JOM RESEARCH

SYSTEMATIC REVIEW

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About me

Lead academic trainer at **Jom Research**

Background

- PhD (Public Health Epidemiology) from USM, 2024
- MSc (Medical Statistics) from USM, 2019
- MBBCh from Al-Azhar University, 2015

Interest:

- Medical statistics, meta-analysis, bibliometrics, scientometrics, text analysis
- Machine learning and deep learning application in medical sciences
- Application of R on health/medical data

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Jom Research promotion

JOM RESEARCH

Systematic Review

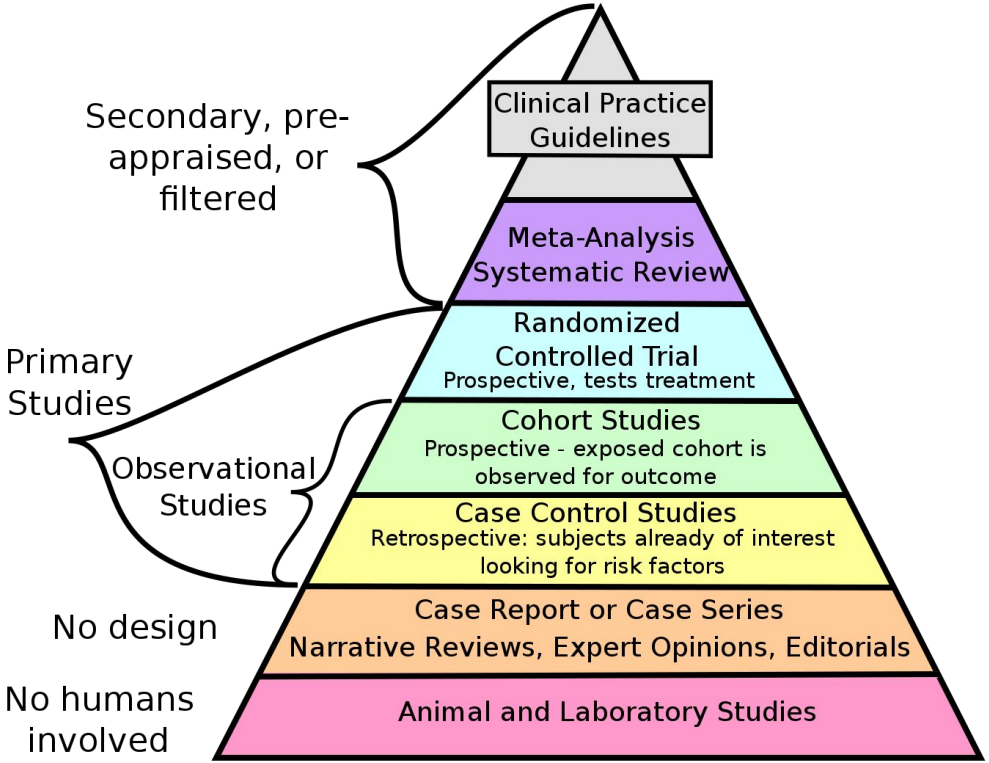
PART 1

JOM RESEARCH

Outline for Part 1

- Hierarchy of evidence
- Type of review papers
- What is a systematic review?
- Aims of a systematic review
- Step by step
- Common mistakes
- Common biases

Hierarchy of evidence



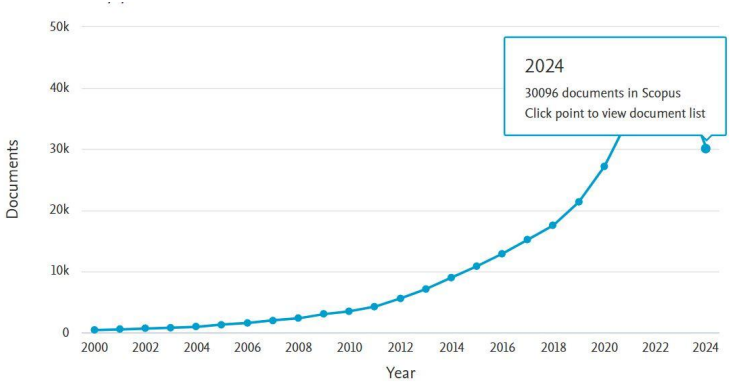
Type of review papers

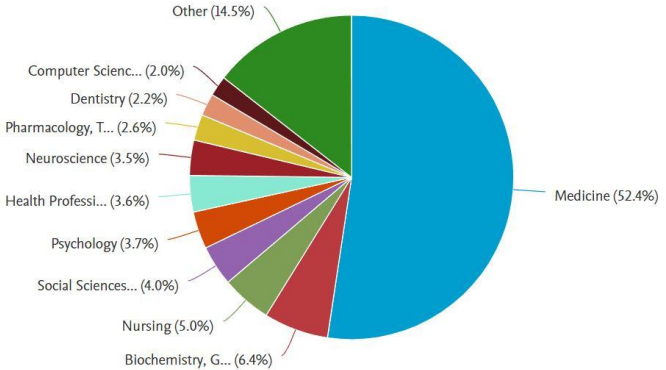
- There are at least 14 types of review paper (Grant et al., 2009)
- The most common ones:
  - Narrative review/non-systematic review*
  - Systematic review*
  - Scoping review*
  - Bibliometric review
  - Meta-analysis

**no statistical analysis involved*

What is a systematic review?

- A review of previous articles that uses **systematic methods** to collect and synthesise the finding to answer a **well-defined question**
  - Systematic: transparent and comprehensive, so that others able to replicate and update the review





Scopus data: 2000-2024

Aims of a systematic review

- Answer a specific objective
- Summarise the studies according to the objectives

Step by step
(10 steps)

1. Formulate a research question

- General idea/question that needs a specific answer
- May come by:
  - Reading a lot of literature
  - Practical experience
- Example:
  - Does drug A effective for diabetic patients?
  - Does e-learning is a good alternative for student during COVID19?

2. Develop a review plan

- A review plan should contain:
  - Objectives
  - Data/variables to be collected
  - Databases
  - Selection criteria
  - Search terms and strategy
  - Quality of study assessment tool
- The plan must be developed and discussed early with collaborators

Review plan - objectives

- Be specific
- Use PICO/PICOT/PICOS
  - Participant, intervention, comparison, outcome, time*, study design*
- Example:
  - To study the effectiveness of drug A in comparison to drug B among diabetic patients in controlling blood glucose
  - To study the impacts of e-learning course/lecture in comparison to physical lecture among medical students on their grades during COVID-19

**optional*

Review plan - data to be collected

- Determine the main and related data/variables to be collected
- Main data is the data that directly related to the objectives:
  - Type of e-learning, characteristic of normal physical lecture
- Related data is the data that indirectly related to objectives:
  - Country, characteristics of participants, type of school, study design, etc
- List all the variable that need to be collected in a list
- All the data can be collected in Microsoft Excel or Google Sheets

Review plan - databases

- Databases:
  - Free: Google Scholar, PubMed, Dimension, Cochrane, etc
  - Paid: Scopus, Web of science, Embase, etc
- Pick 3-5 databases
- Include Google Scholar if the expected number of papers are low

Review plan - selection criteria

- May further divided into:
  - Inclusion criteria
  - Exclusion criteria
- Based on the objectives
- Example (based on effectiveness of drug A previously):
  - Inclusion - RCT, include drug A and B
  - Exclusion - Non-diabetic patients

Review plan - search terms and strategy

- Based on the research objectives
- Include alternatives terms, MESH terms (medical), boolean operator
- Common boolean operator:
  - AND, OR
  - “Wild behavior” - find exact phrase wild behavior
  - Wildcards: behav* - find behave, behavior, behaviour, behavioural, behaviourism, etc
- Boolean operator guidelines for:
  - Scopus
  - Google Scholar
  - PubMed

- Compartmentalise the search strings:
  - Search strings/objectives: **To study the effect of physical exercise during pregnancy among diabetic women**
  - Search terms 1: exercise OR “physical activit*” OR sport OR fitness
  - Search terms 2: pregnancy OR “gestation*”
  - Search terms 3: diabetes OR “diabetic patients” OR “glucose intolerance”
  - Taylor to each database
- Example:
  - Google Scholar - use “allintitle:”
  - Scopus
  - PubMed

Review plan - quality of study assessment tool

- To assess risk of bias in the included studies:
  - ROBINS-I: non-randomised intervention studies
  - RoB 2: randomised trials/studies
  - NOS: non-randomised studies, observational studies
  - CASP: RCT, cohort, case-control, etc
  - JBI: RCT, cohort, case-control, etc

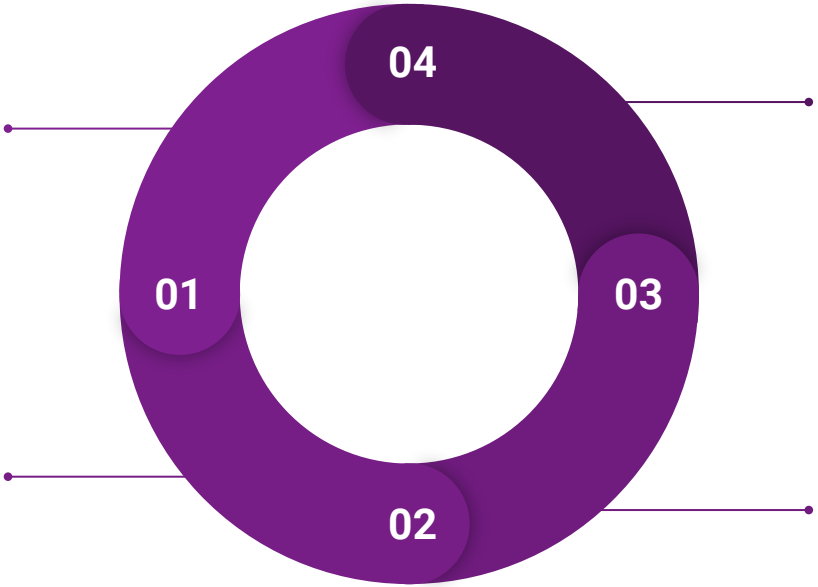
3. Paper searching and extraction

Paper searching

- Take note the date and number of paper for each database
- Make sure the search is extensive and avoid missing a paper:
  - If not, reduce generalisability

Data extraction

Extract relevant bibliographic information:
1) author
2) year
3) title
4) abstract
5) type of paper



Export data for screening

- Rayyan, reference manager, Google Sheet, Excel, etc
- Export as csv or export as BibTex then change to csv using online converter - for Google Sheet and Excel

Import data to reference manager

- Remove duplicates in reference manager: Mendeley, EndNote, Zotero, JabRef
- So far the best options - JabRef and Mendeley Dekstop (the old one)

4. Paper screening

- Removes duplicates if still has not been done yet
- Apply predefined selection criteria
- Start with the title, abstract and full-text (if needed)
- At least two independent reviewers - important!
- Suggested strategy:
  - 2 phases:
    - 1st phase: only screen title and abstract
    - 2nd phase: full-text
  - Increase number of reviewers as needed
- Can be done:
  - Rayyan - not totally free, need to remove duplicate first in Reference Manage

- Microsoft Excel
- Google Sheet

Author, year	Title	Abstract	Reviewer 1	Reason R1	Reviewer 2	Reason R2	Reviewer 3	Reason R3	Consensus
Ahmad, 2023	Title 1	Abstract 1	Yes		No	Not RCT	Yes		Yes
Kyle, 2000	Title 2	Abstract 2	Yes		Yes		Yes		Yes

5. Download the papers

- Download the final papers that meet the selection criteria

6. Register the protocol

- Register systematic review:
  - PROSPERO:
    - Only accepted SR protocol related to human and animal studies
    - Must be submitted before data extraction
  - Peer reviewed journals - use PRISM-P to guide the write-up
  - Non-peer reviewed sources:
    - Preprints - multidisciplinary
    - medRxiv - medical
    - arXiv - more general but non-medical
    - OSF
      - Generalised systematic review form; Google Docs, Google Sheets
      - Example in OSF

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

7. Data extraction

- Extract relevant data from the full-text/paper
- At least two independent extractors
- Make a characteristic table while reviewing
- Extract data based on the plan formulated in Step 2 - review plan

Table 1 Descriptive characteristics and findings of included studies in stroke subcategory

		Sample	Intervention	Comparison	Outcome	Test	Results	Conclusion	User feedback / follow-up info
[29]	Adomaviciene 2019 RCT	N=42 Subacute Mean age= 64.6	VR Kinect + conventional 2 weeks 5 times/ week	Conventional with robot-assisted trainer "Armeo Spring" 2 weeks 5 times/ week	UE mobility Function* Psycho-emotional	FMA, MAS BBT, HTT ROM, FIM HAD	No between group difference in FIM, but p<0.05 in self-care in VR. UE function significant improvement p<0.05 in both groups VR p<0.05 in HAD	Both groups improved in function, UE mobility and cognitive abilities.	Great user satisfaction, improved psycho-emotional state in VR/ No follow-up
[20]	Fishbein 2019 RCT	N=22 Chronic Mean age= 65.2	VR dual task walking 4weeks 2 times/ week	Conventional treadmill single task walking 4weeks 2 times/ week	Gait Balance Function	10MWT, TUG FRT, BBS ABC	VR p<0.01 in BBS, FRT, 10MWT, ABC	VR is effective in improvement of balance, gait and function. Advised combination with conventional training with multitasking	Follow-up 4 weeks – effect maintained
[32]	Kiper 2018 RCT	N = 136 Chronic, subacute Mean age= 63.9	VR + conventional 4 weeks 5 times/ week	Conventional 4 weeks 5 times/week	UE mobility Function	FMA FIM NIHSS ESAS	VR + conventional p<0.05 in all outcomes	VR combined with conventional has greater effect on UE function	No follow-up

8. Analyse the data (quantitatively)

- Descriptive – summary of characteristics table
- Report the results (related to the research question and objectives)
- Interpret the result and draw a conclusion
- Make sure to answer the research question and achieve the objectives

9. Assess the quality of the study

- At least two independent reviewers
- Use the critical appraisal tool selected in the review plan (Step 2)
- Recommend to present a traffic light plot (if possible)
- Can use robvis:
  - RoB 2 - randomised trials/studies
  - ROBINS-I - Non-randomised interventional studies
  - ROBINS-E - Non-randomised exposure/observational studies
  - QUIPS - prognostic studies
- Other tools:
  - Newcastle-Ottawa scale (NOS) - Non-randomised non-interventional studies
  - JBI critical appraisal tools

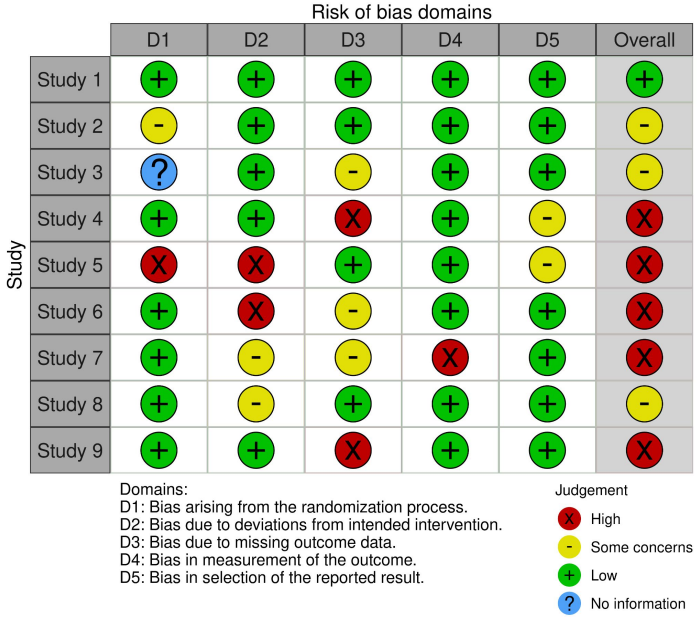
- Quality assessment can be presented in text, table or in figure

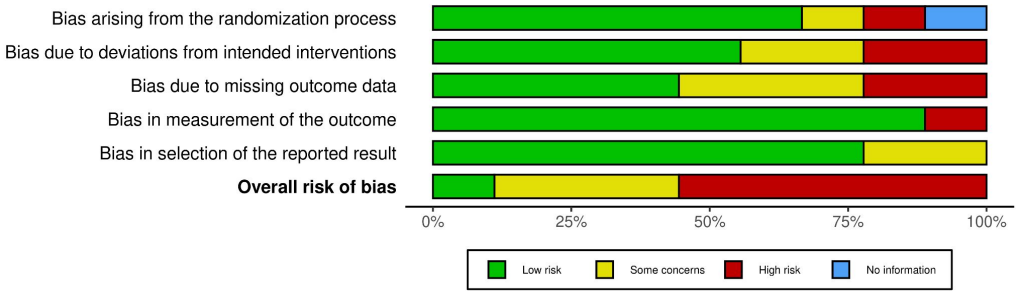
Quality assessment

Filtered and selected for a full-text reading articles (n = 59) were assessed for methodological quality by the CASP tool for randomized controlled trials [19]. Articles included in the final list for the review were graded 9–11 (high quality), assuming that double blinding was not possible in such experimental studies. The grading was not affected if the RCT was at least single-blinded. Five studies [20–24] did not provide a sample size/ power calculations but this limitation was not determinant in the grading. All studies reported on correct randomization procedures, low drop-out rates and few losses to follow-up. Few studies had selective reporting of effects for some secondary outcomes. All studies had limited generalizability of results.

Table 3. Newcastle-Ottawa scale of studies included in the systematic review.

	Selection			Comparability		Outcome			
Study	Representativeness	Selection exposed cohort	Ascertainment	Result not present at start of the study	Comparability for confounders	Assessment of outcome	Follow-up duration	Adequacy of follow-up	Total
*Baricich et al. 2021	*		*	*	*	*	*	-	6
Blanco et al. 2021	*		*	*	*	*			5
Bellan et al. 2021		*	*	*	*	*	*		6
Cao et al. 2021		*	**	*		*	*		6
Cortés-Telles et al. 2021			*	*		*			3
Debeaumot et al. 2021		*	*	*	*	*	*	*	7
Guler et al. 2020	*		*	*	*	*	*	*	7
Huang et al. 2021	*	*	*	*	**	*	*		8
*Iqbal et al. 2021		*	*	*		*	*	-	5
*Leite et al. 2021			*	*	*	*	*	-	5
Parker et al. 2021	*	*	*	*					4
PHOSP-COVID et al. 2021	*		**	*	*	*	*		7
Piquet et al. 2021	*	*	*	*		*		*	6
Puchner et al. 2021	*		*	*	**	*	*		7
Qu et al. 2021	*		**	*		*	*	*	7
Rass et al. 2021			*	*	*	*		*	5
Taboada et al. 2021	*	*	*	*			*	*	6
Todt et al. 2021	*	*		*	*	*	*	*	6
*Townsend et al. 2021	*		*	*	**	*	*	-	7





Traffic light plot (right) and summary plot (left)

10. Write-up

- Use PRISMA checklist to guide the write-up
- JBI manual for evidence synthesis:
  - Extensive
  - Provides guideline for each type of systematic review

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 model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	

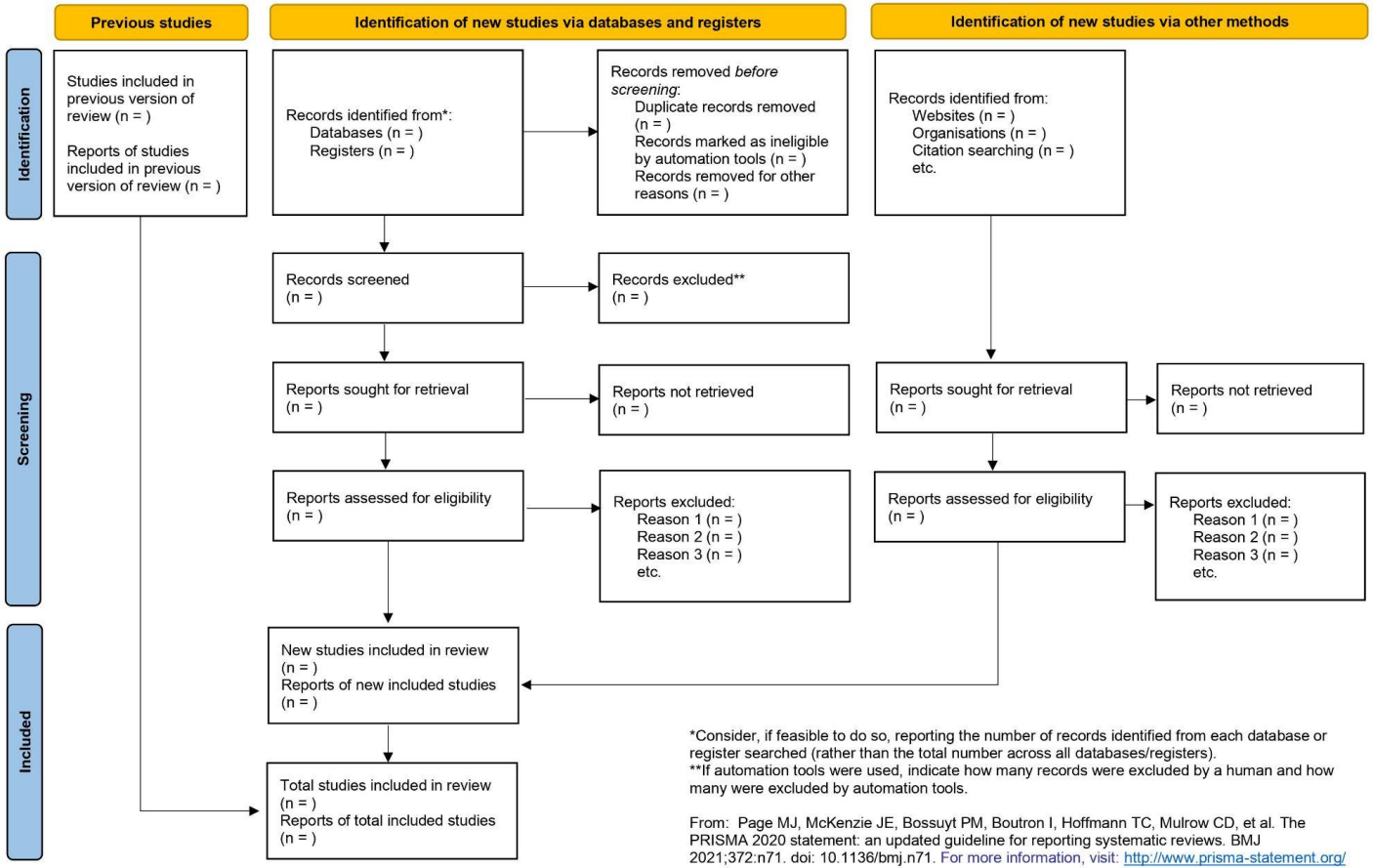
PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	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.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 flow diagram for updated systematic reviews which included searches of databases, registers and other sources



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Any question?

JOM RESEARCH

Systematic Review

PART 2

Common mistakes in systematic review

- Risk of bias or quality assessment are not done
- Search strategy is not well-planned or exhaustive enough
- Not registering the protocol

Common biases in a systematic review

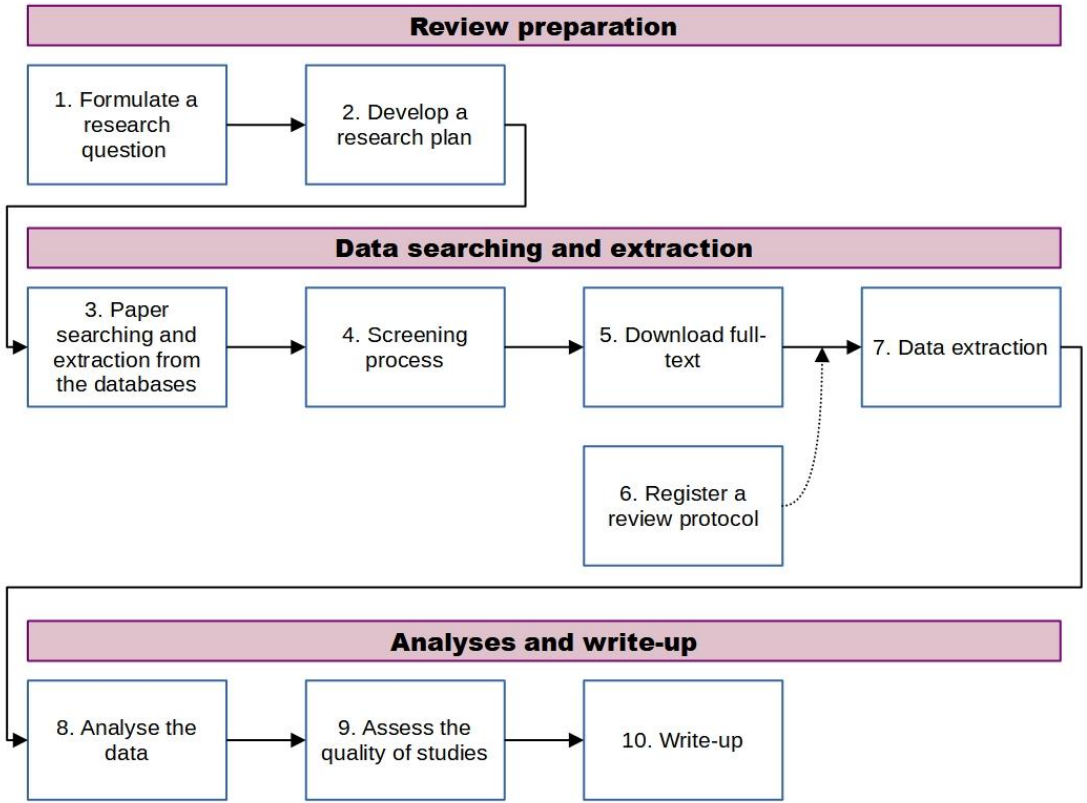
- Bias = deviation from truth

Biases	Details	How to overcome
Publication bias	- Papers with non-significant/non-desirable result are not published	Include preprint, thesis and non-published sources

Selection bias	- Included papers are not representative:
	  - Search not exhaustive
	  - Improper inclusion and exclusion criteria
	  - Include only English language
		Discuss extensively with all the collaborators and develop a proper review plan

Language bias	- Positive finding more likely to be published in international journals - Negative findings are more likely to be published in local journals	Include papers from different languages (may not be possible)

Summary


Review preparation
1. Formulate a research question
2. Develop a research plan
Data searching and extraction
3. Paper searching and extraction from the databases
4. Screening process
5. Download full-text
7. Data extraction
6. Register a review protocol
Analyses and write-up
8. Analyse the data
9. Assess the quality of studies
10. Write-up

References

- Grant, M.J. and Booth, A. (2009). A typology of reviews: an analysis of 14 review types and associated methodologies. Health Information & Libraries Journal. 26: 91-108. https://doi.org/10.1111/j.1471-1842.2009.00848.x
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- Meo, S. A. (2018). Anatomy and physiology of a scientific paper. Saudi Journal of Biological Sciences. 25(7): 1278–1283. https://doi.org/10.1016/j.sjbs.2018.01.004
- Rodzlan Hasani WS, Muhamad NA, Hanis TM, Maamor NH, Wee CX, Omar MA, et al. (2023). The burden of premature mortality from cardiovascular diseases: A systematic review of years of life lost. PLoS ONE 18(4): e0283879. https://doi.org/10.1371/journal.pone.0283879 (example of systematic review)

Acknowledgement

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Any question?

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