SEPSIS RESEARCH (SNAPSHOT AUGUST 2024)

Seminal Sepsis Research Papers

A. Sepsis epidemiology and disease burden:

1. WHO Global report on the epidemiology and burden of sepsis (who.int). 2020. This report highlights the public health impact of sepsis and the fact that many sepsis cases are preventable through infection control measures. It also underscores the importance of strengthening health systems.

2. **Kumar A**, et. al. (2024) Accuracy of the modified Global Burden of Disease and Angus International Classification of Diseases coding methods for identifying sepsis: A prospective multicentre cohort study (manuscript under preparation).
This is the world's first study to prospectively evaluate the accuracy of an ICD coding method for sepsis identification in 450 patients across nine NSW hospitals.

3. **Kumar, A.,** et.al. (2024) Sources of error in modified Global Burden of Disease method in sepsis identification: An analysis of a prospective cohort study (manuscript under preparation). *This is the world first study to describe in details various sources of an error ICD coding method for sepsis identification.*

4. Heldens M, Schout M, **Hammond NE**, Bass F, Delaney A, **Finfer SR**. Sepsis incidence and mortality are underestimated in Australian intensive care unit administrative data (wiley.com). Medical Journal of Australia. 2018 Sep;209(6):255-60. *This study concluded that an accurate, reliable, and reproducible method is needed to determine the incidence and mortality rates of sepsis and septic shock in Australian ICUs.*

5. **Thompson KJ, Finfer SR**, Woodward M, Leong RN, Liu B. Sex differences in sepsis hospitalisations and outcomes in older women and men: A prospective cohort study - Journal of Infection. 2022 Jun 1;84(6):770-6. *In older adults, compared to women, men are at an increased risk of sepsis hospitalisation, sepsis-related ICU admission, death and readmission to hospital within one year after a sepsis hospitalisation. Understanding these sex differences and their mechanisms may offer opportunities for better prevention and management and improved patient outcomes.*

6. Nunnally ME, Ferrer R, Martin GS, Martin-Loeches I, Machado FR, De Backer D, Coopersmith CM, Deutschman CS, Surviving Sepsis Campaign Research Committee. The Surviving Sepsis Campaign: research priorities for the administration, epidemiology, scoring and identification of sepsis (springer.com). Intensive care medicine experimental. 2021 Dec;9:1-26. *This paper provides a framework for priorities in research to address the following questions: (1) What is the optimal model of delivering sepsis care?; (2) What is the epidemiology of sepsis susceptibility and response to treatment?; (3) What information identifies organ dysfunction?; (4) How can we screen for sepsis in various settings?; (5) How do we identify septic shock?; and (6) What in-hospital clinical information is associated with important outcomes in patients with sepsis?*

7. **Kumar A, Hammond N, Abbenbroek B, Thompson K, Taylor C, Venkatesh B, Delaney A, Finfer S**. Sepsis-coded hospitalisations and associated costs in Australia: a retrospective analysis. BMC Health Services Research. 2023 Nov 29;23(1):1319. *This study reported a significant increase in sepsis-coded hospitalisations over the last 20 years and also, where data is available, in associated costs in Australia. The increase in incidence has occurred mainly in those aged 65 years and over, and predominantly due to an increase in coding of unspecified sepsis.*

8. **Kumar A, Abbenbroek B, Delaney A, Hammond N, Grattan S, Finfer S**. Sepsis triggers and tools to support early identification in healthcare settings: An integrative review - Australian Critical Care. 2023 Nov 1;36(6):1117-28. *This review showed that no single sepsis tool or trigger is applicable across various settings and populations, but considering efficacy and ease of implementation, there is evidence to use lactate plus qSOFA for adult patients. More research is needed in maternal, paediatric, and neonatal populations.*

9. **Hammond NE, Kumar A**, Kaur P, Vijayaraghavan BK, Ghosh A, Grattan S, **Jha V**, Mathai D, **Venkatesh B**, Bhatia P, Todi S. Estimates of sepsis prevalence and outcomes in adult patients in the ICU in India: a cross-sectional study. Chest. 2022 Jun 1;161(6):1543-54. *This multi-centre point prevalence study in Indian ICUs showed a high burden of sepsis using both Sepsis-2 and Sepsis-3 criteria, with associated high rates of antimicrobial resistance and mortality. These findings have implications for public health and future research.*

B. Sepsis diagnosis and management:

1. **Thompson K, Venkatesh B, Finfer S**. Sepsis and septic shock: current approaches to management (wiley.com). Internal medicine journal. 2019 Feb;49(2):160-70. *This paper highlights that although acute case fatality rates of sepsis are decreasing, the ageing population and increasing incidence, together with greater appreciation that sepsis is followed by longer term physical, psychologic and cognitive impairment, means that sepsis poses an increasing public health problem. While early recognition and improved management of the acute episode will pay dividends, a substantial reduction in the burden of sepsis-related disease requires action across the healthcare system. Strategies to prevent and treat sepsis sequelae are less well developed and should be a priority for future research.*

2. **Venkatesh B, Finfer S**, Cohen J, Rajbhandari D, Arabi Y, Bellomo R, **Billot L, Correa M, Glass P,** Harward M, Joyce C. Adjunctive Glucocorticoid Therapy in Patients with Septic Shock (nejm.org). NEJM. 2018 Mar 1;378(9):797-808.
This is the world's largest study conducted in septic shock patients evaluating the efficacy of steroids in the management of septic shock patients.

3. Peake SL, **Delaney A**, Finnis M, **Hammond N, Knowles S**, McDonald S, Williams PJ, ARISE FLUIDS Investigators, The George Institute for Global Health and the Australian and New Zealand Intensive Care Society Clinical Trials Group. Early sepsis in Australia and New Zealand: A point-prevalence study of haemodynamic resuscitation practices (wiley.com). Emergency Medicine Australasia. 2023 Dec;35(6):953-9. *This study showed that ICU patients presenting to the ED with sepsis receive less fluids than current international*

recommendations. Study finding supports conduct of trials evaluating optimal fluid dose and vasopressor timing for early sepsis-induced hypotension.

4. ARISE Investigators and the ANZICS Clinical Trials Group. Goal-Directed Resuscitation for Patients with Early Septic Shock (nejm.org). New England Journal of Medicine. 2014 Oct 16;371(16):1496-506. *This landmark trial evaluated the effectiveness of early goal-directed therapy (EGDT) in patients with sepsis in Australia. The results contributed significantly to the ongoing debate on the best management practices for sepsis.*

5. Pirracchio R, Annane D, Waschka AK, Lamontagne F, Arabi YM, Bollaert PE, **Billot L**, Du B, Briegel J, Cohen J, **Finfer S**. Patient-level meta-analysis of low-dose hydrocortisone in adults with septic shock. NEJM evidence. 2023 May 23;2(6):EVIDoa2300034.

6. Spaeth, B., Taylor, S., Shephard, M., Reed, R. L., Omond, R., Karnon, J., **Abbenbroek, B.**,... & **Finfer, S**. (2024). Point-of-care testing for sepsis in remote Australia and for First Nations peoples. *Nature Medicine*, 1-2.

C. Sepsis and AMR:

1. Fitzpatrick F, Tarrant C, Hamilton V, Kiernan FM, Jenkins D, Krockow EM. Sepsis and antimicrobial stewardship: two sides of the same coin (bmj.com). BMJ Quality & Safety. 2019 Sep 1;28(9):758-61. *The article suggests that a change in mindset is required to integrate the management of sepsis and the promotion of antimicrobial stewardship as complementary strategies in the fight against AMR.*

2. Inglis TJ, Urosevic N. Where sepsis and antimicrobial resistance countermeasures converge. Frontiers in Public Health. 2017 Feb 6;5:6. *This document outlines key strategies, including faster and more accurate phenotypic antimicrobial susceptibility testing, incentives for physicians to use evidence-based antimicrobial therapy, and the development of a sepsis/AMR registry to harmonize regional surveillance data.*

Ongoing sepsis research:

1. National Sepsis Program Extension: This program aims to improve the awareness, recognition and support for people at risk of or diagnosed with sepsis in Australia. It is a collaborative effort involving The George Institute for Global Health, Sepsis Australia, and the Australian Commission on Safety and Quality in Health Care to extend the National Sepsis Program.

2. National Critical Care Sepsis Program: This program led by Prof Andrew Udy aims to:
    a. Establish a learning health care system to improve the outcome for patients diagnosed with sepsis
    b. Build capacity and infrastructure aimed at improving the experiences and outcomes of patients diagnosed with sepsis who are admitted to an intensive care unit
    c. Co-design future sepsis projects and build an Australian Critical Care Sepsis Research Roadmap
    d. Develop IT infrastructure to allow sustainable data integration
    e. Translate and develop benchmarking, evidence summaries and, potentially, clinical guidelines

3. **Post-sepsis model of care**: Led by Associate Prof Naomi Hammond, Program Head, Critical Care, The George Institute, this program aims to build effective post-sepsis model of care in Australia.

4. **Automated sepsis coding project**: This project is led by Dr Ashwani Kumar, Research Fellow, Sepsis Australia, The George Institute and aims to develop a Machine Learning algorithm for automated coding of sepsis.

5. **Sepsis awareness longitudinal survey:** Three surveys to gauge sepsis awareness in Australian public have been conducted so far as part of this project with next one planned for 2025.