Comparison of Rapid Diagnostic Tests for Bloodstream Infections using Desirability of Outcome Ranking Management of Antimicrobial Therapy (DOOR-MAT)

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Background:
- Rapid diagnostic tests (RDTs) for bloodstream infection (BSIs) are increasingly common
- Decisions regarding which RDT to implement remains a clinical challenge given the diversity of organisms and resistance mechanisms detected by different platforms
- Desirability of Outcome Ranking Management of Antimicrobial Therapy (DOOR-MAT) has been proposed as a framework to compare RDT platforms but reports of clinical application are lacking
  - The DOOR-MAT is a partial credit scoring system to compare potential antimicrobial decisions with phenotypic susceptibility patterns
  - Treatment selection desirability placed on ordinal classes based on antimicrobial susceptibility results
  - Compare score distribution between competing RDTs
  - Partial credit scoring allows for variation based on institutional values (i.e. different scoring systems penalize under versus-over treatment)
- This study compared potential antibiotic decisions based on results of two different RDTs for BSI using DOOR-MAT

Overall Example of Scoring System

<table>
<thead>
<tr>
<th>Antibiotic/Spectrum</th>
<th>SS</th>
<th>SS</th>
<th>RR</th>
<th>SR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrow</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Intermediate I</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Intermediate II</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Broad</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Last Resort</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>

Optimal Score = 100
Slight Overtreatment Score = 50
Moderate Overtreatment Score = 25
Under treatment Score = 0

Comparison of Rapid Diagnostic Tests:

- GenMark ePlex BCID Panels
- Verigen® BC Panels

Comparison of Clinical Isolates by Susceptibility Phenotype

<table>
<thead>
<tr>
<th>Gram-positive Organisms</th>
<th>Staphylococcus aureus</th>
<th>Enterococcus faecalis</th>
</tr>
</thead>
<tbody>
<tr>
<td>GenMark ePlex</td>
<td>Staphylococcus aureus</td>
<td>Enterococcus faecalis</td>
</tr>
<tr>
<td>Verigen®</td>
<td>Staphylococcus aureus</td>
<td>Enterococcus faecalis</td>
</tr>
</tbody>
</table>

- Gram-negative Organisms

<table>
<thead>
<tr>
<th>Acinetobacter baumannii</th>
<th>Haemophilus influenzae</th>
</tr>
</thead>
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<tr>
<td>GenMark ePlex</td>
<td>Acinetobacter baumannii</td>
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<tr>
<td>Verigen®</td>
<td>Haemophilus influenzae</td>
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</tbody>
</table>

Study Design & Methods:
- Retrospective single-center study at University of Maryland Medical Center
- Adult patients with at least one positive blood culture for a bacterial organism from 8/2018 to 4/2019
  - GenMark ePlex (VBC) was run as part of routine clinical testing
  - GenMark ePlex® (Research Use Only) was run on discarded fresh/frozen samples
- Two ID-trained pharmacists independently reviewed RDT results and used local susceptibility information to make decisions regarding theoretical antimicrobial management decisions
- A DOOR-MAT was applied to these decisions and the scores averaged across reviewers
- Sensitivity analysis with varied point assignment among gram-negatives (AmpC producers) conducted

Example gram-negative: E. coli and Klebsiella spp.

Example gram-positive: Staphylococcus spp.

For Gram and micrococcus: MIC panels for ampicillin, 100 for oxacillin classification (assume no clinical reasons for continuation)

Results:
- 110 clinical isolates included; 41 gram-negative, 69 gram-positive organisms

Study Materials Provided by GenMark Diagnostics

Funding Support provided by: Society of Infectious Disease Pharmacists

Take-home Points:

- Use of a partial credit scoring system such as the DOOR-MAT allows for comparisons between RDT systems beyond sensitivity and specificity allowing for enhanced clinical interpretation.
- GenMark ePlex resulted in higher DOOR-MAT scores for both gram-positive and gram-negative organisms.

Comparison of validation of theoretical antimicrobial management decision based on GenMark ePlex RDT result by final organism susceptibility profile

Comparison of theoretical antimicrobial management decision based on GenMark ePlex Dx ePlex RDT result by final organism susceptibility profile

Score Difference between RDTs as Function of Over Treatment

Clinical Isolates By Susceptibility Phenotype (GenMark Dx ePlex)

- Overall agreement between ID-trained pharmacist reviewers was ~82% for assigned scores
- Overall, average score for VBC was 86.1 (SD 31.3) vs ePlex 92.9 (SD 22.9), P = 0.004
- Among gram-negatives, the average score for VBC was 79.9 (SD 32.1) vs ePlex 88.1 (SD 28.8), P = 0.032
- Sensitivity analysis demonstrated average score of 89.9 (SD 30.4) for VBC vs 95.8 (SD 18.3) for ePlex, P = 0.27
- Among gram-positives, the average score for VBC was 89.9 (SD 30.4) compared to ePlex 95.8 (SD 18.3), P = 0.048

Comparison of theoretical antimicrobial management decision based on GenMark ePlex RDT result by final organism susceptibility profile

Comparison of theoretical antimicrobial management decision based on GenMark ePlex Dx ePlex RDT result by final organism susceptibility profile