

SOLES codeRs

Meta-analysis 1: searching & screening literature

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What is a meta-analysis?

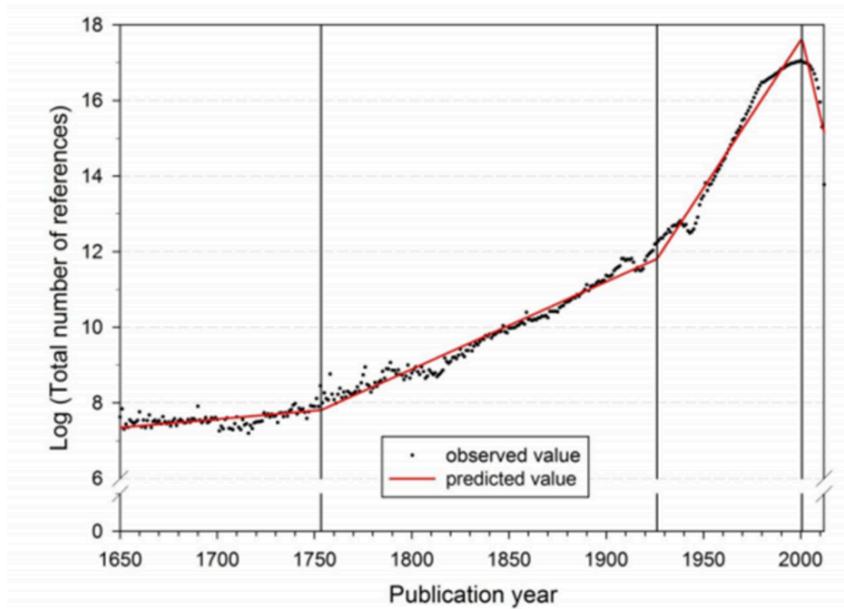
A form of **evidence synthesis**, which entails statistically synthesising the results of related studies to summarise research knowledge, and generate or test new ideas with greater power than any single study.



In its ideal form, it sits atop the ‘evidence pyramid’

Why do we meta-analyses?

Grappling with an ever-increasing evidence base



Thousands of scientists publish a paper every five days

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Scientists are drowning in COVID-19 papers.

Stop the deluge of science research

The increasing pace of human discovery is a curse - we need to rethink what it means to publish the results of research

Why do we do evidence synthesis?

Reconciling conflicting evidence and evaluating reliability.

(see also: calling out bs)

Mini-Review

Potential use of hydroxychloroquine, ivermectin and azithromycin drugs in fighting COVID-19: trends, scope and relevance

R. Choudhary  A.K. Sharma 

Therapeutic potential of ivermectin as add on treatment in COVID 19: A systematic review and meta-analysis

Ivermectin in COVID-19: A meta-analysis

However, this should be inferred cautiously as the quality of evidence is very low. Currently, many clinical trials are on-going, and definitive evidence for repurposing this drug for COVID-19 patients will emerge only in the future.

ICON (Ivermectin in COvid Nineteen) Study: Use of Ivermectin Is Associated with Lower Mortality in Hospitalized Patients with COVID-19

24 Pages • Posted: 21 Aug 2020

Ivermectin: potential candidate for the treatment of Covid 19



Outcomes of Ivermectin in the treatment of COVID-19: a systematic review and meta-analysis

the mean age was 47.5 (SD 9.5) years, and 4283 (58%) were male. Ivermectin was not associated with reduced mortality (logRR: 0.89, 95% CI 0.09 to 1.70, p = 0.04, $I^2 = 84.7\%$), or reduced patient recovery (logRR 5.52 , 95% CI -24.36 to 35.4, p = 0.51, $I^2 = 92.6\%$). All studies had a high risk of bias, and showed a very low certainty of the evidence.

Why do we do evidence synthesis?

Advancing fundamental knowledge



Informing evidence-based applications & policy



Why do we do evidence synthesis?

Personal empowerment and information literacy

The screenshot shows the Cochrane Library website interface. At the top, there is a navigation bar with links for "Cochrane Reviews", "Trials", "Clinical Answers", "About", "Help", and "About Cochrane". To the right of the navigation bar is a search bar with fields for "Title Abstract Keyword" and a magnifying glass icon, along with "Browse" and "Advanced search" buttons. The main content area is titled "Browse by Topic" and features a grid of categories organized by letter (a through w). Each category is a link to a detailed page. The categories include:

Category	Sub-categories
a	Allergy & intolerance
b	Blood disorders
c	Cancer, Child health, Complementary & alternative medicine, Consumer & communication strategies
d	Dentistry & oral health, Developmental, psychosocial & learning problems, Diagnosis
e	Ear, nose & throat, Effective practice & health systems, Endocrine & metabolic, Eyes & vision
g	Gastroenterology & hepatology, Genetic disorders, Gynaecology
h	Health & safety at work, Health professional education, Heart & circulation
i	Infectious disease, Insurance medicine
k	Kidney disease
l	Lungs & airways
m	Mental health, Methodology
n	Neonatal care, Neurology
o	Orthopaedics & trauma
p	Pain & anaesthesia, Pregnancy & childbirth, Public health
r	Reproductive & sexual health, Rheumatology
s	Skin disorders
t	Tobacco, drugs & alcohol
u	Urology
w	Wounds

At the bottom of the page, there is a link "...or Browse by Cochrane Review Group".

Approaches to evidence synthesis

Traditional reviews:

- Haphazard synthesis of literature
- Suffers from selection, discussion, and quality biases
- Not transparent, hence less robust, reproducible

Systematic reviews/meta-analyses:

- ‘Gold standard’
- Exhaustive, comprehensive collation of evidence
- Transparent, reproducible methods & analyses
- Akin to empirical research process

Approaches to evidence synthesis

- *Systematic review or map*
- Comprehensive map and/or critical analysis an evidence base
- Scope: broader
- E.g. What are the effects of land protection on human wellbeing?
- *Meta-analysis*
- Statistical analysis of the results of individual studies
- Scope: narrower
- E.g. What are the non-target effects of neonicotinoid pesticides?

All underlain by a **systematic search**

The meta-analysis pipeline

1: Formulate & refine question

2: Design & execute search

3: Screen results

4: Extract data

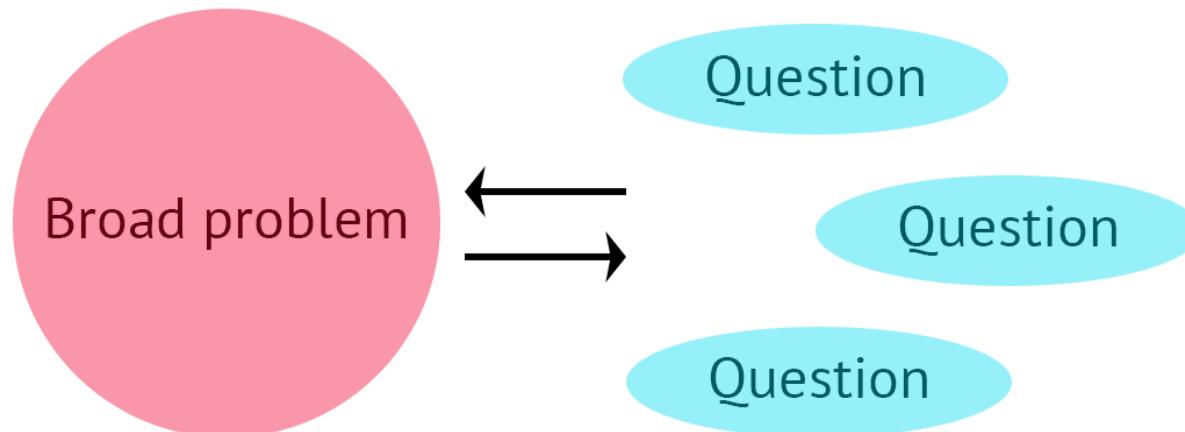
5: Meta-analyse & interpret results

Formulating questions



How do we formulate questions?

- Evidence needs often manifest as a broad, open-framed problem
- Typical initial phase:



How do we formulate questions?

1: Identify broad problem

2: Explore and refine narrow questions

3: Deconstruct and assess suitability of questions for ES (P.I.C.O.S)

Deconstructing and assessing suitability

PICOS

PICOS is a framework to guide thinking, not a set of hard-and-fast rules. It stands for:

- **P**opulation
- **I**ntervention/exposure
- **C**omparator
- **O**utcome
- **S**tudy design

Deconstructing and assessing suitability

- **P**opulation: The unit of study (e.g. ecosystem, habitat, species).
- **I**ntervention/exposure: In eco/evo, any independent variable of interest. Often absent in observational studies.
- **C**omparator: A control, baseline, or means of comparison between groups or timepoints. Often absent in observational studies.
- **O**utcome: The objectives that can be reliably measured (i.e. the dependent variables).
- **S**tudy design: The method of data collection, particularly experimental vs observational designs.

Deconstructing and assessing suitability

What is the effect of neonicotinoid pesticides on pollinator productivity?

- P:
- I:
- C:
- O:
- S:

Deconstructing and assessing suitability

What is the effect of neonicotinoid pesticides on pollinator productivity?

- **P:** Pollinators
- **I:** Neonicotinoid
- **C:** Non-exposed pollinators
- **O:** Productivity
- **S:** Experimental

Deconstructing and assessing suitability

What is the prevalence (ppm) of neonicotinoid pesticides in irrigation runoff?

- P:
- I:
- C:
- O:
- S:

Deconstructing and assessing suitability

What is the prevalence (ppm) of neonicotinoid pesticides in irrigation runoff?

- **P:** Irrigation runoff
- **I:** NA
- **C:** NA
- **O:** Prevalence (ppm) of neonicotinoid pesticides
- **S:** Observational

Systematically searching



Planning a search

Crucial to get right!

Key questions:

- **Where** to search
- **How** to search
- Balance **sensitivity** and **specificity**

Where to search

- Bibliographic databases
 - WoS, Scopus, Pubmed
- Web-based searched
 - Google, Google scholar
- Grey literature
 - Organisational websites
 - Thesis repositories



WEB OF SCIENCE™



EThOS
ELECTRONIC THESES ONLINE SERVICE
Opening access to UK theses



Where to search

Bibliographic databases

- Web of Science
 - Core collection
 - PubMed
 - SciELO
 - Zoological Record
- Scopus
- Agricola
- CAB Abstracts
- Biological Abstracts
- NOT Google Scholar

mean ~7 (2-75) databases

Where to search

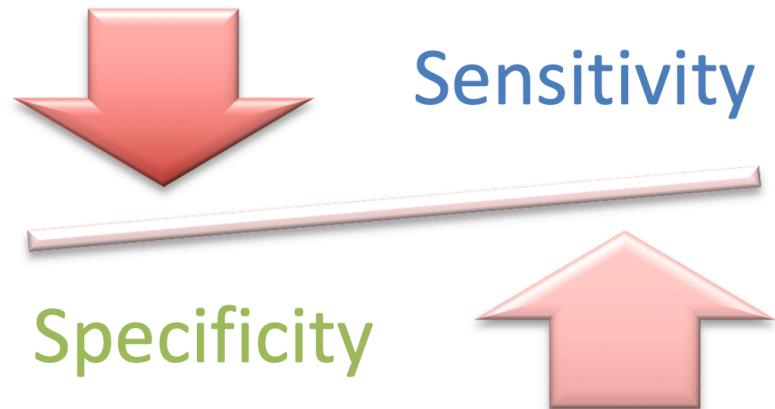
Grey literature

- Preprints
 - bioRxiv
 - arXiv
 - EcoEvoRxiv
- Google Scholar
- Unpublished data
 - Public calls
 - Email researchers
- Theses
 - University repositories
 - Public repositories
- Policy documents
- Biological Abstracts



Designing your search

Searching is always a balance between the *number of results retrieved* and *available resources*



Sensitivity: getting more potentially relevant material (use broad search terms).

Specificity: proportion of captured material that is relevant (narrow search terms).

Designing your search

Establish a **test-set** of studies

- Studies which *you know will be included*
- Informally retrieved from your own reading, experts, etc.
- n = 10+? But may vary greatly.
- Valuable for assessing general feasibility & tractability of meta-analysis, and designing & validating search.

Designing your search

Building a basic search:

- Guided by the review question & PICOS elements
- Databases generally search for keywords in the TITLE, ABSTRACT and KEYWORDS
- Databases often have a range of search options
- Databases use phrasing, Boolean operators (AND, OR, NOT) and nesting differently

Example

How effective is wetland restoration for reducing nitrogen and phosphorus?

Designing your search

How effective is wetland restoration for reducing nitrogen and phosphorus?

- **P:** Wetland
- **I:** Restoration
- **C:** Unrestored/degraded/non-existent wetlands
- **O:** Nitrogen, phosphorus
- **S:** Experimental, observational

Designing your search

A Boolean refresher:

- **OR** terms (synonyms)
 - wetland **OR** bog
- **AND** terms (synonyms)
 - wetland **AND** restoration
- Quotation marks (exact phrases)
 - “wet meadow”
- Wildcards (word variations)
 - phosph* [phosphate, phosphorous]
- **NOT**

Designing your search

How effective is wetland restoration for reducing nitrogen and phosphorus?

Compile synonyms for PIO

Term 1	AND	Term 2	AND	Term 3
wetland*		construct*		nitrogen
OR pond	OR	creat*	OR	phosph*
OR mire*	OR	restor*	OR	nitrate
OR marsh	OR	man*made	OR	TKN
OR fen	OR	flooding	OR	ammoni*
OR "wet meadow"	OR	inundation		
OR riparian	OR	artificial		
OR "flood plain"				
OR reed				

(wetland* OR pond OR mire* OR marsh OR fen OR "wet meadow" OR riparian OR "flood plain" OR reed) AND (construct* OR creat* OR restor* OR man*made OR flooding OR inundation) AND (nitrogen OR phosph* OR nitrate OR TKN OR ammoni)

Designing your search

Test search terms individually for efficacy

Term 1	AND Term 2
wetland*	construct*
OR pond	
OR mire*	
OR marsh	
OR fen	
OR "wet meadow"	
OR riparian	
OR "flood plain"	
OR reed	

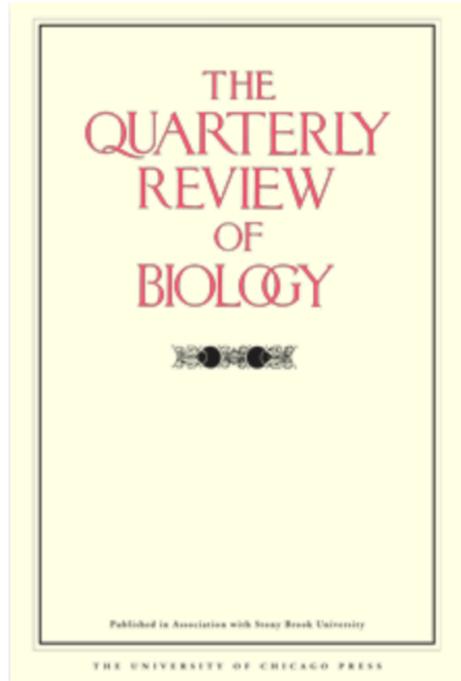
n=13,141

Term 1	AND Term 2
wetland*	construct*
OR pond	OR creat*
OR mire*	OR restor*
OR marsh	OR man*made
OR fen	OR flooding
OR "wet meadow"	OR inundation
OR riparian	OR artificial
OR "flood plain"	
OR reed	

n=36,363

Designing your search

Backward (cited) <—> Forward (citing) search



Validating your search

- Test search results against known studies
 - Gather a benchmark list of studies (10-20+)
 - Check against bibliographies of existing reviews
 - Finalise search when threshold no. studies found
 - Untenable for grey literature

Documenting your search

- What databases?
 - Name, URL, subscribing institution, date ranges
- What websites?
 - Name, URL, affiliation
- What search strings?
 - *Exact* strings used
- What options?
 - Terms searched (topic, title, abstract)
 - Date ranges
- When did you search?
- Who searched?

Repeatability



Screening and appraising studies



Screening and appraising studies

- Lots of results! But what's relevant?
- Screen against **predetermined inclusion criteria** in **two stages**
 1. Title & abstract screening
 2. Full-text screening

Common inclusion rates

- Title & abstract: ~52% (10-74)
 - Full text: ~29% (0-56)

Inclusion & quality criteria

A priori, justifiable criteria to minimise bias, and ensure maintain quality and transparency

Inclusion & quality criteria

- *Inclusion* criteria
 - Let PICOS be your (partial) guide
 - Relevant **population(s)**?
 - Necessary **intervention**?
 - Appropriate **comparator**?
 - Suitable **outcome**?

Inclusion & quality criteria

- *Inclusion* criteria
 - Let PICOS be your (partial) guide
 - Relevant **population(s)**?
 - Necessary **intervention**?
 - Appropriate **comparator**?
 - Suitable **outcome**?
- *Quality* criteria (see R.O.B. and R.O.S.E.S)
 - Suitable controls?
 - Appropriate treatment assignment?
 - Minimum sample sizes?
 - Confounding variables?
 - Typically at **full-text** stage only

The screening process

The two-step (though can be three, if ++ records)

Title + Abstract

∨

(Text retrieval)

∨

Full text

The screening process

Keeping note:

- Title + abstract
 - Efficiency key, often MANY reasons for exclusion
 - Include / Exclude
- Full text
 - Need precise reasons for *all* studies
 - Include
 - Exclude P, I, C, O, S
 - Exclude review / no primary data / commentary / modelling study / etc

Free software to help along the way

R packages

- [Litsearchr](#): search term design
- [Revtools](#): screening
- [metaDigitise](#): extract data from figures
- [CRAN task-view](#) for meta-analysis (50+ packages)

Other

- [Rayyan](#): screening
- [Sysrev](#): screening

Thanks!

