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Effects of Non-statin Lipid-Modif Agents on Cardiovascular Morbic and Mortality Among Statin-Treat Patients: A Systematic Review ar Network Meta-Analysis

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Background: Currently, there is a lack of information on the comparati and safety of non-statin lipid-lowering agents (NST) in cardiovascular (C risk reduction when added to background statin therapy (ST). This study the relative treatment effects of NST on fatal and non-fatal CV even statin-treated patients.

Methods: A network meta-analysis based on a systematic review of ra controlled trials (RCTs) comparing non-statin lipid-modifying agents among sta patients was performed. PubMed, EMBASE, CENTRAL, and Clinicaltrial searched up to April 10, 2018. The primary outcomes were CV and all-cause Secondary CV outcomes were coronary heart disease (CHD) death, non-fatal infarction (MI), any stroke, and coronary revascularization. Risks of discontinua secondary safety outcomes.

Results: Sixty-seven RCTs including 259,429 participants with eight int were analyzed. No intervention had significant effects on the primary outc mortality and all-cause mortality). For secondary endpoints, proprotein subtilisin/kexin type 9 inhibitor (PCSK) plus statin (PCSK/ST) significantly re risk of non-fatal MI (RR 0.82, 95% CI 0.72–0.93, $p = 0.003$), stroke (RR CI 0.65–0.85, $p < 0.001$), coronary revascularization (RR 0.84, 95% CI $p = 0.003$) compared to ST. Combinations of ST and all NST except ezetimibe showed higher rate of discontinuation due to adverse events comp

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Effects of pharmacist interventions on heart failure outcomes: A systematic review and meta-analysis

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Abstract

Heart failure (HF) patients tend to have multiple comorbidities resulting in complex therapy regimens and medication adherence issues. Nevertheless, the evidence of pharmacists' contributions to improving clinical outcomes in HF is limited. To assess the impact of pharmacist intervention on all-cause hospitalization, mortality, and quality of life (QoL) in HF) patients. A systematic search of PubMed, Embase, the Cochrane Central Register of Controlled Trials, Scopus, and CINAHL was performed up to April 30, 2020. Randomized controlled trials (RCTs) evaluating pharmacist interventions compared with usual care in adult HF patients were selected. Data were extracted independently by two authors. Random effects meta-analysis models were used to pool treatment effects and confidence intervals (CIs). Twenty-nine trials identified 6965 predominantly HF with reduced ejection fraction (HFrEF) patients. The average age was 72.0 years (interquartile range [IQR] 66.0-76.0) and 48% were men (IQR 40.0%-68.0%). The majority were New York Heart Association (NYHA) Functional class (FC) II-III with median left ventricular ejection fraction (LVEF) of 38.5% (IQR 34.5%-49.5%). Pharmacist interventions were associated with a significant reduction of all-cause mortality (risk ratio [RR] 0.72; 95% CI 0.58-0.89; $P = 0.003$) and all-cause hospitalizations (RR 0.87; 95% CI 0.77-0.99; $P = 0.041$). A significant increase in the 36-item Short form Health survey (SF-36) on role physical (Mean deviation [MD], 8.5; 95% CI, 1.00 to 16.01, $P = 0.026$) and mental health (MD, 7.49; 95% CI, 3.88 to 11.10, $P < 0.001$) were observed. In addition, a significant improvement in Minnesota Living with Heart Failure Questionnaire score was observed (MD -3.55; 95% CI -6.28 to −0.82; $P = 0.01$). Pharmacist interventions in patients with HF significantly reduced all-cause mortality and hospitalizations and improved QoL. Integration of a pharmacist into a HF care team or care pathway should be strongly considered as an important element of a multidisciplinary team.

KEYWORDS
heart failure, hospitalization, meta-analysis, pharmacist, quality of life

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How to conduct a systematic review and meta-analysis

- Research questions
- Article searching strategy
- Eligible criteria
- Study selection
- Data extraction
- Quality assessment

Systematic review

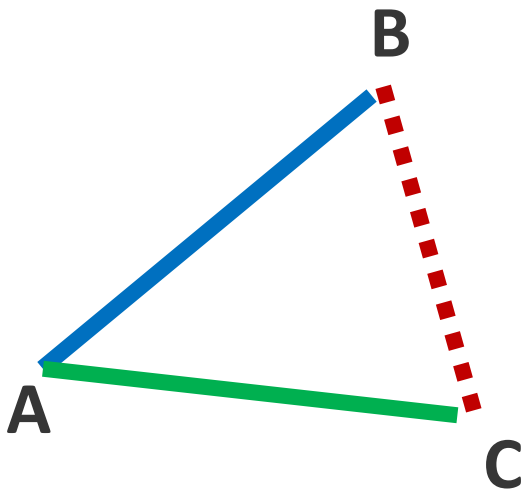
- Data synthesis
- Publication bias
- GRADE

Meta-analysis

Network meta-analysis

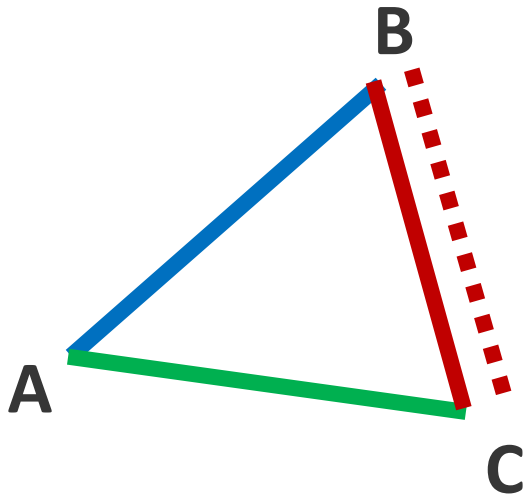
- NMA is an extension of pairwise meta-analysis by including multiple pairwise comparisons across interventions

1. Indirect comparison



Indirect comparison: B-C

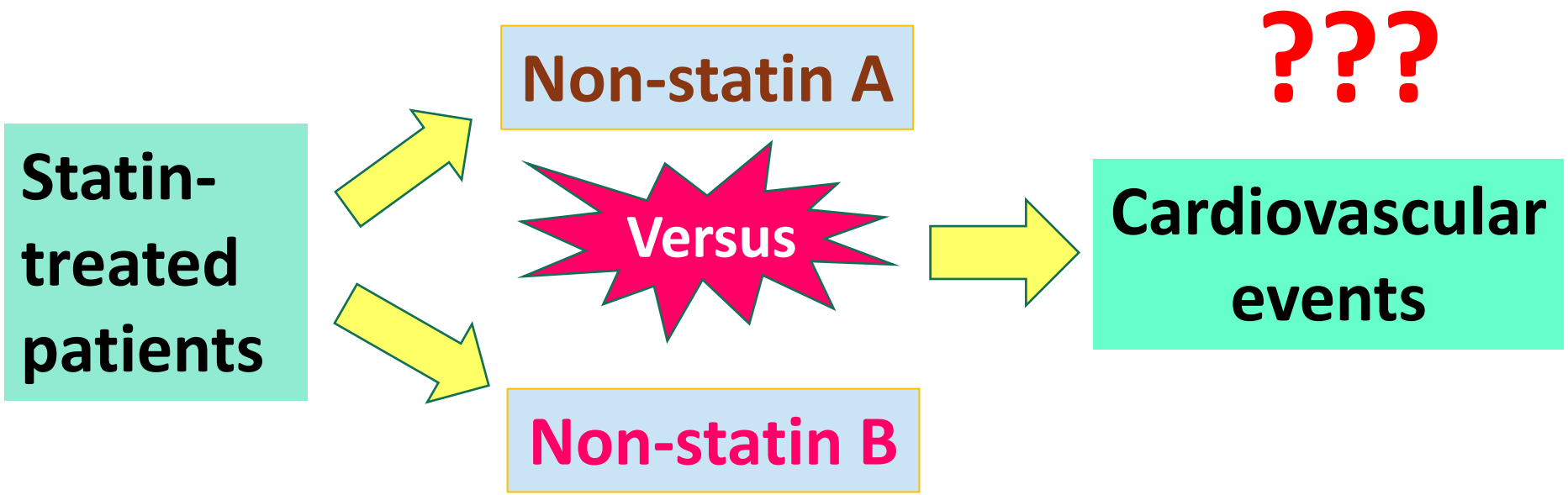
2. Mixed treatment comparison



Indirect comparison: B-C is combined with head to head B-C to produce overall estimate of B-C

Gap of knowledge

A lack of sufficient head-to-head large clinical study



Research topic

- Effects of non-statin lipid-modifying agents on cardiovascular morbidity and mortality in statin-treated patients: A systematic review & network meta-analysis

Research question

- What is the most effective non-statin lipid-modifying agent to further reduce cardiovascular events in statin-treated patients?

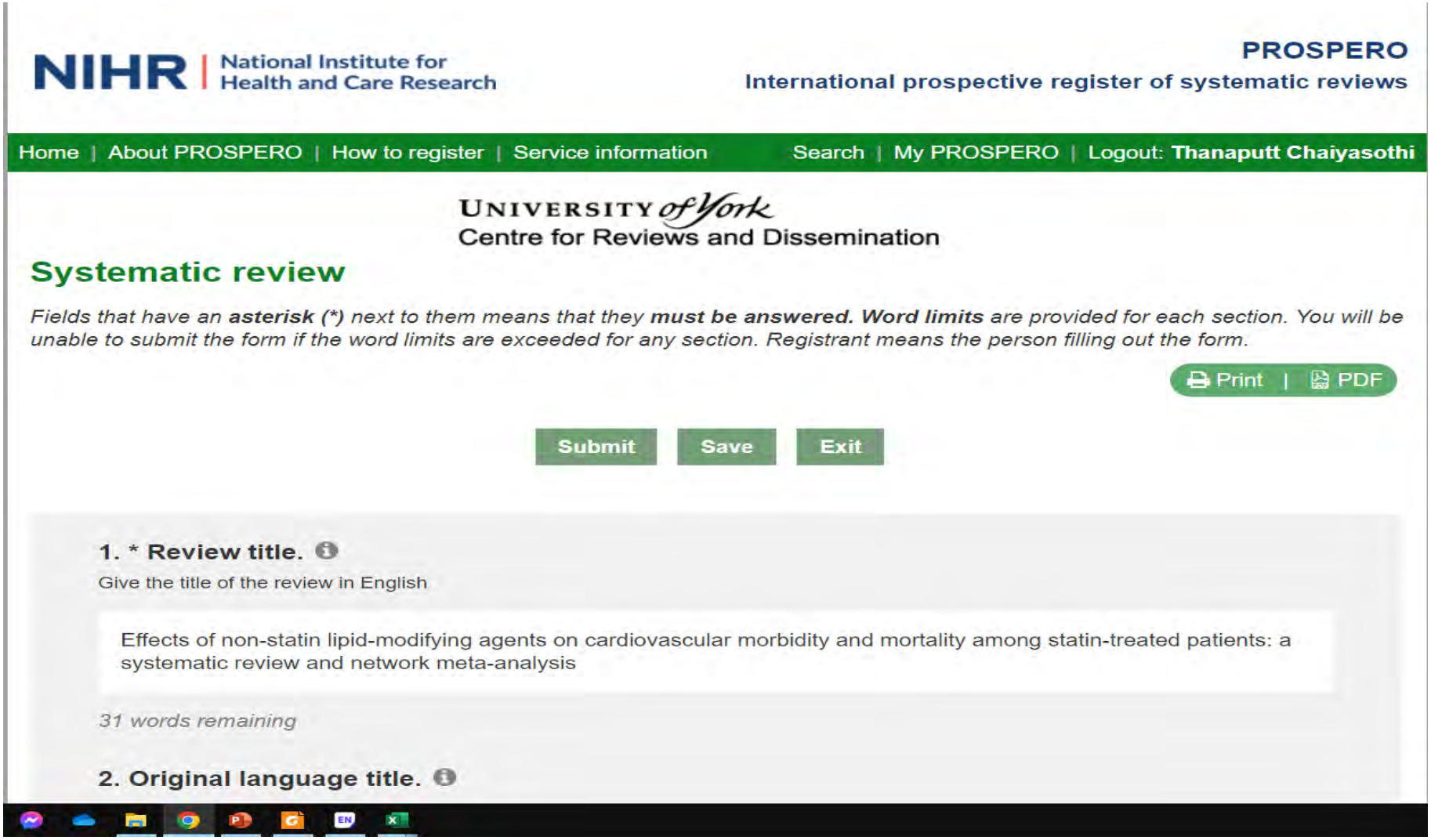
PICO

P	Patients receiving statin therapy
I	Non-statin lipid-modifying agent(s) among statin-treated patients
C	Statin alone or combined therapy
O	Efficacy = CV events Safety endpoints

Inclusion of Criteria of study selection

1. **Age ≥ 18 years**
2. **Randomized controlled trials** (RCTs)
3. **Non-statin agent(s)+statin *vs* statin** (alone or combination)
4. **Reported any event of outcomes of interest** (including all-cause mortality, CV mortality, CHD mortality, nonfatal MI, any stroke, or coronary revascularization)
5. **Follow-up duration ≥ 24 weeks**

https://www.crd.york.ac.uk/prospero/



Steps in systematic review

- Search strategies
- Eligible criteria
- Study selection
- Data extraction
- Risk of bias

Two reviewers (TC and PD) independently performed

Search Strategies

1. Electronic databases searching
   - PubMed
   - EMBASE
   - Cochrane Central Register of Control Trials (CENTRAL)
   - ClinicalTrials.gov
2. References of papers derived for full text review to identify potential studies not indexed in the above databases

No language restriction

Searching terms

The MeSH term and keywords

- Ezetimibe
- Omega-3 fatty acid
- Fibrate
- Niacin
- Bile acid sequestrant
- Proprotein convertase subtilisin/kexin 9
- Cholesteryl ester transfer protein
- Lomitapide
- Mipomersen
- Phytosterol
- Non-statin

+

- Statin
- Atorvastatin
- Simvastatin
- Pravastatin
- Fluvastatin
- Rosuvastatin
- Pitavastatin
- Lovastatin

+

- Cardiovascular
- Vascular
- Death
- Mortality
- Myocardial infarction
- Stroke

Appendix 1 Search strategies

eTable 1.1 search algorithm

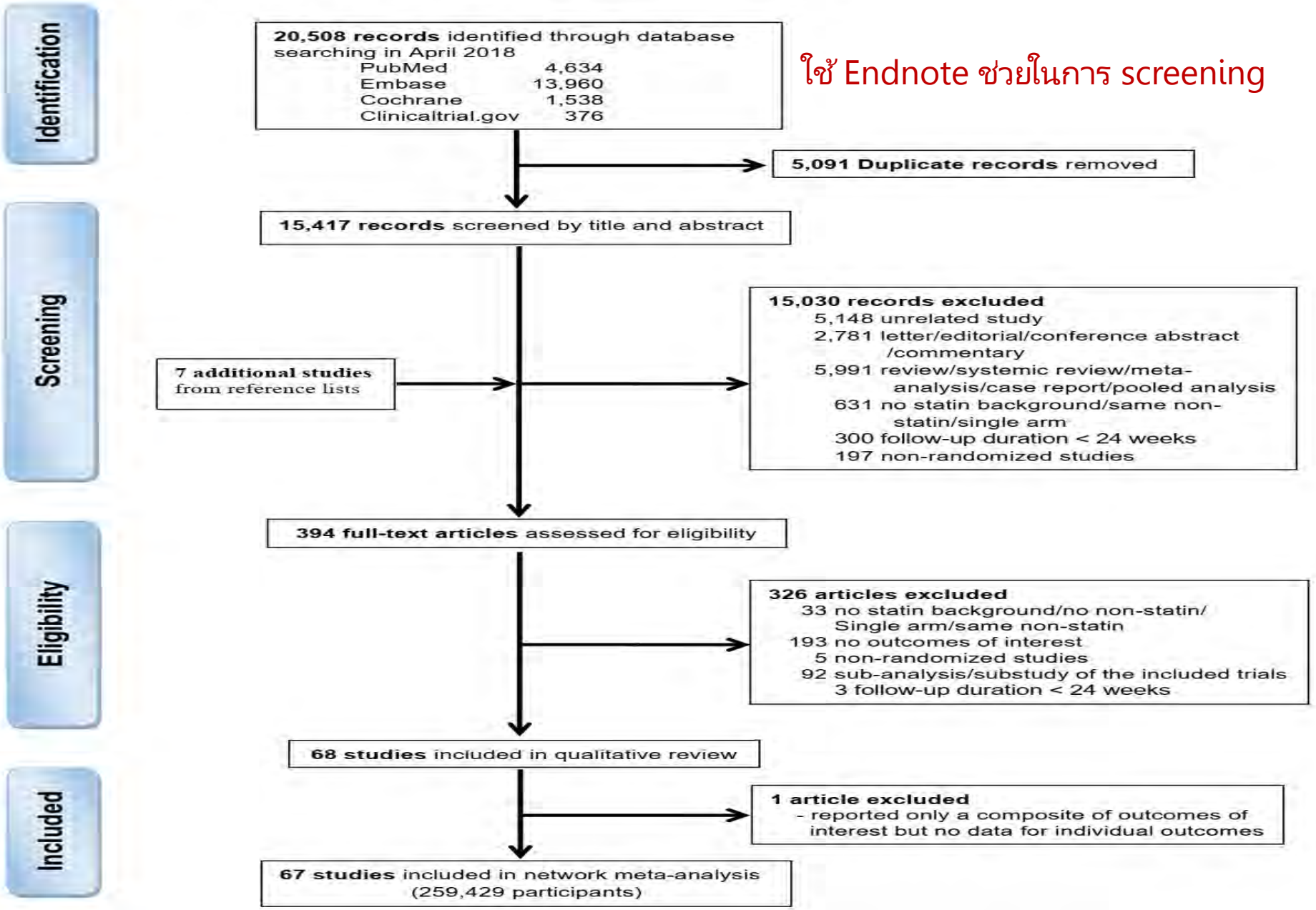
Database	Step	Keyword	Item found
PubMed	#1	Ezetimibe OR "cholesterol absorption" OR "Niemann-Pick C1-like 1" OR NPC1L1	4,726
	#2	Omega-3 OR "fish oil" OR "Omega-3 fatty acid" OR "n-3 fatty acid" OR "Alpha-Linolenic acid" OR "eicosapentaenoic acid" OR "docosahexaenoic acid"	35,496
	#3	Fibrate OR "fibric acid" OR Fenofibrate OR Gemfibrozil OR Bezafibrate OR Ciprofibrate OR Clofibrate OR Clinofibrate	11,714
	#4	"Nicotinic acid" OR niacin OR acipimox	16,575
	#5	"Bile acid sequestrant" OR resin OR Cholestyramine OR Colestipol OR Colesevelam	67,547
	#6	"Proprotein convertase subtilisin/kexin" OR "Proprotein convertase subtilisin kexin" OR "Proprotein convertase subtilisin-kexin" OR PCSK9 OR alirocumab OR evolocumab	2,658
	#7	"Cholesteryl ester transfer protein" OR CETP OR Torcetrapib OR Dalcetrapib OR Anacetrapib OR Evacetrapib	3,548
	#8	"Microsomal triglyceride transfer protein" OR "microsomal transfer protein" OR MTP OR Lomitapide	3,475
	#9	"Antisense oligonucleotide" OR "Apoprotein B-100" OR "apo B-100" OR Mipomersen	5,038
	#10	Phytosterol OR "plant sterol" OR monacolin OR "red yeast rice" OR "dietary fiber" OR "soy protein" OR policosanol OR berberine	25,567
	#11	Non-statin OR nonstatin OR "non statin"	623
	#12	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)	109,484
	#13	Statin OR "3-hydroxy-3-methylglutaryl coenzyme-A" OR "HMG-CoA" OR atorvastatin OR simvastatin OR pravastatin OR fluvastatin OR rosuvastatin OR pitavastatin OR lovastatin	50,944
	#14	Cardiovascular OR cerebrovascular OR cardiac OR coronary OR heart OR vascular OR "myocardial infarction" OR "unstable angina" OR stroke OR death OR mortality OR fatal OR arterial OR artery OR "peripheral artery" OR "peripheral arterial" OR event	4,753,872
	#15	(#12 AND #13 AND #14)	4,634
Embase	#1	Ezetimibe OR "cholesterol absorption" OR "Niemann-Pick C1-like 1" OR NPC1L1	12,040
	#2	Omega-3 OR "fish oil" OR "Omega-3 fatty acid" OR "n-3 fatty acid" OR "Alpha-Linolenic acid" OR "eicosapentaenoic acid" OR "docosahexaenoic acid"	58,336
	#3	Fibrate OR "fibric acid" OR Fenofibrate OR Gemfibrozil OR Bezafibrate OR Ciprofibrate OR Clofibrate OR Clinofibrate	32,763
	#4	"Nicotinic acid" OR niacin OR acipimox	30,661
	#5	"Bile acid sequestrant" OR resin OR Cholestyramine OR Colestipol OR Colesevelam	93,651
	#6	"Proprotein convertase subtilisin/kexin" OR "Proprotein convertase subtilisin kexin" OR "Proprotein convertase subtilisin-kexin" OR PCSK9 OR alirocumab OR evolocumab	4,573
	#7	"Cholesteryl ester transfer protein" OR CETP OR Torcetrapib OR Dalcetrapib OR Anacetrapib OR Evacetrapib	5,387
	#8	"Microsomal triglyceride transfer protein" OR "microsomal transfer protein" OR MTP OR Lomitapide	5,586
	#9	"Antisense oligonucleotide" OR "Apoprotein B-100" OR "apo B-100" OR Mipomersen	19,875
	#10	Phytosterol OR "plant sterol" OR monacolin OR "red yeast rice" OR "dietary fiber" OR "soy protein" OR policosanol OR berberine	39,626
	#11	Non-statin OR nonstatin OR "non statin"	989
	#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	15,921
	#13	Statin OR "3-hydroxy-3-methylglutaryl coenzyme-A" OR "HMG-CoA" OR atorvastatin OR simvastatin OR pravastatin OR fluvastatin OR rosuvastatin OR pitavastatin OR lovastatin	98,608
	#14	Cardiovascular OR cerebrovascular OR cardiac OR coronary OR heart OR vascular OR "myocardial infarction" OR "unstable angina" OR stroke OR death OR mortality OR fatal OR arterial OR artery OR "peripheral artery" OR "peripheral arterial" OR event	6,069,281
	#15	#12 AND #13 AND #14	13,960
CENTRAL	#1	Ezetimibe OR "cholesterol absorption" OR "Niemann-Pick C1-like 1" OR NPC1L1	937
	#2	Omega-3 OR "fish oil" OR "Omega-3 fatty acid" OR "n-3 fatty acid" OR "Alpha-Linolenic acid" OR "eicosapentaenoic acid" OR "docosahexaenoic acid"	5,399
	#3	Fibrate OR "fibric acid" OR Fenofibrate OR Gemfibrozil OR Bezafibrate OR Ciprofibrate OR Clofibrate OR Clinofibrate	1,927
	#4	"Nicotinic acid" OR niacin OR acipimox	1,477
	#5	"Bile acid sequestrant" OR resin OR Cholestyramine OR Colestipol OR Colesevelam	4,802
	#6	"Proprotein convertase subtilisin/kexin" OR "Proprotein convertase subtilisin kexin" OR "Proprotein convertase subtilisin-kexin" OR PCSK9 OR alirocumab OR evolocumab	208
	#7	"Cholesteryl ester transfer protein" OR CETP OR Torcetrapib OR Dalcetrapib OR Anacetrapib OR Evacetrapib	282
	#8	"Microsomal triglyceride transfer protein" OR "microsomal transfer protein" OR MTP OR Lomitapide	180
	#9	"Antisense oligonucleotide" OR "Apoprotein B-100" OR "apo B-100" OR Mipomersen	180
	#10	Phytosterol OR "plant sterol" OR monacolin OR "red yeast rice" OR "dietary fiber" OR "soy protein" OR policosanol OR berberine	3,244
	#11	Non-statin OR nonstatin OR "non statin"	86
	#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	17,642
	#13	Statin OR "3-hydroxy-3-methylglutaryl coenzyme-A" OR "HMG-CoA" OR atorvastatin OR simvastatin OR pravastatin OR fluvastatin OR rosuvastatin OR pitavastatin OR lovastatin	9,688
	#14	Cardiovascular OR cerebrovascular OR cardiac OR coronary OR heart OR vascular OR "myocardial infarction" OR "unstable angina" OR stroke OR death OR mortality OR fatal OR arterial OR artery OR "peripheral artery" OR "peripheral arterial" OR event	298,357
	#15	#12 AND #13 AND #14	1,538
Clinicaltrial.gov	1	Ezetimibe OR "cholesterol absorption" OR "Niemann-Pick C1-like 1" OR NPC1L1	343
	2	Omega-3 OR "fish oil" OR "Omega-3 fatty acid" OR "n-3 fatty acid" OR "Alpha-Linolenic acid" OR "eicosapentaenoic acid" OR "docosahexaenoic acid"	1,442
	3	Fibrate OR "fibric acid" OR Fenofibrate OR Gemfibrozil OR Bezafibrate OR Ciprofibrate OR Clofibrate OR Clinofibrate	258
	4	"Nicotinic acid" OR niacin OR acipimox	989
	5	"Bile acid sequestrant" OR resin OR Cholestyramine OR Colestipol OR Colesevelam	362
	6	"Proprotein convertase subtilisin/kexin" OR "Proprotein convertase subtilisin kexin" OR "Proprotein convertase subtilisin-kexin" OR PCSK9 OR alirocumab OR evolocumab	163
	7	"Cholesteryl ester transfer protein" OR CETP OR Torcetrapib OR Dalcetrapib OR Anacetrapib OR Evacetrapib	117
	8	"Microsomal triglyceride transfer protein" OR "microsomal transfer protein" OR MTP OR Lomitapide	104
	9	"Antisense oligonucleotide" OR "Apoprotein B-100" OR "apo B-100" OR Mipomersen	159
	10	Phytosterol OR "plant sterol" OR monacolin OR "red yeast rice" OR "dietary fiber" OR "soy protein" OR policosanol OR berberine	2,689
	11	Non-statin OR nonstatin OR "non statin"	16
	12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	6,684
	#13	Statin OR "3-hydroxy-3-methylglutaryl coenzyme-A" OR "HMG-CoA" OR atorvastatin OR simvastatin OR pravastatin OR fluvastatin OR rosuvastatin OR pitavastatin OR lovastatin	2,461
	#14	Cardiovascular OR cerebrovascular OR cardiac OR coronary OR heart OR vascular OR "myocardial infarction" OR "unstable angina" OR stroke OR death OR mortality OR fatal OR arterial OR artery OR "peripheral artery" OR "peripheral arterial" OR event	107,898
	#15	#12 AND #13 AND #14	376

Results from database searching

20,508 records identified through database searching in April 2018

• **PubMed**	**4,634**
• **Embase**	**13,960**
• **Cochrane**	**1,538**
• **Clinicaltrial.gov**	**376**

eFigure 1.1 Flow diagram and references of included studies



ใช้ Endnote ช่วยในการ screening

Data extraction

The included RCTs using a standard extraction form

1) Characteristics of the study such as year or publication, country, number of arms, study design, period of follow up
2) Characteristic of participant such as age, gender, number of patients included in analysis, preexisting cardiovascular diseases, cardiovascular risk factors, level of lipid profile
3) Type of intervention and type of comparator(s) such as dosing regimen, concomitant medication, intensity of statin
4) Outcomes measure such as outcomes of interest as stated above including primary and secondary outcomes

Two reviewers (TC and PD) independently extracted data

Appendix 3

Risk of bias assessment

- The Revised Cochrane Risk of Bias Tool for randomized trials (RoB 2.0)

Table 1. Reaching an overall risk-of-bias judgement for a specific outcome.

Overall risk-of-bias judgement	Criteria
Low risk of bias	The study is judged to be at **low risk of bias for all domains** for this result.
Some concerns	The study is judged to raise **some concerns** in at least one domain for this result, but not to be at high risk of bias for any domain.
High risk of bias	The study is judged to be at **high risk of bias** in at least one domain for this result. Or The study is judged to have **some concerns** for **multiple domains** in a way that substantially lowers confidence in the result.

- Low risk of bias, some concerns, or high risk of bias

Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne
on behalf of the RoB2 Development Group

22 August 2019

Dedicated to Professor Douglas G Altman, whose contributions were of fundamental importance to development of risk of bias assessment in systematic reviews

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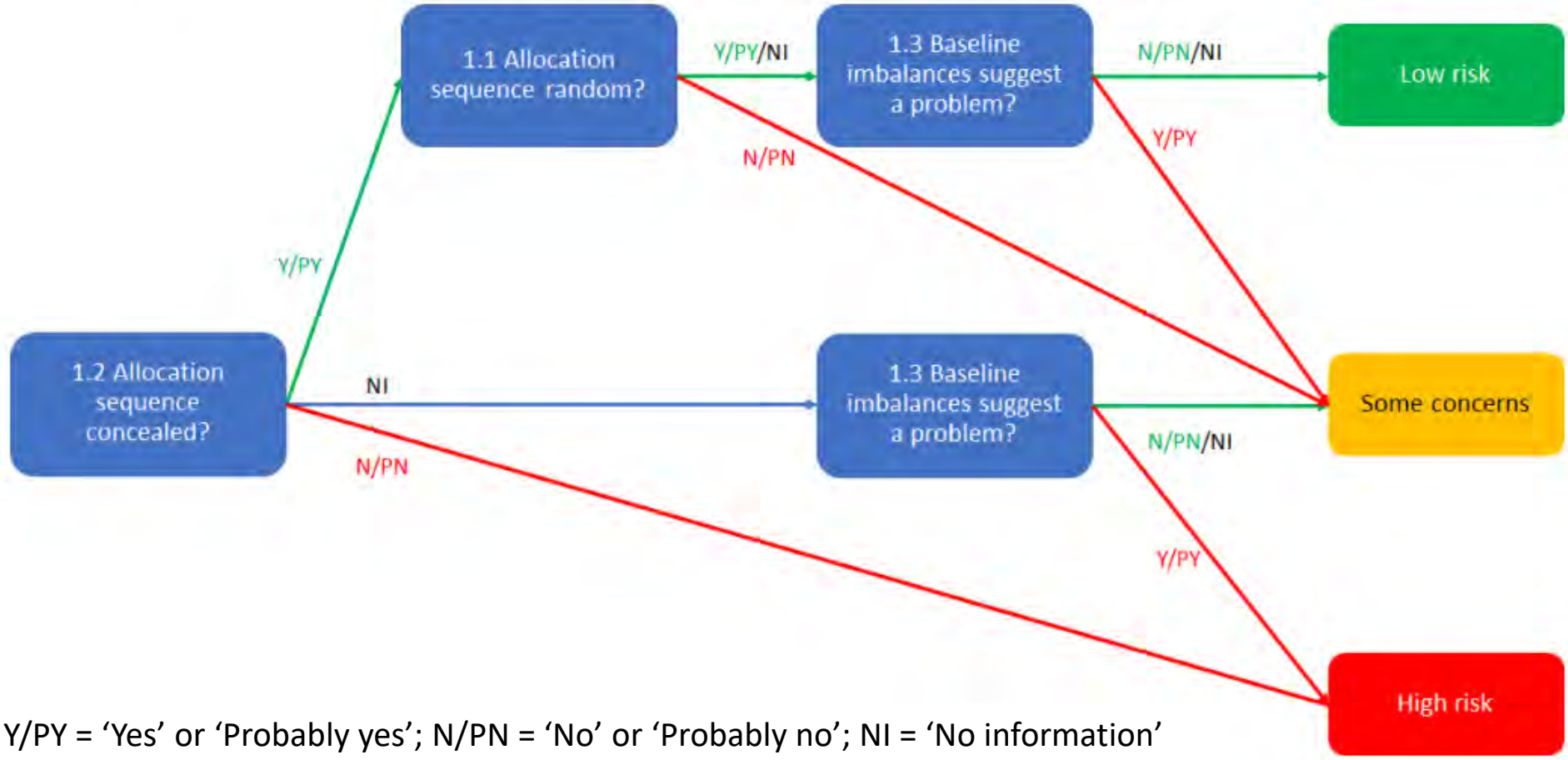
Contents

1 Introduction 2
1.1 Signalling questions 3
1.2 Risk-of-bias judgements 3
1.3 Specifying the nature of the effect of interest 5
2 Issues in implementation of RoB 2 6
2.1 Multiple assessments 6
2.2 The data collection process 7
2.3 Presentation of risk-of-bias assessments 7
2.4 Rapid assessments 7
3 Detailed guidance: preliminary considerations 8
4 Detailed guidance: bias arising from the randomization process 10
4.1 Background 10
4.2 Empirical evidence of bias arising from the randomization process 11
4.3 Using this domain of the tool 12
4.4 Signalling questions and criteria for judging risk of bias 16
5 Detailed guidance: bias due to deviations from intended interventions 21
5.1 Background 21
5.2 Empirical evidence of bias due to deviations from intended interventions 26
5.3 Using this domain of the tool 26
5.4 Signalling questions and criteria for judging risk of bias 27
6 Detailed guidance: bias due to missing outcome data 39
6.1 Background 39
6.2 Empirical evidence of bias due to missing outcome data 44
6.3 Using this domain of the tool 44
6.4 Signalling questions and criteria for judging risk of bias 44
7 Detailed guidance: bias in measurement of the outcome 49
7.1 Background 49
7.2 Empirical evidence of bias in measurement of the outcome 52
7.3 Using this domain of the tool 52
7.4 Signalling questions and criteria for judging risk of bias 53
8 Detailed guidance: bias in selection of the reported result 58
8.1 Background 58
8.2 Empirical evidence of bias in selection of the reported result 60
8.3 Using this domain of the tool 60
8.4 Signalling questions and criteria for judging risk of bias 62
9 Acknowledgements 68
10 Contributors 68
11 References 68

Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne
on behalf of the RoB2 Development Group

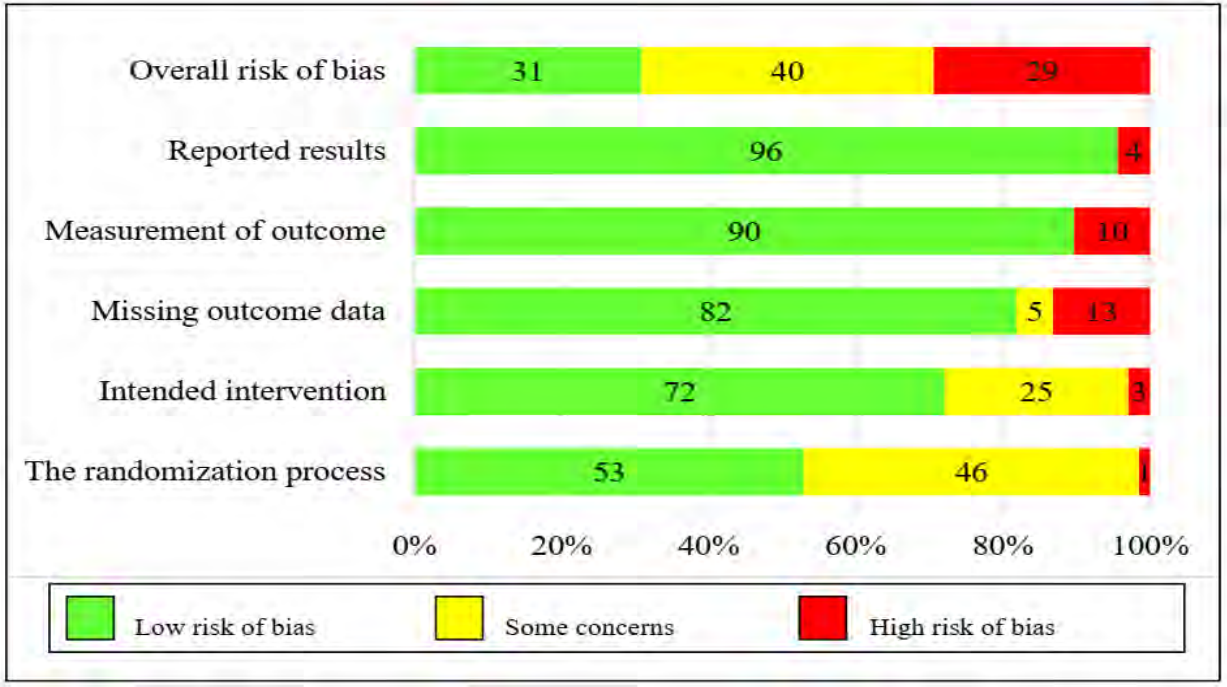
Figure 1. Algorithm for suggested judgement of risk of bias arising from the randomization process.



Y/PY = 'Yes' or 'Probably yes'; N/PN = 'No' or 'Probably no'; NI = 'No information'

eFigure 4.1 Risk of bias graph

Rview authors' judgements (Low, Some concerns and High) about each risk of bias item presented as percentages across all included studies.



	1. The randomization process	2. Intended intervention	3. Missing outcome data	4. Measurement of outcome	5. Reported results	6. Overall risk of bias
Arimura, 2012 [26]	?	−	+	−	+	−
Ballantyne, 2008 [16]	?	+	−	+	+	−
Ballantyne, 2008 [42]	+	+	−	+	+	−
Ballantyne, 2017 [48]	?	+	+	+	+	?
Ballantyne, 2017 [65]	?	+	+	+	+	?
Barter, 2007 [9]	?	+	+	+	+	?
Bays, 2015 [39]	+	+	+	+	+	+
Blom, 2014 [24]	?	+	+	+	+	?
Boden, 2011 [4]	+	+	−	+	+	−
Bots, 2007 [27]	+	+	−	+	+	−
Bowman, 2017 [57]	+	+	+	+	+	+
Brunner, 2013 [15]	?	+	−	+	+	−
Cannon, 2010 [29]	?	+	−	+	+	−
Cannon, 2015 [1]	+	+	+	+	+	+
Cannon, 2015 [23]	+	+	+	+	+	+
Davidson, 2014 [30]	+	+	+	+	+	+
Derosa, 2004 [32]	+	+	+	+	+	+
Durrington, 2001 [33]	?	+	+	+	+	?
Farnier, 2016 [22]	?	+	+	+	+	?
Fayad, 2011 [40]	?	+	+	+	−	−
Gingberg, 2010 [6]	+	+	+	+	+	+
Gingberg, 2016 [47]	+	+	−	+	+	−

Data synthesis in MA

- Estimates for outcomes of interests
- Pairwise meta-analysis
- Subgroup and Sensitivity analyses
- Publication bias
- GRADE

STATA 14.2 software

DOI: 10.1002/jac5.1442

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Effects of pharmacist interventions on heart failure outcomes: A systematic review and meta-analysis

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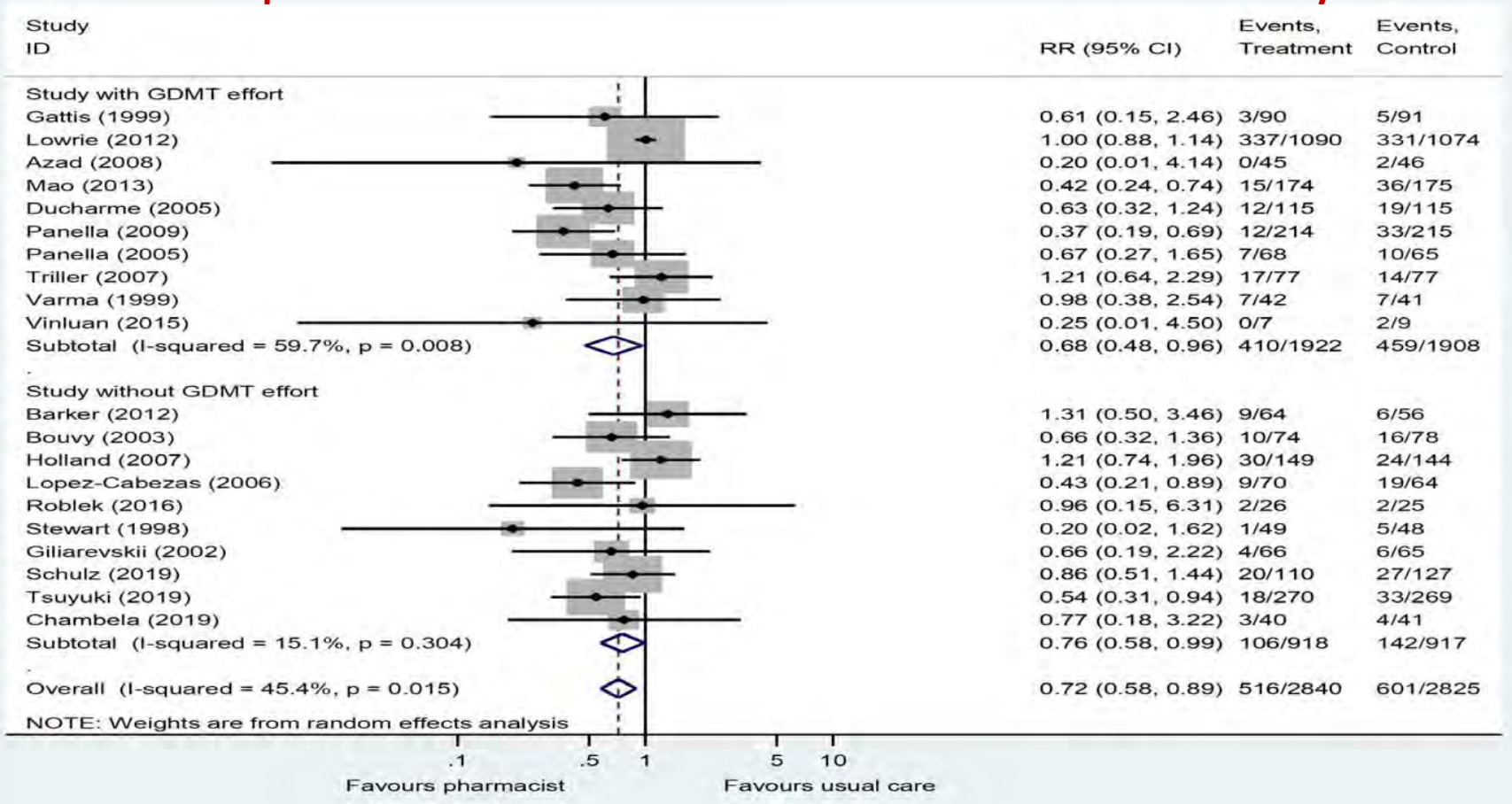
(A) **Effect of pharmacist interventions vs usual care on All-cause mortality**



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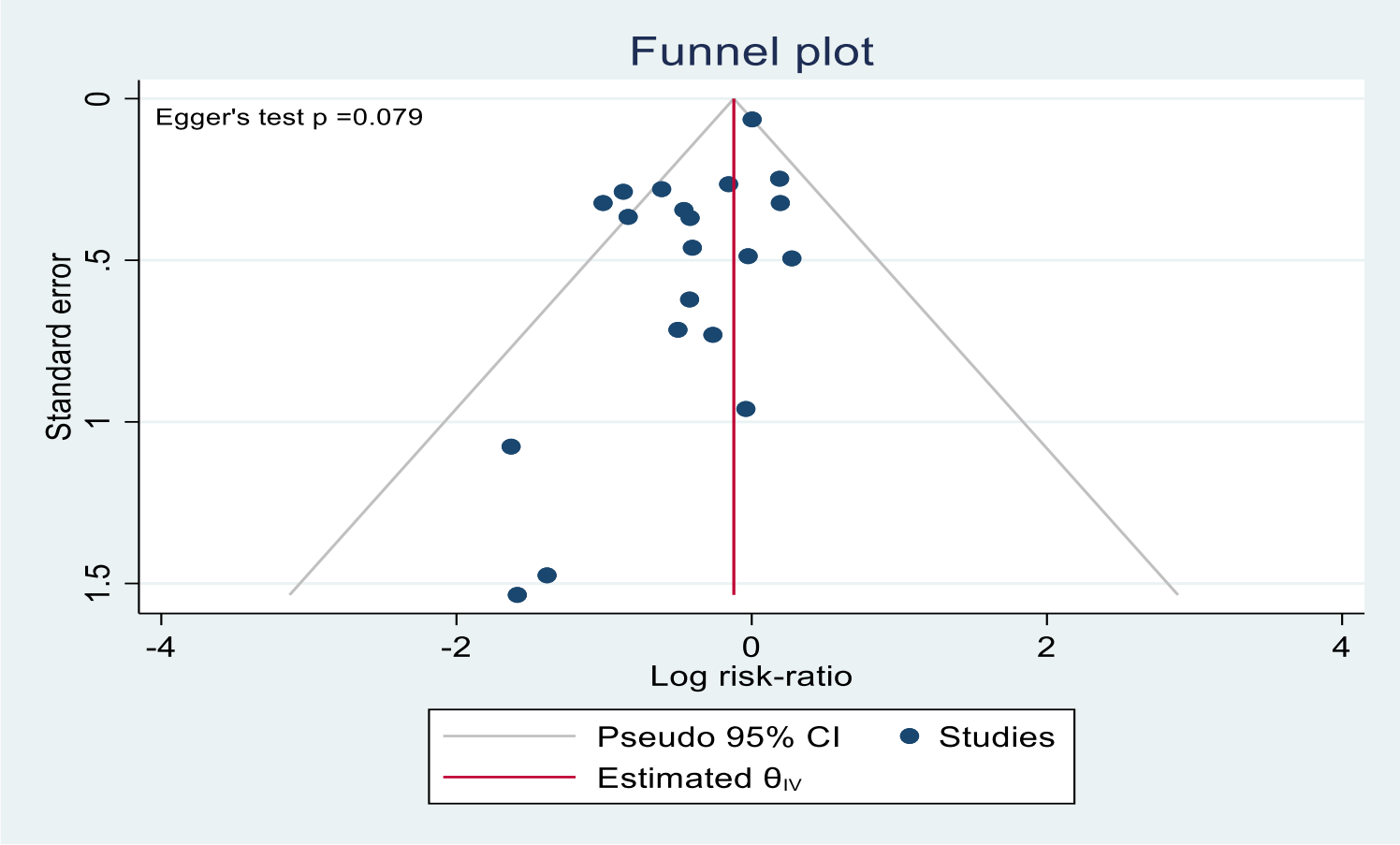

The GRADE approach

- To determine quality of evidence

Study Design	Quality of Evidence	Lower if	Higher if
Randomized trial →	High (four plus: ⊕⊕⊕⊕)	Risk of bias -1 Serious -2 Very serious Inconsistency -1 Serious -2 Very serious Indirectness -1 Serious -2 Very serious Imprecision -1 Serious -2 Very serious Publication bias -1 Likely -2 Very likely	Large effect +1 Large +2 Very large Dose response +1 Evidence of a gradient All plausible confounding +1 Would reduce a demonstrated effect or +1 Would suggest a spurious effect when results show no effect
	Moderate (three plus: ⊕⊕⊕◯)		
Observational study →	Low (two plus: ⊕⊕◯◯)		
	Very low (one plus: ⊕◯◯◯)		

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TABLE 2 Grading of recommendation assessment, development, and evaluation (GRADE) for main analyses

Outcomes	Illustrative comparative risks[a] (95% CI) Assumed risk[a] Usual care	Corresponding risk[a] Pharmacist intervention	Relative effect (95% CI)	Number of participants (No. of studies)	Quality of the evidence (GRADE)
All-cause mortality	160 per 1000	115 per 1000 (93 to 102)	RR 0.72 (0.58 to 0.89)	5665 (20 studies)	⊕⊕⊕◯[b] MODERATE
Hospitalization	452 per 1000	389 per 1000 (339 to 447)	RR 0.86 (0.75 to 0.99)	5203 (18studies)	⊕⊕⊕◯[b] MODERATE

[a]The basis for the assumed risk (eg, the median control group risk across studies). The corresponding risk is based on the assumed risk in the comparison group and the relative effect of the intervention.

[b]Moderate quality evidence is due to serious inconsistency (heterogeneity).

frontiers in Pharmacology

SYSTEMATIC REVIEW
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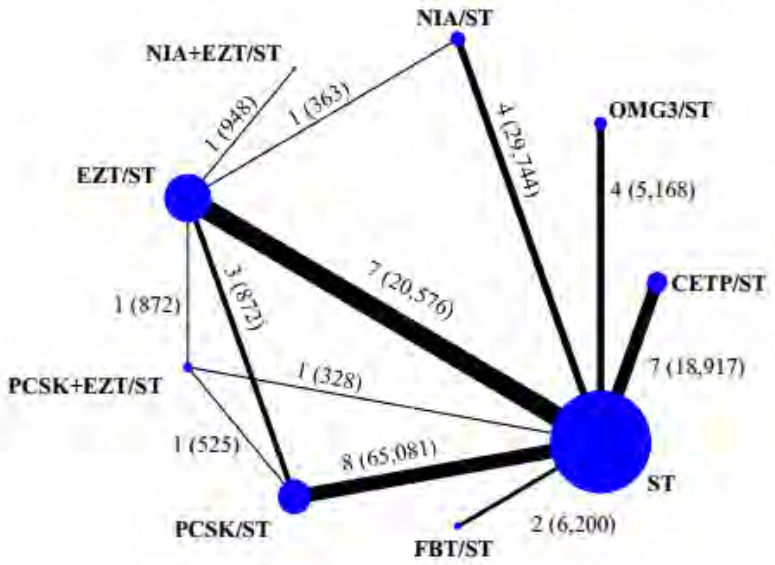
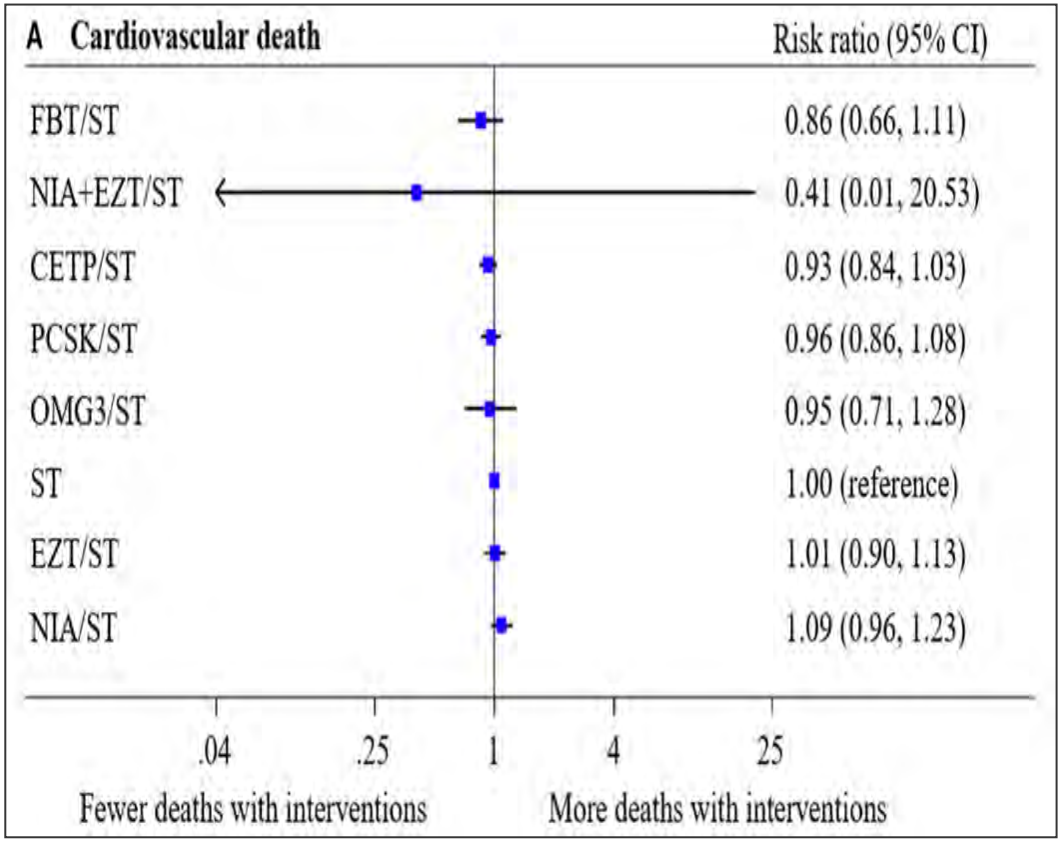
Effects of Non-statin Lipid-Modifying Agents on Cardiovascular Morbidity and Mortality Among Statin-Treated Patients: A Systematic Review and Network Meta-Analysis

Thanaputt Chaiyasothi[1,2], Surakit Nathisuwan[1], Piyameth Dilokthornsakul[3], Prin Vathesatogkit[4], Ammarin Thakkinstian[5], Christopher Reid[6,7], Wanwarang Wongcharoen[8] and Nathorn Chaiyakunapruk[3,9,10,11]**

Cardiovascular mortality





PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	

PRISMA 2020 Checklist

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

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

https://training.cochrane.org/handbook/current

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Cochrane Handbook for Systematic Reviews of Interventions

Search Handbook

- Overview
- Part 1: About Cochrane Reviews
- Part 2: Core methods
- Part 3: Specific perspectives in reviews
- Part 4: Other topics

Version 6.3, 2022

Senior Editors: Julian Higgins[1], James Thomas[2]
Associate Editors: Jacqueline Chandler[3], Miranda Cumpston[4,5], Tianjing Li[6], Matthew Page[4], Vivian Welch[7]

Part 1: About Cochrane Reviews

I. Introduction
II. Planning a Cochrane Review
III. Reporting the review
IV. Updating the review
V. Overviews of Reviews

Part 2: Core methods

1. Starting a review
2. Determining the scope and questions
3. Inclusion criteria & grouping for synthesis
4. Searching & selecting studies
5. Collecting data
6. Effect measures
7. Bias and conflicts of interest
8. Risk of bias in randomized trials
9. Preparing for synthesis
10. Meta-analyses
11. Network meta-analyses
12. Synthesis using other methods
13. Bias due to missing results
14. 'Summary of findings' tables & GRADE
15. Interpreting results

Part 3: Specific perspectives in reviews

16. Equity
17. Intervention complexity
18. Patient-reported outcomes
19. Adverse effects
20. Economic evidence
21. Qualitative evidence

Part 4: Other topics

22. Prospective approaches
23. Variants on randomized trials
24. Including non-randomized studies
25. Risk of bias in non-randomized studies
26. Individual participant data

สิ่งที่ควรคำนึงในการทำ MA กับ NMA คือ...

...ความรวดเร็ว !!!

…End…