Studies examining biomarker use for early detection of AKI have shown modest performance, potentially due to non-selective testing and misclassification when using small changes in serum creatinine as a reference standard for tubular damage. We hypothesized that targeted biomarker measurement in a high-risk population to measure clinically meaningful endpoints would demonstrate improved utility. We further hypothesized that leveraging early changes in serum creatinine to guide testing would improve predictive performance compared to previous testing in unselected populations. We examined the ability of urine L-fatty acid binding protein (uL-FABP), neutrophil gelatinase-associated lipocin (uNGAL), Interleukin-18 (uIL-18), and Kidney Injury Molecule-1 (uKIM-1) to provide prognostic information in patients with early AKI.

- **BACKGROUND**
  - Area Under the Receiver Operating Characteristic (AUC-ROC) curves hypothesized that leveraging early changes in serum creatinine to guide testing would improve predictive performance compared to previous testing in unselected populations. We examined the ability of urine L-fatty acid binding protein (uL-FABP), neutrophil gelatinase-associated lipocin (uNGAL), Interleukin-18 (uIL-18), and Kidney Injury Molecule-1 (uKIM-1) to provide prognostic information in patients with early AKI.
  - The Area Under the Curve (AUC) was calculated to assess the predictive ability of each biomarker to clinical predictors alone. Multivariable logistic regression was used to assess biomarker ability to predict the composite outcome. The Integrated Discrimination Index (IDI) was calculated to assess the added predictive ability of each biomarker to clinical predictors alone.

- **OBJECTIVES**
  - To evaluate the ability of a panel of biomarkers to predict persistent doubling of creatinine, dialysis, or death within 7 days of biomarker measurement in patients with suspected early injury.
  - To evaluate the incremental prognostic utility of this biomarker panel beyond that of known clinical predictors.

- **METHODS**
  - This study was performed within the Validation of biomarkers for Acute Lung Injury Diagnosis (VALID) study cohort, and included 152 adults admitted to ICUs at Vanderbilt University Medical Center.
  - Key Inclusion criteria:
    - Known baseline creatinine 7-365 days prior to admission
    - Urinary biomarkers measured at enrollment and 48 hours later
    - KDIGO Stage 1 AKI (creatinine increase of 0.3 mg/dl or 50% from baseline) at the time of biomarker measurement
  - Key Exclusion Criteria:
    - Stage 2 or 3 AKI
    - History of renal transplant
    - Chronic dialysis or eGFR < 15 mL/min/1.73 m² at the time of ICU enrollment
    - Primary composite outcome (within 7 days of biomarker measurement)
      - Persistent doubling of baseline serum creatinine (52 days),
      - Dialysis, or death
    - A priori selected variables for the clinical model
      - Age, serum creatinine at the time of biomarker measurement, APACHE II score, and presence of sepsis.

- **RESULTS**
  - Table 1. Characteristics of the study subjects by composite outcome—persistent doubling of serum creatinine, dialysis, or death
  - Table 2. Odds Ratios for logistic regression model of individual biomarkers, adjusted for clinical predictors which included age, APACHE II score, serum creatinine at KDIGO Stage I, and presence of absence of sepsis. Biomarkers were natural log transformed. ORS are represented per interquartile range of corresponding biomarker concentration.
  - Table 3. Integrated Discrimination Index and Category Free Net Reclassification index for individual biomarkers

- **CONCLUSIONS**
  - Modest early changes in serum creatinine can help target biomarker measurement for prediction of clinically relevant outcomes.
  - uL-FABP has independent and incremental prognostic value in combination with known clinical predictors to discriminate between patients with early AKI who develop proximately relevant outcomes.
  - uNGAL, uIL-18, and uKIM-1 had modest discrimination and did not improve significantly upon the clinical model alone.
  - uL-FABP was particularly effective in correctly reclassifying non-events to a lower level of risk, while uNGAL was effective in correctly reclassifying events to higher level of risk.
  - Total cNRI was significant for uL-FABP, uNGAL, and uKIM-1; however only uL-FABP showed statistical significance using IDI.