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### Evidence-Based Care in the Intensive Care Unit



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By taking the Hippocratic Oath, physicians commit to practising their art according to the current best scientific knowledge. For that purpose, all physicians need full access to the best knowledge (see **Figure 1**). The necessary steps include continuous innovation in healthcare, followed by appropriate translation of innovative care into routine practice and eventually reassessment of remaining gaps in knowledge to foster new innovations. Ideally this chain makes the wheel of progress by which people live longer in good health. In practice, a substantial number of routinely used health interventions have never been tested in a rigorous scientific manner. Moreover, interventions used routinely for decade eventually demonstrated harm to people.

It is a complex task to define what the current best scientific knowledge is. First, a clear-cut and relevant clinical question needs to be formulated. The most common clinical scenarios are how best to diagnose a specific disease or condition, and how to treat the patient. Then, these clinical scenarios should be translated into a research question that should be meaningful for both physicians and researchers. Typically, in the diagnostic domain, questions are formulated as: "In patients with disease or condition X, is diagnostic test A better than diagnostic test B? For therapeutic interventions, research questions are usually formulated as: "In patients with disease or condition X, is intervention A superior to intervention B? The systematic approach to formulate research questions is usually referred to as the PICOM approach. Briefly, this approach requires defining a precise population (P), explicit experimental intervention (I) and comparator (C), patient-centered outcomes (O) and study designs that are relevant to address the question (M).

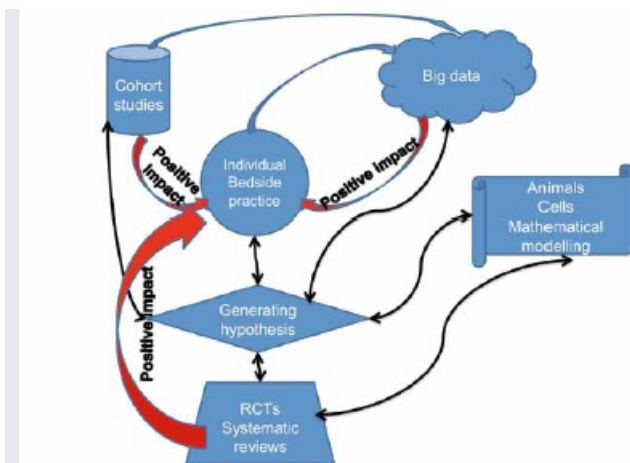


Figure 1

Generating evidence in medicine, and more specifically in the intensive care unit, always started with clinical observations. Obviously, research questions arise mainly from clinical observations. In addition, observational studies are part of the process of addressing relevant research questions not only in the diagnostic domain, but also for therapeutic interventions. For example, at the time of the polio pandemics, observations of patients dying from respiratory paralysis raised the issue of compensating lung function. The introduction of artificial ventilation, mainly by iron lungs, prevented death in almost all patients. In this case, clinical observations allowed the generation of evidence-based care for these patients without the need for more convincing data. Owing to an international effort - STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) – [www.strobe-statement.org](http://www.strobe-statement.org) – the conduct of cohort, case-control and cross-sectional studies may now follow high quality standards minimising biases. More interestingly, recent years have been characterised by the emergence of 'Big Data' in the field of critical care medicine. The concept of big data followed the rapid development of health electronic records with automatic and systematic storage

of almost all data for all patients. Thus, the way to perform observational studies may be revolutionised. Indeed, there are no longer concerns about sampling, sample size, selection bias and generalisability, as all data from all patients are used. However, there are still several issues that need to be addressed before evidence generated via big data can be translated into routine practice. First, tools to standardise collection of data and in particular qualitative information are still lacking. Second, traditional statistics in medicine are based on the concept of sampling a population according to the probability of rejecting or not the null hypothesis. In the big data era, data from the whole population are used. Subsequently, sample size and power are no longer relevant issues. Obviously, the use of massive data also likely decreases the clinical relevance of type I errors. Finally, defining a null hypothesis might be also meaningless. Even more, it might be a limiting factor to innovation. Indeed, getting access to all information from all patients may disclose characteristics of a disease or a condition, or of an intervention, that would never be seen in selected samples of a population. Thus, the use of big data may result in new concepts and new ideas beyond traditional views in the field of critical care medicine.

Information from observational studies and information derived from big data may still not be sufficient to generate firm evidence that an intervention should be used in routine practice. While they play a major role in correctly defining the population of interest, the experimental intervention and best comparator, and outcomes, randomised controlled trials remain so far the gold standard for establishing evidence-based treatments. Unsurprisingly, thousands of randomised trials have been conducted in the field of critical care medicine, and their number is continuously growing as well as the number of related systematic reviews. Yet the proportion of evidence-based interventions in the intensive care unit remains worryingly low. Moreover, the way experimental interventions are tested through randomised controlled trials is far from being efficient. Indeed, for each specific research question, almost everything has to be restarted from zero, i.e. building a new group of investigators and methodologists, finding new funding, designing new case report forms and new data management processes, recruiting new centres, new patient populations, contracting new insurance, and so on. Then, usually it may take from 5 to 10 years to get a research question answered. Of note, if the trial appeared to be positive a confirmatory trial would likely be requested before adopting the evidence. Running a second trial will add more years before people may consider that the research question has been fully addressed. Therefore, a growing number of trialists are considering moving away from this conventional view of conducting randomised studies. Some of them are suggesting, whenever relevant, doing adaptive clinical trials that may allow saving time and money. For example, in a single adaptive trial, several interventions or several doses of an intervention may be tested simultaneously for the same disease or condition. In such trial design, it is the accumulation of information during the conduct of the trial that may be used to adapt tested interventions or, sometimes, the targeted population. Others are considering building large population-based cohorts to be followed up for decades within a prospectively designed framework. Then, within these cohorts, interventions may be easily tested in random samples along the way of the cohort follow-up. This concept may also be of interest in the critical care field. For example, it may have the advantage of getting the full trajectory of the critically ill including pre-illness and long term post-illness followup. Such 'within population-based cohort' randomised trials use the cohort infrastructure, and allow investigation of different interventions in parallel, thus saving time and money. Finally, within the population-based cohort, patients may be always benefiting from best evidence-based care.

Undoubtedly, we need to improve the efficiency of methods to generate evidence-based care for the critically ill. Big data and innovative designs for clinical trials are likely to become more and more diffused among critical care researchers, and ICU physicians are likely to be adopting more and more the conclusions generated from these new tools. In recent years, it has become obvious that medical education still poorly prepares physicians for evidence-based practice. There is a need to teach medical students early how to accurately formulate clinical and research questions, how to accurately search and summarise the available literature, and how to generate evidence-based practice.

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