

Persistent inflammation in sepsis survivors linked to higher mortality rates

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One out of four sepsis patients who survive their hospital stay have elevated levels of inflammation a year after discharge, and they are at higher risk for major health problems and death, according to a study led by physician-scientists at the University of Pittsburgh School of Medicine and the Veterans Affairs Pittsburgh Healthcare System.

The results, published today in *JAMA Network Open*, give tantalizing clues to future treatments that may improve outcomes for sepsis survivors.

Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs, and affects more than 30 million people worldwide every year, according to the World Health Organization.

"Sepsis is the leading cause of death among hospitalized patients. Patients discharged from the hospital aren't out of the woods yet. Approximately 1 out of every 3 sepsis survivors will die in the following year," said lead author Sachin Yende, M.D., M.S., professor of critical care medicine and clinical and translational science at Pitt's School of

Medicine, and vice president of critical care and deputy chief of staff at the Veterans Affairs
Pittsburgh Healthcare System. "Our new findings about chronic inflammation post-discharge suggest that addressing this condition may be important to improve patients' long-term outcomes."

Nearly all patients with sepsis have increased inflammation in their bloodstream during the first few days of their hospitalization. Whether this inflammation resolves or persists is poorly understood. Yende and his team followed 483 people who had been hospitalized with sepsis at one of 12 U.S. hospitals between 2012 and 2017 and survived to be discharged. Detailed information was gathered on the study participants, and they were contacted by telephone and home visits three, six and 12 months after enrollment for health interviews and a blood sample.

Approximately a quarter of the participants showed persistently elevated levels of inflammation and a half showed elevated levels of immunosuppression biomarkers up to a year after hospitalization. These patients had higher rates of readmission—particularly due to heart disease and stroke—and death compared to their peers whose inflammation and immunosuppression biomarkers had returned to normal after hospitalization.

"The participants with increased inflammation had levels that were twice as high as levels in healthy individuals and that elevated inflammation persisted long after hospital discharge," said senior author Derek Angus, M.D., M.P.H., professor and chair of Pitt's Department of Critical Care Medicine and director of Pitt's Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center. "Sepsis increases risk of heart disease and stroke, and, for the first time, we've linked these adverse outcomes to persistent inflammation. This opens the door to future studies into why high levels of inflammation persist for at least a year after hospital discharge and the development of



treatments aimed at modifying the inflammation with the hope that will improve health."

The researchers cautioned that they did not have blood tests on the study participants before their sepsis diagnosis. It is possible that they had elevated levels prior to hospitalization that may have contributed to the development of sepsis and continued to persist after hospitalization.

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