Sepsis hysteria: excess hype and unrealistic expectations

"Sepsis kills over 52 000 every year—each death a preventable tragedy", tweeted Matt Hancock, UK Secretary of State for Health and Social Care, in March, 2019.[1] Many other non-contextualised or fictitious claims regularly fill media pages and airwaves, creating a distorted picture of sepsis epidemiology and unrealistic expectations of outcomes. This hype has generated an unhealthy climate of fear and retribution in both the UK and the USA. Patients and families fear the so-called hidden killer and their confidence in health-care providers is undermined. Hospitals are criticised, penalised, and litigated against for failing to give patients antibiotics within 1 h of presumptive diagnosis. Doctors are reported for not giving antibiotics to patients they deem non-infected. It is thus worth summarising available data and providing a more balanced perspective. Without belittling the problem, patient care must be informed by facts.

Sepsis—"life-threatening organ dysfunction caused by a dysregulated host response to infection"[2]—only develops in a tiny minority of patients. Nature, with or without a short course of antibiotics, deals well with most infections (figure). A small proportion of patients with infection are admitted to intensive care units, of whom approximately 70% survive their hospital stay. Although hard data are unavailable, most patients with substantial organ dysfunction who receive full, active management are likely to be admitted to intensive care. Patients with infection who die outside of intensive care (and many who die inside it) are predominantly older, frail, and at the end of life. Indeed 77·5% of sepsis-related deaths in England are in patients aged 75 years or older. By comparison, approximately 150 sepsis-related deaths occur annually in children aged 0–18 years: a hospital mortality of 0·075% (figure; National Health Services Digital Hospital Episodes Statistics, unpublished data).

The high incidence of frailty and severe comorbidities makes most sepsis-related deaths neither attributable to sepsis, nor preventable through timely and effective health care. In a point prevalence study in Welsh hospitals including 521 patients with sepsis and 136 deaths, only 40 deaths were directly or possibly attributable to sepsis.[6] Of these 40 deaths, 77·5% were in patients who had substantial frailty, and 70% were in patients who were not for cardiopulmonary resuscitation in the event of cardiac arrest. A US study found 12% of sepsis deaths were possibly-to-definitely preventable.[7] Sir William Osler[8] noted in 1901 that "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". Pneumonia in this context could nowadays be replaced by sepsis.

Aside from prompt source control, timely antibiotic administration is the measurable metric of optimal sepsis care. Timely (avoiding unnecessary delays) is often distorted and misinterpreted as early. The Surviving Sepsis Campaign[9]

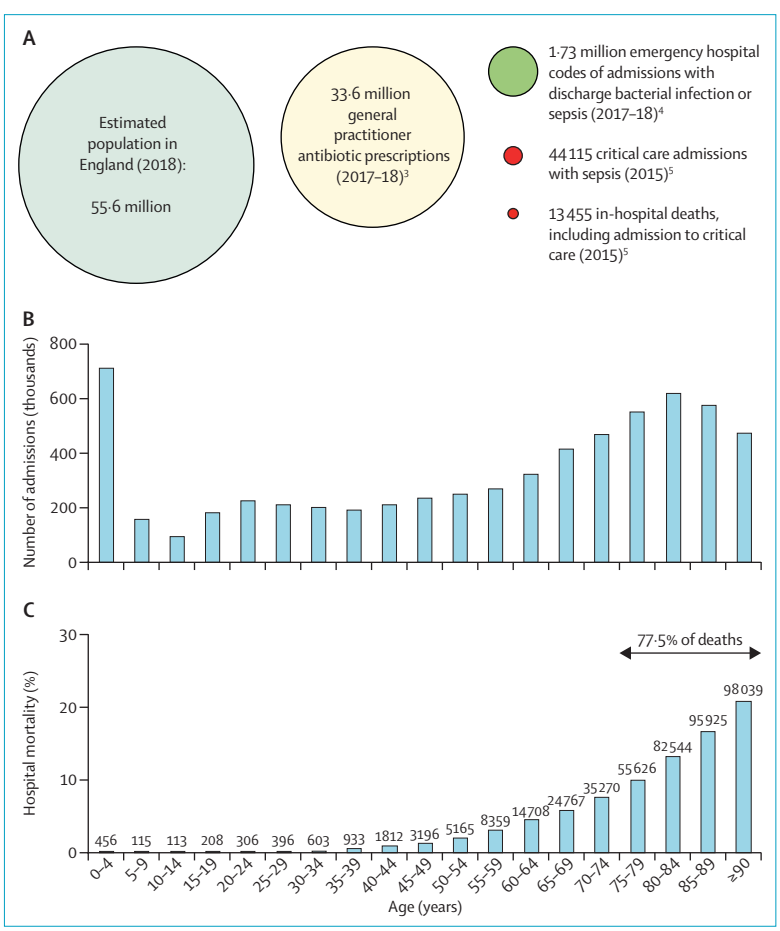

***Figure*: Data for infection, sepsis, and emergency hospital admissions for sepsis or bacterial infection in England**

Bacterial infection and sepsis data in England (A), number of emergency admissions to English hospitals with a discharge code of sepsis or bacterial infection (B), and mortality among these emergency admissions, by age, 2011–17 (numbers above the bars in are total number of deaths; C).

strongly recommends antimicrobial administration within an hour of presentation, contending that each hour's delay costs lives. However, the evidence base is underwhelming and openly challenged by the Infectious Diseases Society of America,[10] among others. Evidence for the benefits of this recommendation is solely from retrospective analyses of databases with inherent residual confounding and biases, and questionable plausibility.[11] No prospective study to our knowledge, including a large randomised trial[12] and multicentre quality improvement programmes,[13,14] has shown outcome benefit. Antibiotic use in emergency departments in English hospitals has doubled since 2015 (Howard P, Rx-Info Define, personal communication), coinciding with the introduction of the Commissioning for Quality and Innovation quality improvement initiative mandating antibiotic prescription within 1 h of presentation, yet no clear effect on mortality has been shown.

For the **Commissioning for Quality and Innovation guidance** see https://www.england.nhs.uk/wp-content/uploads/2018/04/cquin-guidance-2018-19.pdf

Accurate sepsis epidemiology is a major concern and is heavily dependent on data source and case definition. In both the USA[15] and the UK (NHS Digital, unpublished data), the supposed number of admissions for suspected sepsis has increased by approximately 50% in 6 years, and mortality by 27%. Yet, far more modest changes are seen using clinical criteria,[16] intensive care unit admissions,[5] or death certifications.[16] A spike in sepsis-coded deaths coincided with the implementation in April, 2017, of new NHS Digital Coding Guidance[2] and with financial incentives to code a patient's diagnosis as sepsis. A similar effect has been noted in the USA.[17] Furthermore, up to 40% of patients initially diagnosed as having sepsis were later judged as not likely to be infected.[18]

In summary, it is crucial to expose the fictions surrounding sepsis, to provide a proper perspective for better understanding of the condition, and to create realistic expectations about outcomes. A balanced strategy must be delivered in policy, public messaging, and frontline care, to reduce excessive, inappropriate antibiotic use with concurrent risks of resistance and toxicity. Hospitals and clinicians should neither be castigated nor penalised by imposition of time-to-antibiotic targets. The rare cases of severe infection (eg, in patients with shock) should be promptly recognised and treated, as with any emergency condition, and unnecessary delay should be avoided in less sick patients. Patients with sepsis might die despite the best care, yet the large majority who are salvageable do survive. Coding of infection and organ dysfunction must be improved to ensure consistency, to measure quality metrics, and to benchmark strategies that increase the likelihood of desired health outcomes.

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