Review

Accuracy of Large Language Models When Answering Clinical Research Questions: Systematic Review and Network Meta-Analysis

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Abstract

Background: Large language models (LLMs) have flourished and gradually become an important research and application direction in the medical field. However, due to the high degree of specialization, complexity, and specificity of medicine, which results in extremely high accuracy requirements, controversy remains about whether LLMs can be used in the medical field. More studies have evaluated the performance of various types of LLMs in medicine, but the conclusions are inconsistent.

Objective: This study uses a network meta-analysis (NMA) to assess the accuracy of LLMs when answering clinical research questions to provide high-level evidence-based evidence for its future development and application in the medical field.

Methods: In this systematic review and NMA, we searched PubMed, Embase, Web of Science, and Scopus from inception until October 14, 2024. Studies on the accuracy of LLMs when answering clinical research questions were included and screened by reading published reports. The systematic review and NMA were conducted to compare the accuracy of different LLMs when answering clinical research questions, including objective questions, open-ended questions, top 1 diagnosis, top 3 diagnosis, top 5 diagnosis, and triage and classification. The NMA was performed using Bayesian frequency theory methods. Indirect intercomparisons between programs were performed using a grading scale. A larger surface under the cumulative ranking curve (SUCRA) value indicates a higher ranking of the corresponding LLM accuracy.

Results: The systematic review and NMA examined 168 articles encompassing 35,896 questions and 3063 clinical cases. Of the 168 studies, 40 (23.8%) were considered to have a low risk of bias, 128 (76.2%) had a moderate risk, and none were rated as having a high risk. ChatGPT-4o (SUCRA=0.9207) demonstrated strong performance in terms of accuracy for objective questions, followed by Aeyeconsult (SUCRA=0.9187) and ChatGPT-4 (SUCRA=0.8087). ChatGPT-4 (SUCRA=0.8708) excelled at answering open-ended questions. In terms of accuracy for top 1 diagnosis and top 3 diagnosis of clinical cases, human experts (SUCRA=0.9001 and SUCRA=0.7126, respectively) ranked the highest, while Claude 3 Opus (SUCRA=0.9672) performed well at the top 5 diagnosis. Gemini (SUCRA=0.9649) had the highest rated SUCRA value for accuracy in the area of triage and classification.

Conclusions: Our study indicates that ChatGPT-4o has an advantage when answering objective questions. For open-ended questions, ChatGPT-4 may be more credible. Humans are more accurate at the top 1 diagnosis and top 3 diagnosis. Claude 3 Opus performs better at the top 5 diagnosis, while for triage and classification, Gemini is more advantageous. This analysis offers valuable insights for clinicians and medical practitioners, empowering them to effectively leverage LLMs for improved decision-making in learning, diagnosis, and management of various clinical scenarios.

Trial Registration: PROSPERO CRD42024558245; https://www.crd.york.ac.uk/PROSPERO/view/CRD42024558245

(J Med Internet Res 2025;27:e64486) doi: 10.2196/64486

KEYWORDS

large language models; LLM; clinical research questions; accuracy; network meta-analysis; PRISMA

Introduction

Recent research has demonstrated the considerable success of large language models (LLMs) in a multitude of natural language tasks, including automatic summarization (the generation of a condensed version of a passage of text), machine translation (the automatic translation of text from one language to another), and question-and-answer systems (the construction of a system to automatically answer questions based on a passage of text) [1]. In this context, with the development of big biomedical data and artificial intelligence, the emergence of flexible natural language processing models such as ChatGPT provides a number of new possibilities for health care and biomedical research and has the potential to be a turning point in the field [2-4].

Although LLMs have shown great potential in the medical field, medicine is a demanding field, it is associated with life, and its complexity as well as specificity mean that any application must meet extremely high standards of accuracy. Controversy remains about whether LLMs can be applied to the medical field. Mu and He [5] reviewed the potential applications and challenges of ChatGPT in health care, noting that a lack of understanding of medical knowledge and specialized medical backgrounds hinder the ability of ChatGPT to delve into the complexity of medical concepts and terminology. Consequently, the capacity of ChatGPT to address specific medical queries, diagnose ailments, or furnish precise medical recommendations is restricted. Another study noted that the role of LLMs in health care may be limited by the presence of bias in training materials, their tendency to "hallucinate," and ethical and legal considerations when LLMs provide inaccurate advice that leads to patient harm, as well as patient privacy issues [6].

Given the controversy over the application of LLMs in medicine and the continuous emergence and versioning of LLMs, more research has been devoted to evaluating the performance of various LLMs in medicine to provide stronger evidence. In addition to ChatGPT developed by OpenAI, the performance of many other LLMs such as Microsoft (eg, Copilot [7]), Google (eg, Gemini [8]), and Meta (eg, LLaMA [9]) in the medical domain has also been compared. Many aspects of assessment have been included, such as medical exams [10], case text diagnosis [11], and disease classification or grading [12].

Unfortunately, there are differences in the performance of different LLMs in different studies. For example, in a study by Vaishya et al [13] that explored the performance of ChatGPT-3.5, ChatGPT-4, and Google Bard when answering 120 multiple-choice questions, the results showed that Google Bard had 100% accuracy and was significantly more accurate than both ChatGPT-3.5 and ChatGPT-4 (P<.001). Another study showed that ChatGPT-4 was more accurate than Google Bard (83% vs 76%) [14]. At present, most related research is limited to a single type of LLM [15,16] or a specific domain area [17,18], and there is no high-level evidence comparing the accuracy rankings of different LLMs when responding to clinical research questions.

Therefore, this study aimed to compare the accuracy of different LLMs when answering clinical research questions, including objective questions, open-ended questions, top 1 diagnosis, top 3 diagnosis, top 5 diagnosis, and triage and classification. This study aimed to provide high-level evidence-based support for future clinical applications, enabling clinical workers to better use LLMs to make more accurate and informed decisions for future learning, diagnosis, and different clinical scenarios.

Methods

Network Meta-Analysis

The network meta-analysis (NMA) was based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guidelines. The PRISMA checklist is shown in Multimedia Appendix 1. The Bayesian approach permits the indirect comparison of performance between a range of LLMs that were not explicitly articulated throughout the experiment. The study protocol was defined and registered in the PROSPERO database prior to the commencement of the study.

Search Strategy and Selection Criteria

A computer search of the PubMed, Embase, Web of Science, and Scopus databases was conducted to identify relevant studies on the accuracy of different LLMs when answering questions in the medical field. The last search was updated to October 14, 2024, to identify studies published since the first search, with no restrictions on the type of study. When the results of a study were reported in multiple publications, we included the study with the richest and most recent findings. We also searched the list of literature on LLMs in medicine-related systematic reviews and manually searched the references included in the reviews for additional access to relevant literature. The search subject terms were "LLM," "generative AI," "open AI," "Large language model," "ChatGPT-3.5," "ChatGPT-4," "Google

Bard," and "Bing," without any language restriction. The complete search strategies for all databases are shown in Multimedia Appendix 2.

A combination of EndNote X9 deduplication and manual deduplication was used to screen the literature in accordance with the developed inclusion criteria. The results of the literature searches conducted in different databases were then combined to create a new information database, which could be downloaded in full text. Independent review and assessment of the titles, abstracts, and full texts of the relevant literature were undertaken by 4 authors (LW, JL, BZ, and SH). The review encompassed studies using disparate LLMs systems to respond to medical queries. Letters, conference abstracts, editorials, reviews, and expert opinions for which no information was available were excluded from the review. In addition, the following studies were excluded: those that evaluated the performance of only 1 LLM; those that assessed the performance of 2 or more LLMs without specifying the LLM versions used (eg, the article only mentioned evaluating ChatGPT without mentioning ChatGPT-3.5, ChatGPT-4, or other versions), with the updated versions and timelines of various LLMs so far shown in Multimedia Appendix 3; those that assessed the performance of 2 or more LLMs but did not provide data isolating their accuracy when answering different types of questions; and the questions included in the study contained images. In addition, to reduce bias, we excluded research on accessing LLMs through an application programming interface (API).

Assessment of Results

The primary outcomes were the accuracy of LLMs when answering medical questions. These included objective questions, open-ended questions, top 1 diagnosis, top 3 diagnosis, top 5 diagnosis, and triage and classification accuracy. Objective questions are exam questions with a clear, quantifiable answer that is usually predetermined, unique, or with a limited number of options. Open-ended questions are a type of question that does not have a fixed answer nor standardized answer. Diagnosis and triage and classification are open-ended questions, but most diagnostic questions end with "What is the most probable diagnosis?" whereas triage and classification questions end with "How would you classify this disease?" Corresponding examples are shown in Multimedia Appendix 4.

Accuracy for objective questions was calculated as the number of correctly answered questions divided by the total number of questions. For diagnosis and classification, accuracy was defined as the number of cases correctly diagnosed or triaged divided by the total number of cases. Specifically for open-ended questions, accuracy was determined based on the number of questions rated "good" or "accurate" on the accuracy scale divided by the total number of questions.

Data Extraction

The 4 researchers jointly extracted and verified the following data: (1) basic information about the included studies, such as study title and first author; (2) baseline characteristics and interventions of the study population; (3) key elements evaluated for risk of bias; and (4) outcome indicators and relevant outcome measure data. Our study involved extracting raw data from each study. In cases of disagreement, these were resolved through discussion and consultation with a third party.

Quality Assessment

Because they were cross-sectional studies, the quality of the included studies was evaluated using the Newcastle-Ottawa Scale [19]. The quality assessment was conducted by 3 independent researchers (LW, JL, and BZ), with a fourth researcher (SH) resolving any disagreements. A low overall risk of bias was determined when the Newcastle-Ottawa Scale score ranged from 7 to 9, moderate risk was determined when the score was between 4 and 6, and high risk was determined when the score was 0 to 3.

Statistical Analyses

Statistical analyses were performed using Stata 18.0 and R (version 4.3.1), with the odds ratio (OR) as the analytical statistic. Accuracy was assessed using 95% CIs and the credible interval. NMA analyses were performed on different types of LLMs.

The confidence of the NMA results estimates was assessed according to the Confidence in Network Meta-Analysis (CINEMA) methodology, which is broadly based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). An NMA was conducted within a Bayesian framework using Markov chain Monte Carlo methods and was computed using the BUGSnet and GeMTC packages in R (V.4.3.1) software. A network graph was constructed for each LLM included in the experiment in order to facilitate a comparison of the performance of multiple LLMs. The consistency between direct and indirect evidence was evaluated using a node-splitting method when there was a closed loop. If the *P* value between the direct, indirect, and network comparisons of the 2 interventions was >.05, we concluded that there was no statistical difference and consistency was good. The convergence of the network models derived from the Markov chain Monte Carlo simulations was assessed using trace and density plots. We used noninformative priors for all parameters and assumed common heterogeneity. Furthermore, for all LLMs, we determined the ranking probabilities, which were articulated as the surface under the cumulative ranking curve (SUCRA). Higher SUCRA values suggest superior accuracy in model ranking.

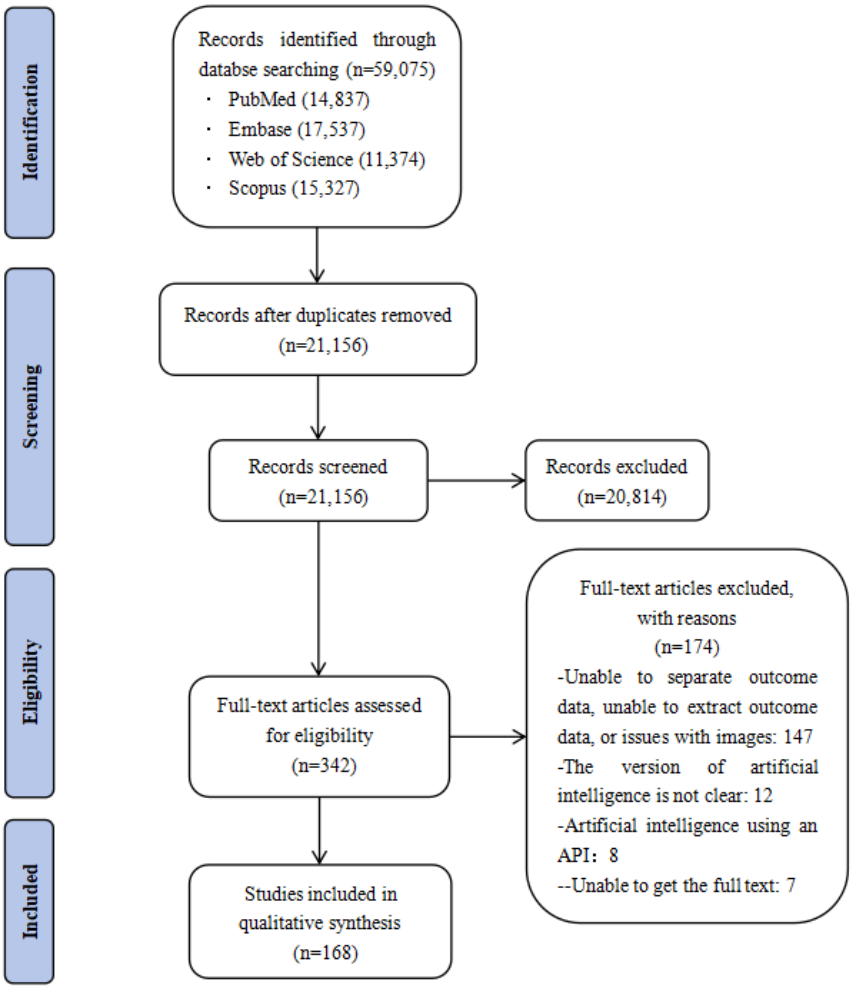
Results

Literature Search and Selection

A bibliographic search yielded 59,075 citations, of which 21,156 studies were identified as potential conditions based on abstract screening and retrieved for full text evaluation. Manual reading of the titles and abstracts of the remaining literature excluded 20,814 papers whose topics and interventions did not match the inclusion criteria for this study. Further reading of the full texts excluded the following: 174 articles that could not be separated nor extracted from the ending; 147 articles in which we were unable to separate outcome data, unable to extract outcome data, or detected issues related to images; 12 articles with unclear versions of the LLMs; and 8 articles that used an API to access

LLMs. In addition, the full text of 7 articles was not available, resulting in the final inclusion of 168 articles from the literature. The literature screening process is shown in Figure 1.

Figure 1. Literature screening flowchart. API: application programming interface.



Basic Characteristics of the Incorporated Literature

To assess the accuracy of different LLMs when answering medical questions, a total of 168 studies underwent a screening process to determine their suitability for inclusion. A total of 35,896 questions and 3063 clinical cases were included in the study. The basic information of the 168 studies is presented in Multimedia Appendix 5.

Quality Assessment of the Included Studies

In the quality assessment, 40 (40/168, 23.8%) studies were assessed as having a low overall risk of bias, while 128 (128/168, 76.2%) had a moderate overall risk of bias. No studies were identified as having a high overall risk of bias. The detailed quality assessment results for each study can be found in Multimedia Appendix 6.

Network Meta-Analysis

Objective Questions

The accuracy of LLMs when answering objective questions was reported in 105 studies [10,13,14,20-121]. The evidence network relationships are plotted in Figure 2A and involve 30 LLMs and a total of 33,838 multiple choice questions. Direct and indirect comparisons were formed for each LLM, partially forming a closed loop. The results of the indirect comparison are shown in Figure 3 and Multimedia Appendix 7. The red cells indicate there are statistically significant differences between the column-defining regimen and the row-defining regimen. The values in the green and blue cells are the logOR and 95% CI, respectively, from the comparison of the LLMs represented in the columns with the LLMs represented in the rows. A logOR value <0 indicates that the accuracy of the LLM corresponding to a column is lower than the LLM corresponding to a row. A value >0 indicates a higher accuracy. There was no evidence of statistically significant inconsistency (all $P>.05$) in the node-splitting test for NMA, except for Claude 2 versus ChatGPT-4 ($P=.04$), Bing chat versus people ($P=.004$), and Perplexity versus people ($P=.04$; Multimedia Appendix 8). The convergence of iterations was evaluated as good in trace and density plots, with the bandwidth tending toward 0 and reaching stability (Multimedia Appendix 9). The best probability ranking showed that ChatGPT-4o (SUCRA=0.9207) ranked first in terms of accuracy when answering objective questions, Aeyeconsult (SUCRA=0.9187) ranked second, and ChatGPT-4 (SUCRA=0.8087) ranked third (Table 1, Figure 4A).

Figure 2. Comparison network diagram of different outcomes, where larger nodes indicate more questions and thicker line segments indicate more questions between 2 types of large language models (LLMs) when answering (A) objective questions, (B) open-ended questions, (C) a top 1 diagnosis, (D) a top 3 diagnosis, (E) a top 5 diagnosis, and (F) triage and classification questions.

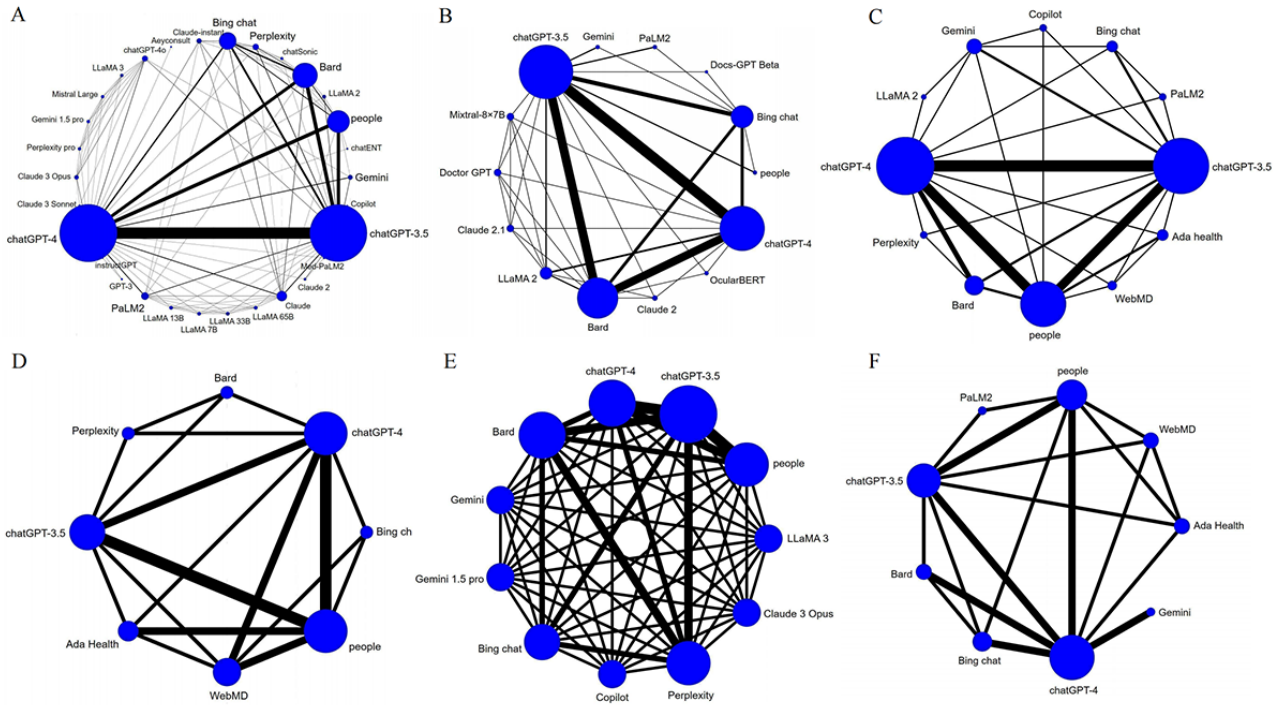


Figure 3. Indirect comparison of the accuracy of large language models (LLMs) when answering objective questions: A: instructGPT; A1: LLaMA 2; B: GTP-3; B1: LLaMA 3; C: ChatGPT-3.5; D: ChatGPT-4; D1: Mistral Large; E: ChatGPT-4o; E1: people; F1: chatENT; G: Bard; G1: ChatSonic; H: PaLM2; H1: Aeyeconsult; I: Gemini; I1: Med-PaLM 2; K: Gemini 1.5 pro; L: Bing chat; M: Copilot; N: Perplexity; O: Perplexity Pro; P: Claude; Q: Claude-instant; R: Claude 2; T: Claude 3 Opus; U: Claude 3 Sonnet; W: LLaMA 7B; X: LLaMA 13B; Y: LLaMA 33B; Z: LLaMA 65B.

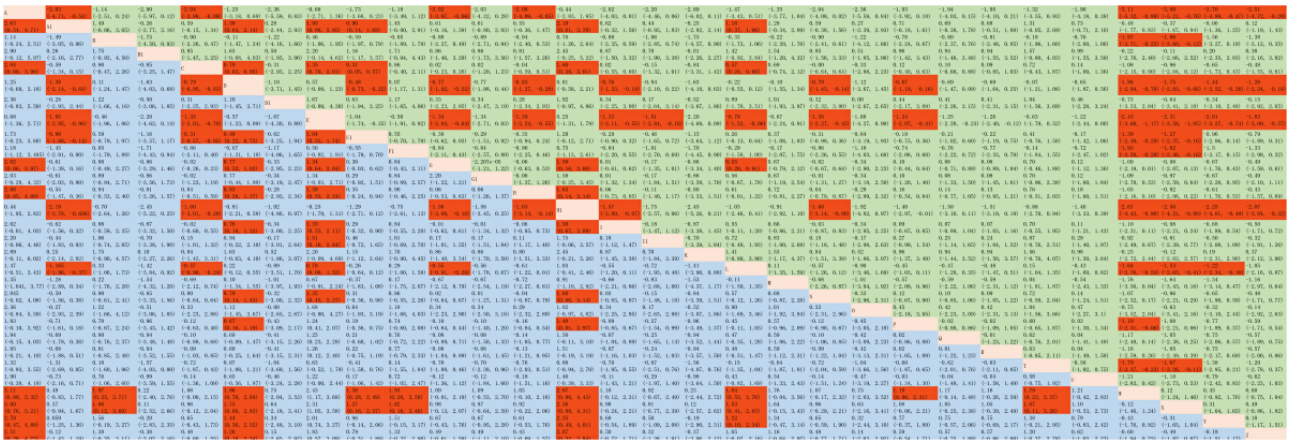
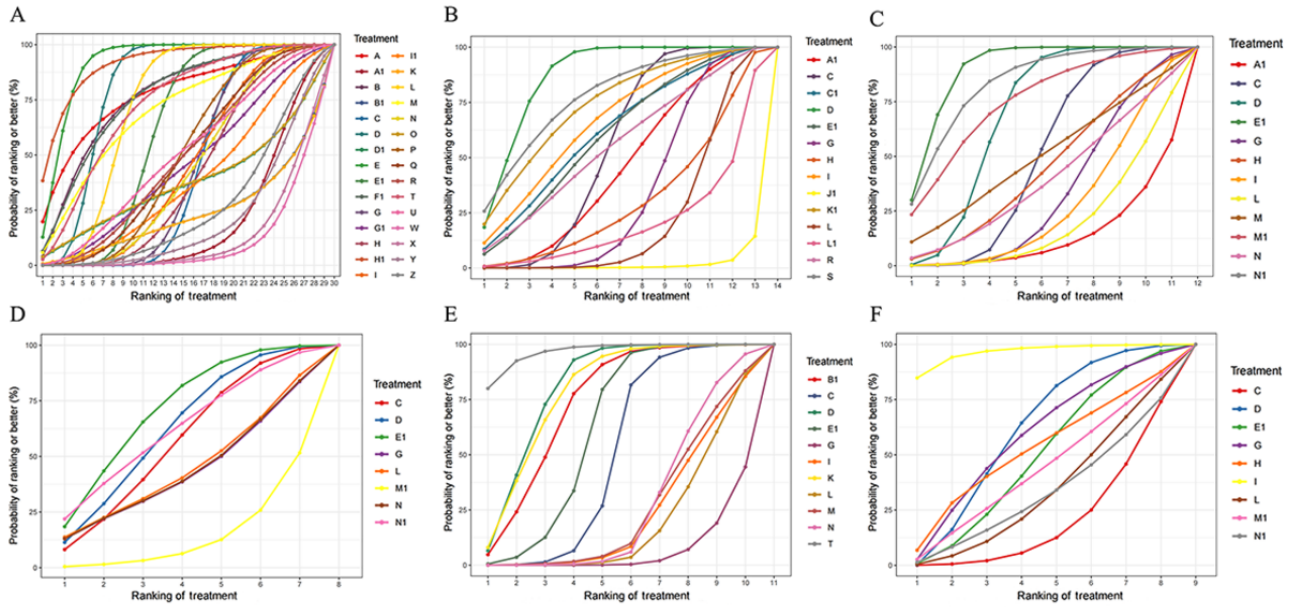


Table 1. Bayesian ranking results (surface under the cumulative ranking curve [SUCRA] value) of the network meta-analysis for each large language model (LLM).

LLM	SUCRA					
	Objective questions	Open-ended questions	Top 1 diagnosis	Top 3 diagnosis	Top 5 diagnosis	Triage and classification
instructGPT (A)	0.7805	__[a]	—	—	—	—
LLaMA 2 (A1)	0.2086	0.4629	0.1395	—	—	—
GTP-3 (B)	0.7704	—	—	—	—	—
LLaMA 3 (B1)	0.239	—	—	—	0.7405	—
ChatGPT-3.5 (C)	0.4343	0.5548	0.5039	0.565	0.5084	0.2093
Mixtral-8x7B (C1)	—	0.6224	—	—	—	—
ChatGPT-4 (D)	0.8087	0.8708	0.693	0.6302	0.8089	0.6185
Mistral Large (D1)	0.3842	—	—	—	—	—
ChatGPT-4o (E)	0.9207	—	—	—	—	—
People (E1)	0.6172	0.6067	0.9001	0.7126	0.6241	0.4934
chatENT (F1)	0.7687	—	—	—	—	—
Bard (G)	0.4443	0.3512	0.3353	0.4329	0.0722	0.5885
ChatSonic (G1)	0.4617	—	—	—	—	—
PaLM2 (H)	0.421	0.312	0.4496	—	—	0.5197
Aeyeconsult (H1)	0.9187	—	—	—	—	—
Gemini (I)	0.4543	0.6703	0.2812	—	0.2405	0.9649
Med-PaLM 2 (I1)	0.3919	—	—	—	—	—
OcularBERT (J1)	—	0.0176	—	—	—	—
Gemini 1.5 pro (K)	0.2449	—	—	—	0.7905	—
Doctor GPT (K1)	—	0.745	—	—	—	—
Bing chat (L)	0.728	0.23	0.2073	0.4499	0.2042	0.3391
Docs-GPT Beta (L1)	—	0.212	—	—	—	—
Copilot (M)	0.7038	—	0.5048	—	0.2633	—
WebMD (M1)	—	—	0.7511	0.1452	—	0.4348
Perplexity (N)	0.4424	—	0.3980	0.4367	0.2801	—
Ada Health (N1)	—	—	0.8363	0.6273	—	0.3319
Perplexity Pro (O)	0.3821	—	—	—	—	—
Claude (P)	0.5048	—	—	—	—	—
Claude-instant (Q)	0.4949	—	—	—	—	—
Claude 2 (R)	0.4928	0.5647	—	—	—	—
Claude 3 Opus (T)	0.7365	—	—	—	0.9672	—
Claude 3 Sonnet (U)	0.5094	—	—	—	—	—
LLaMA 7B (W)	0.1131	—	—	—	—	—
LLaMA 13B (X)	0.1365	—	—	—	—	—
LLaMA 33B (Y)	0.2147	—	—	—	—	—
LLaMA 65B (Z)	0.2721	—	—	—	—	—

[a]Not applicable because the LLM was not in the network.

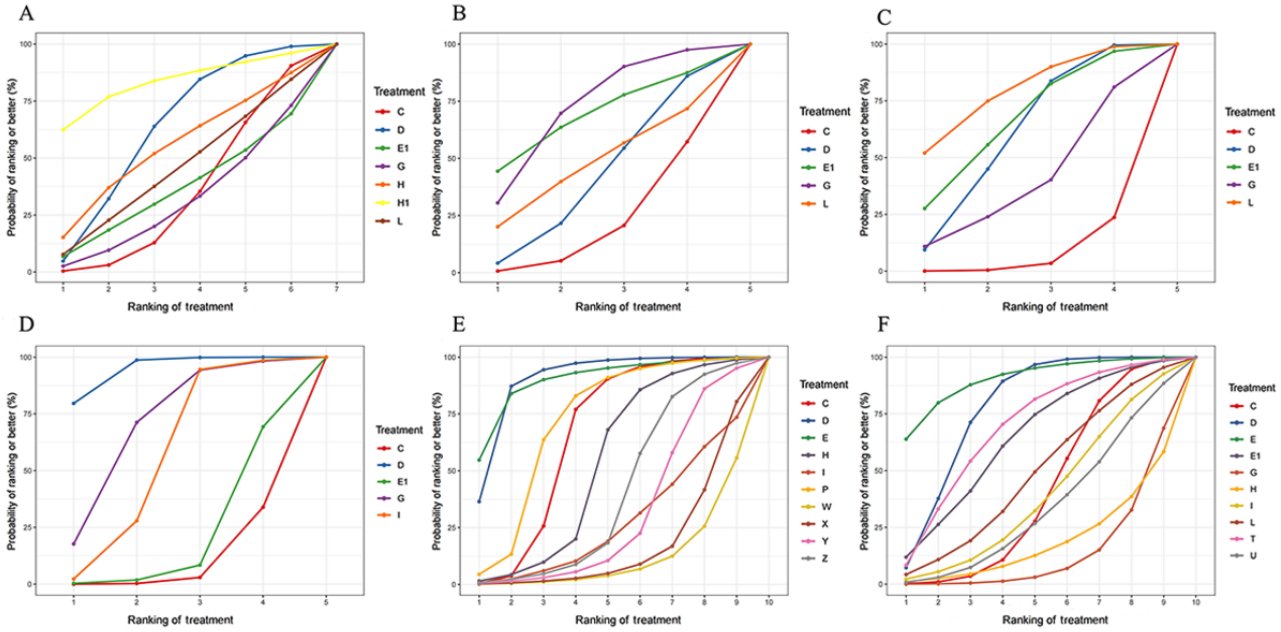
Figure 4. Surface under the cumulative ranking curve (SUCRAs) for the accuracy, with higher rankings associated with larger outcome values, of different large language models (LLMs) when answering (A) objective questions, (B) open-ended questions, (C) the top 1 diagnosis, (D) the top 3 diagnosis, (E) the top 5 diagnosis, and (F) triage and classification questions. The letters in the keys indicate the following LLMs: A: instructGPT; A1: LLaMA 2; B: GTP-3; B1: LLaMA 3; C: ChatGPT-3.5; C1: Mixtral-8x7B; D: ChatGPT-4; D1: Mistral Large; E: ChatGPT-4o; E1: people; F1: chatENT; G: Bard; G1: ChatSonic; H: PaLM2; H1: Aeyeconsult; I: Gemini; I1: Med-PaLM 2; J1: OcularBERT; K: Gemini 1.5 pro; K1: Doctor GPT; L: Bing chat; L1: Docs-GPT Beta; M: Copilot; M1: WebMD; N: Perplexity; N1: Ada Health; O: Perplexity Pro; P: Claude; Q: Claude-instant; R: Claude 2; S: Claude 2.1; T: Claude 3 Opus; U: Claude 3 Sonnet; W: LLaMA 7B; X: LLaMA 13B; Y: LLaMA 33B; Z: LLaMA 65B.



Subgroup Analysis

We stratified the results based on the fields of the problem (Multimedia Appendix 10). Based on the results, we compared the accuracy of LLMs in 6 fields: ophthalmology, orthopedics, urology, dentistry, oncology, and radiology. In ophthalmology, the LLM with the highest accuracy was Aeyeconsult (SUCRA=0.8334), followed by ChatGPT-4 (SUCRA=0.6331) and PaLM2 (SUCRA=0.5517). In the field of orthopedics, the LLM accuracy rates, from highest to lowest, were for Bard (SUCRA=0.7219), people (SUCRA=0.6802), and Bing chat (SUCRA=0.4732). For urology, Bing chat (SUCRA=0.7905) was the most accurate, followed by people (SUCRA=0.6587) and ChatGPT-4 (SUCRA=0.5941). In dentistry, ChatGPT-4 (SUCRA=0.9473) was the most accurate, followed by Bard (SUCRA=0.7068) and Gemini (SUCRA=0.5535). ChatGPT-4 (SUCRA=0.9002) performed the best in oncology, followed by ChatGPT-4o (SUCRA=0.8998) and Claude (SUCRA=0.7159). In radiology, ChatGPT-4o (SUCRA=0.9053) performed the best, ChatGPT-4 (SUCRA=0.7777) was second, and Claude 3 Opus (SUCRA=0.6935) ranked third. The SUCRAs are shown in Figure 5.

Figure 5. Surface under the cumulative ranking curve (SUCRAs) for the accuracy, with higher rankings associated with larger outcome values, of different large language models (LLMs) in (A) ophthalmology, (B) orthopedics, (C) urology, (D) dentistry, (E) oncology, and (F) radiology. The letters in the keys indicate the following LLMs: C: ChatGPT-3.5; D: ChatGPT-4; E: ChatGPT-4o; E1=people; G: Bard; H: PaLM2; H1: Aeyeconsult; I: Gemini; L: Bing chat; P: Claude; T: Claude 3 Opus; U: Claude 3 Sonnet; W: LLaMA 7B; X: LLaMA 13B; Y: LLaMA 33B; Z: LLaMA 65B.



Open-Ended Questions

The accuracy of the LLMs when responding to open-ended questions was examined in 34 studies [122-155]. The relationships within the evidence network are plotted in Figure 2B and include 14 LLMs and a total of 2026 open-ended questions. Direct and indirect comparisons were formed for each LLM, partially forming a closed loop. The results of the indirect comparison are presented in Multimedia Appendix 10, where red cells indicate statistically significant differences between the column-defining regimen and the row-defining regimen (Multimedia Appendix 7). There was no evidence of a statistically significant inconsistency (all P>.05) in the node-splitting test for the NMA, except for Bard versus ChatGPT-3.5 (P=.02; Multimedia Appendix 8). The trace and density plots are shown in Multimedia Appendix 9**,** and from the results, the iterative convergence was good. The best probability ranking indicated that ChatGPT-4 (SUCRA=0.8708) exhibited the highest accuracy when answering open-ended questions, followed by Claude 2.1 (SUCRA=0.7796) and Doctor GPT (SUCRA=0.7450; Table 1, Figure 4B).

Top 1 Diagnosis, Top 3 Diagnosis, and Top 5 Diagnosis

The accuracy of the top 1 diagnosis in clinical cases by LLMs was reported in 19 studies [11,156-173]. The evidence network relationship diagram is shown in Figure 2C and involves 12 LLMs and a total of 1266 clinical cases. The accuracy of LLMs for the top 3 diagnosis was reported in 7 studies [158,161,169,171,174-176]. The evidence network relationships are plotted in Figure 2D and involve 8 LLMs and a total of 453 clinical cases. The accuracy of LLMs for the top 5 diagnosis in clinical cases was reported in 7 studies [158,167,168,173,177-179]. The evidence network relationships are plotted in Figure 2E and involve 11 LLMs and a total of 443 clinical cases. Each LLM formed direct and indirect comparisons, partially closing the loop.

In terms of the top 1 diagnosis and top 5 diagnosis, the results of the indirect comparison are presented in Multimedia Appendix 7, where red cells indicate statistically significant differences between the column-defining regimen and the row-defining regimen. For the top 3 diagnosis, there was no statistical difference (all P>.05) in the comparisons between the LLMs (Multimedia Appendix 7). There was no evidence of a statistically significant inconsistency (all P>.05) for the top 1 diagnosis, except for Ada Health versus ChatGPT-3.5 (P=.04). For the top 3 diagnosis and top 5 diagnosis, all P were >.05 in the node-splitting test for the NMA (Multimedia Appendix 8). Iterative convergence was good, as shown by the trace and density plots (Multimedia Appendix 9). The best probability ranking showed that, in terms of accuracy of the top 1 diagnosis in clinical cases, people ranked first (SUCRA=0.9001), Ada Health ranked second (SUCRA=0.8363), and WebMD ranked third (SUCRA=0.7511; Table 1, Figure 4C). In terms of the accuracy of the top 3 diagnosis, people ranked first (SUCRA=0.7126), ChatGPT-4 ranked second (SUCRA=0.6302), and Ada Health ranked third (SUCRA=0.6273; Table 1, Figure 4D). For the accuracy of the top 5 diagnosis, Claude 3 Opus ranked first (SUCRA=0.9672), ChatGPT-4 ranked second (SUCRA=0.8089), and Gemini 1.5 pro ranked third (SUCRA=0.7905; Table 1, Figure 4E).

Triage and Classification

The accuracy of LLMs in triage and classification was reported in 7 studies [12,167,169,174,180-182]. The evidence network relationships are plotted in Figure 2F and involve 9 LLMs and a total of 901 clinical cases. Each LLM formed direct and indirect comparisons, partially closing the loop. The results of the indirect comparison are shown in Multimedia Appendix 7.

There were significant differences between Gemini and ChatGPT-3.5, ChatGPT-4, or Bing chat ($P<.05$). There was no evidence of a statistically significant inconsistency (all $P>.05$) in the node-splitting test for the NMA, except for ChatGPT-3.5 versus ChatGPT-4 ($P=.045$; Multimedia Appendix 8). Iterative convergence was good, as shown by the trace and density plots (Multimedia Appendix 9). The best probability ranking showed that, for the accuracy of triage and classification, Gemini ranked first (SUCRA=0.9649), ChatGPT-4 ranked second (SUCRA=0.6185), and Bard ranked third (SUCRA=0.5885), as shown in Table 1 and Figure 4F.

Discussion

Principal Findings

This study presents the most comprehensive meta-analysis to date on the accuracy of various LLMs when responding to medical queries, encompassing objective questions, open-ended questions, top 1 diagnosis, top 3 diagnosis, top 5 diagnosis, and triage and classification. Variations in accuracy among different LLMs were observed. ChatGPT-4o demonstrated the highest accuracy when answering objective questions, while ChatGPT-4 excelled at open-ended questions. The superior performance of people at the top 1 diagnosis and top 3 diagnosis suggests that human expertise is generally more dependable than LLMs in complex medical scenarios, while Claude 3 Opus seems to perform the best in the top 5 diagnosis. In terms of triage and classification, Gemini appeared to be more reliable.

In addition, we stratified LLMs according to the medical field in which the objective questions were located and explored their accuracy in 6 fields: ophthalmology, orthopedics, urology, dentistry, oncology, and radiology. We found that Aeyeconsult performed the best in ophthalmology, Bard performed the best in orthopedics, Bing chat performed the best in urology, ChatGPT-4 performed the best in both dentistry and oncology, and ChatGPT-4o had the highest accuracy in radiology.

At present, language models based on transformer architecture, whether pretrained or fine-tuned using biomedical corpora, have been proven effective in a series of natural language processing benchmarks in the biomedical field [183]. We attempted to analyze the reasons for the performance differences when different LLMs answer questions. Parameter size is an important factor affecting the accuracy of LLMs when answering questions. Research has found that, when the parameter size of the PaLM model is expanded from 8B to 40B, the accuracy of answering medical questions is doubled [184]. However, the practicality of a model depends not only on its number of parameters but also on many factors such as its training data and architecture, fine-tuning protocols, and overall architecture [185]. Taking GPT-4 as an example, it achieved a higher performance than its predecessor by adopting more advanced training data and architecture. The timeliness and accuracy of training data are also crucial for model performance. Today, models can not only rely on a limited set of pretraining data but also obtain the latest knowledge from the internet in real time. For example, Bing AI and Google Bard already have the ability to obtain real-time updates, and ChatGPT has also begun to follow suit by accepting plugins to expand its capabilities [185,186].

In addition, we found that some models fine-tuned on the backend LLM can achieve higher accuracy and less energy consumption in specific fields. For example, in the field of ophthalmology, Aeyeconsult integrates many ophthalmic data sets based on GPT-4 for training and generation [24]. This targeted training can significantly improve its performance in ophthalmic clinical tasks. Other possible data sources include clinical texts and accurate medical information, such as guidelines and peer-reviewed literature. In fact, there are already some models built or fine-tuned based on clinical text, such as SkinGPT-4 and ChatDoctor, which perform better overall than various general LLMs at biomedical natural language processing tasks [187,188].

Progress on various grand prognostic models has been very rapid, with a newer, more arithmetically powerful version being released every few months. However, our results show that the newer versions do not necessarily outperform the older ones in terms of performance when measured as accuracy, possibly because the newer versions incorporate fewer studies, which may have biased the results somewhat. In addition, updated versions such as ChatGPT-4V provided multimodal models (eg, that can evaluate image problems), and these models may have a greater advantage for image evaluation, for example.

Studies indicate LLMs outperform humans at exams like medical licensing, orthopedics, and pediatrics globally, highlighting LLMs' potential as a study aid. For the top 1 diagnosis and top 3 diagnosis, human accuracy is higher than that of LLMs. Despite the fact that Claude 3 Opus outperformed humans in the top 5 diagnostic results, due to the high level of accuracy required in the medical field and the multifaceted information and complex decision-making involved in medical diagnosis, we still recommend that LLMs should only be used as an auxiliary tool to assist doctors with more efficient data analysis and preliminary diagnostic recommendations.

Several meta-analyses have been conducted to assess the accuracy of LLMs in health care [15,189,190]. However, it is very unfortunate that the LLMs included in these studies included ChatGPT only and that some of the studies simply evaluated its performance on exams. Some studies did not differentiate between the types of questions answered by ChatGPT, which led to a significant amount of heterogeneity between the studies, resulting in biased results.

We acknowledge certain limitations in our study. First, for the top 3 diagnosis, top 5 diagnosis, and triage and classification, this may bias the results due to the number of included studies as well as the sample size, so caution is needed when interpreting these results. Although we minimized the heterogeneity of the research as much as possible, we cannot deny that the inclusion of different fields of study and the complexity of LLMs (such as different instructions and questioning dates) can affect the results of the study and generate heterogeneity. Therefore, caution should be exercised when interpreting the results. In addition, we did not assess the accuracy of multimodal grand prognostic models when solving medical image–related problems; with the development of

artificial intelligence, more multimodal models are being developed, and in the future, these models will become indispensable in the exploration of image-based problems in the medical field.

Conclusion

Existing studies suggest that ChatGPT-4o has an advantage for answering objective questions. For open-ended questions, ChatGPT-4 may be more credible. Humans are more accurate in the top 1 diagnosis and top 3 diagnosis of clinical cases. Claude 3 Opus performs better in the top 5 diagnosis, while for classification accuracy, Gemini is more advantageous. Although some LLMs excel at addressing medical queries, caution is advised due to the critical need for precision and rigor in medicine. Future high-quality studies and trials are necessary to gather more scientific evidence.

Acknowledgments

This work was supported by the Training Program for Young and Middle-aged Backbone Talents of Fujian Provincial Health Commission (grant number 2022GGA001), Natural Science Foundation of Fujian Province (grant number 2021J01395 and 2024J011032), Foundations of Department of Finance of Fujian Province (grant number Min Cai Zhi (2023) 830 and Min Cai Zhi (2024) 881), Joint Funding Projects for Innovation in Science and Technology of Fujian Province (grant number 2023Y9330), and Internal Supporting Project of Fuzhou University Affiliated Provincial Hospital (grant number 0080072220).

Data Availability

The data sets generated or analyzed during this study are available from the corresponding author on reasonable request.

Authors' Contributions

All authors were involved in the conceptualization and design of the study and reviewed all documents and materials. LW, JL, BZ, and SH collected the data, performed data analysis, interpreted the results, and wrote the first draft of the manuscript. CW, WL, and MZ were involved in the development of the protocol for the systematic review and critically reviewed the results and the manuscript. MF and SG were involved in the development of the protocol and revised the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

PRISMA checklist.
[DOCX File , 28 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Search strategy.
[DOCX File , 14 KB-Multimedia Appendix 2]

Multimedia Appendix 3

Versions and timelines of LLMs iterations.
[DOCX File , 20 KB-Multimedia Appendix 3]

Multimedia Appendix 4

Examples of the outcomes.
[DOCX File , 1341 KB-Multimedia Appendix 4]

Multimedia Appendix 5

Description of 168 studies included.
[DOCX File , 196 KB-Multimedia Appendix 5]

Multimedia Appendix 6

Quality assessment of observational study.
[DOCX File , 66 KB-Multimedia Appendix 6]

Multimedia Appendix 7

Indirect comparison results.
[DOCX File , 1355 KB-Multimedia Appendix 7]

Multimedia Appendix 8

Node splitting inconsistency test.
[DOCX File , 2606 KB-Multimedia Appendix 8]

Multimedia Appendix 9

Trace and density plots.
[DOCX File , 3634 KB-Multimedia Appendix 9]

Multimedia Appendix 10

Objective questions are stratified according to different fields of the questions.
[DOCX File , 13 KB-Multimedia Appendix 10]

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Abbreviations

API: application programming interface
CINEMA: Confidence in Network Meta-Analysis
GRADE: Grading of Recommendations Assessment, Development, and Evaluation
LLM: large language model
NMA: network meta-analysis
OR: odds ratio
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SUCRA: surface under the cumulative ranking curve

Edited by X Ma; submitted 18.07.24; peer-reviewed by M Lotfinia, X-M Zhang; comments to author 14.10.24; revised version received 04.02.25; accepted 03.04.25; published 30.04.25

Please cite as:
Wang L, Li J, Zhuang B, Huang S, Fang M, Wang C, Li W, Zhang M, Gong S
Accuracy of Large Language Models When Answering Clinical Research Questions: Systematic Review and Network Meta-Analysis
J Med Internet Res 2025;27:e64486
URL: https://www.jmir.org/2025/1/e64486
doi: 10.2196/64486
PMID: 40305085