



Medical Research Council

### The problems with systematic reviews

#### Updates on a living systematic review

Evidence Synthesis Ireland 21<sup>st</sup> March 2024

Dr Lesley Uttley

Senior Research Fellow, Sheffield Centre for Health and Related Research (SCHARR)

l.uttley@sheffield.ac.uk



@LesleyUttley



#### Coming up

- Overview of the project
- Other relevant work and contextual factors
- Unpublished updates!

### Funding

- UKRI MRC Career Development Award to Lesley Uttley (MR/T009861/1; 2020-2024): *Investigating human influences in systematic reviews and metaanalyses* which could prove a direct or indirect conflict of interest in the context or content of this presentation.
- Views are my own and not necessarily representative of the MRC/UKRI

#### Disclosures

- Systematic review advocate
- Not an *ad hominem* researcher

#### Evidence-based hierarchy





#### Susceptibility to Fraud in Systematic Reviews

Lessons from the Reuben Case

Emmanuel Marret, M.D.,\* Nadia Elia, M.D., M.Sc.,† Jørgen B. Dahl, M.D., D.MSc., M.B.A.,‡ Henry J. McQuay, M.A., D.M., F.R.C.A., F.R.C.P. (Edin.),§ Steen Møiniche, M.D.,∥ R. Andrew Moore, M.A., D.Phil., C.Chem., F.R.S.C., F.R.C.A., D.Sc.,# Sebastian Straube, B.M., B.Ch., M.A., D.Phil.,\*\* Martin R. Tramèr, M.D., D.Phil.††

Healthcare Economics, Policy, and Organization

Section Editor: Nancy Borkowski

Publication Bias and Nonreporting Found in Majority of Systematic Reviews and Meta-analyses in Anesthesiology Journals

Riley J. Hedin, MPH,\* Blake A. Umberham,\* Byron N. Detweiler,\* Lauren Kollmorgen,\* and Matt Vassar, PhD†

#### ORIGINAL ARTICLE

Systematic Reviews in Burns Care: Poor Quality and Getting Worse

Créquit et al. BMC Medicine (2016 DOI 10.1186/s12916-016-0555-0 Jared M. Campbell, PhD,\* Sheila Kavanagh, OAM, RN,† Rochelle Kurmis, MClinSci,† Zachary Munn, PhD\*

#### RESEARCH ARTICLE

#### **Open Access**

CrossMark

Wasted research when systematic reviews fail to provide a complete and up-to-date evidence synthesis: the example of lung cancer

Perrine Créquit<sup>12†</sup>, Ludovic Trinquart<sup>1,2,3,4\*†</sup>, Amélie Yavchitz<sup>1,2,3</sup> and Philippe Ravaud<sup>1,2,3,4,5</sup>









**ROBIS** 

GRADE





# A living systematic review of problems with systematic reviews

Systematic Q Search Reviewlution Framework of problems Eligibility Criteria Definitions About Contact Systematic Reviewlution Systematic reviews are the best way to assess scientific evidence from multiple studies. But if they aren't done properly systematic reviews can be misleading or serve conflicted interests. This website is a living systematic review bringing together evidence of problems with published systematic reviews. The aim is to inform, educate and improve practice in the future. Explore

#### Website: https://systematicreviewlution.com/

**Published paper:** <u>Uttley, L., Quintana, D. S., Montgomery, P., Carroll, C., Page, M. J., Falzon, L.,</u> ... & Moher, D. (2023). The problems with systematic reviews: a living systematic review. *Journal* <u>of Clinical Epidemiology</u>.

### Why do living research?

### My model of living research



#### The Web App Behind the Database

Systematic Reviewlution	Overview												
A Home	Assig	Assign Tasks											
Cverview													
ப் Logout	ID	Title	First Author	Journal	Publishing								
	1	Incorrect inclusion of individual studies and methodological flaws in systematic review and meta-analysis	R. Aabenhus	BRITISH JOURNAL OF GENERAL PRACTICE	2014								
	2	Systematic reviews of adverse effects of drug interventions: a survey of their conduct and reporting quality	V. Cornelius	PHARMACOEPIDEMIOLOGY AND DRUG SAFETY	2009								
	5	Mounting evidence that librarians are essential for comprehensive literature searches for meta-analyses and Cochrane reports	A. C. Weller	JOURNAL OF THE MEDICAL LIBRARY ASSOCIATION	2004								
	6	Factors predicting completion and time to publication of Cochrane reviews	A. C. Tricco	OPEN MEDICINE	2009								
	7	Epidemiology and Reporting Characteristics of Systematic Reviews of Biomedical Research: A Cross-Sectional Study	M. J. Page	PLOS MEDICINE	2016								
	8	Financial Conflicts of Interest and Reporting Bias Regarding the Association between Sugar-Sweetened Beverages and Weight Gain: A Systematic Review of Systematic Reviews	M. Bes-Rastrollo	PLOS MEDICINE	2014								

### **Open Science Framework page**

(2020-01-06): <u>https://osf.io/2hmv9/</u>

🛟 OSF <b>HOME <del>-</del></b>	Search	Support	Donate	Sign Up	Sign In				
The range and prevalence of problems	Files	Wiki	Analytics	Registrations					
The range and prevalence	e of	-				99.0KE	B Public	۳ O م	

### The range and prevalence of problems with systematic reviews

Contributors: Lesley Uttley, Daniel Quintana, Paul Montgomery, Matthew James Page, Christopher Carroll, Sarah Dawson

Date created: 2020-01-06 10:55 AM | Last Updated: 2020-12-03 09:52 AM

#### Category: Project

Description: Systematic review of published evidence investigating problems in the conduct or reporting of systematic reviews. These problems, errors, biases or influences may potentially be attributable to stakeholders, sponsors and publishers as well as individuals comprising the project team. They may also affect the reliability or validity of the systematic review conclusions.

This project aims to identify published evidence which examines these issues which could include systematic reviews, primary studies or meta-epidemiological analyses of systematic reviews. In order to avoid publication bias, grey literature from unpublished evidence will also be considered. Comprehensive bibliography searches will be used to search for relevant papers. Literature searches to expand thesaurus and free-text terms related to bias, misconduct or errors will also be complemented with pearl growing searches of relevant papers and contact with experts.

This project is funded through a UK Medical Research Council Career Development Award to Lesley Uttley, University of Sheffield.

Wiki 🕑	Citation	~
If you know of any papers or studies that may be relevant to this review please email l.uttley@sheffield.ac.uk.	Tags	

#### **PROSPERO** registration

#### (March 8<sup>th</sup> 2020): <u>CRD42020181371</u>

#### **NIHR** National Institute for Health Research

#### PROSPERO

International prospective register of systematic reviews



The problems with systematic reviews: a living methodological systematic review

Lesley Uttley, Daniel Quintana, Paul Montgomery, Christopher Carroll, Matthew Page, Sarah Dawson, David Moher

#### Citation

Lesley Uttley, Daniel Quintana, Paul Montgomery, Christopher Carroll, Matthew Page, Sarah Dawson, David Moher. The problems with systematic reviews: a living methodological systematic review. PROSPERO 2020 CRD42020181371 Available from: https://www.crd.york.ac.uk/prospero/display\_record.php?ID=CRD42020181371

#### **Review question**

What problems are published systematic reviews (either with or without meta-analysis) susceptible to which may compromise their reliability or validity?

This includes:

- 1. Methodological or reporting quality
- 2. Adherence to guidelines
- 3. Author conduct including questionable research practices
- 4. Presence of conflicts of interest, researcher allegiance and disclosure
- 4. Methodological limitations

Searches

#### Inclusion criteria

 Academic journal articles highlighting problems with published systematic reviews

### Exclusion criteria

- Articles that discuss theoretical problems in systematic reviews but not in relation to examples in the published literature
- Articles of problems with meta-analyses not conducted in the context of a systematic review

# Literature searches from first iteration



### Systematic reviews included in the 485 included articles





1. **COMPREHENSIVE** (does not miss relevant studies)

#### 2. RIGOROUS

(uses appropriate methods for data synthesis)

3. **TRANSPARENT** (reports methods to enable replication)

#### 4. OBJECTIVE

(is conducted fairly and without vested interests)

- Overly stringent inclusion criteria affecting external validity
- Insufficient literature searches
- Grey literature excluded
- Language restriction
- Lack of supplementary searches beyond databases
- Errors or omissions in search strategy
- Outdated searches
- Perpetuates citation of poor quality primary study data
- Ignores setting or context of included studies which limits review applicability
- Errors in study inclusion or omission of relevant studies
- Reliance on randomised controlled trials for harms / safety data
- Poor consideration of publication bias
- Redundant / overlapping / duplicated review question; leads to research waste
- Untimely (taking too long) or resource intensive
- Not updated regularly

### COMPREHENSIVE

- Intervention not described / defined
- Data extraction errors and double counting
- Inclusion of observational / non-randomised studies
- Conflicts of interest or funding of included studies not assessed
- Flawed risk of bias undertaken
- No quality assessment undertaken or reported
- Limited quality assessment or no risk of bias
- Meta-analyses and forest plots presented without considering risk of bias / quality
- Incorrect interpretation or statistical inference error from meta-analysis
- Inadequate analysis of heterogeneity
- Unplanned or unjustified subgroup or sensitivity analyses
- Small number of trials in meta-analyses
- Errors in effect estimate calculations or data synthesis
- Risk of bias not incorporated into conclusions of review
- Poor execution of narrative synthesis
- Low methodological (AMSTAR) quality
- Weaknesses identified in some Cochrane reviews
- Cochrane reviews more rigorous/higher quality than non-Cochrane reviews
- Low reporting or methodological quality (OTHER GUIDANCE)
- Lack of guidance or consistency in systematic overview / umbrella / review of systematic reviews
- Following guidelines is no guarantee of a rigorous systematic review

RIGOROUS

- No registered or published protocol
- Methods not described to enable replication
- Lack of prespecification in eligibility criteria
- Multiplicity of outcomes and lack of pre-specification for outcome reporting
- Undocumented or unjustified deviations to the review protocol
- Funding or sponsor of systematic review not reported
- Conflict of interest statement or disclosures for review authors missing
- Search strategy not provided
- Reasons for excluding potentially eligible studies not provided
- Individual study characteristics not reported sufficiently
- Selective reporting of harms / safety / adverse events / side effects
- Failure to address missing outcome data in analyses
- Errors in systematic review abstracts or plain language summaries
- Unwieldy/ difficult to read
- Low reporting (PRISMA) quality

### TRANSPARENT

- Lack of clinical expert/ stakeholder/ user perspective
- Review question not justified / important
- Inflexible methods to complex questions
- Failure to consider equity, different socioeconomic groups or disadvantaged populations
- Failure to define clinically meaningful outcomes
- Literature searches not validated by information specialist
- Single reviewer / lack of double checking
- Lack of statistical expertise in handling of quantitative data
- Spin or subjective interpretation of findings
- Unpublished or "zombie" reviews (the file-drawer effect)
- Interpreted without considering certainty or overall quality of the evidence base
- Inconclusive or lack of recommendations
- Guest / gift / ghost authorship
- Non-financial conflicts of interest of review authors
- Financial conflicts of interest of review authors
- High risk of bias (ROBIS)

#### OBJECTIVE

Wordcloud of Frequently Ascribed Keywords Across Included Articles Indicating Problems With Systematic Reviews

Rheumatologicow reporting quality bservational studies Reproducibility Gynaecology Grey literature Chicology Subgroup Nursing Missing data Paediatrics Ophthalmology CognitionAnimal studiesCardiology EquityMental health Abstract / summary mergency medicine Covid Allegiance Covid Non-Cochrane review OtolaryngologDisclosure Dimentary & Alternative ror Influence Spin Immunology Orthopaed Cxternal validit / MisconductOpen data Retraction Telemedicine Public healthPsychology Spin Pulmonology Searching Sponsorship bias

#### Secondary research outpacing primary research



Fontelo, P., & Liu, F. (2018). A review of recent publication trends from top publishing countries. Systematic reviews, 7(1), 1-9.

Ioannidis, J. P. (2016). The mass production of redundant, misleading, and conflicted systematic reviews and meta-analyses. *The Milbank Quarterly*, 94(3), 485-514.

Meta-analysis and systematic reviews all PubMed-indexed publications from 1995 to 2015. Numbers next to the country name indicate 20-year totals

#### Retrospective meta-analyses: please stop





Fontelo, P., & Liu, F. (2018). A review of recent publication trends from top publishing countries. Systematic reviews, 7(1), 1-9.

Niforatos, J. D., Chaitoff, A., Weaver, M., Feinstein, M. M., & Johansen, M. E. (2020). Pediatric literature shift: Growth of meta-analyses was 23 times greater than growth of randomized trials. *Journal of Clinical Epidemiology*, *121*, 112-114.

#### Why so many sub-optimal systematic reviews?



### The influence of the research environment



Innovative (5%)





#### Solutions?

for excluding potentiality studies not provided       prespecification for outcome choice       Methods in production choice       methods in production systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not systematic review not suthors       Methods in review not suthors       Subjective systematic review not suthors       No suthors	Reasons	No		1	Errors	Difficult	Failure		Inflexible		
pectentially studies not provided       prespectification reproducted study or systematic review       interaction reproducted study or systematic review       interaction reproducted study or systematic review       interaction reproducted study or systematic review       interaction reproducted study or systematic review       interaction reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported study reported reported study reported study reported study reported study repo	for	no			in ostracts	to	consider equity	clinical expert/stakeholder/user	methods to	Gift/ghost authorship	
potentially studies provided       0'''       not choice       10'''       not choice       10'''       10'''       10'''       10''''       10''''''         No provided       Fundingsponsor of systematic reported       Fundingsponsor of systematic reported       Individual subtraction       Search subtraction       Faller the systematic reported       Single review authors       Individual subtraction       Single review authors       Individual subtraction       Single reviewer/no data       Individual subtraction       Individual subtraction       Single reviewer/no double checking       No statistical reviewer/no double       No stati	excluding	prespecification	Method	ls 🛛		Teau	or disadvantaged	perspective	complex		
eligible such provided No provided No provided No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality authors No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality assessment undertaken/reported No quality authors No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No track No tr	potentially	tor	not		lective	Unjustified deviations	populations	Failure	questions	No information	
studies provided       choice       or       or <thor< th="">       or       or       <tho< td=""><td>eligible</td><td>outcome</td><td>reproduci</td><td>ret</td><td>oorting</td><td>to the</td><td>without</td><td>to define</td><td></td><td>specialist input</td><td></td></tho<></thor<>	eligible	outcome	reproduci	ret	oorting	to the	without	to define		specialist input	
not provided       Funding/sponsor of systematic review not reported       Funding/ addition systematic review authors       Funding/ addition reported       Funding/ systematic review authors       Funding/ systematic review systematic for review authors       Funding/ systematic review systematic for review systematic for reviews       Funding/ systematic for review systematic for reviews       Funding/ systematic for reviews       Funding/systematic for reviews	studies	choice			of	review protocol	certainty of	clinically	Inconclusive or no	High	
provide       of       systematic review not reported       Search bits       Search added       Faller added       Following added       Following review added       Following review addedd       Following review addedd <td>not</td> <td>Funding/sponsor</td> <td></td> <td>h</td> <td>arms</td> <td></td> <td>the evidence base</td> <td>meaningful</td> <td>recommendations</td> <td>of blas</td> <td></td>	not	Funding/sponsor		h	arms		the evidence base	meaningful	recommendations	of blas	
No protococi       systematic review not reported       subdy output sufficiently       Starter provided       Spin/subjective missing       Collicity sufficiently       No provided       Spin/subjective missing       Collicity sufficiently       No sufficiently       No sufficient	provided	of	Individua			Eailura		Financial	<u> </u>		
No protocol       No review reported       Contractensities appendix reported       Single provided       Weight of madrigs       No statistical review review       No statistical review         No presentence indication provided       No review authors instring       No review review authors       No review indication provided       Low prespectification indication provided       Low prespectification review authors       No review review authors       No statistical copertise for review synthesis         Weaknesses identified in some Cochrane reviews authors       Cochrane therewate the some cochrane reviews author indication interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding author interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding author interestrunding interestrunding interestrunding interestrunding author interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrunding interestrund		systematic	study	Se	arch	to	Spin/subjective	conflicts (	Jnpublishe	d conflicts	
No protococol       not reported Disclosures for review authors missing       not sufficiently messed for review authors       not sufficiently messed for review authors       not sufficiently reported for review authors       not sufficiently reported for review authors       not sufficiently reported for review authors       not sufficiently reported for review authors       not sufficiently reported for review authors       not sufficiently reported for authors       not sufficiently review authors		review	characteris	stics stra	ategy	address	interpretation	interest	"zombie"	of interest	
No       reported       sufficiently       provided       data         protocol       Disclosures for review authors       No       Low prespecification in ssing       Low prespecification in ssing       Low reporting (PRISMA) quality       Single reviewer/no double checking       No         Weaknesses identified in some Cochrane reviews       Cochrane wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wighter wigh		not	reported	d I	10t	outcome	findings	Of	review protocols	of review	
No       Disclosures for review authors       No       Low repertise in eligibility classing       Low reporting percention (particular)       Single reviewer/no double checking       No statistical expertise for double checking         Weaknesses identified in some Cochrane reviews       Cochrane reviews       Cochrane reviews       Use the reviewer undertaken/reported of data       Cochrane reviews       Use the reviews       No effect estimates of data       Cochrane reviews       Use the reviews       Cochrane reviews       Cochrane reviews       Cochrane reviews       Errors reviews       Cordical reviews       Errors reviews       Cordical reviews       Corov reviews       Cordical reviews	No	reported	sufficient	tly pro	vided	data		authors		authors	
protocollfor review authors missingNo prespecification in eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility criterial eigibility eigibility criterial eigibility criterial eigibility eigibility criterial eigibility eigibility eigibility no-cochrane reviewsNo eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility eigibility e	INU	Disclosures					Si	nale		No	
Protococolreview authors missingprespecification in eligibility criteriareporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) qualityreporting (PRISMA) (Prisma) (Prisma) (Primary (Primary (Primary (Primary))reporting (PRISMA) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) (Primary) <br< td=""><td>nrotocol</td><td>for</td><td>N</td><td>c</td><td>L</td><td>ow</td><td>rovio</td><td>worlng</td><td>.  </td><td>statistical</td><td></td></br<>	nrotocol	for	N	c	L	ow	rovio	worlng	.	statistical	
No       Cochrane       Cochrane <thcochrane< th="">       Cochrane       Cochra</thcochrane<>	protocor	roviow	prespeci	fication	repo	ortina			<b>,</b>	expertise	
Autorors missing       eligibility criterio insising       (1) (1) (1) (1) (1) (1) (1) (1) (1) (1)			in		(PRI	SMA	do	uble		101 Mantitative	
MissingCriteriaQualityCriteriaQualityWeaknesses identified in some Cochrane reviews duality assessment undertaken/reportedCochrane reviews quality mon-Cochrane reviews estimatesCochrane reviews intervention red or or or or or or or data or or data or or data or or data or or data or or data or or data or or data or or or data or or or data or or data or or data or or or data or or data or or data or or or data or or or data or or or or or or or or or or or or or or or or or or or data or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or or <br< td=""><td></td><td>authors</td><td>eligib</td><td>oility</td><td></td><td></td><td>che</td><td>cking</td><td>  Y</td><td>synthesis</td><td></td></br<>		authors	eligib	oility			che	cking	Y	synthesis	
Weaknesses identified in some Cochrane reviews       Cochrane reviews       Ungusted addyses       Inageographic of addition that addies       Inageographic of addies       Inageographic of addies <thinageographic of addies       Inag</thinageographic 		missing	crite	eria	yu,	anty		oning	Untime	- <b>)</b>	
Identified in some Cochrane reviews       Usualise intervention not       Usualise intervention intervention not       Usualise intervention not       Usualise interventinutin       Usualise intervention int	Weaknesse	2		Inappropri	iate			No	(taking too	Outdated	
Identified in some cochrane reviews       Ingher quality some reviews       Ingher quality assessment undertaken/reported       Ingher quality than non-Cochrane reviews       Ingher quality than non-Cochrane reviews       Ingher quality than non-Cochrane reviews       Ingher quality than non-Cochrane reviews       Ingher quality thereinfor not       Ingher quality thereinfor quality       Ingher quality thereinfor quality       Ingher quality		Cochrane	Jnjustified	use of			Language	supplementar	/ iong) or resource	searches	
in some Cochrane reviews reviews undertaken/reported (AMSTAR) quality ality ality ality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality quality qualit	Identified	higher	analyses	observatio studies	nal	rede-scalpes	restriction	Scaluics		ne Livi	Domain
Some Cochrane reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention reviewsIntervention	in	quality		Poor			-	Ignores	string	ent Not	Domain
Cochrane reviewsreviewsintervention not describeddefinedintervention reviewsintervention reviewsintervention not describeddefinedintervention reviewsintervention reviewsintervention not methodological understatesintervention reviewsintervention not methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological methodological <b< td=""><td>some</td><td>non-Cochrane</td><td></td><td>of</td><td>"   •</td><td>incorrect interpretation or</td><td>Pernetuates</td><td>or</td><td>inclus</td><td>ion regularly</td><td>Comprehensive</td></b<>	some	non-Cochrane		of	"   •	incorrect interpretation or	Pernetuates	or	inclus	ion regularly	Comprehensive
Coordinate reviewsImage: Coordination of the studies in effect estimates assessment undertaken/reportedImage: Coordination of the studies is in effect or data or or data or data synthesis of the studies of the studies of the studies or or data of the studies or or data or or or data or or or data of the studies of the studies or or or data or or o	Cashrana	reviews Ir	tervention	synthesi	\$ S	inference error	citation	of included	criter	ria	Bigourous
reviewsEntrops in effect estimatesLimited quality assessment undertaken/reportedLimited quality assessment or data synthesisLimited quality assessment of biasLimited quality estimatesImited quality assessment of biasData etrops/dubic conflicts of biasData etrops/dubic conflicts of biasData etrops/dubic conflicts of biasData etrops/dubic conflicts of biasData etrops/dubic conflicts of biasData etrops/dubic conflicts of biasData etrops/dubic conflicts of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of 	Cochrane	Creara desc	not ribed/defined	Low reporti	ng	Following guidelines	of	studies	Relian	ce Errore	Transparent
No quality assessment undertaken/reportedIff effect estimatesLimited quality assessment or dataLimited quality assessment or dataConflicts of biasData extraction errors/violutePrimary studyConflicts of dataSearch strategyLow methodological (AMSTAR) qualityErrors assessedRisk of biasConflicts of biasData evtraction of of biasData evtraction errors/violuteGrey utataErrors studyLow methodological (AMSTAR) qualityFlawed biasInadequate analysis of biasData evtraction of of interest/funding of of of of of of biasData evtraction of of of of of of of of of biasData evtraction of of of of of of of of of biasData evtraction of of of of of of of of of of of biasData evtraction of of of of of of of of of of of heterogeneityData evtraction of of of of of of of of heterogeneityData evtraction of publication biasInsufficient literature searches	reviews	Errors		or	gical	is no	quality		randomi	sed in	
No quality assessment undertaken/reportedeffect estimatescurdertaken or no data or isk synthesiscurdertaken or no data or isk of biascurdertaken/cepbiascurdertaken or or or tata extraction continesion or or not incorporated into conclusionscurdertaken risk of of biascurdertaken risk of of of of of of of of of interest/funding of of interest/funding of of interest/funding of of of incorporated into of of of of of of incorporated into of of of incorporated into of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of of 			Limited	qualit (OTHE	r I	guarantee of	primary	review neview	trials	eu search	
No quality assessment undertaken/reportedestimates or data synthesisassessment or or his biasMeta-anayses prisk or risk biasData extraction enors/double countingGrey literature or or data extraction enors/double counting of interest/funding of incorporated into conclusionsErrors sind prisk or or time countingLow methodological (AMSTAR) qualityLow Flawed risk of into conclusionsConflicts of interest/funding of studiesConflicts of interest/funding of interest/funding of interest/funding of interest/funding of into conclusionsData extraction extraction entrest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of interest/funding of publication biasInsufficient interest/funding of publication bias		eneci	quality	GUIDAN	CE)	rigour	study		for harms	s	
And quality assessment undertaken/reportedOr data synthesisOr not biasOr not biasOr not conflicts of biasextraction errors/double countingGrey Iterature of understation errors/double countingErrors in study incusion/omission of relevant studiesLow methodological (AMSTAR) qualityLow Flawed risk of of biasConflicts of of interest/funding of not incorporated studies not into of conclusionsConflicts of of interest/funding of not assessedPoor consideration of publication biasErrors in understation of eevant	No	estimates as	sessment	Meta-anal presente	yses ed	Data			<u> </u>		
assessment undertaken/reporteddata synthesisrisk of biaserrors/double counting biasIterature counting countingLow methodological (AMSTAR) qualityRisk of biasConflicts of interest/funding of included studies not incorporated into of of biasConflicts of of interest/funding of included studies not included studies not conclusionsIterature countingLow methodological (AMSTAR) qualityFlawed risk of of biasInadequate analysis of heterogeneityPoor consideration of publication biasInsufficient literature searches	quality	I OP	no	without	i ex	draction	G	ev		Errors	
undertaken/reportedsynthesisor biasor biasconflicts of interest/funding of included studiesItterature excludedintustromission of relevant studiesLow methodological (AMSTAR) qualityLow Flawed risk of biasInadequate analysis of heterogeneityInadequate of heterogeneityPoor consideration of publication bias	assessment	data	risk	risk	enc C	ounting				in study	
Risk of bias not incorporated (AMSTAR) qualityRisk of tincerst/funding of included studies not included studies not assessedConflicts of interest/funding of included studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies not assessedIncorductorio of tincluded studies tincluded studies tincluded studies not assessedIncorductorio tincluded studiesIncorductorio tincluded studiesLow methodological (AMSTAR) qualityFlawed of tisk of biasInadequate analysis of heterogeneityPoor consideration of publication biasInsufficient literature searches	undertaken/report	ed	bias	bias			litera	ature	) inclu	sion/omission	
Low methodological (AMSTAR) qualityof bias not incorporated into conclusionsof interest/funding of not assessedPoor consideration of of publication biasInsufficient literature searches	andertakernopen	Risk		С	onflicts					or relevant	
Low methodological (AMSTAR) quality ind their since into conclusions flawed risk of bias of bias (AMSTAR) quality ind their since into conclusions flawed bias into conclusions flawed bias into conclusions flawed bias into conclusions flawed bias into conclusions flawed bias into conclusions flawed bias into conclusions flawed bias into conclusions flawed bias into conclusions into conclusions into conclusions into conclusions into consideration bias into consideration bias into consideration bias		of		intor	01 http://jupd	ina	oveli	Ida		studies	
Low methodological (AMSTAR) quality into conclusions Flawed risk of bias undertakon		bias		intore	of	ing		JUC			
Low methodological (AMSTAR) quality of bias of bias heterogeneity windowned into into into into into into into into		incorporate	ad	in	cluded						
Low methodological (AMSTAR) quality		into		S	tudies		_				
methodological (AMSTAR) quality		conclusior	ns	as	sessed		Poo	or			
(AMSTAR) quality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duality duali		, Flawe	bd				conside	ration	Insu	fficient	
(AMSTAR) quality bias bias heterogeneity (AMSTAR) quality bias heterogeneity	methodologic	R) risk		Inadequate		of		liter			
quality of of bias heterogeneity bias bias	(AMSTAR)							Inter	ature		
bias heterogeneity bias	quality	of		analysis		publication sea		sea	rches		
blas heterogeneity blas	quality				of		bia	•			
underteken		bias		heter	ode	neitv	Dia	5			
		underta	ken		- 3-						

#### Comprehensive

- Team inclusivity
  - Appropriate methodological representation: information specialist/librarian, statistician
  - Public involvement
  - Content/ clinical expertise
- Search reflexivity

### Rigour

- Guideline consultation/adherence (e.g. MECIR)
- Planning for heterogeneity in the protocol
- Statistical expertise for quantitative syntheses

#### Transparency

- Pre-specification (e.g. PROSPERO, Open science framework)
- Reporting guidelines (e.g. PRISMA)
- Timely and complete reporting regardless of direction/magnitude of findings; Pre-prints
- Data sharing
- Especially for publicly funded research

### Objective

- Diverse research teams for generalizable research
- Engaged representation = clinically meaningful research questions
- Acknowledging own potential conflicts (financial and nonfinancial)
- Knowing when to step back
- Managing conflicted experts in the team
- Accountability

#### New developments for this work (1)

• Update performed 2023: now 637 included studies



#### New developments for this work (2)

 New problem identified: Lack of diversity in review authorship teams



New keywords: Immunology, Living, Environment, Haematology

#### New developments for this work (3)

- Systematic Reviewlution to live a bit longer!
- (MRC Transition Support Award 2025-2026)



#### Journal of Clinical Epidemiology Special Issue: Methodological Aspects of Research Integrity & Culture

Journal of Clinical Epidemiology   Supports open access								
Articles & Issues 🗸 🛛 About 🗸	Publish 🗸 🛛 Order journal 🛛	Q Search in this journal	Guide for authors					
r 19 March 2024 Methodological aspects of research integrity and culture Submission deadline: <b>02 September 2024</b>	19 March 2024 Methodological aspe This series aims to cover misconduct, and questio Guest editors: • Gowri Gopalakrish University of Maas	19 March 2024 Methodological aspects of research integrity and culture This series aims to cover a broad range of methodological issues of relevance to research i misconduct, and questionable research practices. Guest editors: • Gowri Gopalakrishna, PhD						
24 February 2023 Special Issue: Methodological Considerations Related to Equity, Diversity, and Inclusion in Clinical Epidemiology Submission deadline: <b>01 April 2024</b>	<ul> <li>Research ethics, Research Integrity, Open Science, Responsible Conduct of Research</li> <li>Limbanazo Matandika, PhD         <ul> <li>Interim Steering Committee Member. Africa Research Integrity Network (ARIN)</li> <li>Research Integrity, Decolonising Global Health, Embedded Ethics Approaches, Informed Consent, Clinical ethics, Distributive Justice, Authorship, Conflict of Interest</li> <li>David Moher, PhD             <ul></ul></li></ul></li></ul>							





Medical Research Council

## Thank you for listening. Questions? https://systematicreviewlution.com/

Uttley, L., Quintana, D. S., Montgomery, P., Carroll, C., Page, M. J., Falzon, L., ... & Moher, D. (2023). The problems with systematic reviews: a living systematic review. *Journal of Clinical Epidemiology*.

Dr Lesley Uttley Senior Research Fellow, ScHARR <u>l.uttley@sheffield.ac.uk</u> @LesleyUttley

