Phenotype Development and Validation for a Maternal Early Warning System

Megan Richards\(^1\), Michael Gao, MS\(^1\), William Knechtle, MBA\(^1\), Namita Kansal\(^1\), Vaishakhi Mayya, PhD\(^1\), Mark Sendak, MD\(^1\), Ashraf Habib, MBBCCh, MSc, FRCA\(^1\), Terrence Allen, MBBS\(^2\), Sarah McWay Boling, RN\(^2\), Melissa Bauer, DO\(^2\), Jennifer Gilner, MD, PhD\(^3\), Suresh Balu, MBA, MS\(^3\), Courtney Mitchell, MD\(^3\), Brenna Hughes, MD, MSc\(^2\)

\(^1\)Duke Institute for Health Innovation, \(^2\)Duke University Medical Center

Background.

The maternal mortality rate in the United States has increased from 9.9 per 100,000 births in 1999 to 26.4 per 100,000 births in 2015 [1] making it one of the highest maternal mortality rates among industrialized nations. Severe maternal morbidity (SMM) is a significant indicator of maternal mortality risk and is defined by 18 indications of peripartum complications. SMM has also significantly increased over the last 2 decades, from 49.5 per 10,000 births in 1993 to 144.0 per 10,000 births in 2014 [2]. Delay in diagnosis has been identified as a factor leading to SMM and maternal mortality, prompting calls for the creation of early warning systems to quickly identify patients in need of escalation of care [3]. However, several systemic and technical challenges have inhibited the creation and adoption of such predictive systems in the United States. Existing efforts in prediction of obstetric complications vary widely in the prediction task, complication definitions, and data used [2]. In this work, we model distinct, clinically actionable phenotypes for eight of the most common and dangerous complications for maternal morbidity, showing strong predictive capacity for each in real time. This work presents clinically actionable phenotypes for eight SMM outcomes: hemorrhage, sepsis, acute heart failure (AHF), acute renal failure (ARF), adult respiratory distress syndrome (ARDS), eclampsia, air and thrombotic embolism, and disseminated intravascular coagulation (DIC).

Methods.

A trans-disciplinary team lead by clinicians developed a set of phenotype criteria for each SMM outcome, shown in the figure to the left, and a team of data scientists created models for time-series prediction of eight SMM phenotypes. These phenotypes were evaluated on a retrospective cohort of 19,419 perinatal obstetric encounters, whose characteristics are shown in Table 1. Patient data was formatted hourly, with predictions representing the patient’s likelihood of meeting the phenotype within the following 4 hours. Input data included 142 features, including comorbidities, vitals, demographic information, and labs. Preliminary gradient-boosted models were used to show actionability, and exhibited strong predictive capacity summarized in Table 2. A comparison was made with the Maternal Early Warning Criteria (MEWC), and model prediction significantly outperformed MEWC early onset prediction. These results indicate that these phenotypes represent significantly predictive and actionable criteria for the development of algorithmic maternal early warning systems.

Results.

Table 1: Model Performance Comparison with MEWC Baseline

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Hemorrhage</th>
<th>Sepsis</th>
<th>AHF</th>
<th>ARDS</th>
<th>Embolism</th>
<th>Eclampsia</th>
<th>DIC</th>
<th>ARF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model AUROC</td>
<td>0.765</td>
<td>0.915</td>
<td>0.851</td>
<td>0.811</td>
<td>0.894</td>
<td>0.923</td>
<td>0.811</td>
<td></td>
</tr>
<tr>
<td>MEWC AUROC</td>
<td>0.522</td>
<td>0.608</td>
<td>0.614</td>
<td>0.557</td>
<td>0.572</td>
<td>0.547</td>
<td>0.564</td>
<td>0.562</td>
</tr>
<tr>
<td>Model Average Precision</td>
<td>0.0277</td>
<td>0.0403</td>
<td>0.3641</td>
<td>0.0643</td>
<td>0.0021</td>
<td>0.0544</td>
<td>0.0203</td>
<td>0.0439</td>
</tr>
<tr>
<td>MEWC Average Precision</td>
<td>0.0059</td>
<td>0.0051</td>
<td>0.0007</td>
<td>0.0037</td>
<td>0.0003</td>
<td>0.0039</td>
<td>0.00027</td>
<td>0.0015</td>
</tr>
</tbody>
</table>

Conclusion.

This set of criteria represent clinically actionable phenotypes that can be algorithmically predicted and are represent a promising basis of future maternal early warning systems to improve patient care.

References

1. Nicholas Rasekhbaum, Ryan Barber, Zulfigar Bhatta, Lalit Dandona, Peter Gething, Simon Hay, Yohannes Kifru, Heidil Larson, Xiaojiong Liang, Stephen Lin, Alan Lopez, Rafael Louzao, George Mensah, Ali Mokdad, Mohsen Naghavi, Christine Pinho, Joshua Salomon, Nicholas Kassebaum, Ryan Barber, Zulfiqar Bhutta, Lalit Dandona, Ashraf Habib, MBBCh,MSc, FRCA, Terrence Allen, MBBS, Sarah McWay Boling, RN, Melissa Bauer, DO, Jennifer Gilner, MD, PhD, Suresh Balu, MBA, MS, Courtney Mitchell, MD