

Artificial Intelligence in Nephrology: Clinical Applications and Challenges

Prabhat Singh, Lokesh Goyal, Deobrat C. Mallick, Salim R. Surani, Nayanjoti Kaushik, Deepak Chandramohan, and Prathap K. Simhadri

Artificial intelligence (AI) is increasingly used in many medical specialties. However, nephrology has lagged in adopting and incorporating machine learning techniques. Nephrology is well positioned to capitalize on the benefits of AI. The abundance of structured clinical data, combined with the mathematical nature of this specialty, makes it an attractive option for AI applications. AI can also play a significant role in addressing health inequities, especially in organ transplantation. It has also been used to detect rare diseases such as Fabry disease early. This review article aims to increase awareness on the basic concepts in machine learning and discuss AI applications in nephrology. It also addresses the challenges in integrating AI into clinical practice and the need for creating an AI-competent nephrology workforce. Even though AI will not replace nephrologists, those who are able to incorporate AI into their practice effectively will undoubtedly provide better care to their patients. The integration of AI technology is no longer just an option but a necessity for staying ahead in the field of nephrology. Finally, AI can contribute as a force multiplier in transitioning to a value-based care model.

Complete author and article information provided before references.

Correspondence to P. Singh (Drprabhatsingh@hotmail.com)

Kidney Med. XX(XX):100927. Published online month xx, xxxx.

doi: 10.1016/j.xkme.2024.100927

© 2024 The Authors. Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Artificial intelligence (AI) is a branch of science that enables machines to mimic basic human cognitive behavior, making it possible to think, learn, reason, and act based on prior experience. It has different subsets, including machine learning (ML), robotics, and natural language processing (NLP). ML has further subdivisions, including supervised, unsupervised, deep, and reinforcement learning. Figure 1 shows the major subtypes of ML.

ML is the most common form of AI currently used in medical science. It is essentially defined as a type of program or algorithm that learns from prior experience and continues to improve performance based on the learning. Key definitions in the field of AI have been included in Figure 2.

Clinical scoring systems and other statistical techniques have long been used in medicine. Sometimes, they are mislabeled as AI. AI or ML has some similarities with these systems, but it also differs significantly in that it can adjust the weightage of each variable and produce results without any human intervention.¹ Some of the algorithms in this field, such as random forests, decision trees, naive Bayes, and logistic regression, are adapted from the field of statistics.

An ML algorithm uses a backbone of artificial neurons, and the arrangement of these neurons in a layer makes an artificial neural network.² Each artificial neural network consists of 1 input layer, 1 output layer, and 1-2 hidden layers. These neurons are interconnected with each other in layers in a similar fashion to that in our brain cells. These artificial neural networks must be trained with specific data before they are used for application. This also involves choosing the adequate number of neurons in each

layer and the number of layers.³ A typical lifecycle of AI-based clinical decision support is depicted in Figure 3.

TYPES OF ML

Supervised ML algorithms must be trained on a previously structured data set. ML requires raw data that experts must process to feed into the algorithm. It essentially requires a programmer to arrange the data into a spreadsheet with multiple variables.⁴ ML has the disadvantage of requiring processed data to feed into its algorithm, which can be a resource- and time-consuming undertaking, especially if it is large data set. Unsupervised learning is used to identify relationships between random variables in a large data set. It requires no neural network training because there is no predefined objective. As a result, this kind of ML is well suited for complex big data, such as in health care and genomics. In these cases, the data are usually unstandardized, highly granular, and contain a large number of variables, making it extremely difficult for a human to identify a pattern.⁵

Reinforcement learning uses a model that rewards the desired outcome and minimizes the undesired outcome until it reaches an optimal solution. This is extensively used in video games, in which it collects data proactively. However, this proactive data collection and experimentation is not possible in a health care setting owing to ethical issues. So, data collection is limited to retrospective data.⁶

This type of ML has been used in optimizing antiretroviral therapy in human immunodeficiency virus patients⁷ and adjusting antiepilepsy drugs for seizure control.⁸ Figure 4 shows practical examples of applications in ML.

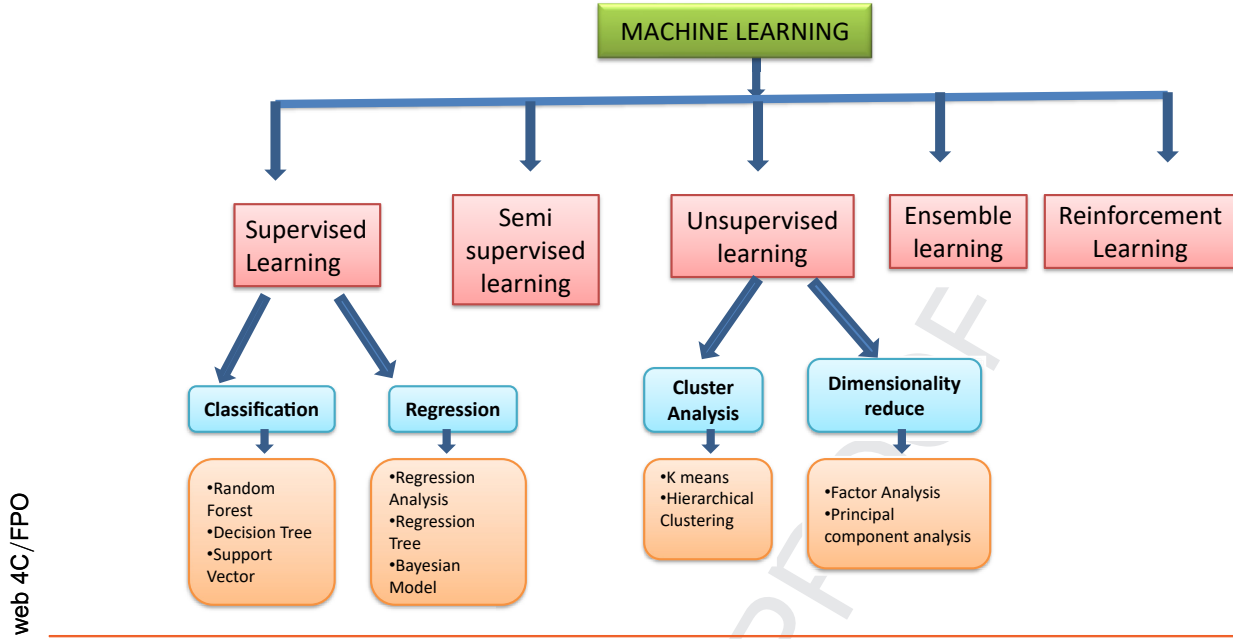


Figure 1. Subtypes of machine learning.

AI IN ACUTE KIDNEY INJURY

Acute kidney injury (AKI) is a term that represents a syndrome of various pathophysiologic processes that eventually lead to an elevation in serum creatinine (Cr) or decreased urine with or without an elevation of serum biomarkers. The challenge with AKI detection is the heterogeneous nature of pathophysiology leading to AKI and multiple AKI phenotypes, which finally manifest as elevated Cr. This poses a major challenge in developing algorithms or statistical models to detect early AKI.

Traditional statistical methods have used various techniques, such as logistic regression analysis or risk scoring, to predict AKI. The use of AI and ML, however, can augment and largely refine this ability.

ML has been used to predict AKI in postoperative heart surgery patients. Lee et al⁹ performed a retrospective analysis of 2,010 patients undergoing vascular and thoracic aortic procedures, as well as cardiac surgery to predict postoperative AKI in these patients. They used various AI techniques, including deep learning, random forest,

Cycle of AI Based Clinical Decision Support

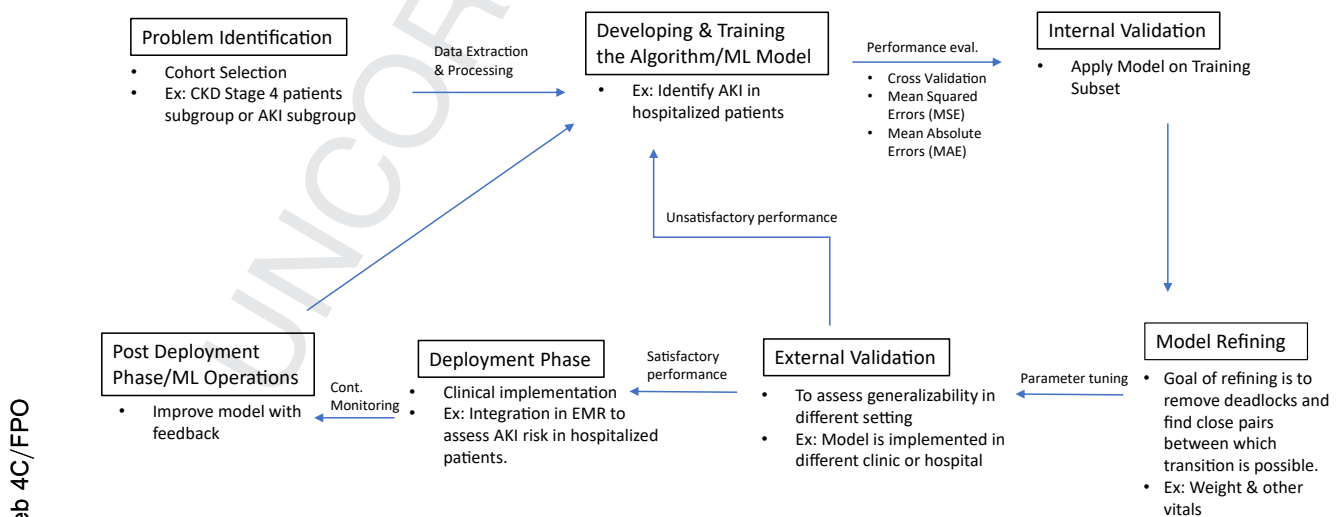


Figure 2. Cycle of AI-based clinical decision support. Abbreviations: AI, artificial intelligence; AKI, acute kidney injury; CKD, chronic kidney disease; EMR, XXX; MAE, mean absolute error; ML, machine learning; MSE, mean squared error.

Algorithm	A set of rules that defines a sequence of operations for computers
Machine learning (ML):	Process by which an algorithm encodes statistical regularities from a database of examples into parameter weights for future prediction
Deep learning (DL)	Deep learning (DL) is a type of machine learning that uses multiple layers of computations to learn from large data sets and extract information without needing human intervention or specific training data sets. It uses CNN, where not all layers are fully connected to each other and has deeper layers, allowing it to efficiently handle complex tasks with less processed data and resources
Artificial neural network (ANN)	Arrangement of neurons in a layer form, which are interconnected with each other in a similar fashion to our brain cells.
Convolutional neural network (CNN)	CNN is distinct from ANN in that not all layers are fully connected to each other. CNN has many deeper layers than ANN, and the number of neurons in each layer decreases with depth.
Decision tree	A type of supervised learning method in which choices and outcomes are represented as a tree, and each tree contains nodes (attributes in groups) and branches (values in a node).
Hierarchical clustering	An algorithm that forms groups of elements that are like one another and different from others by iteratively merging points according to pairwise distances
Random forest	An artificial intelligence model that assembles outputs from a set of decision trees and uses the majority vote or average prediction of the individual trees to produce a final prediction
Gradient boosting	An artificial intelligence (AI) technique for iteratively improving predictive performance by ensuring that the next permutation of the AI model, when combined with the prior permutation, offers a performance improvement.
Support vector machine (SVM)	SVMs are used to identify patterns in complex labeled datasets and classify data transformations. In non-medical fields, SVMs detect subtle patterns, such as handwriting recognition, identifying fraudulent credit cards, and facial detection.
Ensemble model	A model that assembles outputs from multiple algorithms to achieve predictive performance that is greater than that of individual algorithms.

web 4C/FPO

Figure 3. Important AI-related terms and definitions. Abbreviation: AI, artificial intelligence.

decision tree, etc, and demonstrated that extreme gradient boosting was better than traditional analytical models in predicting postoperative AKI.

Another deep learning–based model was developed using a data set of 703,782 patients. Tomašev et al¹⁰ predicted AKI in 55% of cases with AKI and 90.2% of

cases with AKI requiring dialysis. This model could predict AKI 48 hours before dialysis. However, it had a high false-positive rate of 1 in 2. Another issue with this study was regarding generalizability, as the model was trained on almost all male individuals, so external validity remains a concern.¹⁰

Machine learning types	Examples
Supervised learning is used to predict a known outcome and is frequently used in risk estimation tools	<ul style="list-style-type: none"> ➤ Renal mass detection and classification based on radiologic images such as CT scans and MRI scans. ➤ Identification of cancer and pathologic images based on the training data
Unsupervised learning is useful for identifying patterns and data, and usually, there is no predefined predicted outcome.	<ul style="list-style-type: none"> ➤ Identify a common pattern in a group of patients with unexplained acute kidney injury. ➤ Classification of heart failure with preserved ejection fraction based on genetic variations.
Reinforcement learning is based on learning from interactions and is designed to take steps to maximize rewards. A Reward Model can be designed to target clinical improvement.	<ul style="list-style-type: none"> ➤ Optimizing the dosing of immunosuppressive medication in transplant patients. ➤ Dosing of erythropoietin in hemodialysis patients
Natural language Processing allows to extract selected information from a large text.	Symptom identification from a clinical note

Figure 4. Practical examples of various subdivisions of machine learning. Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

Al-Jaghbeer et al¹¹ performed a multicenter observational study using a clinical decision support system to determine its effect on length of stay and in-hospital mortality in the case of AKI. They demonstrated a reduction in hospital length of stay by 1.2 days and a slight modest decrease in mortality outcomes.¹¹ Not all such clinical decision support system studies have yielded positive results. Most recently, in 2021, a randomized control trial involving 6,030 patients using clinical decision support systems and continuing on popup alerts in electronic health records (EHRs) for AKI did not show any improvement in length of stay or mortality.¹²

Unsupervised learning can also be used to analyze large clusters of complex data and identify meaningful relationships or patterns. Chaudhary et al¹³ used unsupervised ML to identify 3 different types of phenotypes in sepsis-related AKI in intensive care unit patients. This

was a unique study of its kind, using ML to better understand sepsis-related AKI.¹³

AI has been used to risk stratify patients with immunoglobulin A nephropathy to identify those with a higher risk of progression. Chen et al¹⁴ used the extreme gradient boosting algorithm in a multicenter retrospective cohort study of 2,047 patients with immunoglobulin A nephropathy. They used an ML method called extreme gradient boosting. This system used multiple clinical variables, such as urine protein excretion, hematuria, serum albumin, and serum Cr, as well as kidney biopsy findings of tubular interstitial fibrosis and global sclerosis to identify those at a higher risk of kidney function loss.¹⁴

The majority of AKIs cannot be prevented because, in many cases, an AKI would have already occurred before coming into the hospital or they would have had an evolving AKI that had not yet manifested. AI can help refine and process the current systems to help identify not

only AKI but also patients who are at a high risk of developing AKI, resulting in the creation of early intervention plans. Newer AI techniques such as NLP can review many clinical notes and gather information based on preset parameters. This can be used to make strategies and assessments from the review of such medical records and ultimately assist clinicians in improving diagnostic accuracy and saving time.¹

AI IN CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) remains underrecognized and underreported partly owing to a lack of cost-effective screening measures. In addition, there is a wide variation in the referral patterns to nephrology, ranging across a spectrum of estimated glomerular filtration rate values. There is a big unmet need for the early and accurate diagnosis of CKD. AI- or ML-driven algorithms integrated with EHRs, especially in primary care settings, can help address this issue, triggering early nephrology referral and improving outcomes in such patients with diabetic kidney disease (DKD).

A logistic regression analysis-based AI model has been developed to predict the progression of DKD. Makino et al¹⁵ used data from 64,059 diabetes patients from EMR to develop a predictive model, which is based on albuminuria and other biomarkers such as urinary L-type fatty acid-binding protein and serum tumor necrosis factor- α . AI was able to predict the DKD progression with 71% accuracy.¹⁵ ML can also be used to predict complications from diabetes mellitus using variables such as gender, age, time from diagnosis, body mass index, glycated hemoglobin, hypertension, and smoking habits. Dagliati et al¹⁶ used the random forest model to detect the onset of diabetic retinopathy, neuropathy, and nephropathy with accuracy of 0.838.

A predictive model-based AI approach has been used to identify patients with a higher risk of Fabry disease. Jeffries et al¹⁷ used a mix of phenotypic signals, as well as other clinical characteristics, to screen patients who have the highest risk of Fabry disease.

Recently, there has been a proliferation of AI models in CKD care. One such model is pulse data, which received a patent in 2021 and uses ML to determine the risk of CKD progression. It uses a combination of laboratory data, genetic tests, patient symptoms, and biomarkers. It requires at least 1 result on tumor necrosis factor receptor 1 and kidney injury molecule 1. This model showed excellent results in terms of predicting CKD progression with a C statistic of 0.84 at 1 year, 0.81 at 2 years, and 0.79 at 5 years.¹⁸

Another model developed by Renalytix AI, KidneyIntelX, has been developed to assist in managing DKD. This model uses plasma biomarkers, including tumor necrosis factor receptor 1, tumor necrosis factor receptor 2, and kidney injury molecule 1, along with 27 other laboratory values, 20 International Classification of Diseases diagnostic codes,

30 medications, and vital signs measured at 3 separate times. This model also showed decent accuracy in terms of CKD progression with a C statistic of 0.77.¹⁹ KidneyIntelX test was integrated into the EHR at Mount Sinai Health Care System in New York in 2020. A subsequent economic study based on that data revealed that the cost of KidneyIntelX and related preventative measures could be offset by cost savings arising from the decreased need for dialysis, decreased “crash dialysis” starts, and reduction in DKD progression.²⁰

AI IN DIALYSIS

Dialysis delivery in the United States is a highly standardized process, and, especially, in-center dialysis is provided in a monitored setting. It generates lots of patient-related data, which is particularly attractive from an ML standpoint. Dialysis-related data include prescriptions (treatment time, ultrafiltration rate, and dialysate flow rate) and medications administered during dialysis (such as erythropoiesis-stimulating agents). In addition to this, patient-related data are also available in a standardized format and stored digitally in EHRs.

NLP software can extract relevant information from these big data, which can be used to train the ML algorithm to improve dialysis performance, predict intradialytic hypotension, and perform many other roles.²¹ Chan et al²² used NLP to extract data from EHRs to identify 7 common hemodialysis-related symptoms in a large set of dialysis patients. Some of the symptoms included fatigue, pain, and nausea or vomiting. They demonstrated that NLP had higher sensitivity as compared to the International Classification of Diseases code in terms of identifying these symptoms, although the specificity was the same.²²

Recurrent neural networks have been used to predict the risk for intradialytic hypotension in a sample data of 261,647 hemodialysis sessions. Lee et al²³ developed a model that could predict intradialytic hypotension with higher accuracy than other models, such as logistic regression models and boosting machines.

Chaudhuri et al²⁴ developed an ML model to predict the risk of hospitalization in outpatient hemodialysis patients. This resulted in the development of an intervention pathway with the assistance of the interdisciplinary team, and they were able to lower hospitalization rates.²⁴

Yang et al²⁵ used a full-adjusted Cox proportional hazards model to predict mortality in hemodialysis patients. In this model, they used 8 parameters, including age, Cr, potassium, Kt/V hemoglobin, albumin, diabetes mellitus, and cardiothoracic ratio, to determine the risk of mortality.²⁵

There is growing literature on the use of ML or deep learning in dialysis, and standardized delivery of dialysis makes it an attractive area of AI application. Despite this, AI or ML is not routinely used in dialysis yet, barring a few exceptions, such as the anemia model. One of the reasons for the slow adoption of AI in the field of dialysis is the

lack of regulations around AI applications in medicine, data privacy, and its integration into clinicians' daily workflow. One of the challenges is related to technology, which requires technical experts and infrastructure to analyze these data to feed into the ML algorithm.

AI IN KIDNEY TRANSPLANT

Q8 Kidney transplant is the treatment of choice for most patients with kidney failure. However, the short supply of organ donors, the risk of kidney rejection, and long-term allograft survival remain significant issues in this field. AI has been applied in almost every aspect of kidney transplantation, including organ allocation, immunosuppressive therapy transplant imaging, and transplant pathology.

A recent study used a prediction system called "iBox" to predict the long-term risk of allograft failure. It showed that iBox could predict allograft failure better than nephrologists.²⁶ This algorithm uses random forest or ML and has been the only model so far that has been externally validated in various clinical trials in the United States and Europe.²⁷

AI can play a role in donor matching and organ allocation, and address health care equity concerns. The United Network for Organ Sharing manages organ allocation in the United States. The current tier-based system has raised concerns about inequitable access to transplants.²⁸ A new AI-based framework called continuous distribution, which uses a point system to prioritize patients, has been launched for lung allocation. It aims to make organ transplants more equitable and is currently being done for only lung transplants, but it may act as a primer for other organ transplants, such as kidneys, pancreas, etc.²⁹

Similarly, AI algorithms can be used to improve donor-recipient matching in organ transplants. Bae et al³⁰ developed an online tool using a random survival forest. This algorithm assists transplant physicians in deciding whether to accept or reject marginal kidney offers. It uses the expected posttransplant survival score and Kidney Donor Profile Index and can predict waitlist survival and postkidney transplant survival.³⁰

Q9 Another model used an ML or gradient boosting survival model to predict long-term survival in liver transplant patients. Yasodhara et al³¹ developed a model to predict both general and cardiac mortality and also analyzed the effects of pretransplant and posttransplant diabetes mellitus on mortality in liver transplant patients. This is the largest study to date examining the impact of diabetes mellitus on the mortality of liver transplant recipients. This model was also externally validated using data from the University Health Network data set from Toronto, Canada (see Table 1).³¹ Figure 5 shows clinical applications of AI across multiple domains in nephrology.

CHALLENGES IN AI IMPLEMENTATION

Despite these benefits of AI, multiple challenges affect the integration of AI into clinical settings. Some of the

significant challenges are listed below. Figure 6 highlights some of the challenges in AI implementation.

Bias

AI technology is not immune to biases and can introduce biases at various stages, starting with data collection and processing. Biases can stem from nonrepresentative data samples and existing health care inequities, leading to inaccurate outcomes. For example, race-based glomerular filtration rate adjustments in clinical practice may result in delayed kidney disease detection and care for Black patients.^{42,43}

Data Quality Issues

Health care data are heterogeneous, nonstandardized, and embedded in clinical notes and other patient-related data. This makes it challenging for AI professionals to process them in a way that an ML algorithm can understand. In addition, these data are segregated, unlabeled, and stored locally, and are highly variable owing to multiple EHR platforms.

Missing data on certain patient groups can lead to poor data quality, causing ML models to underperform. This can exaggerate biases and inaccuracies, affecting the models' generalizability.

One way to address data entry and processing requirements is to integrate AI models into EHR to gather data in real time. These accurate data can be passed through a preprocessed algorithm, which can identify outliers, missed values, and other sampling errors and reduce the workload on the human operator.⁵

Lack of Openness

Black box decision making raises trust issues. Black box AI refers to AI models that lack clarity about how the data are processed in the model after entering them. It could be because the algorithm has not been shared by the developer, or, in some instances, the developers or engineers themselves do not fully understand how their own model functions.⁴⁴ This lack of transparency in understanding how a particular decision was reached by Black box AI has raised doubts in the medical community. This skepticism is also appropriate, especially if these algorithms are involved in medical decision making, including life and death decisions.

Safety Issues

Generally, clinicians are risk averse, and if faced with a diagnostic dilemma in which there is a possibility of adverse outcomes, clinicians tend to take a path of safety. The same is not true for AI.

ML models can have problems with distribution shifts. In other words, machines have difficulty understanding changes in context. Machine models may perform poorly if trained on one distribution set and applied to another. This problem can be minimized, although not eliminated,

617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672

Table 1. Key Publications of AI Applications in Nephrology

Domain	Author (Year)	AI Techniques Used	No. of Patients	Outcome Predicted	Performance	Reference
AKI	Lee et al (2018)	Decision tree, RF, XGBoost	2,010	Risk of AKI postcardiac surgery	Lowest test error rate (26.0%) and the largest AUC (0.78; 95% CI, 0.75-0.80)	9
AKI	Tomašev et al (2019)	Embedding modules, recurrent neural network core	703,782	Prediction of future AKI	55.8% of inpatient AKI events of any severity were predicted early within a window of up to 48 hours in advance, with a ratio of 2 false predictions for every true positive. ROC AUC of 92.1% and PR AUC of 29.7%	10
AKI	Zimmerman et al (2019)	Multivariate logistic regression, RF, and ANNs	23,950	Early prediction of AKI following ICU admission	ML models can predict AKI onset with a competitive AUC (mean AUC, 0.783 by all-feature, LR model)	32
CKD	Dagliati et al (2018)	LR, NB, SVMs, and RFs	1,000	Predict diabetes complications nephropathy, neuropathy, and retinopathy	Provided accuracy up to 0.838	16
CKD	Chauhan et al (2020)	RF	T2D (<i>n</i> = 871) and APOL1-HR (<i>n</i> = 498)	Predict progression of CKD in T2DM and APOL1-HR genotypes	AUC of the ML model was 0.77 (95% CI, 0.75-0.79) in T2D and 0.80 (95% CI, 0.77-0.83) in APOL1-HR, outperforming the clinical models	33
CKD	Chan et al (2021)	RF	1,146	Predict the progression of diabetic kidney disease	The AUC of the ML model was 0.77 (95% CI, 0.74-0.79) compared with the AUC for the clinical model, 0.62 (95% CI, 0.61-0.63)	19
CKD	Kanda et al (2019)	SVMs	7,465	Identifying progressive CKD from healthy population	SVMs including time-series data of the prognostic category of CKD from 3 y later detected the high possibility of the outcome not only in patients at very high risks but also in those at low risks at baseline	34
Dialysis	Kim et al (2022)	LR, deep-learning model, RF, XGBoost	63,640 dialysis sessions involving 387 patients	Predict intradialytic hypotension	Deep-learning model performed better than other models in terms of the AUROCs (Nadir90: 0.905; Fall20: 0.864; Fall20/ MAP10: 0.863)	35
Dialysis	Barbieri et al (2016)	ACM based on ANN	653 (control) 640 (observation)	Clinical decision support to optimize anemia management in HD patients	In the observation phase, median darbepoetin consumption significantly decreased from 0.63-0.46 µg/kg/mo, whereas on-target hemoglobin values significantly increased from 70.6%-76.6%, reaching 83.2% when the ACM suggestions were implemented	36
Dialysis	Zhang et al (2017)	SVMs, ANNs, and RFs	83 PD patients	Define pathogen-specific local immune fingerprints in PD patients with bacterial infections	RF-based feature elimination showed the best average performance, with the optimum biomarker combination comprising 8 features (AUC = 0.993; sensitivity = 98.5%; and specificity = 92.6)	37

(Continued)

785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840**Table 1 (Cont'd).** Key Publications of AI Applications in Nephrology

Domain	Author (Year)	AI Techniques Used	No. of Patients	Outcome Predicted	Performance	Reference
Dialysis	Chaudhuri et al (2021)	XGBoost modeling	182	To decrease hospitalization rates in HD patients	ML model–based risk-directed interdisciplinary team interventions are associated with lower hospitalization rates and hospital day rates in HD patients compared with controls	24
Kidney transplant	Bae et al (2019)	RF, Weibull regressions	Deceased-donor KT recipients (N = 120,818) and waitlisted candidates (N = 376,272) between 2005 and 2016	Predicting survival after deceased-donor KT by donor-recipient combination	For candidates with EPTS = 80, 5-y waitlist survival was 47.6%, and 5-y post-KT survival was 78.9% after receiving kidneys with KDPI = 20 and 70.7% with KDPI = 80	30
Kidney transplant	Yasodhara et al (2021)	CoxPH model GBS	18,058	Identifying modifiable predictors of long-term survival in liver transplant recipients with DM	CoxPH achieves a concordance index of 0.60 (SD, 0.00) for predicting mortality in patients with no DM, 0.59 (SD, 0.00) for patients with pre-DM, and 0.70 (SD, 0.01)	31
Kidney pathology	Zheng et al (2021)	Deep CNN	349	Automatic assessment of glomerular pathologic findings in lupus nephritis	The proposed model achieved an accuracy of 0.951 and Cohen's kappa of 0.932 (95% CI, 0.915-0.949) for the entire test set for classifying the glomerular lesions	38
Kidney pathology	Pan et al (2021)	MTL with CNNs	1,289	MLT-based IF classification of kidney disease	The proposed MTL-IF method was more accurate than the common MTL method in diagnosing kidney disease when applied to blurred IF images. Its overall accuracy rate was 0.94 ($P < 0.01$), and the AUC was 0.993	39
Imaging	Xi (2020)	ResNet50	1,162	Distinguish benign from malignant kidney lesions based on routine MR imaging	Compared with a baseline 0-rule algorithm, the ensemble deep-learning model had a statistically significant higher test accuracy (0.70 vs 0.56; $P = 0.004$)	40
Imaging	Kuo et al (2019)	ResNet101	1,299	Prediction of kidney function and CKD through kidney ultrasound imaging using deep learning	Overall CKD status classification accuracy of AI-based model was 85.6%—higher than that of experienced nephrologists (60.3%-80.1%)	41
Imaging	Potretzke et al (2022)	Multivariate LR	170	To evaluate the MR-derived TKV in ADPKD	AI algorithm–based segmentation showed high levels of agreement and was not inferior to interobserver variability and other methods for determining TKV using MR	41

Abbreviations: ACM, anemia control model; ADPKD, autosomal dominant polycystic kidney disease; AI, artificial intelligence; AKI, acute kidney injury; ANN, artificial neural network; AUC, area under the curve; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; CKD, chronic kidney disease; CNN, convolutional neural network; CoxPH, Cox proportional hazards model; DM, diabetes mellitus; EPTS, expected post-transplant survival; GBS, gradient boosting survival; HD, hemodialysis; ICU, intensive care unit; IF, immunofluorescence; KDPI, Kidney Donor Profile Index; KT, kidney transplantation; LR, logistic regression; ML, machine learning; MR, magnetic resonance; MTL, multitask learning; NB, naive Bayes; PD, peritoneal dialysis; PR, XXX; RF, random forest; ROC, receiver operating characteristic; SD, standard deviation; SVM, support vector machine; TKV, total kidney volume.

Q19

841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896

Artificial Intelligence in Nephrology

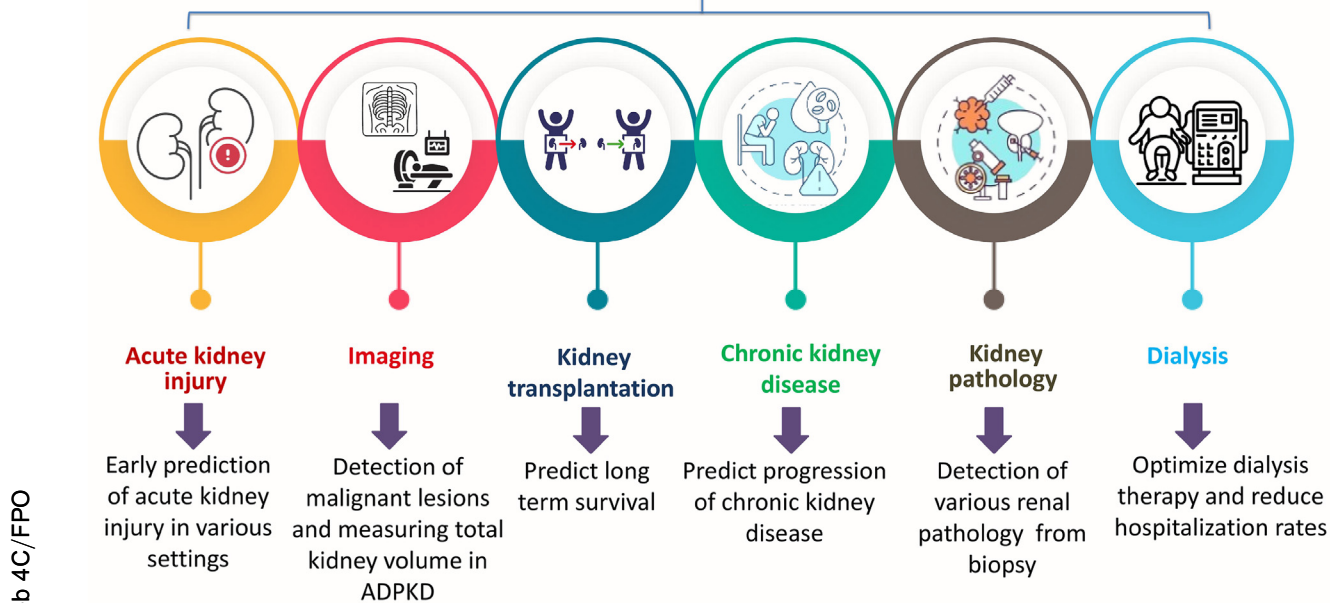


Figure 5. Artificial intelligence in nephrology. Abbreviation: ADPKD, autosomal dominant polycystic kidney disease.

by training on multiple distributions and teaching the model to respond when out of distribution.⁴⁵

Liability Issues

AI algorithms are regulated by the Food and Drug Administration, and ML is considered software as a medical device. In 2019, the Food and Drug Administration proposed a regulatory framework for AI-based software such as software as a medical device. The Food and Drug Administration intends to use a similar regulatory process for AI software as traditional medical devices.⁴⁶ The American Medical Association released a policy statement on the role of physicians and organizations in implementing AI and proposed extending liability to developers and organizations mandating AI use without risk mitigation.⁴⁷ Medicolegal and ethical issues are a reality in the day-to-day practice of medicine, and this extends to AI. We believe AI model development should prioritize innovation and maintain health care equity.

Ethical Issues

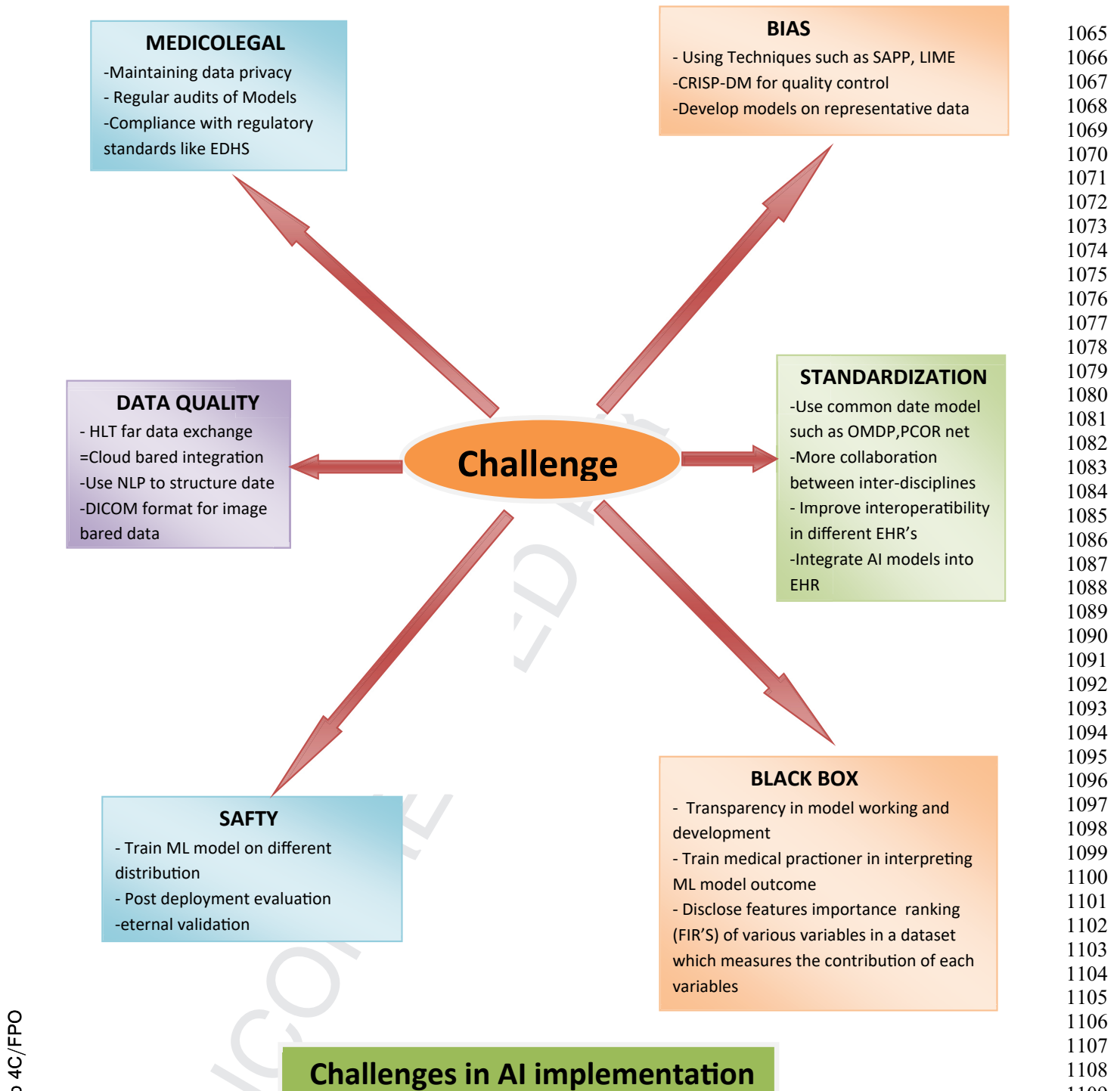
Moreover, ethical challenges include accountability, algorithm fairness, transparency, and data privacy issues. For example, with the increasing use of ML, insurance providers may depend on automated decision-making tools to approve or deny treatment. This raises ethical and accountability concerns as it can hinder independent medical decision making and patient participation.⁴⁸ Accountability is a primary ethical concern, especially in cases of adverse events related to ML-based medical decisions. In such instances, who should be held liable: the physician or the developer?

FUTURE OF ML IN NEPHROLOGY

There has been a rapid expansion of AI applications in the field of medicine, and nephrology does not remain elusive. Significant advances in the computing ability of ML or AI have made it possible to analyze big data, which otherwise would not have been possible with traditional statistical methods. AI offers a lot of promise as it can analyze big data and identify unknown patterns that would otherwise have not been possible with conventional statistical models. AI is underused in nephrology compared with other fields in medicine. More research and funding are required for validation studies. In addition, initiatives are needed to introduce AI or ML in the nephrology training curriculum so that future nephrologists are well versed in using AI to deliver individualized, high-quality care.⁴⁹

AI training in medical education is almost nonexistent. EHRs are crucial for AI algorithms, but most clinicians lack a deep understanding of data collection and processing in clinical settings. Their EHR training is often limited to basic charting tasks. As AI has entered this space, we believe there is a need to develop standardized training and curriculum to train the workforce. This will enable trainees to become well versed in data collection and other aspects and equip them with the ability to independently analyze how a specific algorithm reaches a conclusion.

As the practice of nephrology moves toward value-based care, improving outcomes and efficiency will be the driving factors. AI can play a significant role in bridging the gap between health care worker shortages and



web 4C/FPO

Figure 6. Challenges in AI implementation. Abbreviations: AI, artificial intelligence; CRISP-DM, XXX; DICOM, XXX; EDHS, XXX; EHR, electronic health record; FIR, XXX; HLT, XXX; LIME, XXX; ML, machine learning; NLP, natural language processing; OMDP, XXX; PCOR, XXX; SAPP, XXX.

enhancing patient experience. AI-driven models can help save nursing time spent in charting and review, which in turn translates to more time devoted to direct patient care. Similarly, physicians can benefit from a decrease in administrative and redundant EHR-related tasks and can focus on complex, high-value items.

AI in Evidence-Based Medicine and Clinical Trials

AI is increasingly used in the realm of clinical trials to create the next generation of evidence-based medicine. Randomized controlled trials are costly and time-consuming, but real-world data and real-world evidence can help address this. ML can be applied to real-world data

to generate real-world evidence.⁵⁰ EHRs provide diverse data for ML models to conduct simulated trials at lower costs and in less time. For example, synthetic control arms derived from real-world data use ML models that mimic traditional clinical trials' control arm.⁵¹

AI is crucial in expediting clinical trials by monitoring patient data in real time and quickly analyzing clinical images and scans. Deep-learning models can process pathologic images, radiology scans, and multiple other clinical data in a short period of time, which is humanly impossible. Hence, ML can be applied to real-world data to generate real-world evidence.

AI has immense potential to revolutionize the field of nephrology, including early diagnosis, prognostication, detection of high-risk patients, monitoring, and developing optimized and personalized treatment plans. It can transform the workflow of a nephrologist who is already overburdened by huge volumes of data, alert fatigue, and other bureaucratic tasks. Before AI can be widely used in clinical practice, we must address concerns around privacy, ethics, and transparency. Clinicians need to understand how AI arrives at conclusions and the decision-making process behind it.

CONCLUSION

In conclusion, AI has tremendous potential to transform the delivery of kidney care and ultimately improve patient outcomes. It can address many unmet needs in areas such as early detection of AKI, drug dosing, dialysis, kidney transplant, and kidney pathology. In its current form, AI is not intended to replace nephrologists; rather, it is intended to enhance the capabilities of physicians and other health care professionals. However, specific challenges, such as ethical issues and algorithm transparency, must be overcome before its seamless integration into clinical practice. It is of utmost importance to understand the core principles of AI model development and functions. The nephrology community needs to invest in training a competent workforce that will drive the next generation of AI innovation and practice. In coming times, integration of AI into medicine will no longer be just an option but a necessity to stay ahead and achieve better outcomes. Finally, we believe that medicine should remain on the humanistic side and not be replaced by automated procedures despite the value of more precise data analysis.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Prabhat Singh, MD, Lokesh Goyal, MD, Deobrat C. Mallick, MD, Salim R. Surani, MD, Nayanjyoti Kaushik, MD, Deepak Chandramohan, MD, and Prathap K. Simhadri, MD

Authors' Affiliations: Department of Nephrology (PS), Kidney Specialist of South Texas, Corpus Christi, TX; Department of Internal Medicine (LG, DCM), Christus Spohn Hospital, Corpus Christi, TX; Department of Pulmonary Medicine (SRS), Texas A&M University-Corpus Christi, College Station, TX; Catholic Health Initiatives Health Nebraska (NK), Heart Institute, Lincoln, NE;

Division of Nephrology, Department of Medicine (DC), University of Alabama at Birmingham, Birmingham, AL; and Division of Nephrology (PKS), Florida State University School of Medicine, Tallahassee, FL.

Address for Correspondence: Prabhat Singh, MD, Kidney Specialist of South Texas, 1521 Staples St, Corpus Christi, TX 78403. Email: Drprabhatsingh@hotmail.com

Authors' Contributions: Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Support: None.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Peer Review: Received March 7, 2024. Evaluated by 2 external peer reviewers, with direct editorial input from the Editor-in-Chief. Accepted in revised form September 5, 2024.

REFERENCES

1. Ting Sim JZ, Fong QW, Huang W, Tan CH. Machine learning in medicine: what clinicians should know. *Singapore Med J*. 2023;64(2):91-97.
2. Niel O, Bastard P. Artificial intelligence in nephrology: core concepts, clinical applications, and perspectives. *Am J Kidney Dis*. 2019;74(6):803-810.
3. Thomas LB, Mastorides SM, Viswanadhan NA, Jakey CE, Borkowski AA. Artificial intelligence: review of current and future applications in medicine. *Fed Pract*. 2021;38(11):527-538.
4. Badrouchi S, Bacha MM, Hedri H, Ben Abdallah T, Abderrahim E. Toward generalizing the use of artificial intelligence in nephrology and kidney transplantation. *J Nephrol*. 2023;36(4):1087-1100.
5. Loftus TJ, Shickel B, Ozragat-Baslanti T, et al. Artificial intelligence-enabled decision support in nephrology. *Nat Rev Nephrol*. 2022;18(7):452-465.
6. Mnih V, Kavukcuoglu K, Silver D, et al. Human-level control through deep reinforcement learning. *Nature*. 2015;518(7540):529-533.
7. Parbhoo S, Bogojeska J, Zazzi M, Roth V, Doshi-Velez F. Combining kernel and model based learning for HIV therapy selection. *AMIA Jt Summits Transl Sci Proc*. 2017;2017:239-248.
8. Guez A, Vincent RD, Avoli M, Pineau J. Adaptive Treatment of Epilepsy via Batch-mode Reinforcement Learning. *AAAI*. 2008.
9. Lee HC, Yoon HK, Nam K, et al. Derivation and validation of machine learning approaches to predict acute kidney injury after cardiac surgery. *J Clin Med*. 2018;7(10):322.
10. Tomašev N, Glorot X, Rae JW, et al. A clinically applicable approach to continuous prediction of future acute kidney injury. *Nature*. 2019;572(7767):116-119.
11. Al-Jaghbeer M, Dealmeida D, Bilderback A, Ambrosino R, Kellum JA. Clinical decision support for in-hospital AKI. *J Am Soc Nephrol*. 2018;29(2):654-660.
12. Wilson FP, Martin M, Yamamoto Y, et al. Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial. *BMJ*. 2021;372:m4786.
13. Chaudhary K, Vaid A, Duffy Á, et al. Utilization of deep learning for subphenotype identification in sepsis-associated acute kidney injury. *Clin J Am Soc Nephrol*. 2020;15(11):1557-1565.
14. Chen T, Li X, Li Y, et al. Prediction and risk stratification of kidney outcomes in IgA nephropathy. *Am J Kidney Dis*. 2019;74(3):300-309.

15. Makino M, Yoshimoto R, Ono M, et al. Artificial intelligence predicts the progression of diabetic kidney disease using big data machine learning. *Sci Rep*. 2019;9(1):11862. 1233 1234 1235 1236 1237 1238 1239 1240 1241 1242 1243 1244 1245 1246 1247 1248 1249 1250 1251 1252 1253 1254 1255 1256 1257 1258 1259 1260 1261 1262 1263 1264 1265 1266 1267 1268 1269 1270 1271 1272 1273 1274 1275 1276 1277 1278 1279 1280 1281 1282 1283 1284 1285 1286 1287 1288
16. Dagliati A, Marini S, Sacchi L, et al. Machine learning methods to predict diabetes complications. *J Diabetes Sci Technol*. 2018;12(2):295-302.
17. Jefferies JL, Spencer AK, Lau HA, et al. A new approach to identifying patients with elevated risk for Fabry disease using a machine learning algorithm. *Orphanet J Rare Dis*. 2021;16(1):518.
18. Cha T, Son HP, Kipers C, Fielding O, Son JH, Lee E. Machine Learning Systems and Methods for Predicting Risk of Renal Function Decline. *United States Patent and Trademark Office*. 2021.
19. Chan L, Nadkarni GN, Fleming F, et al. Derivation and validation of a machine learning risk score using biomarker and electronic patient data to predict progression of diabetic kidney disease. *Diabetologia*. 2021;64(7):1504-1515.
20. Datar M, Burchenal W, Donovan MJ, Coca SG, Wang E, Goss TF. Payer budget impact of an artificial intelligence in vitro diagnostic to modify diabetic kidney disease progression. *J Med Econ*. 2021;24(1):972-982.
21. Kotanko P, Zhang H, Wang Y. Artificial intelligence and machine learning in dialysis: ready for prime time? *Clin J Am Soc Nephrol*. 2023;18(6):803-805.
22. Chan L, Beers K, Yau AA, et al. Natural language processing of electronic health records is superior to billing codes to identify symptom burden in hemodialysis patients. *Kidney Int*. 2020;97(2):383-392.
23. Lee H, Yun D, Yoo J, et al. Deep learning model for real-time prediction of intradialytic hypotension. *Clin J Am Soc Nephrol*. 2021;16(3):396-406.
24. Chaudhuri S, Han H, Usvyat L, et al. Machine learning directed interventions associate with decreased hospitalization rates in hemodialysis patients. *Int J Med Inform*. 2021;153:104541.
25. Yang CH, Chen YS, Moi SH, Chen JB, Wang L, Chuang LY. Machine learning approaches for the mortality risk assessment of patients undergoing hemodialysis. *Ther Adv Chronic Dis*. 2022;13:20406223221119617.
26. Divard G, Raynaud M, Tatapudi VS. Comparison of artificial intelligence and human-based prediction and stratification of the risk of long-term kidney allograft failure. *Commun Med*. 2022;2(1):150.
27. Aubert O, Divard G, Pascual J, et al. Application of the iBox prognostication system as a surrogate endpoint in the TRANSFORM randomised controlled trial: proof-of-concept study. *BMJ Open*. 2021;11(10):e052138.
28. Peloso A, Moeckli B, Delaune V, Oldani G, Andres A, Compagnon P. Artificial intelligence: present and future potential for solid organ transplantation. *Transpl Int*. 2022;35:10640.
29. Kasiske BL, Pyke J, Snyder JJ. Continuous distribution as an organ allocation framework. *Curr Opin Organ Transplant*. 2020;25(2):115-121.
30. Bae S, Massie AB, Thomas AG, et al. Who can tolerate a marginal kidney? Predicting survival after deceased donor kidney transplant by donor-recipient combination. *Am J Transplant*. 2019;19(2):425-433.
31. Yasodhara A, Dong V, Azhie A, Goldenberg A, Bhat M. Identifying modifiable predictors of long-term survival in liver transplant recipients with diabetes mellitus using machine learning. *Liver Transpl*. 2021;27(4):536-547.
32. Zimmerman LP, Reyfman PA, Smith ADR, et al. Early prediction of acute kidney injury following ICU admission using a multivariate panel of physiological measurements. *BMC Med Inform Decis Mak*. 2019;19(suppl 1):16.
33. Chauhan K, Nadkarni GN, Fleming F, et al. Initial validation of a machine learning-derived prognostic test (KidneyIntelX) integrating biomarkers and electronic health record data to predict longitudinal kidney outcomes. *Kidney360*. 2020;1(8):731-739. 1289 1290 1291 1292 1293 1294 1295 1296 1297 1298 1299 1300 1301 1302 1303 1304 1305 1306 1307 1308 1309 1310 1311 1312 1313 1314 1315 1316 1317 1318 1319 1320 1321 1322 1323 1324 1325 1326 1327 1328 1329 1330 1331 1332 1333 1334 1335 1336 1337 1338 1339 1340 1341 1342 1343 1344
34. Kanda E, Kanno Y, Katsukawa F. Identifying progressive CKD from healthy population using Bayesian network and artificial intelligence: a worksite-based cohort study. *Sci Rep*. 2019;9(1):5082.
35. Kim HW, Heo SJ, Kim M, et al. Deep learning model for predicting intradialytic hypotension without privacy infringement: a retrospective two-center study. *Front Med (Lausanne)*. 2022;9:878858.
36. Barbieri C, Molina M, Ponce P, et al. An international observational study suggests that artificial intelligence for clinical decision support optimizes anemia management in hemodialysis patients. *Kidney Int*. 2016;90(2):422-429.
37. Zhang J, Friberg IM, Kift-Morgan A, et al. Machine-learning algorithms define pathogen-specific local immune fingerprints in peritoneal dialysis patients with bacterial infections. *Kidney Int*. 2017;92(1):179-191.
38. Zheng Z, Zhang X, Ding J, et al. Deep learning-based artificial intelligence system for automatic assessment of glomerular pathological findings in lupus nephritis. *Diagnostics (Basel)*. 2021;11(11):1983.
39. Pan S, Fu Y, Chen P, et al. Multi-task learning-based immunofluorescence classification of kidney disease. *Int J Environ Res Public Health*. 2021;18(20):10798.
40. Kuo CC, Chang CM, Liu KT, et al. Automation of the kidney function prediction and classification through ultrasound-based kidney imaging using deep learning. *NPJ Digit Med*. 2019;2:29.
41. Potretzke TA, Korfiatis P, Blezek DJ, et al. Clinical implementation of an artificial intelligence algorithm for magnetic resonance-derived measurement of total kidney volume. *Mayo Clin Proc*. 2023;98(5):689-700.
42. Vyas DA, Eisenstein LG, Jones DS. Hidden in plain sight—reconsidering the use of race correction in clinical algorithms. *N Engl J Med*. 2020;383(9):874-882.
43. Eneanya ND, Boulware LE, Tsai J, et al. Health inequities and the inappropriate use of race in nephrology. *Nat Rev Nephrol*. 2022;18(2):84-94.
44. Rudin C, Radin J. Why are we using black box models in AI when we don't need to? A lesson from an explainable AI competition. *Harvard Data Science Review*. 2019;1(2).
45. Amodei D, Olah C, Steinhardt J, Christiano P, Schulman J, Mané D. Concrete problems in AI safety. *ArXiv*. 2016. abs/1606.06565.
46. US FDA. Good Machine Learning Practice for Medical Device Development: Guiding Principles. Accessed October 1, 2024. <https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles>
47. American Medical Association. AMA issues new principles for AI development, deployment & use. Accessed October 1, 2024. <https://www.ama-assn.org/press-center/press-releases/ama-issues-new-principles-ai-development-deployment-use>
48. Vayena E, Blasimme A, Cohen IG. Machine learning in medicine: addressing ethical challenges. *PLoS Med*. 2018;15(11):e1002689.
49. Cassol C, Sharma S. Nephrology lagging behind in machine learning utilization. *Kidney Med*. 2021;3(5):693-695.
50. Liu F, Panagiotakos D. Real-world data: a brief review of the methods, applications, challenges and opportunities. *BMC Med Res Methodol*. 2022;22(1):287.
51. Subbiah V. The next generation of evidence-based medicine. *Nat Med*. 2023;29(1):49-58.