AMR surveillance in LMICs: The pressing need for quality laboratory data

Paul Turner
Cambodia Oxford Medical Research Unit, Angkor Hospital for Children
Antimicrobial Resistance

For the purposes of this talk:

AMR = non-susceptibility of rapidly growing clinically-relevant bacteria to antimicrobial agents

(i.e. the organisms that WHO GLASS are interested in, not TB etc.)
Why do AMR surveillance?

- To estimate burden of disease
- To characterise trends in space and time
- To serve as benchmark to measure the impact of interventions
- To provide local evidence for empiric treatment guidelines and clinical decision making
Why are we involved: Clinical microbiology in SE Asia
The AMR problem...

**ESSAY**

Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050?

Marieke E. A. de Kraker1*, Andrew J. Stewardson2, Stephan Harbarth1

1 Infection Control Program, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland,
2 Infectious Diseases Department, Austin Health, Heidelberg, Australia

- Current global estimates of the burden of AMR are not very informative; we need detailed, reliable data to be able to improve AMR control measures, preferably based on comprehensive, population-based surveillance data from low-, middle-, and high-income countries.
...is hard to define

Improving the estimation of the global burden of antimicrobial resistant infections

Direk Limmathurotsakul, Susanna Dunachie, Keiji Fukuda, Nicholas A Feasey, Iruka N Okeke, Alison H Holmes, Catrin E Moore, Christiane Dolecek, H Rogier van Doorn, Nandini Shetty, Alan D Lopez, Sharon J Peacock, Surveillance and Epidemiology of Drug Resistant Infections Consortium (SEDRIC)

Panel: Key actions to improve the estimation of the global burden of AMR infections

**Strengthen health systems**

- Increase country capability and capacity to:
  - Reliably detect the global priority list of AMR bacteria reported by WHO
  - Document clinical outcomes and link to laboratory data
WHO Global AMR Surveillance System

GLASS is a platform for global data sharing on AMR worldwide

Specimen-based denominator
- Desire to have case-based surveillance
- Trying to avoid just isolate-based data

Enrolment unit
- Country

**Thailand**
Population 69,626 (2019)

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Community origin</th>
<th>Hospital origin</th>
<th>Unknown origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOD</td>
<td>27524</td>
<td>6199</td>
<td>110</td>
</tr>
<tr>
<td>GENITAL</td>
<td>3578</td>
<td>202</td>
<td>1</td>
</tr>
<tr>
<td>STOOL</td>
<td>1529</td>
<td>530</td>
<td>N.R.</td>
</tr>
<tr>
<td>URINE</td>
<td>16894</td>
<td>5502</td>
<td>25</td>
</tr>
</tbody>
</table>

**Number of infected patients**

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Pathogen name</th>
<th>Community origin</th>
<th>Hospital origin</th>
<th>Unknown origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOD</td>
<td>Acinetobacter spp.</td>
<td>156</td>
<td>220</td>
<td>1</td>
</tr>
<tr>
<td>E. coli</td>
<td></td>
<td>996</td>
<td>134</td>
<td>1</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td></td>
<td>354</td>
<td>124</td>
<td>2</td>
</tr>
<tr>
<td>S. aureus</td>
<td></td>
<td>308</td>
<td>117</td>
<td>1</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td></td>
<td>105</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td></td>
<td>84</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>GENITAL</td>
<td>N. gonorrhoeae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STOOL</td>
<td>Salmonella spp.</td>
<td>375</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shigella spp.</td>
<td></td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>URINE</td>
<td>E. coli</td>
<td>2,563</td>
<td>754</td>
<td>5</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td></td>
<td>645</td>
<td>334</td>
<td></td>
</tr>
</tbody>
</table>

**Brazil**
Population 211,050 (2019)

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Community origin</th>
<th>Hospital origin</th>
<th>Unknown origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOD</td>
<td>1055</td>
<td></td>
<td>N.R.</td>
</tr>
<tr>
<td>URINE</td>
<td>1051</td>
<td>9148</td>
<td>N.R.</td>
</tr>
</tbody>
</table>

**Number of infected patients**

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Pathogen name</th>
<th>Community origin</th>
<th>Hospital origin</th>
<th>Unknown origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOD</td>
<td>Acinetobacter spp.</td>
<td>3</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>E. coli</td>
<td></td>
<td>12</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td></td>
<td></td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>S. aureus</td>
<td></td>
<td></td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>URINE</td>
<td>E. coli</td>
<td>446</td>
<td>2,254</td>
<td></td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td></td>
<td>14</td>
<td>385</td>
<td></td>
</tr>
</tbody>
</table>
LMICs – often not so many (good) microbiology laboratories

Population by province

Laboratory coverage by province

Challenges of Maintaining Good Clinical Laboratory Practices in Low-Resource Settings

A Health Program Evaluation Framework Case Study From East Africa

Helen L. Zhang,1 Michael W. Omondi, MSc,2 Augustine M. Musyoka, MSc,1,4 Isaac A. Afgamba,3 Renigii P. Swai,3 Francis P. Karia, MPH/MBA,1,4 Charles Mumere, MPH,2 Elizabeth A. Reddy, MD,2 John A. Crump, MD,1,4,6 and Matthew P. Rubash, MD

Service provision hampered by:
• Delays in biomedical engineer support
• Delays and extra costs in commodity procurement
• Low testing throughput
• High personnel turnover

Am J Clin Pathol (2016)
LMICs – often not so many (busy) microbiology laboratories

Emerg Inf Dis (2018)
Clinical bacteriology in low-resource settings: today’s solutions

- Availability of equipment and consumables adapted for use in low-resource settings
- Rationalised bacterial identification and antimicrobial susceptibility testing
- Communication between the laboratory and clinicians
- Prioritisation of clinically relevant specimens
- Provision of accessible and affordable training and reference materials
- Onsite validation and field adoption
Lack of IT infrastructure is often cited as a barrier to comprehensive AMR surveillance and antibiotic usage stewardship programmes in LMICs.

Few open access software options that might support an IT infrastructure for AMR surveillance are available.
How do labs store and share data?

An online survey to collect information on laboratory data management

- 5th March and 29th April 2019

The intention was to capture one response per laboratory from 50 – 100 diagnostic microbiology laboratories in LMICs

Sampling was purposive

- Organisations and colleagues known to be working in, or associated with, such laboratories
Storage of laboratory test result data

Does your laboratory routinely store test results electronically?

- All results: 20
- Some results: 15
- None: 5

<1/2 recorded all results electronically

Primary system used for storage of laboratory data

- Dedicated LIMS system: 10
- Microsoft Excel spreadsheet: 5
- WHONET: 4
- Other: 3
- Microsoft Access database: 3

Only 1/3 had a dedicated lab information management system
AMR surveillance information flow
We need a better LIMS – fit for LMICs

• Needs to include microbiology-specific functionality
  • Multiple results are generated per specimen
  • Tests are added dynamically based on initial microscopic and culture findings
  • Result reporting is complex
  • Bacterial nomenclature changes over time
  • Periodic generation of antibiograms

• Intuitive to use but with excellent support

• Deployable in a range of settings / IT infrastructures
  • Single machine
  • Local server
  • Cloud

• Should not cost US$25,000 (or more) + annual maintenance costs
  • Must be free AND open source
  • Developers need to have funding for on-going development
Analytics – make it simple

Dashboards - ACORN

Automated reports - AMASS

1. Download AMASS
2. Obtain raw data sets
3. *Configure data dictionary files
   - Microbiology data
   - Hospital admission data
   - Dictionary for microbiology data
   - Dictionary for hospital admission data

4. Double-click on the AMASS.bat

5. Review reports
   - PDF report
   - Summary data

6. Share reports
   - National
   - International
   - Open Access

Automatically generate reports

www.acornamr.net / Well Open Res (2020)
Published data quality...

...there are issues to be aware of

<table>
<thead>
<tr>
<th>Organism</th>
<th>Region</th>
<th>Africa</th>
<th>South-East Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>Amoxycillin (AMX)</td>
<td>60.0</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Ampicillin (AMP)</td>
<td>40.0</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Cefotaxime (CTX)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Cefazidime (CAZ)</td>
<td>100.0</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone (CRO)</td>
<td>--</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin (CIP)</td>
<td>--</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Gentamicin (GEN)</td>
<td>80.0</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Imipenem (IMP)</td>
<td>100.0</td>
<td>--</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Amoxycillin (AMX)</td>
<td>73.0</td>
<td>--</td>
</tr>
<tr>
<td><em>Klebsiella species</em></td>
<td>Amoxycillin (AMX)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Ampicillin (AMP)</td>
<td>--</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>Cefotaxime (CTX)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Cefazidime (CAZ)</td>
<td>--</td>
<td>22.0</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone (CRO)</td>
<td>--</td>
<td>71.4</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin (CIP)</td>
<td>--</td>
<td>64.0</td>
</tr>
<tr>
<td></td>
<td>Gentamicin (GEN)</td>
<td>100.0</td>
<td>42.0</td>
</tr>
<tr>
<td></td>
<td>Imipenem (IMP)</td>
<td>--</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* Averages were taken when more than one variant’s sensitivity patterns were reported.
Klebsiella pneumoniae

Results look good?

“For interpretation of AST results, CLSI guideline (version X) was followed”

Nothing to worry about then...

Keep reading the CLSI doc until page 218...

Is this an isolated issue or part of a larger quality management problem?
Staphylococcus aureus

<table>
<thead>
<tr>
<th></th>
<th>Amoxycillin (AMX)</th>
<th>–</th>
<th>–</th>
<th>–</th>
<th>–</th>
<th>–</th>
<th>–</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin (AMP)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Cefotaxime (CTX)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ceftazidime (CAZ)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>66.7</td>
<td>–</td>
</tr>
<tr>
<td>Ceftriaxone (CRO)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>90.0</td>
<td>–</td>
</tr>
<tr>
<td>Ciprofloxacin (CIP)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>80.0</td>
<td>–</td>
</tr>
<tr>
<td>Gentamicin (GEN)</td>
<td>85.8</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>90.0</td>
<td>29.0</td>
</tr>
<tr>
<td>Imipenem (IMP)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>90.0</td>
<td>–</td>
</tr>
</tbody>
</table>

How much MRSA: no cefoxitin / oxacillin results?
- Could just guess from the imipenem or ceftriaxone data?
- But how were these results generated?

Ceftazidime for *S. aureus*: might be ok 2/3 of the time...really?

Are these isolated issues or part of a larger quality management problem?
Tackling antimicrobial resistance (AMR) is a Global Health priority

Poor quality data hampers efforts to understand the burden of AMR

Use the MICRO framework to enhance the quality and scientific reporting of clinical microbiology data:

- Increase data utility and comparability
- Improve AMR surveillance
- Facilitate meta-analyses
- Inform policy and interventions from local to global levels
To sum up...

- Laboratory-based AMR surveillance in LMICs is hampered by many things

- Local data management is a major road block to progress
  - Urgently need better LIMS and IT infrastructure to support this
  - User friendly analysis tools would unlock local data use

- Perhaps more focus on the local situation might improve uptake and usefulness of global surveillance
  - If we don’t get the site level data sorted, then the global data will be wrong anyway
Thank you.