Core outcome sets in intensive care—what are they and why do we need them? An example for delirium

Rose, L., Burry, L., & Blackwood, B. (2021). Core outcome sets in intensive care—what are they and why do we need them? An example for delirium. Nursing in Critical Care, 26(3), 144-146. https://doi.org/10.1111/nicc.12627
Core outcome sets in intensive care—what are they and why do we need them? An example for delirium

Delirium in critically ill patients is common with an unclear pathogenesis and with known short- and long-term adverse physiologic, emotional, and cognitive outcomes. Because delirium is potentially preventable, it can be considered a useful quality metric. Standardization of interventions targeting delirium prevention, such as the intensive care unit (ICU) liberation (ABCDEF) bundle, is likely to lead to improvement in patient outcomes.

Variation across ICUs in the method chosen to assess and document delirium, may make comparisons of performance towards quality metrics problematic. As a hypothetical example, one ICU counts delirium days from the first day a positive delirium screen is documented to the first day without a positive screen. Another ICU considers delirium days to include all days with a positive screen until ICU discharge. This second ICU will record more days of delirium as it is known to reoccur. From a quality performance perspective, if days with delirium is the quality metric, this second ICU would be considered as underperforming compared with the first, despite using a more accurate method for recording the number of days with delirium.

Variation in the way we measure delirium and other outcomes of importance is also highly problematic in studies that investigate the effect of interventions to either prevent or treat delirium in the critically ill. Our Delirium Core Outcome Set team led a systematic review evaluating variability of outcomes, definitions, measures, and measurement time-points in published clinical trials of pharmacological or non-pharmacological interventions. We found substantial heterogeneity and multiplicity of trial outcome selection with 12 different delirium-specific and 94 non-delirium-specific outcomes reported in three or more of the 195 included studies. Measures and timing of measurement also varied. The need for standardization of outcomes and measures in delirium trials has been highlighted in the 2017 intensive care delirium research agenda and the 2019 Scientific Think Tank of the Network for Investigation of Delirium: Unifying Scientists (https://deliriumnetwork.org/).

Selection of different trial outcomes and measures is not unique to the study of interventions to prevent or treat delirium. Indeed, similar findings across numerous health conditions have been documented over the last three decades. Unfortunately, this lack of standardization has impaired the ability to statistically pool and compare results from trials of interventions addressing the same health condition to draw conclusions in relation to effective treatments, which is the purpose of a meta-analysis. Thus, selection of different outcomes and measures reduces statistical power and precision of meta-analyses, and importantly for critical care clinicians, precluding the ability to make evidence-based clinical or health policy decisions. Core outcome sets (COS) are designed to improve homogeneity of outcome selection and reporting for trials of interventions for similar health conditions. A COS is an agreed-upon minimum set of outcomes that should be measured and reported in all studies relating to a specific health condition or intervention.

Besides improving the precision of meta-analyses, COS development offers the opportunity for health service users (i.e., patients and families), policy makers, health technology assessors, research and health system funders, and those delivering health services (i.e., healthcare professionals) to participate in outcome selection efforts. It is essential to obtain broad representation in COS development as there are often differences in the perceived importance of outcomes. For example, ICU clinicians may view survival as an outcome of utmost importance. Patients, on the other hand, may perceive ability to return to prior functional capabilities as of greater importance than survival on its own. Therefore, broad stakeholder involvement enhances research relevance, value and patient centredness, and may facilitate more rapid understanding of effective treatments and their adoption into clinical practice. Although COS originated and are generally aimed at improving clinical research, more recently COS are being developed for use in quality improvement and performance measurement related to clinical practice. Therefore, we urge the readers of Nursing in Critical Care to look out for opportunities to contribute to COS development.

Core outcome set development commences with determination of “what to measure” (i.e., study outcomes) and culminates with determination of “how to measure” (i.e., instruments or measures) for the core outcomes. Measures may include patient-reported questionnaires; performance-based tests, assessments, or clinical rating scales completed by health professionals; imaging and laboratory tests including biomarkers. A COS does not mandate the primary outcome of a trial, nor prohibit the measurement of additional outcomes not in the COS.

To date, only a handful of COS specific to critically ill patients have been published. These include a COS for studies conducted in acute respiratory failure survivors, the COVenT COS—designed for
trials of interventions intended to modify the duration of ventilation,\textsuperscript{13} and a COS for research in critically ill patients received extracorporeal membrane oxygenation.\textsuperscript{14} Most recently published are a COS for paediatric critical care\textsuperscript{15} and two for COVID-19 trials.\textsuperscript{16,17} Several other protocols of COS have been published that are relevant to adult and paediatric critical care\textsuperscript{18,19} including our own protocol for a delirium COS.\textsuperscript{20} This COS is now complete and published in Critical Care Medicine.\textsuperscript{21}

In this special issue of the journal, there are three research studies, one integrative review, and a quality improvement project focused on delirium, emphasizing the importance of this topic among the journal’s readership. In reading these papers, and indeed all delirium-related studies in the critically ill, we urge readers to pay particular attention to reported outcomes, measures, and the time horizon of each measurement (i.e. when did measurement commence and when was it discontinued). Habeeb-Allah and colleagues\textsuperscript{22} report delirium incidence in post-operative cardiac surgery patients using the Arabic version of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and the Brief Confusion Assessment Method in surgical wards. The authors’ definition of delirium was at least one positive CAM-ICU in ICU, or at least one positive brief CAM in a surgical ward. In both cases, the maximum duration of delirium assessment was five post-operative days. Gravante and colleagues\textsuperscript{23} report delirium prevalence in general ICU patients using the Intensive Care Delirium Screening Checklist each admitted patient was evaluated for up to a maximum of 5 days after waking up from sedation. Delirium assessment did not continue after ICU discharge.

Both studies laudably use validated delirium screening tools as recommended by the Society of Critical Care Medicine Pain Agitation Delirium Immobility and Sleep guidelines.\textsuperscript{24} Although the estimates of delirium occurrence in these two studies are not comparable given the different patient populations, we encourage readers to reflect on the different measurement time horizons. Studies that continue delirium assessment into the wards may result in a different (and arguably more accurate) estimate of delirium occurrence than one that discontinues assessment on ICU discharge.

In conclusion, awareness of the impact and consequences of differences in the selection of outcomes and the methods used to measure outcomes is important not only for researchers designing trials but also for clinicians as consumers of research and those involved in quality improvement activities. In the future, we anticipate more core outcome sets relevant to critical care to be developed and encourage the journal’s readership to seek out opportunities to participate in their development.

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