**BME 580.670-671 Precision Care Medicine**

**Project Title: Delirium Prediction and Subtype Identification Using a Large Multi-Center ICU Database**

**Problem Statement**:

Delirium, a syndrome of acute brain dysfunction, is prevalent critically ill patients and has been associated with adverse outcome1-3, however its biological mechanisms and pathophysiology remain poorly understood. Many predictive biomarkers currently viewed as having high potential (e.g. advanced neuroimaging, high throughput proteomics, next generation gene sequencing) are not routinely available in the ICU. In this proposal, we intend to extract readily available physiological signatures and electronic health records from eICU, a large multicenter data set of ICU patients. **The principal hypothesis is that delirium risk is encoded in physiological signatures which can accurately predict delirium risk, onset, severity, duration and outcome.** Specific aims are fourfold: **Aim 1:** Data extraction, curation, and pre-processing**. Aim 2:** Unsupervised clustering and delirium subtype discovery. This will be an important exercise not only to identify novel risk factors within the dataset but to divide the identified delirium population into subtypes with differing outcome trajectories. **Aim 3:** Development of statistical and machine learning models to predict delirium risk and outcome. **Aim 4:** (If time permits)Further extension of state change models to include transitions between non-delirium, delirium, and comatose states.

**Project Team:**

Domain PIs/Mentors

1. Dr. Robert Stevens, Associate Professor of Anesthesiology and Critical Care Medicine
2. Dr. Jose Suarez, Director, Division of Neurosciences Critical Care

**Background**:

Delirium is a common and deleterious neuropsychiatric impairment characterized by reduced an acute onset of behavioral changes, a fluctuating course, and inattention5. Depending on the population studied up to 80% of patients admitted to the ICU develop delirium, typically in the setting of major physiological disturbances such as surgery, trauma, infection, and organ dysfunction, with an increased likelihood observed in elderly patients with chronic comorbid conditions3, 4, 8. The prevalence of delirium is associated with two to three times increased likelihood of mortality3, unfavorable recovery, longer length of hospitalization, higher healthcare expenses (estimated US annual expenditure of 150 billion)4,6, and increased burden for caregivers7. Medication, environmental changes, and other treatments improve the time course and outcome of patients with delirium. However, prevention is widely seen as the most effective method to reduce the burden of delirium (30-40% of delirium cases are deemed preventable)10. Thus, early prediction of delirium risk, time of onset, duration, severity and outcome are important goals in intensive care medicine9. In terms of prediction, multivariable logistic regression models such as PRE-DELIRIC have been reported and externally validated, however the performance of such models is unsatisfactory (e.g. AUROC of PRE-DELERIC is 0.77). In this proposal, we will develop entirely novel delirium prediction approaches by applying advanced statistical and supervised machine learning methods to high-dimensional physiologic and demographic features recorded in a large data set of critically ill patients labeled using standard delirium scoring systems. In addition, we plan to identify clinically meaningful delirium subtypes using unsupervised approaches, linking subtypes with outcome trajectories. Taken together, we expect these novel methods could increase the specificity of delirium management in critically ill patients.

**Potential Solution:**

Students will work with domain and engineering faculty to refine the study aims and hypotheses. They will identify novel subtypes of delirium based on physiologic and demographic features, and they will link subtypes to specific clinical trajectories such as the development of coma, resolution of delirium, survival, and death. They will build innovative models to predict delirium risk, onset, duration, and outcome. They will model transitions between the non-delirium and delirium states. Thus, we expect the students will work not only with machine learning algorithms but also that they will develop a Markov chain model or an equivalent model that can predict the probability of state changes in and out of delirium.

**Preliminary Data/Relevant Experience**:

Feasibility of this work is supported by the fact the PIs Drs Stevens and Suarez have successfully mentored a Precision Care Medicine student group (2018-2019) working with the same eICU data set to build a computational prediction model in cardiac arrest patients. Results generated from that effort are in a manuscript to be submitted imminently for peer review.

In addition, a recently conducted screen of eICU data shows that the database contains several indicators of delirium which will be considered as labels in the supervised modeling exercise:

1. Symptoms of Delirium Present: 8,766 patients with at least one positive indication of delirium.
2. Delirium scale/score: (CAM-ICU and ICDSC scores). An estimated 25,000 patients were evaluated using one of these scoring systems, with approximately 5500 patients who screened positive for delirium during their ICU stay.

**Data Set Identification**:

Data for the study will come from the Philips eICU Research Institute database which aggregates patient electronic health record and low frequency physiological time series data of 200,859 ICU patients in more than 200 ICUs22. A brief introduction of the eICU database can be found on the MIT hosted web page ([https://eicu-crd.mit.edu](https://eicu-crd.mit.edu/about/eicu/)). Access for this database has already been procured by Dr. Robert Stevens and querying of the entire database has already been initiated.

This project will also consider using the MIMIC-III database for external validation purposes. MIMIC-III contains 38,645 patient health records along with high frequency physiological time series data23. MIMIC-III will serve as an external data set to determine the generalizability and robustness of models created using the eICU database. An overview of the MIMIC-III database can be found here: ([https://mimic.physionet.org](https://mimic.physionet.org/gettingstarted/overview/)).

**References:**

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