

1 **Supplementary file**2 **PRISMA-P Checklist**

Section and topic	Item No	Checklist item	Information reported	Line number(s)
ADMINISTRATIVE INFORMATION				
Title:				
Identification	1a	Identify the report as a protocol of a systematic review	Yes	1-3
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes	45
Authors:				
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes	8-15
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes	307-311
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	Yes	320-321
Support:				
Sources	5a	Indicate sources of financial or other support for the review	Yes	312-313
Sponsor	5b	Provide name for the review funder and/or sponsor	NA	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA	
INTRODUCTION				
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes	62-95
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes	96-98
METHODS				
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes	100-205
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes	208-214
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Yes	Supplementary file 12-18
Study records:				
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes	231-237
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes	215-226
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes	232-237
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes	Table 1

Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes	191-205 and Table 1
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes	238-242
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	Yes	257-258
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	Yes	259-281
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	Yes	282-287
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Yes	253-256
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	Yes	248-250
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	Yes	296-298

3 *** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P**
4 **Explanation and Elaboration (cite when available) for important clarification on the items.**
5 **Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P**
6 **(including checklist) is held by the PRISMA-P Group and is distributed under a Creative**
7 **Commons Attribution Licence 4.0.**

8 *From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L,*
9 *PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols*
10 *(PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

11 Search strategy

Data search strategy for embase.com

#	Searches	
#1	'antilipemic agent'/exp	
#2	'anticholesteremic':ab,kw,ti,tn OR 'antihypercholesteremic':ab,kw,ti,tn OR 'altacor':ab,kw,ti,tn OR 'atorvastatin':ab,kw,ti,tn OR 'baycol':ab,kw,ti,tn OR 'bervastatin':ab,kw,ti,tn OR 'canef':ab,kw,ti,tn OR 'cerivastatin':ab,kw,ti,tn OR 'compactin':ab,kw,ti,tn OR 'cranoc':ab,kw,ti,tn OR 'crestor':ab,kw,ti,tn OR 'crilvastatin':ab,kw,ti,tn OR 'dalvastatin':ab,kw,ti,tn OR 'fluidostatin':ab,kw,ti,tn OR 'fluvastatin':ab,kw,ti,tn OR 'glenvastatin':ab,kw,ti,tn OR 'hmg coa':ab,kw,ti,tn OR 'hydroxymethylglutaryl':ab,kw,ti,tn OR 'hypochole':ab,kw,ti,tn OR 'hypolipidemic':ab,kw,ti,tn OR 'lescol':ab,kw,ti,tn OR 'lipitor':ab,kw,ti,tn OR 'lipex':ab,kw,ti,tn OR 'lipostat':ab,kw,ti,tn OR 'livalo':ab,kw,ti,tn OR 'local':ab,kw,ti,tn OR 'lovostatin':ab,kw,ti,tn OR 'lochol':ab,kw,ti,tn OR 'medostatin':ab,kw,ti,tn OR 'mevacor':ab,kw,ti,tn OR 'mevalotin':ab,kw,ti,tn OR 'mevinacor':ab,kw,ti,tn OR 'mevinolin':ab,kw,ti,tn OR 'monacolin':ab,kw,ti,tn OR 'pitava':ab,kw,ti,tn OR 'pitavastatin':ab,kw,ti,tn OR 'pravachol':ab,kw,ti,tn OR 'pravasin':ab,kw,ti,tn OR 'pravastatin':ab,kw,ti,tn OR 'rosuvastatin':ab,kw,ti,tn OR 'simvastatin':ab,kw,ti,tn OR 'zocor':ab,kw,ti,tn OR 'statin':ab,kw,ti,tn	Statins
#3	#1 OR #2	
#4	'muscle disease'/exp	
#5	((muscl* OR muscu*) NEAR/3 (pain* OR fatigue OR intoler* OR symptom*)):ti,ab,kw) OR ((statin* NEAR/3 (induc* OR relat* OR associ* OR intoler* OR symptom* OR 'side effect*' OR side-effect* OR 'adverse effect*'))):ti,ab,kw) OR sams:ti,ab,kw OR sas:ti,ab,kw OR sinam:ti,ab,kw OR myopath*:ti,ab,kw OR myalg*:ti,ab,kw OR myosit*:ti,ab,kw OR necrot*:ti,ab,kw OR rhabdomyo*:ti,ab,kw	SAMS
#6	#4 OR #5	
#7	#3 AND #6	
#8	'dosage schedule comparison'/exp OR 'drug choice'/exp OR 'drug dose comparison'/exp OR 'drug dose escalation'/exp OR 'drug dose increase'/exp OR 'drug dose intensification'/exp OR 'drug dose reduction'/exp OR 'drug dose regimen'/exp OR 'drug dose titration'/exp OR 'drug intermittent therapy'/exp OR 'drug megadose'/exp OR 'drug microdose'/exp OR 'drug pulse therapy'/exp OR 'low drug dose'/exp OR 'loading drug dose'/exp OR 'maintenance drug dose'/exp OR 'recommended drug dose'/exp OR 'optimal drug dose'/exp	Managements
#9	((daily OR everyday OR quotidian OR 'every other' OR 'every second' OR rotat* OR alternat* OR 'non daily' OR nondaily OR non-daily OR hebdomad* OR weekly OR intermit* OR escalat* OR build-up OR intensif* OR reduct* OR puls*) NEAR/3 (therap* OR dos* OR treatment OR prescript*)):ti,ab,kw) OR reinitation:ti,ab,kw OR challeng*:ti,ab,kw OR rechalleng*:ti,ab,kw OR 're challeng*':ti,ab,kw OR monotherap*:ti,ab,kw	
#10	#8 OR #9	
#11	#7 AND #10	
#12	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	RCT
#13	cohort:ab,ti OR (case:ab,ti AND (control:ab,ti OR controll*:ab,ti OR comparison:ab,ti OR referent:ab,ti)) OR risk:ab,ti OR causation:ab,ti OR causal:ab,ti OR 'odds ratio':ab,ti OR etiol*:ab,ti OR aetiol*:ab,ti OR 'natural history':ab,ti OR predict*:ab,ti OR prognos*:ab,ti OR outcome:ab,ti OR course:ab,ti OR retrospect*:ab,ti OR 'epidemiology'/de	Observational studies
#14	#12 OR #13	
#15	#11 AND #14	

Filter: <https://blocks.bmi-online.nl/catalog/106>

Creator: Ket JCF and Vries R de

Notes: PubMed drafted in 2009 from: Etiology, causation, harm; and: Natural history and prognosis. In: McKibbin KA, Eady A, Marks S. PDQ evidence-based principles and practice. Hamilton etc.: B.C. Decker; 1999, p. 91, 110. PubMed revised in 2015 by adding '[ot]'. Embase.com drafted by De Vries, 2015. PubMed and Embase.com for non-randomized and observational designs from: <http://guides.library.harvard.edu/c.php?g=309982&p=2079546> (Countway Library of Medicine, 31 Aug 2016).

Date: 2016-08-31

University Library Vrije Universiteit Amsterdam

12

Data search strategy for Ovid Medline®

#	Searches	
1	exp hypolipidemic Agents/ (Anticholesteremic or antihypercholesteremic or altacor or atorvastatin or baycol or bervastatin or canef or cerivastatin or compactin or cranoc or crestor or crilvastatin or dalvastatin or fluidostatin or fluvastatin or glenvastatin or hmg coa* or hydroxymethylglutaryl* or hypochole* or hypolipidemic* or lescol or lipitor or lipex or lipostat or livalo or local or lovostatin or lochol or medostatin or mevacor or mevalotin or mevinacor or mevinolin or monacolin or pitava or pitavastatin or pravachol or pravasin or pravastatin or rosuvastatin or simvastatin or zocor or statin*).ab,kw,ti,nm.	Statins
2		
3	1 or 2	
4	exp muscular diseases/	
5	((muscl* or muscu*) adj3 (pain* or fatigue or intoler* or symptom*)) or (statin* adj3 (induc* or relat* or associ* or intoler* or symptom* or side effect* or side-effect* or adverse effect*)) or sams or sas or sinam or myopath* or myalg* or myosit* or necrot* or rhabdomyo*).ti,ab,kw.	SA
6	4 or 5	
7	3 and 6	
8	exp drug therapy/	^

3

9 (((daily or everyday or quotidian or every other or every second or rotat* or alternat* or non daily or nondaily or non-daily or hebdomad* or weekly or intermit* or escalat* or build-up or intensif* or reduct* or puls*) adj3 (therap* or dos* or treatment or prescript*)) or reinitiation or challeng* or rechalleng* or re challeng* or monotherap*).ab,kw,ti.

10	8 or 9	
11	7 and 10	
12	Randomized controlled trial.pt.	RCT
13	controlled clinical trial.pt.	
14	Randomi?ed.ab.	
15	placebo.ab.	
16	drug therapy.fs.	
17	randomly.ab.	
18	trial.ab.	
19	groups.ab.	
20	or/12-19	
21	exp animals/ not humans.sh.	
22	20 not 21	
23	Epidemiologic studies/	Observational studies
24	exp case control studies/	
25	exp cohort studies/	
26	Case control.tw.	
27	(cohort adj (study or studies)).tw.	
28	Cohort analy\$.tw.	
29	(Follow up adj (study or studies)).tw.	
30	(observational adj (study or studies)).tw.	
31	Longitudinal.tw.	
32	Retrospective.tw.	
33	Cross sectional.tw.	
34	Cross-sectional studies/	
35	or/23-34	
36	22 or 35	
37	11 and 36	

Filters

https://training.cochrane.org/handbook/current/chapter-04-technical-supplement-searching-and-selecting-studies#_Ref19195060
<https://www.sign.ac.uk/what-we-do/methodology/search-filters/>

13

Database search strategy for Cochrane library

#	Searches	
#1	(Anticholesteremic or antihypercholesteremic or altocor or atorvastatin or baycol or bervastatin or canef or cerivastatin or compactin or cranoc or crestor or crivastatin or dalvastatin or fluintostatin or fluvastatin or glenvastatin or hmg coa* or hydroxymethylglutaryl* or hypochol* or hypolipidemic* or lescol or lipitor or lipex or lipostat or livalo or locol or lovostatin or lochol or medostatin or mevacor or mevalotin or mevinacor or mevinolin or monacolin or pitava or pitavastatin or pravachol or pravasin or pravastatin or rosuvastatin or simvastatin or zocor or statin*);ti,ab, kw	Statins
#2	(((muscl* OR muscu*) NEAR/3 (pain* OR fatigue OR intoler* OR symptom*)) OR ((statin* NEAR/3 (induc* OR relat* OR associ* OR intoler* OR symptom* OR "side effect" OR side-effect* OR "adverse effect")) OR sams OR sas OR sinam OR myopath* OR myalg* OR myosit* OR necrot* OR rhabdomyo*));ti,ab,kw	SAM
#3	#1 AND #2	
#4	(((daily or everyday or quotidian or "every other" or "every second" or rotat* or alternat* or "non daily" or nondaily or non-daily or hebdomad* or weekly or intermit* or escalat* or build-up or intensif* or reduct* or puls*) near/3 (therap* or dos* or treatment or prescript*)) or reinitiation or challeng* or rechalleng* or "re challeng*" or monotherap*).ab,kw,ti.	Managements
#5	#1 AND #2 AND #4	

14

Database search strategy for Scopus

Searches

4

15 TITLE-ABS-KEY (anticholesteremic OR antihypercholesteremic OR altacor OR atorvastatin OR baycol OR bervastatin OR canef OR cervastatin OR compactin OR cranoc OR crestor OR crilvastatin OR dalvastatin OR fluindostatin OR fluvastatin OR glenvastatin OR "hmg coa*" OR hydroxymethylglutaryl* OR hypochole* OR hypolipidemic* OR lescol OR lipitor OR lipex OR lipostat OR livalo OR locol OR lovostatin OR lochol OR medostatin OR mevacor OR mevalotin OR mevinacor OR mevinolin OR monacolin OR pitava OR pitavastatin OR pravachol OR pravasin OR pravastatin OR rosuvastatin OR simvastatin OR zocor OR statin*) AND TITLE-ABS-KEY (((muscl* OR muscu*) W/3 (pain* OR fatigue OR intoler* OR symptom*)) OR ((statin* W/3 (induc* OR relat* OR associ* OR intoler* OR symptom* OR "side effect*" OR side-effect* OR "adverse effect*"))) OR sams OR sas OR sinam OR myopath* OR myalg* OR myosit* OR necrot* OR rhabdomyo*)) AND TITLE-ABS-KEY (((daily OR everyday OR quotidian OR "every other" OR "every second" OR rotat* OR alternat* OR "non daily" OR nondaily OR non-daily OR hebdomad* OR weekly OR intermit* OR escalat* OR build-up OR intensif* OR reduct* OR puls*) W/3 (therap* OR dos* OR treatment OR prescript*)) OR reinitiation OR challeng* OR rechalleng* OR "re challeng*" OR monotherap*)

Database search strategy for Clinicaltrials.gov

Searches

1 (atorvastatin OR fluvastatin OR pitavastatin OR pravastatin OR rosuvastatin OR simvastatin OR statin) AND (pain OR fatigue OR intolerance OR symptom OR side OR adverse OR myopathy OR myalgia OR myositis OR rhabdomyolysis OR muscular OR muscle)

16

Datadbse search strategy for Proquest

Searches

1 AB,TI,IF(anticholesteremic OR antihypercholesteremic OR altacor OR atorvastatin OR baycol OR bervastatin OR canef OR cervastatin OR compactin OR cranoc OR crestor OR crilvastatin OR dalvastatin OR fluindostatin OR fluvastatin OR glenvastatin OR "hmg coa*" OR hydroxymethylglutaryl* OR hypochole OR hypolipidemic OR lescol OR lipitor OR lipex OR lipostat OR livalo OR locol OR lovostatin OR lochol OR medostatin OR mevacor OR mevalotin OR mevinacor OR mevinolin OR monacolin OR pitava OR pitavastatin OR pivastatin OR pravachol OR pravasin OR pravastatin OR rosuvastatin OR simvastatin OR zocor OR statin*) AND AB,TI,IF(muscl* OR muscul* OR pain* OR fatigue OR intoler* OR symptom* OR SAMS OR SAS OR SINAM OR rhabdomyo* OR myosit* OR myopath* OR myalg* OR necrot*)

17