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Artificial Intelligence for the Prediction of Sepsis in Adults



Authors: Robyn Haas, Sarah C. McGill

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Key Messages

- Horizon Scan reports provide brief summaries of information regarding new and emerging health technologies; Heath Technology Update articles typically focus on a single device or intervention.
- These technologies are identified through the CADTH Horizon Scanning Service as topics of potential interest to health care decision-makers in Canada.
- This Horizon Scan summarizes the available information regarding an emerging technology, artificial intelligence algorithms, for the prediction of sepsis in adults.

Predicting Sepsis Using Artificial Intelligence

Named as a global health priority in 2017 by the World Health Assembly and WHO, sepsis is a leading cause of morbidity and mortality around the world. Artificial intelligence (AI) algorithms could play important role in addressing this worldwide health threat.

Globally, sepsis affects about 49 million people each year.¹ Sepsis is a life-threatening condition that occurs as a result of the body's overwhelming systemic response to infection, and can cause tissue damage, organ failure, and death.²³ There is a range in its severity from sepsis to septic shock.² Sepsis can be difficult to detect because many people present with nonspecific symptoms, which can be easily mistaken for other illnesses (e.g., influenza), and clinical presentations of sepsis can vary from patient to patient.²³ Timely and accurate detection of sepsis is crucial as every hour that treatment is delayed is associated with an increased risk of mortality.² Al algorithms have the potential to predict sepsis hours before its onset.² Harnessing this technology may help clinicians quickly and accurately diagnose sepsis, which could decrease time to treatment, and ultimately improve a person's chance of recovery.

How It Works

Al algorithms for the prediction of sepsis are machine learning models that are developed using clinical data collected in electronic health records (EHR).⁴ The use of Al predictive algorithms is meant to improve the accuracy and timeliness of sepsis prediction in a clinical setting.⁴ The technology may be particularly useful in intensive care units (ICUs) where sepsis is present in a notable number of patients.³ There are currently numerous Al algorithms in development for this purpose.⁴ The exact mechanisms of these algorithms vary from model to model, but most typically examine key variables that can play a role in the development of sepsis. These variables may include vital signs, demographics, laboratory tests, comorbidities, and administrative data (e.g., length of stay in the ICU).⁵ Predictive Al algorithms work by continuously monitoring a patient's EHR data and assessing the aforementioned variables in real time to determine the likelihood that sepsis will occur.⁴ Earlier and more accurate sepsis prediction allows for timely clinical intervention, such as the administration of antibiotics.⁴ By optimizing the management of sepsis, Al predictive algorithms can contribute to a reduction in sepsis-associated morbidity and mortality.⁴



Who Might Benefit?

All individuals who have an existing infection are at risk for developing sepsis. As of 2011, sepsis was involved in 1 in 18 deaths in Canada.⁶ In 2020, sepsis was the 14th leading cause of death in Canada among all age groups,⁷ and the in-hospital rate of sepsis was 4.3 per 1,000 patients.⁸ Some populations are at a higher risk of sepsis and may experience greater benefits from Al predictive algorithms. Examples of risk factors include chronic conditions, immunodeficiency, pregnancy, and use of immunosuppressive drugs.⁶ Additionally, sepsis-associated mortality increases with age, except for in individuals under the age of 1, who have an increased risk of developing sepsis.⁶ Health care providers might also benefit from the use of Al algorithms as this technology is meant to assist in clinical decision-making regarding the management of sepsis, including timing of treatment initiation and choice of appropriate antibiotics.

Availability in Canada

In Canada, Al algorithms to predict sepsis are not currently authorized to be integrated into hospitals' clinical workflows. There are several algorithms under development; however, this technology may still be some time away from real-world application. Researchers at McMaster University recently created an Al algorithm called BiLSTM (Bidirectional Long Short-Term Memory). They planned to launch a pilot project to investigate its clinical effectiveness in November 2021.9

Some of the AI algorithms currently in development outside of Canada are InSight, DeepAISE, and Sepsis Watch. InSight was developed by Dascena, a start-up company based in the US, and has been investigated in both a randomized controlled trial and a post-marketing study. ¹⁰ DeepAISE was developed by a research lab at the University of California, San Diego, and is seeking prospective validation. ¹¹ Sepsis Watch was developed by Duke University and has been implemented in hospitals across the Duke University Health System. ¹²

What Does It Cost?

Information on the cost of AI algorithms for the prediction of sepsis was not found.

Sepsis itself is a costly condition. Health care costs for people with sepsis are generally higher than for those without sepsis. ¹³ Additionally, rehospitalization rates and length of hospital stay in the ICU are higher among patients with sepsis than those without sepsis. ¹³ There is evidence to suggest that early and accurate prediction of sepsis using machine Al models has the potential to decrease both rehospitalization rates and length of hospital stay. ^{14,15} Therefore, the use of Al predictive algorithms may result in reduced health care costs.



Current Practice

In 2021, the Surviving Sepsis Campaign released updated international guidelines for the management of sepsis and septic shock. These guidelines include screening for patients with sepsis and septic shock; the guidelines also discuss prediction using rules-based tools or scoring systems. ¹⁶ Common screening tools include systemic inflammatory response syndrome (SIRS) criteria, National Early Warning Score (NEWS), Modified Early Warning Score (MEWS), and quick Sequential Organ Failure Score (qSOFA) or Sequential Organ Failure Score (SOFA). ¹⁶ As of 2021, the Surviving Sepsis Campaign recommends against the use of qSOFA as a single-screening tool. ¹⁶ These screening tools use manual methods or are digital, automated assessment tools that use EHR data to assess the risk of sepsis occurring. ¹⁶ These tools differ from AI algorithms, which go beyond risk assessment and aim to identify sepsis itself. They can be used in numerous locations, including the ICU, emergency departments, or in-patient wards. ¹⁶ The guidelines note that sensitivity and specificity of the screening tools vary, but that their use is an important part of early sepsis identification. ¹⁶ The strength of the recommendations for screening is strong, with moderate-quality evidence.

What Is the Evidence?

Several retrospective studies have investigated the ability of AI algorithms to predict sepsis hours before its onset in adult patients staying in the ICU. While results are generally favourable for the use of this technology, 2 systematic reviews of these studies have found a range in the predictive performance of these models. Even with the variation in performance, 1 review concluded that AI models could accurately predict sepsis onset in retrospective data. The other review found similar variation in AI model performance and concluded that the studied AI models had better predictive performance than the existing SIRS, MEWS, SOFA, and gSOFA scoring systems.

One prospective clinical outcomes evaluation examined the effects of an AI algorithm for the prediction of severe sepsis on in-hospital mortality, length of stay, and 30-day readmission. AR Researchers collected data from EHR systems across 9 hospitals over 2 years. Pollowing implementation of an AI algorithm, researchers found a 39.50% reduction in in-hospital mortality, a 32.27% reduction in length of stay, and a 22.74% reduction in 30-day readmission. Ar randomized controlled trial also used a machine learning—based sepsis prediction system to evaluate average length of stay and in-hospital mortality in adults. Researchers found that patients in the experimental group had a shorter average length of stay and reduced in-hospital mortality than those in the control group. Results from both studies suggest implementation of an AI algorithm to predict sepsis has the potential to improve patient-related outcomes.

A qualitative study examined the factors that influence the integration of an Al algorithm for the prediction of sepsis into clinical workflows. ¹⁸ Through semi-structured interviews with physicians and nurses in the emergency department, researchers found that perceived utility and trust, the implementation process of the algorithm, and workforce considerations were notable factors influencing technology integration. ¹⁸ Therefore, to maximize the adoption of the technology, these are areas that may be useful to target for education and learning.



Safety

No evidence on the safety of Al algorithms for the prediction of sepsis was identified in the literature.

Issues to Consider

While there is not yet information on the exact cost of AI algorithms for the prediction of sepsis, this technology will not be free. Given the widespread nature of sepsis, affordable technologies would be needed if AI algorithms are adopted for use. This would help to ensure hospitals across all settings could access predictive AI algorithms and ensure equitable patient care.

There may be technical limitations to integrating Al algorithms into hospital information systems. Al technologies tend to require a lot of data and a robust IT infrastructure to run, which existing information systems may not possess. 19,20

Finally, clinician perception and acceptance of AI algorithms may be a barrier to the successful implementation of these systems. Results of a 2019 study found that overall perception of 1 machine learning—based early warning system were poor, where more than half of respondents did not report any change in their evaluation of a patient's risk of sepsis.²¹ AI algorithms are intended to be decision support tools for clinicians; therefore, a lack of acceptance from clinicians may hinder both the implementation and intended utilization of this technology.

Related Developments

Al for Mortality Prediction of Sepsis in the ICU

Al models to predict in-hospital mortality due to sepsis in patients the ICU are currently under development. Using retrospective data, researchers are investigating the predictive performance of various Al models. ²²⁻²⁴ Research in this area is in the early stages of development and is focused on identifying the best-fitting type of model. ²²⁻²⁴ Accurate prediction of mortality may help clinicians intervene and choose appropriate treatment methods. ²² It may also lead to better prognoses for patients. ²²

Al for the Prediction of Sepsis in Infants in the Neonatal Intensive Care Unit

Al technology for the prediction of sepsis is being investigated for infant populations as well as adult populations. In 2019, researchers performed a retrospective study of infants who were hospitalized for 48 hours or more in the neonatal intensive care unit.²⁵ They used variables from electronic health record data to develop 8 machine learning models and found that 6 of them had strong abilities with respect to predicting sepsis.²⁵ Researchers concluded



that the models were able to identify infants with sepsis hours before clinical recognition was possible.²⁵

Looking Ahead

The creation of AI algorithms to predict sepsis is a field undergoing rapid development. Numerous models are being created and tested; however, there are a notable lack of prospective studies. There is a need for further research on the integration of this technology in clinical settings. Prospective clinical studies can provide information regarding the effect of AI algorithms on patient-related outcomes. Studies that examine the implementation of this technology in a variety of settings (e.g., ICU, emergency departments, in-patient wards) would also be beneficial as they may demonstrate where the use of this technology is most effective. Clinical studies can also provide insight into how health care providers interact with this technology, and the degree to which it influences practice. Perspectives of clinicians can provide unique insight into the development and implementation of AI algorithms for the prediction of sepsis. Finally, while AI predictive algorithms are intended to be support tools for clinicians, who ultimately guide the course of treatment, it may also be valuable to explore patient perspectives on the use of this technology.



References

- 1. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *The Lancet*. 2020;395(10219):200-211. PubMed
- 2. Persson I, Ostling A, Arlbrandt M, Soderberg J, Becedas D. A machine learning sepsis prediction algorithm for intended intensive care unit use (NAVOY Sepsis): proof-of-concept study. JMIR Form Res. 2021;5(9):e28000. PubMed
- 3. Moor M, Rieck B, Horn M, Jutzeler CR, Borgwardt K. Early prediction of sepsis in the ICU using machine learning: a systematic review. *Frontiers in Medicine*. 2021;8:607952. PubMed
- 4. Islam MM, Nasrin T, Walther BA, Wu CC, Yang HC, Li YC. Prediction of sepsis patients using machine learning approach: A meta-analysis. Comput Methods Programs Biomed. 2019:170:1-9. PubMed
- 5. Hassan N, Slight R, Weiand D, et al. Preventing sepsis; how can artificial intelligence inform the clinical decision-making process? A systematic review. *Int J Med Inform*. 2021;150:104457. PubMed
- Navaneelan T, Alam S, Peters PA, Phillips O. Deaths involving sepsis in Canada. Statistics Canada Health at a Glance. 2016. https://www150.statcan.gc.ca/n1/pub/82-624-x/2016001/article/14308-eng.htm. Accessed 2022 Feb 22.
- Statistics Canada. Leading causes of death, total population, by age group. Table 13-10-0394-01. 2022 Jan 24; https://www150.statcan.gc.ca/t1/tbl1/en/tv.action
 Ppid=1310039401. Accessed 2022 Feb 17.
- 8. Canadian Institute for Health Information (CIHI). In-hospital sepsis details for New Brunswick. 2022; https://yourhealthsystem.cihi.ca/hsp/indepth?lang=en#/indicator/016/2/C300/. Accessed 2022 Feb 17.
- 9. McMaster DeGroote School of Business, Research Institute of St. Joe's Hamilton. Researchers create AI algorithm to improve timeliness, accuracy of sepsis predictions. 2021; https://www.degroote.mcmaster.ca/articles/researchers-create-ai-algorithm-to-improve-timeliness-accuracy-of-sepsis-predictions/. Accessed 2022 Feb 24.
- 10. Dascena. Predictive algorithms for better care: InSight. 2022; https://www.dascena.com/insight. Accessed 2022 Feb 15.
- 11. Nemati S, Holder A, Razmi F, Stanley MD, Clifford GD, Buchman TG. An interpretable machine learning model for accurate prediction of sepsis in the ICU. Crit Care Med. 2018;46(4):547-553. PubMed
- 12. Duke Health. Duke's augmented intelligence system helps prevent sepsis in the ED. 2020: https://physicians.dukehealth.org/articles/dukes-augmented-intelligence-system-helps-prevent-sepsis-ed. Accessed 2022 Feb 17.
- 13. Farrah K, McIntyre L, Doig CJ, et al. Sepsis-associated mortality, resource use, and healthcare costs: A propensity-matched cohort study. *Crit Care Med.* 2021;49(2):215-227. PubMed
- 14. Burdick H, Pino E, Gabel-Comeau D, et al. Effect of a sepsis prediction algorithm on patient mortality, length of stay and readmission: a prospective multicentre clinical outcomes evaluation of real-world patient data from US hospitals. BMJ Health Care Inform. 2020;27(1). PubMed
- 15. Shimabukuro DW, Barton CW, Feldman MD, Mataraso SJ, Das R. Effect of a machine learning-based severe sepsis prediction algorithm on patient survival and hospital length of stay: a randomised clinical trial. BMJ Open Respir Res. 2017;4(1):e000234. PubMed
- Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181-1247. PubMed
- 17. Fleuren LM, Klausch TLT, Zwager CL, et al. Machine learning for the prediction of sepsis: a systematic review and meta-analysis of diagnostic test accuracy. *Intensive Care Med.* 2020;46(3):383-400. PubMed
- 18. Sandhu S, Lin AL, Brajer N, et al. Integrating a machine learning system into clinical workflows: Qualitative study. J Med Internet Res. 2020;22(11):e22421. PubMed
- 19. Garnacho-Montero J, Martin-Loeches I. Clinical management of sepsis can be improved by artificial intelligence: no. Intensive Care Med. 2020;46(2):378-380. PubMed
- 20. Sendak MP, Ratliff W, Sarro D, et al. Real-world integration of a sepsis deep learning technology into routine clinical care: implementation study. *JMIR Med Inform*. 2020;8(7):e15182. PubMed
- 21. Ginestra JC, Giannini HM, Schweickert WD, et al. Clinician perception of a machine learning-based early warning system designed to predict severe sepsis and septic shock. Crit Care Med. 2019;47(11):1477-1484. PubMed
- 22. Kong G, Lin K, Hu Y. Using machine learning methods to predict in-hospital mortality of sepsis patients in the ICU. *BMC Med Inform Decis Mak.* 2020;20(1):251. PubMed
- 23. Garcia-Gallo JE, Fonseca-Ruiz NJ, Celi LA, Duitama-Munoz JF. A machine learning-based model for 1-year mortality prediction in patients admitted to an Intensive Care Unit with a diagnosis of sepsis. *Med Intensiva*. 2020;44(3):160-170. PubMed
- 24. Wernly B, Mamandipoor B, Baldia P, Jung C, Osmani V. Machine learning predicts mortality in septic patients using only routinely available ABG variables: a multicentre evaluation. *Int J Med Inform.* 2021;145:104312. PubMed
- 25. Masino AJ, Harris MC, Forsyth D, et al. Machine learning models for early sepsis recognition in the neonatal intensive care unit using readily available electronic health record data. *PLoS One*. 2019;14(2):e0212665. PubMed