SYSTEMATIC REVIEWS AND META-ANALYSES

Shelley Facente, PhD, MPH
Sara Durán, MPH

Virtual Session 1 of 3

COURSE WEBSITE

- Slides and all other resources you'll need for the course are available at:

https://facenteconsulting.com/srmacourse/

INTRODUCTIONS

Instructors:

Shelley Facente, PhD, MPH

- Principal of Facente Consulting
- Adjunct Professor at the University of California, Berkeley

Sara Durán, MPH

- Senior Consultant at Facente Consulting
- MPH in Epidemiology & Biostatistics University of Southern California

CURRICULUM

Wednesday

- Overview of SRs and MAs
- PROSPERO and PRISMA
- Defining the review question
- PICOS

Thursday

- Searching for records and studies
- Practice!

Friday

- Extracting and organizing data
- Summarizing data and meta-analysis
- Evaluating bias

In person, Week of Dec 1

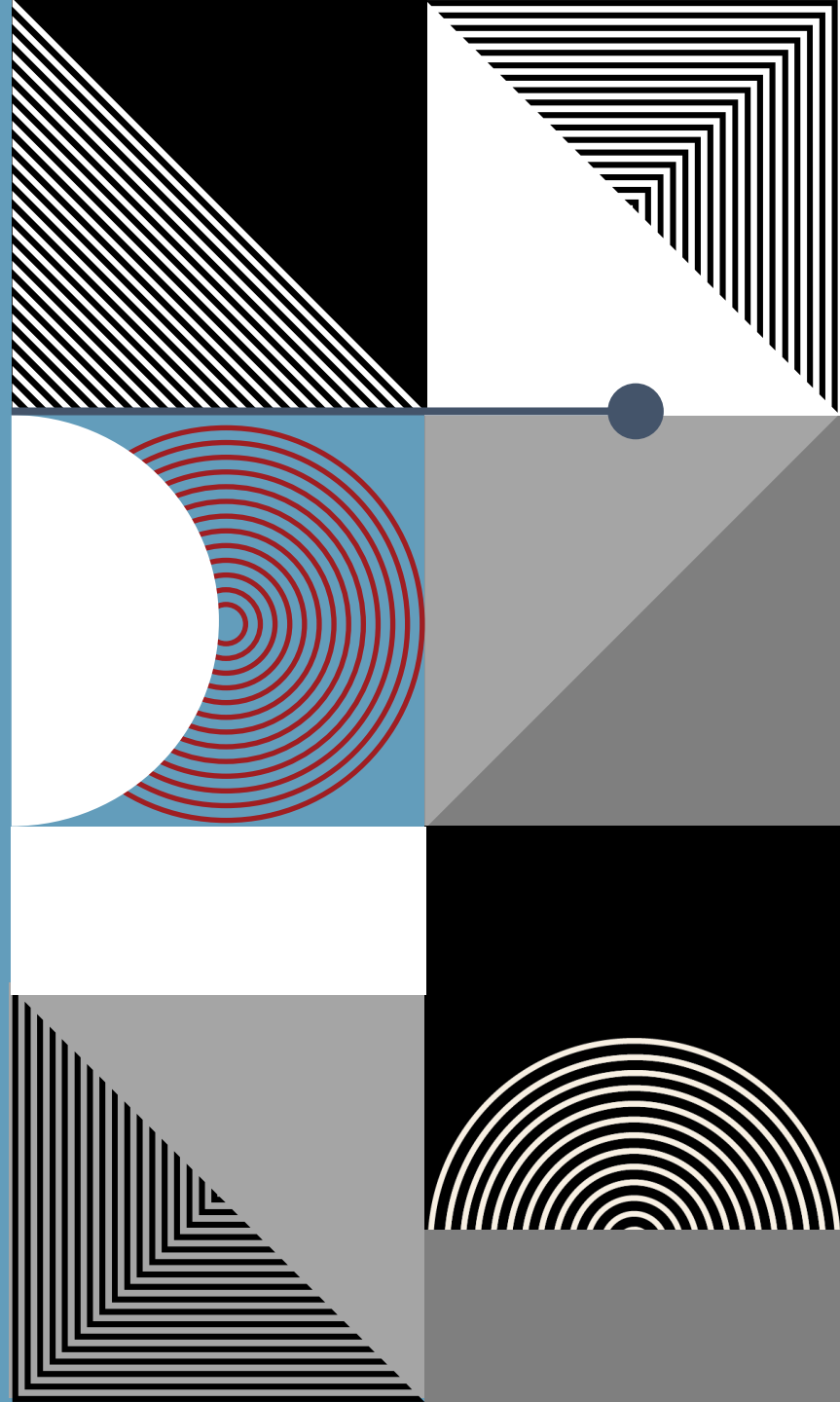
- Review and practice defining the review question and PICOS criteria to be used
- Practice searching for records and screening returned studies
- Review of evaluating bias
  Practice extracting data
- Sensitivity analyses & stratified analyses
  Understanding SRMA limitations
  Interpreting and reporting results
- Reviewing special types of SRs and MAs
  Final chance for Q&A from the course

WHAT IS A SYSTEMATIC REVIEW?

"Systematic reviews seek to collate all evidence that fits pre-specified eligibility criteria in order to address a specific research question."

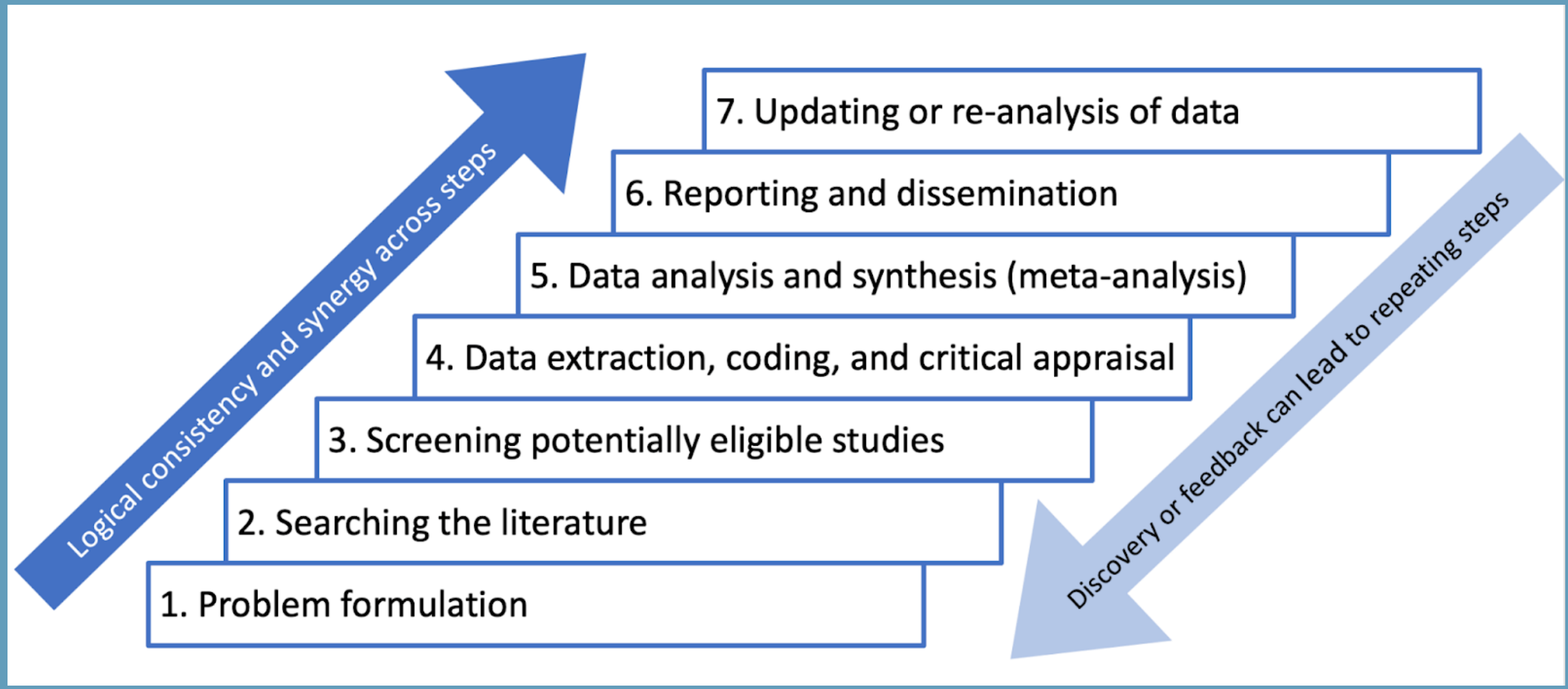
A systematic review is:

- a summary of all available studies based on a pre-defined research question and criteria;
- systematic in how to identify studies, evaluate, and summarize those studies; and
- a type of secondary analysis that uses data from existing studies.



https://training.cochrane.org/handbook/current/chapter-i
https://oli.cmu.edu/jcourse/workbook/activity/page?context=79edf8310a0001dc0a6f12f3d846b74f

SYSTEMATIC REVIEWS PROCESS



https://oli.cmu.edu/courses/systematic-reviews-and-meta-analysis-o-f/#

ARCHIBALD COCHRANE AND THE INVENTION OF SYSTEMATIC REVIEWS

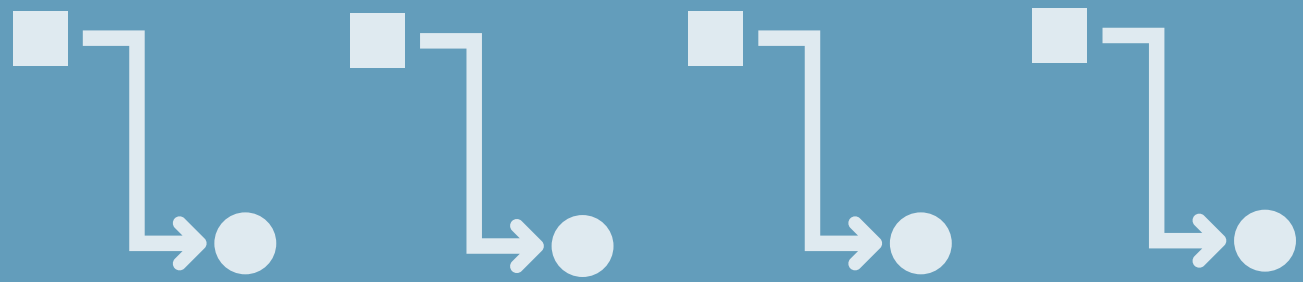
Three years later the British physician and epidemiologist Archie Cochrane drew attention to the fact that people who want to make informed decisions about health care do not have ready access to reliable reviews of the available evidence.[15] In the 1980s meta-analysis became increasingly popular in medicine, particularly in the fields of cardiovascular disease,[16,17] oncology,[18] and perinatal care.[19] Meta-analysis of epidemiological studies[20,21] and "cross design synthesis",[22] the integration of observational data with the results from meta-analyses of randomised clinical trials was also advocated.

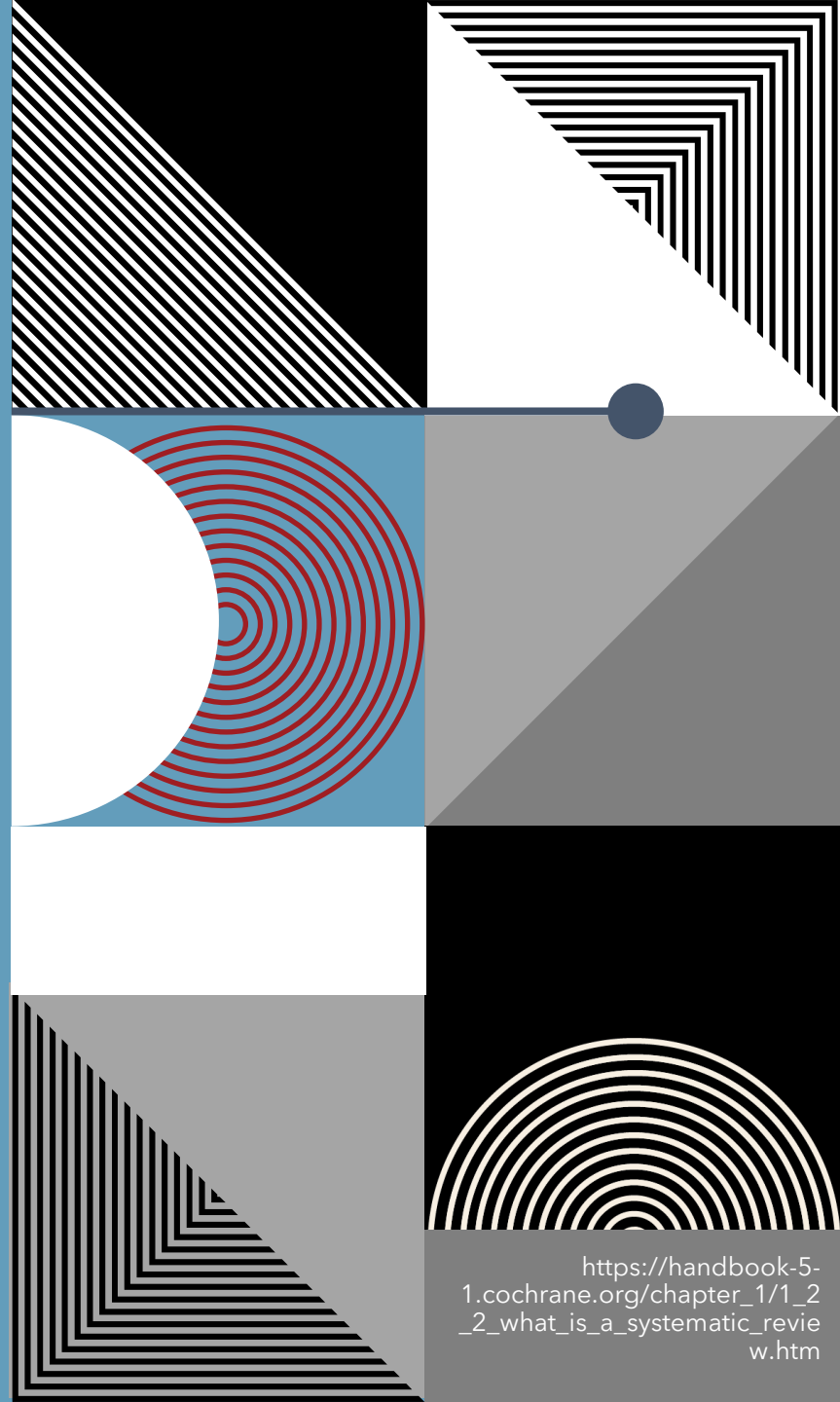
THE COCHRANE COLLABORATION®

EGGER, M., DAVEY-SMITH, G. & ALTMAN, D. 2008. *Systematic reviews in health care: meta-analysis in context*, John Wiley & Sons.

SYSTEMATIC REVIEWS SHOULD HAVE:

- Explicit objectives with pre-specified eligibility criteria
- A method that can be reproduced
- A methodical search to identify every available study that meets eligibility criteria
- An evaluation of the validity of study findings, including assessing risk of bias
- An organized synthesis and presentation of included studies





https://handbook-5-1.cochrane.org/chapter_1/1_2_2_what_is_a_systematic_review.htm

WHY AND HOW ARE SRs USED?

SRs are used to collect and condense research and information on a topic to help inform providers, academia, policymakers, and the general public.

Some reasons to conduct a systematic review:

- Resolve conflicting evidence and study findings
- Address uncertain clinical questions
- Explore differences in clinical practice
- Provide evidence that supports decision making (whether for clinical or community interventions)
- Highlight areas for future research

https://handbook-5-1.cochrane.org/chapter_1/1_2_1_the_need_for_systematic_reviews.htm

WHY AND HOW ARE SRs USED?

SRs go beyond the individual study

- Randomized clinical trials always have some sort of bias
- All studies have random error
- Individual studies cannot always be generalized (external validity issues)

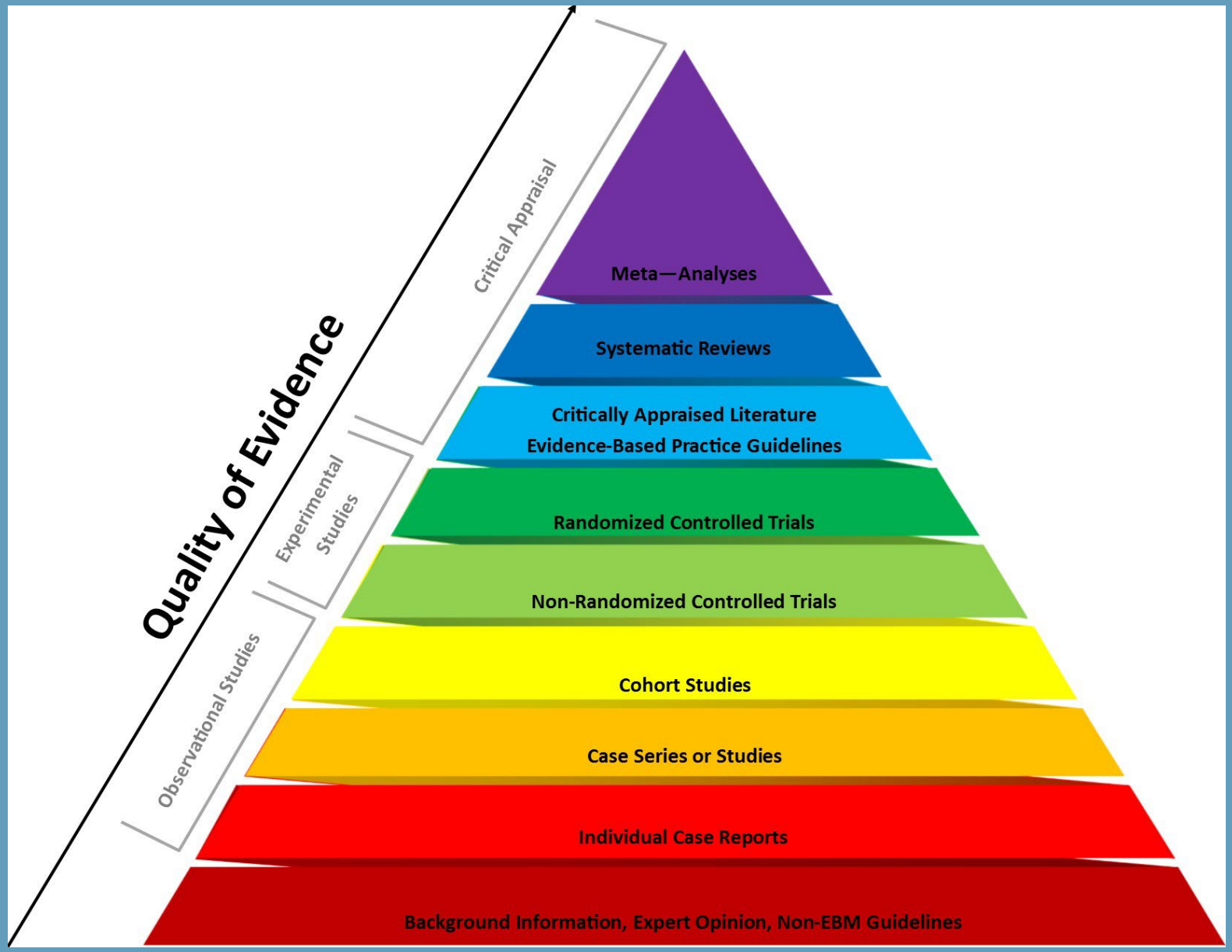
https://handbook-5-1.cochrane.org/chapter_1/1_2_1_the_need_for_systematic_reviews.htm

WHAT IS META-ANALYSIS?

- “Meta-analysis is the statistical combination of results from two or more separate studies.”
- Meta-analyses are often a part of systematic reviews
- Some advantages:
  - MAs improve accuracy by increasing the available information (i.e. pooling the sample sizes)
  - MAs can sometimes provide answers to questions that individual studies do not address
  - MAs support developing new hypotheses and help to address conflicting study findings/results

https://training.cochrane.org/handbook/current/chapter-10

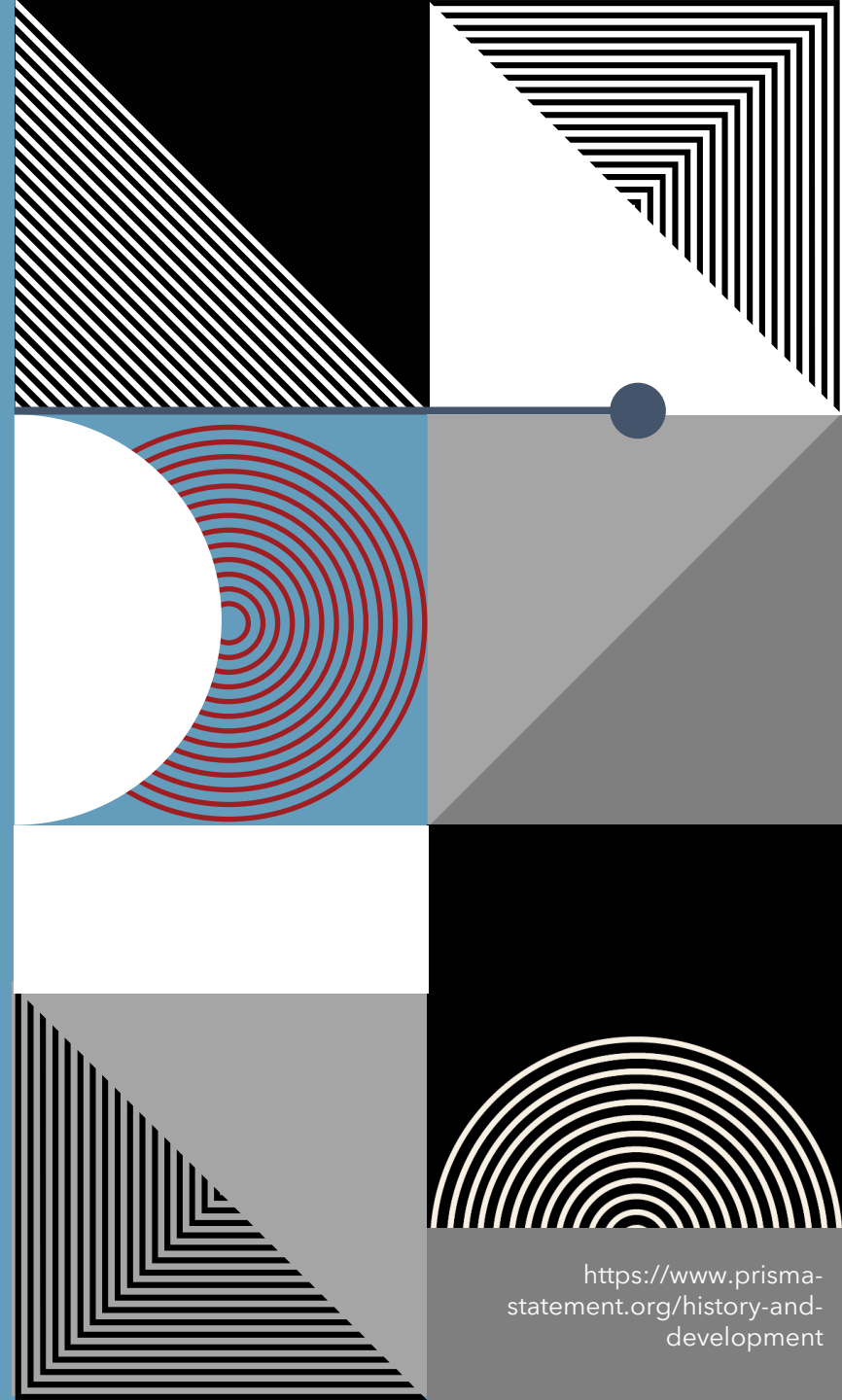
ROLES OF SR AND MA



- To accurately conduct SRMAs, it is vital to understand the role of critical appraisal
- Critiquing published trials, including assessing for risk of bias, is integral to this process
- SRMA studies and combines our understanding from individual studies and therefore increases their combined power

PRISMA HISTORY

- SRMAs are important in healthcare, clinical practice guidelines, and public health. People see them as a shortcut to understanding the literature, which might be complex!
- Studies have been conducted on the quality of SRMAs and early studies found poor quality in reporting.
- As a result, the QUOROM (Quality of Reporting of Meta-analyses) Statement was developed as a guiding document in 1999.



https://www.prisma-statement.org/history-and-development

THE LANCET

REVIEW · Volume 354, Issue 9193, P1896-1900, November 27, 1999

Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement

Dr David Moher, MSc [a] · Deborah J Cook, MD [b] · Susan Eastwood, EL(D) [c] · Ingram Olkin, PhD [d] · Drummond Rennie, PhD [e] · Donna F Stroup, PhD [f] · et al. Show more

Summary

Background

The Quality of Reporting of Meta-analyses (QUOROM) conference was convened to address standards for improving the quality of reporting of meta-analyses of clinical randomised controlled trials (RCTs).

Methods

The QUOROM group consisted of 30 clinical epidemiologists, clinicians, statisticians, editors, and researchers. In conference, the group was asked to identify items they thought should be included in a checklist of standards. Whenever possible, checklist items were guided by research evidence suggesting that failure to adhere to the item proposed could lead to biased results. A modified Delphi technique was used in assessing candidate items.

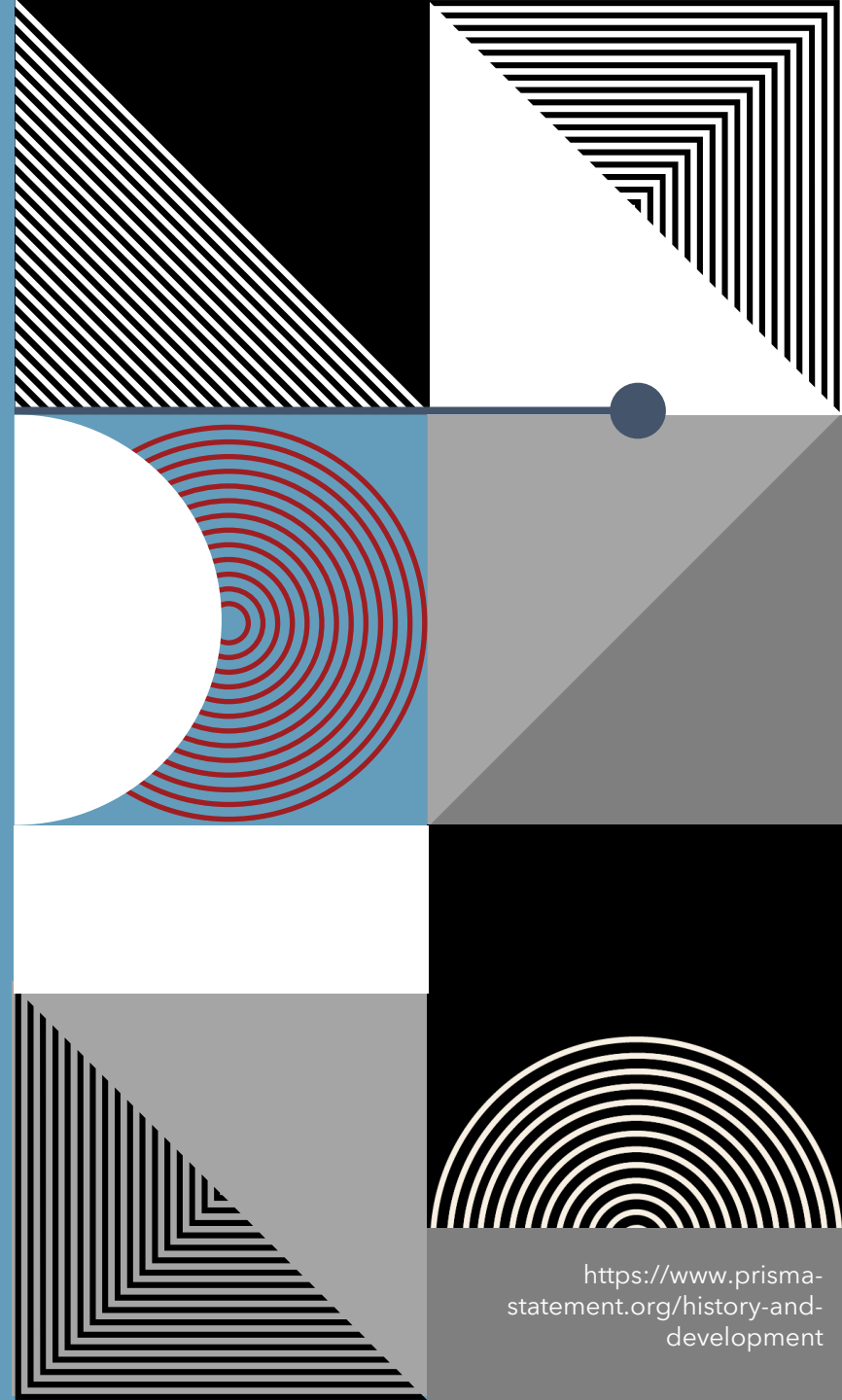
Findings

The conference resulted in the QUOROM statement, a checklist, and a flow diagram. The checklist describes our preferred way to present the abstract, introduction, methods, results, and discussion sections of a report of a meta-analysis. It is organised into 21 headings and subheadings regarding searches, selection, validity assessment, data abstraction, study characteristics, and quantitative data synthesis, and in the results with "trial flow", study

https://www.prisma-statement.org/history-and-development

PRISMA HISTORY CONT.

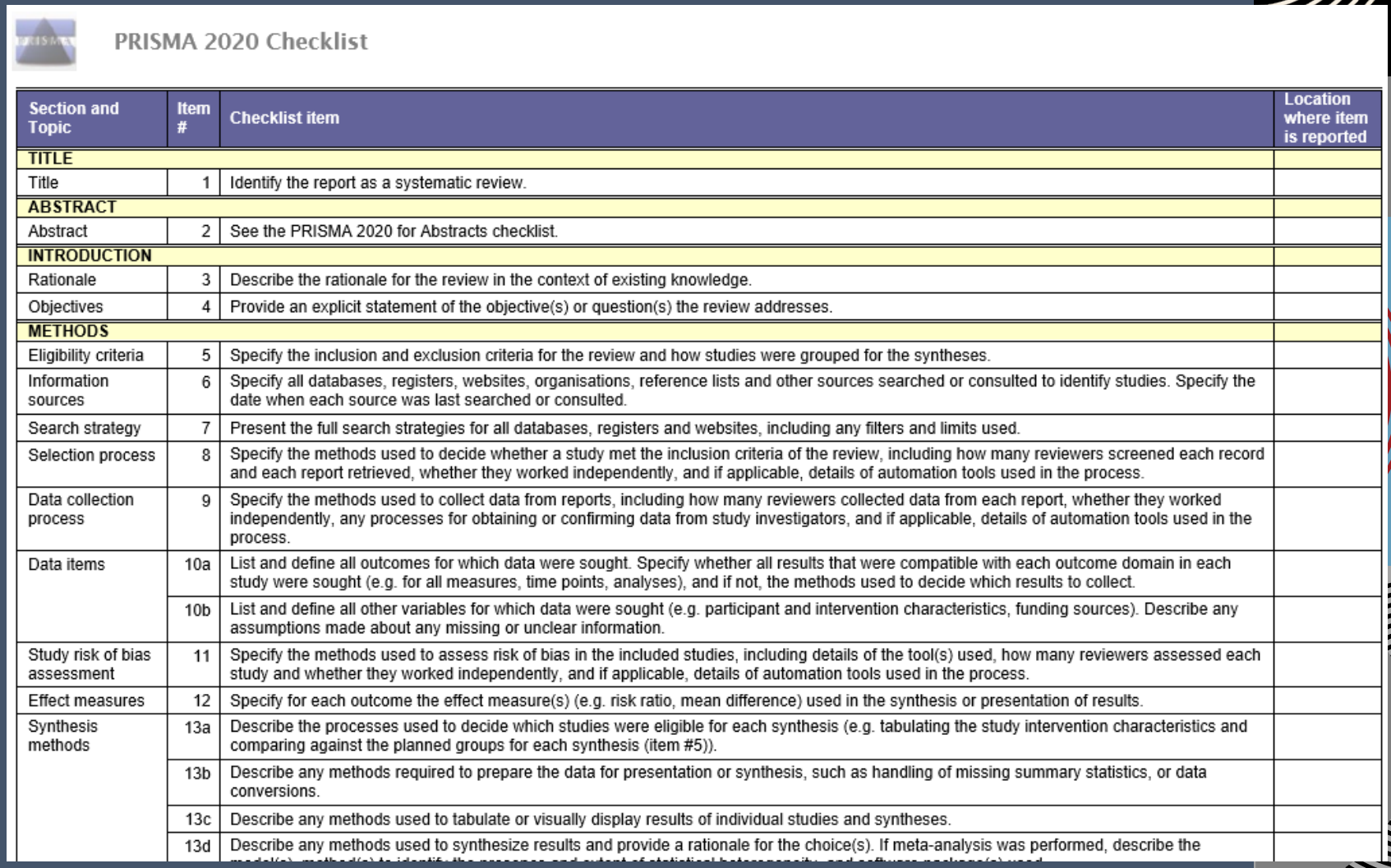
- In 2009, this was updated and renamed to PRISMA and was published in multiple journals and accompanied by an Explanation and Elaboration paper.
  - *PLoS Medicine, BMJ, Ann Intern Med, Journal of Clinical Epidemiology, International Journal of Surgery, Open Med, Phys Ther*
- The statement was then updated in 2020 to integrate updates in methodology and terminology and published in March 2021.
  - *MetaArXiv (preprinted in 2020), BMJ, PLoS Medicine, Journal of Clinical Epidemiology, Systematic Reviews, Int Journal of Surgery*



https://www.prisma-statement.org/history-and-development

PRISMA GUIDELINES

- https://www.prisma-statement.org/
- Intended mainly for SRs of health interventions
- Consists of a checklist https://www.prisma-statement.org/prisma-2020-checklist and flow diagram (will cover more in December)

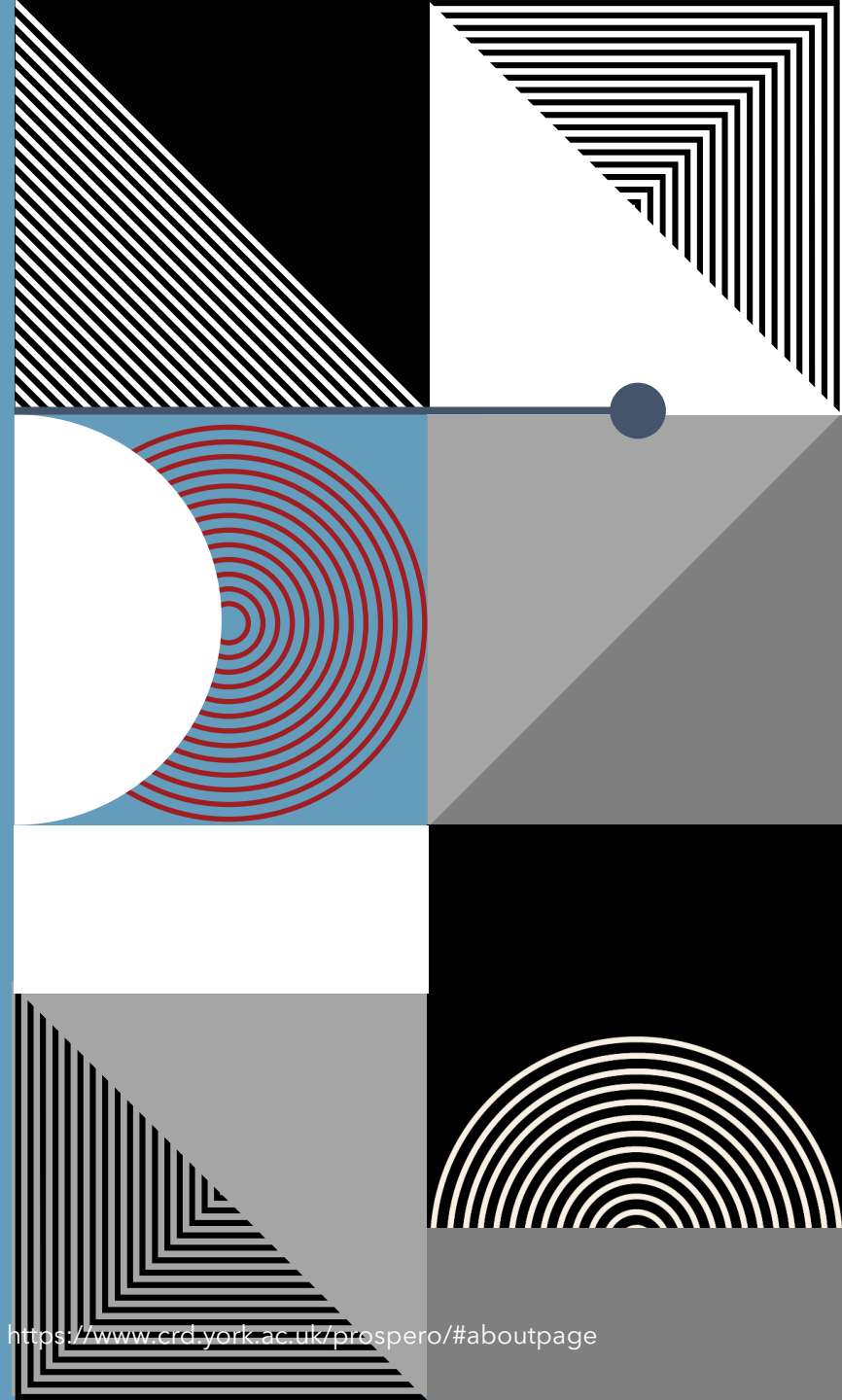


PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	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.	
Data collection process	9	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.	
Data items	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.	
Study risk of bias assessment	11	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.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the	

PROSPERO REGISTRATION

- PROSPERO was founded in 2014, with the aim to provide a comprehensive listing of systematic reviews with health outcomes, registered at inception.
- Systematic reviews should be prospectively registered in PROSPERO to ensure transparency, reduce possible duplication of efforts, and address publication bias, as it records all SRs regardless of eventual publication.
- Registration in PROSPERO has 27 mandatory and 14 optional fields.



https://www.crd.york.ac.uk/prospero/#aboutpage

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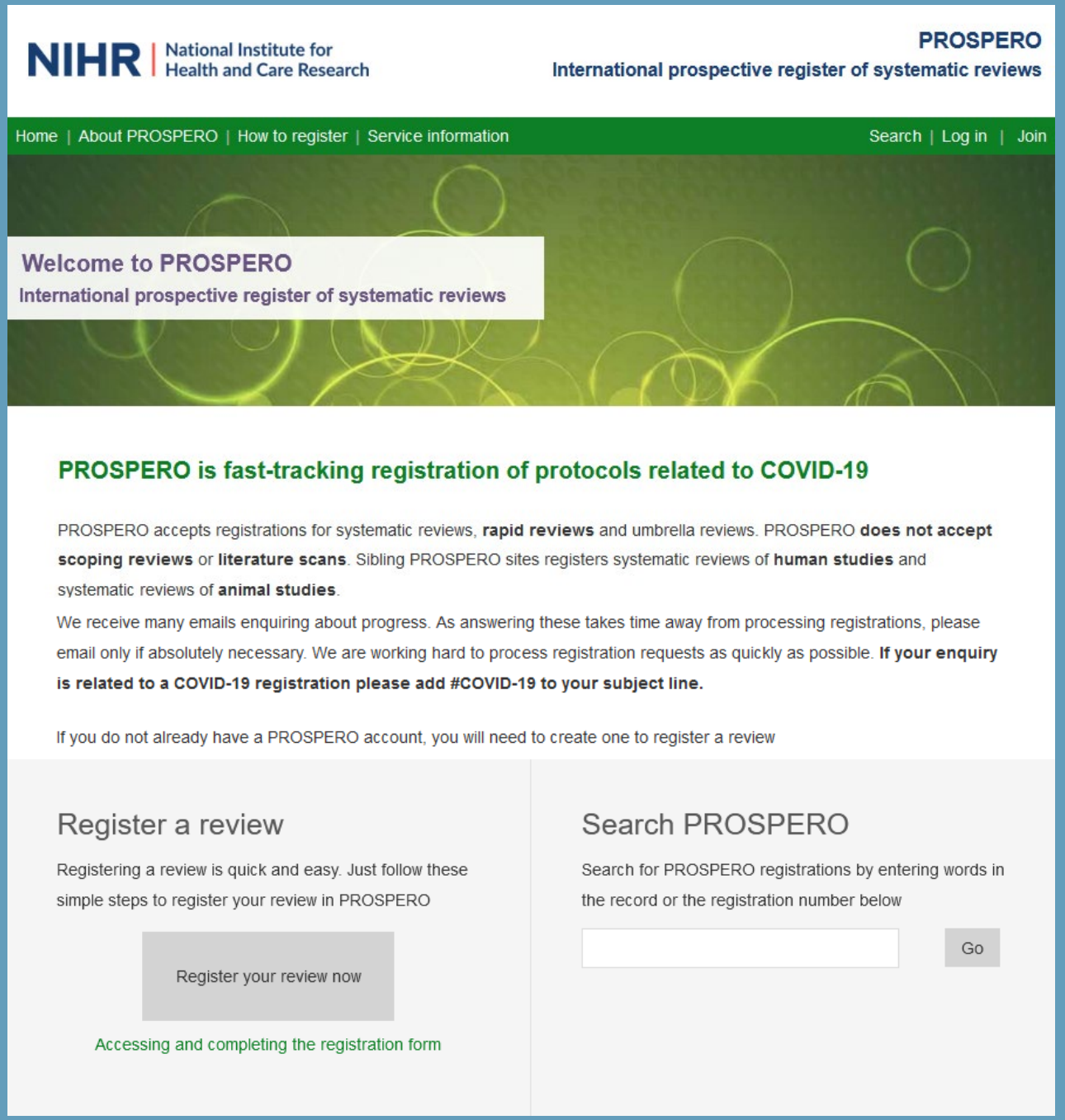
- Registration in PROSPERO has 27 mandatory and 14 optional fields
- Registration requirements
  - The full protocol needs to be ready
  - Registration must be completed prior to the beginning of data extraction
  - Registration form must be complete and in English

https://www.crd.york.ac.uk/prospero/#aboutpage


NIHR | National Institute for Health and Care Research
PROSPERO
International prospective register of systematic reviews
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Welcome to PROSPERO
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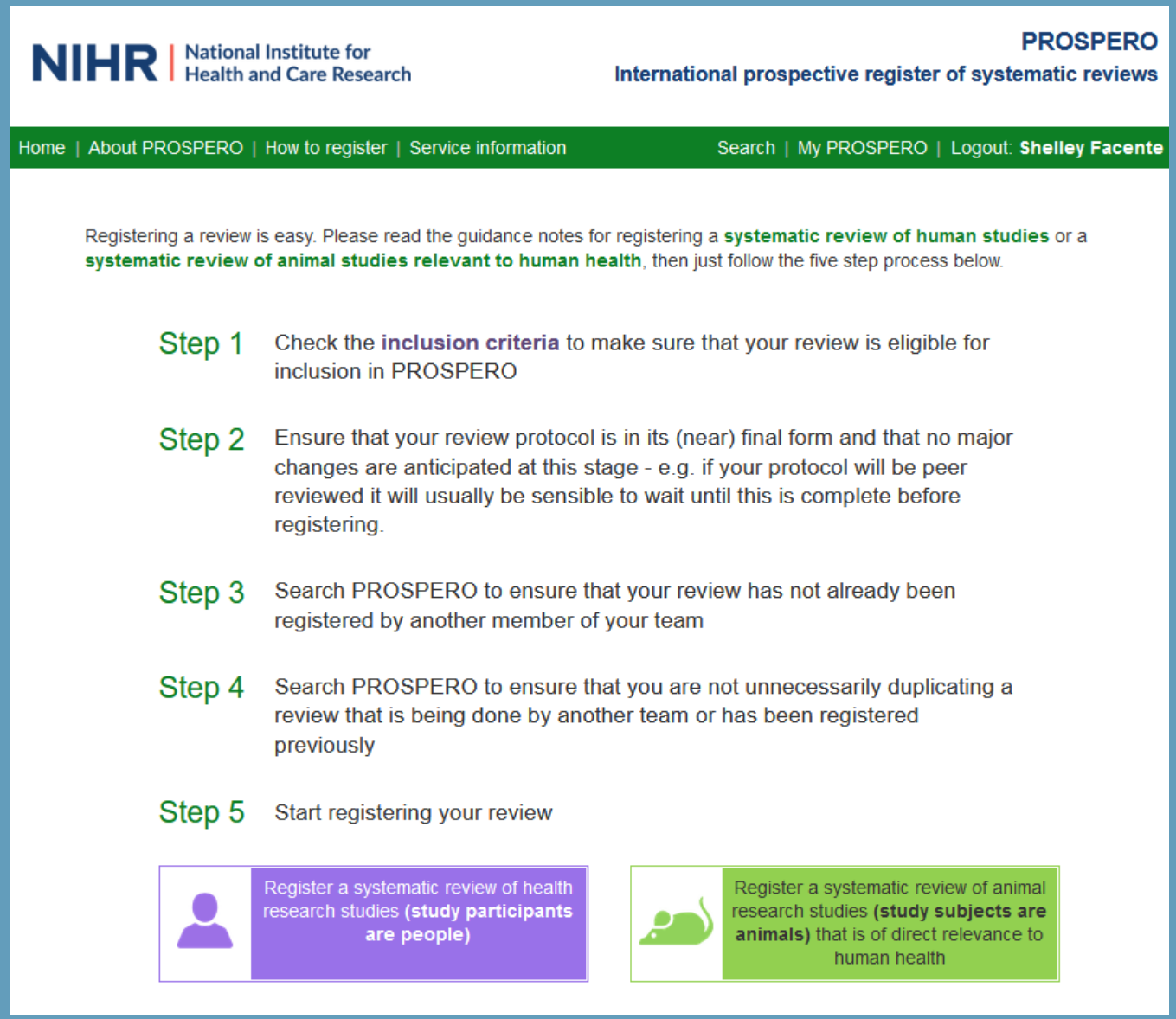
PROSPERO is fast-tracking registration of protocols related to COVID-19
PROSPERO accepts registrations for systematic reviews, rapid reviews and umbrella reviews. PROSPERO does not accept scoping reviews or literature scans. Sibling PROSPERO sites registers systematic reviews of human studies and systematic reviews of animal studies.
We receive many emails enquiring about progress. As answering these takes time away from processing registrations, please email only if absolutely necessary. We are working hard to process registration requests as quickly as possible. If your enquiry is related to a COVID-19 registration please add #COVID-19 to your subject line.
If you do not already have a PROSPERO account, you will need to create one to register a review
Register a review
Registering a review is quick and easy. Just follow these simple steps to register your review in PROSPERO
Register your review now
Accessing and completing the registration form
Search PROSPERO
Search for PROSPERO registrations by entering words in the record or the registration number below
Go


NIHR | National Institute for Health and Care Research
PROSPERO
International prospective register of systematic reviews
Home | About PROSPERO | How to register | Service information
Search | My PROSPERO | Logout: Shelley Facente
Registering a review is easy. Please read the guidance notes for registering a systematic review of human studies or a systematic review of animal studies relevant to human health, then just follow the five step process below.
Step 1
Check the inclusion criteria to make sure that your review is eligible for inclusion in PROSPERO
Step 2
Ensure that your review protocol is in its (near) final form and that no major changes are anticipated at this stage - e.g. if your protocol will be peer reviewed it will usually be sensible to wait until this is complete before registering.
Step 3
Search PROSPERO to ensure that your review has not already been registered by another member of your team
Step 4
Search PROSPERO to ensure that you are not unnecessarily duplicating a review that is being done by another team or has been registered previously
Step 5
Start registering your review
Register a systematic review of health research studies (study participants are people)
Register a systematic review of animal research studies (study subjects are animals) that is of direct relevance to human health

NIHR | National Institute for Health and Care Research

PROSPERO
International prospective register of systematic reviews

Home | About PROSPERO | How to register | Service information Search | My PROSPERO | Logout: **Shelley Facente**

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

*Fields that have an **asterisk (*)** next to them means that they **must be answered. Word limits** are provided for each section. You will be unable to submit the form if the word limits are exceeded for any section. Registrant means the person filling out the form.*

Print | PDF

Submit Save Exit

1. * Review title.
Give the title of the review in English

50 words remaining

2. Original language title.
For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

50 words remaining

3. * Anticipated or actual start date.
Give the date the systematic review started or is expected to start.

4. * Anticipated completion date.
Give the date by which the review is expected to be completed.

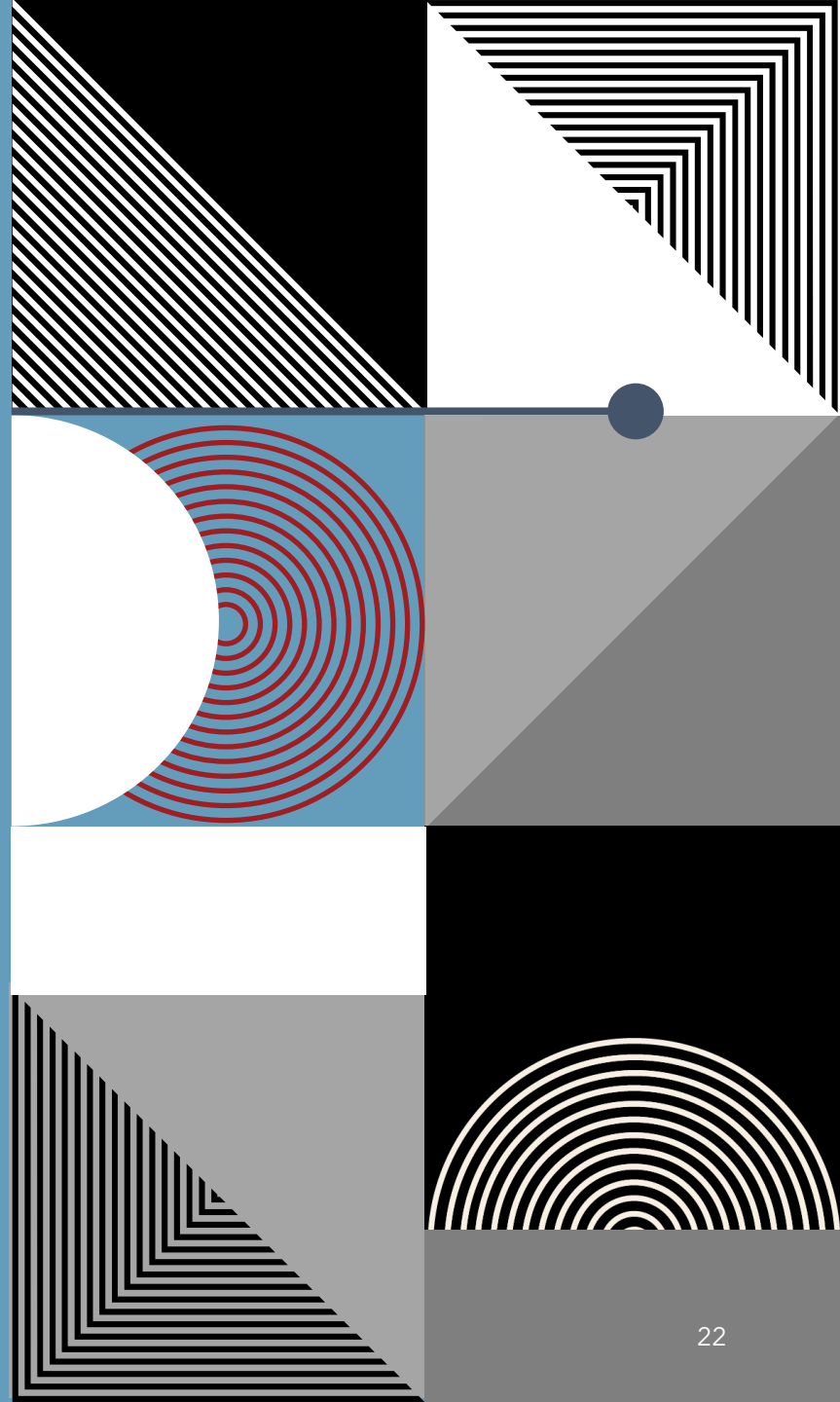
5. * Stage of review at time of this submission.

MANDATORY

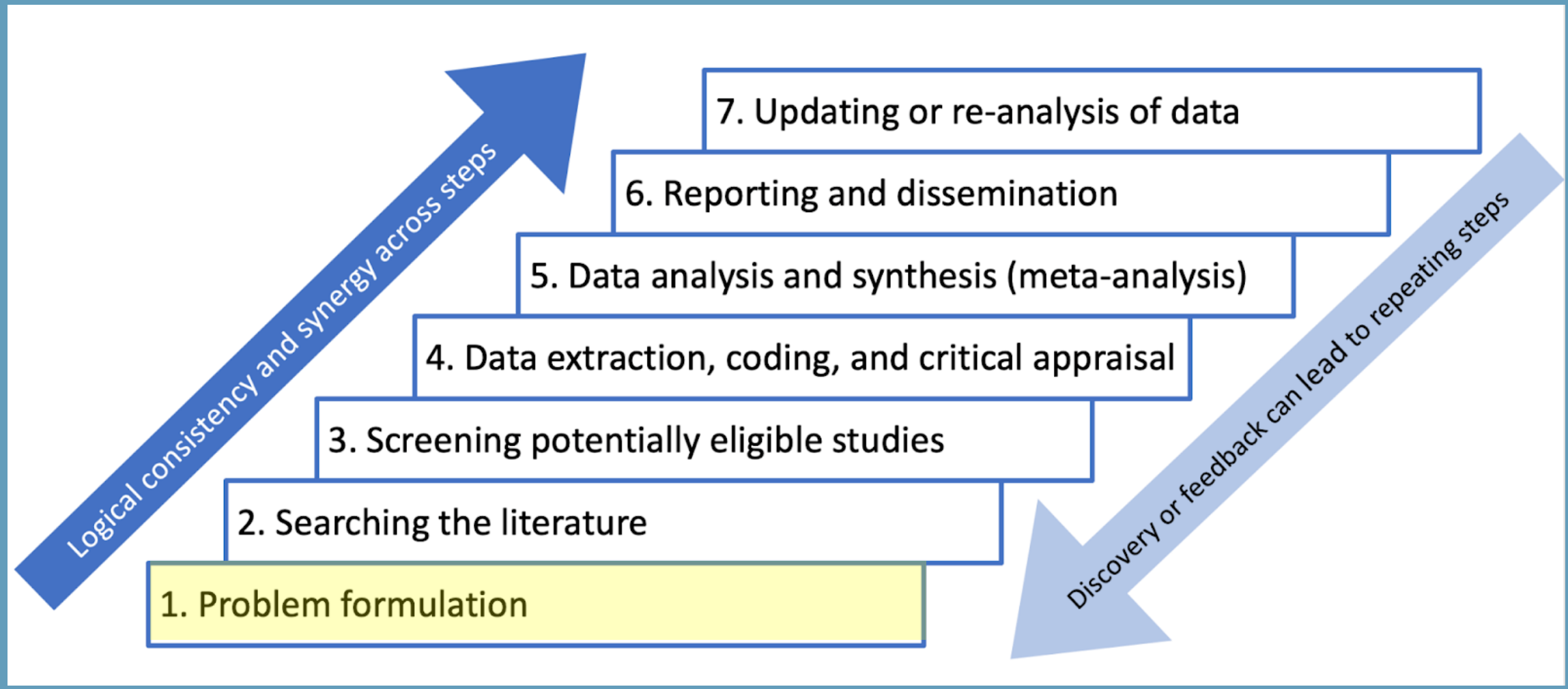
1. Title
2. Anticipated or actual start date
3. Anticipated completion date
4. Stage of review at time of PROSPERO submission
5. Contact name
6. Contact email
7. Organizational affiliation for the review
8. Review team members (name, affiliation, email, and country)
9. Funding sources/sponsors (names and grant numbers)
10. Real or perceived conflicts of interest
11. Collaborators (name, email, and country)
12. Review question (research question)
13. Search sources, dates, and any restrictions
14. Condition or domain being studied
15. Participants/population (**P**ICOS)
16. Interventions/exposures (P**I**COS)
17. Comparators/control (PI**C**OS
18. Main outcomes (PIC**O**S), with measures of effect if applicable
19. Additional outcomes (if any)
20. Types of studies to be included (PICO**S**)
21. Data extraction (selection and coding)
22. Risk of Bias (quality) assessment plans
23. Strategy for data synthesis
24. Analysis of subgroups or subsets
25. Type and method of review (checkboxes to choose from)
26. Country (or countries) carrying out the review
27. Current review status

OPTIONAL

1. Original language title
2. Contact address
3. Contact phone number
4. URL to a file with your full search strategy
5. Context of setting (inclusion/exclusion criteria)
6. Health area of the review
7. Language of the review
8. Other registration details (including any other places the review title, protocol, or extracted data are or will be registered)
9. Reference and/or URL for published protocol (if any)
10. Dissemination plans
11. Keywords
12. Details of any existing review of the same topic by the same authors
13. Any additional information
14. Details of final report/publication(s) or pre-print – add when done!



SYSTEMATIC REVIEWS PROCESS



https://oli.cmu.edu/courses/systematic-reviews-and-meta-analysis-o-f/#

DEFINING THE REVIEW QUESTION

- What is your motivation and rationale for conducting a systematic review? Be clear about why you want to complete a review.
- Before embarking on a review, search to see if this has already been done or if it is currently being worked on.

Scoping search

1. Has this already been done?
   a. Google Scholar
   b. PubMed
   c. Cochrane
   d. Others
2. Is this currently being conducted?
   a. PROSPERO

DEFINING THE REVIEW QUESTION

- Select a topic
- Develop a question (that can be answered)
- Set the scope (PICO)
- Create the criteria (eligibility – both inclusion and exclusion)
- Write the protocol

https://oli.cmu.edu/jcourse/workbook/activity/page?context=79edf8800a0001dc4b1c83a8e13ea0c1

DEFINING THE REVIEW QUESTION - PICO

https://libguides.lb.polyu.edu.hk/syst_review/PICO

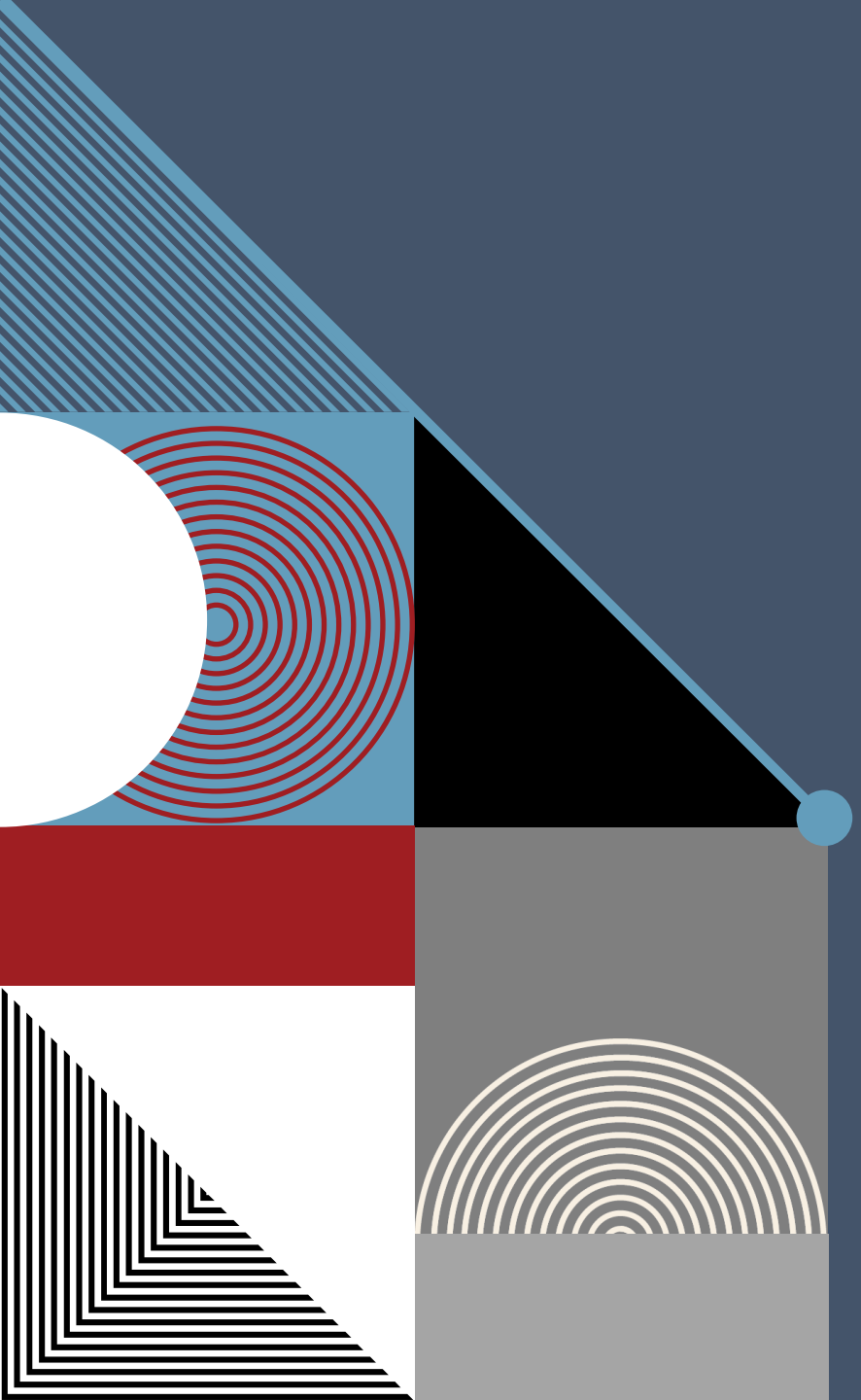
DEFINING THE REVIEW QUESTION - PICO

P = Patient, Population, Problem

Intention = Specify the condition and/or specific characteristics of the subgroup of people of interest

What are examples you can think of?

https://libguides.lb.polyu.edu.hk/syst_review/PICO

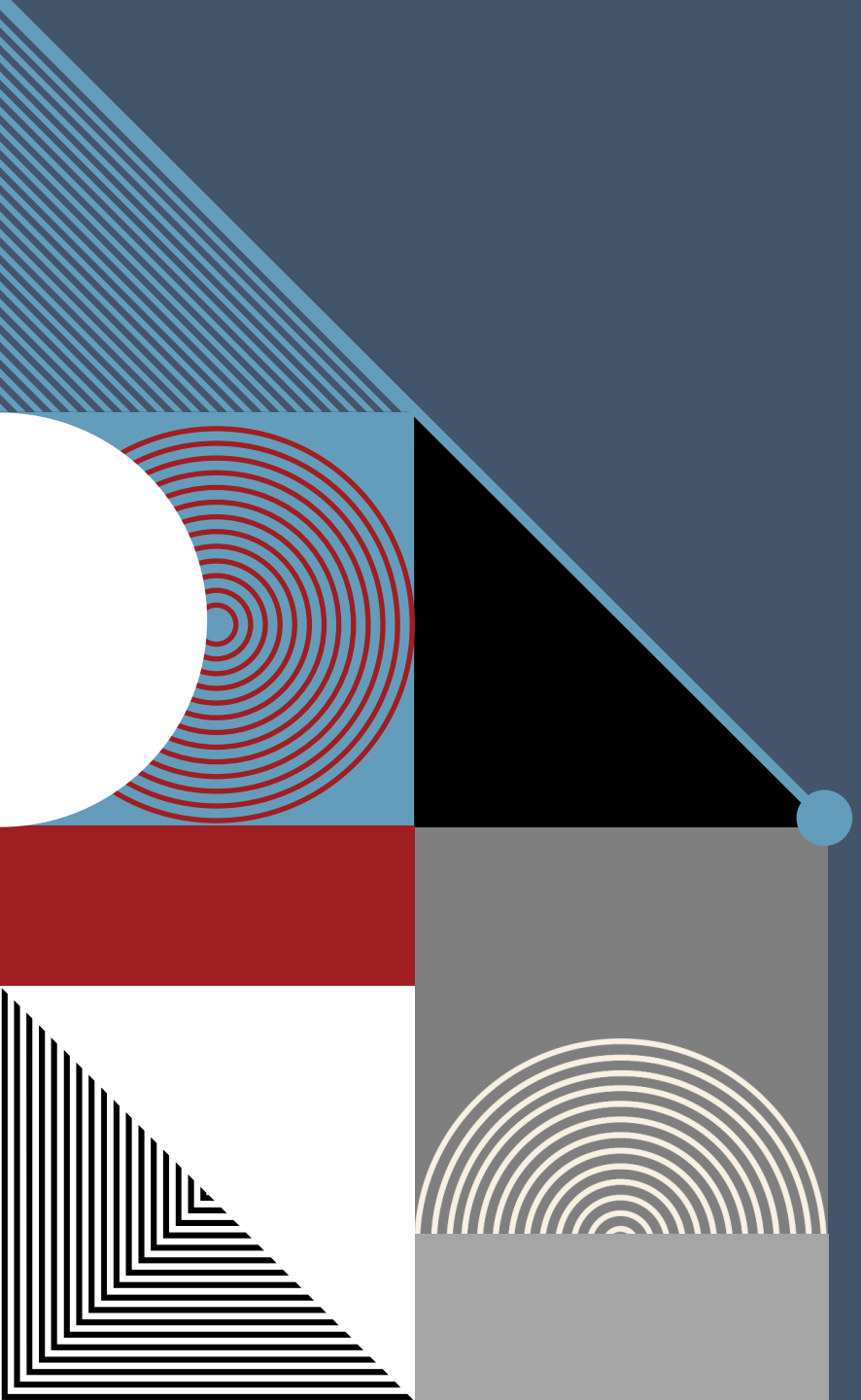


DEFINING THE REVIEW QUESTION - PICO

I = Intervention (Prognostic factor or exposure)

Intention = Specify the intervention and its specifics

What are examples you can think of?

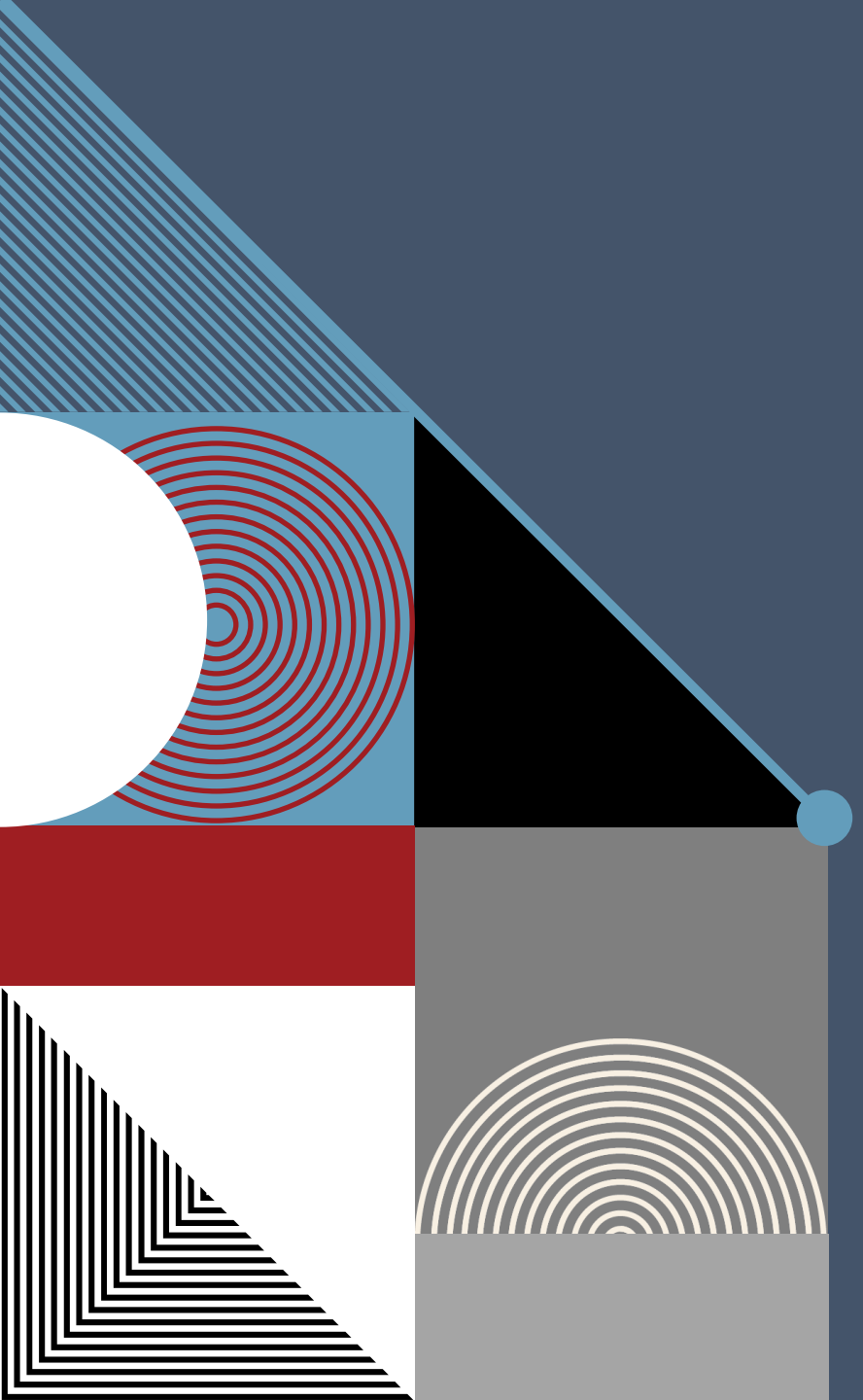


DEFINING THE REVIEW QUESTION - PICO

C = Comparison or Control

Intention = Specify the comparison for the intervention. This may be the standard of care

What are examples you can think of?

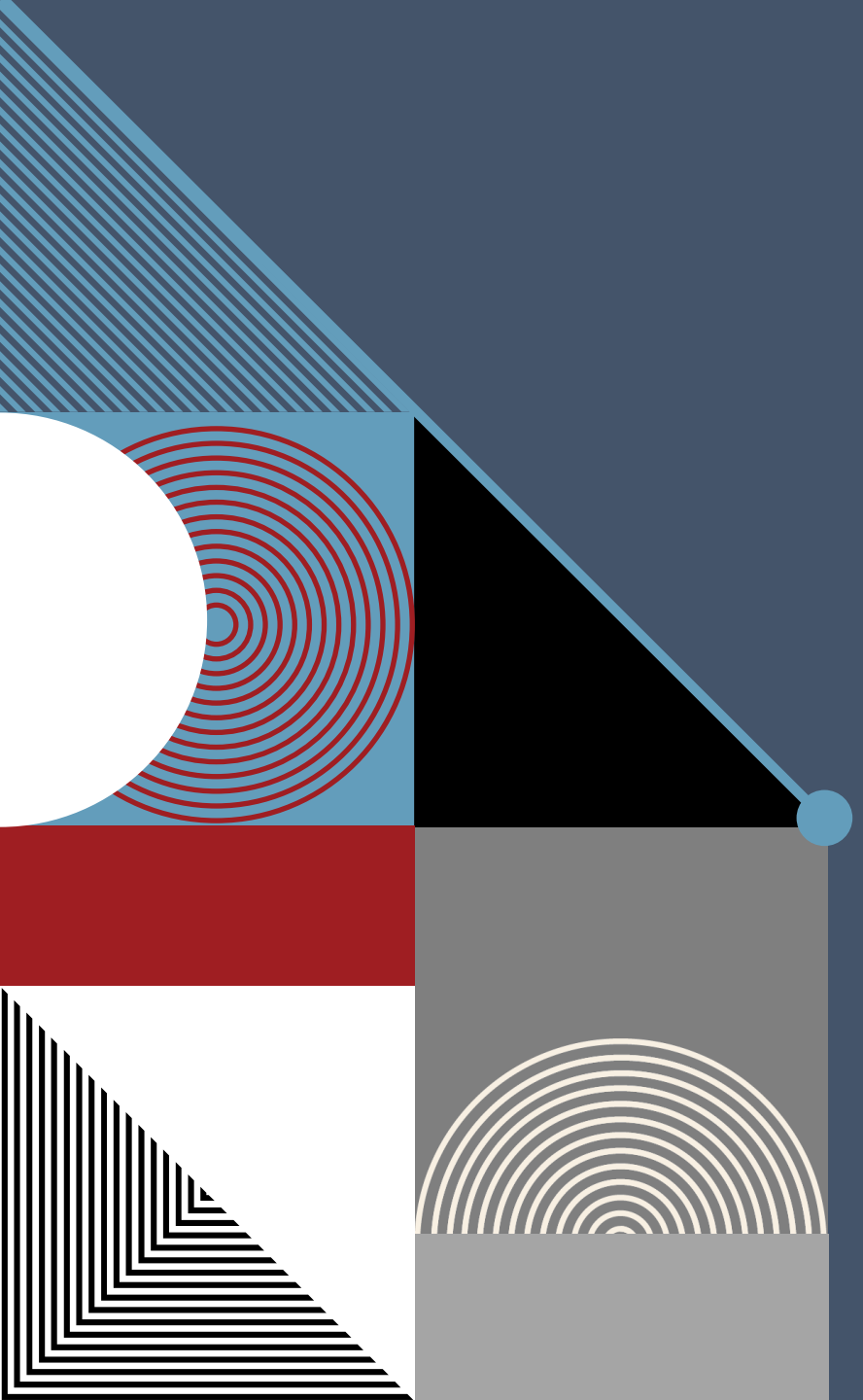


DEFINING THE REVIEW QUESTION - PICO

O = Outcomes

Intention = Specify what is being measured

What are examples you can think of?



DEFINING THE REVIEW QUESTION - PICOS

S = Study Design

- This is an addition to PICO that can be important to increase specificity of your search (less results overall but more specific to what you are interested in)

Intention = Specify the study type to include

What are examples you can think of?

PICO

	P (Patient or Population or Problem)	I (Intervention, prognostic factor, exposure)	C (Comparison)	O (Outcomes)
Intention	State the disease, age and gender, if appropriate, of the population.	State the intervention and specifics related to it.	A therapeutic question always has a comparator (even if it is standard care).	What is being looked for or measured?
Example (a therapeutic question)	Women who have experienced domestic violence	Advocacy programmes	General practice or routine treatment	Quality of Life (measured by the SF-36 scale)
	Research question: For women who have experienced domestic violence, how effective are advocacy programmes as compared with routine general practice treatment for improving women's quality of life (as measured by the SF-36 scale)?			
	Objective: The purpose of this review is to evaluate the effectiveness of advocacy programmes as compared with routine general practice on the quality of life of women who have experienced domestic violence.			
	Title: The effectiveness of advocacy compared with routine general practice treatment for women who are or have previously experienced domestic violence: a systematic review of women's quality of life.			

Reproduced from: Bettany-Saltikov, J, (2010). Learning how to undertake a systematic review: part 1. Nursing Standard. 24(50), 47-55.

https://libguides.lb.polyu.edu.hk/syst_review/PICO

SELECTION CRITERIA: DEGREES OF RIGOR

What study types/design will be included?

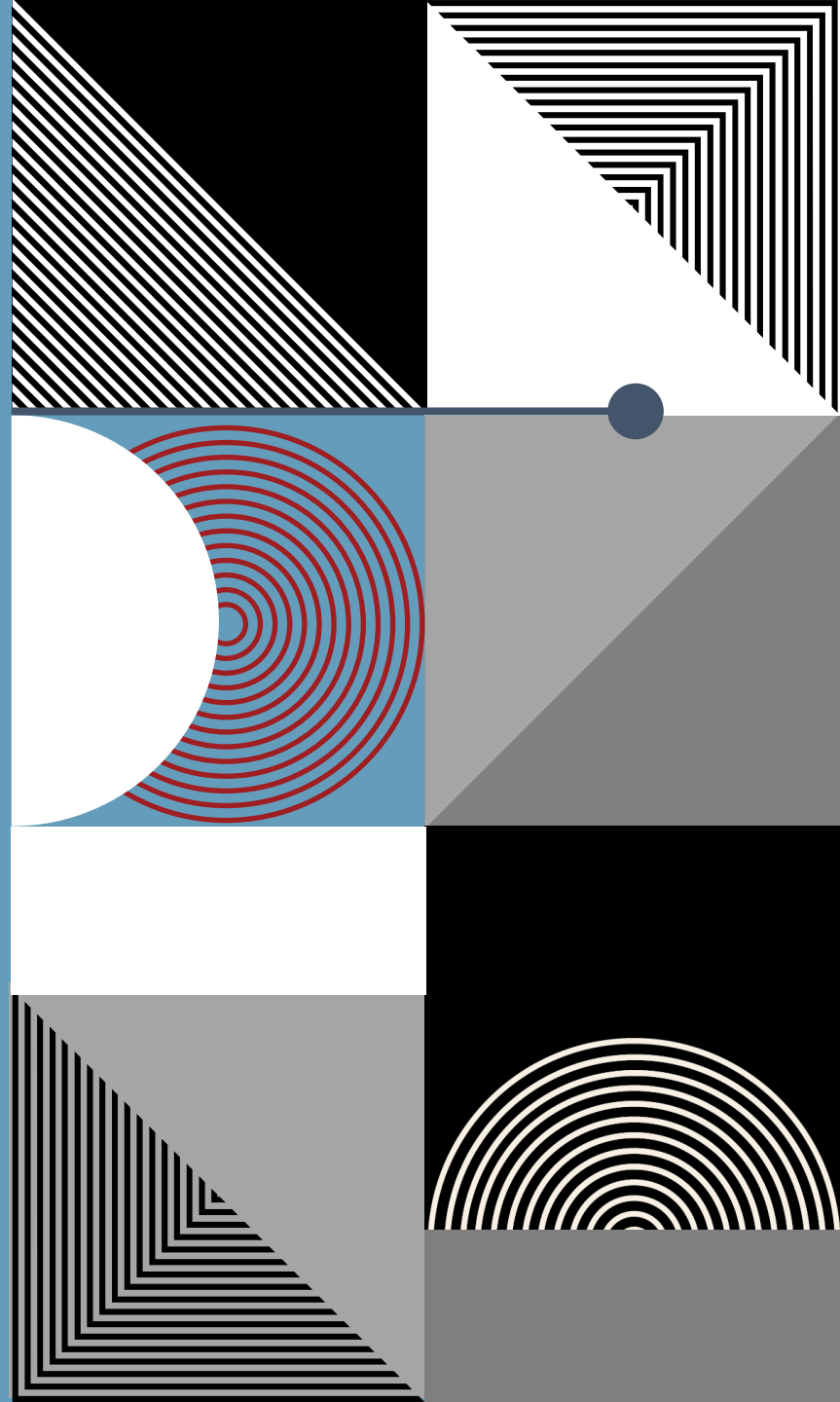
What date range will be included (limit to a specific date range or all publications)?

What languages will be included?

Search primary databases or include regional databases?

Will you plan to contact authors for data?

Will grey literature be included? Or only published? Or only peer-reviewed published?



CRITERIA PRACTICE

Case Studies

Identify the inclusion and exclusion criteria for each study.

Any questions?

CRITERIA PRACTICE

What did you think?

What questions do you have?

DEFINING THE RESEARCH QUESTION PRACTICE

Define the research question and PICOS criteria for your own project. Prepare to report back to other groups!