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Machine Learning in Neurocritical Care – Overview, Pitfalls, and Potential Solutions

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Abstract

Artificial Intelligence and Machine Learning (ML) are increasingly being used in the Neurocritical Care and healthcare in general. The ML model algorithms have many existing and potential uses in triage, diagnosis, clinical decision support, monitoring, and prevention of clinical syndromes. Combining and appropriately analyzing the vast number of neurocritical care data parameters, ranging from clinical (including electronic medical record), laboratory, imaging, multimodal monitoring, and many others is beyond human capability. ML algorithms can help the providers and patients in analyzing these data parameters to address certain defined problems. Machine learning does have limitations in several aspects (technical, medico-legal, financial, clinical, ethical, social, etc.), which can prevent realization of its full potential. Addressing these pitfalls with appropriate solutions in a timely manner is important to get the maximum benefit out of this valuable technological advancement.

Keywords: Machine Learning; Neurocritical Care; Healthcare; Solutions

Introduction and Background

Artificial Intelligence (AI) and its use in healthcare have seen a significant rise in the past few years, including Neurology. Neurocritical care deals with a vast number of parameters that need to be assessed and used in clinical decision support (CDS) and is well suited to have machine learning (ML) play a key role in patient care. Not surprisingly, ML in this field has seen a significant rise in interest and usage, particularly since the Covid pandemic [1].

Definition

Historically, the term 'artificial intelligence' was first coined by Dr. John McCarthy at the Dartmouth Conference in 1956. It is defined as a branch of the computer science that attempts to understand and build intelligent entities, in the form of software programs. In other words, it is the computer algorithm' s ability to interpret external data correctly, to learn from such data, and to achieve specific goals and tasks using flexible adaptations.

AI includes 'Machine Learning' (ML) which is a type of artificial intelligence that enables computers to independently initiate and execute learning when exposed to new data and identify patterns in it. Deep Learning (DL) is a subspecialty of Machine Learning, that uses multiple layers of data representations generated by nonlinear transformations, instead of individual task-specific algorithms, to build and train neural network models. It uses artificial neural networks (NN) with many intervening layers and nodes to identify patterns in data [2]. Subcategories of machine learning and its classification is described in the figure 1 [3,4,5,6].

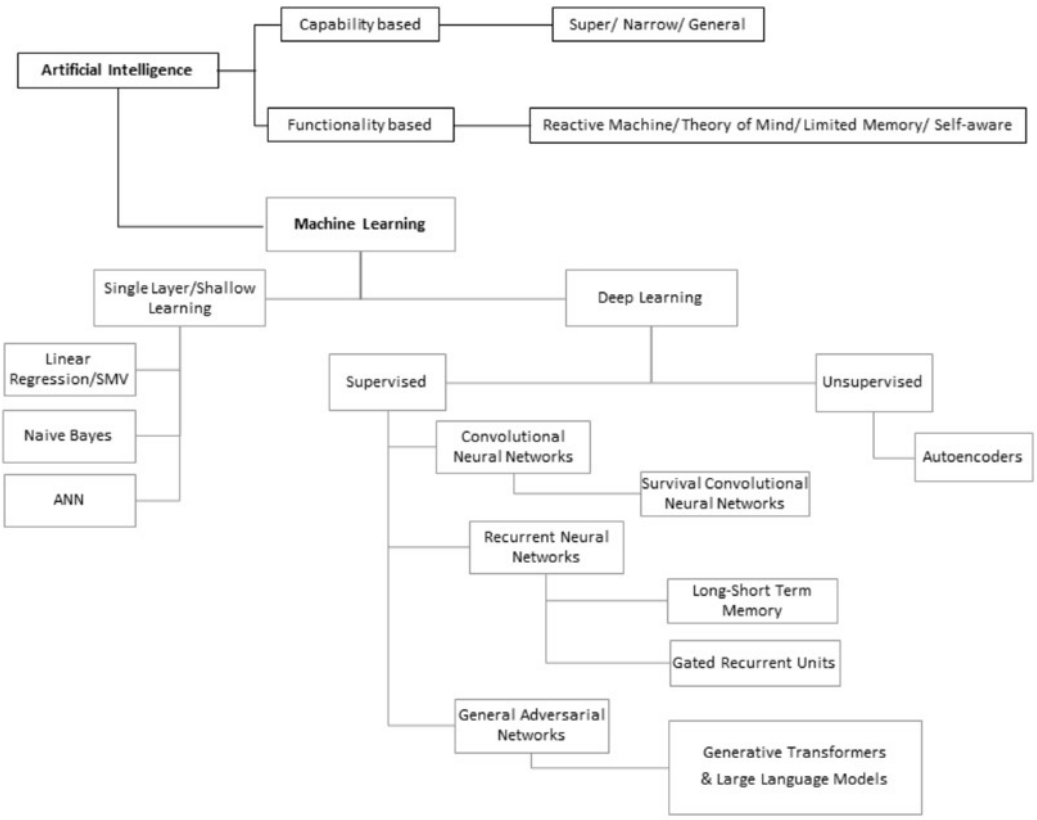

Figure 1: Classification of Machine Learning [5, 6].

(ANN: Artificial Neural-Network, CNN: Convolutional Neural Network, RNN: Recurrent Neural Network, SMV: Support Vector Machine); Adapted with permission from Aly Al-Amyn Valliani et al (Deep Learning and Neurology: A Systematic Review,Neurol Ther (2019) 8:351-365. (http://creativecommons.org/licenses/by-nc/4.0/)

Like the information technology 'Big Data', the healthcare data, has: volume, velocity, variety and veracity. Volume is the vast number of parameters that need to be monitored in the neurocritical care field, velocity indicates the rapid data acquisition speed in real time for it to be useful in CDS. Variety denotes the information collected from vast number of data sources, like clinical, laboratory, imaging, waveforms (like electrocardiogram, electroencephalogram, ventilator, intracranial pressure monitors) etc. Veracity stands for the data quality, and ML models are expected to have better reliability versus humans due to relative lack of human interference. Other important features in this series include- Validity (data's accuracy and correctedness), variability (relevance of the data to the clinical case), volatility (the frequency of change in the data), vulnerability (level of data security), visualization (presentation of data). Value is the end-goal to help improve the patient outcome, by predictive analysis of data and efficient resource use to serve the 'quadruple aim of healthcare'- i.e. enhancing patient experience, improving population health, cost reduction and improving the work life of healthcare providers [7, 8, 9, 10].

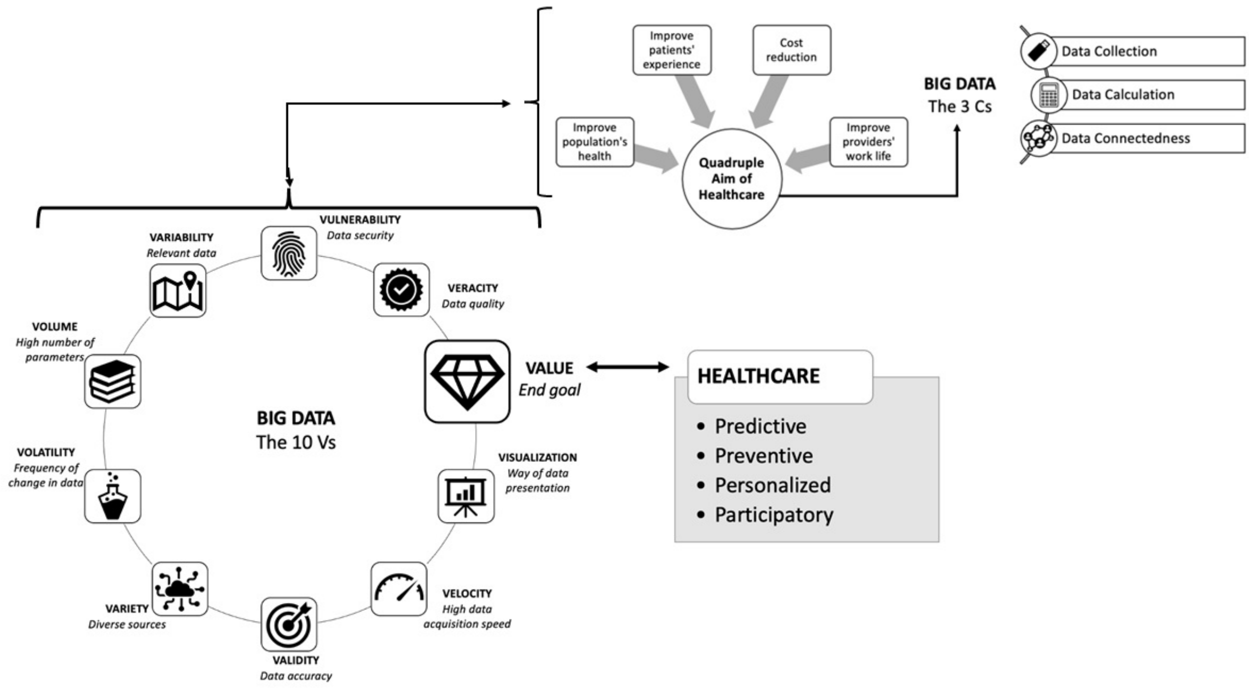

Figure 2: Big Data properties and workflow to the Healthcare Goals

'Big data' (BD) traditionally defined by volume, i.e. when log(n x p) is equal to or more than 7. BD and AI/ ML applications together can help in achieving the 'P4 medicine' goal, i.e. 'predictive, preventive, personalized and participatory' healthcare. Neurocritical care too has a similar goal in 'Precision Medicine'[10]. Potential ML healthcare applications include basic biomedical, translational research to clinical practice, using techniques of classification, regression, outcome labeling (with supervised learning), or clustering, outlier identification (with unsupervised learning), or predictive research (with predictive analytical models) [2, 10].

Basics of ML Modeling

Clinical approach typically includes analysis of clinical, laboratory and imaging data, using provider knowledge of evidence-based medicine and the experience of the team. Based on this, a clinical hypothesis is generated, evaluated and modified based on the treatment response. However, there is always an element of uncertainty, as each patient is unique.

Many ML models have a black-box hidden layer architecture, that providers and patients may regard it as hinderance in its trust worthiness. As many of the existing clinical approaches, despite being not explaniable are used due to their robust verification and validation clinical trial outcomes. Similar trials with ML models can help win patient & provider trust. There is concern that making the ML models more explainable may drop their accuracy [11,12].

Large Language Models (LLM) are a type of neural network (NN) softwares that are evolving rapidly. Recent unveiling of the Generative Pretrained Transformers (DL models that can differentialy adjudge the input data components), like the ChatGPT, GEMINI and GPT-4 with open source availability by OpenAI™, Alphabet™, and other companies is a game changing development, and is expected to have a significant impact on the future of ML including its healthcare applications.

Data Collection, Calculation and Connectedness

In Healthcare-AI evolution, the first step was the widespread adoption of the electronic medical records (EMR), with 'collection' of large scale data, even though it was 'unstructured' and not readable by computers. In last 10-15 years, a major growth in the computer processing power and mathematical algorithm improvement has allowed real-time, data 'calculation' (processing) to find relationships (correlation or causation), even with unstructured data providing actionable assistance in clinical decision support (CDS).

After the initial emergence of multiple EMR software companies, the field has now a few handful of leaders amongst them, which helped in improving the chances of solving the next problem, i.e. data 'connectedness'. Evolution from data 'collection', data 'calculation' (or processing) to the current stage of data 'connectedness' has been remarkable, providing many effective healthcare solutions [7].

Currently, there is a vast amount of medically relevant data that is collected by a multitude of sources. They include both public and private entities with little interoperability between them. Even the electronic medical records (EMR) are not compatible with each other between regional and national institutions, due to being on different digital platforms, like EPIC™ and Cerner™.

Factors leading to lack of interoperability include- (besides the software model used), variable pace of modernization and adoption of healthcare data collection and storage (e.g. EMR) between medical facilities, lack of uniform data governance standards, lack of coordination between the government, medical facilities and the technology companies. There is an emergent need to establish a system for healthcare data collection, storage and analysis, that is equitable, reliable, fair, efficient, effective and adaptable to future technological developments. With such a system in place, the AI applications in healthcare can be utilized to their full potential [13]. The federal government's efforts to provide a uniform standard using the Fast Health Interoperability Resources (FHIR) has been helpful [14].

Applications of Machine Learning Models in Healthcare

There are numerous ways that Machine Learning models are used in healthcare application. Enlisting all of them is outside the scope of this article but for simplicity, it can be broadly divided into- clinical applications and population healthcare applications.

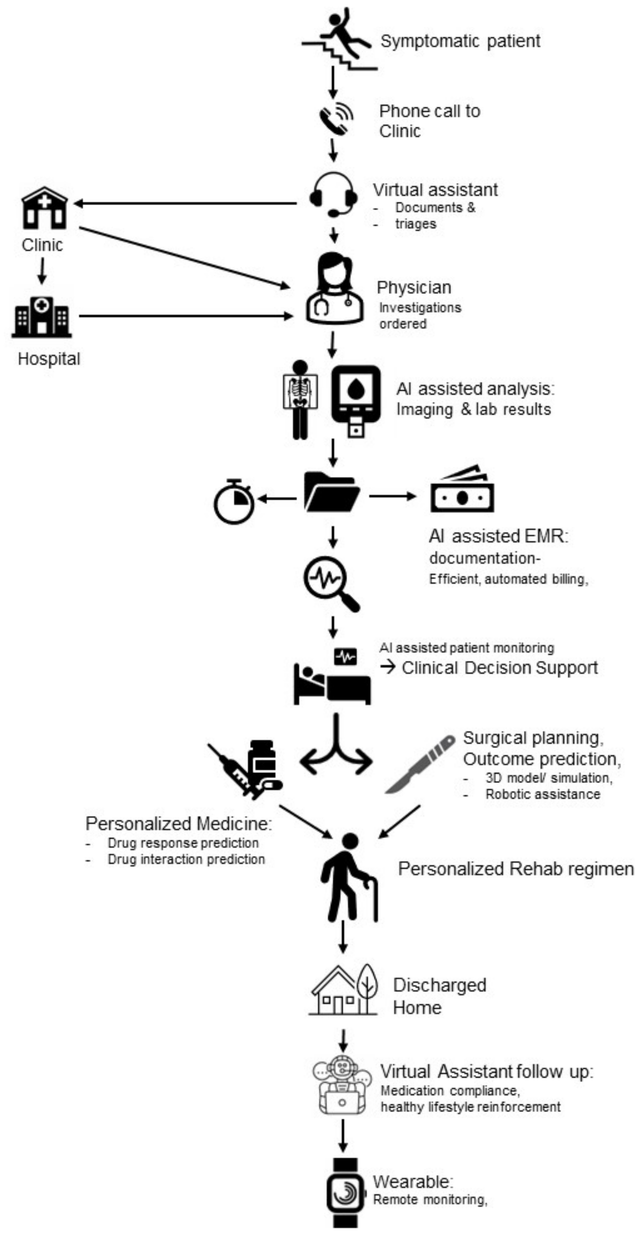

Figure 3: Applications of Machine Learning models in healthcare: journey of a hypothetical patient in digitalized healthcare.

Clinical application of ML models: If we follow a hypothetical patient who, when symptomatic, makes a phone call to the clinic. This call may be attended by a virtual assistant, which collects the basic clinical information, is able to document it, and then triage the patient, directing this patient to either a clinic or a hospital emergency department, based on the severity of the symptoms. Once in the clinic/ hospital, the patient is assessed by the physician, who will formulate a management plan, including laboratory and/ or imaging intervention to establish a clinical diagnosis. These investigation results are/ can be analyzed by the ML algorithms to expedite the clinical decision-making. The documentation of these results in the EMR can be automated, which is cost-effective. The billing of these EMR documents can also be automated, reducing burden on the coding personnel.

The clinical decision support may lead to medical interventions, which can be personalized (with prediction of drug-response and highlight any potential drug-interactions using the past medical data using ML algorithms). For patients planned for surgery, the surgical outcome prediction ML models can be utilized to improve decision making. The surgery itself can be improved with use of ML assisted surgical techniques, like 3D model simulation and robotic-assisted surgery.

During the hospitalization, and in the post-discharge phase, the rehabilitation program can be personalized using ML models. Post-discharge, the patient behavior can be modulated by phone calls from the virtual assistant about medication compliance and healthier lifestyle. Patient health can be monitored at home and remotely with the help of wearable smart sensors, many of them available now with smartwatches/ phones to assist the primary care physician with preventive care [15].

Population Healthcare Applications of Machine Learning Models

Population healthcare data is collected by various government agencies via multiple sources. This data fulfills the 'big data' definition and can be (and is) analyzed using ML algorithms. This analysis helps in preparation of the 'clinical practice guidelines', efficient allocation of the resources, especially during a public health crisis, like the COVID pandemic. They have also been helpful in prioritized use of the supply chain management resources based on the population needs, and surveillance of any potential outbreaks.

One of the primary goals of the population data collection and analysis is 'Risk Prediction' to forewarn the authorities about a health crisis like the onset of an epidemic/ pandemic. During the COVID pandemic, use of ML assisted healthcare interventions led to an expedited discovery, and development of COVID specific drugs and vaccines. ML algorithms were utilized in optimizing the clinical trials of these drug and vaccine candidates to ensure a safe, effective and accelerated deployment of these medications thus helping save millions of lives. Similar methodology can be used for rapid and safe drug discovery and development in the post-COVID era too [16].

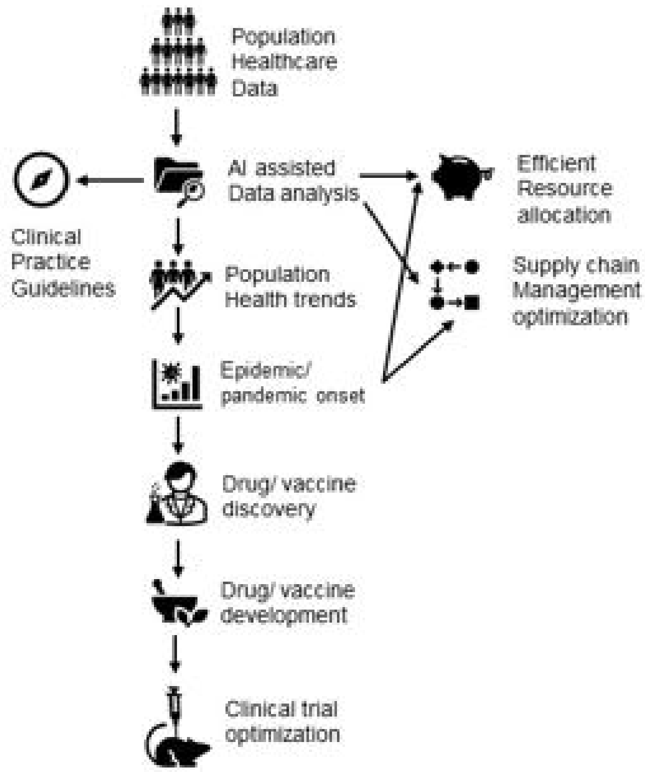

Figure 4: Applications of Machine Learning models in population healthcare

Machine Learning and its Applications in the Neurocritical Care

An easy way to elaborate the ML applications in the Neurocritical Care field would be to look at different disease syndromes where they have been used already or are likely to be used in the near future.

Stroke

Use of machine learning applications in Stroke medicine has several existing and many potential uses, including stroke prevention, screening, management and rehabilitation. Clinical data based patient screening to differentiate stroke and stroke-mimics using artificial NN was found to be superior than the traditional screening tool in Abedi et al study[17]. Similarly, study by JoonNyung Heo et al, showed that deep NN's using the clinical and laboratory data can be used to predict the outcome of stroke patients proving their superiority over the traditional methods [18].

By now, the ML based stroke identification from the imaging (eg. CT scan) is an established practice in many hospitals using the ML-based imaging tools (RAPID™, Viz.ai™) as shown in studies by Lee et al and Feng et al [19, 20]. Now, accurate identification of the stroke subtypes is possible with the help of ML and NLP tools as demonstrated by Garg et al in 2019 [21].

Stroke outcome studies have been performed using Big Data including entire nation's Stroke Registry. Taiwan Stroke Registry study by Lin et al of 58,496 patients using ML models showed outcome prediction with good accuracy, improving further with follow-up data addition with area-under-the-receiver-curve (AUC) at 0.97 for both ischemic and hemorrhagic stroke patients [22]. Similarly, the South Korean study by Cheon et al used the Korean National Hospital Discharge Data of 15,104 patients using Deep NN model for early detection of high stroke risk patients [22, 23]. A Japanese study, by Teoh et al, evaluated EMR data of 8000 patients to better predict their stroke risk [24].

Subarachnoid Hemorrhage

Delayed cerebral ischemia (DCI) in subarachnoid hemorrhage (SAH) cases is common and the leading cause of morbidity in the survivors. Its timely prediction can be immensely helpful. A study of 131 patients, by Meghjhani et al used real-time intra-cranial pressure (ICP), cerebral perfusion pressure and related ICU multimodal parameters analyzed using a validated time-varying temporal signal angle measurement (TTSAM) algorithm. During the study, 48.5% patients had DCI with balanced accuracy of algorithm at 67.3%, with a consistent performance above 60% even after 105 hours post bleed [25].

Another study by Tanioka et al using extracellular proinflammatory biomarker proteins like osteopontin, periostin, and galactin-3. Three different ML models using clinical, biomarker and both clinical and biomarker parameters were compared achieving prediction accuracy of 93.9%, 87.2% and 95.1% respectively [26, 27]. These studies highlight the potential utility of ML models in more accurate prediction of DCI in aneurysmal SAH compared to the conventional management.

AI in Cardiac Arrest:

Deep Transfer Learning (DTL) is a human brain-mimicking ML technique, where knowledge learned at one task helps improve performance at another task. It transfers learned tasks and applies it to the data provided. In 54 patients' study by Ali Mansour et al, DTL was used to assess head CT scans read by radiologists as normal. DTL was able to accurately identify progression to hypoxic ischemic brain injury with AUC value at 0.90, performing better than the human radiologists [28]. Ongoing PRECICECAP trial aims to investigate the optimal duration for post cardiac arrest hypothermia, using ML model to analyze the multimodal data including novel biomarkers, with goal to provide personalized neurocritical care improving their clinical outcome [29].

Epilepsy

ML has made enormous progress in the field of epilepsy with quantitative electroencephalogram (EEG) analysis, automated seizure detection, imaging analysis for seizure focus localization, and making more accurate prediction of medical and surgical therapy effectiveness (Jeppesen et al) [30, 31]. ML models have helped in better prediction of early versus late seizure remissions by medical management in new onset seizure cases in a study of 287 patients by Yao et al [32]. Other possible uses include- seizure prediction in admitted patients, neuro prognostication in post cardiac arrest cases, and even prediction of brain age from the sleep EEG recording [33-35]. Modern wearables have shown efficacy in personalized seizure detection using heart-rate variability-based ML models, though there is a significant room for improvement [30]. If applied with better analytics, qualitative EEG interpretation can decrease the burden on neurologists and help resource deprived areas.

Traumatic Brain Injury

Traumatic Brain injury (TBI) is a worthy cause of morbidity and mortality across the globe especially amongst young adults. Predicting acute respiratory failure due to complications like acute respiratory distress syndrome (ARDS), pneumonia, neurogenic pulmonary edema etc. can be challenging in these cases. Rui Na Ma et al. study of 312 patients with abnormal CT head due to brain trauma, had multiple clinical severity scores analyzed using XGBoost ML model, which was then compared with the conventional logistic regression (LR) for prediction of acute respiratory failure onset. The XGBoost model was superior with AUC value at 0.903 versus logistic regression AUC value at 0.798. Use of this ML model can help improve the length of stay, morbidity, and mortality outcome of such patients, and decrease the healthcare cost by better triage and risk stratification [36].

Concept of variable endotype (patients with a common biologic mechanism for a given disease) and endophenotype (patients sharing a measurable indicator or disease pattern along the causal pathway between gene expression and the phenotype) is the basis of understanding and providing ‘precision medicine.’ For example, ARDS is now known to have at least 2 endotypes- hyperinflammatory and hypoinflammatory, and each of them responds differently to ventilation pressures and fluid therapy. Similarly, ML models can be helpful in identifying endotype variations in TBI, also known to be a heterogeneous syndrome, as shown in Azad et al study [37]. Acute severe TBI cases can be monitored non-invasively using automated Trans-Cranial Doppler (TCD), for extended periods. Mainali et al have completed a study that establishes safety and feasibility of prolonged TCD monitoring with automated data analysis [38]. This modality has an immense potential as an adjunct to other multimodal parameters in the neurocritical care setting.

Pitfalls of the Machine Learning Applications in the Healthcare

Despite the multiple advantages of the ML applications in the healthcare, there are several drawbacks of this technology. They can be broadly divided into:

i. Technical

ii. Medico-legal

iii. Financial

iv. Ethical

v. Clinical

vi. Social

There is an overlap in many of these categories. Each of these categories generates a different degree of concern depending on the problem associated with it. Many of them have solutions that are available, or being implemented but there are others where the solution needs to be formulated and/ or implemented.

Table 1: ML Healthcare: Pitfalls and potential solutions

	Pitfalls	**Potential Solutions**
A. Technical		
1. Data quality	Lack of high-quality data	Advanced ML model
		Development,
		Better data collection
2. Interoperability	Lack of interoperability,	Legislative measures
	Data harmonization	for universal data format
3. Black-Box format	Lack of model transparency	Explainable AI models,
		Verification & validation
		trials for AI/ ML models
	Risk of bias	Education and
		awareness
B. Medico-Legal		
1. AI model error in medical	Patient harm from AI error	Robust studies and legislature
decision making		rules based on them
	Privacy concern &	Regulations and laws to
	Security breach	manage such breaches
C. Financial		
1. Data ownership	Control over financial support	Legal & legislative
	& data ownership	regulations to define
		responsibilities
D. Ethical		
1. Clinical Decision Support	Errors in Clinical Decision	Regular feedback between all
(CDS)	Support	stakeholders
E. Clinical		
1. Patient-Provider	Unpredictable changes in this	Education and
Relationship	relationship	communication about the
		evolving field
2. Comparison with	Different format of outcome	Robust ML model studies
traditional Versus AI model	presentation	
studies		
F. Social		

1. Job realignment	Jobs in healthcare	Better awareness about jobs
	subspecialties will realign	that may be lost & gained due.
		to AI/ ML models
2. AI model Acceptability	Provider and patient	Better education & awareness
	acceptability for clinical	
	decision support	

Artificial Intelligence (AI), Machine Learning (ML), Clinical Decision Support (CDS)

Technical Pitfalls and Potential Solutions [39]

i. Access to High Quality Data: For training of the ML models, data needed should be inclusive, relevant, and applicable to the general population. As most of the EMR's currently have 'noisy' data, not readable by the software, it may not be usable by the ML models. Use of advanced ML models and better data collection can be used to resolve this problem [39, 40, 41].

ii. Interoperability and Data Harmonization: Most of the current EMR systems do not communicate with other similar systems effectively. There is lack of data harmonization between different EMR platforms, including regionally within the same EMR platform. Data harmonization is the process that makes various file formats, coding and naming systems etc. to effectively communicate with each other in a universal format [42]. With the help of legal guidelines and regulations, this problem can be resolved, making the format universally readable and accessible as proven with the healthcare imaging regulations (DICOM™ and HL7) [40, 41, 42].

iii. Lack of Transparency/ Explainability of the ML Model: With the DL models having the 'black-box' architecture, there is a lack of trust in them by the providers and patients. Use of an 'explainable AI' (xAI) with human comprehensible hidden layers and interface will help resolve this. Use of an AI passport, a traceability tool, for documenting the model's key information, with input from the clinical end-user for the ML model re-certification can be key to solve this. Robust trial based verification and validation of ML models can win the patient-provider trust, even in the absence of explainability [6, 11, 39].

iv. Risk of Bias and Inequality: The data collected, when not uniform and representative of the population being studied, there will be a biased conclusion about the underrepresented subgroups. Even if the data is accurate, a systemic bias in the ML model developers leads to biased models, which can perpetuate and exacerbate the social inequality [43]. On a societal level, bigger healthcare institutions in future may have better ML models increasing the urban-rural, rich-poor gap and inequity in the quality of care provided by the smaller institutions. The Executive Order on AI by the US President prioritizes the equity and fairness for the US citizens [44]. The European Parliament's AI Act formally accepted as law in March 2024 emphasizes 'risk-based' regulation, upholding protection of fundamental rights, democracy and the rule of law [45].

Medico Legal Issues

AI models intended for use in healthcare need to have important properties, that include robustness, interpretability, accountability, with use of 'responsible AI' models, that are transparent and explainable.

Multiple medico-legal challenges are anticipated in the use of ML models in healthcare applications. They include:

i. Lack of Transparency: Deep Learning based Clinical Decision support involves lack of transparency of the algorithm (the 'black box' phenomena) due to the inaccessibility to the physician of reason/s behind the medical decision-making process by the algorithm.

ii. Medicolegal Liability When AI/ML Applications are Used: Currently, there are no laws on professional liability for AI systems use in healthcare. The current laws shield the physicians from liability if they follow the current standard of care, and that includes the safest use of medical AI applications in healthcare by them.

iii. Legal Status of AI Model in Healthcare: There is uncertainty about recognition of artificial intelligence as a distinct legal entity given its autonomous decision-making skills, leading to contention about its merit for legal subjectivity. A potential solution for this problem is human supervision of all AI recommendations before their application in healthcare [46].

iv. Patient Harm From AI Error: ML models can make errors (from noisy data, data gap/shift between training and real-world data, unexpected clinical variations) leading to missed diagnosis, incorrect diagnosis, or inappropriate prioritization of the planned interventions, leading to patient morbidity and mortality. Comprehensive scientific studies, with close participation by the clinicians in ML model development, and traceable ML models can be helpful in correcting this [39].

v. Data Privacy and Security: Data privacy (right to keep information from being disclosed), data confidentiality (right to have protection from unauthorized access), data integrity (information is kept accurate and consistent), and data availability (right to access data when it is needed) are all features required for a secure healthcare database. Risks of data breach include disclosure, fraud, and incorrect medical intervention. Measures to avoid this include better awareness, improved regulations, federated models, regular surveillance and strict punishment of the offenders. Both the USA Presidential Executive Order and the EU Parliament's AI Act mention protection of their citizens' privacy as a major goal [39, 44, 43, 47].

Financial Issues:

i. Financial Support and Data Ownership: Development, deployment, and maintenance of ML healthcare models is expensive, needing large financial input and only wealthy companies may be able to afford this. Therefore, the end-user (provider or patient) may not have much control over the ownership of the data and its usage. The European parliament's AI Act helps regulate the big data companies from misusing this data and provides a framework for the rest of the world [39, 45]. In July 2023, the White House received assurance from the top 7 tech companies on voluntray measures to safeguard the AI safety and transparency.

Ethical Issues

ii. Clinical Decision Support (CDS) Errors: Once the ML models are put into practice, they will be directly or indirectly involved in the clinical decision making. In case of an adverse outcome, figuring out the proportion of responsibility on the ML algorithm can be challenging. This would require a continuous feedback between all the stakeholders including the provider and algorithm developer [48].

Clinical Issues

i. Patient-Provider Relationship: With integration of the ML-assisted CDS into the clinical practice, there will be unpredictable changes in the patient-provider relationship. Depending on the context, these changes may be positive or negative. Better communication, transparency and education about the role and extent of the ML model use to all the stakeholders would be helpful to prevent a potential conflict [39].

ii. Research Study Comparison: Conventional research study outcomes are presented in scores or measurements that are different than those where the ML models are used. Due to this mismatch, providers may have difficulty in comparing the results of studies done using the conventional methodology versus the ML associated trials. Extensive multi-center robust clinical trials of the ML models and educating the providers about them can resolve this problem [48].

Social Issues

i. Job Realignment: Certain subspecialties within the healthcare will be impacted more than others by the rise of AI. This realignment will impact the choices that the current and prospective physicians will have. Better education and awareness about this will help in better job satisfaction [39].

ii. Acceptability by the Provider and the Patient: ML algorithm-assisted clinical decision support is likely to meet with varying degrees of resistance by different strata of providers and patients, based on their beliefs, experiences, readiness to change, the clinical and financial impact that they encounter. Better education about the way the models work, and their applicability to different clinical cases would be instrumental in improving their acceptance [48].

The recent legislative measures (the US Presidential Executive Order on AI and the EU Parliament's AI Act, March 2024) lay down the framework for the tech companies and the stakeholders. The former emphasizes advancement of AI safety, security, protection of it's citizens' privacy, while enhancing equity and fairness, and promoting responsible innovation to facilitate American leadership in this field [44]. The EU AI Act adopts a 'risk-based' regulatory approach, to uphold the fundamental rights of its citizens, promote innovation, enhance governance and effective enforcement of existing laws and facilitate AI application development for its market [45, 47].

Conclusion

Machine Learning applications in the Neurocritical Care field are rising and have great potential in improving the patient care experience, heathcare cost and providers' well-being. Despite several challenges in their widespread use, the potential benefits of their use in healthcare are immense and multifaceted therefore their wider use in daily healthcare is inevitable in future. With appropriate steps by all the stakeholders, including the legislature, this tool can be instrumental in helping us achieve the universal, affordable, accessible, effective and efficient healthcare, that we all aspire.

Highlights

•Machine Learning (ML) is increasingly being used in healthcare, including Neurocritical Care.

•ML models can be applied to several neurocritical disease syndromes, to help understand the complexity of clinical data, better predict clinical deterioration, and improve the outcomes.

•Despite several advantages, ML models have limitations that need to be resolved before their application in daily patient care and improve their acceptance by providers and the public.

•This study tries to suggest solutions to the common problems, present and expected with clinical applicability of ML models in healthcare.

•The main domains where ML models face problems are- clinical applicability, technical difficulties, medico-legal hurdles, financial responsibility, ethical dilemma, and social accountability.

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