How do clinicians become informed about how to treat their patients?

> How do governments and institutions make health policy decisions?

How do clinicians become informed about how to treat their patients?

# **Systematic Reviews**

How do governments and institutions make health policy decisions?

# Systematic Reviews

- Guide clinical decisions
  Inform practice and policy
- Provide evidence

Systematic Reviews

Critically Appraised Individual Articles

Randomised Controlled Trials (RCTs)

**Cohort Studies** 

Case-controlled Studies / Case Reports

Background Information / Expert Opinion

# Systematic review creation is hard!











# Why such little research on queries?

(("Thyroid Neoplasms" [MeSH] OR "Adenocarcinoma, Follicular" [MeSH] OR "Adenocarcinoma, Papillary" [MeSH] OR OPTC OR ((Thyroid[tiab] OR Follicular[tiab] OR Papillary[tiab] OR hurtle cell[tiab]) AND (cancer[tiab] OR cancers[tiab] OR carcinoma[tiab] OR carcinomas[tiab] OR Adenocarcinoma[tiab] OR Adenocarcinomas[tiab] OR neoplasm[tiab] OR neoplasms[tiab] OR nodule[tiab] OR nodules[tiab] OR tumor[tiab] OR tumour[tiab] OR Tumors[tiab] OR Tumours[tiab] OR cyst[tiab] OR cysts[tiab]))) AND ("Autopsy"[MeSH] OR "Autopsy"[tiab] OR "Autopsies" [tiab] OR "Postmortem" [tiab] OR Post-mortem [tiab] OR "step-sectioned"[tiab] OR "step sectioned"[tiab] OR (Post[tiab] AND mortem[tiab])) AND (Prevalence"[MeSH] OR Prevalence"[tiab] OR Prevalences"[tiab] OR Incidence[tiab] OR Epidemiology[tiab] OR Epidemiological[tiab] OR Frequency[tiab] OR Detected[tiab]) AND ("Incidental Findings" [MeSH] OR Incidental [tiab] OR Unsuspected [tiab] OR Discovery[tiab] OR Discoveries[tiab] OR Findings[tiab] OR Finding[tiab] OR Occult[tiab] OR Hidden[tiab] OR Latent[tiab] OR Consecutive[tiab]))



Why are Boolean queries used?

Reproducibility -> double check screening

# Understandability -> control set size

## Lecture Content Overview

# Formulating Boolean queries

- Use decoder model to automatically formulate Boolean queries
- Translating Boolean queries
  - Use decoder model to translate Boolean queries to alternative representations
- Automatically assessing documents
  - Use decoder model to automatically assess the relevance of documents

Overview

Use ChatGPT to formulate Boolean queries [Wang et al. 2023].

- □ Existing methods for Boolean query formulation use many heuristics.
- □ Use ChatGPT instead to automatically formulate Boolean queries.
- □ Compare effectiveness of all formulation methods to humans.

Formulating Boolean Queries How Humans Formulate Queries

- Conceptual method [Clark 2013] → Human expertise Objective method [Hausner et al. 2012] → More algorithmic
- Both methods → Seed studies

### Automating the conceptual method

#### Systematic review statement + seed studies



High level concepts → broaden search → iterate until satisfied

#### Automating the conceptual method

#### Systematic review statement + seed studies



POS tagger -> parse grammar & segment words into noun phrases

### Automating the conceptual method

#### Systematic review statement + seed studies



MetaMap → extract CUIs from UMLS ontology

### Automating the conceptual method

#### Systematic review statement + seed studies



Skipgram model → broaden scope

### Automating the conceptual method

#### Systematic review statement + seed studies



# Map concepts (CUIs) to terms

#### Automating the objective method



# Find prominent terms from docs → Add these terms to query

#### Automating the objective method



Extract list of keywords from seed studies

#### Automating the objective method



# Rank documents using term frequency

#### Automating the objective method



Add keywords from documents to query

Conceptual versus objective results

CLEF TAR [Kanoula	as et al. 2017, 20	)18]	Seed study	/ collection [Wang et al. 2022]
	Precision	Recall	Precision	Recall
Conceptual Objective	0.0014 0.0002	0.6996 0.9128	0.0018 0.0057	0.4138 0.5192
num. queries=72			num. queries	=40

Conceptual versus objective results

### CLEF TAR [Kanoulas et al. 2017, 2018]

	Precision	Recall
Human	0.0207	0.8317
Conceptual	0.0014	0.6996
Objective	0.0002	0.9128

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#### Seed study collection [Wang et al. 2022]

Precision	Recall
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# Objective provides highest recall, but larger trade-offs than conceptual

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Both methods are highly sensitive to initial seed studies

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Both methods are highly sensitive to initial seed studies

# Conceptual method better starting point for precision, and objective for recall

Can ChatGPT formulate effective queries?

Hey ChatGPT, formulate a query for me!

Sure, no problem! ;-)

- $\Box$  Translation task: prompt  $\rightarrow$  query
- Two methods to formulate queries:
  - Unguided prompt one shot to generate query
  - Guided prompt follows objective approach
- Prevalence of Differentiated Thyroid Cancer in Autopsy Studies Over Six Decades: A Meta-Analysis

**Unguided Prompt Examples – Simple** 

For a systematic review titled "{review\_title}", can you generate a systematic review Boolean query to find all included studies on PubMed for the review topic?

("Prevalence of Differentiated Thyroid Cancer" AND "Autopsy Studies"AND "Six Decades") AND (systematic review OR meta-analysis)

# **Formulating Boolean Queries** Unguided Prompt Examples – Detailed

You are an information specialist who develops Boolean queries for systematic reviews. You have extensive experience developing highly effective queries for searching the medical literature. Your specialty is developing queries that retrieve as few irrelevant documents as possible and retrieve all relevant documents for your information need. Now you have your information need to conduct research on "{review\_title}". Please construct a highly effective systematic review Boolean query that can best serve your information need.

> ("Differentiated Thyroid Cancer" OR "Papillary Thyroid Cancer" OR "Follicular Thyroid Cancer") AND "Autopsy Studies" AND "Prevalence" AND (("1960/01/01"[PDAT] : "2023/01/30"[PDAT]) OR ("1960"[PDAT]:"2023"[PDAT]))

## **Formulating Boolean Queries** Unguided Prompt Examples – With Example

You are an information specialist who develops Boolean queries for systematic reviews. You have extensive experience developing highly effective queries for searching the medical literature. Your specialty is developing queries that retrieve as few irrelevant documents as possible and retrieve all relevant documents for your information need. You are able to take an information need such as: "{example\_review\_title}" and generate valid pubmed queries such as: "{example\_review\_query}". Now you have the information need to conduct research on "{review\_title}", please generate a highly effective systematic review Boolean query for the information need.

("Differentiated Thyroid Cancer"[Mesh] OR (differentiated[All Fields] AND thyroid[All Fields] AND cancer[All Fields]) OR Papillary Thyroid Cancer"[Mesh] OR (papillary[All Fields] AND thyroid[All Fields] AND cancer[All Fields]) OR Follicular Thyroid Cancer"[Mesh] OR (follicular[All Fields] AND thyroid[All Fields] AND cancer[All Fields])) AND ((prevalence[All Fields] OR incidence[All Fields]) AND (autopsy[All Fields] OR post-mortem[All Fields] OR mortuary[All Fields]) AND (study[All Fields] OR studies[All Fields]) AND (six[All Fields] OR 60[All Fields] OR decades[All Fields]))

**Previous Query Formulation Results** 

CLEF TAR [Kanoulas et al. 2017, 2018]

Seed study collection [Wang et al. 2022]

	Precision	Recall
Human	0.0207	0.8317
Conceptual	0.0014	0.6996
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Precision	Recall
0.0367	0.7366
0.0018	0.4138
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**Unguided Query Formulation Results** 

#### CLEF TAR [Kanoulas et al. 2017, 2018]

Seed study collection [Wang et al. 2022]

	Precision	Recall
Human	0.0207	0.8317
Conceptual	0.0014	0.6996
Objective	0.0002	0.9128
Simple	0.0543	0.1293
Detailed	0.1166	0.1310
Example	0.0752	0.5035

Precision	Recall
0.0367	0.7366
0.0018	0.4138
0.0057	0.5192
0.0501	0.0528
0.0983	0.0394
0.0283	0.1290

**Unguided Query Formulation Results** 

#### CLEF TAR [Kanoulas et al. 2017, 2018]

Seed study collection [Wang et al. 2022]

	Precision	Recall
Human	0.0207	0.8317
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Objective	0.0002	0.9128
Simple	0.0543	0.1293
Detailed	0.1166	0.1310
Example	0.0752	0.5035

Precision	Recall
0.0367	0.7366
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Collection contains **seed studies** 

→ Use ChatGPT for objective method

Guided Prompt Examples - 1

Follow my instructions precisely to develop a highly effective Boolean query for a medical systematic review literature search. Do not explain or elaborate. First, Given the following statement and text from a relevant study, **identify 50 terms or phrases that are relevant**. The terms you identify should be used to retrieve more relevant studies, so be careful that the terms you choose are not too broad. You are not allowed to have duplicates in your list. Statement: {statement}. Text: {text}

#### 1. Differentiated thyroid cancer

- 2. Prevalence
- 3. Autopsy studies
- 4. Meta-analysis
- 5. Occult carcinomas

. . .

50. Parameters.
Guided Prompt Examples – 2

... 50. Parameters.

For each item in the list you created in Step 1, **classify it into three categories**: terms relating to health conditions (A), terms relating to a treatment (B), terms relating to types of study design (C). When an item does not fit one of these categories, mark it as (N/A). Each item needs to be categorised into (A), (B), (C), or (N/A).

#### 1. (A) Differentiated thyroid cancer

- 2. (N/A) Prevalence
- 3. (C) Autopsy studies
- 4. (C) Meta-analysis
- 5. (A) Occult carcinomas

•

50. (N/A) Parameters.

Guided Prompt Examples – 3

#### 50. (N/A) Parameters.

. . .

Using the categorised list you created in step 2, create a Boolean query that can be submitted to PubMed which groups together items from each category. For example: ((**itemA1** OR **itemA2** or **itemA3**) AND (itemB1 OR itemB2 OR itemB3) AND (itemC1 OR itemC2 OR itemC3))

(((differentiated[Title/Abstract] OR thyroid[Title/Abstract] OR carcinoma[Title/Abstract] OR papillary[Title/Abstract] OR microcarcinoma[Title/Abstract]) AND (cancer[Title/Abstract] OR incidence[Title/Abstract] OR etiology[Title/Abstract] OR risk[Title/Abstract] OR gender[Title/Abstract] OR hormonal[Title/Abstract] OR nodular[Title/Abstract] OR goiter[Title/Abstract] OR Hashimoto's[Title/Abstract] OR malignancy[Title/Abstract] OR concomitant[Title/Abstract] OR tumor[Title/Abstract] OR infiltrate[Title/Abstract] OR fibrosis[Title/Abstract] OR development[Title/Abstract] OR frequency[Title/Abstract] OR material[Title/Abstract] OR series[Title/Abstract] OR specimens[Title/Abstract] OR cases[Title/Abstract]]

Guided Prompt Examples - 4

...AND (autopsy[Title/Abstract] OR surgical[Title/Abstract] OR material[Title/Abstract] OR series[Title/Abstract] OR specimens[Title/Abstract] OR cases[Title/Abstract]))

Use your expert knowledge to **refine the query**, making it retrieve as many relevant documents as possible while minimising the total number of documents retrieved. Also add relevant MeSH terms into the query where necessary, e.g., MeSHTerm[MeSH]. Retain the general structure of the query, however, with each main clause of the query corresponding to a PICO element. The final query still needs to be executable on PubMed, so it should be a valid query.

> (((differentiated thyroid cancer[MeSH] OR "differentiated thyroid"[All Fields] OR "thyroid carcinoma"[All Fields] OR "papillary microcarcinoma"[All Fields]) AND (prevalence[All Fields] OR incidence[MeSH] OR "etiology of"[All Fields] OR "risk factors"[All Fields] OR gender[All Fields] OR hormonal[All Fields] OR "nodular goiter"[All Fields] OR "Hashimoto's thyroiditis"[MeSH] OR malignancy[MeSH] OR "concomitant lesion"[All Fields] OR tumor[All Fields] OR infiltrate[All Fields] OR fibrosis[All Fields] OR "early stages of development"[All Fields] OR frequency[All Fields])) AND (autopsy[MeSH] OR surgical[All Fields] OR material[All Fields] OR series[All Fields] OR specimens[All Fields] OR cases[All Fields]))

Query Formulation Results on Seed Study Collection [Wang et al. 2022]

	Precision	Recall
Human	0.0367	0.7366
Conceptual	0.0018	0.4138
Objective	0.0057	0.5192
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ChatGPT is more effective than automatic conceptual and objective methods

Query Formulation Results on Seed Study Collection [Wang et al. 2022]

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ChatGPT is more effective than automatic conceptual and objective methods

# ChatGPT is highly dependent on prompt and prone to hallucination

Overview

Use decoder models to translate Boolean queries into alternative representations [Wang et al. 2023].

- □ Translate the Boolean query into a natural language query.
- □ Rank documents retrieved by Boolean query using natural language query.
- Compare ranking effectiveness across baseline approaches from the literature.

Method Overview



#### Method Overview



Single Query versus Multiple Queries

Decoder models have a temperature parameter that introduces randomness into token prediction.

- □ Single query generation sets temperature to 0.
  - Translation will produce the same query every time.
- □ Multiple query generation uses the default temperature parameter.
  - Translation will produce a different query every time.
  - Generate ten natural language queries per Boolean query.

Single Query versus Multiple Queries

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  - Translation will produce the same query every time.
- □ Multiple query generation uses the default temperature parameter.
  - Translation will produce a different query every time.
  - Generate ten natural language queries per Boolean query.

What is the effectiveness of thyroid neoplasms, including adenocarcinoma, papillary neoplasms, and hurtle cell neoplasms, in the treatment of thyroid neoplasms? Specifically, I am interested in articles that discuss thyroid neoplasms in terms of cancer, neoplasms, carcinoma, or cysts, as well as articles that include thyroid neoplasms in step-sectioned or post-mortem studies. What is the effectiveness of autopsy, postmortem, and stepsectioned neoplasms in the diagnosis of thyroid neoplasms, including Adenocarcinoma, Follicular Neoplasia, and Papillary Neoplasia? Specifically, I am interested in articles that discuss thyroid neoplasms, cancer, tumors, or cysts with respect to autopsy, postmortem, or step-sectioned. What is the effectiveness of thyroid neoplasms, including adenocarcinoma, papillary thyroid neoplasm, and hurtle cell, in preventing or treating thyroid cancer, including subtypes of thyroid cancer such as papillomavirus, adenocarcinoma, and tumor? What is the effectiveness of thyroid neoplasms, including adenocarcinoma, in cancer detection? Specifically, I am interested in studies that focus on the use of thyroid neoplasms in detecting hepatic fibrosis or cancer, as well as studies that utilize thyroid neoplasms to uncover latent or hidden thyroid conditions.

Instruction fine-tuning

ChatGPT is a closed model, research with it has many limitations.

- Llama is a useable model trained on publicly available data [Touvron et al. 2023].
- □ However, on its own, Llama is 'just' a very large decoder-only transformer.
  - Adjusts aspects like the activation function and positional embeddings.
  - Several instances of the model, each with more parameters, 7B-65B.
  - For comparison, BERT has 110M parameters.
- □ Can fine-tune Llama in a similar way to make GPT-3 work like ChatGPT.
  - Self-instruct used to induce instruction following capabilities with minimal human-labelled data [Wang et al. 2023].
  - Bootstrap a model to generate instructions for itself and then learn to predict outputs for instructions.
- □ Alpaca is an instruction fine-tuned Llama model [Taori et al. 2023]
  - Here, Alpaca is further instruction fine-tuned for generating natural language queries.

Single Query Results on Seed Collection [Wang et al. 2022]

Query	Method	MAP
Boolean terms	BM25	0.087
Boolean terms	QLM	0.085
Boolean terms	BioBERT	0.199

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Boolean terms	BM25	0.087
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ChatGPT	BioBERT	0.217
Alpaca	BioBERT	0.221

Single Query Results on Seed Collection [Wang et al. 2022]

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ChatGPT	BioBERT	0.217
Alpaca	BioBERT	0.221
ChatGPT+Boolean terms	BioBERT	0.219
Alpaca+Boolean terms	BioBERT	0.230

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Instruction fine-tuned Alpaca produces most effective queries.

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Instruction fine-tuned Alpaca produces most effective queries.

Adding terms from the Boolean query improved ranking.

Multiple Query Results on Seed Collection [Wang et al. 2022]



Systematic Review Topics

Multiple Query Results on Seed Collection [Wang et al. 2022]



Systematic Review Topics

# Fusion of multiple generated queries typically results in higher ranking effectiveness.

Multiple Query Results on Seed Collection [Wang et al. 2022]



Systematic Review Topics

Fusion of multiple generated queries typically results in higher ranking effectiveness.

Oracle suggests that individual queries exist that are highly effective.

Use decoder models to automatically classify documents retrieved by Boolean query as relevant or non-relevant [Wang et al. 2024].

- Prompts a decoder-only model with instructions to output whether a document is relevant to a given systematic review.
- □ Everything done in a 'zero-shot' fashion: Models are not fine-tuned.
- □ Use token probabilities to determine degree of relevance to review.
- □ Learn a threshold to tighten the bound on precision.

**Overview** 

#### Automatically Assessing Documents Overview



**Decoder Models** 

Following large decoder models used in a zero-shot setting:

- 🛛 LLaMa
- Alpaca
- 🗅 LLaMa-2
  - Identical model architecture to LLaMa, but trained on more data.
- Guanaco
  - Memory-efficient fine-tuned LLaMA model.
- Falcon
  - First 'open' model of its kind, freely available and permissive license.
  - Decoder-only model with different yet architectures to LLaMA and GPT.

Every document retrieved by the query requires a forward pass through each model.

□ Using GPT-3.5-turbo would cost USD\$4,000 and GPT-4 USD\$80,000.

Uncalibrated Results on Seed Collection [Wang et al. 2022]

Model	Precision	Recall	F3
BioBERT	0.04	0.93	0.24
Alpaca-7b	0.04	0.90	0.22
Falcon-7b	0.04	0.93	0.22
Guanaco-7b	0.04	1.00	0.23
LLaMA-2-7b	0.05	0.90	0.27
LLaMA-2-13b	0.13	0.48	0.28

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LLaMa-2-7b gives best trade-off between precision and recall.

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LLaMa-2-7b gives best trade-off between precision and recall.

LLaMa-2-13b can dramatically increase precision at the cost of recall.

Calibrated Results on Seed Collection [Wang et al. 2022]

Model	Precision	Recall	F3
BioBERT (unc)	0.04	0.93	0.24
BioBERT (cal)	0.04	0.83	0.22
LLaMA-2-7b (unc)	0.05	0.90	0.27
LLaMA-2-7b (cal)	0.05	0.97	0.26
LLaMA-2-13b (unc)	0.13	0.48	0.28
LLaMA-2-13b (cal)	0.06	0.87	0.25

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LLaMA-2-13b (unc)	0.13	0.48	0.28
LLaMA-2-13b (cal)	0.06	0.87	0.25

Calibrated LLaMa-2-7b assesses documents better than calibrated LLaMa-2-13b.

Calibrated Results on Seed Collection [Wang et al. 2022]

Model	Precision	Recall	F3
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BioBERT (cal)	0.04	0.83	0.22
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LLaMA-2-7b (cal)	0.05	0.97	0.26
LLaMA-2-13b (unc)	0.13	0.48	0.28
LLaMA-2-13b (cal)	0.06	0.87	0.25

Calibrated LLaMa-2-7b assesses documents better than calibrated LLaMa-2-13b.

Similar results can be observed on other test collections.