Med-R^2: Crafting Trustworthy LLM Physicians through Retrieval and Reasoning of Evidence-Based Medicine

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Abstract

In recent years, Large Language Models (LLMs) have exhibited remarkable capabilities in clinical scenarios. However, despite their potential, existing works face challenges when applying LLMs to medical settings. Strategies relying on training with medical datasets are highly cost-intensive and may suffer from outdated training data. Leveraging external knowledge bases is a suitable alternative, yet it faces obstacles such as limited retrieval precision and poor effectiveness in answer extraction. These issues collectively prevent LLMs from demonstrating the expected level of proficiency in mastering medical expertise. To address these challenges, we introduce **Med-R^2**, a novel LLM physician framework that adheres to the Evidence-Based Medicine (EBM) process, efficiently integrating retrieval mechanisms as well as the selection and reasoning processes of evidence, thereby enhancing the problem-solving capabilities of LLMs in healthcare scenarios and fostering a trustworthy LLM physician. Our comprehensive experiments indicate that **Med-R^2** achieves a 14.87% improvement over vanilla RAG methods and even a 3.59% enhancement compared to fine-tuning strategies, without incurring additional training costs. Code and datasets are available at https://github.com/8023looker/Med-RR.

1 Introduction

In recent years, Large Language Models (LLMs) have emerged as pivotal tools in the medical domain, redefining the contours of healthcare practice and research (Abd-Alrazaq et al., 2023; Yang et al., 2023; Thirunavukarasu et al., 2023). Their ability to process and understand vast amounts of unstructured medical data positions them at the forefront of medical research (Clusmann et al., 2023; Mumtaz et al., 2024), clinical decision-making (Hager et al., 2024; Kim et al., 2024), and patient care (Busch et al., 2024; Tripathi et al., 2024).
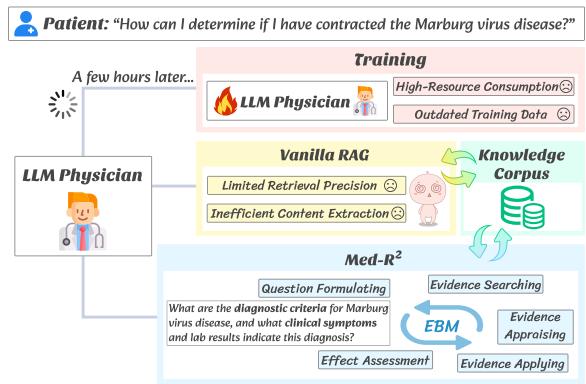

Figure 1: Comparison of Med-R^2 with existing strategies for medical problem solving.

However, despite their remarkable capabilities, LLMs encounter several challenges when applied specifically to healthcare settings:

C1: Inefficiency in Knowledge Acquisition. Existing approaches predominantly rely on pretraining and fine-tuning LLMs with datasets from the medical domain, the process of which is inherently compute-intensive and resource-demanding, especially as model sizes increase (Singhal et al., 2023b; Luo et al., 2022). Moreover, training with outdated datasets can result in a lack of highly specialized expertise, which can lead to suboptimal clinical recommendations or misinform healthcare professionals (He et al., 2022; Kandpal et al., 2023).

C2: Limited Precision for Medical Retrieval. Compared to domain-specific training, Retrieval-Augmented Generation (RAG) systems provide a cost-efficient solution, leveraging the external knowledge base to enhance content generation (Lewis et al., 2020). The retrieval quality is critical in RAG systems, where inaccuracy or misinformation can heavily influence the effectiveness of LLMs' augmentation. While some efforts (Wang et al., 2024; Jeong et al., 2024; Long et al., 2024) have been made to improve the retrieval precision, they neglect the specific and highly professional

nature of medical knowledge, where *tailored retrieval enhancement* for distinct medical scenarios remains insufficiently explored.

C3: Low Effectiveness in Answer Extraction. Considering the constraints imposed by the models' context window length, it is essential to critically appraise the retrieved medical evidence for its validity, impact, as well as applicability, and integrate the most pertinent ones with existing clinical expertise for problem-solving (Case and Swanson, 1998; Guyatt et al., 1992). Nonetheless, current studies fail to develop targeted answer extraction methods tailored for healthcare scenarios, where the nuanced evaluation of evidence hierarchies and intricate reasoning are required (Sackett et al., 1996).

To address these challenges, we introduce **Med-R^2**, a noval medical LLM framework designed in accordance with the principles of Evidence-Based **Med**icine (EBM), conducting outstanding **R**etrieval and **R**easoning aligned with distinct phases of EBM. **1)** For *C1*, we have established a comprehensive external knowledge base to enhance models' medical performances, offering a more cost-effective and flexible alternative to domain-specific training. **2)** For *C2*, we improve the retrieval precision by refining the original queries according to their respective medical scenarios, while iteratively incorporating chain-of-thought sequences generated from the retrieved content. **3)** For *C3*, we adopt a coarse-to-fine strategy for document appraising and filtering, and select the most pertinent ones supplemented with chain-of-thought demonstrations to assist medical queries addressing. In summary, our contributions are as follows:

- *Challenges in Medical Scenarios.* Through conducting a quantitative analysis of strategies aimed at enhancing models' medical capabilities, we underscore the challenges prevalent in healthcare scenarios, including high computational consumption as well as poor efficiency in knowledge retrieval and extraction (Figure 1).

- *LLM Physician Framework.* We present *Med-R^2*, a novel LLM physician that integrates the Evidence-Based Medicine (EBM) principles for clinical problem-solving, bolstering models' performances within medical contexts (Section 3).

- *Performance and Effectiveness.* Our comprehensive experiments indicate that *Med-R^2* achieves a 14.87% improvement over the vanilla RAG methods, and even a 3.59% enhancement compared

to the fine-tuning strategies without additional training expenses (Section 4 and Section 5).

2 Background and Related Work

Evidence-Based Medicine (EBM) EBM refers to the application of the best available research to healthcare, which requires evidence integration with clinical expertise and patient values (Sackett et al., 1996; Guyatt et al., 1992; Sackett, 1997). Clinical questions can be categorized into several types, including *diagnosis, therapy, prognosis, etiology, prevention, cost,* etc. (Case and Swanson, 1998). Each category intersects with EBM principles by emphasizing the systematic collection, evaluation, and application of the best retrieved evidence to inform medical decision-making (Guyatt et al., 2000), detailed in Appendix A.

LLMs for Medical Domain As the application of LLMs expands, their deployment in the medical domain has become a widely discussed topic (Clusmann et al., 2023; Zeng et al., 2020). Recent studies have concentrated on the direct use of real or synthetic medical data for the pretraining or fine-tuning of LLMs (Thirunavukarasu et al., 2023; Singhal et al., 2023a). Prominent open-source milestones include ChatDoctor (Li et al., 2023) which integrates real-world doctor-patient communication data for training, PMC-LLaMA (Wu et al., 2024) pretrained on 4.9 million medical literature records, and MEDITRON (Chen et al., 2023), a scaling series of medical pretrained models. However, such extensive training can be computationally intensive. In contrast, Retrieval-Augmented Generation (RAG) systems offer a more efficient alternative, achieving comparable results with reduced training costs and enhancing the model's precision in locating and leveraging knowledge.

Retrieval-Augmented Generation (RAG) The concept of RAG (Lewis et al., 2020) was introduced as a powerful framework for integrating external knowledge into natural language generation tasks, enhancing the accuracy and relevance of generated outputs across various domains (Gao et al., 2023; Zhao et al., 2024). In the medical field, RAG has been widely used to improve LLMs' analytical performances by utilizing external medical knowledge from sources such as medical papers, textbooks, guidelines, and entries (Jin et al., 2023; Zakka et al., 2024; Xiong et al., 2024). However, while there has been efforts dedicated to optimizing the individual components of RAG pipelines (Wang et al., 2024; Jeong et al., 2024),
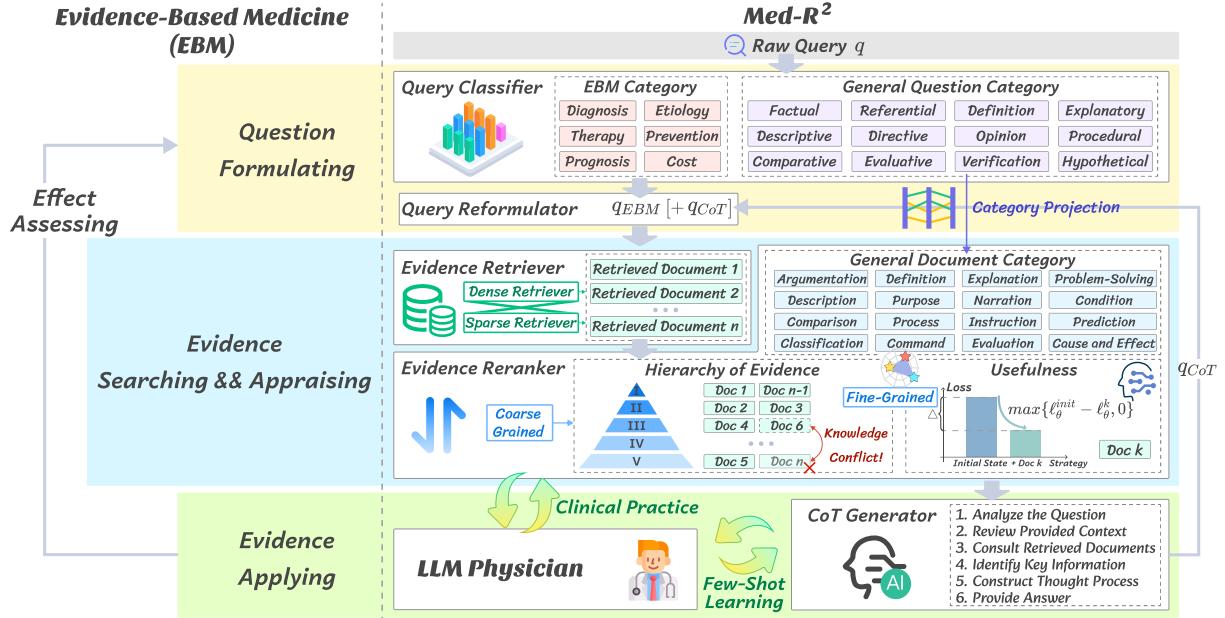
Figure 2: An illustration of Med-R^2's process, adhering to the Evidence-Based Medicine (EBM) workflow. We first categorize the query by EBM and general question types. Queries are then reformulated according to established EBM classification templates to ensure precision and relevance. In the evidence searching and appraising stages, we employ a coarse-to-fine strategy to retrieve, filter, and re-rank the evidence documents within the knowledge base. CoT sequences are then generated from processed evidence to refine retrieval space, iterating to ensure robustness.

research that integrates the unique characteristics and requirements of the medical domain remains in its infancy. In this study, we incorporate the principles of *Evidence-Based Medicine* (*EBM*) into medical RAG systems to better address the special demands of healthcare.

3 Med-R^2

In this section, we discuss our Med-R^2 framework, illustrated in Figure 2. Med-R^2 is designed around the Evidence-Based Medicine (EBM) workflow, encompassing the stages of clinical question formulation (Section 3.1), evidence retrieval and appraisal (Section 3.2), evidence application (Section 3.3), and effect assessment (Section 3.4).

3.1 Question Formulation

In the medical domain, the efficacy of information retrieval is closely tied to the professionalism of the query. A well-crafted, professional query that includes precise descriptions of medical symptoms can markedly enhance the accuracy and relevance of the documents retrieved from knowledge bases. Conversely, non-standard terms and isolated numerical values frequently hinder effective information retrieval. Moreover, the focus of the desired response varies depending on the type of clinical

consultation. For instance, in queries pertaining to *etiology*, users seek insights into potential causes of a condition, including risk factors, pathogens, or genetic predispositions. In contrast, for *prognosis*-related queries, users are interested in understanding the long-term outcomes or patient prognoses, such as survival rates or recurrence probabilities.

The clinical question formulation stage consists of two components: **query classifier** and **query reformulator**. The query classification encompasses two dimensions: *Evidence-Based Medicine (EBM) categories* and *general natural language question types*. Specifically, we have delineated six distinct EBM categories and twelve general question categories, as illustrated in Figure 2. The application of this classification scheme to the MedQA-USMLE dataset yielded the categorized results presented in Figure 3. For the classification task, we employed Qwen2.5-72B-Instruct[1] as our classifier. We perform domain-specific reformulations of the original queries based on their respective classes of the EBM categories to align with the professional context. Meanwhile, the general question categories are utilized as one of the criteria to rerank retrieved documents, thereby prioritizing those that best match the current query's intent and document

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[1] https://huggingface.co/Qwen/Qwen2.5-72B-Instruct

type preferences described in Figure 8. Further details regarding the method and implementation can be found in Appendix B.


Query Categories of *MedMCQA*
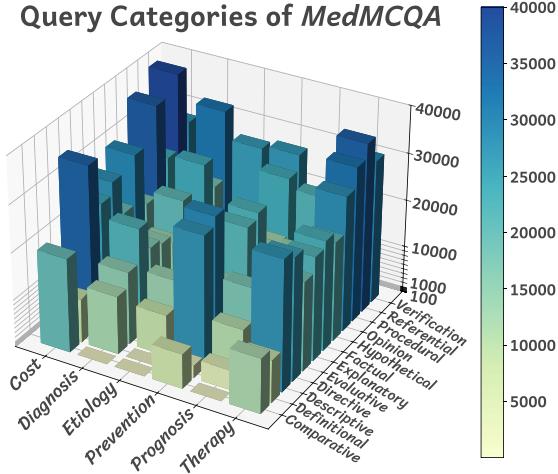
Figure 3: Query category of **MedMCQA**. We employ a logarithmic scale (base 10) on the z-axis, ranging from 1 to 40000, to represent the wide range of values.

3.2 Evidence Searching && Appraising

The retrieval and appraisal of evidence constitute one of the most critical stages in EBM. The professional reformulating of queries in the preceding stages (Section 3.1) aims to enhance the precision of retrieving relevant evidence documents. This stage comprises two key components: **evidence retriever** and **evidence reranker**.

3.2.1 Evidence Retriever

Knowledge Corpus To construct a more comprehensive medical knowledge base adaptable to diverse healthcare scenarios, we have amassed a collection of both open-source and in-house medical data to build our retrieval corpus. The final medical knowledge base employed for retrieval comprises four distinct types of resources: *academic papers*, *entries*, *books*, and *guidelines*, with details of the statistics depicted in Table 1. For resources with extensive content such as academic papers, books, and guidelines, we first perform content segmentation with a threshold set at 10,000 tokens. We prioritize dividing the content based on natural chapters. If natural chapters cannot be identified or exceed the threshold, we resort to truncation according to the predefined limit.

We integrate multiple types of retrievers to optimize our retrieval performance, including BGE-

Source Type	# Volume
Academic Papers	6,000,000
Entries	470,000
Books	10,000
Guidelines	10,000

Table 1: Overall statistics of the data volumes from different medical knowledge resources.

Large-EN-v1.5[2] for dense retrieval and SPLADE-v3[3] for sparse retrieval. We then consolidate the documents retrieved through both methods into a unified collection that contains n documents, $\mathcal{D} = \{d_i\}_{i=1}^n = \mathcal{D}^D \cup \mathcal{D}^S$, where $\mathcal{D}^D$ comprises documents obtained by dense retrieval, and $\mathcal{D}^S$ represents those acquired via sparse retrieval.

3.2.2 Evidence Reranker

For the document collections retrieved in Section 3.2.1, we employ a ***coarse-to-fine*** strategy for reranking. we initially utilize the BGE-Reranker-v2-M3[4] to rerank $\mathcal{D} = \{d_i\}_{i=1}^n$ based on their semantic relevance to the current query at a *coarse* granularity, returning the top k documents, denoted as $\mathcal{S}^c = \{d_i\}_{i=1}^k$. At this stage, the total length of these k documents significantly exceeds the context limit of the model. Then we conduct a *fine*-grained reranking that integrates three distinct criteria for the current k documents to get $\mathcal{S}^f = \{d_i\}_{i=1}^k$, enabling the model to provide answers based on the most effective retrieved documents within the limited length of the context window. The fine-grained reranking score can be formulated as:

$$\mathcal{F}(x) = f_h(x) \cdot f_g(x)(1 + \alpha \cdot f_u(x)) \quad (1)$$

where $f_h(x)$, $f_u(x)$ and $f_g(x)$ refer to scores of each refined evaluation criteria, while α is the nonnegative hyper-parameter for weight controlling.

Hierarchy of Evidence This criterion serves dual purposes: scoring and conflict filtering. The recalled documents that have undergone coarse-grained reranking are first categorized according to their evidence levels. Subsequently, contents of these documents are analyzed for conflicting facts, where the documents that contain conflicting facts and have lower evidence ratings are filtered out. Formally, each retrieved document $d_i \in \mathcal{S}^c$ is associated with an integer evidence level e, where

$e \in \{x \in \mathbb{Z} \mid 1 \leq x \leq 9\}$, with 1 indicating the highest level of credibility:

$$f_h(x) = 9 - (e_x - 1) \tag{2}$$

Usefulness   The usefulness ranker is employed to assess the contribution of retrieved documents to the answering process. Specifically, we quantify the usefulness of a document by measuring the difference in loss before and after using the retrieved document to answer the question. This is achieved with a lightweight proxy model that evaluates the impact of the document on the answer's quality, which can be written as:

$$f_u(x) = \max\left\{\ell_\theta^{init} - \ell_\theta^x, 0\right\} \tag{3}$$

where ℓ_θ^{init} indicates the loss without referring to any retrieved documents, while ℓ_θ^x represents that informed by document x.

General Document Category   It corresponds to the mapping of *general natural language question* types discussed in Section 3.1. Different categories of questions desire distinct answer structures. For instance, questions regarding procedural steps are ideally answered by documents that describe processes rather than those that define concepts. To address this, we categorize the retrieved documents into 16 document types, denoted as C, as outlined in Table 5, and score them based on their alignment with the response type preferred by the original query. The scoring function is defined as follows:

$$f_g(x) = \sum_{j=1}^{|C^e|} p(x|c_j) \tag{4}$$

where $C^e = \{c_j\}_{j=1}^{|C^e|}$ stands for the list of expected document types ($C^e \subset C$), and $p(x|c_j)$ represents the probability that the document x belongs to the current expected type c_j from C^e. Details of computational procedures are provided in Algorithm 1.

3.3 Evidence Applying

Through the comprehensive evaluation and reranking of retrieved documentary evidence in Section 3.2.2, we aim to ensure the application of the highest-quality available evidence to decision-making in the medical field. This process extends beyond merely applying research findings, where integrating the professional reasoning and judgment is essential. Therefore, it is imperative to make *professional and reasoned inferences* based on the question retrieved documents.

CoT Generator   This module constructs a chain-of-thought reasoning process based on the original medical query and the retrieved evidence documents. It serves dual functions: (1) *Component of Query Reformulation*: It contributes to the subsequent query reformulation process, facilitating the retrieval of evidence documents relevant to the question. (2) *Few-Shot Learning Instance*: It provides few-shot examples for the LLM physician (target model) intended for downstream task evaluating, demonstrating how to analyze the retrieved evidence and address medical queries effectively.

3.4 Effect Assessment

Our assessment of evidence encompasses two key aspects: the *accuracy* of the CoT generator in responding to queries and the *stability* of evidence document retrieval across different stages, described in Algorithm 2. This dual focus ensures that when evaluating the LLM physician (target model) on medical tasks, the retrieved evidence documents provided are both effective and robust.

4 Experiments and Results

In this section, we first describe the details of our experimental setup (Section 4.1). We then outline the baseline methods we use for comparison (Section 4.2) and our experimental results to prove the effectiveness of Med-R^2 (Section 4.3).

4.1 Experimental Setup

Model Details. We employ the latest open-source LLMs from LLaMA (Touvron et al., 2023; Dubey et al., 2024) and Qwen (Yang et al., 2024) series as our target language models for evaluation. We assessed models including Qwen2.5-7B, LLaMA3.1-8B, LLaMA2-13B, Qwen2.5-14B, Qwen2.5-32B and LLaMA3.1-70B, scaling from 7B to 70B. The default setting of context window for our main experiments is 4K, with an in-depth scaling analysis presented in Section 5.

Datasets.   We have selected five medical datasets including PubMedQA (Jin et al., 2019), MedQA-USMLE, MedQA-MCMLE (Jin et al., 2020), MedMCQA (Pal et al., 2022), and MMLU-Med (Hendrycks et al., 2021), and use accuracy as evaluation metrics. More details about the datasets can be found in Appendix E.1.

Implementation. We constructed the medical knowledge corpus by establishing the FAISS vector library (Johnson et al., 2019). Experiments related

Model	Method	MedQA-USMLE	MedQA-MCMLE	MedMCQA	PubMedQA	MMLU-Med	Average
		Within-Dataset Fine-Tuning			*Cross-Dataset Fine-Tuning*		
Qwen2.5-7B	Direct Response	22.58	39.14	28.77	54.16	44.45	37.82
	Vanilla RAG	58.28	64.78	32.78	55.68	54.97	53.30
	Fine-Tuning	<u>78.56</u>	**84.94**	<u>47.43</u>	54.40	<u>56.09</u>	<u>64.28</u>
	LLM-AMT	70.44	72.39	43.86	<u>56.02</u>	54.43	59.43
	Med-R^2	**81.06**	<u>81.07</u>	**49.27**	**56.06**	**72.39**	**67.97**
LLaMA3.1-8B	Direct Response	31.16	41.45	30.02	36.17	37.12	35.18
	Vanilla RAG	55.80	59.38	35.91	<u>47.10</u>	43.54	48.35
	Fine-Tuning	<u>76.53</u>	**85.24**	<u>47.38</u>	42.78	42.92	<u>58.97</u>
	LLM-AMT	52.91	66.63	45.08	44.60	**45.39**	50.92
	Med-R^2	**77.79**	<u>85.01</u>	**49.84**	**55.53**	<u>44.58</u>	**62.55**
LLaMA2-13B	Direct Response	25.84	23.00	29.68	40.71	43.57	32.56
	Vanilla RAG	36.97	22.15	35.14	52.67	45.81	38.55
	Fine-Tuning	**39.51**	<u>26.65</u>	**43.35**	<u>55.37</u>	45.70	<u>42.12</u>
	LLM-AMT	<u>38.65</u>	25.03	39.87	52.36	<u>48.67</u>	40.92
	Med-R^2	38.06	**29.34**	<u>41.96</u>	**57.12**	**48.89**	**43.07**
Qwen2.5-14B	Direct Response	50.01	65.23	42.85	56.93	71.60	57.32
	Vanilla RAG	<u>54.88</u>	75.60	42.06	60.38	79.46	62.48
	Fine-Tuning	**55.87**	**85.52**	<u>47.64</u>	54.29	<u>80.41</u>	<u>64.75</u>
	LLM-AMT	51.48	77.11	43.09	<u>62.42</u>	78.78	62.58
	Med-R^2	53.28	<u>82.67</u>	**48.85**	**67.99**	**83.20**	**67.20**
Qwen2.5-32B	Direct Response	16.23	87.07	66.44	<u>68.66</u>	80.19	63.72
	Vanilla RAG	19.33	<u>89.30</u>	67.63	67.06	<u>83.85</u>	65.43
	Fine-Tuning	**25.57**	**89.97**	66.17	66.69	82.40	<u>66.16</u>
	LLM-AMT	19.38	88.08	<u>68.33</u>	68.61	82.06	65.29
	Med-R^2	<u>23.27</u>	89.21	**70.50**	**69.05**	**84.53**	**67.31**
LLaMA3.1-70B	Direct Response	46.43	58.36	62.33	66.81	71.33	61.05
	Vanilla RAG	62.66	77.91	66.63	68.78	76.95	70.59
	Fine-Tuning	**87.17**	**86.21**	<u>71.65</u>	74.72	79.46	<u>79.84</u>
	LLM-AMT	79.18	68.59	70.12	**79.05**	<u>80.74</u>	75.54
	Med-R^2	<u>85.52</u>	<u>85.01</u>	**74.48**	<u>78.01</u>	**84.65**	**81.53**

Table 2: Comparison of Med-R^2 with baselines. The best and second best results are in **bold** and <u>underlined</u>.

to model training were conducted based on full-parameter fine-tuning, during which we utilized a learning rate scheduler featuring linear warm-up and cosine decay, peaking at a learning rate of 2e-5, alongside a warmup ratio of 0.03, a weight decay of 0.0 and a batch size of 128 for 3 epochs. We conducted all training and evaluation experiments on NVIDIA RTX H800 with 80G memory.

4.2 Baselines

We compare Med-R^2 with the following baselines: (1) The simplest baseline is ***Direct Response***, where the model answer medical questions directly without the aid of external knowledge bases or dataset fine-tuning. (2) ***Vanilla RAG*** (Lewis et al., 2020) utilizes raw queries for evidence searching, and the retrieved documents are then directly integrated into the generation process without any further manipulation. (3) ***Fine-Tuning*** leverages medical datasets to further train the model under supervised conditions. Here we have employed two distinct strategies: *within-dataset fine-tuning*, where

the datasets for training and evaluation are derived from different parts of the same data corpus, and *cross-dataset fine-tuning*, where the model is fine-tuned on one medical dataset (e.g., MedMCQA) and then evaluated on different datasets (e.g., PubMedQA). (4) ***LLM-AMT*** (Wang et al., 2024) is a dedicated process tailored for biomedical question answering, which includes typical modules such as query augmenter, hybrid retriever, knowledge refiner, etc. Details are discussed in Appendix E.2.

4.3 Main Results

We conduct evaluations to validate the efficiency of Med-R^2 across different open-source models. We summarize the observations below.

Med-R^2 is effective across different models. Table 2 shows that the incorporation of external knowledge bases significantly enhances the model's ability to address medical queries, where even the most basic *vanilla RAG* method depicts an average enhancement of 17.92% over *direct responses*. Furthermore, Med-R^2 provides an added

layer of the enhancement by adhering to the EBM process, which outperforms all baselines across various benchmarks, achieving an average improvement of 35.46% over the *direct response* strategy. It is Notably, for lightweight models such as Qwen-2.5-7B and LLaMA3.1-8B, Med-R^2 demonstrates increases of 79.72 and 77.80% respectively. We surmise that this is due to the fact that while lightweight models inherently lack comprehensive domain-specific medical knowledge, they possess the capability to efficiently read and identify information from external medical documents. Consequently, effective augmentation from external knowledge bases substantially bolsters the models' capacity to tackle medical domain questions. We also ablate components of Med-R^2 in Table 8 to further identify the contribution of each module.

Med-R^2 shows superiority compared to fine-tuning. From Table 2, we find that Med-R^2 stands out as the only approach among those leveraging external knowledge bases that surpasses the average performance of *fine-tuning* methods. Specifically, Med-R^2 exhibits nearly equivalent performance to fine-tuning strategies in *within-dataset training*, yet it significantly outperforms in *cross-dataset training*, achieving an enhancement of 7.02% and an overall capability improvement of 3.59%. One contributing factor is that during within-dataset fine-tuning, the training and testing datasets are of the same origin, thus a model trained on homogeneous data should logically achieve substantial performance gains on the test set. Conversely, in cross-dataset fine-tuning, the heterogeneity between the training and testing datasets more rigorously assesses the model's ability to generalize within the same domain. Under these circumstances, the utilization of a comprehensive external medical knowledge base and the effective retrieval and extraction of pertinent information becomes particularly crucial. Additionally, considering that fine-tuning necessitates additional training time and computational resources, Med-R^2 emerges as a more efficient approach for enhancing the model's performance on medical domain-related issues.

5 Ablations and Analysis Across Scales

Previously in Section 4, we have established the efficacy of Med-R^2 in improving models' medical performances. Here we further analyze the impact of *model scale* and *context window length* on Med-R^2, and provide rationale for incorporating the
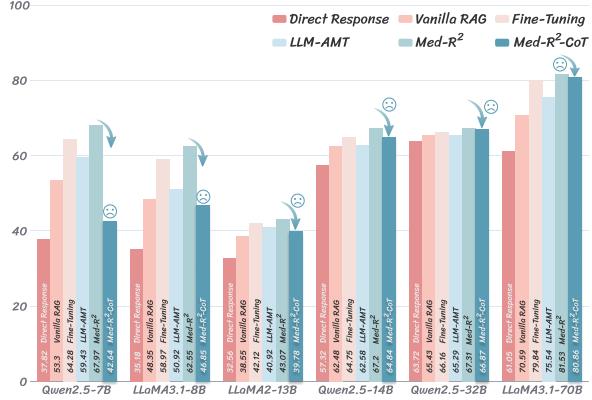

Figure 4: Grouped bar chart depicting the average evaluation results of baselines from Table 2 and Med-R^2-CoT. Compared to Med-R^2, Med-R^2-CoT involves the immediate incorporation of models' CoT sequence into the query reformulator for retrieval during the initial round.

CoT sequences of models into the retrieval process starting from the second iteration.

Integrating CoT at the onset may bring adverse effects. We ablate the components of query reformulator q_{EBM} $[+q_{CoT}]$ through integrating the chain-of-thought (CoT) sequences generated by models into the initial evidence retrieval phase, which is denoted as **Med-R^2-CoT**. Figure 4 presents a grouped bar chart illustrating the medical task performance of Med-R^2-CoT and all baselines included in our main experiments. It is observed that Med-R^2-CoT exhibits a decline in performance compared to Med-R^2, with the disparity increasing as the model parameter scale decreases. Notably, at the 7-8 billion parameter level (e.g., Qwen2.5-7B and LLaMA3.1-8B), the performance of Med-R^2-CoT is even inferior to that of *vanilla RAG* strategy. We hypothesize that one contributing factor is that the lightweight models' less solid grasp of medical knowledge. Consequently, without the aid of an external medical knowledge base, these models are unable to think in the direction of the original query, and thus, the generated CoT sequences may even negatively impact the retrieval effectiveness. However, this phenomenon is somewhat mitigated as the model parameter scale increases.

Effect of context window scale on model's performance. We compared the performance of Med-R^2 across models with varying parameter scales and different context window lengths on medical tasks, as shown in Table 7, and then plotted heatmaps illustrating the percentage improvement of Med-R^2 over *direct responses*, as depicted in Figure 5. It reveals that Med-R^2 exhibits an optimal

context window length for enhancing the model's medical performance, which increases with the growth of model parameter size. Concurrently, the enhancement of Med-R^2 follows a trend of initial decline followed by an increase with the escalation of model scale. Specifically:

- For models of 8B parameters, the most pronounced enhancement was observed at a 4K context window, but this benefit diminished sharply as the context length increased.

- For 14B models, the 8K length stands out, where a measurable decrease in performances is observed as the context window expanded. Moreover, the improvement provided by Med-R^2 at this scale is *the most modest* compared to others.

- Models with 32B and 70B parameters achieved optimal performance at a 16K context length, demonstrating relatively stable improvement across various context window lengths.

We hypothesize that as the context length increases, the role of Med-R^2's reranker diminishes since most retrieved evidence documents are fed into the same context window of the model. At this point, lightweight models, particularly those around 8B, which may not have a solid grasp of medical knowledge, and overly long evidence sequences could reduce the model's efficiency in extracting key information, potentially leading to the generation of hallucinations and adversely affecting the model's medical performance. However, the addition of other modules, such as the query reformulator, can help improve the precision of knowledge retrieval, thereby mitigating this negative impact to some extent. In contrast, models with 32B and above scales exhibit greater robustness, and the impact of increasing window length on Med-R^2's effectiveness is less pronounced.

6 Conclusion

Despite the promising applications of Large Language Models (LLMs) in the medical field, the highly professional nature of medical knowledge poses several challenges, including inefficiency in knowledge acquisition, low precision in medical evidence retrieval, and low effectiveness in key information extraction. In this study, we follow the Evidence-Based Medicine (EBM) process to design a novel LLM physician framework, which
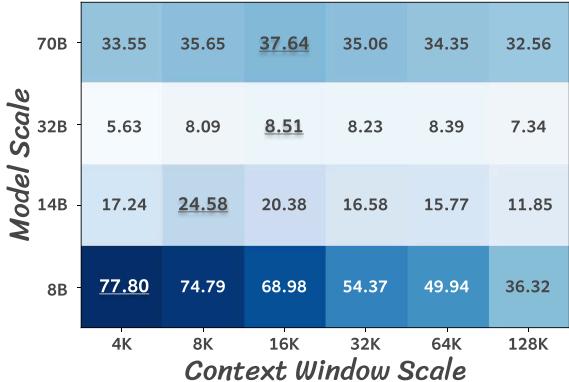
Figure 5: The percentage increase of performance achieved by Med-R^2 over *direct responses* across various context window sizes and model scales.

effectively leverages the retrieval, filtering, and reasoning processes inherent to EBM, thereby significantly enhancing the model's performance in medical scenarios. Comprehensive experiments demonstrate that our Med-R^2 holds superior advantages over existing strategies, particularly in achieving performance nearly on par with models trained on corresponding datasets, while also reducing the substantial computational costs associated with model training. Furthermore, our analysis of model scale and context window size also highlights the scaling capabilities of Med-R^2.

7 Limitations

There are some limitations in our work. Firstly, due to the professional nature and rapid evolution of medical knowledge, the medical knowledge corpus we construct may not ensure complete coverage of medical information, potentially limiting the upper bound of retrieval precision. Additionally, the classification framework of our query classifier may not be comprehensive in scope, and since the classifier relies on advanced language models, it cannot guarantee the absolute accuracy in classification. Concurrently, during the fine-grained reranking phase, to balance the computational cost and effectiveness, we employ a lightweight proxy model to calculate the usefulness score of the current evidence document, yet it does not fully represent the performance tendencies of the target model during actual evaluating.

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A Evidence-Based Medicine (EBM)

Evidence-Based Medicine (EBM) is defined as the conscientious, explicit, and judicious application of the best current evidence in making decisions regarding the care of individual patients. This practice entails the integration of individual clinical expertise with the most reliable external clinical evidence derived from systematic research (Sackett et al., 1996). The EBM process typically includes five stages, *question formulating*, *evidence searching*, *evidence appraising*, *evidence applying* and *effect assessing*, which aims to make the best possible health care decision through iterative improvements.

To utilize "best evidence", researchers assess the quality of trials by determining the grading system based on the likelihood that the methods used and the results obtained are less prone to bias and more reliable. The ***hierarchy of evidence*** guides the clinical decision-making, since not all evidence is created equal, as described in Figure 6. The evidence hierarchy establishes the priority of references, particularly when conflicting facts are present within the retrieved evidence.
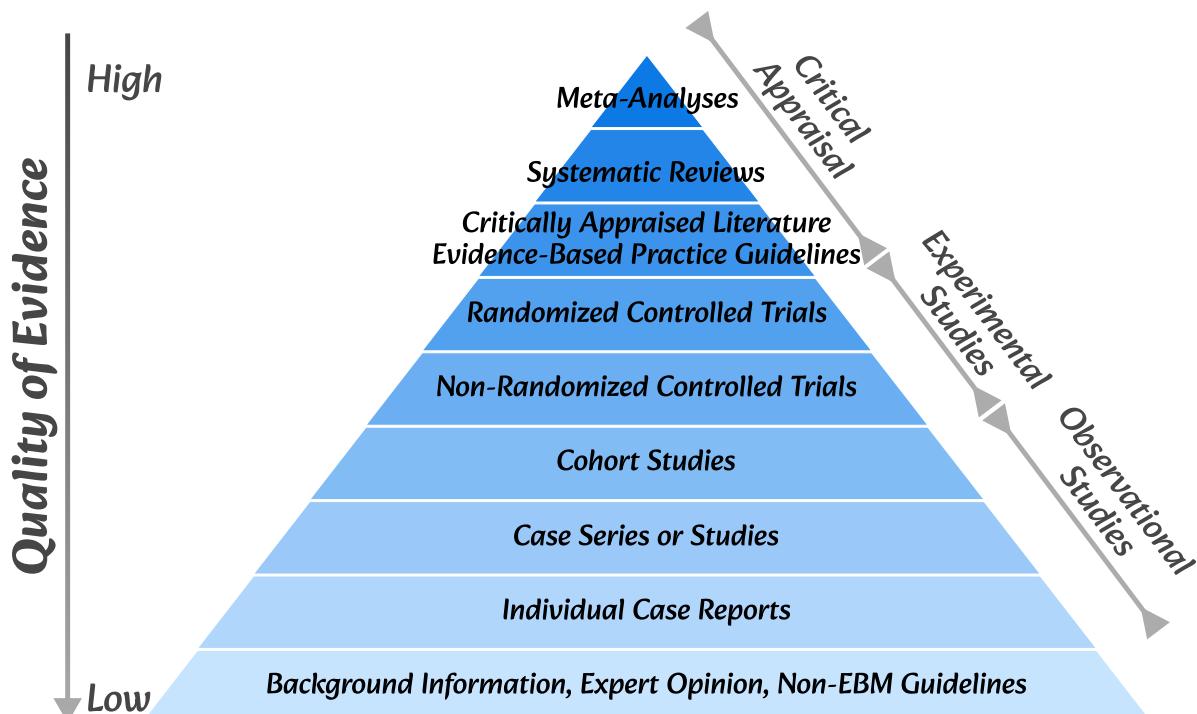

Figure 6: Illustration for ***Hierarchy of evidence***. The base of the pyramid represents the lowest quality and highest risk of bias in research design, while the apex signifies the highest quality and lowest risk of bias.

The construction and rationale behind the hierarchical structure of evidence grading is outlined from the highest to the lowest levels:

- **Systematic Reviews/Meta-Analyses (SR/MA)** represent *the highest* tier of evidence. These assessments evaluate the consistency and risk of bias across all research findings within the medical domain, demonstrating the overall effect of interventions or exposures.
- **Randomized Controlled Trials (RCTs)** constitute *the second-highest* level of evidence. These trials aim to minimize confounding biases and examine the causal relationships between intervention measures and outcomes across groups.
- **Cohort Studies** fall into *the third-highest* category of evidence. Both retrospective and prospective cohort studies are prone to various biases. Prospective cohort studies are considered more reliable, less susceptible to information biases (selection, misclassification, recall), and can establish temporal associations (outcomes following exposure). However, both types of cohort studies may suffer from confounding biases, which is a major concern that can undermine the validity of their findings.
- **Case-Control Studies** are a form of observational research and rank as *the fourth-highest* level of evidence. These studies attempt to identify associations between outcomes and exposure to

risk factors after the outcomes have occurred. Case-control studies are susceptible to selection, information, and confounding biases, reducing their credibility compared to cohort studies.

- **Individual Case Reports** are of *the second-lowest* evidence level, essentially uncontrolled cohort studies lacking a comparison group. The absence of a control group affects the correlation between study variables and interventions/exposures/risk factors and outcomes.
- **Expert Opinion** is considered *the lowest* level of evidence due to its high susceptibility to bias. Compared to other levels, experts are more likely to selectively choose evidence that confirms their preconceived hypotheses or beliefs, potentially leading to conflicts of interest and a focus on a specific domain while overlooking broader contexts, thereby introducing bias into their perspectives.

B Question Formulation Details

B.1 Details of Query Classification

We categorize the medical queries along two orthogonal dimensions: *Evidence-Based Medicine (EBM) categories* and *general natural language question types*.

Evidence-Based Medicine (EBM) Categories Non-professional queries may fail to clearly articulate the current medical symptoms, thereby hindering the effective retrieval of the necessary medical evidence. Here we classify the medical queries into several types according to the categories of Evidence-Based Medicine (EBM) questions, including *diagnosis*, *therapy*, *prognosis*, *etiology*, *prevention*, *cost*, etc., and then conduct and professional medical query reformulations based on their EBM categorization to emphasize specialized retrieval. Instructions for targeted augmentation of clinical queries are outlined in Table 4, where we employ Qwen2.5-72B-Instruct[5] as our question reformulator.

General Natural Language Question Types It serves as a crucial reference for filtering and reranking the evidence documents retrieved in response to a query, since the emphasis of the expected answer varies with different question types. We categorize queries into 12 natural language classes, as illustrated in Table 3, establishing a mapping between the types of questions and the types of retrieved evidence documents to form a question-answer typology (depicted in Figure 8).

Category	Details of Description
Factual	Inquiring into specific and objective facts or data.
Referential	Seeking answers by referencing specific documents, resources, or other information.
Definition	Inquiring about the definition or explanation of a concept or entity.
Explanatory	Seeking explanations for the causes of phenomena, processes, or events.
Descriptive	Requesting a description of the characteristics, properties, and features of an entity.
Directive	Seeking guidance or recommendations.
Opinion	Pertaining to individual feelings, attitudes, or preferences.
Procedural	Inquiring about the specific steps to complete a particular task or activity.
Comparative	Inquiring comparison of the differences between two or more entities.
Evaluative	Assessing the validity or quality of a statement or viewpoint.
Verification	Confirming or verifying the authenticity or accuracy of certain information.
Hypothetical	Presenting a hypothetical scenario and requesting predictions of outcomes.

Table 3: Explanations and descriptions for each category within the general question classification.

We have categorized the question of each instance within the datasets utilized for our experiments. For detailed statistical values of the data samples, please refer to Table 6. We employed the complete set of

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instances ("# Total Instance" in Table 6) from each dataset for the classification process. The 3D bar charts of the classification results are shown in Figure 3 and Figure 7.

(a) Query category of **MedQA-USMLE**.

(b) Query category of **MedQA-MCMLE**.

(c) Query category of **PubMedQA**.

(d) Query category of **MMLU-Med**.
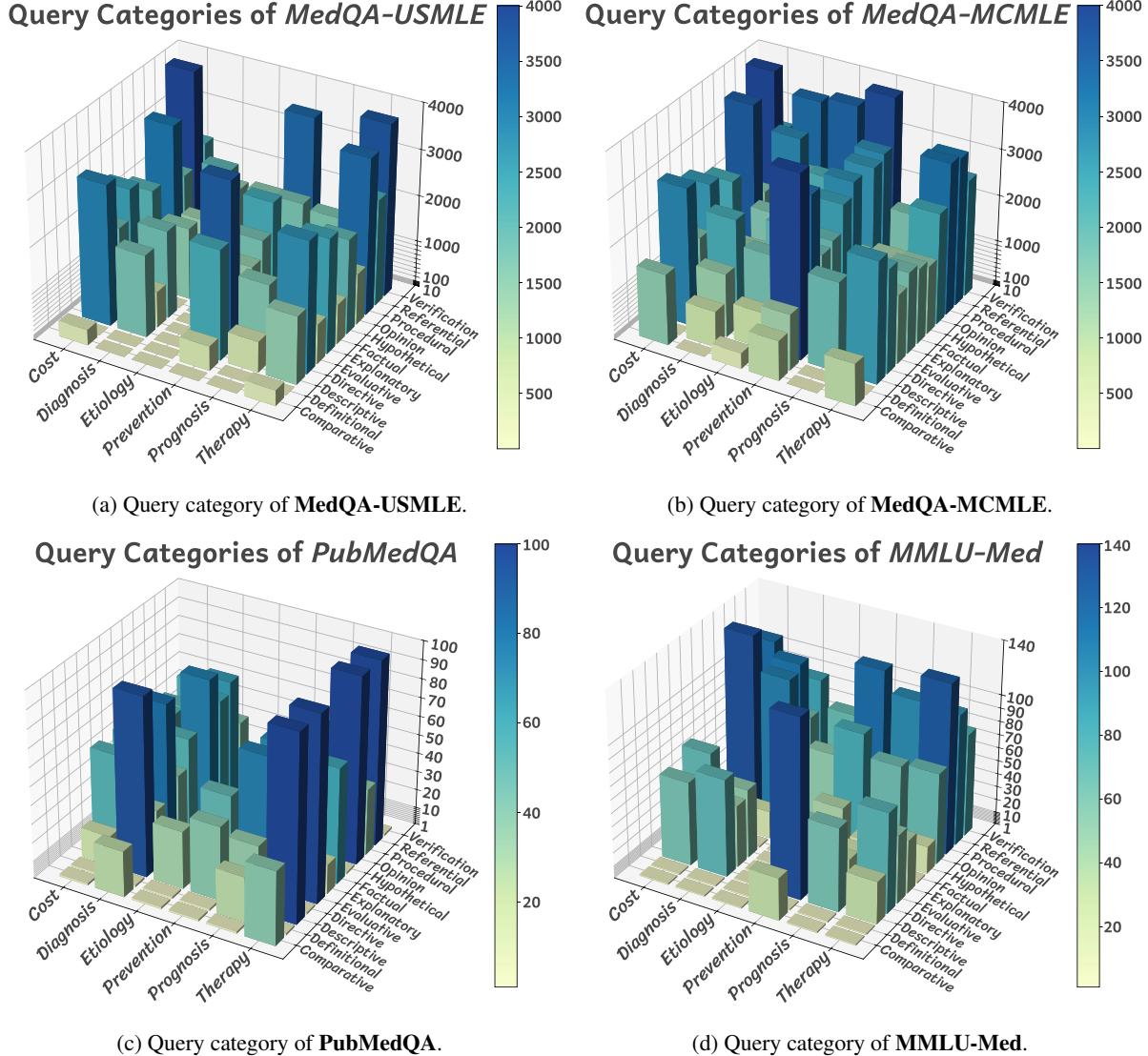
Figure 7: Query categories of different medical datasets. We employ a 3D bar chart to represent the number of instances in each category within the two distinct classification systems of the current dataset. A logarithmic scale (base 10) on the z-axis, ranging from 1 to z $(z = 100, 140, 4000)$, is utilized to represent the wide range of values.

B.2 Details of Query Reformulator

Following the instructions outlined in Table 4, we have employed Qwen2.5-72B-Instruct to professionally reformulate the queries within the medical datasets to enhance the subsequent retrieval of relevant evidence pertaining to the current query from the knowledge corpus.

C   Evidence Reranking Details

We detail the scoring implementation for the fine-grained reranking phase of retrieved documents, which is based on the categorization and mapping to general document categories, as depicted in Algorithm 1.

D   Evidence Assessment Details

Here, we provide the details of the iterative multi-document retrieval process, as illustrated in Algorithm 2.

Category	Instructions for Query Reformulation
Diagnosis	Specify the condition you need to diagnose and ask about the accuracy, sensitivity, or specificity of specific diagnostic tests.
Therapy	Specify the disease or symptom along with the therapy being considered, and inquire about its effectiveness, safety, or comparison with other therapies.
Prognosis	Specify the disease or condition and ask about long-term outcomes such as survival rates, recovery chances, or disease progression.
Etiology	Describe the health issue and ask about potential causes, including risk factors, pathogens, or genetic background.
Prevention	Specify the disease or health issue and ask about the effectiveness of preventive measures or recommendations.
Cost	Specify the medical intervention or service and ask about cost-effectiveness analyses, including direct and indirect costs and cost-effectiveness ratios.

Table 4: Prompts for query reformulation of each category within the Evidence-Based Medicine (EBM) categories.

Category	Details of Description
Argumentation	Presenting a viewpoint or argument, potentially accompanied by supporting evidence.
Definition	Providing a clear definition of a term or concept.
Description	Describing the characteristics or attributes of an object or event.
Explanation	Explaining a concept, process, or cause.
Purpose	Elucidating the purpose or intent behind a particular action or event.
Narration	Providing a narrative account of an event, experience, or story.
Process	Describing a process or a sequence of steps.
Instruction	Providing steps or guidance for executing a task or operation.
Command	Conveying a request that requires the listener to take action.
Problem-Solving	Proposing methods or strategies for addressing specific issues.
Comparison	Comparing the similarities or differences between two or more entities.
Evaluation	Articulating a judgment on a particular subject or behavior.
Classification	Categorizing objects or concepts into specific categories systems.
Condition	Describing the assumptions under which a particular event occurs.
Prediction	Forecasting future events or trends.
Cause and Effect	Describing the causal relationships between events.

Table 5: Explanations and descriptions for each category within the general document classification.

E Experiments Details

E.1 Details of Medical Datasets

To evaluate the performance of our proposed Med-R^2 in medical scenarios, we chose five knowledge-intensive medical question-answering tasks for comparison with other approaches, the statistical description of which is provides in Table 6.

- **MedQA-USMLE** and **MedQA-MCMLE** (Jin et al., 2020): The MedQA dataset is derived from the professional medical board exams, covering languages of English, simplified Chinese, and traditional Chinese. In this study, we employ the subsets collected from US and Mainland China. The MedQA-USMLE dataset includes text materials from 18 English medical textbooks, while the MedQA-MCMLE dataset is constructed from 33 simplified Chinese medical textbooks.

- **MedMCQA** (Pal et al., 2022): The MedMCQA dataset is a large-scale multi-choice question answering data corpus that covers 2,400 healthcare topics and 21 medical subjects. Topics of MedMCQA span from medicine (endocrinology, infection, haematology, respiratory, etc.), surgery (general surgery, endocrinology, breast, and vascular surgery, etc.) to radiology & biochemistry, which are sourced from both real-world scenarios and simulated examinations.
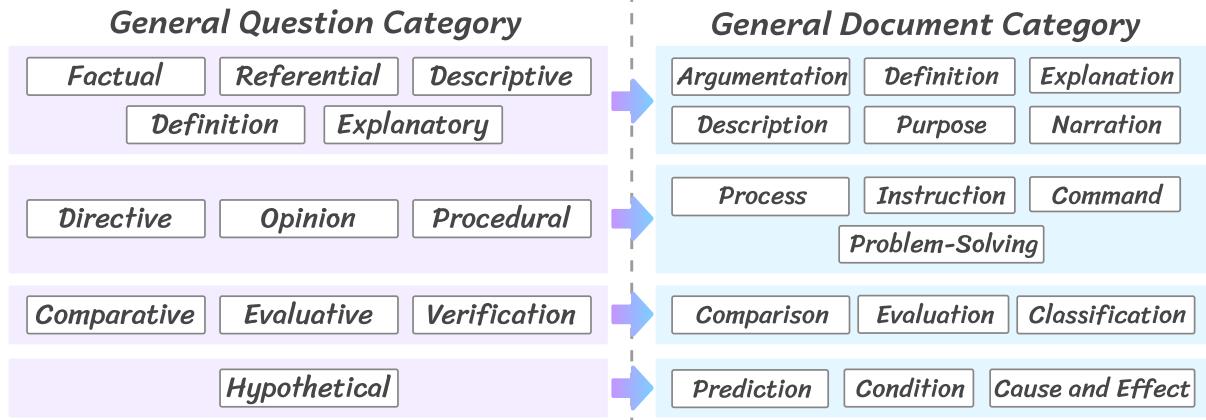
Figure 8: Query Document Projection.

Algorithm 1 Scoring Based on General Document Category Classification

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Input: Coarsely reranked documents $\mathcal{S}^c$, Query-document mapping $\mathcal{A}$ based on Figure 8, classifier M_P, List of general document categories C
Parameter: List of current expected document categories C^e, $C^e \subset C$
Output: Scores based on document category $f_g(S^c)$
Define q^c: category of the query used for retrieving
Define $\vec{p}$: category probability distribution of document d

1: **for** each document d_i in $\mathcal{S}^c$ **do**
2:     /* Step 1: Expected Category Mapping */
3:     Obtain expected categories $C^e = \mathcal{A}(q^c_{d_i})$, where $C^e \subset C$
4:     /* Step 2: Document Category Probability Inference */
5:     Provide category probability distribution of d_i referring to M_P: $\vec{p_i} = \{p(d_i|c_j)\}_{j=1}^{|C|} \leftarrow M_P(d_i)$
6:     /* Step 3: Statistics Aggregation */
7:     Calculate the sum of probabilities across all expected categories:
$$f_g(d_i) = \sum_{j=1}^{|C^e|} p(d_i|c_j), \text{ where } c_j \in C^e$$
8: **end for**
9: **Return** $f_g(S^c) = \{f_g(d_i)\}_{i=1}^{|S^c|}$

- **PubMedQA** (Jin et al., 2019): The PubMedQA dataset is a novel biomedical question answering dataset originated from PubMed abstracts. To ensure equity, we exclude the origin-given contexts during the retrieval phase. Here we choose the 1,000 expert-annotated instances for downstream task evaluation. PubMedQA is included only in our test set due to the limited number of instances.

- **MMLU-Med** (Hendrycks et al., 2021): MMLU-Med is a set of six medical tasks (anatomy, clinical knowledge, professional medicine, human genetics, college medicine, college biology) derived from the MMLU dataset. MMLU-Med is also included only in our test set due to its limited quanity.

For the MedQA-USMLE and MedQA-MCMLE datasets, the original data is divided into three parts: train, dev, and test. We utilize the training part directly for model fine-tuning. The dev and test subsets are merged for evaluation, from which we selected 10 (or 11) instances as Chain-of-Thought (CoT) demonstration examples. Since the test portion of MedMCQA does not provide ground truth answers, we use the development set for evaluation. We employ MedQA-USMLE, MedQA-MCMLE, and MedMCQA datasets for *within-dataset fine-tuning*. For instance, we train with the training subset of MedQA-USMLE and subsequently evaluate with its corresponding test partitions. For *cross-dataset fine-tuning* setting, we utilize PubMedQA and MMLU-Med. Specifically, we train on MedMCQA and assess performance on PubMedQA and MMLU-Med to test the model's generalizability across disparate data sources.

Algorithm 2 Evidence Assessment and Iterative Retrieval Loop for Query Corpus

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Input: Query corpus $\mathcal{Q}$, CoT generator M_{CoT}, Context window length w, Hyperparameters: alteration threshold δ, maximum iterations T

Parameter: Coarsely reranked documents $\mathcal{S}^c$, finely reranked documents $\mathcal{S}^f$

Output: Selected evidence documents $\mathcal{S}^f_{\mathcal{Q}-top}$ and CoT sequences $\mathcal{Q}^{CoT}$

Define q^{CoT}: chain-of-thought sequence generated based on query and associated evidence documents

Define $E(d)$: embedding of document d

1: $\mathcal{S}^f_{\mathcal{Q}-top}, \mathcal{Q}^{CoT} \leftarrow [\,], [\,]$
2: **for** each query q_i in $\mathcal{Q}$ **do**
3:      **for** $t = 1, 2, \ldots, T$ **do**
4:          Reformulate query q_i (Section 3.1), search and appraise the retrieved evidence (Section 3.2)
5:          /* *Step 1: CoT Generation* */
6:          Select top k documents from $\mathcal{S}^{f^{(t)}}_i$ referring to w: $\mathcal{S}^{f^{(t)}}_{i-top} \leftarrow \text{SelectTopK}(\mathcal{S}^{f^{(t)}}_i, k, w)$
7:          Generate chain-of-thought sequence based on q_i and $\mathcal{S}^{f^{(t)}}_{i-top}$: $q^{CoT^{(t)}}_i =\leftarrow M_{CoT}(q_i, \mathcal{S}^{f^{(t)}}_{i-top})$
8:          /* *Step 2: Evidence Assessment* */
9:          Compute answer accuracy: $Acc^{(t)}_i \leftarrow \text{CalculateAccuracy}(q^{CoT^{(t)}}_i)$
10:         Compute semantic stability of documents retrieved in consecutive iterations:
$$\vec{\mu}^{(t)}_i \leftarrow ||\tfrac{1}{|\mathcal{S}^{c^{(t)}}_i|} \textstyle\sum_{d_i \in \mathcal{S}^{c^{(t)}}_i} E(d_i) - \tfrac{1}{|\mathcal{S}^{c^{(t-1)}}_i|} \textstyle\sum_{d_i \in \mathcal{S}^{c^{(t-1)}}_i} E(d_i)||$$
11:         /* *Step 3: Termination Condition Evaluation* */
12:         **if** $Acc^{(t)}_i / \vec{\mu}^{(t)}_i > \delta$ **then**
13:             $\mathcal{S}^f_{\mathcal{Q}-top}.append(\mathcal{S}^{f^{(t)}}_{i-top})$, $\mathcal{Q}^{CoT}.append(q^{CoT^{(t)}}_i)$
14:             **Break**
15:         **end if**
16:       **end for**
17:      $\mathcal{S}^f_{\mathcal{Q}-top}.append(\mathcal{S}^{f^{(T)}}_{i-top})$, $\mathcal{Q}^{CoT}.append(q^{CoT^{(T)}}_i)$
18: **end for**
19: **Return** Selected evidence documents $\mathcal{S}^f_{\mathcal{Q}-top}$ and CoT sequences $\mathcal{Q}^{CoT}$

E.2   Details of Baselines

- **Direct Response**: In this instance, we employ the base model to directly respond to medical queries without the aid of additional training on any dataset or augmentation from external knowledge bases.

- **Vanilla RAG**: It represents the most traditional and fundamental strategy for utilizing external knowledge bases to assist models in answering questions. In this study, we employ the same medical knowledge base as Med-R^2 , but directly utilizing the raw text retrieved by FAISS and combining it with the original query to test the model's performance on medical tasks.

- **Within-Dataset Fine-Tuning**: During the within-dataset training, where the training and test sets originate from the same distribution, models fine-tuned on this data naturally exhibit strong performance gains due to the homogeneity of the datasets. Consequently, both Med-R^2 and fine-tuning methods perform comparably well in this setting.

- **Cross-Dataset Fine-Tuning**: Cross-dataset training poses a greater challenge by testing the model's ability to generalize across different distributions. This scenario demands robust transfer learning capabilities, which are significantly bolstered by the integration of rich external medical knowledge bases. Med-R^2 excels in this context by effectively retrieving and extracting relevant information from these resources, thereby enhancing its performance on diverse datasets.

- **LLM-AMT**: LLM-AMT is a RAG system specifically designed for clinical question answering. It incorporates common RAG components such as a query augmentor, textbook retriever, knowledge

Dataset	# Training Instance	# Testing Instance	# N-Shot for CoT	# Total Instance
MedQA-USMLE (Jin et al., 2020)	10178	2535	10	12723
MedQA-MCMLE (Jin et al., 2020)	27400	6840	11	34251
MedMCQA (Pal et al., 2022)	182822	4170	13	187005
PubMedQA (Jin et al., 2019)	-	990	10	1000
MMLU-Med (Hendrycks et al., 2021)	-	1080	9	1089

Table 6: Details of the experimental datasets. We utilize MedQA-USMLE, MedQA-MCMLE and MedMCQA for *within-dataset fine-tuning*, while employing PubMedQA and MMLU-Med for *cross-dataset fine-tuning*.

refiner, and an LLM reader. LLM-AMT leverages a collection of medical textbooks as an external indexable medical knowledge base. However, in this comparison, we aim to assess the RAG's capability to retrieve, filter, and apply evidence text from the same external knowledge base. To control variables, we employ the LLM-AMT's process but replace the externally indexable medical knowledge base with our own constructed medical retrieval corpus.

E.3 Hyper-Parameters Setting

In the fine-grained reranking phase, we treat each factor as having equal importance, hence we set the weight controlling hyper-parameter α in Equation (1) to 1. As for retrieval iteration settings, we performed iterative retrieval on each query within the dataset presented in Table 6 and visualized the dimensionality reduction of the retrieved document vectors across different iterations using t-SNE. Our analysis revealed that after approximately 5 iterations, the distribution of the retrieved document vectors stabilizes. Consequently, we set the maximum iterations T to 5 in Algorithm 2. As depicted in Figure 9, we selected a sample query retrieval result from the MedQA-USMLE dataset to illustrate this stabilization. It is evident that after $t = 5$ iterations, the vector space of the retrieved document clusters has become relatively stable. After conducting iterative retrieval for all samples in the dataset and calculating the average of the minimum distances in the retrieval space during the iterations, we obtained a value of 6.85, which we adopted as our termination alteration threshold δ in Algorithm 2.

F   Scaling Analysis and Ablation Details

In this section, we conduct a more detailed analysis of the impact of context window size and model parameter scale on our Med-R^2 . Additionally, we evaluate the contribution of each component within Med-R^2 to the model's performance in the medical domain.

F.1 Scaling for Context Window

We have selected 4 models of varying parameter scales from our main experiments to examine the impact of context window length. Considering that the training context window length for the LLaMA2 series is relatively short, at only 8K, whereas the LLaMA3.1 series models are explicitly designed to extend up to a context length of 128K. The Qwen2.5 series, trained at a 32K context length, can also be extended to 128K by modifying the `max_position_embedding` in the `config.json` file through `Yarn`. Consequently, we have chosen two models each from the LLaMA3.1 series and the Qwen2.5 series to conduct inference tests on context window length expansion. Experimental results are outlined in Table 7 and Figure 5.

F.2 Module Impact Analysis

We have analyzed the contributions of various modules in Med-R^2 to the model's performance in the medical domain using a default context window size of 4K, sequentially incorporating components onto the vanilla RAG framework. As shown in Table 8, we decompose the modules into three components: **query reformulator**, **evidence reranker**, and **CoT generator**. The optimal performance values for models with single and dual component additions are highlighted with background colors ▭ and ▭, respectively. Overall, the evidence reranker contributed the most to models' performances among the individual components. When combined with the query reformulator, the performance gains were even more pronounced, demonstrating a synergistic effect. The addition of the CoT generator further enhanced
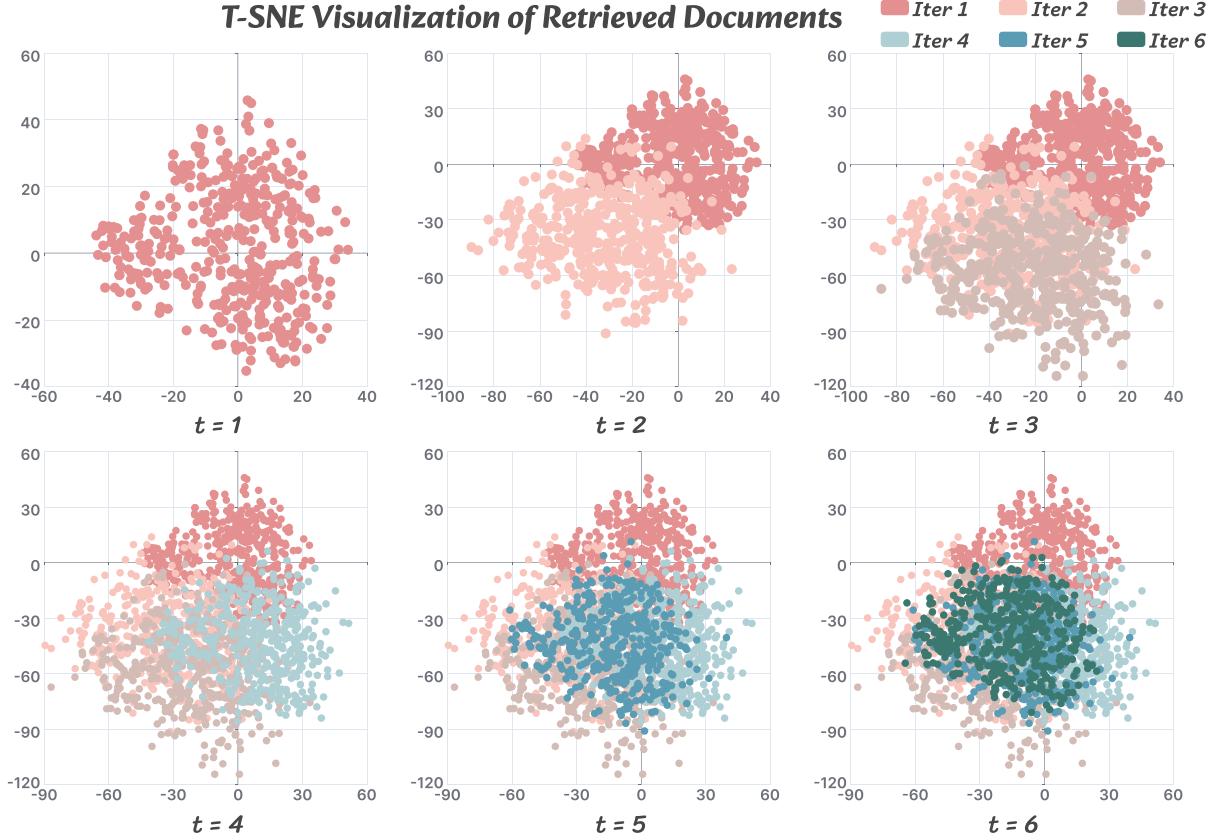
Figure 9: A case of the t-SNE visualization for retrieved documents. We visualized the projections of document embeddings onto a 2-D plane across different iterations. It is evident that aside from the significant variation in the retrieval document vector space at $t = 2$, the semantics of the retrieved documents tend to stabilize in subsequent iterations. It occurs because we did not incorporate the model's CoT sequence for the initial retrieval round ($t = 1$). Instead, we began to include it starting from the second iteration onwards ($t = 2$) to avoid the generation of sequences that are not only unrealistic but also detrimental to the precision of evidence document retrieval.

the model's ability to effectively utilize retrieved medical evidence documents, providing substantial added value. However, we observed that the performance of Qwen2.5-14B on MedQA-USMLE and Qwen2.5-32B on MedQA-MCMLE was not entirely satisfactory. Upon closer examination, we found that even the base model's direct responses were comparable to those augmented by external knowledge bases via the RAG strategy. We hypothesize that these models may have been pretrained on the MedQA dataset, thereby already possessing a robust understanding of the medical knowledge contained within such data corpus, which makes the incremental benefit from the external knowledge base less noticeable.

Model	Method	MedQA-USMLE	MedQA-MCMLE	MedMCQA	PubMedQA	MMLU-Med	Average
			4K				
LLaMA3.1-8B	Direct Response	31.16	41.45	30.02	36.17	37.12	35.18
	Med-R^2	77.79	85.01	49.84	55.53	44.58	62.55
Qwen2.5-14B	Direct Response	50.01	65.23	42.85	56.93	71.60	57.32
	Med-R^2	53.28	82.67	48.85	67.99	83.20	67.20
Qwen2.5-32B	Direct Response	16.23	87.07	66.44	68.66	80.19	63.72
	Med-R^2	23.27	89.21	70.50	69.05	84.53	67.31
LLaMA3.1-70B	Direct Response	46.43	58.36	62.33	66.81	71.33	61.05
	Med-R^2	85.52	85.01	74.48	78.01	84.65	81.53
			8K				
LLaMA3.1-8B	Direct Response	31.34	41.64	29.54	36.71	38.65	35.58
	Med-R^2	73.16	82.61	47.72	58.72	48.74	62.19
Qwen2.5-14B	Direct Response	50.21	64.21	41.34	57.18	70.28	56.64
	Med-R^2	58.50	86.86	53.40	69.74	84.29	70.56
Qwen2.5-32B	Direct Response	15.75	86.82	66.39	68.64	79.73	63.51
	Med-R^2	25.28	89.36	75.55	68.87	84.21	68.65
LLaMA3.1-70B	Direct Response	47.99	57.78	61.69	67.20	70.69	61.07
	Med-R^2	85.72	86.80	78.21	78.66	84.82	82.84
			16K				
LLaMA3.1-8B	Direct Response	31.39	41.43	29.72	36.70	37.78	35.40
	Med-R^2	72.54	77.22	45.13	57.45	46.75	59.82
Qwen2.5-14B	Direct Response	49.69	66.44	41.84	57.07	69.10	56.83
	Med-R^2	55.46	83.01	52.67	67.23	83.68	68.41
Qwen2.5-32B	Direct Response	15.46	86.83	66.52	68.48	80.07	63.47
	Med-R^2	28.02	89.32	70.79	70.51	85.72	68.87
LLaMA3.1-70B	Direct Response	47.46	57.61	61.62	67.45	69.09	60.65
	Med-R^2	86.43	88.15	74.64	80.94	87.24	83.48
			32K				
LLaMA3.1-8B	Direct Response	31.25	40.51	30.58	36.62	38.44	35.48
	Med-R^2	62.86	68.67	41.65	57.22	43.44	54.77
Qwen2.5-14B	Direct Response	50.40	66.31	41.27	58.24	69.31	57.11
	Med-R^2	54.78	78.41	50.76	65.73	83.23	66.58
Qwen2.5-32B	Direct Response	15.61	86.85	64.98	69.16	80.10	63.34
	Med-R^2	27.05	89.29	70.80	71.07	84.56	68.55
LLaMA3.1-70B	Direct Response	46.31	57.89	61.87	67.32	69.96	60.67
	Med-R^2	83.36	85.58	75.93	78.22	86.61	81.94
			64K				
LLaMA3.1-8B	Direct Response	31.92	39.85	30.24	36.68	37.52	35.24
	Med-R^2	62.57	62.51	40.97	52.44	45.73	52.84
Qwen2.5-14B	Direct Response	49.88	64.76	42.02	57.06	69.42	56.63
	Med-R^2	54.84	78.75	50.64	63.06	80.51	65.56
Qwen2.5-32B	Direct Response	15.89	86.81	65.12	68.65	79.29	63.15
	Med-R^2	27.87	88.75	70.42	70.65	84.54	68.45
LLaMA3.1-70B	Direct Response	47.17	57.43	61.79	67.18	69.37	60.59
	Med-R^2	83.55	84.86	74.09	78.79	85.70	81.40
			128K				
LLaMA3.1-8B	Direct Response	31.14	39.97	30.69	36.43	38.26	35.30
	Med-R^2	56.06	59.58	32.48	47.64	44.82	48.12
Qwen2.5-14B	Direct Response	51.38	65.04	40.73	57.50	70.90	57.11
	Med-R^2	52.79	75.53	49.52	63.96	77.61	63.88
Qwen2.5-32B	Direct Response	16.11	85.77	66.29	68.12	79.84	63.23
	Med-R^2	27.09	88.21	69.17	70.99	83.87	67.87
LLaMA3.1-70B	Direct Response	47.26	57.37	63.28	68.12	70.03	61.21
	Med-R^2	83.84	84.07	74.97	77.87	84.93	81.14

Table 7: Scaling analysis of context window and model size for Med-R^2 .

Model	Method	MedQA-USMLE	MedQA-MCMLE	MedMCQA	PubMedQA	MMLU-Med	Average
Qwen2.5-7B	Direct Response	22.58	39.14	28.77	54.16	44.45	37.82
	Vanilla RAG	58.28	64.78	32.78	55.68	54.97	53.30
	+ Query Reformulator	64.34	67.77	37.99	55.01↓	59.64	56.95
	+ Evidence Reranker	68.37	70.81	38.43	55.78	62.38	59.15
	+ CoT Generator	63.12	66.98	35.64	55.62↓	56.88	55.65
	+ Query Reformulator, Evidence Reranker	77.85	78.67	45.62	55.99	70.74	65.77
	+ Query Reformulator, CoT Generator	73.36	74.54	40.21	55.54↓	63.02	61.33
	+ Evidence Reranker, CoT Generator	75.89	73.36	42.88	55.92	68.96	63.40
	Med-R^2	81.06	81.07	49.27	56.06	72.39	67.97
LLaMA3.1-8B	Direct Response	31.16	41.45	30.02	36.17	37.12	35.18
	Vanilla RAG	55.80	59.38	35.91	47.10	43.54	48.35
	+ Query Reformulator	62.47	72.85	41.66	48.72	43.98	53.94
	+ Evidence Reranker	68.62	75.74	43.84	49.97	43.76	56.34
	+ CoT Generator	59.87	65.63	39.45	47.71	43.61	51.25
	+ Query Reformulator, Evidence Reranker	74.41	81.68	47.71	53.96	44.23	60.40
	+ Query Reformulator, CoT Generator	70.86	77.43	44.83	51.75	44.02	57.78
	+ Evidence Reranker, CoT Generator	72.69	79.84	45.12	52.25	44.00	58.78
	Med-R^2	77.79	85.01	49.84	55.53	44.58	62.55
LLaMA2-13B	Direct Response	25.84	23.00	29.68	40.71	43.57	32.56
	Vanilla RAG	36.97	22.15	35.14	52.67	45.81	38.55
	+ Query Reformulator	37.32	25.64	36.98	53.83	46.67	40.09
	+ Evidence Reranker	37.54	25.98	38.74	54.04	46.94	40.65
	+ CoT Generator	37.44	23.12	35.93	53.22	46.03	39.15
	+ Query Reformulator, Evidence Reranker	37.99	29.28	40.17	56.73	48.63	42.56
	+ Query Reformulator, CoT Generator	37.58	26.88	39.65	54.94	46.98	41.21
	+ Evidence Reranker, CoT Generator	38.00	27.43	41.79	56.08	47.72	42.20
	Med-R^2	38.06	29.34	41.96	57.12	48.89	43.07
Qwen2.5-14B	Direct Response	50.01	65.23	42.85	56.93	71.60	57.32
	Vanilla RAG	54.88	75.60	42.06	60.38	79.46	62.48
	+ Query Reformulator	54.93	78.96	45.43	64.85	81.73	65.18
	+ Evidence Reranker	55.03	78.83	45.97	65.08	81.56	65.29
	+ CoT Generator	54.62↓	76.72	43.86	62.13	80.02	63.47
	+ Query Reformulator, Evidence Reranker	55.38	82.04	48.29	67.02	83.17	67.18
	+ Query Reformulator, CoT Generator	54.77↓	80.58	47.61	66.98	82.21	66.43
	+ Evidence Reranker, CoT Generator	54.81↓	81.79	47.87	67.48	82.95	66.98
	Med-R^2	53.28↓	82.67	48.85	67.99	83.20	67.20
Qwen2.5-32B	Direct Response	16.23	87.07	66.44	68.66	80.19	63.72
	Vanilla RAG	19.33	89.30	67.63	67.06	83.85	65.43
	+ Query Reformulator	20.14	89.42	68.72	68.41	83.97	66.13
	+ Evidence Reranker	20.83	89.88	68.88	68.47	83.99	66.41
	+ CoT Generator	19.78	88.69↓	67.94	67.72	83.92	65.61
	+ Query Reformulator, Evidence Reranker	23.04	89.25↓	70.35	68.89	84.46	67.20
	+ Query Reformulator, CoT Generator	21.97	89.56	69.06	68.56	84.08	66.65
	+ Evidence Reranker, CoT Generator	23.01	89.75	69.75	69.00	84.39	67.18
	Med-R^2	23.27	89.21↓	70.50	69.05	84.53	67.31
LLaMA3.1-70B	Direct Response	46.43	58.36	62.33	66.81	71.33	61.05
	Vanilla RAG	62.66	77.91	66.63	68.78	76.95	70.59
	+ Query Reformulator	70.82	80.64	69.72	71.82	73.56	73.31
	+ Evidence Reranker	73.96	80.78	70.87	74.64	75.28	75.11
	+ CoT Generator	68.08	78.65	68.85	70.09	73.72	71.88
	+ Query Reformulator, Evidence Reranker	80.41	84.09	73.01	77.80	80.68	79.20
	+ Query Reformulator, CoT Generator	78.62	82.56	72.71	76.06	78.56	77.70
	+ Evidence Reranker, CoT Generator	81.93	82.97	72.88	76.52	81.62	79.18
	Med-R^2	85.52	85.01	74.48	78.01	84.65	81.53

Table 8: Module analysis of Med-R^2 . We sequentially integrate various modules onto the *vanilla RAG* systems to conduct comparative analyses. ↓ indicates a decrease in downstream scores comparing to the *vanilla RAG* strategy.