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The Future ICU

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The Intersection of Big Data, Artificial Intelligence, Precision and Predictive Medicine to Create the Future of Critical Care

Over the next 50 years, critical care will evolve from a system that reacts to patient deterioration into a system that predicts and prevents these events. The application of real-time analytics to large-scale integrated ICU patient data will facilitate creation of learning healthcare systems and delivery of personalised and even predictive critical care medicine.

Over the next 50 years, critical care will evolve from a system that reacts to patient deterioration into a system that predicts and prevents these events. The pathway to proactive critical care involves technical and computing advances that integrate large-scale clinical data from critically ill patients and applies complex analytics in real-time to personalise care and predict untoward events. These advances will facilitate creation of learning healthcare systems and delivery of personalised and even predictive critical care medicine. In the not-so-distant future, ICU patients will look vastly different than the patients we see today with multiple organ dysfunction, as we predict and prevent critical illness and become an environment where individualised care is delivered to patients recovering from unforeseen traumatic injuries, increasingly complex surgeries and unpredictable acute illnesses.

Already in the present day, patients in critical care units generate extraordinary amounts of data, from diagnostic and laboratory testing, provider notes, intermittent and continuous monitoring equipment, and myriad support devices such as mechanical ventilators. In the near future, the panoply of monitoring devices will take advantage of secure wireless connections to facilitate contactless patient monitoring that functions seamlessly across healthcare environments such as the ED, radiology, OR and the ICU. Outside of healthcare, in the consumer market we are already experiencing the explosion of internet-connected devices known as the internet of things (IoT). Those devices, estimated to be as many as 200 billion by 2020 (Intel 2019), are now using a small fraction of internet traffic but non-human, but the coming global rollout of 5G connectivity will increase exponentially machine-to-machine traffic to more than 50% of internet traffic by 2022 (Cisco 2019; McKinsey 2017a; McKinsey 2017b). The IoT already exists in healthcare, being used to track equipment, patients and even providers throughout the hospital. Although the evolution of IoT devices and other monitoring equipment complement the developments outside of healthcare, such as in computing technology and the consumer markets, they have unique needs in healthcare. For example, healthcare has greater demands on secure communications as well as reliability and safety across patient environments such as the ICU, OR, radiology, emergency department, pre-hospital setting and more.

Imagine for healthcare to adopt the manufacturing production principles of big data, where the introduction of comprehensive, real-time data collection and analysis results in fantastically more responsive production systems. In healthcare, in order for the growing constellation of monitoring, testing and data to be clinically valuable, it must be integrated in real-time with the entire spectrum of clinical data in order to ensure the delivery of timely, high quality patient care. An important next step in handling the impending explosion of data generated by critical care patients is data harmonisation. Our current lack of inter-operability between electronic health record (EHR) systems is confounded by multiple instances of duplicated data. For example, in the data warehouse for one of our hospitals, there are multiple entries for haemoglobin, each recorded with a different label: ED-Hgb, OB-Hgb, STAT-Hgb and regular inpatient-Hgb, outpatient-Hgb, neonatal-Hgb and point-of-care-Hgb! Harmonising data variables and concatenating these instances is one step towards clinically effective data reporting and utilisation.

Harnessing the full spectrum of clinical data needed to care for ICU patients requires advancing the underlying technologies that make it feasible. Computing power is now in the realm where basic streams of real-time data can be aggregated and reported, such as clinical lab testing, nurse-recorded vital signs and intravenous infusion pump data. The next steps require the computing and storage capabilities to handle the entire *river* of real-time data, and the associated analytic capacity to efficiently drive patient care. In the coming years, the application of artificial intelligence and machine learning will solve some of the vexing problems we experience in healthcare, such as early detection of critical illness, alarm fatigue, and variability or subjectivity in test interpretation. While advances in natural language processing may underpin the future of radiology and pathology data systems, AI will be used to solve some of our most challenging problems. For example, the inability to consistently acquire and interpret ultrasound images limits the application of one of our most available technologies. The ubiquitous nature of ultrasound in the future of critical care makes it necessary to solve this problem, and the combination of AI and computing interfaces makes this possible.

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The effective integration of clinical critical care data at scale with real-time analytics is the foundation for changes at each end of the medical care spectrum. At the level of *healthcare systems*, it enables iterative system-level improvements that produce consistent, cutting-edge, reliable, high quality care. At the level of the *individual patient*, it enables care to be customised for each patient according to the current state of their acute and chronic conditions, while taking into account other relevant factors such as social support and other determinants of health. In essence, aggregation and utilisation of clinical data promote the creation of *learning healthcare systems and personalised medicine*. Taken together, these embody the axiom that the public health is represented by the point estimate while each individual patient is represented within the confidence interval. In other words, data collected from groups of patients will appear as the mean (e.g. the point estimate from a clinical study) and are amenable to system-level interventions, whilst individual patients rarely fall exactly at the exact point estimate but are likely to fall within the range of results from the group (e.g. the confidence interval), and individual responses may be optimised or predicted by fully characterising each unique patient.

Integration of data permits the conversion of the traditional ICU to a learning healthcare system. A learning healthcare system (LHS) is defined by the Institute of Medicine as a system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience (Institute of Medicine 2007). A LHS is a sociotechnical system with afferent and efferent components where the afferent component assembles, analyses and interprets data from various sources, and the efferent component returns these findings to the healthcare system in order to favourably change clinical practice. The afferent side is made possible by recent technical innovations such as EHR data and the IoT, and efferent side incorporates elements such as behavioural psychology, implementation science, behavioural economics, policy and organisational theory in order to effect change. The collision of big data harmonisation, EHR interoperability and AI will make easier the transition of each hospital from a traditional healthcare environment to a learning healthcare system.

The creation of learning healthcare systems sets the foundation for personalised medicine on an international scale. Personalised medicine is a medical model that individualises the care of patients according to their risk of disease or their predicted response to an intervention, and thus has the potential to ensure the best

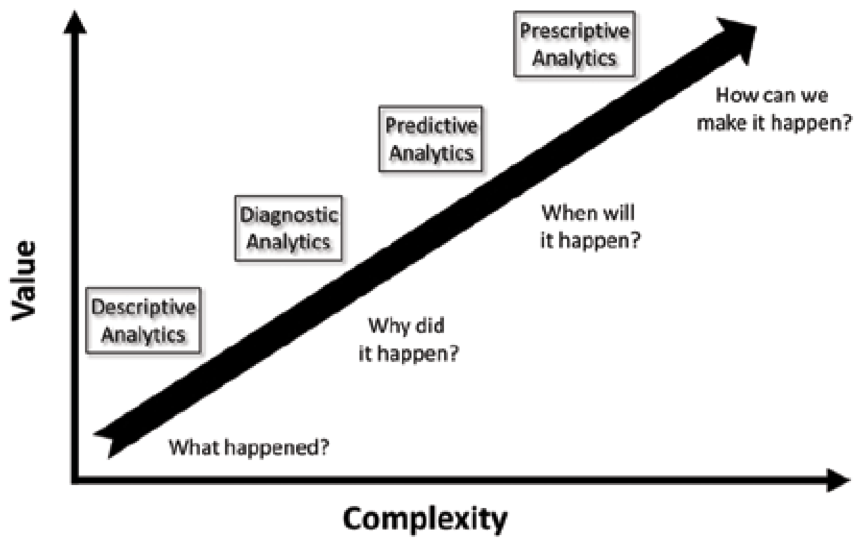

Figure 1. The penultimate approach to personalised medicine.

response and highest safety margin for patient care. This last feature is particularly important in critical care units, where medical care is often time sensitive, where high-stakes decisions are made with incomplete information and imperfect knowledge, and where "decision fatigue" may occur because of the large number of decisions made per hour (McKenzie et al. 2015). Ensuring the highest probability of a favourable response to an intervention effectively tailors medical treatment to the individual characteristics of each patient. While the claim that personalised medicine requires scientific breakthroughs in areas such as genetic profiling and molecular medicine to deliver individualised patient care, the earliest phases of personalised medicine already exist in oncology and in the treatment of rare diseases, whilst the fullest expression of personalised medicine requires both additional scientific discovery and the real-time integration and analysis of these large-scale data to overcome the human limitations of information overload and cognitive processing. For example, systematic application of surveillance and biomonitoring methods using the metabolome can measure 20,000 chemicals and combine that profile with genomic information for our 20,000 genes to provide an array yielding 400 million interactions, thus having sufficient resolution to define an individual as an individual (Martin and Jones 2013). This leads to an even more exciting element beyond personalised medicine – the advent of predictive medicine where we will predict human disease before it is clinically apparent. This characterises the penultimate approach to personalised medicine—the ability to predict disease in individuals and target interventions that restore and optimise health **(Figure 1)**. This approach has also entered reality, in the Emory Predictive Health Institute and with well-documented examples of high-dimensional phenotyping permitting early, effective interventions that favourably benefit human health (Chen et al. 2012). In critical care, predictive medicine creates opportunities across several time scales, from predicting arrhythmias or cardiac arrest in minutes, to respiratory or renal failure in hours, to hospital complications and readmissions in the months following critical care discharge.

Effectuating personalised medicine leads to, as one example, immunotherapy of critical illnesses like sepsis. Immunotherapy is already taking hold in oncology, with many of the latest and some of the most effective cancer drugs using this method, and drawing substantial public, private and philanthropic investment. As one of the most common conditions in critical care, sepsis has recently been redefined with a focus on the dysregulation of the immune system (Singer et al. 2016). We no longer consider sepsis to be a unilateral immunological response of hyperinflammation causing organ failure, but rather a dynamic immune response that continuously changes in the balance between inflammation and anti-inflammation (Pickers and Kox 2017). In sepsis, personalised immunotherapy could address dynamic biological events such as T-cell exhaustion, decreased cellular expression of HLA-DR, and macrophage phenotypes shifted away from inflammation, each tied to an intervention that is individually tailored to the patient (Hotchkiss and Moldawer 2014). In combination with integrated big data and artificial intelligence, predictive medicine will lead to a landmark change in sepsis care. The ability to predict organ dysfunction changes the face of clinical sepsis care from one of reactive care to one of proactive and even preventive critical care (Kempker et al. 2018).

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The application of artificial intelligence and advanced machine learning to the big data generated from myriad sources in the care of critically ill patients will facilitate the evolution of learning healthcare systems and predictive medicine. The combination of data and complex computer-assisted analysis will advance us from unsophisticated analytics where the goal is simply to describe what happened, through the more difficult phase of diagnosis where we seek to understand why something happened **(Figure 1)**. As discussed earlier, we are now at the stage of predictive analytics, accurately predicting when an event will occur, and nearing the stage of prescriptive analytics: how can we control events or make events happen. Taken together, these will change the face of critical care from our familiar systems that react to injury, illness, infection and organ dysfunction, to a system of prediction and prevention. With the power of analytics and prediction, we can advance to prescriptive medicine, effectively controlling the response of our patients starting with the earliest phases of an incipient critical illness and extending throughout the course of their care. With the prediction, prescription and prevention of severe illness and organ dysfunction, the most common and vexing problems of critical care medicine can be eliminated. We will no longer manage severe organ dysfunction, having effectively predicted and prevented it in most patients. In so doing, the ICU will become an environment where we care for the unpredictable and the unpreventable complications of life, such as traumatic injuries and recovery from complex surgeries and other insults.

Conflict of Interest

Greg Martin's institution (Emory University) has received funds from the National Institutes of Health, the Marcus Foundation and Cheetah Medical to conduct studies, and he has served as a consultant or medical advisor to Becton Dickinson, Grifols and Regeneron.■

Key Points

- Over the next 50 years, critical care will evolve from a system that reacts to patient deterioration into a system that predicts and prevents these events.
- The effective integration of clinical critical care data at scale with real-time analytics is the foundation for changes at each end of the medical care spectrum.
- In combination with integrated big data and artificial intelligence, predictive medicine will lead to a landmark change in sepsis care.
- The application of artificial intelligence and advanced machine learning to the big data generated from myriad sources in the care of critically ill patients will facilitate the evolution of learning healthcare systems and predictive medicine.
- The ICU will become an environment where we care for the unpredictable and the unpreventable complications of life, such as traumatic injuries and recovery from complex surgeries and other insults.

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