Systematic Reviews, Episode 3: PREPARE to LAUNCH!

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1 Defining your DATA SOURCES

2 Defining your SEARCH TERMS

3 Planning DATA EXTRACTION and ASSESSMENT

4 Developing a STATISTICAL ANALYSIS plan

+ Q&A: YOUR questions!

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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 Scott McCleary

- Creator of Edanz Learning Lab
- Instructional designer with 18 years' experience in lifelong learning and career skills development for professionals
- Lecturer at Kaetsu University, Tokyo
- has developed and delivered training programs for more than 50 organizations worldwide in medicine, pharma, business, science, technology, government, K12, and higher education

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To plan your research question and search strategy:

❑ Ask a specific 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?"

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SLR2: Planning Systematic Reviews
⏱ 1 hour · Learn how to define your research question and plan a search and analysis strategy.

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Defining DATA SOURCES

One key feature of a systematic literature review (SLR) is **objectivity** -- to minimize bias wherever possible.

The **selection criteria** of studies must be predefined to match the research question. Relevant variables include the **sources, date span, language,** and **types of data searched for,** and the **search-engine keywords** you used.

Your data extraction and analysis methods also need to be planned in advance.

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To show that the methods were not changed so as to manipulate the results, a full systematic review **protocol** must be carefully designed in advance.

Your protocol should contain specific items and follow **PRISMA** guidelines. (More about this later, in Episode 4)

Ideally, your protocol should also be made **public**. You can upload it to a public preprint registry or review registry, or you can submit it for peer review as a registered report or **protocol article**. (More about this later, in Episode 6)

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Q: How much, if any, data can/should be collected at the time of protocol writing?

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A: To maintain the integrity of the review, data should <u>not</u> be collected, selected, or analyzed at the protocol stage.

Q: Can I do some pilot research to survey the existing literature?

Q: Can I do some preliminary research to survey the existing literature?

A: You can do some desk research to see if there are already any SLRs for your topic. You can also do a scoping review.

The existing literature determines what data are available for your review. Your review criteria will depend on features of past studies such as **exact treatments, interventions, or exposures; settings and participants; study quality and design types;** or **languages**.

To survey the available primary data, you can do a **literature precheck**, which is sometimes called an **environment scan, situation analysis, evidence gap mapping, or gap analysis.**

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Q: I don't have time to do a literature pre-check. Can I change my protocol later, if I need to?

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A: Yes, but is important that protocol changes be fully documented in both the protocol and final report.

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A contingency plan within a protocol can address the possibility that your original research question might not be answerable from the available primary data.

This shows that you are planning to avoid bias, while maximizing the usefulness of your systematic review.

In a contingency plan, your **PICO question** is modified slightly. You might also require alternative changes to the **data sources, search terms, inclusion/exclusion criteria,** and **data analysis plans.**

Adjusting your PICO question (narrow vs broad)

P (Population/Patients)

Narrow scope: "To assess the effect of X on women older than 60 years".

Broad scope: "To assess the effect of X on men and women older than 60 years".

I (Intervention)

Narrow scope: "To assess the effect of taking acetaminophen by mouth before procedure X on postoperative pain".

Broad scope: "To assess the effect of taking a nonsteroidal anti-inflammatory drug by mouth before procedure X on postoperative pain".

C (Comparison/Comparator)

Narrow scope: "To assess the effects of drug X compared with drug Y".

Broad scope: "To assess the effects of drug X compared with any drug of class Z".

O (Outcome)

Narrow scope: "To assess the effect of drug X on coughing during the common cold".

Broad scope: "To assess the effect of drug X on symptoms of the common cold".

Listing Data Sources

For each research question (and contingency plan), the **relevant data sources**, both online and in print, **should be listed**.

The included sources **should be as wide as possible at the start** to capture as many potentially relevant studies as possible. The studies **can then be filtered later** according to search terms and inclusion/exclusion criteria.

The name of the database source used, search period (date span of the literature searched), and any language restrictions **should be recorded in the review protocol and final report**.

Mayo-Wilson et al. suggest using **Multiple Data Sources** (**MUDS**) and offer the following **six tips**:

(1) **Specify** which sources you will use.

(2) **Link** individual trials with multiple sources.

(3) **Follow** a pre-specified protocol for extracting trial characteristics from multiple sources

(4) **Pre-specify** outcomes and results to examine in the review and meta-analysis

(5) **Identify** which data sources were included in the review, and any possible impact on results

(6) **Share** the data used in your review, to reduce bias, and to reduce research waste

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5888128/

Q: I don't have time to do a literature pre-check. Can I change my protocol later, if I need to?

A: Yes, but is important that protocol changes be fully documented in both the protocol and final report.

Ask our
expert panel!

Ask us ANYTHING about DATA SOURCES and/or doing a LITERATURE PRE-CHECK!

Click the 'raise hand' icon, or type your question into the 'Questions' panel

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Searching Databases for Evidence to Extract

Search strings:
(UVW AND XYZ AND (ABC OR DEF [MeSH terms])

Systematic reviews & meta-analyses

Primary Literature

Evidence review map

'Raw' databases
(Medline, Embase, Scopus, Web of Science…)

15-Point Search Strategy:

1. Focus and clarify your question
2. Describe articles that can answer your question
3. Choose keywords + key concepts
4. Choose the best elements
5. Choose an appropriate database
6. Document your search process
7. Identify appropriate index terms in the thesaurus of the first database
8. Identify synonyms in the thesaurus
9. Add variations in search terms
10. Use database-appropriate syntax
11. Repeat the search with synonyms
12. Evaluate the initial results
13. Check for errors
14. Translate to other databases
15. Test and reiterate (Try again)

based on CC BY, Bramer et al, J Med Libr Assoc 2018;106:531-541;
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6148622/

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"Fifteen Point Search Strategy"

learning.edanz.com/ebooks/

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SLR2: Planning Systematic Reviews

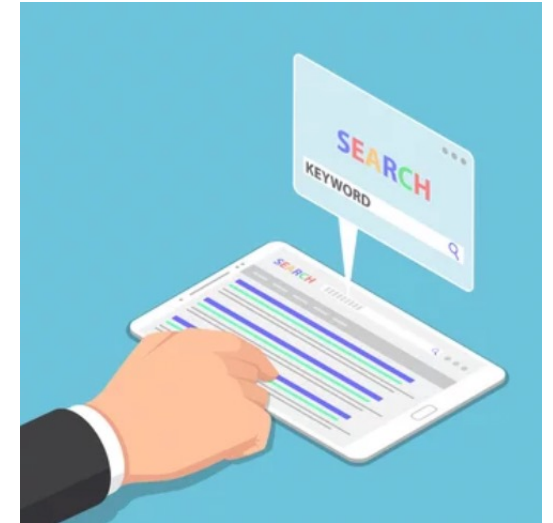⏱ 1 hour • Learn how to define your research question and plan a search and analysis strategy.

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How to define SEARCH TERMS

Search Terms / Keywords

For each of the data sources chosen, literature searches must be performed using **search terms** or **keywords** (or phrases). Your search strategy should be **logical, systematic, and repeatable**.

These search terms / keywords will depend on the research question and topic, as well as elements of **PICO** (Patient, Intervention, Comparator, Outcome)

Search terms should be as comprehensive as possible to capture all potentially relevant studies, which can be filtered later. You may need to use synonyms (eg, "old", "senior", and "elderly") and different parts of speech (related words such as "elder" and "elderly").

Here are **MeSH keywords** for the article "Prostate-Specific Antigen-Based Screening for Prostate Cancer: Evidence Report and Systematic Review for the US Preventive Services Task Force"

Fenton et al, JAMA 2018;319:1914-1931 retrieved from
https://www.ncbi.nlm.nih.gov/pubmed/29801018/

- Age Factors
- Aged
- Biopsy/adverse effects
- Early Detection of Cancer*/methods
- Early Detection of Cancer*/standards
- False Positive Reactions
- Humans
- Male
- Medical Overuse
- Middle Aged
- Practice Guidelines as Topic
- Prostate-Specific Antigen/blood*
- Prostatic Neoplasms/diagnosis*
- Prostatic Neoplasms/mortality
- Prostatic Neoplasms/therapy
- Risk Factors
- Watchful Waiting

(*) means that the term is a major topic of the article
(/) means subtopics)

Q: Do you have any tips for choosing search terms / keywords for a particular search engine?

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Q: Do you have any tips for choosing search terms / keywords for a particular search engine?

A: Find an indexed article in that search engine that is close in topic or scope to your research question

Example MeSH (Medical Subject Headings) Keywords

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Fenton et al, JAMA 2018;319:1914-1931 retrieved from
https://www.ncbi.nlm.nih.gov/pubmed/29801018/

- Age Factors
- Aged
- Biopsy/adverse effects
- Early Detection of Cancer*/methods
- Early Detection of Cancer*/standards
- False Positive Reactions
- Humans
- Male
- Medical Overuse
- Middle Aged
- Practice Guidelines as Topic
- Prostate-Specific Antigen/blood*
- Prostatic Neoplasms/diagnosis*
- Prostatic Neoplasms/mortality
- Prostatic Neoplasms/therapy
- Risk Factors
- Watchful Waiting

(*) means that the term is a major topic of the article
(/) means subtopics)

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Each search engine may use slightly different syntax (logical language) in the search string

Most use the basic **Boolean operators (OR, AND, NOT)**, in combination with **quotes** and **parentheses.**

OR
AND
AND + OR
NOT
Truncation and wild cards [*] [?] [$]
Proximity operator [NEAR]

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[mh]   the term is from the MeSH dictionary

[tiab]   restricts a term to the title or abstract of a paper

[au]   author

[dp]   date of publication

[pt]   publication type

[tw]   text words, or words in any associated record, including non-MeSH keywords (also called free text)

A full list of PubMed tags can be found at:
https://www.ncbi.nlm.nih.gov/books/NBK3827/#pubmedhelp.Search_Field_Descriptions_and

Examples of Boolean logic

Here are some examples of **Boolean logic** with or without **PubMed tags**, taken from the PubMed help page:

Find citations on DNA that were authored by Dr. Crick in 1993:
dna [mh] AND crick [au] AND 1993 [dp]

Find citations on the effects of heat or humidity on multiple sclerosis:
(heat OR humidity) AND multiple sclerosis

Find citations about arthritis excluding the Publication Type Letter:
arthritis NOT letter [pt]

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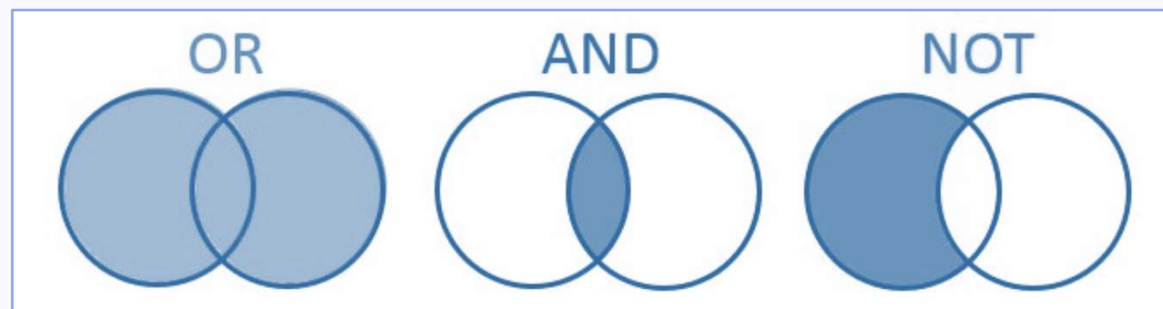
Ask our expert panel!

Ask us ANYTHING about how to define SEARCH TERMS

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Planning DATA EXTRACTION and ASSESSMENT

Eligibility (inclusion and exclusion) criteria

The protocol should state your **eligibility criteria** (how you will filter retrieved studies)

Inclusion criteria: Retrieved studies are checked for relevance to PICO terms, and your exact research question and topic

Exclusion criteria: Studies are excluded if certain features are present, such as if patients are not within the target age range

A compromise may be needed for how general or specific the inclusion criteria are. Keywords that are too specific and narrow may not yield enough studies to analyze. Keywords that are too general may yield too many studies, of variable quality. The criteria also need to appear in the final report.

For more help with eligibility criteria, try our course, "SLR2: Planning Systematic Reviews": free for all Researcher users!)

Q: How are inclusion and exclusion criteria organized and presented?

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A: It's common to list your inclusion and exclusion criteria in terms of your PICO question, or simply as a tabled list.

This table show inclusion and exclusion criteria based on **PICOs** (Patients/ Population, Intervention, Comparator/Comparison, Outcome, Study design)

Parameter	Inclusion criteria	Exclusion criteria
Patients	Patients of any age with prostate cancer/treatment associated gynecomastia	Other types of gynecomastia
Intervention	Pharmacological, surgical or radiotherapeutic treatments	
Comparator	How effective are the different treatment methods	
Outcomes	*Primary outcome measures*: Treatment results and number of complications/side effects. *Secondary outcome measures*: QoL	
Study design	Randomized controlled trials, non-randomized controlled trials, retrospective, prospective, or concurrent cohort studies. At least 20 patients. At least 1 year follow-up. Published in English.	Reviews, expert opinion, comments, letter to editor, case reports, studies on animals, conference reports. Less than 20 patients. Shorter follow-up than 1 year. Studies with no outcomes reported. Published before 2000. Published in any other language than English.

doi:10.1371/journal.pone.0136094.t001

This table shows inclusion and exclusion criteria that are listed **without** PICOs:

Inclusion Criteria:

1. Multi-disciplinary interventions of any duration.

2. Study participants included adults only (minimum of 18 years). If studies included children younger than 18 years, these were considered if they reported results specific for adults.

3. Language was limited to those understood by the authors–English, French, Dutch and German.

4. Chronic pain of any aetiology. Studies involving both acute and chronic pain were considered if they reported results specific to chronic pain.

5. The intervention was a randomised or controlled study design that involved an educational component of any form (e.g. lectures, online links, leaflets, apps and books) about any topic (e.g. medication management, pain control, understanding pain, etc.)

Exclusion Criteria:

1. Interventions were not multi-disciplinary.

2. Identified articles had no element of educational intervention for patients and/or were only pharmacological in nature.

3. Studies involving only acute pain.

4. Studies involving only cancer pain.

5. Study participants involving children and adolescents only (younger than 18 years).

6. Languages other than English, French, Dutch and German.

https://doi.org/10.1371/journal.pone.0223306.t001

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Agree on list of eligible studies

Separate literature searches

There are usually at least two reviewers who search the literature independently according to the search string and eligibility criteria, and then check each other's work.

A third reviewer can be asked to resolve remaining differences.

How the researchers search and retrieve literature must be documented in the review protocol and final report. Author initials are usually used in the text to indicate who did what.

- GRADE: Grading of Recommendations Assessment, Development and Evaluation
- PROBAST: Prediction model Risk Of Bias ASsessment Tool
- CHARMS: CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies
- Cochrane risk of bias in randomized trials tool
- Quality Assessment of Systematic Reviews and Meta-Analyses (US NIH)

For observational and nonrandomized studies:
- NOS: Newcastle-Ottawa Scale to assess nonrandomized studies in meta-analyses
- Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (US NIH)

For qualitative studies:
The Critical Skills Appraisal Programme (CASP) qualitative research checklist or GRADE Confidence in Evidence from Reviews of Qualitative research (GRADE-CERQual) can be used. For health care evaluation studies, the Cochrane Effective Practice and Organisation of Care (EPOC) tool can be used. There is also QUADAS-2, the Quality Assessment of Diagnostic Accuracy Studies.

Protocol Title: Quality of life of women who practice dance: a systematic review protocol

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6040078

Data Extraction: **"Two reviewers will independently screen the studies identified by the searches following a three-phase procedure. After each phase, the reviewers will check inclusions and exclusions, and, in case of disagreements, a third reviewer will be involved as an adjudicator."**

Recording and Tracking Your Data Sources

Tip: use reference management software (eg, Edanz's MY manuscript, EndNote, Reference Manager, RefWorks) to help record and track your identified studies.

MYmanuscript

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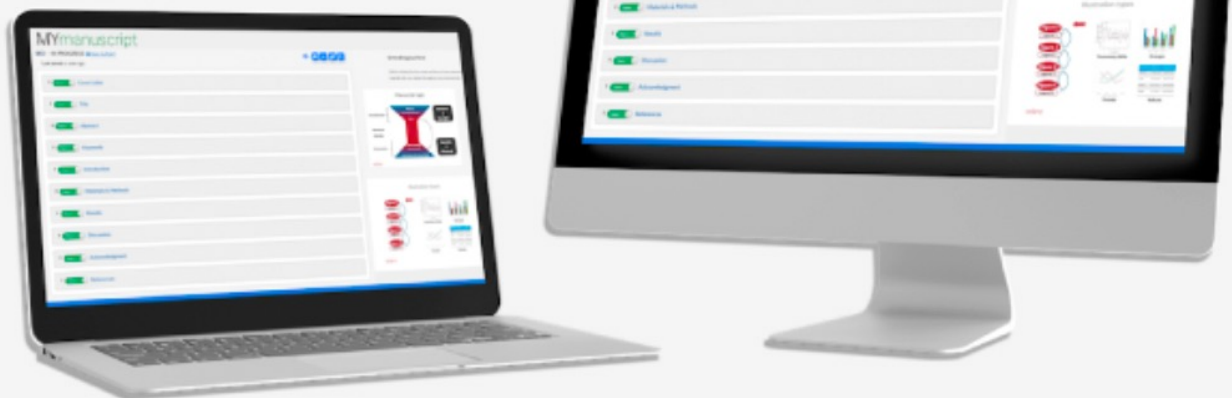
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Developing a STATISTICAL ANALYSIS plan

To achieve full transparency and objectivity, researchers must document their data management plan in advance.

Aiming for full transparency and objectivity

Your **data management plan** needs to define all **variables** and cover your **data selection and extraction**.

Your plan should also include **data analyses** both **descriptive/qualitative** and **quantitative** (pooled statistical testing as a meta-analysis), plus any **subgroup analyses**.

You also need to plan and define the **outcome measure** (eg, observed primary and secondary treatment outcomes), an appropriate **effect measure** or **effect size** (eg, standardized mean difference, risk difference, odds ratio, risk ratio, or correlation coefficient such as Pearson r statistic), and **how studies are combined for meta-analysis** (eg, how studies are weighted).

Effect sizes for individual and pooled studies are summarized in a **forest plot**.

Meta-analyses can use either a **fixed-effect** or **random-effects** statistical model for pooling data, and the appropriate one must be chosen. The random-effects model is the more conservative and usually more plausible model. Initially, both models can be performed.

Fixed-effect model

Random-effects model

Heterogeneity (or noncombinability) is how variable the outcomes (effect sizes) of the different studies are. A common cause for heterogeneity is small sample size.

Tests for heterogeneity include the **Cochran Q test, Higgins I^2 test, chi-squared (χ^2) test, and Kendall tau (τ) test**.

Heterogeneity can be further assessed by:
- a sensitivity analysis
- subgroup analyses (by specified categories or study types)
- meta-regression analysis

Publication/dissemination bias is another important bias to check for. Authors feel pressured to publish only positive findings and to publish them earlier than negative studies, if at all.
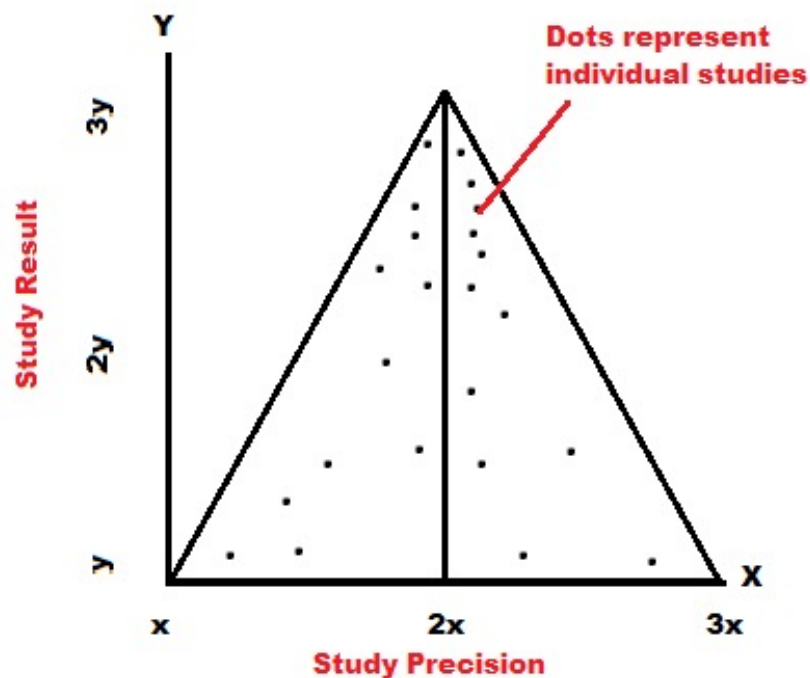
A common test for publication bias is to produce a **funnel plot**, which is a graph of the estimated treatment effect of each individual plotted against the study precision.

A **symmetrical** funnel shape in the graph will indicate a **low risk** of publication bias.

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Documenting Your Analyses

The review and statistical software package and version number should be named in the review protocol if possible. Commonly used statistical software include: DistillerSR, Stata (StataCorp), SAS, SPSS, Matlab, and "R".

In addition, your protocol needs to include specific statistical test names and assumptions/conditions relevant to the dataset, such as whether one- or two-tailed tests* will be done, depending on the research hypothesis being tested.

Full details of your analyses (descriptive and statistical) also need to be given in your final SLR report (as per PRISMA or MOOSE guidelines).

Your datasets may also need to be made available to readers.

*Try our **SLR2 course** to review PICO research questions, and one- vs. two-tailed tests.

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Click the 'raise hand' icon, or type your question into the 'Questions' panel

Thank you Dr Victor Popoola!

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