Survey of Artificial Intelligence (AI) in Medicine

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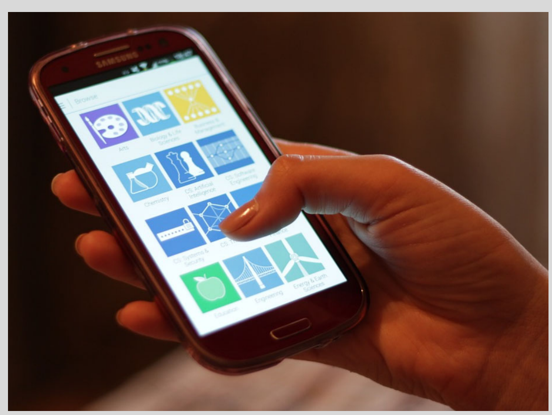
Thought Experiment – Everyday Life

- Unlock mobile device with facial recognition
- Ask smart home device about commute/weather with chatbots
- Autonomous-driving cars using real-time object detection



How is AI already here in our day-to-day lives?

Océanos y dados, CC0, via Wikimedia Commons

Thought Experiment 2 – Medical Clinic

- Patient Encounters
  - Unclear diagnosis
  - Expensive testing
- Clinical trial identification
- Time-consuming documentation
- High volume of patient queries

How can AI improve clinical care in the future?

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Objectives

- Brief Overview of AI Concepts
- Examples AI in Medicine
- AI for Drug Development
- Generative AI
- Pitfalls and Explainability

Alenoach, Public domain, via Wikimedia Commons

Brief Overview of AI Concepts

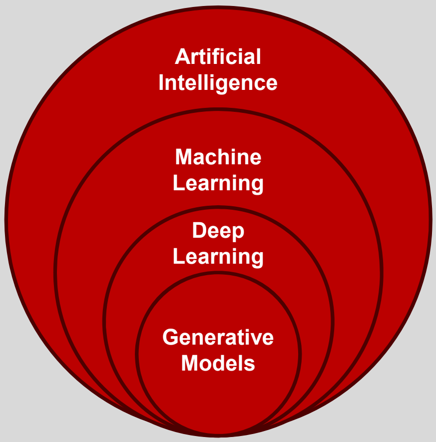
Definitions, Frameworks, and Timeline of AI in Medicine

Informal Definitions

- **Artificial Intelligence (AI):** "Science and engineering of making intelligent machines"
  - Coined in 1955
- **Machine Learning (ML):** Study of how computer agents can improve perception, knowledge, or actions based on experience or data
- **Deep Learning (DL):** The use of large multi-layer neural networks

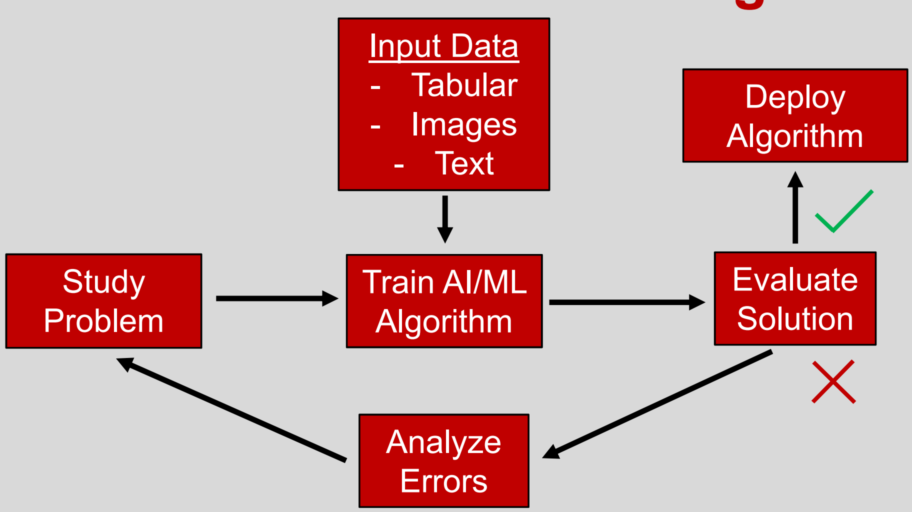
Adapted from Christopher Manning, Stanford University's Human-Centered Artificial Intelligence Department, September 2020.

Framework for Terminology



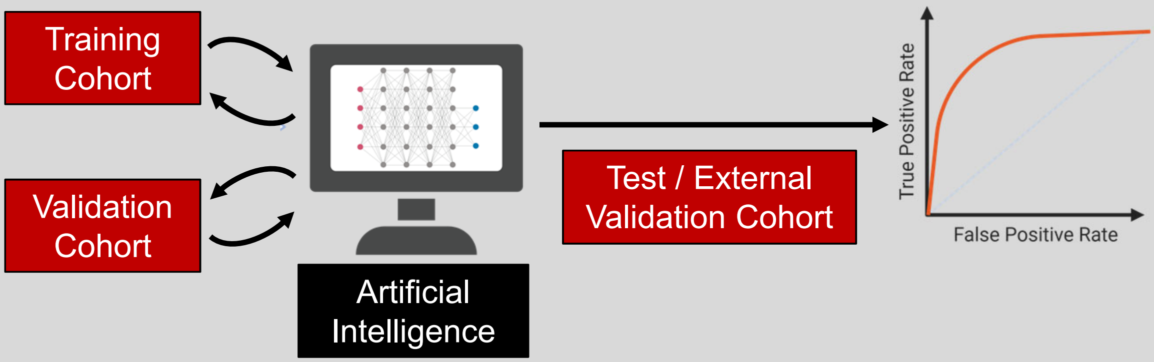
- Subsets of one another
- Syntax is imperfect:
  - Deep Learning often involves neural networks
  - Not every model in the Deep Learning era is a “neural network”
- Framework is rapidly changing

Framework for Machine learning



Géron. Hands-on machine learning with Scikit-Learn and TensorFlow, 2017.

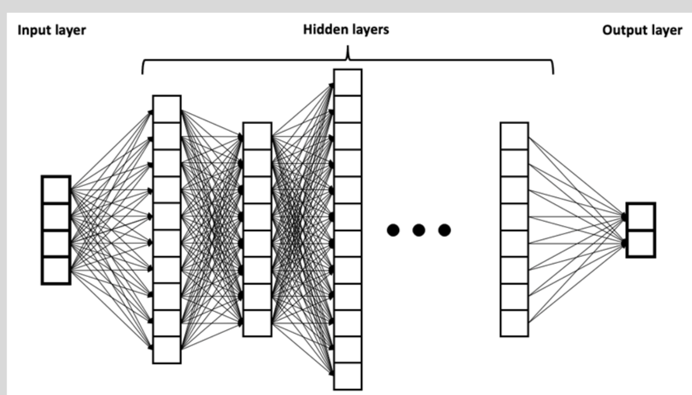
Dataset Subgroups for AI Development



Created in BioRender. Srisuwananukorn, A. (2024)

Basics of a Neural Network

- Loosely modeled after neural connections of human brain
- Data are encoded as numbers
- Efficient algorithms to change internal algorithms for optimal outcome prediction



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Distinct Eras of AI

- AI 1.0: Symbolic AI
- AI 2.0: Deep Learning
- AI 3.0: Foundation Models

Howell MD, et al. Three Epochs of Artificial Intelligence in Health Care. JAMA, 2024.

Distinct Eras of AI

1 **Symbolic AI**
- Follows direct rules
- Based on expert knowledge hard-encoded in programming

2 **Deep Learning**
- Predicts/classifies information
- Learns patterns from ground-truth examples

3 **Foundation Models**
- Generates new content (text, sound, images)
- Self-supervised learning from large datasets

Howell MD, et al. Three Epochs of Artificial Intelligence in Health Care. JAMA, 2024.

AI Models in Medicine

Examples of Research-only and FDA-approved
AI Algorithms in Clinical Medicine

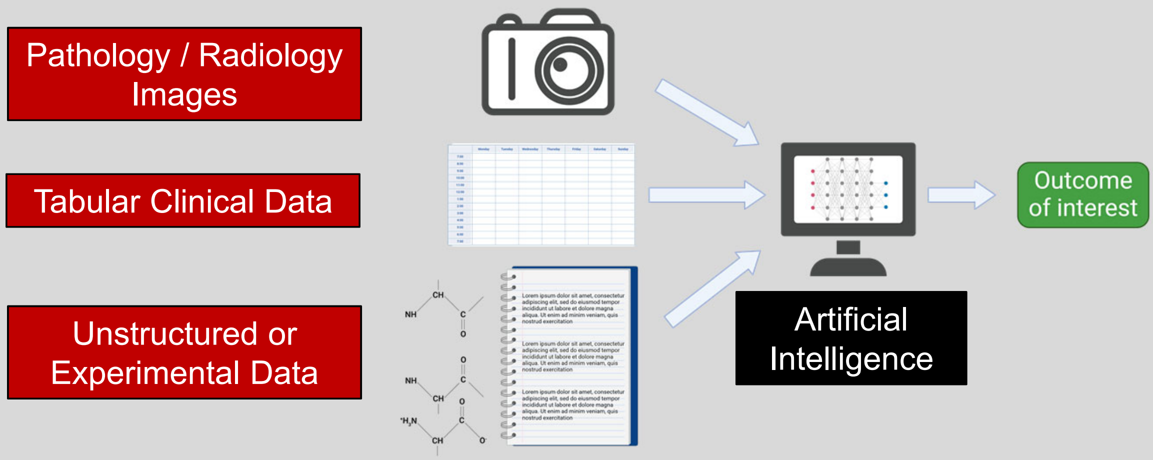
Clinical Dilemmas Addressed with AI

Operational / Automation

Diagnostic

Predictive

Modalities of Data in Clinical AI Models



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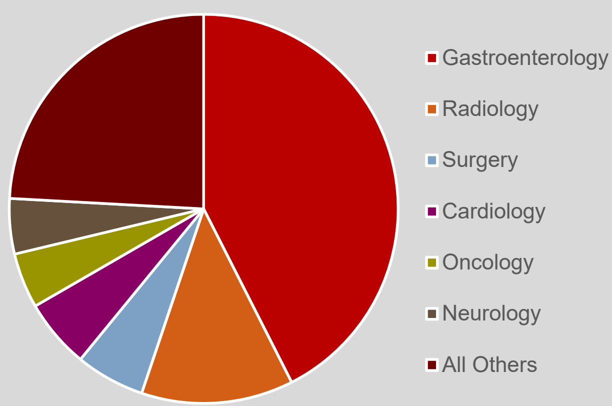
Domains in Medicine Utilizing AI

- Review of 86 AI-related Randomized Controlled Clinical Trials (RCTs)
  - Geography:
    - 31% in USA
      30% in China
  - Domain:
    - 43% Gastroenterology
    - 13% Radiology
    - 6% each Surgery or Cardiology



Han, et al. Randomised controlled trials evaluating artificial intelligence in clinical practice: a scoping review. The Lancet Digital Health, 2024.

FDA-Approved AI/ML Devices

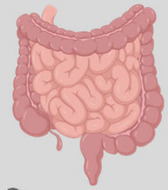
- U.S. Food and Drug Administration (FDA) continues to publish a database of all AI/ML-enabled medical devices
- As of **September 2024**, FDA has approved **over 900 AL/ML-enabled devices**
- At least 285 devices prior to December 2021 have been approved due to being “substantially equivalent” to formerly cleared devices

Muehlematter, et al. FDA-cleared artificial intelligence and machine learning-based medical devices and their 510(k) predicate networks. The Lancet Digital Health, 2023.

Example Implementations of AI in Medicine in Advanced Development

- **Gastroenterology**
- **Dermatology**
- **Radiology**
- **Pathology**

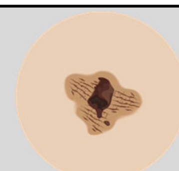
Example: Gastroenterology



- AI-aided colonoscopy has been explored to increase adenoma detection rate
- In a systematic review of 33 RCTs undergoing AI-aided colonoscopy
  - 50.5 - 52.5% decrease in polyp / adenoma missed detection rate
  - 23.8 – 24.2% increase in polyp / adenoma detection rate
- AI **significantly enhanced** colorectal neoplasia detection

Lou, et al. Artificial intelligence for colorectal neoplasia detection during colonoscopy: a systematic review and meta-analysis of randomized clinical trials. eClinicalMedicine, 2023.

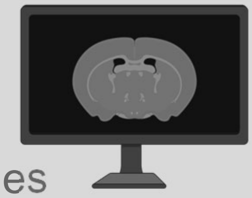
Example: Dermatology



- AI recognition of suspicious skin lesions from routine photographs may expedite diagnosis from mobile devices
- Prior work noted potentially high performance for skin cancer detection
- In a cross-sectional study of 41 readily-available mobile device applications for skin cancer diagnosis
  - No app was FDA-approved
  - In general, mobile device apps **lacked evidence, clinician input, transparency, and user/data privacy**

Wongvibulsin, et al. Current State of Dermatology Mobile Applications With Artificial Intelligence Features. JAMA Dermatology, 2024.

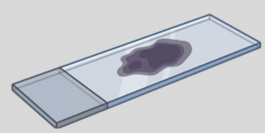
Example: Radiology



- AI algorithms can "upscale" low resolution images
- AI may improve quality of low-resolution radiology images obtained with reduced radiation dose
- In a systematic review of pediatric computed tomography (CT) studies,
  - Two AI algorithms for CT image reconstruction proposed a **reduction in radiation dose by 40-76%**
  - There is still need for prospective evaluation

Gupta, et al. Complex Relationship Between Artificial Intelligence and CT Radiation Dose. Academic Radiology, 2022.

Example: Pathology



- Across oncologic diseases, genomic assessment is critical for diagnosis, prognosis, and therapeutic considerations
- Genomic assessment is costly and may not be readily available in certain clinical settings
- AI upon digital pathology may accurately link genotype with cancer phenotype
  - A subset of **clinically actionable mutations** across multiple cancer types may be **inferred from histology**

Kather, et al. Pan-cancer image-based detection of clinically actionable genetic alterations. Nature Cancer, 2020.

AI for Drug Development

Expediting the development of novel therapeutics

AI for Therapeutic Development

- In a cross-sectional study of 165 AI-developed therapeutics
  - Domain:
    - 32% developed for Oncology
    - 28% developed for Neurology
  - Scope:
    - 76% for drug molecule discovery
    - 22% for drug target discovery

Druedahl, et al. Use of Artificial Intelligence in Drug Development. JAMA Network Open, 2024.

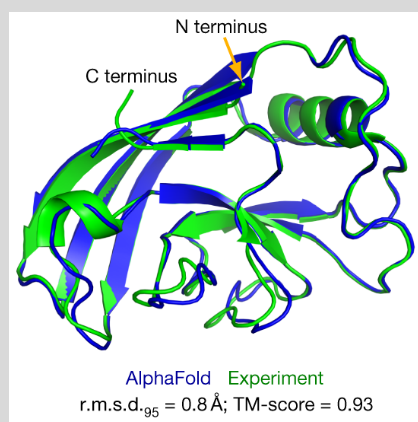
The Time is Now: AI-designed Drugs in Clinical Trials

- **INS018_055** for idiopathic pulmonary fibrosis on an undisclosed target with positive phase 1 trial
  - The first AI-designed molecule entered into a clinical trial
- **EXS-21546**, a highly selective A2A receptor antagonist, currently in Phase 1 trials for solid tumors carrying high adenosine signatures
- **EXS4318**, a selective protein kinase C-theta inhibitor, currently in phase 1 in healthy participants

Arnold, et al. Inside the nascent industry of AI-designed drugs. Nature Medicine, 2023.

AI for Protein Structure Prediction

- RoseTTAFold and AlphaFold
  - Highly accurate prediction of 3-dimensional protein structure from amino acid sequence
- Database of > 200 Million predicted structures are readily-available
  - https://alphafold.ebi.ac.uk/
- Wide-ranging implications for drug development



John Jumper et al, CC BY 4.0, via Wikimedia Commons

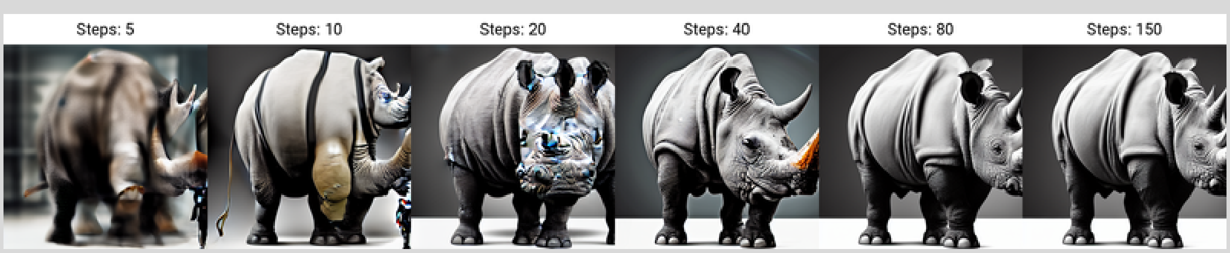
Baek, et al. Accurate prediction of protein structures and interactions using a three-track neural network. Science, 2021.
Abramson, et al. Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature, 2024.

Generative AI

Using Foundation models to generate information

Domains of Generative AI

- Imaging
  - Models such as **Generative Adversarial Networks** (GANs) and **Diffusion models** can create new images from initial images or text

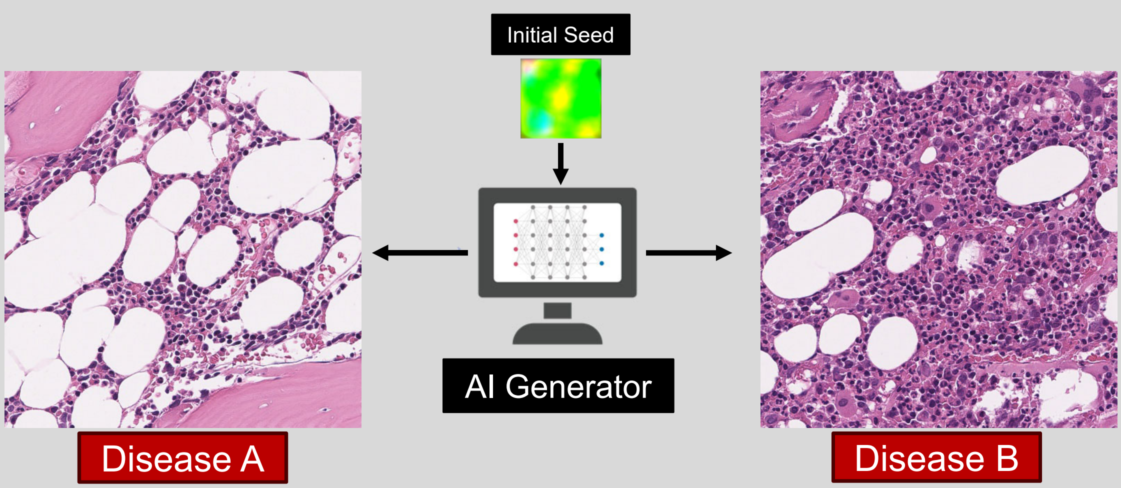


Stable Diffusion WebUI - Automatic1111, Public domain, via Wikimedia Commons

Domains of Generative AI

- Imaging
  - Models such as **Generative Adversarial Networks** (GANs) and **Diffusion models** can create new images from initial images or text
- Text
  - **Large Language Models** (LLMs) are trained to predict the next word in a sequence, which allow the model to generate new text from input prompts and questions.

Image Generation: Synthetic Histology



Srisuwananukorn, et al. Interpretable Artificial Intelligence (AI) Differentiates Prefibrotic Primary Myelofibrosis (prePMF) from Essential Thrombocythemia (ET). Blood, 2023.

Text Generation: Ambient AI Scribe for Clinical Note Documentation

- AI upon ambient listening of patient encounters allow automatic transcription into structured clinical notes
- In a study of 3400 physicians across 300,000 encounters:
  - Transcriptions acceptable by physicians and patients
  - Some physicians note transformative experience
  - Transcriptions still produce inconsistencies, requiring physician review

AI-based transcription services are available at OSU

Tierney, et al. Ambient Artificial Intelligence Scribes to Alleviate the Burden of Clinical Documentation. NEJM Catal Innov Care Deliv, 2024.

Text Generation: Patient Query Response

> "Physician responses were 41% less empathetic than chatbot responses…
>
> The proportion of responses rated ***empathetic*** or ***very empathetic*** was [9.8 times] higher for chatbot than for physicians."

Ayers, et al. Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum. JAMA Internal Medicine, 2023.

Pitfalls and Explainability

Why it is important to "Open the Black Box"

AI Tends to Find the Shortcut

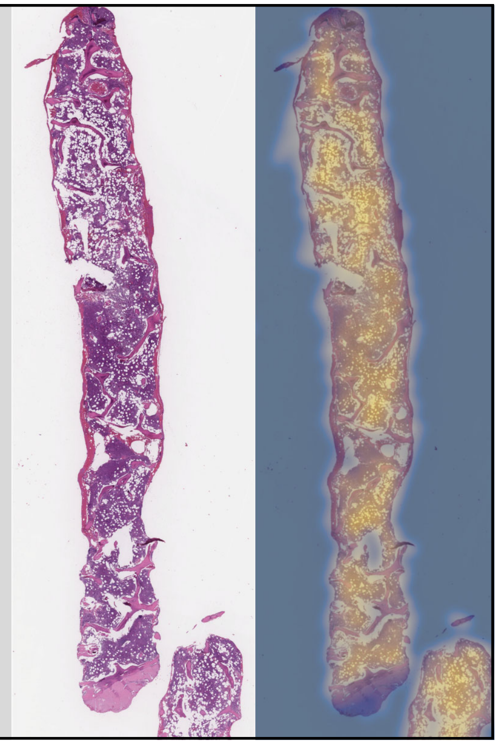
- Example:
  Highly accurate AI classifier for "Husky vs Wolf"
- Upon further analysis, AI relies only on background snow

Ribeiro, et al. "Why Should I Trust You?" Explaining the Predictions of Any Classifier. arXiv, 2016.

Techniques for Explainability

- Numeric scores of image regions associated with the desired outcome of interest can be plotted as a heatmap
  - Saliency Maps
  - Attention score heatmaps
- Allows for interpretability of AI's reliance on various image regions

Srisuwananukorn, et al. Interpretable Artificial Intelligence (AI) Differentiates Prefibrotic Primary Myelofibrosis (prePMF) from Essential Thrombocythemia (ET). Blood, 2023.



Worsening Inherent Biases

- AI may exacerbate the inherent biases within the available data
- In a study upon a widely deployed algorithm to identify patients with complex health needs,
  - Significant unintentional racial biases resulted in ~ 30% of patients not receiving the intended additional assistance
- **It is critical to assure the training datasets and training labels are representative and equitable for the desired task**

Obermeyer, et al. Dissecting racial bias in an algorithm used to manage the health of populations. Science, 2019.

Guidelines for AI reporting

How to critique AI literature

Reporting Guidelines for AI Publications

Study design	Reporting Guideline	AI-related Extension
Clinical Trial Protocol	SPIRIT	SPIRIT-AI
Diagnostic Accuracy Studies	STARD	STARD-AI
		CLAIM
		MINIMAR
Prediction models for diagnostic or prognostication purposes	TRIPOD	TRIPOD-AI/ML
	PROBAST	PROBAST-ML
Randomised Controlled Trials (Interventional Study Design)	CONSORT	CONSORT-AI
Systematic reviews and meta-analyses	PRISMA PRISMA-DTA	PRISMA-AI
Critical appraisal and data extraction of publications relating to prediction models	CHARMS	Applicable to machine learning
Evaluation of human factors in early algorithm deployment	Not applicable	DECIDE-AI
Assess Bias and Applicability in Diagnostic Accuracy Studies	QUADAS-2	QUADAS-AI
Ethical use, disclosure, and reporting of AI in scholarly publication	Not applicable	CANGARU
Assess use of chatbots and LLMs for health information	Not applicable	CHART

Shelmerdine et al. Review of study reporting guidelines for clinical studies using artificial intelligence in healthcare. *BMJ Health Care Inform,* 2021.
Flanagin, et al. Reporting Use of AI in Research and Scholarly Publication—JAMA Network Guidance. JAMA, 2024

Conclusion

Review of AI in Medicine Survey

Key Takeaways

- Terminology in AI is ambiguous and ever-changing
- AI in Medicine examples are highly heterogenous with promising outcomes
- AI in drug development has led to breakthroughs and early-phase development of novel therapeutics
- Generative AI can be helpful in clinical operations
- Healthcare professionals must be vigilant and knowledgeable to critique novel AI algorithms