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Harnessing AI to boost the fight against hospital-acquired sepsis

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One in five global deaths are related to sepsis, and many cases are linked to hospitalization and medical devices.

Sepsis can progress quickly, and is hard to treat in the later stages, so speed of diagnosis is critical. AI and machine learning bring a new dimension to clinical decision support, predicting a patient's likelihood of developing sepsis so diagnosis and treatment can happen sooner.

While AI and machine learning have the potential to improve the survival rate of hospital-acquired sepsis, there are challenges preventing widespread uptake. We unravel the complexity and identify issues that medical equipment manufacturers may need to overcome to aid the fight against sepsis.

Hospital-acquired infections (HAIs), also known as healthcare-associated infections, are a major burden for global healthcare. In the UK, they represent an annual cost of around £1billion to the NHS[1]. And in the US, the Centers for Disease Control and Prevention estimates that HAIs account for 1.7million infections and 99,000 associated deaths each year[2].

Much of the time, HAIs are a result of invasive treatments or procedures involving devices, surgical equipment or monitoring technologies. The very equipment that has revolutionized healthcare, improving patient outcomes and saving lives, can result in life-threatening conditions. Inadequate cleaning, maintenance or design can have fatal consequences.

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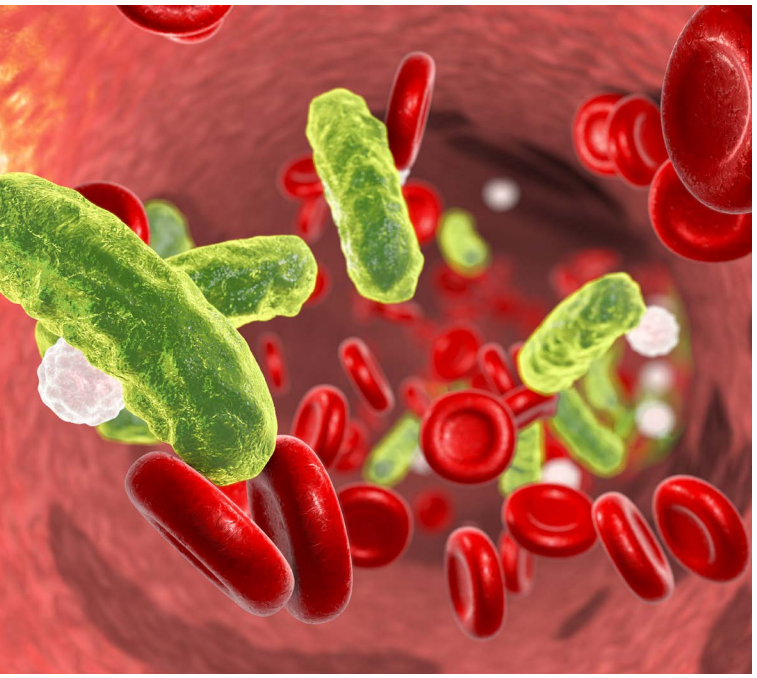
HAIs and the global burden of sepsis

HAIs are a leading cause of sepsis. A study recently published in the Lancet says that 11million sepsis related deaths were reported in 2017, representing 19.7% of all global deaths. The authors conclude that 'the global burden of sepsis is larger than previously appreciated, requiring further attention'. Furthermore, they clearly highlight a link with HAIs:

"...many of these cases of sepsis are suspected to be due to nosocomial infections; patients admitted to hospital for non-infectious conditions could be exposed to infection risk either from invasive devices such as central venous or urinary catheters or through inadequate handwashing practices among healthcare workers."[3]

The study's authors conclude that clinicians and public health policy makers must implement cost-effective measures to improve sepsis outcomes. A critical success factor is early detection and treatment. This presents a major challenge with sepsis, so medical device and healthcare providers are increasingly looking at how clinical decision support (CDS) software can incorporate AI and machine learning to augment and accelerate the diagnostic process.



The sepsis diagnosis challenge

In the early stages, sepsis is easy to treat but hard to diagnose. In later stages it is easy to diagnose but very hard to treat. This impedes the fight against the illness, especially as it progresses so quickly. Every hour that treatment is delayed represents an 8% reduction in the average survival rate. Often, by the time sepsis is diagnosed, it is too late to prevent tissue damage, organ failure or death.

Sepsis: key facts

Sepsis is a life-threatening illness caused by the body's response to an infection.

It can injure internal organs, and is a major contributor to disability, death and healthcare costs worldwide.

The survival rate is 80% when treatment is administered within the first hour, but every hour of delay decreases the average survival rate by 8%.

In a hospital environment, people being treated in an intensive care or emergency department setting are at greatest risk, as are people exposed to invasive devices such as intravenous catheters or breathing tubes.

Symptoms of sepsis include low blood pressure, elevated white blood cell count, an increased heart rate and shallow breathing. However, these are also associated with typical infections, so they don't necessarily trigger healthcare professionals to request scans or screen for acid or bacteria in blood or other bodily fluids.

It's not practical or desirable to screen every patient that presents infection symptoms. However, there is a need for an efficient and effective way to understand when there is a higher likelihood of sepsis, for instance after invasive procedures or when certain factors converge. This could optimize the timing and workflow of diagnosis and treatment. It would mean patients that do have sepsis are identified and receive antibiotic treatment in the critical early hours when a positive outcome is more likely.

A fine balance needs to be achieved here: early prediction of sepsis can be lifesaving but predicting sepsis in non-sepsis patients risks wasting valuable hospital resources.

How AI can optimize the sepsis diagnostic pathway

Machine learning and AI offer new ways to overcome this challenge with more accurate predictions surrounding a patient's chances of developing sepsis following treatment. The development of CDS software rooted in this capability could potentially drive significant improvements in patient outcomes.

Healthcare generates large amounts of data surrounding vital signs, lab test results, progress notes and medication, but it's often held in disparate and remote systems. Applying machine learning and AI to this big data can yield important insights and predictive capabilities that have previously been out of reach. This can be leveraged via CDS software to drive benefits in three core areas:

Diagnosis - predictive capabilities enable earlier diagnosis and intervention when a patient has sepsis.

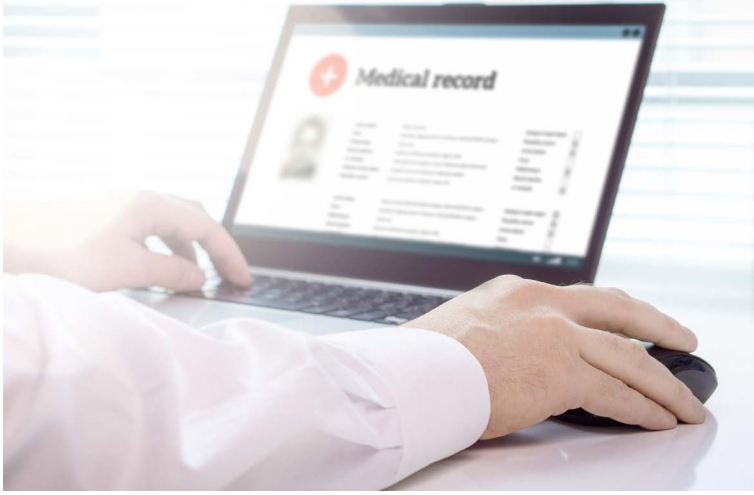
Prognosis - predicting readmission due to sepsis can ensure patients most at risk are identified and closely monitored.

Treatment - data surrounding treatments and outcomes can be harnessed to devise optimal treatment strategies for sepsis in intensive care.

In the wider medical community, there's much interest in the use of data for improved and predictive sepsis diagnosis. Pockets of activity in various fields of medicine are already making some headway.

For instance, the PhysioNet Computing in Cardiology Challenge 2019[4] focused on the early prediction of sepsis using clinical data. Participants were challenged to accurately predict sepsis using physiological data six hours before the clinical prediction of sepsis. A report discussing the outcomes of the challenge concludes that:

"Diverse computational approaches predict the onset of sepsis several hours before clinical recognition, but generalizability to different hospital systems remains a challenge."[5]



Advancements in healthcare technologies

Several large healthcare providers and electronic health record (EHR) software providers are integrating AI and machine learning with their efforts to reduce sepsis-related mortality.

A collaborative project between Geisinger Health System and IBM analyzed deidentified EHR data for more than 10,500 sepsis patients in the US. This has resulted in the creation of an AI model to predict sepsis mortality, which will aid the development of personalized clinical care plans for at-risk patients.

Additional developments in this space range from sepsis prediction tools to real-time evaluation of patient condition:

SPOT (Sepsis Prediction and Optimization of Therapy) is an electronic information and alert system developed by HCA Healthcare. Embedded in a patient's EHR, it analyzes real-time data from bedside monitoring equipment and medical lab test results. HCA claims it can identify sepsis approximately 18 hours earlier than the best clinicians, alerting physicians and caregivers accordingly.

Sepsis Watch developed by Duke Institute for Health Innovation, is an AI-enabled system which pulls information from a patient's EHR every five minutes to evaluate condition and offer real-time analysis that human doctors cannot provide.

Jvion, a healthcare AI company, pinpoints individual patients on a sepsis risk trajectory. It then determines whether the trajectory can be changed and provides patient-specific recommendations.

EPIC and Cerner, EHR specialists, have developed sepsis predictive tools and alerts that are gaining attention in the US.

These developments are promising, and progress is certainly being made. However, assessing the true value of any AI-informed decision is challenging. When the algorithm and clinicians disagree, it's difficult to reliably estimate what would have happened to the patient in an alternative reality. Furthermore, achieving meaningful improvements in nosocomial sepsis outcomes at scale will require a more widespread, joined-up approach than we have seen to date.

What's hindering AI-led sepsis diagnosis?

As it stands, there are many obstacles preventing large-scale use of AI and machine learning in CDS software. From a technical perspective, these range from insufficient data standardisation and integration to poor inter-device communication in healthcare settings. There are also important regulatory matters that need to be considered at an early stage of device development.

Technical issues

Standardization of data is a major challenge preventing scaled use of AI for predictive sepsis diagnosis. Overcoming barriers to standardisation is critical so that data can be converted into a common format that is understood across multiple implementations. Interoperability between different workflow components is also essential to facilitate the storage and retrieval of data from EHRs.

Another related issue is the need for external validation of AI algorithms. This demands access to and interoperability between different datasets by an independent party. Randomized controlled trials comparing 'clinicians alone' to 'clinicians assisted by the algorithm' may be necessary for regulatory approval.

The dataset shift phenomenon also needs to be considered. An AI algorithm is typically 'trained' within a stationary environment. Introducing AI to sepsis management is likely to introduce changes in practice which in turn will result in a new distribution, different to that used when training the algorithm. To counter this, methods need to be put in place to identify performance deterioration.

One of the greatest challenges of AI is reliable Generalization. Generalization can be hard due to technical differences between hospitals (including differences in equipment, coding definitions and EHR systems as well as laboratory equipment and assays). Variations in local clinical and administrative practices and the population itself are another factor. So site-specific training will be required to adapt existing systems for new populations. Methods to detect out-of-distribution inputs and provide a reliable measure of model confidence will be important to prevent clinical decisions being made on inaccurate model outputs.

Communication between devices provided by different vendors and where AI algorithms are hosted is another important concern. This is particularly true for sepsis where AI diagnosis tests may be conducted at five minute intervals. It's likely that many manufacturers will aim to make their product the linchpin of a connected AI ecosystem, drawing in data from other devices. So common standards for good device integration will be essential.

Regulatory matters

In 2019, the FDA released new draft guidance on CDS software[6]. It includes a category dedicated to 'Device CDS', which uses the same risk classification framework as 'Software as a Medical Device'. While the final details are yet to be announced, the FDA clearly indicates an intention to focus its regulatory oversight on Device CDS functions for healthcare practitioners (HCPs) that:

"...'inform clinical management' for 'serious or critical situations or conditions' and that, in addition, are not intended for the HCP to be able to independently evaluate the basis for the software's recommendations."

This suggests that the use of AI and machine learning in devices geared towards the diagnosis of sepsis will come under intense scrutiny.

Finally, Article 22 of the EU's General Data Protection Regulation (GDPR), giving people the right to receive an explanation for algorithmic decisions, must be considered. This potentially limits the deployment of devices if people operating them cannot understand or interpret how the AI algorithm reached a certain decision or prediction.

These technical challenges and regulatory matters are not insurmountable. But addressing them effectively will require focused attention from a broad range of specialists. Collaborative effort involving experts in AI, machine learning, software development and data as well as healthcare is needed to help CDS software achieve the required standards for improved nosocomial sepsis diagnosis and treatment.

The future of sepsis management

AI and machine learning present an exciting opportunity to facilitate the early detection and treatment of hospital-acquired sepsis.

There are opportunities for a broad spectrum of equipment manufacturers to optimize or future-proof products so they can play an active role in sepsis management. Those on the hardware side of the healthcare ecosystem might obtain more frequent and automated monitoring of vital signs, which can be uploaded to EHRs and accessed by AI tools. Many IVD companies are already investing in better and quicker infection testing, so embracing predictive sepsis diagnosis could be a natural next step.

Predictive diagnosis can be hugely beneficial, even if it doesn't provide a firm diagnosis. For instance, it might prompt caregivers to run an initial blood or urine test to establish whether an infection is present, before confirming whether the patient has sepsis. The patient could be started on a broad-spectrum antibiotic ahead of a confirmatory test identifying the infectious organism so that targeted antibiotic therapy can be administered.

In time, patients with sepsis will be optimally managed by a combination of AI algorithms and human clinicians working hand-in-hand. The same will be true of other infections and health issues related to hospital treatment, from postoperative cardiovascular events to opioid addiction. Medical device companies that find ways to address the technical and regulatory factors limiting AI and machine learning will be at the forefront of this new reality.

Earlier detection of hospital-acquired sepsis is critical to saving lives, but infection prevention needs to be addressed too. In a future paper, we'll focus on how the risk of infection from hospital equipment can be reduced through better design.

1 https://www.lifescienceindustrynews.com/money/funding-to-fight-hospital-acquired-infections/
2 https://patientcarelink.org/improving-patient-care/healthcare-acquired-infections-hais/
3. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32989-7/fulltext
4. https://www.physionet.org/content/challenge-2019/1.0.0/
5. https://www.physionet.org/content/challenge-2019/1.0.0/physionet_challenge_2019_ccm_manuscript.pdf
6. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-decision-support-software

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