Annals of Internal Medicine RESEARCH AND REPORTING METHODS

Development of Prompt Templates for Large Language Model–Driven Screening in Systematic Reviews

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Background: Systematic reviews (SRs) are hindered by the initial rigorous article screen, which delays access to reliable information synthesis.

Objective: To develop generic prompt templates for large language model (LLM)–driven abstract and full-text screening that can be adapted to different reviews.

Design: Diagnostic test accuracy.

Setting: 48 425 citations were tested for abstract screening across 10 SRs. Full-text screening evaluated all 12 690 freely available articles from the original search. Prompt development used the GPT4-0125-preview model (OpenAI).

Participants: None.

Measurements: Large language models were prompted to include or exclude articles based on SR eligibility criteria. Model outputs were compared with original SR author decisions after full-text screening to evaluate performance (accuracy, sensitivity, and specificity).

Results: Optimized prompts using GPT4-0125-preview achieved a weighted sensitivity of 97.7% (range, 86.7% to 100%) and specificity of 85.2% (range, 68.3% to 95.9%) in abstract screening and weighted sensitivity of 96.5% (range, 89.7% to 100.0%) and specificity of 91.2% (range, 80.7% to 100%) in full-text screening across 10 SRs. In contrast, zero-shot prompts had poor sensitivity (49.0% abstract, 49.1% full-text). Across LLMs, Claude-3.5 (Anthropic) and GPT4 variants had similar performance, whereas Gemini Pro (Google) and GPT3.5 (OpenAI) models underperformed. Direct screening costs for 10 000 citations differed substantially: Where single human abstract screening was estimated to require more than 83 hours and $1666.67 USD, our LLM-based approach completed screening in under 1 day for $157.02 USD.

Limitations: Further prompt optimizations may exist. Retrospective study. Convenience sample of SRs. Full-text screening evaluations were limited to free PubMed Central full-text articles.

Conclusion: A generic prompt for abstract and full-text screening achieving high sensitivity and specificity that can be adapted to other SRs and LLMs was developed. Our prompting innovations may have value to SR investigators and researchers conducting similar criteria-based tasks across the medical sciences.

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Systematic reviews (SRs) are rigorous forms of knowledge synthesis that involve the gathering, critical appraisal, and analysis of evidence. As the gold standard in evidence-based practice, SRs bolster decision making across various domains, including medicine, business, and agriculture, among others (1). However, SRs are resource intensive, typically requiring 1 year and upwards of $100 000 to complete due to the comprehensive processes of conducting detailed searches, screening articles, extracting data, analyzing findings, and report writing (2–4). The screening phase is particularly demanding and typically involves 2 investigators working independently, and in duplicate, to identify articles that meet predefined eligibility criteria through title and abstract and then full-text screening stages (1, 5). Despite a growing catalog of tools and resources (6), SR automation remains elusive. Existing tools only supplement human workflows, lack the performance required for independent decision making, and require extensive historical training data that is not available when conducting a new review (7, 8).

The rise of large language models (LLMs), such as generative pretrained transformer (GPT; OpenAI), creates new horizons for SR screening (9, 10). MedPrompt (Microsoft) (11), a collection of prompting techniques to optimize GPT4 performance on medical benchmarks, has shown that well-prompted generalist models can surpass fine-tuning methods. However, previous LLM

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Supplement

assessments for SR screening relied on basic zero-shot prompting—where LLMs are only given task instructions without examples—and demonstrated low sensitivity and recall or specificity that precludes their use (12–16).

Here, we aimed to develop generic prompt templates for LLM-driven SR abstract and full-text screening that could be used for future SRs. We evaluated the sensitivity and specificity of the prompt templates using *BenchSR*, our newly created database of published SRs. If successful, LLM-driven SR abstract screening can be implemented as a single reviewer vote or "prescreen" citations before human screening (**Supplement Figure 1**, available at Annals.org). Large language model–based full-text screening may directly screen articles from the original search, bypassing the initial abstract screening step.

Methods

An overview of our workflow is provided in the **Appendix Figure** (available at Annals.org).

BenchSR Database and Data Acquisition

We created a database (*BenchSR*) of 10 previously published SRs spanning 9 unique clinical domains collected through convenience sampling based on Oxford Centre for Evidence-Based Medicine SR question types (**Appendix Table 1** and **Supplementary Methods**, available at Annals.org) (17–26). We acquired the complete set of citations retrieved from the search strategies for each SR. Citations were downloaded from Covidence (Veritas Health Innovation) and contained complete reference information (for example, title, authors, and digital object identifier) and abstracts. Duplicate citations, and citations missing identifiers (digital object identifier) or abstracts, were discarded (**Figure 1**). We obtained all freely available PubMed Central (PMC) full texts from the complete set of citations for each review with the BioC application programming interface (API). We extracted information concerning review objectives from the published manuscript or PROSPERO protocol and contacted study authors for a priori study eligibility criteria.

The *BenchSR* database is available at https://github.com/JZSang/srma. The eligibility criteria and objectives for each review are provided in Supplementary Note 1 (available at Annals.org). We invite researchers to contribute to *BenchSR*.

Prompt Testing Workflow

Our reference standard was the final article inclusion or exclusion decisions of the original review authors after full-text screening. "Included" articles represented the final set of articles included in each review, and "excluded" articles represented articles excluded from title and abstract and full-text screening in each review. This reference standard was applied in both LLM-based abstract and full-text screening.

We evaluated our LLM approach as an independent single reviewer across 2 different screening scenarios. For LLM-based abstract screening, we evaluated the complete set of eligible titles and abstracts retrieved from the original SR search. For LLM-based full-text screening, we evaluated all full texts that were freely available on PMC from the original SR search. An overview of our article selection workflow is provided in **Figure 1**.

In our prompt development phase (**Figure 1**), we determined a minimum sensitivity (included) sample size of 196 articles and minimum specificity (excluded) sample size of 196 articles with the Cochran sample size formula (**Supplementary Methods**) (27). We oversampled balanced train (*n* = 200 included, *n* = 200 excluded) and validation (*n* = 200 included, *n* = 200 excluded) samples from the SeroTracker (ST) data set with random sampling (**Figure 1**). Our iterative prompt development was performed only on the ST train sample with the GPT4-0125-preview model (OpenAI). We then validated the performance of our optimized prompting strategy on the ST validation sample.

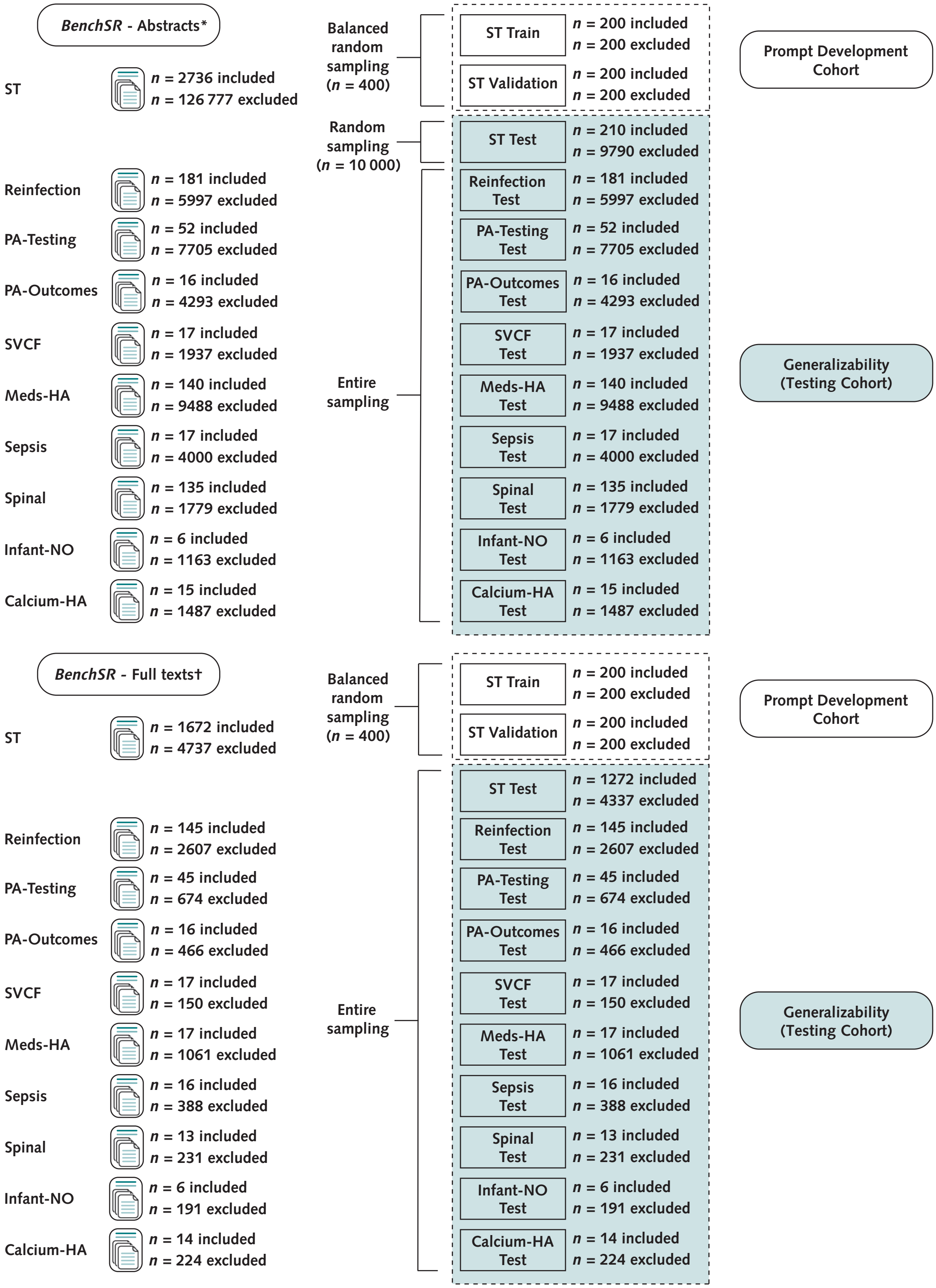
After prompt development, we tested the performance of the optimized prompt on our testing cohort (**Figure 1**). These data sets represented novel data not seen in the prior prompt development steps. For 9 of the SRs, we performed testing on the entire set of included and excluded articles in abstract and full-text screening. Given the size of the ST data set and associated cost of testing, the abstract ST test sample consisted of a large sample (*n* = 10 000) of 210 included and 9790 excluded abstracts (**Supplementary Methods**). The full-text ST test sample consisted of all retrievable full texts not involved in prompt development.

Prompt Development Method

We sought to develop generic prompt templates that could be adapted by SR investigators for abstract and full-text screening, in both new and existing SRs (that is, living SRs). During prompt development, we focused on developing decision-making instructions that would apply across SRs. The review-specific elements—objectives and eligibility criteria—were inserted verbatim into our prompt template. When iteratively testing prompts, we prioritized changes that increased sensitivity (minimizing false negatives) while maintaining specificity (limiting false positives), as missing relevant articles could bias review findings, whereas false positives could be corrected during human review.

In abstract screening, we first tested 3 established prompting techniques: zero-shot, few-shot, and Chain-of-Thought (CoT) (**Supplement Table 1**, available at Annals.org). We then iteratively refined our prompts to enhance LLM decision making, while keeping review-specific elements unchanged. For full-text screening, we addressed the "lost-in-the-middle" phenomenon—where LLMs may overlook key information in lengthy documents—by strategically restructuring prompt instructions without modifying their content (that is, repositioning, numbering). We assessed the generalizability of our

Figure 1. Flow diagram of *BenchSR* data sets for prompt development (train cohort) and prompt generalizability (test cohort) in abstract (*top*) and full-text screening (*bottom*).



HA = hospital admissions; NO = nitric oxide; PA = primary aldosteronism; ST = SeroTracker; SVCF = superior vena cava flow.

* Citations missing abstract content or digital object identifiers were discarded.

† All PubMed Central free full-text articles retrieved from original systematic review search.

optimized prompt templates by testing their performance across 10 different SRs, inserting review-specific elements verbatim from each protocol.

All prompt templates and definitions are provided in **Supplement Table 1**. The final optimized abstract screening (*Abstract ScreenPrompt*) and full-text screening (*Instruction Structure Optimized* (*ISO*)*-ScreenPrompt*) templates are provided in Supplementary Notes 2 and 3 (available at Annals.org).

Time and Cost Analysis

We estimated the direct cost and time of LLM-based screening compared with traditional human screening approaches. Our analysis focused on the resources needed to screen a defined number of abstracts or PMC full texts; we did not consider indirect costs, including initial programming time, human screening software licenses, and full-text retrieval costs.

We used a time estimate for abstract screening (30 seconds per abstract) reported by Perlman-Arrow and colleagues (28), which measured human screening time during completion of the ST review. These estimates are conservative relative to other reported screening times in literature, ranging from 20 to 461 seconds per abstract (5, 28, 29). We obtained a time estimate for full-text screening from the literature (12 minutes 9 seconds per article). This represents the median of estimates we identified searching the literature (4.3 to 20 minutes for a single full-text article) (29, 30). Details of the search are reported in our **Supplementary Methods**.

We assumed a compensation rate of $20 USD per hour for human reviewers. We did not consider the additional costs of conflict screening (additional abstracts and full texts screened due to conflicts between reviewers). For our abstract screening (*Abstract ScreenPrompt*) and full-text screening (*ISO-ScreenPrompt*) approach with GPT4-0125-preview, we calculated the cost for each run ($10 per million input tokens, $30 per million output tokens, OpenAI pricing). We applied the OpenAI Batch API, which offered a 50% cost discount and completed all screening runs within 24 hours.

LLM API and Evaluations

We tested the performance of GPT3.5-Turbo-0125 (GPT3.5; OpenAI), GPT4-0125-preview, GPT4-Turbo-0409 (OpenAI), GPT4-o-0513 (OpenAI), Gemini Pro (Google), open Mixtral-8x22-0424 (Mistral AI), Mistral-Large-0224 (Mistral AI), and Claude-3.5-Sonnet-1022 (Claude-3.5-Sonnet; Anthropic) models for abstract and full-text screening with our final optimized abstract (*Abstract ScreenPrompt*) and full-text (*ISO-ScreenPrompt*) prompt templates. For all models, we set the maximum output tokens (upper limit of output text units) to 2048 and used default model settings (**Supplementary Methods**). All model evaluations were performed through standardized API calls, ensuring a controlled environment for LLM interactions. This approach enabled consistent testing conditions and reproducible results across models. Detailed information about our API call infrastructure is provided in the **Supplementary Methods**.

Data Analysis

We assessed the performance of our prompts by analyzing accuracy ($[TP + TN]/[TP + TN + FP + FN] \times 100$), sensitivity ($[TP]/[TP + FN] \times 100$), and specificity ($[TN]/[TN + FP] \times 100$), and reported true positives (TPs), true negatives (TNs), false positives (FPs), and false negatives (FNs). We calculated 95% CIs for sensitivity and specificity using the Clopper-Pearson method (31) with the binom package in R (R Foundation for Statistical Computing).

Role of the Funding Source

This study did not receive direct funding support.

Results

Data Sets and *BenchSR*

We curated *BenchSR*, a collection of 10 SR data sets comprising more than 170 000 articles, spanning 4 of 6 Oxford Centre for Evidence-Based Medicine question types (32, 33) and 9 different clinical domains (34) (**Appendix Table 1**). This compilation includes SR metadata (inclusion and exclusion criteria and study objectives) and the complete set of articles (included and excluded) for each review.

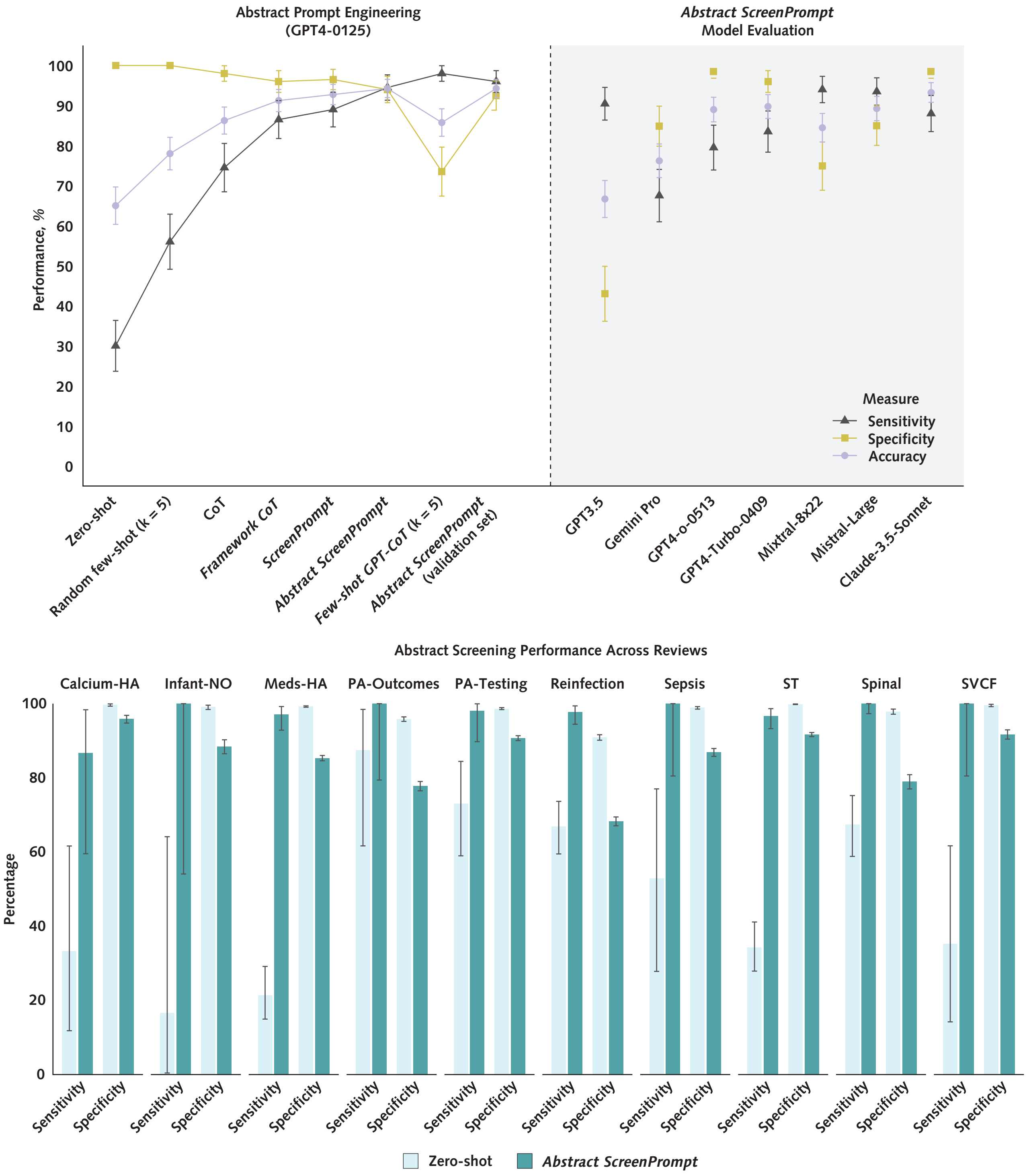
Abstract Prompt Engineering

We iteratively evaluated the performance of 7 different prompting methods on our ST train sample with the GPT4-0125-preview model (**Figure 1,** ***top***; **Figure 2,** ***top***; **Supplement Table 2**, available at Annals.org). Prompt definitions and templates are provided in **Supplement Table 1**.

Zero-shot prompting approaches adapted from Guo and colleagues (12) had suboptimal performance (30% sensitivity, 100% specificity) (**Figure 2,** ***top***). We then tested few-shot prompts, which incorporated additional labeled examples, and *zero-shot CoT* prompts, which added instructions to "think step-by-step." Although we saw performance improvements with *zero-shot CoT* (74.5% sensitivity, 98.0% specificity), the model outputs were inconsistent and occasionally failed to reason against exclusion criteria (**Supplement Table 3**, available at Annals.org). In response, we incorporated additional instructions for the LLM to reason using the predefined inclusion and exclusion criteria. This approach, termed *Framework CoT*', improved the consistency of our model outputs and had performance gains (86.5% sensitivity, 96% specificity) (**Figure 2,** ***top***).

When reviewing *Framework CoT* outputs, we found that LLMs often inferred incorrect SR objectives (**Supplement Table 3**). We then refined our prompt by including unmodified SR objectives (termed

Figure 2. Iterative abstract prompt template development and testing.



CoT = Chain-of-Thought; GPT = Generative Pretrained Transformer; HA = hospital admissions; NO = nitric oxide; PA = primary aldosteronism; ST = SeroTracker; SVCF = superior vena cava flow. **Top.** Left: Performance comparison of different abstract prompting methods on the ST train data set (n = 400) tested with GPT4-0125-preview (OpenAI), showing accuracy, sensitivity, and specificity. The *Abstract ScreenPrompt* is also separately evaluated on the ST validation data set (n = 400). The order of prompts reflects the temporal progression of our prompt development process. Right: *Abstract ScreenPrompt* is evaluated on the ST train data set (n = 400) across GPT3.5 (OpenAI), Gemini Pro (Google), GPT4-o-0513 (OpenAI), GPT4-Turbo-0409 (OpenAI), Mixtral-8x22 (Mistral AI), and Mistral-Large (Mistral AI) large language models. Error bars represent 95% CIs for binomial proportions. **Bottom.** Bar plot displaying sensitivity and specificity of zero-shot and *Abstract ScreenPrompt* across 10 different systematic review data sets from *BenchSR*. Error bars represent 95% CIs for exact proportions with the Clopper–Pearson method.

ScreenPrompt) (89.0% sensitivity, 96.5% specificity) and further increased the sensitivity of the prompt by including additional abstract screening instructions (*Abstract*) (**Supplement Tables 3** and **4**, available at Annals.org). The final optimized abstract prompt (*Abstract ScreenPrompt*) had the best performance on the ST train sample (94.3% accuracy, 94.5% sensitivity, and 94% specificity) and similar performance on the ST validation sample (94.3% accuracy, 96% sensitivity, and 92.5% specificity), indicating that we did not overfit the training sample (**Figure 2,** ***top***). An example *Abstract ScreenPrompt* is provided in Supplementary Note 2. Key components of the prompt are highlighted in **Figure 3**.

Although few-shot prompting (adding additional labeled examples) is traditionally believed to enhance LLM performance (35), our balanced *few-shot GPT-CoT* prompt was associated with decreased performance (85.8% accuracy, 98.0% sensitivity, and 73.5% specificity) (**Figure 2,** ***top***). Adjusting the ratio of included and excluded few-shot examples (9:1 inclusion- or exclusion-favored *GPT-CoT few-shot* examples) did not alter performance (**Supplement Figure 2b** and **Supplement Table 5**, available at Annals.org).

Generalizability of Abstract Prompting

Across LLMs, the GPT4-0125-preview model had the best performance (94.5% sensitivity and 94% specificity) (**Figure 2,** ***top***; **Supplement Table 6**, available at Annals.org). The Gemini Pro model had the lowest performance (67.5% sensitivity and 84.8% specificity). *Abstract ScreenPrompt* was associated with improvements in accuracy and sensitivity relative to zero-shot prompting, regardless of the LLM used (**Supplement Table 7**, available at Annals.org).

We applied our optimized abstract prompt template (*Abstract ScreenPrompt*) to 10 SRs using GPT4-0125-preview (**Figure 2,** ***bottom***; **Appendix Table 2**, available at Annals.org). *Abstract ScreenPrompt* achieved high sensitivity across reviews (weighted, 97.7% [range, 86.7% to 100.0%]), outperforming zero-shot prompting (weighted, 49.0% [range, 16.7% to 87.5%]). Zero-shot prompting had higher specificity (weighted, 97.9% [range, 90.9% to 99.8%]) compared with *Abstract ScreenPrompt* (weighted, 85.2% [range, 68.3% to 95.9%]). Across all 10 reviews, zero-shot prompting incorrectly excluded a median of 12.5 eligible articles (IQR, 8.5 to 56) that were included by original SR authors. In contrast, *Abstract ScreenPrompt* incorrectly excluded a median of 0.5 eligible articles (IQR, 0 to 3.5) per review.

Full-Text Prompt Engineering

We then evaluated LLM-based full-text article screening using our full-text ST train sample with the GPT4-0125-preview model (**Figure 4,** ***top***; **Supplement Tables 8** and **9**, available at Annals.org). Prompt definitions and templates are provided in **Supplement Table 1**.

Zero-shot prompting had the worst performance (37.7% sensitivity and 100.0% specificity) (**Figure 4,** ***top***). Our experiments repositioning our prompt instructions (**Supplement Figure 3a**, available at Annals.org, and **Supplement Table 9**) found the best performance with our *ScreenPrompt (init + fin)* prompt, where prompt instructions were repeated before and after the full-text article (94.8% accuracy, 95% sensitivity, and 94.5% specificity) (**Figure 4,** ***top***). We also saw improvements with our *Numbered ScreenPrompt* prompt, where we numbered each eligibility subcriterion—without modifying the criteria content (95.2% accuracy, 98% sensitivity, and 92.4% specificity) (**Figure 4,** ***top***). Applying the same prompting strategies (that is, repeating and numbering prompts) to abstract screening did not notably improve results (**Supplement Figure 3b** and **Supplement Table 10**, available at Annals.org), possibly because abstracts are too short to manifest the lost-in-the-middle phenomenon.

We combined the *Numbered Framework CoT* prompt with the optimal prompt structure (init + fin) to create the optimized full-text screening prompt (*ISO-ScreenPrompt*). The *ISO-ScreenPrompt* had the best overall performance on the ST train sample (95.5% accuracy, 94% sensitivity, and 98% specificity) and similar performance on the ST validation sample (96.3% accuracy, 97.5% sensitivity, and 95% specificity) (**Figure 4,** ***top***, and **Supplement Table 8**). A full example *ISO-ScreenPrompt* is provided in Supplementary Note 3 (available at Annals.org). Key components of the prompt are highlighted in **Figure 5**.

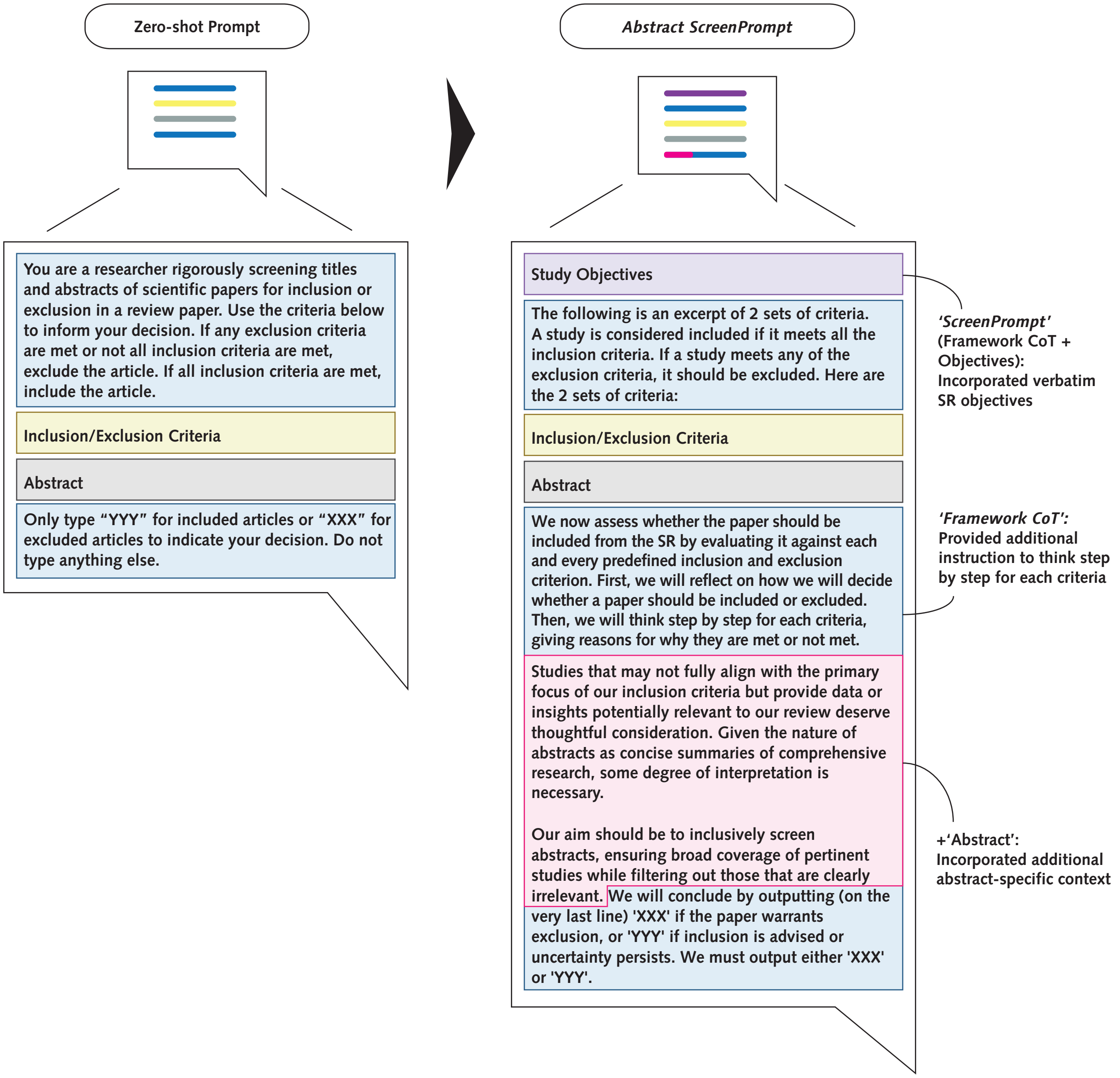
Generalizability of Full-Text Prompting

Across LLMs, GPT4-0125-preview, GPT4-Turbo-0409, GPT4-o-0513, and Claude-3.5-Sonnet models demonstrated similar performance when prompted with *ISO-ScreenPrompt* (93.0% to 93.5% sensitivity and 97.5% to 99% specificity). Other models (Gemini Pro, Mistral-Large, and GPT3.5) performed worse (69.1% to 77.8% sensitivity and 65.4% to 96% specificity) (**Figure 4,** ***top***; **Supplement Table 11**, available at Annals.org).

We applied our optimized full-text prompt template (*ISO-ScreenPrompt*) to 10 SRs using GPT4-0125-preview (**Figure 4,** ***bottom***; **Appendix Table 3**, available at Annals.org). Of all citations from the SR search, 7.56% (*n* = 12 690) had freely available full texts. These 12 690 articles represented 59.16% of articles that original reviews included in their final study. All final included articles were available as free full texts for 5 reviews, 94% (16 of 17) for 1 review, and 80% (145 of 181) for 1 review (**Figure 1,** ***bottom***).

ISO-ScreenPrompt demonstrated high sensitivity across 10 reviews (weighted, 96.5% [range, 89.7% to 100.0%]), in contrast to zero-shot prompting (weighted, 49.1% [range, 11.8% to 93.8%]). Zero-shot prompting had higher specificity (weighted, 97.5% [range, 89.5% to 100.0%]) than *ISO-ScreenPrompt* (weighted, 91.2%

Figure 3. Key components of *Abstract ScreenPrompt*, relative to zero-shot.



You are a researcher rigorously screening titles and abstracts of scientific papers for inclusion or exclusion in a review paper. Use the criteria below to inform your decision. If any exclusion criteria are met or not all inclusion criteria are met, exclude the article. If all inclusion criteria are met, include the article.

Inclusion/Exclusion Criteria

Abstract

Only type “YYY” for included articles or “XXX” for excluded articles to indicate your decision. Do not type anything else.

Study Objectives

The following is an excerpt of 2 sets of criteria. A study is considered included if it meets all the inclusion criteria. If a study meets any of the exclusion criteria, it should be excluded. Here are the 2 sets of criteria:

Inclusion/Exclusion Criteria

Abstract

We now assess whether the paper should be included from the SR by evaluating it against each and every predefined inclusion and exclusion criterion. First, we will reflect on how we will decide whether a paper should be included or excluded. Then, we will think step by step for each criteria, giving reasons for why they are met or not met.

Studies that may not fully align with the primary focus of our inclusion criteria but provide data or insights potentially relevant to our review deserve thoughtful consideration. Given the nature of abstracts as concise summaries of comprehensive research, some degree of interpretation is necessary.

Our aim should be to inclusively screen abstracts, ensuring broad coverage of pertinent studies while filtering out those that are clearly irrelevant. We will conclude by outputting (on the very last line) 'XXX' if the paper warrants exclusion, or 'YYY' if inclusion is advised or uncertainty persists. We must output either 'XXX' or 'YYY'.

‘ScreenPrompt’ (Framework CoT + Objectives): Incorporated verbatim SR objectives

‘Framework CoT’: Provided additional instruction to think step by step for each criteria

+‘Abstract’: Incorporated additional abstract-specific context

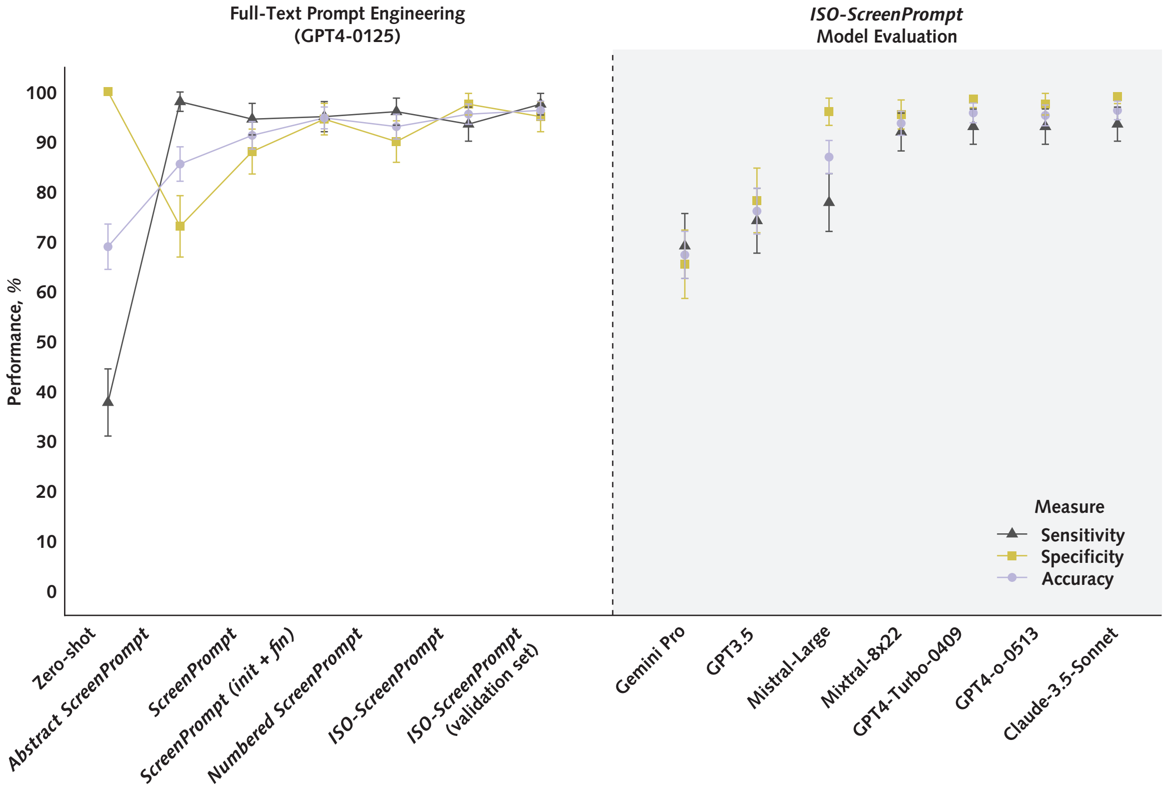
CoT = Chain-of-Thought; SR = systematic review.

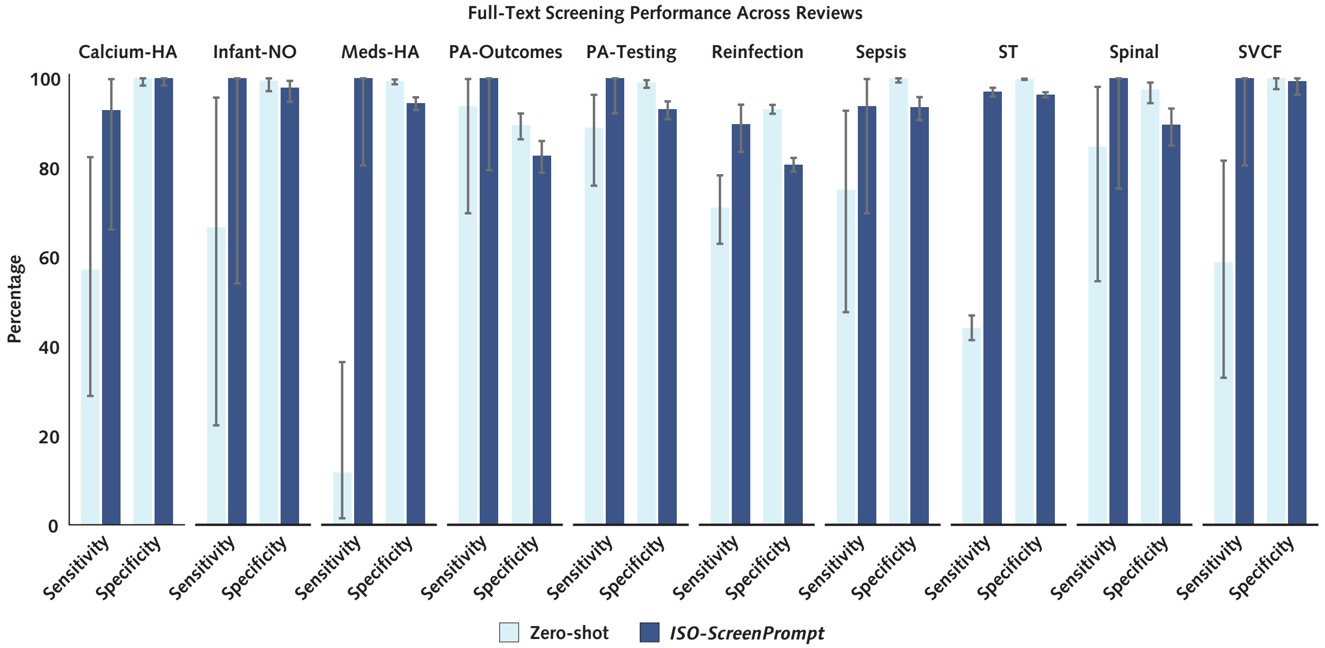
[range, 80.7% to 100%]). Across all 10 reviews, zero-shot prompting incorrectly excluded a median of 5.5 eligible articles (IQR, 2.5 to 13) per review that were included by original SR authors. In contrast, *ISO-ScreenPrompt* incorrectly excluded a median of 0 eligible articles (IQR, 0 to 1) per review.

Cost and Time Savings of LLM-Driven Screening

Direct screening costs for *Abstract ScreenPrompt* ranged from $16.74 to $157.02 USD depending on the number of articles in the SR, compared with $194.83 to $1666.67 USD for single human-reviewer abstract screening (**Supplement Table 13**, available at Annals.org). Direct screening costs for *ISO-ScreenPrompt* ranged from $14.53 to $622.12, compared with $676.35 to $25 956.40 USD for single human-reviewer full-text screening (**Supplement Table 14**, available at Annals.org). Single human reviewers were estimated to require 9.74 to 83.33 hours (abstracts) and 33.82 to 1297.82 hours (full texts), whereas *Abstract ScreenPrompt* and *ISO-ScreenPrompt* completed screening for all reviews within 24 hours. The *Abstract ScreenPrompt* prescreen approach was estimated to reduce screening duration by 17.15 to 149.70 hours and reduce abstract screening

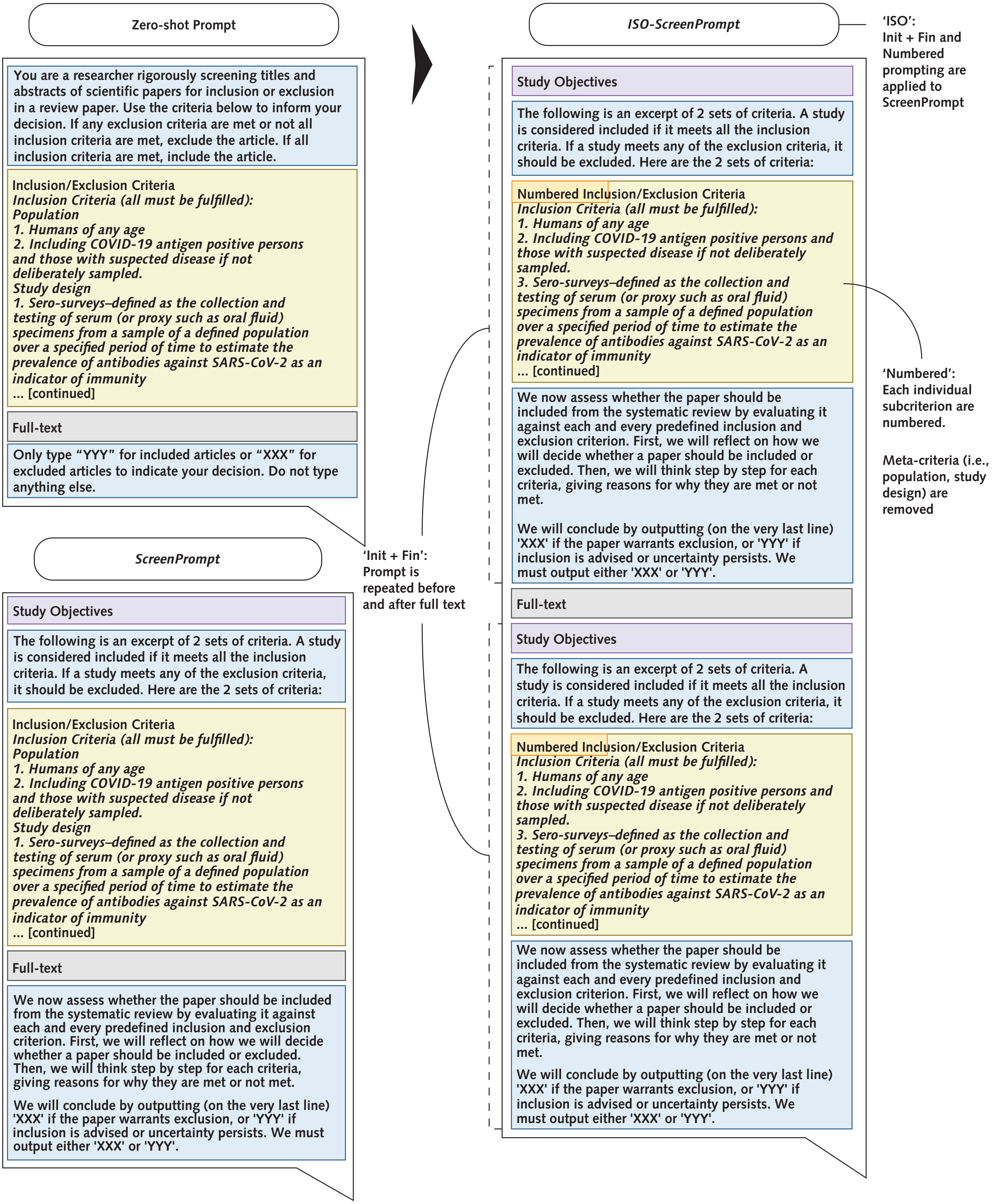
Figure 4. Iterative full-text prompt template development and testing.





GPT = Generative Pretrained Transformer; HA = hospital admissions; init + fin = initialize + finalize; ISO = Instruction Structure Optimized; NO = nitric oxide; PA = primary aldosteronism; ST = SeroTracker; SVCF = superior vena cava flow. **Top.** Left: Performance comparison of different full-text prompting methods on the ST train data set (n = 400) tested with GPT4-0125-preview (OpenAI), showing accuracy, sensitivity, and specificity. *ISO-ScreenPrompt* is also separately evaluated on the ST validation data set (n = 400). The order of prompts reflects the temporal progression of our prompt development process. Right: *ISO-ScreenPrompt* is evaluated on the ST train data set (n = 400) across GPT3.5 (OpenAI), Gemini Pro (Google), GPT4-o-0513 (OpenAI), GPT4-Turbo-0409 (OpenAI), Mixtral-8x22 (Mistral AI), and Mistral-Large (Mistral AI) large language models. Error bars represent 95% CIs for binomial proportions. **Bottom.** Bar plot displaying sensitivity and specificity of zero-shot and *ISO-ScreenPrompt* across 10 different systematic review data sets from *BenchSR*. Error bars represent 95% CIs for exact proportions with the Clopper–Pearson method.

Figure 5. Key components of *ISO-ScreenPrompt*, relative to zero-shot and *ScreenPrompt*.



Zero-shot Prompt

You are a researcher rigorously screening titles and abstracts of scientific papers for inclusion or exclusion in a review paper. Use the criteria below to inform your decision. If any exclusion criteria are met or not all inclusion criteria are met, exclude the article. If all inclusion criteria are met, include the article.

Inclusion/Exclusion Criteria
Inclusion Criteria (all must be fulfilled):
Population
1. Humans of any age
2. Including COVID-19 antigen positive persons and those with suspected disease if not deliberately sampled.
Study design
1. Sero-surveys–defined as the collection and testing of serum (or proxy such as oral fluid) specimens from a sample of a defined population over a specified period of time to estimate the prevalence of antibodies against SARS-CoV-2 as an indicator of immunity
... [continued]

Full-text

Only type “YYY” for included articles or “XXX” for excluded articles to indicate your decision. Do not type anything else.

ScreenPrompt

Study Objectives

The following is an excerpt of 2 sets of criteria. A study is considered included if it meets all the inclusion criteria. If a study meets any of the exclusion criteria, it should be excluded. Here are the 2 sets of criteria:

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Inclusion Criteria (all must be fulfilled):
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1. Sero-surveys–defined as the collection and testing of serum (or proxy such as oral fluid) specimens from a sample of a defined population over a specified period of time to estimate the prevalence of antibodies against SARS-CoV-2 as an indicator of immunity
... [continued]

Full-text

We now assess whether the paper should be included from the systematic review by evaluating it against each and every predefined inclusion and exclusion criterion. First, we will reflect on how we will decide whether a paper should be included or excluded. Then, we will think step by step for each criteria, giving reasons for why they are met or not met.

We will conclude by outputting (on the very last line) 'XXX' if the paper warrants exclusion, or 'YYY' if inclusion is advised or uncertainty persists. We must output either 'XXX' or 'YYY'.

'Init + Fin': Prompt is repeated before and after full text

ISO-ScreenPrompt

'ISO': Init + Fin and Numbered prompting are applied to ScreenPrompt

Study Objectives

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... [continued]

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Full-text

Study Objectives

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3. Sero-surveys–defined as the collection and testing of serum (or proxy such as oral fluid) specimens from a sample of a defined population over a specified period of time to estimate the prevalence of antibodies against SARS-CoV-2 as an indicator of immunity
... [continued]

We now assess whether the paper should be included from the systematic review by evaluating it against each and every predefined inclusion and exclusion criterion. First, we will reflect on how we will decide whether a paper should be included or excluded. Then, we will think step by step for each criteria, giving reasons for why they are met or not met.

We will conclude by outputting (on the very last line) 'XXX' if the paper warrants exclusion, or 'YYY' if inclusion is advised or uncertainty persists. We must output either 'XXX' or 'YYY'.

'Numbered': Each individual subcriterion are numbered.

Meta-criteria (i.e., population, study design) are removed

Init + fin = initialize + finalize; ISO = Instruction Structure Optimized.

costs by $343.00 to $2994.00 USD (**Supplement Table 15**, available at Annals.org), depending on SR size.

Discussion

Systematic review workflows are encumbered by resource- and time-intensive article screening processes.

Unlike other traditional machine learning approaches that require extensive labeled training data, our LLM-based method bypasses the need for prior classifier training. Reviewers can immediately begin screening articles after they insert their eligibility criteria and SR objectives into the prompt template. Our generic template offers an alternative for investigators seeking to automate screening with minimal upfront effort rather than relying on review-specific customized prompts (16, 36).

The optimized abstract prompt template (*Abstract ScreenPrompt*) achieved a weighted sensitivity of 97.7% and weighted specificity of 85.2% across 10 diverse reviews, surpassing previous tools (for example, Abstrackr [Agency for Healthcare Research and Quality], Rayyan [Rayyan], and RobotAnalyst) (37, 38) and estimates of single human-reviewer performance (86.6% sensitivity and 79.2% specificity) (39). The optimized full-text prompt template (*ISO-ScreenPrompt*) achieved even higher performance (weighted, 96.5% sensitivity and 91.2% specificity).

While maintaining high sensitivity across reviews, our LLM approach showed lower specificity in the Reinfection (abstract: 68.3%, full-text: 80.7%) and (PA)-Outcomes (abstract: 77.8%, full-text: 82.6%) reviews. The Reinfection SR's lower performance may stem from its reliance on supplementary data not included in abstracts or full texts. The PA-Outcomes SR had broad outcomes inclusion criteria (for example, major adverse cardiovascular events), which may have led to overly inclusive LLM decisions. For instance, studies reporting on hypertension control were incorrectly included due to potential cardiovascular associations. Although more specific outcomes may have improved performance, we maintained the original investigators' criteria as part of our goal to create generalizable prompt templates. Future investigators may see better results by specifically defining all aspects of PICO (population, intervention, comparator, outcomes) as part of their inclusion and exclusion criteria.

Previous studies evaluating LLM performance for abstract screening have primarily used zero-shot prompting approaches with unsatisfactory results. Sensitivity and specificity with GPT3.5 has ranged from 38% to 69% (14) and 2.1% to 45.5% (16), respectively, and sensitivity with GPT4 somewhat improved at 59.3% to 100% (12). Zero-shot prompting, akin to assessing a race car's performance without shifting gears, may underestimate the capabilities of LLMs for downstream tasks. Our prompt templates showed improved accuracy and sensitivity compared with zero-shot prompting across all tested LLMs.

GPT4-0125-preview achieved the highest performance with the optimized abstract and full-text prompts compared with other LLMs. This likely stems from our prompt development being conducted with GPT4-0125-preview. Kojima and colleagues (40) found that minor variations in prompt phrasing could influence GPT3 performance by up to 8.4%. This suggests potential opportunities for model-specific prompt optimization through refined word choice and phrasing. In contrast, Gemini Pro and GPT3.5 models had consistently lower performance, which may reflect fundamental model limitations, as evidenced by their lower performance on established reasoning benchmarks, such as multitask language understanding (GPT3.5, 70%; Gemini Pro, 71.8%; and GPT-4o, 88.7%) (41).

We offer several prompt engineering insights. First, we developed *Framework CoT*, which guides LLMs to produce structured reasoning on the basis of a priori criteria, reducing errors in unstructured freeform reasoning. Second, we found that providing additional task-specific context (that is, review objectives) can improve the model understanding and performance. Third, few-shot prompting can underperform zero-shot approaches, and adjusting the proportion of *GPT-CoT few-shot* label distributions (that is, balanced, exclusion-favored, and inclusion-favored) did not affect model performance. Finally, for lengthy documents (that is, full-text articles), our *ISO-ScreenPrompt* approach addresses the lost-in-the-middle phenomenon (42–44) by repeating and numbering instructions at the start and end of the prompt (43).

We highlight 2 potential implementation pathways for LLMs in abstract screening (**Supplement Figure 1**). First, mirroring our study, the LLM could serve as an independent single reviewer, either complementing a human reviewer to halve the traditional screening workload or enabling full automation of rapid reviews where single screening is accepted. Second, *Abstract ScreenPrompt* could be used to prescreen citations before 2 human reviewers begin abstract screening, reducing screening volume by 66.4% to 95.1%, while only incorrectly excluding a median of 0.5 studies at the full-text stage. Implementation decisions should be guided by available resources, risk tolerance for missed citations, and cost–benefit analysis specific to each review's context.

In contrast, full-text screening faces major practical barriers. Our full-text analysis was limited to PMC full-texts, which made up only 7.56% of all citations. Journal paywalls, copyright concerns, and other associated costs preclude complete full-text retrieval. It is premature to support a workflow bypassing title and abstract screening.

Our study has several limitations. First, although our analysis was validated across a range of SRs, further research is needed to assess the generalizability to other clinical questions (for example, harms, screening), non-English SRs, and different review methods like scoping reviews. Second, we tested only a sample of the ST data set in abstract screening due to cost barriers, and our full-text analysis was limited to freely accessible PMC texts. Consequently, the true sensitivity and specificity of our LLM-based template may differ from the reported results. As barriers to full-text accessibility persist, LLM-based full-text screening may not yet be feasible. Third, our LLM approach focused on text content; incorporating figures and tables could enhance performance and should be explored in future research. Fourth, our cost and time estimates for human screening were based on literature estimates rather than direct measurement, and we only considered the direct costs of screening a defined number of citations. Other external factors (that is, programming time, conflicts, and full-text costs) were not considered. Fifth, we limited few-shot prompting to abstracts due to LLM context length limitations. Finally, although we surveyed various prompting techniques, we did not explore every possible method, and subtle optimizations could further enhance model performance. While future model advancements will likely continue to enhance LLM reasoning abilities and downstream task performance, researchers may explore further prompt optimization for model-specific refinements.

In conclusion, our study provides generic prompt templates (*Abstract ScreenPrompt* and *ISO-ScreenPrompt*) that can achieve high sensitivity and specificity for abstract and full-text screening across diverse systematic reviews. Future research should expand validation to a broader spectrum of SRs and conduct prospective studies that evaluate our prompts' performance against human reviewers. Future research could also explore use of these prompting techniques for other criteria-based tasks across the medical sciences. Exploration of LLMs for other SR tasks, such as data extraction and meta-analysis, may allow for more dynamic, continuously updated knowledge repositories supporting greater evidence-based practices for researchers, clinicians, and patients.

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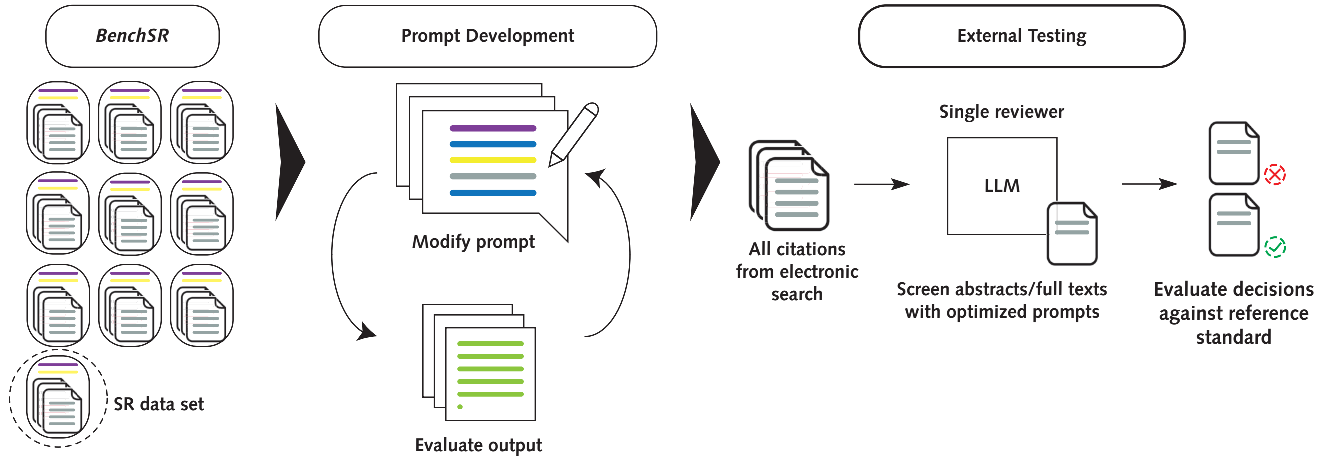
Appendix Figure. Infographic of study design.


BenchSR
SR data set
Prompt Development
Modify prompt
Evaluate output
External Testing
All citations from electronic search
Single reviewer
LLM
Screen abstracts/full texts with optimized prompts
Evaluate decisions against reference standard

We created *BenchSR*, a systematic review screening benchmark comprising 10 diverse systematic reviews with detailed study metadata and complete citation data. During prompt development, we iteratively assessed various prompting techniques, with the LLM making include or exclude decisions for abstracts and full texts on the basis of review eligibility criteria. Model outputs were compared against the reference standard (final article decisions after full-text screening by original study authors) to evaluate performance. During external testing, we evaluated our optimized prompt templates using unaltered study metadata (objectives, inclusion criteria) from each review, comparing model outputs against the same reference standard. LLM = large language model; SR = systematic review.

Appendix Table 1. Descriptive Overview of *BenchSR* Data Sets

CEBM Type	Data Set	Clinical Domain (Web of Science) (34)	Population	Intervention/ Exposure	Study Types Included	Citations Identified From Electronic Search (After Deduplication), *n*	Citations Included After Title/ Abstract Screening, *n*	Citations Included After Full-Text Screening, *n*
Prevalence *How common is the problem?*	SeroTracker	Infectious diseases	Humans of any age	Prevalence of SARS-CoV-2 antibodies	Cross-sectional, repeated cross-sectional, and cohort study designs	130 436	3659	2736
Diagnostic test accuracy *Is this diagnostic or monitoring test accurate?*	PA-Testing	Endocrinology and metabolism	Patients with primary aldosteronism	Confirmatory tests used to diagnose primary aldosteronism	Case–control, diagnostic testing	8000	248	52
	Spinal	Neurosciences and neurology	Adolescents (aged 12–17 y) or adults (aged ≥18 y) undergoing any type of spine surgery	Neuromonitoring of postoperative neurologic status	RCTs or comparative observational studies (comparative cohorts, case–control studies)	2233	296	135
Prognosis *What will happen if we do not add a therapy?*	SVCF	Pediatrics cardiovascular system and cardiology	Preterm infants <32 wk gestational age	Low SVC flow identified by Doppler assessment in the first 48 h after birth	RCTs, cohort or case-control studies	2257	95	17
	Infant-NO	Pediatrics respiratory system	Preterm infants born <34 wk of gestational age without congenital anomalies or genetic disorders	Treatment with inhaled nitric oxide	Prospective and retrospective cohort studies	1317	53	6
Intervention benefits *Does this intervention help?*	Reinfection	Infectious diseases	Humans of any age, in any geographic setting	Persons with previously confirmed SARS-CoV-2 infection that have documented vaccination status	Test-negative case-control, traditional case-control, cross-sectional, cohort, non-RCTs, and RCTs	6724	1256	181
	Sepsis	General and internal medicine	Persons aged ≥16 y with septic shock (sepsis and use of at least 1 vasopressor)	Treatment with hydrocortisone alone, hydrocortisone-fludrocortisone, placebo, or usual care.	RCTs	5034	59	17
	Meds-HA	Pharmacology and pharmacy	Adults (aged >16 y)	Administration of any medication during emergency hospital admissions	Systematic reviews of RCTs	9707	1563	140

Continued on following page

Appendix Table 1–Continued

CEBM Type	Data Set	Clinical Domain (Web of Science) (34)	Population	Intervention/ Exposure	Study Types Included	Citations Identified From Electronic Search (After Deduplication), *n*	Citations Included After Title/ Abstract Screening, *n*	Citations Included After Full-Text Screening, *n*
	Calcium-HA	Cardiovascular system and cardiology	Adults and children in any setting with cardiac arrest	Administration of calcium (intravenous or intraosseous) during cardiac arrest	RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) with a control group	1939	37	15
	PA-Outcomes	Endocrinology and metabolism surgery	Patients with primary aldosteronism	Surgical adrenalectomy and medical treatment with a mineralocorticoid receptor antagonist	RCTs, observational studies	5376	74	16
Intervention harms *What are the common/rare harms?*	N/A	N/A						
Screening *Is this (early detection) test worthwhile?*	N/A	N/A						

CEBM = Oxford Centre for Evidence-Based Medicine; HA = hospital admissions; N/A = not available; NO = nitric oxide; PA = primary aldosteronism; RCT = randomized controlled trial; SCVF = superior vena cava flow.

Appendix Table 2. Generalizability of Abstract *ScreenPrompt* Across SRs

Data Set	Abstracts, *total n* (Include/ Exclude, *n*)	Prompt	True Positives, *n*	True Negatives, *n*	False Negatives, *n*	False Positives, *n*	Sensitivity (95% CI), %	Specificity (95% CI), %
SeroTracker (test sample)	10 000 (210/9790)	Zero-shot	72	9775	138	15	34.3 (27.9–41.1)	99.8 (99.7–99.9)
		Abstract ScreenPrompt	203	8975	7	815	96.7 (93.3–98.6)	91.7 (91.1–92.2)
Reinfection	6180 (181/5999)	Zero-shot	121	5453	60	546	66.9 (59.5–73.7)	90.9 (90.1–91.6)
		Abstract ScreenPrompt	177	4096	4	1903	97.8 (94.4–99.4)	68.3 (67.1–69.5)
PA-Testing	7757 (52/7705)	Zero-shot	38	7603	14	102	73.1 (59.0–84.4)	98.7 (98.4–98.9)
		Abstract ScreenPrompt	51	6990	1	715	98.1 (89.7–100.0)	90.7 (90.1–91.4)
PA-Outcomes	4309 (16/4293)	Zero-shot	14	4115	2	178	87.5 (61.7–98.4)	95.9 (95.2–96.4)
		Abstract ScreenPrompt	16	3339	0	954	100.0 (79.4–100.0)	77.8 (76.5–79.0)
Meds-HA	9628 (140/9488)	Zero-shot	30	9415	110	73	21.4 (14.9–29.2)	99.2 (99.0–99.4)
		Abstract ScreenPrompt	136	8096	4	1392	97.1 (92.8–99.2)	85.3 (84.6–86.0)
Sepsis	4017 (17/4000)	Zero-shot	9	3956	8	44	52.9 (27.8–77.0)	98.9 (98.5–99.2)
		Abstract ScreenPrompt	17	3475	0	525	100.0 (80.5–100.0)	86.9 (85.8–87.9)
Spinal	1914 (135/1779)	Zero-shot	91	1742	44	37	67.4 (58.8–75.2)	97.9 (97.1–98.5)
		Abstract ScreenPrompt	135	1405	0	374	100.0 (97.3–100.0)	79.0 (77.0–80.8)
Infant-NO	1169 (6/1163)	Zero-shot	1	1153	5	10	16.7 (0.4–64.1)	99.1 (98.4–99.6)
		Abstract ScreenPrompt	6	1029	0	134	100.0 (54.1–100.0)	88.5 (86.5–90.3)
Calcium-HA	1502 (15/1487)	Zero-shot	5	1483	10	4	33.3 (11.8–61.6)	99.7 (99.3–99.9)
		Abstract ScreenPrompt	13	1426	2	61	86.7 (59.5–98.3)	95.9 (94.8–96.8)
SVCF	1954(17/1937)	Zero-shot	6	1929	11	8	35.3 (14.2–61.7)	99.6 (99.2–99.8)
		Abstract ScreenPrompt	17	1777	0	160	100.0 (80.5–100.0)	91.7 (90.4–92.9)

HA = hospital admissions; NO = nitric oxide; PA = primary aldosteronism; SR = systematic review; SVCF = superior vena cava flow.

Appendix Table 3. Generalizability of *ISO-ScreenPrompt* Across SRs

Data Set	Full text, *total n* (Include/ Exclude, *n*)	Prompt	True Positives, *n*	True Negatives, *n*	False Negatives, *n*	False Positives, *n*	Sensitivity (95% CI), %	Specificity (95% CI), %
SeroTracker (test sample)	5609 (1272/4337)	Zero-shot	561	4329	711	8	44.1 (41.4–46.9)	99.8 (99.6–99.9)
		ISO-ScreenPrompt	1234	4178	38	159	97.0 (95.9–97.9)	96.3 (95.7–96.9)
Reinfection	2752 (145/2607)	Zero-shot	103	2427	42	180	71.0 (62.9–78.3)	93.1 (92.1–94.0)
		ISO-ScreenPrompt	130	2103	15	504	89.7 (83.5–94.1)	80.7 (79.1–82.2)
PA-Testing	719 (45/674)	Zero-shot	40	667	5	7	88.9 (75.9–96.3)	99.0 (97.9–99.6)
		ISO-ScreenPrompt	45	627	0	47	100.0 (92.1–100.0)	93.0 (90.8–94.8)
PA-Outcomes	482 (16/466)	Zero-shot	15	417	1	49	93.8 (69.8–99.8)	89.5 (86.3–92.1)
		ISO-ScreenPrompt	16	385	0	81	100.0 (79.4–100.0)	82.6 (78.9–85.9)
Meds-HA	1078 (17/1061)	Zero-shot	2	1054	15	7	11.8 (1.5–36.4)	99.3 (98.6–99.7)
		ISO-ScreenPrompt	17	1002	0	59	100.0 (80.5–100.0)	94.4 (92.9–95.7)
Sepsis	404 (16/388)	Zero-shot	12	388	4	0	75.0 (47.6–92.7)	100.0 (99.1–100.0)
		ISO-ScreenPrompt	15	363	1	25	93.8 (69.8–99.8)	93.6 (90.6–95.8)
Spinal	244 (13/231)	Zero-shot	11	225	2	6	84.6 (54.6–98.1)	97.4 (94.4–99.0)
		ISO-ScreenPrompt	13	207	0	24	100.0 (75.3–100.0)	89.6 (84.9–93.2)
Infant-NO	197 (6/191)	Zero-shot	4	190	2	1	66.7 (22.3–95.7)	99.5 (97.1–100.0)
		ISO-ScreenPrompt	6	187	0	4	100.0 (54.1–100.0)	97.9 (94.7–99.4)
Calcium-HA	238 (14/224)	Zero-shot	8	224	6	0	57.1 (28.9–82.3)	100.0 (98.4–100.0)
		ISO-ScreenPrompt	13	224	1	0	92.9 (66.1–99.8)	100.0 (98.4–100.0)
SVCF	167 (17/150)	Zero-shot	10	150	7	0	58.8 (32.9–81.6)	100.0 (97.6–100.0)
		ISO-ScreenPrompt	17	149	0	1	100.0 (80.5–100.0)	99.3 (96.3–100.0)

HA = hospital admissions; ISO = Instruction Structure Optimized; NO = nitric oxide; PA = primary aldosteronism; SR = systematic review; SVCF = superior vena cava flow.