Diagnostic innovation to improve patient outcomes from global infectious diseases, including AMR infection

Sharon Peacock, University of Cambridge
Panel 2: Catalyzing innovation and access to AMR diagnostics for humans and animals, 14th April 2023
Defining areas for diagnostic innovation to improve global outcomes from infectious diseases, including AMR infection

- What are the leading causes of infection death
- When are diagnostic tests recommended
- When are current tests sub-optimal
- When could new tests improve human health
Defining areas for diagnostic innovation to improve global outcomes from infectious diseases

- What are the leading causes of infection death
- When are diagnostic tests recommended
- When are current tests sub-optimal
- When could new tests improve human health
Top 10 causes of death globally, overall

Fact sheet 9 Dec 2020

Source: WHO Global Health Estimates.
Top 10 causes of death

### Leading causes of death in high-income countries

1. Ischaemic heart disease
2. Alzheimer’s disease and other dementias
3. Stroke
4. Trachea, bronchus, lung cancers
5. Chronic obstructive pulmonary disease
6. Lower respiratory infections
7. Colon and rectum cancers
8. Kidney diseases
9. Hypertensive heart disease
10. Diabetes mellitus

### Leading causes of death in low-income countries

1. Neonatal conditions
2. Lower respiratory infections
3. Ischaemic heart disease
4. Stroke
5. Diarrhoeal diseases
6. Malaria
7. Road injury
8. Tuberculosis
9. HIV/AIDS
10. Cirrhosis of the liver

Number of deaths (in millions)

Focus on diagnostic areas for health outcomes

3 syndromes and 3 specific conditions:

- Neonatal conditions
- Lower respiratory tract infections
- Diarrhoeal diseases
- TB
- HIV
- Malaria
Table 1. Recent large-scale, multicentre observational studies of the pathogens causing neonatal sepsis and their findings

<table>
<thead>
<tr>
<th>Author, year, Country(ies), Setting</th>
<th>Population</th>
<th>Dates of recruitment</th>
<th>Incidence of culture-positive sepsis, %</th>
<th>Most frequent pathogen causing neonatal sepsis (from neonates with culture-positive sepsis)</th>
<th>Proportion that were MDR or resistance to key antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeNIS collaboration, 2016*</td>
<td>India, Three urban tertiary hospitals</td>
<td>2011–2014</td>
<td>6.2% (640/10,500)</td>
<td>Acinetobacter spp. (22.1%; 222/1005)</td>
<td>81.2% (181/222)</td>
</tr>
<tr>
<td>Saha et al. (The ANISA Study), 2018*</td>
<td>Bangladesh, India, Pakistan, Community settings across five sites</td>
<td>2011–2014</td>
<td>2.7% (1,324/48,723)</td>
<td>Escherichia coli (13.4%; 1,657/12,005)</td>
<td>53.9% (691/1,291)</td>
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<tr>
<td>Sands et al. (BANAROS network), 2021*</td>
<td>Bangladesh, Ethiopia, India, Nigeria, Pakistan, Rwanda, South Africa, Network of 12 urban hospitals</td>
<td>2015–2017</td>
<td>6.8% (2,483/36,285)</td>
<td>K. pneumoniae (10.4%; 258/2,483)</td>
<td>67.0% (50/75)</td>
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<td>Huynh et al. (RIKSTudy Group), 2017*</td>
<td>Cambodia, Madagascar, Senegal, Nine urban and rural hospitals</td>
<td>2012–2016</td>
<td>Culture-positive incidence per 1,000 live births: Cambodia, 6.5 (95% CI: 2.7–15.6); Madagascar, 15.2 (95% CI: 16.1–21.8); Senegal, 10.2 (95% CI: 4.8–21.3)</td>
<td>Acinetobacter spp. (22.2%; 94/420)</td>
<td>71.4% (50/70)</td>
</tr>
<tr>
<td>Russell et al. (NeoDBS network), 2022*</td>
<td>Bangladesh, Brazil, China, Greece, India, Italy, Kenya, South Africa, Thailand, Uganda, Vietnam, 19 urban and rural hospitals</td>
<td>2018–2020</td>
<td>Culture-positive incidence per 1,000 live births: Brazil, 6.5 (95% CI: 2.7–15.6); China, 15.2 (95% CI: 16.1–21.8); Greece, 5.0 (95% CI: 4.8–21.3)</td>
<td>Acinetobacter spp. (12.8%; 72/564)</td>
<td>37.7% (37/1,144)</td>
</tr>
</tbody>
</table>

*Proportion that were MDR or resistance to key antibiotics: 25.0% of all 50 tested pathogenic gram-negative isolates not susceptible to penicillin, ampicillin, or gentamicin. Incidence of gram-negative organisms higher among hospital-born than community-born infants (1.3/1,000 live births vs 0.7/1,000 live births).

WHO Guidelines on testing

- What are the leading causes of infection death?
- When are diagnostic tests recommended?
- When are current tests sub-optimal?
- When could new tests improve human health?

https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2022.02

https://www.who.int/publications/i/item/9789240019102
WHO AWaRe antibiotic book: management of infection

• Evidence-based guidance on antibiotic dose, route and duration for 34 common clinical infections in children and adults in primary health care and hospitals
• Complements the *WHO Model list of essential medicines* and *WHO Model list of essential medicines for children*
• A book in three sections: Primary healthcare, Hospital facility, Reserve antibiotics

https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2022.02
When to do a diagnostic test

- Severe pneumonia*
- Suspected TB*
- Sexually transmitted diseases*
- Symptomatic urinary infection*
- Pharyngitis if high risk of Group A strep infection
- Selected gastroenteritis (eg. suspected cholera, bloody diarrhoea)
- Some eye diseases

* Risk of AMR
When to do a diagnostic test

- Most acute conditions*
- These conditions require patients to have blood culture

* Risk of AMR
Last-resort reserve antibiotics. Restricted to very selected cases of confirmed or suspected infection with multidrug-resistant pathogen

**RESERVE ANTIBIOTICS**
- Cefiderocol ................................................................. 147
- Ceftazidime+avibactam .............................................. 148
- Fosfomycin ................................................................. 149
- Linezolid ................................................................ 150
- Meropenem+vaborbactam ........................................... 151
- Plazomicin ................................................................. 152
- Polymyxin B and colistin (polymyxin E) ..................... 153

WHO AWaRe antibiotic book: management of infection
What tests to perform? WHO essential tests

1. Disease-specific diagnostics in community health facilities without labs (point of care tests)

2. Health care facilities with clinical labs:
   - Clinical microbiology (staining, culture, blood culture, identification, susceptibility testing)
   - Viral tests (eg HIV, hepatitis, flu, measles)
   - Sexually transmitted diseases
   - Neglected tropical diseases
   - Malaria
   - TB

https://www.who.int/publications/i/item/9789240019102
Mind the gap: lack of utilization of tests that work

• Many diagnostic tests have already been described but are not used, or not used effectively to guide antibiotic use (e.g. blood culture, susceptibility testing):
  • Lack of sustainable lab capacity, funding, training

• How can diagnostic innovation be directed to improve uptake of existing tests – which would then inform personalized prescribing and improve antibiotic use and stewardship?
Mind the gap – importance of surveillance

• Most prescribing in the community for bacterial infections is based on surveillance data rather than diagnostic testing

• Prescribing in hospitals for bacterial infections also depends on surveillance data combined with a variable amount of testing depending on availability

• How can innovation create stronger diagnostic surveillance networks for empiric prescribing and better patient outcome from all infection, including AMR infection?
When current tests are sub-optimal

1. When tests are not available to direct antimicrobial prescribing
2. When tests are available but are not performed (or do not perform) correctly and lead to sub-optimal prescribing
3. When tests are performed but the data is not used again to inform empiric prescribing and provide population-based AMR data
Innovation focused on appropriate prescribing through stronger diagnostics systems

1. Strengthen diagnostics ecosystems in the community to preserve existing and new antibiotics (e.g. point of care tests for STIs)
2. Strengthen diagnostics ecosystems in hospitals (introducing essential tests, improved diagnostics systems) to reduce death from severe infections (including neonatal and respiratory)
3. Empower on the ground diagnostic surveillance to improve empiric prescribing and use of local data (networks, digital tools, etc)
4. Improving ease of accurate susceptibility testing for the reserve antibiotic list
5. Focus on TB to find the missing millions
Innovation focused on local empowerment of test manufacture

1. Bringing local innovation in diagnostic test manufacturing at scale
2. Sustainable, local markets for quality assured and affordable diagnostics
3. Taming the testing ‘wild west’ [see FIND Strategy] associated with the use of poor-quality assays
Summary highlights for diagnostic innovations

• Innovation that strengthens diagnostics ecosystems in the community e.g. POC tests
• Innovation that strengthens diagnostic test utilization and data networks in the hospitals
• Innovation that strengthens on the ground surveillance and use of data for empiric prescribing
• Diagnostic innovation in local test manufacturing to provide affordable high-quality tests