



PRINCIPLE AND METHODS FOR WRITING SYSTEMATIC REVIEW AND META-ANALYSIS.



MSc of Epidemiology

SANA Institute for avian health and disease research

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LEARNING OUTCOMES / OBJECTIVES



- At the end of this session, you will be able to:
- Understand the **purpose and methodology of systematic reviews**, including the PRISMA guidelines, and apply them to design a systematic review.
- Develop clear search strategy and eligibility criteria,
- Extract and synthesize data from included studies (Meta-analysis), including conducting meta-analysis and assessing statistical heterogeneity.
- Assess risk of bias in studies using appropriate tools, and evaluate the certainty of evidence for each outcome.
- Interpret and discuss findings in the context of existing literature, addressing study limitations and implications for practice, policy, and future research.



1. INTRODUCTION

- Definition of Systematic Review
- Cochrane Collaboration definition:
- A systematic review uses **systematic** methods to **identify**, **select**, **critically appraise**, and **extract and analyze data from relevant research** [Higgins & Green 2011].
- Institute of Medicine (US)
- Meta-analysis is a scientific research methodology consisting of the analysis and synthesis (combination) of data obtained from previously conducted independently from each other studies on the same problem.

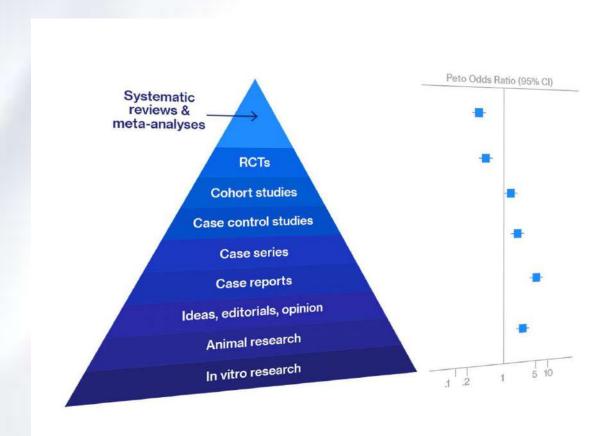


WHY WE NEED SYSTEMATIC REVIEWS

- Minimize the impact of bias/errors
- Can help to end confusion
- Highlight where there is not sufficient evidence
- Combining findings from different studies can highlight new findings
- Can mitigate the need for further trials



STUDIES PYRAMID





BEFORE STARTING REVIEW: CHECK IF SIMILAR STUDIES HAVE BEEN CONDUCTED

Avoid Redundancy

• Before starting a new review, check if similar systematic reviews or studies have already been conducted on the same topic.

Why Check?

- Save time: Prevent repeating work that has already been done.
- **Identify gaps**: Find areas where research is lacking or where new questions can be explored.
- Improve efficiency: Build on existing knowledge rather than duplicating efforts.

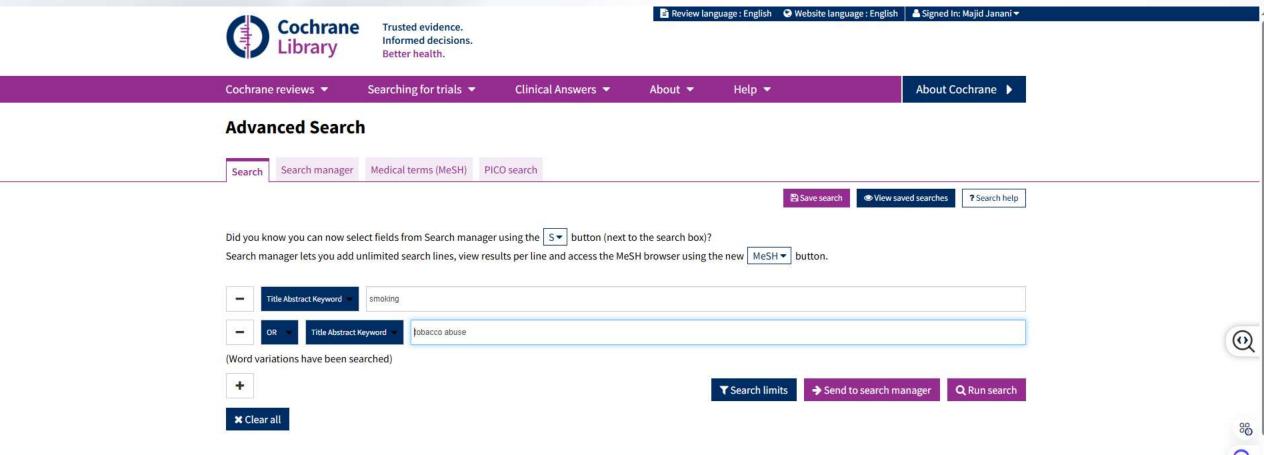
• How to Check for Previous Studies:

- Literature Databases: Search major databases like PubMed, Cochrane, Google Scholar, and Scopus.
- Systematic Review Registries: Check platforms like PROSPERO for already registered reviews.
- **Review Past Studies' Protocols**: Check if protocols exist that match your research question.

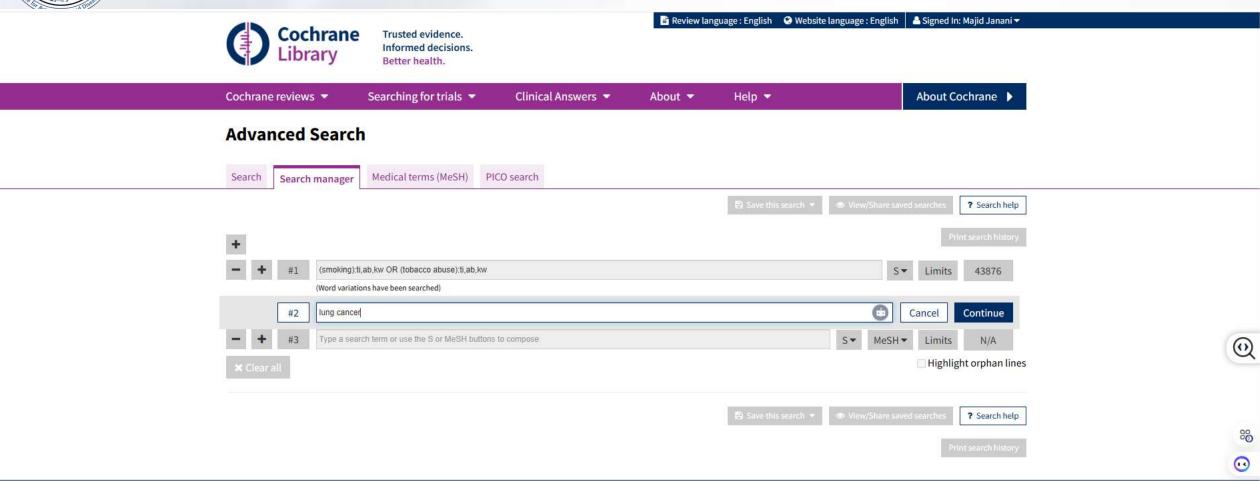
When You Find Similar Studies:

- Evaluate the scope: Are your review objectives different? Can you provide a more detailed synthesis?
- **Refine your focus**: Identify areas that were **under-explored or overlooked**.

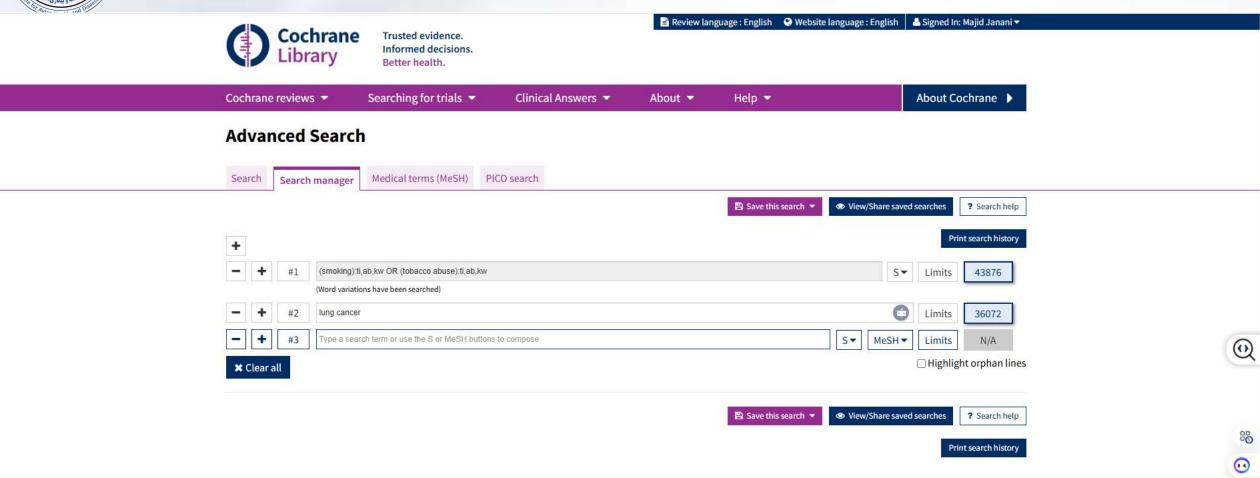














SEARCHING IN COCHRANE LIBRARY

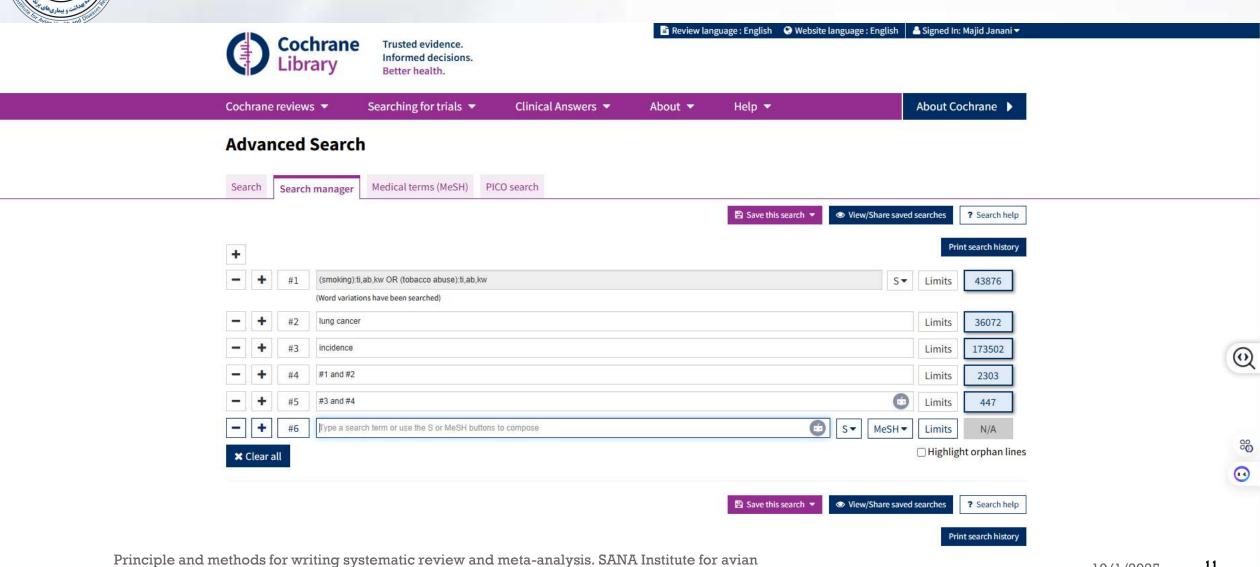
	Search limits	×	
	Content type Cochrane Reviews	CENTRAL Trials only Original publication year 1	
	☐ Cochrane Protocols ☐ Trials ☐ Clinical Answers	 ○ All years ○ Between	
	☐ Editorials ☐ Special Collections	Search word variations (e.g. "paid" will find pay, pays, paying, payed)	
■ #1 (smoking):ti,ab,kw OR	(tobacco abuse):ti,ab,kw		S▼ Limits
(Word variations have he	The last month The last 3 months The last 6 months The last 9 months The last 9 months The last 2 years Between YYYYY and YYYYY	Cnoose Gochrane Group ▼	

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health and disease research

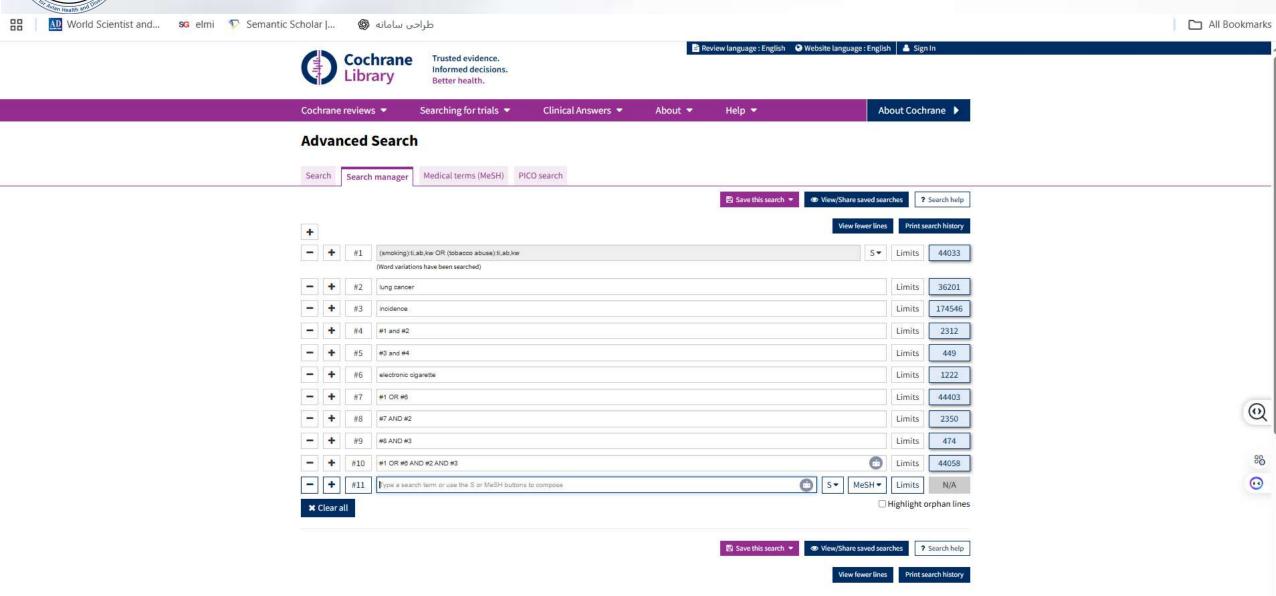
SEARCHING METHOD



10/1/2025



WHY WE SHOULD TO SEARCH BLOCK BY BLOCK





S	earch Search manager	Medical terms (MeSH)	PICO search					
					 View saved searches 	P Search help		
			e on the Search manager tab by selecting results per line, and select fields using the					1
36	arch manager lets you add t	untilinited Search lines, view i	esuits per tille, and select fields using the	button (next t	o the search box).			
C	igarette Smoking		Select subheadings / qualifiers		Look up	Clear		
	Definition							
	Cigarette Smoking - The SM	MOKING of CIGARETTES.						
_					A SERVICE BOOK BOOK BOOK BOOK			
	Thesaurus Matches	~	MeSH Trees MeSH term - Cigarette Smoking	¥3	Search Results There are 321 results for your search on			
	Exact Term Match	î	Explode all trees		- MeSH descriptor: Cigarette Smoking			
	Cigarette Smoking	•	Single MeSH term (unexploded)		- Explode all trees			
	Synonyms: Smoking, Cigaret	te	Explode selected trees	Select	Add to search manager			@
	Phrase Matches		☑ Tree number 1	B 🙃		-		
	Cigarette Smoking		Behavior and Behavior Mechanisms [+	16]	Trials	321		_
	Synonyms:		Behavior [+43] Smoking [+5]		Cochrane Reviews	0		90
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Principle and metal health and disease	nods for writing sy	stematic review an	d meta-analysis d meta-analysis fonaccouse[+1]	itute for avian			10/1/2025	13
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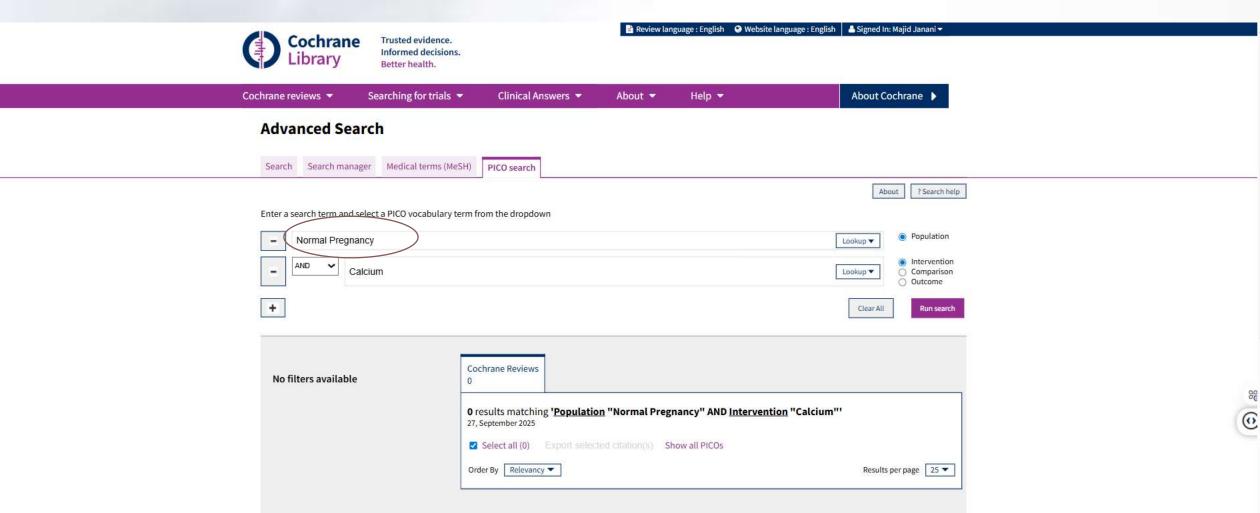


SEARCH BY PICO

Advanced Search			
Search manager Medical ter	rms (MeSH)	PICO search	
			About ? Search help
er a search term and select a PICO vocabulary t	term from the	dropdown	
			Population
Pregnancy		Looku	○ Intervention ○ Comparison
			Outcome
AND Calcium	Looku	● Intervention ○ Comparison ○ Outcome	
_			Outcome
		C	lear All Run search
ondition	6 results 27, Septemb	matching 'Population "Pregnancy " AND Intervention "Calcium"' per 2025	
ondition	27, Septemb	per 2025	
Pregnancy5	☐ Select	all (6) Export selected citation(s) Show all PICOs	
Pregnant1	Order By	Relevancy ▼	Results per page 25 ▼
Normal Blood Pressure1	1 🗆	Vitamin D supplementation for women during pregnancy	
Leg Cramps1		ShowPICOs = 30 July 2024	
ntervention / Comparison	2 🗆	Rest during pregnancy for preventing pre-eclampsia and its complications in normal blood pressure	women with
ntervention Name		ShowPiCOs + 01 February 2006	
Calcium6	3 🗆	Calcium supplementation (other than for preventing or treating hypertensio	n) for improving
inoleic Acid Supplementation1		pregnancy and infant outcomes ShowPICOs = 25 February 2015	
Soy Proteins1	Fig. 1225		7.7.40.20.3
Saline1	4 🗆	Calcium supplementation commencing before or early in pregnancy, for prev hypertensive disorders of pregnancy	venting
Multivitamins With Minerals1		ShowPICOs - 16 September 2019	
Magnesium1	5 🗆	Interventions for leg cramps in pregnancy	
/itamin D and analogues1		ShowPICOs → 01 January 2002	
Vitamins, Other Combinations1	6 🗆	Calcium supplementation during pregnancy for preventing hypertensive disc	orders and related



CARE ABOUT YOUR KEYWORDS



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EXAMPLE OF PICO IN ONE STUDY

PICOs[®]

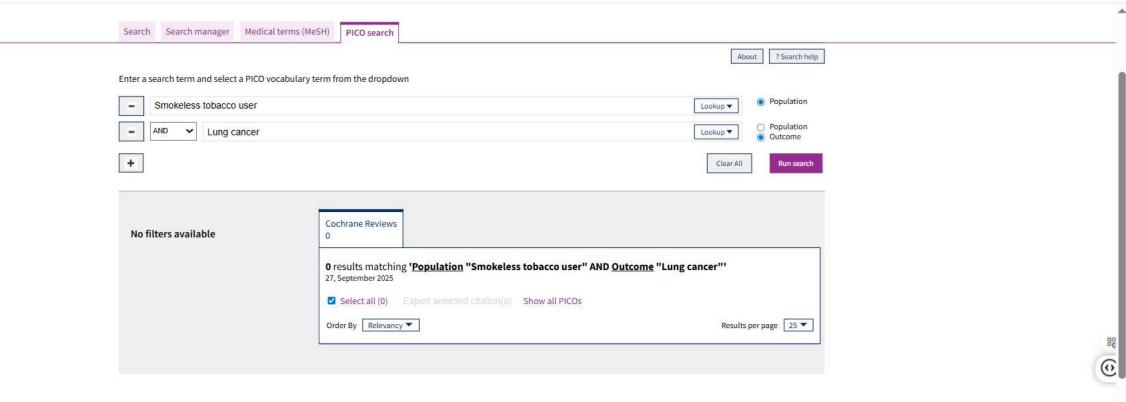
Population (5)	Intervention (1)	Comparison (1)	Outcome (11)
Adult 19-44 years Middle Aged 45-64 years Young Adult 19-24 years Pregnancy	Calcium	Placebo	Cesarean Section Birth Weight Morbidity Index Apgar Score
Adolescent 13-18 years			Stillbirth Perinatal Death Neonatal Death Pre-eclampsia Pregnancy Loss Intensive Care Maternal Death

1 The PICO model is widely used and taught in evidence-based health care as a strategy for formulating questions and search strategies and for characterizing clinical studies or meta-analyses. PICO stands for four different potential components of a

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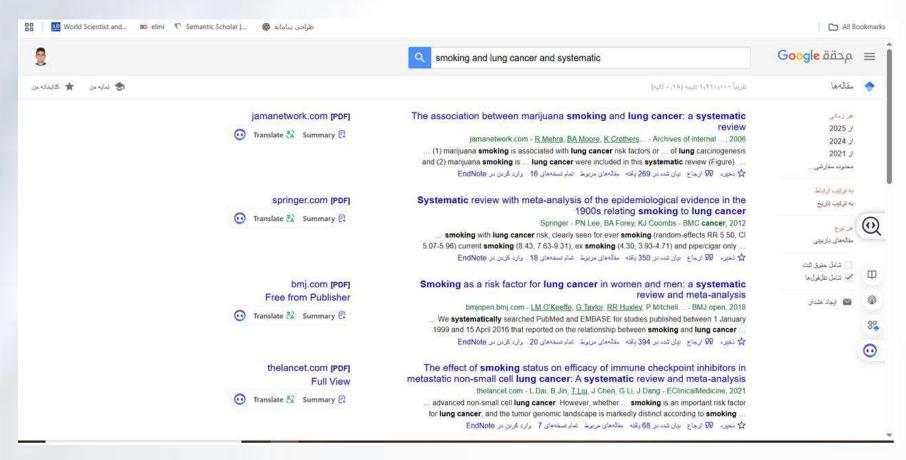
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REVIEW OF GOOGLE SCHOLAR





WHEN TO CONDUCT A NEW META-ANALYSIS (AFTER PREVIOUS META-ANALYSES)

When New Evidence Emerges

- New studies published since the last meta-analysis that may change the overall conclusions.
- A significant increase in the sample size or the inclusion of more diverse populations might lead to more accurate and generalizable results.

Advancements in Methodology

- New statistical methods or improvements in meta-analysis techniques (e.g., network meta-analysis, Bayesian methods) may allow for a more robust or refined analysis.
- More appropriate data handling (e.g., different effect size metrics) or adjustment for confounders that were not previously considered.

Inconsistent or Conflicting Results from Previous Meta-Analyses

- If different meta-analyses have conflicting conclusions on the same topic.
- A new meta-analysis might reconcile the differences, especially if new studies with higher quality or better data are available.



WHEN TO CONDUCT A NEW META-ANALYSIS (AFTER PREVIOUS META-ANALYSES)

Revised Research Questions or Scope

- If the **research question** or focus of the review has shifted (e.g., you want to focus on a specific subgroup or outcome that wasn't analyzed previously).
- If **new subgroups** or **differing intervention effects** need to be considered.

Changes in Study Design or Population Characteristics

- If there's a **shift in study design** (e.g., new trials using more rigorous methods or larger sample sizes).
- When the population of interest has changed or studies now focus on a different demographic or geographic region.

When the Previous Meta-Analysis Is Outdated

• If the prior meta-analysis is **several years old**, it may no longer reflect the current evidence. A new meta-analysis can provide a more up-to-date and relevant synthesis.



STEP BY STEP TO WRITING THE REPORTS

- PRISMA is a checklist designed to help authors report systematic reviews and metaanalyses transparently and comprehensively.
- Section 1: Title (PRISMA Item 1)
- The title should clearly identify the report as a title might say "Systematic Review of..." or "...
- This helps readers immediately understand the t

Welcome to the PRISMA website

PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) is a guideline designed to improve the reporting of systematic reviews. PRISMA provides authors with guidance and examples of how to completely report why a systematic review was done, what methods were used, and what results wer found. The main PRISMA reporting guideline (PRISMA 2020) primarily provides guidance for the reporting of systematic reviews evaluating the effects of interventions. PRISMA 2020 is complemented by various PRISMA extensions, which provide guidance for the reporting of different types or aspects of systematic reviews and other types of evidence synthesis (e.g. scoping reviews).

Key PRISMA 2020 documents

- Checklist
- Expanded checklist
- Flow diagram
- Statement pape
- Explanation and elaboration paper





ABSTRACT (PRISMA ITEM 2)

• This should be written at the end of the article. So, it will be described at the end or the presentation.



IMPORTANCE AND RATIONAL (PRISMA ITEM 3)

Checklist Item:

- "Describe the rationale for the review in the context of existing knowledge."
- Purpose of the Rationale: This section explains why the systematic review is necessary. It provides the **context** for the review by identifying gaps or inconsistencies in the existing literature.

• What to Include:

- Context: Briefly describe the existing body of research on the topic.
- Gap in Knowledge: Highlight any unresolved issues, contradictory findings, or areas where more evidence
 is needed.
- Importance: Explain the significance of conducting the review and how it will contribute to the field.



OBJECTIVES (PRISMA ITEM 4)

Checklist Item:

- "Provide an explicit statement of the objective(s) or question(s) the review addresses."
- Purpose of the Objectives: This section clearly defines the primary research question(s) the review aims to answer.

• What to Include:

- **Research Question**: Clearly state the main question the review seeks to answer (e.g., "What is the effect of intervention X on outcome Y in population Z?").
- **Scope**: Define the specific areas or populations the review will cover.
- **Hypotheses** (if applicable): If there is a hypothesis being tested, clearly state it.



METHODS: ELIGIBILITY CRITERIA (PRISMA ITEM 5)

Checklist Item:

- "Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses."
- Purpose of Eligibility Criteria: The eligibility criteria define which studies will be included in the review. This ensures that the studies selected meet certain standards and are relevant to the review question.
- It also ensures **transparency** in the review process, so readers understand how studies were selected.



WHAT TO INCLUDE?

- Inclusion Criteria:
- Describe the characteristics of studies that will be included.
- This may include aspects like:
 - Study design (e.g., randomized controlled trials, observational studies).
 - Population characteristics (e.g., age, gender, health condition).
 - Interventions (e.g., types of treatments, drugs, or behavioral interventions).
 - Outcomes (e.g., reduction in blood pressure, improvement in quality of life).



EXCLUSION CRITERIA

- Specify the characteristics of studies that will be excluded.
- This could be based on factors such as:
 - Study design (e.g., case reports, conference abstracts).
 - **Population** (e.g., studies focusing on children if your review is about adults).
 - Intervention or outcome (e.g., different treatment modalities not relevant to the review).
 - Time frame or language restrictions (e.g., studies published only in English, studies from the past 10 years).



EXAMPLE

• 1. Inclusion Criteria:

Study Design:

• Randomized controlled trials (RCTs) that assess the effectiveness of vaccines in preventing CPV in dogs.

Population:

• Dogs of all ages, including puppies and adult dogs, that are at risk of or exposed to CPV infection.

• Intervention:

- Vaccination strategies for preventing CPV, including both single-agent CPV vaccines and combination vaccines (e.g., DHPP, which includes distemper, hepatitis, parvovirus, and parainfluenza).
- Vaccines administered via SC or IM injection.

Outcomes:

- Primary outcome: **Incidence of CPV infection** (diagnosed through PCR, ELISA, or clinical symptoms).
- Secondary outcomes: Survival rate following infection, duration of immunity, or seroconversion rates (percentage of dogs that develop antibodies after vaccination).

Language:

• Studies published in **English**, **Spanish**, or **French**.

• Time Frame: until 2025

So A H D P

EXAMPLE

2. Exclusion Criteria:

Study Design:

- Non-randomized studies (e.g., retrospective studies or expert opinions).
- Studies without a **control group** (e.g., studies that only include dogs that were vaccinated, with no comparison group of unvaccinated dogs).

Population:

- Studies focused on **non-canine species** (e.g., feline, equine, or other livestock).
- Dogs with pre-existing **immune disorders**, as vaccination effectiveness may vary in immunocompromised dogs.

• Intervention:

- Studies evaluating **non-vaccine-based prevention methods** (e.g., antiviral drugs or other treatments).
- Studies using **homemade vaccines** or vaccines **not approved** by regulatory agencies (e.g., USDA or European Medicines Agency).

Outcomes:

- Studies that do not measure **CPV** infection or do not report clinical or laboratory evidence of infection.
- Studies where **vaccine efficacy** is not the primary outcome or does not report any measurable results.

Other Exclusions:

• Studies that are **not peer-reviewed**, **conference abstracts**, or **case reports** without sufficient data.



METHODS: INFORMATION SOURCES (PRISMA ITEM 6)

Checklist Item:

- "Specify all databases, registers, websites, organisations, reference lists, and other sources searched or consulted <u>to identify studies</u>. Specify the date when each source was last searched or consulted."
- Purpose of Information Sources: The goal of this section is to provide transparency about where and how you searched for studies.
- Report all the sources you used, you enable others to replicate your search process if necessary.



WHAT TO INCLUDE:

- Databases: List all the electronic databases searched (e.g., PubMed, Scopus, Cochrane Library), specifying the date of the last search.
- **Registers**: Specify any trial registries (e.g., ClinicalTrials.gov) used to find ongoing or unpublished studies, along with their last searched date.
- Websites: Mention any websites consulted for additional sources, including gray literature or guidelines from veterinary organizations, with the date of the last consultation.



WHAT TO INCLUDE:

- Organizations: Include any organizations whose publications, guidelines, or recommendations were consulted, including the date of consultation.
- Reference Lists: State whether you reviewed the reference lists of the included studies to identify additional relevant studies.
- Other Sources: Include any gray literature, unpublished studies, and conference proceedings reviewed for relevant data.



EXAMPLES

Databases:

- PubMed (Last searched: January 2024)
- Cochrane Library (Last searched: January 2024)
- Scopus (Last searched: January 2024)
- Web of Science (Last searched: January 2024)

Trial Registers:

- ClinicalTrials.gov (Last searched: December 2023)
- PROSPERO (Last searched: December 2023)

Websites:

- World Health Organization (WHO) website (Last checked: January 2024)
- International Companion Animal Network (ICAN) website (Last checked: January 2024)



EXAMPLE

Organizations:

Veterinary Information Network (VIN) (Last consulted: December 2023)

Reference Lists:

Reference lists of included studies were manually reviewed to identify additional studies.

Other Sources:

- Google Scholar search for unpublished studies or theses (Last searched: December 2023)
- Conference proceedings from the American Veterinary Medical Association (AVMA)
 (Last checked: January 2024)



METHODS: SEARCH STRATEGY (PRISMA ITEM 7)

Checklist Item:

- "Present the full search strategies for all databases, registers, and websites, including any filters and limits used."
- Purpose of the Search Strategy: This section provides a detailed description of how the search for relevant studies was conducted.
- It ensures **transparency**, enabling others to **replicate** your search process. A clearly documented search strategy helps establish that the review's study selection is comprehensive and unbiased.



2. CONSTRUCTING THE SEARCH STRATEGIES

Structure of the Sea

PROBLEM, POPULATION OR PATIENT

What is the **problem** you want to study? Which **population** with a certain disease or health event are you investigating?

INTERVENTION OR EXPOSURE

If you are conducting a trial, what is the **intervention** you plan to implement? Or, is there a specific **exposure** you think is causing a certain health phenomenon?

P – Patient, Population or Problem	I – Interventic	P	I/E O	phenomenon?	ıe	S – Study Design
What are the characteristics of the patient or population? What is the condition or disease you are interested in?	What do you v this patient diagnose,	Commence of the Commence of th	occ ce	OUTCOME t is the outcome you want to investigate? Is it the urence of a disease after ertain exposures? Or, an evement in health outcomes after your proposed intervention?	evant orbidity, ions)?	- Meta-analysis - Systematic Review - Randomized Control Trials



STRUCTURE OF THE SEARCH STRATEGY

- To find 2 or 3 most important concepts
- Focus on those most likely to be found in title and abstract
- Example of a clinical question that outlines the PICOS components: Helmets for preventing head and facial injuries in cyclists

P – Patient, Population or Problem	I – Intervention or Exposure	C – Comparison	O – Outcome	S – Study Design
?	?	?	?	?

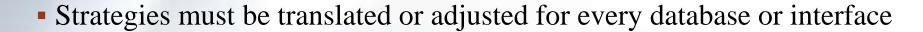
P – Patient, Population or Problem	I – Intervention or Exposure	C – Comparison	O – Outcome	S – Study Design
		(Not specified)		Systematic Review

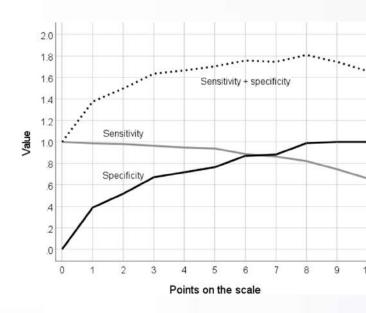


BROADENING SEARCH TERM/KEYWORD

Aim for high sensitivity

- Express each concept in as many ways as possible
- Minimize the risk of missing a relevant study
- Will lead to lower precision find a balance
- Preliminary searching may help your test strategy







TEXT WORDS

- Words appearing in title and/or abstract of the record
- Include synonyms, related terms, international terms, alternative spellings, plurals
- e.g., brain injury, head injury, skull fracture
- Truncation and wildcards: <u>"*, ?"</u>
- protect* = protects, protective, protection, ...
- but beware: car* = cars (but also carcinoma)
- wom?n= women, woman,
- Proximity operators NEAR, NEXT, ADJ
- e.g., liver ADJ cancer = liver cancer, liver and bowel cancer

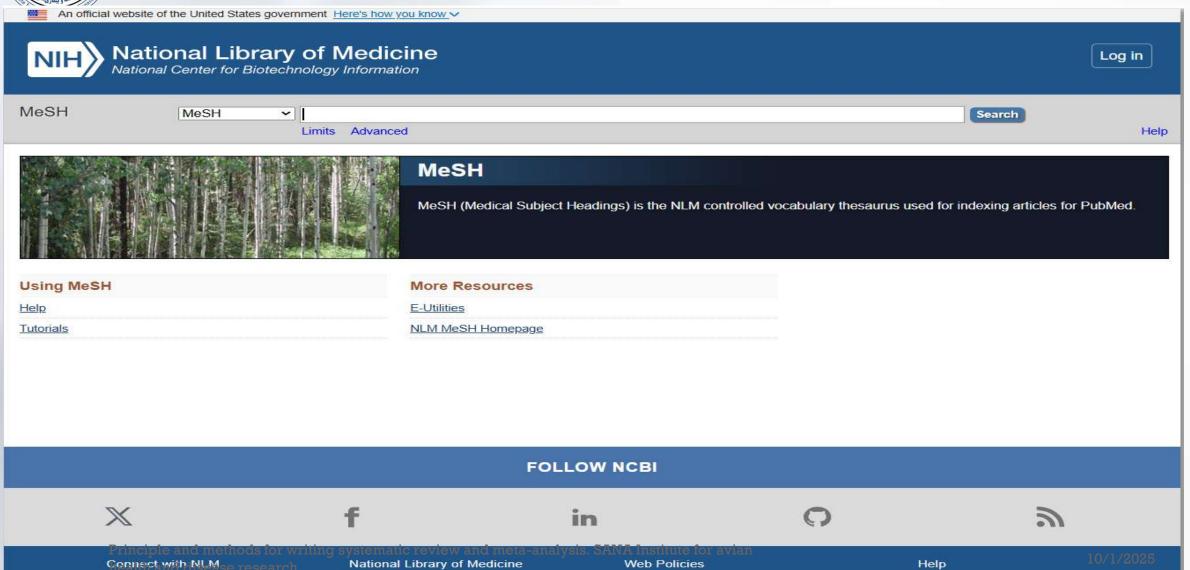


CONTROLLED VOCABULARY, SYNONYMS

- Standardized subject terms assigned by indexes
- e.g., Medline = MeSH, Embase = EMTREE
- Identifies relevant articles even if different terms are used for the same concept



FINDING SYNONYMS, MESH TERMS (MEDICAL SUBJECT HEADING)





MESH

Full - Send to: -

Bicycling

The use of a bicycle for transportation or recreation. It does not include the use of a bicycle in studying the body's response to physical exertion (BICYCLE ERGOMETRY TEST see EXERCISE TEST).

Year introduced: 1990(1983) Date introduced: April 28, 1982

PubMed search builder options

Subheadings:

classification	history	□ psychology
economics	□ injuries	standards
education	 legislation and jurisprudence 	\square statistics and numerical data
ethics	□ physiology	☐ trends

- Restrict to MeSH Major Topic.
- ☐ Do not include MeSH terms found below this term in the MeSH hierarchy.

Tree Number(s): I03.450.642.845.140 MeSH Unique ID: D001642 Previous Indexing:

- Exercise Test (1966-1982)
 - Exertion (1966-1982)

All MeSH Categories

Anthropology, Education, Sociology and Social Phenomena Category, Human Activities

Leisure Activities
Recreation

Sports

Bicycling

Add to search builder AND ~ Search PubMed You Tube Tutorial Related information PubMed PubMed - Major Topic Clinical Queries NLM MeSH Browser Recent Activity Turn Off Clear Bicycling MeSH Sports MeSH Q bicycle (4) MeSH See more...

PubMed Search Builder

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MESH TERMS

MeSH	MeSH v helmet		⊗ Search
	Create alert Limits Advanced		Help
Full +		Send	d to: → PubMed Search Builder •
Head Protective De	evices		
Personal devices for protect Year introduced: 1991(1975) Date introduced: December		ng objects, and from limited electric shock and burn.	
PubMed search builder opti Subheadings:	tions		Add to search builder AND ✓ Search PubMed
□ adverse effects	□ microbiology	☐ supply and distribution	You Tube Tutorial
classification economics	□ parasitology □ standards	trends veterinary	Related information PubMed
ethics history	☐ statistics and numerical data	□ virology	PubMed - Major Topic
_			Clinical Queries
☐ Restrict to MeSH Major ☐ Do not include MeSH te	Topic. erms found below this term in the MeSH hierarchy.		NLM MeSH Browser
	560.750, J01.637.708.560.750		
MeSH Unique ID: D006260 Entry Terms:)		Recent Activity Turn Off Clear
Device, Head ProtectDevices, Head Protect	ective		Head Protective Devices MeSH
Head Protective Device, H Protective Device, H	Head		Q helmet (1)
Protective Devices, IHelmetsHelmet	Head		Bicycling MeSH
All MeSH Categories	s iagnostic and Therapeutic Techniques and Equipment Cate	dory	Sports MeSH
Principle and meti	ment and Supplied Systematic review and meta-an hods for writing Protective Devices Preseatchonal Protective Equipment	nalysis. SANA Institute for avian	Q bicycle (4) 10/1/2025 ^{SH}

Head Protective Devices

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See more...



MESH TERMS

☐ Do not include MeSH terms found below this term in the MeSH hierarchy.

Tree Number(s): E07.700.560.750, J01.637.708.560.750

MeSH Unique ID: D006260

Entry Terms:

· Device, Head Protective

· Devices, Head Protective

· Head Protective Device

Protective Device, Head

· Protective Devices, Head

Helmets

Helmet

All MeSH Categories

Analytical, Diagnostic and Therapeutic Techniques and Equipment Category

Equipment and Supplies

Protective Devices

Personal Protective Equipment

Head Protective Devices

All MeSH Categories

Technology and Food and Beverages Category

Technology, Industry, and Agriculture

Manufactured Materials

Protective Devices

Personal Protective Equipment

Head Protective Devices





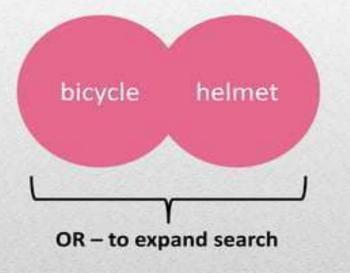
HOW TO SEARCH

- **Search Terms**: List all the **keywords** used in the search.
- **Boolean Operators**: **Boolean operators** (AND, OR, NOT) used to combine search terms. These operators help refine the search to capture the most relevant studies.
 - AND: Narrows the search (e.g., "canine parvovirus AND vaccine").
 - **OR**: Expands the search (e.g., "canine parvovirus OR CPV").
 - NOT: Excludes unwanted terms (e.g., "vaccine NOT flu").
- Filters: Specify any filters used, such as:
 - Date range (e.g., studies published from 2010 to present).
 - Language restrictions (e.g., studies in English, Spanish).
 - **Study type** (e.g., RCTs, observational studies).
- Limits: List any limits applied to the search, such as:
 - Age group (e.g., studies involving adult dogs, not puppies).
 - Study design (e.g., limiting to randomized controlled trials or cohort studies).
 - Species (e.g., only studies on dogs, excluding other animals).



BOOLEAN OPERATORS

Boolean Operators

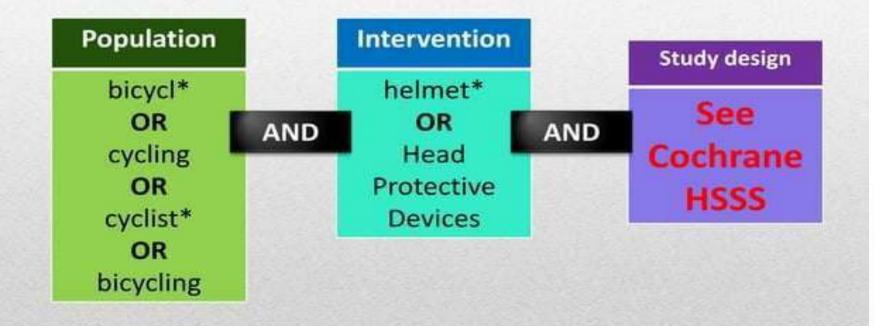






COMBINING OF TERMS

Combining terms



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health and disease research

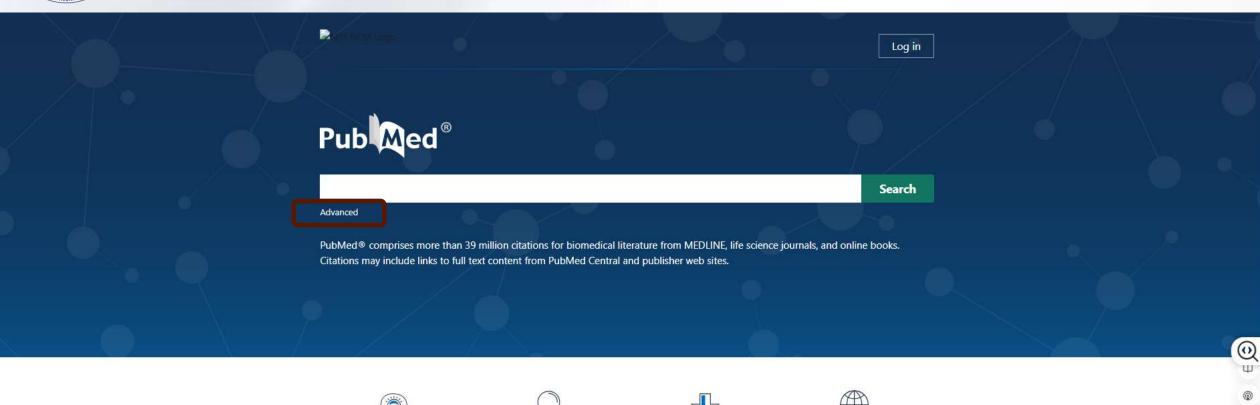
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HOW TO COMBINE AND SEARCH IN DIFFERENT DATABASES



SEARCH IN PUBMED



Learn

About PubMed FAQs & User Guide Finding Full Text



Find Advanced Search Clinical Queries Single Citation Matcher



Download E-utilities API FTP

Batch Citation Matcher



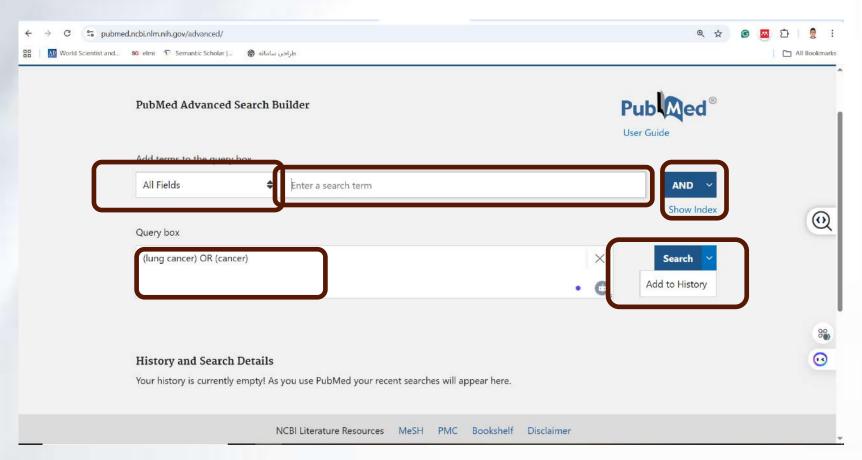
Explore MeSH Database

Journals

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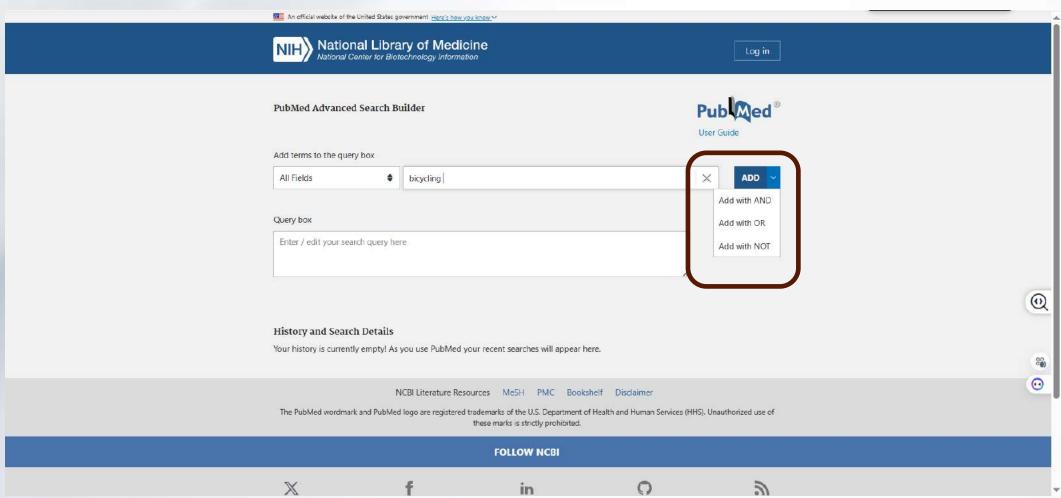


SEARCH IN PUBMED



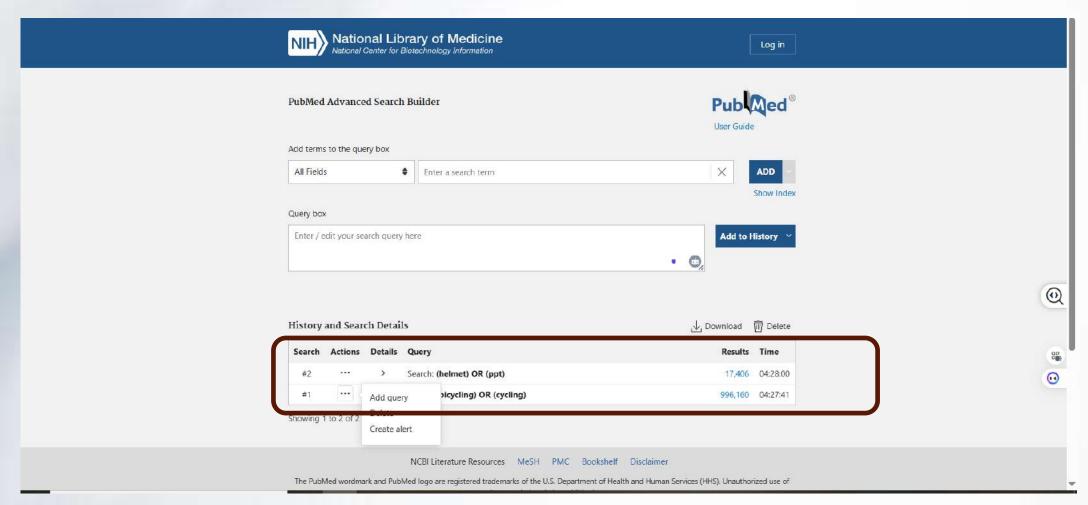


SEARCH IN PUBMED





COMBINING THE SEARCH



10/1/2025

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COMBINING THE SEARCH

Enter / edit your search query here Add to History

History and Search Details

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Search	Actions	Details	Query	Results	Time
#10	•••	>	Search: (children) AND ((((bicycling) OR (cycling)) AND ((helmet) OR (ppt))) AND (((head trauma) OR (face injury)) OR (hand injury)) OR (injur*)))	761	04:33:16
#9	•••	>	Search: children	3,467,447	04:33:07
#8	•••	>	Search: (((bicycling) OR (cycling)) AND ((helmet) OR (ppt))) AND ((((head trauma) OR (face injury)) OR (hand injury)) OR (injur*))	1,368	04:32:24
#7	•••	>	Search: #6 and #3	1,368	04:32:15
#6	•••	>	Search: #1 and #2	2,004	04:32:03
#5		>	Search: #1 AND #2	2,004	04:31:54
#4	•••	>	Search: ((bicycling) OR (cycling)) AND ((helmet) OR (ppt))	2,004	04:31:34
#3	•••	>	Search: (((head trauma) OR (face injury)) OR (hand injury)) OR (injur*)	1,645,645	0 1.50. 13
#2	•••	>	Search: (helmet) OR (ppt)	17,406	04:28:00
#1		>	Search: (bicycling) OR (cycling)	996,160	04:27:41

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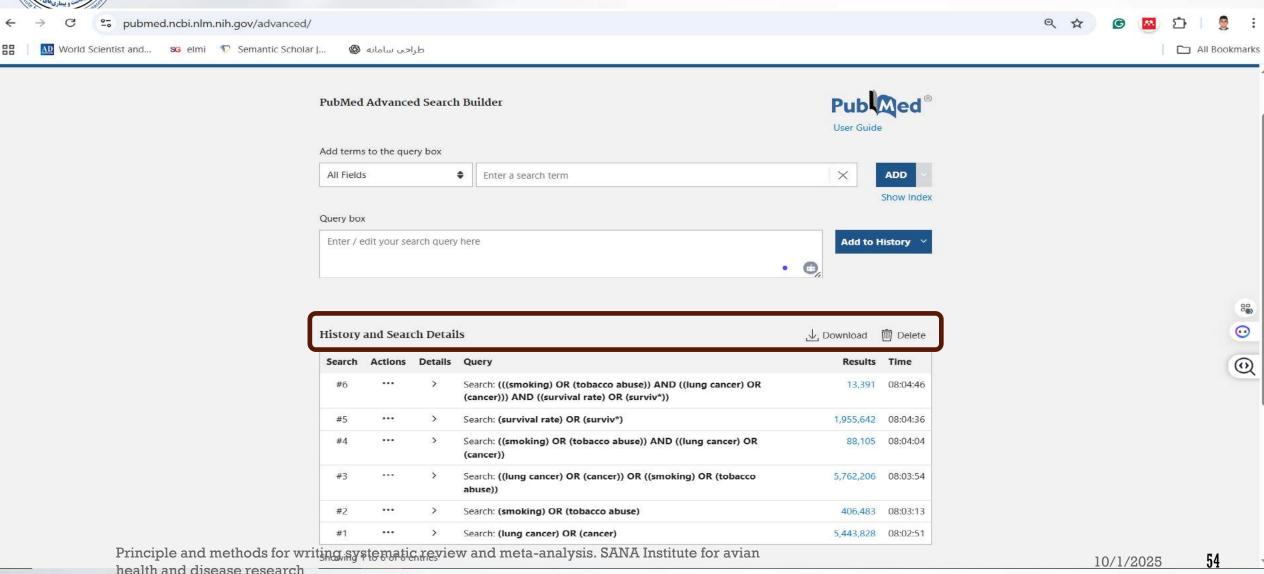
Showing 1 to 10 of 10 entries

53

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HISTORY OF SEARCH IN PUBMED





DETAIL OF SEARCH

#8 *** Search: (((bicycling) OR (cycling)) AND ((helmet) OR (ppt))) AND (((head trauma) OR (face injury)) OR (hand injury)) OR (injur*))

("bicycle" [All Fields] OR "bicycled" [All Fields] OR "bicycles" [All Fields] OR "bicvcling"[MeSH Terms] OR "bicvcling"[All Fields] OR ("bicvcling"[MeSH Terms] OR "bicycling"[All Fields] OR "cycling"[All Fields] OR "cycle"[All Fields] OR "cycle s"[All Fields] OR "cycled"[All Fields] OR "cycles"[All Fields] OR "cyclings"[All Fields])) AND ("head protective devices"[MeSH Terms] OR ("head"[All Fields] AND "protective"[All Fields] AND "devices" [All Fields]) OR "head protective devices"[All Fields] OR "helmet"[All Fields] OR "helmets" [All Fields] OR "helmet s" [All Fields] OR "helmeted" [All Fields] OR "ppt"[All Fields]) AND ("craniocerebral trauma"[MeSH Terms] OR ("craniocerebral"[All Fields] AND "trauma"[All Fields]) OR "craniocerebral trauma" [All Fields] OR ("head" [All Fields] AND "trauma" [All Fields]) OR "head trauma"[All Fields] OR ("facial injuries"[MeSH Terms] OR "facial" [All Fields] AND "injuries" [All Fields]) DR "facial injuries" [All Fields] OR ("face" [All Fields] AND "injury" [All Fields]) OR "face injury" [All Fields]) OR ("hand injuries"[MeSH Terms] OR ("hand"[All Fields] AND "injuries"[All Fields]) OR "hand injuries"[All Fields] OR ("hand"[All Fields] AND "injury" [All Fields]) OR "hand injury" [All Fields]) OR "injur*" [All Fields])

Translations

bicycling: "bicycle" [All Fields] OR "bicycled" [All Fields] OR "bicycles" [All Fields] OR "bicycling" [MeSH Terms] OR "bicycling" [All Fields] or "cycling" [MeSH Terms] OR "bicycling" [All Fields] OR "cycling" [All Fields] OR "cycleig" [All Fields] OR "head [All Fields] OR "head [All Fields] OR "head [All Fields] OR "helmet: "All Fields] OR "helmets" [All Fields] OR "head trauma" [All Fields] OR ("head" [All Fields] AND "trauma" [All Fields]) OR "head trauma" [All Fields]

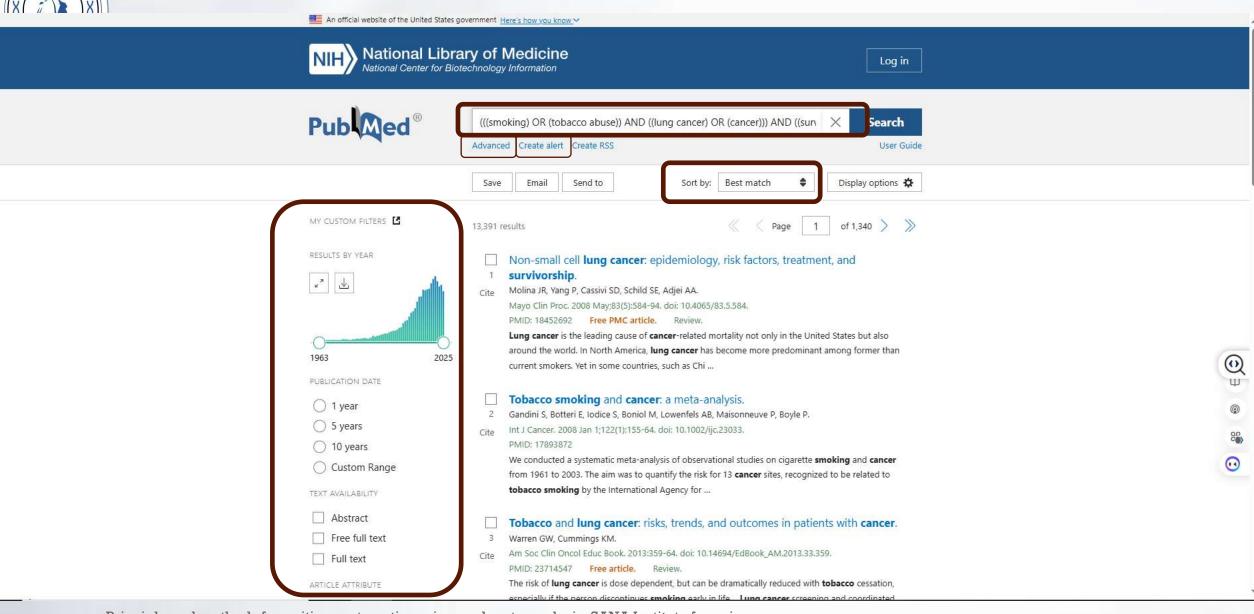
face injury: "facial injuries" [MeSH Terms] OR ("facial" [All Fields] AND

AND "injury" [All Fields]) OR "face injury" [All Fields]

"injuries"[All Fields]) OR "facial injuries"[All Fields] OR ("face"[All Fields]

1,368 04:32:24



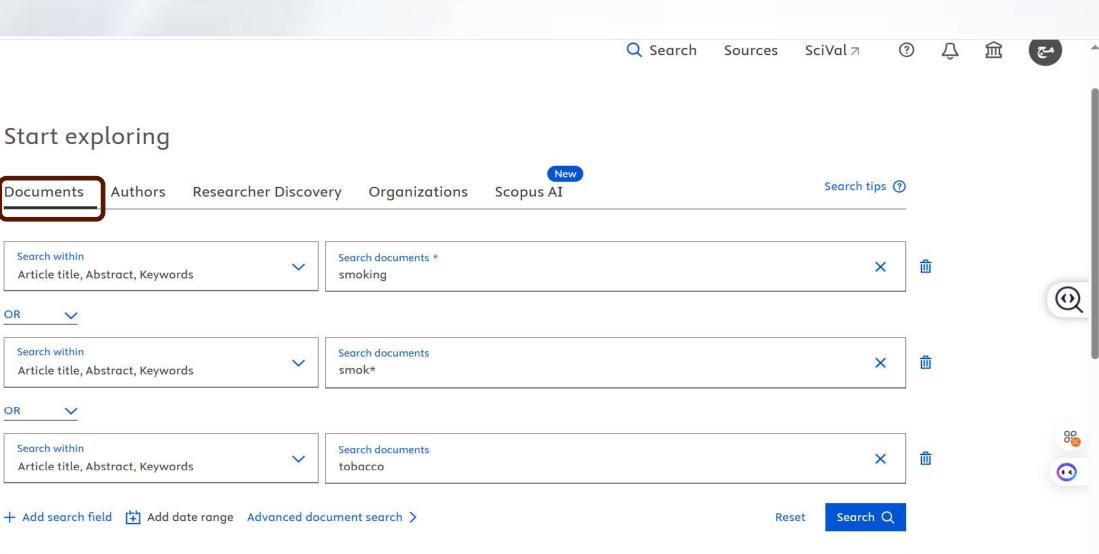




EXAMPLE OF SEARCH STRATEGY HGF AND CANCER AND SURVIVAL

- Pubmed
- **2295** 12/1/2025
- **9/9/2025**:
- 53 added

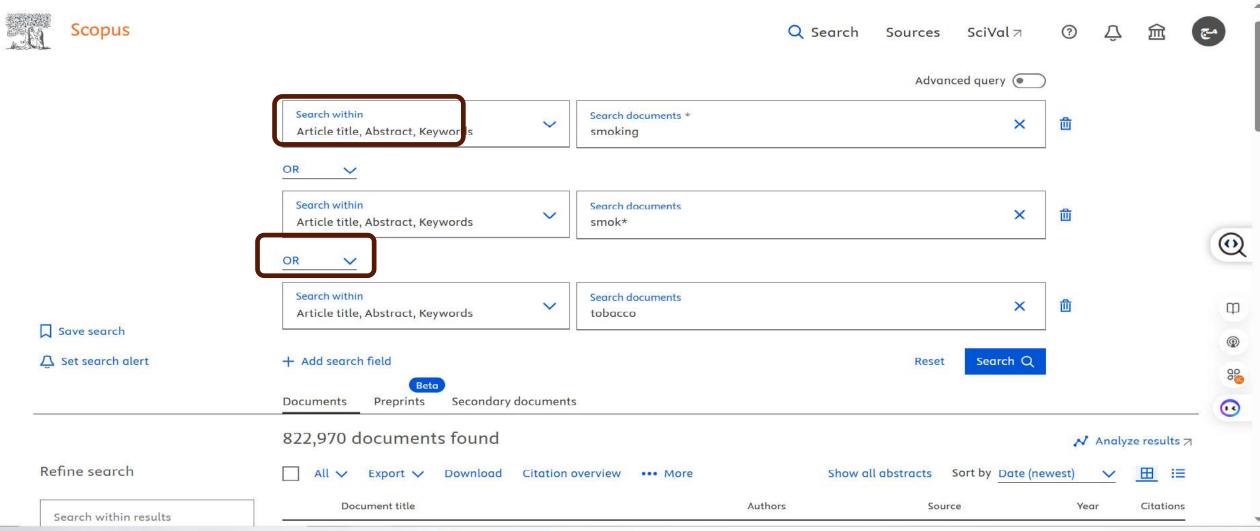




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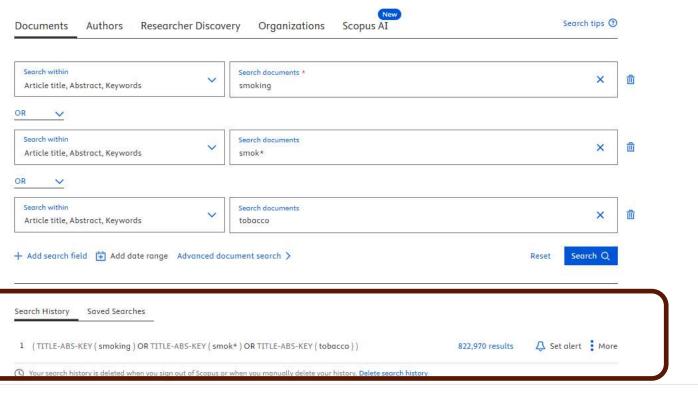


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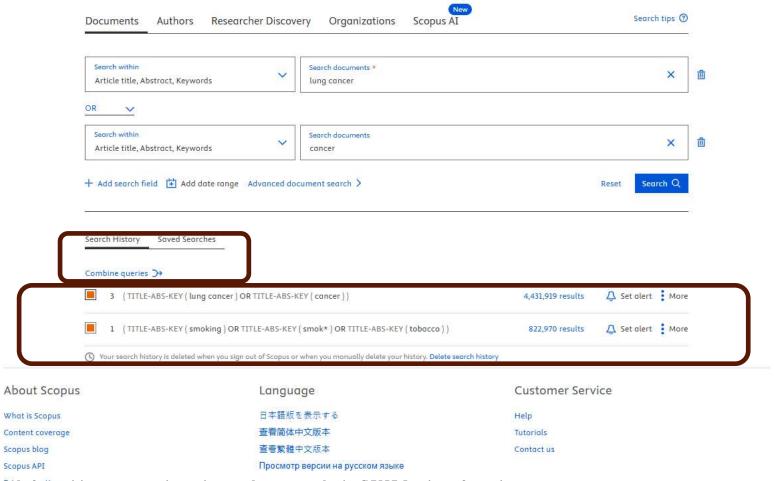


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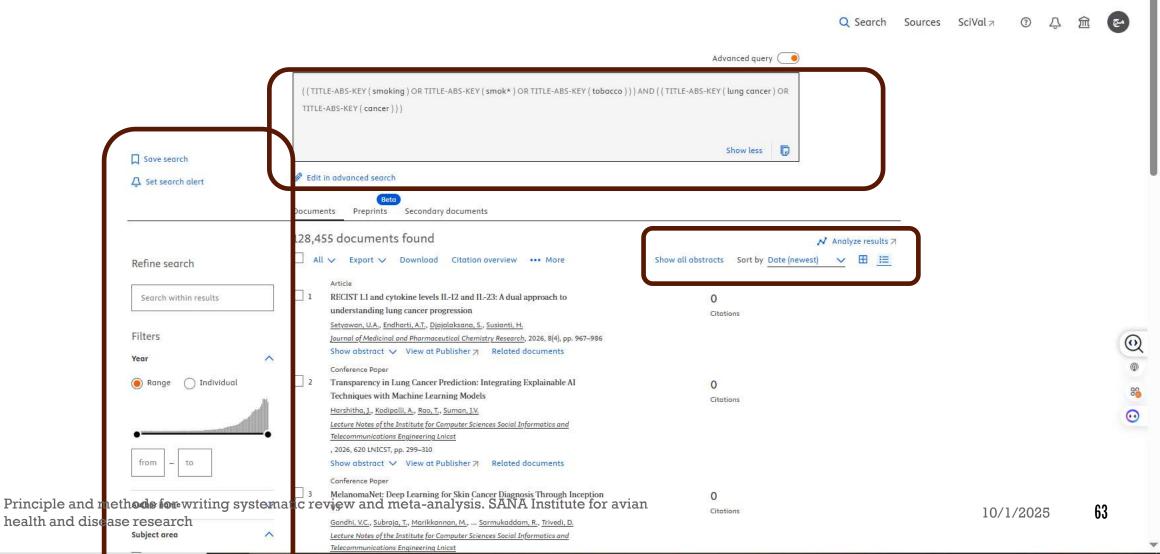






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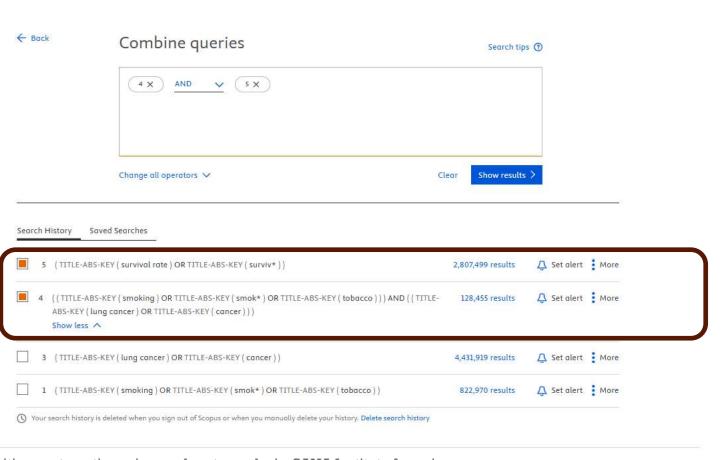






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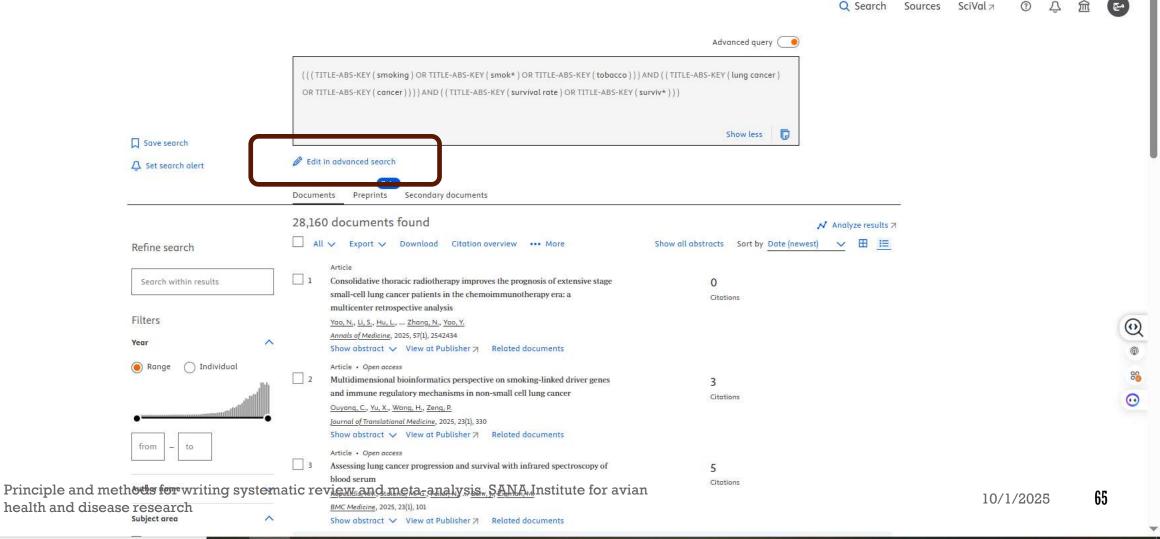
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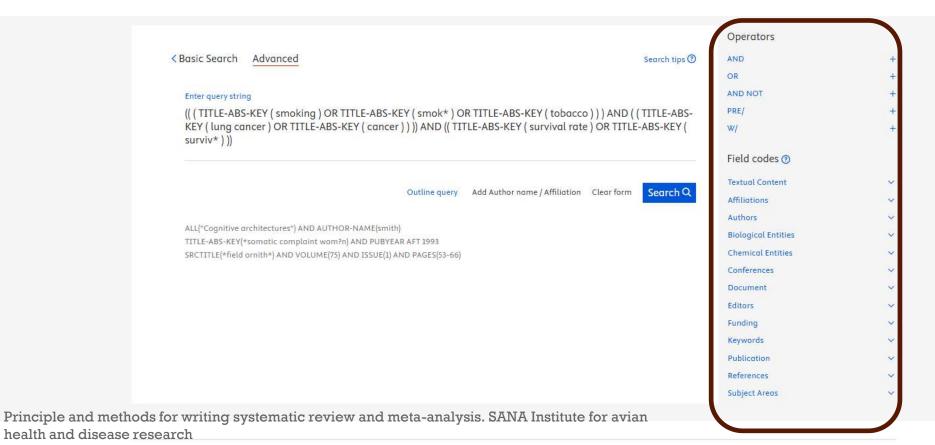
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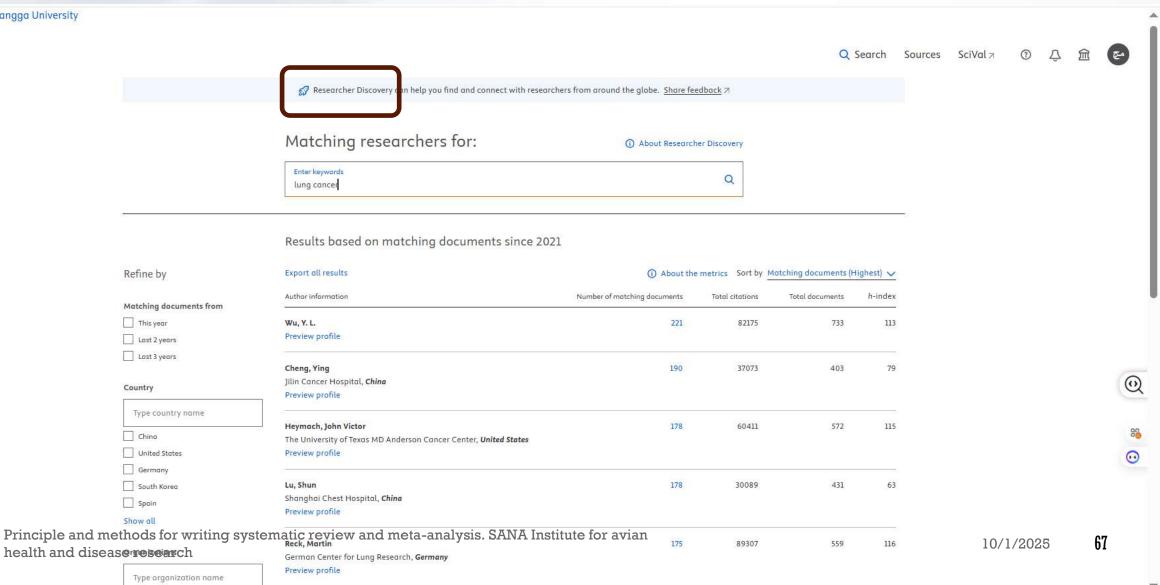
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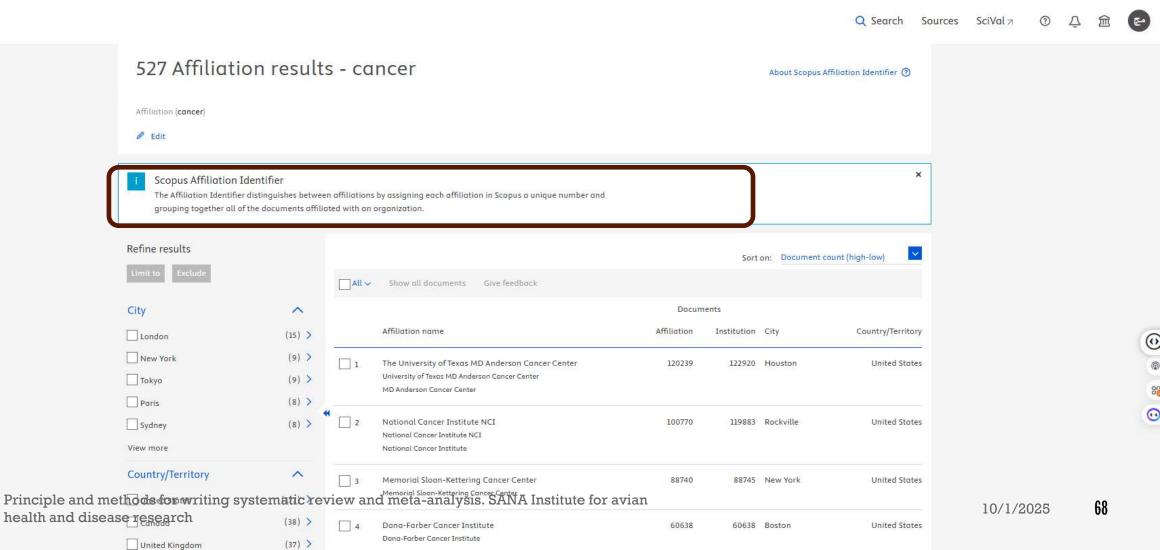






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Lung cancer and smoking relationship ...

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Lung cancer and smokin...

lung cancer and smoking

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Summary

Lung Cancer and Smoking

The relationship between smoking and lung cancer is well-established, with smoking being the leading cause of lung cancer, responsible for approximately 90% of cases 1 2 3 4 5 . This strong correlation is supported by numerous epidemiological studies and experimental findings 4

Key Points:

- . Causal Relationship: Smoking is the primary risk factor for lung cancer, with tobacco smoke containing carcinogens that lead to genetic mutations and molecular changes in lung cells 7 8 9 10. These changes include alterations in tumor suppressor genes, proto-oncogenes, and growth factors 7.
- · Genetic Susceptibility: Despite the high risk associated with smoking, only a minority of smokers develop lung cancer, suggesting that genetic factors play a role in individual susceptibility 7 11. Gene-environment interactions are thought to explain some of the variability in lung cancer risk among smokers 11.
- . Impact of Smoking Cessation: Quitting smoking significantly reduces the risk of developing lung cancer and improves outcomes for those already diagnosed with the disease 1 8 10 12 13 . Smoking cessation interventions, including behavioral counseling and pharmacotherapy, are effective in helping individuals quit smoking and should be integrated into lung cancer treatment and prevention strategies 12 13 14.

Additional Risk Factors: Besides smoking, other risk factors for lung cancer include environmental

References

Tratamiento de la Dependencia del Tabaco en un Fumador Oue ha Tenido un Cáncer de Pulmón

Neiro B.P., Becoña E.

Psicooncologia 7 2012

Reference 2

Smoking cessation and the success

of lung cancer surgery

Erhunmwunsee L., Onaitis M.W.

Current Oncology Reports 7 2009

Online public interest in smoking and lung cancer: A comparative study in Google Trends

Tas F., Erturk K.

Journal of Cancer Research and Therapeutics 7

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Share feedback

Foundational documents

606 citations

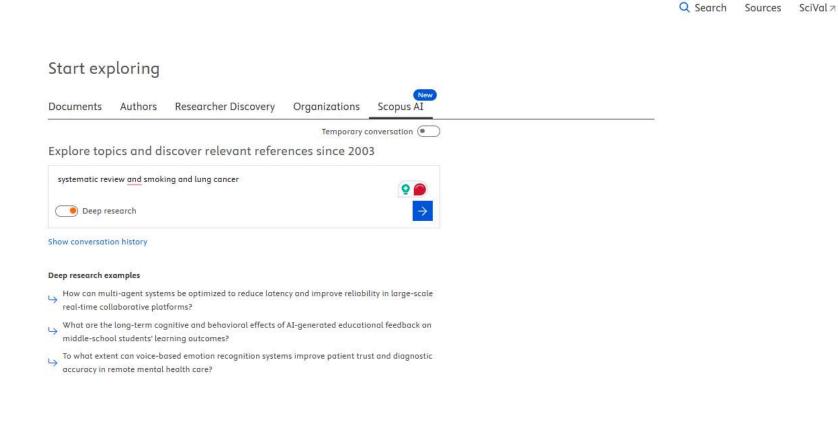
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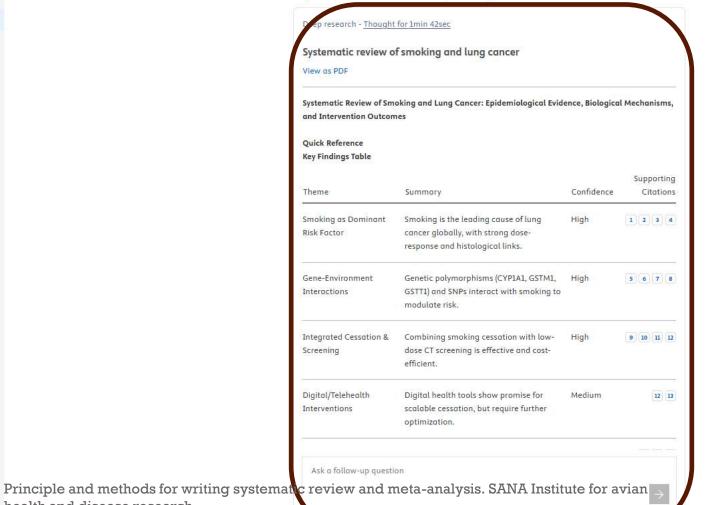
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health and disease research

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EXAMPLE OF SEARCH STRATEGY HGF AND CANCER AND SURVIVAL

- Scopus
- (((TITLE-ABS-KEY (survival AND analysis) OR TITLE-ABS-KEY (survival AND rate) OR TITLE-ABS-KEY (progression AND free AND survival) OR TITLE-ABS-KEY (disease AND free AND survival) OR TITLE-ABS-KEY (overall AND survival) OR TITLE-ABS-KEY (survival AND analysis) OR TITLE-ABS-KEY (kaplan AND meier) OR TITLE-ABS-KEY (cox AND regression) OR TITLE-ABS-KEY (recurrence AND free AND survival) OR TITLE-ABS-KEY (survival AND time) OR TITLE-ABS-KEY (survival AND time) OR TITLE-ABS-KEY (survival AND factors) OR TITLE-ABS-KEY (neoplasm) OR TITLE-ABS-KEY (tumors) OR TITLE-ABS-KEY (neoplasms) OR TITLE-ABS-KEY (neoplasia) OR TITLE-ABS-KEY (malignancy) OR TITLE-ABS-KEY (malignancies) OR TITLE-ABS-KEY (malignancy) OR TITLE-ABS-KEY (hepatocyte AND growth AND factor) OR TITLE-ABS-KEY (human AND hgf AND cytokine) OR TITLE-ABS-KEY (human AND hgf) OR TITLE-ABS-KEY (hgf AND cytokine)))
- **3555** 12/1/2025

• In 9/9/2025, 111 added



EXAMPLE OF SEARCH STRATEGY HGF AND CANCER AND SURVIVAL

- Web of sciences:
- survival analysis (All Fields) or survival rate (All Fields) or progression free survival (All Fields) or disease free survival (All Fields) or overall survival (All Fields) or survival analysis (All Fields) or kaplan meier (All Fields) or cox regression (All Fields) or recurrence free survival (All Fields) or survival time (All Fields) or survival factors (All Fields) or survival curves (All Fields) or survival (All Fields)
- AND
- cancer (All Fields) or neoplasm (All Fields) or tumor (All Fields) or neoplasm (All Fields) or neoplasia (All Fields) or malignancy (All Fields) or malignancy (All Fields) or malignance (All Fields)
- AND
- https://www.webofscience.com/wos/woscc/summary/9d2ad057-b1c4-4a7c-94ad-8e84d9807a35-0178bd1f54/relevance/1
- hepatocyte AND growth AND factor (All Fields) or hgf (All Fields) or human AND hgf AND cytokine (All Fields) or human AND hgf (All Fields) or human AND hgf (All Fields) or hgf AND cytokine (All Fields)
- **2506** 12/1/2025
- IN 9/9/2025, 46 ADDED
- https://www.webofscience.com/wos/woscc/summary/65467de6-3ca3-4095-ac28-f9ead4b88a2f-0178bdc23d/relevance/1

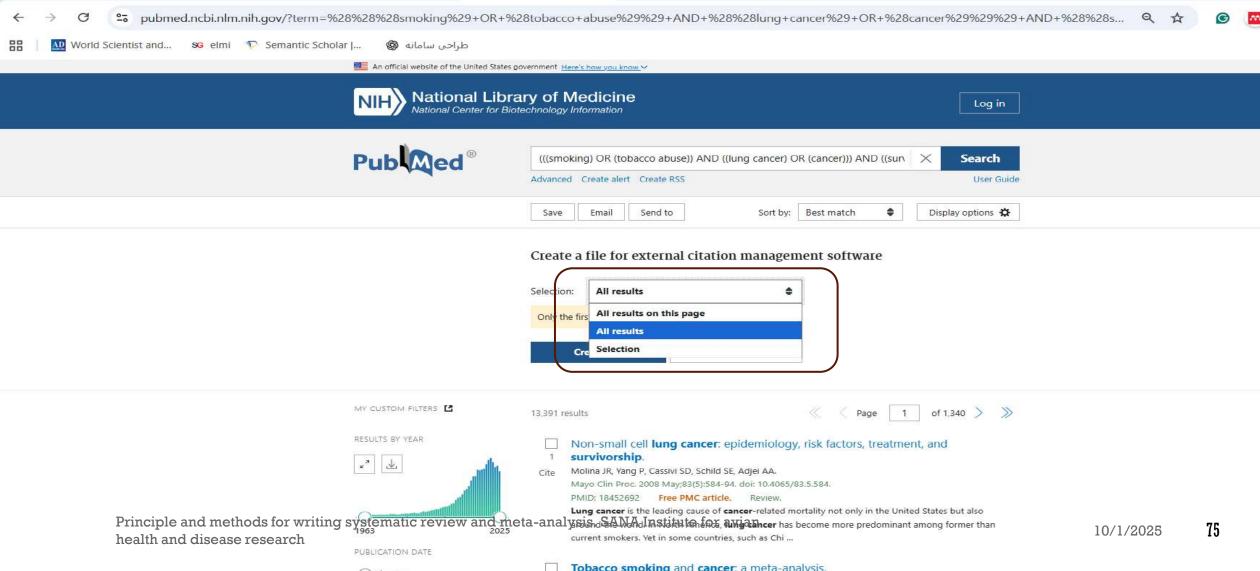


LIMIT & RESTRICTIONS

- *t* To avoid bias, do **not** limit by:
- Language ask your research group about translation
- Year unless there is a clear point of change or availability
- Format there may be additional information about a study in letters

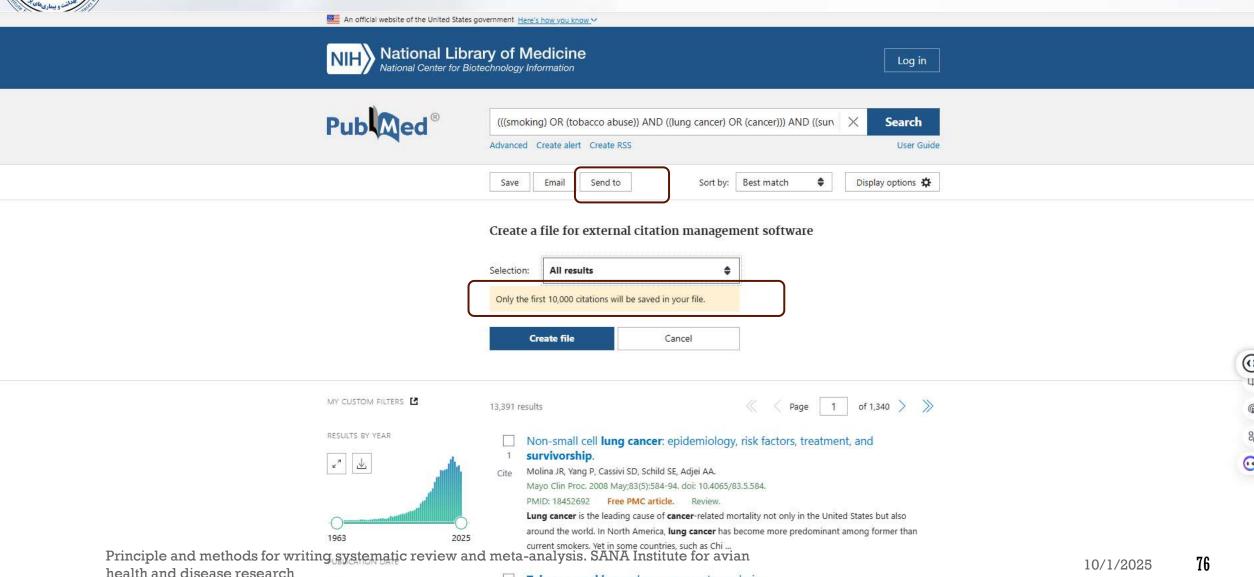


EXTRACTING REFERENCES FROM PUBMED





EXTRACTING REFERENCES FROM PUBMED



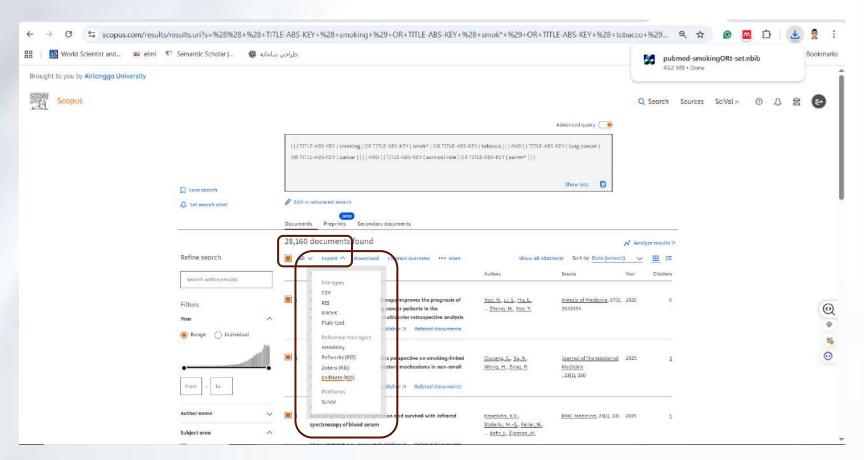
Tobacco smoking and cancer: a meta-analysis.

2 Gandini S, Botteri E, Iodice S, Boniol M, Lowenfels AB, Maisonneuve P, Boyle P.

1 year



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health and disease research

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DOI



3. DEDUPLICATION

- Automatic removal of duplicate records (common when searching multiple databases)
- Example: PubMed + Embase often retrieve the same studies
- Critical before moving to screening



4. MANAGING YOUR SEARCH RESULTS

- Store results from each source
- Download all available fields for each record
- Use bibliographic/reference management software:
 - e.g., EndNote, Mendeley, ProCite, Reference Manager, RefWorks, Zotero
- Sort and de-duplicate
- Move to screening stage (title/abstract, then full-text review)



1. EXPORTING SEARCH RESULTS

- From each database (PubMed, Embase, Cochrane, etc.),
- export results in compatible formats:
- RIS (.ris) BibTeX (.bib) EndNote XML (.xml)



IMPORTING INTO REFERENCE MANAGEMENT SOFTWARE

- Common tools (reference managers):
 - EndNote
 - Zotero
 - Mendeley

• Functions:

- Organize references
- Attach PDFs
- Annotate notes
- Sync across devices



4. PREPARING FOR SCREENING

- Export cleaned reference list to systematic review software if available:
 - Rayyan (free web-based tool)
 - Covidence (subscription)
 - **RevMan** (Cochrane)
- These tools help to conduct:
 - Title/abstract screening
 - Full-text review
 - Conflict resolution



5. DOCUMENTING THE SEARCH

- Report full search strategy for transparency
- Note:
 - Database name
 - Date searched
 - Search terms used
 - Number of results retrieved



METHODS: SELECTION PROCESS (PRISMA ITEM 8)

Checklist Item:

- Specify the methods used to decide whether a study met the inclusion criteria of the review
- including how many reviewers screened each record and each report retrieved,
- whether they worked independently,
- and if applicable, details of automation tools used in the process.



KEY ELEMENTS TO REPORT OF SELECTION PROCESS

- Screening Process: Explain how records were screened (e.g., first by title/abstract, then by full text).
- **Reviewers:** State how many reviewers were involved (usually at least two), and whether they worked independently.
- **Disagreements:** Describe how disagreements between reviewers were resolved (e.g., through discussion or a third reviewer).
- Automation Tools (if used): Mention any software (e.g., Rayyan, Covidence) or machine learning tools that assisted in the screening process.
- **Documentation:** Highlight that reasons for exclusion were recorded, and a PRISMA flow diagram was used to illustrate the process



EXAMPLE (VETERINARY MEDICINE — CANINE PARVOVIRUS REVIEW):

Screening Process:

- All studies identified through database searches (n = 2,345) were imported into Rayyan software for initial screening. First, duplicates were removed automatically. Then, titles and abstracts were screened to exclude clearly irrelevant studies. Full texts of the remaining 183 studies were assessed for eligibility based on predefined inclusion/exclusion criteria.
- Reviewers: *Two independent reviewers* screened each record and full-text report.
- **Disagreements:** Any disagreements regarding eligibility were **resolved through discussion.** If consensus could not be reached, a **third reviewer** made the final decision.
- Automation Tools: Rayyan's artificial intelligence-assisted screening function was used to prioritize potentially relevant studies, but final decisions were made manually by the reviewers.
- **Documentation: Reasons for excluding studies** at the full-text stage (e.g., wrong population, irrelevant intervention) were recorded in a separate table. The entire process was summarized in a PRISMA flow diagram showing the number of records identified, screened, included, and excluded.



INTRODUCTION TO RAYYAN

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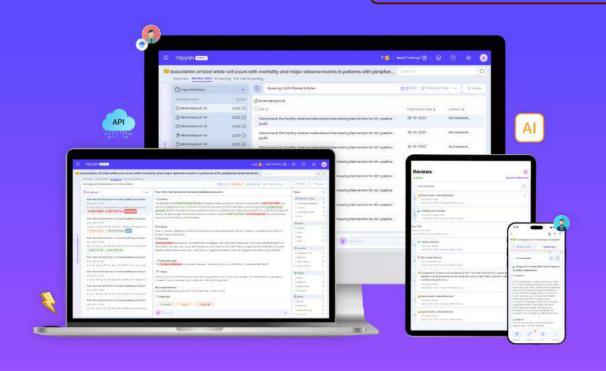
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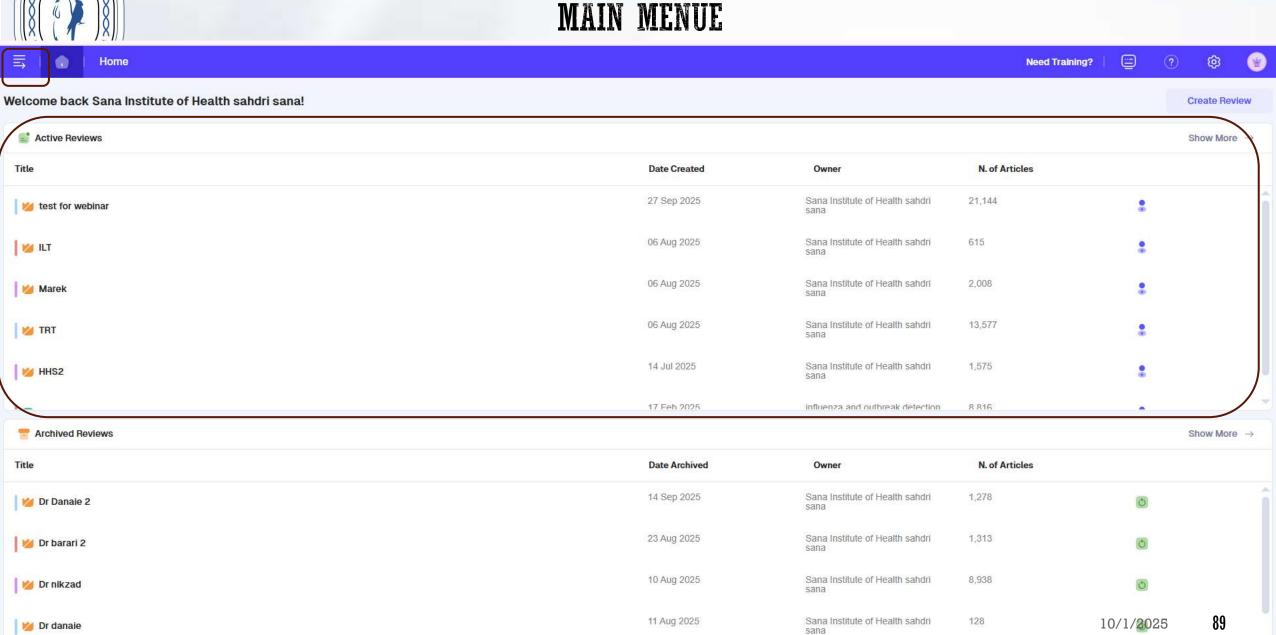
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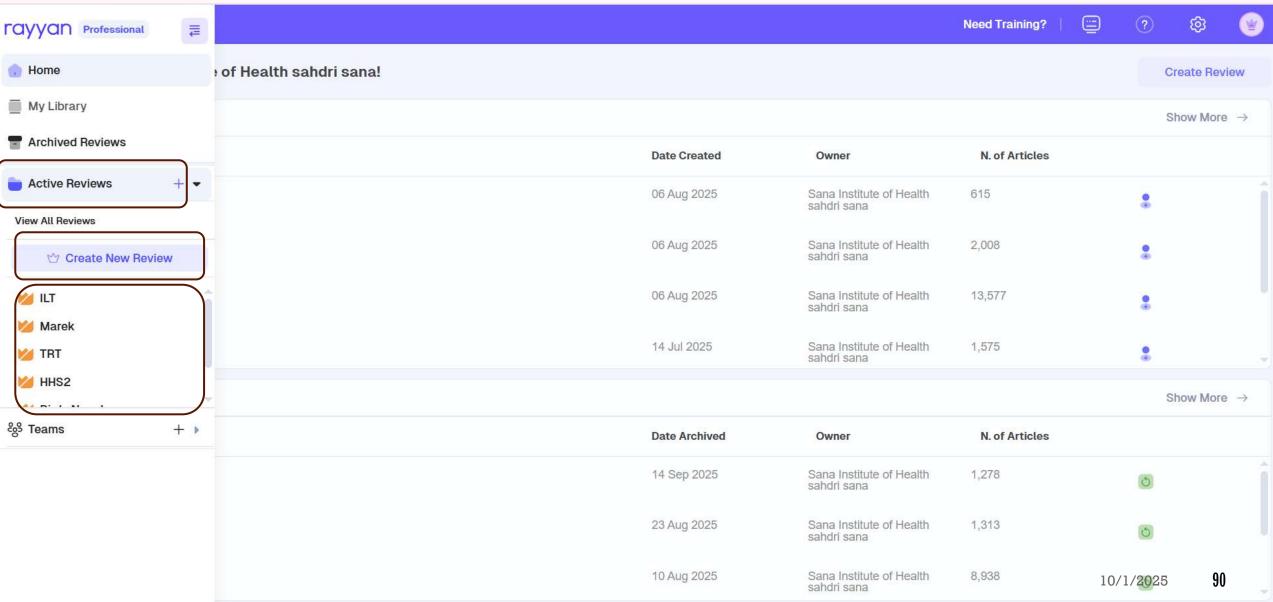
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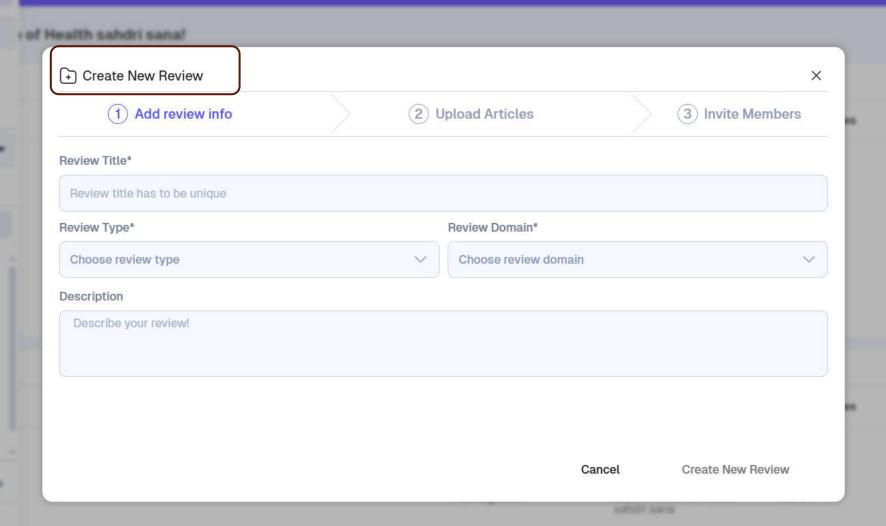
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STEP BY STEP FOR NEW REVIEW DEFINITION



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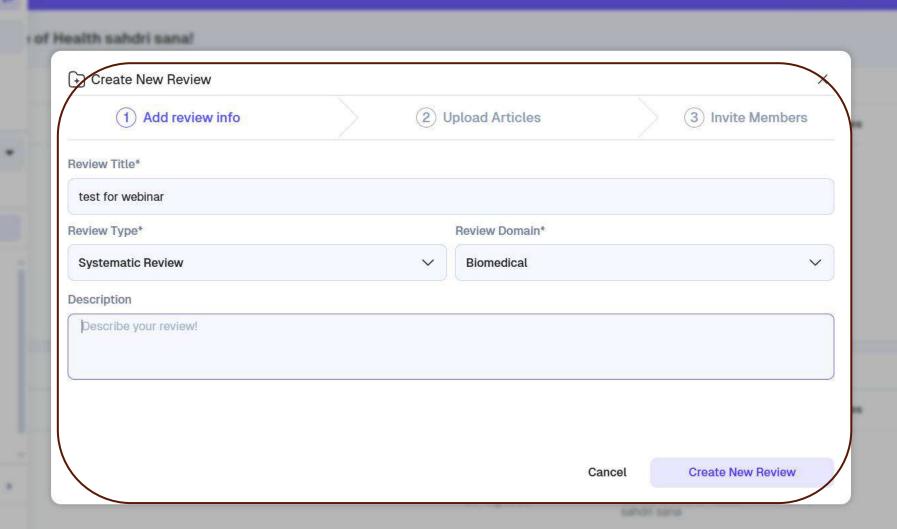
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STEP BY STEP FOR NEW REVIEW DEFINITION



10 Aug 2025

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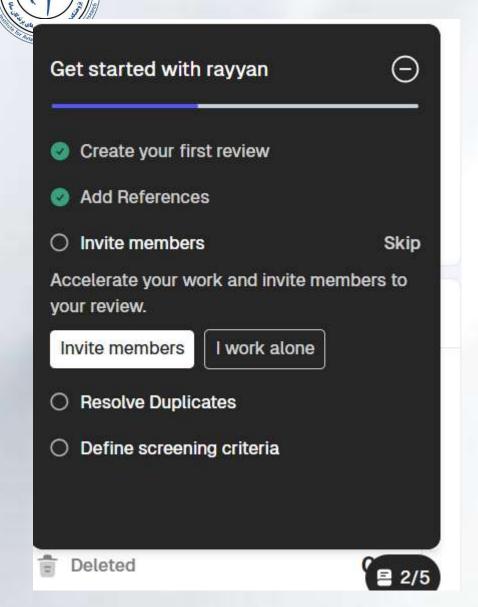
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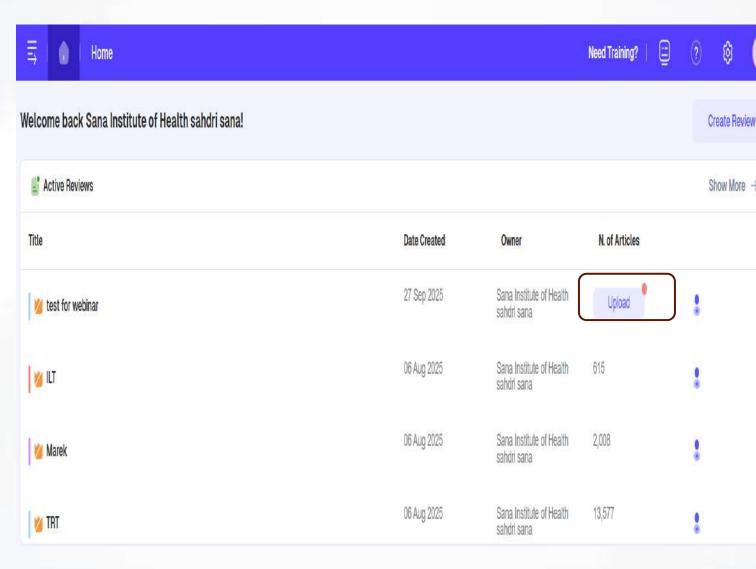
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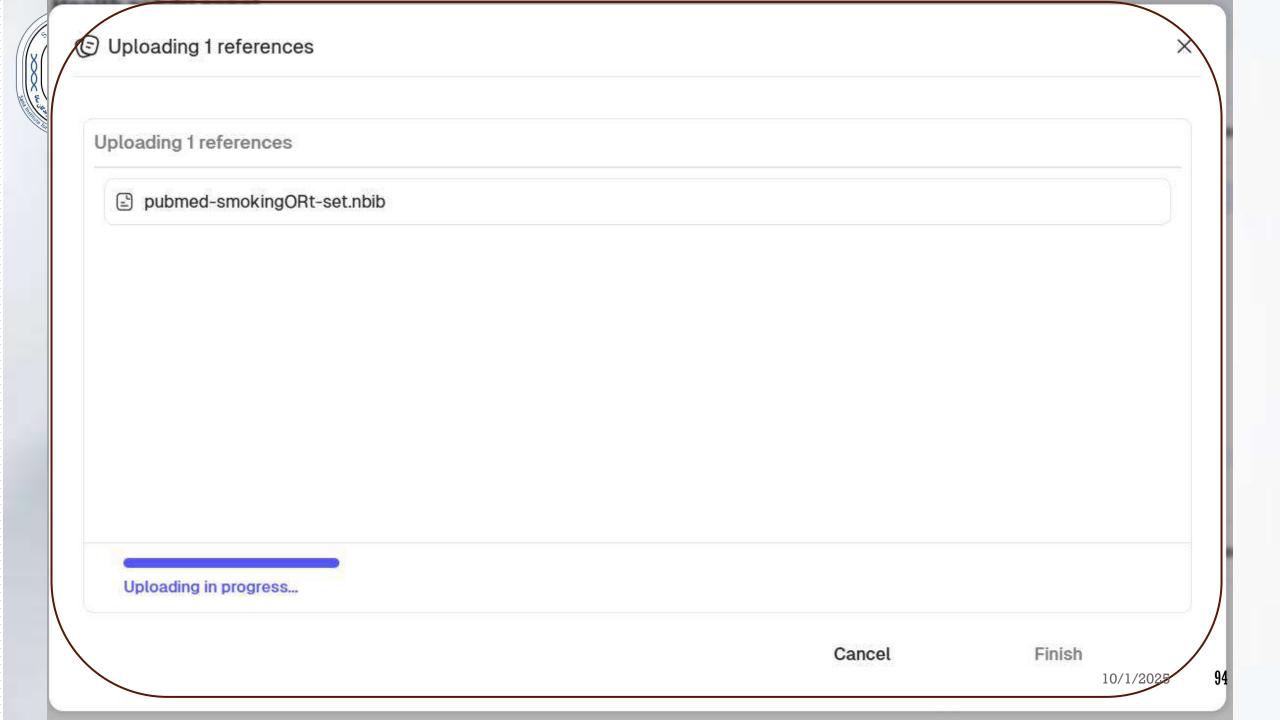
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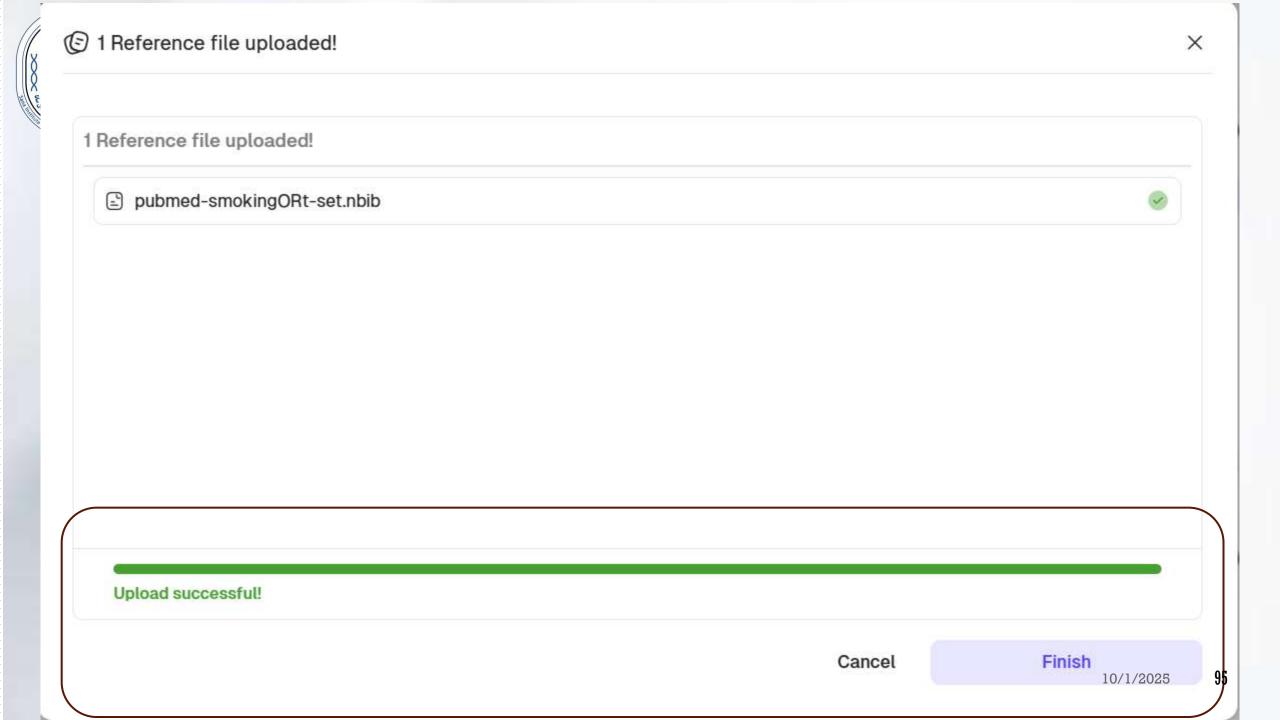
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STEP BY STEP FOR NEW REVIEW DEFINITION









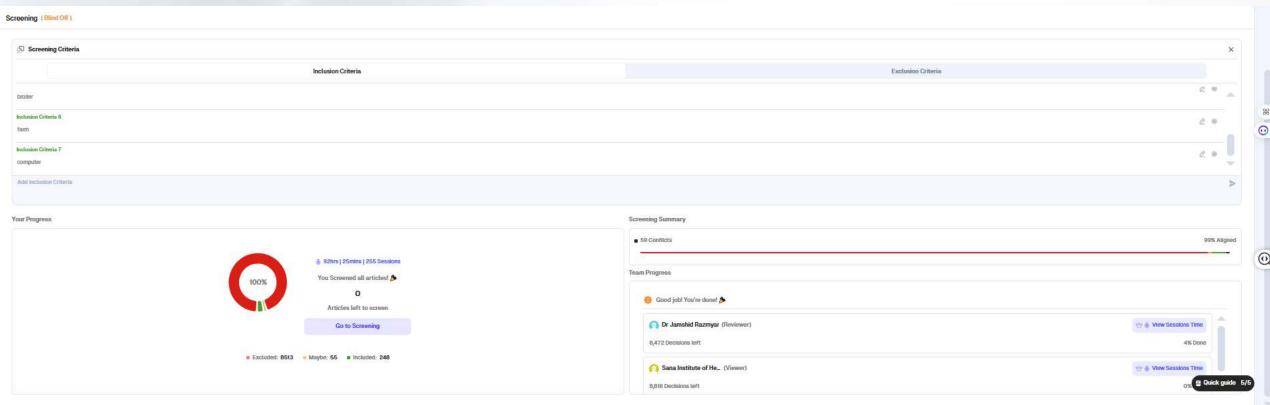


INFORMATION OF NEW REVIEW



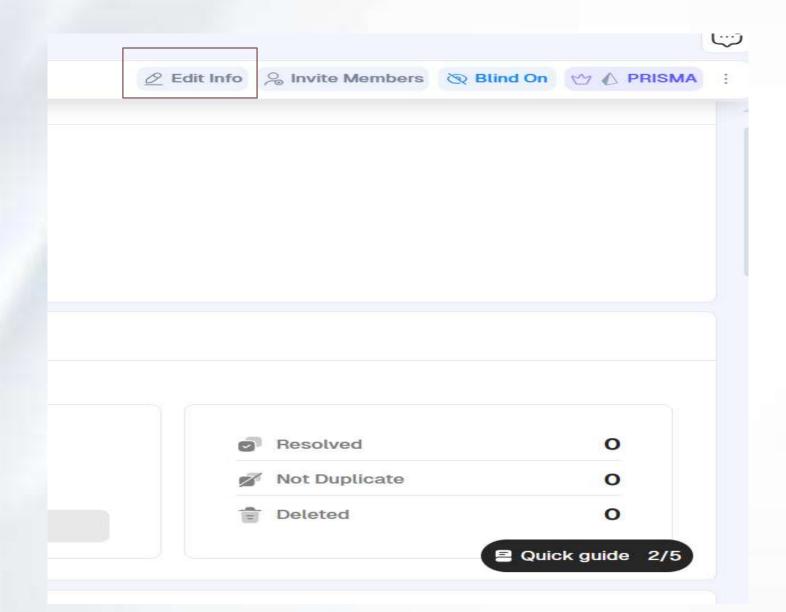


INFORMATION OF REVIEW



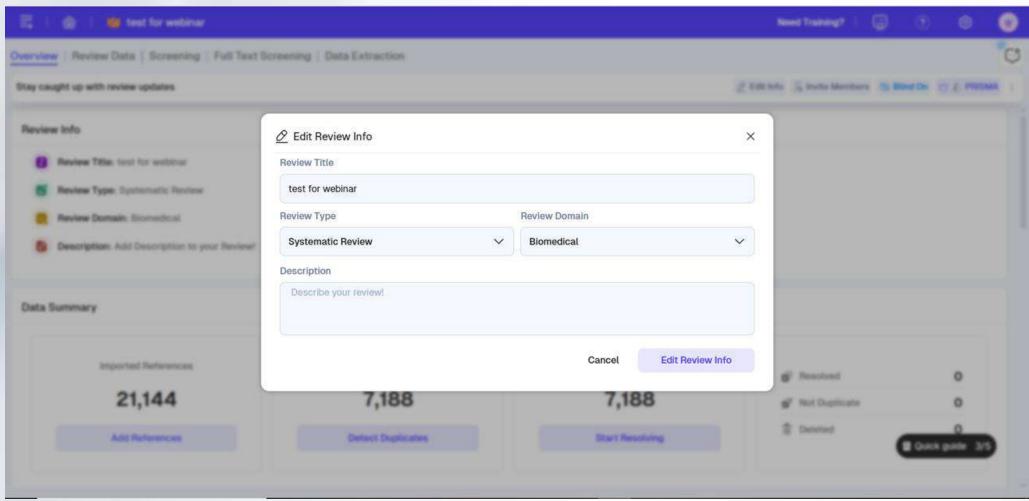


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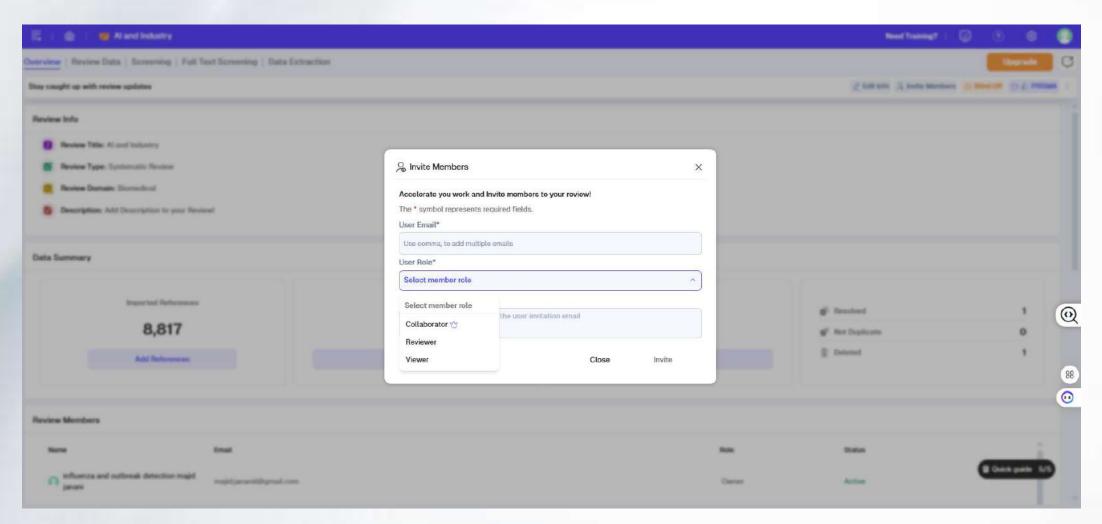


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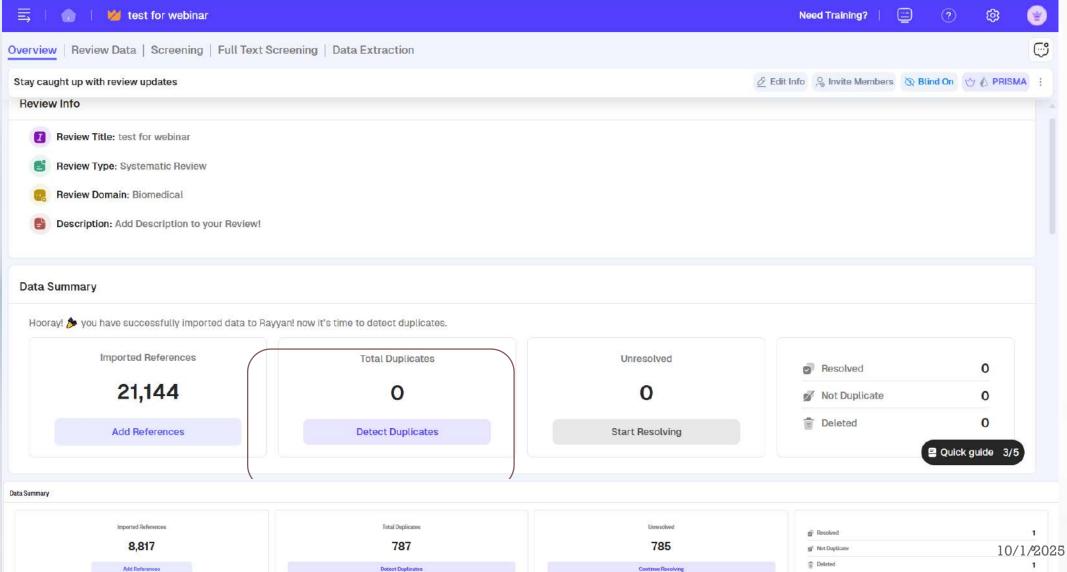


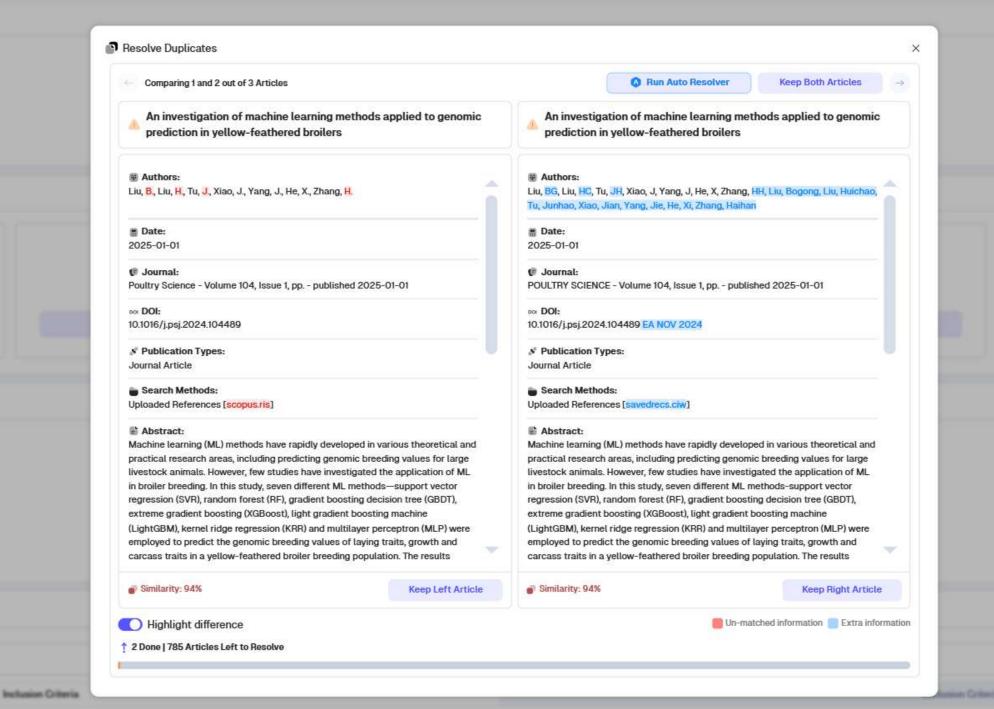
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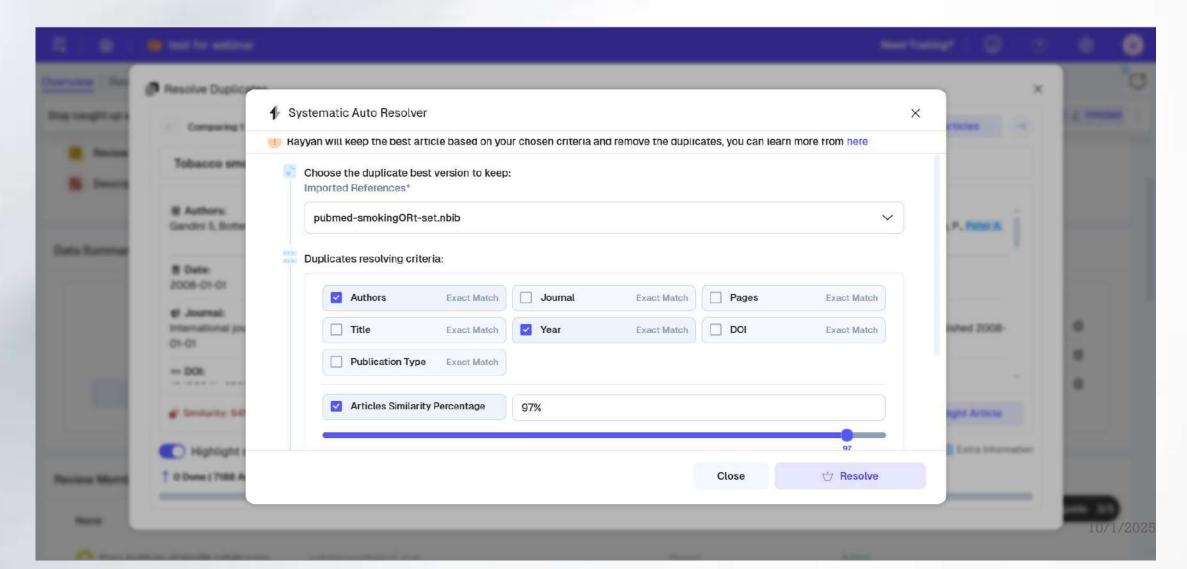




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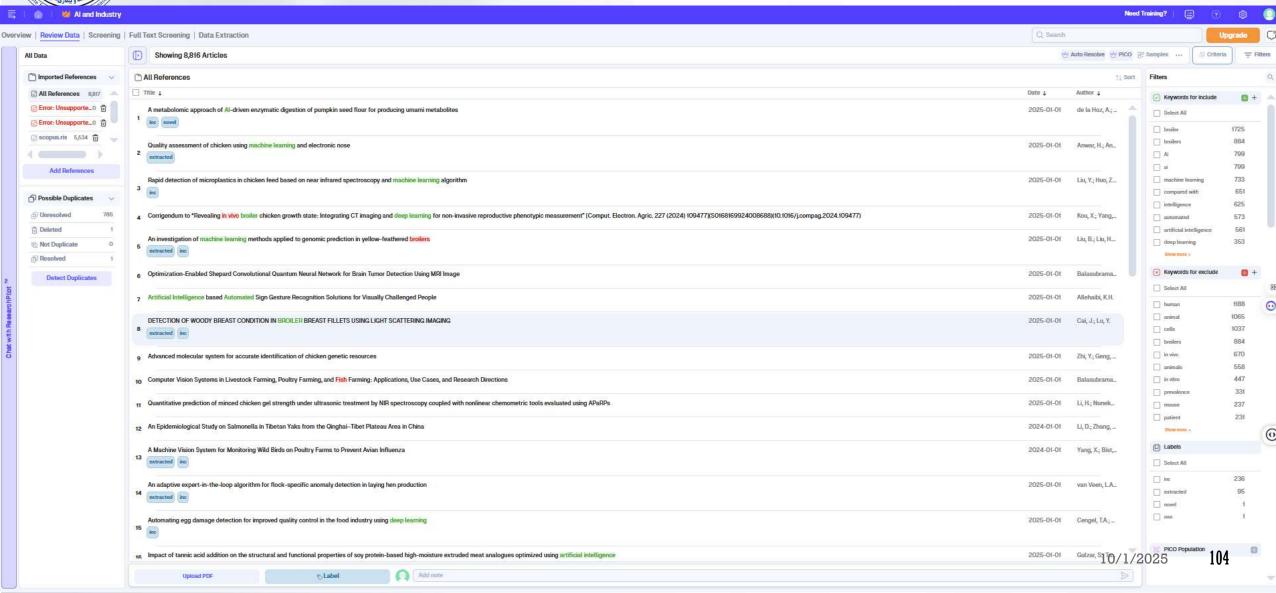


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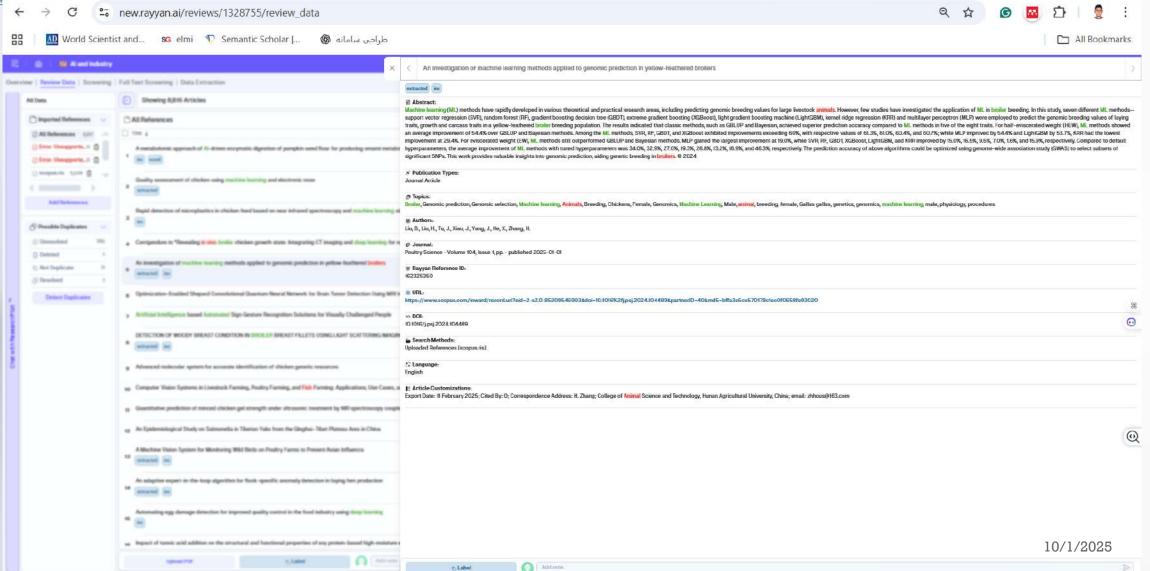


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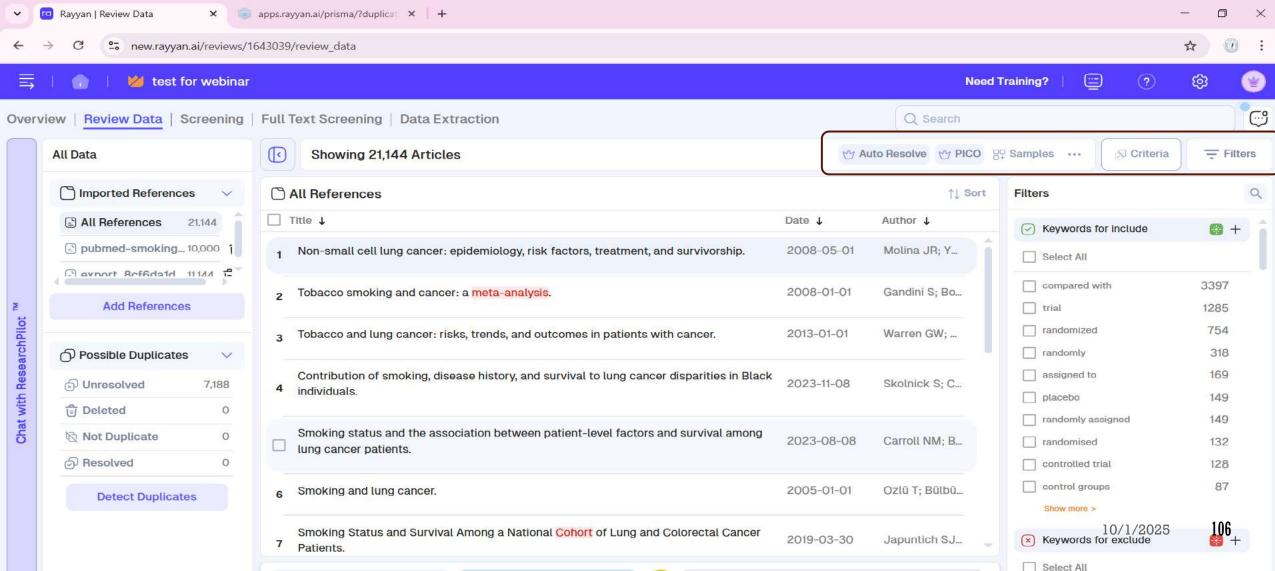


REWIEW OF DATA- INFO ASSESSMENT



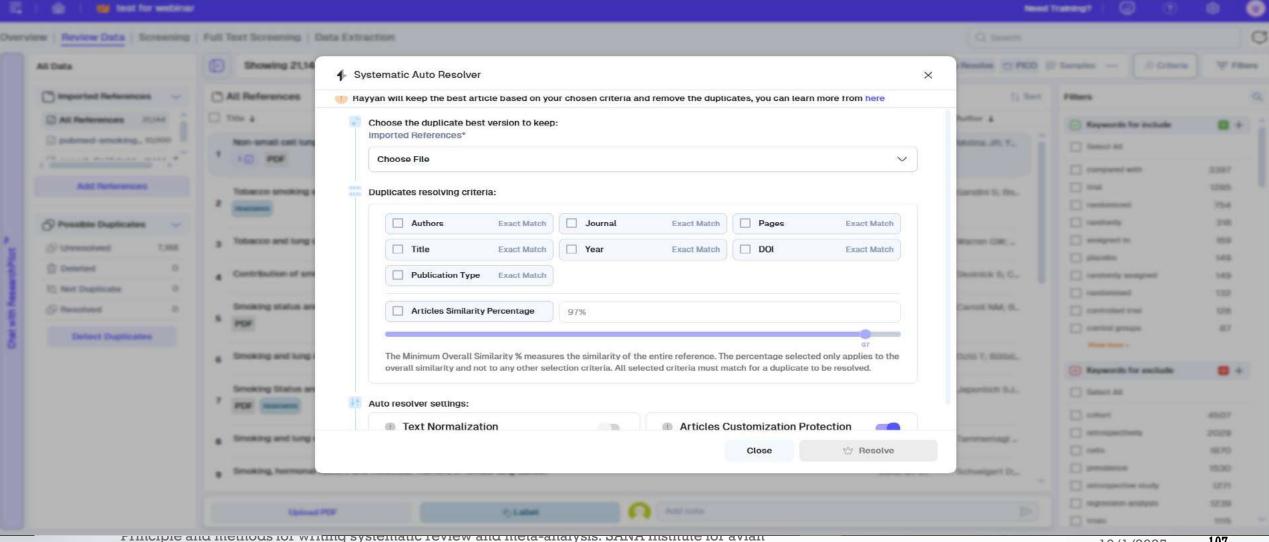


CRITERIA DEFINITION, PICO AND AUTO RESOLVE

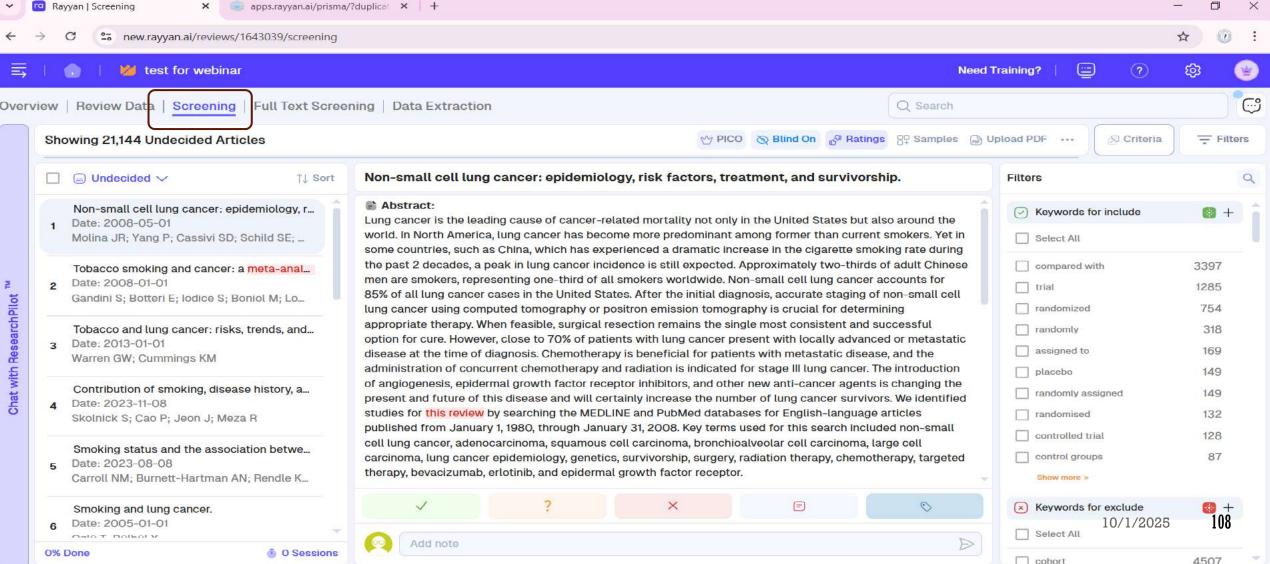




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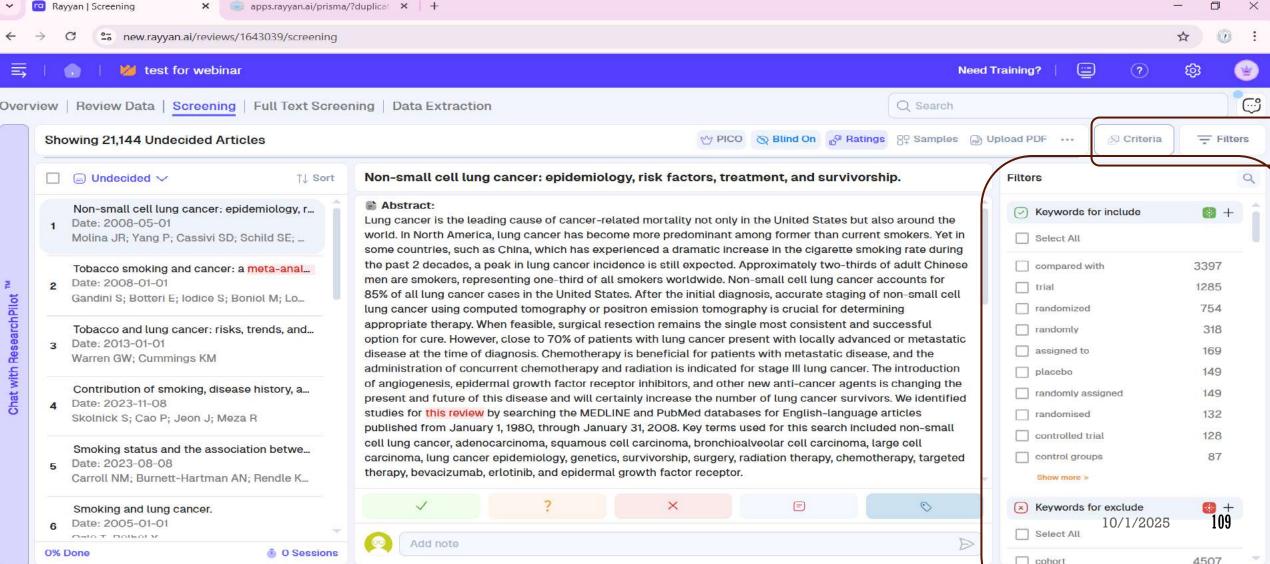


CRITERIA



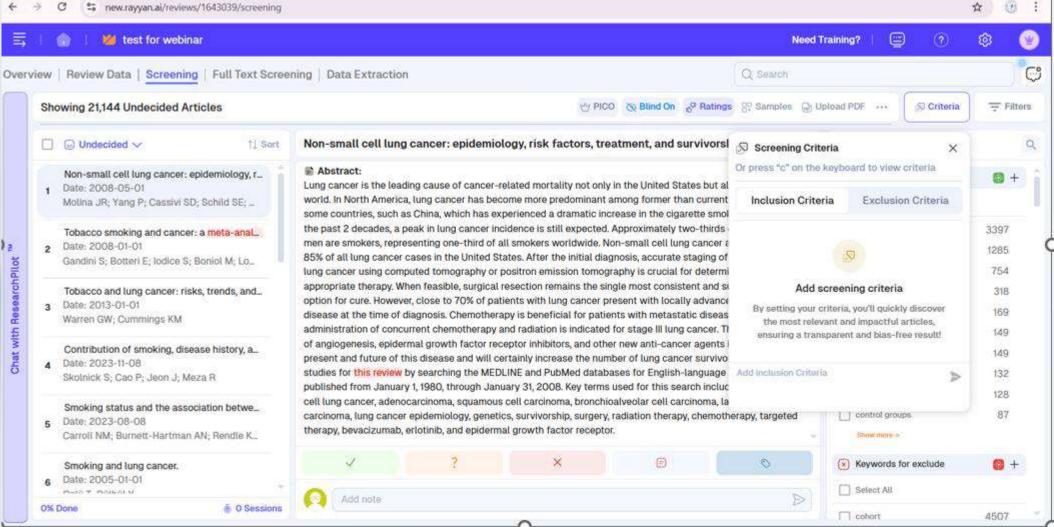


CRITERIA





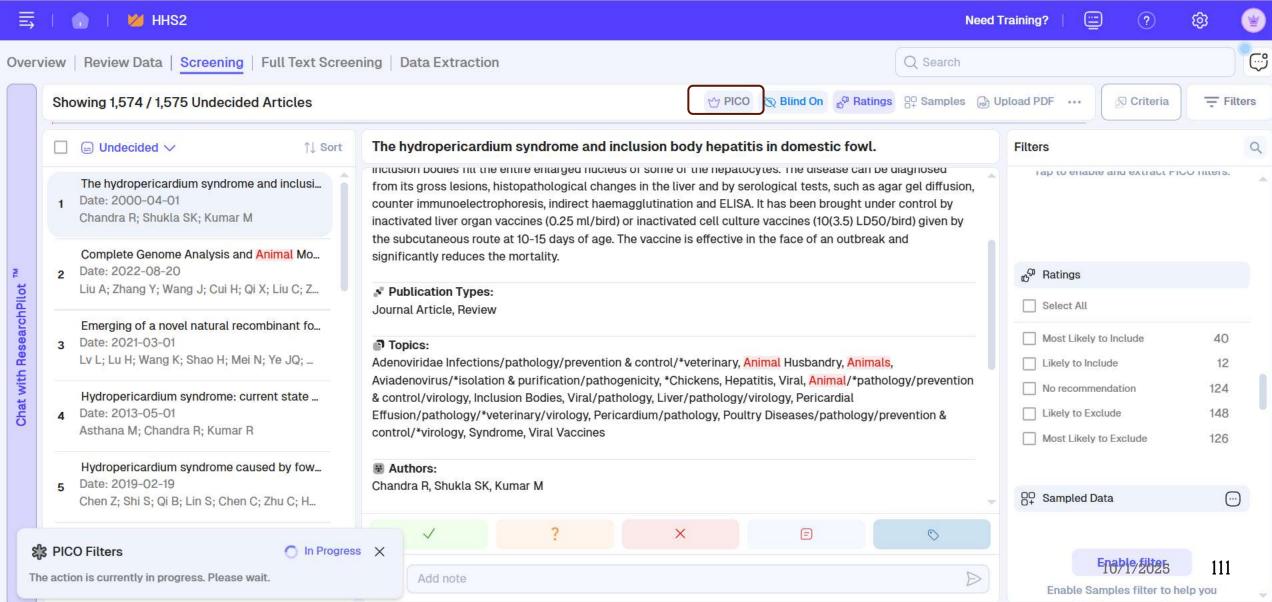
CRITERIA DEFINITION



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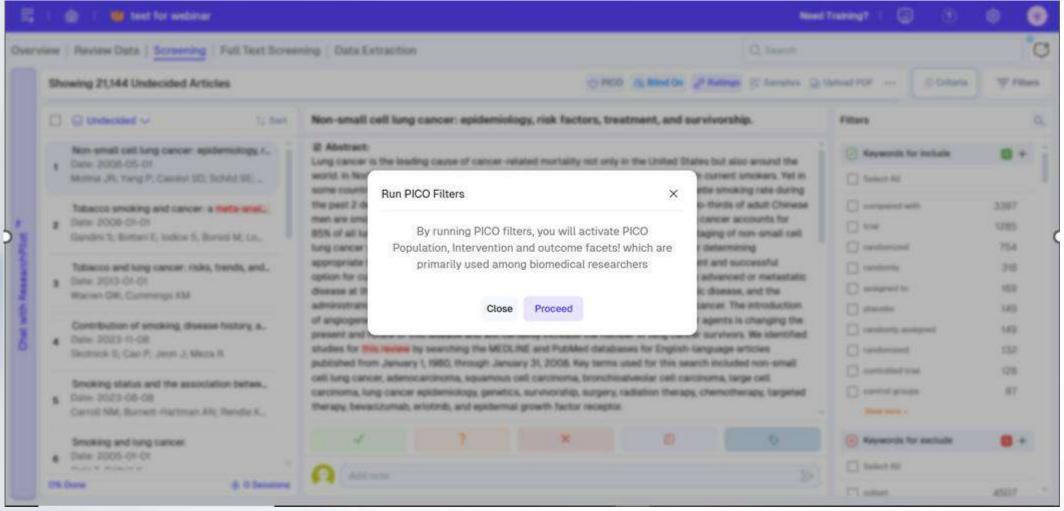


RATING OF THE STUDIES



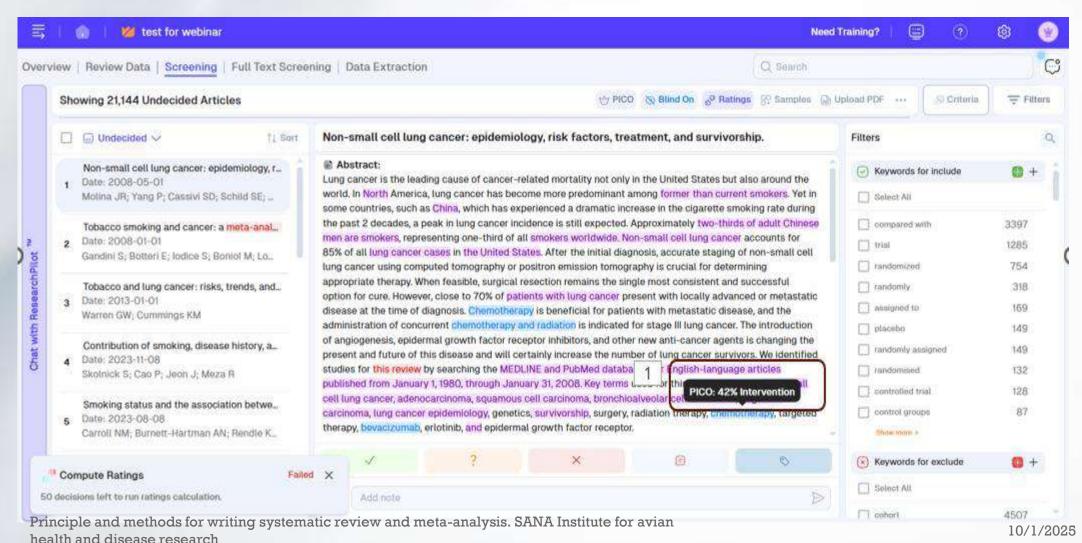


PICO DEFINITION



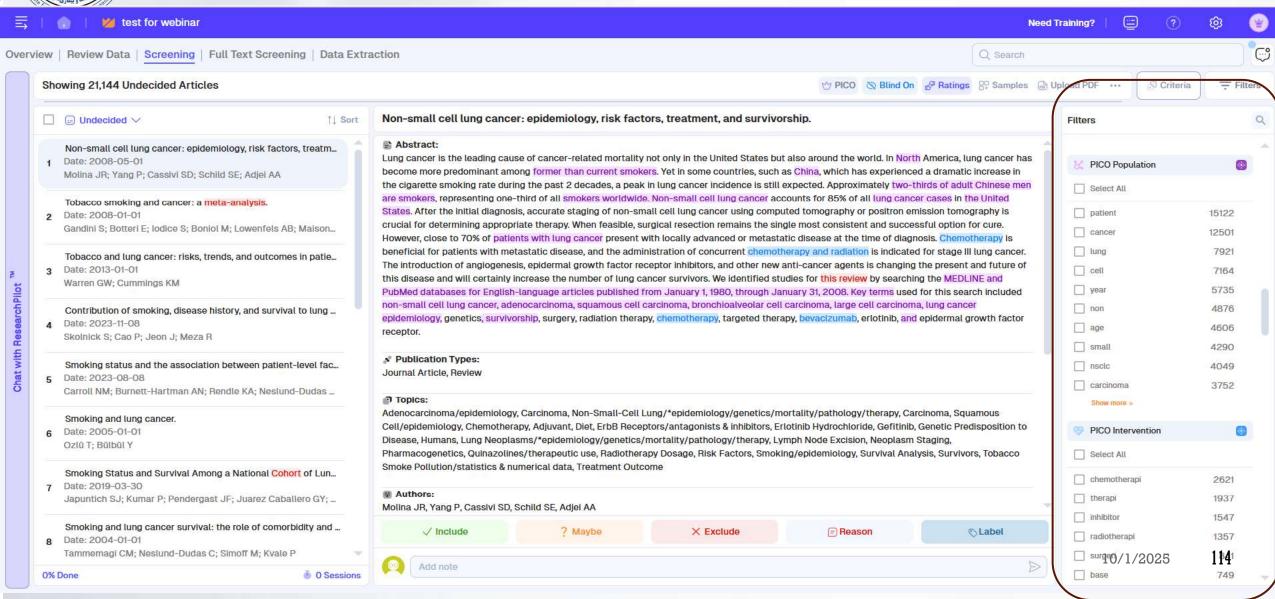


PICO REVEAL IN ABSTRACT



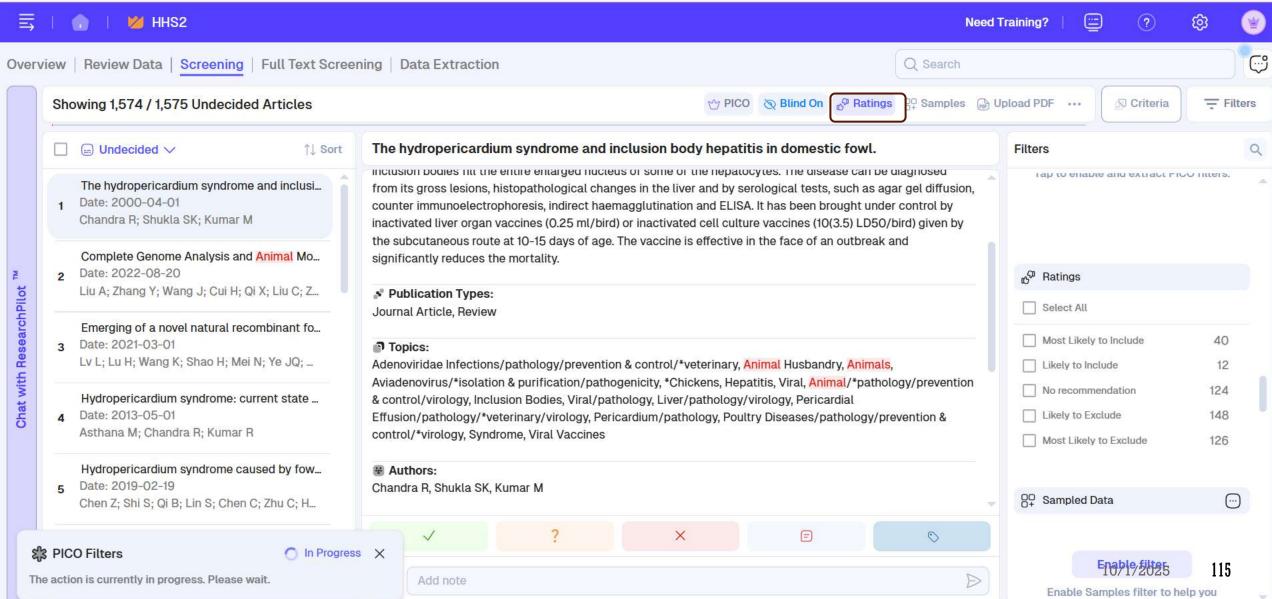


PICO CRITERIA



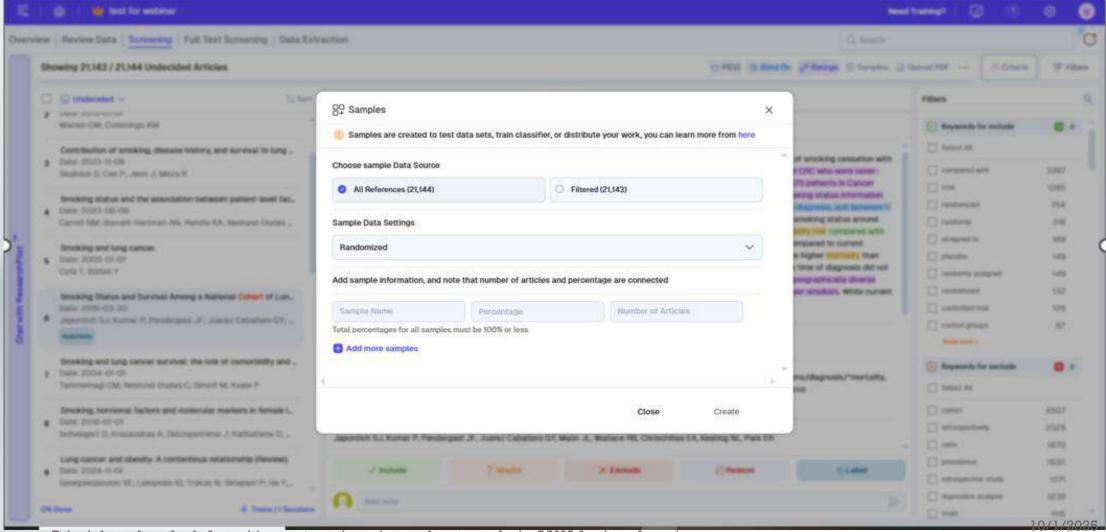


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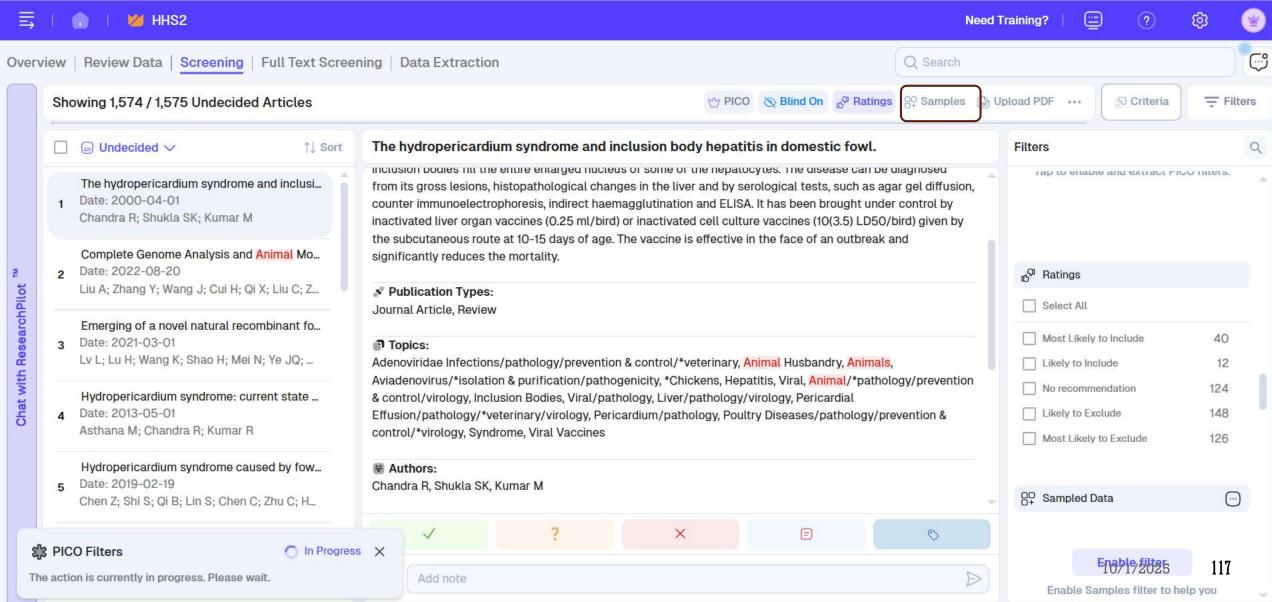
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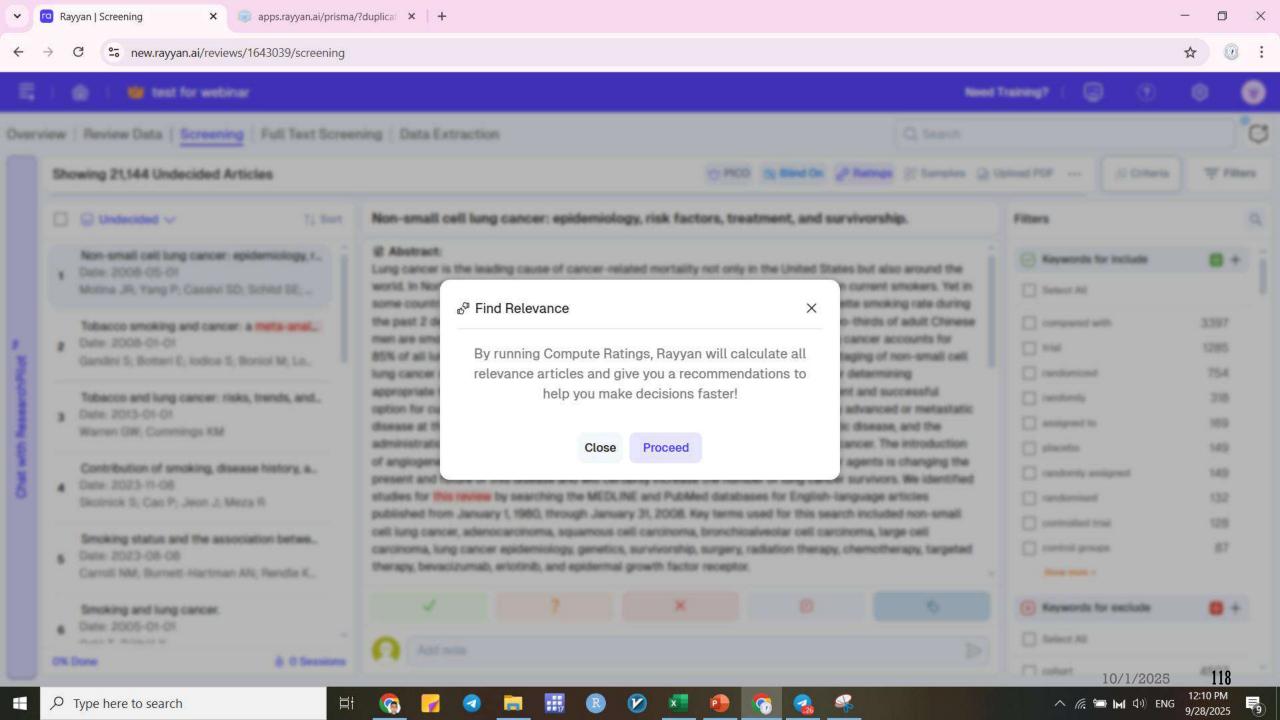


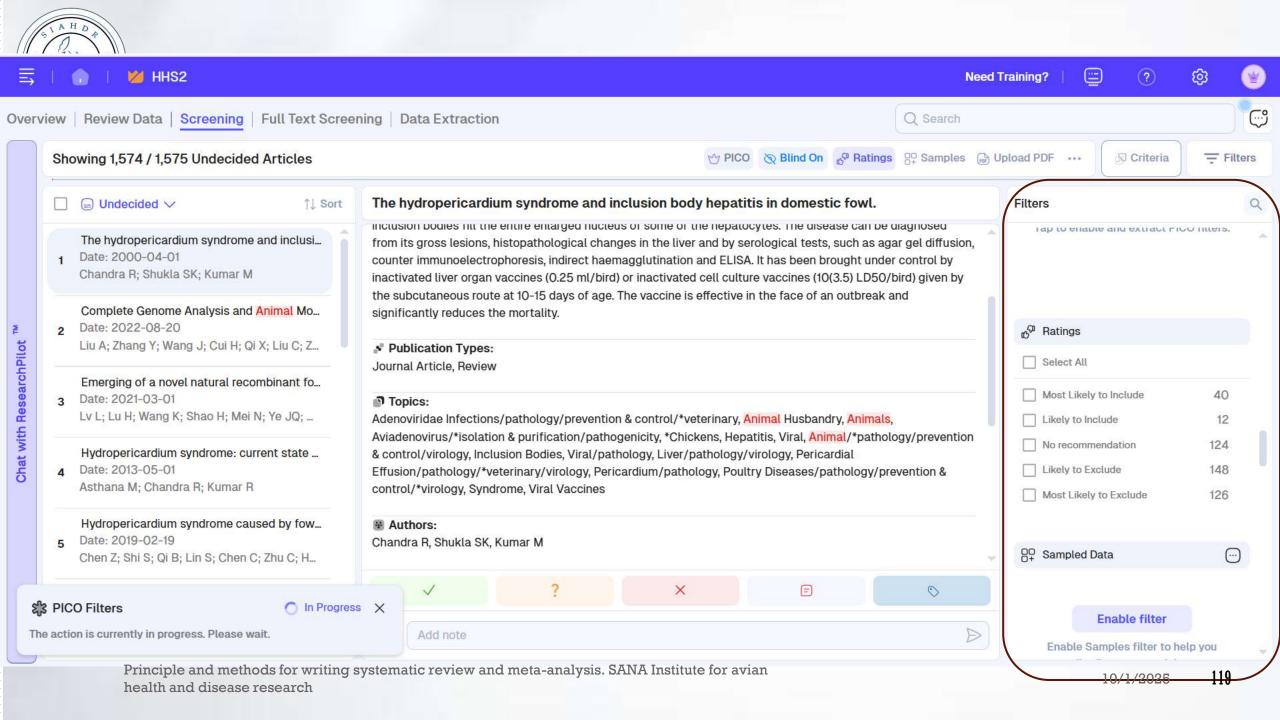
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RATING OF THE STUDIES

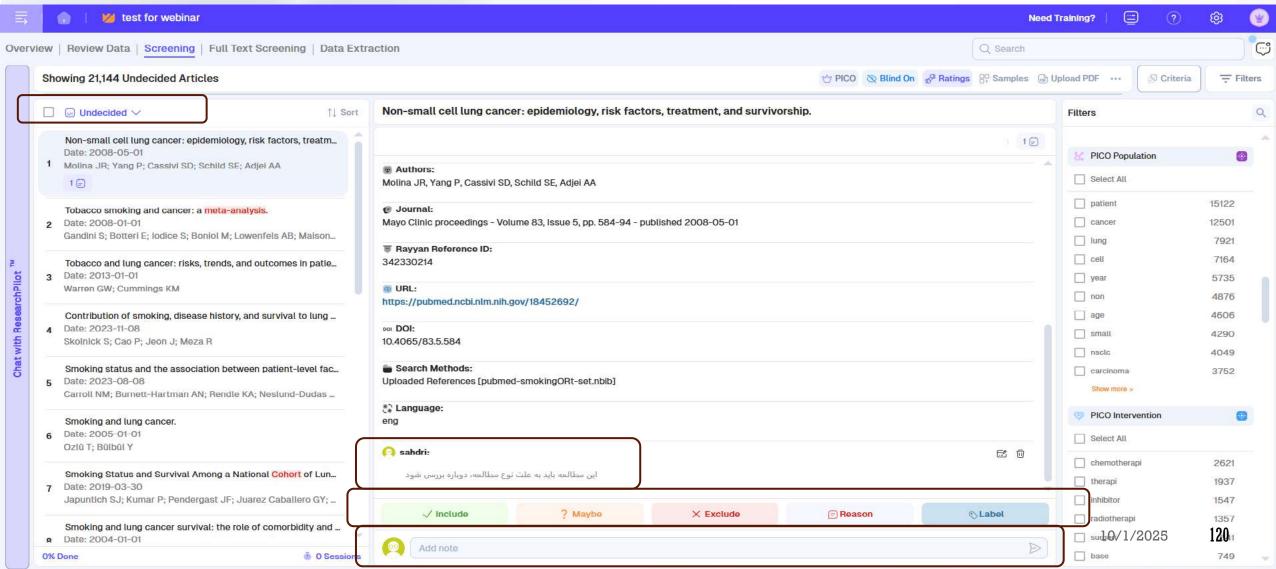






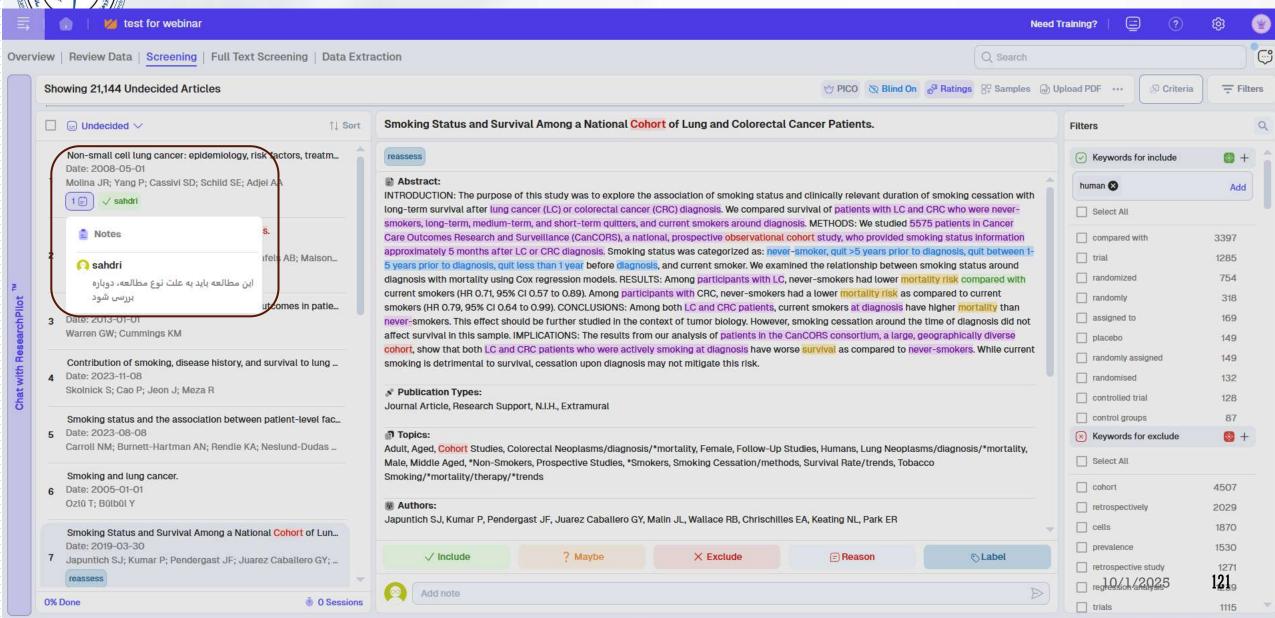


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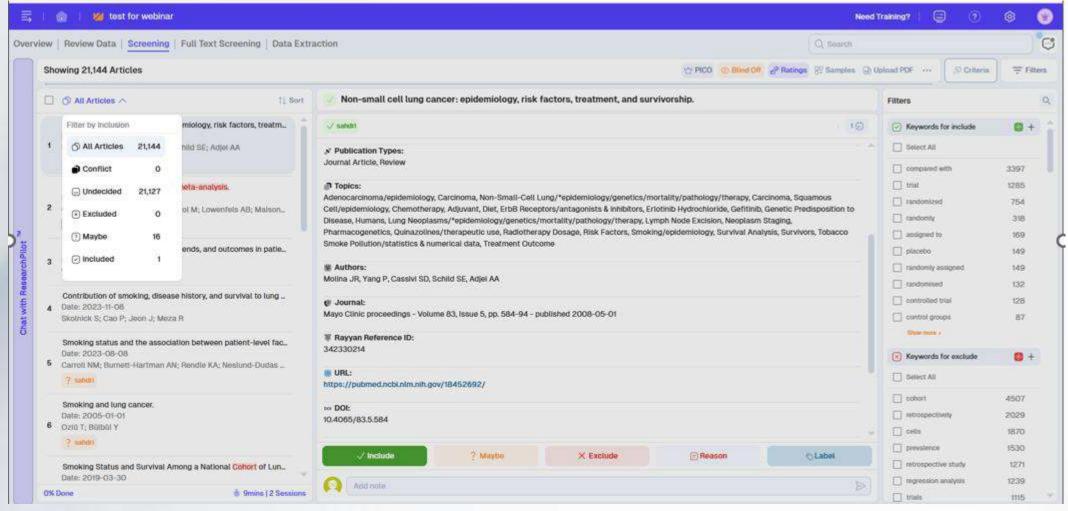


NOTE FOR THE ARTICLES





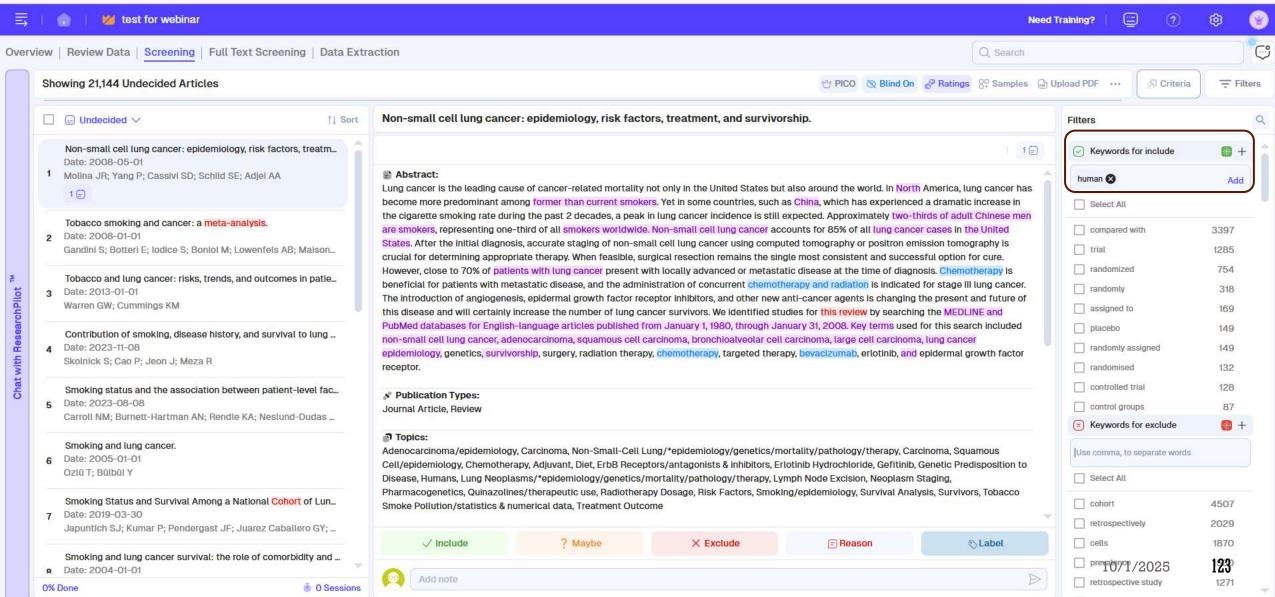
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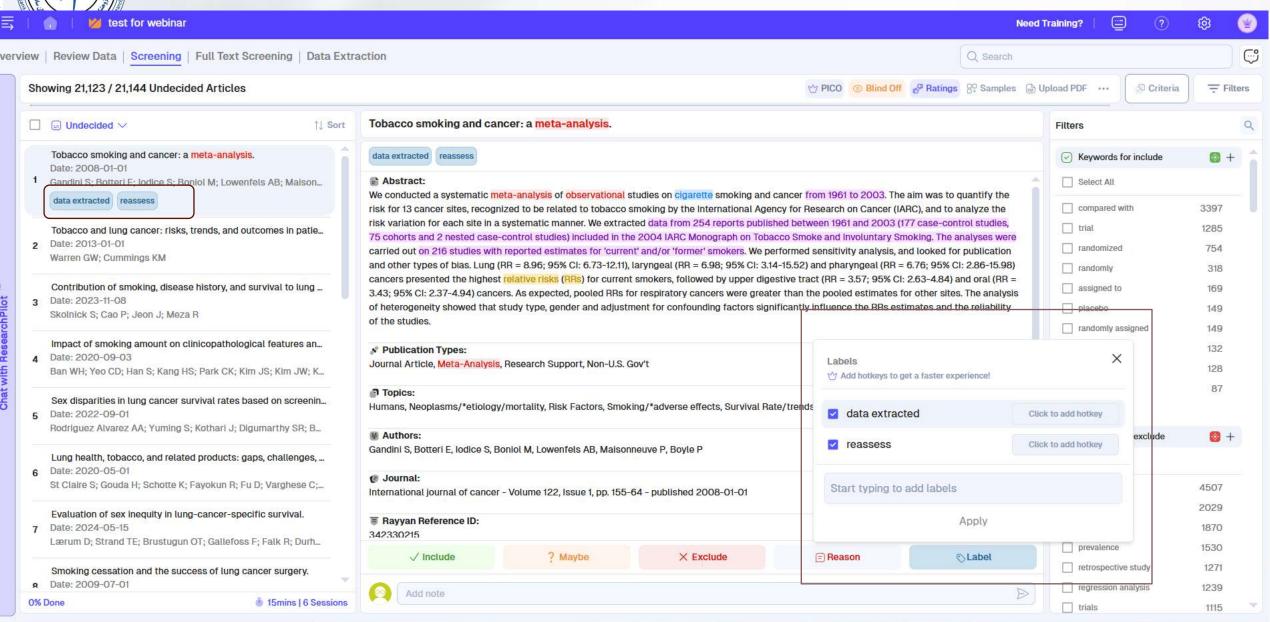


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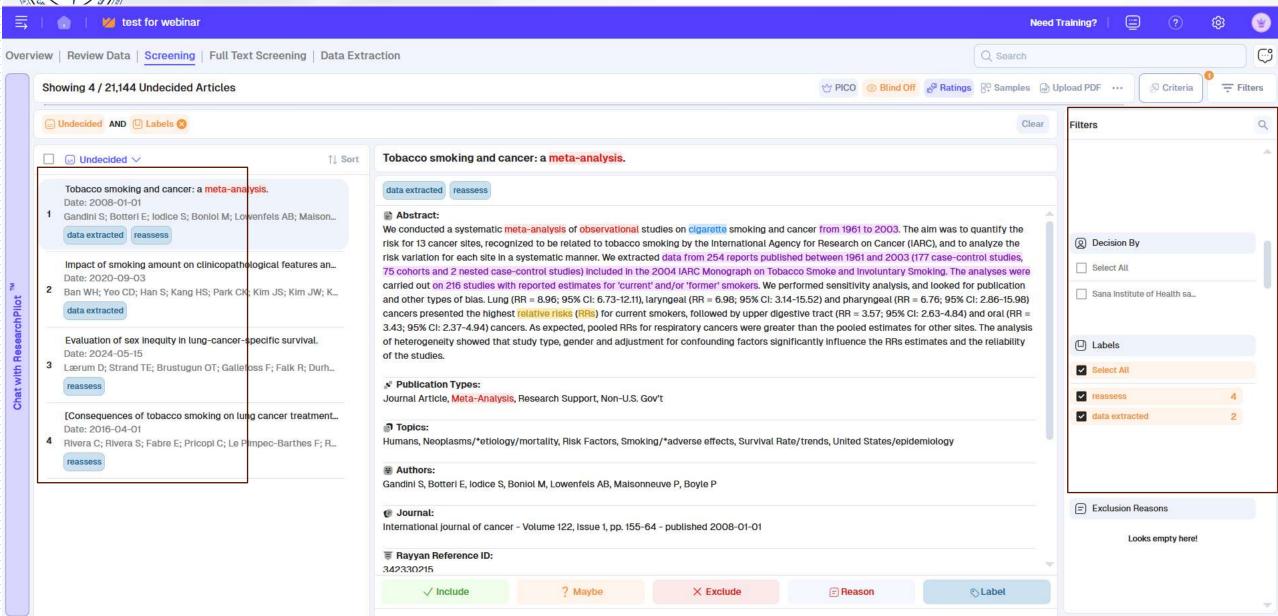


LABEL TO ARTICLES





FILTER BY LABELS



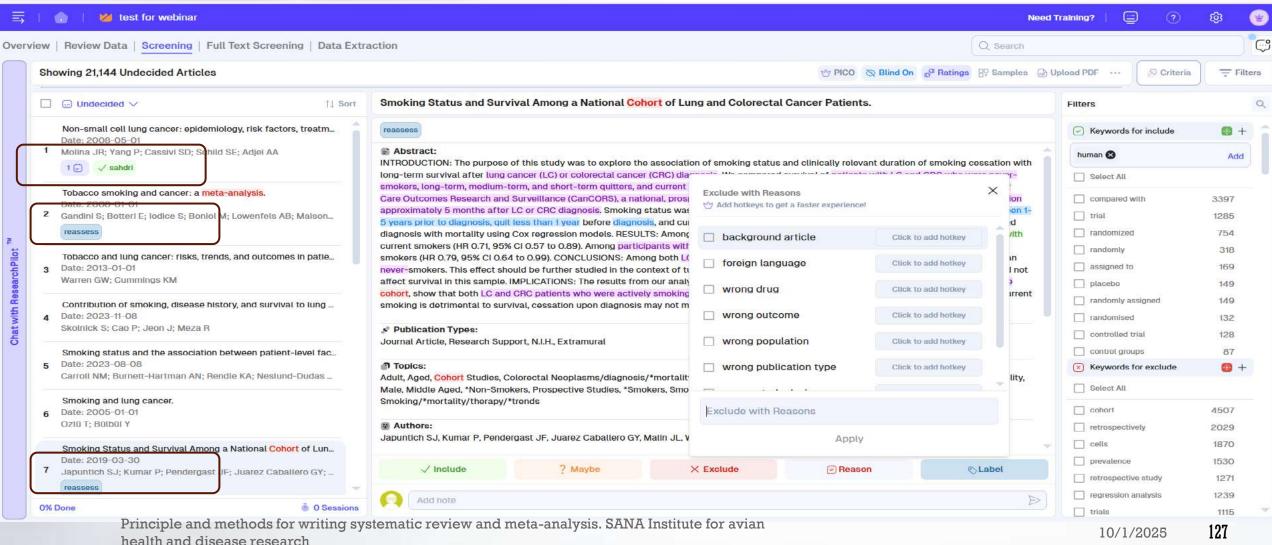


REASON OF EXCLUSION

verview | Review Data | Screening | Full Text Screening | Data Extraction Q Search Showing 21,144 Undecided Articles PICO Solind On Ratings Soling Samples De Upload PDF ... Criteria = Filters Tobacco smoking and cancer: a meta-analysis. ☐ Undecided ∨ 1 Sort **Filters** Non-small cell lung cancer: epidemiology, risk factors, treatm... reassess Keywords for include **8** + Date: 2008-05-01 1 Molina JR; Yang P; Cassivi SD; Schild SE; Adjei AA Abstract: human 🔇 Add We conducted a systematic meta-analysis of observational studies on cigarette smoking and cancer from 1961 to 2003. The aim was to quantify the 1 (=) ✓ sahdri risk for 13 cancer sites, recognized to be related to tobacco smoking by the International Agency for Decearch on Concer (IADO), and to enable the Select All risk variation for each site in a systematic manner. We extracted data fr Tobacco smoking and cancer: a meta-analysis. **Exclude with Reasons** 75 cohorts and 2 nested case-control studies) included in the 2004 IAF vere compared with 3397 Date: 2008-01-01 Add hotkeys to get a faster experience! carried out on 216 studies with reported estimates for 'current' and/or 'f ion 2 Gandini S; Botteri E; Iodice S; Boniol M; Lowenfels AB; Maison... trial 1285 and other types of bias. Lung (RR = 8.96; 95% CI: 6.73-12.11), laryngeal (.98)reassess cancers presented the highest relative risks (RRs) for current smokers, 3R = randomized 754 background article Click to add hotkey 3.43; 95% CI: 2.37-4.94) cancers. As expected, pooled RRs for respirato lysis randomly 318 Tobacco and lung cancer: risks, trends, and outcomes in patie... of heterogeneity showed that study type, gender and adjustment for co lity foreign language Click to add hotkey assigned to Date: 2013-01-01 169 of the studies. Warren GW: Cummings KM placebo wrong drug Click to add hotkey Publication Types: randomly assigned Contribution of smoking, disease history, and survival to lung ... Journal Article, Meta-Analysis, Research Support, Non-U.S. Gov't wrong outcome Click to add hotkey Date: 2023-11-08 randomised 132 Skolnick S; Cao P; Jeon J; Meza R Topics: controlled trial wrong population Click to add hotkey Humans, Neoplasms/*etiology/mortality, Risk Factors, Smoking/*adver Smoking status and the association between patient-level fac... control groups Date: 2023-08-08 Authors: wrong publication type Keywords for exclude Click to add hotkey Carroll NM; Burnett-Hartman AN; Rendle KA; Neslund-Dudas ... Gandini S, Botteri E, Iodice S, Boniol M, Lowenfels AB, Maisonneuve P, B Select All Smoking and lung cancer. Journal: Exclude with Reasons cohort 4507 6 Date: 2005-01-01 International journal of cancer - Volume 122, Issue 1, pp. 155-64 - publis Ozlů T: Bůlbůl Y retrospectively 2029 Rayyan Reference ID: Apply cells 1870 Smoking Status and Survival Among a National Cohort of Lun... 342330215 7 Date: 2019-03-30 prevalence 1530 ✓ Include ? Maybe X Exclude Reason C Label Japuntich SJ; Kumar P; Pendergast JF; Juarez Caballero GY; ... retrospective study 1271 Add note 0% Done O Sessions trials

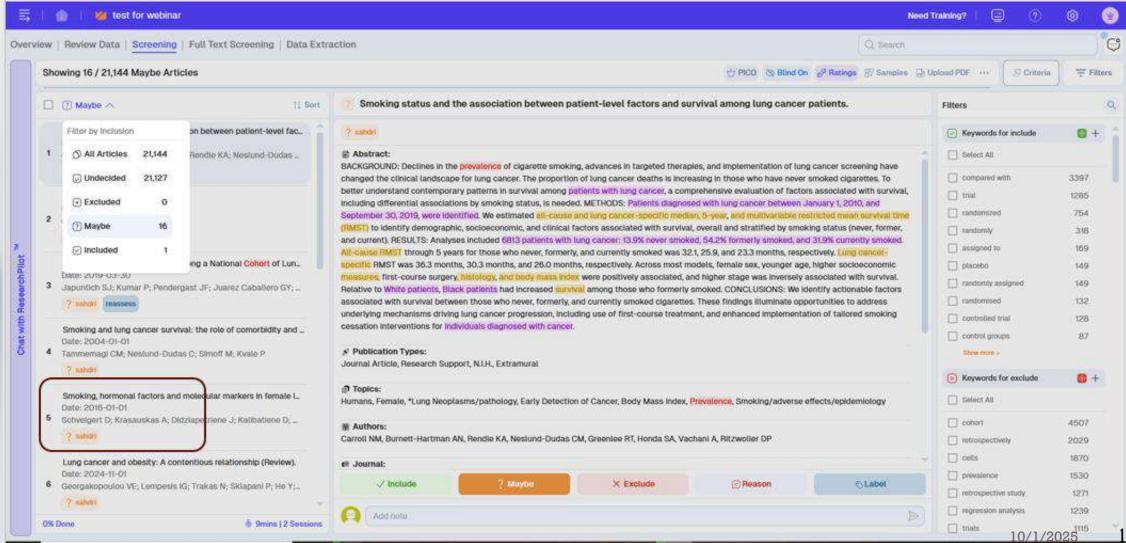


TAG OF ARTICLES, SHOW THE SITUATION



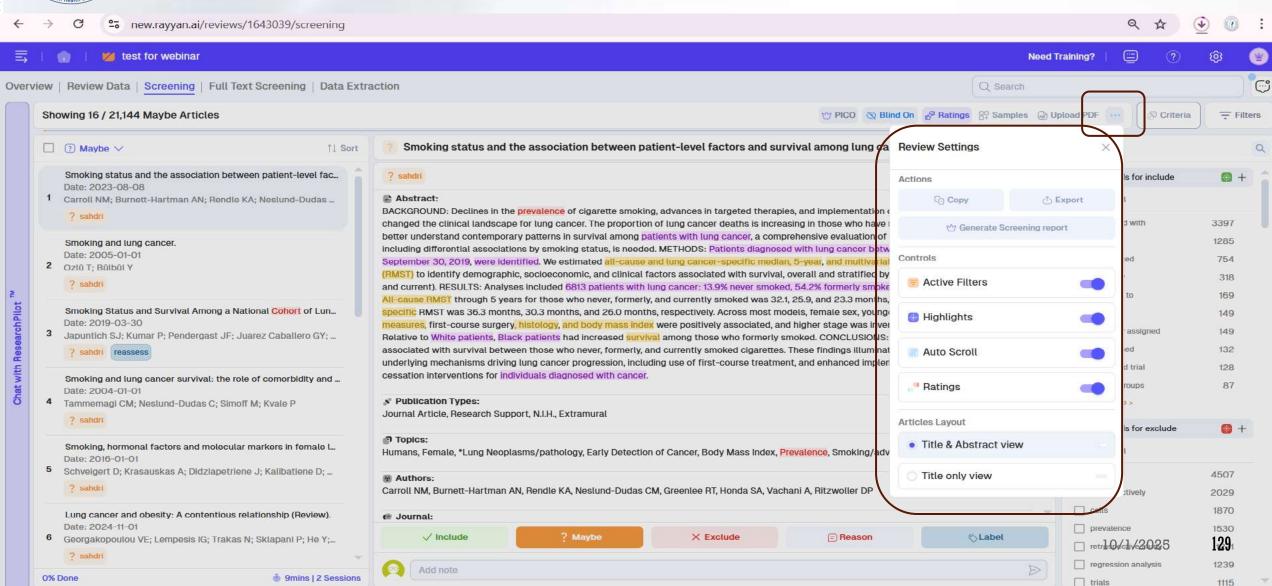


SUBGROUP SHOWS OF THE ARTICLES



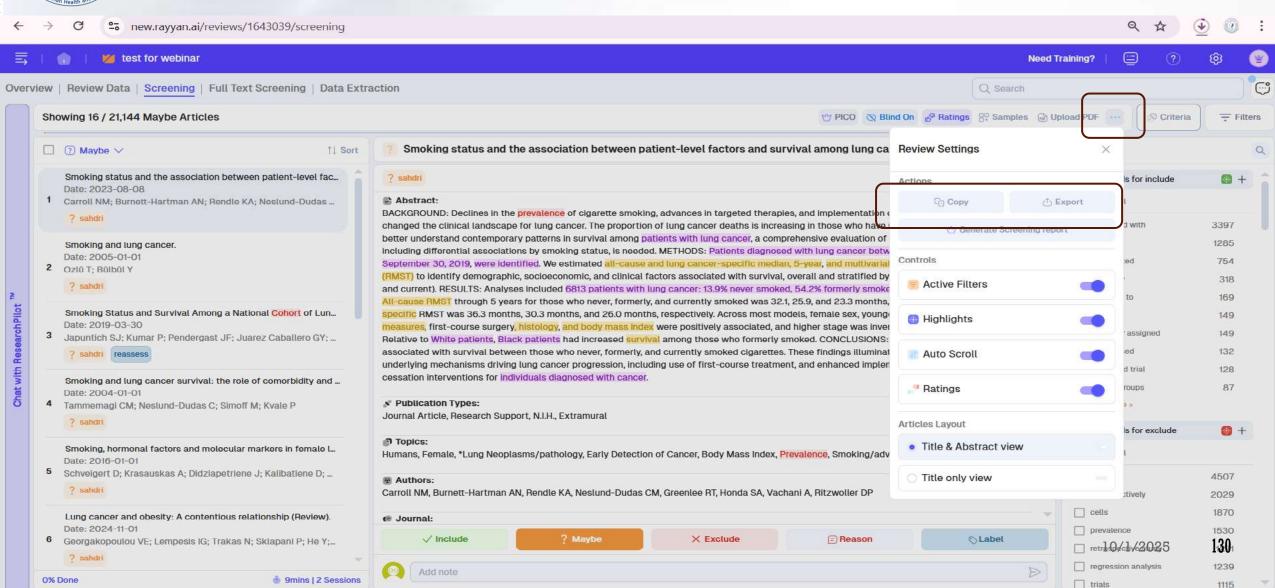


REVIEW SEETING



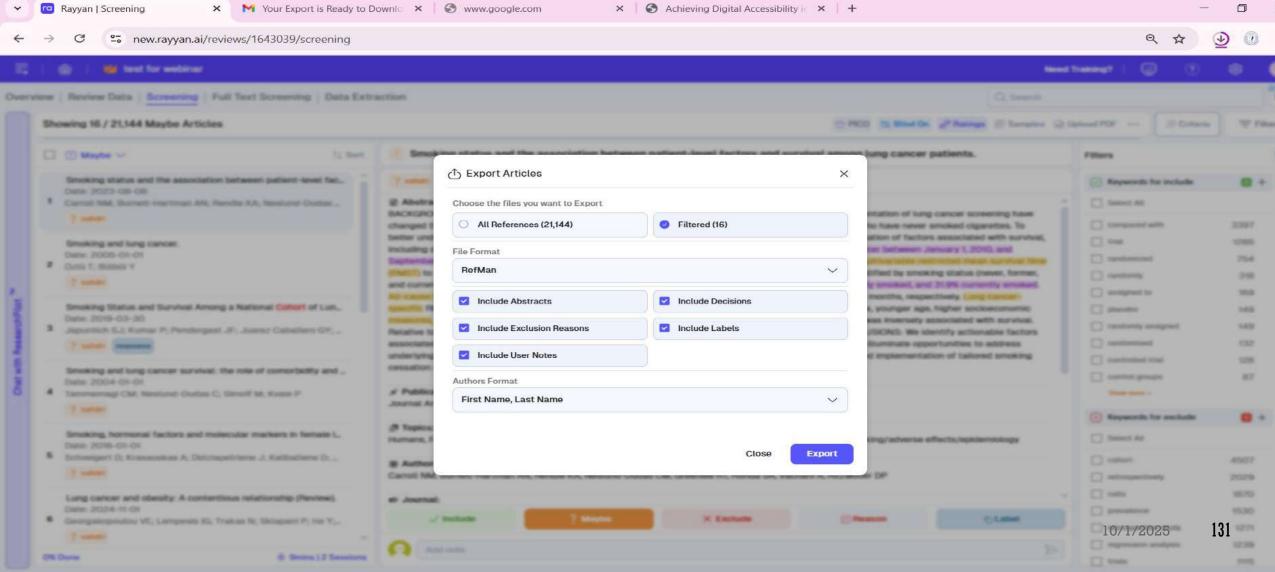


EXPORT ARTICLES





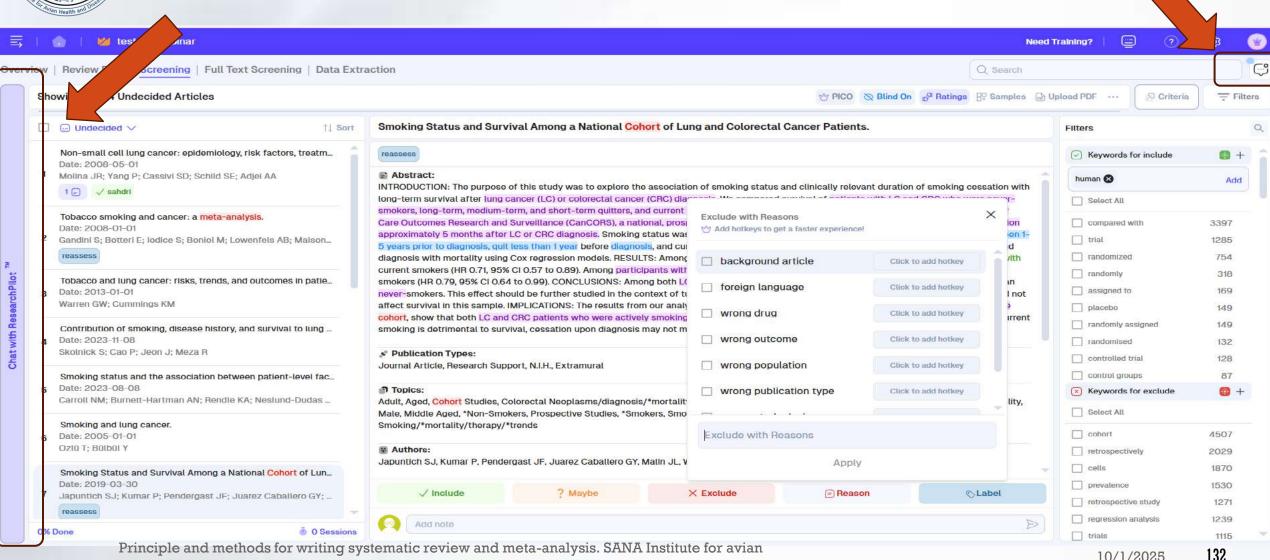
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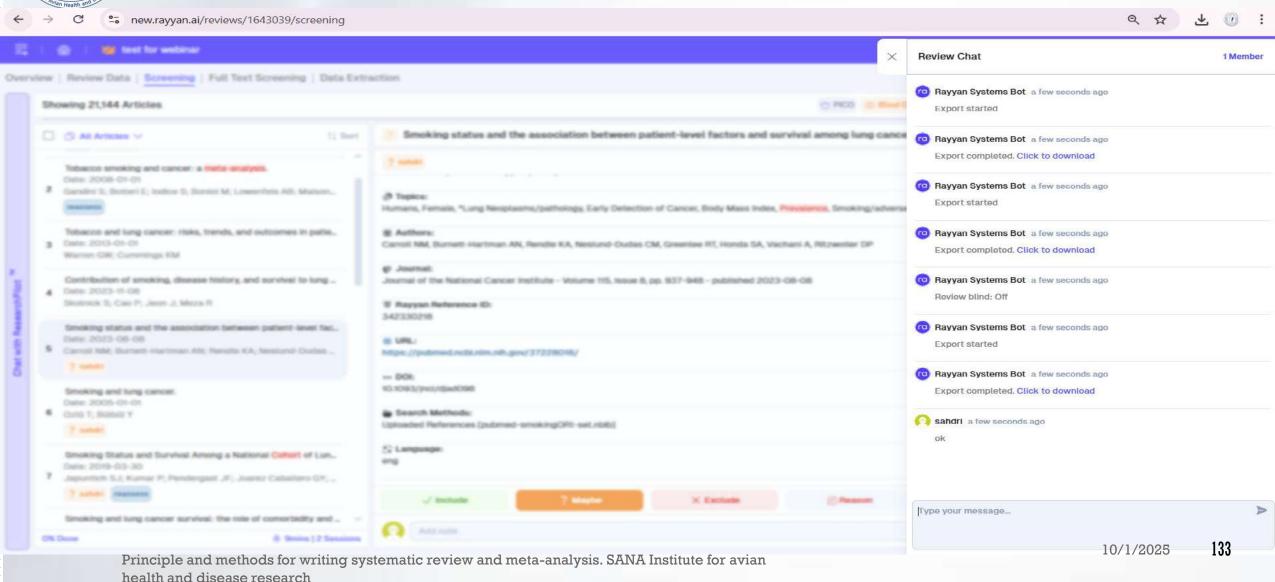
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AI AND CHAT BOX OF THE RAYYAN



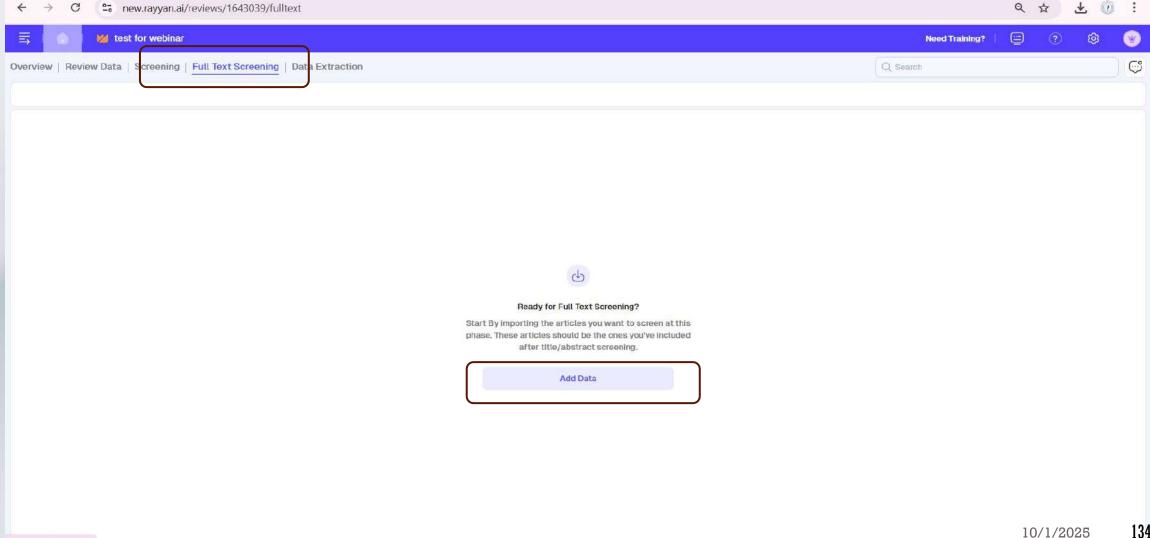


CHAT BOX OF THE RAYYAN





FULL TEXT ASSESSMENT

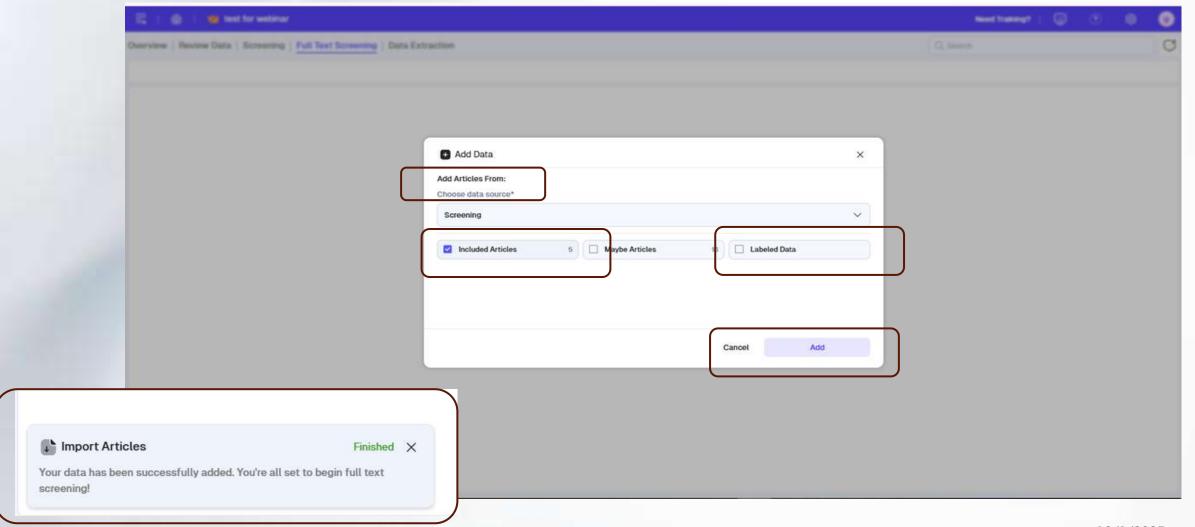


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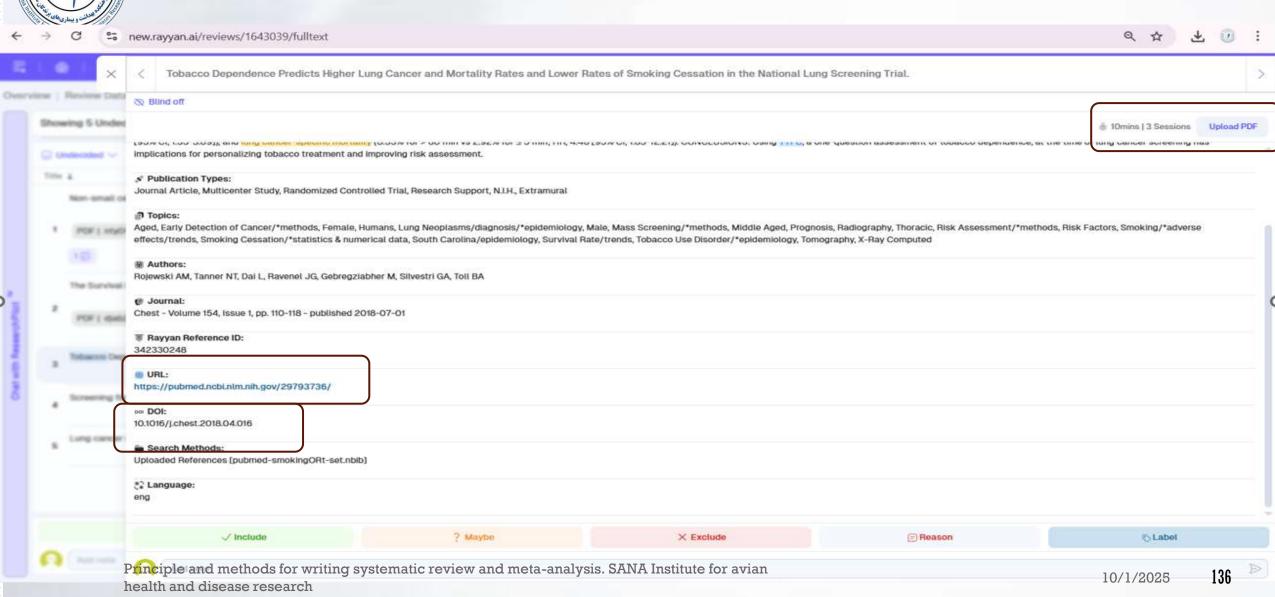


ADD THE DATA FOR FULL TEXT



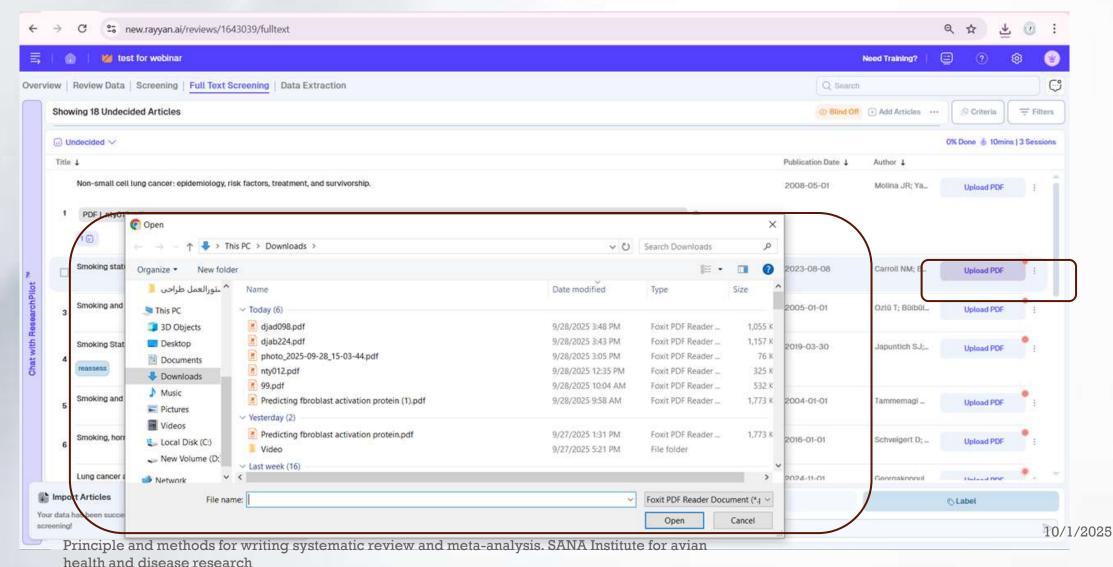


FULL TEXT DOWNLOAD AND UPLOAD



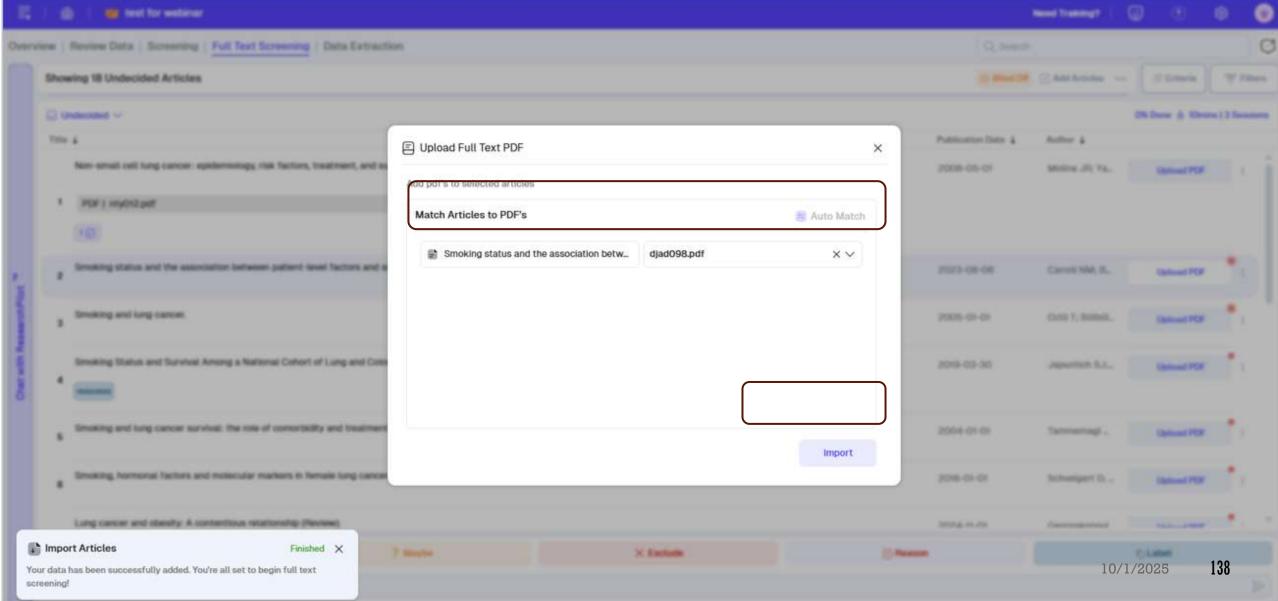


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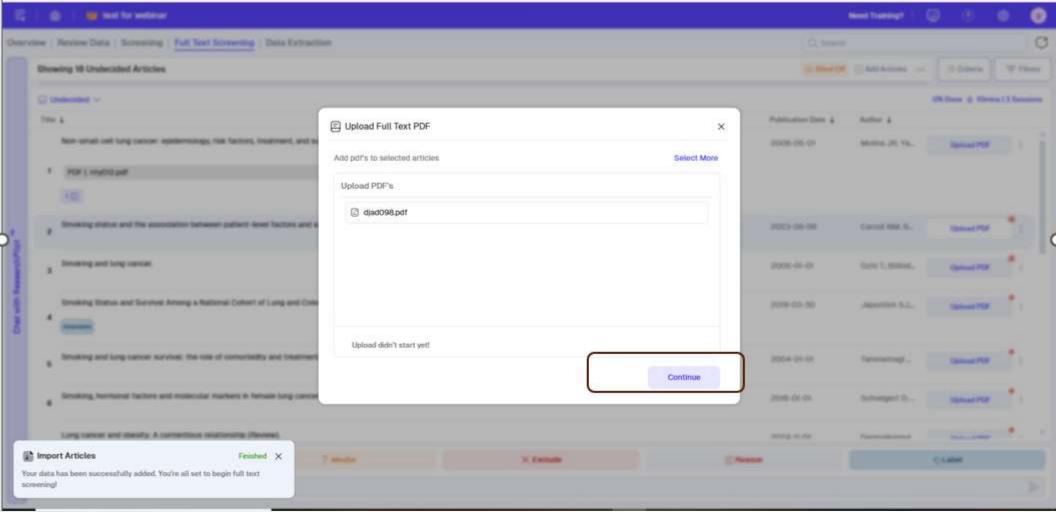


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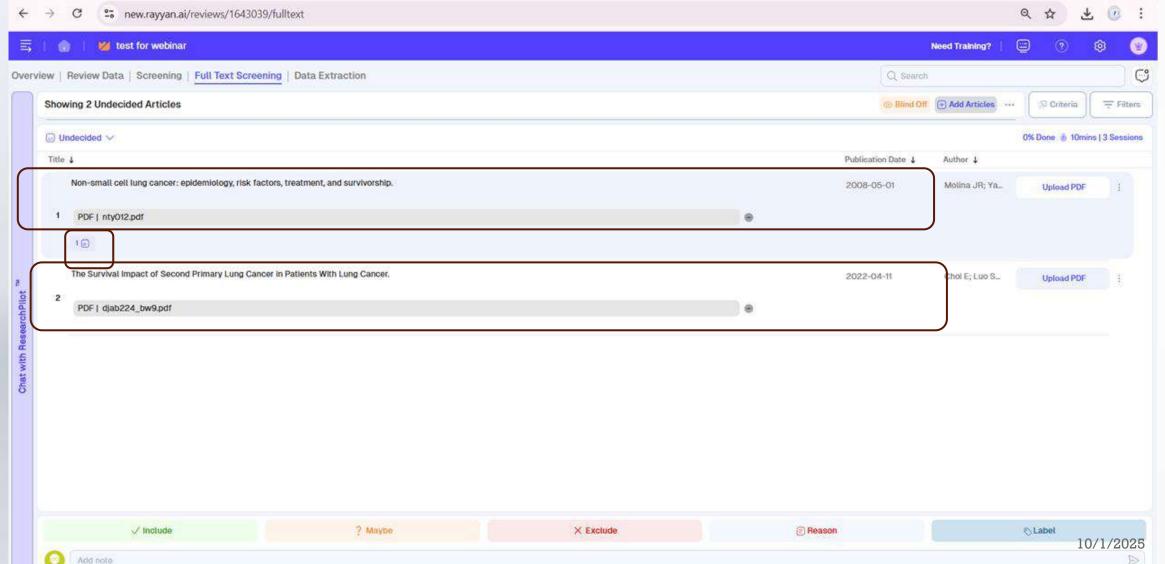


UPLOAD THE FILE





UPLOADED FILE





METHODS: DATA ITEMS (PRISMA ITEMS 10A & 10B)

Checklist Item:

- 10a: "List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect."
- 10b: "List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information."



PURPOSE AND KEY ELEMENTS:

• This section explains exactly what data you collected from included studies, both for outcomes and other variables (study and participant details, interventions, funding, etc.).

Key Elements:

- Outcomes (10a)
 - List primary outcomes (the main variables of interest in your review).
 - List secondary outcomes (additional, supportive variables).



EXPLANATION:

- Other Variables (10b)
- Describe additional variables collected to give context to your review, such as:
 - Participant characteristics (species, breed, age, sex, health status).
 - Intervention details (type, dosage, administration route).
 - Study characteristics (year, country, design, sample size).
 - Funding sources and conflicts of interest.



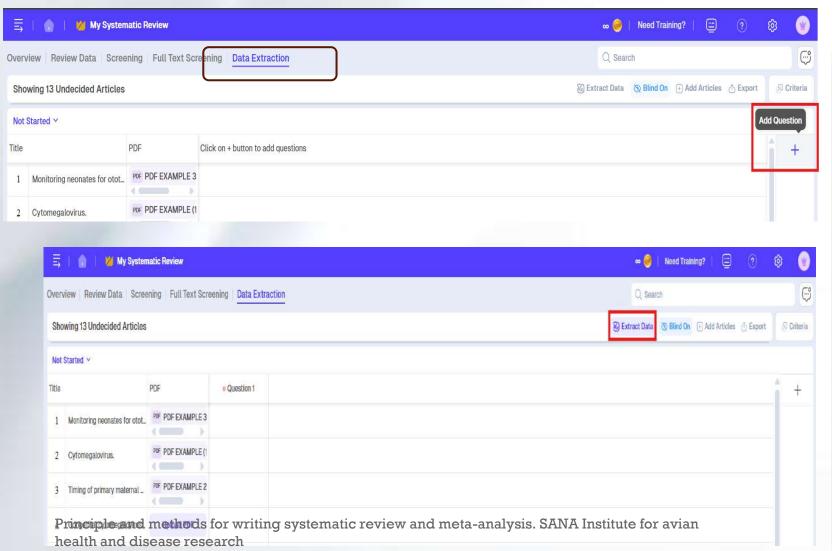
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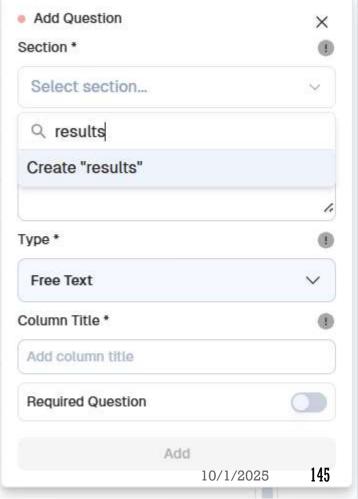
EXAMPLE: MORTALITY IN BIRDS WITH AVIAN INFLUENZA

Tilling of Shoot	The state of the s															<u> </u>		
Record N	First Author (APA)	Year	Country	Species	Disease	Sample size	Study design	Age mean (SD)	Sex (M/F)	Detectio n method	Viral load cut-off	Infected (n)	Non-	Mortalit y OR (95% CI)		Sheddin g duratio n HR (95% CI)	P value	Note
1	Hassan, M. (2015)	2015	Egypt	Chicken (broiler)	HPAI H5N1	200	Cohort	6 wk (±1)	Mixed	RT-PCR	Ct ≤ 35	120	80	3.50 (2.00– 6.10)	<0.001	2.10 (1.30– 3.45)	0.002	Media FU: 21
2	Alvarez, J. (2017)	2017	Spain	Turkey	HPAI H7N9	150	Experim ental	8 wk (±2)	Mixed	Virus isolation	≥10^3 EID50	90	60	2.85 (1.65– 4.95)	<0.001	1.75 (1.05– 2.90)	0.03	Adjuste for housir
3		_	China d methods		HPAI H5N6 g systema	100 tic review	Case- control	10 wk (±2.5) analysis. S	Mixed	ELISA + RT-PCR tute for avi	≥1:80 titer	55	45	1.95 (1.00– 3.80)	0.048	1.40 (0.85– 2.30)	0.18 5 14 4	Duck had lower mortal y



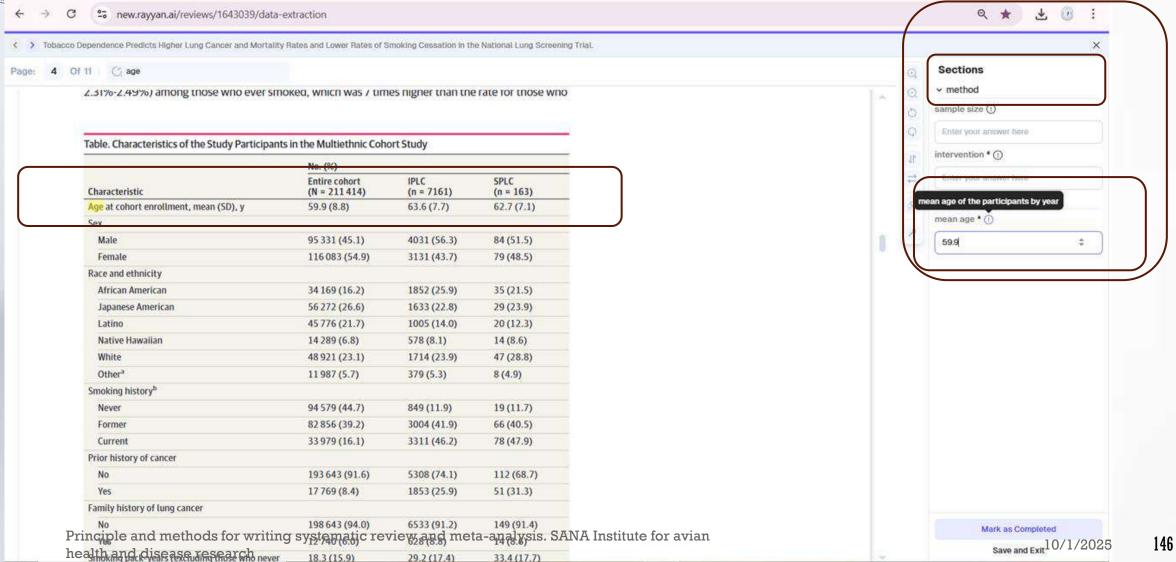
DATA EXTRACTION





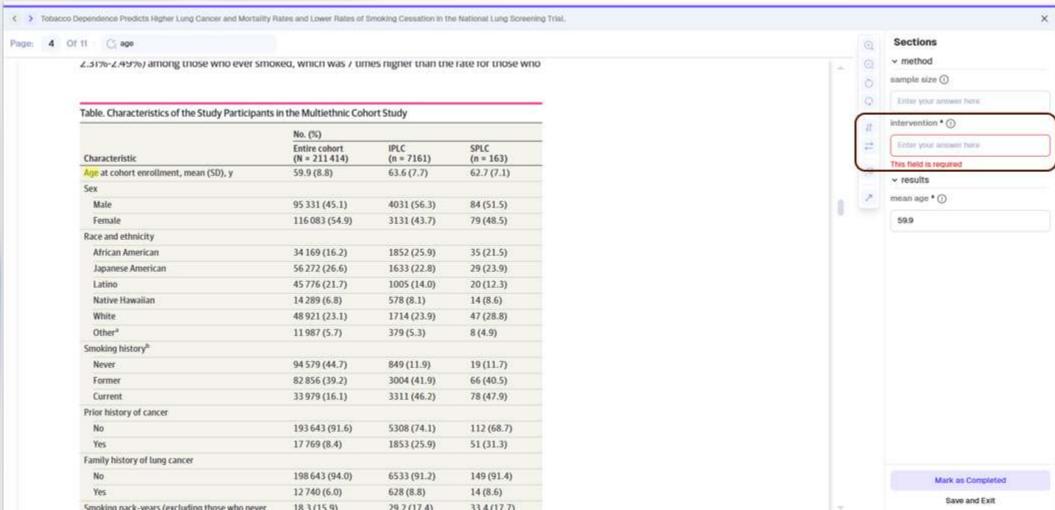


DATA EXTRACTION





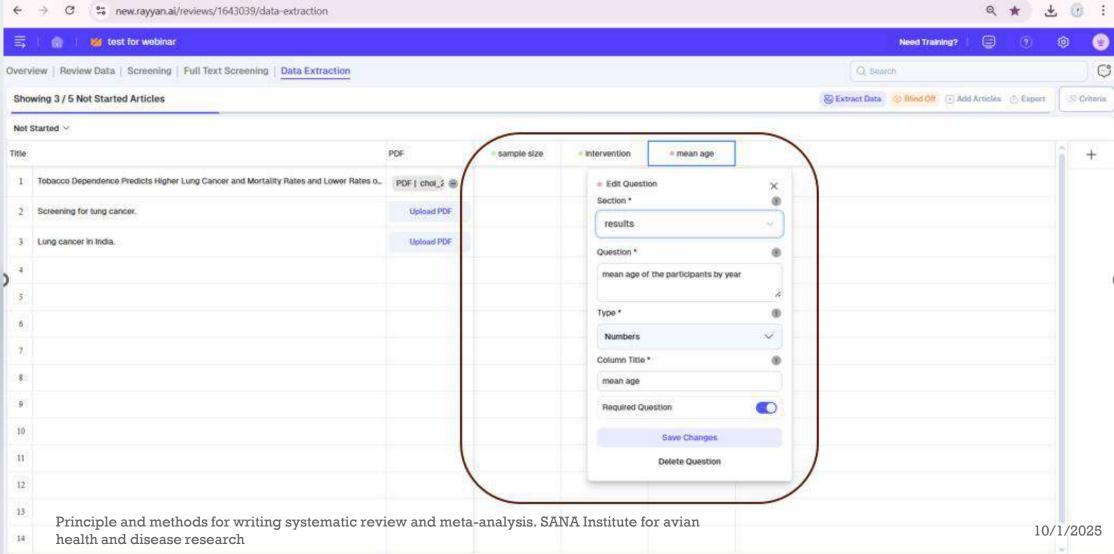
DATA EXTRACTION



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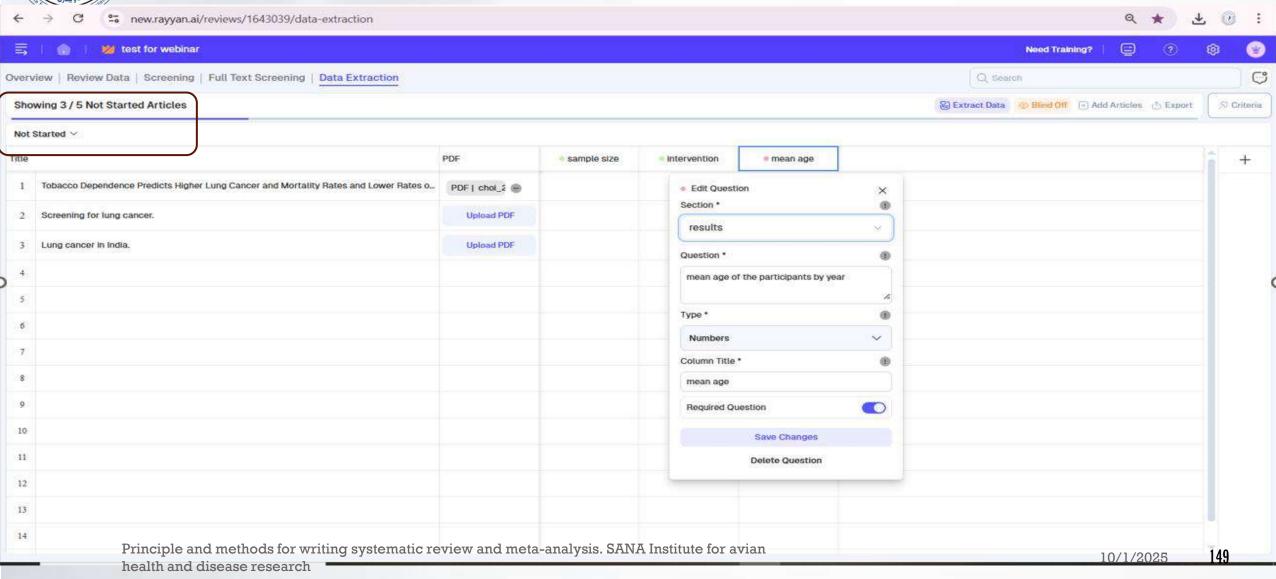


ITEM DETAILS





ITEMS SITUATION



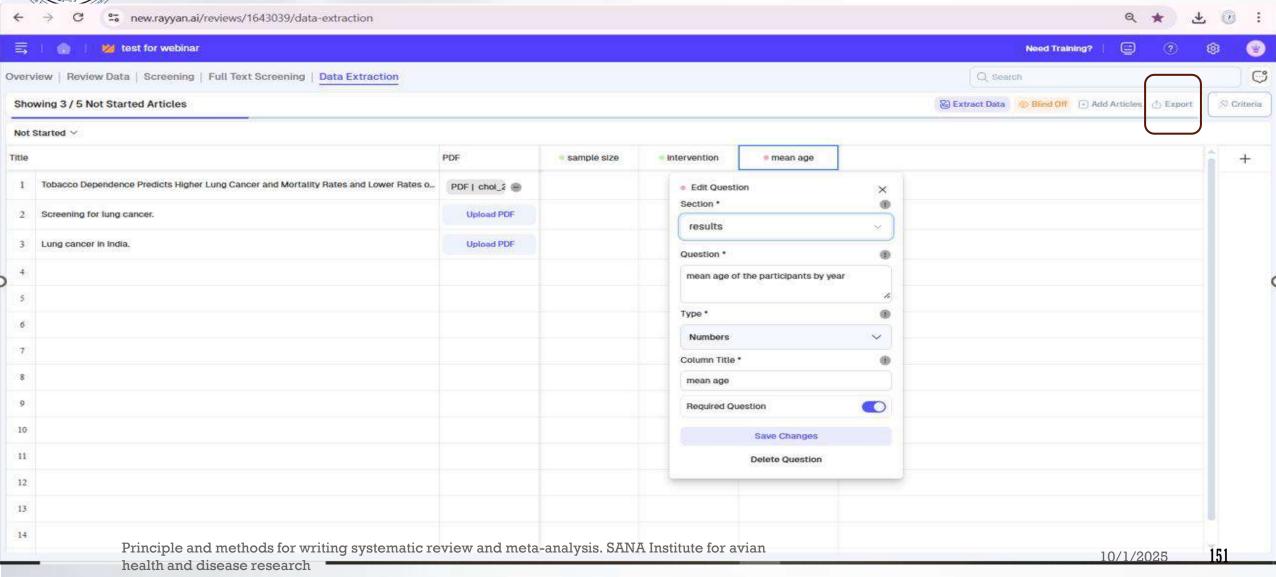


ITEMS SITUATION

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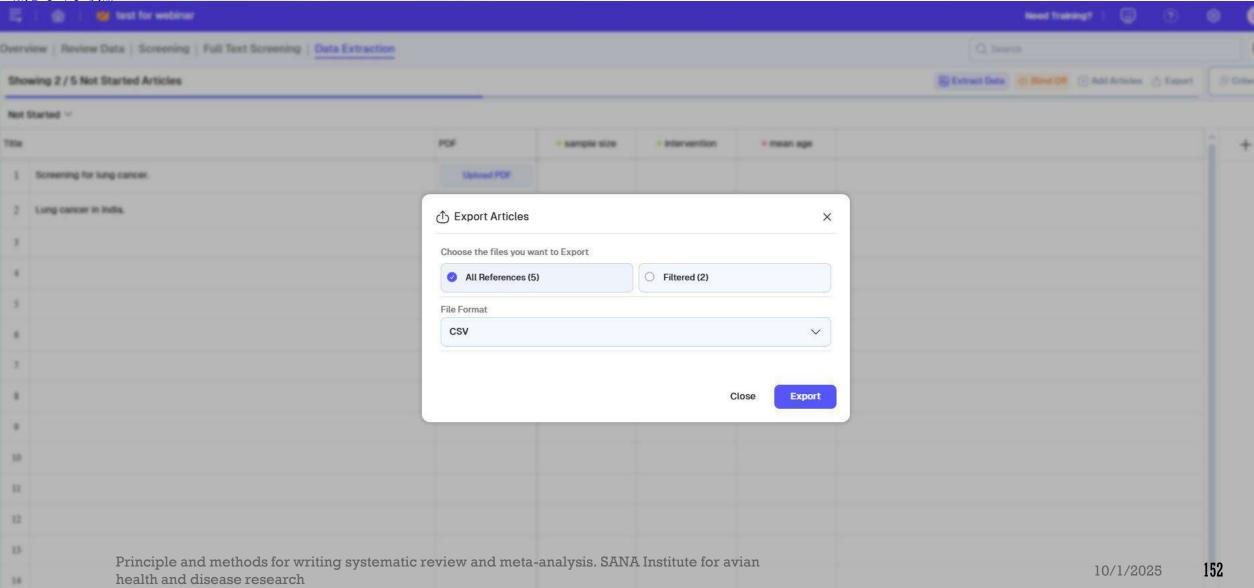


EXPORT THE DATA



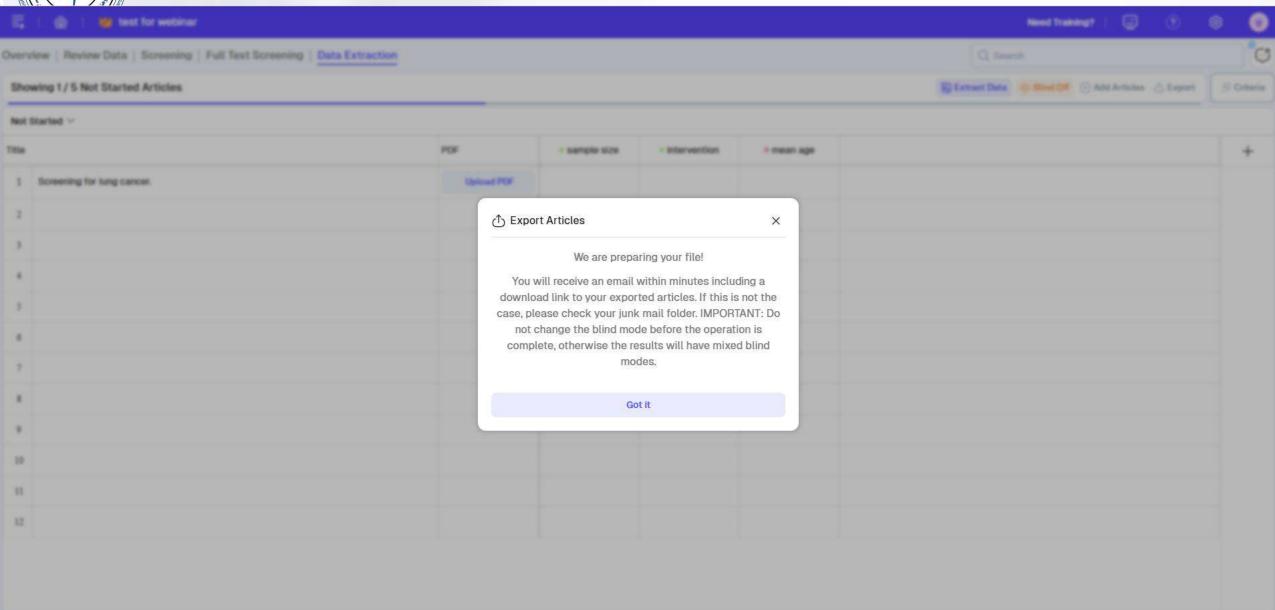


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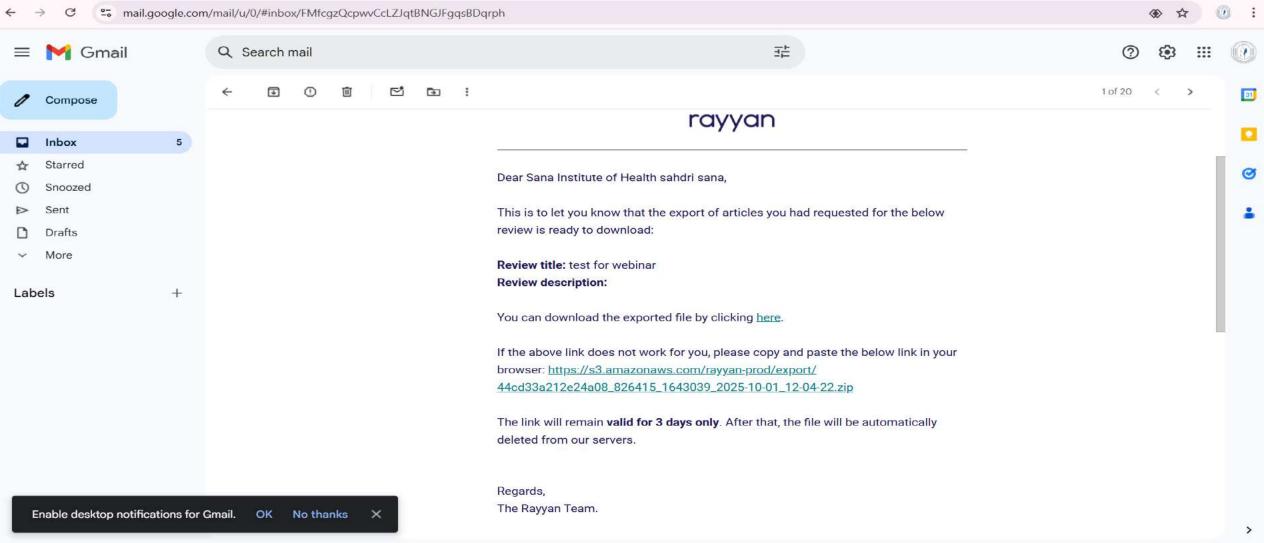
EXPORT THE ARTICLES





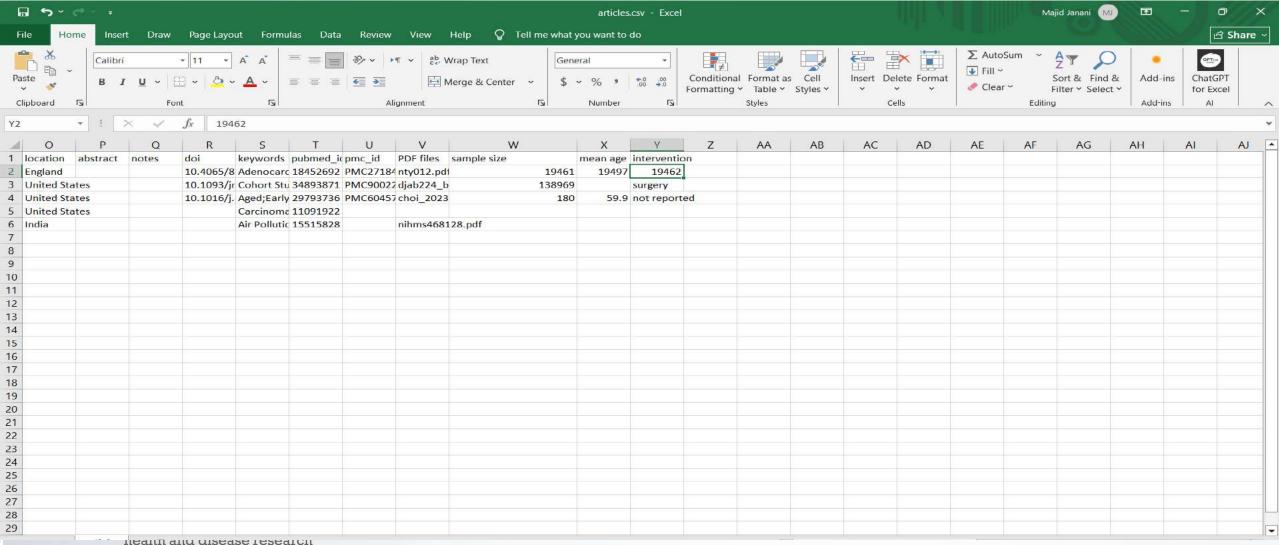
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DOWNLOAD DATA





REPORTED EXCEL





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ARTICLES INCLUDED/EXCLUDED REPORTS

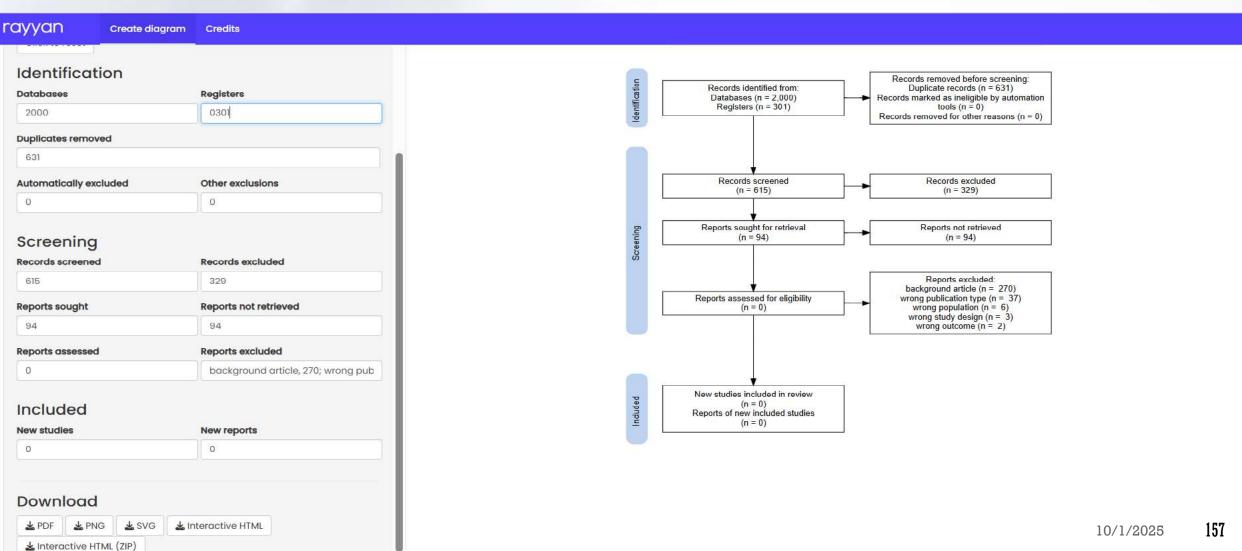


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10/1/2025



ARTICLES INCLUDED/EXCLUDED REPORTS





METHODS: STUDY RISK OF BIAS ASSESSMENT (PRISMA ITEM 11)

- Checklist Item:
- "Specify the methods used to assess risk of bias in the included studies,
- Including:
- details of the tool(s) used,
- how many reviewers assessed
- each study and whether they worked independently,
- and if applicable, details of automation tools used in the process".



PURPOSE OF RISK OF BIAS ASSESSMENT:

- This section explains how the risk of bias in individual studies was evaluated.
- The goal is to assess the quality of the studies included in your review, identifying potential biases that might affect the findings.
- Bias could arise from various factors such as poor randomization, incomplete outcome reporting, or funding sources influencing study results.



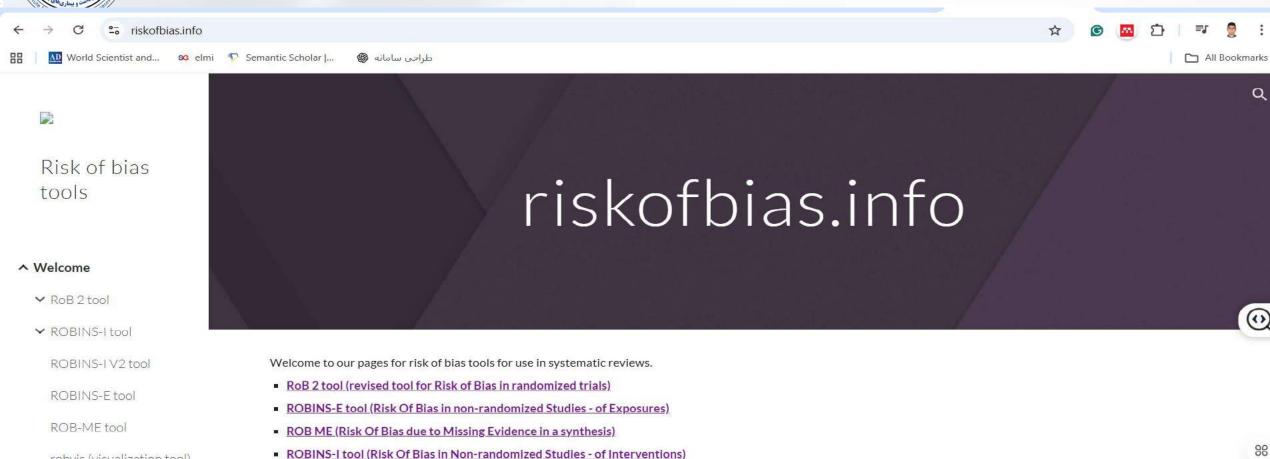
KEY ELEMENTS TO REPORT:

- 1. **Risk of Bias Tools**: Specify the tool(s) used to assess risk of bias (e.g., Cochrane Risk of Bias Tool, ROBINS-I for non-randomized studies).
- 2. **Reviewers**: State how many reviewers assessed the risk of bias for each study and whether they worked independently.
- 3. **Disagreements**: Describe how disagreements between reviewers were resolved (e.g., through discussion, third reviewer).
- 4. **Automation Tools**: Mention if any software tools (e.g., Covidence, RevMan) were used to assist with the risk of bias assessment.



robvis (visualization tool)

RISK OF BIAS TOOLS



robvis (visualization tool for risk of bias assessments in a systematic review)



EXAMPLE

Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1a: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options		
1a.1 Was the allocation sequence random?		Y/PY/PN/N/NI		
1a.2 Was the allocation sequence concealed until clusters were enrolled and assigned to interventions?		Y/PY/PN/N/NI		
1a.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y/PY/PN/N/NI		
Risk-of-bias judgement		Low / High / Some concerns		
Optional: What is the predicted direction of		NA / Favours experimental /		
bias arising from the randomization process?		Favours comparator / Toward null /Away from null / Unpredictable		



METHODS: DATA COLLECTION PROCESS (PRISMA ITEM 9)

Checklist Item:

- "Specify the methods used to collect data from reports,
- including how many reviewers collected data from each report,
- whether they worked independently,
- any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process."



KEY ELEMENTS TO REPORT:

- Data Extractors: State how many reviewers were involved in the data extraction process and whether they worked independently.
- Consistency: Mention if a standardized data extraction form (manual or electronic) was used.
- **Verification:** Describe how extracted data were checked for accuracy (e.g., cross-checking by a second reviewer).
- Contacting Authors: Note whether you contacted study investigators for missing or unclear data.
- Automation Tools: Specify if any software tools (e.g., Covidence, Rayyan, Excel spreadsheets, DistillerSR) were used to assist in data collection



METHODS: EFFECT MEASURES (PRISMA ITEM 12)

Checklist Item:

- "Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference)
 used in the synthesis or presentation of results."
- Purpose: Effect measures describe how the results of individual studies were quantified and compared.



KEY ELEMENTS TO REPORT:

- Primary Outcomes: For each outcome, state the exact measure used (e.g., risk ratio, odds ratio, mean difference).
- **Secondary Outcomes**: Provide effect measures for additional outcomes of interest (e.g., survival rate, antibody titers).
- Precision: Indicate how precision was reported, typically with 95% confidence intervals (CI) or credible intervals (for Bayesian analyses).
- Consistency: If different studies reported outcomes in different ways (e.g., some used odds ratios, others relative risk), describe how you standardized them for comparison.



METHODS: SYNTHESIS METHODS (PRISMA ITEMS 13A-13F)

- 13a: Explain how studies were chosen for each synthesis.
- 13b: Describe how missing or incompatible data were handled.
- 13c: Explain how results were tabulated or visualized.
- 13d: Detail **how results were synthesized** (model, heterogeneity, software).
- 13e: Report how heterogeneity was explored (subgroups, meta-regression).
- 13f: Mention sensitivity analyses for robustness



13A. DECIDING WHICH STUDIES WERE ELIGIBLE FOR EACH SYNTHESIS

• How to Report:

- Tabulate study characteristics (e.g., intervention type, outcome measures).
- Compare against your planned groups (from eligibility criteria).

Example (Veterinary CPV Vaccination Review):

- RCTs comparing monovalent CPV vaccines with placebo contributed to the primary infection incidence analysis.
- Studies reporting **antibody titers** only were included in the *immunogenicity synthesis*.



METHOD, STUDY SELECTION:

Study selection

The study selection process involved multiple stages, including duplicate elimination, screening, eligibility assessment at full-text assessment, and selection for review. Database search results were imported into End-Note version×9 at initial screening. Duplicates were identified and removed. Two independent reviewers (Z. A, and K. P) screened the remaining records based on titles and abstracts. Studies that did not meet the inclusion criteria were excluded at this stage. Two independent reviewers evaluated and reviewed full-text articles of potentially relevant studies (Z. A, and K. P). Any disagreements regarding study eligibility were resolved through discussion with the third reviewer to make the final decision.



13B. PREPARING DATA FOR PRESENTATION/SYNTHESIS

• How to Report:

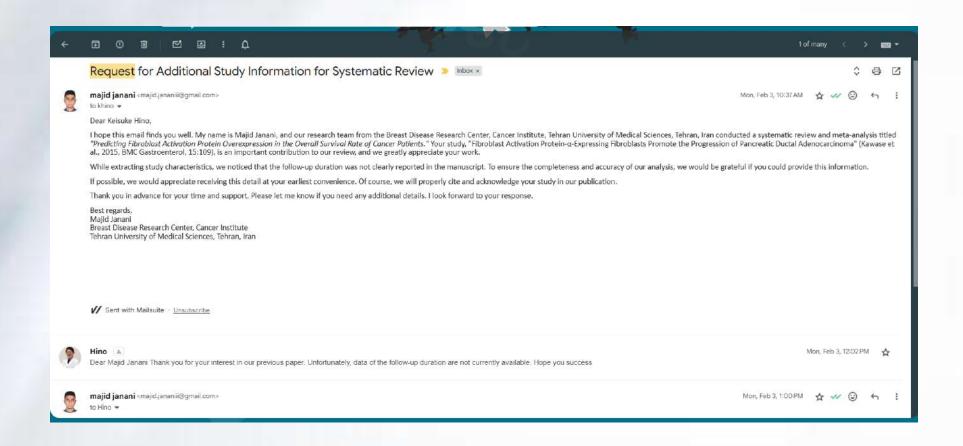
- Describe handling of missing data (e.g., imputing standard deviations).
- Note any data conversions (e.g., converting antibody titers from log scale to linear).

• Example:

- If a study reported mean **follow up by month**, we can synthesis and **convert all data to year+-Sd.**
- When outcome data were missing, attempts were made to **contact study authors**; if unsuccessful, the study was excluded from meta-analysis but included in narrative synthesis



EXAMPLE OF CONTACT STUDY AUTHORS





CALCULATE OR BY NUMBER OF PATIENTS

	Cases		Controls		
	N	%	N	%	
Smoking pattern ^c					
Non-filter	102	32.2	35	13.8	
Ex-smoker	50	15.8	87	34.3	
Filter	165	52.1	132	52.0	
Type of tobacco					
Only blond	8	2.5	26	10.2	
Black/both types	309	97.5	228	89.8	
Total	317	100	254	100	

a Adjusted for age (categorized as in Table 1), socioeconomic level (categorized as I–II, III, IVa, IV variable in the Table.

b Adjusted for age (categorized as in Table I), socioeconomic level (categorized as I-II, III, IVa, IVband for the other variable in the Table.

^c Smoking pattern: ex-smoker (>5 years since cessation), filter (exclusive filter cigarette use during



13C. TABULATING/DISPLAYING RESULTS

• Purpose: Readers should easily see individual study results before synthesis.

• How to Report:

Describe the methods used (tables, forest plots, summary of findings tables).

• Example:

• A **Summary Table** was created to display study characteristics and outcomes (sample size, intervention, effect estimate).



EXAMPLE



Table 1 Characteristics of the included studies in the systematic review

First author name (year)	Country	Follow up duration	Sample size	Mean age	Gender	Cancer type	Tumor stage	Patients under treatment	FAP detection method, Cut off of FAP	Number of patients with high FAP level	Main results
Ariga, N. (2001) [41]	Japan		112			Breast cancer		1271	IHC is focally positive (10%), positive (10% to 50%), or strongly positive (50%)	61	Higher expression of FAP/ seprase in invasive ductal carcinoma cases is associated with longer OS and DFS Multivariate analysis has shown FAP/seprase expression as an independent prognostic factor for survival
_	Germany and method d disease re		77 g systematic :	64.6 (Mean), 65.2 (Median), Range (37.6–82.9)	(female)	Lung cancer A Institute fo			IHC, negative (score 0) = 0%; low (score 1) = 1-10%; moderate (score 2) = 11-50%; high (score 3) = > 50%	46	Two-year OS was 51.7% in the high FAP expression compared to 29.6% in the low expression (cutoff: 95 counts; p=0.012; HR: 1.93; 95%)/ CF:200263.24). Median OS in high FAP



13D. SYNTHESIZING RESULTS

- Purpose: Explain how results were combined polled across studies.
- How to Report if a meta-analysis was performed:
 - Specify the model (fixed-effect vs. random-effects).
 - Report heterogeneity methods (I² statistic, chi-square test).
 - Mention the software used (RevMan, STATA, R).

• Example:

- A random-effects model was used due to expected variability in vaccine types and populations.
- Heterogeneity was assessed using I²; values >50% were considered moderate to high heterogeneity.
- Analyses were performed using RevMan 5.4 software.



13E. EXPLORING CAUSES OF HETEROGENEITY

- **Purpose**: If results vary, explain how you explored the reasons.
- How to Report:
- Subgroup analyses (e.g., by age group, vaccine type).
- Meta-regression (if enough studies).
- **Example:**
- Subgroup analyses compared puppies vs. adult dogs to assess whether age influenced vaccine effectiveness.
- Subgroup analyses also compared monovalent vs. combination vaccines

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13F. SENSITIVITY ANALYSES

- Purpose: Check how robust your findings are.
- How to Report:
- Describe analyses excluding certain studies (e.g., low-quality studies, small sample sizes) to see if results change.

• Example:

- Sensitivity analysis was performed by excluding studies at high risk of bias. Results remained consistent, strengthening confidence in the findings.
- Another sensitivity analysis excluded studies with fewer than 20 animals per group.



EXAMPLE

Statistical analysis

After data extraction, data were synthesized for meta-analysis. In the first step, we standardized variable units across studies. Besides, all reported HR were adjusted for the hazards of the high FAP- α group compared to the low FAP- α group based on study reports. Then, we took the logarithm of the HRs along with their 95% confidence intervals (CIs) due to the asymmetry in the HR range [13]. The primary method involved pooling HRs for overall survival. The effect size was calculated by fixed-effect and random-effects models based on the between-study variability [14].

The homogeneity and heterogeneity among studies were assessed by Cochran's Q test and I^2 statistics that quantify the percentage of total variation due to heterogeneity rather than chance. For the categorization of I^2 , an I^2 value of 25%, 50%, and 75% was defined to indicate low, moderate, and high levels of heterogeneity, respectively [15]. In addition, Begg's [16] and Egger's [17] tests were used to detect publication bias, and the funnel plot was reported as a visual representation of potential asymmetry [18]. Moreover, the Trim and Fill method was used to estimate and adjust for missing studies. In cases of heterogeneity ($I^2 \ge 50\%$ and significant Q test P-value) in studies, sensitivity analysis was conducted to assess to the conductivation of the property of a sensitivity analysis was conducted to assess the conductivation of the property of the property of the conductivation of the property of



METHOD: REPORTING PUBLICATION BIAS ASSESSMENT (PRISMA ITEM 14), CERTAINTY ASSESSMENT (PRISMA ITEM 15)

Checklist Item:

"Describe any methods used to assess risk of **publication bias** due to missing results in a synthesis (arising from reporting biases)."

• Why publication bias assessed?

- Studies with *negative or null results* are not published ("publication bias").
- Only selective outcomes from a study are reported ("outcome reporting bias").

• Why It Matters:

• If not addressed, reporting bias can inflate the perceived effectiveness of an intervention and mislead conclusions.



HOW TO ASSESS AND REPORT THAT

- Statistical Methods: Describe how you checked for reporting bias across studies.
 - Funnel plots can reveal asymmetry suggestive of bias.
 - Egger's test or Begg's test can be applied for small-study effects.
- **Protocol Comparison**: If protocols or trial registrations exist (e.g., ClinicalTrials.gov), compare planned vs. reported outcomes.
- Sensitivity Analyses: Report whether excluding small or lower-quality studies changed conclusions.
- **Automation Tools:** Mention if software (e.g., RevMan, STATA, R packages like metafor) was used to generate funnel plots or run bias tests.
- Certainty assessment: Describe any methods used to assess confidence interval and weight of the studies



RESULTS: STUDY SELECTION (PRISMA ITEM 16A & 16B)

- 16a. Search and Selection Results
- Purpose: Report what happened after you conducted your search how many records you found, how many were excluded, and how many studies were finally included.
- How to Report:
 - Present the numbers at each stage:
 - Records identified (from databases, registers, websites).
 - Records after duplicates removed.
 - Records screened by title/abstract.
 - Full-text reports assessed for eligibility.
 - Studies included in the final review.
 - Ideally, show this in a **PRISMA flow diagram** for clarity to visually show selection process
- 16b. Excluded but Relevant-Looking Studies
- **Purpose**: Some studies *looked eligible* but were excluded after closer inspection. It is important to cite them and explain why.
- **How to Report**: Provide a list (often in a table) of excluded studies with clear reasons.

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EXAMPLE

Results

General data

Figure 1 shows that 5,757 articles were included in the first search for this systematic review. In the next step, 513 studies were identified as duplicates. Following the evaluation of titles, abstracts, and keywords, 4,371 articles were excluded due to irrelevant patient populations (n=2,896), exposures (n=864), outcomes (n=589), or study design (n=22). Furthermore, 873 articles that initially met the inclusion criteria were re-evaluated with full-text assessment, 41 articles were included in this systematic review, and 25 studies were considered in this meta-analysis. Table 1 presents the characteristics of the included articles.

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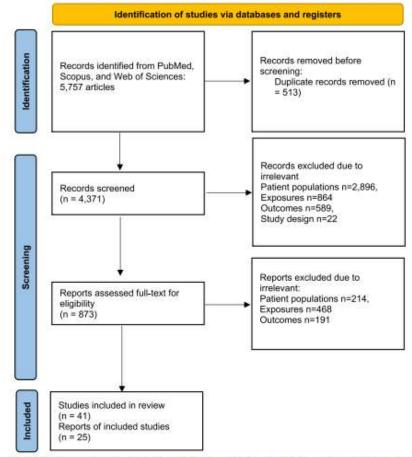


Fig. 1 PRISMA flowchart illustrating the selection process of studies, from initial identification (5,757 articles) to final inclusion in the systematic review (41 articles) and meta-analysis (25 studies)



RESULTS: STUDY CHARACTERISTICS (PRISMA ITEM 17)

Checklist Item:

- "Cite each included study and present its characteristics."
- Purpose: Once you've selected the studies, you need to give readers a clear picture of what they look like.
- This allows comparison between studies and helps readers judge whether the findings are applicable to their context.



WHAT TO INCLUDE:

- Citation details: Author, year, journal.
- Study design: RCT, cohort, case-control, cross-sectional, etc.
- **Population**: Species, breed, age, sex, sample size.
- **Intervention(s)**: Type of vaccine/treatment, dose, schedule.
- Comparator(s): Placebo, no treatment, alternative intervention.
- Outcomes measured: Infection incidence, antibody response, survival, etc.
- **Setting**: Country, clinical vs. laboratory conditions.



EXAMPLE

Systematic review

Table 1 shows the study characteristics. The studies were published between 2001 and 2024. The sample size was 908 (min=31, max=939). Among the reviewed articles, all of them were conducted in cohort design, and 16 studies had sample sizes of less than 100 participants. There were 17 studies between 101 and 200 participants, 2 studies between 201 and 300 participants, and 6 studies with sample sizes of more than 300 participants. The included studies were published in China (18 studies) [9, 19–33], South Korea (7 studies) [34–40], Japan (5 studies) [41–45], Germany (3 studies) [46–48], the USA (2 studies) [49, 50]. Other countries, Switzerland [51], Spain [52], Sweden [53], Egypt [54], Brazil [55], and Taiwan [56], were each study 1.

The mean/median age of participants was distributed between 51 and 70 years old, and cancer types of participants included lung cancer (7 studies), breast cancer (6 studies), colorectal cancer (5 studies), ovarian cancer (5 studies), gastric cancer (4 studies), pancreatic cancer (3 studies), oral squamous cell carcinomas (2 studies), rectal cancer (2 studies), bladder cancer (2 studies), hepatocarcinoma (2 studies), ampullary carcinoma (1 study), esophageal cancer (1 study), and nasopharyngeal carcinoma (1 study) (Table 1).

Surgical interventions were the most common treatment, among 23 studies that described treatment; 10 studies just investigated surgery as treatment [19, 24, 27, 30, 31, 38, 40, 53, 54, 57], 9 studies combined surgery and chemotherapy [23, 28, 33, 42, 43, 45, 47, 48, 52] and chemotherapy-only treatments were observed in 4 studies [25, 49, 50, 56]. In addition, 41 studies reported the FAP-α detection method. All of the interstation register and the studies and the station of the interstation register and the station of the interstation method.

Principle and methods for writing systematic reviewends meta-analysis. SANA Institute foodvire to chemistry as health and disease research an assessment method of FAP-a expression level, and



RESULTS: RISK OF BIAS IN STUDIES (PRISMA ITEM 18)

- Checklist Item:
- Report assessments of risk of bias for each included study.
- Purpose: This section summarizes how much confidence we can place in the individual study results.
- The risk of bias assessment (described earlier in Methods, **Item 11**) is now presented for each included study.



COMMON TOOLS:

- Cochrane RoB 2.0 (for randomized controlled trials).
- ROBINS-I (for observational studies).

Domains typically assessed:

- Randomization / selection bias.
- Allocation concealment.
- Blinding (participants, personnel, outcome assessors).
- Incomplete outcome data.
- Selective reporting.
- Other sources of bias (e.g., funding).



HOW TO REPORT:

- Text Summary: Describe overall risk of bias patterns across studies.
- Tables: Present study-level judgments (low / some concerns / high risk).
- Figures: Traffic light plots or bar charts are highly recommended for teaching and publication.



PUBLICATION BIAS, HOW TO REPORT?

TABLE 2 Quality assessment of the included studies

F:	Item number on the checklist											Total			
First author	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Byrling et al. (2020) (15)	1	1	1	1	1	1	1	1	1	0	1	1	NR	1	12
Chen et al. (2018) (17)	1	1	1	1	1	1	1	1	1	0	1	1	NR	1	12
Coto-Lierena et al. (2020) (18)	1	1	1	1	1	1	1	1	1	0	1	0	NR	0	10
Errarte et al. (2016) (19)	1	1	1	1	1	1	1	1	1	0	1	0	NR	0	10
Gao et al. (2017) (20)	1	1	1	1	1	1	1	1	1	0	1	0	NR	0	10
Ha et al. (2014) (21)	1	1	1	1	1	1	1	1	1	0	1	1	NA	1	12
Henry et al. (2007) (37)	1	1	1	1	1	1	1	1	1	0	1	1	NR	1	12
Higashino et al. (2019) (22)	1	1	1	1	1	1	1	1	1	0	1	1	NR	1	12
Ma et al. (2017) (26)	1	1	1	1	1	1	1	1	1	0	1	0	NA	0	10
Son et al. (2019) (30)	1	1	1	1	1	1	1	1	1	0	1	0	NA	1	11
Song et al. (2016) (31)	1	1	1	1	1	1	1	1	1	0	1	0	NR	1	11
Wen et al. (2019) (34)	1	1	1	ĭ	1	1	1	1	1	0	1	1	NR	1	12
Yuan et al. (2013) (38)	1	1	1	1	1	1	1	1	1	0	1	1	NR	1	12
Zhang et al. (2015) (35)	1	1	1	1	1	1	1	1	1	0	1	0	NR	1	11
Zou et al. (2018) (36)	1	1	1	1	1	1	1	1	1	0	1	1	NR	1	12

2.3 Publication quality assessment

We evaluated the quality of the studies by employing the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies from the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH) (7), which is suitable for risk of bias assessment of cohort and case-control studies (8). This is a standardized and structured tool consisting of 14 criteria that include aim description (item 1), study population description (item 2), participation rate (item 3), homogeneity of study population (item 4), sample size and power (item 5), exposure measurement (item 6), adequate timeframe (item 7), varied exposure levels (item 8), clear exposure measures (item 9), repeated exposure assessment (item 10), clear outcome measures (item 11), blinding of outcome assessors (item 12), loss to follow-up

3.2 Quality assessment

The quality assessment of the included studies showed a mean score of 11.07, with the highest score being 12 and the lowest score being 10. Considering that the maximum score possible on the checklist was 14, the findings suggest that the overall quality of the studies was within the range of fair to acceptable quality (Table 2).

10/1/2025



PUBLICATION BIAS, HOW TO REPORT?



Study (first author)	Group Compara hiliry	Exposur a Assuss mont Consist othery	Exposure Measure ment Validity	Confinent sters (dontifie st	Continu ndur Control Strategi es.	Outco me- firm at Boseli me	Outcome Measure more Validity	Fuffew -up Durati on Adoqu acy	Follow- up Comple tion	Handli ug of Incomp lete Follow -up	Appropriat eness of Statistical Analysis
Arign, N. (2001) (42)		Î	1	1							
Borchert, S. (2023) (47)											
Cabrette, J. (2019) (53).											
Chén, L. (2018) (19)				i i					i i		
Jiang, K. (2023) (22)											
Jung, Y.Y. (2015) (36)	2		0		3 1						2
Kawase, T. (2015) (43)											
Kripper, K. (2023) (48)			Ĭ								
Lee, P. J. (2022) (57)											
Li, F. (2020) (23)											
Li, M. (202m)(23)	9		9		1			2			
Lise, Y. (2013) (24)											
Lyu, S.I. (2024) (49)											
Moreso- Ruiz, P. (2021) (54)											
Nam, V. (2022) (39)	3										
Rosg, X. X. (2022) (25)											
Son. G.M. (2019) (41)											
Song, Z. (2016) (27)								1			
Telogi, K. (2023) (45)				1							
Tong, Y. (2022) (28)	3		8			ij					
Waki, Y. (2023) (46)											
Wen, X. (2017) (30)											
Wen, Z. (2019) (58)											
Zhuo, Z. (2023) (33)											
Zou, B. (2018) (34)	4	8	4	9	9 1	- 0		6		2	

🔲: Yes, 💻 No, 🔼 Unclear

Risk of bias assessment

The risk of bias was assessed for studies included in the meta-analysis. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist was used for risk of bias assessment and was designed explicitly for cohort studies. This tool evaluates key methodological aspects, including study design, exposure and outcome measurement validity, confounding control, and completeness of follow-up. Based on the checklist guideline, each parameter was classified as Yes (low risk), No (high risk), Unclear (insufficient data), or Not Applicable [12].

Risk of bias assessment

The risk of bias assessment showed that most studies had a low risk of bias in group comparability, exposure measurement, and outcome reliability. However, a high risk of bias was observed in confounder control and follow-up completeness, with several studies lacking proper adjustments or having incomplete follow-up data and unclear risk in handling missing data and follow-up sufficiency (Table 2).



RESULTS: RESULTS OF INDIVIDUAL STUDIES (PRISMA ITEM 19)

Checklist Item:

- "For all outcomes, present, for each study:
- (a) summary statistics for each group (where appropriate) and
- (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots."

• Explanation:

 Purpose: Readers should see the raw study-level findings before you combine them in synthesis or meta-analysis

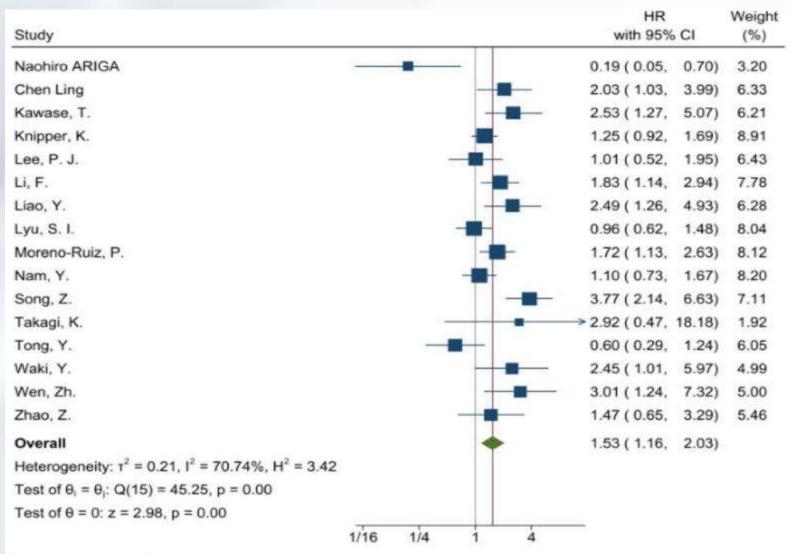


VISUAL PRESENTATION:

- Forest plots: Useful for comparing effect estimates and confidence intervals across multiple studies.
- Bar charts / scatter plots: Helpful for outcomes like antibody titers over time



FOREST PLOT



Random-effects REML model



20A. SUMMARIZE CHARACTERISTICS

- Summarize their designs, interventions, outcomes, and populations.
- Provide an overview of their risk of bias for example, whether most were randomized trials or observational studies, and whether common bias issues were present (e.g., lack of blinding, incomplete reporting).
- The purpose is to give context before presenting pooled results.



20A. SUMWARIZE CHARACTERISTICS

Systematic review

Table 1 shows the study characteristics. The studies were published between 2001 and 2024. The sample size was 908 (min=31, max=939). Among the reviewed articles, all of them were conducted in cohort design, and 16 studies had sample sizes of less than 100 participants. There were 17 studies between 101 and 200 participants, 2 studies between 201 and 300 participants, and 6 studies with sample sizes of more than 300 participants. The included studies were published in China (18 studies) [9, 19–33], South Korea (7 studies) [34–40], Japan (5 studies) [41–45], Germany (3 studies) [46–48], the USA (2 studies) [49, 50]. Other countries, Switzerland [51], Spain [52], Sweden [53], Egypt [54], Brazil [55], and Taiwan [56], were each study 1.

The mean/median age of participants was distributed between 51 and 70 years old, and cancer types of participants included lung cancer (7 studies), breast cancer (6 studies), colorectal cancer (5 studies), ovarian cancer (5 studies), gastric cancer (4 studies), pancreatic cancer (3 studies), oral squamous cell carcinomas (2 studies), rectal cancer (2 studies), bladder cancer (2 studies), hepatocarcinoma (2 studies), ampullary carcinoma (1 study), esophageal cancer (1 study), and nasopharyngeal carcinoma (1 study) (Table 1).

Surgical interventions were the most common treatment, among 23 studies that described treatment; 10 studies just investigated surgery as treatment [19, 24, 27, 30, 31, 38, 40, 53, 54, 57], 9 studies combined surgery and chemotherapy [23, 28, 33, 42, 43, 45, 47, 48, 52] and chemotherapy-only treatments were observed in 4 studies [25, 49, 50, 56]. In addition, 41 studies reported the FAP- α detection method. All of the included studies employed immunohistochemistry as an assessment method of FAP- α expression level, and



20B. STATISTICAL SYNTHESES

- Present the results of any quantitative syntheses (meta-analyses).
- Report the summary effect size (e.g., risk ratio, odds ratio, mean difference) with precision estimates such as confidence or credible intervals.
- Include measures of heterogeneity (e.g., I^2 , τ^2 , Chi-square test).
- If groups were compared, state the direction of effect (e.g., intervention group performed better, worse, or no difference).
- If no meta-analysis was possible, describe how findings were synthesised narratively.



EXAMPLE

Table 3 Pooled hazard ratios (HRs) for overall survival, disease-free survival (DFS), lymph node metastasis (LNM), and distant metastasis (DM) based on high FAP expression compared to low FAP expression

Associated factor	Number of studies	Sample size	HR	95% Confidence Interval	P-Value	l ² (%)
Crude FAP (univariable)	18	2452	1.486	(1.194—1.847)	< 0.001	74.31
Adjusted FAP (Multivariable)	16	2550	1.534	(1.158—2.034)	0.003	70.74
DFS	6	1018	1.361	(0.750—2.469)	0.311	84.30
PFS	2	112	6.619	(5.844, 7.496)	< 0.001	98.93
LNM	12	2341	2.053	(1.603—2.630)	< 0.001	29.26
DM	7	1168	2.630	(1.902—3.637)	< 0.001	20.59



20C. INVESTIGATING HETEROGENEITY

- When study results vary, explain how you explored possible causes.
- This can be done with subgroup analyses (e.g., by age, intervention type, or setting)
- Or meta-regression (testing whether study-level factors explain differences in results).
- Report what factors were considered, and what the findings showed about variation across studies.



20D. SENSITIVITY ANALYSES

- Sensitivity analyses test the robustness of your conclusions.
- Typical approaches include:
 - Excluding studies judged to be at high risk of bias.
 - Comparing different statistical models (fixed vs. random effects).
 - Handling of studies with missing data or zero events.
 - Running leave-one-out analyses (removing one study at a time to check influence).



EXAMPLE

Table 4 Subgroup analysis of hazard ratios (HRs) based on potential sources of heterogeneity for crude HR, adjusted HR, and disease-free survival

Subgroups	No. of studies	HR (95% of CI)	Heterogeneity I ² (%)	P-value heterogeneity	P-value between subgroups
Survival (crude, based on univariable analys	sis)				
Age					< 0.001
65 or under	4	1.45 (1.05-1.99)	51.65	0.102	
Over 65	6	1.73 (1.05-2.86)	81.91	< 0.001	
Mean follow-up duration					0.013
60 months or lower	4	1.79 (1.28-2.50)	34.92	0.174	
Over 60 month	2	1.01 (1.03-2.00)	0.00	0.420	
Treatment in Participants					< 0.001
Not reported	4	1.43 (0.79-2.59)	87.16	< 0.001	
Participants with treatment	13	1.52 (1.20-1.92)	67.08	0.001	
High FAP %					0.003
50% or under	8	1.40 (0.96-2.05)	68.09)	0.003	
Over 50%	8	1.67 (1.14-2.44)	82.04	< 0.001	
Nodal metastasis in patients					< 0.001
50% or under	7	1.78 (1.29-2.47)	60.91	0.014	
Over 50%	5	1.30 (0.67-2.50)	77.90	0.003	
Cancer type					< 0.001
Gastrointestinal and head & neck cancers*	12	1.53 (1.16-2.03)	69.10	0.002	
Ovarian cancer	1	2.10 (1.23-3.57)	1 -2)	i s	
Pr incipleance methods for writing systematic r	eview and meta-ana	lysis2 8AOVA8In309) te f	or assalt9	< 0.001	
healthand disease research	1	1.68 (0.99-2.85)	1867	=	



SUBGROUP ANALYSIS REPORT EXAMPLE

Subgroup analysis for heterogeneity

A subgroup analysis assessed potential heterogeneity in survival outcomes between the included studies.

The subgroup analysis showed older participants (over 65) had higher HR (HR of age > 65 years = 1.73 vs. HR of age < 65 years = 1.45). Also, studies with 60 months or less follow-up periods reported a higher HR (HR of follow-up≤60 months=1.79 vs. HR of followup > 60 months = 1.01). Studies conducted on untreated participants showed a lower HR (HR for untreated participants = 1.43 vs. HR for treated participants = 1.52). Moreover, studies with more than 50% high FAP-α expression in participants reported higher HR (HR of $\leq 50\% = 1.40$, HR of > 50% = 1.67). The HR was significantly increased in studies in which more than half of the participants had nodal metastases compared to the studies in which less than half had nodal metastases (HR of $\leq 50\% = 1.78$, HR of > 50% = 1.30). In addition, cancer type reported significant heterogeneity and various HR were reported between cancer type subgroups (Table 4).

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Heterogeneity assessment

The heterogeneity across the studies that examined crude HR with FAP-α was moderate to high, with I²=74.31% and a significant Q-test for heterogeneity (Q=64.68, P=0.00). In addition, studies that reported adjusted analyses ($I^2 = 70.74\%$, Q=45.25, P=0.00), PFS $(I^2 = 98.93\%, Q = 93.41, P < 0.001)$, and DFS $(I^2 = 84.30\%, Q = 93.41, P < 0.001)$ Q=23.44, P=0.001) were statistically significant. However, studies reporting an association between LNM with HR ($I^2 = 29.26\%$, Q=16.89, P=0.11) and DM with HR $(I^2 = 20.59\%, Q = 6.48, P = 0.37)$ showed non-significant heterogeneity (Table 3).



RESULTS: REPORTING BIASES (PRISMA ITEM 21) (PUBLICATION)

 This section showed whether your findings may be affected by reporting biases when not all results are available or selectively reported.

Types of Reporting Bias:

- Publication bias: Studies with positive findings are more likely to be published.
- Outcome reporting bias: Only favorable outcomes within a study are reported, while negative or null results are omitted.
- Selective time-point reporting: Only certain follow-up periods are reported.



WHAT TO INCLUDE:

- Assessment methods used to detect reporting bias. Common approaches:
 - Funnel plots (visual check for asymmetry across studies).
 - Statistical tests (Egger's test, Begg's test).
 - Protocol comparison (e.g., trial registry outcomes vs. published outcomes).

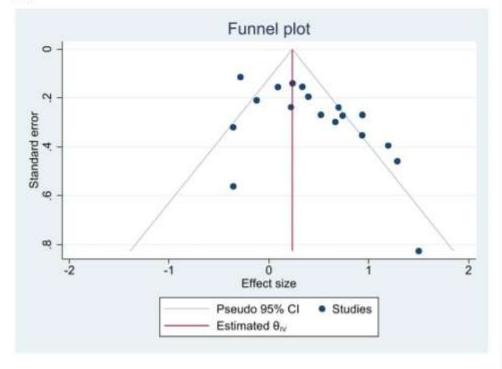


PUBLICATION BIAS ASSESSMENT EXAMPLE

Publication bias

The publication bias assessment for studies that reported crude HR suggests significant small-study effects with the Egger test (beta1 = 2.09, P = 0.009), Begg's test (Kendall's score = 55.00, P = 0.041), and for studies that reported PFS (Egger test beta1 = -18.33, P < 0.001, Begg's test Kendall's score = not assessed due to insufficient observation); however, the trim-and-fill analysis reports that the effect size remains consistent. Also, publication bias assessment showed insignificant publication bias for studies that assessed adjusted HR (Egger test beta1 = -0.18, P = 0.866, Begg's test Kendall's score = 12.00, P = 0.620), for studies that reported DFS (Egger test beta1 = -1.17, P = 0.662, Begg's test Kendall's score = -1.00, P = 1.000), for studies that assessed the association of LNM with HR (Egger test beta1 = -1.35, P = 0.185, Begg's test Kendall's score = -14.00, P = 0.373), and DM with HR (Egger test beta1=1.15, P=0.439, Begg's test Kendall's score=3.00, P = 0.7639) (Fig. 3).







RESULTS: CERTAINTY OF EVIDENCE (PRISMA ITEM 22)

- Even when you have multiple studies and meta-analyses, not all estimates is equally and 100% trustworthy.
- You should to report confidence interval of the estimates (usually 95% CI) even while you import high number of sample size and P-value reported.



DISCUSSION (PRISMA ITEMS 23A-23D)

- 23a. General Interpretation of Results in the Context of Other Evidence
- Here, you interpret your review's findings in light of the broader body of literature.
- Compare your results with previous systematic reviews, meta-analyses, or large primary studies.
- Point out whether your findings are consistent or divergent, and suggest possible reasons.
- Keep the tone **balanced** not just what was found, but how it fits into the bigger picture.



23B. LIMITATIONS OF THE EVIDENCE INCLUDED IN THE REVIEW

- Critically appraise the quality of the included studies:
 - Were they small, underpowered, or poorly reported?
 - Was there risk of bias (e.g., poor randomization, lack of blinding)?
 - Were the populations, interventions, or outcomes heterogeneous?
 - Was there evidence of publication bias?
- The goal is to report the weaknesses in the available evidence base, not <u>your own</u> methods yet.



23C. LIMITATIONS OF THE REVIEW PROCESSES USED

- Here, reflect on your own review methods:
 - Were there language restrictions (e.g., only English studies included)?
 - Were databases limited (e.g., missed grey literature, conference proceedings)?
 - Was screening or data extraction performed by a limited number of reviewers?
 - Did you face time/resource constraints that may have influenced comprehensiveness?
- Transparency about process limitations helps readers judge reliability and validity of your study



23D. IMPLICATIONS FOR PRACTICE, POLICY, AND FUTURE RESEARCH

Practice:

• How can your findings be applied in clinical, veterinary, or public health practice?

Policy:

• Are there policy-level recommendations (e.g., vaccination programs, screening guidelines)?

Future Research

 Identify knowledge gaps — e.g., need for more RCTs, better standardization of outcomes, longer follow-ups.



REGISTRATION AND PROTOCOL (PRISMA ITEMS 24A-24C)

- 24a. Provide Registration Information for the Review
- 24b. Indicate Where the Review Protocol Can Be Accessed
- 24c. Describe and Explain Any Amendments to the Registration or Protocol

24A. PROVIDE REGISTRATION INFORMATION FOR THE REVIEW

- 24a. Provide Registration Information for the Review
- It's essential to be transparent about whether and where your review was **pre-registered**.
- Why Register?: Pre-registration improves transparency and reduces risk of selective reporting or outcome switching. It allows others to track your research methods and ensure you're following your original plan.

• What to Include:

- Register Name: Name of the platform where the review was registered (e.g., PROSPERO, Cochrane Database).
- Registration Number: The unique identification number assigned when the review was registered (e.g., CRD42019112345).

• Example:

• "This systematic review was registered with PROSPERO (registration number: CRD42020123456)." Principle and methods for writing systematic review and meta-analysis. SANA Institute for avian



24B. INDICATE WHERE THE REVIEW PROTOCOL CAN BE ACCESSED

- Provide the location where others can access the detailed protocol of your review.
- This enhances transparency and helps prevent issues like outcome reporting bias.

• What to Include:

- Location/URL: Direct readers to the repository where your protocol is available (e.g., PROSPERO website, institutional repository).
- State if No Protocol: If you did not prepare a protocol, explicitly mention this.

• Example:

- "The protocol for this systematic review is available at PROSPERO (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020123456)."
- "A protocol for this review was not prepared."



REGISTRATION NUMBER REPORT

METHODS

Registration and search strategy

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (online supplemental table 1) and was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42024505533). As per the registered protocol, two researchers (LL and ZL) conducted searches in Ovid MEDLINE, Embase and the Cochrane Central Register of Controlled Trials up to 15 June 2025. The search strategy was developed with assistance from experts at the Sichuan University Library, as detailed in online supplemental table 2. The main search terms included 'heart failure', 'incidence', 'risk' and 'cohort study'.



24C. DESCRIBE AND EXPLAIN ANY AMENDMENTS TO THE REGISTRATION OR PROTOCOL

- If any changes were made after the review was registered or the protocol was written, that **must** be documented and justified.
- This improves transparency by showing whether the review adhered to the original plan and helps others understand why the changes were necessary.

• What to Include:

- Amendments: List the changes made to the original protocol (e.g., changes in eligibility criteria, outcomes assessed).
- Reasons for Changes: Explain why the changes were necessary (e.g., additional relevant studies discovered, data availability issues).
- **Timeline:** When the changes occurred (e.g., date of amendment).



ABSTRACT (PRISMA ITEM 2)

- **Purpose of the Abstract**: The abstract should summarize the essential elements of your systematic review in a concise manner.
- It serves as a **brief overview for the reader** to understand the review's aims, methods, and key findings quickly.



WHAT TO INCLUDE IN THE ABSTRACT:



PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE	•		
Title	1	Identify the report as a systematic review.	
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	
Synthesis of results	6	Specify the methods used to present and synthesise results.	
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	
Interpretation	10	Provide a general interpretation of the results and important implications.	
OTHER			
Funding	11	Specify the primary source of funding for the review.	
Registration	12	Provide the register name and registration number.	



ABSTRACT EXAMPLE

	el.	ABSTRACT	
	e	Objective To identify comorbidities associated with	
	red itic	incident heart failure with preserved ejection fraction	
	ıf	(HFpEF) and quantify their HRs for early risk stratification and prevention.	
	136/	Design PROSPERO-registered (CRD42024505533)	
		systematic review and meta-analysis. Primary analysis prioritised unadjusted HRs; exploratory analysis	
	ıf	incorporated adjusted HRs.	
		Data sources Ovid MEDLINE, Embase and the Cochrane	
	ese	Central Register of Controlled Trials through 15 June 2025	
	1	Eligibility criteria for selecting studies Cohort studies	
	136/	of adults (≥18 years) without prior HF reporting HRs for incident HFpEF-associated comorbidities. Exclusions:	N.
	24	non-English publications, reviews, non-clinical studies an studies without HR data.	(
		Data extraction and synthesis Two reviewers independently extracted data and assessed quality	
		(Newcastle-Ottawa Scale). Random-effects models poole	
		HRs. Heterogeneity was investigated using Galbraith/	
		Baujat plots, meta-regression and subgroup analyses.	
		Publication bias assessed via funnel plots, Egger's and	
a:	r	Begg's tests.	A Institute for
-		33	

Results Among 61 eligible studies, 22 reporting unadjusted HRs formed the primary analysis, identifying five comorbidities with significant incident HFpEF risk: atrial fibrillation (AF) (HR 2.92, 95% CI 1.94 to 4.37, I²=86.6%), hypertension (HR 2.28, 95% CI 1.35 to 3.84, I2=96.9%), diabetes (HR 1.88, 95% CI 1.54 to 2.30, I2=58.2%), obesity (HR 1.70, 95% CI 1.45 to 2.00, I2=69.7%) and myocardial infarction (MI) (HR 1.62, 95% CI 1.18 to 2.23, I²=72.1%). Conversely, chronic kidney disease (CKD) (HR 1.44, 95% CI 0.68 to 3.06, I2=86.6%) and cerebrovascular disease (HR 1.72, 95% Cl 0.93 to 3.18, I²=77.2%) showed non-significant associations. Exploratory analysis integrating unadjusted HRs from primary studies and adjusted HRs from 39 additional studies confirmed these five comorbidities as significant risk factors, with CKD again demonstrating non-significant association.

Conclusion AF, hypertension, diabetes, obesity and MI constitute evidence-based targets for HFpEF risk stratification and preventive management. The CKD-HFpEF association requires validation in larger cohorts.

PROSPERO registration number CRD42024505533.



SUPPORT (PRISMA ITEM 25)

 Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review."

• Explanation:

- This section ensures transparency about any external funding or support for the review.
- It helps to assess whether the findings could be influenced by any external interests.

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s13643-025-02929-6.



WHAT TO INCLUDE:

- **Financial Support:** List any funding sources, such as grants from universities, research councils, or industry sponsors.
- Non-financial Support: Include non-financial contributions, like access to data, databases, or technical support (e.g., software access).
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• What to Include:

- Financial Conflicts: Any financial interests, such as funding from companies that may benefit from the review's findings.
- Non-financial Conflicts: Any professional or personal relationships that could be seen as a conflict of interest (e.g., authors having close ties with organizations that may be impacted by the review's conclusions).
- Blank Declaration: If the second of the secon

Competing interests



AVAILABILITY OF DATA, CODE, AND OTHER MATERIALS (PRISMA ITEM 27)

- "Report which of the following are publicly available and where they can be found, this include:
- template data collection forms
- Data extracted from included studies
- data used for all analyses
- analytic code
- any other materials used in the review.



WHAT TO INCLUDE:

- Data Collection Forms: If you used a standard form to extract data, provide a link or reference to the form.
- Extracted Data: Share the raw data that was extracted from included studies, where possible (e.g., study characteristics, outcome data).
- Analytic Code: If any software or code was used for analysis (e.g., for statistical synthesis), provide access to it.
- Other Materials: Any supplementary materials, such as study protocols, full search strategies, or supplementary analyses.
- Example:

Data availability

The data supporting this study's findings are available on request from the corresponding author.







THANKS FOR YOUR ATTENTION

