# Artificial Intelligence and Clinical Deterioration

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## Abstract

### *Purpose of review*

To provide an overview of the systems being used to identify and predict clinical deterioration in hospitalised patients, with focus on the current and future role of Artificial Intelligence (AI).

### *Recent findings*

There are five leading AI driven systems in this field: the Advanced Alert Monitor (AAM), the electronic Cardiac Arrest Risk Triage score (eCART), Hospital wide Alert Via Electronic Noticeboard (HAVEN), the Mayo Clinic Early Warning Score (MC-EWS) and the Rothman Index (RI). Each uses Electronic Patient Record (EPR) data and Machine Learning (ML) to predict adverse events. Less mature but relevant evolutions are occurring in the fields of Natural Language Processing, Time and Motion Studies, AI Sepsis and COVID-19 algorithms.

### *Summary*

Research based AI driven systems to predict clinical deterioration are increasingly being developed, but few are being implemented into clinical workflows. Escobar et al. (AAM) provide the current gold standard for robust model development and implementation methodology. Multiple technologies show promise, however the pathway to meaningfully affect patient outcomes remains challenging.



### *Key words*

Artificial Intelligence, Machine Learning, Clinical Deterioration, Predictive Modelling.

## Introduction

This review gives an overview of the systems being used to identify and predict clinical deterioration in hospitalised patients, with focus on the current and future role of Artificial Intelligence (AI).

## Artificial Intelligence

AI is defined as the intelligence demonstrated by machines. AI can be subclassified into Artificial General Intelligence (AGI) and Artificial Narrow Intelligence (ANI). AGI is designed to mimic humans by demonstrating reason when problem solving. (2) ANI is the execution of single, highly constrained tasks, such as recognising patterns in large datasets. Machine Learning (ML) is a form of ANI and extracts knowledge from large datasets. There are two main subgroups of ML - supervised and unsupervised. Supervised ML typically employs multiple input variables (e.g., data extracted from the Electronic Patient Record (EPR)) to predict a pre-defined outcome (e.g., an outcome such as unplanned Intensive Care Unit (ICU) admission). To ensure generalisability, the algorithm is tested on an independent (but comparable) dataset. Supervised ML is commonly used for research on clinical deterioration and comes in various forms (tree-based models, K-nearest neighbour and neural networks are three well known forms). (3) Unsupervised ML uses unlabelled data and finds patterns within that data (e.g., clustering). It is less often used in research on clinical deterioration but has applications that are relevant. (4)

## Clinical Deterioration

There is no internationally recognised definition of *patient deterioration*. Jones et al. defined a deteriorating patient as 'one who moves from one clinical state to a worse clinical state which increases individual risk of morbidity…and mortality'. (5) Historically, studies have focussed on hard outcomes that represent end-stage deterioration, also called in-hospital adverse events. Typically, these are defined by the triad of in-hospital death, unplanned ICU admission and cardiac arrest. Medical Emergency Response (MER) calls are also used occasionally in research to characterise the deteriorating patient cohort. Each outcome has its strengths and weaknesses when being used as an outcome measure for the development of algorithms to predict deterioration. (6) However, identification should be targeted at the earliest stage of deterioration where interventions are most likely to change patient outcomes.

## Rapid Response Systems & Early Warning Scores

Rapid Response Systems (RRS) and Early Warning Scores (EWS) were developed thirty years ago to improve the management of patient deterioration, supported by analysis that showed in-hospital cardiac arrests (IHCA) were commonly preceded by periods (e.g., minutes to hours) of unnoticed physiological instability.(7–9) The linked RRS/EWS system was designed to optimise the allocation of specialist clinical resources to those most in need, thus reducing IHCA and preventable death in patients admitted to the general hospital ward. (10)

In the UK, despite improvements made using RRS, untreated clinical deterioration in hospitalised ward patients persists. (11) Moreover, while many thousands of patients trigger an RRS alert annually only a small percentage suffer an adverse event or require a significant escalation in care. (12) An emphasis on high sensitivity, at the expense of lower specificity, has been tolerated because of the associated reduction in adverse events. However current systems, developed in the pre-EPR (paper-based) era, reveal a mismatch between hospital resource availability and patient demand. Improved recognition of early signs of deterioration has the potential to reduce avoidable mortality, unnecessary ICU admissions and length of hospital stay.

Late recognition of in-hospital patient deterioration is associated with worse outcomes, including higher mortality. (13–15) In the UK, around 45,000 patients per year deteriorate on hospital wards to the extent they require urgent admission to an ICU. (16) Analysis of the UK Intensive Care National Audit and Research Centre database shows up to 80% of these unplanned ICU admissions have a preceding period of untreated clinical deterioration, despite the implementation of the National Early Warning Score in more than 75% of National Health Service Hospitals. (17) Recent Australian data also shows that deterioration within 72 hours of admission increases treatment costs irrespective of diagnosis, age and hospital length of stay. (18)

## Electronic Patient Records & Algorithms

Since 2005, increasing numbers of hospitals have implemented Electronic Patient Records (EPR), creating opportunities to develop advanced digital risk algorithms that use rich and contemporaneous patient data sets including vital signs, laboratory results, demographics, comorbidities, and hospital administrative data. (19,20) In 2008, Tam et al. developed a nomogram based on available administrative patient data to predict unplanned ICU admission but neither validated it nor published any follow up analysis. (21) Bailey et al. derived and implemented an EPR based prognostic risk score. (22) They found patients with a positive alert had a 5.3 times higher likelihood of needing ICU admission and had a significantly longer hospital length of stay. However, when implemented there was no difference between clinical outcomes of the intervention (EPR based alert ward patients) and control groups (standard RRS ward patients). In 2013, Alvarez et al. developed and validated an automated model that was more sensitive, specific and with a better Area Under the Receiver Operator Curve

Characteristic than contemporary systems. The model also identified patients destined to have adverse events on average 16 hours before they occurred. (23)

## Advanced Alert Monitor

Escobar et al, in Oakland USA, are the most advanced team regarding real-world deployment of a predictive algorithm, which in their hospitals is called the Advanced Alert Monitor (AAM). (1,24) AAM is a nonlinear logistic regression model, which includes laboratory data, vital signs and comorbidities. They developed an intervention program where nurses remotely reviewed the medical notes, and implemented a care plan, in patients identified by AAM as high risk. This system was implemented in a staggered fashion into 19 hospitals in the US and showed a reduction in mortality (Adjusted Relative Risk 0.84, 95% CI 0.78-0.90; p<0.001). This study was the culmination of multiple sequential studies describing the development, validation and implementation of AAM. (25–27)

## Electronic Cardiac Arrest Risk Triage

Churpek et al., in Chicago USA developed a predictive algorithm called the electronic Cardiac Arrest Risk Triage score (eCART). (3) eCART2 is a nonlinear logistic regression model, which includes laboratory data and vital signs. The authors have also developed a random forest model, although this does not appear to have been implemented into real-time clinical systems. (28) eCART has been evaluated in multiple retrospective validation studies against widely used EWS, including Between The Flags (BTF), NEWS and the Modified Early Warning Score (MEWS) and was shown to better predict IHCA, unplanned ICU admission and death. (29,30) They demonstrated eCART detected four times as many IHCAs and 50% more ICU admissions than their current RRS. eCART also demonstrated detection of deterioration 8 hours in advance of the standard RRS activation thresholds. (31) It has been tested in a prospective feasibility study however this did not involve using the algorithm to alter current RRS clinical workflows. (32)

## The Hospital-wide Alerts Via Electronic Noticeboard

The Hospital-wide Alerts Via Electronic Noticeboard (HAVEN) was developed by the University of Oxford in collaboration with two National Health Service Trusts. HAVEN uses a supervised machine learning model (gradient boosted machines) that imputes 76 routinely available, EPR-based variables. (33) These data were divided into two categories: static variables that do not change during an admission (e.g., age, past medical history), and dynamic variables that do change during a patient's admission and are repeatedly updated (e.g., vital signs, laboratory results). A risk estimate of deterioration in the next 24 hours was derived from these data. The risk estimate is then used to rank hospital ward patients from most to least likely to deteriorate in the coming 24 hours. Using a combined outcome of in-hospital cardiac arrest and unplanned ICU admission, HAVEN has a c-statistic of 0.901 and, at a precision of 10%, was able to identify 42% of cardiac arrests with a lead time of 48 hours. The algorithm development process was thorough, but it awaits implementation into clinical workflows. (34–39)

## Mayo Clinic Early Warning Score

MC-EWS is a gradient boosting machine, which includes laboratory data, vital signs, patient demographics and nursing assessments. (40) The algorithm was developed in datasets from three hospitals totalling almost 132,000 hospitalisations. Using a composite outcome cardiac arrest call, RRS team activation of unplanned ICU admission, the algorithm had a c-statistic of 0.937 and with a sensitivity of 73% generated 45% less alerts than NEWS. In a pilot study, published as pre-print (41), the authors have developed the Bedside Patient Rescue (BPR) which is a weighted combination of MC-EWS and “nurse worry factor” (entered by nurses when vital signs are recorded at the bedside).

### Rothman Index

The Rothman Index (RI) combines vital signs, laboratory tests, cardiac rhythm and nursing assessments. (42) The RI transforms each input variable into a “risk function” that quantifies the excess risk of one year mortality. Individual risk functions are then combined into a weighted score, which also accounts for how recently laboratory tests were measured.

Each of these systems complies with the generic approach represented in **Figure 1**.

## Time and Motion Analysis

Time and motion analysis show the movement and activities of hospital staff as they deliver care to patients. It is plausible that hospital staff alter their movements and activities in response to patient demand (i.e., increase physical proximity because of the need to manage deterioration). These data may hypothetically be used independently, or be incorporated with existing models, to aid in the prediction of patient deterioration. To date this form of analysis has not occurred but steps have been taken towards developing methods that could enable it. Traditionally, data is collected manually by external observers, but recently automated computerised systems have become available. (43–47) Within the ICU, analysis has shown significant differences between the pattern of work in an ICU as compared to other medical and surgical units. (48) Likewise the impact of strain on ICU workflow may influence patient care. (49) ICU registrar activity outside the unit has been automatically quantified using Real Time Location Devices and may represent activity associated with deteriorating patients. (50) Time and motion analysis has also been applied to patient journeys through the hospital. (51,52)

## Natural Language Processing

The analysis of free text in the EPR relies on natural language processing (NLP). NLP, also a form of AI, can model a range of clinically relevant data (e.g., symptoms, examination findings, clinical diagnosis), which may in turn be incorporated into models predicting clinical deterioration. This process combines two forms of AI: NLP and ML. Korach et al. showed that unsupervised machine learning methods can successfully identify meaningful content in free-text nursing notes. (53) They demonstrated models using demographics and vital signs better predicted mortality when augmented by nursing note NLP. (54) In ICU patients, NLP also augments mortality prediction model performance and prolonged length of stay prediction performance. (55–58) However, despite these promising findings NLP is yet to be implemented in real-time clinical workflows specific to deteriorating patients.

## Patient Subgroups

Sepsis is a large and important subgroup of the deteriorating patient cohort. Two recent reviews showed there are more than 130 sepsis algorithms currently being tested. (59,60) Both found methodological inconsistency and population heterogeneity and there remains a large gap between the creation of AI algorithms and their implementation into clinical practice. Further, in 2021 Wong et al. externally validated the Epic Sepsis Model (ESM) which has been implemented in hundreds of hospitals in the United States. ESM was found to have low sensitivity compared to current clinical practice, with low discrimination and calibration when predicting the onset of sepsis. (61)

COVID-19 has presented institutions with unique challenges, particularly with respect to the prediction and management of demand for ICU resources. AI has been applied in multiple domains with respect to COVID-19 including institution-level predictions, diagnosis, and prognostication. Systematic reviews of machine learning strategies applied to COVID-19 have been conducted previously. (62)(63) Noteworthy applications include the use of AI, such as autoregressive models and time-delay artificial neural networks, in the prediction of case numbers and ICU bed availability. (64)(65) With respect to individual-level prediction of deterioration, models have been developed aiming to predict transfer to ICU, (66) intubation (67) and mortality.(68) The potential application of such models to the large numbers of individuals affected by COVID-19 highlights the importance of taking a deliberate approach aiming to use these models in an ethical manner that minimises bias and maximises public good. (69)

## Additional Relevant Research

The high stakes involved in the clinical decision making around deteriorating patients emphasise the importance of having an ethical framework for the development and implementation of AI models. The potential for unintended ethical consequences associated with medical AI models is a pressing concern in multiple areas, including bias, confidentiality and fiduciary incentives. (70) Potential sources of bias include: biased datasets, models being developed that reflect human biases and automation bias adversely affecting human decision making. (71) Multiple strategies may be employed to help minimise these issues, including improving the interpretability of AI models and post-authorisation monitoring. (72) It is imperative that such models are researched and employed with transparency to maintain and support public trust in medical AI applications. Finally, AI applications to wearable, remote vital sign monitoring equipment are expected to play an important role in future health care systems but remain experimental. (73)

## Real world implementation

AI has revolutionised operations in personal banking, investment, manufacturing and news media but has not made comparable progress in health. (74) Despite the large increase in AI related clinical research over the last decade, very few algorithms and/or AI clinical applications progress through to the level of real-time clinical implementation. (2) This is demonstrated in the medical literature but also in FDA applications and approvals. (75) As of 2020, only 29 medical AI/ML specific applications were made and of these, none related to clinical deterioration (nearly all related to radiology or cardiology) (76) demonstrating that AI is still some way from being ubiquitous in health.

## AI Research guidelines

The Consolidated Standards of Reporting Trial - Artificial Intelligence (CONSORT-AI) extension was released in 2020. (77) It was developed in parallel with its companion statement SPIRIT-AI (both developed via consensus). (78) CONSORT-AI contains 14 new items that are specific to reporting AI research. These items include how the AI was integrated into the trial setting, data input and validity methodology, how the algorithm contributed to decision making, accessibility of algorithm code and algorithm performance error. CONSORT-AI is an important development in this field because research methodologies to date have been of varying quality and heterogenous. (75)

## Conclusions

AI driven systems predicting clinical deterioration are increasingly being developed in research, but few are being implemented into clinical workflows. Escobar et al. provide the gold standard for robust model development and implementation methodology. (1) Multiple technologies show promise, however the pathway to meaningfully affect patient outcomes remains challenging.

## Key Points

- Electronic Patient Record data are increasingly being used to develop predictive algorithms for clinical deterioration using Machine Learning techniques.
- There are five leading examples of this research with Escobar et al. providing the gold standard for robust model development and implementation methodology.
- Relevant research is occurring in the fields of Time and Motion analytics and Natural Language Processing, as well as in evaluating subgroups like sepsis and COVID-19.
- Many barriers still exist in the implementation of AI driven technology in this field and widespread adoption is still some years in the future

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## Conflicts of Interest

James Malycha and Oliver Redfern are both members of the HAVEN research team.

## References and recommended reading

Papers of particular interest, published within the last 18 months, have been highlighted as:

* of special interest

** of outstanding interest

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