

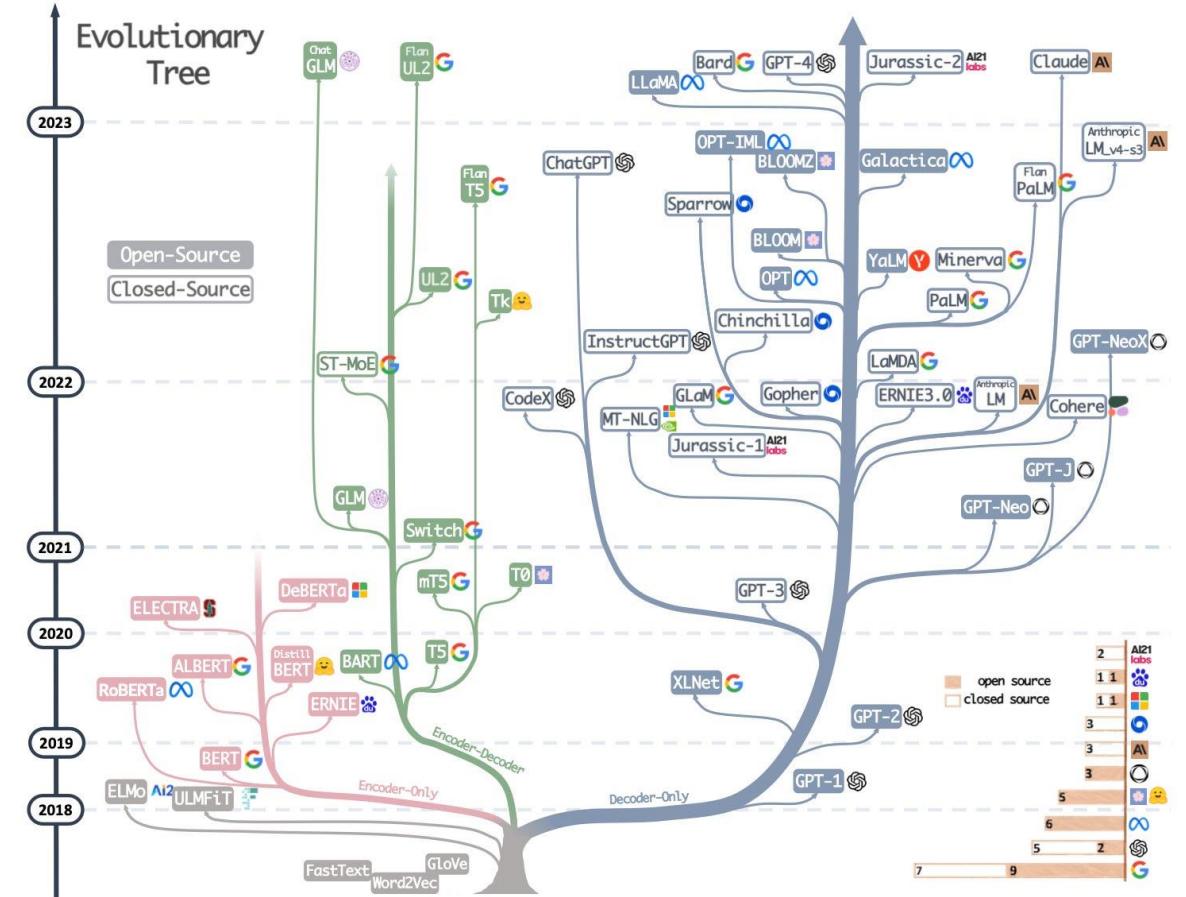
Large Language Models in Molecular Tumor Boards

Manuela Benary | May 21st, 2024
Core Unit Bioinformatics / Comprehensive Cancer Center
Charité / BIH

manuela.benary@bih-charite.de

Large Language Models as Subset of advanced deep learning models

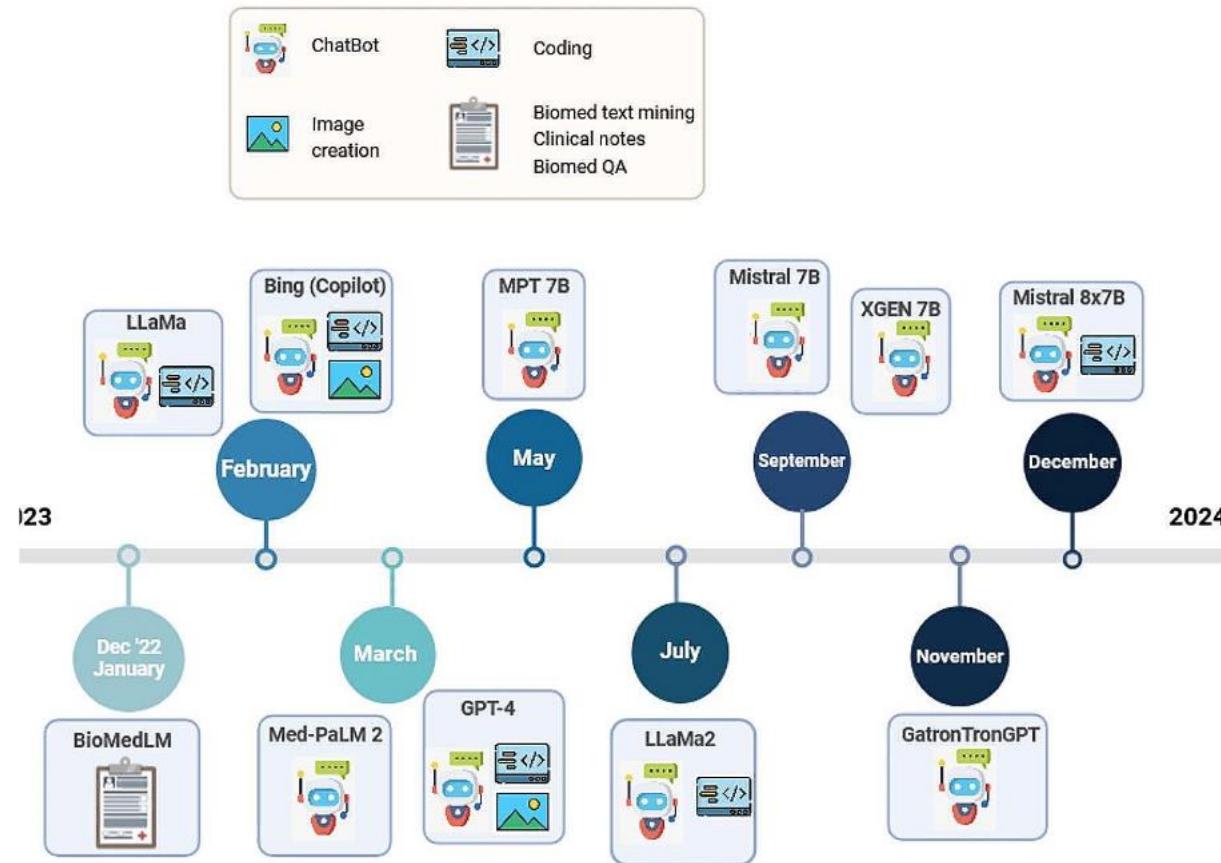
- **Variational autoencoder (VAE):**
 - Combining two Neural Networks (encoder and decoder)
 - Mostly focusing on images
- **Generative Adversarial Network (GAN):**
 - Combining two DNN – a generator and a discriminator
 - Competing against each other to generate images
 - Introduced 2014 (Ian Goodfellow)
- **Generative Pre-trained Transformer (GPT):**
 - semi-supervised learning (generative pretraining)
 - Autoregressive – predicting one token at a time
 - Decoder only models



Yang et al, 2023 <https://arxiv.org/pdf/2304.13712>

LLMs for Medicine: 1-Year Timeline and Perspectives

Cascella et al, 2024 (<https://doi.org/10.1007/s10916-024-02045-3>)

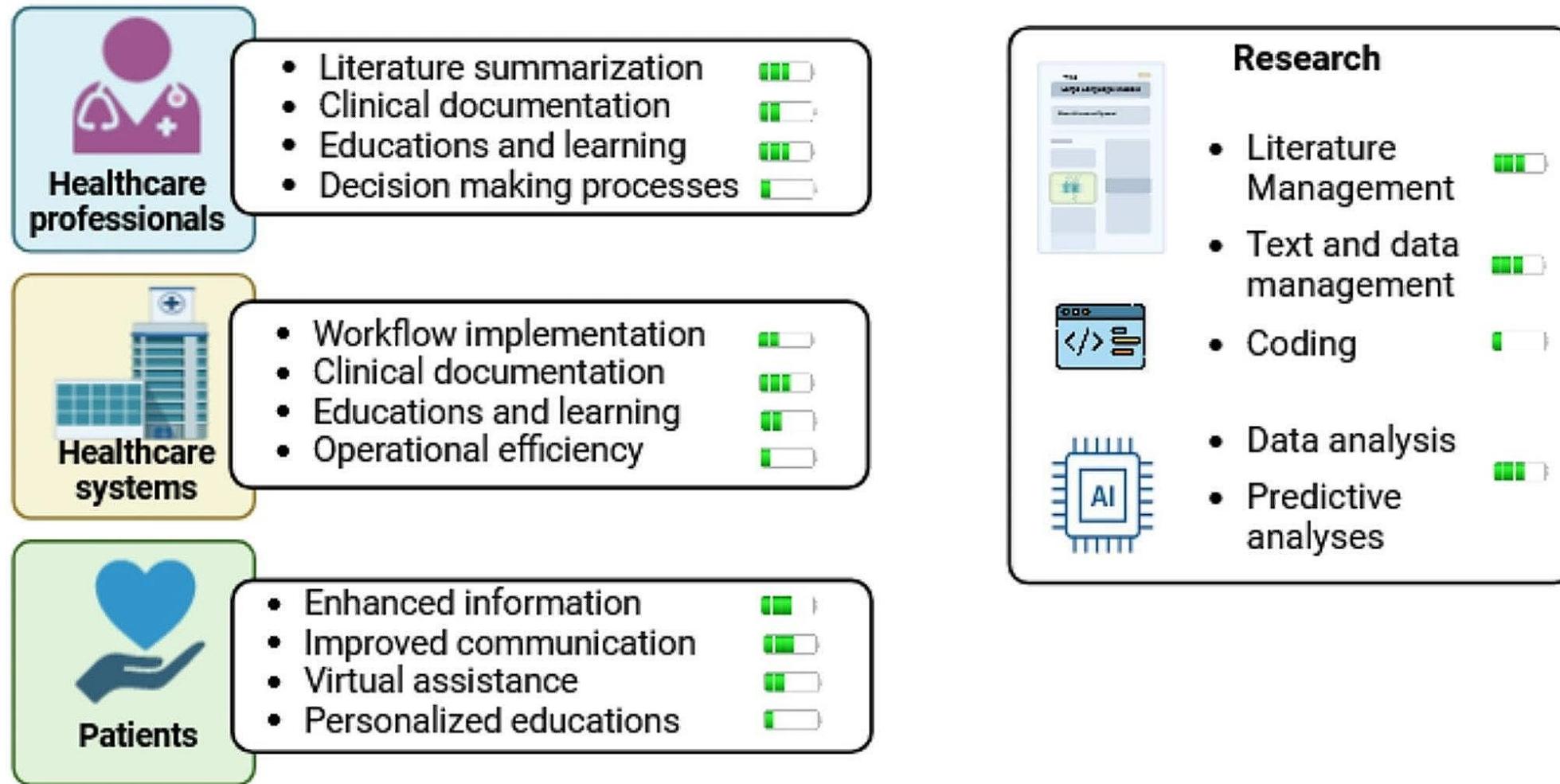


Six ways LLMs are changing healthcare

Webster, Nature Medicine, 2023, <https://doi.org/10.1038/s41591-023-02700-1>

- **Virtual nurses:** Conversation with patients, reminder of medications, care plans
- **Clinical note-taking:** Managing electronic health records (EHRs) and categorization of emails
- **Adverse-event detection:** Unearthing adverse events from clinical notes -> redaction of personal data necessary
- **Predicting cancer metastasis:** Using computer tomography reports to predict metastatic disease
- **Social determinants of health:** EHRs, discharge summary, social work, ...
- **Conversational AI diagnostics:** Combine machine learning (AI tools) in medical imaging domain with conversational Chatbots
- Not yet part of healthcare: **Personalized treatment recommendations using LLMs**

How chatbots (Large Language Models) support personalized medicine



What is precision oncology?

- ... determine therapies depending on **molecular characterization** of an individual patient
- Tumors are driven by genomic variations (“mutations”)
- **Different variants** – different prognosis & treatment
- **Targeted therapies:** **Drugs** whose applicability depend on the presence / absence of certain variants
 - 90% of all current late-stage anti-cancer drugs in developments
- For **rare cases**, often no clinical guidelines are available
 - Lack of sufficient patients for designing clinical trials
- only **14%** of cancer patients in the United States are treated with precision medicine, and only **7%** benefit (Paul Workman, Experts Forecast 2024, AACR)

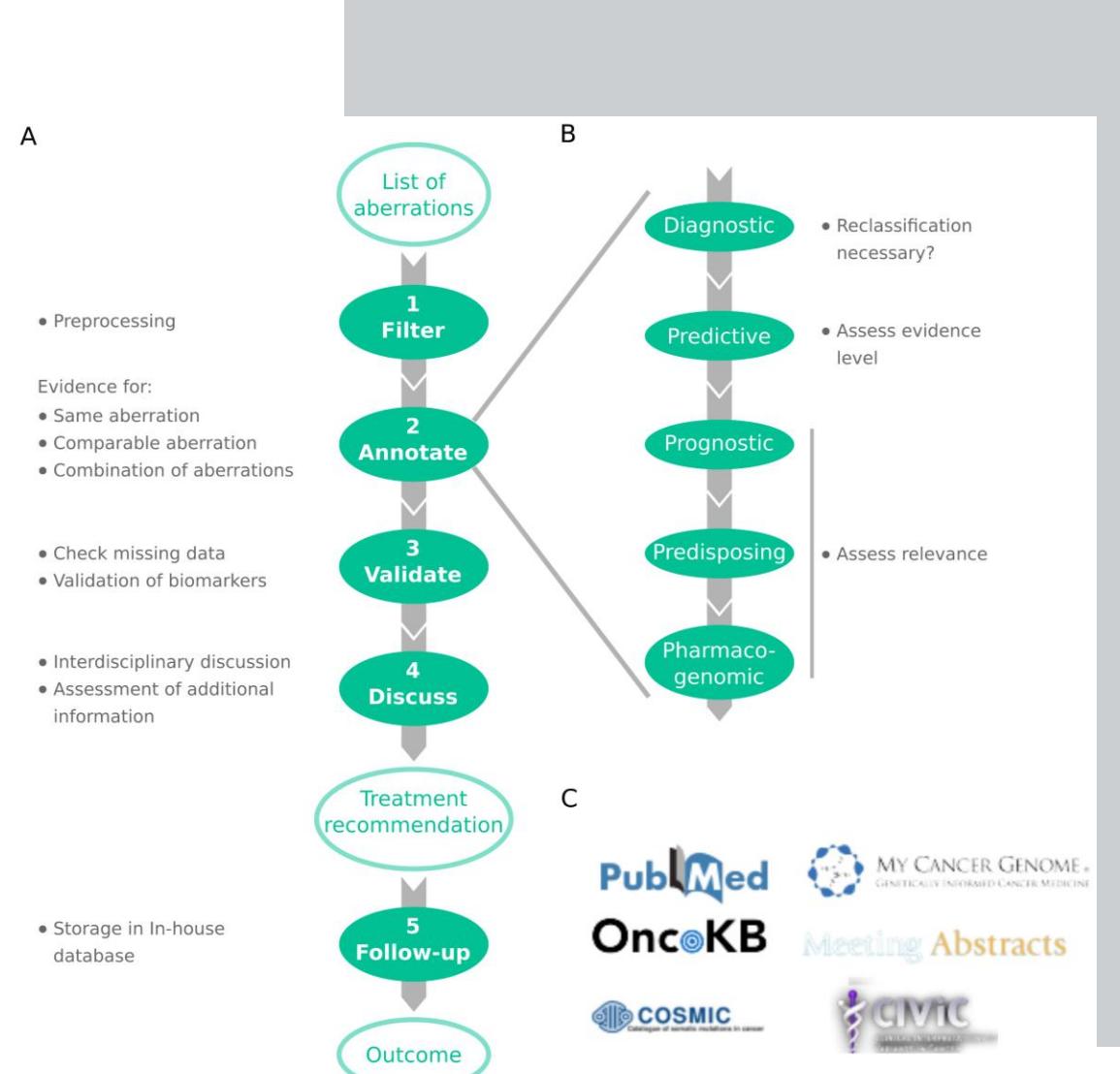
How can large language models help precision oncology?

What ChatGPT (3.5) says it can do

- **Data Analysis:** Large language models can analyze vast amounts of medical literature, research papers, and patient records related to oncology.
- **Identifying Patterns:** They can identify patterns in genetic mutations, treatment responses, and patient outcomes, aiding in the discovery of new insights and correlations.
- **Personalized Treatment Recommendations:** LLMs can assist oncologists in recommending personalized treatment options based on a patient's genetic profile, medical history, and current research findings.
- **Clinical Decision Support:** By analyzing patient data and clinical guidelines, LLMs can provide decision support to oncologists, helping them make informed decisions about treatment plans and interventions.
- **Natural Language Processing (NLP) for Patient Records:** LLMs can process unstructured text from electronic health records (EHRs) and pathology reports, extracting relevant information about diagnoses, treatments, and outcomes, which can facilitate research and improve patient care.
- **Drug Discovery and Development:** Large language models can aid in drug discovery by analyzing molecular structures, predicting drug interactions, and suggesting potential therapeutic targets based on genetic data and biomedical literature.
- **Patient Education and Communication:** LLMs can generate easy-to-understand educational materials for patients, explaining their diagnosis, treatment options, and prognosis in plain language, thus improving patient understanding and engagement in their own care.

Improving the decision process in precision oncology

- Preparing an MTB report is mostly manual work
- Expert knowledge influences recommendations
→ MTBs will differ in their suggestions
(Rieke et al, JCO PO 2018, Rieke et al, BMC Med 2022)
- Data bases are a great resource, but there is no “one-fits-all” solution (Pallarz et al, JCO PO 2019)



Lamping et al., Support of a molecular tumour board by an evidence-based decision management system for precision oncology, EJC 2020

1 Create fictional patients

Table. Patient Characteristics of Mock Patients in Analyzing of Artificial Intelligence Large Language Models

Variable	Participants, No. (%) (N = 10)
Age, median (IQR) [range], y	57 (48-59) [26-79]
Sex	
Female	3 (30)
Male	3 (30)
Unknown	4 (40)
Diagnosis	
Lung adenocarcinoma	4 (40)
Other	6 (60)
Tumor purity, median (IQR) [range], %	60 (50-77.5) [30-80]
Type of sequencing	
Panel	9 (90)
Whole exome sequencing	1 (10)
TMB, median (IQR) [range]	7.2 (3.2-11.1) [3.2-12.8]
Total variants, median (IQR) [range], No.	3.5 (3.0-4.75) [2.0-18.0]

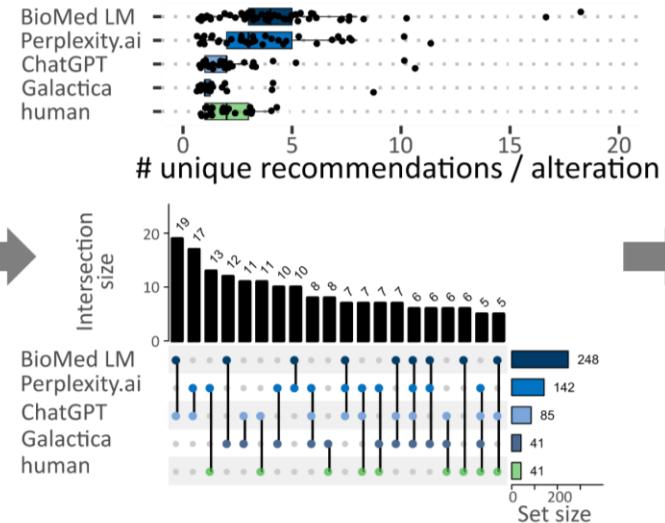
Abbreviation: TMB, tumor mutational burden.

2 Prepare annotations

Manual preparation
using standard procedures for discussion in molecular tumor board

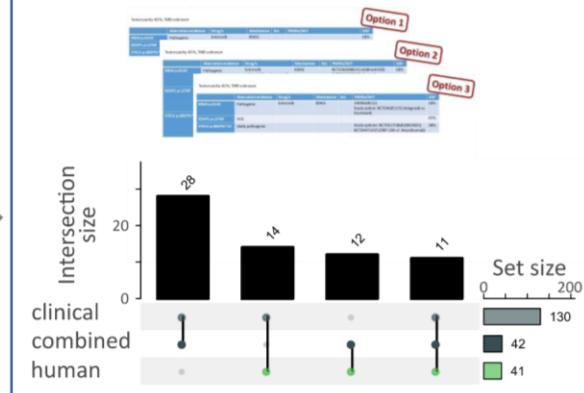
ChatGPT
175 B GPT 3.5, closed
Perplexity.ai
175 B GPT 3.5, closed
Galactica
30 B parameters
BioMed LM
2.7 B parameters

3 Condensed MTB slide



4 Survey to understand relevance in MTB

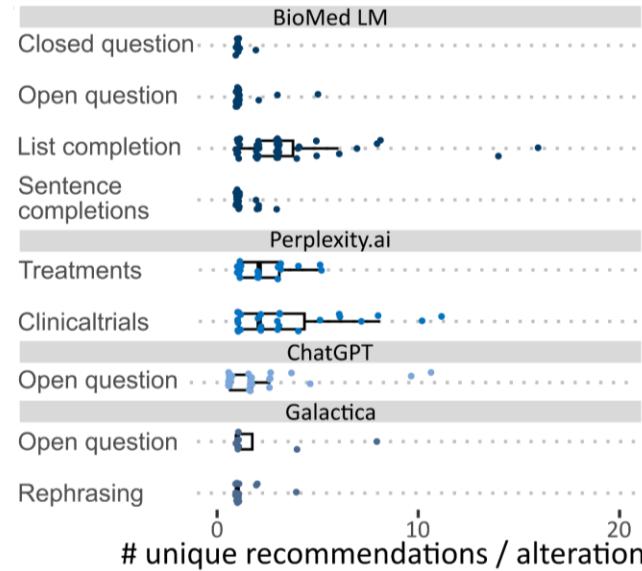
Condensed presentation



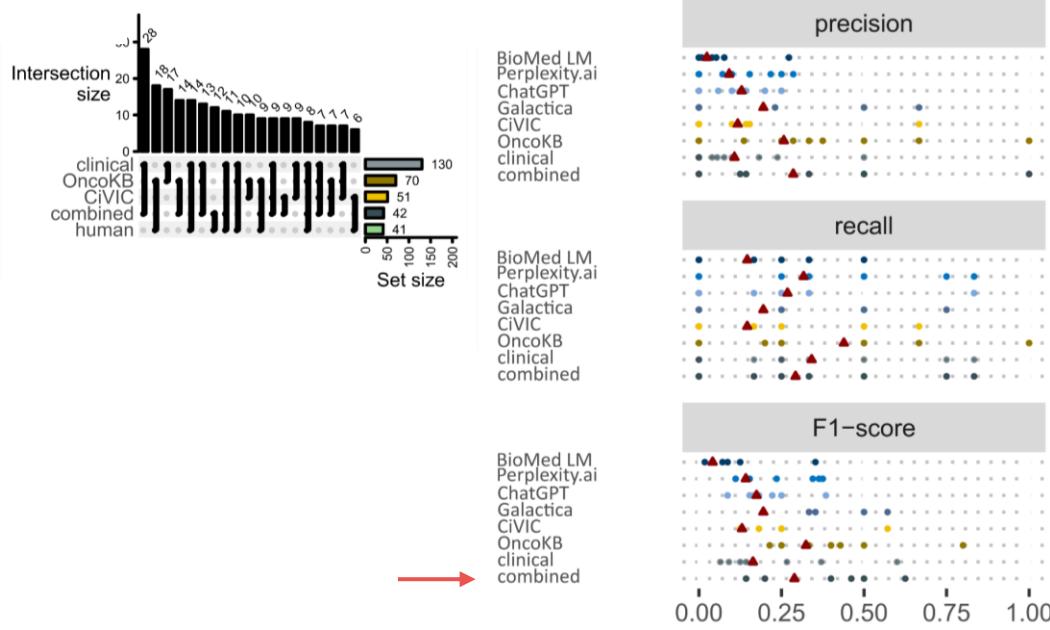
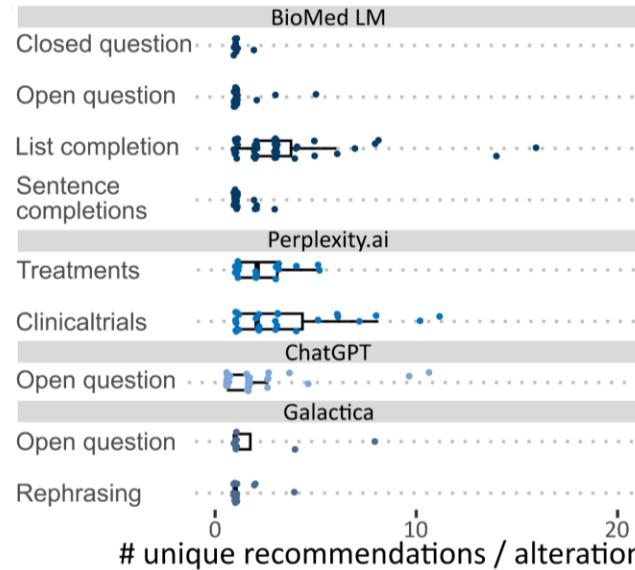
survey to understand presented options

- Number of recommendations vary between different LLMs
- Overlap with expert knowledge is very low
- Recommendations from LLMs are easily spotted by clinical experts

Type of prompting affects number of results from an LLM



Condensing recommendations improves concordance with expert knowledge



- **Precision:** how many of the predictions made are (clinically) correct?
- **Recall:** how many of the clinical recommendations were correctly predicted?
- **F1-score:** harmonic mean of precision and recall

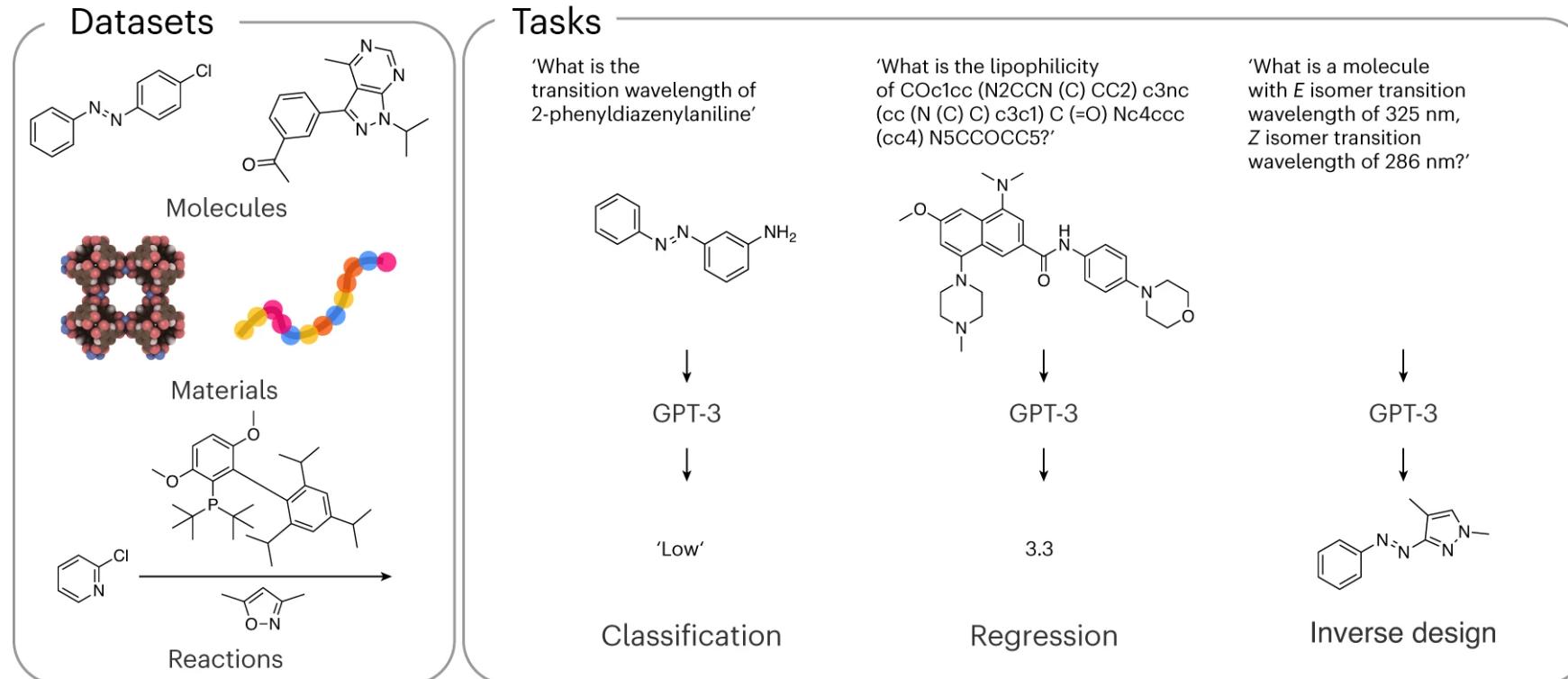
How can large language models help precision oncology?

What ChatGPT says it can do

- **Data Analysis:** Large language models can analyze vast amounts of medical literature, research papers, and patient records related to oncology.
- **Identifying Patterns:** They can identify patterns in genetic mutations, treatment responses, and patient outcomes, aiding in the discovery of new insights and correlations.
- **Personalized Treatment Recommendations:** LLMs can assist oncologists in recommending personalized treatment options based on a patient's genetic profile, medical history, and current research findings.
- **Clinical Decision Support:** By analyzing patient data and clinical guidelines, LLMs can provide decision support to oncologists, helping them make informed decisions about treatment plans and interventions.
- **Natural Language Processing (NLP) for Patient Records:** LLMs can process unstructured text from electronic health records (EHRs) and pathology reports, extracting relevant information about diagnoses, treatments, and outcomes, which can facilitate research and improve patient care.
- **Drug Discovery and Development:** Large language models can aid in drug discovery by analyzing molecular structures, predicting drug interactions, and suggesting potential therapeutic targets based on genetic data and biomedical literature.
- **Patient Education and Communication:** LLMs can generate easy-to-understand educational materials for patients, explaining their diagnosis, treatment options, and prognosis in plain language, thus improving patient understanding and engagement in their own care.

AI chatbot shows surprising talent for predicting chemical properties and reactions

Jablonka et al. Nature Machine Intelligence, 2024



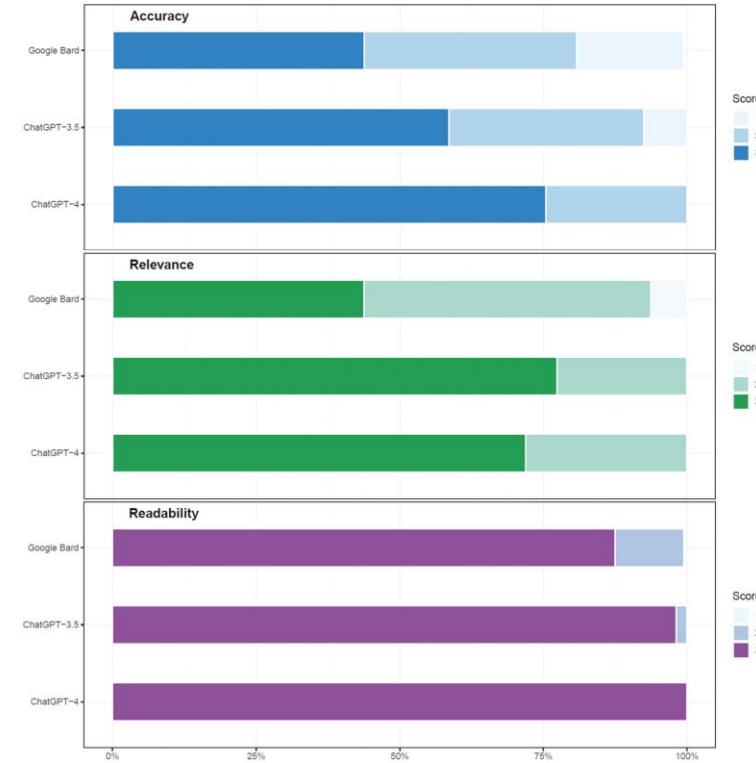
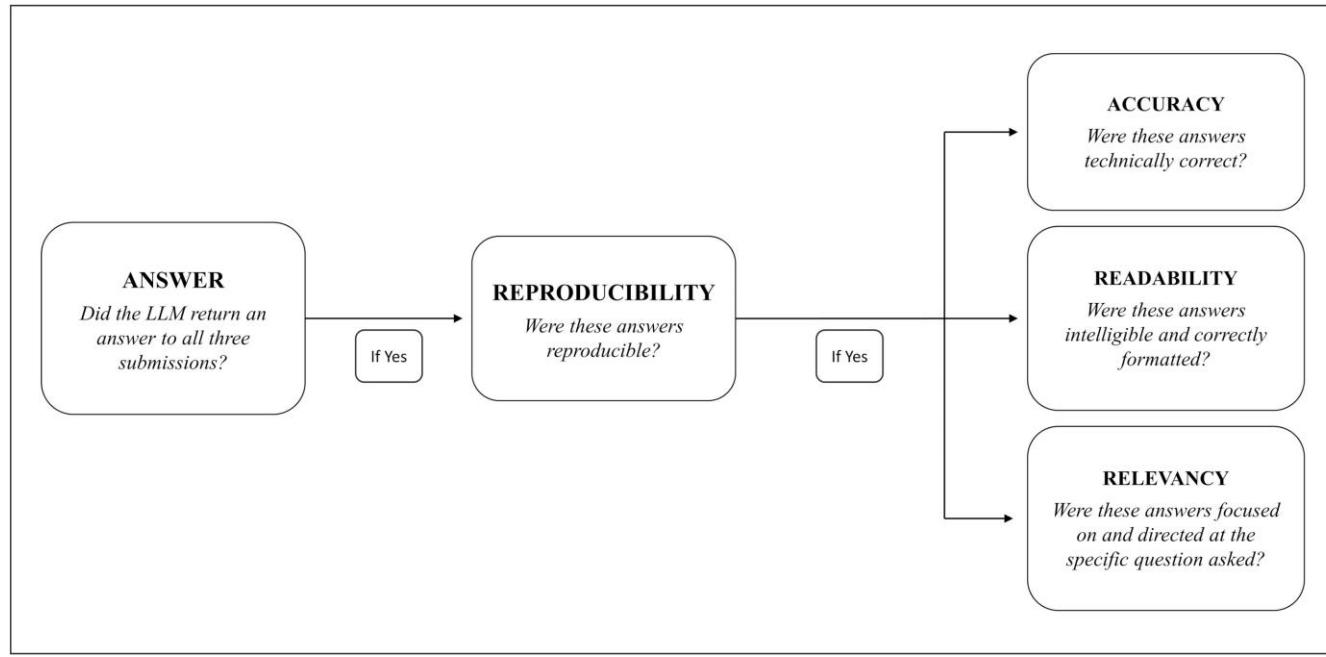
How can large language models help precision oncology?

What ChatGPT says it can do

- **Data Analysis:** Large language models can analyze vast amounts of medical literature, research papers, and patient records related to oncology.
- **Identifying Patterns:** They can identify patterns in genetic mutations, treatment responses, and patient outcomes, aiding in the discovery of new insights and correlations.
- **Personalized Treatment Recommendations:** LLMs can assist oncologists in recommending personalized treatment options based on a patient's genetic profile, medical history, and current research findings.
- **Clinical Decision Support:** By analyzing patient data and clinical guidelines, LLMs can provide decision support to oncologists, helping them make informed decisions about treatment plans and interventions.
- **Natural Language Processing (NLP) for Patient Records:** LLMs can process unstructured text from electronic health records (EHRs) and pathology reports, extracting relevant information about diagnoses, treatments, and outcomes, which can facilitate research and improve patient care.
- **Drug Discovery and Development:** Large language models can aid in drug discovery by analyzing molecular structures, predicting drug interactions, and suggesting potential therapeutic targets based on genetic data and biomedical literature.
- **Patient Education and Communication:** LLMs can generate easy-to-understand educational materials for patients, explaining their diagnosis, treatment options, and prognosis in plain language, thus improving patient understanding and engagement in their own care.

Comparison of Large Language Models in Answering Immuno-Oncology Questions: A Cross-Sectional Study

Iannantuono et al, The Oncologist, 2024



the risk of inaccuracy or incompleteness in the responses was evident in all 3 LLMs, highlighting the importance of expert-driven verification

Topics I haven't talked about

Practical challenges for precision medicine

The prediction of individual treatment responses with machine learning faces hurdles

FREDERIKE H. PETZSCHNER [Authors Info & Affiliations](#)

SCIENCE • 11 Jan 2024 • Vol 383, Issue 6679 • pp. 149-150 • DOI: 10.1126/science.adm9218

NEWS | 11 January 2024

Medical AI falters when assessing patients it hasn't seen

Physicians rely on algorithms for personalized medicine – but an analysis of schizophrenia trials shows that the tools fail to adapt to new data sets.

NATURE PODCAST | 22 December 2023

How AI works is often a mystery – that's a problem

The inner workings of many AIs are mysterious, but with increasing use of such technologies in high stakes scenarios, how should their inscrutable nature be dealt with?

Generative AI's environmental costs are soaring – and mostly secret



First-of-its-kind US bill would address the environmental costs of the technology, but there's a long way to go.



Research Square

Revolutionizing Personalized Medicine with Generative AI: A Systematic Review

Hans Mielke & Thomas Selhorst (Bundesinstitut für Risikobewertung)

Exploring AI and its Limits: Can Current Chatbots Truly Enhance Statistical Work? - von ChatGPT generiert

NEWS EXPLAINER | 16 February 2024

What the EU's tough AI law means for research and ChatGPT

The EU AI Act is the world's first major legislation on artificial intelligence and strictly regulates general-purpose models.

Thanks to ...



Ulf Leser

Xing Wang



Comprehensive Cancer Center
Universitätstumorzentrum

Ulrich Keilholz

Damian Rieke

Georg Hilfenhaus

Mani Nassir

Dominik Soll

Max Schmidt

Team of the MTB



Dieter Beule



Thanks for your attention!