# Big Data for Critical Care

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# 1. ABSTRACT


## 1.1. Background

Like other scientific fields, such as cosmology or high-energy physics, biology as a whole and medicine and healthcare in particular are facing the challenge of an extremely quick transformation into data-centered sciences. This challenge entails the daunting task of putting these data to work through computer-based methods capable of transforming them into workable knowledge. In the medical context this could, for instance, take the form of the design of medical decision support systems for diagnosis, prognosis, and patient management. Arguably, one of the most data-dependent clinical environments is the intensive care unit (ICU) and by extension the whole area of critical care.

## 1.2. Methods

The increasing availability of complex and heterogeneous data at the point of patient attention in critical care environments makes the development of fresh approaches to data analysis almost compulsory. Methods from the field of Big Data Analytics (BDA) can provide such approaches and have already shown their usefulness in tackling problems in the area. This paper reviews the state-of-the-art on the use and application of such methods to critical care problems. Such review is presented from the viewpoint of the different subfields of critical care, but also from the viewpoint of the different available BDA techniques.

## 1.3. Conclusions

In this paper, we have provided a structured state-of-the-art that illustrates the broad-ranging ways in which BDA methods can make a difference in problems affecting the manifold areas of critical care.



## 1.4. Keywords

Critical Care, Big Data Analytics, Intensive Care Unit, Machine Learning.

# 2. INTRODUCTION

We are witnessing an epochal change in Biology as it quickly evolves from being a wet laboratory-centered science towards becoming a data-centered one [1], a process that could be seen as a pertinent example of the pervasive Big Data (BD) paradigm [2]. Medicine draws heavily from the biological sciences and does not escape from this transformation. On the contrary, it can be argued that the transformation is enhanced by the increasing accessibility to medically-relevant data, mediated by the fast development of novel and increasingly sophisticated non-invasive data acquisition methods, and by the rapid accommodation of medical practice to advanced information technology networked systems. A further issue to consider in the context of data-centric medicine is the convergence of medicine and the omics sciences, called to fulfill the promises of truly personalized medicine.

Data is thus quickly becoming a core concern in healthcare and stands to improve it by providing insights into the causes and outcomes of disease [3], better drug targets for precision medicine, and enhanced disease prediction and prevention. Moreover, citizen-scientists will increasingly use this information to promote their own health and wellness. BD can improve our understanding of health behaviors (smoking, drinking, etc.) and accelerate the knowledge-to-diffusion cycle [4]. Data availability to medical experts is the main building block for the development of medical decision support systems (MDSS) [5,6,7,8].

Medical decision making in clinical environments is often made on the basis of multiple and heterogeneous parameters and, obviously, in the context of patient presentation. This includes the setting and the specific conditions related to the reason for admission as well as the procedures involved. Importantly, the data used in such decision making may originate from manifold sources and at multiple scales: devices in and around the patient, medical images, laboratory information, blood tests, omics analyses, and a potential wealth of ancillary information available both prior to and during the hospitalization.

One of the medical environments in which data dependency comes to the fore is the critical care department (CCD) in any of its general or specialized forms: intensive care unit (ICU), pediatric intensive care unit (PICU), neonatal intensive care unit (NICU) or surgical intensive care units (SICU), and this involves very practical implications for MDSS at the point of care [9]. As obvious as it may seem to say, the ICU cares for acutely ill patients. Many of these, and particularly SICU patients, are technologically dependent on life-sustaining devices such as infusion pumps, mechanical ventilators, catheters and so on. Beyond treatment, assessment of prognosis in critical care and patient stratification combining different data sources is extremely important in a patient-centric environment such as this.

The CCD conditions obviously put a strain on data acquisition and management tasks. The assessment of clinical needs changes depending on the acuity of the patient and the conditions present at the point of care. Changes in patient status unavoidably drive the quantity of data captured within the bedside documentation, either through flow sheets or paper and electronic records. The medical team, though, must ultimately define what is required and, in order to support clinical decision making, it may also be necessary to include further data from the electronic health record and from monitoring devices. These include fluid intake and patient output, demographic information, laboratory blood draw assessments, medical images, and so on. These high-volume, high-velocity, and high-variety information assets that demand cost-effective, innovative forms of information processing for enhanced insight and decision making fall under the umbrella term BD [10]. BD are worthless in a vacuum. Its potential value is unlocked only when leveraged to drive decision making. To enable such evidence-based decision making, organizations need efficient processes to turn high volumes of fast-moving and diverse data into meaningful insights [11].

In any case, medical device connectivity in the different types of ICU is essential for providing a complete clinical decision support framework. While electronic medical records in and of themselves offer enormous work flow benefits, the documentation and charting systems are only as good as the data they convey. Due diligence by care providers can be augmented by automated and validated data collection, achieved through a seamless form of medical device connectivity and interoperability that is supported both inside and outside the hospital premises, and that follows the patient throughout the assisting process. That is, it can be augmented through standardized ICU data curation.

Fresh approaches to data analysis that are tailored to the specific needs and limitations of the ICU environments are thus required, and some of the most interesting of such approaches are currently based on the acquisition of intelligence from data, which have already shown its relevance both as the basis for MDSS design and development [12] and as tools to improve hospital inpatient care [13].

This paper aims to provide a detailed up-to-date survey on the use of BD methods for data analysis in critical care environments, using [14] as source for state-of-the-art machine learning (ML) applications on critical are.

According to this goal, the remaining of the paper is structured as follows. A state-of-the-art of the application of BDA to critical care is first presented, followed by individual reviews devoted to patient monitoring and alarm algorithms; to neonatal critical care; and to sepsis management. We conclude by highlighting how BDA can have a significant impact in the area of critical care.

# 3. APPLYING BIG DATA ANALYTICS IN CRITICAL CARE

BDA techniques under the umbrella concept of Artificial Intelligence (AI) have, over the last decades, demonstrated not just their promise, but their actual value as data analysis tools in different fields of biology and health. These fields include, amongst others, bioinformatics [15,16], genetics and genomics [17,18], clinical applications [19], medical decision support and clinical diagnosis [20,21], oncology [22,23], psychiatry and neurological disorders [24,25], or cytopathology [26]. Note that in many of these fields, data analysis has traditionally been dispensed by statisticians and the integration of both scientific cultures has not always been a seamless process [27].

Critical care might seem too narrow a field to provide by itself a particular perspective on the use of BDA. The situation is actually the opposite: these types of methods are being applied to critical care problems with a variety of approaches of astonishing depth and breadth. This is not a new situation: Hanson and Marshall [28] were already reviewing the use of AI in critical care back in 2001, stating that the ICU environment was particularly well suited to the deployment of AI-based analytical strategies due to the wealth of available data and the promise they hold of increased efficiency in inpatient care due to their specific characteristics.

The current paper aims to provide a state-of-the-art compact survey of BD applications to problems in the area of critical care. A similar attempt by Johnson and colleagues [29] takes a different route and emphasizes the challenges posed by critical care data themselves, which is a very interesting point of view according to which researchers in the field should consider the need to focus as much on data-related challenges as on the development and application of appropriate data modelling techniques. That is, from a Data Mining perspective, we are advised to shift part of our focus from the data modelling stage to the data understanding and pre-processing stages. Three main challenges are considered, namely *compartmentalization*, *corruption* and *complexity*. Compartmentalization includes problems related to data privacy and anonymization, data integration from potentially heterogeneous databases, and data harmonization in terms of consistent definition of concepts throughout databases. Corruption involves different types of data errors, including issues such as data missingness and data imprecision (usually due to mismatching goals in the data acquisition and data modelling processes). Finally, complexity includes issues of prediction, state estimation and data multi-modality. This latter challenge bridges the stages of data pre-processing and modelling.

In the current study, instead, we categorize published studies according to several different critical care subfields, singling out in sub-sections those to which more attention has been paid, and collecting the rest in a separate sub-section.

# 3.1. Big Data Analytics for Patient Monitoring and Alarm Algorithms in Critical Care

As described in the introduction, critical care patients are often technologically dependent on monitoring or life-sustaining devices. The assessment of prognosis and patient stratification making use of these combined data sources is extremely important, which highlights the importance of medical device connectivity in this patient-centric environment as an essential element of a complete clinical decision support framework.

The data made available by these devices often takes the form of signal, making it the perfect target for signal processing techniques based on ML and related methods. One of the key ICU problems addressed with this approach is patient monitoring and the related design of algorithms for the implementation of patient alarms. A position editorial paper by Walsh *et al.* [30] recently highlighted what possibly is the single most challenging problem of this type: the potential negative effects derived from alarm fatigue; that is, from false positive alarms that might unduly mask true positive ones.

The field of alarm algorithms in critical care monitoring was considered in some detail in [31]. There, three levels at which these algorithms could operate were described, namely *signal acquisition*, *alarm generation* and *alarm validation*. Requirements for these algorithms were also listed, including: robustness against artifacts and missing values, real-time operation capabilities, predictable behavior and methodological rigor. Imhoff and colleagues describe their own previous early experience with ML methods in this area [32,33]: a combination of time series analysis with support vector machines (SVM) and knowledge bases.

Artificial neural networks (ANNs) were, from very early on, picked up as building blocks of the design of monitoring alarms, specifically for monitoring of patients under anesthesia [34,35]. More recent work in this sub-field [36] proposed the use of ANNs and Decision Trees (DT) for the design of patient-specific alarm algorithms in real time. DTs [37] and Random Forests (RF) [38], an extension of DTs, have also recently been proposed for the reduction of false cardiac arrhythmia alarms.

Other somehow less standard methods applied to this area include early work using Bayesian Networks (BN) [39] for event detection in patient monitoring. More recently, Gaussian Processes (GP) have also been used in patient vital signals monitoring after surgery [40] and unsupervised hierarchical clustering was used in [41] for the identification of physiologic patient states at the ICU. Fuzzy systems, which could be characterized under the umbrella term of AI, have been shown to be specifically well suited for the design of alarm systems at the ICU [42].

Recent work by Joshi and colleagues [43] in the design of alarms for the NICU is described in the next section, which is devoted to neonatal critical care. Another similar interesting line of research is that of Temko and co-workers concerning the NICU problem of neonatal seizure detection from EEG (see, for instance [44] and [45]). In the latter study, authors state that “Technologies for automated detection of neonatal seizures are gradually moving towards cot-side implementation”. For this, they propose an interesting MDSS that involves audified EEG and several ML-supported information output visualization approaches, where the output is generated through the post-processing of several EEG channel-specific SVM classifiers. Fuzzy systems for the design of NICU alarms for preterm infants were also proposed in [46].

## 3.2. Neonatal Critical Care

Despite the fact that we are highlighting the most popular areas of application of BDA in critical care, this categorization is, to some extent, artificial because some studies cross over such categorization. An excellent example of this is the recent work by Joshi and colleagues [43] who apply clustering and state-transition methods for the analysis of alarm systems in neonatal intensive care. Given that, as previously mentioned, the main problem in alarm management in critical care is the preponderance of false positive alarms, leading to “alarm fatigue”, this problem becomes specially acute in the neonatal critical care population and for premature neonates in particular due to their often far more irregular physiological signals. Another example defying easy categorization can be found in recent work by Mani and co-workers [47], who investigated the use of ML methods for the early detection of late-onset neonatal sepsis. This work is not just an example of crossover topics, but also of the appropriate use of a broad selection of different BDA methodologies and related approach for formal comparison, including SVM, Naïve Bayes (NB) in different variants, K-Nearest Neighbor (KNN), decision trees (CART), RF, Logistic Regression (LR) and Bayesian methods.

There are certain patterns to be found in the use of BDA and related methods at the NICU, both from the point of view of the specific problems addressed using these methods and from the point of view of the type of methods used. Beyond the aforementioned design and development of automated alarm systems and sepsis management, the former include problems such as risk-of-death (RoD) prediction and brain development, and neurology issues in neonates, amongst others.

RoD or mortality prediction in the NICU has for instance been investigated for over a decade by Frize and co-workers. In both [48] and [49], for example, ANNs, in their standard feed-forward multilayer perceptron (MLP) form trained by back-propagation, were used for this purpose. Interestingly, the authors define an MDSS that involves neonates' parents in the decision loop, which is a quite unique and highly sensitive way to comply (even if inadvertently) with the new European Union General Data Protection Regulation (GDPR) that went into effect in April 2018 [50]. The GDPR includes an article on “Automated individual decision making, including profiling” that establishes a policy on the right of citizens to receive an explanation for algorithmic decisions that may affect them.

ANNs in the latest work by Frize and colleagues [49] used in-built missing data imputation and treated mortality prediction as a heavily unbalanced binary classification problem (due to the comparative low mortality rate of patients in the analyzed database). Unsurprisingly in such setting, the achieved sensitivity (ratio of true positives to all positive cases) is far lower than the achieved specificity (ratio of true negatives to all negative cases). Even if surpassing clinical expectations, this reveals a typical difficulty faced by these models: if no proactive class-rebalancing procedures are used, the most relevant indicators (in this case sensitivity) are bound to under-perform.

A somehow different approach can be found in the use of BDA methods for the development of MDSS for neonatal critical care assistance by Cerqueira and colleagues [51], where the explicit target is the prediction of the RoD for newborns admitted to NICUs, but where the emphasis is placed on the BD pipeline of the MDSS (including data preprocessing) as a simulation tool to investigate the problem beyond actual prediction. The proposed MDSS uses

ANN (standard MLP) and SVM classifiers. Mortality prediction has also been addressed using DTs in [52] and Fuzzy Systems in [53].

BDA has also been used for the assessment of brain development in preterm neonates at the NICU. Recent examples of this include [54] and [55]. The former focuses on brain maturity prediction from functional MRI data in a dual approach that involves the use of SVM classifiers to discriminate between term- and preterm-born infants and the use of Support Vector Regression for the automated estimation of birth gestational age of neonates. The latter provides a different twist to the problem of preterm *vs.* term-born neonates classification, finding discriminative pattern of alterations in basal ganglia and frontal connections, first by focusing on functional connectivity patterns and, second, by assisting SVM classifiers with Independent Component Analysis (ICA)-based source extraction, in a combined source extraction-classification analytical pipeline suitable for the problem at hand. Temko and co-workers have a long track of research in neurological issues related to neonates at the NICU. These include for instance the recent work on neonates' seizure detection [45] from EEG that has been described in the previous section devoted to patient monitoring and alarm algorithms in critical care. In related work dealing with neonatal neurological pathologies, Ahmed, one of Temko's co-workers [56] investigates the non-trivial problem of grading the severity of hypoxic-ischemic encephalopathy in neonates from EEG data. Hypoxia is the lack of oxygen and ischemia the decreased blood supply to the brain near the time of birth. This severity grading analysis is understood as a multi-class problem addressed using a combination of Gaussian mixture models and SVMs.

## 3.3. BDA for sepsis management at the ICU

One of the medical problems in critical care to which more attention has been paid from the point of view of BDA techniques is that of the management of the sepsis pathology. This has been accomplished mostly from the point of view of diagnosis and prognosis.

Fuzzy systems and rule extraction, mostly as strategies for increasing the interpretability and usability of the results have been proposed: a Fuzzy DSS for the management of post-surgical cardiac intensive care unit (CICU) patients was described in [57]. The problem of rule generation was addressed in [58] and [59], the former together with an ANN.

Beyond [58], the initiatives related to the application of ANNs to the study of Sepsis have also resulted in expert systems such as the one called SES, in early work described in [60], designed for the diagnosis of pathogens and prescription of antibiotics. Ross and co-workers [61] later derived a system of ordinary differential equations together with an ANN model of inflammation and Septic Shock. Other studies have deployed ANNs for the study of sepsis. They include [62], who presented a clinical study examining SIRS and Multiple organ dysfunction syndrome (MODS) in the ICU after cardiac and thoracic surgery. A state-of-the-art application of a Deep Learning (DL) technique, namely Deep Reinforcement Learning (DRL) has recently been proposed in by Raghu and co-workers [63] for the definition of continuous-space models for sepsis treatment, in a twist that goes beyond the more traditional development and use of discriminative classifiers.

SVM models have also been used for the prediction of sepsis. Kim and co-workers [64] applied them to study the occurrence of sepsis in post-operative patients. Wang *et al*. [65] went a step further to build a DSS for the diagnosis of sepsis. Tang and colleagues [66] presented an SVM-based system for sepsis and SIRS prediction from non-invasive cardiovascular spectrum analysis.

BDA methods have also been used with varying success for the more specific problem of the prediction of mortality caused by Sepsis. A diagnostic system for Septic Shock based on ANNs (Radial Basis Functions -RBF- and supervised Growing Neural Gas) was presented in [67]. Also in this area, Brause and colleagues [68] applied an evolutionary algorithm to an RBF network (the MEDAN Project) to obtain, over a retrospective dataset, a set of predictive attributes for assessing mortality for Abdominal Sepsis. Relevance Vector Machines (RVM), SVM variants with embedded feature selection, were used in [69], DTs were used in [70], while BN models were used in [71] and [72]. Finally, kernel methods were used in [73].

## 3.4. Further applications of BDA in critical care

The previous topic-specific sub-sections are, arguably, devoted to those critical care-related problems to which more attention has been paid from the point of view of BDA approaches. All these reviews reflect not only the manifold areas of application to critical care, but also the broad palette of methods available to practitioners in critical care.

Other problems, to which perhaps less attention has been paid from this point of view include, among others, general mortality prediction using ANN models [74,75,76] and SVMs [77]. Another problem is that of medicine dosing, to which less standard methods such as BN [78], or DRL [79] have been used. Other applications of Deep Learning techniques (the current *reincarnation* of ANNs, very much in vogue but which is usually restricted by large data requirements) include that for the unsupervised learning of phenotypical features in longitudinal sequences of serum uric acid measurements, as investigated in [80]. The application of Fuzzy Systems for disease-based modeling for fluid resuscitation and vasopressor use in ICUs has also been investigated in [81].

# 4. CONCLUSIONS

In this short overview paper, we have described the increasingly complex challenge posed by the current data availability surplus in medicine in general and critical care in particular. Advanced BDA methods have provided evidence of their value in extracting usable knowledge from these data. The many different approaches to the use of these methods in the CCD have been surveyed and the main challenges they face have been outlined.

One of the main limitations of the quantitative methods for the assessment of ROD currently in use at the ICU is their lack of specificity (i.e. the high number of false positive cases they incur), which not only puts an extra risk on an already severely affected patient population, but also results in an unnecessary burden for National Health Systems. In this regard, BDA techniques can play an important role as they improve the overall performance by combining the indicators already in place with other clinical variables, which are routinely measured.

Attending to the nature of clinical data available in the ICU, it is possible to better assess prognosis through a proper embedding of the data. Recent studies have revealed that 80% of medical data is unstructured, although clinically relevant [82]; and these data can be traced in multiple locations like physician notes, medical correspondence, individual EMRs, lab and imaging systems, CRM systems, finance and claims. Despite the fact that healthcare organizations are leveraging Big Data technology to capture all of the information about a patient to get a more complete view about the medical data, getting access to this valued data and categorizing it into clinical and advanced analytics is crucial for building sustainable healthcare systems that are more accessible.

In conclusion, we believe that Big Data Analytics methods prove to be valuable in an extremely data-intensive environment such as the ICU. They can provide actionable and interpretable prognostic indicators and also give insight about the relevance of different clinical traits that are not recommended to be used in the current protocols. In this regard, we believe that future work in Big Data to study the role of “omics” (transcriptomics, proteomics and metabolomics) during the inflammatory cascade during sepsis may further improve our understanding of the mechanisms and physiopathology of sepsis.

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