

INPLASY PROTOCOL

Associations between statin use and osteoarthritis risk and progression: a systematic review and meta-analysis

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No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Review question / Objective: Populations: Included participants were over 18 years of age, had a prescription or a medication of statins. Non-users were in the same population as statin users and with no any statin medication. Interventions: Use of statin (regardless of kind, duration, and dosage), may be in any baseline condition, any co-medication, or any time-history of use. Comparison: Osteoarthritis risk, progression and/or other available indexes like operations due to osteoarthritis, conditions of statin use (duration, dosage) were also estimated if data were available. Outcomes: OR/HR/RRs concerning OA incidence, progression and/or others obtained from included subjects that were expected.

Condition being studied: Osteoarthritis (OA) is the most common form of degenerative joint disease, and the major cause of pain and disability in the elderly. In addition to a low quality of life, OA imposes a huge social and economic burden. The etiopathogenesis of OA is currently believed to be multifactorial, involving ageing, mechanical loading, metabolism and inflammation. Metabolic factors, such as dyslipidemia and hypercholesterolemia, have also been proved to be significantly associated with OA. The proinflammatory effects of lipids, adipokine-linked proinflammatory cytokines and pathways, and atherosclerotic vascular disease, have been reported associated with OA pathogenesis. There is now a growing interest in the use of statins as potential disease-modifying agents for OA. However, in previous reported clinical studies, statin use may be linked to adverse effects in musculoskeletal system and metabolisms, but it remains controversial. Meanwhile, it is inconclusive whether statin use is related to OA development and progression. Therefore, the purpose of this study was to conduct a systematic review and meta-analysis to estimate the effect of statin use on OA risk and progression.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 April 2020 and was last updated on 23 April 2020 (registration number INPLASY202040160).

INTRODUCTION

Review question / Objective: Populations: Included participants were over 18 years of

age, had a prescription or a medication of statins. Non-users were in the same population as statin users and with no any statin medication. Interventions: Use of

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METHODS

Participant or population: Included participants were over 18 years of age, had a prescription or a medication of statins.

Intervention: Use of statin (regardless of kind, duration, and dosage), may be in any baseline condition, any co-medication, or any time-history of use.

Comparator: Non-users of statin were in the same population as statin users and with no any statin medication.

Study designs to be included: Randomized controlled trials, prospective or retrospective cohort studies, case-control and cross-sectional studies were included.

Eligibility criteria: Studies were selected based on the following criteria: (1) data of relevant studies concerning statin use and OA risk and/or progression, including baseline data of other related studies; (2) studies with available data or conclusion (systematic reviews only).

Information sources: An online systematic search was conducted using the electronic databases of MEDLINE (PubMed), Cochrane library, Embase, Web of Science and Scopus, from the date of database inception until January 1, 2020. Search strategy: ("osteoarthritis"[MeSH Terms] OR "osteoarthritis"[All Fields] OR "degenerative arthritis"[All Fields]) AND ("hydroxymethylglutaryl-coa reductase inhibitors"[Pharmacological Action] OR "hydroxymethylglutaryl-coa reductase inhibitors"[MeSH Terms] OR statin[MeSH Terms] OR "atorvastatin"[All Fields] OR "cerivastatin"[All Fields] OR "crivastatin"[All Fields] OR "Lovastatin"[All Fields] OR "mevastatin"[All Fields] OR "pitavastatin"[All Fields] OR "Pravastatin"[All Fields] OR "Rosuvastatin"[All Fields] OR "Simvastatin"[All Fields]). No language limitation was set. After the process of primary retrieval and study selection, the references of relevant studies and grey literature were also searched to avoid omission.

Main outcome(s): OR/HR/RRs of OA incidence or progression of the statin users versus non-users of population studied.

Additional outcome(s): Trend tests of duration/dosage-related risk.

Quality assessment / Risk of bias analysis: Cross-sectional, case-control and cohort studies are assessed using the Newcastle-

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AND ("hydroxymethylglutaryl-coa reductase inhibitors"[Pharmacological Action] OR "hydroxymethylglutaryl-coa reductase inhibitors"[MeSH Terms] OR ("hydroxymethylglutaryl-coa"[All Fields] AND "reductase"[All Fields] AND "inhibitors"[All Fields]) OR "hydroxymethylglutaryl-coa reductase inhibitors"[All Fields] OR "statin"[All Fields]) OR ("hydroxymethylglutaryl-coa reductase inhibitors"[Pharmacological Action] OR "hydroxymethylglutaryl-coa reductase inhibitors"[MeSH Terms] OR ("hydroxymethylglutaryl-coa"[All Fields] AND "reductase"[All Fields] AND "inhibitors"[All Fields]) OR "hydroxymethylglutaryl-coa reductase inhibitors"[All Fields] OR "statin"[All Fields]) OR *statin OR ("atorvastatin"[MeSH Terms] OR "atorvastatin"[All Fields]) OR ("cerivastatin"[Supplementary Concept] OR "cerivastatin"[All Fields]) OR ("crilvastatin"[Supplementary Concept] OR "crilvastatin"[All Fields]) OR ("lovastatin"[MeSH Terms] OR "lovastatin"[All Fields]) OR ("mevastatin"[Supplementary Concept] OR "mevastatin"[All Fields]) OR ("pitavastatin"[Supplementary Concept] OR "pitavastatin"[All Fields]) OR ("pravastatin"[MeSH Terms] OR "pravastatin"[All Fields]) OR ("rosuvastatin calcium"[MeSH Terms] OR ("rosuvastatin"[All Fields] AND "calcium"[All Fields]) OR "rosuvastatin calcium"[All Fields] OR "rosuvastatin"[All Fields]) OR ("simvastatin"[MeSH Terms] OR "simvastatin"[All Fields])).

Cochrane library - (In the topic of orthopedics& trauma, endocrine &metabolic, and rheumatology)

(Statin OR *statin OR Atorvastatin OR cerivastatin OR crilvastatin OR Lovastatin OR mevastatin OR pitavastatin OR Pravastatin OR Rosuvastatin OR Simvastatin) AND (Osteoarthrit* OR osteoarthrit* OR osteoarthro* OR osteo-arthro* OR "degenerative arthritis" OR osteoarthritis)

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'mevastatin'/exp OR mevastatin OR 'pitavastatin'/exp OR pitavastatin OR 'pravastatin'/exp OR pravastatin OR 'rosuvastatin'/exp OR rosuvastatin OR 'simvastatin'/exp OR simvastatin) AND ('osteoarthritis'/exp OR osteoarthritis)

Web of Science - ((Statin OR *statin OR Atorvastatin OR cerivastatin OR crilvastatin OR Lovastatin OR mevastatin OR pitavastatin OR Pravastatin OR Rosuvastatin OR Simvastatin) AND (Osteoarthrit* OR osteo-arthrit* OR osteoarthro* OR osteo-arthro* OR "degenerative arthritis" OR osteoarthritis))

Scopus - ((Statin OR *statin OR Atorvastatin OR cerivastatin OR crilvastatin OR Lovastatin OR mevastatin OR pitavastatin OR Pravastatin OR Rosuvastatin OR Simvastatin) AND (Osteoarthrit* OR osteoarthro* OR "degenerative arthritis" OR osteoarthritis)).