*\*\*\*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 usually 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 support integrating hypercapnia on VBG 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 Emergency Department (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 (hypercapnia ≥ 45 mmHg; hypocapnia < 35 mmHg) and VBG (hypercapnia ≥ 50 mmHg; hypocapnia < 35 mmHg). To mitigate confounding by test selection, we trained gradient-boosted models on encounter-type, demographics, comorbidities, triage vital signs, and labs to derive inverse propensity-of-sampling weights. Outcomes were within-encounter diagnosis code for hypercapnic respiratory failure, within-encounter procedure codes for Non-invasive ventilation (NIV) or invasive mechanical ventilation (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 (85% inpatient, 15% ED) compared with VBG (68% inpatient, 32% ED). Figure 1 displays the propensity-weighted odds ratios for each outcome stratified by the presence of hypocapnia, normal CO2 (referent), and hypercapnia. Hypercapnia by ABG and VBG were associated with similarly increased odds of NIV and diagnosis of hypercapnic respiratory failure, while weighted rates of those outcomes amongst patients with hypocapnia were roughly the same as normocapnia, supporting adequate control of sampling by inverse-propensity weighting. Both hypocapnia and hypercapnia by either type of blood gas were associated with similar increased rates of IMV and 60-d all cause mortality, as compared to normocapnia.

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

*A graph with red and blue dots

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**Conclusions:**  
After controlling for test-ordering patterns, VBG-identified hypercapnia showed similar prognostic associations for ventilatory support and mortality. VBG results were also similarly associated with subsequent diagnostic labeling, suggesting clinicians currently use VBGs to support the diagnosis, 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.