An Assessment of the Validity of the Comprehensive Severity Index as a Measure of Severity of Influenza Infection in Children

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• Influenza is an important illness associated with significant morbidity, mortality and healthcare burden.
• There is significant variation in severity of influenza infection, including among healthy individuals.
• A standardized quantitative severity score that reflects the breadth of influenza complications would prove valuable in epidemiologic analyses of risk factors for severe influenza infection.
• The maximum Comprehensive Severity Index score (maxCSI) is a composite, continuous measure of illness severity, based on the degree of individuality of all individual symptoms and signs of a patient’s disease or illness.
• The Comprehensive Severity Index contains metrics of age-specific criteria for influenza as well as related complications.²

### Background

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Participant</th>
<th>Total (n)</th>
<th>Stratified by maxCSI</th>
<th>MaxCSI</th>
<th>AUC (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>&lt;60</td>
<td>206/312</td>
<td>0.88 (0.84–0.91)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥60</td>
<td>105/312</td>
<td>0.77 (0.73–0.81)</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>157/317</td>
<td>0.89 (0.86–0.92)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>157/317</td>
<td>0.72 (0.69–0.75)</td>
<td>0.008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza type</td>
<td>Pandemic H1N1</td>
<td>264/312</td>
<td>0.91 (0.88–0.93)</td>
<td>0.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seasonal influenza A</td>
<td>115/317</td>
<td>0.86 (0.82–0.89)</td>
<td>0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seasonal influenza B</td>
<td>128/317</td>
<td>0.85 (0.82–0.88)</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Results

#### Table 3. Association of maxCSI and other variables with hospitalization for influenza.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza complications</td>
<td>1.67 (1.39–2.01)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Presence of hospitalization</td>
<td>1.49 (1.27–1.73)</td>
<td>0.002</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.31 (1.25–1.38)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>African ancestry</td>
<td>1.43 (1.01–1.85)</td>
<td>0.04</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>1.72 (1.22–2.40)</td>
<td>0.002</td>
</tr>
<tr>
<td>High-school education</td>
<td>1.39 (1.21–1.58)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hospitalization adjusted for maxCSI</td>
<td>1.72 (1.16–2.55)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

### Discussion

• maxCSI and influenza subtype were independently associated with influenza complications.
• maxCSI and antiviral treatment were independently associated with hospitalization.
• maxCSI had good discriminatory ability (AUC = 0.88) for influenza complications and excellent discriminatory ability (AUC = 0.84) for hospitalization.
• maxCSI was well calibrated for both outcomes.
• maxCSI (alone) was as good as a predictor of both outcomes as the multivariable model comprising maxCSI age, household crowding, influenza type/subtype, and antiviral therapy.

### Conclusion

maxCSI can be leveraged to increase statistical power in epidemiologic studies aimed at identifying factors associated with severe influenza.

### References


### Acknowledgments

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### Contact

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**Figure 1. ROC curves for the prediction of influenza complications and hospitalization.**

**Table 4. AUC and Hosmer-Lemeshow goodness of fit test for the prediction of influenza complications and hospitalization.**

**Table 2. Association of maxCSI and other variables with respiratory and/or extra-respiratory influenza complications.**

**Table 1. Characteristics of participants in the study sample.**

**Methods**

• To assess the performance of the maxCSI in a population of children medically-attended, laboratory-confirmed influenza.

**Ethics**

• Ethics approval obtained from SickKids Research Ethics Board

**Participants**

• 321 children prospectively recruited from 12/2007 through 3/2010

**Procedure**

• Collection of standard data collection form

**Study Outcomes**

• Primary outcome: respiratory and/or extra-respiratory influenza complications based on physician diagnosis

**Statistical Methods**

• Descriptive statistics produced for participant characteristics

• Univariate (maxCSI as sole predictor variable) and multivariable logistic regression (maxCSI, age, sex, household crowding, influenza type/subtype, early antiviral therapy) models constructed for each outcome

• Presence of household crowding defined as equalized crowding index (applying the Canadian Disadvantaged Occupancy Standard): ≤ 1.0

• Early antiviral therapy defined as receipt within 48 hours of illness onset

• Assessment of discrimination by plotting the receiver operating characteristic (ROC) curve and calculating the area under the ROC curve (AUC): AUC values ‘ranked’ as excellent [>0.90], good [0.80 and <0.90], fair [0.70 and <0.80] and poor (<0.70)

• Assessment of calibration using the Hosmer-Lemeshow C statistic²

• AUCs of univariate and multivariable models compared using method of DeLong et al³

• P < 0.05 considered statistically significant

• Data analyzed in SPSS (SPSS version 24, SPSS Inc, Chicago, IL, USA)