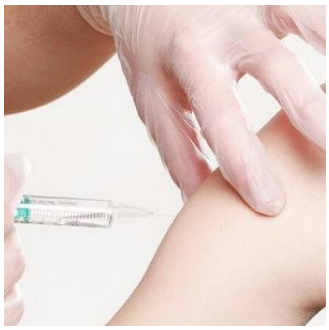
ICU MANAGEMENT & PRACTICE

Precision critical care for all?



All of medicine aspires to be precise, where a greater understanding of individual data will lead to personalised treatment and improved outcomes. However, precision medicine faces many challenges in critical care. These challenges include confusion about terminology, uncertainty about how to divide patients into discrete groups, and the need for timely interventions, according to a review paper in the journal Critical Care.

"Complex acute illness among patients with multimorbidity, integrated systems biology data with daunting scope and scale, and critical illness syndromes that lack gold-standard criteria are just some of the many barriers to newer precision strategies. To move past the failures of molecularly targeted therapeutics, novel trial designs will need to embrace and explore heterogeneity of treatment during phase 2/3 evaluation," write report authors led by Christopher W. Seymour, MD, MSc, Assistant Professor, Departments of Critical Care and Emergency Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA.

Traditional medicine has always sought to divide patients into groups, but this is also a key element for precision medicine. What is often overlooked in both is that assigning a patient to a particular group is non-trivial. Clinicians are long familiar with diagnostic challenges, differential diagnoses and vague syndromic presentations. Regrettably, the authors say, that challenge is not easily solved by precision medicine.

The authors explain how multimorbidity may also challenge the development of precision critical care. First, multimorbidity may be present and measurable, but unrelated to the discrete clusters that may guide precision treatment. Second, multimorbidity could itself be part of the set of variables evaluated when identifying discrete groups. In chronic obstructive pulmonary disease (COPD) phenotyping using principal components analysis, the presence of obesity, cardiovascular comorbidities and diabetes were included in the hierarchical clustering algorithm and ultimately found to be key features in a subgroup with a higher risk of mortality but less severe airflow limitation.

Also, research in precision medicine is faced with an enormous burden of information. To develop new scientific knowledge from large-scale studies that explore phenotypes or endotypes, a wealth of data must be gathered, analysed, and integrated across many levels. For example, a hypothetical study which seeks to gather data across a platform of system biology data types could generate more than one million SNPs from single cell genome sequencing, 40,000–50,000 microarray transcripts in transcriptomic analyses, 700 results from proteomic analyses, and 4000–7000 named and unnamed metabolites. Rather than 1000 patients, precision medicine studies have proposed enrolment of over one million patients in whom multiple organs can be sampled at more than one time point. The resulting scale of data, in which to search for important subgroups, would exceed a trillion data points. Such an increase would directly impact computational time to estimate even simple queries across relational datasets.

The report points to a variety of potential solutions to the problems of scale in precision critical care, including the use of state-of-the-art software to coordinate and index omics datasets (e.g., format, store, calibrate). "In the end, critical care may solve the immense problem of scale through both system level analyses that search for emergent properties in complex, electronic data and reductionist approaches that isolate single mechanisms with rare phenotypes," the authors say.

To make gains towards precision medicine for all of critical care, the authors emphasise that a multidisciplinary, collaborative approach is needed that spans three research domains: preclinical work, novel clinical trials, and implementation science. In addition, the authors say the changing pace of discovery work in precision critical care will mandate that trials of candidate therapies are nimble, accessible, and designed to test multiple therapies across heterogeneous patients.

"Future real-world testing and implementation of precision medicine will also require close partnership with electronic health record systems to reduce cost, improve timeliness of patient screening and treatment, and contribute to broader learning healthcare networks," the authors write.

Source: Critical Care
Image Credit: Pixabay

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