When Chain-of-Thought Backfires: Evaluating Prompt Sensitivity in Medical Language Models

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Abstract

Large language models are increasingly deployed in medical settings, yet their sensitivity to prompt formatting remains poorly characterized. We evaluate MedGemma (4B and 27B variants) on MedMCQA (4,183 questions) and PubMedQA (1,000 questions). Our experiments reveal concerning findings: chain-of-thought prompting *decreases* accuracy by 5.7% compared to direct answering; few-shot examples degrade performance by 11.9% while increasing position bias from 0.14 to 0.47; shuffling answer options causes the model to change predictions 59.1% of the time with accuracy dropping up to 27.4 percentage points; and truncating context to 50% causes accuracy to plummet below the no-context baseline. These results demonstrate that prompt engineering techniques validated on general-purpose models do not transfer to domain-specific medical LLMs.

1 Introduction

Large language models have achieved impressive performance on medical licensing exams, with GPT-4 exceeding passing thresholds by over 20 points [Nori et al., 2023] and Med-PaLM 2 reaching 86.5% on MedQA [Singhal et al., 2023b]. These results have fueled enthusiasm for deploying LLMs in clinical decision support. However, benchmark accuracy tells only part of the story—how models respond to variations in prompt format, question ordering, and context presentation remains poorly understood, despite being critical for real-world deployment where inputs are rarely formatted identically to benchmark conditions.

We focus on MedGemma [DeepMind, 2024], Google's medical-specialist LLM built on the Gemma architecture. A widely held belief in the LLM community is that certain prompting strategies reliably improve performance. Chain-of-thought prompting, which instructs models to reason step-by-step before answering, has shown consistent gains on mathematical and logical reasoning tasks [Wei et al., 2022]. Few-shot learning, where examples are provided in-context, helps models understand desired output formats [Brown et al., 2020]. These techniques are often treated as "best practices" that should transfer across domains and model families.

But should they? Domain-specific models may have internalized different patterns during training. A model trained extensively on medical literature might already encode structured clinical reasoning, making explicit chain-of-thought prompts redundant or even counterproductive. Similarly, few-shot examples drawn from one medical specialty might prime the model with concepts that are irrelevant or misleading for questions in other specialties.

We present a systematic evaluation of MedGemma's sensitivity to prompt variations across three experimental conditions. First, we conduct a prompt ablation study comparing zero-shot, chain-of-thought, and few-shot strategies on 4,183 MedMCQA questions, measuring both accuracy and position bias. Second, we test option order sensitivity by shuffling answer choices and measuring how often the model changes its prediction—a direct test of whether responses reflect semantic understanding or superficial position cues. Third, we evaluate evidence conditioning on 1,000 PubMedQA questions, systematically varying context completeness to understand how partial information affects accuracy. Our findings challenge conventional assumptions about prompt engineering in medical AI and have important implications for clinical deployment.

2 Related Work

Medical Language Models and Benchmarks. Medical language models often demonstrate impressive benchmark scores on exam-style question answering. For example, GPT-4 performs strongly on medical challenge sets [Nori et al., 2023], and Med-PaLM and Med-PaLM 2 report high scores on MedQA [Singhal et al., 2023a,b]. Open, domain-tuned models have also emerged, including MedGemma [DeepMind, 2024] and BioMistral [Labrak et al., 2024]. However, most reporting still emphasizes a single headline accuracy, while deployment inputs vary in formatting, context quality, and answer presentation.

Prompting for Reasoning. Chain-of-thought (CoT) prompting can improve performance on general reasoning tasks by eliciting intermediate steps [Wei et al., 2022]. Follow-up work such as self-consistency explores sampling multiple reasoning paths and aggregating answers [Wang et al., 2023]. These techniques are now common defaults, despite their added token cost and their sensitivity to output parsing.

When CoT Backfires. Recent work challenges the idea that CoT helps everywhere. Sprague et al. [2024] identify settings where step-by-step prompting reduces accuracy, connecting these failures to cases where deliberate reasoning hurts humans as well. Meincke et al. argue that the gains from CoT have diminished for newer models and can even reverse on some tasks [Meincke et al., 2024]. In medical question answering, Omar et al. compare multiple CoT-style prompts and find that improvements depend on the specific method and dataset, rather than following a simple monotonic trend [Omar et al., 2024].

Prompt Sensitivity and Few-shot Formatting. Even without CoT, small prompt changes can shift performance. Lu et al. [2022] show that few-shot example order can materially affect accuracy, and Zhao et al. [2021] propose calibration methods that reduce sensitivity to label and prompt priors. ProSA provides a more systematic view by measuring how model outputs vary across prompt templates [Zhuo et al., 2024]. Together, this work suggests that comparisons between models can be misleading if prompt choices are not controlled.

Multiple-choice Artifacts. Multiple-choice evaluation introduces its own failure modes. Zheng et al. [2024] show that LLMs exhibit selection bias, preferring certain option identifiers even when content is balanced. Our option reordering experiments build on this line of work by separating changes in answer position from changes in distractor content.

Retrieval and Context Quality. Retrieval-augmented generation (RAG) augments a model with external documents at inference time. In medicine, benchmarking work finds large variation in RAG performance across retrievers and corpora, and it reports a pronounced "lost-in-the-middle" effect in biomedical settings [Xiong et al., 2024, Liu et al., 2024]. Retrieval can also introduce new failure modes. ClashEval shows that models can be led astray by incorrect retrieved context, even when it conflicts with the question [Wu et al., 2024]. Recent medical RAG methods aim to improve reliability under imperfect retrieval, for example by training models to cite supporting evidence and by evaluating failure cases explicitly [Sohn et al., 2024, Barnett et al., 2024].

Summary. Our work complements prior studies by focusing on a single medical model family and quantifying how concrete prompt and context variations affect both accuracy and bias, rather than reporting only peak performance under one prompt choice.

3 Methods

3.1 Models and Datasets

We evaluate MedGemma-4B, the 4-billion parameter instruction-tuned variant at bfloat16 precision, and MedGemma-27B, the 27-billion parameter model requiring full bfloat16 precision on 80GB A100 GPUs.

Initial experiments with 4-bit quantization on the 27B model produced NaN logits—a notable finding suggesting that quantization techniques validated on general models may not transfer to medical-specialist architectures.

We use two standard medical QA benchmarks. MedMCQA [Pal et al., 2022] contains questions from Indian medical entrance examinations across 21 subjects; we use the 4,183-question validation split. PubMedQA [Jin et al., 2019] contains research questions derived from PubMed titles that must be answered using abstracts; we use the 1,000-question labeled subset.

3.2 Experimental Conditions

Experiment 1: Prompt Ablation. We test five prompting strategies on MedMCQA: (1) zero-shot direct, presenting the question and requesting only the answer letter; (2) zero-shot CoT, adding "think step by step"; (3) few-shot direct, providing three example Q&A pairs; (4) few-shot CoT, providing three examples with reasoning traces; and (5) answer-only, a minimal prompt with no instructions.

Experiment 2: Option Order Sensitivity. We apply five transformations to each question: original order, random shuffle, rotate-1 (cyclic shift by one), rotate-2 (shift by two), and distractor swap (exchange incorrect options while preserving correct answer position). We measure the flip rate—how often the model changes its answer when options are reordered.

Experiment 3: Evidence Conditioning. On PubMedQA, we vary context: question-only (no context), full abstract, truncated 50%, truncated 25%, background-only (introduction sentences), and results-only (conclusion sentences). This tests how context completeness and type affect accuracy.

3.3 Metrics

We report accuracy with 95% bootstrap confidence intervals (1,000 iterations). Position bias is computed as the absolute difference between predicted and ground truth answer distributions across positions A-D. For option-order experiments, we compute the flip rate: the proportion of questions where the model's prediction changes when options are reordered.

4 Results

4.1 Prompt Ablation

Table 1 shows accuracy across prompting strategies. Zero-shot direct achieves the highest accuracy at 47.6%, while chain-of-thought *reduces* accuracy by 5.7 percentage points. Few-shot examples cause an even larger degradation of 11.9%, while simultaneously increasing position bias from 0.137 to 0.472—indicating the model learns spurious patterns from examples rather than useful formats.

Table 1: Prompt ablation results on MedMCQA (n=4,183). Random baseline is 25%.

Condition	**Accuracy**	**95% CI**	**Pos. Bias**
Zero-shot direct	47.6%	[46.1%, 49.1%]	0.137
Zero-shot CoT	41.9%	[40.4%, 43.3%]	0.275
Few-shot direct	35.7%	[34.3%, 37.0%]	0.472
Few-shot CoT	40.8%	[39.4%, 42.3%]	0.413
Answer-only	43.0%	[41.5%, 44.6%]	0.096

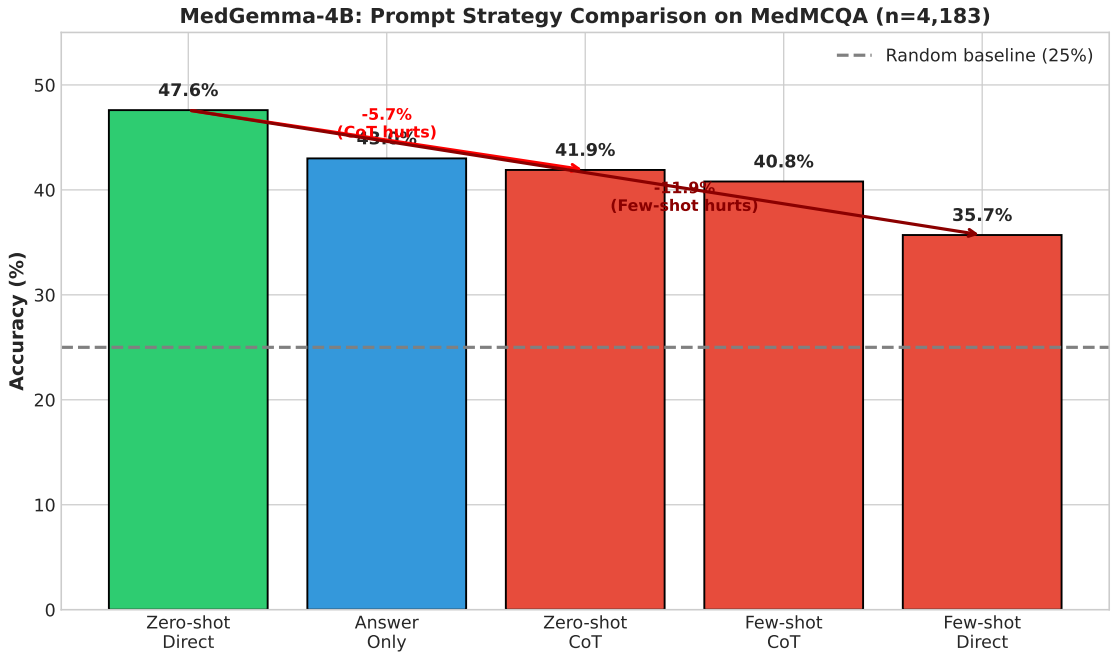

Figure 1: MedGemma-4B accuracy across prompt strategies. Zero-shot direct outperforms all other strategies including chain-of-thought (−5.7%) and few-shot (−11.9%).

4.2 Option Order Sensitivity

Table 2 reveals extreme sensitivity to option ordering. The mean flip rate is 59.1%—the model changes its answer more often than not when options are shuffled. Rotation perturbations cause the largest accuracy drops (up to 27.4%), while distractor swaps show smaller impact (−8.9%), confirming that position rather than distractor content drives fragility.

Table 2: Option order sensitivity on MedMCQA (n=4,183). Random baseline is 25%.

Perturbation	**Accuracy**	**Drop**
Original	47.6%	—
Random shuffle	29.2%	−18.4%
Rotate-1	20.2%	−27.4%
Rotate-2	24.3%	−23.3%
Distractor swap	38.7%	−8.9%
Mean flip rate	59.1%	

4.3 Evidence Conditioning

Table 3 shows context substantially affects PubMedQA performance. Most critically, truncated context performs *worse* than no context: 50% truncation yields 14.1% (4B) and 23.4% (27B), far below question-only baselines of 36.7% and 31.0%. This indicates partial context actively misleads rather than simply providing less information.

Surprisingly, MedGemma-27B achieves its best performance with results-only context (40.0%), which *exceeds* its full-context accuracy (38.2%). The 27B model also underperforms 4B on most conditions, suggesting scale does not guarantee robustness.

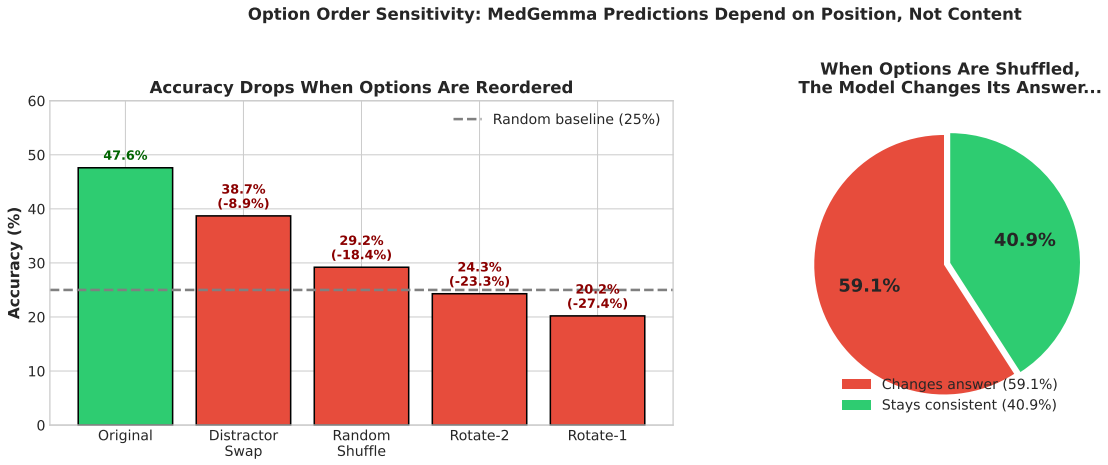

Figure 2: Left: Accuracy drops substantially when options are reordered. Right: The model changes its answer 59.1% of the time when options are shuffled.

Table 3: Evidence conditioning on PubMedQA (n=1,000). Random baseline is 33.3%.

Condition	MedGemma-4B	MedGemma-27B
Question only	36.7%	31.0%
Full context	45.0%	38.2%
Truncated 50%	14.1%	23.4%
Truncated 25%	13.1%	18.6%
Background only	26.5%	19.8%
Results only	41.7%	**40.0%**

5 Discussion

5.1 Why Chain-of-Thought Hurts

The 5.7% accuracy drop from CoT prompting aligns with recent findings that deliberation can reduce performance on certain tasks [Sprague et al., 2024]. MedGemma was trained extensively on medical text and may have internalized domain reasoning patterns; forcing explicit step-by-step logic may override these learned patterns with less reliable deliberation.

Case-level analysis reveals the mechanism: CoT prompting changed answers on 1,262 of 4,183 questions, hurting 750 (direct correct, CoT wrong) while helping only 512—a net loss of 238 questions. The predominant failure pattern involves verbose reasoning (90.7% exceeded 500 characters) where longer chains create opportunities for errors to compound. We also observed self-contradiction (25.6% contained hedge words introducing conflicting logic) and confident wrong conclusions (11.1% stated "therefore" before incorrect answers).

The characteristic failure mode: the model correctly identifies relevant medical concepts early in reasoning, considers alternatives, then talks itself into the wrong answer. In one case involving organophosphate poisoning, CoT correctly identified the condition and atropine's role as antidote, then continued deliberating and selected neostigmine—which would worsen the condition.

5.2 The 59% Flip Rate Problem

MedGemma changes its answer 59.1% of the time when options are shuffled, far exceeding random noise. The maximum flip rate of 72.9% for certain perturbations means that for nearly three-quarters of questions, answers depend more on option position than content. This magnitude exceeds typical findings [Zheng et al.,

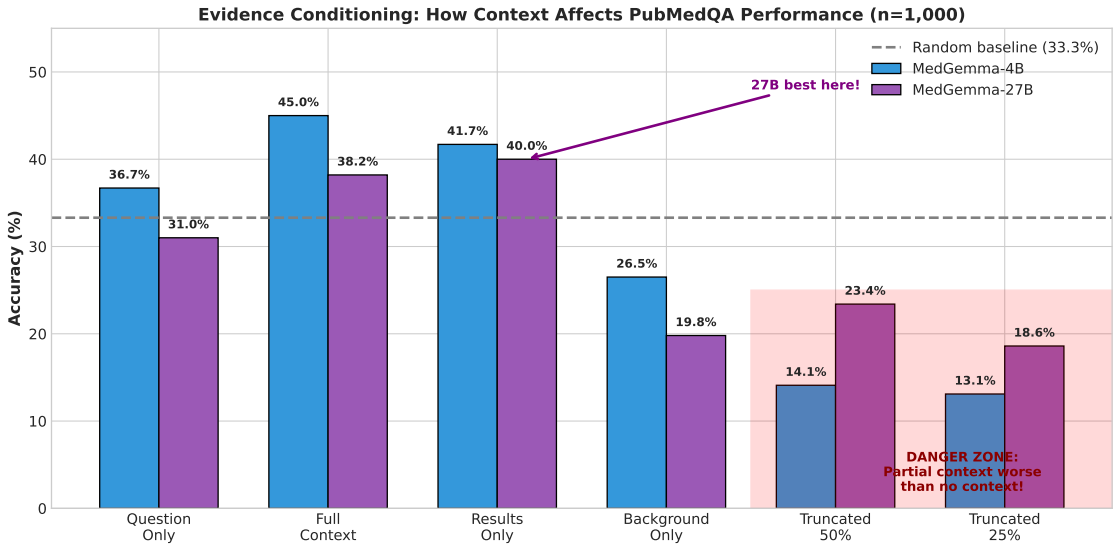

Figure 3: Evidence conditioning results. Truncated context performs worse than no context (danger zone). MedGemma-27B achieves best performance with results-only context.

2024], suggesting medical-specialist training may not mitigate—and could exacerbate—position bias.

For clinical applications, this fragility is unacceptable. A diagnostic support system that changes recommendations based on option ordering provides no reliable signal to clinicians and undermines the premise of using AI to assist medical decision-making.

5.3 Partial Context Actively Misleads

Truncating context to 50% yields 14.1% accuracy while no context achieves 36.7%. This 22.6 point gap suggests that partial context can mislead the model. This matters for retrieval-augmented systems in medicine, where retrieval can surface incomplete or misleading snippets. Prior work shows that models can be led astray by incorrect retrieved evidence, and that retrieval pipelines have multiple failure points that affect end-to-end quality [Wu et al., 2024, Barnett et al., 2024].

Interestingly, results-only context (41.7% for 4B, 40.0% for 27B) nearly matches or exceeds full context, while background-only achieves just 26.5%/19.8%. Both models benefit from conclusions rather than methodological background, suggesting RAG systems should prioritize high-information-density content.

5.4 Scale and Robustness

MedGemma-27B underperforms 4B on evidence conditioning (38.2% vs 45.0% with full context), demonstrating that medical benchmark performance does not scale uniformly with model size. However, 27B shows a different pattern: its best performance comes from results-only (40.0%), exceeding full-context accuracy. This "less is more" finding suggests larger models may be more susceptible to distraction from verbose context but respond well to concentrated information. For deployment, this implies larger models may require selective rather than comprehensive retrieval strategies.

6 Conclusion

Our evaluation reveals that standard prompt engineering techniques do not reliably improve—and may actively harm—medical question answering performance. Chain-of-thought decreases accuracy by 5.7% while increasing position bias; few-shot examples decrease accuracy by 11.9% while tripling position bias; shuffling options causes 59.1% flip rates with accuracy drops up to 27.4 percentage points; and truncated context performs worse than no context.

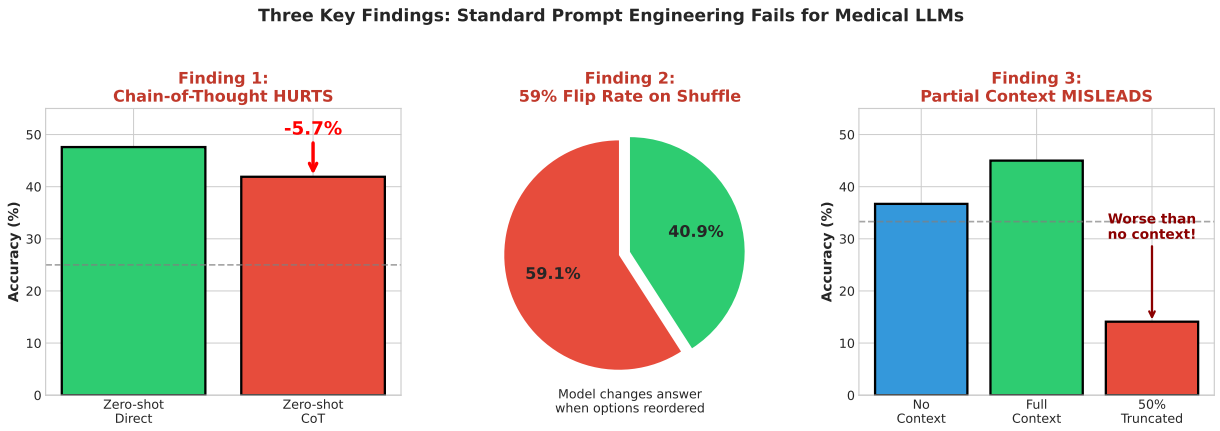

Figure 4: Summary: CoT reduces accuracy 5.7%; option shuffling causes 59.1% flip rate; truncated context performs worse than no context.

For practitioners deploying medical LLMs, we recommend: (1) default to zero-shot direct prompting until evidence justifies added complexity; (2) test option order sensitivity before deployment and consider averaging across orderings or using debiasing techniques [Zheng et al., 2024]; (3) validate retrieval completeness for RAG systems, as incomplete context can be worse than none; and (4) for larger models, prefer selective retrieval of high-density information over comprehensive retrieval.

The extreme sensitivity to prompt variations raises fundamental questions about what benchmark accuracy measures. Before deploying medical LLMs, rigorous empirical validation on specific use cases is essential—assumed best practices from general-purpose models do not transfer.

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A Detailed Analysis

A.1 Chain-of-Thought Failure Patterns

Of 4,183 questions, CoT changed 1,262 answers: 750 hurt vs. 512 helped. Failure patterns:

Verbose reasoning (90.7%): 680 cases exceeded 500 characters. Longer chains create compounding error opportunities.

Self-contradiction (25.6%): 192 cases contained "however" or "but" introducing conflicting mid-reasoning logic.

Confident wrong conclusions (11.1%): 83 cases stated "therefore" before incorrect answers.

A.2 Position Bias Details

MedMCQA ground truth: A: 32.2%, B: 25.1%, C: 21.4%, D: 21.3%. Zero-shot direct predicts A 45.9% (overweight 13.7%). Few-shot direct predicts A 76% despite 32% correct rate.

A.3 Threats to Validity

Parsing errors: <2% across conditions. CoT slightly harder (2.1% vs 1.4%), but cannot explain 5.7% gap.

Dataset imbalance: We report differences from ground truth. The 59.1% flip rate cannot be explained by imbalance.

Contamination: We focus on relative robustness. Memorized answers should be prompt-robust; large degradations indicate genuine sensitivity.

A.4 Limitations

Limited model coverage (MedGemma, BioMistral-7B); 27B requires 80GB GPUs; MCQ and yes/no/maybe formats only; English only; single-turn evaluation.