*\*\*\*400 word limit\*\*\**

**Title:**

Propensity-weighted prognostic associations of hypercapnia by Arterial and Venous Blood Gas: A retrospective, multicenter health records study

**Rationale:**  
Arterial blood gases (ABGs) are the gold standard for assessing hypercapnia but are invasive, technically challenging, and associated with various complications. Venous blood gases (VBGs) are easier to obtain and increasingly used, yet few studies have compared their prognostic utility in hypercapnic respiratory failure. This study aims to evaluate the associations of hypercapnia measured by ABG and VBG with hypercapnia-related outcomes such as receipt of a diagnosis code for hypercapnia respiratory failure, invasive mechanical ventilation (IMV), non-invasive ventilation (NIV) and 60-day any-cause mortality, after adjusting for propensity to receive each type of blood gas sampling.

**Methods:**  
A multicenter retrospective cohort study using 2022 data from the TriNetX research network was conducted. Adult patients with encounters suggestive of hypercapnia in emergency or inpatient settings were eligible. Hypercapnia was defined as PaCO₂ ≥45 mmHg on ABG and PvCO₂ ≥50 mmHg on VBG. Outcomes included diagnosis of hypercapnic respiratory failure, receipt of NIV or IMV, and 60-day all-cause mortality. To mitigate selection bias, inverse propensity weights were estimated by modeling the likelihood of obtaining arterial or venous blood gas based on encounter type, demographic variables, comorbidities, vital signs and labs. Associations between pCO₂ and outcomes were examined using logistic regression and restricted cubic spline models.

**Results:**  
A total of \*\*\* patients met inclusion criteria, including \*\*\* with ABG and \*\*\* with VBG. Baseline characteristics differed between groups with ABG more often obtained in inpatient setting and VBG in emergency setting. ABG patients additionally had higher prevalence of multiple comorbidities. After propensity weighting, covariate balance was achieved. Figure 1 displays the continuous relationship between pCO₂ and outcomes for VBG and ABG. ABG and VBG had comparable predicted probability for non-invasive ventilation, invasive mechanical ventilation and 60-day mortality. However, diagnosis of hypercapnic respiratory failure had higher likelihood of being diagnosed for VBG group compared to ABG group.

*\*will submit Figure 1 – superimposed ABG and VBG restricted cubic splines*

**Conclusions:**  
Hypercapnia identified by VBG demonstrated prognostic associations similar to those measured by ABG for ventilatory support and mortality. These findings suggest VBG may be sufficient for risk stratification and management of hypercapnic patients, potentially reducing the need for invasive arterial sampling. Prospective studies are warranted to confirm these findings and inform clinical practice guidelines.