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Advances in evidence synthesis without meta-analysis

Advances in PRISMA and the PRISMATIC Initiative

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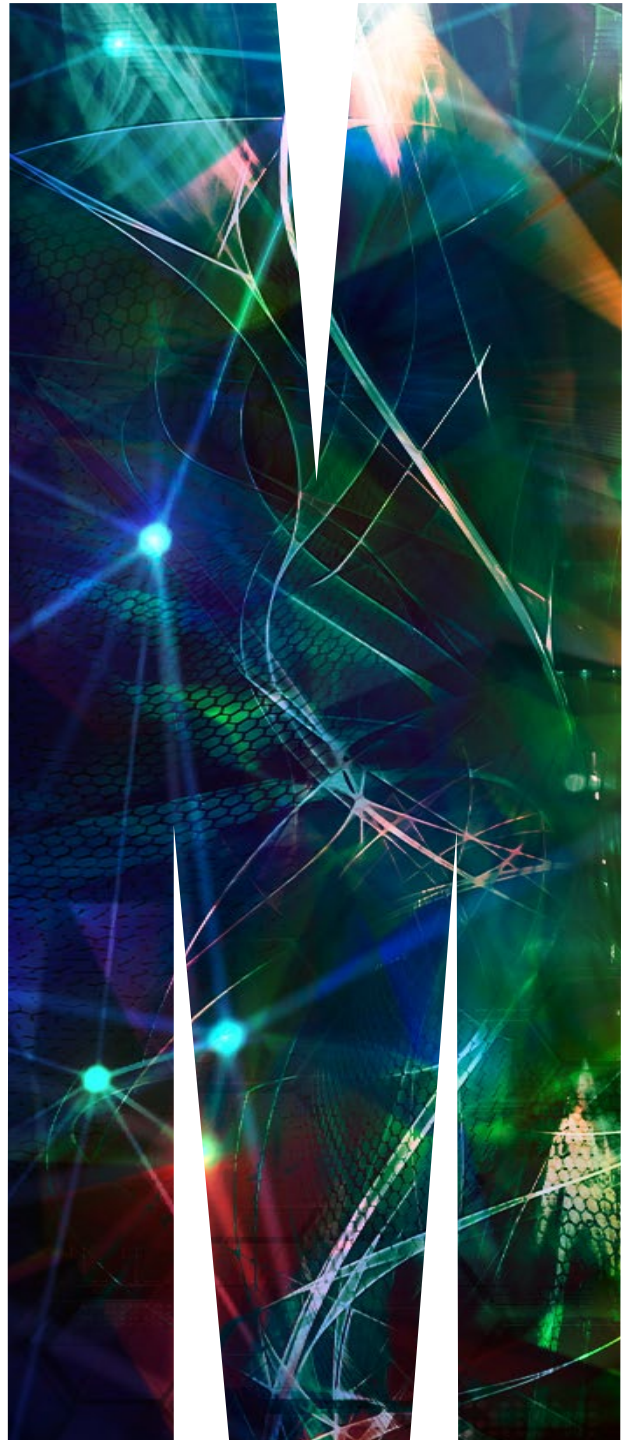
National Academies Webinar on Recent Advances in Evidence Synthesis

27th February 2026

Acknowledgements: Matthew Page and Sue Brennan, Monash University



Advances in evidence synthesis without meta-analysis

- Why statistical synthesis methods beyond meta-analysis of effect estimates are needed
- Guidance in the Cochrane Handbook
- Discussion questions

Context

- 35% - 56% of systematic reviews do not use meta-analysis at all

Page PLoS Med 2016, Campbell JCE 2019

- Many more reviews have at least one outcome for which meta-analysis is not used

- What can happen when meta-analysis is not undertaken …

Effects of patient-held medical records for patients with chronic disease

"… a statistical meta-analysis was not appropriate, so we undertook a narrative synthesis"

The approach the authors used to present and summarise the results was to:

- Structure the review by chronic condition
- Within condition, they reported the individual results for each outcome within each study
- Report results completely (effect estimate + CI) only when they were statistically significant

?

"There is no clear benefit of implementing patient-held medical records …"

Diabetes

Three studies, represented by four articles, in diabetes as summarised in table 1 include a total of 3807 patients. All three studies have a moderate to high risk of bias. See table 2 for details about the methodological limitations.

Each of the studies reports a small number of benefits of PHRs. Dijkstra *et al*[8] reported significant differences for five out of 17 outcomes. These include increases patients receiving foot examinations (OR: 1.68; 95% CI 1.12 to 2.50), having physical exercise advised (OR: 1.84; 95% CI 1.16 to 2.92), smoking discussed or non smoking advised (OR: 1.82; 95% CI 1.15 to 2.89), decreases in HbA1c ($p<0.001$) and a decrease in diastolic blood pressure ($p<0.05$). In Dijkstra *et al*[10] there are differences in seven out of 21 outcome measures. There are benefits in the PHR group for process indicators of checking HbA1c (OR: 1.8; 95% CI 1.2 to 2.7), creatinine (OR: 2.1; 95% CI 1.5 to 3.1), eye exam (OR: 1.7; 95% CI 1.1 to 2.5), cholesterol (OR: 1.9; 95% CI 1.3 to 2.7), weight measured (OR: 2.2, 95% CI 1.5 to 3.4) and glucose exam (OR: 1.6, 95% CI 1.0 to 2.6) within certain time frames.[10] Patients in the PHR group also have better knowledge of their own HbA1c level than control patients (OR: 1.7; 95% CI 1.0 to 2.9). In Simmons *et al*[11] there are differences in only two out of the 19 outcomes—relative reductions in HbA1c levels (p0.017) and increases in body mass index ($p=0.028$) favouring the PHR group. The other outcomes are not different between groups. As investigated by Dijkstra *et al*,[9] even though life expectancy and quality-adjusted life years increased with PHR use, by 0.63 years and 0.59, respectively, the economic outcomes presented suggest that any potential small benefit of PHRs in this population is not justified by the additional cost required to

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Journal of Clinical Epidemiology

Journal of Clinical Epidemiology 156 (2023) 42–52

ORIGINAL ARTICLE

Synthesis methods other than meta-analysis were commonly used but seldom specified: survey of systematic reviews

Miranda S. Cumpston[a], Sue E. Brennan[a], Rebecca Ryan[b], Joanne E. McKenzie[a,*]

[a]*School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, 3004, Australia*
[b]*Centre for Health Communication and Participation, La Trobe University, Melbourne, Victoria, 3086, Australia*

Accepted 1 February 2023; Published online 8 February 2023

A random sample of 100 systematic reviews of public health and health systems interventions (published 2018)

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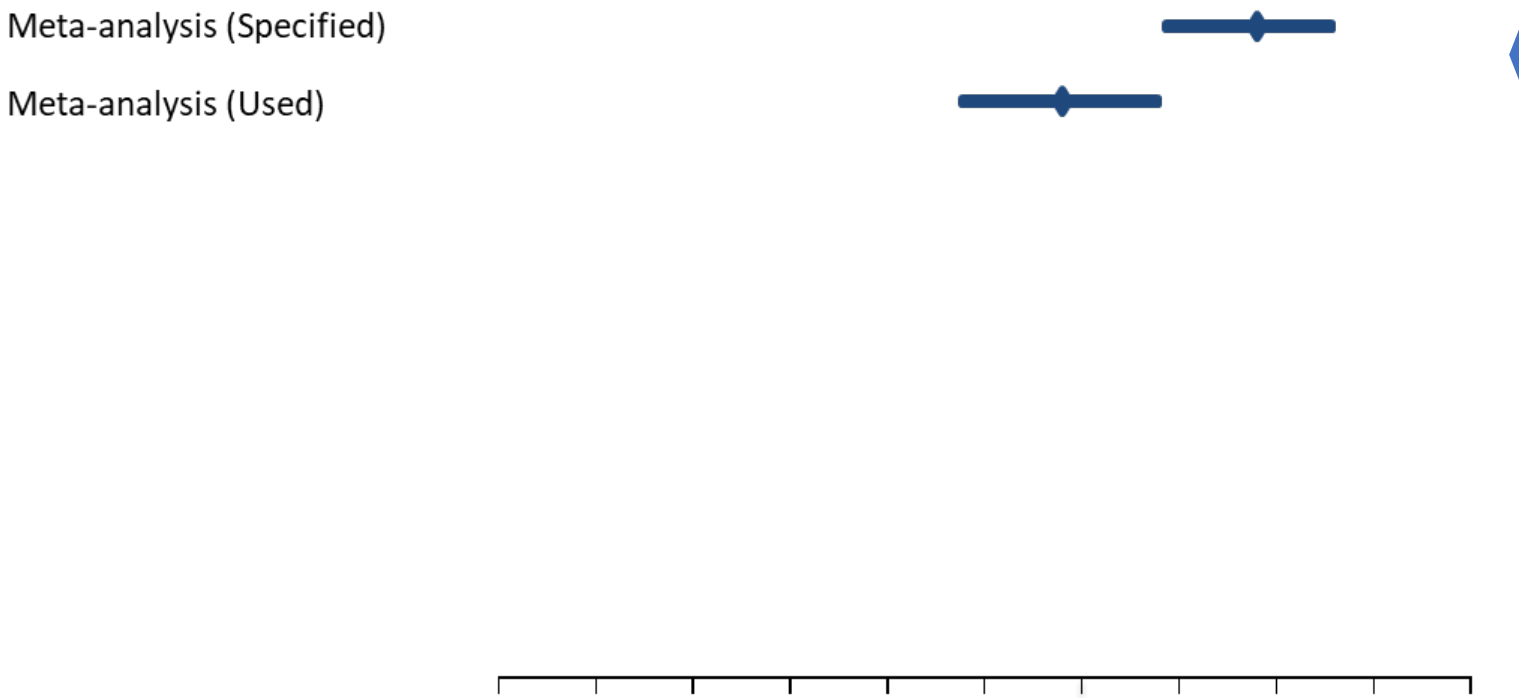

Large percentage of reviews specified meta-analysis (78%), a smaller percentage used meta-analysis (58%)

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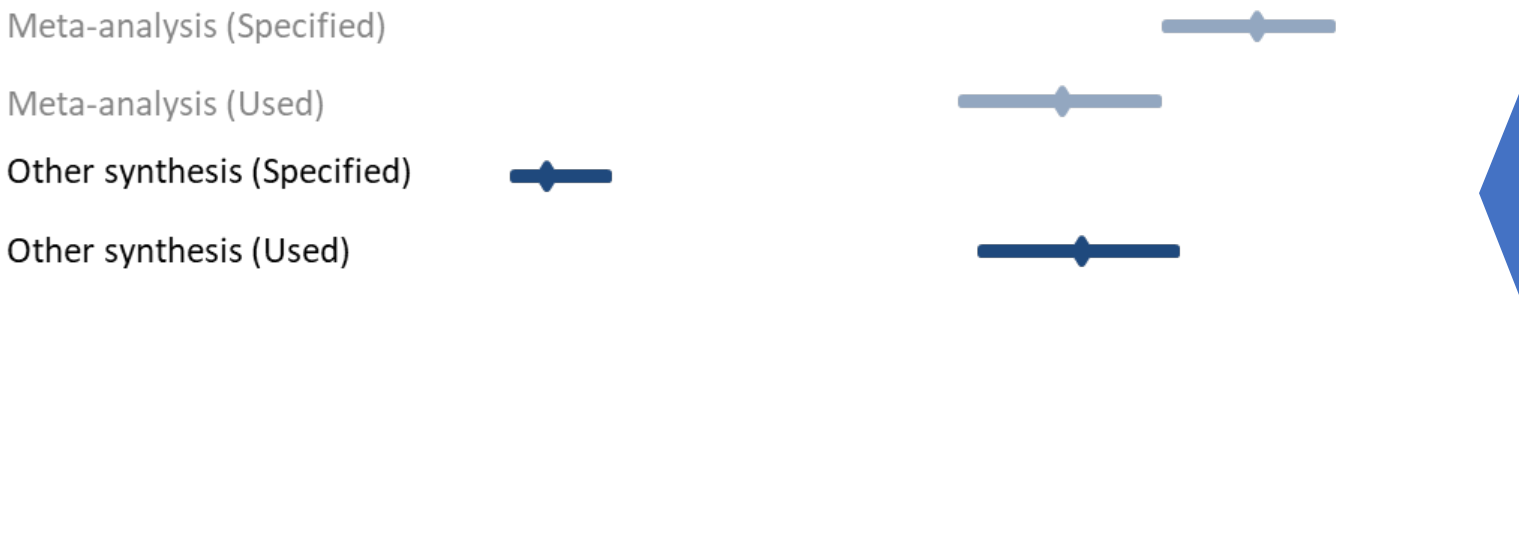

Other synthesis methods rarely specified (5%), but they were commonly used (60%)

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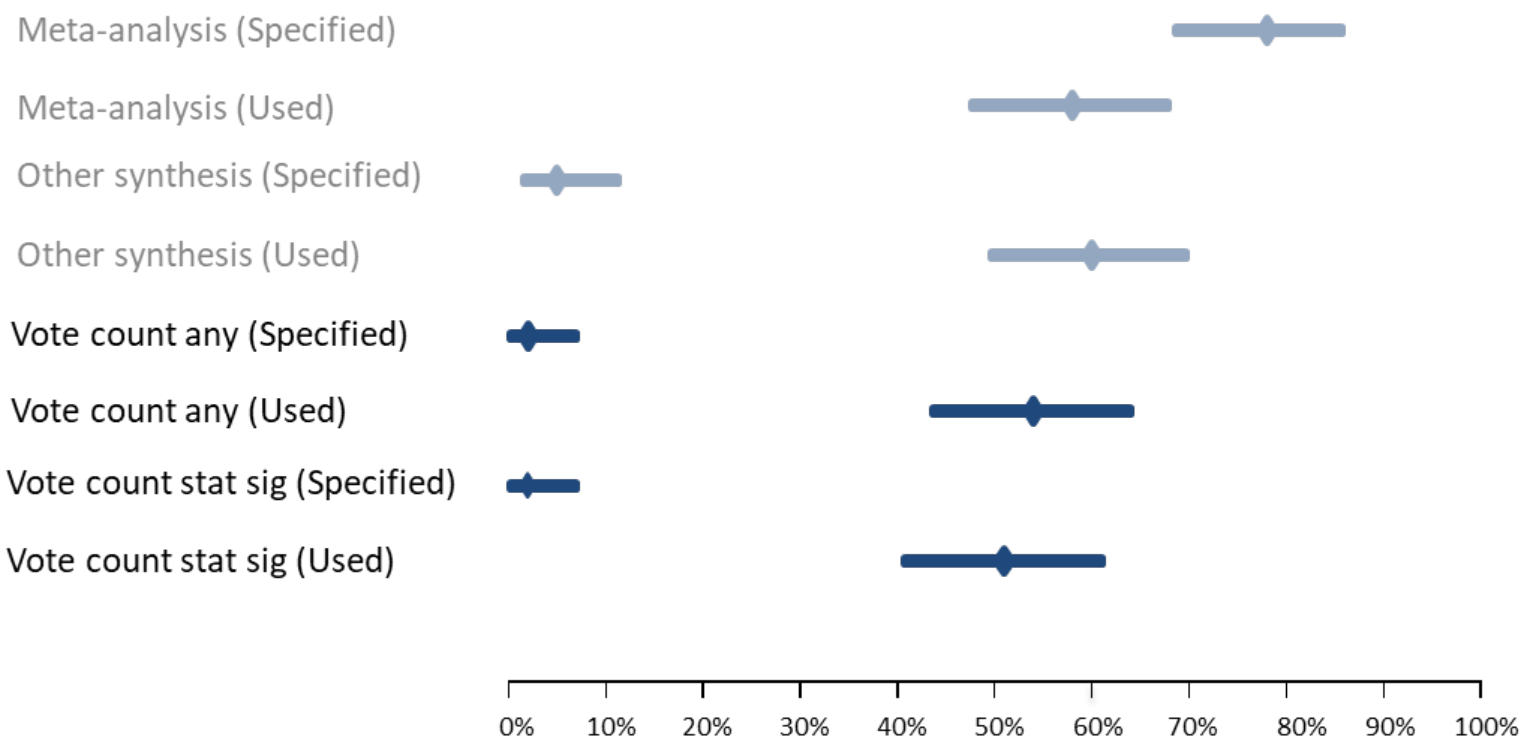

When other synthesis methods were used it was nearly always vote counting (54%), with the count based on:

- statistical significance (36%)
- unclear basis (15%)
- direction of effect (3%)

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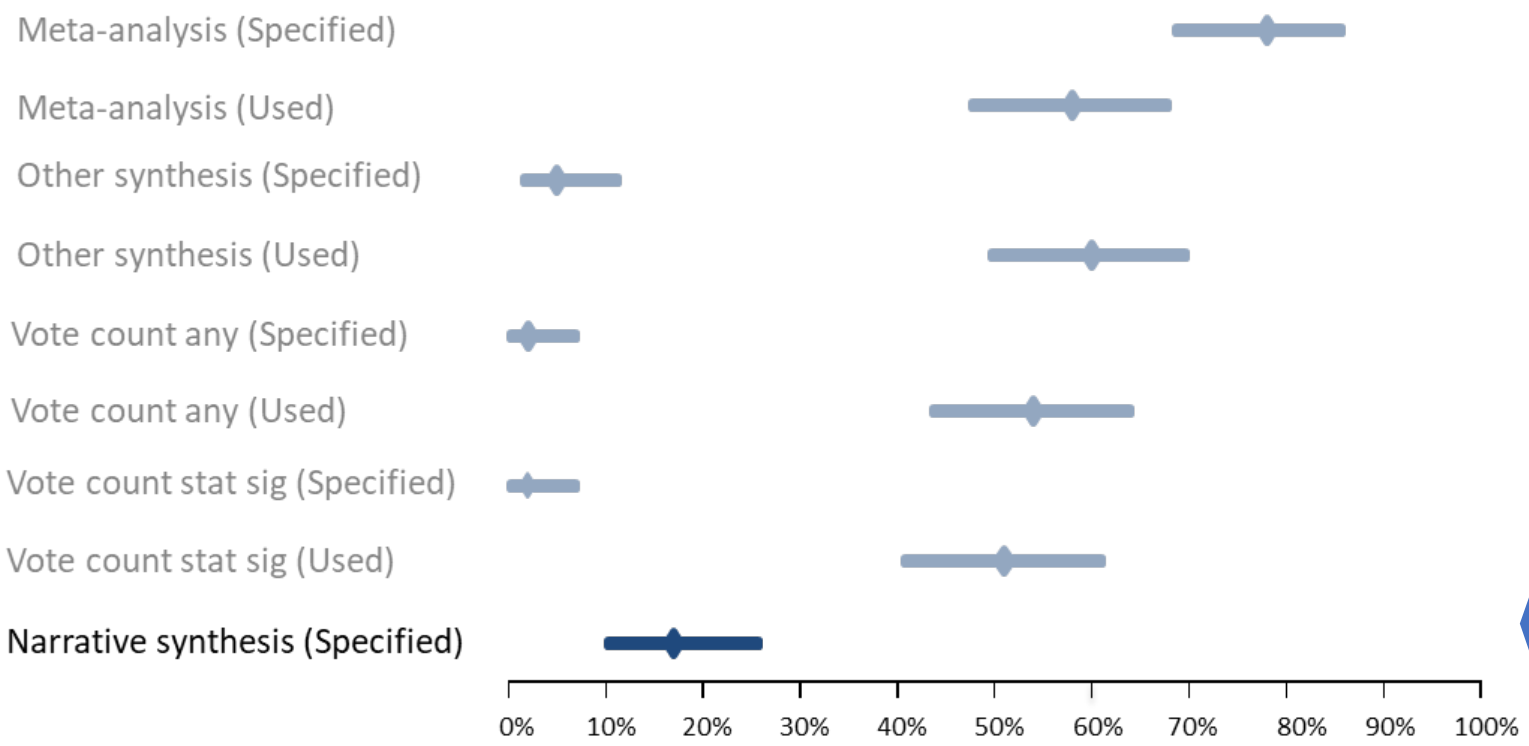
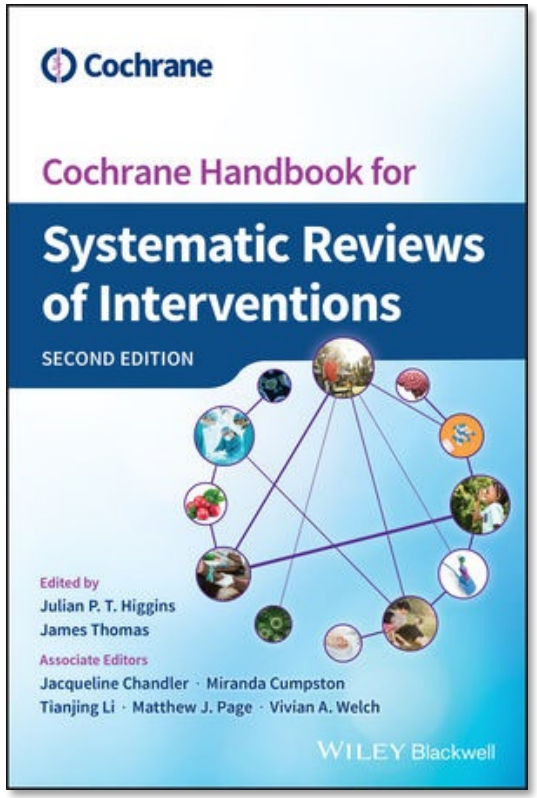


"Narrative synthesis" (or similar) specified in 17 of 100 reviews, of which 15 used vote counting (all based on statistical synthesis or an unclear basis)

Guidance in the Cochrane Handbook on other synthesis and presentation methods



Chapter 12: Synthesizing and presenting findings using other methods

Chapter 12: Synthesizing and presenting findings using other methods

Search within the Handbook

Table of contents

Joanne E McKenzie, Sue E Brennan

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Guidance covers

- Reasons why a meta-analysis of effect estimates may not be possible

Legitimate reasons	Commonly cited reasons where meta-analysis should be considered
Limited evidence for a pre-specified comparison (one or no studies)	Clinical or methodological diversity (consider modifying comparisons with rationale)
Incompletely reported outcome or effect estimate	Statistical heterogeneity (attempt to reduce or explain; present prediction intervals)
Different effect measures across studies (e.g. some dichotomize time-to-event, others do not, leading to hazard ratios and risk ratios)	
Bias in the evidence (missing studies, missing outcomes, or bias in studies)	

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Guidance covers

- Reasons why a meta-analysis of effect estimates may not be possible
- Provides a range of preferred, acceptable and unacceptable statistical synthesis methods
- Provides examples of accompanying methods for displaying results

Overview of available methods for summary and synthesis

Table 9.5.a Overview of available methods for summary and synthesis

	Summary	Acceptable statistical synthesis methods			Preferred statistical synthesis methods		
Methods	Text/Tabular	Vote counting	Combining P values	Summary of effect estimates	Pairwise meta-analysis	Network meta-analysis	Subgroup analysis/ meta-regression
Questions addressed	Structured summary of evidence presented in either text of tabular form	Is there any evidence of an effect?	Is there evidence that there is an effect in at least one study?	What is the range and distribution of observed effects?	What is the common intervention effect? (fixed-effect model) What is the average intervention effect? (random effects model)	Which intervention of multiple is most effective?	What factors modify the magnitude of the intervention effects?
Example plots	Forest plot (plotting individual study effects without a combined effect estimate)	Harvest plot Effect direction plot	Albatross plot	Box and whisker plot Bubble plot	Forest plot	Forest plot Network diagram Rankogram plots	Forest plot Box and whisker plot Bubble plot

Table 9.5.a (modified). McKenzie JE, Brennan SE, Ryan RE, Thomson HJ, Johnston RV. Chapter 9: Summarizing study characteristics and preparing for synthesis. Cochrane Handbook for Systematic Reviews of Interventions version 6.3.

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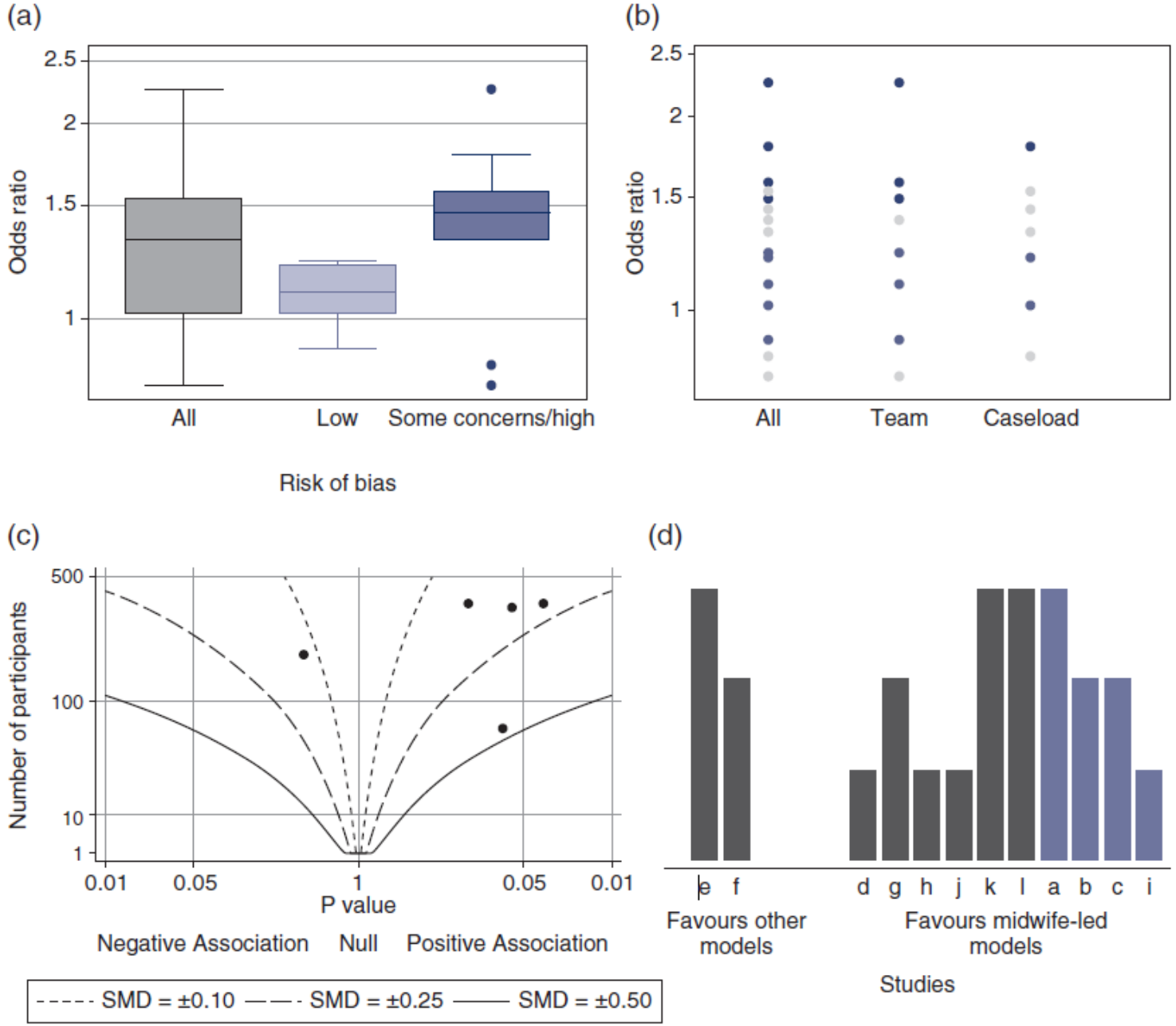
Four examples of methods to display results



Guidance covers

- Reasons why a meta-analysis of effect estimates may not be possible
- Provides a range of preferred, acceptable and unacceptable statistical synthesis methods
- Provides examples of accompanying methods for displaying results
- Provides a description of each method, data required, what to report, limitations

Table 12.2.a Summary of preferable and acceptable synthesis methods

Synthesis method	Question answered	Minimum data required				Purpose	Limitations
		Estimate of effect	Variance	Direction of effect	Precise P value		
Combining P values	Is there evidence that there is an effect in at least one study?			✓	✓	Can be used to synthesize results when studies report: ▪ no, or minimal, information beyond P values and direction of effect; ▪ results of non-parametric	Provides no information on the magnitude of effects. Does not distinguish between evidence from large studies with small effects and small studies with large effects.

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Guidance covers

- Reasons why a meta-analysis of effect estimates may not be possible
- Provides a range of preferred, acceptable and unacceptable statistical synthesis methods
- Provides examples of accompanying methods for displaying results
- Provides a description of each method, data required, what to report, limitations
- Worked example

Box 12.4.e How to describe the results from this synthesis

Scenario 4. Synthesis using vote counting based on direction of effects

'There was evidence that midwife-led models of care had an effect on satisfaction, with 10 of 12 studies favouring the intervention (83% (95% CI 55% to 95%), P = 0.039) (Figure 12.4.a, Panel D). Four of the 12 studies were judged to be at a low risk of bias, and three of these favoured the intervention. The available effect estimates are presented in [review] Table X.'

Advances in evidence synthesis without meta-analysis: discussion questions

- How has methodological guidance changed since the 2011 IOM standards were released?
  → Yes – this topic is not covered in the 2011 standards
  → Increasing imperative to ensure syntheses are reproducible
- Are there aspects of narrative (or qualitative) synthesis that would benefit from further guidance?
  → Yes – without guidance review authors revert to vote counting based on statistical significance
  → Guideline complemented by Chapter 9, which outlines qualitative synthesis of study characteristics
- What standards can make a systematic review report more engaging and readable?
  → Better use of tables (particularly in reviews without meta-analysis) and visual displays

Advances in PRISMA and the PRISMATIC initiative

- PRISMA 2020 statement
- PRISMATIC Initiative
- Discussion questions

How is PRISMA 2020 different to PRISMA 2009?

- PRISMA 2020 retained all items in the PRISMA 2009 checklist (wording of some items revised)
- PRISMA 2020 covers new aspects
  - Data availability, analytic code and other review materials (item 27)
  - Automation tools throughout the review process (items 7, 8, 9 and 11)
  - Declaration of competing interests (item 26)
  - Assessments of the certainty of evidence (methods and results items, 15 and 22)
  - Other statistical synthesis and presentation methods (item 13a – f)

RESEARCH METHODS AND REPORTING

OPEN ACCESS

Check for updates

The PRISMA 2020 statement: an updated guideline for reporting systematic reviews

Matthew J Page,[1] Joanne E McKenzie,[1] Patrick M Bossuyt,[2] Isabelle Boutron,[3] Tammy C Hoffmann,[4] Cynthia D Mulrow,[5] Larissa Shamseer,[6] Jennifer M Tetzlaff,[7] Elie A Akl,[8] Sue E Brennan,[1] Roger Chou,[9] Julie Glanville,[10] Jeremy M Grimshaw,[11] Asbjørn Hróbjartsson,[12] Manoj M Lalu,[13] Tianjing Li,[14] Elizabeth W Loder,[15] Evan Mayo-Wilson,[16] Steve McDonald,[1] Luke A McGuinness,[17] Lesley A Stewart,[18] James Thomas,[19] Andrea C Tricco,[20] Vivian A Welch,[21] Penny Whiting,[17] David Moher[22]

RESEARCH METHODS AND REPORTING

PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews

Matthew J Page,[1] David Moher,[2] Patrick M Bossuyt,[3] Isabelle Boutron,[4] Tammy C Hoffmann,[5] Cynthia D Mulrow,[6] Larissa Shamseer,[7] Jennifer M Tetzlaff,[8] Elie A Akl,[9] Sue E Brennan,[1] Roger Chou,[10] Julie Glanville,[11] Jeremy M Grimshaw,[12] Asbjørn Hróbjartsson,[13] Manoj M Lalu,[14] Tianjing Li,[15] Elizabeth W Loder,[16] Evan Mayo-Wilson,[17] Steve McDonald,[1] Luke A McGuinness,[18] Lesley A Stewart,[19] James Thomas,[20] Andrea C Tricco,[21] Vivian A Welch,[22] Penny Whiting,[18] Joanne E McKenzie[1]

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How is PRISMA 2020 different to PRISMA 2009?

Box. Example of an item and its elements from PRISMA 2020

Item 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 (for example, for all measures, time points, analyses), and, if not, the methods used to decide which results to collect
Essential elements	• List and define the outcome domains and time frame of measurement for which data were sought. • Specify whether all results that were compatible with each outcome domain in each study were sought, and, if not, what process was used to select results within eligible domains. • If any changes were made to the inclusion or definition of the outcome domains or to the importance given to them in the review, specify the changes, along with a rationale. • If any changes were made to the processes used to select results within eligible outcome domains, specify the changes, along with a rationale.
Additional element	• Consider specifying which outcome domains were considered the most important for interpreting the review's conclusions (such as "critical" versus "important" outcomes) and provide rationale for the labelling (such as "a recent core outcome set identified the outcomes labelled 'critical' as being the most important to patients").

ITEM: Synopsis of what should be reported for a particular aspect of the review

ELEMENT: Specific reporting recommendations for an item

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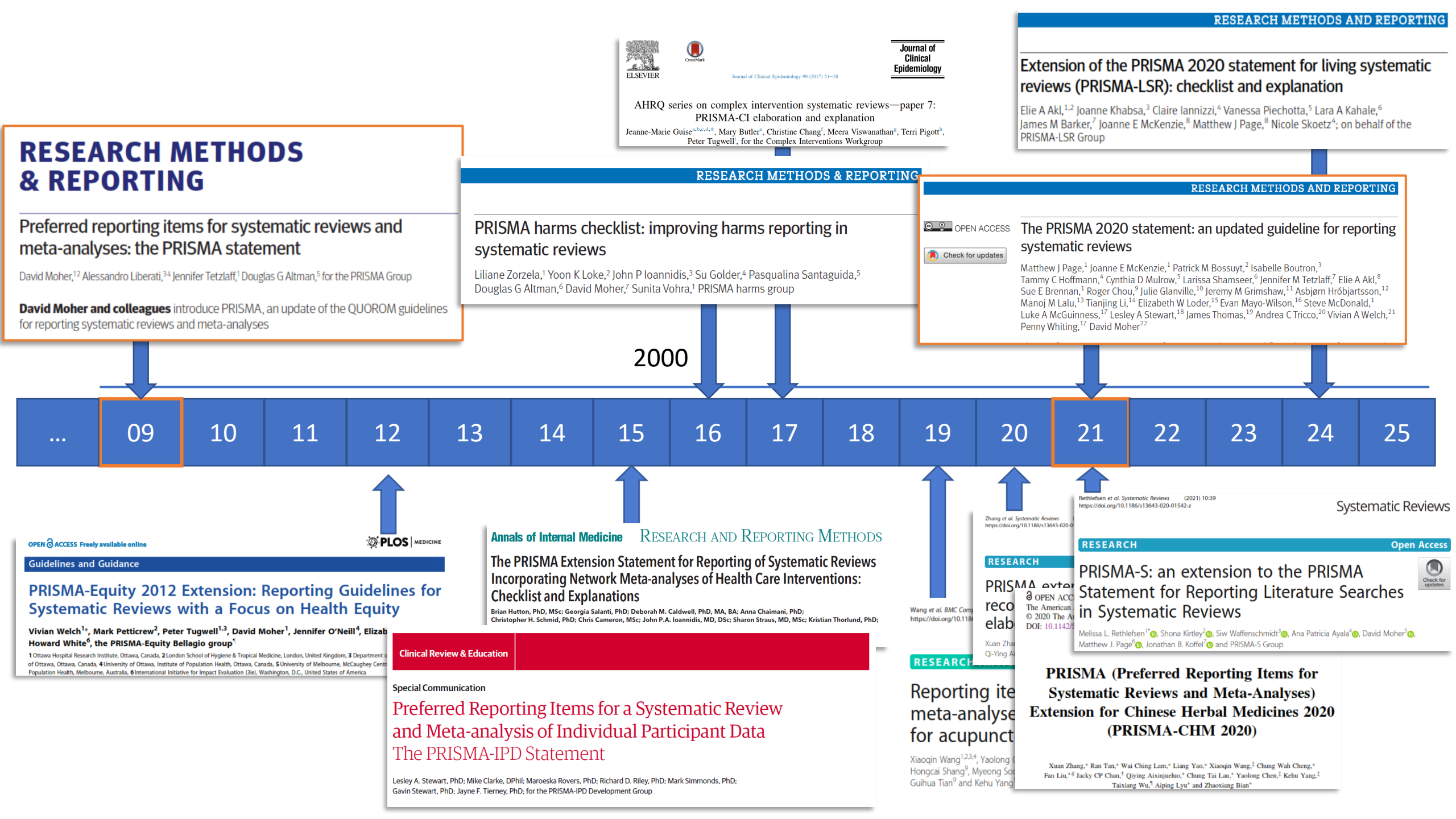
RESEARCH METHODS & REPORTING
Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement
David Moher,[1,2] Alessandro Liberati,[3,4] Jennifer Tetzlaff,[1] Douglas G Altman,[5] for the PRISMA Group
David Moher and colleagues introduce PRISMA, an update of the QUOROM guidelines for reporting systematic reviews and meta-analyses
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CrossMark
Journal of Clinical Epidemiology 90 (2017) 51–58
Journal of Clinical Epidemiology
AHRQ series on complex intervention systematic reviews—paper 7: PRISMA-CI elaboration and explanation
Jeanne-Marie Guise, Mary Butler, Christine Chang, Meera Viswanathan, Terri Pigott, Peter Tugwell, for the Complex Interventions Workgroup
RESEARCH METHODS & REPORTING
PRISMA harms checklist: improving harms reporting in systematic reviews
Liliane Zorzela,[1] Yoon K Loke,[2] John P Ioannidis,[3] Su Golder,[4] Pasqualina Santaguida,[5] Douglas G Altman,[6] David Moher,[7] Sunita Vohra,[1] PRISMA harms group
RESEARCH METHODS AND REPORTING
Extension of the PRISMA 2020 statement for living systematic reviews (PRISMA-LSR): checklist and explanation
Elie A Akl,[1,2] Joanne Khabsa,[3] Claire Iannizzi,[4] Vanessa Piechotta,[5] Lara A Kahale,[6] James M Barker,[7] Joanne E McKenzie,[8] Matthew J Page,[8] Nicole Skoetz[4]; on behalf of the PRISMA-LSR Group
RESEARCH METHODS AND REPORTING
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The PRISMA 2020 statement: an updated guideline for reporting systematic reviews
Matthew J Page,[1] Joanne E McKenzie,[1] Patrick M Bossuyt,[2] Isabelle Boutron,[3] Tammy C Hoffmann,[4] Cynthia D Mulrow,[5] Larissa Shamseer,[6] Jennifer M Tetzlaff,[7] Elie A Akl,[8] Sue E Brennan,[1] Roger Chou,[9] Julie Glanville,[10] Jeremy M Grimshaw,[11] Asbjørn Hróbjartsson,[12] Manoj M Lalu,[13] Tianjing Li,[14] Elizabeth W Loder,[15] Evan Mayo-Wilson,[16] Steve McDonald,[1] Luke A McGuinness,[17] Lesley A Stewart,[18] James Thomas,[19] Andrea C Tricco,[20] Vivian A Welch,[21] Penny Whiting,[17] David Moher[22]
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Guidelines and Guidance
PRISMA-Equity 2012 Extension: Reporting Guidelines for Systematic Reviews with a Focus on Health Equity
Vivian Welch, Mark Petticrew, Peter Tugwell, David Moher, Jennifer O'Neill, Howard White, the PRISMA-Equity Bellagio group
Annals of Internal Medicine RESEARCH AND REPORTING METHODS
The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations
Brian Hutton, PhD, MSc; Georgia Salanti, PhD; Deborah M. Caldwell, PhD, MA, BA; Anna Chaimani, PhD; Christopher H. Schmid, PhD; Chris Cameron, MSc; John P.A. Ioannidis, MD, DSc; Sharon Straus, MD, MSc; Kristian Thorlund, PhD;
Clinical Review & Education
Special Communication
Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data
The PRISMA-IPD Statement
Lesley A. Stewart, PhD; Mike Clarke, DPhil; Maroeska Rovers, PhD; Richard D. Riley, PhD; Mark Simmonds, PhD; Gavin Stewart, PhD; Jayne F. Tierney, PhD; for the PRISMA-IPD Development Group
Wang et al. BMC Com
https://doi.org/10.118
Zhang et al. Systematic Reviews
https://doi.org/10.1186/s13643-020-0
RESEARCH
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Hongcai Shang, Myeong So
Guihua Tian and Kehu Yang
Rethlefsen et al. Systematic Reviews (2021) 10:39
https://doi.org/10.1186/s13643-020-01542-z
Systematic Reviews
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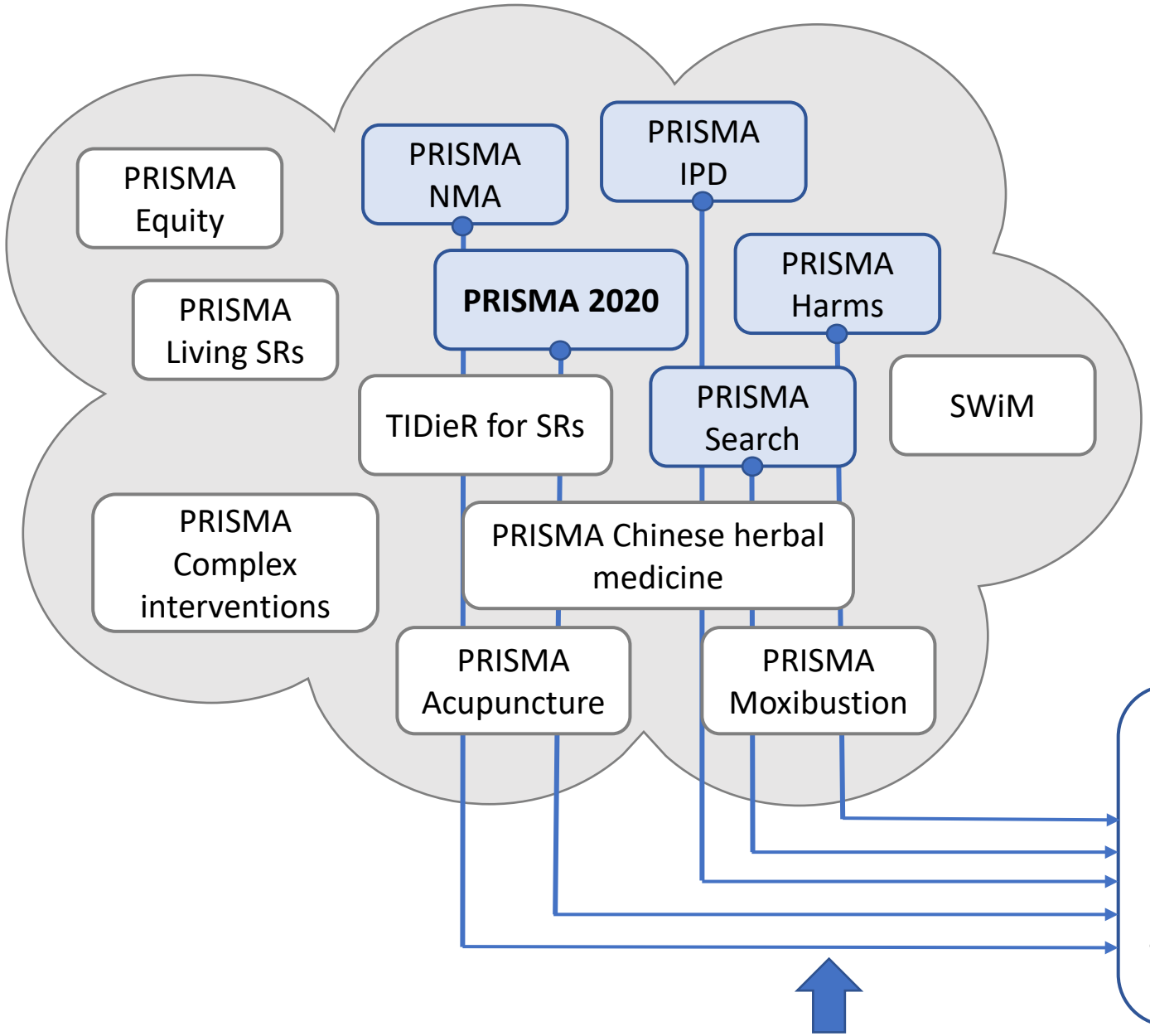
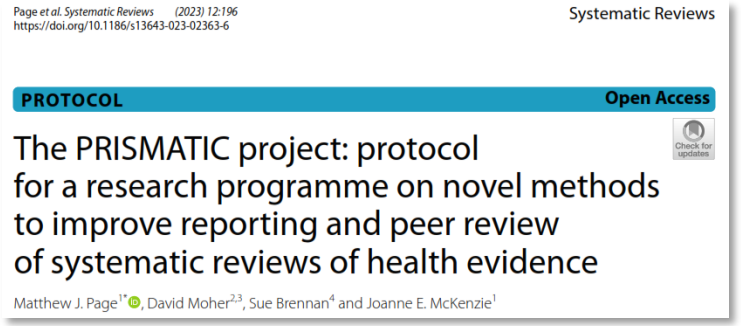
PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews
Melissa L. Rethlefsen, Shona Kirtley, Siw Waffenschmidt, Ana Patricia Ayala, David Moher, Matthew J. Page, Jonathan B. Koffel and PRISMA-S Group
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Extension for Chinese Herbal Medicines 2020 (PRISMA-CHM 2020)
Xuan Zhang, Ran Tan, Wai Ching Lam, Liang Yao, Xiaoqin Wang, Chung Wah Cheng, Fan Liu, Jacky CP Chan, Qiying Aixinjueluo, Chung Tai Lau, Yaolong Chen, Kehu Yang, Taixiang Wu, Aiping Lyu and Zhaoxiang Bian



PRISMATIC (PRISMA, Technology, and Implementation to enhance reporting Completeness) project

Aim: Streamline the process of reporting SRs of the effects of interventions


Page et al. Systematic Reviews (2023) 12:196
https://doi.org/10.1186/s13643-023-02363-6

Systematic Reviews

PROTOCOL Open Access

The PRISMATIC project: protocol for a research programme on novel methods to improve reporting and peer review of systematic reviews of health evidence

Matthew J. Page[1*], David Moher[2,3], Sue Brennan[4] and Joanne E. McKenzie[1]

To achieve this, we have had to first harmonise the structure and reporting recommendations from each extension with PRISMA 2020

Matt Page
Monash University

Harmonise extensions → **unified PRIMSA statement**

PRISMA 2020 Section and Topic	PRISMA-Harms Item #	PRISMA-Harms Element text	PRISMATIC Proposal (see "PRISMA-Harms unified checklist" for element cited)	If you have any comments on the wording of element text or the proposal, include them here
Methods: Eligibility criteria	6	Clearly indicate if specific study designs and lengths of follow-up were chosen specifically to address harms.	Include element in unified checklist (see 5.3H).	
Methods: Information sources	7	Report if only published data were sought, or if data from unpublished sources, from authors, drug manufacturers and regulatory agencies were also sought.	Do not include element in unified checklist as it overlaps with PRISMA 2020 (see 6.3, 6.5 and 6.6).	
Methods: Information sources	7	If unpublished data were included, provide the source and the process of obtaining it.	Do not include element in unified checklist as it overlaps with PRISMA 2020 (see 6.3, 6.5 and 6.6).	
Methods: Search strategy	8	If additional searches were used specifically to identify adverse events, present the full search process so it can be replicated.	Do not include element in unified checklist as it overlaps with PRISMA 2020 (see 7.1).	
Methods: Selection process (all reviews)	9	If the systematic review only includes studies reporting on adverse events of interest, report whether screening was based on adverse event reporting in the title or abstract or in the full text.	Include element in unified checklist (see 8.3H).	
Methods: Selection process (all reviews)	9	If no information on harms was reported in text, report if any attempt was made to retrieve relevant data from authors.	Do not include element in unified checklist as it overlaps with PRISMA 2020 (see 8.2).	
Methods: Data items (outcomes)	11	Report the definition of the harm and seriousness used by each included study (if applicable). Report if multiple adverse events occurred in the same individuals, if this information is available. When reporting on adverse events, consider whether the incidence of adverse events is related to factors	Include element in unified checklist (see 8.3H) but reframe as a Methods-Data collection item (see 10a.2H).	

For each extension:

- Extracted reporting recommendations from the extension checklist + E&E
- Provided extension team with proposals for reporting recommendations
- Sought feedback (most harmonisation proposals were reviewed 2 or 3 times)

Section and Topic	Item #	Unified list of PRISMA 2020 and PRISMA-IPD items and elements recommended for reporting
TITLE		
TITLE	**1**	**Item: Identify the report as a systematic review.** Elements: 1.1 Identify the report as a systematic review in the title. 1.2 Report an informative title that provides key information about the main objective or question that the review addresses (for reviews of interventions, this usually includes the population and the intervention(s) that the review addresses). 1.3 *Consider providing additional information in the title to capture key methodology, such as the method of analysis used (e.g. "a systematic review with network meta-analysis of individual participant data"), the designs of included studies (e.g. "a systematic review of randomised trials"), or an indication that the review is an update of an existing review or a continually updated ("living") systematic review.*
ABSTRACT		
ABSTRACT	**2**	**Item: See the PRISMA 2020 for Abstracts checklist.** Elements: 2.1 Identify the report as a systematic review. 2.2 Provide an explicit statement of the main objective(s) or question(s) the review addresses. 2.3 Specify the inclusion and exclusion criteria for the review. 2.4 Specify the information sources (e.g. databases, registers) used to identify studies and the date when the primary information source(s) were last searched. 2.4.I1 PRISMA-IPD: Note that individual participant data (IPD) were sought. 2.5 Specify the methods used to assess risk of bias in the included studies. 2.6 Specify the methods used to present and synthesise results. 2.7 Give the total number of included studies and participants and summarise relevant characteristics of studies. 2.7.I1 PRISMA-IPD: Give the number (%) of studies and the number (%) of participants for which IPD were obtained. 2.8 Present results for the main comparison(s) and outcome(s), indicating for each the number of included studies and participants, the summary estimate, confidence/credible interval and a measure of statistical heterogeneity if meta-analysis was done, and the direction of effect. 2.9 Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision). 2.10 Provide a general interpretation of the results and important implications. 2.11 Specify the primary source of funding for the review.

Across PRISMA 2020 + 12 extensions:

- 50 unique items & 465 unique elements

Unified PRISMA statement

- Unified statement will ensure that users will not need to sift through redundant or conflicting recommendations when multiple extensions apply
- Next step is to develop web applications that will generate manuscript templates and checklists that are customised to the characteristics and methods of the systematic review

Advances in PRISMA and the PRISMATIC initiative: discussion questions

- How has methodological guidance changed since the 2011 IOM standards were released?

  → Yes – 2011 standards use PRISMA 2009 + additional recommendations

- How do you envision the future of systematic reviews, and are there any emerging practices or methods that you would recommend considering?

  → Yes – generative AI will be instrumental in helping authors report and others assess the quality of reporting