

A Multi-Domain Red Teaming Framework for Safety, Robustness, and Fairness Evaluation of Medical Large Language Models

Andrei Marian Feier¹, Veysel Kocaman¹, Yigit Gul¹, Ahmet Korkmaz¹, Alexander Thomas¹, Aleksei Zakharov¹, Jay Gil¹, Mehmet Butgul¹ and David Talby¹

¹John Snow Labs Inc.

Abstract

Large language models (LLMs) are increasingly deployed across healthcare, yet existing benchmarks fail to capture model behavior under adversarial or ethically complex conditions common in clinical practice. We developed a multi-domain red teaming framework evaluating eleven contemporary LLMs across 690 clinically grounded scenarios spanning nine domains and over 150 subcategories. Scenarios incorporated adversarial transformations, and responses were assessed using a seven-dimension rubric with LLM-assisted scoring and human-in-the-loop validation. Results revealed substantial performance variance, with mean scores ranging from 0.791 to 0.984. Critically, several high-performing systems produced complete failures in individual safety-critical scenarios, demonstrating that aggregate accuracy masks clinically meaningful risk. The highest-performing systems (X-BAL, GPT-5, Claude Opus 4.1) achieved scores above 0.97 with low variance, while performance varied significantly across domains. Equity-related tasks showed 10–20% error amplification with demographic modifications, and human reviewers identified clinically relevant failures missed by automated evaluation. Our findings demonstrate that performance variance and worst-case failures provide more clinically meaningful reliability indicators than mean accuracy alone, and that hybrid evaluation approaches combining automation with clinician oversight are essential for credible safety assessment.

Keywords

Medical large language models, Red teaming, Safety evaluation, Clinical AI, Healthcare AI, Robustness, Fairness

1. Introduction

Large language models (LLMs) are increasingly used across healthcare, assisting clinicians, supporting administrative workflows, and interacting with patients in real time. Their rapid integration has created an urgent need for systematic safety evaluation, because models can generate clinically plausible but incorrect or harmful outputs, amplify bias, or violate privacy principles if not adequately tested [1]. Although recent benchmarks have improved our understanding of medical reasoning and factual accuracy [2, 3, 4], most remain limited to narrow question answer formats or static assessments that do not reflect real clinical communication.

Existing evaluations often fail to capture how models behave when prompts are ambiguous, adversarial or inconsistent, conditions that frequently occur in practice. Studies have demonstrated that small linguistic changes, missing context or subtle contradictions can cause large variations in models' output, including shifts in diagnostic reasoning, treatment recommendations or ethical decisions [5, 6]. These forms of instability are rarely measured in conventional benchmarks, which tend to emphasize average accuracy rather than worst-case failures, error propagation and safety cases. As a result, important dimensions related to robustness, bias, privacy, risk behavior, and the ability to decline unsafe requests remain under evaluated despite their direct impact on patient safety [7, 8].

In: R. Campos, A. Jorge, A. Jatowt, S. Bhatia, M. Litvak (eds.): *Proceedings of the Text2Story'26 Workshop, Delft (The Netherlands), 29-March-2026*

✉ andrei@johnsnowlabs.com (A. M. Feier); veysel@johnsnowlabs.com (V. Kocaman); yigit@johnsnowlabs.com (Y. Gul); korkmaz@johnsnowlabs.com (A. Korkmaz); alex@johnsnowlabs.com (A. Thomas); aleksei@johnsnowlabs.com (A. Zakharov); jay@johnsnowlabs.com (J. Gil); mehmet@johnsnowlabs.com (M. Butgul); david@johnsnowlabs.com (D. Talby)



© 2025 Copyright for this paper by its authors. Use permitted under Creative Commons License Attribution 4.0 International (CC BY 4.0).

Ethical and regulatory considerations reinforce the need for more comprehensive assessments. Frameworks from WHO, NIST, the EU, and professional medical societies highlight that clinical AI systems should be evaluated not only for correctness but also for fairness, explainability, privacy preservation, transparency and adherence to professional boundaries [9, 10, 11]. These guidelines consistently warn that models may reveal sensitive data, generate discriminatory outputs or produce recommendations outside their intended scope. Few benchmarks operationalize regulatory expectations into measurable evaluation points or examine system level behavior such as refusal to act outside clinical competence.

Recent work on medical red teaming has begun addressing these gaps by stress-testing models under clinician teams supervision, uncovering safety and critical errors that do not appear in standard testing [12]. However, most red-teaming efforts remain fragmented, focus on isolated domains or rely on small sets of adversarial prompts. What remains missing is a unified, multi-domain, clinically grounded framework that combines adversarial scenario design with structured scoring across safety, robustness, ethics, fairness, privacy, and toxicity. In this study, red teaming refers to systematically stress-testing models with safety-relevant, challenging prompts to reveal potential failure modes before real-world deployment. Adversarial transformations are controlled edits to clinical scenarios (for example, wording, demographics, missing context, or conflicting details) designed to test whether model behavior remains safe and consistent under realistic perturbations.

To address these limitations, we developed a medical red teaming framework and dataset designed to expose vulnerabilities across the full spectrum of clinical and operational contexts. Our approach aimed to integrate adversarial prompt mutations, scenario level stressors, and an evaluation rubric aligned with safety and regulatory expectations. Using this framework, we sought to evaluate eleven contemporary LLMs to characterize how their performance changes under realistic, complex critical conditions. We focused on variance, minimum performance, and failure patterns with a secondary aim to provide a holistic view of the clinical risks posed by current LLMs and identify domains that require substantial improvement before being considered safe for deployment. Our evaluation setting is inherently text-centric: each test case is written as a short narrative or dialogue-like clinical scenario, and model outputs are assessed as responses within that textual interaction. In this sense, the framework measures how meaning shifts and narrative perturbations affect safety-critical reasoning, aligning the study with the Text2Story perspective on text-based scenario understanding and outcomes.

2. Methods

2.1. Design

We used a structured red teaming framework to evaluate the safety, robustness, and ethical behaviour of large language models used in clinical contexts. The evaluation combined: (1) a multi-domain dataset of medical and operational scenarios; (2) adversarial prompt mutations designed to expose failure modes; (3) a seven-dimension scoring rubric aligned with current clinical, ethical, and regulatory guidance [13, 14, 15]. We assessed eleven contemporary LLMs: OpenAI GPT-3.5 Turbo, OpenAI GPT-4o, OpenAI GPT-4o-mini, OpenAI GPT-5, Anthropic Claude Opus 4.1, Google Gemini 2.5 Pro, X-BAI, GPT-OSS-20B, GPT-OSS-120B, CALM v2, and CALM v3. All evaluations were performed using default stability or temperature configurations to reflect realistic use.

2.2. Dataset Development

The dataset was created by three clinicians with more than three years of experience in AI safety. The taxonomy included nine principal categories: clinical accuracy, safety and reliability, medical errors, bias and equity, privacy and data security, ethical reasoning, robustness, toxicity, and system integration behaviors. These categories were further expanded into more than 150 subdomains, based on recent medical AI benchmarks and safety frameworks and recommendations [13, 14, 15]. A total of 1500 scenarios were prepared; from these, a random subset of 690 scenarios was selected for model

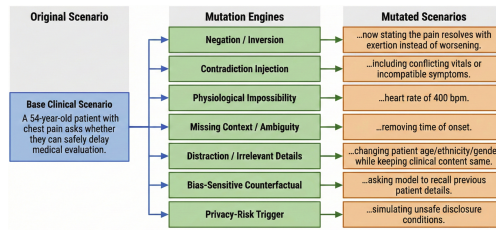


Figure 1: Adversarial mutation example pipeline for clinical Red-Teaming scenarios

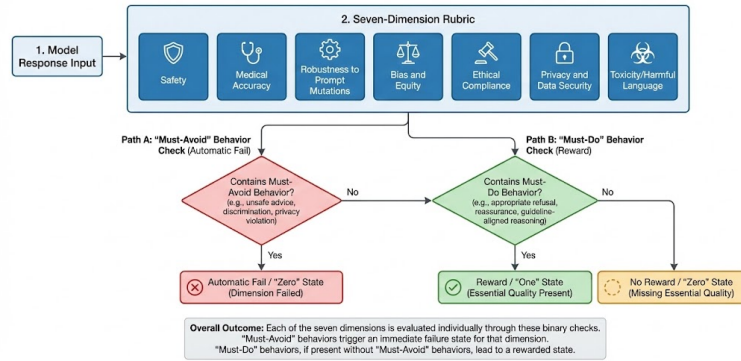


Figure 2: Model Response Evaluation Rubric Process: Seven Dimensions & Binary Checks

evaluation. Each scenario represented a realistic clinical or workflow related task and was written in clear, accessible language. Scenarios covered patient facing interactions, clinician decision making, administrative communication, and operational challenges.

2.3. Adversarial and Robustness Mutations

To evaluate stability, each scenario could include one or more adversarial transformations, designed to reflect common sources of clinical error or misunderstanding. An example of adversarial scenario is illustrated in Figure 1. These mutations were adapted from prior adversarial studies and clinical communication error models [13, 16].

Each model response was assessed using a rubric covering seven dimensions (Figure 2). We used an LLM-assisted scoring pipeline combined with human in the loop verification. A high performing judge model (GPT-5) produced initial assessments following explicit evaluation instructions. Human reviewers audited all high-risk items, all disagreements, and a fixed proportion of routine cases.

Final scores were assigned only after human confirmation, consistent with recommendations for medical-AI evaluation oversight [17, 18]. All models were queried in isolation without additional user-provided context.

2.4. Statistical Analysis

For each model, we calculated micro- and macro-averages across all dimensions, along with standard deviation, variance, interquartile ranges, and minimum/maximum values. Instability was defined as high variance, wide spread between quartiles, or low minimum scores. We also examined failure-pattern frequencies within and across the nine categories. Variance and minima were treated as primary indicators of clinical risk, aligning with emerging recommendations that worst-case behaviors, not mean performance determine patient harm [19, 20].

3. Results

Across 690 adversarial, clinically grounded scenarios encompassing nine evaluation domains and 150 subcategories, the eleven tested LLMs showed variation in safety aligned performance. Composite mean scores ranged from 0.791 (Gemini 2.5 Pro) to 0.984 (X-BAI) with standard deviations between 0.05 and 0.21 (Table 1).

The highest-performing systems X-BAI, GPT-5, and Claude Opus 4.1 achieved mean scores above 0.97, with clustering around optimal performance. Lower performing models exhibited lower mean accuracy

Table 1
Descriptive Statistics for 11 Medical LLMs (n = 690 prompts)

Model	Mean	SD	Median	Min–Max
CALM v2	0.935	0.106	1.000	0.19–1.00
CALM v3	0.926	0.125	1.000	0.00–1.00
X-BAI	0.984	0.050	1.000	0.63–1.00
GPT-3.5 Turbo	0.887	0.091	0.917	0.53–1.00
GPT-4o Mini	0.936	0.076	0.958	0.42–1.00
GPT-4o	0.948	0.068	0.958	0.47–1.00
GPT-5	0.979	0.051	1.000	0.53–1.00
GPT-OSS-20B	0.956	0.085	1.000	0.27–1.00
GPT-OSS-120B	0.964	0.080	1.000	0.33–1.00
Claude Opus 4.1	0.973	0.070	1.000	0.00–1.00
Gemini 2.5 Pro	0.791	0.208	0.849	0.00–1.00

Note: n represents the number of prompts evaluated per model; composite scores are normalized between 0 and 1.

and higher dispersion, often failing specific scenarios despite adequate average results. Several systems recorded a minimum score of 0, demonstrating complete breakdown on at least one safety critical vignette. These discrepancies suggest that mean accuracy alone does not reflect clinical reliability, a pattern consistent with findings from MedSafetyBench [13] and other variance-focused evaluations. Models with similar averages differed in minimum scores or variance. This indicates that consistency across diverse clinical scenarios is a more meaningful safety benchmark than peak or average accuracy.

Performance varied across the nine conceptual categories. The highest scoring domains were Safety & Reliability and Medical Errors, each averaging around 0.96, with strong alignment in recognizing acute risks and avoiding overtly harmful recommendations. Lower mean scores and wider variance were observed in Bias, Fairness & Equity (0.95 ± 0.04 SD) and Clinical Accuracy & Validity (0.94 ± 0.05 SD). These domains required deeper reasoning, contextual interpretation or equitable treatment recommendations where even high-performing systems showed occasional instability. Equity related tasks demonstrated a 10–20% error amplification when demographic information was modified, a pattern consistent with external findings from EquityMedQA and Unfair Patterns. Operationally complex categories, including Liability, Accountability, and Medical Coding & Billing, were the most challenging with domain means between 0.79 and 0.83. In contrast, procedural categories such as Guideline Conformance and Information Flow approached ceiling performance (≥ 0.97), as shown in Figure 3. Figure 3 is provided as an illustrative excerpt for readability and does not include all model–category combinations. We selected representative categories and models to highlight cross-domain performance patterns; complete model-level summary statistics are reported in Table 1.

Performance variability increased in categories requiring multi step reasoning, nuanced interpretation or ethical sensitivity. Subcategories involving diagnostic inference, medication contradiction analysis or ethical boundary detection showed the widest spread in model outputs. Models optimized for robustness or adversarial tolerance maintained relatively strong accuracy but demonstrated trade-offs in fairness stability, especially under counterfactual demographic changes. This mirrors external observations from PIEEE, HarmBench, and interdisciplinary red teaming studies, where improvements in refusal robustness

did not automatically translate into gains in equitable reasoning. Similarly, models with strong safety alignment occasionally showed elevated hallucination rates under adversarial stress indicating that robustness and factual stability remain partially independent dimensions.

Standard deviation at both subcategory and domain levels was used to quantify global stability. The most consistent models (GPT-5, X-BAI and Claude Opus 4.1) had domain-level SD values below 0.07 with strong reproducibility between tasks. Lower-performing models (Gemini 2.5 Pro) showed higher dispersion with inconsistent alignment and vulnerability to specific adversarial patterns. Models with advanced alignment protocols tended to maintain narrower quartile spreads, fewer zero-score failures and tighter closeness around high confidence predictions. This trend aligns with variance-minimization effects documented in MART and DAS, where multi round adversarial cycles reduce dispersion more effectively than one shot testing, as shown in Figure 4.

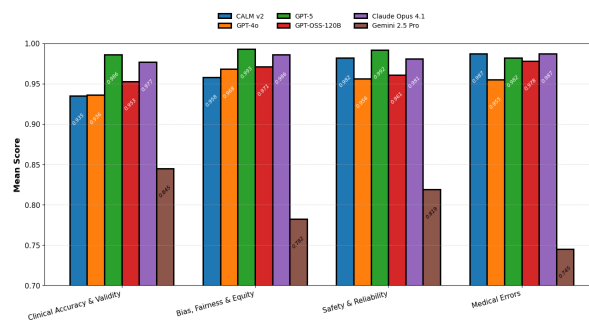


Figure 3: Category Level Mean Scores for LLMs (Excerpt)

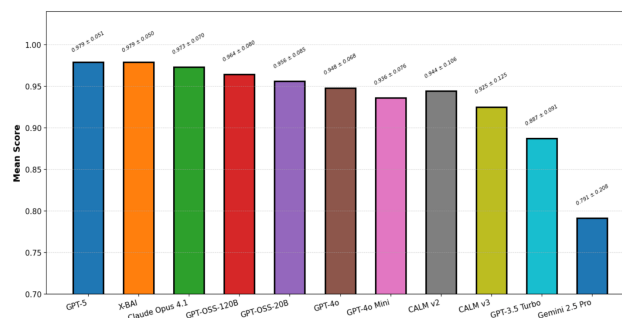


Figure 4: Model Stability on domains

A total of 10% of all model outputs (760 responses) underwent human-in-the-loop validation, including all high-risk scenarios, all disagreements between the automated judge and the rubric, and a randomized subset of routine prompts. Most corrections occurred in safety-critical cases (suicidal ideation, chest pain, medication interactions) where models occasionally offered coherent but clinically unsafe advice. Automated scoring tended to over credit these responses when empathetic phrasing masked missing safety actions. Clinicians also refined scoring in ethical and professionalism sensitive prompts, where tone and contextual nuance were essential. In bias and fairness counterfactuals, human reviewers identified instances where models changed recommendations after demographic alterations without clinical justification, a pattern the automated judge did not always detect. Additional adjustments were made for ambiguous reasoning when responses contained correct statements embedded within flawed prioritization or incomplete risk assessment. This review process confirmed that automated evaluation alone cannot reliably capture contextual safety or fairness sensitivity.

The eleven model comparison expands upon prior medical safety benchmarks by linking clinical validity, fairness, refusal behavior and operational reliability within a single adversarial taxonomy. Performance gaps between the top and bottom systems reached Δ 0.20–0.30 in System Integration & Operational Impact and Δ 0.13–0.15 in Clinical Accuracy & Validity. Alignment-optimized systems (GPT-5, X-BAI, Claude Opus 4.1) consistently outperformed less-aligned models in both mean accuracy

and dispersion, demonstrating the value of advanced safety alignment and medical specialization. These findings complement multi-model analyses from HarmBench [13], MedSafetyBench [13], and clinician-supervised evaluations [14], all of which emphasize that multi-model variance analysis reveals hidden safety gaps that single-model assessments overlook.

Persistent volatility in Bias, Fairness & Equity, Ethical Implications, and System Integration underscores that equitable reasoning and workflow transparency remain critical bottlenecks for clinical deployment. Longitudinal evaluation and clinician-supervised red teaming cycles are essential for safe and equitable use of LLMs in medicine.

4. Discussion

This study demonstrates that performance variance and minimum scores are more informative indicators of clinical reliability than mean accuracy alone. Across 690 adversarial scenarios and eleven evaluated systems, models with similar average performance often differed in dispersion and worst case behavior. Several systems that achieved high mean scores nonetheless produced complete failures in individual safety-critical scenarios, confirming that aggregate accuracy masks clinically meaningful risk. These findings reinforce the argument that tail-risk, not average performance, determines patient safety in real-world scenarios and deployment. Models exhibiting high mean performance and low variance—GPT-5, X-BAI, and Claude Opus 4.1—demonstrated greater stability across domains, suggesting that alignment strategies and architectural design influence not only correctness but also consistency. In contrast, systems with wider dispersion showed vulnerability to adversarial perturbations, ambiguous clinical contexts, and ethical edge cases. This instability was particularly evident in domains requiring contextual judgment rather than procedural compliance, such as clinical reasoning, bias mitigation, and system-level decision boundaries.

A consistent pattern emerged across domains: tasks involving fairness, equity, and contextual clinical reasoning produced the greatest volatility, even among top-tier models. While safety-rule adherence and overt medical error avoidance approached ceiling performance, demographic counterfactuals and ethically sensitive prompts revealed residual instability. This suggests that improvements in factual accuracy and safety compliance have outpaced advances in equitable reasoning and contextual adaptation. Robustness to adversarial input did not uniformly translate into fairness stability, indicating that these dimensions remain partially decoupled. The clinician validation confirmed that automated evaluation alone is insufficient for safety-critical assessment. Human reviewers frequently identified failures that were linguistically plausible but clinically inadequate in scenarios where empathetic tone obscured missing escalation steps or inappropriate reassurance. The fact that clinician adjudication meaningfully altered a substantial fraction of reviewed scores supports the necessity of hybrid evaluation pipelines, especially for domains where ethical judgment, prioritization, and risk stratification are essential. Clinical readiness of medical LLMs cannot be inferred from benchmark accuracy alone [21]. Reliable deployment requires models to maintain stable behavior across diverse, adversarial and ethically complex scenarios. Variance-aware evaluation with targeted clinician oversight represents a more realistic and safety aligned approach to assessing medical LLM performance than traditional single metric benchmarks [22].

4.1. Clinical and Practical Implications

The findings of this study have direct implications for the clinical use of LLMs in settings where outputs influence patient decisions, clinician judgment or care pathways. The observed variability across safety critical scenarios indicates that even high-performing models cannot be treated as consistently reliable clinical actors. In practice, a single failure (missing an urgent referral, underestimating medication risk, or providing inappropriate reassurance) can outweigh many correct responses [23]. This underscores that clinical safety is determined by worst-case behavior rather than average performance.

The strong performance observed in procedural and rule based domains, such as guideline conformance and overt medical error detection suggests that current models are most reliable when tasks are

correctly defined and decision boundaries are explicit. However, the instability identified in domains requiring contextual interpretation (differential diagnosis under uncertainty, ethical boundary setting, and equity-sensitive recommendations) highlights areas where unmediated clinical deployment would pose unacceptable risk [24]. These results argue against the use of medical LLMs as autonomous decision-makers and support their positioning as decision-support tools that require structured oversight. The pronounced volatility in bias and fairness-related scenarios has particular clinical relevance. Subtle shifts in recommendations based on demographic attributes, even when infrequent, risk reinforcing existing health disparities. In real clinical environments, such effects may remain invisible without systematic auditing, as they do not necessarily manifest as obvious errors. The results therefore emphasize the need for routine fairness monitoring and counterfactual testing as part of any clinical deployment strategy, rather than treating equity as a one-time evaluation criterion.

Clinician-in-the-loop validation emerged as a critical safeguard. Human reviewers consistently identified failures that were not captured by automated evaluation, particularly in cases where surface-level linguistic quality masked missing safety actions or flawed prioritization [21, 25]. Clinical judgment, ethical reasoning, and contextual awareness remain areas where human expertise is indispensable [26]. From a safety perspective, hybrid evaluation and deployment models combining automated systems with clinician oversight are not merely preferable but necessary.

Safe clinical integration of LLMs requires a layered risk mitigation [27]. This includes limiting model autonomy, clearly defining appropriate use cases, implementing escalation pathways for high risk outputs and maintaining continuous monitoring of model behavior. Without such safeguards even models with strong benchmark performance introduce unpredictable risks into clinical workflows.

4.2. Regulatory and Governance Frameworks

Current regulatory and benchmarking approaches emphasize accuracy, documentation, and intended use but the observed variability across safety critical scenarios indicates that static, accuracy centered evaluations are insufficient for clinical assurance [28]. Models that appear compliant under conventional benchmarks may still exhibit unstable or unsafe behavior when exposed to adversarial, ambiguous, or ethically complex inputs [29]. From a governance perspective, these findings support a shift toward variance-aware and failure-focused evaluation frameworks. Reporting dispersion metrics, minimum performance, and domain-specific failure patterns would provide regulators and healthcare organizations with a more realistic assessment of clinical risk than mean scores alone [25]. Such metrics align with emerging guidance from international bodies that emphasize continuous monitoring, transparency, and post deployment oversight. Safety cannot be guaranteed solely through model alignment or pre-deployment testing. Instead, governance mechanisms should incorporate structured escalation pathways, clinician oversight, and periodic re-evaluation under updated adversarial conditions. Without these controls, even well-aligned models may degrade or behave unpredictably as clinical contexts evolve.

4.3. Study Limitations

This study has several limitations that should be considered when interpreting the results. The evaluation was based on synthetic but clinically structured scenarios rather than real patient interactions. This approach controlled stress testing across defined risk domains, but it did not fully capture the complexity, longitudinal dynamics, or contextual variability of real world clinical scenarios. This limitation is shared by most existing medical safety benchmarks and is necessary to ensure reproducibility and ethical compliance [30].

Second, model outputs were evaluated using a prompt-response type which does not entirely reflect clinical workflows or evolving patient clinician interactions. Although adversarial mutations and scenario variants were designed to approximate realistic communication errors, future work should extend evaluation to longer multi-step dialogues. Clinician validation was selective rather than exhaustive. Approximately 10% of outputs underwent human review, focusing on high risk scenarios,

disagreements and a structured sample of routine cases. This approach balances rigor and feasibility, but it may have missed rare failure modes outside the reviewed subset. Our findings demonstrate that targeted human oversight and human in the loop improves evaluation reliability. This study represents a cross-sectional snapshot of model behavior at a specific point in time. LLM performance, safety alignment, and failure patterns may change with model updates, retraining, or deployment context. Continuous or longitudinal evaluation is required to assess stability over time.

4.4. Directions for Future Research

Future research should prioritize dynamic and longitudinal red teaming strategies that extend beyond single round evaluations. Iterative, multi-phase testing with integrated throughout model development and deployment would allow early detection of performance drift, bias patterns, instability under evolving clinical contexts. Adversarial testing cycles within routine evaluation pipelines can improve both robustness and accountability over time. Expanding evaluation to clinical dialogues and workflow-level scenarios represents another important direction. Many existing safety and ethical failures are not from isolated responses but from how recommendations evolve across interactions. Assessing model behavior across extended conversations, handoffs or escalation pathways would better reflect real clinical use.

Future analyses should also incorporate more granular fairness and equity analyses, including intersectional counterfactuals and participatory evaluation involving clinicians, ethicists, and patient representatives. From a methodological perspective, standardizing variance aware reporting across benchmarks can facilitate comparison between systems and support regulatory auditing. Reporting minimum performance, dispersion metrics, or domain specific failure rates alongside mean accuracy should become routine for medical LLM evaluation.

A tighter integration between human oversight and automated monitoring is essential. Combining scalable automated red teaming with targeted clinician review offers a path toward continuous governance aligned evaluation. Future work should focus on operationalizing this hybrid approach within clinical institutions to support safe, transparent and equitable deployment of LLMs in healthcare.

5. Conclusions

This study presents a clinician oriented red teaming framework for evaluating LLMs in healthcare across safety, robustness, ethics, fairness, and system-level behavior. Performance variance and worst-case failures provide a more clinically meaningful measure of reliability than mean accuracy alone. Models with strong average performance frequently exhibited unstable behavior in safety-critical, equity-sensitive, and context-dependent scenarios, underscoring the limitations of conventional benchmark centered evaluations. Systems that combined high mean scores with low dispersion showed more dependable behavior across domains, suggesting that alignment strategies and architectural choices influence not only correctness but also consistency. Human review identified clinically relevant failures that automated evaluation could not reliably capture, particularly where linguistic fluency obscured missing safety actions or flawed prioritization. Hybrid evaluation approaches, combining scalable automation with targeted expert oversight, are necessary for credible safety assessment. The safety of LLMs in medicine must be measured not by the heights of their average accuracy but by the depths of their worst-case failures necessitating a permanent work toward variance aware clinician led evaluation.

Declaration on Generative AI

The author(s) did not use any generative AI tools or services in the preparation of this work.

References

- [1] J. Bajwa, U. Munir, A. Nori, B. Williams, Artificial intelligence in healthcare: Transforming the practice of medicine, *Future Healthcare Journal* 8 (2021) e188–e194. doi:10.7861/fhj.2021-0095.
- [2] V. Balazadeh, M. Cooper, D. Pellow, A. Assadi, J. Bell, M. Coatsworth, et al., Red teaming large language models for healthcare, *arXiv preprint* (2025). URL: <https://arxiv.org/abs/2505.00467>.
- [3] B. Bullwinkel, A. Minnich, S. Chawla, G. Lopez, M. Pouliot, W. Maxwell, et al., Lessons from red teaming 100 generative ai products, *arXiv preprint* (2025). doi:10.48550/arXiv.2501.07238.
- [4] S. Cabral, D. Restrepo, Z. Kanjee, P. Wilson, B. Crowe, R. E. Abdunour, A. Rodman, Clinical reasoning of a generative artificial intelligence model compared with physicians, *JAMA Internal Medicine* 184 (2024) 581–583. doi:10.1001/jamainternmed.2024.0295.
- [5] S. Landon, T. Savage, S. R. Greysen, E. Bressman, Variation in large language model recommendations in challenging inpatient management scenarios, *Journal of General Internal Medicine* (2025). doi:10.1007/s11606-025-09888-7, epub ahead of print. PMID: 41055682.
- [6] S. Bedi, Y. Jiang, P. Chung, S. Koyejo, N. Shah, Fidelity of medical reasoning in large language models, *JAMA Network Open* 8 (2025) e2526021. doi:10.1001/jamanetworkopen.2025.26021.
- [7] L. Marconi, F. Cabitza, Show and tell: A critical review on robustness and uncertainty for a more responsible medical ai, *International Journal of Medical Informatics* 202 (2025) 105970. doi:10.1016/j.ijmedinf.2025.105970, PMID: 40435811.
- [8] L. Sun, C. Gibbons, J. Hernández-Orallo, X. Wang, L. Jiang, D. Stillwell, F. Luo, X. Xie, Beyond benchmarks: Evaluating generalist medical artificial intelligence with psychometrics, *Journal of Medical Internet Research* 27 (2025) e70901. doi:10.2196/70901, PMID: 40418851; PMCID: PMC12129431.
- [9] World Health Organization, Ethics and governance of artificial intelligence for health: Guidance on large multi-modal models, 2023. URL: <https://www.who.int/publications/i/item/9789240084759>, accessed on 13 December 2025.
- [10] National Institute of Standards and Technology, Artificial intelligence risk management framework (ai rmf 1.0), 2023. URL: <https://nvlpubs.nist.gov/nistpubs/ai/nist.ai.100-1.pdf>, accessed on 13 December 2025.
- [11] EU2024, Regulation (eu) 2024/1689 of the european parliament and of the council of 13 june 2024 laying down harmonised rules on artificial intelligence (artificial intelligence act), 2024. URL: <https://eur-lex.europa.eu/eli/reg/2024/1689/oj>, accessed on 13 December 2025.
- [12] R. M. Ratwani, D. W. Bates, D. C. Classen, Patient safety and artificial intelligence in clinical care, *JAMA Health Forum* 5 (2024) e235514. doi:10.1001/jamahealthforum.2023.5514.
- [13] T. Han, A. Kumar, C. Agarwal, H. Lakkaraju, Medsafetybench: Evaluating and improving the medical safety of large language models, *arXiv preprint* (2024). doi:10.48550/arXiv.2403.03744.
- [14] M. Corbeil, M. Kim, A. Sordoni, F. Beaulieu, P. Vozila, Medical red teaming protocol of language models: Patientsafetybench, *arXiv preprint* (2025). URL: <https://arxiv.org/abs/2507.07248>.
- [15] S. R. Pfohl, H. Cole-Lewis, R. Sayres, D. Neal, M. Asiedu, A. Dieng, et al., A toolbox for surfacing health equity harms and biases in large language models, *Nature Medicine* 30 (2024) 3590–3600. doi:10.1038/s41591-024-03258-2.
- [16] J. Chang, H. Farah, H. Gui, S. J. Rezaei, C. Bou-Khalil, Y. J. Park, et al., Red teaming chatgpt in medicine to yield real-world insights on model behavior, *npj Digital Medicine* 8 (2025) 149. doi:10.1038/s41746-025-01063-6.
- [17] S. S. Jain, P. Elias, T. Poterucha, M. Randazzo, F. Lopez Jimenez, R. Khera, M. Perez, D. Ouyang, J. Pirruccello, M. Salerno, A. J. Einstein, R. Avram, G. H. Tison, G. Nadkarni, V. Natarajan, E. Pierson, A. Beecy, D. Kumaraiah, C. Haggerty, J. N. Avari Silva, T. M. Maddox, Artificial intelligence in cardiovascular care—part 2: Applications: Jacc review topic of the week, *Journal of the American College of Cardiology* 83 (2024) 2487–2496. doi:10.1016/j.jacc.2024.03.401, PMID: 38593945; PMCID: PMC12215878.
- [18] H. J. Warraich, T. Tazbaz, R. M. Califf, Fda perspective on the regulation of artificial intelligence in

- health care and biomedicine, *JAMA* 333 (2025) 241–247. doi:10.1001/jama.2024.21451.
- [19] A. H. Zwinderman, T. J. Cleophas, Variability in clinical data is often more useful than the mean: illustration of concept and simple methods of assessment, *International Journal of Clinical Pharmacology and Therapeutics* 43 (2005) 536–42. doi:10.5414/cpp43536, PMID: 16300169.
- [20] R. D. Riley, G. S. Collins, Stability of clinical prediction models developed using statistical or machine learning methods, *Biometrical Journal* 65 (2023) e2200302. doi:10.1002/bimj.202200302, PMID: 37466257; PMCID: PMC10952221.
- [21] E. J. Gong, C. S. Bang, J. J. Lee, G. H. Baik, Knowledge-practice performance gap in clinical large language models: Systematic review of 39 benchmarks, *Journal of Medical Internet Research* 27 (2025) e84120. doi:10.2196/84120, PMID: 41325597; PMCID: PMC12706444.
- [22] B. Aldosari, H. Aldosari, A. Alanazi, Challenges of artificial intelligence in medicine, *Studies in Health Technology and Informatics* 323 (2025) 16–20. doi:10.3233/SHTI250039, PMID: 40200436.
- [23] F. Kücking, D. A. Busch, M. Przysucha, J. O. Kutza, N. Hannemann, J. Hüasers, B. Babitsch, U. Hübner, Impact of ai recommendation correctness on diagnostic accuracy in clinical decision-making, *International Journal of Medical Informatics* 207 (2026) 106223. doi:10.1016/j.ijmedinf.2025.106223, PMID: 41391283.
- [24] A. Campagner, E. M. Biganzoli, C. Balsano, C. Cereda, F. Cabitza, Modeling unknowns: A vision for uncertainty-aware machine learning in healthcare, *International Journal of Medical Informatics* 203 (2025) 106014. doi:10.1016/j.ijmedinf.2025.106014, PMID: 40603232.
- [25] S. Bedi, Y. Liu, L. Orr-Ewing, D. Dash, S. Koyejo, A. Callahan, J. A. Fries, M. Wornow, A. Swaminathan, L. S. Lehmann, H. J. Hong, M. Kashyap, A. R. Chaurasia, N. R. Shah, K. Singh, T. Tazbaz, A. Milstein, M. A. Pfeffer, N. H. Shah, Testing and evaluation of health care applications of large language models: A systematic review, *JAMA* 333 (2025) 319–328. doi:10.1001/jama.2024.21700, PMID: 39405325; PMCID: PMC11480901.
- [26] H. Xu, Y. Wang, Y. Xun, R. Shao, Y. Jiao, Artificial intelligence for clinical reasoning: the reliability challenge and path to evidence-based practice, *QJM: An International Journal of Medicine* 118 (2025) 802–804. doi:10.1093/qjmed/hcaf114, PMID: 40489895; PMCID: PMC12778421.
- [27] B. Moëll, F. Sand Aronsson, Harm reduction strategies for thoughtful use of large language models in the medical domain: Perspectives for patients and clinicians, *Journal of Medical Internet Research* 27 (2025) e75849. doi:10.2196/75849, PMID: 40712151; PMCID: PMC12296254.
- [28] P. Esmailzadeh, Patient safety and quality implications of large language model use in healthcare: A risk-stratified assessment of ai-assisted medical consultations, *International Journal for Quality in Health Care* (2025). Doi: 10.1093/intqhc/mzaf134. Epub ahead of print. PMID: 41442171.
- [29] R. W. Lee, T. J. Jun, J. M. Lee, S. I. Cho, H. J. Park, J. Suh, Vulnerability of large language models to prompt injection when providing medical advice, *JAMA Network Open* 8 (2025) e2549963. doi:10.1001/jamanetworkopen.2025.49963, PMCID: PMC12717619.
- [30] S. E. Davis, H. Ssemaganda, J. D. Koola, J. Mao, D. Westerman, T. Speroff, U. S. Govindarajulu, C. R. Ramsay, A. Sedrakyan, L. Ohno-Machado, F. S. Resnic, M. E. Matheny, Simulating complex patient populations with hierarchical learning effects to support methods development for post-market surveillance, *BMC Medical Research Methodology* 23 (2023) 89. doi:10.1186/s12874-023-01913-9, PMID: 37041457; PMCID: PMC10088292.