

Artificial Intelligence: Implications for Clinical Practice, Research, and Education

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William Hersh, MD
Professor

Department of Medical Informatics & Clinical Epidemiology
School of Medicine
Oregon Health & Science University
Portland, OR, USA

<https://www.ohsu.edu/informatics>

Email: hersh@ohsu.edu

Web: <http://www.billhersh.info/>

Blog: <https://informaticsprofessor.blogspot.com/>

X/Twitter: [@williamhersh](https://twitter.com/williamhersh)

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Artificial Intelligence: Implications for Clinical Practice, Research, and Education

William Hersh, MD
Professor
Department of Medical Informatics & Clinical Epidemiology
Oregon Health & Science University
Portland, OR, USA

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Objectives and disclosures

- After this talk, you will to be able to
 - Define the major types of AI and their applications, successes, and limitations
 - Discuss the evidence base for AI, its limitations, and how to improve it
 - Follow a pathway for application of AI and its role in clinical practice, research, and education
- Disclosures
 - None

AI Implications

2



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Artificial intelligence (AI) defined

- AI – “information systems and algorithms capable of performing tasks associated with human intelligence” (Rajpurkar, 2022)
- Some classify AI into two broad categories (Khare, 2023)
 - Predictive AI – use of data and algorithms to predict some output (e.g., diagnosis, treatment recommendation, prognosis, etc.)
 - Generative AI – generates new output based on prompts (e.g., text, images, etc.)
- A large part of modern success of AI due to machine learning (ML) – “computer programs that learn without being explicitly programmed” (McCarthy, 1990, attributed to Samuel, 1959; Shah, 2023)
 - Most success with deep learning, based on many-layered neural networks



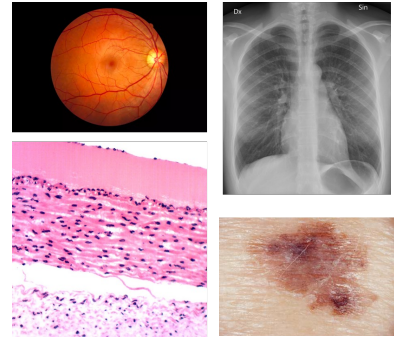
History of AI – first era in mid-20th century

- Earliest paper related to AI and biomedical informatics attributed to Ledley and Lusted (1959, 1960) aiming to model physician reasoning through symbolic logic and probability
- Warner (1961) developed mathematical model for diagnosing congenital heart disease
- In 1960s-1970s, emergence of “expert systems” – computer programs aiming to mimic human expertise (historical overview – Lea, 2023)
 - Rule-based systems – PhD dissertation of Shortliffe (1975) and subsequent work (Clancey, 1984)
 - Disease profiles and scoring algorithms – INTERNIST-1 (Miller, 1982) and DxPlain (Barnett, 1987)
- Limited by approach of manual construction and maintenance of knowledge
 - Not scalable or sustainable
 - Led to “AI winter” between 1990-2010
 - Main remnant is clinical decision support (CDS) for electronic health records (EHRs) that emerged in 1990s for electronic health records (Greenes, 2023)



Re-emergence of AI in 21st century

- “Predictive AI” driven by advances in ML, increasing availability of data, and more powerful computers and networks (Topol, 2019; Rajpurkar, 2022)
 - Deep learning in imaging breakthroughs by Hinton (2006)
- Most success in image interpretation (Rajpurkar, 2023); examples include
 - Radiology – chest x-rays for diagnosis of pneumonia and tuberculosis
 - Ophthalmology – retinal images for diagnosis of diabetic retinopathy
 - Dermatology – skin lesions for diagnosis of cancer
 - Pathology – breast cancer slides to predict metastasis



Predictive AI not limited to imaging

- Adverse events in hospitalizations from EHR data (Rajkomar, 2018)
- Generating clinical notes from patient and physician verbal interaction (Rajkomar, 2019)
- Protein folding from amino acid sequences (Jumper, 2021)
- Model based on past ICD-10 codes and lab results to predict future diagnoses in office visits (Mukherjee, 2023)
- Semantic reconstruction of continuous language from fMRI brain recordings (Tang, 2023)
- Map chemicals to odors perceived by humans (Lee, 2023)

Predictive AI (cont.)

- Assist in detection of inappropriate 16% duplicate images in papers in toxicology journal (David, 2023)
- Perform initial screening of medical school applicants comparable to faculty (Triola, 2023)
- Next-generation sequencing (NGS) data able to predict cancer of unknown primary with high confidence for 41% of tumors, leading to improved survival for those patients (Moon, 2023)
- Predict Alzheimer's Disease from EHR data up to 7 years before diagnosis (Tang, 2024)
- The list goes on and on, especially with addition of generative AI...

AI Implications

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Also success in “seeing” where humans cannot (Topol, 2022)

- Retinal images
 - Age, biological sex, and cardiovascular risk determination from retinal images (Poplin, 2018)
 - Race (Coyner, 2023)
- Electrocardiograms (ECGs)
 - Age and biological sex determination (Attia, 2019)
 - Chronic kidney disease (Holmstrom, 2023)
- Chest x-rays
 - Race (Gichoya, 2022)
 - Cardiac function and valvular heart diseases (Ueda, 2023)
 - Diabetes (Pyrros, 2023)
 - Correlation with chronological age in healthy cohorts and, for various chronic diseases, difference between estimated age and chronological age (Mitsuyama, 2023)
 - Cardiac risk as accurately as common models, e.g., atherosclerotic cardiovascular disease (ASCVD) (Weiss, 2024)



Using AI techniques, a computer can determine from a 12-lead ECG:



Whether you are male or female with an accuracy of over 90%

Your age, if you're healthy, within 7 years ... And may determine your physiologic age if you have other comorbidities

AI Implications

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And now, “generative AI”

- Introduction of ChatGPT on November 30, 2022 brought new type of AI into focus: generative AI
- Based on large language models (LLMs) processed by deep neural networks using large amounts of training data and tuned for specific tasks (Omiye, 2024)
 - Trained on massive amounts of text and other content, e.g., large Web crawls, books, Wikipedia, and more for GPT (Roberts, 2022)
 - Use transformer models that predict words in sequence from billions/trillions of words and add measure of importance to “attention” words (Raschka, 2023)
 - Fine-tuned with reinforcement learning from human feedback (RLHF) (Lambert, 2022)
 - Activated by (and importance of) prompting (Liu, 2023; Meskó, 2023)



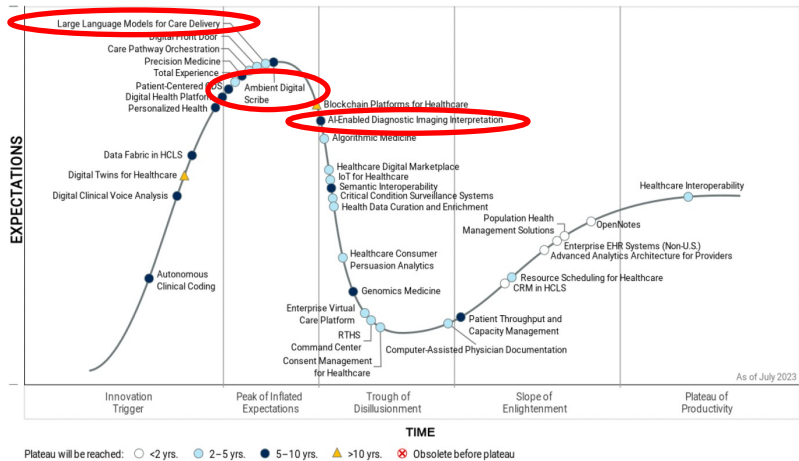
Generative AI is more than ChatGPT

- Adding generative AI to search, including retrieval-augmented generation (RAG) (King, 2023)
 - CoPilot – GPT-4 integrated into Microsoft Bing
 - Google – Bard and now Gemini
- Many products adding generative AI, e.g., Microsoft Office, Adobe Acrobat, etc.
- “Small” language models – Phi-2, Mistral, etc.
 - Clinically-oriented models, e.g., Almanac (Zakka, 2024)
- Many roles and challenges in academia, business, etc. (Mollick, 2024)



Generative AI at peak of inflated expectations (Meyer, 2023)

Hype Cycle for Healthcare Providers, 2023



AI Implications

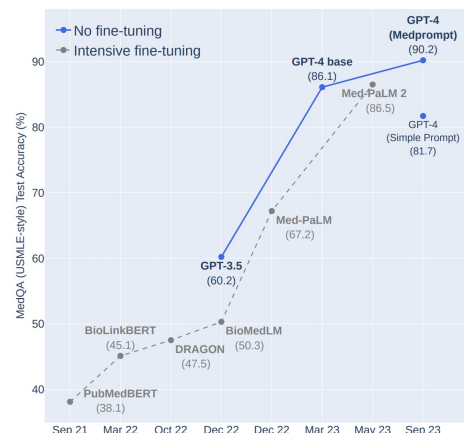
Gartner



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Results of ChatGPT and other LLMs

- Medical board exam questions
 - USMLE “arms race,” starting with (Kung, 2023)
 - Now best with GPT-4 and specific types of prompting (Nori, 2023)
 - Even on “soft skills” (e.g., communication skills, ethics, empathy, and professionalism) questions (Brin, 2023)
 - Passing level on most board exam questions (clinical informatics – Kumah-Crystal, 2023; radiology – Bhayana, 2023; neurology – Schubert, 2023) but not others (neonatology – Beam, 2023, used only GPT-3.5)
- Answering questions
 - Vary by subject domain and type, but sometimes wrong and/or incomplete (e.g., Antaki, 2023; Chen, 2023; Goodman, 2023)
- Solving clinical cases
 - Comparable to but not better than expert humans (e.g., Levine, 2023; Kanjee, 2023; Rao, 2023; Benoit, 2023; Levkovich, 2023)



AI Implications

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Results of LLMs (cont.)

- In simulated (text-based) objective structured clinical exam (OSCE) format, Articulate Medical Intelligence Explorer (AMIE) outperformed primary care physicians in text-based dialogue in history-taking, diagnostic accuracy, management reasoning, communication skills, and empathy (Tu, 2024)
- For 20 clinical cases, GPT-4 performed comparable to attending physicians and residents in diagnostic accuracy, correct clinical reasoning, and cannot-miss diagnosis inclusion (Cabral, 2024)



Results of LLMs (cont.)

- Communicating with patients
 - Answering questions in public forums (Sarraj, 2023; Ayers, 2023)
 - Writing letters with comparable or better empathy (Ali, 2023, Ayers, 2023)
 - Generating surgical consent forms better than surgeons (Decker, 2023)
- Closing the loop with predictive AI
 - Classifying CXR findings based on previous images and reports (Xu, 2023)
 - Generating CXR reports from new images in ED from prior images and reports (Huang, 2023)
 - Predicting cardiovascular risk comparable to Framingham models (Han, 2023)
 - Designing and validating easily synthesizable and structurally novel antibiotics (Swanson, 2024)



But there are some downsides to generative AI

- Dictionary.com 2023 word of year: hallucinate
 - <https://content.dictionary.com/word-of-the-year-2023/>
- Fabrication and errors in the bibliographic citations – asked to produce short literature reviews on 42 multidisciplinary topics (Walters, 2023)
 - 55% of GPT-3.5 citations and 18% of GPT-4 citations fabricated
 - 43% of real (non-fabricated) GPT-3.5 citations and 24% of real GPT-4 citations include substantive errors
- LLMs reflect content (and bias) of text used for training (Schaul, 2023)



Downsides to generative AI (cont.)

- 8 clinical questions asked of 4 LLMs recapitulated “harmful, race-based medicine” (Omiye, 2023)
- Equally compelling disinformation – humans cannot distinguish between true and false tweets generated by GPT-3 and written by real Twitter users (Spitale, 2023)
- Automated GPT detectors have mixed results (Sadasivan, 2023; Odri, 2023; Desaire, 2023; Tang, 2024)
 - More likely to classify non-native English writing as AI-generated (Liang, 2023)
 - Humans not able to discern AI writing either (Dell'Acqua, 2023)



And some downsides to AI in general

- After clinical models deployed, performance may decline due to actual real-world use (Vaid, 2023; Palmer, 2023)
- Implementing diabetic retinopathy screening in rural Thailand and India found (Widner, 2023)
 - Challenges related to equipment operation, workflows, and image quality
 - Need for training and attention to human factors



Downsides to AI in general (cont.)

- Variable impacts on different levels of radiologists, leading to automation bias and detrimental effects of incorrect AI (Dratsch, 2023; Yu, 2024)
- Concerns about reproducibility (Ball, 2023)
 - Data bias (especially from EHR – Lewis, 2023; Chin, 2023)
 - Data leakage (Kapoor, 2023)
 - Data drift/shift (Finlayson, 2021; Li, 2024)



Will AI help or hinder healthcare?

- Real-world use still modest
 - As of Sept 2023, only 21% of medical groups using AI applications in practice (MGMA, 2023)
 - EHR usability, patient communications, and billing outrank AI as top tech priorities among medical groups (MGMA, 2023)
 - AI tools used by only 38% of physicians (AMA, 2023)
- “AI won’t replace radiologists, but radiologists who use AI will replace radiologists who don’t,” (Langlotz, 2019)
 - (Plug in your health profession)



What do we need for AI applications to make it to the plateau of productivity?

- Translational AI (Hersh, 2024)
 - Show us the evidence
 - How do we learn about it
- Search still matters (Hersh, 2024)
 - In many circumstances, who said what is more important than providing a generated answer

A screenshot of a webpage titled "MUSINGS from the MEZZANINE" from the National Library of Medicine. The page features a header with the NIH logo and the title. Below the header, there is a navigation bar with "HOME", "ABOUT", and "NATIONAL LIBRARY OF MEDICINE". The main content area is titled "Translational AI: A Necessity and Opportunity for Biomedical Informatics and Data Science" and is dated February 7, 2024. The author is listed as William Hersh, MD. The page also includes logos for AMIA and OXFORD. The text of the article is partially visible, including an abstract and a conclusion.

How do we “show the evidence?”

- From evidence-based medicine (EBM), best evidence for any clinical intervention is from randomized controlled trials (RCTs) or systematic reviews of RCTs
- Although not as easy to carry out as RCTs of drugs or devices (and placebos), AI must demonstrate benefit for patient outcomes and/or healthcare delivery improvement
 - Additional issues for RCTs of AI (Liu, 2020)
- As with drugs and devices, we need to move from “basic science” to “clinical science”
- Not everything can be studied in an RCT and RCTs cannot be done for every last clinical question (Greenhalgh, 2022)



What is the evidence so far?

- Many, many papers published about models and simulated use (basic science), including systematic reviews of those papers
- Very few RCTs demonstrating value from real-world use (clinical science) – systematic reviews of RCTs show (Zhou, 2021; Plana, 2022; Han, 2023)
 - Much smaller numbers of RCTs – about 100, depending on how we count
 - 65-82% of RCT showed positive outcomes
 - Many RCTs showed aspects of “risk of bias”



Learning from some specific examples

- Computer-aided detection (CAdE) of polyps in colonoscopy
 - One of earliest and most widely-studied applications of AI
 - Recent systematic review shows polyps missed by colonoscopists are discovered, but mostly small and clinically inconsequential (Hassan, 2023)
 - RCT of CAdE found no increased detection of advanced neoplasias (Mangas-Sanjuan, 2023)
- 30-day hospital readmissions
 - After implementation of CMS penalty, proliferation of highly accurate predictive models published in mid-2010s
 - Recent RCT showed use of high-quality model and implementation of program around it did not reduce readmissions (Donzé, 2023)



Examples (cont.)

- RCT to assess whether use of previously validated hospital-acquired venous thromboembolism (HA-VTE) prognostic model, together with pediatric hematologist review, could reduce pediatric inpatient rates of HA-VTE (Walker, 2023)
 - No difference for intervention group randomized to use model
 - Reluctance to use model by primary physicians – used only 26% of time
 - For children in intervention arm, model mostly not used, AI's “Cassandra problem” (Wilson, 2023)?
- Pragmatic trial of predictive algorithm and practice facilitators in outpatient practices did not reduce hospitalization rate in chronic kidney disease over 1 year compared with usual care (Vazquez, 2024)



How do we get to “translational AI?”

- In pediatric critical care ML research, “the literature demonstrates incomplete reporting, absence of external validation, and infrequent clinical implementation” (Heneghan, 2023)
- Singh, X/Twitter, Feb 8 2024: “Researched models aren’t implemented. Implemented models aren’t researched.”
- Postmarket surveillance, e.g., algorithmovigilance (Embi, 2021)
- Responsible use (Dorr, 2023) and code of conduct (Adams, NAM, 2024) for AI
- Building the evidence base (Hersh, 2024)



Also critical is education of clinicians and informaticians

- AI should build on competencies in clinical informatics (Hersh, 2014; Hersh 2020; Hersh, 2023)
- Others note
 - Clinicians must be prepared to practice in a world of AI (James, 2022)
 - Medical schools face dual challenges of needing to teach about AI in practice but also adapt to its use by learners and faculty (Cooper, 2023)
- AI-specific competency frameworks (Russell, 2023; Liaw, 2023)

1. Find, search, and apply knowledge-based information to patient care and other clinical tasks
2. Effectively read from, and write to, the electronic health record (EHR) for patient care and other clinical activities
3. Use and guide implementation of clinical decision support (CDS)
4. Provide care using population health management approaches
5. Protect patient privacy and security
6. Use information technology to improve patient safety
7. Engage in quality measurement selection and improvement
8. Use health information exchange (HIE) to identify and access patient information across clinical settings
9. Engage patients to improve their health and care delivery through personal health records and patient portals
10. Maintain professionalism in use of information technology tools, including social media
11. Provide clinical care via telemedicine and refer patients as indicated
12. Apply personalized/precision medicine
13. Participate in practice-based clinical and translational research
14. Use and critique artificial intelligence (AI) applications in clinical care

Search still matters (Hersh, 2024)

- Generative AI systems such as ChatGPT are cool and fun, but
 - For some tasks that many of us do, need more than answers, e.g.,
 - Clinical – patient-care questions
 - Research – methods and insights
 - Teaching – synthesizing knowledge for our students
 - Where the information comes from is as important what it says
- Information retrieval (IR) systems “do not inform user about a subject; indicate the existence (or nonexistence) and whereabouts of documents related to an information request” (Lancaster, 1978)

AI Implications

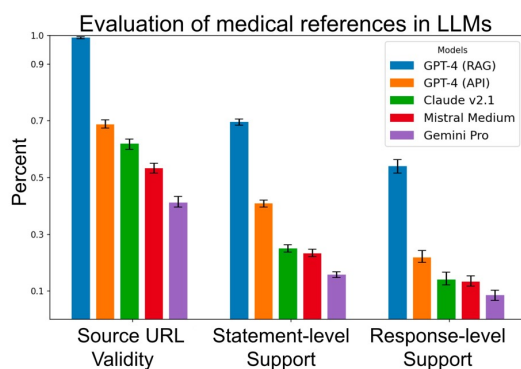
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Search in the era of generative AI

- Another adage of EBM?
 - Gen AI for background questions
 - Search and critical appraisal for foreground questions
- Retrieval-augmented generation (RAG) for improving Gen AI but do we need “generation-augmented retrieval” for LLMs to aid search?
 - Evidence modest so far, e.g., using ChatGPT for generating Boolean queries did not improve search results (Wang, 2023)
 - Best LLM with RAG (GPT-4 in CoPilot) achieved about 70% statement-level support and <50% for others (Wu, 2024)



AI Implications

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Conclusions

- AI will profoundly impact the practice and education of all health professions
- Translational AI is a necessity and opportunity for clinicians, researchers and others
- Healthcare, informatics, and educational professionals must be competent with AI as much as any other tool in clinical practice
- Generative AI systems must provide attribution for their assertions



Questions?

William Hersh, MD
Professor
Department of Medical Informatics & Clinical Epidemiology
Oregon Health & Science University
Portland, OR, USA
Email
hersh@ohsu.edu
Web
<http://www.billhersh.info>
Blog
<https://informaticsprofessor.blogspot.com/>
Textbook
<http://www.informaticsbook.info>
What is Informatics?
<http://informatics.health>

