# Title:

Estimation of Medical Diagnostic Likelihood Ratios Using Artificial Intelligence

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Dr. Locke had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Conflicts of Interest**

B.W.L. claims an equity interest in Mountain Biometrics, a startup focused on machine learning medical time series data.

Shuhan He: Dr. Shuhan He is employed by Mass General Physician Organization and Mass General Institute of Health Professions and has received consulting fees from Franchise Medicine. He is an unpaid volunteer at Health Tech Without Borders and ConductScience.org. No other disclosures are reported.

Boyu Peng: Mr. Boyu Peng was employed by ConductScience Inc. and serves as Adjunct Faculty at the Massachusetts General Hospital Institute of Health Professions. These affiliations are not relevant to the work presented in this article. No other conflicts of interest are declared.

The remaining authors have no conflict of interest to declare.

**Use of AI:**

Generative AI tools were used solely for language editing of the manuscript. All content, interpretations, and final decisions were made by the authors, who take full responsibility for the work.

**Description:**

Large language model-estimated diagnostic likelihood ratios showed negligible bias bounded disagreement with 700 literature-reported likelihood ratios, demonstrating their potential to supply evidence weights for Bayesian reasoning in clinical diagnosis.

# Abstract:

*Importance:*

Bayesian diagnostic reasoning requires likelihood ratios (LRs), but empiric LR estimates are often unavailable or context-specific.

*Objective:*

To evaluate whether large language models (LLMs) can estimate diagnostic likelihood ratios that approximate values reported in the literature.

*Design, Setting, and Participants:*

Methodologic diagnostic comparison study. We extracted 700 finding–condition likelihood ratios from TheNNT.com (April 1, 2025 snapshot) and generated LLM-estimated LRs using three OpenAI models (GPT-4o, o3, GPT-5). No human participants were involved.

*Exposures:*

Constrained few-shot prompting of three LLMs to output numeric LRs for each finding–condition pair.

*Main Outcomes and Measures:*

Agreement between literature-reported LRs (LR\_Reported) and LLM-estimated LRs (LR\_LLM) on the log scale measured by Bland-Altman analysis (mean bias and multiplicative 95% limits of agreement); calibration (regression of log-LR\_LLM on log-LR\_Reported); and categorical agreement across LR evidence bands (quadratic-weighted Cohen’s κ).

*Results:*

Among 700 finding–condition pairs covering 30 conditions, all 3 models showed negligible mean bias. GPT-5 had the narrowest 95% limits of agreement (0.26×–3.70×) compared with o3 and GPT-4o. Agreement varied by finding type, with laboratory test LRs showing larger dispersion than history, signs/symptoms, and imaging.

*Conclusions and Relevance:*

Modern LLMs can estimate diagnostic likelihood ratios with low bias and bounded dispersion; LLM-derived LRs may be useful as auditable evidence weights to support Bayesian reasoning when empirical LRs are scarce. Prospective validation against embargoed or novel diagnostic accuracy studies is needed.

Key Points:

Question:

Do large language models generate diagnostic likelihood ratios that approximate values reported in the literature?

Findings:

Across 700 finding–condition pairs from 30 conditions, all 3 models demonstrated negligible mean bias; GPT-5 showed the tightest agreement (95% limits of agreement 0.26×–3.70×).

Meaning:

LLM-generated likelihood ratios may provide usable evidence weights for Bayesian clinical reasoning when empirical estimates are unavailable.

# Introduction:

Medical diagnosis requires integrating history, examination, and test findings to identify the condition that best explains a patient’s presentation1,2. Bayesian reasoning provides a principled framework for this task because it is information-efficient, broadly applicable, and transparent.3–5. Instruction in Bayesian methods can improve clinicians’ diagnostic reasoning 6, yet broader clinical adoption remains modest and many clinicians continue to rely on intuition, heuristics, and pattern recognition.7,8

A major barrier to routine Bayesian updating at the bedside is the scarcity of accurate, context-specific likelihood ratios (LRs). LRs quantify how the presence or absence of a finding (history, symptom, examination sign, or test result) changes the odds of disease3,4. However, empirical LR estimates require diagnostic accuracy studies, which are difficult to perform and interpret9,10; consequently, reliable LRs for many common clinical findings are unavailable. and true likelihood ratios often vary substantially by clinical context11. Because the condition–finding–context space is combinatorially large, exhaustive empirical measurement is infeasible. For applied Bayesian reasoning to scale, a rapid and sufficiently accurate method of estimating LRs is necessary.

Recent advances in generative artificial intelligence suggest a potential means to generate such estimates directly from encoded clinical knowledge. Large language models (LLMs) are neural networks trained on extensive text corpora that capture clinical concepts and associations12,13. They can generalize to new tasks through zero-shot or in-context learning14,15,, suggesting they might infer LRs when empirical data are absent. There is growing interest in using large language models (LLMs) for diagnostic reasoning, and recent studies show impressive stand-alone performance.16-18. Yet integrating these systems as physician adjuncts remains difficult, in part because their reasoning processes are opaque. If LLMs can produce quantitative LR estimates, this would represent a different mode of application where models supply explicit, clinician-interpretable evidence weights that can be combined through well-established Bayesian updating, whether algorithmically or at the bedside. Such outputs could also populate decision-support tools and serve as prior predictions for future diagnostic studies.

Despite its rigor, Bayesian reasoning remains underused in practice, owing both to the absence of applicable LR estimates and the difficulty of applying them at the bedside. The ability of LLMs to approximate diagnostic LRs could bridge a long-standing translational gap between data and decision-making. 3,4,27 A precondition to evaluating LR-estimation in situations where current empiric data is missing is assessing how well LLMs encode existing LR estimates from the scientific literature. In this study, we evaluated successive generations of LLMs to determine how closely their inferred LRs align with published values, and to explore whether AI-generated estimates can serve as credible, inspectable surrogates for empirical diagnostic evidence.

**Methods:**

*Study Design:*

We conducted a retrospective comparative study assessing the agreement between diagnostic LRs generated by three LLMs and empirically derived LRs reported by theNNT.com (© The NNT Group, 2010–2022). This study followed the STARD-AI reporting guidelines for studies involving artificial intelligence in diagnostic evaluation. No human participants were involved.

### Data Sources:

On April 1, 2025, we compiled a reference-standard dataset of likelihood ratios (LRReported) from theNNT.com, a curated repository diagnostic likelihood ratios from published medical literature. For each condition, point estimates of all LRs were recorded directly or, when only a range was provided, derived as the geometric mean (e.g., “1–2” recorded as 1.41; “1.5 [95% CI 1–2]” recorded as 1.5). LRs were initially extracted using an automated script and then manually validated with duplicate independent review (PC and BWL). Each LR was categorized as a patient historical element, a sign/symptom, a test result, an imaging finding, and/or a diagnostic adjudication (e.g. “diagnosis based on ultrasound”). Scores (e.g. Centor criteria for Strep pharyngitis) were counted as each of the constituent findings. We qualitatively describe the strength of findings as strong (LR- ≤ 0.10 or LR+ ≥ 10), moderate (0.1 < LR- ≤ 0.2 or  5 ≤ LR+ < 10), weak (0.2 ≤ LR- < 0.5 or 2 ≤ LR+ < 5), or negligible (0.5 < LR < 2), consistent with prior literature3,4.

The intended sample size was determined by the total number of distinct likelihood ratios available from TheNNT.com at the time of data collection. Because this study was exploratory and descriptive rather than hypothesis-testing, no formal sample size calculation was performed; instead, all 700 available finding–condition pairs were included to maximize coverage across clinical domains.

Date and Code availability:

The full pipeline for collating likelihood ratios (LRs) from TheNNT.com and generating large‑language‑model (LLM) estimates is available at: <https://github.com/reblocke/llm_estimate_lrs>

### LLM Comparators

On August 25, 2025, we generated comparator likelihood ratios (LRLLM) for all findings listed on theNNT.com using a constrained, few-shot prompting procedure. To represent a range of model ages, complexity, and inference costs, we queried three OpenAI LLMs (OpenAI, LP; San Francisco, California, USA) using the OpenAI API: GPT-4o (model release Nov 20, 2024), o3 (release Apr 16, 2025), and GPT-5 (release Aug 7, 2025). A full description of the prompting strategy is included in the supplement. In brief, the system prompt defined the LR, ‘P(finding | diagnosis) / P(finding | not diagnosis)’, gave qualitative LR strength descriptions3, and required a numeric-only response. We used 8 (non-reasoning model, GPT-4o) or 2 (reasoning models, o3 and GPT-5) clinician-estimated few-shot examples. These were clinician-estimated finding-clinical state-LR groups that were not in the evaluation set. Inference settings were temperature = 0.2 (non-reasoning model) and ‘reasoning effort’ = "medium" (reasoning models); text.verbosity = "low" was applied where supported (GPT-5 only). Internet search was not

enabled for any models. No model fine-tuning was performed.

LLM queries were executed without providing the models any TheNNT.com data or study identifiers; model outputs were generated independently of the reference standard to ensure index-test/ reference-standard independence.

Indeterminate or invalid index test outputs, defined as non-numeric, non-finite, or non-positive model responses, were automatically rejected and re-queried until a valid value was obtained, as detailed in the Supplemental Methods. Because reference-standard likelihood ratios were derived directly from curated numeric values on TheNNT.com and manually validated, no indeterminate reference-standard data were present.

No missing data occurred for either the reference-standard or index-test likelihood ratios. Each LRReported entry received a corresponding valid model-generated value, ensuring a one-to-one comparison set for all analyses.

*Outcomes and Measures*

The primary outcome was agreement between generated LR (LRLLM) and Reported LR. Agreement was evaluated on the log-transformed LR scale using Bland-Altman analysis to estimate mean bias and multiplicative 95% limits of agreement. Secondary measures included calibration (linear regression of log-LR\_LLM on log-LR\_Reported) and categorical agreement across qualitative LR evidence bands (strong, moderate, weak, negligible), evaluated using quadratic-weighted Cohen’s κ.

Intended use is clinician decision support when empirical LR unavailable.

### Statistical Analysis

We assessed the agreement between reported likelihood ratios (LRReported) and LLM-estimated likelihood ratios (LRLLM) using Bland-Altman analysis19 on log-transformed LR values, as strength of evidence is additive on the log scale4,20. We calculated multiplicative (ratio) limits of agreement, which indicate the range within which LRLLM is expected to lie within an x-fold difference of the LRReported in 95% of cases. 50%, 75%, 90%, and 99% limits of agreement are also tabulated in the supplemental materials.

We compared models using paired t-test for mean differences (bias) and the Pittman-Morgan test for differences in the width (variance) of the limits of agreement21,22. Subgroup analyses were conducted by information type (historical element, symptom/sign, examination finding, test result, or diagnostic adjudication), and by direction of evidence (positive: LR >1; negative: LR < 1) using Welch’s t-test for bias and Levene’s test for differences in width. Calibration was evaluated by linear regression of log-transformed LLM estimates on reported log LRs, yielding the intercept, slope, 95% confidence intervals, and R². Agreement between qualitative LR strength categories (e.g. strong, moderate, weak)3,4 was assessed using Cohen’s Kappa with quadratic weights, which penalizes large disagreements more heavily and approximates squared-error on the underlying likelihood ratio scale23,24. Statistical significance was set at α = 0.05 without adjustment for multiple testing.Analyses were conducted in Python 3.11.11 and Microsoft Excel. Code is available at <https://github.com/reblocke/llm_estimate_lrs> .

The evaluation has several limitations. Models were compared to published likelihood ratios (LRs) that may have influenced pretraining, though direct memorization was not observed. Reference LRs lacked confidence intervals, study-level context, and methodological assessment, and models did not have sufficient clinical detail to match patient populations precisely. Additionally, only quantitative agreement was measured, without categorizing model errors. Despite these constraints, the results indicate that LLMs can meaningfully predict LR..

*Ethical Considerations:*

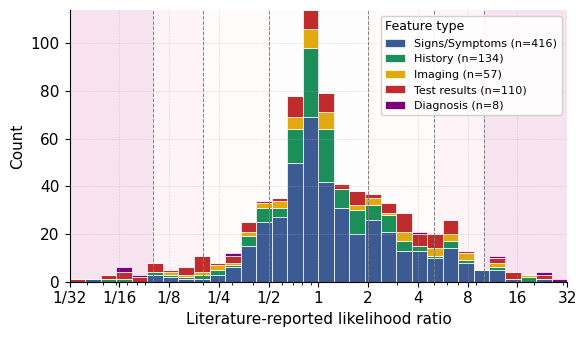
This study used publicly available aggregated data and did not involve human participants; therefore, it was exempt from institutional review board oversight.

# Results:

Seven hundred LRReported exploring the 30 available medical conditions were compiled from theNNT.com. Signs/symptoms were the most common type of LR (59%, n=416), followed by historical element (19% , n=134) and test results (16% , n=110)

LRReported values ranged from 0.01 to 145.9, with a median of 1 (interquartile range 0.7 to 2.2) and a geometric mean of 1.21. Figure 1 shows the distribution of strength of evidence in the LRReported. Most (n=400) findings offered negligible strength of evidence (0.5 < LR < 2; 56.5%), with the next most common being weak evidence in favor of a diagnosis (n=120, 17.4%), weak evidence against (n=60, 8.7%) and moderate evidence for (n=52, 7.5%). Diagnostic adjudications tended to provide the strongest evidence, while signs/symptoms were the weakest (Supplemental Table 1).

**Figure 1:** Distribution of likelihood ratios reported in the literature, as collected from theNNT.com. Background shading represents strong, moderate, weak, and negligible strength of evidence categories3,4. Most of the LRreported cluster near 1, showing they offer negligible or weak evidence.

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Three sets of LRLLM were generated (for GPT-4o, o3, and GPT-5) for each of the 700 LRReported. Figure 2 shows the 95% multiplicative limits of agreement. All 3 models showed excellent mean bias (GPT-4o 1.02x, o3 0.99x, GPT-5 0.99x; no differences in pairwise comparisons). LR estimates from GPT-5 had the narrowest limits of agreement to the values reported on theNNT.com (95% limits of agreement from 0.26x to 3.7x, *P* < .001 vs both o3 and GPT-4o ), followed by o3 (0.23x to 4.28x), and GPT-4o (0.23x to 4.53x, *P* = .58 for o3 vs GPT-4o). Other coverage ranges (50, 75%, 90%, and 99%) are presented in the supplementary materials.

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**Figure 2: Agreement between literature-reported and LLM-generated likelihood ratios:** Each panel shows the agreement between reported and model-generated likelihood ratios (LRs). The y-axis shows the ratio of LRs (reported/model), and the x-axis shows the geometric mean of paired LRs. Solid black lines represent mean bias; Dashed lines indicate the multiplicative (i.e. x-fold) range in which 95% of estimates would be expected to be from a value reported on theNNT.com. Narrower coverage intervals represent closer agreement, and deviations of the mean line from unity indicate systematic bias. Shaded areas indicate the confidence intervals on each bound of agreement. All models showed negligible bias. GPT-5 had the tightest agreement with reported likelihood ratios.

Figure 3 shows the limits of agreement by finding type. Estimates of the strength of evidence followed similar patterns across models. Estimates of the importance of sign/symptoms, historical elements, and imaging findings were all similarly accurate, while test results agreed less closely with reported estimates.

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**Figure 3: Agreement between LLM-estimated and literature-reported likelihood ratios** by type of clinical finding. Rows represent clinical finding categories (laboratory, imaging, history, sign-symptom, and diagnosis); columns represent LLM versions (GPT-4o, o3, and GPT-5). Categories were assigned by manual review, and likelihood ratios could be categorized as multiple types (e.g. scores integrating multiple findings).

When analyzed by the direction of evidence, patterns differed between models (Supplemental Figure 2). For GPT-4o, mean bias differed between negative (LRreported < 1) evidence (mean 1.13x) vs. positive (LRreported > 1) findings (mean 0.92x, *P* < .001). No difference in mean bias was observed for o3 (0.95x vs. 1.03x; *P* = 0.15). GPT-5 showed the opposite pattern of mean bias (negative evidence 0.88x vs positive evidence 1.12x; *P* < .001). The width of the limits of agreement did not differ by evidence direction for any of the models (GPT-4o *P* = .11; o3 *P* = .40; GPT-5 *P* = .37). For all 3 models, the calibration slope of predictions on the logarithmic scale suggested predictions were slightly less extreme than literature reported values (Supplemental Figures 2a-c)

Agreement between qualitative evidence categories was moderate for all models (Supplemental Figures 3a-c). The quadratic-weighted Cohen’s κ for GPT-5 was highest (0.775, 95% confidence interval [CI] 0.728-0.821), followed by o3 (0.745, 95% CI 0.702 – 0.789), and GPT-4o (0.734, 95% CI 0.691 – 0.778).

# Discussion:

We found that modern LLMs can estimate diagnostic likelihood ratios with negligible mean bias and bounded dispersion. Across 700 finding–condition pairs covering 30 conditions, GPT-5 demonstrated the closest agreement with literature-reported values (95% limits of agreement of 0.26×–3.70×). Agreement varied by finding type, with laboratory test results showing looser agreement than history, signs/symptoms, or imaging results. Qualitative category agreement was substantial (κ = 0.78 for GPT-5*).*25 Collectively, these findings indicate that LLM-derived likelihood ratios could help shift clinical AI from opaque end-to-end reasoning toward transparent, clinician-interpretable Bayesian updating by linking model inference to established frameworks for decision support.27,31

Prior work shows that AI can complement human diagnostic reasoning by offering distinct strengths.26 Because Bayesian reasoning depends on accurate likelihood ratios that are often unknown or difficult to access at the point of care,27,28 our results suggest that LLM-derived estimates could help operationalize structured reasoning in an array of situations, education, decision-support, or diagnostic test accuracy study planning.

This study, to our knowledge, provides the first large-scale evaluation of 700 finding–condition pairs across 30 conditions, resolving LLM clinical reasoning into a quantitative unit: the LR4. Unlike black-box outputs17, quantitative of estimates permits their inspection and integration within human or algorithmic reasoning pipelines. Whether the observed limits of disagreement is acceptable depends on the use case: it may be too wide when a single, high-stakes finding drives a decision, the negligible mean bias implies that serial Bayesian updating across multiple findings would yield unbiased posteriors if independence among findings approximately holds, analogous to the resilience of naïve Bayes classifiers.29.

A primary strength of this work is introducing a paradigm whereby LLM’s diagnostic contribution is resolved to a single component of the clinical reasoning pipeline, the LR. Prior studies show that LLMs can match or exceed clinician performance in structured pretest estimation tasks.31 Thus, resolving LLMs to generating of explicit evidence weights, which can then be combined through the established machinery of Bayesian updating, may yield performance comparable to more opaque reasoning approaches while remaining substantially more interpretable.

We used a reproducible evaluation methodology across a broad set of comparators and multiple model generations and quantified agreement of both qualitative categories and continuous metrics. Both showed similar performances. Interestingly, using long-standing qualitative strength of evidence classification 3, most of the LRs studied represented “negligible or weak evidence”, underscoring that individual findings may generally be less diagnostic than creators of the classification scheme anticipated.

Several limitations warrant mention. First, the evaluation compares model outputs to published LRs that may have been used in model pretraining, introducing potential contamination. Although we observed no verbatim reproduction and disabled web access, prior exposure could influence model weights and tighten observed agreement.30 Nonetheless, the observed results demonstrate the capacity of LLMs to encode information about studied LRs, and the improvement in performance across model generations, variation by finding type, and bounded dispersion suggest that the results capture meaningful aspects of model behavior rather than memorization alone.

Additionally, we did not manually extract LR confidence intervals or study-level context from the primary sources compiled by TheNNT.com, so our reference standards include hidden uncertainty, and models lacked the clinical detail necessary to match the precise patient spectrum to which a given LR applies.11 We also did not assess the methodological rigor of those studies10 and reported only quantitative agreement, not a taxonomy of model errors.

LLM-estimated LRs could serve multiple roles in clinical medicine. Beyond providing immediate quantitative estimates for Bayesian updating, model-generated LRs may act as prior hypotheses for future diagnostic-accuracy studies, offering predictions that can inform power calculations or serve as prior distributions for Bayesian designs.32 In practice, model-derived LRs could populate decision-support tools, inform pretest probabilities in diagnostic pathways, and extend to educational settings as structured reasoning aids, and collectively advancing evidence-weighted clinical decision-making at scale.

Looking ahead, the critical question is prospective: can LLMs generate likelihood ratios for findings not yet studied and anticipate the results of future diagnostic-accuracy research? Addressing this will require leakage-controlled, preregistered benchmarks with embargoed targets to test true predictive ability.17,18,30 Future work should evaluate whether tighter specification of patient context and care setting improves the precision of LLM-estimated LRs, whether model biases mirror those of clinicians, and whether calibrated uncertainty estimates can be generated. Comparative studies should benchmark LLM performance against clinicians across expertise levels, and implementation studies should assess how embedding model-generated LRs into workflows affects diagnostic accuracy, cognitive load, and patient outcomes.16,31,32

Ethical Considerations:

This study used publicly available aggregated data and did not involve human participants; therefore, it was exempt from institutional review board oversight.

# Conclusion:

Our findings suggest that large language models can be used to approximate a core element of diagnostic reasoning, the likelihood ratio. While the ability to generalize to unstudied LRs will require prospective validation, the capability of models to encode existing diagnostic information suggests they could be used to bridge the long-standing gap between probabilistic theory and routine clinical decision-making.Rather than replacing empirical research, model-derived likelihood ratios could support future diagnostic studies, guide hypothesis generation, and support transparent clinical reasoning in clinical care.15,16

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# Supplemental Materials

## Prompt Details

Code availability. The full pipeline for collating likelihood ratios (LRs) from TheNNT.com and generating large‑language‑model (LLM) estimates is available at: <https://github.com/reblocke/llm_estimate_lrs>

**Overview:** We prompted the LLMs to produce a single numeric likelihood ratio (LR) for a clinical finding with respect to a diagnosis, under a constrained output schema (only a numerical response) and with minimal verbosity.

**Prompt specification:**

* System role: “You are a Bayesian diagnostic assistant. Estimate a numeric likelihood ratio (LR) for a finding with respect to a diagnosis. Return only a JSON object matching the schema: {“value”: }, where value > 0.”
* Definition shown to the model: LR = P(finding | diagnosis) / P(finding | not diagnosis)
* Qualitative evidence bands provided as context. >10 strong for; 5–10 moderate for; 2–5 weak for; 0.5–2 negligible; 0.2–0.5 weak against; 0.1–0.2 moderate against; ≤0.1 strong against.
* Inputs to the model are plain text pairs: ”Condition: <diagnosis>\nFinding: <finding>”
* preceded by the system prompt, definition/bands, and few‑shot examples.

**Few‑shot strategy:** We include exemplar (Condition, Finding → LR) pairs to anchor scale:

* Non‑reasoning models (e.g., GPT‑4o): 8 examples.
* Reasoning models (o3 series; GPT‑5 family): 2 examples.

Example LRs were clinician‑estimated, not scraped values, to reduce the chance that exemplars appear in the evaluation set or anchor to relevant model pretraining data.

Prompt engineering and prompt validation were performed by two investigators (B.W.L. and P.C.), both trained in evidence-based medicine and experienced in Bayesian diagnostic reasoning.

**Inference settings:**

* Non‑reasoning models: temperature = 0.2.
* Reasoning models: reasoning = {"effort": "medium"}; no temperature.
* Verbosity control: where supported (GPT‑5 family), text.verbosity = "low". The JSON‑only response format further suppresses extraneous text.

**Output schema and validation**:

* Schema. Structured output {"value": float}; parser enforces numeric type.
* Requests use the Responses API with a Pydantic schema (LRResponse { value: float }) to enforce structure.
* Validity rule. Accept only finite, strictly positive values.
* Retry logic. If the response is non‑numeric, malformed, non‑finite, or ≤0, the call is retried with exponential backoff and jitter until a valid LR is obtained (or up to the configured maximum, if set).

**Code:**

from \_\_future\_\_ import annotations

import os

import logging

from pathlib import Path

from typing import Optional

import time, math

from random import random

import pandas as pd

from pydantic import BaseModel

from openai import OpenAI

# -----------------------------------------------------------------------------

# 0) Configuration

# -----------------------------------------------------------------------------

logging.basicConfig(level=logging.WARNING)

client = OpenAI(api\_key=os.getenv("OPENAI\_API\_KEY"))

# Model registry:

MODEL\_CAPABILITIES = {

# GPT‑5 series (reasoning; supports text.verbosity; no temperature)

"gpt-5" : {"reasoning": True, "verbosity": True, "allow\_temp": False},

"gpt-5-mini" : {"reasoning": True, "verbosity": True, "allow\_temp": False},

"gpt-5-nano" : {"reasoning": True, "verbosity": True, "allow\_temp": False},

# GPT‑4.1 family (non‑reasoning; temperature OK); include snapshots + aliases

"gpt-4.1-2025-04-14" : {"reasoning": False, "verbosity": False, "allow\_temp": True},

"gpt-4.1-mini-2025-04-14": {"reasoning": False, "verbosity": False, "allow\_temp": True},

"gpt-4.1-nano-2025-04-14": {"reasoning": False, "verbosity": False, "allow\_temp": True},

# GPT‑4o family (non‑reasoning; temperature OK); prefer latest snapshot or alias

"gpt-4o-2024-11-20" : {"reasoning": False, "verbosity": False, "allow\_temp": True},

"gpt-4o-mini-2024-07-18": {"reasoning": False, "verbosity": False, "allow\_temp": True},

# o‑series (reasoning; no temperature)

"o3-2025-04-16" : {"reasoning": True, "verbosity": False, "allow\_temp": False},

"o3-mini-2025-01-31": {"reasoning": True, "verbosity": False, "allow\_temp": False},

"o4-mini-2025-04-16": {"reasoning": True, "verbosity": False, "allow\_temp": False},

}

MODELS = list(MODEL\_CAPABILITIES)

# -----------------------------------------------------------------------------

INPUT\_FILE = "nnt\_lrs\_processed.xlsx"

OUTPUT\_FILE = "nnt\_lrs\_with\_estimated.xlsx"

# -----------------------------------------------------------------------------

# 1) Prompt

# -----------------------------------------------------------------------------

SYSTEM\_CORE = """You are a Bayesian diagnostic assistant.

Estimate a numeric likelihood ratio (LR) for a finding with respect to a diagnosis.

Return only a JSON object matching the schema: {"value": <float>}, where value > 0.

"""

DEFINITION = """Definition:

LR = P(finding | diagnosis) / P(finding | not-diagnosis)

"""

BANDS = """LR evidence bands (reference):

>10 strong for; 5-10 moderate for; 2–5 weak for;

0.5–2 negligible;

0.2-0.5 weak against; 0.1-0.2 moderate against; ≤0.1 strong against"""

# Few‑shot examples - these are human guestimates (to avoid seeding the dataset and inflating performance)

FEW\_SHOT\_RICH = [

("deep vein thrombosis", "femoral vein noncompressaible on ultrasound", 16.0), # some data this might be higher?

("pericarditis", "pleuritic chest pain improved by leaning forward", 5.2),

("pulmonary embolism", "tachycardia >100 bpm", 2.2),

("urinary tract infection", "malodorous urine", 1.1),

("myocardial infarction", "enjoys playing chess", 1.0),

("appendicitis", "no RLQ tenderness", 0.45),

("pneumothorax", "bilateral lung sliding present on US", 0.18), # some data this might be lower?

("HIV infection", "4th‑generation Ag/Ab screen negative beyond window",0.05),

]

FEW\_SHOT\_MIN = [

("deep vein thrombosis", "femoral vein noncompressaible on ultrasound", 16.0),

("myocardial infarction", "enjoys playing chess", 1.0),

]

def build\_messages(diagnosis: str, finding: str, reasoning: bool) -> list[dict]:

msgs: list[dict] = [

{"role": "system", "content": SYSTEM\_CORE.strip()},

{"role": "system", "content": DEFINITION.strip()},

{"role": "system", "content": BANDS.strip()},

]

examples = FEW\_SHOT\_MIN if reasoning else FEW\_SHOT\_RICH

for dx\_ex, f\_ex, v\_ex in examples:

msgs.append({"role": "user", "content": f"Condition: {dx\_ex}\nFinding: {f\_ex}"})

msgs.append({"role": "assistant", "content": f'{{"value": {float(v\_ex)}}}'})

msgs.append({"role": "user", "content": f"Condition: {diagnosis}\nFinding: {finding}"})

return msgs

# -----------------------------------------------------------------------------

# 2) Structured Outputs schema (Pydantic)

# -----------------------------------------------------------------------------

class LRResponse(BaseModel):

value: float

# -----------------------------------------------------------------------------

# 2b) Retry wrapper (exponential backoff with jitter)

# -----------------------------------------------------------------------------

def estimate\_lr\_until\_positive(

diagnosis: str,

finding: str,

model: str,

client: Optional[OpenAI] = None,

max\_retries: Optional[int] = None, # None ⇒ retry indefinitely

base\_backoff: float = 0.5, # seconds

max\_backoff: float = 30.0 # seconds

) -> float:

attempt = 0

while True:

attempt += 1

try:

lr = estimate\_lr(diagnosis, finding, model, client)

if isinstance(lr, (int, float)) and math.isfinite(lr) and lr > 0:

return float(lr)

raise ValueError(f"Non‑positive or non‑finite LR: {lr!r}")

except Exception as e:

logging.warning(

f"[retry {attempt}] sheet finding='{finding[:80]}' | "

f"model={model} → {e}"

)

if (max\_retries is not None) and (attempt >= max\_retries):

raise

# exponential backoff with jitter

delay = min(base\_backoff \* (2 \*\* (attempt - 1)), max\_backoff)

time.sleep(delay \* (0.5 + random())) # 0.5–1.5× jitter

# -----------------------------------------------------------------------------

# 3) Estimator call (Responses API)

# -----------------------------------------------------------------------------

def estimate\_lr(diagnosis: str, finding: str, model: str, client: Optional[OpenAI] = None) -> float:

if client is None:

client = OpenAI()

cfg = MODEL\_CAPABILITIES[model]

msgs = build\_messages(diagnosis, finding, reasoning=cfg["reasoning"])

kwargs = {}

if cfg["reasoning"]:

kwargs["reasoning"] = {"effort": "medium"} # for GPT‑5 and o‑series

# no temperature/top\_p

elif cfg["allow\_temp"]:

kwargs["temperature"] = 0.2 # allowed for 4o / 4.1

# Apply verbosity only where supported (GPT‑5 family)

if cfg["verbosity"]:

kwargs["text"] = {"verbosity": "low"}

resp = client.responses.parse(

model=model,

input=msgs,

text\_format=LRResponse, # Structured Outputs → Pydantic

\*\*kwargs,

)

return float(resp.output\_parsed.value)

# -----------------------------------------------------------------------------

# 4) Main pipeline: read workbook → append model columns → write output

# -----------------------------------------------------------------------------

def run\_batch(input\_file: str | Path, output\_file: str | Path, models: list[str]) -> None:

sheets = pd.read\_excel(input\_file, sheet\_name=None, header=None)

for sheet\_name, df in sheets.items():

diagnosis = str(df.iloc[0, 0]).strip()

for model in models:

new\_header = "lr\_" + model

col = []

print(f"→ {diagnosis[:60]} | {model}")

for i in range(len(df)):

if i == 0:

col.append("") # top-left cell (sheet label row)

elif i == 1:

col.append(new\_header) # column header row

else:

finding = str(df.iloc[i, 0]).strip()

if not finding:

col.append("") # keep blank rows blank

continue

try:

# retry until a strictly positive, finite float is returned

lr = estimate\_lr\_until\_positive(

diagnosis, finding, model, client,

max\_retries=None # set to an int (e.g., 8) to cap retries

)

except Exception as e:

lr = "ERROR"

logging.warning(

f"Error on sheet '{sheet\_name}', row {i}, model {model} after retries: {e}"

)

col.append(lr)

# Insert as object dtype to accommodate strings like "ERROR"

df.insert(df.shape[1], new\_header, pd.Series(col, dtype="object"))

sheets[sheet\_name] = df

with pd.ExcelWriter(output\_file, engine="openpyxl") as writer:

for name, frame in sheets.items():

frame.to\_excel(writer, sheet\_name=name, index=False, header=False)

print(f"Done – results saved to '{output\_file}'")

if \_\_name\_\_ == "\_\_main\_\_":

run\_batch(INPUT\_FILE, OUTPUT\_FILE, MODELS)

## Supplemental Table 1: Distribution of Reported Likelihood Ratios, by type

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Statistic | Overall | Test results | Imaging | History | Signs Symptoms | Diagnosis |
| Count | 700 | 110 | 57 | 134 | 416 | 8 |
| Geometric mean | 1.206 | 1.071 | 1.322 | 1.065 | 1.267 | 1.164 |
| 5th percentile | 0.190 | 0.060 | 0.200 | 0.226 | 0.360 | 0.064 |
| 25th percentile | 0.700 | 0.312 | 0.680 | 0.755 | 0.700 | 0.077 |
| 50th percentile | 1.000 | 1.000 | 1.000 | 0.995 | 1.000 | 2.057 |
| 75th percentile | 2.200 | 3.675 | 3.300 | 1.675 | 2.100 | 16.300 |
| 95th percentile | 7.905 | 15.550 | 12.000 | 5.085 | 7.225 | 26.300 |
| Min | 0.010 | 0.010 | 0.010 | 0.050 | 0.040 | 0.060 |
| Max | 145.894 | 145.894 | 34.400 | 18.500 | 57.000 | 27.000 |

## Supplemental Figure 1: Limits of Agreement by Direction of Evidence

Rows separate positive (LRreported > 1) from negative findings (LRreported < 1).

A group of colored dots

AI-generated content may be incorrect.

## Supplemental Table 2: Coverage Intervals

Limits of Agreement that bound 50%, 75%, 90%, 95%, and 99% of model-generated likelihood ratios relative to literature-reported values. Intervals are expressed as multiplicative factors (“×”), indicating how far each model can be expected to deviate reported LRs. Parentheses show 95% confidence intervals for the estimate of each coverage limit..

**Model: GPT-4o**

|  |  |  |
| --- | --- | --- |
| Coverage | Lower edge (95% CI) | Upper edge (95% CI) |
| 50% | 0.61x (0.57x - 0.65x) | 1.70 (1.60x - 1.81x) |
| 75% | 0.42x (0.39x - 0.46x) | 2.44 (2.27x - 2.63x) |
| 90% | 0.29x (0.27x - 0.32x) | 3.56 (3.27x - 3.88x) |
| 95% | 0.23x (0.21x - 0.25x) | 4.53 (4.11x - 4.99x) |
| 99% | 0.14x (0.13x - 0.16x) | 7.24 (6.43x - 8.14x) |

**Model: o3**

|  |  |  |
| --- | --- | --- |
| Coverage | Lower edge (95% CI) | Upper edge (95% CI) |
| 50% | 0.60x (0.56x - 0.63x) | 1.64 (1.54x - 1.74x) |
| 75% | 0.42x (0.39x - 0.45x) | 2.33 (2.17x - 2.51x) |
| 90% | 0.29x (0.26x - 0.31x) | 3.38 (3.10x - 3.68x) |
| 95% | 0.23x (0.21x - 0.25x) | 4.28 (3.89x - 4.71x) |
| 99% | 0.14x (0.13x - 0.16x) | 6.79 (6.05x - 7.62x) |

**Model: GPT-5**

|  |  |  |
| --- | --- | --- |
| Coverage | Lower edge (95% CI) | Upper edge (95% CI) |
| 50% | 0.63x (0.59x - 0.66x) | 1.56 (1.47x - 1.65x) |
| 75% | 0.46x (0.43x - 0.49x) | 2.15 (2.01x - 2.29x) |
| 90% | 0.33x (0.30x - 0.35x) | 2.99 (2.77x - 3.23x) |
| 95% | 0.26x (0.24x - 0.29x) | 3.70 (3.40x - 4.03x) |
| 99% | 0.17x (0.16x - 0.19x) | 5.61 (5.05x - 6.22x) |

## Supplemental Figure 2 (a-c): Calibration Plots

## Calibration of log-transformed likelihood ratios (LRs) generated by each model against literature-reported LRs, with the calibration intercept, slope, 95% Wald confidence intervals, and R² reported. Perfect calibration on the log scale corresponds to the intercept=0 and the slope=1; A slope <1 indicates shrinkage toward less-extreme LRs. Each panel shows the identity line (dashed), model predictions (solid), binned means (quantile bins), and non-parametric smoothers (LOWESS and isotonic regression) as descriptive complements. All regressions used complete (x,y) pairs; residual diagnostics showed no material heteroskedasticity, so standard OLS inference was retained. LRs are presented on the logarithmic scale.

(Panels A–C: GPT-4o, o3, GPT-5, respectively.).



## Supplemental Figure 3(a-c): Qualitative Agreement between LLMs and Literature-reported LRs



