SLR PRO Series, Episode 1:

Systematic Reviews:
REACH the PEAK of EVIDENCE
1. What are systematic reviews?
2. Who uses systematic reviews?
3. How are they conducted?
4. How are they evaluated?

+ 4x Q&A: Ask YOUR questions!
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  - MY manuscript (formerly AuthorPath)
About our expert panel

About Dr Victor Popoola

- Physician-epidemiologist
- Over 16 years of experience in medicine, public health, and academic research
- Obtained masters and doctoral education at Johns Hopkins University in Maryland, United States
- >20 peer-reviewed publications
- Owns a services marketplace startup (providing research consulting and other services) – OmniBios Inc.

https://omnibios.com/

About Dr Tim Spelman

- Assistant Professor
- a PhD biostatistician and clinician with 20+ years experience in statistics, epidemiology
- one of the world’s leading registry/real-world data analysis and pharmaco-epidemiologists
- has authored or co-authored over 250 publications
- currently senior statistician at the Department of Surgery, St Vincent’s Hospital and leader of statistics at a several international organizations
What are systematic reviews?
A systematic literature review (‘SLR’) is a methodical summary of past research.

“Systematic” means that the review methods are planned in advance, as a protocol

Methods are transparent and repeatable

SLRs are a convenient source of high-level evidence

The names of systematic review study types can vary widely, so check the methods used!
The primary aim of an SLR is to try to answer a specific question or need.

"In patients aged 70 years or older, how does the administration of an influenza vaccine compared with not administering a vaccine affect the risk of developing influenza during the winter?"
“In patients aged 70 years or older, how does the administration of an influenza vaccine compared with not administering a vaccine affect the risk of developing influenza during the winter?”

PICO:
Patient or Population
Intervention
Comparator or Control
Outcome
(timeframe or setting)
What’s the difference between **systematic** and **traditional** literature reviews?
What’s the difference between **systematic** and **traditional** literature reviews? 

<table>
<thead>
<tr>
<th>Systematic Literature Reviews</th>
<th>Traditional Literature Reviews</th>
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<tr>
<td>are methodical</td>
<td>are usually descriptive</td>
</tr>
<tr>
<td>are repeatable</td>
<td>may not include all the available data</td>
</tr>
<tr>
<td>are comprehensive</td>
<td>do not analyze the data</td>
</tr>
<tr>
<td>require at least two authors so that judgments and interpretations can be cross-checked and discussed</td>
<td>rigorously are commonly performed by one author</td>
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Types of systematic reviews

- Qualitative
- Quantitative
- Mixed-Methods
Qualitative systematic reviews evaluate, summarize, and interpret data that are not numerical such as descriptive results, observations, texts, and transcripts.

Observational study types:
- Interviews
- Surveys
- Questionnaires
- Focus-group studies
- Diary studies
- Case studies/reports
**Quantitative systematic reviews** or meta-analyses involve pooling the numerical data from two or more studies and using appropriate statistical tests to analyze the combined data.

**Study types included:**

- Quantitative case studies/reports/series
- Observational epidemiologic studies clinical trials
A “mixed-methods systematic review” or “systematic review and meta-analysis” contains an initial general qualitative summary followed by a sub-analysis of relevant numerical data in a meta-analysis.
Other types of systematic reviews

- Diagnostic test accuracy review
- Network meta-analysis
- Umbrella review (‘systematic review of systematic reviews’)
- Scoping reviews and integrative reviews
What are some of the advantages and disadvantages of systematic reviews?
Advantages and Disadvantages of systematic literature reviews

**Advantages**
- Are comprehensive
- Save time for readers
- Are more reliable and useful than any single study
- Can boost a researcher’s career
- Inform “evidence-based” practice and decision-making

**Disadvantages**
- The process may take many months
- An SLR can quickly become outdated
- There may not be enough research in the literature to analyze
- An SLR’s quality depends on what has been published in the literature
Publication bias can affect the quality of your systematic review.

Some studies are biased or simply never published (called “publication bias”) because researchers and journals tend to prefer to publish only ‘positive’ results.

Dr. Daniel McGowan, Edanz Science Director
Ask our expert panel!

Ask us ANYTHING about systematic review types, features, strengths and weaknesses... etc.

Raise your hand to step up to the podium!
Who benefits from systematic reviews?
Who uses SLRs, and why?

Readers of SLRs

Direct
- Nurses
- Therapists
- Trainers
- Doctors

Indirect
- Public Policy Makers
- Business Decision Makers
- Researchers
- Consumers
What do people use SLRs for?

- To find the highest-level evidence
- To make informed decisions about health care provision
- For convenience and reliability
- To contribute to the research community
- For career advancement
SLRs are used in evidence-based practice

Evidence-based practice in health care is the policy to use scientific information in treatment, intervention, support, and advice. It is important in areas such as medicine, nursing, and dentistry.

Systematic reviews provide the highest level of research evidence.
Health Care Providers and systematic reviews

HCPs can formally or informally form teams of interested colleagues to perform systematic reviews.

The information may not be up-to-date; providers may need to conduct their own secondary research of new primary research studies.
Databases of systematic reviews for evidence-based practice

- The Cochrane Library (https://www.cochranelibrary.com/)
- JBI Evidence-based Practice Database (https://joannabriggs.org/ebp#database)
- Campbell Collaboration (https://www.campbellcollaboration.org/library.html)
- Turning Research into Practice (https://www.tripdatabase.com/).

Some peer-reviewed journals are dedicated to evidence-based practice:

- BMJ Evidence-Based Medicine, https://ebm.bmj.com/
Q&A/Discussion #2

Ask our expert panel!

Ask us ANYTHING about SLRs, uses, benefits... their use in evidence-based practice...

Raise your hand to step up to the podium!
How are systematic reviews conducted? What is the basic process?
To plan the research question and search strategy:

- Ask a precise research question
- Define eligibility criteria of studies
- Decide on search strategy and sources/databases

P.I.C.O.T. question:

“What is the relative efficacy of treatment X vs. treatment Y for condition Z?”
Develop a synopsis and protocol

The synopsis can be used as

- a guide for developing the protocol into several other items:
  - a **registered protocol** submitted to an online registry (i.e., PROSPERO)
  - a **protocol paper** for posting to a preprint server or publishing in a journal
  - a protocol for journal preregistration as a **registered report**
  - (after finishing your review) the Introduction and Methods sections of the **manuscript of your final report**
Perform data extraction and analysis

- Retrieve and select studies
- Extract relevant data
- Evaluate study quality
- Analyze the data
- Generate forest plots and funnel plots
The SLR is published as a report giving a critical summary of the secondary research.

The report follows an IMRaD structure:

- **Introduction**
- **Methods** (with a flow diagram)
- **Results**
- **Discussion**
What are **forest plots** and **flow diagrams**?
What is a **forest plot**?

A forest plot summarizes the effects (effect sizes) and 95% confidence intervals of individual primary studies that are included in the review.

![Forest plot example](https://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-10-47)

What is a flow diagram?

Literature search: Mainstream databases (e.g. MEDLINE, EMBASE) and other databases

Search results combined (n=154)

Excluded (n=117)
- Devoid of relevant maternal or infant outcomes
- No control group
- No lifestyle, dietary, health education or exercise intervention
- GDM, Pre-Pregnancy diabetes or PCOS

Included (n=37)

Excluded (n=18)
- Trial protocol (2)
- Data not complete (4)
- Duplicate publication data (2)
- Observational study (1)
- Outcome data not relevant (8)
- Pilot RCT with small sample size (1)

Articles screened on basis of title and abstract

Full test manuscript review and application of inclusion criteria

RCTs (n=13) Non-RCTs (n=6)
Checklists to include with your report: **PRISMA vs MOOSE**

For **systematic reviews** in general and for **meta-analyses of randomized controlled trials**, the relevant guidelines are the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (**PRISMA**) guidelines.

For meta-analyses of data from **observational studies**, the Meta-analysis of Observational Studies in Epidemiology (**MOOSE**) guidelines should be used.
Q&A / Discussion #3

Ask the Edanz experts!

Ask our expert panel!

Ask us ANYTHING about conducting systematic reviews and writing the report!

Raise your hand to step up to the podium!
Questions to think about:

What is the “evidence pyramid”?

Why do systematic reviews generally sit on top of the pyramid?

...But, can all systematic reviews be trusted as high-quality evidence?
The “Evidence Pyramid”

What is the "evidence pyramid"?

Why do systematic reviews generally sit on top of the pyramid?

Can all systematic reviews be trusted as high-quality evidence?
How are systematic reviews evaluated for quality?
Table 1. Grading the level of evidence obtained using different study methodologies to answer specific questions

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Study design</th>
<th>Study type</th>
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<tbody>
<tr>
<td>I</td>
<td>Systematic Reviews</td>
<td>Structured review</td>
</tr>
<tr>
<td>II</td>
<td>Randomized Clinical trials</td>
<td>Experimental</td>
</tr>
<tr>
<td>III</td>
<td>Cohort studies</td>
<td>Observational</td>
</tr>
<tr>
<td>IV</td>
<td>Challenge trials</td>
<td>Experimental</td>
</tr>
<tr>
<td>V</td>
<td>Case-control studies</td>
<td>Observational</td>
</tr>
<tr>
<td>V</td>
<td>Cross-sectional studies</td>
<td>Observational</td>
</tr>
<tr>
<td>VI</td>
<td>Descriptive studies, case reports/case series,</td>
<td>Descriptive</td>
</tr>
<tr>
<td></td>
<td>opinion of respected authorities, reports of</td>
<td></td>
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<td></td>
<td>expert committees.</td>
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Readers must check the quality of an SLR before applying its conclusions to daily practice.

Randomized controlled trials (RCTs) are the gold standard of experimental studies, but still need to be checked for quality.

**PRO TIP:** To know what data were actually used in a quantitative SLR, check the methods carefully!

But WHAT should we check for...?
What are some things to look for when checking the **quality** of systematic reviews?
Authors of systematic reviews often use the GRADE framework when assessing the quality of individual primary research studies in their reviews (and when appraising the quality of their own review).
Assess the quality of a review before relying on its conclusions for practical application.

- Was the research question clear and focused?
- Was the literature search comprehensive and up-to-date?
- Can the search be repeated consistently?
- Were the inclusion and exclusion criteria reasonable and clear?
- Were the correct types of studies included?
- Were included studies appraised for their design and quality?
Are the conclusions supported by the data?

Is the clinical relevance of the conclusions reported?

Do the benefits outweigh harms/costs?

Are the results applicable now?
Are data pooled, analyzed, and presented appropriately?

Were additional analyses conducted to test for the degree of study variability (heterogeneity)?

Is a minority of the studies biasing the results?

Are the effect size (size of the effect of an intervention) and precision reported?
What are some examples of bias or conflicts of interest that might appear in systematic reviews?
Checking studies for bias and conflicts of interest

**Bias:**
- Publication bias
- Hypothesizing after the results are known (HARK)
- p hacking or fishing trips/expeditions
- Cherry-picking and data manipulation

**Conflicts of interest:**
- Financial
- Non-financial
The AMSTAR checklist for checking quality of SLRs

Protocol for the systematic review was preplanned and registered before the start of the review (item 2)

The literature search was adequate (item 4)

Excluded studies were listed and their exclusion was justified (item 7)

Included studies were assessed for risk of bias (item 9)

Methods used in any meta-analysis were appropriate (item 11)

Risk of bias was accounted for when interpreting the results of the review (item 13)

Publication bias was assessed, and its likely impact was discussed (item 15)
Ask our expert panel!

Ask us ANYTHING about systematic reviews! Evidence levels... how to check for quality of reviews or individual studies...

Raise your hand to step up to the podium!
About our expert panel

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SLR1: Understanding Systematic Reviews

1 hour of self-study
- Rich text and illustrations
- Try-it-yourself activities
- Real-world examples and links