https://doi.org/10.1590/1806-9282.20220177

Artificial intelligence and machine learning in pediatrics and neonatology healthcare

Felipe Yu Matsushita[1*], Vera Lucia Jornada Krebs[1], Werther Brunow de Carvalho[1]

Medicine has evolved dramatically over the past century. There have been several discoveries, from the invention of antibiotics to the identification of DNA, antipsychotics, and oral rehydration therapy. However, medicine is currently involved by a perplexing paradox: rising spending and worsening health outcomes. Over the past few decades, healthcare has been in the middle of three significant trends: increase in complexity, growing data volumes, and burnout among healthcare professionals. We discussed each of these trends, as well as how artificial intelligence (AI) might aid in the resolution of these issues.

DETERIORATING HEALTH OUTCOMES WITH INCREASING COST

Despite improvements in life expectancy over the past century, mortality trends have remained stagnant in recent decades. In the United States, life expectancy stopped increasing in 2011 and surprisingly began to fall after 2014. Individuals aged 25–64 years have seen an increase in mortality since 2010. The death rates for hypertension and obesity grew by 78.9% and 114%, respectively, between 1999 and 2017. Heart and lung disease, stroke, diabetes, and Alzheimer's disease all contributed to an increase in mortality in early studies[1]. Two reasons why life expectancy stopped improving are the absence of new therapies and higher complexity.

Many clinical disorders still have limited treatment options. The discovery of new therapies and drugs is expensive. Each new medicinal drug was estimated to cost almost a billion dollars in research and development[2]. Moreover, higher costs do not equate to improved essential health outcomes[3]. Pharmacological discovery and development are time-consuming and expensive, with complex processes that can take decades to be approved[4]. Furthermore, the majority of clinical studies for a new drug fail, with efficacy (52%) and safety (24%) being the most common reasons for failure[5].

Moreover, patient heterogeneity cannot be ignored anymore. Medicine in past centuries has focused on developing universal therapies that can treat the maximum number of patients with similar symptoms[6]. However, a wide range of different diseases have similar symptoms, but with distinct mechanisms[7]. It is not a surprise that patients evolve differently, even with the same treatment. Individual variability must be taken into consideration[8]. Precision medicine allows healthcare interventions to be tailored to individuals on the basis of their individuality[4]. Medicine should focus on prevention, personalization, and precision rather than devising therapies for populations and making the same medical decisions on the basis of a few similar physical traits among patients[6]. However, a side effect of evaluating patient heterogeneity is that complexity increases exponentially.

VOLUME OF HEALTHCARE DATA

A physician's ability to examine all healthcare data or stay updated has become impractical. A massive amount of healthcare data is generated every second. Approximately 30% of the world's data volume is created only by the healthcare industry. Data for healthcare will expand at a compound annual growth rate of 36% by 2025, far faster than any other industry[9]. This massive data generation is happening mainly due to the digitalization of healthcare data, high-resolution medical imaging, biosensors with continuous physiologic metrics output, and the OMICS science (genomics, proteomics, metabolomics, and transcriptomics).

The human capacity for analyzing these vast amounts of data has certainly been exceeded. Furthermore, not only the volume of data has increased, but also the variety. Different

[1]Universidade de São Paulo, Faculty of Medicine, Department of Pediatrics – São Paulo (SP), Brazil.
*Corresponding author: felipe.matsushita@hc.fm.usp.br
Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on February 09, 2022. Accepted on February 09, 2022.

types of health data sources have emerged, such as sensor data, new images techniques, gene arrays, laboratory tests, free text, and demographics[6].

BURNOUT

Burnout is becoming more prevalent among healthcare practitioners. Between 30% and 50% of physicians are thought to be affected. Burnout is linked to lower patient safety, outcomes, and the occurrence of serious medical errors[10]. In addition, physicians with burnout have a higher risk of substance addiction, stress, depression, and suicide[11].

One leading cause of physician burnout is inefficient time management owing to administrative tasks. Without receiving additional incentives, the physician has done an additional 1–2 h of administrative work for every hour spent on patient engagement[11]. An average nurse in the United States spends approximately 25% of her time on regulatory and administrative tasks[12].

The need for providing high-quality care is the first significant component in burnout in healthcare professionals[10]. But how can we deliver high-quality care if we cannot even analyze all the data and spend maximum time on administrative tasks while slowly moving away from the doctor-patient connection, which is (or should be) the heart of medicine? Furthermore, medical error is on the rise in the United States, and it is now the third leading cause of death. It is virtually impossible to completely avoid human error. However, as complexity grows and physicians become overloaded, there is an increase in the number of preventable lethal incidents.

HOW CAN ARTIFICIAL INTELLIGENCE HELP?

Artificial intelligence and machine learning can assist in the resolution of these three fundamental issues by generating new complex insights, increasing computational capacity, and lowering physician workload.

WHAT IS ARTIFICIAL INTELLIGENCE?

Laurence Moroney is an AI lead at Google and explains what AI is in an easy-to-understand manner: A programmer constructs an algorithm by generating a set of rules, expressing them in a programming language, and then using a computer to implement those rules. However, most individuals do not learn a game by being given a set of rules and then blindly obeying them. You play, and then you learn the rules and strategies through experience. So, rather than writing a code that works on the data to get the answers, you will give examples and then let the computer figure out the patterns. They could then turn those patterns into a model that can be used to predict future patterns. In other words, the AI revolution was the idea of using computing power to figure out the rules. Machine learning and big data are already influencing almost every aspect of life. Netflix knows which movies people like to watch and Amazon knows what people want to shop[4].

The AI revolution was only possible because of the increase in computational power. Over time, performance of the computers improved at an exponential rate. Cellphones are currently more powerful than computers were 25 years ago. AI applications can handle massive amounts of data and uncover hidden patterns that would otherwise be lost in the avalanche of wide medical data[13], enabling healthcare professionals to solve complex problems. AI applications are expected to save US$150 billion by 2026 in the US healthcare industry. The shift from a reactive to a proactive healthcare strategy, focused on health management rather than treatment of disease, is responsible for a substantial portion of these cost savings[4]. Also, by reducing mistakes and boosting precision, AI could reduce workload for healthcare personnel while also improving the quality of work provided[14].

EXAMPLES OF ARTIFICIAL INTELLIGENCE APPLICATIONS IN PEDIATRICS

In the past few years, research studies on AI in healthcare skyrocketed. We listed a few examples of applications of machine learning in pediatrics and neonatology.

Machine learning and identification of subphenotypes in extremely low birth weight preterm[7]

Problem

Critically ill patients are the most diverse group in the hospital, with a high prevalence of morbi-mortality. Patients with the same diagnosis often receive the same therapy and strategies, yet their outcomes vary. Patients with various illness mechanisms may be grouped together if they are organized into shallow disorder-based groups.

Population
A total of 215 extremely low birth weight infants who did not have severe congenital malformation.

Artificial intelligence solution
The authors identified six distinct sub-phenotype clusters with different clinical and laboratory characteristics. This means that all preterm infants should not be treated in the same manner.

Machine learning and autism screening in toddlers[15]

Problem
Autism spectrum disorder (ASD) is a neurodevelopmental disorder that affects 1 out of every 59 children. Early detection and management can enhance a patient's prognosis. However, early detection is difficult, and in the United States, the average age of diagnosis is still 4 years.

Population
A total of 16168 toddlers aged between 16 and 30 months.

Artificial intelligence solution
M-CHAT-R scoring was comparable to that of the machine learning system. The M-CHAT-R can be scored objectively and automatically using machine learning.

Artificial intelligence and pediatric head trauma decision rules[16]

Problem
Computed tomography (CT) scanning is the gold standard for quickly diagnosing intracranial damage, but it is expensive, requires sedation, and exposes patients to ionizing radiations. It is quite impossible to avoid unnecessary CT scans.

Population
Between 2004 and 2006, 42,412 children with head trauma and no altered mental status were enrolled in PECARN from 25 emergency departments.

Artificial intelligence solution
Machine learning algorithms may outperform PECARN rules in terms of predictive performance and deliver more tailored and detailed risk estimates.

Machine learning and pediatric sepsis[17]

Problem
In the United States, pediatric sepsis is responsible for about 6500 deaths per year. Early and aggressive treatment of pediatric sepsis is linked to better outcomes.

Population
Children aged 2–17 years, between 2011 and 2016, from a single-center unit, inpatient, and emergency department.

Artificial intelligence solution
Machine learning surpassed the Pediatric Logistic Organ Dysfunction score (PELOD-2) in the prediction of severe sepsis 4 h before the start of the treatment.

Machine learning and neonatal sepsis[18]

Problem
One of the leading causes of morbidity and mortality in neonates is late-onset sepsis. Very preterm infants are more vulnerable, with 10–25% of them developing late-onset sepsis at least once. Antibiotics administered promptly after a diagnosis can significantly reduce mortality, whereas antibiotics administered indiscriminately are counterproductive.

Population
Between 2017 and 2019, 49 preterm (gestational age less than 30 weeks) newborns were admitted to six university NICUs in France.

Artificial intelligence solution
A machine learning system that analyzes heart rate variability in real time (noninvasive) may detect late-onset sepsis with an AUROC of 87.7% as early as 6 h before starting the antibiotics, and with predictive potential (AUROC > 70%) as early as 42 h before starting the antibiotics.

Machine learning and young febrile infants[19]

Problem
Despite the fact that 10% of febrile children aged less than 60 days have serious bacterial infections (SBIs), a considerable majority of those without SBI are categorized as false-positives on the basis of previous decision standards, resulting in wasteful procedures.

Population
A total of 1470 children aged less than 60 days with fever in the emergency department.

Solution
A machine learning algorithm may be able to risk-stratify well-appearing febrile infants aged less than 60 days. This model could have spared 849 (68.5%) of the 1240 individuals who had lumbar punctures.

Machine learning and asthma[20]

Problem
Asthma is the world's most frequent chronic disease among children. It is a multifactorial illness with numerous risk factors. It may be possible to design asthma prevention measures by identifying children who are at a higher risk of acquiring asthma.

Population
A total of 202 children aged between 7 months and 12 years.

Artificial intelligence solution
With an accuracy of 84.9%, a machine learning algorithm could predict asthma in children.

Deep learning and grading hydronephrosis[21]

Problem
Subjective assessment of renal ultrasonography images is used to grade the degree of hydronephrosis.

Population
Children aged 0–116 months with sagittal renal ultrasonography scans were included in the study.

Artificial intelligence solution
The deep learning algorithm correctly graded 94% of the hydronephrosis images.

Machine learning and speech analysis[22]

Problem
Anxiety and depression in children are frequently underdiagnosed. These diseases, if left untreated, are linked to long-term unfavorable effects such as substance abuse and an increased risk of suicide.

Population
Children aged between 3 and 8 years and who spoke English fluently.

Artificial intelligence solution
With an accuracy of 80%, a machine learning analysis of a 3-min speech can be used to detect children with anxiety or depression.

Machine learning and neonatal mortality[23]

Problem
For most poor countries, neonatal mortality is still a major problem. Between 2018 and 2030, an estimated 27.8 million children will die in the 1st month of their birth worldwide.

Population
Between 2012 and 2017, all live births in the Municipality of São Paulo, Brazil (N=1,202,843) were analyzed.

Artificial intelligence solution
Using only normally gathered data, a machine learning algorithm with an AUC of 0.97 could predict the probability of newborn mortality with a very high accuracy.

Machine learning and obesity[24]

Problem
In the United States, childhood obesity is increasing at an alarming rate. Obesity in adults has a number of negative health consequences. Preventing childhood obesity could be essential.

Population
A total of 7519 children aged between 2 and 10 years with at least one BMI percentile recorded.

Artificial intelligence solution
Machine learning system predicted childhood obesity with good accuracy (85%) and sensitivity (90%).

ETHICAL ISSUES INVOLVING ARTIFICIAL INTELLIGENCE

Although we highlighted a few examples of the usefulness of AI in healthcare, it is important to cite some ethical dilemmas.

Artificial intelligence systems will likely make errors in patient diagnosis and treatment. If an AI system makes an incorrect prediction, who is to be blamed? When it comes to health, this becomes a far more serious ethical issue[6].

Transparency may be the most challenging issue to address with AI. Many AI systems, particularly deep learning image analysis algorithms, are nearly impossible to analyze or explain why the algorithm made a certain prediction. How can we be sure that there are no biases if we cannot explain or interpret the model? Machine learning systems in healthcare may be prone to algorithmic bias, such as predicting a higher risk of disease based on gender or ethnicity when those aspects are not truly relevant[12]. In the context of biomedicine, such systems can strengthen existing sociocultural discriminations that encourage inequities[25].

Artificial intelligence will not replace doctors, as we are dealing with human lives, not simply data. Decisions regarding healthcare are complex and there are many other factors involved, such as communication, doctor-patient relationship, spirituality, and others. However, AI tools will definitely assist healthcare workers with a wide range of duties, namely administrative tasks, clinical documentation, patient outreach, as well as specialized assistance in areas such as image analysis, medical device automation, and patient monitoring.

It is time for pediatricians and neonatologists to embrace AI in order to improve health quality while lowering expenses and administrative workload.

AUTHORS' CONTRIBUTIONS

FYM: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **VLJK:** Conceptualization, Methodology, Supervision, Writing – review & editing. **WBC:** Conceptualization, Supervision, Writing – review & editing.

REFERENCES

1. Woolf SH, Schoomaker H. Life expectancy and mortality rates in the United States, 1959-2017. JAMA. 2019;322(20):1996-2016. https://doi.org/10.1001/jama.2019.16932
2. Wouters OJ, McKee, M, Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. JAMA. 2020;323(9):844-53. https://doi.org/10.1001/jama.2020.1166
3. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat. Med. 2019;25(1):44-56. https://doi.org/10.1038/s41591-018-0300-7
4. Bohr A, Memarzadeh K. The rise of artificial intelligence in healthcare applications. Artificial Intelligence in Healthcare. 2020;2020:25-60. https://doi.org/10.1016/b978-0-12-818438-7.00002-2
5. Harrison RK. Phase II and phase III failures: 2013-2015. Nat Rev Drug Discov. 2016;15(12):817-8. https://doi.org/10.1038/nrd.2016.184
6. Mesko B. The role of artificial intelligence in precision medicine. Expert Rev Precis Med Drug Dev. 2017;2(5):239-41. https://doi.org/10.1080/23808993.2017.1380516
7. Matsushita FY, Krebs VLJ, de Carvalho WB. Identifying clinical phenotypes in extremely low birth weight infants—an unsupervised machine learning approach. Eur J Pediatr. 2022;181:1085-97. https://doi.org/10.1007/s00431-021-04298-3
8. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015;372(9):793-5. https://doi.org/10.1056/NEJMp1500523
9. Dash S, Shakyawar SK, Sharma M, Kaushik S. Big data in healthcare: management, analysis and future prospects. J Big Data. 2019;6:54. https://doi.org/10.1186/s40537-019-0217-0
10. Bridgeman PJ, Bridgeman MB, Barone J. Burnout syndrome among healthcare professionals. Am J Heal Pharm. 2018;75(3):147-52. https://doi.org/10.2146/ajhp170460
11. Patel RS, Bachu R, Adikey A, Malik M, Shah M. Factors related to physician burnout and its consequences: a review. Behav Sci (Basel). 2018;8(11):98. https://doi.org/10.3390/bs8110098
12. Puaschunder JM. The potential for artificial intelligence in healthcare. SSRN Electron J. 2020;6(2):94-8. https://doi.org/10.7861/futurehosp.6-2-94
13. Secinaro S, Calandra D, Secinaro A, Muthurangu V, Biancone P. The role of artificial intelligence in healthcare: a structured literature review. BMC Med Inform Decis Mak. 2021;21:125. https://doi.org/10.1186/s12911-021-01488-9
14. Aung YYM, Wong DCS, Ting DSW. The promise of artificial intelligence: a review of the opportunities and challenges of artificial intelligence in healthcare. Br Med Bull. 2021;139(1):4-15. https://doi.org/10.1093/bmb/ldab016
15. Achenie L, Scarpa A, Factor RS, Wang T, Robins DL, McCrickard DS. A machine learning strategy for autism screening in toddlers. J Dev Behav Pediatr. 2019;40(5):369-76. https://doi.org/10.1097/DBP.0000000000000668
16. Bertsimas D, Dunn J, Steele DW, Trikalinos TA, Wang Y. Comparison of machine learning optimal classification trees with the pediatric emergency care applied research network head trauma decision rules. JAMA Pediatr. 2019;173(7):648-56. https://doi.org/10.1001/jamapediatrics.2019.1068
17. Le S, Hoffman J, Barton C, Fitzgerald JC, Allen A, Pellegrini E, et al. Pediatric severe sepsis prediction using machine learning. Front Pediatr. 2019;7:413. https://doi.org/10.3389/fped.2019.00413
18. Leon C, Carrault G, Pladys P, Beuchee, A. Early detection of late onset sepsis in premature infants using visibility graph analysis of heart rate variability. IEEE J Biomed Health Inform. 2021;25(4):1006-17. https://doi.org/10.1109/JBHI.2020.3021662
19. Ramgopal S, Horvat CM, Yanamala N, Alpern ER. Machine learning to predict serious bacterial infections in young febrile infants. Pediatrics. 2020;146(3):e20194096. https://doi.org/10.1542/peds.2019-4096

20. Jeddi Z, Gryech I, Ghogho M, Hammoumi MEL, Mahraoui C. Machine learning for predicting the risk for childhood asthma using prenatal, perinatal, postnatal and environmental factors. Healthcare (Basel). 2021;9(11):1464. https://doi.org/10.3390/healthcare9111464
21. Smail LC, Dhindsa K, Braga LH, Becker S, Sonnadara RR. Using deep learning algorithms to grade hydronephrosis severity: toward a clinical adjunct. Front Pediatr. 2020;8:1. https://doi.org/10.3389/fped.2020.00001
22. McGinnis EW, Anderau SP, Hruschak J, Gurchiek RD, Lopez-Duran NL, Fitzgerald K, et al. Giving voice to vulnerable children: machine learning analysis of speech detects anxiety and depression in early childhood. IEEE J Biomed Health Inform. 2019;23(6):2294-301. https://doi.org/10.1109/JBHI.2019.2913590
23. Batista AFM, Diniz CSG, Bonilha EA, Kawachi I, Chiavegatto Filho ADP. Neonatal mortality prediction with routinely collected data: a machine learning approach. BMC Pediatr. 2021;21(1):322. https://doi.org/10.1186/s12887-021-02788-9
24. Dugan TM, Mukhopadhyay S, Carroll A, Downs S. Machine learning techniques for prediction of early childhood obesity. Appl Clin Inform. 2015;6(3):506-20. https://doi.org/10.4338/ACI-2015-03-RA-0036
25. Cirillo D, Catuara-Solarz S, Morey C, Guney E, Subirats L, Mellino S, et al. Sex and gender differences and biases in artificial intelligence for biomedicine and healthcare. NPJ Digit Med. 2020;3:81. https://doi.org/10.1038/s41746-020-0288-5