# Comparative Effectiveness of Riociguat versus Treprostinil in Chronic Thromboembolic Pulmonary Hypertension: A Propensity-Matched Analysis Using the TriNetX Research Network

*Ekow Arhin Essien MD, Karldon Nwaezeapu MD, Abena Agyekum MD, Justice Owusu-Achiaw MD, Edmund Mireku Bediako MD*

Advocate Aurora Health Care, Trinity Health Ann Arbor, SUNY Downstate Health Sciences University, 37 Military Hospital, The Shelburne Hospital

Contact: Ekow Essien, MD | ekowe94@gmail.com

## Background

Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive form of pulmonary hypertension with significant morbidity and mortality. Both riociguat and treprostinil are approved treatments, but comparative effectiveness data remain limited.

## Objective

To compare the effectiveness and safety of riociguat versus treprostinil in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

## Methods

- **Design:** Retrospective cohort study using TriNetX Global Collaborative Network (129 healthcare organizations)
- **Population:** Patients diagnosed with CTEPH (ICD-10 code I27.24)
- **Treatment groups:** Treprostinil (n=314) vs Riociguat (n=2,371)
- **Analysis:** Propensity score matching for demographics and clinical characteristics
- **Final cohorts:** 310 patients in each matched group
- **Primary outcome:** All-cause mortality
- **Secondary outcomes:** Cardiovascular events, arrhythmias, hospitalizations
- **Follow-up:** Five-year period

## Primary Outcome

**All-cause mortality:**

**Treprostinil: 29.3%**

**Riociguat: 17.1%**

Risk Ratio: 1.715
95% CI: 1.270-2.316
$p < 0.001$

**Hazard Ratio:**

**1.975**

95% CI: 1.406-2.773
$p < 0.001$

**72%**

Higher Mortality Risk with Treprostinil

## Secondary Outcomes

Cerebrovascular Disease — **RR 0.464**

**Cerebrovascular disease incidence:** Lower in treprostinil group (5.5% vs 11.8%; RR 0.464, 95% CI 0.253-0.852; p=0.011)

**No significant differences observed in:**

- Heart failure outcomes
- Cardiac arrhythmias
- Acute kidney injury
- Hospitalizations requiring coronary interventions

## Results Summary

In this large propensity-matched analysis of CTEPH patients, riociguat treatment was associated with significantly lower all-cause mortality compared to treprostinil.

**Key findings:**

- 72% higher mortality risk with treprostinil vs riociguat
- Reduced cerebrovascular disease risk with treprostinil
- No significant differences in other cardiovascular outcomes

## Conclusion

Riociguat treatment was associated with significantly lower all-cause mortality compared to treprostinil in CTEPH patients. The differential impact on cerebrovascular outcomes suggests complex mechanisms of action that warrant further investigation.

**Clinical Implications:** These findings provide real-world evidence to inform treatment selection in CTEPH management, suggesting potential survival advantages of riociguat over treprostinil in this high-risk population.

## Strengths and Limitations

**Strengths:**

- Large sample size
- Propensity matching
- Real-world evidence
- Multi-center data
- Five-year follow-up

**Limitations:**

- Retrospective design
- Potential residual confounding
- Medication adherence unknown
- Disease severity not captured