The Clinical Need for Antibiotic Resistance Related Diagnostics

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Facts (i)

• IVDs will be the world’s largest med-tech sector in 2018
• Beating cardiology and diagnostic imaging to the top spot
• Annual sales of $54.5 billion
• 5 yr compounded annual growth rate 4.8%
• Roche is the clear IVD market leader (18% market share)
• Projected 2018 sales $9.9 billion

Facts (ii)

[Graph showing IVD Market Growth Forecast 2011–2016*]

*Five-year compound annual growth rate
Abbreviations: POC, point-of-care; POL, physician office lab.
Source: Enterprise Analysis Corporation

[Graph showing the fastest growing market segments: Molecular 11%, Anatomic Pathology 10%, POCT/POL 9%, and regions: Asia Pacific 12%, Latin America 8%, North America 6.5%, Europe, Middle East, and Africa 4.8%, Japan 2%]

[Images of market segments: Immunohemistry, Clinical Chemistry, Molecular Diagnostics, Hematology, Microbiology, Coagulation, Other Clinical Instruments]

http://www.aacc.org/publications/cln/2012/ExpolIssue/Pages/RecordBreaking2012ClinicalLab.aspx#
NATIONAL STRATEGY
FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

GOAL 1: Slow the Development of Resistant Bacteria and Prevent the Spread of Resistant Infections .................................................................

GOAL 2: Strengthen National One-Health Surveillance Efforts to Combat Resistance ...........

GOAL 3: Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria ......................................................

GOAL 4: Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines ............................................................................................................................

GOAL 5: Improve International Collaboration and Capacities for Antibiotic Resistance Prevention, Surveillance, Control, and Antibiotic Research and Development ...........

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‘diagnostics’ are mentioned 40 times in the UK’s Five Year Antimicrobial Resistance (AMR) Strategy 2013–18.
CE marking diagnostics (IVDs)

- CE Marking based **only on self-declaration**

- **No systematic safety net** to identify poor IVD performance

- **No clear requirement to demonstrate** IVD has good clinical utility

BMJ 2013;346:f836 doi: 10.1136/bmj.f836
Widely used molecular pathogen detection / screening tests

- HPV 16/18
- Influenza
- HSV
- RSV

- *M. tuberculosis*
- *C. trachomatis, N. gonorrhoeae, T. vaginalis*
- MRSA screening
- *C. difficile ‘screening’*
- Group A Strep
Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae
Each rectal swab (n=816) was cultured using:

- Chromogenic media for CRE (Carba-SMART ChromID, BioMerieux)
- Non-chromogenic media (MacConkey with an ertapenem disc)
- PCR assay (CheckDirect, Checkpoints)
What could be the impact of modern and future diagnostics on antibiotics stewardship?

Which would you prefer to know?

- There is an infection
- There is not an infection
- There is a specific pathogen
- There is not a specific pathogen
- There is a specific resistance profile
- There is not a specific resistance profile
Molecular diagnostics

Rapid
Sensitivity
Specificity
Cost-effectiveness

Negative predictive value
Positive predictive value
Multivariate sensitivity analyses:
Cost-effectiveness of POC CD4 testing compared with laboratory testing

POC CD4 test cost = S13
POC CD4 test cost = S26
POC CD4 test cost = S52

CD4 test and result return (%)

Cost-saving
ICER< 1 x GDP (very cost-effective)
ICER< 3 x GDP (cost-effective)
ICER> 3 x GDP or more expensive, less effective
(not cost-effective)

http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0117751
Potential of molecular tools for antibiotic stewardship
Surviving Sepsis Campaign

NATIONAL STRATEGY FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA
Randomized Trial of Rapid Multiplex Polymerase Chain Reaction–Based Blood Culture Identification and Susceptibility Testing

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Effect of testing strategy/stewardship on time to organism id, phenotypic susceptibility results, & first appropriate modification of antimicrobial therapy

<table>
<thead>
<tr>
<th>Median time in hours (IQR) to:</th>
<th>control</th>
<th>rmPCR</th>
<th>rmPCR + stewardship</th>
</tr>
</thead>
<tbody>
<tr>
<td>organism id</td>
<td>22.3 (17–28)</td>
<td>1.3 (0.9–1.6)*</td>
<td>1.3 (0.9–1.6)*</td>
</tr>
<tr>
<td>de-escalation</td>
<td>39 (19–56)</td>
<td>36 (22–61)</td>
<td>20 (6–36)**</td>
</tr>
<tr>
<td>escalation</td>
<td>18 (2–63)</td>
<td>4 (1.5–24)*</td>
<td>4 (1.8–9)*</td>
</tr>
</tbody>
</table>

Data for subset of subjects with organisms represented on rapid multiplex (rmPCR) panel (n = 481). Time 0 = positive Gram stain result reported. *P < .05 vs control; **P < .05 vs control & rmPCR groups.

Rapid, comprehensive, and affordable mycobacterial diagnosis with whole-genome sequencing: a prospective study


Summary

Background Slow and cumbersome laboratory diagnostics for Mycobacterium tuberculosis complex (MTBC) risk delayed treatment and poor patient outcomes. Whole-genome sequencing (WGS) could potentially provide a rapid and comprehensive diagnostic solution. In this prospective study, we compare real-time WGS with routine MTBC diagnostic workflows.
• Full WGS diagnostics could be generated in a median of 9 days (IQR 6–10)
• Median 21 days (IQR 14–32) faster than final reference laboratory reports
• Cost of £481 per culture-positive specimen versus £518 for routine diagnosis
The number needed to test