

Sepsis hysteria – a need to rebalance hype and unrealistic expectations

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*"Sepsis kills over 52,000 every year – each death a preventable tragedy"*

tweeted Matt Hancock, UK Secretary of State for Health, in March 2019. Many other non-contextualised or downright fictitious claims regularly fill media pages and airwaves, creating a distorted picture of sepsis epidemiology and unrealistic expectations. This hype has generated an unhealthy climate of fear and retribution in both Britain and America. Patients and families fear 'the hidden killer' with confidence in healthcare providers undermined. Hospitals are criticised, penalised and litigated against for failing to give within-the-hour antibiotics. Doctors are reported for not giving antibiotics to patients they deem non-infected. It is thus worth summarizing available data and providing a more balanced perspective. Without belittling the problem, patient care must be informed with facts.

Sepsis – 'life-threatening organ dysfunction caused by a dysregulated host response to infection'<sup>1</sup> – is the tip of a large infection iceberg. Nature, with or without a short course of antibiotics, deals perfectly well with most infections (Figure 1a). A relatively small proportion are admitted to intensive care units (ICU), of whom approximately 70% survive their hospital stay. Though hard data are unavailable, most patients with significant organ dysfunction receiving full active management would likely be admitted to critical care. Those who die outside the ICU (and many inside) are predominantly elderly and/or frail and at the end of life. Unpublished data (NHS Digital Hospital Episodes Statistics) show 77.5% of sepsis-related deaths in England affect patients aged  $\geq 75$  years, while approximately 150 deaths occur annually in children aged 0-18 years, a hospital mortality rate of 0.075% among children admitted with a suspicion of sepsis (Figure 1b).

The high incidence of frailty and severe comorbidities makes most sepsis-related deaths neither *attributable* to sepsis, nor *preventable* through timely and effective healthcare. A point-prevalence study in Welsh hospitals identified 521 septic patients and 136 deaths, of whom only 40 were directly or possibly attributable to sepsis.<sup>2</sup> Of these 40, 77.5% had significant frailty and 70% were not for cardiopulmonary resuscitation. A US study found 12% of sepsis deaths were possibly-to-definitely preventable.<sup>3</sup> Osler noted "*Pneumonia may well be called the friend of the aged. Taken off by it in an acute, short, not often painful*

*illness, the old man escapes those "cold gradations of decay" so distressing to himself and to his friends."* In today's parlance, 'pneumonia' could be replaced by 'sepsis'.

Aside from prompt source control, timely antibiotic administration remains the measurable metric of optimal sepsis care. *Timely* - avoiding unnecessary delays - is often conflated as *early*. The Surviving Sepsis Campaign strongly recommends antimicrobial administration within an hour of presentation, contending that each hour's delay costs lives.<sup>4</sup> However, the evidence base is underwhelming and openly challenged by the Infectious Diseases Society of America<sup>5</sup> among others. Purported benefits arise solely from retrospective analyses of databases with inherent residual confounding and biases and questionable plausibility.<sup>6</sup> Every prospective study to our knowledge, including a large randomised trial<sup>7</sup> and multicentre quality improvement programs<sup>8,9</sup> have not shown outcome benefit. Antibiotic use in English hospitals has doubled since 2015 (courtesy Philip Howard, Rx-Info Define, [www.rx-info.co.uk/products/define/](http://www.rx-info.co.uk/products/define/)). This coincides with introduction of the CQUIN quality improvement initiative mandating antibiotics within one hour of presentation, yet no clear mortality impact has been demonstrated.

Finally, accurate sepsis epidemiology remains a major concern and is heavily dependent on data source and case definition. Both in the US<sup>10</sup> and UK (NHS Digital, unpublished), the supposed number of admissions for suspected sepsis has risen by approximately 50% in six years and mortality by 27%. Yet far more modest changes are seen using clinical criteria<sup>10</sup>, ICU admission rates<sup>11</sup>, or death certification.<sup>12</sup> A spike in sepsis-coded deaths coincided with implementation of new NHS Digital Coding Guidance in April 2017<sup>13</sup> and financial incentivization to code a patient as 'sepsis'. A similar effect has been noted in the US.<sup>14</sup> Furthermore, up to 40% of patients initially diagnosed as sepsis were later adjudicated as not likely to be infected.<sup>15</sup>

In summary, it is crucial to lay bare the fictions, to provide a proper perspective for better understanding of the condition, and to create realistic expectations about outcomes. We must deliver a balanced strategy in policy, public messaging and front-line care, reducing excessive, inappropriate antibiotic usage with concurrent risks of resistance and toxicity. Hospitals and clinicians should neither be castigated nor penalized by imposition of time-

to-antibiotic targets. The relatively rare cases of severe infection, e.g. those with shock, should be promptly recognized and treated, as with any emergency condition, and unnecessary delay avoided in the less sick patient. We must accept that septic patients will die despite best current care, yet highlight that the large majority who are salvageable do survive. We must improve coding of infection and organ dysfunction to ensure consistency, measure quality metrics, and benchmark strategies that increase the likelihood of desired health outcomes.

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## Figure legend

Figure 1:

- (a) English infection and sepsis data. \*<https://improvement.nhs.uk/resources/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur/>
- (b) Emergency admissions to English hospitals 2011-2017 with a discharge code of sepsis or bacterial infection. Top panel: age-related admissions. Lower panel: age-related mortality (NHS Digital Hospital Episodes Statistics)