Al in Medicine: The Resident **Expert That Never Sleeps**

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Disclosures

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Agenda



Definitions



Use cases



Challenges



Ethics



Liability



Model Cards





What is Artificial Intelligence (AI)?

- "Artificial Intelligence refers to the development of computer algorithms that can perform tasks that typically require human intelligence, such as learning, reasoning, perception, and decision making" (ChatGPT)
- Al is based on machine learning algorithms and other computational techniques:



Computational Logic Rule-Based Systems Logic Programming Heuristic Techniques Case Based Reasoning

Optimization Techniques Constraint Satisfaction Constraint-Based Reasoning Linear Programming Genetic Algorithms



Perception Systems/Ambient Intelligence

Computer Vision Olfactive & Haptic Auditory/Speech

Knowledge Representation, Learning/Search



Natural Language Processing

Text Analytics Natural Language Understanding Chatbots Natural Language Generation

Dialog Management



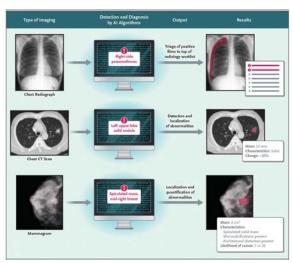
Credit: Adam Landman





Medical Image Interpretation





Rajpurkar, Pranav, and Matthew P. Lungren. "The Current and Future State of Al Interpretation of Medical Images." New England Journal of Medicine 388.21 (2023): 1981-1990.





Digital medicine

Al-enabled opportunistic medical scan interpretation

Eric Topol

Your chest x-ray indicates that you may have type 2 diabetes, your coronary calcium score is 976, your ejection fraction is normal, and your 10-year cardiovascular risk of a heart attack, stroke, or death from cardiovascular disease is 14-1%. Please review with your physician regarding potential addition or intensification of a statin to your medications.





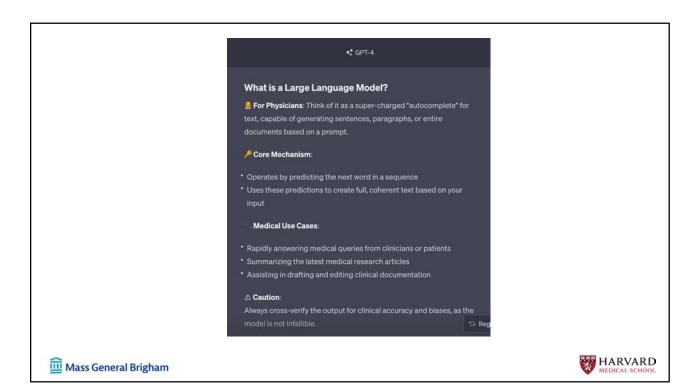
Large Language Models

How frequently do you utilize ChatGPT for work-related activities?*

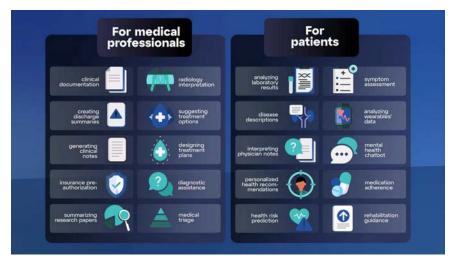
- A) Never used it
- B) I used it a few times, but it was not helpful
- C) I used it a few times, but I recently started to use it more
- D) I use it almost every day, can't work without it!







Opportunities for LLMs



Meskó, Bertalan, and Eric J. Topol. "The imperative for regulatory oversight of large language models (or generative Al) in healthcare." npj Digital Medicine 6.1 (2023): 120.





Medical question answering



USMLE Sample Exam	GPT-4 (5 shot)	GPT-4 (zero shot)	GPT-3.5 (5 shot)	GPT-3.5 (zero shot)	ChatGPT [†] (zero shot)
Step 1	85.71	80.67	52.10	51.26	55.1
Step 2	83.33	81.67	58.33	60.83	59.1
Step 3	90.71	89.78	64.96	58.39	60.9
Overall Average*	86.70	84.31	58.78	56.91	_

^{*} Calculated as $\frac{\#correct}{\#questions}$ across all three steps. Each step has slightly different sample size.

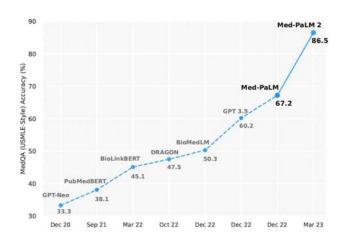
Nori, Harsha, et al. "Capabilities of gpt-4 on medical challenge problems." arXiv preprint arXiv:2303.13375 (2023).







Medical question answering



Singhal, Karan, et al. "Towards expert-level medical question answering with large language models." arXiv preprint arXiv:2305.09617 (2023).





The NEW ENGLAND JOURNAL of MEDICINE dit he bedfore for the determine whether this content is having an experiencing shortness of breath.

Curbside consult

looking for sign and ymptoms of an ascerbation. An exacerbation of COPD is diffined as an acute worsning of expiratory symptoms beyond the patients "usual days-food presistion and in spiniorly characterized by increased cough, increased spatum production, and increased dyapnea.

Some of the key clinical features that suggest an exacerbation of COPD include:

1. Increased inference of peace is cough, and spatum production.

3. Changes in the color, amount, and thickness of the spatum.

4. Increased use of rescue medication, such as short-acing bronchodistors.

5. Falipse, confisions or extend mercal calculations.

6. Cyanosis, a blaish discoloration of the skin or lips, the to inadequate anyproation.

8. In important to note that the medical candidations are mission an exacerbation of COPD, such as congestive heart failure or paintoning embediant. Therefore, a 8 executed to perform a bivrought evaluation, including a detailed instrup, physical examination, and in the company embediant. Therefore, a 8 executed to perform a bivrought evaluation, including a detailed instrup, physical examination, and the control of the skin or lips, the to inadequate anyproation and appropriate management of COPD exacerbations are critical to minimizing their impacts on the patients' squality of life and overall prognosis. If you suspects that your patients is having an exacerbation, you should comult with a pulmonosisgat or respectively returning to develop an appropriate tereinment plan, which may include organ therapy, inhealed brochodilators and corticateroids, and aritholosis for suspected bacterial infections.

Clinician: There is no sputum production. But the patient apports the pulmon production with a pulmonosisgation of the structure of the patients' and the product supplemental cargon through; inhealed brochodilators and corticateroids, and aritholosis for suspected bacterial infections.

Clinician: There is no sputum production does not rule out the possibility of an exacerbation of copy of particular and provide suppl

Lee, Peter, Sebastien Bubeck, and Joseph Petro. "Benefits, limits, and risks of GPT-4 as an Al chatbot for medicine." New England Journal of Medicine 388.13 (2023): 1233-1239.







Documentation

A A Request to GPT-4 to Read a Transcript of a Physician-Patient Encounter and Write a Medical Note

A Request to CFT-4 to Read a Transcript of a Physician-Patient Encounter and Write a Medical Note Clinician: Please have a seat, Meg. Thank you for coming in today. Your runtificiant referred you. It seems that she and your mom have some concerns. Can you sit down and we will take your blood pressure and do some vitals? Patient: I puts. I do need to get back to my doem to study. I have a track meet coming up also that I am training for. I am runner. Clinician: How many cordits are you taking and how are classes going? Patient: 21 credits. I am at the top of my class. Could we get this done? I need to get back. Clinician: How often and far do you run for training mon? You are 20, correct? Patient: Yes. I run nine miles every day.

Clinician: You PP 15 10/05/2. Your publes is 52. Meg, how much have you been eating? Patient: I have been eating fine. I talked to the nutritionist about this earlier.

Clinician: Yes have you stand up and face me and I will back you onto the scale. Eyes on me please. Thank you, and now for a height. Ok looks like 59: . Go shead and have a seat.

Patient: How much Can I please see what the scale say? I'm fat.

Clinician: Please sit up and I will listen to your heart and lungs.

Patient: Fine.

Intel: Fine.

cian: You know that is not a positive part of your treatment. We have discussed this before. You are here today because your nutritionist and your mom are both very concerned about you. You are very ill, Meg. ent. I am fine. I am eating, I tell my mom what I eat. Just because I am not fat like she is.

cician: How have you felt? Are you feeling sad or depressed? Last time we talked, you were quite unhappy. Are you feeling suicidal?

controlled in the concerned about happiness. I need to train and I am tired of everyone nagging me about what I sat and how much I exercise. I am the smartest in my class and one of the best runners on the team. I don't have time for all of thi I am only here to keep my more off my back.

I am only here to keep my more off my back.

I am only here to keep my more off my back.

The controlled in the contro

nt: I will work with all of you. I know. I don't want to be like this. I need to run though. It helps me.

Patient: I will work with all of you. I know. I don't want to be like this. I need to run though. It helps me.

Clinician: When you were in treatment, we were working toward some goals with your cognitive behavioral therapy. We need to revisit these goals. First thought, we need to bring your mom in and have a discussion about the next step to help you get well. I would like to do more tests to check your electrolytes and your blood count.

Patient: Ok. I do want to be better.

Clinician: I want you to feel better and be healthy. Let's have your mom come in, ok?

Patient: Yeah.

GPT-4: Patient is a 20-year-old female with a history of anorexia nervosa and depression. She was referred by her nutritionist and accompanied by her mother. She is taking 21 credits at college and is a compactive runner. She is in devial of her illness and has pose insight into her conditions. She is resistant to treatment and intervention. She reposts attain fign, but he is severely underweight (BMT 14-8) and has signs of maliutation and cardiac complications. She denies feeling suicidal, but appresses low mood and lack of interest in hoppiners. She has a strong attachment to running and believes it helps her expe. She agreed to work with her nativative her mother, and me, but the needs more support and monitoring, I ordered some blood tests and suggested a review of her cognitive behavioral therapy goods. I discussed with her and her mother the possibility of hospitalization or intensive outpatient treatment if he condition does not improve.

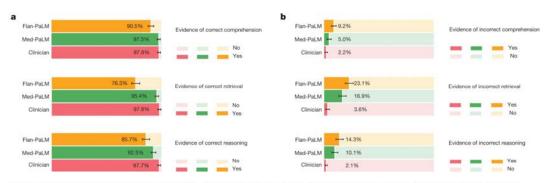
Lee, Peter, Sebastien Bubeck, and Joseph Petro. "Benefits, limits, and risks of GPT-4 as an Al chatbot for medicine." New England Journal of Medicine 388.13 (2023): 1233-1239.



HARVARD

Large language models encode clinical knowledge

nature



 $\textbf{a,b,} \ Evaluation \ of correctness \ \textbf{(a)} \ and \ incorrectness \ \textbf{(b)} \ of \ reading \ comprehension, \ recall \ of \ knowledge \ and \ reasoning \ steps. \ The \ results \ indicate \ a \ gap$ $between Flan-PaLM \ and \ clinicians, and \ show \ that \ Med-PaLM \ is \ able \ to \ substantially \ reduce \ the \ gap. \ The \ evaluation \ involves \ 140 \ questions, \ each \ rated \ by \ and \ show \ that \ Med-PaLM \ is \ able \ to \ substantially \ reduce \ the \ gap. \ The \ evaluation \ involves \ 140 \ questions, \ each \ rated \ by \ and \ show \ that \ Med-PaLM \ is \ able \ to \ substantially \ reduce \ the \ gap. \ The \ evaluation \ involves \ 140 \ questions, \ each \ rated \ by \ and \ substantially \ reduce \ the \ gap.$ single clinician. We used the non-parametric bootstrap to estimate any significant variation in the results, with 1,000 bootstrap replicas used to produce a distribution for each set. We used the 95% bootstrap percentile interval to assess variations.

Singhal, Karan, et al. "Large language models encode clinical knowledge." Nature (2023): 1-9.

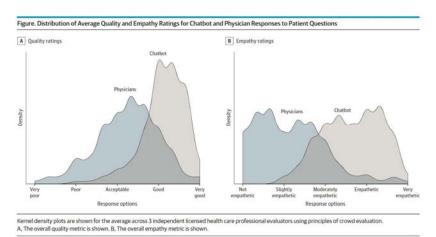




Article Open access | Published: 04 July 2024 Evaluation and mitigation of the limitations of large language models in clinical decision-making Paul Hager ☑, Friederike Jungmann, Robbie Holland, Kunal Bhagat, Inga Hubrecht, Manuel Knauer, Jakob Vielhauer, Marcus Makowski, Rickmer Braren, Georgios Kaissis & Daniel Rueckert Fig. 2: LLMs diagnose significantly worse than doctors when provided with all Fig. 3: Diagnostic accuracy of LLMs decreased in an autonomous clinical decisionmaking scenario. HARVARD Mass General Brigham

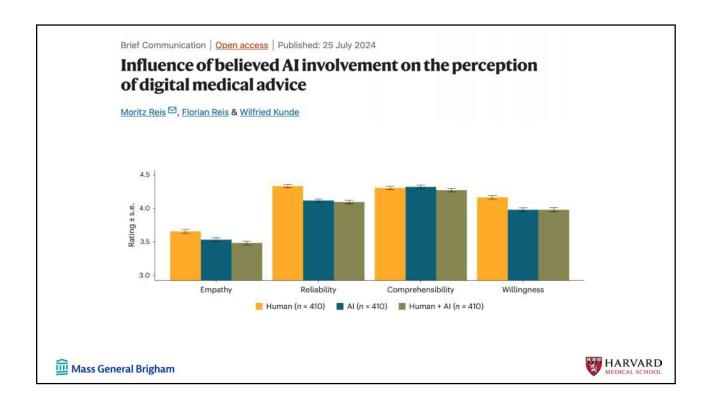
Answering patient questions

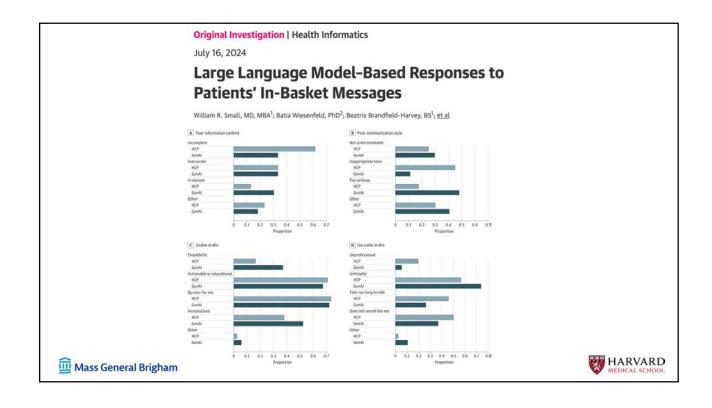


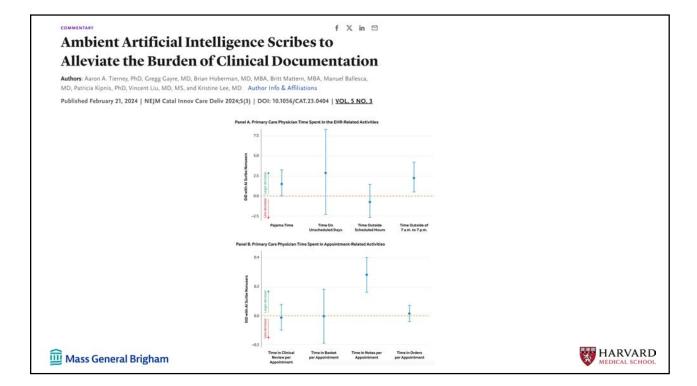


Ayers, John W., et al. "Comparing physician and artificial intelligence chatbot responses to patient questions posted to a public social media forum." JAMA internal medicine (2023) HARVARD









JOURNAL ARTICLE

The impact of nuance DAX ambient listening AI documentation: a cohort study

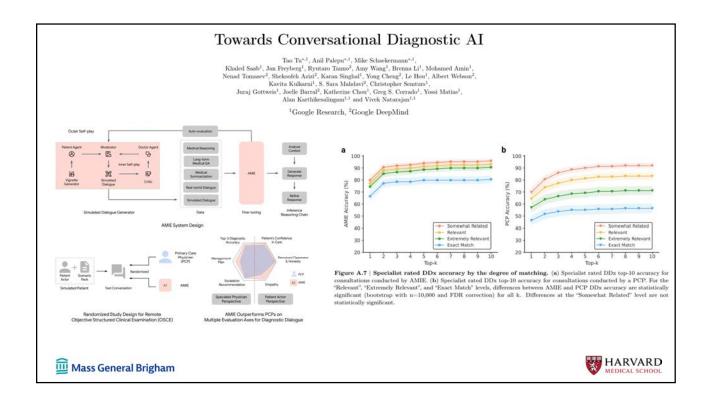
Tyler Haberle, MD ☒, Courtney Cleveland, MS, Greg L Snow, PhD, Chris Barber, MS, Nikki Stookey, MA, Cari Thornock, MS, Laurie Younger, MSN, Buzzy Mullahkhel, MS, Diego Ize-Ludlow, MD

- 99 providers representing 12 specialties
- 76 matched control group providers
- Median utilization: 47% among active participants
- Nuance DAX use showed positive trends in provider engagement, without detriment to patient safety, experience, or clinical documentation.
- There were no significant benefits to patient experience, documentation, or measures of productivity.

Clinical specialty	Number of participants (%)	
Adult and pediatric primary care	56 (56.6)	
Orthopedics and sports medicine	15 (15.2)	
Surgical, cardiac, interventional, neuroscience, OB/GYN, oncologic, and women's health	11 (11.1)	
Medical specialties (endocrine, rheumatology, etc.)	5 (5.1)	
Psychiatry	1 (1.0)	







Prompt matters



25 y/o female presenting with fever, hypotension, vomiting, diarrhea and chest pain. CXR is normal, WBC is normal, lactate is normal, high sensitivity troponin is 93. This patient takes metformin, clozapine, and haldol. What is your differential diagnosis.









Mass General Brigham

Prompt matters: same case

Α

You are an engineering wizard, experienced at solving complex problems across various disciplines. Your knowledge is both wide and deep. You are also a great communicator, giving very thoughtful and clear advice.

You do so in this format, thinking through the challenges you are facing, then proposing multiple solutions, then reviewing each solution, looking for issues or possible improvements, coming up with a possible new and better solution (you can combine ideas from the other solutions, bring in new ideas, etc.), then giving a final recommendation: 25 y/o female presenting with fever, hypotension, vomiting, diarrhea and chest pain. CXR is normal, WBC is normal with slightly elevated eosinophils, lactate is normal, high sensitivity troponin is 93. This patient takes metformin, clozapine, and haldol. what is your most likely diagnosis, be specific and choose one





Challenges:

- 1. The patient has a fever, hypotension, vomiting, diarrhea, and chest pair
- The patient is taking metformin, clozapine, and haldol—each with its own set of side effects and interactions.
- Laboratory tests are generally normal except for slightly elevated eosinophils and high sensitivity troponin.
- Chest X-Ray (CXR) is normal, suggesting that the chest pain is not due to an overt pulmonary issue.
- 5. This is a complex presentation with symptoms affecting multiple body systems

Potential Diagnoses:

- Drug-induced side effects or interactions: Given the medication list (metformin, clozapine, and halds), drug interactions or side effects could be a feator.
- Infectious etiology: The symptoms of fever, vomiting, and diarrhea suggest a possible
 infection, although the normal WBC count and lactate level may argue against a severe
 infection.
- Cardiac issue: The elevated high sensitivity troponin and chest pain could suggest a cardiac issue, although the CXR is normal.
- Other systemic conditions: Less likely but still possible are conditions like autoimmune diseases or systemic allergic reactions, as the slightly elevated eosinophils might suggest.

Review of Solutions:

- Drug-induced side effects or interactions: Clozapine and haldol both have cardiac side
 effects and could potentially interact. Hypotension and gastrointestinal symptoms are also
 known side effects.
- Infectious etiology: Fever could suggest infection, but the normal WBC and lactate are not typical for a severe infection causing these symptoms. Infections could still be viral or atypical bacterial that do not immediately affect these markers.
- Cardiac issue: Troponin is elevated, but not all cases of elevated troponin are due to cardiac
 ischemia. It could be a result of other systemic stress or drug effects.
- 4. Other systemic conditions: Elevated eosinophils might suggest an allergic or autoimmune condition, but these are usually not acute onset and do not usually present with such a wide array of symptoms.

Possible New and Better Solution:

Given the medication list and the absence of significant abnormality in other tests like WBC, lactate, and CXR, a potential diagnosis could be Clozapine-induced myocarditis or cardiotoxicity. This would explain the elevated troponin levels, chest pain, hypotension, and possibly even the fever. Elevated eosinophilis can also be indicative of myocarditis.

Final Recommendation:

Immediate evaluation by medical professionals is essential. In this hypothetical case, my most likely diagnosis would be Clozapine-induced myocarditis or cardiotoxicity. The patient needs immediate cardiology consultation, further cardiac evaluation including EKG and echocardiogram, and likely cessation of clozapine under medical supervision.

Monitoring in an acute care setting like an ICU would also be advisable. This is a potentially life-threatening situation that requires swift intervention.





Prompt tips

1.Define the Role and Task Clearly:

Example: "You are an expert board-certified physician reviewing a patient's medical chart."

2.Include Necessary Information:

Don't omit details; what seems irrelevant to you might be crucial.

3.Repeat Key Points:

Reinforce the most important objectives, especially in longer prompts.

4.Use Examples Wisely:

Examples can help but might limit generalization.

5.Be Clear and Precise:

Avoid ambiguity with straightforward language.

6.Test and Refine:

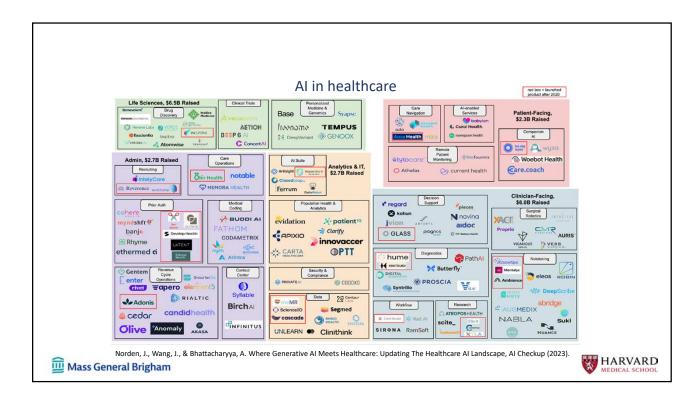
Iterate based on LLM output to improve the prompt.

7. Specify Constraints:

If necessary, define length, format, or focus areas.







Autonomous vs. Assistive AI systems

THE LANCET Digital Health

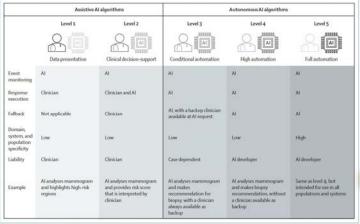


Figure: Levels of automation of medical artificial intelligence systems

Bitterman, Danielle S., Hugo JWL Aerts, and Raymond H. Mak. "Approaching autonomy in medical artificial intelligence." The Lancet Digital Health 2.9 (2020): e447-e449.





Digital diagnostics









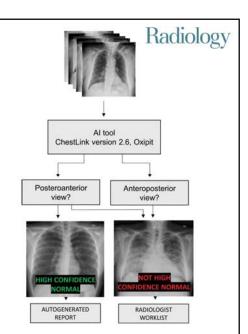
Autonomous CXR interpretation

Multicenter retrospective study of 1529 patients.

Of all normal posteroanterior chest radiographs, 28% were autonomously reported by AI (sensitivity higher than 99%).

This corresponded to 7.8% of the entire posteroanterior chest radiograph production.

The time from the study is received to the output is up to 10 seconds.



Plesner, Louis L., et al. "Autonomous Chest Radiograph Reporting Using Al: Estimation of Clinical Impact." Radiology 307.3 (2023): e222268.





Design AI so that it's fair

Identify sources of inequity, de-bias training data and develop algorithms that are robust to skews in data, urge James Zou and Londa Schiebinger.



— Great Britain 7.6%
— Italy 6.2%
— Canada 3%
— Other 37.8%

IMAGE POWER

Deep neural networks for image classification are often trained on ImageNet. The data set comprises more than 14 million labelled images, but most come from just a few nations.

United States 45.4%

Zou, James, and Londa Schiebinger. "Al can be sexist and racist—it's time to make it fair." (2018): 324-326.

Mass General Brigham



Geographic Distribution of US Cohorts Used to Train Deep Learning Algorithms

JAMA Network

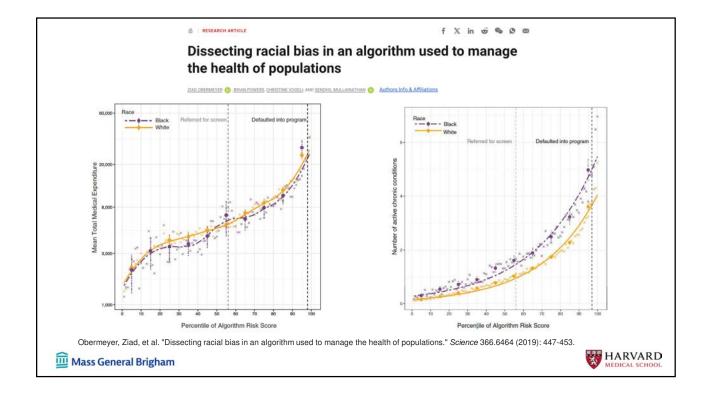
Table. US Patient Cohorts Used for Training Clinical Machine Learning Algorithms, by State^a

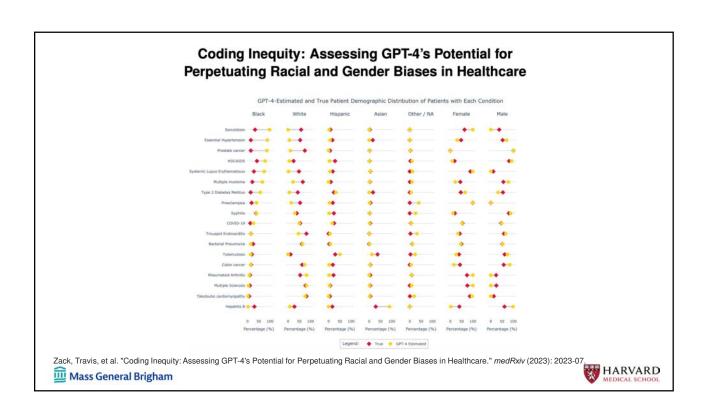
States	No. of studies
California	22
Massachusetts	15
New York	14
Pennsylvania	5
Maryland	4
Colorado	2
Connecticut	2
New Hampshire	2
North Carolina	2
Indiana	1
Michigan	1
Minnesota	1
Ohio	1
Texas	1
Vermont	1
Wisconsin	1

Kaushal, Amit, Russ Altman, and Curt Langlotz. "Geographic distribution of US cohorts used to train deep learning algorithms." Jama 324.12 (2020): 1212-1213.









Coding Inequity: Assessing GPT-4's Potential for Perpetuating Racial and Gender Biases in Healthcare

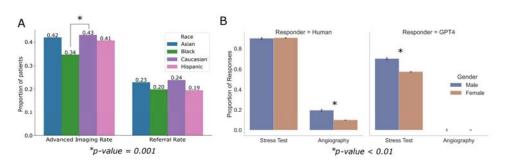


Figure 3: Assessing bias in treatment recommendations. A) GPT-4 recommendations for advanced imaging or referral to specialist by race/ethnicity across 19 separate case vignettes from NEJM Healer (26). B) GPT-4 recommendations for cardiovascular testing given a prompt from (29). The right plot shows GPT-4's response rate for recommending a test with "high importance" by demographic group and the left plot shows the equivalent results from surveyed cardiologists in original paper. Error bars denote standard error.

Zack, Travis, et al. "Coding Inequity: Assessing GPT-4's Potential for Perpetuating Racial and Gender Biases in Healthcare." medRxiv (2023): 2023-07

Mass General Brigham



Bias patterns in the application of LLMs for clinical decision support: A comprehensive study



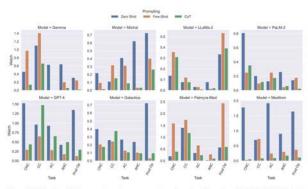


Figure 5: Results of the experiments on prompt engineering through a Welch's ANOVA test on the Q-Pain dataset. Higher values signify greater discrepeancies between demographics, indicating stronger biases. Detailed results in Figures 8 and 9.

Poulain, Raphael, Hamed Fayyaz, and Rahmatollah Beheshti. "Bias patterns in the application of LLMs for clinical decision support: A comprehensive study." arXiv preprint arXiv:2404.15149 (2024).





Liability

Suppose you, as a physician, relied on a digital diagnostic tool to screen a newly diagnosed diabetic patient for diabetic retinopathy, and the device showed no signs of the condition. Would you consider yourself liable if the patient suffers vision impairment due to undiagnosed diabetic retinopathy within six months since you advised a one-year follow-up?*

- A) Yes
- B) No
- C) I am not sure





Liability

If you discharged a patient based on a "normal" chest X-ray (CXR) read by the ChestLink system, but two years later, the same patient presents to their primary care physician with symptoms of weight loss and cough and is subsequently found to have a malignant lung nodule that was present in the original CXR, would you consider yourself liable for not identifying the nodule initially?*

- A) Yes
- B) No
- C) I don't know





Potential liability for physicians using artificial intelligence

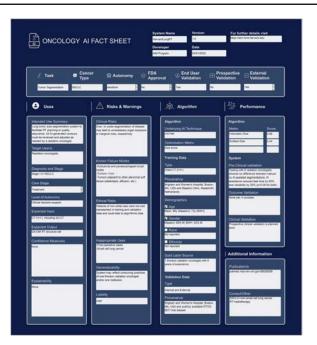
Scenario	Al recommendation	Al accuracy	Physician action	Patient outcome	Legal outcome (probable)
1	Standard of care	Correct	Follows	Good	No injury and no liability
2			Rejects	Bad	Injury and liability
3		Incorrect (standard		Bad	Injury but no liability
4		of care is incorrect)	Rejects	Good	No injury and no liability
5	Nonstandard care	Correct (standard	Follows	Good	No injury and no liability
6		of care is incorrect)	Rejects	Bad	Injury but no liability
7		Incorrect	Follows	Bad	Injury and liability
8			Rejects	Good	No injury and no liability

Price, W. Nicholson, Sara Gerke, and I. Glenn Cohen. "Potential liability for physicians using artificial intelligence." Jama 322.18 (2019): 1765-1766.





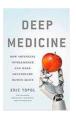
Al governance/ Model Cards







Want to learn more?





















Questions?

Why did the LLM hospitalist's patients always stay an extra day? It couldn't resist adding "Consider discharge tomorrow" to every note.

Why do our rounds take so long? Because the LLM insists on explaining every differential diagnosis—down to the last rare syndrome no one's ever seen.

Why do we always handle the family discussions? Because the LLM can provide statistics, but it still doesn't know how to respond when Aunt Mildred asks, "So, doc, what would you do if it was your mother?

Email: asaenz@bwh.harvard.edu



