

# Language Models are Surprisingly Fragile to Drug Names in Biomedical Benchmarks

**Jack Gallifant<sup>1\*</sup>, Shan Chen<sup>2,3,4\*</sup>, Pedro Moreira<sup>1,8</sup>, Nikolaj Munch<sup>1,5</sup>, Mingye Gao<sup>1</sup>**  
**Jackson Pond<sup>2,3</sup>, Hugo Aerts<sup>2,3,7</sup>, Leo Anthony Celi<sup>1,2,9</sup>,**  
**Thomas Hartvigsen<sup>1,6</sup>, Danielle S. Bitterman<sup>2,3,4†</sup>**

<sup>1</sup>MIT, <sup>2</sup>Harvard, <sup>3</sup>Mass General Brigham, <sup>4</sup>Boston Children’s Hospital,

<sup>5</sup>Aarhus University <sup>6</sup>University of Virginia, <sup>7</sup>Maastricht University,

<sup>8</sup>Universitat Pompeu Fabra, <sup>9</sup>Beth Israel Deaconess Medical Center

## Abstract

Medical knowledge is context-dependent and requires consistent reasoning across various natural language expressions of semantically equivalent phrases. This is particularly crucial for drug names, where patients often use brand names like Advil or Tylenol instead of their generic equivalents. To study this, we create a new robustness dataset, **RABBITS**, to evaluate performance differences on medical benchmarks after swapping brand and generic drug names using physician expert annotations.

We assess both open-source and API-based LLMs on MedQA and MedMCQA, revealing a consistent performance drop ranging from 1-10%. Furthermore, we identify a potential source of this fragility as the contamination of test data in widely used pre-training datasets.<sup>1</sup>

## 1 Introduction

Large Language Models (LLMs) are poised to transform medicine by providing data processing and decision support capabilities (Jiang et al., 2023b; Clusmann et al., 2023). However, the medical deployment of LLMs demands high accuracy and reliability, as errors can result in severe health consequences (Chen et al., 2024a; Goodman et al., 2024; Yan et al., 2024). A key challenge is the synonymy and context-specific nature of medical language; for instance, patients might use brand names like Advil or Tylenol instead of pharmaceutically equivalent generic terms such as ibuprofen or acetaminophen. LLMs must, therefore, be able to provide consistent and accurate advice in the face of this variability. Fluctuations could lead to risks like medical misinformation, medication

errors due to incorrect medication advice, and biases toward or against proprietary products. Our study investigates the effects of substituting drug names—from brand to generic and vice versa—on LLM performance.

Building on the need for robustness in medical LLM applications, numerous efforts have developed knowledge benchmarks (Jin et al., 2019; Hendrycks et al., 2021; Jin et al., 2020; Liu et al., 2023; Wang et al., 2024). Yet, these initiatives primarily tackle general language tasks and often neglect the unique challenges of medical terminology in real-world settings. There is an unmet need to overcome this research gap, as the variability in medical language implies that conventional robustness evaluations might not sufficiently cater to specialized healthcare demands.

A key reason for this gap is the lack of publicly available, expert-annotated datasets specific to the healthcare domain. To address this issue, our work leverages existing medical benchmarks and employs physician expert annotators to substitute brand names with their generic counterparts and vice versa.

Our findings reveal a surprising drop in the performance of LLMs on common medical benchmarks when the drug names are swapped from generic to brand names: **4% drop in accuracy on average**. This is concerning given that patients commonly use brand names and are less likely to spot errors, especially given existing misconceptions that brand drugs are superior to equivalent generics (Colgan et al., 2015; Sewell et al., 2012). Furthermore, we identify a potential source for this fragility: Open pretraining datasets contain substantial amounts of benchmark test data.

Our research introduces a novel category of robustness evaluation centered on drug name interchangeability. We present **RABBITS** (**R**obust **A**sessment of **B**iomedical **B**enchmarks **I**nvolving **d**rug **T**erm **S**ubstitutions for **L**anguage **M**odels) a

\*Co-first authors: Jack Gallifant and Shan Chen

†Corresponding author: dbitterman@bwh.harvard.edu

<sup>1</sup>All code is accessible at <https://github.com/BittermanLab/RABBITS>, and a HuggingFace leaderboard is available at [https://huggingface.co/spaces/ AIM-Harvard/rabbits-leaderboard](https://huggingface.co/spaces/AIM-Harvard/rabbits-leaderboard).

specialized dataset and leaderboard to aid in evaluating LLM performance in healthcare. Specifically, our study combines and modifies select questions from the MedMCQA (Pal et al., 2022) and MedQA (Jin et al., 2020) benchmarks to:

- Assess model robustness in understanding clinical knowledge across drug synonyms.
- Detect potential dataset contamination in biomedical benchmarks.
- Highlight the importance of robustness to nomenclature variations in the healthcare domain.

## 2 Related Work

### 2.1 Dataset Contamination

Dataset contamination in training data is a well-documented issue and can affect the performance and generalizability of LLMs. Many studies have aimed to detect benchmark questions within LLM training data (Shi et al., 2024; Xu et al., 2024; Zhou et al., 2023). For instance, research by Recht et al. (2019) illustrated that models trained on contaminated datasets often exhibit inflated performance metrics that do not generalize well to new, unseen data. This problem is particularly concerning for medical LLMs, where inaccurate information can harm patients (Chen et al., 2024a; Yan et al., 2024).

Various strategies have been employed to mitigate dataset contamination. These include removing data with high n-gram overlap with benchmark datasets (Brown et al., 2020) and employing embedding similarity to filter out similar data (Shi et al., 2024). More advanced approaches involve functional evaluations, such as generating new, unique problem instances for each evaluation (Srivastava et al., 2024). Addressing contamination is crucial for ensuring that LLMs provide reliable outputs, especially in sensitive domains like healthcare.

### 2.2 Evaluating Model Robustness

LLMs gain broad capabilities from large-scale data ingestion (Wei et al., 2022), but this also introduces significant challenges (Lu et al., 2023; Chen et al., 2024b). While larger models often perform better, these improvements are not always consistent across domains (Magnusson et al., 2023). Moreover, recent research has questioned the actual reasoning abilities of LLMs, suggesting that their performance may be inflated by dataset contamination

rather than genuine problem-solving skills (Zhang et al., 2024).

Some works have looked into LLMs' robustness in terms of faithfulness (Han et al., 2024) and fairness (Zack et al., 2024; Guevara et al., 2024) under clinical settings. Medfuzz introduced a method to test LLMs' robustness in medical question answering by revealing vulnerabilities through modified benchmark questions (Ness et al., 2024). However, these studies do not specifically address the unique challenges associated with clinical drug terminology and the relationship between robustness and contamination. Hence, there is a significant gap in evaluating LLM robustness for medical applications, particularly in the context of brand and generic drug name interchangeability. This gap underscores the need for focused robustness evaluations tailored to the healthcare sector.

## 3 Methodology

### 3.1 Brand-Generic Pairs

Figure 1 demonstrates the overall workflow of the study. Appendix A details the full data quality assurance and dataset curation process. To create the dataset of brand and generic drug name pairs, we used the RxNorm (National Library of Medicine, 2024) ontology, which links normalized drug names with many pharmaceutical vocabularies. We extracted combinations of brand and generic drug names using the "ingredient of" and "tradename of" relations, resulting in 2,271 generic drugs mapped to 6,961 brands. For each generic drug, there are often multiple associated brand names. Multiple rounds of expert annotation were performed to derive a final list of 1:1 mapped brand-generic pairs for use in the transformed datasets described below.

### 3.2 Dataset Transformation

We used regular expressions to identify and replace brand and generic drug names in the questions and answers of MedQA, MedMCQA, MMLU, PubMedQA, and USMLE. MMLU and PubMedQA had fewer than 100 instances of identified drug names in the test split and were excluded from further analysis. USMLE was excluded due to its overlap with MedQA. Thus, the two datasets included in the final RABBITS benchmark are **MedQA** and **MedMCQA**.

The quality of the transformed datasets were iteratively reviewed by 2 physician authors (JG, DB),

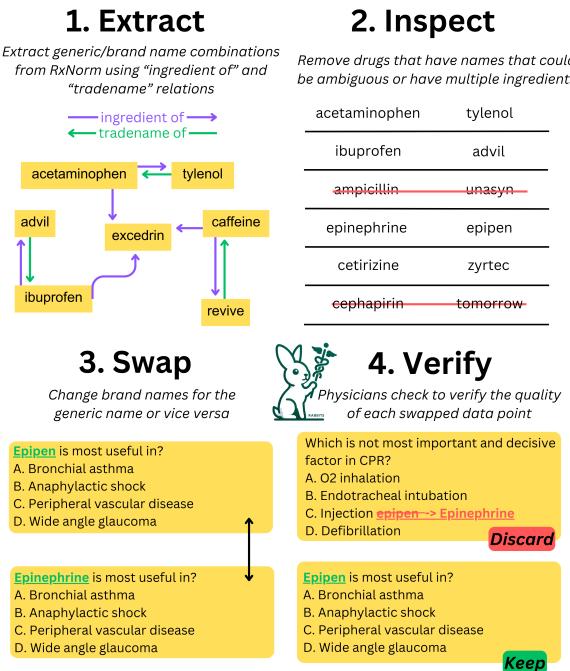


Figure 1: RABBITS dataset generation workflow.

removing instances where replacements introduced inaccuracies, ambiguities, and/or logical inconsistencies in context. This process is described in detail in Appendix A. For the rest of the paper, we will refer to the generic-to-brand swapped benchmark as **g2b** and the brand-to-generic swapped benchmark as **b2g**.

To prevent further data contamination, we will not release the full dataset directly. The HuggingFace leaderboard will be the best way to assess new models' robustness in terms of performance. We evaluated the models using the EleutherAI lm-evaluation harness with zero-shot setting (Gao et al., 2023). We forked this repository, added our transformed datasets as new tasks, and made no other modifications. For API models, we used the same prompt format as the lm-evaluation harness with the default hyperparameters.

Our evaluation focuses on comparing the performance of base models (full list in Appendix Table 3) across the original and transformed datasets to assess the impact of synonym substitution on accuracy. We report results for g2b due to the limited number of b2g swaps observed. By doing so, we aim to determine whether models can maintain performance despite semantically equivalent pharmaceutical terminology.

All datasets and models used in accordance with owners' licenses.

## 4 Results and Discussion

### 4.1 Drug Swapping Results

Figure 2 presents the performance of each model on the original (no-swap) and transformed (g2b) datasets, alongside the average performance and the difference between the two. The line of robustness, with a gradient of 1, represents the ideal scenario where synonym swaps do not affect the selection of answers. The plot reveals that all open-source models from 7B and above fall below this line, indicating decreased performance when drug names are swapped. We also observe a larger drop among MedMCQA over MedQA across models. Refer to Appendix C for a detailed breakdown of individual results in Table 5 and Figure 4.

Table 5 shows that most models experience a decrease in accuracy when generic names are swapped with brand names across different datasets and model sizes. Among large open-source models, the Llama-3-70B model, despite being one of the larger and more accurate models on the original dataset (no-swap accuracy of 76.6%), decreases to 69.7% accuracy with generic-to-brand swaps. Overall, API models perform better than their open-source counterparts with higher accuracy and lower performance drop. While larger open-source series like Qwen2, Llama, and Mixtral are more accurate on original datasets, they exhibit greater sensitivity to g2b swaps. This suggests limitations in true comprehension and reasoning abilities.

### 4.2 Model Knowledge of Drug Pairs via Multi-Choice Questions

We evaluate whether models are able to directly map brand-to-generic drug pairs and vice versa using multiple-choice questions for all drugs that were swapped in our final benchmark dataset. Overall, a clear "scaling law" (Kaplan et al., 2020) is observed in Appendix B Figure 3, where larger models (active parameter size over 13B) consistently outperform smaller models on this task, with larger open-source and API models achieving accuracy over 97%.

### 4.3 Generic and Brand Mentions in Benchmarks and Pre-training Datasets

Table 1 shows our overall dataset swapping statistics where we observe benchmark questions overwhelmingly use generic terms. We also use Infinigram (Liu et al., 2024) to screen the common open-sourced pre-training data, including Redpajama

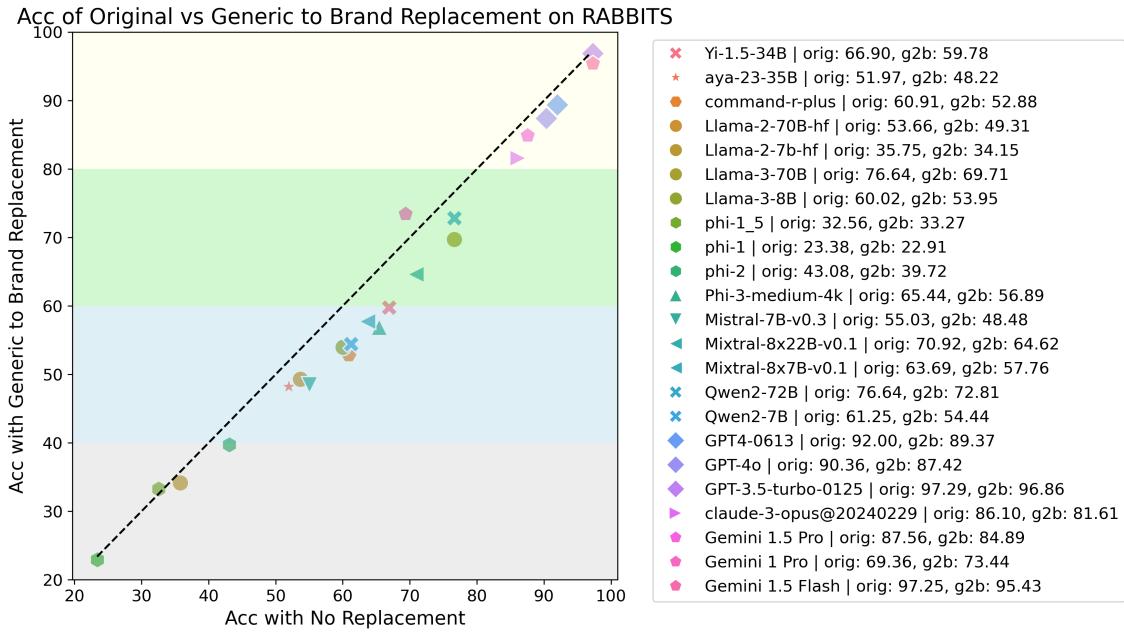


Figure 2: Performance of models on the filtered original datasets compared to the generic-to-brand versions. The dashed diagonal line represents the ideal scenario where synonym swaps do not affect model performance.

(Computer, 2023), C4 train (Raffel et al., 2019), Pile train (Gao et al., 2020), and Dolma 1.6 (Soldaini et al., 2024) for drugs identified in RxNorm, filtered for terms that overlap with common terms (Appendix A, Step 1). Generic names are more common than brand names in these pre-training datasets, as Appendix D table 6 shows.

Table 1: Original and Swapped Dataset Statistics

Dataset	Orig.	Kept	Swap direction	
			b2g	g2b
MedQA	1,271	378	5	816
MedMCQA	4,180	348	24	626

#### 4.4 Contamination Source from Pre-training Dataset

To investigate why we see larger performance drops in MedMCQA than MedQA, we use Infini-gram API (Liu et al., 2024) to identify overlaps with the Dolma 1.6 dataset (3.1T tokens) using size 8 n-grams. Each question’s n-grams are generated and queried through the Infini-gram API.

Dataset contamination are 99.21% and 34.13% in the MedQA and MedMCQA test datasets, respectively, as Table 2 shows. We also benchmark OLMo-1.7-7B-hf, trained only on Dolma, which shows no drop in MedQA (31.22) scores compared

to a 3% drop in MedMCQA (40.90 to 37.93). This likely explains the greater drop in performance in MedMCQA rather than MedQA across models (Appendix C Figure 4).

Table 2: Percentage of contamination of MedQA and MedMCQA benchmarks in Dolma dataset

Dataset	Percentage
MedQA Train	86.92%
MedQA Val	98.10%
MedQA Test	99.21%
MedMCQA Train	22.41%
MedMCQA Val/Test	34.13%

## 5 Conclusion

We find decreased performance on common medical benchmarks when using different names for the same drug, despite LLMs’ ability to match these names, and that these trends scale with LLM size. This suggests that LLM performance may be driven by memorization and not reasoning ability. RABBITS underscores the importance of dataset contamination and model robustness evaluations, particularly in the medical domain. Future research should refine strategies and explore new methods for robustness and fairness evaluation.

## 6 Limitations

Our evaluation is limited to biomedical datasets and focuses only on pharmaceuticals. Future work will extend this approach to other medical synonyms. Although the dataset is smaller, trained physicians have curated it multiple times, ensuring its validity and the accuracy of questions after replacement. Among the pre-training dataset contamination section, we acknowledge none of these models are trained specifically among the pile, C4, RedPajama, or Dolma. However, we use this as a reasonable proxy for estimating the internet distribution.

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## A Brand-Generic Pair Generation and Transformed Dataset Curation

To create the initial dataset of brand and generic drug name pairs, we used the RxNorm ([National Library of Medicine, 2024](#)) ontology, which links normalized drug names with many pharmaceutical vocabularies. We extracted combinations of brand and generic drug names using the "ingredient of" and "tradename of" relations, resulting in 2,271 unique generic names mapped to 6,961 brands. For each generic name, there are often multiple brand names. Keywords were identified using regular expressions and counted in each question within each column (questions and answer choices), and within each dataset split. Datasets with fewer than 100 instances of identified keywords in the test set were excluded from further analysis. We then carried out the following steps to arrive at our dataset of matched brand and generic drug names, and our final transformed QA datasets, as described below.

1. Two authors (SC and JG) reviewed the brand and generic names retrieved from RxNorm and removed keywords that could overlap with common text not referring to drugs. For example, some brand names such as "today" and "perform" could lead to erroneous replacement and were excluded. This resulted in 581 generic keywords mapped to 4297 unique brand keywords.
2. Regular expressions were used to identify and replace names in the medical QA datasets to create 2 initial transformed datasets: generic-to-brand swapped in context, and brand-to-generic swapped in context.
3. Two authors (SC and JP) reviewed the resulting datasets to ensure that the replacements were done correctly.
4. Two physician authors (JG and DB) reviewed the datasets, and identified several areas of ambiguity, errors, and inconsistencies resulting from the regular expression replacement, most commonly: (1) brand names for combination medications swapped to generic names referring to single-agent medications; (2) generic names of combination medications in which a single-agent brand name was swapped for one or both of the drugs in the generic description, for example trimethoprim/sulfamethoxazole replaced with proloprim/sulfamethoxazole; (3) brand names for veterinary formulations; (4) brand names for specific formulations that did not make logical or clinical sense in context, such as brand names for topical formulations replacing descriptions of the drug administered intravenously (either explicitly or implicitly given the clinical context); (5) drug names that are also naturally occurring physiologic compounds, such as amino acids (e.g., tyrosine), vitamins (e.g., Vitamin A); endogenous hormones (e.g., insulin, thyroxine), essential elements (e.g., copper, calcium), etc; and (6) drug names that are also dietary compounds (e.g., caffeine, tryptophan). These questions were annotated, and the drug in question tracked.
5. Given the above identified errors, to facilitate expert review the drug pairs from Step 1 were provided to GPT-4o, which was prompted to check if the brand name's main component is the paired generic drug, and if the brand name drug is used mainly used for humans. 1247 brand drugs were filtered out of the keyword list. This resulted in 563 generic drug mapped to 3050 brand keywords.
6. The remaining drugs in Step 5 were provided to Cohere-RAG, which was prompted to provide a list of brand names for each generic name.
7. A physician author (JG) reviewed the retrieved brand names and selected a single brand name to pair with each generic name. This resulted in 525 generic-to-brand pairs.
8. These 525 generic-to-brand pairs were used to regenerate the transformed dataset using regular expressions to identify and replace names.
9. Two physician authors (JG and DB) reviewed the dataset generated in Step 8, and removed any remaining questions where the replacement resulted in ambiguity or inconsistencies in context to ensure quality of the final dataset.

## B Drug Knowledge

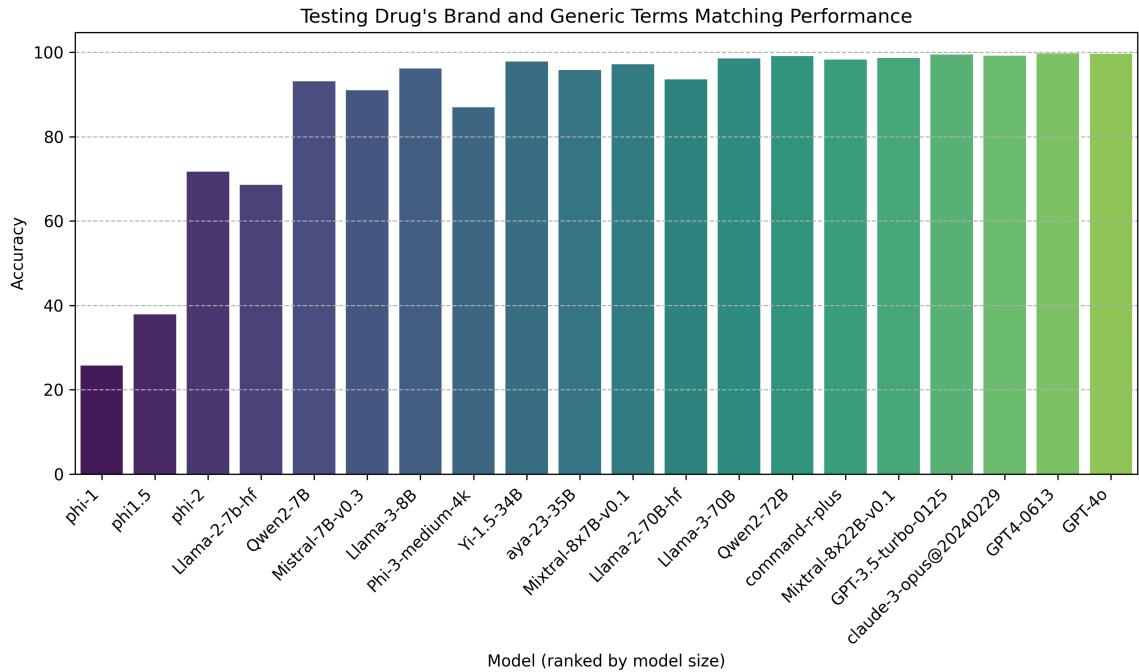


Figure 3: Performance of models on multi-choice question identification of brand-generic drug pairs ordered in increasing model size. Gemini results are missing due to Google’s API safety filters.

## C Drug Swapping results

Figure 4 shows the performance change from the original filtered datasets compared to the dataset where generic drug names are swapped with the brand names (g2b). Notice that the MedMCQA (left) x-axis range is much larger than the MedQA x-axis range, indicating a larger drop across models.

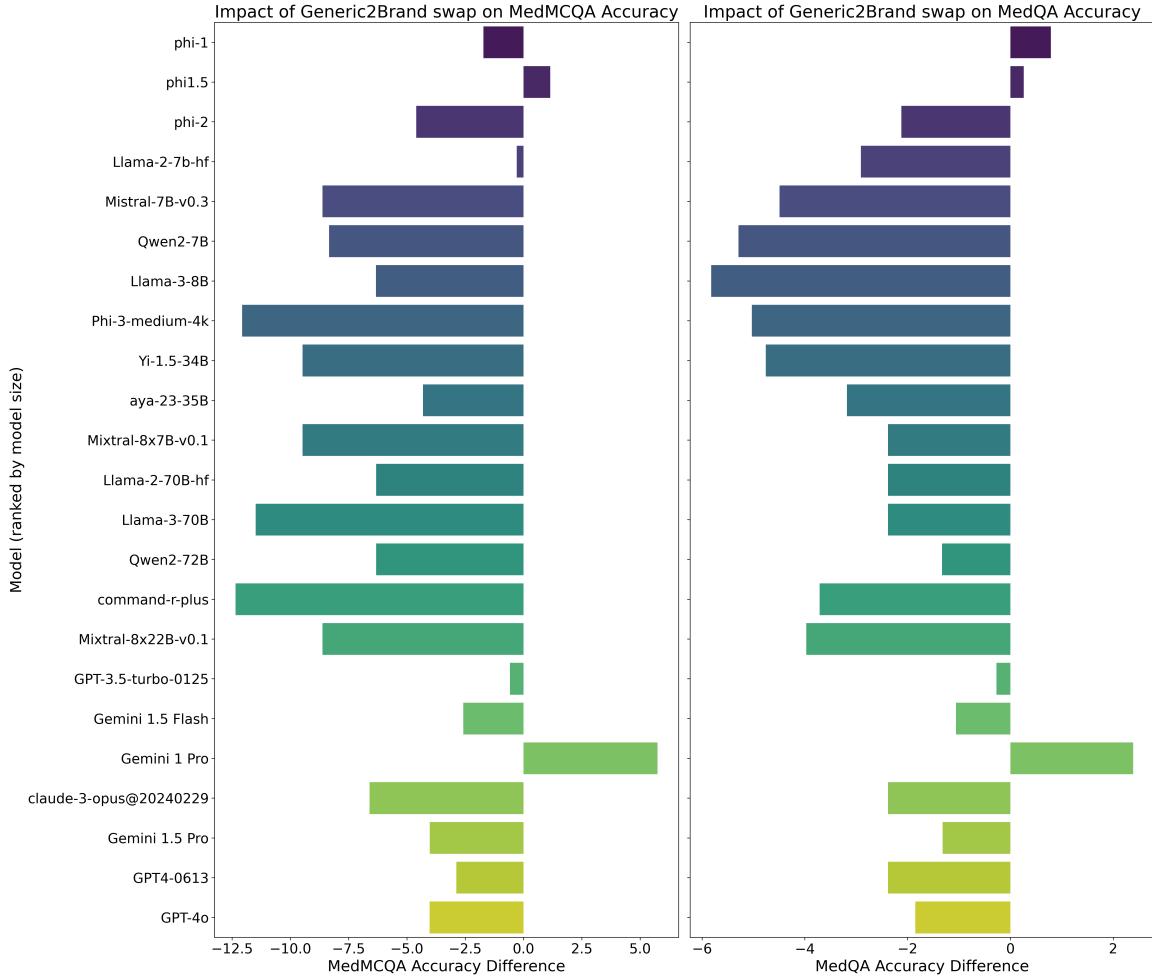


Figure 4: Performance of models on the filtered original datasets compared to the generic-to-brand versions for MedMCQA and MedQA subsets. Negative values indicate worse performance on the swapped dataset.

Table 3: List of Models Used in Experiments, June 12th, 2024

Model Name	Size	MoE	Multi-Modal
phi-1 ( <a href="#">Gunasekar et al., 2023</a> )	1.3B	No	No
phi-1.5 ( <a href="#">Li et al., 2023</a> )	1.3B	No	No
phi-2 ( <a href="#">Li et al., 2023</a> )	2.7B	No	No
phi-3-medium ( <a href="#">Abdin et al., 2024</a> )	14B	No	No
Llama3-8B ( <a href="#">AI@Meta, 2024</a> )	8B	No	No
Llama3-70B ( <a href="#">AI@Meta, 2024</a> )	70B	No	No
llama-2-70B ( <a href="#">Touvron et al., 2023</a> )	70B	No	No
llama-2-7B ( <a href="#">Touvron et al., 2023</a> )	7B	No	No
c4ai-aya-23-35B ( <a href="#">Aryabumi et al., 2024</a> )	35B	No	No
c4ai-r-plus	104B	No	No
Mistral-7B-v0.3 ( <a href="#">Jiang et al., 2023a</a> )	7B	No	No
mixtral-8x22B ( <a href="#">Jiang et al., 2024</a> )	176B	Yes	No
mixtral-8x7B ( <a href="#">Jiang et al., 2024</a> )	56B	Yes	No
qwen2-72B ( <a href="#">Qwen, 2024</a> )	72B	No	No
qwen2-7B ( <a href="#">Qwen, 2024</a> )	7B	No	No
yi-1.5-34B ( <a href="#">Young et al., 2024</a> )	34B	No	No
GPT-3.5-turbo-0125	NA	NA	No
GPT4-0613	NA	NA	Yes
GPT-4o	NA	NA	Yes
Claude 3 Opus	NA	NA	Yes
Gemini 1 Pro	NA	NA	Yes
Gemini 1.5 Flash	NA	NA	Yes
Gemini 1.5 Pro	NA	NA	No

Table 4: Overall and difference of Model performance on RABBITS

Dataset	Model	g2b	original
medmcqa	GPT-3.5-turbo-0125	97.70	98.28
medmcqa	GPT-4o	86.49	90.52
medmcqa	GPT4-0613	88.79	91.67
medmcqa	Gemini 1 Pro	73.85	68.10
medmcqa	Gemini 1.5 Flash	94.83	97.41
medmcqa	Gemini 1.5 Pro	82.47	86.49
medmcqa	Llama-2-70B-hf	45.98	52.30
medmcqa	Llama-2-7b-hf	33.91	34.20
medmcqa	Llama-3-70B	66.67	78.16
medmcqa	Llama-3-8B	52.87	59.20
medmcqa	Mistral-7B-v0.3	48.28	56.90
medmcqa	Mixtral-8x22B-v0.1	61.78	70.40
medmcqa	Mixtral-8x7B-v0.1	55.46	64.94
medmcqa	Phi-3-medium-4k	60.34	72.41
medmcqa	Qwen2-72B	71.55	77.87
medmcqa	Qwen2-7B	55.17	63.51
medmcqa	Yi-1.5-34B	59.77	69.25
medmcqa	aya-23-35B	48.56	52.87
medmcqa	claude-3-opus@20240229	79.89	86.49
medmcqa	command-r-plus	49.14	61.49
medmcqa	phi-1	24.14	25.86
medmcqa	phi-2	37.64	42.24
medmcqa	phi1.5	31.61	30.46
medqa 4options	GPT-3.5-turbo-0125	96.03	96.30
medqa 4options	GPT-4o	88.36	90.21
medqa 4options	GPT4-0613	89.95	92.33
medqa 4options	Gemini 1 Pro	73.02	70.63
medqa 4options	Gemini 1.5 Flash	96.03	97.09
medqa 4options	Gemini 1.5 Pro	87.30	88.62
medqa 4options	Llama-2-70B-hf	52.65	55.03
medqa 4options	Llama-2-7b-hf	34.39	37.30
medqa 4options	Llama-3-70B	72.75	75.13
medqa 4options	Llama-3-8B	55.03	60.85
medqa 4options	Mistral-7B-v0.3	48.68	53.17
medqa 4options	Mixtral-8x22B-v0.1	67.46	71.43
medqa 4options	Mixtral-8x7B-v0.1	60.05	62.43
medqa 4options	Phi-3-medium-4k	53.44	58.47
medqa 4options	Qwen2-72B	74.07	75.40
medqa 4options	Qwen2-7B	53.70	58.99
medqa 4options	Yi-1.5-34B	59.79	64.55
medqa 4options	aya-23-35B	47.88	51.06
medqa 4options	claude-3-opus@20240229	83.33	85.71
medqa 4options	command-r-plus	56.61	60.32
medqa 4options	phi-1	21.69	20.90
medqa 4options	phi-2	41.80	43.92
medqa 4options	phi1.5	34.92	34.66

Table 5: Overall and difference of Model performance on RABBITS

Model	Original	g2b	Average	Difference
GPT-3.5-turbo-0125	97.29	96.86	97.08	-0.42
GPT-4o	90.36	87.42	88.89	-2.94
GPT4-0613	92.00	89.37	90.69	-2.63
Gemini 1 Pro	69.36	73.44	71.40	4.07
Gemini 1.5 Flash	97.25	95.43	96.34	-1.82
Gemini 1.5 Pro	87.56	84.89	86.22	-2.67
Llama-2-70B-hf	53.66	49.31	51.49	-4.35
Llama-2-7b-hf	35.75	34.15	34.95	-1.60
Llama-3-70B	76.64	69.71	73.18	-6.93
Llama-3-8B	60.02	53.95	56.99	-6.08
Mistral-7B-v0.3	55.03	48.48	51.76	-6.55
Mixtral-8x22B-v0.1	70.92	64.62	67.77	-6.29
Mixtral-8x7B-v0.1	63.69	57.76	60.72	-5.93
Phi-3-medium-4k	65.44	56.89	61.16	-8.55
Qwen2-72B	76.64	72.81	74.72	-3.83
Qwen2-7B	61.25	54.44	57.84	-6.82
Yi-1.5-34B	66.90	59.78	63.34	-7.12
aya-23-35B	51.97	48.22	50.09	-3.75
claude-3-opus@20240229	86.10	81.61	83.85	-4.49
command-r-plus	60.91	52.88	56.89	-8.03
phi-1	23.38	22.91	23.15	-0.47
phi-2	43.08	39.72	41.40	-3.36
phi1.5	32.56	33.27	32.91	0.70

## D Pre-training data screening

Table 6: Statistics for occurrence counts of selected brand and generic terms among popular pre-training datasets

<b>Subset</b>	<b>Terms</b>	<b>Average</b>	<b>Median</b>	<b>Std. Dev</b>
Dolma	Generic	564,151	136,682	2,399,928
	Brand	234,138	698	2,543,075
Red Pajama	Generic	161,227	42,549	620,393
	Brand	29,561	84	232,661
Pile train	Generic	96,309	28,074	325,307
	Brand	4,757	19	43,613
C4 train	Generic	27,973	5,454	144,162
	Brand	9,941	26	96,504

## E Biomedical-Supervised Fine-Tuned (SFT) Models

The top 3 accessible models on the leaderboard (all higher than GPT-4 and Med-Palm as of June 1st, 2024) (Pal et al., 2024) are all Llama3 SFT variants. The Llama3-8B-sft2 model achieved the highest original score of 0.85 but showed a performance drop of -0.15 in the g2b category, similar to Llama3-8B-sft1. Both performance decreases are greater than those observed in the base model version. Similar patterns were seen in the Llama-70B models. These degradations among benchmark datasets may be helpful in inspecting SFT models that are over-fitted.

Table 7: Llama-3 Vanilla v.s its Fine-Tuned Variants

Model	None ↑	g2b ↑	$\delta \downarrow$
llama-3-8B (vanilla)	0.60	0.53	-0.07
llama-3-8B-sft1	0.80	0.66	-0.14↑
llama-3-8B-sft2	0.85	0.70	-0.15↑
llama-3-70B (vanilla)	0.77	0.70	-0.07
llama-3-70B-sft1	0.75	0.66	-0.09↑