Artificial Intelligence in Paediatric Urology: A Brave New World?

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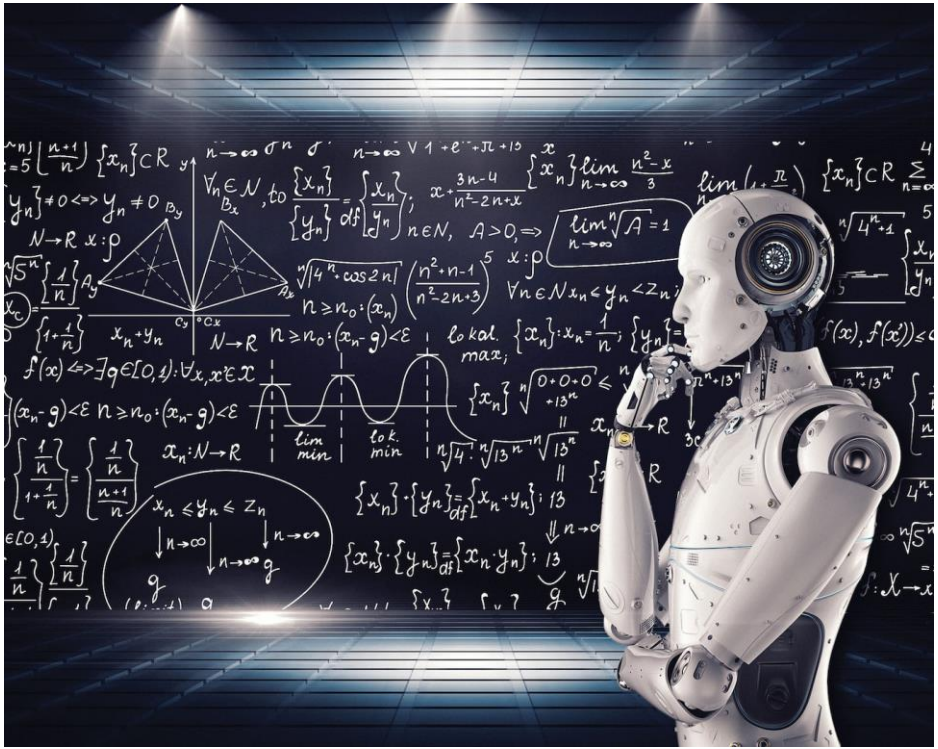
ESPU-RESEARCH COMMITTEE SESSION
18 APRIL 2024

Artificial Intelligence (AI) is transforming medicine and research

What is AI's current and future role in paediatric urology?



Framework of today's discussion

1) Definitions/terminology
2) AI in clinical medicine
3) AI as a research tool
4) AI in education/workforce issues
5) Pitfalls of AI

Definitions and terminology

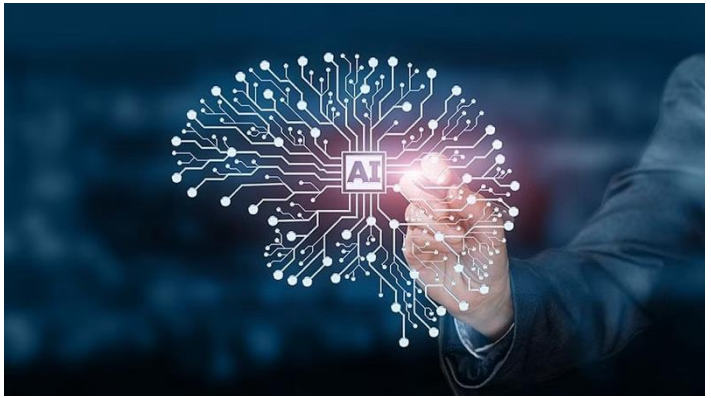
Artificial intelligence

=computer systems performing tasks that typically would require human intelligence

=applications of algorithms and models that

- learn from large data sets
- adapt to new information
- take decisions and make predictions
- generate new, transformed information

=huge variety of applications and ideas



Something „new“? … a short historical perspective

1956: John McCarthy, Dartmouth Conference

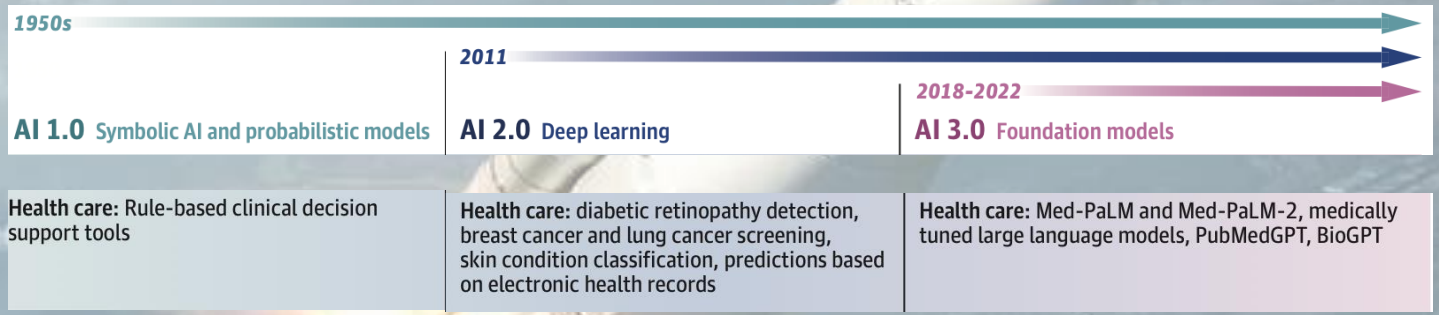
40ies-50ies: early concepts – electronic computers

50ies – 80ies: Symbolic AI – simple algorithms, e.g. „Logic Theorist“

90ies-2000s: Machine Learning resurgence: neuronal networks, Bayesian networks

10s: big data / deep learning, convolutional and recurrent neuronal networks

History of AI in healthcare – 3 Epochs



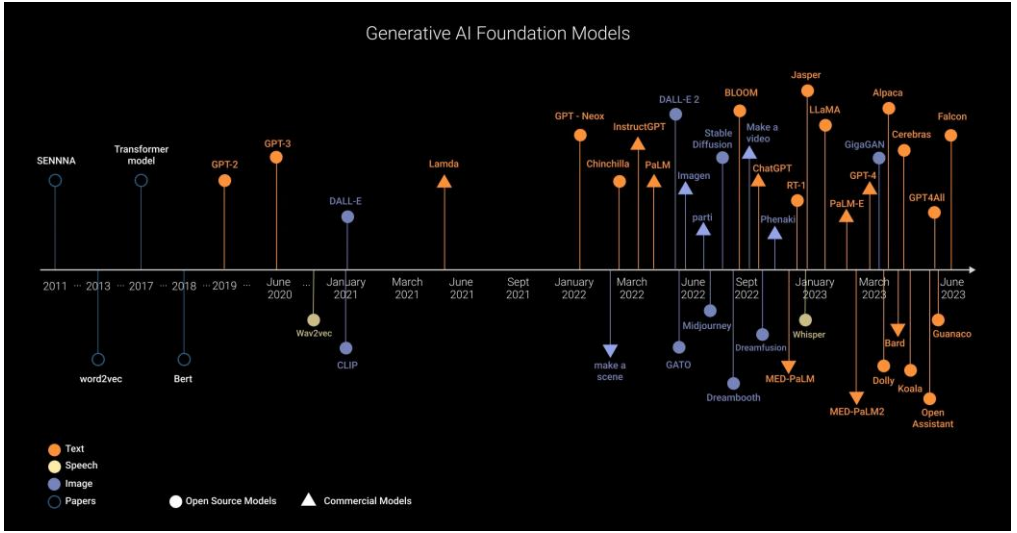
Howell, M. D., Corrado, G. S., & DeSalvo, K. B. (2024). Three Epochs of Artificial Intelligence in Health Care. *JAMA*, *331*(3), 242-244.

Main types of AI

- **machine learning**
  - = learning from experience without being explicitely programmed
  - = an email spam filter learning to identify new spam emails based on previous patterns learned
- **natural language processing / large language models**
  - = understand, interpret and generate human like text (and imagages)
  - = chatbots like ChatGPT **G**enerative **P**retrained **T**ransformer
- **computer vision**
  - = image recongnition, object detection and scene understanding
  - = facial recognition used in security systems
- **robotics**
  - = autonomous mobile and learning devices
  - = Roomba – the autonomous vacuum cleaner

Terms and tools in AI

- **Algorithm**
- **Neural network**: interconnected nodes- inspired by the human brain
- **Deep learning**: use of typically multilayered neuronal
- **Foundation models**: up to trillions of parameters used



AI in clinical medicine

AI in clinical medicine

- Prediction models
  - Algorithms that use clinical or research data to predict patient outcomes in future or concurrent test datasets
- Computer vision
- Signal Analysis
- Prescription models

Prediction models in paediatric urology

- UTI and VUR
  - UTI diagnosis
  - UTI recurrence/VUR incidence after UTI
  - VUR resolution
  - Reflux surgery results
- Renal outcomes in PUV
- Hydronephrosis outcomes
- Hypospadias genotype
- Enuresis incidence
- Rhabdomyosarcoma survival
- Clinic flow and timing

What if we could predict those patients with first febrile UTI who are most at risk of both recurrent UTI and VUR?

- Joint collaboration of BCH and MIT…….  Scott Wang MD
- Use machine learning algorithms to develop prediction models using RIVUR/CUTIE data
- Sort patients into “high-risk” and “low-risk” groups
- Used “optimal classification tree” procedure
- Low-risk of rUTI and VUR: defer VCUG after first febrile UTI
- High-risk of rUTI and VUR: do VCUG after first febrile UTI

NIDDK

THE RIVUR STUDY

Randomized Intervention for children with
Vesico-Ureteral Reflux
(RIVUR)

Multicenter RCT (TMP-SMX vs. placebo) in children at 2-60 months with febrile UTI and VUR

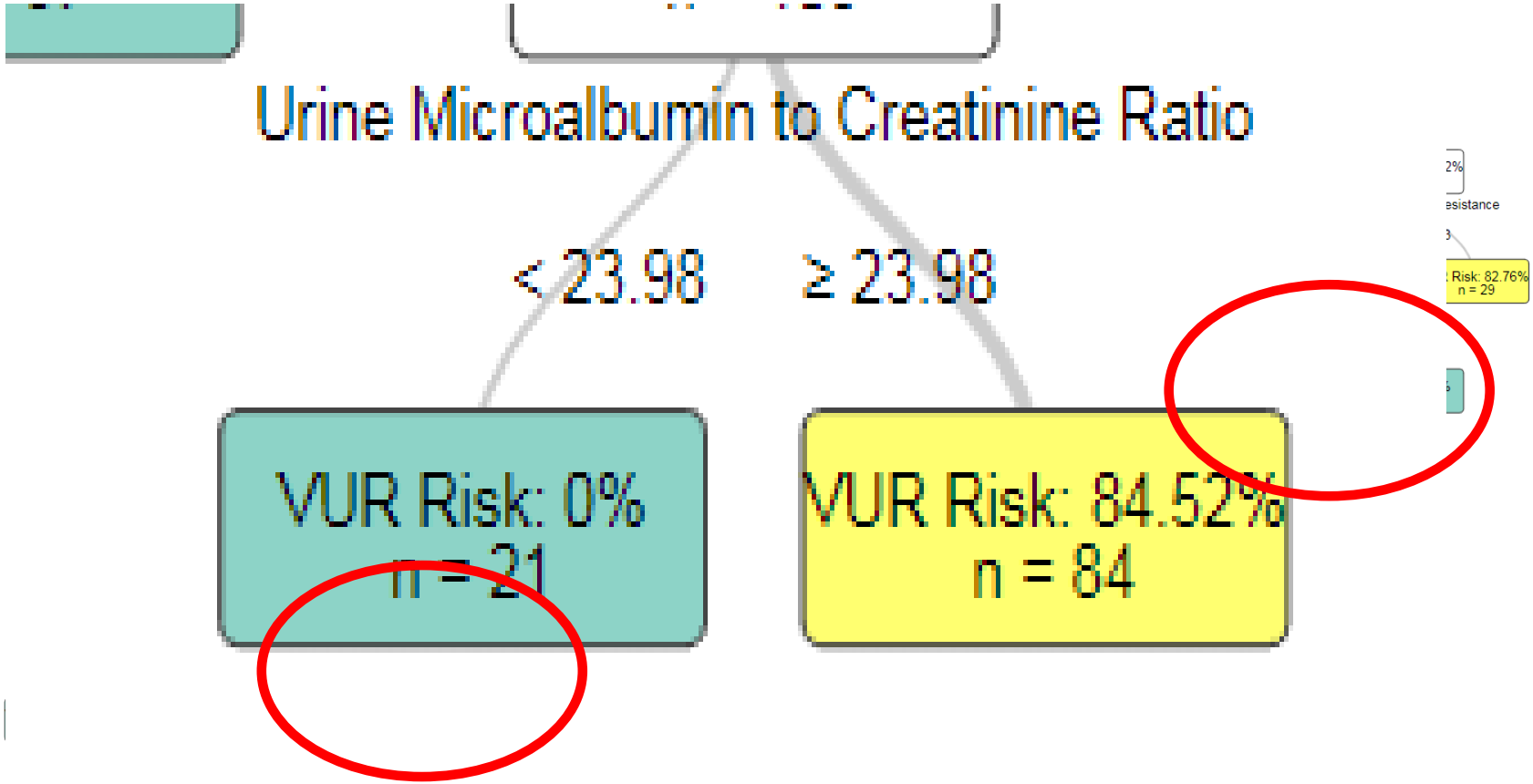
NIDDK

THE CUTIE STUDY

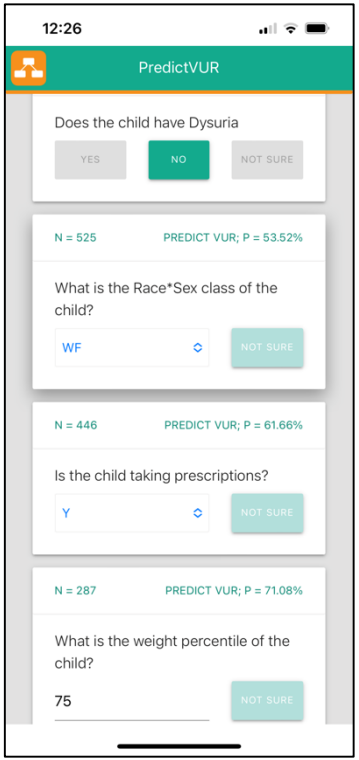
Careful Urinary Tract Infection Evaluation

Observational cohort study of 195 children without VUR but otherwise eligible for RIVUR

Provides a non-VUR “control” group for RIVUR subjects


Urine Microalbumin to Creatinine Ratio
< 23.98
≥ 23.98
VUR Risk: 0%
n = 21
VUR Risk: 84.52%
n = 84

This algorithm available using an App



"PredictVUR" in the App store

This effort illustrates the challenges and promise of AI in clinical medicine

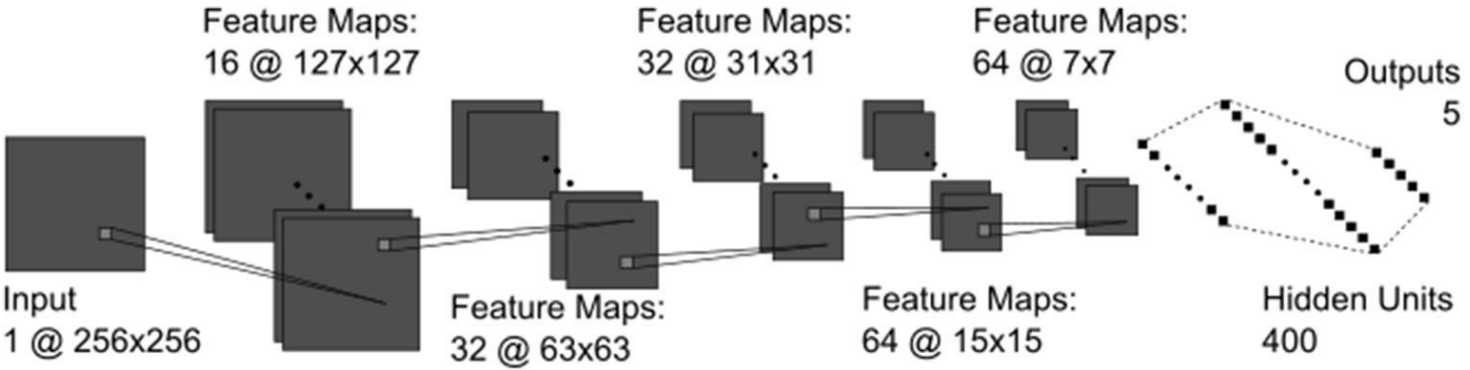
- Low availability of granular, high-quality data on large number of patients
- RIVUR/CUTIE studies: complex expensive studies costing 10’s of millions $
- Still - only provide data on a few hundred patients
- Unbiased data on control/natural history cohorts are extremely hard to obtain

AI in clinical medicine

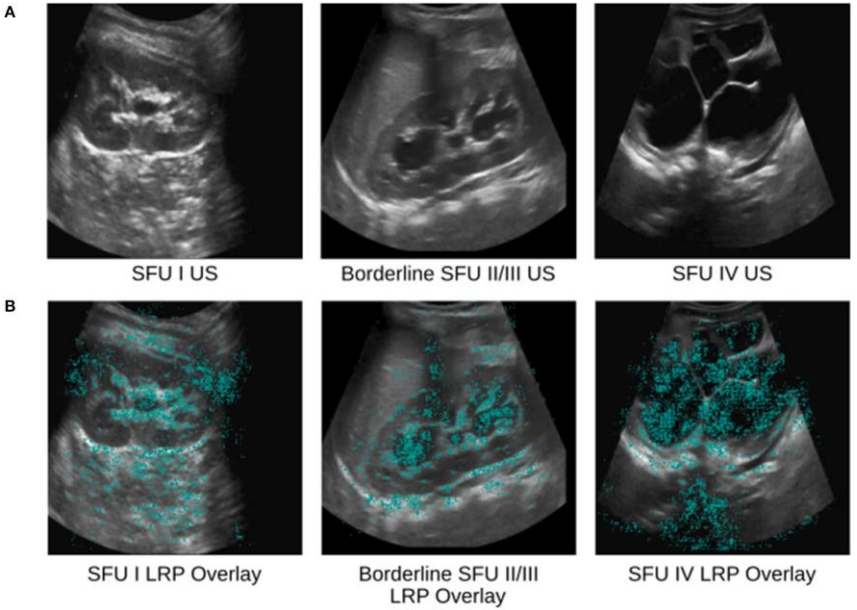
- Prediction models
- Computer vision
  - Use of software algorithms to interpret clinical images (x-rays, ultrasounds, cross-sectional imaging)
- Signal Analysis
- Prescription models

Computer vision in paediatric urology

- Grading of hydronephrosis
  - Segmenting renal parenchyma
  - Ratio of parenchyma to collecting system
  - Classifying SFU score
  - Evaluate need for MAG3
- VUR grade
- Urethral stricture
- Wilms' tumor
- Hypospadias phenotype



Deep learning model
(deep convolutional neural Networks) to assign SFU grades to ultrasound images
[LC Smail 2020]

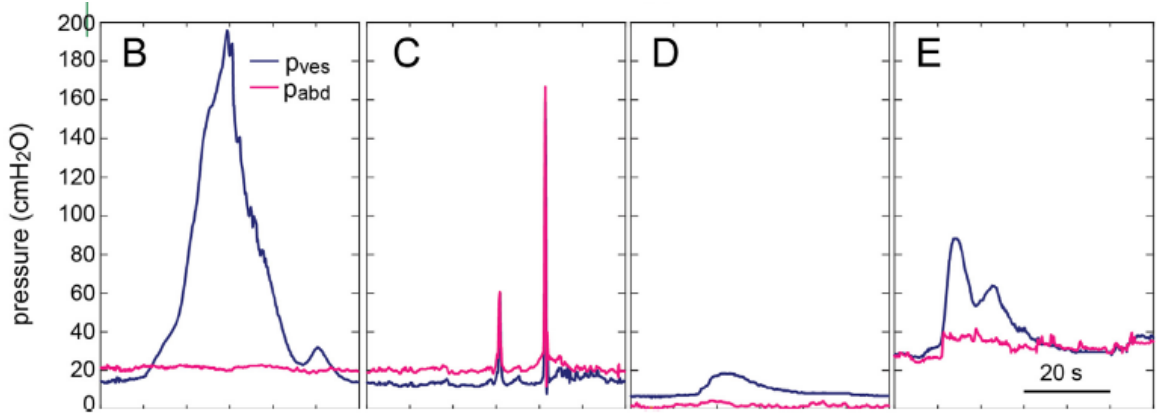


AI in clinical medicine

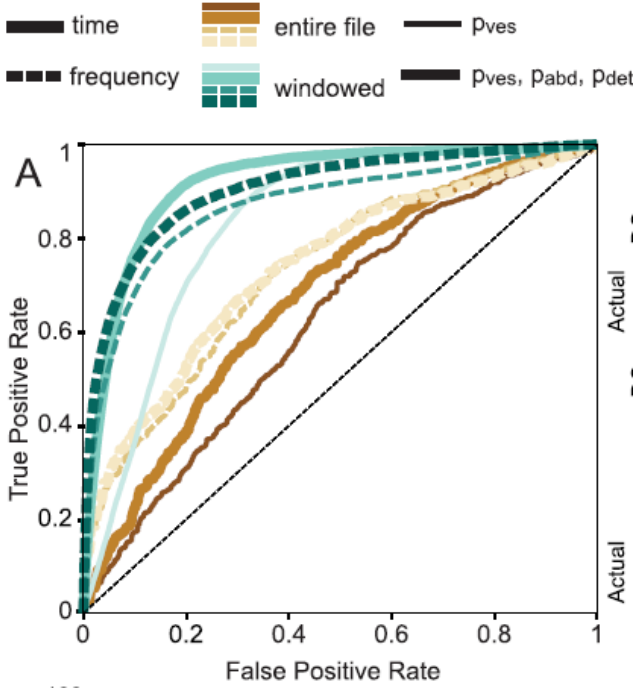
- Prediction models
- Computer vision
- Signal Analysis
  - Field of electrical engineering looking at time series data forms such as music, nerve conduction patterns, or seismic activity
- Prescription models

Signal analysis in paediatric urology

- Urodynamic studies
  - Identification of detrusor overactivity
  - Classification and severity of lower urinary tract dysfunction
  - Measuring bladder compliance
- Drainage curves of diuretic renal scans



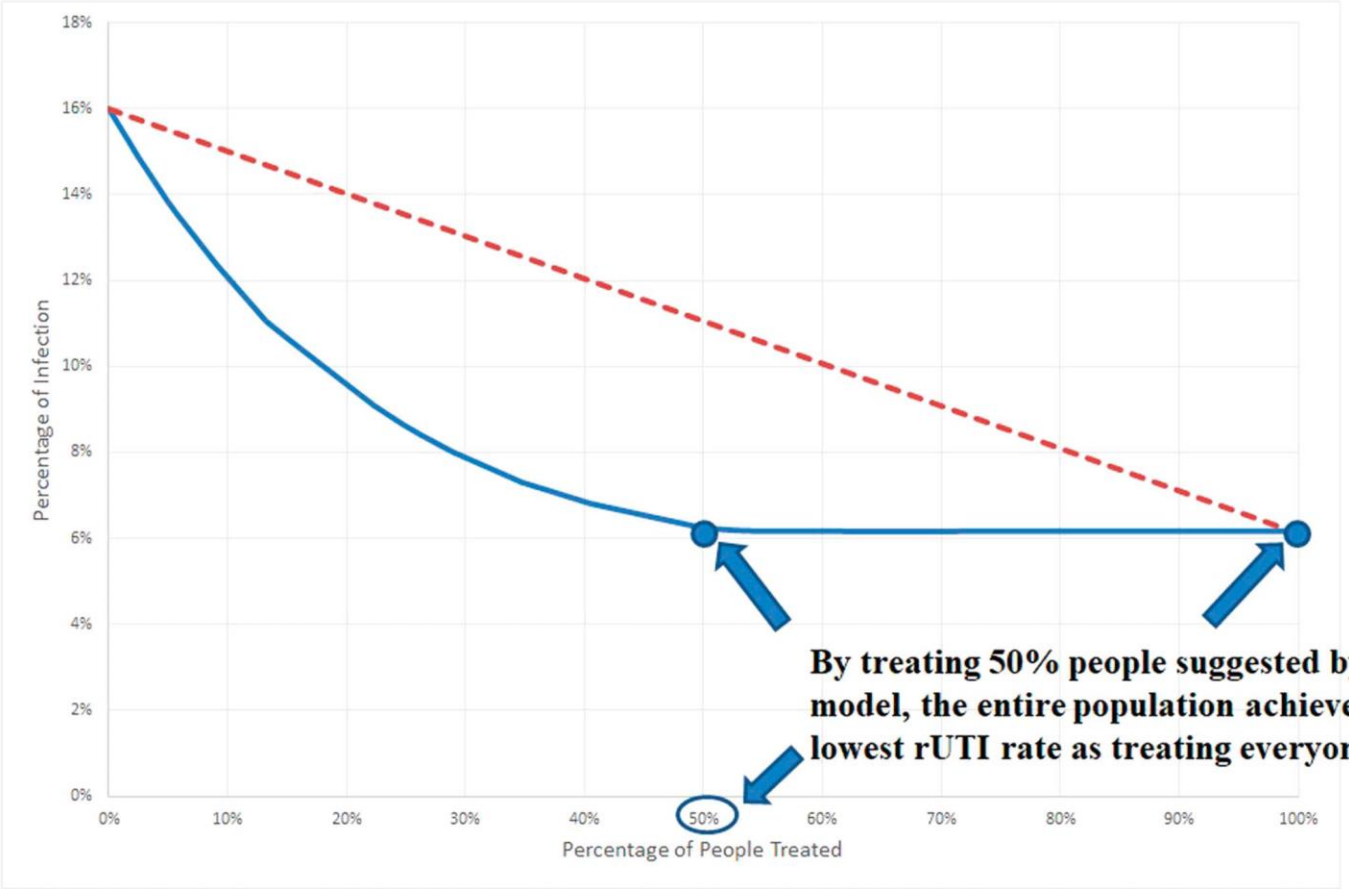
Machine learning pipeline to identify detrusor overactivity during urodynamic studies [KT Hobbs 2021]



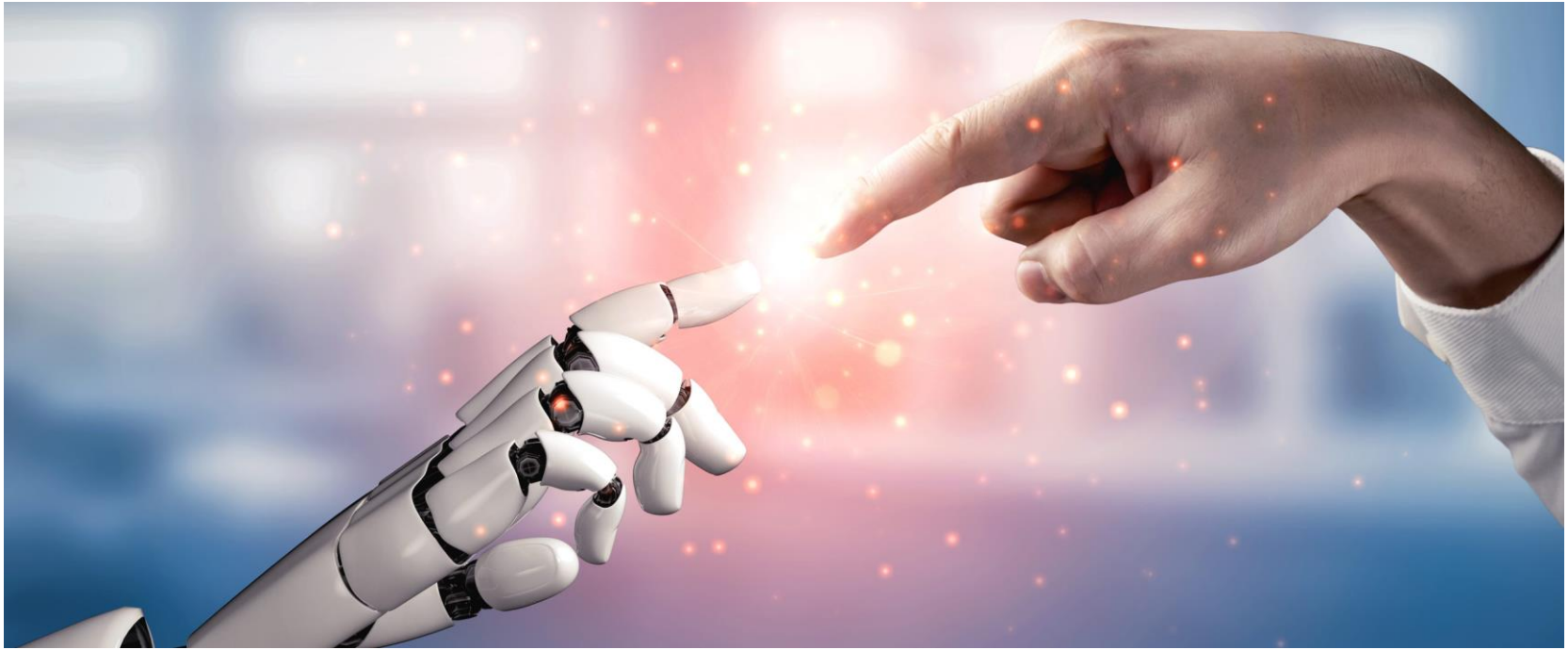
AI in clinical medicine

- Prediction models
- Computer vision
- Signal Analysis
- Prescription models
  - Algorithms that provide treatment recommendations (“prescriptions”) based on patient’s predicted outcome with or without treatment

Machine learning model to identify those most likely to benefit from CAP [D Bertsimas et al. 2021]



AI in Research and Education



AI as a tool for medical research

Study design

Medical writing

Reviewing

Study design

- Optimize the design and execution of clinical trials:
  - Patient Recruitment:
    - Analyze electronic health records to predict potential candidates for clinical trials
    - Natural Language Processing can analyze unstructured medical data
  - Trial Design:
    - Optimizing Protocols using historical data and identifying potential barriers to recruitment
    - Simulate different trial scenarios
  - Site Selection Optimization using historical data

Data retrieval

- Automated Data Extraction
- Predictive Analytics: AI can predict patient responses to treatments
- Real-time data analysis:
  - Facilitate remote patient monitoring through wearable devices and sensors
  - Reduces need for frequent clinic visits and enhances overall trial efficiency
  - Early Detection of Adverse Events: improved participant safety
  - Identifying discrepancies in real-time
  - Adaptive trial designs
- Monitoring of participant behavior and protocol adherence

AI as a tool for qualitative research

- AI has potential for qualitative and Mixed Method research
- Very important in nursing research
- Enhance data collection, analysis, and interpretation
  - *Nashwan AJ, Abukhadijah H. Harnessing Artificial Intelligence for Qualitative and Mixed Methods in Nursing Research. Cureus. 2023 Nov 9;15(11):e48570.*
- Not a statistics tool but can suggest methods

AI for clinical trials

Enhance the efficiency, accuracy, and overall success of clinical trials

Cost savings and a more patient-centric approach

Using Chatgpt to define a research question

What are the knowledge gaps concerning PUV?

- **Etiology and Pathogenesis**: The exact cause of PUV remains unclear.
- **Risk Factors**: Although PUV is considered a sporadic anomaly, there may be certain genetic and environmental factors that contribute to its development.
- **Natural History and Long-Term Outcomes**: While PUV can lead to significant urinary tract issues in infancy and childhood, there's still a need for more comprehensive studies on the long-term outcomes of individuals with PUV. This includes their renal function, risk of urinary tract infections, and potential complications later in life.
- **Optimal Treatment Strategies**: While the primary treatment for PUV is surgical intervention to relieve urinary obstruction, there are ongoing debates about the timing, type, and long-term implications of these procedures.
- **Fetal Intervention**: In cases where PUV is detected prenatally, there's growing interest in fetal intervention to alleviate urinary obstruction and prevent renal damage before birth. However, the efficacy and safety of such interventions are still being investigated,
- **Psychosocial Impact:** Living with a chronic medical condition like PUV can have significant psychosocial implications for affected individuals and their families. Understanding the psychosocial impact of PUV and developing appropriate support systems are essential aspects of holistic care that warrant further exploration.

How do we investigate risk factors?

Genetic Studies: Conduct Genome-Wide Association Studies (GWAS) to identify genetic variations or mutations associated with PUV.

Examine familial clustering of PUV to determine if there's a hereditary component to the condition. Studying families with multiple affected individuals can help identify candidate genes or genetic pathways involved in PUV development.

Epidemiological Studies: Conduct population-based studies to assess the prevalence of PUV in different geographic regions and demographic groups. Investigate potential associations between maternal factors (e.g., age, parity, maternal health conditions) and the risk of PUV development in offspring.

Environmental Studies: Explore potential environmental exposures during pregnancy or early childhood that may increase the risk of PUV. This could include exposure to certain medications, toxins, pollutants, or maternal lifestyle factors (e.g., smoking, diet). Utilize animal models to investigate the effects of specific environmental exposures on the development of PUV.

Multifactorial Analyses: Integrate genetic, epidemiological, and environmental data through multifactorial analyses to identify potential gene-environment interactions or synergistic effects contributing to PUV risk.

Consider the role of epigenetic modifications (e.g., DNA methylation, histone modifications) in regulating gene expression patterns associated with PUV development. Epigenetic studies can provide insights into how environmental factors may influence gene expression and phenotype.

What would the inclusion criteria be?

Confirmed Diagnosis of PUV: Participants should have a confirmed diagnosis of PUV based on clinical evaluation, imaging studies (e.g., ultrasound, voiding cystourethrogram), and/or surgical findings.

Age Range: Depending on the study objectives, the age range of participants may vary. For studies focusing on prenatal risk factors, participants may include pregnant women with a prenatal diagnosis of PUV.

Consent and/or Assent: Participants (or their legal guardians) should provide informed consent (or assent for minors) to participate in the study.

Demographic Characteristics: Inclusion criteria may specify certain demographic characteristics such as ***gender,*** ethnicity, socioeconomic status, or geographic location **to ensure diversity and representativeness** of the study population.

Availability of Clinical Data: Participants should have relevant clinical data available for analysis, including medical records, imaging studies, laboratory test results, and maternal/fetal/neonatal history if applicable.

Willingness to Participate in Follow-Up: For longitudinal studies or studies requiring follow-up assessments, participants should be willing and able to comply with study procedures and follow-up visits.

No Known Major Comorbidities:

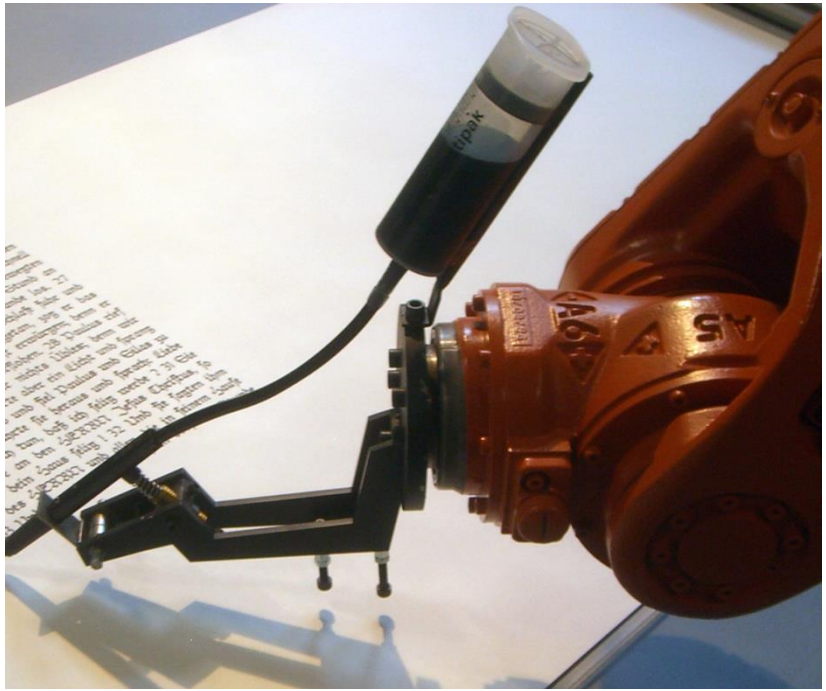
Ability to Communicate and Understand Study Requirements

AI in medical writing

- Can write a paper but there is a risk of hallucinations
  - « seemingly realistic sensory experiences that do not correspond to any real-world input”
  - *Alkaissi H, McFarlane SI. Artificial Hallucinations in ChatGPT: Implications in Scientific Writing. Cureus. 2023 Feb 19;15(2):e35179*
- Useful for translating non-English medical literature
- Useful as an aid for non-English-speaking scientists writing in english
  - *ChatGPT and other artificial intelligence applications speed up scientific writing. Chen TJ. J Chin Med Assoc. 2023;86:351–353.*

Authorship?

- Should Chatgpt be credited as an author?
- Nature editorial published in 2023
- *No LLM tool will be accepted as a credited author on a research paper(…) because any attribution of authorship carries with it accountability for the work, and AI tools cannot take such responsibility.*
- *Researchers using LLM tools should document this use in the methods or acknowledgements sections.*
    - *Tools such as ChatGPT threaten transparent science; here are our ground rules for their use. Editorial Editorial. Nature. 2023;613:612*



AI as a tool for reviewing

- Neural network model trained on a dataset of 3300 reviews
- Capable of predicting future review process results
  - *AI-assisted peer review. Checco A, Bracciale L, Loreti P, et al. Humanit Soc Sci Commun. 2021;8:1–11.*
- *Applicable to research grant applications?*

AI for guidelines?

- Current study by Lisette ‘t Hoen, Allon Van Uitert, Christian Radmayr *from EAU guidelines panel*

- Structured guidelines updates:
  - Methodology given by the Guidelines Office Methods Committee vs ChatGPT

- Interesting results soon to be presented…

AI as a tool for medical education

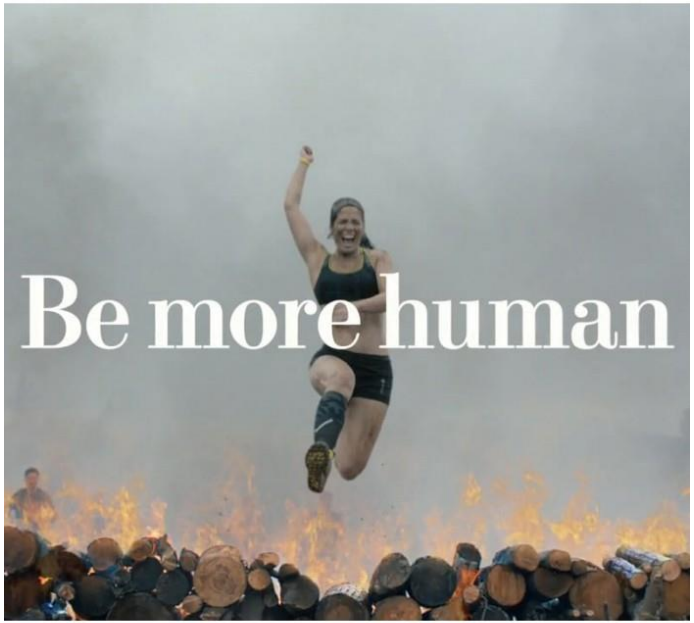
- 30% of college students use ChatGPT for their written homework
  - *Nearly 1 in 3 College Students Have Used ChatGPT on Written Assignments - Intelligent. [Mar; 2023].*
- But does ChatGPT possess the ability to teach medicine?

Can Chatgpt teach medicine?

- Performance of ChatGPT on the United States Medical Licensing Exam
- At or near the passing threshold for all 3 exams !
- Equivalent of a passing score for a third-year medical student
- Showed high internal concordance, low self-contradiction and sound clinical reasoning
  - *Performance of ChatGPT on USMLE: potential for AI-assisted medical education using large language models. Kung TH, Cheatham M, Medenilla A, et al. PLOS Digit Health. 2023;2:0.*
- *If it can think like a student…*

- Interestingly, ChatGPT outperformed PubMedGPT
- Domain-specific training creates ambivalence
- Real-world text that are:
  - inconclusive, contradictory, highly conservative or noncommittal
- ChatGPT, may therefore have an advantage because it is also exposed to broader clinical content that are more definitive and congruent

- Can provide novel and nonobvious concepts



- Can allow students to learn to integrate/use data instead of remembering it
- Can lead to higher level of understanding individual patients
  - Compassionate culturally competent communication
  - Physical exam
- **To be even more human**
  - *Hswen Y, Abbasi J. AI Will—and Should—Change Medical School, Says Harvard's Dean for Medical Education. JAMA. 2023;330(19):1820–1823.*

"A Leap Forward: Harnessing Artificial Intelligence in Medical Research“ title suggested by Chatgpt

Introduction suggested by Chatgpt:

- *"Picture a scenario where a team of researchers is faced with an overwhelming amount of medical data—millions of patient records, countless scientific articles, and complex genomic sequences. It's a daunting task to sift through this vast sea of information, searching for patterns, insights, and breakthroughs. Yet, in this age of artificial intelligence, what once seemed insurmountable is now within reach. Today, I stand before you to unveil the remarkable journey of AI in medical research—a journey marked by innovation, discovery, and the promise of transforming the landscape of healthcare as we know it.“*

Ending phrase:

- *"As we harness the power of artificial intelligence to unlock the mysteries of disease, let us embrace this journey with unwavering curiosity, determination, and compassion, for in our pursuit of knowledge lies the promise of a healthier, more equitable future for all."*

Pitfalls of AI

Data collection

Algorithm development

Accountability and safety

Ethical and social considerations

Data collection

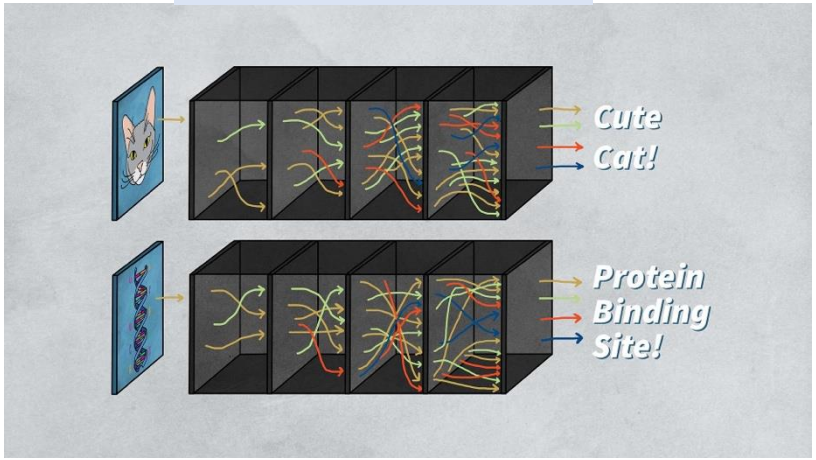
- **Availability** of **large, relevant patient data** is the cornerstone of efficient machine learning and subsequent reliable results
  - data protection / **confidentiality**
  - data **storage and transfer**
- Nonexistent **legislation** on how to obtain and process health data
- No possibility to check the input data for **errors**, which are common in health-care data
- **Short T1/2** of health / biological systems related data

Khan, B., Fatima, H., Qureshi, A., Kumar, S., Hanan, A., Hussain, J., & Abdullah, S. (2023). Drawbacks of Artificial Intelligence and Their Potential Solutions in the Healthcare Sector. *Biomed Mater Devices*, 1-8.

Algorithm / Application development

- **Black-Box**: no explanation for outcomes
- **Systematic errors / biases** if erroneous data informs model creation
- **Balanced input data**: no detection of under-representation of e.g. ethical groups

But why and how? Is this reversible or explainable?



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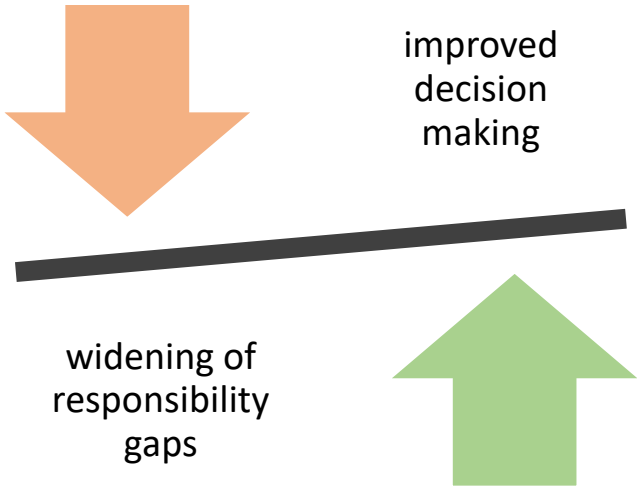
Accountability and Safety

- Any AI tool or its developer is only accountable on the basis of the data included: **„algor-ethics“**
- Data triangulation can re-identify up to 99% even in heavily sampled and incomplete data
- Cybersecurity threat: **us$6trillion**

➢Safety considerations should be seen as a dynamic process to be followed after deployment of any tool as they will not be fully resolvable during development



Habli, I., Lawton, T., & Porter, Z. (2020). Artificial intelligence in health care: accountability and safety. *Bull World Health Organ*, *98*(4), 251-256. Cacciamani, G. E., Chen, A., Gill, I. S., & Hung, A. J. (2024). Artificial intelligence and urology: ethical considerations for urologists and patients. *Nat Rev Urol*, *21*(1), 50-59.

Ethical and social considerations

- 4 **Pillars**
  - Autonomy
  - Beneficience
  - Non-maleficience
  - Justice
- Examples
  - Choosing the right tools – standardized reporting
  - Preserving the autonomy of the urologist taking the decision
  - Ensuring inclusiveness and equity

Cacciamani, G. E., Chen, A., Gill, I. S., & Hung, A. J. (2024). Artificial intelligence and urology: ethical considerations for urologists and patients. *Nat Rev Urol*, *21*(1), 50-59.

Take Home Messages

- AI is much more varied than you might have thought – and much older
- It will shape clinical medicine with prediction models, computer vision, signal analysis and prescription models
- In science, its use in writing has to be scrutinized – it will be useful in data collection, guideline design and reviewing
- Can AI make us „more human“ in teaching and practicing clinical medicine?
- Use it wisely: Know the pitfalls and dangers

Thank You!

The ESPU Research Committee

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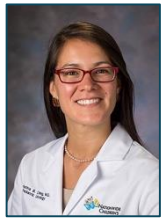

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Get involved in the CyPhy trial!