

# Short-term Gains with Long-term Consequences The Evolving Story of Sepsis Survivorship



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## KEYWORDS

- Sepsis • Cognitive impairment • Physical impairment • Infection • Hospital readmission
- Critical care

## KEY POINTS

- Sepsis survivors frequently experience declines in cognitive and physical function.
- Sepsis survivors experience increased cardiovascular risk and are at increased risk for subsequent infections.
- Health care resource use is high among sepsis survivors given the frequency of postacute services at hospital discharge and hospital readmission.
- Health-related quality of life is decreased, and long-term mortality is increased after sepsis.

Sepsis is an acute, life-threatening condition characterized by the human systemic inflammatory response to infection.<sup>1</sup> Sepsis is common, afflicting millions of patients each year in the United States and countless more internationally.<sup>2–4</sup> The incidence of sepsis seems to be increasing,<sup>3</sup> owing in part to an aging population, age-related impaired immunity, and an increasing burden of comorbid conditions.

Although the proportion of in-hospital deaths attributed to sepsis remains extremely high,<sup>5,6</sup> advances in care and heightened awareness of sepsis have led to substantial declines in in-hospital mortality over the last 20 years.<sup>7–13</sup> A stark example of this phenomenon is the trend in mortality in severe sepsis and septic shock trials. In the original early goal-directed therapy trial conducted

by Rivers and colleagues<sup>8</sup> between 1997 and 2000, the in-hospital mortality in the control arm receiving usual care at the time was 46.5%. In contrast, the in-hospital mortality in the early goal-directed therapy arm was 30.5%. In 3 multicenter trials published in 2014 and 2015, in-hospital mortality had improved to approximately 20% and 90-day mortality ranged from 19% to 29%.<sup>11–13</sup> In parallel, temporal trends of severe sepsis and septic shock mortality outside of the trial context have revealed similar improvement.<sup>4,7,9,10</sup>

At the intersection of an increasing incidence of sepsis and declining short-term mortality is a growing population of sepsis survivors that has been heralded as a “hidden public health disaster.”<sup>14</sup> Over the last decade, an expanding body of literature has emerged to describe the

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Box 1

Long-term consequences of sepsis

Neuropsychological impairment

Physical impairment

Sepsis-induced inflammation and cardiovascular risk

Sepsis-induced immunosuppression

Health care resource use

Long-term health-related quality of life

Long-term mortality

long-term impact of sepsis among survivors. These studies have revealed that long-term cognitive and functional impairment, sustained inflammation and immune dysfunction, increased health care resource use, decreased health-related quality of life, and increased mortality plague many sepsis survivors. The evidence challenges the notion that sepsis is an acute, transient illness, instead revealing that sepsis is an acute illness with lingering consequences that impact one’s long-term health. This article provides a state-of-the-art review of the emerging literature of the long-term consequences of sepsis (Box 1).

LONG-TERM NEUROPSYCHOLOGICAL AND PHYSICAL IMPAIRMENTS

Survivors of critical illness frequently experience cognitive and functional impairments that persist after discharge and impact health-related quality of life. In survivors of critical illness, this is known as the post-intensive care syndrome (PICS) and is defined as new or worsening cognition, mental health, and/or physical health that arises after critical illness and endures.<sup>15,16</sup> Severe sepsis and septic shock are common risk factors for these

impairments, although admission to an intensive care unit (ICU) is not a prerequisite for the development of impairments among sepsis survivors.

Cognitive Impairment

Cognitive impairment seems to be a profound and persistent development in sepsis survivors. In a landmark study, Iwashyna and colleagues<sup>17</sup> examined the impact of severe sepsis on cognitive and physical functions. Using the Health and Retirement Study, a national representative sample of elderly subjects in the United States, serial cognitive and functional assessments were leveraged to compare function after severe sepsis hospitalizations to nonsepsis hospitalizations. The cohort enrolled 1194 elderly patients (mean age, 76.9 years) who experienced 1520 hospitalizations. The rate of moderate to severe cognitive impairment increased from 6.1% before severe sepsis to 16.7% afterward, an absolute increase of 10.6%. After adjustment, for which patients served as their own controls, the odds of moderate to severe cognitive impairment developing after severe sepsis remained 3-fold higher compared with nonsepsis hospitalizations. Approximately 2 years after the initial postsepsis assessment, a nearly identical proportion of severe sepsis survivors were found to have moderately to severely impaired cognition, suggesting that these new impairments persisted (Fig. 1). Because only 43% of the severe sepsis episodes included an ICU stay, cognitive impairment after severe sepsis seems to extend to those cared for outside of the ICU as well.

In the largest prospective study of cognitive impairment in ICU survivors, the Bringing to Light the Risk Factors and Incidence of Neuropsychological Dysfunction in ICU Survivors (BRAIN-ICU) investigators assessed patients for cognitive function at 3 and 12 months after hospitalization.<sup>18</sup>

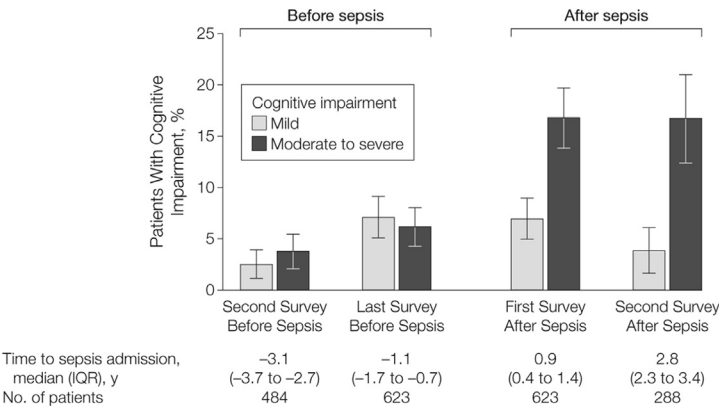


Fig. 1. Cognitive trajectory among elderly severe sepsis survivors. IQR, interquartile range. (From Iwashyna TJ, Ely EW, Smith DM, et al. Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA 2010;304:1790; with permission.)

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