Precision Medicine for Sepsis Management in Low- and Middle-Income Countries – Melioidosis as a Model?

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Advances in translational critical care has revealed limitations in the current clinical management of critical illness which is syndrome based (1). Studies evaluating the host response using immunoassays, multi-omics platforms and bioinformatics analysis have identified heterogenous subgroups (subphenotypes) as well as distinct pathogenic features (endotypes) among patients diagnosed with sepsis (2, 3). This has led to the aim of utilizing a precision medicine approach where targeted therapeutic management is based on utilization of assays to identify subphenotypes or clinical correlates of endotypes. This approach has been used in oncology with significant improvement in outcomes by targeting the underlying biological mechanism in individual patients (1).

The overwhelming majority of studies which have characterized the different subphenotypes or endotypes in sepsis patients have been conducted in high income countries (2, 3). Annually, there are an estimated 49 million cases of sepsis resulting in 11 million deaths, which represents close to 20% of global deaths (4). Almost 85% of the global incidence of sepsis are in low- and middle-income countries (LMICs) with the highest burdens in South Asia, East Asia, Oceania and sub-Saharan Africa (4). The characteristics of sepsis patients in these regions which may affect outcomes differ in demographics, pathogen etiology and co-morbidities compared to developed countries and even between the regions. However, the lack of studies conducted in these settings highlight a major limitation if a precision-based approach to sepsis management is to be implemented globally.

Melioidosis resulting from infection with the gram-negative saprophytic pathogen *Burkholderia pseudomallei* is endemic in Southeast Asia, Northern Australia, and the Indian subcontinent with a poorly defined epidemiology in many parts of the world (5). Melioidosis has distinct clinical features compared to other gram-negative bacterial infections with a varying proportion

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