



Three Major Scientific Societies Confirm Link Between SARS-CoV-2 and Sepsis, Which Causes Vast Majority of COVID-19 Deaths in ICUs

Sepsis is the immune system's response to severe infections, bacterial, fungal, or viral, leading to the damage and failure of organs and death. The uptake by health systems of measures to prevent and treat sepsis, urged by the World Health Assembly in 2017¹, is more urgent than ever, as emphasized in a consensus paper published on Intensive Care Medicine² by the Global Sepsis Alliance (GSA), the European Society for Intensive Care Medicine (ESICM), and the Society for Critical Care Medicine (SCCM).

These leading organizations emphasize the importance of recognizing that patients critically ill with COVID-19 have viral sepsis, despite some differences from sepsis caused by other pathogens. Patients with severe COVID-19 suffer from multi-organ dysfunction, including acute respiratory distress syndrome (ARDS), vasodilatory shock, acute kidney injury, coagulopathy, and impaired brain, heart and gastrointestinal function; these represent the common clinical manifestations that characterize sepsis.

Last year a systematic review led by a research team in Athens, Greece, confirmed that COVID-19 causes death and disability due to sepsis³: 85% of adults critically affected by COVID-19 develop sepsis, 40% of the whole spectrum of cases present with sepsis.

"Sepsis should become a widely used umbrella term for a condition that is caused by different pathogens, including SARS-CoV-2", says Tex Kissoon, GSA President. "This pandemic has showed us the effectiveness of international and horizontal cooperation between healthcare professionals and policymakers. We must keep the focus on infection prevention measures and use the successful trial platforms set up during the pandemic to support research on sepsis. Above all governments should integrate sepsis in the national health systems, as urged by the WHA resolution of 2017", concludes Kissoon.

¹ https://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_13-en.pdf

² <https://link.springer.com/article/10.1007/s00134-021-06409-y>

³ COVID-19 as cause of viral sepsis: A Systematic Review and Meta-Analysis
Eleni Karakike, Evangelos J. Giamarellos-Bourboulis, Miltiades Kyprianou, Carolin Fleischmann-Struzek, Mathias W. Pletz, Mihai G. Netea, Konrad Reinhart, Evdoxia Kyriazopoulou
medRxiv 2020.12.02.20242354; doi: <https://doi.org/10.1101/2020.12.02.20242354>



Greg S. Martin, SCCM President, also stresses on the importance of understanding severe COVID-19 as viral sepsis: “Even before COVID-19, the global impact of sepsis was astonishing and vastly underestimated. With 150 million cases of COVID-19 leading to nearly 50 million deaths in less than 18 months, it is more important than ever to appreciate that COVID-19 may manifest as sepsis.”

Management guidelines for COVID-19 have been directly developed by the Surviving Sepsis Campaign Coronavirus Disease 2019 panel from similar sepsis guidelines⁴. In this regard, Martin reminds that “as with sepsis, a key element for effective treatment of patients with COVID-19 is to recognize the inciting infection and the consequent immune response in order to treat the potentially lethal organ dysfunction that accompanies COVID-19 and is the hallmark of sepsis.”

The three organisations also warns that patients who survive other forms of sepsis suffer longer-term ill-effects similar to those of patients with “long-COVID”, although they are not equally well recognized. Scientific literature demonstrates that longer-term effects of sepsis, known as post-sepsis syndrome, occur in up to 50% of sepsis survivors, who suffer from persisting physical, cognitive, and psychological sequelae.

“COVID-19 will end at some point, but ICU teams will carry on taking care of patients with sepsis. We need to raise awareness of sepsis in the community”, according to Maurizio Cecconi, ESICM President, who adds: “As with patients with long-COVID, patients who survive sepsis have a long journey ahead. Providing the best possible care for patients with sepsis means also looking after sepsis survivors and their families in their journey to get back their lives.”

⁴ <https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19>



SEPSIS FACTS

50 million cases per year - **40%** are children under age 5 - **11 million** deaths - burden concentrated in low- and middle-income countries - leading cause of death in high-income countries⁵ – **3,4 million** cases in Europe, **680.000** deaths per year⁶ (e.g. >100.000 in France⁷, 98.000 in Germany⁸)
\$ 62 billion: average yearly cost for sepsis treatment in the US
> **€ 9 billion**: average yearly cost for sepsis treatment in Germany (3% health budget)⁷
> **€ 15.000**: average treatment cost for single patient in Germany⁹
> **€ 16.000**: average treatment cost for single patient in France⁶

⁵ Rudd, K.E., *Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study*. The Lancet (British edition), 2020. **395**(10219): p. 200 - EOA.

⁶ Extrapolation from Mellhammar L, Wullt S, Lindberg Å, Lanbeck P, Christensson B, Linder A. Sepsis Incidence: A Population-Based Study. *Open Forum Infect Dis*. 2016;3(4):ofw207. Published 2016 Dec 8. doi:10.1093/ofid/ofw207

⁷ Dupuis, C., Bouadma, L., Ruckly, S. *et al*. Sepsis and septic shock in France: incidences, outcomes and costs of care. *Ann. Intensive Care* **10**, 145 (2020). <https://doi.org/10.1186/s13613-020-00760-x>

⁸ Fleischmann, C., Hartmann, M., Hartog, C. *et al*. Epidemiology of Sepsis in Germany: Incidence, Mortality And Associated Costs of Care 2007-2013. *ICMx* **3**, A50 (2015). <https://doi.org/10.1186/2197-425X-3-S1-A50>

⁹ Study currently under review.