

Disclosures

- Grant funding from NIH
- Consultant for Vifor Pharma

Case Presentation

- 56 year old female with a PMH DM and HTN presenting to your outpatient nephrology clinic with newly diagnosed CKD (eGFR 45 and Alb/Cre ratio 100mg/g). She is very concerned about her new diagnosis of CKD and wants to know what her risk of needing dialysis is.
- You respond based on your experience and her eGFR and albuminuria levels, she is at high risk.
- What if we could accurately predict her risk of progression using EHR data from all patients seen at your clinic/hospital?

	eGFR (mL/min/1.73m ²) description and range	Alb/Cre ratio (mg/g)	Persistent albuminuria categories, description and range		
			A1	A2	A3
			Normal to mildly increased <30 mg/g	Moderately increased 30-300 mg/g	Severely increased >300 mg/g
G1	Normal or high ≥90	≤30	Low risk	Modestly increased risk	High risk
G2	Mildly decreased	30-59	Low risk	Modestly increased risk	High risk
G3a	Mildly to moderately decreased	45-59	Modestly increased risk	High risk	Very high risk
G3b	Moderately to severely decreased	30-44	High risk	Very high risk	Very high risk
G4	Severely decreased	15-29	Very high risk	Very high risk	Very high risk
G5	Kidney failure	<15	Very high risk	Very high risk	Very high risk

Objectives

- Provide a general overview of AI
- Examples of how AI can be used in nephrology
- Considerations for AI implementation

AI is everywhere

Customers say
Customers like the softness, softness, and gift value of the top figure. They mention it's very comforting, makes a great gift for any age living donor, and is made incredibly well. Some appreciate the humor and teaching tool.

Select to learn more

- Color
- Softness
- Gift value
- Quality
- Size
- Author
- Teaching tool
- Learning value

Reviews with images

Detect language: English, Spanish, Vietnamese, Chinese (Simplified)

Nephrology is amazing! × Khoa thận học thật tuyệt vời! ☆

What is AI?

Techniques that enable computer to mimic human behavior

Subset of AI which uses statistical models to enable machine to improve with experience

Subset of ML which uses multiple layers of artificial neural networks to learn

AI in Medical Research-Opportunities

Automating or augmenting data and information processing tasks

Raw Data

- User instructions
- Tabular data
- Sensors
- Clinical text
- Imaging

AI Model (embedded knowledge)

Desired Output

- Diagnosis
- Prediction
- Clustering
- Summarization
- Generation
- Decision support

Making data work for patients, physicians and systems

Rajkumar et al. NEJM, 2019.

Types of Machine Learning

TYPES OF MACHINE LEARNING

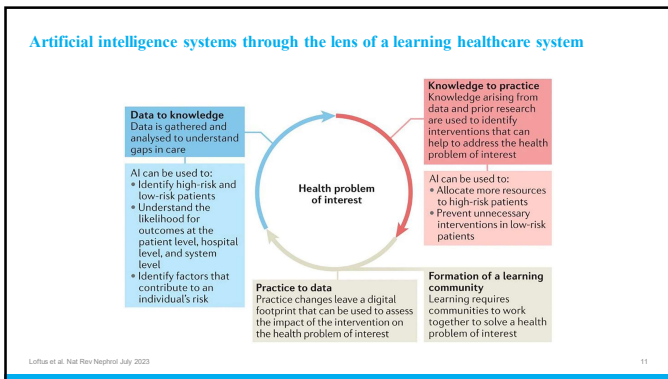
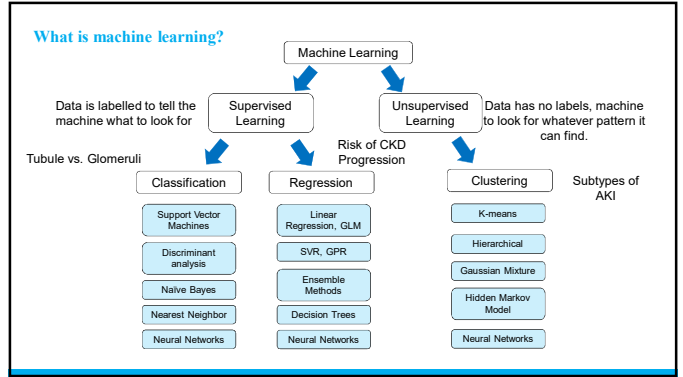
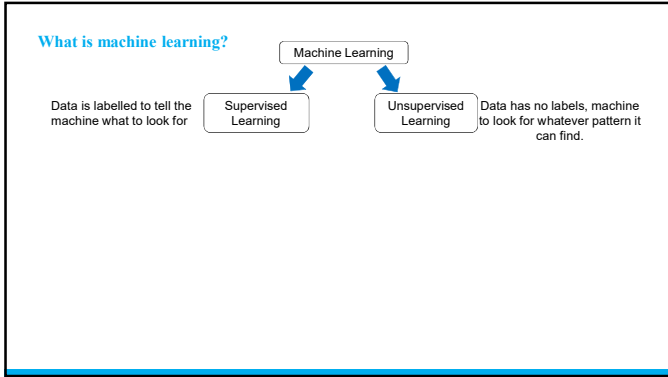
Supervised Machine Learning

Unsupervised Machine Learning

Semi-Supervised Learning

Reinforcement Learning

TOOLBOX



AI Use in Nephrology

AI for AKI Prediction

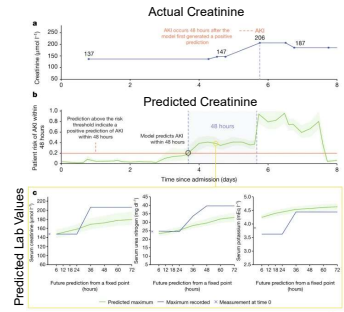
- AKI is common in hospitalized patients and associated in morbidity and mortality
- Early detection may
 - improve patient outcomes
 - More opportunities for treatment
 - Avoidance of further renal insults



13

Prediction of AKI

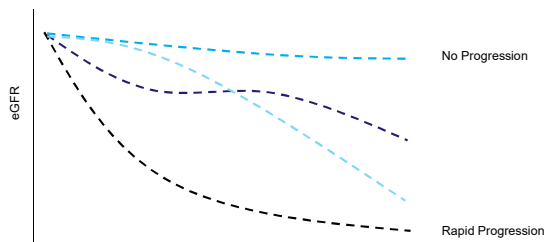
- Study Population:
 - Multi-site retrospective dataset of 703,782 adult patients from all available sites at the US Department of Veterans Affairs, years 2011-2015
 - Age 18-90
- Data types: EHR data
- ML algorithm: Recurrent Neural Network (DL)
- Outcome:
 - AKI by KDIGO Creatinine Criteria



Tomaliev et al. Nature July 2019

AI for CKD Progression Risk Stratification

- One in four adults with type 2 DM have kidney disease
- Existing measures do not precisely identify patients who will experience rapid kidney function decline

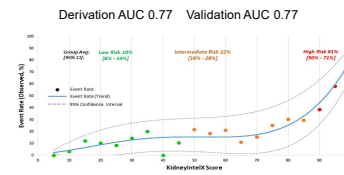


15

Prediction of DKD Progression

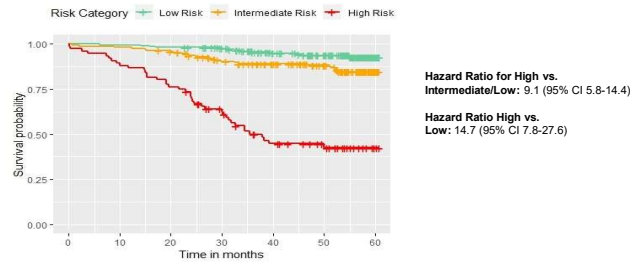
Mount Sinai BioMe Biobank UPenn BIOBANK N=1146

- Data type: EHR data and plasma biomarkers
- ML Algorithm: Random forest model
- Outcome:
 - Primary outcome was composite kidney endpoint at 5 years:
 - eGFR slope decline of $5 \text{ ml min}^{-1} [1.73 \text{ m}]^{-2}$ per year
 - a sustained decline in eGFR of $\geq 40\%$
 - kidney failure defined by sustained eGFR $< 15 \text{ ml min}^{-1} [1.73 \text{ m}]^{-2}$
 - receipt of long-term maintenance dialysis or receipt of a kidney transplant



Chen et al. Diabetologia April 2021

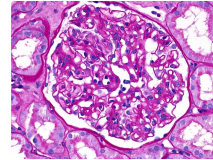
Kaplan-Meier Curves by KidneyIntelX Risk Strata for the Endpoint of Sustained 40% Decline in eGFR or Kidney Failure (Validation n=460)



Chan et al. Diabetologia April 2021

AI in Nephropathology

- Pathology constitutes a cornerstone in the diagnosis and treatment decisions of many kidney diseases.
- It relies on morphology-based histopathological tissue analysis, which remains manual and requires highly trained expert pathologists; which is not always readily available.
- The same is true for nephropathology, a highly specialized area of pathology focusing on the complex diagnostics of kidney diseases.
- Progresses in digitization of pathology enables workflows augmented by advanced image analysis techniques

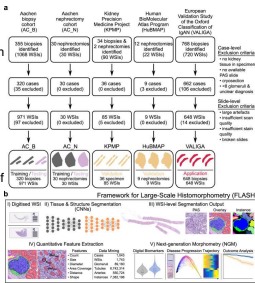


Arkana Labs

18

Automated framework for large scale histomorphometry in nephropathology

- Study Population/Data Types: Using biopsy/nephrectomy data from five different sites
- ML Algorithm: Two CNN were trained to automate segmentation inference: glomeruli, tubules, vessels, and interstitium
- This allowed for large scale comparison of glomerular morphometric features in common native kidney diseases
- Median glomerular tuft area was larger in 20% of lupus nephritis vs. 19% in minimal change, and 41% in membranous compared to normal baseline.
- Morphometric features were associated with progression of IgA nephropathy

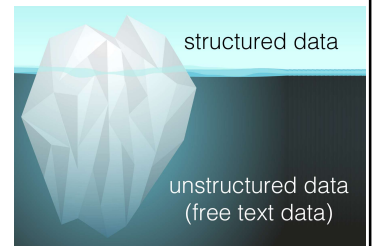


Heller et al. Nat Commun Jan 2023

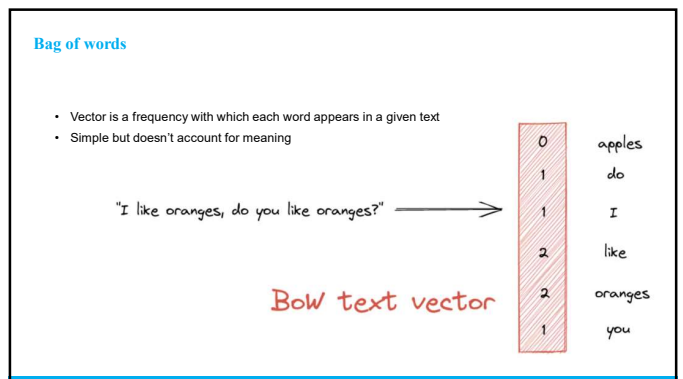
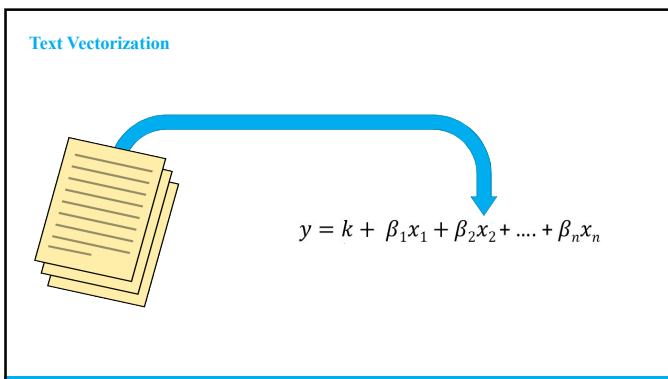
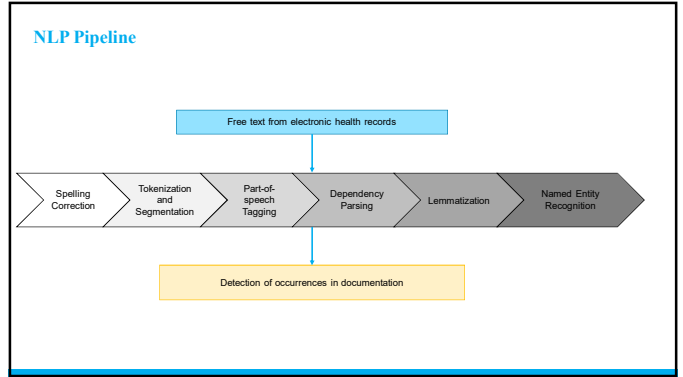
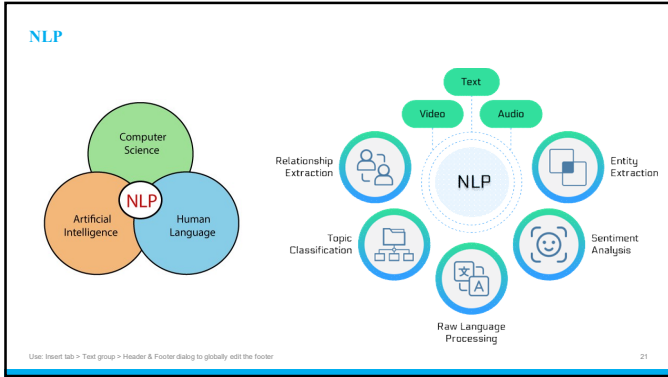
19

Unstructured data > Structure Data

- Lack of meta-information
- Standardization issues
- Data quality and bias
- Infrastructure and human resources
- Lack of suitable analysis tools, methods, and techniques
- Legal and ethical issues

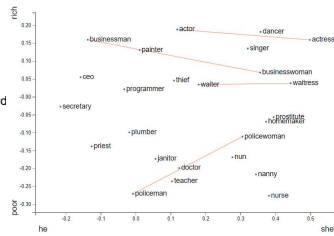


Sedlakova et al. PLOS Digit Health Oct 2023



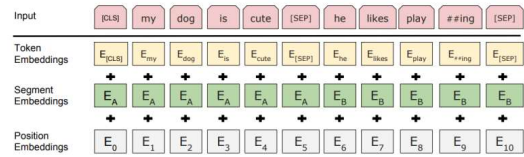
Word2Vec

- Neural net that processes text into vectors
- Model is trained against words that neighbor them in the input corpus
- Similar words are close to each other
- Encodings are rigid: same vector even if a word has different meanings



Bidirectional Encoder Representations from Transformers (BERT)

BERT trained on the entire English-language Wikipedia and the Google Books Corpus, a large collection of unpublished novels.
Leverages transformers to generate word embeddings (word vectors)



Transformers

Attention Is All You Need

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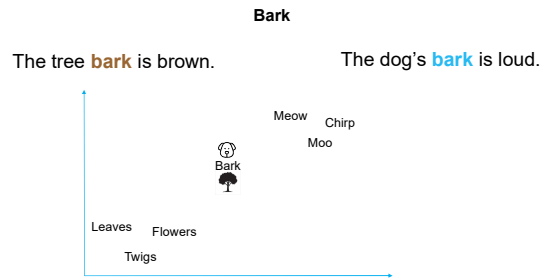
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Why We Need Attention



Self Attention Extracts Relationships Between Words

The tree bark is brown. The dog's bark is loud.

Meow Chirp
Moo

Leaves Flowers
Twigs

Bark

Generative Pre-Trained Transformer (GPT) is a Large Language Model or LLM

Large Language Model (LLM) - Given the statistical distribution of words in the vast public corpus of (English) text, what words are most likely to follow the sequence

- The first person to walk on the moon was...Neil Armstrong

Generate statistically likely sequences of words (tokens).

LLMs do not understand text meaning in a literal sense - just the statistics/mathematical model

Figure 1: The Transformer model architecture.

LLMs to Answer Multiple Choice Questions

- Evaluate the ability of several LLMs to answer multiple choice questions
 - 858 Nephrology Self-Assessment Program (nephSAP) from January 2016 to April 2023

Unstructured Database → Natural Language Tool Kit (NLTK) Preprocessing Steps → Structured JSON File

State-of-the-Art Open-Source LLMs with Claude 2 and GPT-4

Postprocessing Analysis

LLMs: GPT-4, Claude 2, Llama2-70B, Falcon (7B), Stable-Vicuna (13B), Koala (7B), Orca-Mini (1.3B)

LLM Performance

- GPT4 and Claude 2 were far superior to open source LLMs
 - Passing grade for human test takers was 75%
- Majority of open-source LLMs' overall score did not differ from what would be expected if answered at random
- Evaluation of quality of answer explanations:
 - Word error rate (WER, how similar are two texts, lower score better): 0-22%
 - BLEU (quality of generated text compared to ground truth, higher score better): most scoring <0.1
 - Cosine similarity metric (similarity across two texts, higher score better): ~0.3

LLM	Total Qs	N Correct	% Correct	CI
GPT-4	858	629	73.3	70.3–76.3
Claude 2	858	467	54.4	51.1–57.7
Vicuna	858	219	25.5	22.6–28.4
Orca	858	147	17.1	14.6–19.6
Falcon	858	155	18.1	15.5–20.7
Koala	858	204	23.8	21.0–26.6
Llama	858	263	30.6	27.6–33.8

Chatbots for CKD

Kidney Care

This chatbot is designed to provide information and case guidance for patients with Chronic Kidney Disease (CKD) based on the KDIGO 2023 CKD Guidelines.

Instructions:

- The chatbot should provide accurate information aligned with the KDIGO 2023 Guidelines.
- It should maintain patient confidentiality and not store personal health data.
- The chatbot should clarify when the user needs to seek direct medical advice rather than relying solely on information provided through the chat.
- It should avoid providing information outside of its knowledge base and state when it is not able to give a definitive answer.

Knowledge:

repro-ess-oso-ou-ues

Miao et al. *Medicine* Feb 2024

Why
Use medication treatment to help slow progression of CKD to ESKD

Kidney Care
Based on the KDIGO 2023 CKD Guidelines, several medications are recommended to help slow the progression of chronic kidney disease (CKD) to end-stage kidney disease (ESKD). Here are some key recommendations:

- Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i):** These medications are suggested for use in adults and children with CKD but not diabetes. Examples include canagliflozin, dapagliflozin, empagliflozin, and others. They are compared against placebo, usual care, or an active comparator in terms of their effects on the progression of CKD, complications of CKD, and adverse events.
- Nonsteroidal Mineralocorticoid Receptor Antagonists (MRA):** These are recommended for adults with Type 2 Diabetes (T2D), an eGFR ≥ 25 mL/min per 1.73 m², normal serum potassium concentration, and albuminuria despite the maximum tolerated dose of RAS inhibitor (RAI). They can be added to a RAI and an SGLT2i for the treatment of T2D and CKD in adults.
- Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RA):** For adults and children with CKD and T2D, GLP-1 RA like abiraterole, dulaglutide, and tirzepatide may be used. These are compared against other glucose-lowering agents, placebo, or usual care, specifically looking at their impact on kidney failure, all-cause hospitalizations, and other critical outcomes.
- Lipid Management:** In adults aged ≥ 20 years with an eGFR ≥ 30 mL/min per 1.73 m² but not treated with chronic dialysis or kidney transplantation, treatment with a statin or statin/ezetimibe combination is recommended.

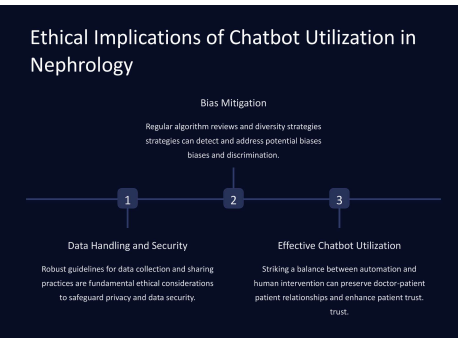
These recommendations are aimed at managing the progression of CKD and its complications, and the choice of specific medication should be made based on individual patient factors and in consultation with a healthcare provider. It's also important to note that these medications are part of a broader management strategy that includes lifestyle changes and management of other health conditions.

If you have CKD or are at risk, it's essential to consult with a healthcare professional for personalized advice and treatment.

Considerations for Implementation



Ethical Implications of Chatbot Utilization in Nephrology



1. Bias Mitigation
Regular algorithm reviews and diversity strategies can detect and address potential biases and discrimination.

2. Data Handling and Security
Robust guidelines for data collection and sharing practices are fundamental ethical considerations to safeguard privacy and data security.

3. Effective Chatbot Utilization
Striking a balance between automation and human intervention can preserve doctor-patient relationships and enhance patient trust.

Valencia et al. *J. Pers. Med* Sept 2023

Additional concerns with AI implementation

- Transparency and Explainability:**
 - Many AI models are "black boxes", making it difficult how they arrived at their decisions.
 - May lead to lack of trust in AI systems
 - Methods to interpret and explain AI driven recommendations are needed
- Informed consent and autonomy:**
 - Patients should have the right to understand and consent to use of AI technology
 - However, AI system complexity may make it difficult for people to fully comprehend the implications of AI-driven interventions.
- Equitable access and resource allocation:**
 - High costs, technological barriers, and unequal distribution of resources could widen the gap between those who can benefit from AI-enabled care and those who cannot.
 - Efforts are needed to ensure that AI technologies are accessible to all populations, regardless of socioeconomic status or geographic location.

