BACKGROUND

OVERVIEW OF CDI
- C. difficile infection (CDI): leading cause of gastroenteritis-related death in USA
- 453,000 infected per year
- 35,000 deaths per year
- Risk of complicated CDI attributable to ICU admission, colectomy, or death is 7–15%

THE DILEMMA WITH NEW & ADVANCED TREATMENTS FOR CDI: WHO SHOULD GET THEM?
- Effective treatments exist to decrease risk of adverse outcomes but there are limitations:
  - Cost (monoclonals, fidaxomicin)
  - Invasiveness (loop ileostomy)
  - Cost/safety (focal transplant)

THE HOPE OF PREDICTIVE MODELING
- Accurately predict adverse outcomes
- Applicable early after diagnosis
- Portable and validated
- Can be used to allocate treatments

PUBLISHED PREDICTIVE MODELS FOR CDI SEVERITY
- Overall poor performance when validated in a small external cohort (n=184) against complicated CDI (Fujitani et al., 2011)
- Best score by kappa: Hines VA but only 73% sensitive (Table 1)
- Other predictive modeling metrics such as net reclassification index (NRI) and area under the curve / discriminant function were not assessed

OBJECTIVE

Validate and assess CDI severity scoring systems in a large, external cohort using multiple metrics

METHODS

Literature search revealed nine scores with objective criteria

Scores applied to pre-existing cohort of 1144 inpatients with CDI

Assessed ability to predict primary outcome of complicated CDI

Compared metrics: sensitivity, specificity, positive/negative predictive values, discriminant function (DF), and net reclassification index (NRI)

Baseline score for NRI comparison was IDSA (Cohen et al., 2010): a 1.5-fold rise in creatinine above baseline [AKI] OR a white blood cell count [WBC] >15,000 cells/mm3

DEFINITIONS OF METRICS

Results of Test

<table>
<thead>
<tr>
<th>Disease Status (Truth)</th>
<th>Positive</th>
<th>Negative Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>a</td>
<td>a+b</td>
</tr>
<tr>
<td>Negative</td>
<td>c</td>
<td>c+d</td>
</tr>
</tbody>
</table>

Sensitivity = a / (a+c)

Specificity = d / (d+b)

Positive Predictive Value = a / (a+b)

Negative Predictive Value = d / (d+c)

Discriminant function = a+d / (a+b+c+d)

NRI = Predictive Value - Predicted Value (P(down|event) - P(down|nonevent))

RESULTS

Table 1. Validation of CDI Severity Scores

<table>
<thead>
<tr>
<th>Index</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Kappa score (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0.87 (0.85, 0.89)</td>
<td>0.94 (0.92, 0.95)</td>
<td>0.98 (0.97, 0.99)</td>
<td>0.93 (0.92, 0.94)</td>
<td>0.17 (0.14, 0.20)</td>
</tr>
<tr>
<td>LMSC</td>
<td>0.89</td>
<td>0.94</td>
<td>0.98</td>
<td>0.93</td>
<td>0.19</td>
</tr>
<tr>
<td>LMSC v1</td>
<td>0.89</td>
<td>0.94</td>
<td>0.98</td>
<td>0.93</td>
<td>0.19</td>
</tr>
<tr>
<td>LMSC v2</td>
<td>0.89</td>
<td>0.94</td>
<td>0.98</td>
<td>0.93</td>
<td>0.19</td>
</tr>
<tr>
<td>Hines VA</td>
<td>0.79</td>
<td>0.91</td>
<td>0.94</td>
<td>0.88</td>
<td>0.12</td>
</tr>
<tr>
<td>Northwell University</td>
<td>0.81</td>
<td>0.93</td>
<td>0.96</td>
<td>0.93</td>
<td>0.18</td>
</tr>
<tr>
<td>University of Colorado</td>
<td>0.78</td>
<td>0.91</td>
<td>0.93</td>
<td>0.89</td>
<td>0.16</td>
</tr>
<tr>
<td>UPenn</td>
<td>0.77</td>
<td>0.90</td>
<td>0.93</td>
<td>0.87</td>
<td>0.16</td>
</tr>
<tr>
<td>University of Temple</td>
<td>0.68</td>
<td>0.86</td>
<td>0.91</td>
<td>0.82</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Note: CI: confidence interval; NRI: net reclassification index; PPV: positive predictive value; NPV: negative predictive value; UPenn, University of Pittsburgh Medical Center

CONCLUSIONS

The in-house model had excellent performance with AUC = 0.83
- All of the published models evaluated performed poorly upon validation in our external cohort
- None significantly improved upon the IDSA guideline (Cohen et al., 2010) scores for severe and complicated CDI
- The relative ranking of the scores depended on the metric used to assess them
- Better scores are needed for severe CDI, and biomarkers may be required to improve performance

REFERENCES AND ACKNOWLEDGEMENTS