

## Rethinking sepsis: from controversy to precision-driven solutions

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John C Alverdy's "Unpacking the Sepsis Controversy" presents a compelling critique of the prevailing sepsis paradigm, particularly the over-emphasis on host-centered immune dysregulation and the limitations of current animal models.<sup>1</sup> The article raises significant concerns about how sepsis is defined, coded, and studied, arguing that flawed assumptions have led to ineffective treatments and a lack of progress in the field. His call for a reassessment of sepsis as a cause of death rather than a coexisting condition in critically ill patients is particularly thought-provoking.

However, although the article successfully challenges outdated perspectives, it does not fully address emerging trends that could reshape sepsis research and treatment. Artificial intelligence (AI) and machine learning are revolutionizing early detection and risk stratification, providing real-time diagnostics that may refine sepsis classification and coding—one of the author's key concerns.<sup>2</sup> Likewise, the rise of immune checkpoint inhibitors and precision medicine offers a more nuanced approach to immune modulation, countering the broad-brush host-targeted therapies the article critiques.<sup>3</sup> Additionally, multiomics and endotype-based classifications are already shifting sepsis management from a one-size-fits-all approach to a personalized framework, directly addressing the issue of heterogeneity in sepsis responses.<sup>4</sup>

Although Dr Alverdy's critique is valuable, incorporating technological and immunological advancements into the conversation could bridge the gap between controversy and innovation. Moving forward, sepsis research should integrate both pathogen-directed approaches and cutting-edge tools in AI, precision medicine, and multiomics to improve patient outcomes.<sup>5 6</sup> A balanced approach—acknowledging the flaws in past research and embracing future possibilities—may offer the breakthrough needed to redefine sepsis care.

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