Scoring systems for identifying patients at risk of resistant Enterobacteriaceae bacteraemia at sepsis onset
Results from a Dutch multicentre nested case-control study

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Introduction
- A balance is needed between minimizing inappropriate antibiotic treatment for 3GC-R EB infections and overuse of carbapenems in patients with other causative pathogens
- This can be achieved by means of risk stratification based on patient characteristics
- For example, Dutch sepsis guidelines consider patients at risk of 3GC-R EB infection in case of prior colonization or prior exposure to cephalosporins or fluoroquinolones
- Sensitivity of these guidelines is limited, whereas many patients are unnecessarily qualified as at risk (Rottier et al., CID 2015)

Aim
To develop better prediction, among patients with sepsis and needing empiric antibiotic therapy, for the occurrence of 3GC-R EB bacteraemia

Methods
1. Identification of all patients ≥18 years with a blood culture and concurrent initiation of intravenous therapy aimed at Gram-negatives in 8 Dutch hospitals between Jan 2008 and Dec 2010
2. Separation of sepsis episodes into those with the outcome 3GC-R EB bacteraemia, and those with all other outcomes
3. Matching each 3GC-R EB bacteraemia (cases) to four controls, based on hospital, CO vs. HO, and date of blood culture
4. Chart review for all cases and controls
5. Creation of separate prediction models for CO and HO sepsis by selecting 10 variables after eyeballing associations, followed by backward stepwise logistic regression (retaining p < 0.2)
6. Conversion into scoring systems
7. Evaluation of scoring systems by selecting a cutoff with sensitivity similar to Dutch sepsis guidelines, and observing improvement attained with regard to prevalence; and vice versa

Cohort
Incidences of 3GC-R EB bacteremia:
- Cases: 90
- Controls: 360

Final model and score
<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio (95% CI)</th>
<th>Derived score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonization with 3GC-R EB</td>
<td>5.55 (4.17-7.39)</td>
<td>100</td>
</tr>
<tr>
<td>Suspected UTI</td>
<td>2.56 (2.13-3.08)</td>
<td>50</td>
</tr>
<tr>
<td>Immuno-compromised</td>
<td>1.54 (1.26-1.87)</td>
<td>25</td>
</tr>
<tr>
<td>Any antibiotic use (prior 2 months)</td>
<td>1.32 (1.11-1.57)</td>
<td>25</td>
</tr>
<tr>
<td>Age (per year increase)</td>
<td>1.02 (1.01-1.02)</td>
<td>1</td>
</tr>
<tr>
<td>Suspected LRTI</td>
<td>0.46 (0.36-0.60)</td>
<td>-50</td>
</tr>
</tbody>
</table>

Score performance - with correction for sampling fraction of controls

Hospital-onset sepsis
Incidences of 3GC-R EB bacteremia:
- Cases: 77
- Controls: 308

Cohort
Incidences of 3GC-R EB bacteremia:
- Cases: 90
- Controls: 360

Final model and score
<table>
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<tr>
<th>Predictor</th>
<th>Odds ratio (95% CI)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Colonization with 3GC-R EB</td>
<td>3.15 (2.39-4.16)</td>
<td>90</td>
</tr>
<tr>
<td>Renal disease</td>
<td>3.12 (2.31-4.22)</td>
<td>90</td>
</tr>
<tr>
<td>Solid malignancy</td>
<td>1.60 (1.30-1.97)</td>
<td>30</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>1.53 (1.22-1.92)</td>
<td>30</td>
</tr>
<tr>
<td>Surgical procedure (prior 30 days)</td>
<td>1.53 (1.25-1.86)</td>
<td>30</td>
</tr>
<tr>
<td>Prior hospital stay (per day increase)</td>
<td>1.01 (1.01-1.02)</td>
<td>1</td>
</tr>
<tr>
<td>Suspected LRTI</td>
<td>0.22 (0.14-0.33)</td>
<td>-90</td>
</tr>
</tbody>
</table>

Score performance - with correction for sampling fraction of controls

Conclusion
- The prediction rules developed improve the trade-off between sensitivity for 3GC-R EB bacteraemia, and proportion qualified as at risk of 3GC-R EB bacteraemia (prevalence), as compared to Dutch sepsis guidelines

Definitions
- Sensitivity = Proportion of 3GC-R EB bacteraemias qualified as at risk
- Prevalence = Proportion of all patients qualified as at risk
- Positive predictive value = Probability of 3GC-R EB bacteraemia for those qualified as at risk

Abbreviations
- 3GC-R EB: 3rd generation cephalosporin-resistant Enterobacteriaceae
- CI: confidence interval
- CO: community-onset sepsis
- HO: hospital-onset sepsis
- LRTI: lower respiratory tract infection
- UTI: urinary tract infection