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Generic Protocol for Environmental Health Systematic Reviews Based on COSTER Recommendations V.1

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COSTER _Reports

Paul Whaley[1]

[1]Lancaster University

Systematic Reviews

Paul Whaley
EBTC

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Protocol status: In development
This is the first attempt at developing a generic protocol based on the COSTER recommendations. Feedback is very welcome!

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Abstract

A protocol template to help researchers follow the **COSTER recommendations** for conduct of systematic reviews. This instance covers the planning steps of a systematic review and will help with writing up the systematic review protocol.

The intent is to convert COSTER from a checklist of things which need to be done into a sequence of actions which can be followed by a research team.

When completing the protocol and either registering it or submitting it to a journal, please cite this instance of the protocol template and the parent manuscript, DOI **10.1016/j.envint.2020.105926**.

Image Attribution

Image by Paul Whaley.

Guidelines

Protocols.io has not yet been optimised as a means for reporting what was done in response to complex instructions such as those found in this protocol. Feedback on use of the protocol, and how to develop it to facilitate reporting of planned methods, would be very much appreciated.

Troubleshooting

Securing capacity, competencies, and tools

1 **Assess the team's combined competence in conduct of a systematic review**.
Recommendation 1.1.1.

	Competency	Team member(s) (initials)
	Information science (for e.g. search strategies)	
	Evidence appraisal methods (i.e. risk of bias assessment)	
	Statistical methods	
	Domain or subject expertise	
	Systematic review methods	

Team member competencies

2 **Identify information management practices and tools for each stage of the review**. *Recommendation 1.1.2*.

	Information management component	Tools or packages
	Reference manager	
	Knowledge management tool	
	Systematic review software	
	Statistics software and packages	
	Aritifical Intelligence support tools (e.g. for screening)	

Information management tools and packages

3 **List the potential conflicts of interest of the authors**. *Recommendations 1.1.3 and 1.1.4*. This should include both financial and non-financial interests which readers should be aware of in order to understand the motivations of the authors of the review.

By listing the interests as *potential*, you are confirming that they are not *apparent* conflicts of interest, i.e. they cannot reasonably be expected to compromise the integrity of the systematic review. People with apparent conflicts of interest should be excluded from decision-making roles in the review.

Interests should be declared using the ICMJE Conflict of Interest Disclosure Forms, as attached. The summary statements generated by the forms for each author can be copy-pasted into the table. ICMJE COI Disclosure Form.pdf

	Author	ICMJE COI Summary

Summary statements of authors declared conflicts of interest.

Setting the research question ("problem formulation")

4 **Demonstrate the need for a new review**. *Recommendation 1.2.1*

4.1 Describe the scientific value of the question(s), i.e. why it is important that it be investigated.

4.2 Describe the importance to stakeholders of the question(s) being asked.

4.3 Summarise relevant existing primary research and evidence syntheses to justify conducting a new systematic review.

5 **Articulate the scientific rationale for each question via development of a theoretical framework**. *Recommendation 1.2.2.* For example, this would describe how the exposure is related to the outcomes of interest if the systematic review is an investigation of an exposure-outcome relationship. The theoretical framework should include discussion of the biological plausibility of the relationship being investigated.

6 **For each research question to be answered by the review, prospectively define a statement of the research objective in terms of Population, Exposure or Intervention, Comparator, Outcome, Study Design, and Target Condition, selected as appropriate**. *Recommendation 1.2.3.*

- Authors may wish to refer to Morgan et al. 2018 for guidance on how to formulate research questions as PECO statements. Conceiving of an ideal study may also help characterise the PECO elements which define what type of study will be informative for your review findings.

Citation

Morgan RL, Whaley P, Thayer KA, Schünemann HJ (2018)
. Identifying the PECO: A framework for formulating good questions to explore the association of environmental and other exposures with health outcomes..
Environment international.

https://doi.org/10.1016/j.envint.2018.07.015 LINK

6.1 **Define the target Population of interest**. These are the objects of investigation, i.e. the entities to which exposures or interventions happen.

	Species	
	Sex	
	Age	
	Health status	
	Additional characteristics	

Characteristics of the population of interest. Add rows to cover other population characteristics relevant to the SR question.

6.2 **Define the target Exposure or Intervention of interest**. This concerns the administered or observed change in conditions of the objects of investigation. It should include timing, duration and dose.

	Exposure or intervention	What is the exposure or intervention?

	Timing	When does the exposure or intervention happen?
	Duration	For how long does the exposure or intervention last?
	Dose	What is the dose regimen (amount, frequency)?

Timing, duration and dose of the exposure / intervention. Add rows to cover other exposure / intervention characteristics relevant to the SR question. Add a new table for each exposure or intervention of interest.

6.3 **Define the target Comparator of interest**. This concerns the characteristics of the exposure or intervention being used as the comparator to which the target exposure or intervention is being compared.

	Comparator	What is the comparator exposure or inter

		vention?
	Timing	When does the comparator happen?
	Duration	For how long is the comparator administered?
	Dose	What is the dose of the comparator (amount, frequency)?

Timing, duration and dose of the comparator. Add rows to cover other comparator characteristics relevant to the SR question.

6.4 **Define the target Outcome(s) of interest**. This concerns the change being measured in the exposure or intervention group. These should be the primary outcomes of interest to the systematic review which form the hypothesis or hypotheses being tested. Secondary outcomes can also be listed.

	Primary outcome 1	
	Primary outcome 2	

Primary outcomes of interest. Add new rows for each outcome of interest.

	Secondary outcome 1	
	Secondary outcome 2	

6.5 **Define the Target Condition**. This is the object of a test method for diagnosis or detection. It is only necessary for a systematic review of a diagnostic or detection test method.

	Target condition characteristic 1	
	Target condition characteristic 2	

Defining the eligibility criteria and designing the process for screening evidence for inclusion

7 **Define and justify unambiguous and appropriate eligibility criteria** for each component of the objective statement. *Recommendation 1.3.1, 1.3.3, 1.3.4, 1.3.5*

	PECO element	**Description of eligibility criteria**
	Eligible populations	Include e.g. age, sex, health status, socioeco

		nomic status, occupation etc.
	Eligible exposures	Include timing, methods for measurement exposure
	Eligible comparators	The populations and exposures against which the exposed populations are being compared
	Eligible primary outcomes	Specify the outcome, whether the outcome is apical (whole

		organism) or intermediate (is a marker of an apical outcome); the acceptable outcome measures (diagnostic criteria, scales, etc.) and timing of outcome measurement
	Eligible secondary outcomes	Specify the outcome, whether the outcome is apical (whole organism) or intermediate

		(is a marker of an apical outcome); the acceptable outcome measures (diagnostic criteria, scales, etc.) and timing of outcome measurement
	Eligible study designs	Define eligibile study designs by design features rather than design labels.

Describe the eligibility criteria for each PECO element. Add additional PECO elements as appropriate.

	PECO element	Description of exclusion criteria	Reasons for exclusion
	Excluded populations		
	Excluded exposures		
	Excluded comparators		
	Excluded outcomes		

Describe the criteria for exclusion of studies, according to each PECO element. Add additional PECO elements as appropriate.

8 **Define the points at which screening for eligibility will take place.** *Recommendation 1.3.2.* Will there be screening at title and abstract, full text, or both?

	Points at which screening will take place
	Describe whether there will be screening at title and abstract, full text, or both

Points at which screening will take place

9 **Include all relevant, publicly-available evidence**, except for research for which there is insufficient methodological information to allow appraisal of internal validity.
Recommendation 1.3.6. **Exclude evidence which is not publicly available**.
Recommendation 1.3.9

	Policy on eligibility of grey literature and unpublished evidence
	Describe how grey literature will be handled in the systematic review. If some or all grey literature is to be excluded, explain why

	and anticipate its implications as a limitation of review methods.

Policy on grey literature for the systematic review.

Note

COSTER recommends that grey literature (i.e. studies that have not been published in peer-reviewed journals) should be included in systematic reviews. This is because the relevance of evidence is determined by the SR objectives, not by the publication status of that evidence, the language the evidence is in, nor its compatibility with the analyses planned by the reviewers.

Only publicly available information about a study should be eligible for inclusion. If the planned SR will bring into the public domain evidence which was previously inaccessible, this makes the evidence eligible for inclusion.

Studies for which there is insufficient information for risk of bias to be evaluated should be excluded from a SR, to prevent the inclusion in a SR of evidence that is potentially misleading but cannot be identified as such by the reviewers.

10 **Include evidence which is relevant to review objectives irrespective of whether its results are in a usable form**. *Recommendation 1.3.7*

	Policy on eligibility of studies with unusable data

	Describe how studies which report their results in a manner incompatible with planned analyses will be handled in the systematic review.

Policy on usability of study data

Note

COSTER recommends that documents be included in a SR regardless of whether their data fit the analysis plan of the reviewers or they are in a language in which the reviewers are fluent. This is to ensure that study documents which may contain information of potential relevance to the SR's research objectives are not excluded from the data extraction step of the SR; however, they may be excluded from specific synthesis steps such as meta-analysis.

11 **Include relevant evidence irrespective of language**. *Recommendation 1.3.8.*

	Policy on eligibilit

	y of studies based on language
	State the language/s in which the systematic review will be written, and how studies not written in that language will be handled.

Policy on language

	Languages to be included in the systematic review

List of included languages in the systematic review

12 **Do not exclude multiple reports of the same research** (e.g. multiple publications, conference abstracts etc.); instead collate the methodological information from each of the reports as part of the data extraction process for each unit of evidence. *Recommendation 3.4*

	Multiple publications policy
	Describe how multiple publications derived from the same study will be aggregated.

Policy on handling of multiple publications from same study

13 **Screening of each piece of evidence for inclusion to be conducted by at least two people working independently**, with an appropriate process (e.g. third-party arbitration) for identifying and settling disputes. *Recommendation 3.1*

	Team members who will conduct screening	Method for resolving disputes

Planned approach to duplicate screening and dispute resolution

14 **Design the PRISMA flow chart for presentation of the results of the screening process**. *Recommendation 3.2*

15 **Pilot test the screening process.** *Recommendation 1.4.7*

Note

A generic protocol for piloting the screening stage of a systematic review is available here: https://www.protocols.io/view/a-general-protocol-for-pilot-testing-the-screening-bkc9ksz6

Defining the strategy for searching for evidence relevant to the review objectives

16 **Design sufficiently sensitive search criteria**, so that studies which meet the eligibility criteria of the review are not inadvertently excluded. Document the search methods in sufficient detail to render them transparent and reproducible. *Recommendations 1.4.1, 2.6*

16.1 **Search all the key scientific databases for the topic**, including national, regional and subject-specific databases. *Recommendation 2.1*

	List of databases
	Database 1
	Database 2

	Data base 3

List of databases searched in the systematic review

16.2 **Structure search strategies for each database**, electronic and other source, using appropriate controlled vocabulary, free-text terms and logical operators in a manner which prioritises sensitivity. Document the search methods and results in sufficient detail to render them transparent and reproducible. *Recommendations 2.3, 2.6*

2d

	Database	Search strategy

Search strategy for each database in the systematic review

Citation

Atkinson KM, Koenka AC, Sanchez CE, Moshontz H, Cooper H (2015)
. Reporting standards for literature searches and report inclusion criteria: making research syntheses more transparent and easy to replicate..
Research synthesis methods.

https://doi.org/10.1002/jrsm.1127 LINK

16.3 **Define reproducible strategies for identifying and searching sources of grey literature** (databases, websites etc.). Document the search methods and results in sufficient detail to render them transparent and reproducible. *Recommendations 2.2 and 2.6*

2d

	Grey literature	Search strategy	Date of search	No. of

	source			results

Search strategy for each source of grey literature in the review

16.4 **Search within the reference lists of included studies and other reviews relevant to the topic** ("hand-searching") and consider searching in the reference lists of documents which have cited included studies. **Search by contacting relevant individuals and organisations**. *Recommendations 2.4 and 2.5*

	Supplementary search strategies	Indicate if will be used
	Hand search references of included studies	
	Hand search references of relevant reviews	
	Hand search references of studies cited by included studies	
	By contacting individuals and organisations	
	Other	

Supplementary search strategies

17 **Plan for re-running all searches and screen the results for potentially eligible studies** within 12 months prior to publication of the review (screening at least at the level of title plus abstract). *Recommendation 2.7*

	Timing	When will the searches be updated prior to

		publication of the review?
	Sources	Which sources will be searched again?
	Level of screening	What level of screening will be conducted?
	Updating findings	How will review findings be updated in context of new studies?

Policy for updating searches

Methods for synthesising and evaluating the evidence

18 **Design the "characteristics of included studies" table**. *Recommendation 1.4.2*

19 **Design and pilot the data extraction forms**. *Recommendation 1.4.7*

20 **Define the risk of bias assessment methods to be used for evaluating the internal validity of the included research**. If observational studies are included, this should cover identification of plausible confounders. *Recommendation 1.4.3*

Note

Review teams may find the **FEAT** (Focus-Extent-Application-Transparency) mnemonic to be useful in defining their risk of bias assessment methods.

- **Focus**: The focus of the tool should be exclusively the internal validity of a study. If other quality constructs are of interest, each should be assessed in a separate process.
- **Extent**: All the important threats to internal validity should be covered by the tool. If observational studies are being appraised, the threats should include all important confounders.
- **Application**: The appraisal process should produce consistent, accurate descriptions of the extent to which a study is vulnerable to each identified threat to internal validity. The judgements should be in a form which can be logically incorporated into the evidence synthesis.
- **Transparency**: The reason for each judgement should be documented, quoting as justification relevant text from the study documentation.

Refer to Section 5 of the COSTER recommendations for detail on how the risk of bias assessment process should be conducted.

20.1 **Define the tool selection and modification process** (how will a suitable tool be identified, and what process will be followed to identify and validate any necessary modifications?) *Recommendation 1.4.3*

	Tool selected	Studies to which it is applied	Modifications made	Method for validating modifications

Selection of tools to be used in systematic review

20.2 **Risk of bias assessment is to be conducted by at least two people working independently**, with an appropriate process (e.g. third-party arbitration) for identifying and settling disputes. *Recommendation 5.3*

	Team members conducting risk of bias assessment	Method for identifying and settling disputes

Approach to conducting risk of bias assessment

20.3 **Define the training and piloting process for the risk of bias assessment** (how will the review team be trained in use of the tool, and what are the conditions under which the piloting process will be determined satisfactory?) *Recommendation 1.4.7*

21 **Design the methods for synthesising the included studies**, to cover: qualitative and quantitative methods (with full consideration given to synthesis methods to be used when meta-analysis is not possible); assessment of heterogeneity; choice of effect measure (e.g. RR, OR etc.); methods for meta-analysis and other quantitative synthesis; pre-defined, appropriate effect modifiers for sub-group analyses. *Recommendations 1.4.4, 6.1*

	Synthesis Component	Planned Methods
	Qualitative or narrative methods	
	Quantitative methods	
	Conditions for combining studies in overall and subgroup analyses	
	Choice of effect measure	
	Assessment of heterogeneity (6.3) and consequences of developing summary results (6.4)	

	Effect modifiers for subgroup analysis	
	Transformation of scales into common measures (6.2)	
	Assessment of publication bias (6.5)	
	Impact of the risk of bias assessment on the synthesis (6.6)	
	Sensitivity analyses (6.7)	
	Other methods	

Methods for synthesising the included evidence

Note

Refer to section 6 of COSTER for detailed recommendations for how evidence should be synthesised in systematic reviews. Popay et al. (2006) attached provides very useful guidance on how to approach the non-quantitive components of the synthesis.

Popay et al. 2006 - Guidance on th...

22 **Define the methods for determining how, given strengths and limitations of the overall body of evidence, confidence in the results of the synthesis of the evidence for each outcome is to be captured and expressed**. (For reviews which include multiple streams of evidence, this may need to be defined for each stream.) *Recommendation 1.4.5*

Note

The components of assessment of confidence or certainty in the evidence are described in section 7 of COSTER.

22.1 **Pilot the process for the assessment of confidence in the results of the synthesis of the evidence.** How will the review team be trained in use of the tool, and what are the conditions under which the piloting process will be determined satisfactory? *Recommendation 1.4.7*

23 **For reviews which include multiple streams of evidence (e.g. animal and human studies), define the methods for integrating the individual streams into an overall result**. *Recommendation 1.4.6*

This should include a description of the relative relevance of populations (e.g. species, age, comorbidities etc.), exposures (e.g. timing, dose), and outcomes (direct or surrogate, acute or chronic model of disease, etc.), as appropriate, per which inferences about predicted effects in target populations can be made from observed effects in study populations.

Registering and publishing the protocol

24 **Create a permanent public record of intent to conduct the review** (e.g. by registering the protocol in an appropriate registry) prior to conducting the literature search. *Recommendation 1.5.1*

25 **As appropriate for review planning and question formulation, secure peer-review and public feedback on a draft version of the protocol,** incorporating comments into the final version of the protocol. *Recommendation 1.5.2*

26 **Publish the final version of the protocol in a public archive**, prior to screening studies for inclusion in the review. *Recommendation 1.5.3*

Note

Publication of the protocol in a journal is equivalent to publication in a public archive.

Citations

Step 16.2

Atkinson KM, Koenka AC, Sanchez CE, Moshontz H, Cooper H. Reporting standards for literature searches and report inclusion criteria: making research syntheses more transparent and easy to replicate. https://doi.org/10.1002/jrsm.1127

Step 6

Morgan RL, Whaley P, Thayer KA, Schünemann HJ. Identifying the PECO: A framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. https://doi.org/10.1016/j.envint.2018.07.015