



Guest Editorial

Sepsis Awareness and Trajectory: Never Forget and Never Stop Fighting

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INTRODUCTION

Sepsis is a global killer. Approximately 49 million sepsis occur annually; 11 million do not survive (Rudd et al, 2020). Of those who survived the initial attack, only 50% survived unscathed beyond two years (Mostel et al, 2019). Close to 33% die in less than two years after the initial sepsis attack, and another 17% have one or more sustained and life-impacting complications (Rudd et al, 2020). Numbers and statistics are undoubtedly devastating, but as Estee Neuwirth, a former colleague and mentor, would often say, "No data without stories and no stories without data."

In 2016, Bob Davis, a 76-year-old California (United States) native, underwent routine abdominal surgery. The surgery went well, and he appeared to be recovering, so his wife went home to check on the dog, get a good night's rest, and freshen up. They lived a little over an hour away. Late night, early morning, Mrs. Davis received a phone call from the hospital asking her to return. When asked if it could wait until the morning, the nurse said, "No, you should come back now." After Mrs. Davis left, Bob's abdomen became swollen, and infection became apparent. Before she could return to the hospital, sepsis took his life. The staff missed the signs of sepsis. They did not even admit to the family that he died of sepsis. How do I know? Because Bob Davis was my uncle. With full permission from my aunt and his sister Kathy (my mom), I tell this story as a reminder that each number and each statistic is a person, and each person has a story.

As my story suggests, the devastating impact of sepsis goes beyond individuals; it affects families. The average household size worldwide is 4.9 (Kramer, 2020). Based on this information, sepsis makes an average of 42.9 million orphans and widows annually (11 million deaths multiplied by 3.9). Less measurable but still unfathomable is the impact on the families of those who survived the initial insult of sepsis but never fully recovered. Consider the

husband who must walk through his wife's major depressive disorder or anxiety attacks. Think about the parents who must care for their child who survived sepsis but lost their leg. What about the global financial impact of sepsis?

In 2022, researchers from the University of Groningen in the Netherlands estimated that the international median interquartile cost per sepsis case was approximately \$38,000 (van den Berg et al 2022). Pause and do the math – \$38,000 x 49 million sepsis cases annually. Sepsis costs the world around 1.9 trillion dollars annually, and that is only healthcare costs. What about the impact on the family because the primary provider died from sepsis? Even if they survived, what if post-sepsis complications prohibit them from working? Again, I ask you to pause to contemplate the cost of sepsis. Are we, as healthcare professionals, as members of the global family, doing enough? The answer is a resounding “no,” but it does not mean we are not trying.

Healthcare professionals (HCP) and sepsis have a long battle history. In the early days of sepsis, HCPs focused on understanding, defining, and identifying evidence-based care. In 1992, the American College of Chest Physicians and the Society of Critical Care Medicine published the first consensus definition and care guidelines for sepsis (Bone et al, 1992). The team defined sepsis as “the systemic response to infection...”. They introduced “systemic inflammatory response syndrome (SIRS)...” as a primary determinant. In 2016, JAMA published the Sepsis-3 international consensus definitions, swapping Systemic inflammatory response syndrome (SIRS) for quick Sepsis organ-related organ failure assessment (qSOFA)(Singer et al, 2016). Then, in 2021, the Surviving Sepsis Campaign (SSC) committee dug deeper into evidenced-based care and published International Guidelines for Management of Sepsis and Septic Shock 2021 (Evans et al, 2021). Surprisingly, the SSC went against Sepsis-3 by recommending that sepsis teams not use qSOFA only. All the while, the Centers for Medicare and Medicaid continued to use SIRS criteria on a publicly reported quality measure (Centers for Medicare & Medicaid Services, 2014). In 2023, the United States-based Centers for Disease Control and Prevention stepped outside the traditional care definitions. They focused on the elements that make a hospital-based sepsis program more effective (CDC, 2023).

Equally important, over the last several years, a concerted effort has been made to “save lives and reduce suffering by improving sepsis awareness and care”(Sepsis Alliance, 2023) To mention a few, in 2011, the Sepsis Alliance designated September as Sepsis Awareness Month in the United States (Sepsis Alliance, 2023). In 2012, The Global Sepsis Alliance, launched by the Sepsis Alliance, established September 13 as Global Sepsis Day Global (Sepsis Alliance, ND). Several years later, the Sepsis alliance took it further by designating April 18 – 24 as Pediatric Sepsis Week and May 14 – 20 as Maternal Sepsis Week (Cech, 2022). These organizations impact care through events, education, grass-roots government

actions, and a strategic social media campaign. But what is the sepsis community doing beyond definitions and awareness?

While herculean efforts are still aimed at definition alignment, evidence-based practice, and awareness, there seems to be a shift. The community is looking at individualized care based on phenotyping, biomarker/cell marker utilization, and artificial intelligence (AI). In my opinion, we are headed in the right direction and should focus on integrating these streams of research. Ideally, we will reach a point of synergy where informatics and sepsis specialists learn to incorporate artificial intelligence with clinical intelligence seamlessly. We will reach a point where there is enough information about a client (health information exchange and real-time data entry) to paint a clear clinical picture (phenotype) so that an AI-driven clinical decision support system can guide care teams toward individualized patient care. Unfortunately, we are not there yet.

In all fairness, healthcare systems like Duke University (Malone, 2020) and Johns Hopkins University (Cech, 2022) lead the pack in AI. Machine learning tools like XGBoost and random forest models show great promise (Yang et al, 2023). FDA-approved Sepsis diagnostic tests like Cytovale's IntelliSep (Hollenbeak, et al, 2023) and Immupress' SeptiCyte RAPID (Graoyrand, et al, 2023) are shaping up to be to sepsis what Troponin I is to myocardial infarction. Researchers like Dr. Georgios Papathanakos in Greece (Papathanakos, et al, 2023) are leading the way in sepsis phenotypes. Professor Dr. Nelson Sanchez-Pinto at Northwestern University guides us toward informatics and phenotyping integration in pediatrics. I am excited to see what the next ten years hold and to experience a leap in safe and effective sepsis care. In the meantime, I challenge HCP worldwide to join or continue the fight against our deadly foe.

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