Antimicrobial Resistance surveillance data: from antibiotic susceptibility testing results to treatment regimen

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The Future of Infectious Diseases in the 1970’s

• “It is time to close the book on infectious diseases, and declare the war against pestilence won”
  • William H Stewart, US surgeon general 1965-1969

• “Even with my great personal loyalty to Infectious Disease, I cannot conceive of the need for 309 more trainees in infectious disease…unless they spend their time culturing each other”
  • Robert Petersdorf, 1978

• “If for the present we retain a basic optimism and assume no major catastrophes occur and that any wars are kept at the 'brush fire' level, the most likely forecast about the future of infectious disease is that it will be very dull.”
  • Frank McFarlane-Burnet, 1972
Antibiotics were discovered – not invented

AMR and AMR genes are selected, not newly evolving or emerging

Antibiotics are like a natural resource – every use, appropriate or inappropriate, eats away at its future / total use – Tragedy of the Commons

AMR is a “wicked problem”

Antibiotics are part of our societal and healthcare infrastructure – losing our ability to rely on their effectiveness will have profound consequences

AMR is a pandemic that has been and will be among us globally for the foreseeable future – “The lobster and the frog”
what do you want to know?
AMR in 2050
10 million

- Tetanus: 60,000
- Road traffic accidents: 1.2 million
- Cancer: 8.2 million
- Measles: 130,000
- Diarrhoeal disease: 1.4 million
- Diabetes: 1.5 million
- Cholera: 100,000–120,000

AMR now: 700,000 (low estimate)
Currently **700,000** deaths (low estimate) due to antimicrobial resistant infection [amr-review.org](http://amr-review.org)
Estimates of Burden of Antibacterial Resistance

European Union
population 500m
25,000 deaths per year
Source: ECDC 2007

Thailand
population 70m
19,000 deaths
Source: Lim 2016

United States
population 300m
>23,000 deaths
Source: US CDC 2013

Global information is insufficient to show complete disease burden impact and costs

www.who.int/antimicrobial-resistance/publications/surveillancereport/en/

Elife 2016 5:e18082
EARSnet / CAESAR

(European Antimicrobial Resistance Surveillance Network – ecdc)
(Central Asian and Eastern European Surveillance of Antimicrobial Resistance – WHO)

• Blood and CSF

• *Escherichia coli* – *Klebsiella pneumoniae* – *Pseudomonas aeruginosa* – *Acinetobacter baumannii* – *Streptococcus pneumoniae* – *Staphylococcus aureus* – *Enterococcus faecium/faecalis*

• Isolate–based

• No differentiation HAI / CAI (date of hospitalization collected)

• No information on previous antibiotics

  [www.euro.who.int](http://www.euro.who.int)
Fig. 7.1 Third-generation cephalosporin-resistant E. coli in the European Region (EARS-Net and CAESAR, 2017).

EARS-Net countries: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

CAESAR countries and areas: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, Uzbekistan and Kosovo (in accordance with United Nations Security Council resolution 1244 (1999)).

Global Antimicrobial Resistance Surveillance System

Blood – Urine – Faeces – Urethra

Isolate based with guidance for sample / case based surveillance data and denominator data collection (sample based)

Option to differentiate between hospital and community origin

No previous antibiotics

www.who.int/glass/en/
Countries enrolled in GLASS
As of 20 May 2020

92 countries, territories and areas
Non-susceptible pathogen-antimicrobial combination frequency

Frequency of infection caused by pathogens under surveillance per specimen and infection origin (left). Frequency of infection caused by pathogens non-susceptible to defined antibiotics under surveillance, per specimen and infection origin (right).

BLU000- Community origin (n tested = 5733)
Weighted-incidence syndromic combination antibiograms (WISCAs)
Figure 1: List of AMR surveillance network implemented in Viet Nam from 1988 to 2018
National AMR surveillance network

- National Hospital for Tropical Diseases
- Bach Mai Hospital
- Vietnam National Children Hospital
- Saint Paul Hospital
- Viet Duc Hospital
- Viet Tiep Hospital
- Viet Nam - Sweden, Uong Bi Hospital
- Binh Dinh Provincial General Hospital
- Da Nang Hospital
- Hue Central Hospital
- Khanh Hoa Provincial General Hospital
- Dak Lak Provincial General Hospital
- Cho Ray Hospital
- Children Hospital No 1
- Hospital for Tropical Diseases, Ho Chi Minh City
- Can Tho Central General Hospital

AMR surveillance in Neisseria gonorrhoeae (since 2017)

- National Hospital of Dermatology and Venereology
- Hospital of Dermato Venereology, Ho Chi Minh City
- Hai Phong Dermato Venereology Center
- Quang Ninh Center of Disease Control
- Quy Hoa Dermato Venereology Hospital

AMR surveillance in Neisseria gonorrhoeae (since 2019)

- Ha Noi Hospital of Dermatology and Venereology
- Dong Nai Hospital of Dermatology and Venereology
- Da Nang Hospital of Dermatology and Venereology
- Thanh Hoa Hospital of Dermatology and Venereology
- Khanh Hoa Hospital of Dermatology and Venereology
## “Bug-drug combinations” – Blood & CSF

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Antibiotic</th>
<th>2016-2017</th>
<th>Thailand</th>
<th>Philippines</th>
<th>Korea</th>
<th>Sweden</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>% (N)</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
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<tr>
<td><strong>Acinetobacter baumannii</strong></td>
<td>Imipenem</td>
<td>56,8 (192)</td>
<td>17</td>
<td>40</td>
<td>69</td>
<td>2</td>
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<tr>
<td></td>
<td>Colistin</td>
<td>2,5 (122)</td>
<td>-</td>
<td>6</td>
<td>0</td>
<td>-</td>
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<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td>Imipenem</td>
<td>36,7 (147)</td>
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<td>-</td>
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<tr>
<td></td>
<td>Ceftazidime</td>
<td>37,3 (150)</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<tr>
<td><strong>Escherichia coli</strong></td>
<td>Imipenem</td>
<td>6,6 (1504)</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>1</td>
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<tr>
<td></td>
<td>ESBL</td>
<td>60,1 (1167)</td>
<td>42</td>
<td>38</td>
<td>36</td>
<td>11</td>
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<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>64,3 (1414)</td>
<td>38</td>
<td>40</td>
<td>40</td>
<td>14</td>
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<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td>Imipenem</td>
<td>19,5 (477)</td>
<td>8</td>
<td>22</td>
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<td>1</td>
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<tr>
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<td>35,0 (380)</td>
<td>50</td>
<td>54</td>
<td>30</td>
<td>8</td>
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<tr>
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<td>Ciprofloxacin</td>
<td>40,1 (431)</td>
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<td>40</td>
<td>25</td>
<td>10</td>
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<td><strong>Staphylococcus aureus</strong></td>
<td>MRSA</td>
<td>69,4 (533)</td>
<td>14</td>
<td>62</td>
<td>53</td>
<td>2</td>
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<tr>
<td></td>
<td>Vancomycin</td>
<td>0,0 (669)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td>Penicillin</td>
<td>43,1 (102)</td>
<td>51</td>
<td>5</td>
<td>21</td>
<td>8</td>
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<td></td>
<td>Ceftriaxone</td>
<td>14,9 (134)</td>
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<td>1</td>
<td>15</td>
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</tr>
</tbody>
</table>

[resistancemap.org](http://resistancemap.org) (CDDEP)

Biases

Underuse of microbiology
Isolate based - No clinical denominator
More severe and unresponsive infections
Transfers
Pre-admission antibiotic use
Hospital vs. community acquired

All bias towards resistance
Why ACORN?

Antibiotic access prior to healthcare visit / hospitalization

Microbiology services only available at higher levels hospitals

Suboptimal use of microbiological diagnostics
  capacity
  culture / trust / toothless
  insurance

Probably preferential culturing of
  severe infection
  unresponsive infections
  hospital acquired infections

No denominator data

No clinical metadata

www.acornamr.net
ACORN

1. Active data collection on wards at day 0, 3 and at day 28 for patients with an infectious syndrome, weekly PPS for HAI
   a. Case based AMR data for specified subgroups that can
   b. inform local treatment guidelines and local / global AMR data
   c. Data on burden of DRI vs non-DRI

2. Diagnostic stewardship
   a. Sampling
   b. Analysis / Interpretation

3. Software solutions
   a. Tablet
   b. LIMS
   c. middleware

www.acornamr.net
Clinical variable selection

Two-day workshop held in May 2019

Key AMR stakeholders asked to provide 10 key clinical variables

• Epidemiologist, ID clinicians, microbiologists, paediatricians, mathematical and economic modellers
• Investigators then developed a consensus list for the pilot surveillance

www.acornamr.net
Simple and scalable

Efficient data capture

• Clinical data captured by smartphone / tablet app
• Carefully defined clinical dataset
• Laboratory data captured via bespoke LIMS or WHONET
Direct & Local Utility
The pilot

National Hospital for Tropical Diseases
350/500 bed governmental hospitals
Tertiary infectious diseases

Mahosot Hospital
365 bed governmental hospital
Primary - tertiary

Angkor Hospital for Children
~100 bed non-governmental hospital
Primary – tertiary

Pilot until May 2020
Extension until October 2020

www.acornamr.net
The next steps...