



Kunutsor, S. K., Seidu, S., & Khunti, K. (2017). Statins and secondary prevention of venous thromboembolism: pooled analysis of published observational cohort studies. *European Heart Journal*.
<https://doi.org/10.1093/eurheartj/ehx107>

Peer reviewed version

Link to published version (if available):
[10.1093/eurheartj/ehx107](https://doi.org/10.1093/eurheartj/ehx107)

[Link to publication record in Explore Bristol Research](#)
PDF-document

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/>

SUPPLEMENTARY MATERIAL

Supplementary Material 1	PRISMA checklist
Supplementary Material 2	MOOSE checklist
Supplementary Material 3	MEDLINE literature search strategy

Supplementary Material 1: PRISMA 2009 check-list

Section/topic	Item No	Checklist item	Reported on page No
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	1
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	2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)	3
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	None
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	Methods
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	Methods
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	Supplementary Material 3
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)	Methods
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	Methods
Data items	11	List and define all variables for which data were sought (such as PICOS, funding sources) and any assumptions and simplifications made	Methods
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	Methods
Summary measures	13	State the principal summary measures (such as risk ratio, difference in means).	Methods
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	Methods
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)	Methods
Additional analyses	16	Describe methods of additional analyses (such as sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-	Methods

Section/topic	Item No	Checklist item specified	Reported on page No
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	Figure 1
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	Table 1
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).	Table 1
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	Results and Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	Results and Figure 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15)	Not applicable
Additional analysis	23	Give results of additional analyses, if done (such as sensitivity or subgroup analyses, meta-regression) (see item 16)	Not applicable
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)	Discussion
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)	Discussion
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	Discussion
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	None

Supplementary Material 2: MOOSE checklist

Statins and secondary prevention of venous thromboembolism: pooled analysis of published observational cohort studies

Criteria	Brief description of how the criteria were handled in the review
Reporting of background	
√ Problem definition	There have been suggestions that statins may have a potential role in secondary prevention of venous thromboembolism (VTE), but the evidence is inconsistent
√ Hypothesis statement	Statins may have a role in the secondary prevention of VTE
√ Description of study outcomes	VTE [which includes deep vein thrombosis (DVT) and pulmonary embolism (PE)]
√ Type of exposure	Statin use
√ Type of study designs used	Prospective (cohort, case-cohort or “nested case control”) population-based studies
√ Study population	Populations with prior VTE
Reporting of search strategy should include	
√ Qualifications of searchers	Setor Kunutsor, MD PhD; Samuel Seidu, MD
√ Search strategy, including time period included in the synthesis and keywords	Time period: from inception of MEDLINE, EMBASE, Web of Science to January 25, 2017. Search strategy: Supplementary Material 3
√ Databases and registries searched	MEDLINE, EMBASE, and Web of Science
√ Search software used, name and version, including special features	Ovid was used to search EMBASE Endnote used to manage references
√ Use of hand searching	We searched bibliographies of retrieved papers
√ List of citations located and those excluded, including justifications	Details of the literature search process are outlined in the flow chart. The citation list for excluded studies is available upon request.
√ Method of addressing articles published in languages other than English	We placed no restrictions on language
√ Method of handling abstracts and unpublished studies	None found
√ Description of any contact with authors	Not applicable
Reporting of methods should include	
√ Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion and exclusion criteria are described in the Methods section.
√ Rationale for the selection and coding of data	Data extracted from each of the studies were relevant to the population characteristics, study design, exposure, outcome, and possible effect modifiers of the association.
√ Assessment of confounding	We assessed confounding by ranking individual studies on the basis of different adjustment levels, and performed sub-group analyses to evaluate differences in the overall estimates according to levels of adjustment.
√ Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Study quality was assessed based on the nine-star Newcastle–Ottawa Scale using pre-defined criteria namely: population representativeness, comparability (adjustment of confounders), ascertainment of outcome.
√ Assessment of heterogeneity	Heterogeneity of the studies was explored with I^2 statistic that provides the relative amount of variance of the summary effect due to the between-study heterogeneity.
√ Description of statistical methods in sufficient detail to be replicated	Description of methods of meta-analyses is detailed in the methods. We performed Knapp-Hartung as well as the DerSimonian–Laird

		random effects meta-analysis with Stata 14.
√	Provision of appropriate tables and graphics	Table 1, Figures 1 and 2
Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	Figure 2
√	Table giving descriptive information for each study included	Table 1
√	Results of sensitivity testing	Sensitivity analysis was conducted to assess the influence of each individual study by omitting one study at a time and calculating a pooled estimate for the remainder of the studies. Results section
√	Indication of statistical uncertainty of findings	95% confidence intervals were presented with all summary estimates, I ² values and results of sensitivity analyses
Reporting of discussion should include		
√	Quantitative assessment of bias	Inability to assess publication bias due to the limited number of studies. Limitations have been discussed.
√	Justification for exclusion	All studies were excluded based on the pre-defined inclusion criteria in methods section.
√	Assessment of quality of included studies	Brief discussion included in 'Methods' section
Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	Discussed in the context of the results.
√	Generalization of the conclusions	Discussed in the context of the results.
√	Guidelines for future research	Well-designed intervention studies are needed to corroborate these findings.
√	Disclosure of funding source	No separate funding was necessary for the undertaking of this systematic review.

Supplementary Material 3: MEDLINE literature search strategy from 1946 to present

Relevant studies, published before January 25, 2017 (date last searched), were identified through electronic searches not limited to the English language using MEDLINE, EMBASE, and the Science Citation Index databases. Electronic searches were supplemented by scanning reference lists of articles identified for all relevant studies (including review articles), by hand searching of relevant journals and by correspondence with study investigators. The computer-based searches combined search terms related to statins and venous thromboembolism without language restriction.

- 1 exp Hydroxymethylglutaryl-CoA Reductase Inhibitors/ (38526)
- 2 statins.mp. (25447)
- 3 exp Thromboembolism/ (55621)
- 4 recurrent venous thromboembolism.mp. (829)
- 5 VenousThrombosis.mp. (1)
- 6 exp Venous Thromboembolism/ (7992)
- 7 exp Pulmonary Embolism/ (39779)
- 8 recurrent pulmonary embolism.mp. (522)
- 9 recurrent deep vein thrombosis.mp. (192)
- 10 3 or 4 or 5 or 6 or 7 or 8 or 9 (91733)
- 11 1 or 2 (47480)
- 12 10 and 11 (200)
- 13 limit 12 to humans (181)

Each part was specifically translated for searching alternative databases.