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AMRC Statement on the initial antimicrobial treatment of sepsis

A pragmatic framework that should support, not dictate, clinical decision-making

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Sepsis is a life-threatening organ dysfunction caused by a dysregulated response to infection.(1) Early treatment with appropriate antimicrobials may improve outcome but antimicrobial overuse can cause harm and contribute to antimicrobial resistance.(2,3) Multiple organisations have produced guidelines, statements, recommendations, and standards around the choice and timing of antimicrobials that are often contradictory and open to challenge.(4-6) Consequently, the Academy of Medical Royal Colleges (AMRC) convened a working group led by the Faculty of Intensive Care Medicine to issue recommendations on the initial antimicrobial management of patients with sepsis.(7)

The resulting statement focusses on the challenge of identifying patients most likely to benefit from early antimicrobials. Early antimicrobial treatment makes sense if the mortality risk is due to the dysregulated response to infection, but as the report highlights, sepsis-related deaths commonly involve pre-existing conditions. Sepsis diagnosis involves evidence of infection and new organ damage. Clinicians often see this combination in people with long-term conditions (8) where a self-limiting or easily treatable infection is exacerbating underlying comorbidity or frailty, rather than causing organ damage through a dysregulated response. In such circumstances, comorbidities and performance status will be the main determinants of mortality, and early antimicrobial treatment will have limited potential to improve outcome. Future research will hopefully generate important insights and ultimately biomarkers to guide treatment decisions, but our current initial assessment tools generally assess illness severity, which may not correlate well with potential to benefit from early antimicrobials.

The statement includes a lengthy narrative review of the literature, which is well worth reading. It carefully considers the many complex issues that clinicians need to consider, and highlights the challenges of an overwhelmingly observational evidence base. There is welcome recognition of the importance of comorbidities, frailty, and patient preference in determining treatment decisions, including treatment intensity limits and end-of-life care, that has often been missing in previous guidance.

The key elements of the statement are two clinical decision support frameworks providing management recommendations based on likelihood of infection and illness severity, using NEWS-2 (National Early Warning Score, version 2) and PEWS (Paediatric Early Warning Score) for adults and children respectively.(9,10) These are pragmatic choices based on current use in healthcare and lack of evidence suggesting any alternative is superior, rather than strong evidence for the scores. NEWS-

2 predicts risk of adverse outcome with reasonable accuracy but we really need to predict benefit from early antimicrobial treatment.(11) Baseline NEWS-2 score is often elevated, so clinicians need to use their judgement to determine the extent to which abnormal early warning scores reflect serious infection or pre-existing conditions.(12) The statement appropriately advises that the early warning scores should support and not replace clinical judgement, in accordance with evidence highlighting the limitations of clinical decision aids compared to expert opinion.(13)

Each framework recommends actions for different risk groups within one, three, and six-hour time periods, based on evidence presented in the literature review. Only patients with the highest severity scores require antimicrobial treatment within one-hour. Longer time periods should facilitate more targeted use of antimicrobials, but only if diagnostic tests are completed in a timely manner. Assessment of undifferentiated patients is challenging, and many cases initially suspected of sepsis are ultimately found to have a non-infectious condition.(14) The previously mandated four-hour benchmark for pneumonia treatment in the United States shows how implementation of arbitrary time targets risks unintended consequences of misdiagnosis and inappropriate antimicrobial use.(15) It is also not clear how the proposed framework aligns to the emergency care pathway, which typically involves triage preceding definitive clinical assessment, nor how it is deliverable in an emergency care system with prolonged waiting times. Emergency departments can only achieve the one and three-hour time targets if people with suspected sepsis are prioritised, which may mean that other patients with time-critical conditions are deprioritised.

The statement ends by inviting national and local organisations to consider introducing and auditing the sepsis clinical decision frameworks, but it is not clear how they should do this. Any discrepancies between clinical decisions and framework recommendations could simply reflect the appropriate use of clinical judgement. Audit requires a robust clinical standard, yet the narrative review reveals the uncertainty and weakness of the evidence. Audit can certainly provide useful insights but we should be cautious about inferring that discrepancies between practice and recommendations reflect poor care.

Overall, the statement represents a pragmatic approach that reflects the complexity of the clinical decision and limitations of the evidence base. Clinical judgement is essential when applying uncertain evidence to complex cases. We advocate using the frameworks to direct senior clinicians to the most urgent cases and then letting them (rather than the framework) make the treatment

decisions. Ultimately, organising and resourcing the emergency care system to deliver timely clinical expertise is the key to improving sepsis care.

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Competing interests

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