

# AI, Machine Learning, and ChatGPT in Hypertension

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**ABSTRACT:** Hypertension, a leading cause of cardiovascular disease and premature death, remains incompletely understood despite extensive research. Indeed, even though numerous drugs are available, achieving adequate blood pressure control remains a challenge, prompting recent interest in artificial intelligence. To promote the use of machine learning in cardiovascular medicine, this review provides a brief introduction to machine learning and reviews its notable applications in hypertension management and research, such as disease diagnosis and prognosis, treatment decisions, and omics data analysis. The challenges and limitations associated with data-driven predictive techniques are also discussed. The goal of this review is to raise awareness and encourage the hypertension research community to consider machine learning as a key component in developing innovative diagnostic and therapeutic tools for hypertension. By integrating traditional cardiovascular risk factors with genomics, socioeconomic, behavioral, and environmental factors, machine learning may aid in the development of precise risk prediction models and personalized treatment approaches for patients with hypertension.

**Key Words:** artificial intelligence ■ cardiovascular diseases ■ hypertension ■ machine learning

Hypertension is the leading cause of cardiovascular disease and premature death worldwide. Despite decades of experimental and clinical efforts, the pathophysiology of hypertension remains incompletely understood. An underlying renal or adrenal disease appears to be the cause of elevated blood pressure in some people with hypertension. In the rest of the patients, however, no single cause can be identified.<sup>1</sup> Blood pressure regulation involves a number of physiological systems, including the cardiovascular system, the renal system, the renin-angiotensin-aldosterone system, and the renal sympathetic nervous system.<sup>2,3</sup> The derangement of some of these systems likely contributes to the development of primary hypertension. In turn, dysregulation of the blood pressure mechanisms and the resulting hypertension may be attributed to numerous interrelated factors, such as aging, diet and salt intake, obesity, insulin resistance, endothelial dysfunction, and neurovascular anomalies. The involvement and relative contributions of these factors differ among individuals.

Despite the availability of numerous drugs, patients with hypertension often fail to achieve adequate blood

pressure control. Why do some treatments work for some patients but not for others with similar symptoms? For a given patient, what is the most effective treatment? To answer these questions, the potential role of artificial intelligence (AI) in cardiovascular medicine and hypertension has received increasing attention. AI is a machine that mimics cognitive functions that humans associate with other human minds, such as learning and problem solving. AI holds promise for developing innovative diagnostic and therapeutic tools for patients with hypertension, who often exhibit diverse symptoms, disease progression, and response to treatment despite having the same diagnosis based on blood pressure measurements. AI-based systems achieve this by applying advanced algorithms to large amounts of data, with the goal of identifying hidden risk factors or phenotypes of hypertension that are difficult to identify or uncover by conventional statistics and study designs. Additionally, AI may aid in developing precise risk prediction models for patients with hypertension by integrating traditional cardiovascular risk factors with multiomics (eg, genomics,

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Nonstandard Abbreviations and Acronyms

<b>AI</b>	artificial intelligence
<b>FN</b>	false negative
<b>FP</b>	false positive
<b>TN</b>	true negative
<b>TP</b>	true positive

proteomics, and metabolomics), socioeconomic, behavioral, and environmental factors, as well as developing personalized treatment approaches for patients with hypertension. Hence, AI-based systems might change clinical practice for hypertension by identifying patient trajectories for new, personalized care plans and predicting patients' risks and necessary therapy adjustments due to changes in disease progression or therapy response.

AI is at the heart of most of the technologies that we use daily. A particularly relevant example is the smart watches or phones that can be paired with blood pressure-measuring devices that allow us to monitor our blood pressure at home. An important subfield of AI is machine learning, which is a series of algorithms that analyze data, learn from it, and make better and more informed decisions as they are exposed to more data over time. Machine learning has gone through many phases of development since the inception of computers. In 1943, Warren McCulloch and Water Pitts developed the first neural network with an electric circuit to demonstrate that it was possible for 2 computers to communicate without human interactions, paving the way for future machine learning development. In the 1950s, Alan Turing proposed the Turing test to determine whether it was possible to distinguish between answers provided by humans and machines. The purpose of the test is to assess the extent to which machines can think intelligently and demonstrate some form of emotional capability. In 1952, Arthur Samuel created the first computer program to play championship-level checkers. In 1957, Frank Rosenblatt developed the perceptron, which is a machine learning algorithm. Arguably, the most memorable development in the history of machine learning, at least to the general public, was that in 1997, the IBM supercomputer Deep Blue defeated chess grandmaster Garry Kasparov in a match. In recent years, the development and applications of machine learning have skyrocketed, in part, due to the computational resources required for handling a huge amount of data that have become available through advances in computer hardware. Now, power is good, but data is king. The large amount of data needed by most machine learning models is made possible by new technologies in data capture and data management. Indeed, it can be said that we are living in the golden age of machine learning.

TYPES OF MACHINE LEARNING

Machine learning approaches can be divided into 3 subcategories: supervised learning, unsupervised learning, and reinforcement learning. In supervised learning, each sample is labeled with an outcome or diagnosis by experts, and this labeled data set is used to train a model to make predictions on new, unseen examples. In contrast, an unsupervised machine learning model is not given labeled outputs. Instead, it seeks to infer the natural structure within the data. Unsupervised models can discover new drug-drug interactions or cluster patients according to their attributes. A third subtype is reinforcement learning, which is an autonomous, self-teaching system that essentially learns by trial and error. Reinforcement learning thus far has limited applications in medicine and is outside the scope of this review.

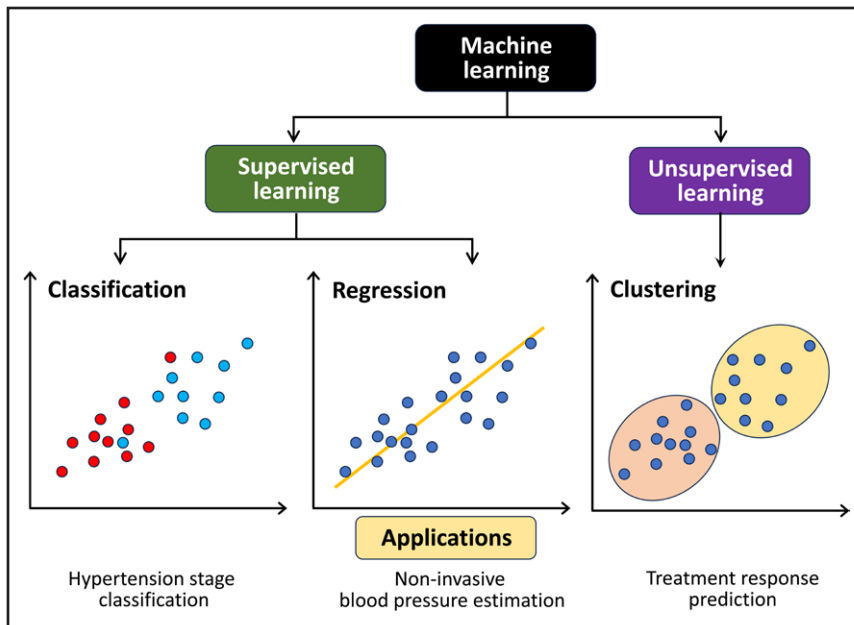
Machine learning problems can generally be divided into 3 types, as illustrated in Figure 1. Regression is used to predict continuous value, for example, blood pressure. In classification, the outputs are categories, typically binary class label, for example, whether a patient will have a cardiovascular event in the next 12 months. Regression and classification are examples of supervised learning. Unsupervised learning, which in the context of machine learning applications often refers to clustering, determines labels by grouping similar information into labeled groups. For instance, longitudinal blood pressure trajectories can be grouped to reveal what characteristics are associated with which blood pressure trajectories. The Table highlights some common machine learning algorithms, the types of machine learning problems they can be applied to, and their pros and cons. Three popular algorithms (K-nearest neighbors, support vector machine, and neural network) are illustrated in Figure 2.

PERFORMANCE METRICS

Suppose a machine learning model is trained using a large volume of electronic health records to predict each patient's likelihood of having a cardiovascular event in the next year. Now further suppose that the prediction for an individual is very likely. How alarmed should they be? If we want to know how much we can trust the predictions of a machine learning model, there are various metrics we can use to assess its performance.

First, consider the classification problems, where the prediction is, for example, either "yes, you will have a cardiovascular event" or "no, you won't, don't worry." In terms of model performance, there are 4 types of outcomes:

- True positive (TP): the model predicts correctly that a patient will have a cardiovascular event.
- True negative (TN): the model predicts correctly that a patient would not have a cardiovascular event.
- False positive (FP): the model predicts that a patient will have a cardiovascular event when, in fact, they would not;



**Figure 1. Types of machine learning algorithms and examples of applications.**

Classification and regression are types of supervised learning algorithm, whereas clustering is a type of unsupervised learning algorithm. When the output variable is continuous, then it is a regression problem. When it contains discrete, often binary, values, it is a classification problem. Clustering algorithms create the clusters based on the characteristics of the data points.

- False negative (FN): a patient will have a cardiovascular event, but the model misses it.

To state the obvious, TP and TN are correct predictions, whereas FP and FN are incorrect. These outcomes are used to define the performance metrics below.

Accuracy is the proportion of the total number of predictions that were correct and is given by the number of correct predictions (TP+TN) divided by the total number of predictions. Accuracy tells us how often the classifier is correct. It is intuitive and is commonly used, sometimes even (misleadingly) used as a synonym for performance. However, accuracy is helpful only when the data are balanced. Consider the scenario where the model is extremely rare, occurring in only 0.1% of cases. Then, a model that blindly predicts no regardless of the input would achieve 99.9% accuracy. Highly accurate but also rather unhelpful.

Precision tackles the data imbalance problem by computing the proportion of all positive predictions by the classifier that were correct, that is, TP/(TP+FP). If the model says yes about an individual, how likely is it that an individual will actually have a cardiovascular event? Even when the event is rare (ie, TP+FP is small), precision should still yield a meaningful measure of the classifier's performance. The downside of precision is that it neglects FNs. Not being able to predict future cardiovascular events (FNs) means missing opportunities to save lives.

Recall takes FNs into account by measuring the proportion of all positive cases that were correctly predicted by the classifier, that is, TP/(TP+FN). How likely is the model to pick out individuals who will have cardiovascular events? The downside of recall is this: a model that assumes everyone will have a cardiovascular event would not miss the actual cases (100% recall) but may cause people to panic unnecessarily.

The F1 score aims for a balance between precision and recall by calculating their harmonic mean:

$$\frac{2}{\frac{1}{\text{Precision}} + \frac{1}{\text{Recall}}}$$

The F1 score is typically a better choice as a performance measure than accuracy, especially when the data are imbalanced.

In clinical problems, we often want to identify all the positive cases so we can treat those patients. False alarms are undesirable, but they are often considered less tragic than missing a positive case. However, there are applications where we cannot tolerate FPs. For example, it would be highly unfortunate for a fraud detection algorithm to put an innocent person behind bars. In medicine, for example, incorrect cancer diagnoses can result in unnecessary surgeries and emotional trauma. For such applications, the models can be assessed by their specificity, which can be viewed as the opposite of recall. It measures the proportion of all negative cases that the model has correctly identified as such, that is, TN/(TN+FP).

Machine learning algorithms for regression problems generate continuous outputs, and their performance is evaluated by some measure of the difference between the predicted numeric value(s) and the actual data. A popular metric is the mean square error, which is the sum of the square of the difference between each data point and the corresponding predicted value. The squaring is done so that negative values do not cancel positive ones. The smaller the mean square error, the better the approximation. Another measure is the root mean square error, which is just the square root of the mean square error. Root mean square has the advantage of having the same unit as the data point. Alternatively, we can compute the

**Table. Common Machine Learning Algorithms With Pros and Cons**

Algorithm	Description
Linear regression	A data set is described using a straight line, $y=ax+b$ . By determining the optimal values of the slope $a$ and the $y$ -intercept $b$ , a linear regression model aims to establish the best-fitting line, so that given a new $x$ value, the model can make optimal prediction for $y$ . Types: Supervised, regression Pros: Simple, easy to understand Cons: Does not capture nonlinearity, easily affected by outliers, subject to overfitting
Lasso regression	A modification of linear regression, where the model is penalized for the sum of absolute values of the weights. Types: Supervised, regression Pros: Select features, avoid overfitting Cons: Unstable, feature selection not intuitive and not robust when there are higher correlated features
Logistic regression	Models the probability of a discrete outcome given an input variable. Types: Supervised, classification Pros: Easy to implement, interpret, and train Cons: Assumes linearity between the dependent and independent variables
K-nearest neighbors	Uses proximity to make classifications or predictions about the grouping of an individual data point. Types: Supervised, classification Pros: Simple to implement, robust to noise in training data, scalable Cons: K can be expensive to determine, difficult to handle high dimensions, expensive to calculate the distance between all points
Decision tree	A tree-like map of the possible outcomes of a series of related choices. Types: Supervised, classification and regression Pros: Simple, intuitive, interpretable Cons: Lacks robustness, computationally expensive
Random forest	Combines the output of multiple decision trees to reach a single result. Types: Supervised, classification and regression Pros: Simple, prevents overfitting Cons: Computationally expensive, not easily interpretable
Support vector machine	Create the best decision boundary that can segregate $n$ -dimensional space into classes. Types: Supervised, classification Pros: Effective in high dimensional spaces, works well when there is a clear margin of separation between classes Cons: Suitable for large data sets, performance tends to suffer when the data set is noisy
K means	Groups $n$ observations into $K$ clusters. Types: Unsupervised, classification Pros: Simple, scalable, easily adapts to new examples Cons: Sensitive to initial conditions, difficulty in determining $k$ , cannot handle categorical data
Neural networks	Processes data in a manner inspired by the human brain. Types: Supervised or unsupervised, classification and regression Pros: Performed well with nonlinear data with large inputs, flexible Cons: Lack interpretability, can be expensive to train

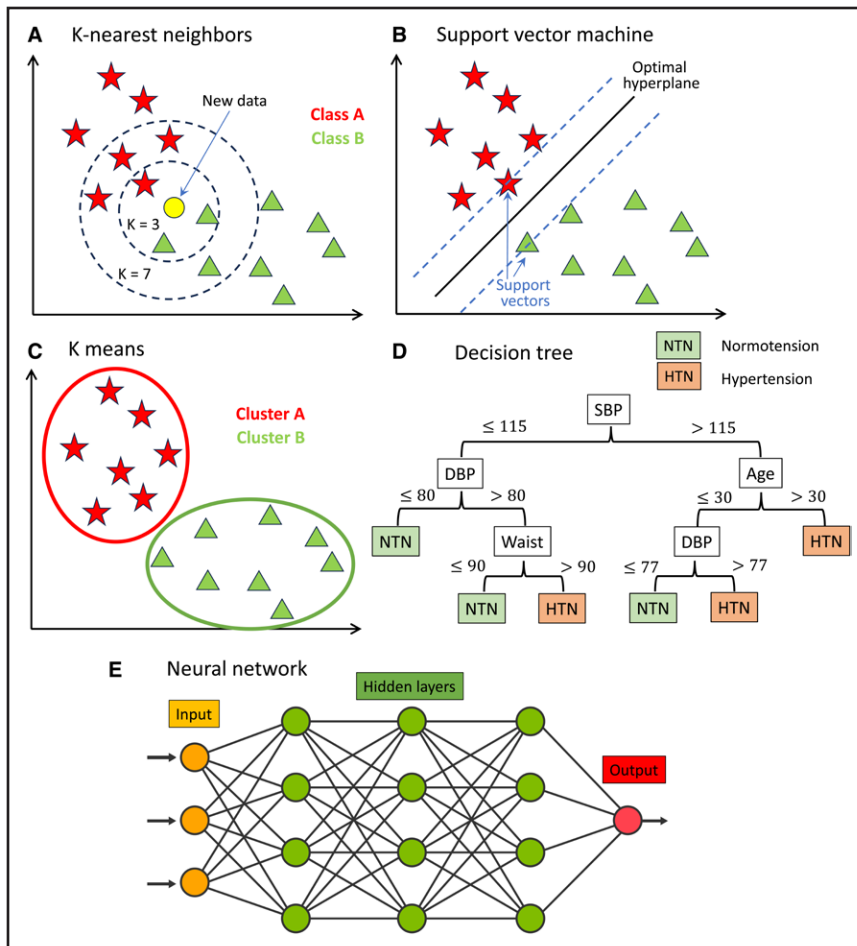
mean absolute error, where we sum the absolute values (instead of squares) of the differences between the data and the predictions.

MACHINE LEARNING APPLICATIONS IN HYPERTENSION

Keeping hypertension at bay may prevent cardiovascular disease, heart attacks, kidney disease, and other health problems. As such, a worthwhile public health goal is to prevent hypertension by identifying risk factors and addressing those that are modifiable. Machine learning algorithms can help reduce the population with hypertension by identifying health, behavioral, socioeconomic, and environmental factors, including diseases such as type 2 diabetes and lipid disorders, dietary habits, physical activity, and educational level, as risk factors for developing hypertension. That potential has been demonstrated using K-nearest neighbors,<sup>4</sup> XGBoost,<sup>5</sup> classification trees,<sup>6</sup> and neural networks.<sup>7</sup> New genes

have been identified that are associated with hypertension using machine learning models.<sup>7</sup> Genetic data can be combined with environmental and behavioral factors to more accurately predict the development of hypertension.<sup>7,8</sup>

Complications of hypertension include atherosclerosis, stroke, heart attacks, other cardiac complications, and kidney damage. Not only are these adverse outcomes serious, but they are also often irreversible. To avoid these complications, patients would benefit from an accurate assessment of their risks for adverse outcomes following a diagnosis of hypertension and receiving interventions that are optimized for them. Traditionally, risk stratification was done using clinical risk scores determined for specific populations and risk groups using linear models.<sup>9</sup> While these scores are still in use, machine learning models can be leveraged to analyze the tremendous amount of health data that have since become available to provide a more accurate prognosis and risk stratification of patients with hypertension.<sup>10–13</sup> By applying a machine learning model trained on electronic medical



**Figure 2. Schematics of popular machine learning algorithms.**

**A**, The K-nearest neighbors model predicts the label of a new data point by considering the labels of its K-nearest neighbors in the training data set. With  $K=3$ , the new data will be classified as class B; with  $K=7$ , it will be classified as class A. **B**, A support vector machine finds a decision boundary (a.k.a., a hyperplane) that can separate n-dimensional space into classes such that one can put the new data points in the right class. A hyperplane maximizes the margin from each of the support vectors. **C**, K means divides data points into clusters such that the distance between each data point and the centroid of its associated cluster is the smallest. **D**, A decision tree for prediction of hypertension (HTN) derived from a training set. **E**, In a neural network, the input is transformed through multiple hidden layers. The output of each node in the deep learning network is a function of the inputs to that node. DBP indicates diastolic blood pressure; NTN, normotension; and SPB, systolic blood pressure.

records, primary care providers may make accurate precision risk predictions based on a single patient's medical record.

The blood pressure response to a given antihypertensive therapy varies greatly among patients. Machine learning models,<sup>14–16</sup> trained using clinical trial data or electronic health records, have been shown to be able to predict patient response and help clinicians identify which patients are more or less likely to benefit from a given treatment. Indeed, machine learning algorithms can accurately predict the likelihood of antihypertensive treatment success in terms of attaining a patient's target blood pressure and help personalize hypertension management. Occasionally, machine learning models discover surprising yet valuable information, such as the blood pressure-lowering effect of protein pump inhibitors.<sup>14</sup>

The popularity of ChatGPT (<https://chat.openai.com/>), a large language model developed by OpenAI, has grown explosively. ChatGPT distinguishes itself from previously developed large language models with its impressive ability to engage in human-like dialogues. The rapid and widespread adoption of ChatGPT is impressive. Since its release on November 30, 2022, ChatGPT has garnered over 180 million monthly users and 100 million weekly active users in a year. For academic

researchers, ChatGPT and its alternatives (eg, Microsoft's Copilot, Cohere's Coral, and Anthropic's Claude) have become increasingly valuable tools. Besides drafting scientific papers, these large language models can also support researchers by sifting through the huge number of publications and gleaning relevant data, a task that has become increasingly daunting given the exponential growth of scientific literature. For patients and health care providers, ChatGPT and similar tools can offer resources to facilitate informed decision-making regarding diagnosis and treatment options. These large language models can also improve access to information on hypertension, including the latest research and treatment options. See Figure 3 for ChatGPT's response to "What are the machine learning applications in hypertension?" obtained on January 4, 2024.

## LIMITATIONS OF MACHINE LEARNING APPLICATIONS IN HYPERTENSION

No doubt machine learning has made tremendous advances in hypertension research and health care. Nevertheless, this approach is not without its limitations and drawbacks. A key piece of building a machine learning



**You**

What are the machine learning applications in hypertension?

**ChatGPT**

Machine learning (ML) applications in hypertension span various areas, ranging from early detection and diagnosis to personalized treatment strategies. Here are some key machine learning applications in hypertension:

1. **Risk Prediction and Prevention:**

- ML algorithms analyze patient data, including demographics, medical history, and lifestyle factors, to predict an individual's risk of developing hypertension.
- Early identification of high-risk individuals allows for targeted preventive interventions and lifestyle modifications.

2. **Diagnostic Support:**

- ML models aid in the early diagnosis of hypertension by analyzing diverse datasets, including medical imaging (e.g., retinal scans, cardiac imaging).
- Automated diagnostic tools can assist healthcare professionals in identifying signs of hypertensive organ damage.

3. **Blood Pressure Monitoring:**

- ML-driven wearable devices continuously monitor blood pressure and other relevant physiological parameters.
- These devices provide real-time data for personalized monitoring, enabling timely interventions and adjustments to treatment plans.

4. **Personalized Treatment Plans:**

- ML algorithms analyze patient-specific data to develop personalized treatment plans for hypertension.
- Factors such as genetics, response to medications, and lifestyle choices are considered to optimize treatment efficacy.

5. **Medication Adherence:**

- ML-based applications help improve medication adherence by sending reminders, providing education, and offering personalized support.
- Addressing medication adherence enhances blood pressure control and reduces the risk of complications.

6. **Genomic Studies:**

- ML assists in the analysis of large-scale genomic data to identify genetic markers associated with hypertension.
- Genomic insights contribute to personalized medicine approaches and the development of targeted therapies.

7. **Clinical Decision Support Systems:**

- ML-driven decision support systems assist healthcare professionals in making informed decisions regarding hypertension diagnosis and treatment.
- These systems integrate the latest research findings, patient data, and clinical guidelines to enhance decision-making.

**Figure 3.** ChatGPT's response to "What are the machine learning applications in hypertension?" obtained on January 4, 2024.

model involves the collection, cleaning, and validation of data, frequently a huge amount of it. The data curation process often represents a significant portion of resources in data science projects, exceeding that required by model construction and optimization. Indeed, ensuring

that the quality of the data used to train machine learning models is sufficiently high is crucial for the development of meaningful medical machine learning projects. Part of the data curation process is to remove erroneous values, such as negative weight or blood pressure below

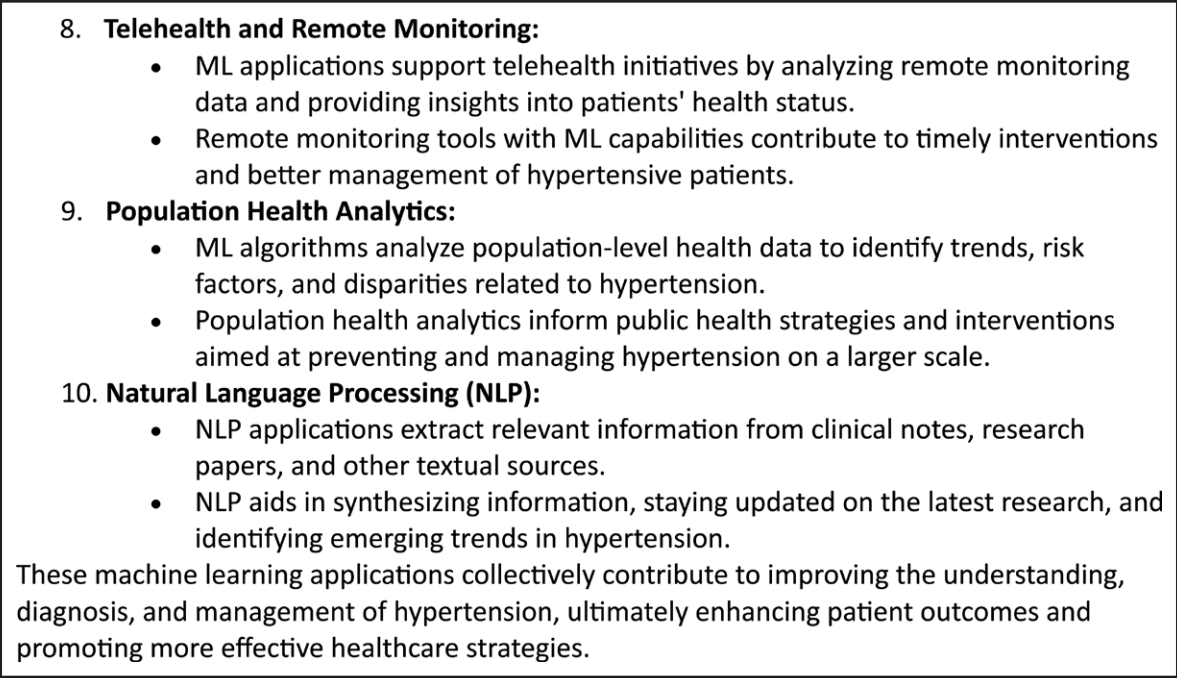


Figure 3 Continued.

10 mm Hg. However, there are less intuitive errors that require the application of clinical expertise. For example, data compatibility issues can arise from a switch between *International Coding of Diseases* versions. Missing these errors can impair model performance.

Model generalizability is a common problem with clinical machine learning models. For example, a model that is trained using electronic health records from 1 hospital may not perform nearly as well when applied to patients in another hospital. This problem may arise from measurement drift due to hardware changes (eg, using a Philips versus GE scanner), different clinical conditions (eg, metropolitan area hospital versus rural clinic), population health changes (eg, increasing diabetes rates), global health challenges (eg, pandemic), economic disparities (eg, health care access), and many others. A related issue is data interoperability, which enables information to flow seamlessly between different solutions and devices. When different parts of the health system are interoperable with each other (eg, hospitals in different provinces or states), they can speak the same language. That is, unfortunately, often not the case. The lack of interoperability may negatively impact continuity of care, collaboration between health providers, and patient access to their health information. Not only do data silos generate inefficiencies and redundancies within the health system, but they also add to errors and incompatibilities and limit the generalizability and performance of machine learning models.

Wide adaptation of machine learning applications is likely hindered by the reservation, shared by many health care professionals, of the inherent black box nature of

many machine learning models, especially neural networks. Indeed, the complexity of deep learning models and their consequent lack of interpretability can foster mistrust, which can be particularly problematic in medicine. Recently, explainable or interpretable machine learning algorithms have been developed that aim to be more comprehensible in terms of their decision-making process,<sup>17</sup> with the eventual goal of promoting trust. This trust is important. Neural networks, of which there are many types, are particularly useful in handling images and have the potential to identify features of those images that are related to hypertension but are not obvious to human observation. This is where explainable algorithms become important to identify exactly what it is within the images that allows the algorithm to determine its categorization. Regardless of how good the categorization might be, if we do not know why, it can be difficult to develop trust.

Another challenge that is common to most machine learning applications is overfitting. Overfitting occurs when a model becomes overly tuned to the training data. Instead of learning the hidden patterns in the data, the model essentially memorizes those data, including any random fluctuations. Even if the model can make highly accurate predictions for that particular data set, overfitting hinders its ability to generalize effectively to new data sets. This is the opposite of underfitting, where the model fails to fully capture the predictive potential of the data. Clinical applications of machine learning often suffer from these problems when samples from the populations of interest are limited. Overfitting and underfitting can be dealt with by refining the model parameters or

introducing modifications to the training set. Splitting the data and leaving aside the test set until the very end, or even having a distinct test set from the outset, is important in this endeavor. The remaining data are split into training and validation sets with the validation set being used as a test during training and tuning of algorithm-specific parameters, known as hyperparameters. Then, the values of the performance metrics when the final model is tested on the brand new test set will give a better indication of its general applicability.

Moreover, while ChatGPT is impressive and powerful, users should be mindful of the possibility of hallucination. An AI model is said to hallucinate when it generates information that is factually incorrect or unrelated to the given context but presents it as if it were a relevant fact.

These outputs often emerge from ChatGPT's inherent biases, lack of ability to apply logic, insufficient training data, or overfitting. The result is that sometimes ChatGPT and other such models can hallucinate information that they have not been explicitly trained on and produce unreliable or misleading responses.

Their potential to enhance health care accessibility notwithstanding, machine learning algorithms also have the capability to perpetuate existing inequities. The effectiveness of machine learning algorithms relies heavily on the data used for training and the associated labels. Consequently, biases may persist, particularly toward underrepresented groups in the training data. Additionally, the labeling process itself is susceptible to biases, as clinicians with diverse interpretations of clinical data may contribute to the labeling process.

Regardless of these limitations, the integration of AI in the field of hypertension has not only accelerated research and enhanced the quality of care delivered by health care professionals but also holds the potential to further elevate it in the near future and beyond. Indeed, the transformative impact of AI and machine learning on hypertension is profound. As these technologies advance, researchers and health care professionals will adapt and learn to collaborate with AI, enhancing their capabilities.

## ARTICLE INFORMATION

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None.

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