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Denver Health Participates in National Trial to Compare Sedatives Used for Intubation

DENVER (Dec. 10, 2025) —To improve outcomes for critically ill patients who require a breathing machine, Denver Health joined health systems across the country in a multicenter study to compare two commonly used sedatives for intubation, etomidate and ketamine and determine if either sedative improves patient outcomes.

Intubation is a bedside procedure where a breathing tube is inserted into the mouth and then into the windpipe. The tube is then connected to a breathing machine or ventilator, which breathes for the patient. Sedatives are needed to keep the patient comfortable and sleepy during the procedure. Almost all patients who require emergent intubation for critical illness or injury are too ill to consent, so clinicians are making decisions on the patient's behalf, underscoring the need for clear evidence to guide those decisions.

The findings of the [Randomized Trial of Sedative Choice for Intubation \(RSI\) study](#) were published in the Dec. 9, 2025, issue of *New England Journal of Medicine*. The trial included 2,365 patients at 14 emergency departments and intensive care units across the United States. The RSI trial found that etomidate is safe to use, meaning it does not increase the risk of death compared with ketamine. Moreover, it found increased cardiovascular risks of ketamine, including low blood pressure and arrhythmias, which are side effects of ketamine that have not been well studied in the past.

"Etomidate and ketamine are both FDA approved and have been used for intubation for almost as long as I have been alive," said Stacy Trent, MD, MPH, an emergency physician and the lead RSI investigator at Denver Health. "When I started practicing emergency medicine, etomidate was the most used sedative for intubation, but over time, ketamine has been increasingly used and sometimes favored without good data to support one drug over the other. The RSI trial is the first large, multicenter study to examine which of these two sedatives results in the best outcomes for patients. While both drugs are similar in terms of the risk of death, the increased cardiovascular risks of ketamine may make clinicians prefer etomidate again."



Concerns in past decades about etomidate's transient effect on cortisol production led some countries to remove it from the market. However, ketamine's cardiovascular risk identified in the RSI trial along with its growing use for other conditions, such as chronic pain, depression, and post-traumatic stress disorder, highlights the need for stronger data. The RSI study's results may prompt some countries to reconsider making etomidate available again.

"Patients receive treatments every day that have never been rigorously evaluated and may be ineffective or even harmful," said lead author Jonathan Casey, MD, of Vanderbilt University Medical Center. "Studies like RSI are critically important to understand the treatments patients are already receiving and to ensure patients receive the treatments that lead to the best outcomes."

Researchers are now studying whether either sedative effect long-term outcomes, including symptoms of post-traumatic stress at 12 months. They are also leading a separate trial, BREATHE, to evaluate whether smaller breathing tubes reduce vocal-cord injury and long-term issues with speaking, swallowing and breathing.

The RSI trial was funded by the Patient-Centered Outcomes Research Institute and the National Institutes of Health.

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About Denver Health

[Denver Health](#) is a comprehensive health and hospital system that provides high-quality care and proudly serves as the city's safety-net hospital. For more than 160 years, Denver Health has been guided by its mission to serve the people of Denver, to educate the next generation of health care professionals and to engage in research and community partnerships to better deliver the services that meet our patients health care needs while strengthening our community.