limitations, the report demonstrates worldwide magnitude of ABR and surveillance gaps.
Summary: Surveillance of Antibacterial Resistance

1. Gaps are largest where health systems are weak

2. There is no agreement on surveillance standards:
   - What samples and information to collect
   - How to analyse samples
   - How to compile and share data

3. Obtained national data was usually based on proportions of resistant bacteria rather than proportions of resistant bacteria causing specific diseases or affecting defined populations

4. The report provides a benchmark for future surveillance progress
AMR in Disease-Specific Programs (Tuberculosis, Malaria, HIV and Influenza)

Epidemiologically sound surveillance systems were established to monitor resistance and disease impact. This has taken many years to build and is dependant on external funding.

Available information verifies that AMR is increasing:

- **Example of mycobacterium:**
  - **Tuberculosis**
  - Increased morbidity and mortality, increased costs, threatened disease control

- **Example of parasite:**
  - **Malaria**
  - Threatened disease control

- **Example of viruses:**
  - **HIV and influenza**
  - Threatened disease control
AMR in Food-Producing Animals and Food Chain

1. Major gaps exist in surveillance and data sharing

2. Integrated surveillance systems would enable data comparison from food-producing animals, food products and humans

3. Surveillance is hampered by lack of implemented global standards

4. WHO is pursuing a multi-sectoral approach by collaborating with the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE) and other stakeholders
Antifungal Drug Resistance: Invasive *Candidiasis*

- Antifungal resistance in *Candidiasis* poses a burden on patients and healthcare systems
- Resistance to fluconazole varies widely by country/species
  - Gaps exist in information
- Resistance to newest class of antifungals (*echinocandins*) is emerging
Surveillance of Antimicrobial Resistance: Needs and Next Steps

Vision

“To achieve a monitoring capacity that will capture the global situation of antimicrobial resistance, and inform decision-making.”


Towards integrated surveillance of AMR

In humans and animals
and in disease specific programs

Immediate steps will focus on ABR

Standards for global surveillance
Collaborative platform for surveillance
Antimicrobial Resistance in a Wider Context

A global problem requiring a global solution

Commitment from stakeholders in all sectors

Comprehensive national plans

Surveillance is key to inform public health actions and strategies
In January 2014, the Executive Board approved a draft resolution co-sponsored by several Member States:

“Combating antimicrobial resistance, including antibiotic resistance”
