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How to conduct and assess a systematic review

Antti Malmivaara, MD, PhD, Chief Physician
Centre for Health and Social Economics
National Institute for Health and Welfare

Trusted evidence.
Informed decisions.
Better health.

Potential conflicts of interests

Finnish Institute for Health and Welfare, Centre for Health and Social Economics, Chief Physician

Current Care Guidelines, Finnish Medical Association Duodecim, Editor

Ministry for Social Affairs and Health, Council for Choices in Health care in Finland, Expert

Hospital ORTON, Scientific Board, Member

European Academy of Rehabilitation Medicine

Cochrane Back and Neck Review Group, Editorial Board

Cochrane Rehabilitation Field, Member of Executive Committee; Chair of the Methodology Committee

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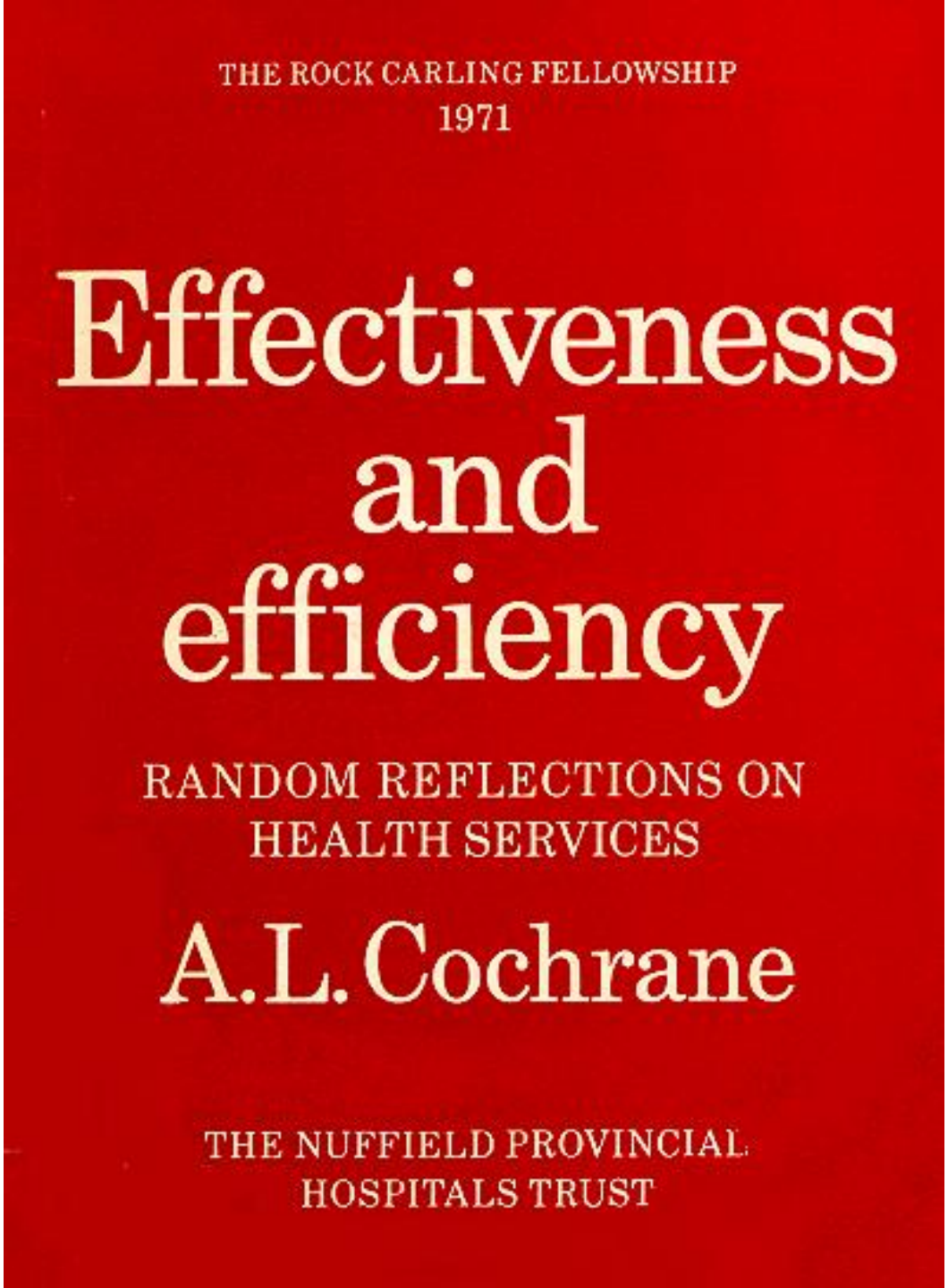

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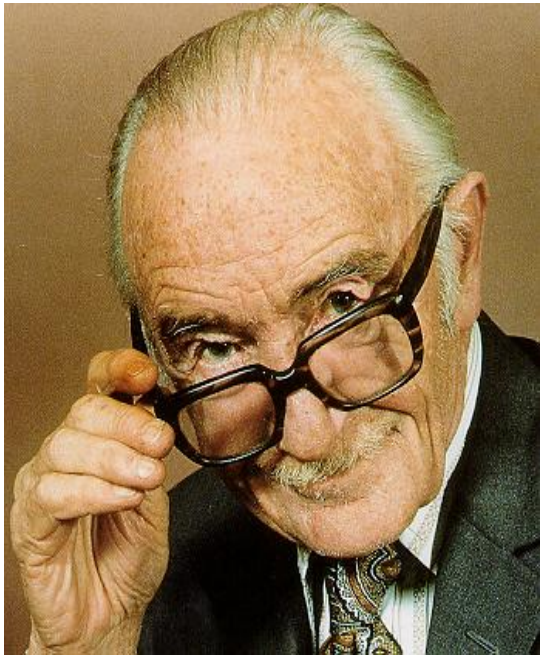
Archie Cochrane



“It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or sub-specialty, adapted periodically, of all relevant randomized controlled trials”

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THE COCHRANE COLLABORATION®

International non-profit organization that prepares, maintains, and disseminates systematic up-to-date reviews of health care interventions

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Systematic review, definitions

A systematic review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review.

Meta-analysis refers to the use of statistical techniques in a systematic review to integrate the results of the included studies.

Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies.

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, et al. (2009) The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. BMJ 2009;339:b2700

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Steps in a systematic review

1. Defining the question
2. Establishing inclusion/exclusion criteria
3. Literature search and choice of articles
4. Data extraction and quality estimation of articles
5. Combining scientific evidence (descriptive or meta-analysis)
6. Drawing conclusions based on evidence

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Assessing a systematic review

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Steps in assessing systematic reviews and meta-analyses

1. What is the study question (PICOS)?
2. Validity - how high is the Risk of Bias (RoB)?
3. What are the results and how precise they are?
4. What is the generalizability of the results?

1. What is the study question (PICOS)

- Patient (population)
- Intervention
- Control intervention
- Outcome
- Study design

2. Validity - how high is the Risk of Bias (RoB)

- Was the study question well defined and were the studies included in the meta-analysis clinically homogenous?
- Was the study design appropriate for anwering the study question?
- Is it probable that all relevant studies are included in the meta-analysis?
- What was the validity of the included studies and were the interpretations based on studies with low risk of bias?
- Are the results of the systematic review/meta-analysis repeatable?

3. What are the results and how precise they are?

1. What are the point estimates?
2. How precise are the point estimates (by 95 per cent confidence intervals) ?

Statistical significance and clinical importance

Trombolysis for MI

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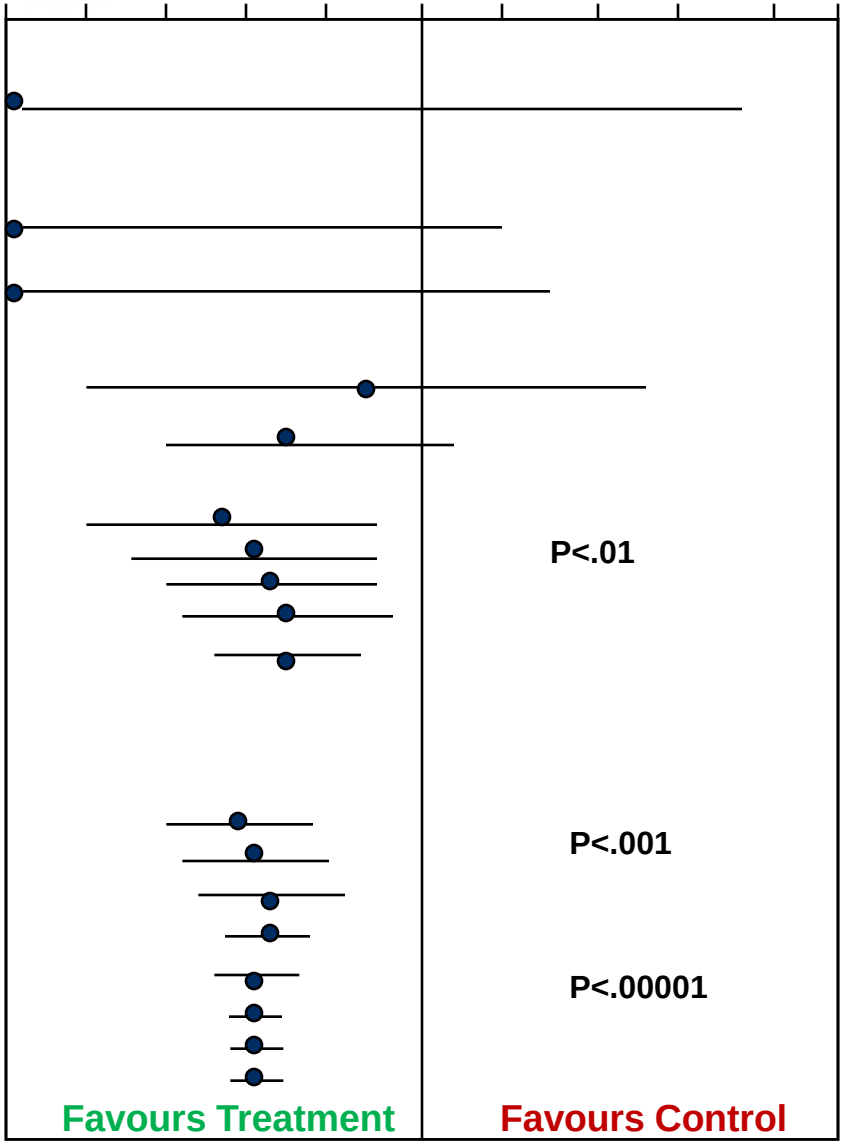
Year	Cumulative RCTs	Pts
1960	1	23
1965	2	65
	3	149
1970	4	316
	7	1793
	10	2544
	11	2651
	15	3311
	17	3929
	22	5452
1980	23	5767
	27	6125
	30	6346
1985	33	6571
	43	21 059
	54	22 051
	65	47 185
	67	47 531
1990	70	48 154



	Textbook/Review Recommendations				
	Routine	Specific	Rare/Never	Experimental	Not Mentioned
					21
					5
				1	10
				1	2
				2	8
					7
					8
		1			12
M		1		8	4
M		1		7	3
M	5	2		2	1
M	15	8			1
M	6	1			

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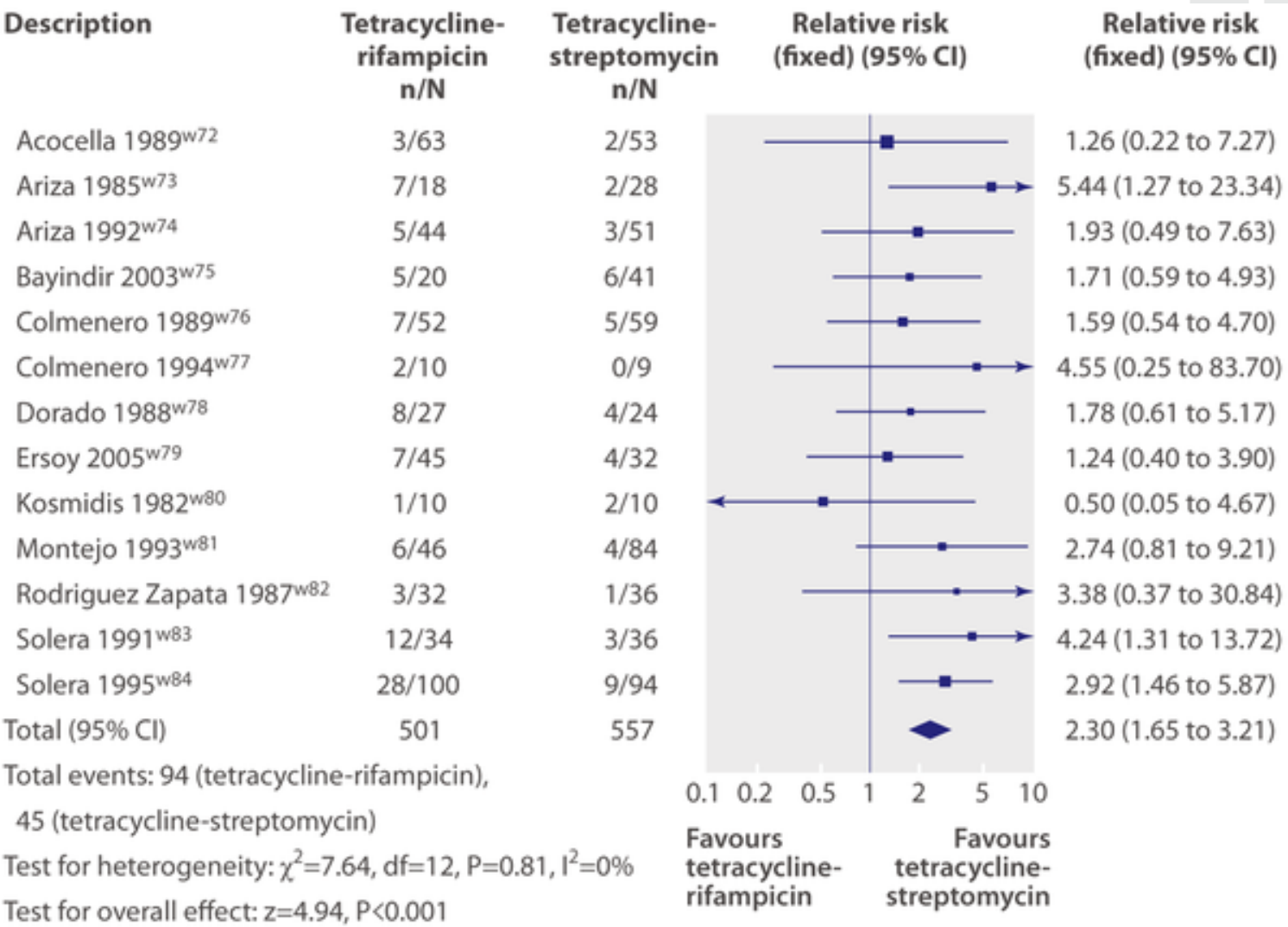
Example Figure: Overall failure (defined as failure of assigned regimen or relapse) with tetracycline-rifampicin versus tetracycline-streptomycin.



4. What is the generalizability of the results?

1. How applicable the results are for my own patients?

- Consider the PICO: how similar are the patients, interventions, control interventions and outcomes in relation to my own patients.
- Putting the question other way round: are my patients so different from those in the systematic review, that the results are not applicabe to my patients

2. Have we enough resources and competence for the intervention?

4. What is the generalizability of the results? (cont'd)

3. Were all important benefits and harms taken into consideration

- Although systematic reviews/meta-analyses provide more decisive information of results than original studies, they may not have covered all benefits or harms important for my patient.

4. What are my patient's values and preferences concerning the benefits and harms

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informa
healthcare

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EDITORIAL

Methodological considerations of the GRADE method

Antti Malmivaara

Centre for Health and Social Economics, National Institute for Health and Welfare, Helsinki, Finland

The GRADE method (Grading of Recommendations, Assessment, Development, and Evaluation) provides a tool for rating the quality of evidence for systematic reviews and clinical guidelines. This article aims to analyse conceptually how well grounded the GRADE method is, and to suggest improvements. The eight criteria for rating the quality of evidence as proposed by GRADE are here analysed in terms of each criterion's potential to provide valid information for grading evidence. Secondly, the GRADE method of allocating weights and summarizing the values of the

Key messages

- The quality of evidence during systematic reviews should be based on the degree of internal validity of each study and the consistency of findings across clinically homogeneous studies and, when feasible, also on publication bias.

Conclusions

Interpretation of systematic reviews and meta-analyses should be based on:

- Clinically homogeneous studies
- Studies with a low risk of bias
- Lack of publication bias

Malmivaara A. Methdological considerations of the GRADE method. Ann Med 2015;47:1-5.

Funnel plot – no publication bias

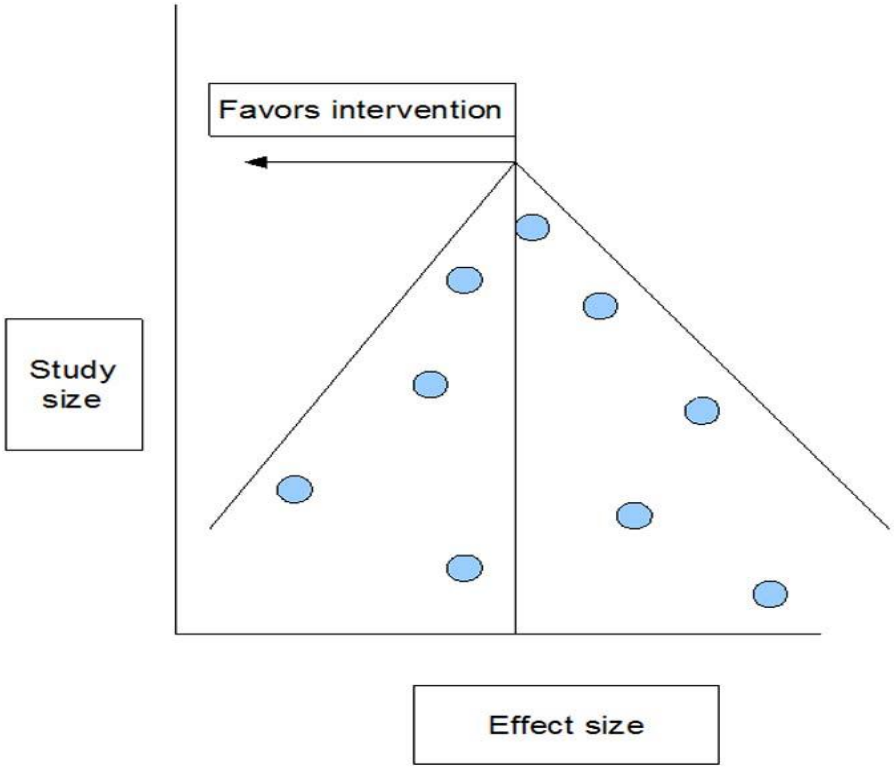


Figure 1 Hypothetical funnel plot
which ***does not*** show publication bias

Turlik M. Evaluating the results of a Systematic Review/Meta-Analysis: Foot and Ankle Online Journal 2009;2:5

Funnel plot – a publication bias

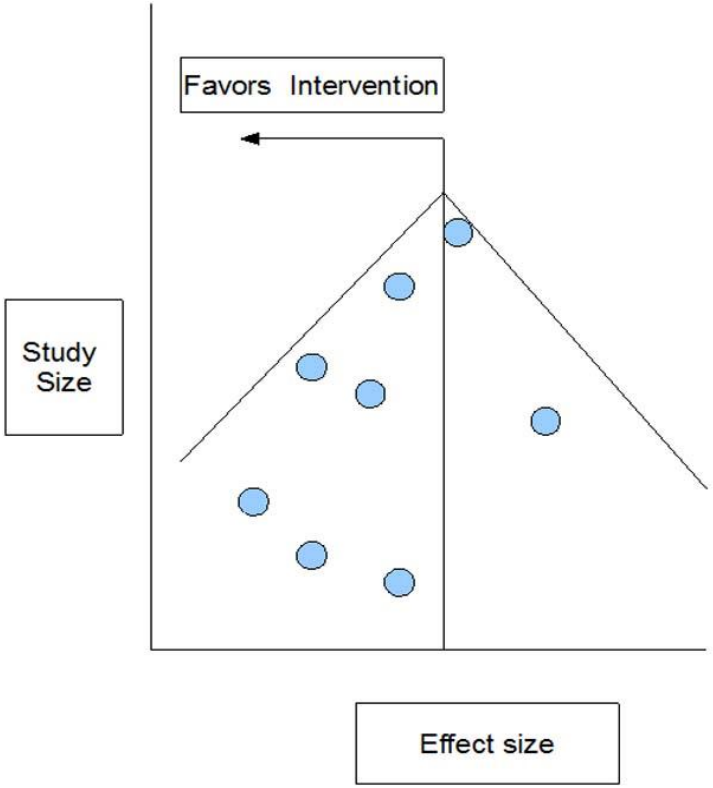
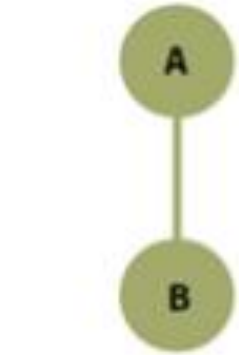


Fig. 2 Hypothetical funnel plot which ***does*** show publication bias

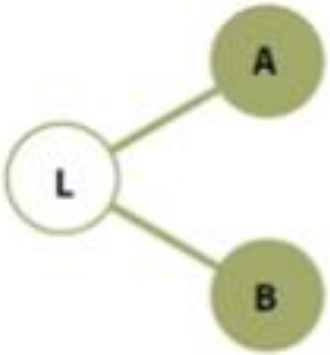
Turlik M. Evaluating the results of a Systematic Review/Meta-Analysis: Foot and Ankle Online Journal 2009;2:5

Direct comparison, undirect comparison, network meta-analysis



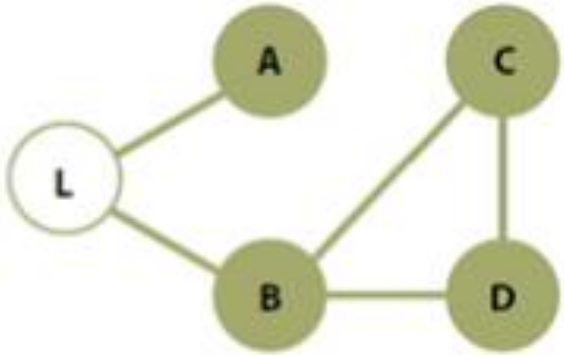
Suora vertailu
(tavanomainen meta-analyysi)

Direct comparison



Epäsuora vertailu

Undirect comparison



Suora ja epäsuora vertailu
(verkostometa-analyysi)

Direct and undirect comparison = Network meta-analysis

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Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis

Andrea Cipriani, Toshi A Furukawa, Georgia Salanti*, Anna Chaimani, Lauren Z Atkinson, Yusuke Ogawa, Stefan Leucht, Henricus G Ruhe, Erick H Turner, Julian P T Higgins, Matthias Egger, Nozomi Takeshima, Yu Hayasaka, Hissei Imai, Kiyomi Shinohara, Aran Tajika, John P A Ioannidis, John R Geddes*

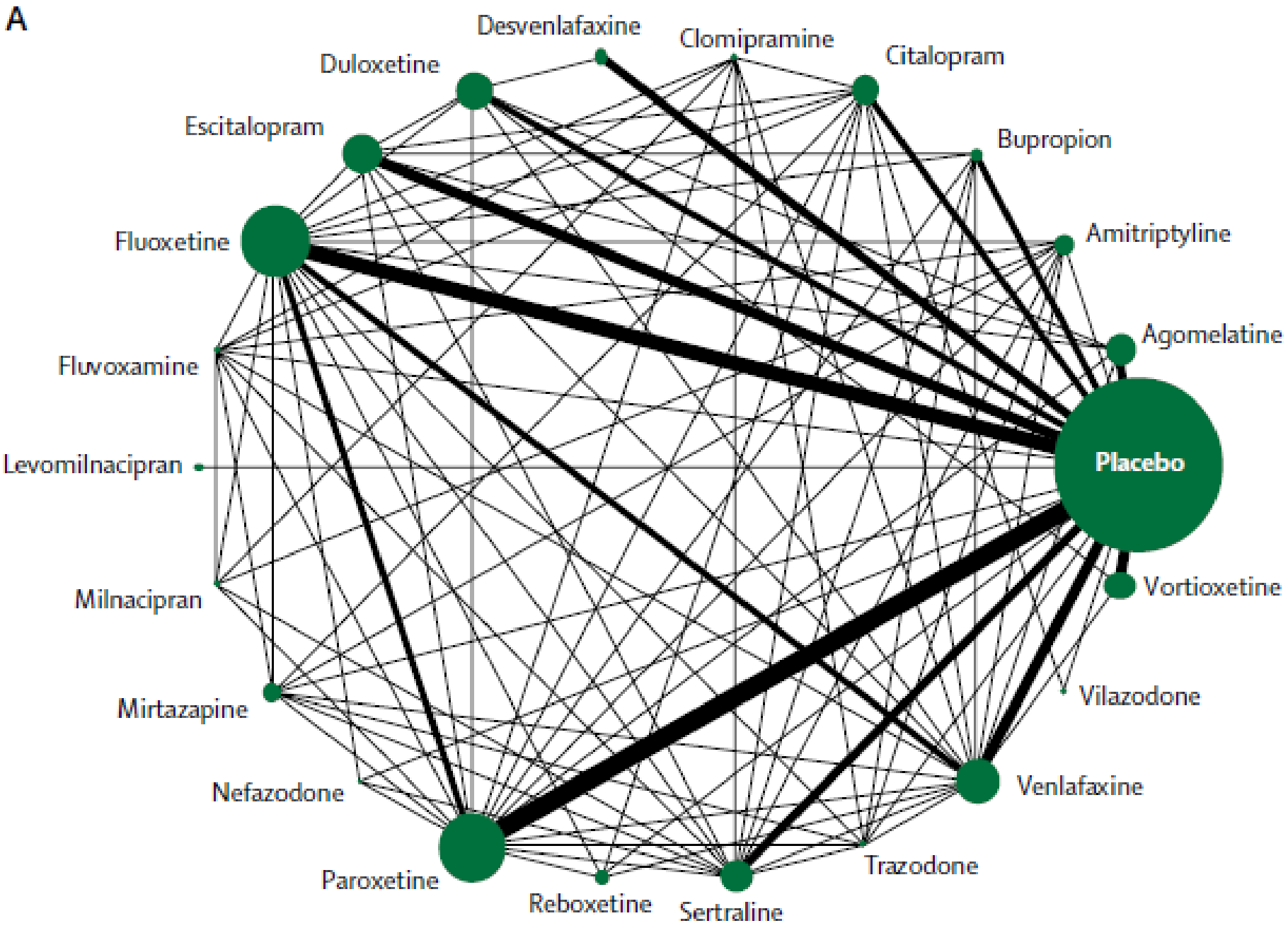
Summary

Background Major depressive disorder is one of the most common, burdensome, and costly psychiatric disorders worldwide in adults. Pharmacological and non-pharmacological treatments are available; however, because of inadequate resources, antidepressants are used more frequently than psychological interventions. Prescription of these agents should be informed by the best available evidence. Therefore, we aimed to update and expand our previous work to compare and rank antidepressants for the acute treatment of adults with unipolar major depressive disorder.

Lancet 2018; 391: 1357–66

Published Online February 21, 2018 http://dx.doi.org/10.1016/S0140-6736(17)32802-7

See Comment page 1333


A
Desvenlafaxine
Clomipramine
Duloxetine
Citalopram
Escitalopram
Bupropion
Fluoxetine
Amitriptyline
Agomelatine
Fluvoxamine
Placebo
Levomilnacipran
Vortioxetine
Milnacipran
Vilazodone
Mirtazapine
Venlafaxine
Nefazodone
Trazodone
Paroxetine
Reboxetine
Sertraline

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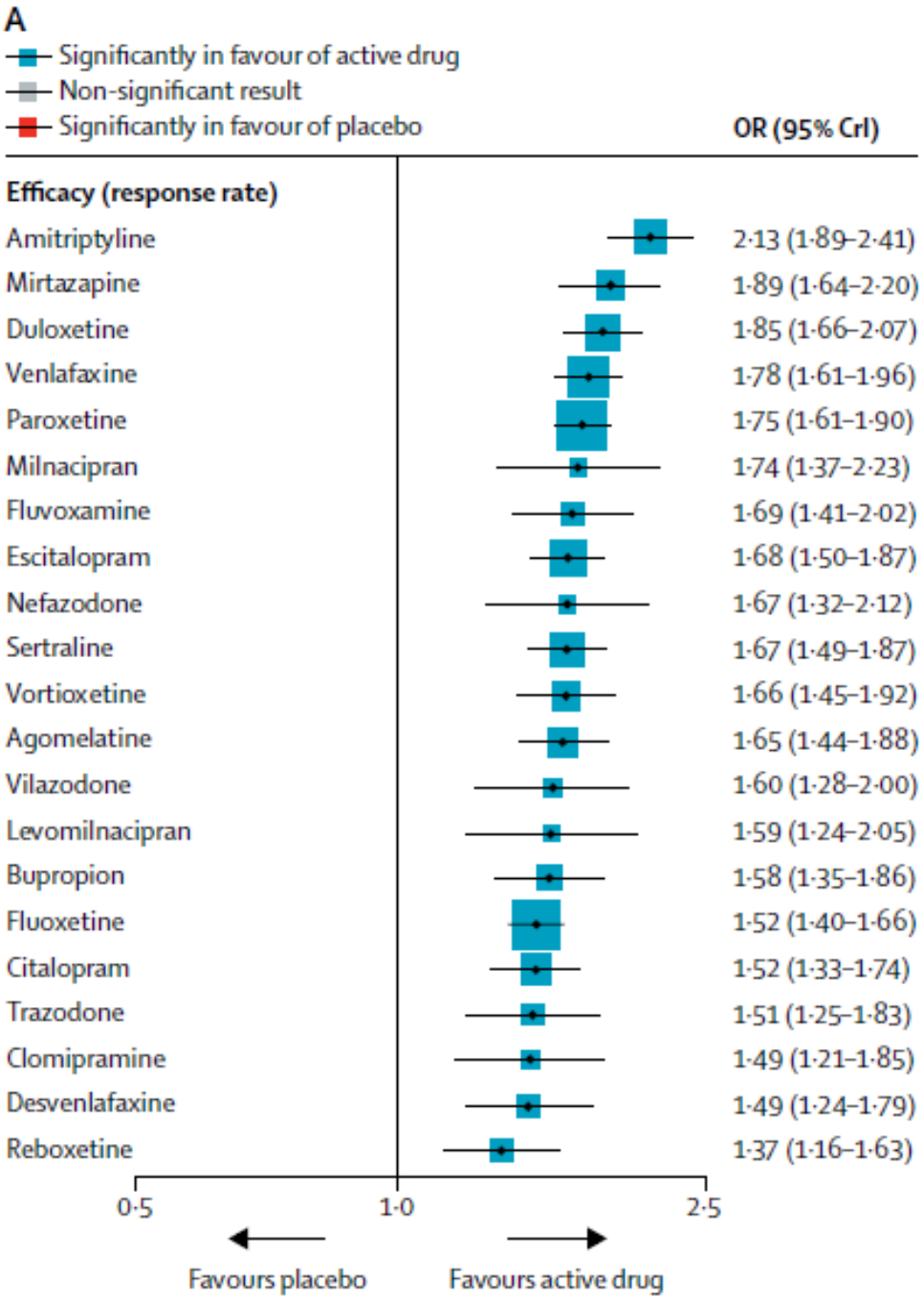

Summary, network meta-analysis

Evidence from direct and undirect comparison can be combined in network analysis

Statistical power and precision of results increases as the patient material increases

The risk of bias in network meta-analyses is greater than in systematic reviews based on direct comparisons, because some of the comparisons are not based on a randomized design

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Conducting a systematic review

Follow the PRISMA statement

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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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PRISMA flow chart

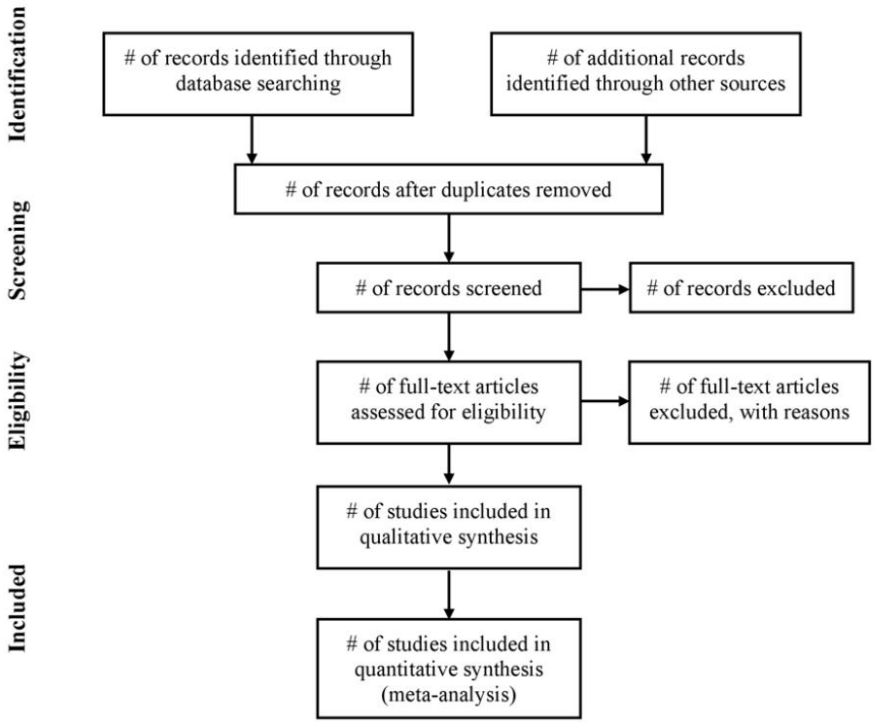

Figure 1. Flow of information through the different phases of a systematic review.
doi:10.1371/journal.pmed.1000100.g001

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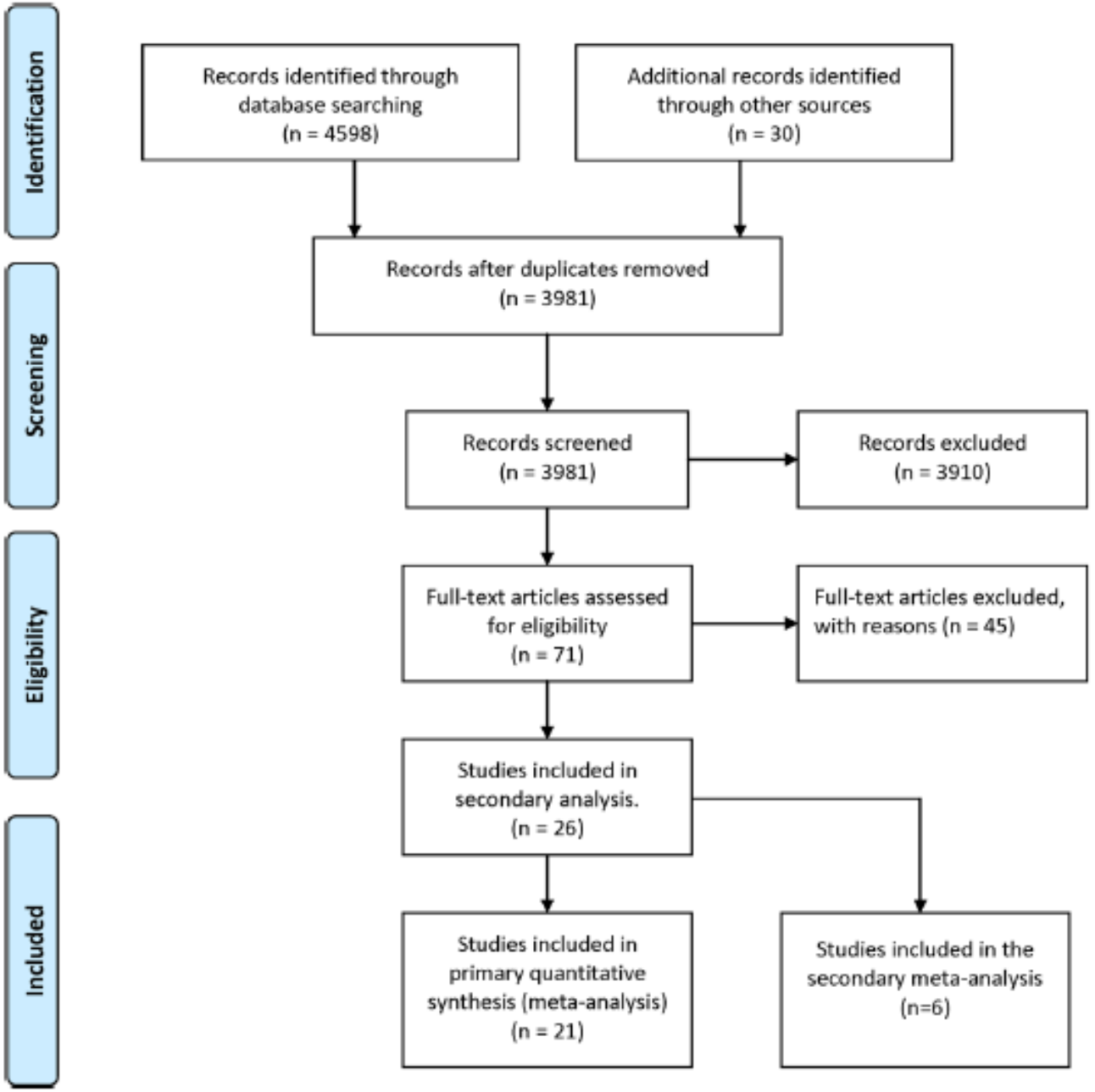

Robotham D, *et al. BMJ Open* 2016;**6**:e012116. doi:10.1136/bmjopen-2016-012116

PRISMA checklist (1)

Section/topic	Item No	Checklist item
Title		
Title	1	Identify the report as a systematic review, meta-analysis, or both
Abstract		
Structured summary	2	Provide a structured summary including, as applicable, background, objectives, data sources, study eligibility criteria, participants, interventions, study appraisal and synthesis methods, results, limitations, conclusions and implications of key findings, systematic review registration number
Introduction		
Rationale	3	Describe the rationale for the review in the context of what is already known
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)

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PRISMA checklist (2)

Methods		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (such as web address), and, if available, provide registration information including registration number
Eligibility criteria	6	Specify study characteristics (such as PICOS, length of follow-up) and report characteristics (such as years considered, language, publication status) used as criteria for eligibility, giving rationale
Information sources	7	Describe all information sources (such as databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated
Study selection	9	State the process for selecting studies (that is, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)
Data collection process	10	Describe method of data extraction from reports (such as piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators
Data items	11	List and define all variables for which data were sought (such as PICOS, funding sources) and any assumptions and simplifications made
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis
Summary measures	13	State the principal summary measures (such as risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (such as I^2 statistic) for each meta-analysis
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies)
Additional analyses	16	Describe methods of additional analyses (such as sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified

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Searched Databases:

- Embase: embase 1980 to april 2015 week 15.
- Medline: 1946 to april 2015 week 2.
- Psychinfo: 1806 to April Week 2 2015.
- Web of science searched 22nd April 2015.
- Cochrane Database of Systematic Reviews : Issue 4 of 12, April 2015
- Cochrane Central Register of Controlled Trials : Issue 3 of 12, March 2015

Appendix 1. MEDLINE (Ovid) search strategy:

1. cellular phone/
2. ((cell* or mobile or wireless) adj (phone* or telephon*)).tw.
3. (cellphone* or mobiles or mhealth or m-health).tw.
4. ((mobile or handheld or hand-held) adj2 (device* or technolog* or app* or health*)).tw.
5. (smart phone* or smartphone* or blackberry or iphone* or android phone* or google android or ipod touch or personal digital assistant* or pda or pdas).tw.
6. 1 or 2 or 3 or 4 or 5
7. (text* or messag* or multimedia or multi-media or imag* or mms or data or input* or application* or app?).tw.
8. 6 and 7
9. text messaging/
10. ((text or short or multimedia or multi-media) adj1 messag*).tw.
11. sms.tw.
12. (texting* or texted or texter*).tw.
13. (mms and (multimedia or multi-media or messag*)).mp.
14. Electronic mail/
15. (electronic adj3 mail$).ab,ti.
16. (electronic adj3 messag$).ab,ti.
17. (email$ or e-mail$).ab,ti.
18. (noti* adj6 (patient* or client* or service-user* or people)).ti,ab,kw.
19. ((remind* or alert* or return* or fail*) adj2 (patient* or client* or service-user* or people)).tw.
20. ((appointment* or attend* or arriv* or consul*) adj2 (patient* or client* or service-user* or people)).tw.
21. (non?attend or non attend* or no show).ti,ab,kw.
22. ((appointment* or attend*) adj6 (complicance or fail* or keep* or miss* or prompt*)).ti,ab,kw.
23. exp Reminder Systems/
24. exp "Appointments and Schedules"/
25. exp Patient Compliance/
26. Outpatients/
27. Outpatient Clinics, Hospital/ut [Utilization]
28. Case Management/
29. Office Visits/
30. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
31. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
32. 30 and 31
33. exp animals/ not humans.sh.
34. 32 not 33
35. limit 34 to yr="1993 -Current"

To cite: Robotham D, Satkunanathan S, Reynolds J, *et al*. Using digital notifications to improve attendance in clinic: systematic review and meta-analysis. *BMJ Open* 2016;**6**: e012116. doi:10.1136/bmjopen-2016-012116

PRISMA checklist (3)

Results		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram
Study characteristics	18	For each study, present characteristics for which data were extracted (such as study size, PICOS, follow-up period) and provide the citations
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present for each study (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15)
Additional analysis	23	Give results of additional analyses, if done (such as sensitivity or subgroup analyses, meta-regression) (see item 16)
Discussion		
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (such as health care providers, users, and policy makers)
Limitations	25	Discuss limitations at study and outcome level (such as risk of bias), and at review level (such as incomplete retrieval of identified research, reporting bias)
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research
Funding		
Funding	27	Describe sources of funding for the systematic review and other support (such as supply of data) and role of funders for the systematic review

QUOROM vs PRISMA

Section/topic and item	QUOROM	PRISMA
Abstract	√	√
Introduction:		
Objective		√
Methods:		
Protocol		√
Search	√	√
Assessment of risk of bias in included studies	√	√
Assessment of risk of bias across studies		√
Discussion	√	√
Funding		√

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Thank you!