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

**Title:**

Prognostic value of hypercapnia by ABG vs VBG: A propensity-weighted, multicenter EHR cohort

**Rationale:**  
Arterial blood gases (ABGs) remain the reference test for hypercapnia but are invasive and difficult to obtain. Venous blood gases (VBGs) are less invasive and more accessible, yet diagnostic and device qualification criteria do not accept VBG evidence. To address this gap, we compared prognostic associations of hypercapnia measured by ABG and VBG with ventilator support and 60-day mortality, adjusting for the likelihood of each test being ordered. If VBG-identified hypercapnia predicts outcomes similarly to ABG, it would justify integrating VBG criteria into diagnostic criteria and clinical decision-making.

**Methods:**  
We conducted a multicenter retrospective study using the TriNetX research network, including adult patients presenting to the ED or admitted to the hospital with a presentation indicating possible hypercapnia (at least 1 factor that should trigger consideration) during calendar year 2022. The exposure was pCO2 measured by ABG and VBG, represented using restricted cubic splines. To mitigate confounding by test selection, we trained gradient-boosted models on encounter-type, demographics, comorbidities, triage vital signs, and labs to derive stabilized inverse propensity-of-sampling weights. Outcomes were within-encounter diagnosis code for hypercapnic respiratory failure, within-encounter procedure codes for NIV or IMV, and 60-day all-cause mortality. Associations between pCO₂ and each outcome were examined using weighted logistic regression.

**Results:**  
We identified a total of 515,286 patients across 107 health systems; 187,242 had a first calendar-day ABG and 149,663 had a VBG documented. Before weighting, ABGs were more commonly obtained in inpatient setting with 17% absolute difference. After propensity weighting, covariate balance improved. Figure 1 displays the weighted odds ratios of outcomes categorized by PCO2 level (below vs. above normal) for ABG and VBG groups. Hypercapnia in ABG and VBG groups was associated with increased odds of NIV and diagnosis of hypercapnic respiratory failure. Compared with ABG, the VBG group showed significantly higher odds for hypercapnic respiratory failure, NIV and IMV. Among hypercapnic patients, mortality did not significantly differ between the VBG and ABG groups.

*Figure 1 – Weight Odds Ratios of Outcomes by PCO2 category (ABG, VBG).*

*A graph with colored dots and lines

Description automatically generated*

**Conclusions:**  
In reweighted cohorts, VBG-identified hypercapnia showed similar prognostic associations similar to ABG for ventilatory support and mortality. VBG results were also similarly associated with subsequent diagnostic labeling, suggesting its use despite current formal criteria. Broader acceptance of VBG-based definitions in billing and device qualification should be considered, pending external validation and associations with post-discharge management.