**Data Studio**
1:30–3:00pm, Wednesday, 23 February 2022

Videoconference:
https://stanford.zoom.us/j/92300593799?pwd=aXNHSUtQcFVmSEsSSVR2N3FRNmx3Zz09
Password: 909614

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**Title:** Biomarker of Acute Kidney Injury for Cardiothoracic Surgery Patients

**Summary:**

The Data Studio Workshop brings together a biomedical investigator with a group of experts for an in-depth session to solicit advice about statistical and study design issues that arise while planning or conducting a research project. This week, the investigator(s) will discuss the following project with the group.

Cardiac surgical patients are at high risk for acute kidney injury (AKI) due to preexisting kidney dysfunction, hemodynamic instability, and the use of cardiopulmonary bypass. Although the initial kidney injury likely occurs in the operating room, current clinical criteria (urine output and serum creatinine) often will not make the diagnosis until post-operative day 1 or 2. Nucleophosmin (NPM) is an intracellular protein that becomes phosphorylated (p-NPM) during ischemic stress and causes cell death of proximal tubular epithelial cells in the kidney. We have previously developed NPM and p-NPM as a marker for AKI and as a therapeutic target in animal models of renal ischemia. We now plan to evaluate its use in humans.

This is a prospective cohort study of patients undergoing cardiothoracic surgery at moderate to high risk of AKI. We will gather urine samples intra- and post-operatively. Samples will be analyzed for urine NPM and p-NPM, common commercially available AKI diagnostics (i.e., Kim-1, NGAL, NephroCheck), and urine creatinine. Our primary outcome of interest will be AKI as diagnosed by established KDIGO criteria up to postoperative day 5.

We have three specific aims. Aim 1 will characterize the kinetics of urinary NPM and p-NPM in cardiothoracic patients at high risk of AKI. Aim 2 will construct a prediction model using urinary NPM, p-NPM, and the p-NPM-to-NPM ratio to predict AKI using currently accepted KDIGO criteria. Aim 3 will compare performance of urinary NPM and p-NPM to currently available urinary diagnostics (Kim-1, NGAL, and NephroCheck) to predict AKI. The kinetics and concentrations of NPM and p-NPM in human urine are currently unknown. Thus, we plan to address Aim 1 first to generate preliminary data that will be used to finalize the design of the study used to achieve Aims 2 and 3.
Questions:

Our questions concern how to design Aim 1 (kinetics and range finding) to inform the study design for Aims 2 and 3 (predictive model performance compared to gold standard and other common biomarkers).

1. Aim 1: Initial pilot cohort to characterize biomarker concentrations and kinetics
   
   (a) Estimate the sample size needed to conduct a range-finding study
   
   (b) Account for issues related to urine concentration of biomarkers given variable urine output during renal injury
   
   (c) Design the range-finding cohort study to inform the following:

   i. Estimate a sample size for a prediction model study
   
   ii. Understand the optimal timing and intervals to gather our samples to allow us to generate high quality predictions using our biomarker, potentially using rate of change information if this improves model performance

2. Aims 2 and 3: Prediction model cohort to identify optimal biomarker thresholds and kinetics

   (a) Sample size calculation (based on results of our first study)
   
   (b) Statistical plan to develop a prediction model for AKI using our biomarkers (either alone or in combination with other variables)
   
   (c) Statistical plan for comparing our prediction model(s) with performance of commercially available biomarkers (Kim-1, NGAL, NephroCheck)
   
   (d) Are adaptive study designs applicable?
Zoom Meeting Information

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