EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome

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ABSTRACT

Objective To develop recommendations for cardiovascular risk (CVR) management in gout, vasculitis, systemic sclerosis (SSc), myositis, mixed connective tissue disease (MCTD), Sjögren's syndrome (SS), systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS).

Methods Following European League against Rheumatism (EULAR) standardised procedures, a multidisciplinary task force formulated recommendations for CVR prediction and management based on systematic literature reviews and expert opinion.

Results Four overarching principles emphasising the need of regular screening and management of modifiable CVR factors and patient education were endorsed. Nineteen recommendations (eleven for gout, vasculitis, SSc, MCTD, myositis, SS; eight for SLE, APS) were developed covering three topics: (1) CVR prediction tools; (2) interventions on traditional CVR factors and (3) interventions on disease-related CVR factors. Several statements relied on expert opinion because high-quality evidence was lacking. Use of generic CVR prediction tools is recommended due to lack of validated rheumatic diseases-specific tools. Diuretics should be avoided in gout and beta-blockers in SSc, and a blood pressure target <130/80 mm Hg should be considered in SLE. Lipid management should follow general population guidelines, and antiplatelet use in SLE, APS and large-vessel vasculitis should follow prior EULAR recommendations. A serum uric acid level <0.36 mmol/L (<6 mg/dL) in gout, and disease activity control and glucocorticoid dose minimisation in SLE and vasculitis, are recommended. Hydroxychloroquine is recommended in SLE because it may also reduce CVR, while no particular immunosuppressive treatment in SLE or urate-lowering therapy in gout has been associated with CVR lowering.

Conclusion These recommendations can guide clinical practice and future research for improving CVR management in rheumatic and musculoskeletal diseases.

INTRODUCTION

Patients with inflammatory rheumatic diseases have an increased risk of cardiovascular disease,[1] in comparison to the general population, which prompted the development (2010) and update (2015/16) of European League against Rheumatism (EULAR) recommendations for cardiovascular risk (CVR) management in patients with rheumatoid arthritis (RA), ankylosing spondylitis and psoriatic arthritis.[2] Accumulating evidence has shown elevated cardiovascular morbidity and mortality in other rheumatic and musculoskeletal diseases (RMDs) including gout, vasculitis, systemic sclerosis (SSc), myositis, mixed connective tissue disease (MCTD), Sjögren's syndrome (SS), systemic lupus erythematosus (SLE) and the antiphospholipid syndrome (APS).[3–13] Estimations of the incidence of cardiovascular events vary among the different disease groups (Supplementary systematic literature review (SLR) report, section II).

The higher CVR in patients with rheumatic diseases is not sufficiently explained by differences in the prevalence of traditional CVR factors,[14–18] suggesting that specific treatment recommendations tailored to patients with these conditions are needed. Chronic inflammation has been considered a key feature in cardiovascular disease pathogenesis in RMDs,[19] demonstrated also in the general population by associations with serum C-reactive protein (CRP) levels[20 21] and the efficacy of medications targeting inflammatory pathways,[22–24] while new links between inflammation, immunity and cardiometabolic factors are being researched.[25] Furthermore, patients with RMDs are often exposed to immunomodulators and glucocorticoids. Although better control of inflammation may reduce CVR in individual patients,[23 24] it is not known if some side effects of these medications might outweigh any anti-inflammatory benefit, thereby increasing the CVR.

Therefore, a EULAR Task Force was formed to develop recommendations for the management of CVR in patients with SLE, APS, gout, vasculitis, SSc, myositis, MCTD and SS based on an evidence-based approach and experts' consensus.

METHODS

Task force

Two convenors (MTN and MGT) guided the task force together with two methodologists (GJM and MMW) and four fellows (DV, GCD, EH and LB), responsible for the SLRs. Furthermore, the task force included 20 members from 11 European countries: 12 rheumatologists, 2 cardiologists, 1 metabolic medicine physician, 1 healthcare professional, 2 patient representatives and 2 EMerging EULAR NETwork members (KS and SS). The process followed the updated EULAR standardised operating procedures[26] and the Appraisal of Guidelines for Research and Evaluation II instrument.[27]

At the initial task force meeting, a first set of research questions, prepared by the convenors, was discussed with the panel and formulated on four major topics: use of cardiovascular prediction tools; interventions targeting traditional CVR factors; interventions targeting disease-related CVR factors and prevalence/incidence of cardiovascular disease. Thereafter, final research questions were developed using the PICO format (P, population; I, intervention; C, comparator; O, outcomes).

Collection of evidence

A comprehensive SLR was performed by two groups working in parallel: the gout, vasculitis, SSc/myositis/MCTD/SS group (convenor: MTN; methodologist: GJM; fellows: DV, EH and LB), and the SLE and APS group (convenor: MGT; methodologist: MMW; fellow: GCD). The protocol for the literature search was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[28] Search terms were developed with the help of experienced librarians of the VU Amsterdam, Northwest Clinics Alkmaar (for gout, vasculitis, SSc, myositis, MCTD and SS SLRs) and the National Institutes of Health, USA (for SLE and APS SLRs). PubMed, Embase and the Cochrane Library were searched for full-length English-language published articles from their inception to March 2020, while searches for incidence and prevalence of cardiovascular events were extended up to November 2020. Exclusion criteria and the search terms for each disease separately are presented in the Supplementary SLR report (section IA). The outcome was cardiovascular events rather than surrogate markers of cardiovascular disease.

Data abstraction is described in Supplementary SLR report (section IB). Retrieved studies were screened by title and abstract and articles selected for full text review were then examined independently by two persons for each group (DV, EH, LB, MN, CM, and GCD, MGT and MMW) with consultation of other task force members. A number of individually searched articles (one for gout,[29] three for SLE/APS[30–32] published after the initial search periods were included due to their importance. Data extraction was performed by the fellows (DV, EH and LB) and CM under supervision of MN and GJM in the gout, vasculitis, SSc, myositis, MCTD and SS group, and by GCD, MGT and MMW in the SLE and APS group. Quality assessment was performed using the Cochrane risk-of-bias tool[33] for randomised clinical trials and the Newcastle-Ottawa Scale[34] for observational studies. Formal pooling and meta-analysis of risks could not be performed due to the diversity of outcomes, exposures and measures of association reported in the primary studies. Evidence summaries and draft recommendations were formulated for review by all task force members before the second meeting.

Consensus on statements

The virtual second task force meeting included the presentation of SLR results and discussion and editing of the first draft of recommendations. Recommendations were accepted when ≥75% of the task force members voted agreement. After additional discussions on wording changes and voting on text, a final set of recommendations and overarching principles was prepared, including the level of evidence (LoE) and grade of recommendation (GoR) according to the Oxford Centre for Evidence Based Medicine system.[35] All task force members indicated their level of agreement (LoA) for each recommendation (0, no agreement at all; 10, full agreement), and results were averaged. The manuscript was reviewed and approved by all task force members and the EULAR Executive Committee before submission.

RESULTS

For gout, vasculitis, SSc, myositis, MCTD and SS, 105 articles were included in the SLR, while for SLE and APS, 75 articles were included (figures 1 and 2). SLR results including the flow chart and evidence tables for each PICO are presented in Supplementary SLR report (section II); all articles included in the SLRs are shown in section III.

Overarching principles

The task force developed four overarching principles emphasising the need for increased awareness of elevated CVR in RMDs, regular CVR screening, assessment and management of modifiable CVR factors, and patient education about CVR, treatment adherence and lifestyle changes (table 1).

Recommendations

Gout, vasculitis, SSc, myositis, MCTD and SS

CVR prediction tools

1. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, we recommend thorough assessment of traditional CVR factors. The use of cardiovascular prediction tools as for the general population is recommended. (LoE: 5, GoR: D)

No studies have investigated the accuracy of cardiovascular prediction tools in patients with gout, vasculitis, SSc, myositis, MCTD and SS. It is currently uncertain to what extent the elevated risk for cardiovascular disease is driven by an increased prevalence of traditional or disease-specific risk factors. Existing tools, such as the Framingham Risk Score (FRS), QRISK3 or Systematic Coronary Risk Evaluation (SCORE) have been based on large general population cohorts with long follow-ups.[36–38] Therefore, for gout, vasculitis, SSc, myositis, MCTD and SS, we recommend the use of prediction tools developed in the general population.

2. For ANCA-associated vasculitis the Framingham score may underestimate the CVR. Information from the European Vasculitis Society (EUVAS) model may supplement modifiable Framingham risk factors and is recommended to take into account. (LoE: 2b, GoR: D)

In patients with ANCA-associated vasculitis the observed incidence of cardiovascular events exceeded Framingham predicted incidence in two studies.[39 40] Furthermore, one study on CVR in ANCA-associated vasculitis found a higher area under the curve (AUC) for the EUVAS model (AUC 0.73) based on age, diastolic

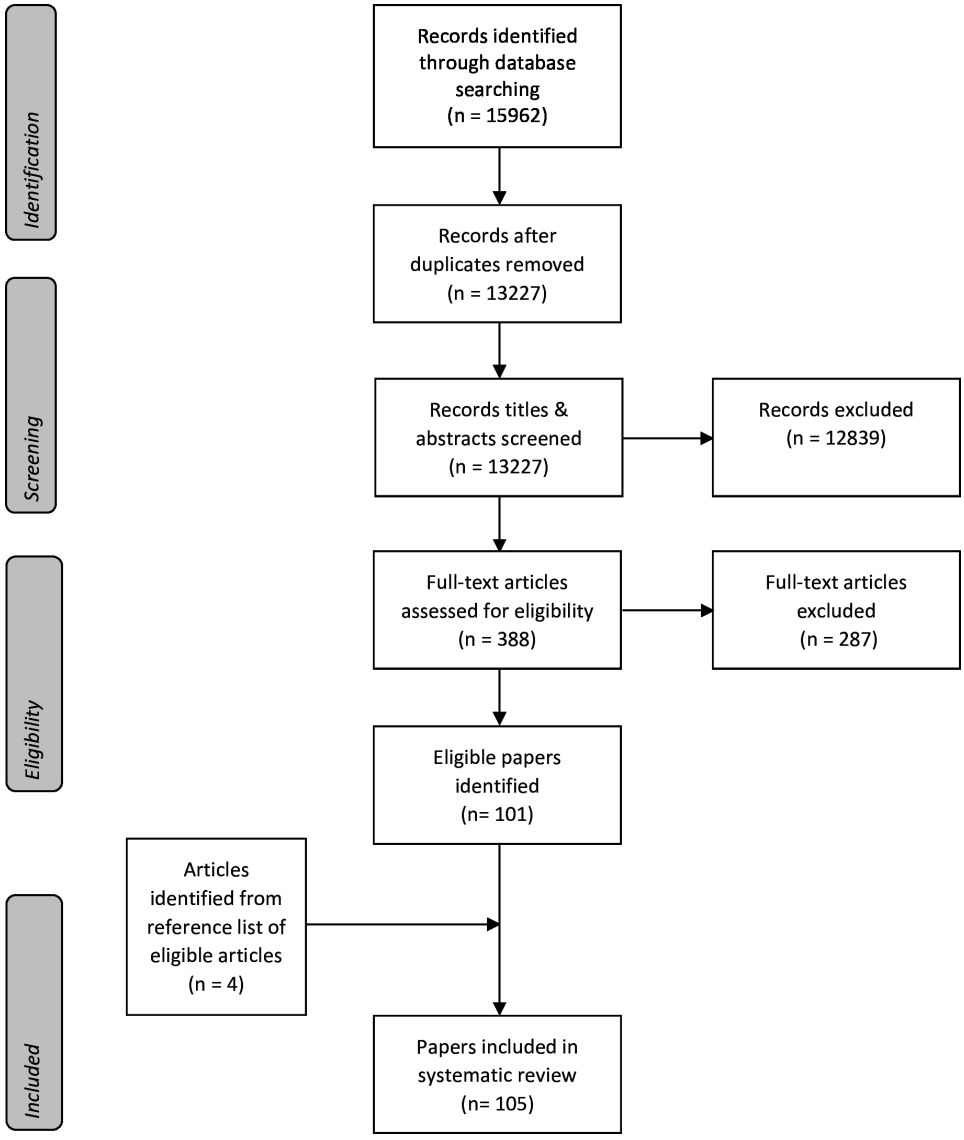

Figure 1 Flow chart of systematic literature review for cardiovascular risk management in gout, vasculitis, systemic sclerosis, myositis, mixed connective tissue disease and Sjögren's syndrome. Articles on cardiovascular incidence and prevalence are also included.

hypertension, and PR3 ANCA status in comparison with the Framingham model (AUC 0.65).[41] Although this study was not designed for the evaluation of CVR, these disease-specific factors could be used for risk assessment in addition to Framingham risk factors but further work is needed to validate these findings.

Interventions targeting traditional CVR factors

3. In patients with gout, vasculitis, SSc, myositis, MCTD, and SS, blood pressure (BP) management should follow recommendations used in the general population. (LoE: 5, GoR: D)

We found no trials that assessed the use of antihypertensive treatment in these patients. One small retrospective cohort study found an increase of severe cranial ischaemic events in patients with giant-cell arteritis (GCA) treated with beta blockers.[42] One large prospective cohort study in SSc found a protective effect of calcium channel blockers (CCB), ACE inhibitors (ACEI), and angiotensin receptor blockers (ARB) with ventricular arrhythmias.[43] Both studies did not control for confounding by indication. Altogether, currently, there is no evidence to modify the hypertension treatment target levels in patients with gout, vasculitis, SSc, myositis, MCTD and SS from those used in the general population.

4. In patients with gout, diuretics should be avoided. (LoE: 5, GoR: D)

Following the EULAR recommendations on management of gout, use of thiazide and loop diuretics should be avoided, if possible, because of their effect to increase serum uric acid (SUA) levels.[44] Instead, the use of CCB or losartan could be considered. This topic was not updated as part of this guideline as the literature search focused on the effect of antihypertensives on cardiovascular outcomes and not on potential effect on SUA levels.

5. In patients with SSc beta blockers should be avoided. (LoE: 5, GoR: D)

Although large trials are lacking and therefore based on expert opinion, beta blockers are considered contraindicated due to their effect on Raynaud's phenomenon.

6. In patients with gout, vasculitis, SSc, myositis, MCTD, and SS, lipid management should follow recommendations used in the general population. (LoE: 5, GoR: D)

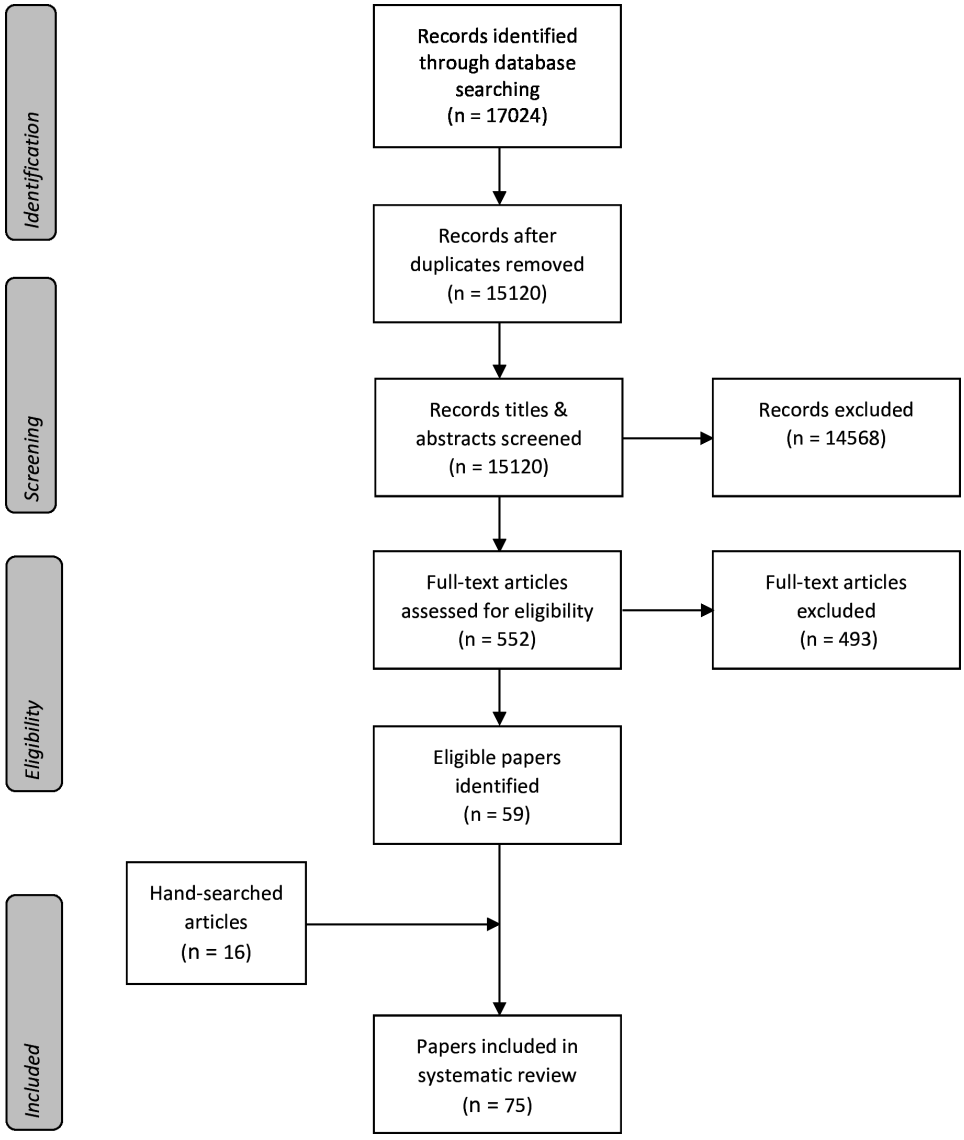

Figure 2 Flow chart of systematic literature review for cardiovascular risk management in systemic lupus erythematosus and the antiphospholipid syndrome.

In gout patients, no studies evaluated the effect of statins on cardiovascular disease or mortality in comparison with the general population. Two retrospective cohort studies suggested a protective effect of statins on mortality in patients with gout after 5 and 10 years, relative to patients not using statins.[45 46] Because of the limited evidence, we recommend following guidelines on lipid management for the general population. Furthermore, myotoxicity as side effect of the combination of a statin and prophylactic colchicine (0.5 mg/day) is rare and routine discontinuation of the statin is not recommended.[47]

Three studies in patients with GCA did not find an association between statins and cardiovascular events,[42 48 49] but a fourth study of 103 patients with GCA, 28 of whom were treated with statins, reported a lower risk of cardiovascular hospitalisations with a longer cumulative duration of statin treatment (HR 0.993 per one additional daily dose).[50] No studies controlled for confounding by indication.

7. In patients with gout, vasculitis, SSc, myositis, MCTD, and SS, standard use of low-dose aspirin for primary prevention is not recommended. Treatment with platelet inhibitors should follow recommendations used in the general population. (LoE: 2b/5, GoR: D)

In 2009 EULAR recommended the use of aspirin for prevention of cardiovascular and cerebrovascular events in individuals with large vessel vasculitis (LoE: 3, GoR: C).[51] More recently the American College of Rheumatology (ACR) has used the same literature base to conditionally recommend the use of aspirin in flow critical large vessel vasculitis.[52] However, in 2020 an update of the 2009 EULAR recommendations reappraised this evidence and concluded that the risk–benefit analysis was not favourable, and blanket use of antiplatelets was not essential unless indicated for other reasons.[53] Based on newly published studies, we agree with the 2020 iteration.[41 48 49] In patients with gout, ANCA-associated vasculitis, SSc, myositis, MCTD and SS we did not find studies on this topic.

8. In patients with gout, we recommend a SUA level below 0.36 mmol/L (6 mg/dL) to potentially lower the risk of cardiovascular events and cardiovascular mortality. (LoE: 2b, GoR: C)

Retrospective cohort studies in patients with gout showed an association between an elevated SUA (per 0.06 mmol/L (1 mg/

Table 1 EULAR overarching principles and recommendations for the management of CVR in gout, vasculitis, SSc, myositis, MCTD, SS, SLE, and APS

Overarching principles	LoA* (SD)
A. Clinicians should be aware of increased CVR in patients with RMDs including gout, vasculitis, SSc, myositis, MCTD, SS, SLE and APS. For all RMDs, reduction of disease activity is likely to lessen CVR.	9.92 (0.39)
B. Rheumatologists are responsible for CVR assessment and management in collaboration with primary care providers, internists or cardiologists and other healthcare providers.	9.55 (1.12)
C. CVR factor screening should be performed regularly in all individuals with RMDs. Risk management should include screening for and strict control of CVR factors (smoking cessation, management of blood pressure, lipids and diabetes). CVR assessment is recommended within 6 months of diagnosis and repeated based on individual patient characteristics and risk levels.	9.55 (0.84)
D. Patient education and counselling on CVR, treatment adherence and lifestyle modifications, such as healthy diet and regular physical activity, are important in the management of CVR in these patients.	9.88 (0.42)
Recommendations for gout, vasculitis, SSc, myositis, MCTD and SS	
1. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, we recommend thorough assessment of traditional CVR factors. The use of cardiovascular prediction tools for the general population is recommended. (LoE: 5, GoR‡: D)	9.48 (0.84)
2. For ANCA-associated vasculitis the Framingham score may underestimate the CVR. Information from the EUVAS model may supplement modifiable Framingham risk factors and is recommended to take into account. (LoE: 2b, GoR: D)	8.59 (1.50)
3. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, blood pressure management should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.66 (0.62)
4. In patients with gout, diuretics should be avoided. (LoE: 5, GoR: D)	8.88 (2.06)
5. In patients with SSc beta blockers should be avoided. (LoE: 5, GoR: D)	8.92 (2.11)
6. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, lipid management should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.48 (1.08)
7. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, standard use of platelet inhibitors for primary prevention is not recommended. Treatment with platelet inhibitors should follow recommendations used in the general population. (LoE: 2b/5, GoR: D)	9.37 (1.14)
8. In patients with gout, we recommend a serum uric acid level below 0.36 mmol/L (6 mg/dL) to potentially lower the risk on cardiovascular events and cardiovascular mortality. (LoE: 2b, GoR: C)	9.03 (1.34)
9. In patients with gout there is no preference for a particular urate-lowering therapy from the cardiovascular point of view. (LoE: 1b, GoR: B)	9.14 (1.35)
10. In patients with ANCA-associated vasculitis, remission induction and remission maintenance will also reduce CVR. (LoE: 2b, GoR: D)	9.07 (1.35)
11. In patients with giant-cell arteritis an optimal glucocorticoid regimen that balances the risk of relapse and glucocorticoid use side effects may also reduce CVR. (LoE: 2b, GoR: D)	9.14 (1.06)
Recommendations for SLE and the APS	
1. In patients with SLE and/or APS, a thorough assessment of traditional CVR factors and disease-related risk factors is recommended to guide risk factor modification. (LoE: 2b, GoR: D)	9.88 (0.32)
2A. In patients with SLE, lower levels of blood pressures are associated with lower rates of cardiovascular events and a blood pressure target of <130/80 mm Hg should be considered. (LoE: 2b, GoR: C)	9.70 (0.54)
2B. In patients with lupus nephritis, ACE inhibitors or angiotensin receptor blockers are recommended for all patients with urine protein-to-creatinine ratio >500 mg/g or arterial hypertension. (LoE: 5, GoR: D)	9.51 (0.64)
2C. In patients with APS, blood pressure management should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.81 (0.39)
3. In patients with SLE and/or APS, lipid treatment should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.70 (0.54)
4A. Patients with SLE may be candidates for preventative strategies as in the general population, including low-dose aspirin, based on their individual CVR profile. (LoE: 2b, GoR: D)	9.29 (1.37)
4B. In asymptomatic aPL carriers (not fulfilling any vascular or obstetric APS classification criteria) with a high-risk aPL profile with or without traditional risk factors, prophylactic treatment with low-dose aspirin (75–100 mg daily) is recommended. (LoE: 2a, GoR: B) In patients with SLE and no history of thrombosis or pregnancy complications: (1) with high-risk aPL profile, prophylactic treatment with low-dose aspirin is recommended (LoE: 2a, GoR: B); (2) with low-risk aPL profile, prophylactic treatment with low-dose aspirin may be considered. (LoE: 2b, GoR: C)	9.44 (0.97)
5. In patients with SLE, low disease activity should be maintained to also reduce CVR. (LoE: 2b, GoR: B)	9.59 (1.11)
6. In patients with SLE, treatment with the lowest possible corticosteroid dose is recommended to minimise any potential cardiovascular harm. (LoE: 2b, GoR: C)	9.59 (0.79)
7. In patients with SLE, no specific immunosuppressive medication can be recommended for the purpose of lowering the risk of cardiovascular events. (LoE: 2b, GoR: C)	9.44 (0.89)
8. In patients with SLE, treatment with hydroxychloroquine (which is recommended for all patients unless contraindicated) should be considered to also reduce the risk of cardiovascular events. (LoE: 2b, GoR: B)	9.66 (0.73)

*LoA, level of agreement; numbers in column indicate the mean (SD) of the LoA among task force members.
†LoE, level of evidence: 1a: systematic review of RCTs; 1b: individual RCT; 2a: systematic review of cohort studies; 2b: individual cohort study (and low-quality RCT); 3a: systematic review of case–control studies; 3b: individual case–control study; 4: case series and poor-quality cohort and case–control studies; 5: expert opinion without explicit critical appraisal, or based on physiology, bench research or 'first principles'.
‡GoR, grade of recommendation: A: consistent level 1 studies; B: consistent level 2 or 3 studies, or extrapolations from level 1 studies; C: level 4 studies or extrapolations from level 2 or 3 studies; D: level 5 evidence or troublingly inconsistent or inconclusive studies of any level.
ACE, angiotensin-converting enzyme; ANCA, antineutrophil cytoplasmic antibodies; aPL, antiphospholipid antibodies; APS, antiphospholipid syndrome; CVR, cardiovascular risk; EULAR, European League against Rheumatism; EUVAS, European Vasculitis Society; MCTD, mixed connective tissue disease; RMDs, rheumatic and musculoskeletal diseases; SLE, systemic lupus erythematosus; SS, Sjögren's syndrome; SSc, systemic sclerosis.

dL)) and cardiovascular events.[54 55] The association might be stronger in patients with SUA levels above 0.48 mmol/L (8 mg/dL),[56] than in patients with SUA levels higher than 0.36 mmol/L (6 mg/dL).[57] Studies on the effect of urate-lowering therapy (ULT) showed conflicting results. Evidence originates predominantly from observational studies and often lacked data on treatment adherence and SUA levels during treatment. One study showed a linear dose response relation with a decline in the CVR

in the group with the highest defined daily dose.[58] This suggests that adequate ULT possibly lowers the CVR. This possibility was supported by two studies that showed a protective association of respectively 'high dose' allopurinol and ULT resulting in SUA <0.36 mmol/L (<6 mg/dL) on cardiovascular events and cardiovascular mortality.[59 60] Altogether, although numbers of events were often low and associations were stronger for the highest SUA quartiles and higher dose ULT, it is possible that achieving lower SUA level decreases the risk on CV events. A cut-off value of 0.36 mmol/L (6 mg/dL) is used in the management of gout activity and could also benefit the risk of cardiovascular events. There is not sufficient evidence to support a threshold lower than 0.36 mmol/L (6 mg/dL) for CVR management.

9. In patients with gout there is no preference for a particular ULT from the cardiovascular point of view. (LoE: 1b, GoR: B)

Current guidelines recommend allopurinol as the first choice of ULT followed by febuxostat. Most studies on CVR compared these two xanthine oxidase inhibitors. Overall, regardless of the used dosage and duration of treatment, no difference was seen in number of cardiovascular events.[61–63] In 2018, the CARES trial reported a higher risk of cardiovascular mortality with febuxostat than allopurinol.[62] However, no difference was seen in the primary composite cardiovascular disease endpoint. Recently, the FAST trial showed no difference in CVR between patients using allopurinol or febuxostat.[29] Because of the limitations of the CARES trial (high number drop-outs, no difference in primary outcome, most events occurred after discontinuation of study) and the non-inferiority results of the FAST trial, we do not recommend the use of a specific ULT regarding cardiovascular outcomes.

Interventions targeting disease-related CVR factors

10. In patients with ANCA-associated vasculitis, remission induction and remission maintenance will also reduce CVR. (LoE: 2b, GoR: D)

In three of four included studies an association was found between high disease activity scores (Birmingham Vasculitis Activity Scores version 3) and a higher risk for cardiovascular events.[64–66]

11. In patients with GCA an optimal glucocorticoid regimen that balances the risk of relapse and glucocorticoid use side effects may be considered to also reduce CVR. (LoE: 2b, GoR: D)

In patients with vasculitis, SSc, myositis, MCTD, and SS the primary goal is disease control with the lowest possible dose of glucocorticoids. In GCA two studies found a higher CVR in patients with a higher (daily/cumulative) prednisone dose. One study found that the use of an immunosuppressant in addition to glucocorticoid was a protective factor against new cardiovascular events.[67 68] The increased CVR associated with glucocorticoids has to be balanced with the risk of relapse. Special attention and frequent evaluation of risks and benefits are warranted for patients with ongoing low dose glucocorticoids.

SLE and/or APS

CVR prediction tools

1. In patients with SLE and/or APS, a thorough assessment of traditional CVR factors and disease-related risk factors is recommended to guide risk factor modification. (LoE: 2b, GoR: D)

The FRS underestimates CVR in SLE patients[18 69–71] with stroke, more often than myocardial infarction (MI), accounting for excess 'missed' risk by the FRS.[69 70] A modified version of the FRS that used a 2.0 multiplier was found, retrospectively, to improve the measure's sensitivity from 0.13 to 0.31 while maintaining good specificity to identify patients with a moderate/high risk of coronary artery disease.[72] A study examining cardiovascular mortality in middle-aged patients with SLE found that SCORE predicted less than half the observed fatal cardiovascular events.[73] The QRISK3 tool included weights for SLE,[38] but validation studies in SLE populations have not yet been performed. Direct comparison of the performance of most commonly used generic risk assessment tools in SLE is currently lacking. A new SLE-specific risk score that included disease-related variables (SLEDAI, lupus anticoagulant and low C3) along with traditional risk factors found higher estimated risks than the American College of Cardiology/American Heart Association risk equation, except among patients whose risk was already moderate/high from traditional risk factors.[74] This prediction equation requires more testing and independent validation. Given the limitations of the current evidence, the task force did not endorse use of any particular CVR assessment tool, but instead recommended a thorough assessment of traditional and disease-related risk factors to guide cardiovascular prevention interventions.

No studies were identified that examined generic CVR prediction scores in APS. The adjusted Global APS Score (aGAPSS), a clinical score including the three major antiphospholipid antibodies (aPL), hypertension and lipidaemia, was developed to predict thrombosis, though data on cardiovascular events were not reported separately.[75] Modification of the aGAPSS by adding points for diabetes mellitus, smoking, and obesity to create a score specific for cardiovascular disease, the $aGAPSS_{CVD}$ score, increased its discriminative ability and accuracy for CVR prediction in one study,[76] but further testing is needed.

Interventions targeting traditional CVR factors

2A. In patients with SLE, lower levels of BP are associated with lower rates of cardiovascular events and a BP target of <130/80 mm Hg should be considered. (LoE: 2b, GoR: C)

2B. In patients with lupus nephritis, ACEi or ARBs are recommended for all patients with urine protein-to-creatinine ratio >500 mg/g or arterial hypertension. (LoE: 5, GoR: D)

2C. In patients with APS, hypertension management should follow recommendations used in the general population. (LoE: 5, GoR: D)

A. SLE. Hypertension is associated with a higher risk of both coronary artery disease events[77] and first ischaemic stroke[78] in SLE. It, therefore, follows that BP control with antihypertensive medications should reduce the risk of cardiovascular events.[79] Recent mean systolic BP ≥132 mm Hg was identified as a determinant of a higher risk of cardiovascular events, and systolic BP had a stronger association than diastolic BP.[80] A recent study of patients with SLE examining three BP categories (normotensive; systolic BP 130–139/diastolic BP 80–89; systolic BP ≥140/diastolic BP ≥90 mm Hg) reported an increased risk of cardiovascular events in both hypertensive groups compared with the normotensive group,[30] suggesting that a target BP of less than 130/80 should be used.

B. Lupus nephritis. Evidence specifically addressing the impact of antihypertensive treatment on cardiovascular events in lupus nephritis is scarce. In a retrospective cohort analysis,[81] risk of a cardiovascular event was not associated with treatment with ACEI/ARB, but 18% in the ACEI/ARB group had end-stage renal disease compared with 2.4% in the comparison group and this imbalance would be expected to affect the comparison of CVRs. The panel endorsed the current EULAR/ERA-EDTA

recommendation on the use of ACEI/ARB for patients with lupus nephritis with concomitant hypertension or high-level proteinuria.[32]

C. APS. No studies were identified on the use of specific antihypertensives for cardiovascular prevention in patients with APS. These patients should be managed according to recommendations for the general population.[82]

3. In patients with SLE and/or APS, hyperlipidaemia treatment should follow recommendations used in the general population. (LoE: 5, GoR: D)

Higher levels of total cholesterol and low-density lipoprotein cholesterol have been associated with a higher risk of MI and stroke in SLE.[74 78 83] One study using national administrative data found that patients with SLE treated with lipid-lowering agents had a significantly lower risk of coronary artery disease during follow-up (mean 8.4 years) than those not treated, while short-duration or long-duration statin use were both associated with a lower risk of stroke.[84] Several other observational studies included statin use as a covariate in prediction of cardiovascular events, and identified statin use as a risk factor for events, likely representing confounding by indication.[71 85–88] Diagnosis of SLE is not sufficient per se for prescribing lipid-lowering treatment for primary cardiovascular prevention.[89] In APS, no study was identified that examined the effect of lipid-lowering agents on cardiovascular events. The task force judged that hyperlipidaemia treatment should follow the recommendations used in the general population.[89]

4A. Patients with SLE may be candidates for preventive strategies as in the general population, including low-dose aspirin, based on their individual CVR profile. (LoE: 2b, GoR: D)

4B. In asymptomatic aPL carriers with a high-risk profile with or without traditional risk factors, prophylactic treatment with low-dose aspirin (75–100 mg daily) is recommended. (LoE: 2 a, GoR: B) In patients with SLE and no history of thrombosis or pregnancy complications, prophylactic treatment with low-dose aspirin is recommended for those with a high-risk aPL profile (LoE: 2a, GoR: B) and may be considered for those with a low risk APL profile. (LoE: 2b; GoR: C)

The panel agreed to include the corresponding statements (and LoE and GoR) about the prophylactic use of antiplatelets in SLE and APS from the recent EULAR recommendations for the management of SLE[90] and APS,[91] respectively. The LoA from our task force group is shown in table 1. Use of low-dose aspirin for cardiovascular prevention in patients with SLE or APS should be individualised (particularly in the presence of a high-risk aPL profile) according to EULAR recommendations.

Interventions targeting disease-related CVR factors

5. In patients with SLE, low disease activity should be maintained to also reduce CVR. (LoE: 2b, GoR: B)

SLE activity has often been reported as a predictor of cardiovascular events. With the exception of two studies,[86 92] higher time-integrated SLEDAI levels were associated with an increased risk of cardiovascular events,[69 77 79 93] more so than baseline or single measurements.[78 94 95] In three studies,[71 96 97] baseline SLEDAI was found to be higher in patients with cardiovascular events, although it was not carried to multivariable analysis. Associations of SLEDAI with cardiovascular events was found to be stronger when considering categories of activity compared with per-unit increases,[69] suggesting a non-linear association of disease activity with cardiovascular events.

Many studies did not consider simultaneously the association of measures of disease activity and SLE medication use; therefore, results may be confounded. In an analysis that adjusted for current prednisone dose, a 1-point increase in SLEDAI was marginally associated with an increased risk of cardiovascular events (relative risk 1.05, 95% CI 1.00 to 1.11).[69] Available evidence indicates that higher disease activity may be associated with a higher risk of cardiovascular events. Thus, in addition to its importance in general patient management,[90] a low-disease activity state may also have a beneficial effect on cardiovascular health.

6. In patients with SLE, treatment with the lowest possible glucocorticoid dose is recommended to minimise any potential cardiovascular harm. (LoE: 2b, GoR: C)

Mean dosage, cumulative exposure and duration of glucocorticoid treatment have all been investigated with reference to cardiovascular events in SLE. Higher current glucocorticoid dose was associated with a higher risk of atherothrombotic events, ischaemic heart disease, and/or stroke in two studies,[69 98] but was protective in one study[79] and not associated with stroke in the SLICC inception cohort.[99] Higher mean daily doses, greater cumulative doses, and ever-use of prednisone 30 mg/day or more were more consistently associated with increased risks of cardiovascular events in both cohort and case-control studies,[71 92 100 101] although glucocorticoid use was not significantly associated with cardiovascular events in two analyses of the Toronto cohort.[95 97] Not all studies adjusted for SLE activity. A retrospective study that adjusted for SLE activity[98] found that higher daily doses (prednisone >10 mg) administered continuously were significantly associated with both MI and stroke. In a retrospective and non-randomised study, patients treated at clinics following a glucocorticoid dose-minimisation strategy had lower prednisone exposures and markedly lower risks of cardiovascular damage by the SLICC measure, particularly for stroke.[102] Most evidence suggests that higher glucocorticoid exposure (cumulative and mean daily dose) increases CVR in SLE. The task force recommended treatment with the lowest possible corticosteroid dose to minimise risks of cardiovascular harm.

7. In patients with SLE, no specific immunosuppressive medication can be recommended for the purpose of lowering the risk of cardiovascular events. (LoE: 2b, GoR: C)

Use of immunosuppressants as a class in SLE have had largely null or conflicting associations with cardiovascular events.[79 99 103] Three studies from the Toronto lupus cohort reported either a protective[96] or null association,[93 97] while one study found that patients treated with immunosuppressants vs those not treated were more likely to develop a cardiovascular event in univariate but not multivariate analyses.[95] Immunosuppressive therapy was also associated to higher odds of ischaemic heart disease and cardiovascular events in the LUMINA[104] and Hopkins lupus cohort.[69]

Studies of individual medications suggest that use of methotrexate, mycophenolate, cyclosporine, or rituximab had neutral associations with cardiovascular events.[88 92 105] Conflicting results have been reported for cyclophosphamide[71 106] and azathioprine.[71 88 106]

A common limitation in many studies was the examination of ever use vs never use of immunosuppressants, which may be too crude an exposure. No studies considered issues of confounding by indication, and positive associations with cardiovascular disease may reflect risks due to associated disease activity or severity, or concomitant glucocorticoid use. Based on current evidence, the task force concluded that no specific immunosuppressive medication can be recommended for reducing the risk of cardiovascular events. Furthermore, the committee call for better quality pharmacoepidemiologic studies in future, using recent advances in this field.

8. In patients with SLE, treatment with hydroxychloroquine (which is recommended for all SLE patients, unless contraindicated) should be considered to also reduce the risk of cardiovascular events. (LoE: 2b, GoR: B)

A large body of evidence has addressed the role of antimalarials in cardiovascular prevention in SLE. In six cohort studies, antimalarial use was associated with lower risk of either atherothrombotic events or coronary artery disease,[69 77 79 88 94 107] although in one study protection was only associated with current long-term use.[69] Several other studies reported null associations.[85 87 92 93 95 103 106] Two of seven case–control studies also reported less use of hydroxychloroquine or antimalarials among cases with cardiovascular events than controls,[100 108] with only one study reporting increased risk.[97] No associations with risk of stroke specifically have been reported.[99 109] Importantly, patients with less active disease are more often treated with antimalarials, while SLE activity may be the risk factor for cardiovascular disease; this possible selection bias was not addressed. Additionally, studies did not report results stratified by the presence of APS or aPL, therefore, it is unclear if any reduced risk is limited to patients with SLE and aPL. The task force endorsed treatment with hydroxychloroquine, as should be provided to all patients with SLE, as it may also reduce the risk of cardiovascular events.

DISCUSSION

The 2021 EULAR recommendations for CVR management in RMDs comprise overarching principles and guidance informed by the currently available evidence on several potential interventions aiming to improve cardiovascular outcomes in these disorders. The LoA for most statements was high, indicating a coherent perspective on behalf of health professionals from different areas of care and patients alike for CVR reduction efforts.

The majority of the included RMDs are uncommon diseases limiting the ability to perform large observational studies to assess the impact of traditional and disease-specific risk factors on cardiovascular disease burden and clinical trials on the long-term cardiovascular effects of preventive treatments. One of the main challenges of these recommendations was the low LoE due to few studies on many of the research questions. Confounding by indication and lack of propensity adjustment was a common limitation in the included studies and therefore several statements relied on expert opinion. Future studies that better identify exposures and outcomes may help overcome these methodological issues.

There are several additional issues that need to be addressed in the future efforts for CVR management in RMDs. Systemic RMDs are complex diseases with a wide range of clinical manifestations of various severity that may affect cardiovascular health in diverse ways. Considering personalised patient care, the potential impact of individual patient clinical phenotype on cardiovascular prognosis also merits further investigation. In guidelines for cardiovascular prevention in the general population, risk stratification represents a prerequisite for CVR management (eg, BP targets or lipid-lowering therapy).[82 89] In this context, it is important to recognise that underperformance of clinical CVR prediction tools used in the general population may hamper CVR prevention and management in RMDs. The use of prediction tools that incorporate CRP[110] (eg, Reynolds risk score[111]), the presence of specific RMDs (RA, SLE) or anti-inflammatory agents (eg, QRISK3)[38] or multipliers of baseline risk (eg, modified SCORE)[112] has been suggested by some guideline committees for CVR stratification in the general population but their use in RMDs needs to be further tested and validated. Thus, studies on disease-specific tools for CVR assessment including disease-specific in addition to traditional CVR factors, as well as risk qualifiers including the evaluation of the predictive value of nonclinical tools, are warranted. These issues, along with other relevant questions such as the pragmatic use of any risk score (simplicity often aids use) will hopefully inspire future research increasing the quality of evidence in CVR management in RMDs, are presented in the Research Agenda (box 1). One of future challenges is the better identification of patient subgroups at higher CVR including for example those with longer disease duration, and number of flares/relapses (eg, in SLE, vasculitis, gout)[55 66 113–115] or those with certain demographic (age, gender, race/ethnicity)[116] and disease characteristics (eg, aPL positivity in SLE, polyarticular or tophaceous phenotype in gout).[55 113 117]

Box 1 Research agenda and future perspectives

1. Validation of existing generic and modified CVR prediction tools in large prospective studies, and development of new disease-specific equations.
2. Additive value of vascular imaging and/or circulating biomarkers in CVR assessment in RMDs.
3. Identification of patient subgroups with higher CVR.
4. Long-term effects of current and new drugs for RMDs on CVR factors and cardiovascular events.
5. Role of antithrombotic agents used in some RMDs (eg, aspirin, LMWH in SLE/APS) to reduce the overall CVR in these patients.
6. Need for large educational campaigns within the rheumatological and other medical specialties and patient associations to increase CVR awareness.
7. Best implementation methods for the CVR recommendations.

APS, antiphospholipid syndrome; CVR, cardiovascular risk; LMWH, low-molecular weight heparin; RMDs, rheumatic and musculoskeletal diseases; SLE, systemic lupus erythematosus.

Long-term effects of current and new drugs for RMDs on CVR need further investigation. The deleterious cardiometabolic effects of the excessive exposure to glucocorticoids are well known.[118] Current recommendations by the ACR[119] and the EULAR[53 90 120 121] for the management of RMDs emphasise the adverse effects and the need of the limited dose of glucocorticoids. Limiting glucocorticoid exposure to the lowest effective dose to control active disease for the shortest duration possible and eventually discontinuation, as well as weighting the benefits and risks before starting systemic glucocorticoids, can help reduce cardiovascular harm. Several anti-inflammatory agents (eg, colchicine,[122] anti-IL1b[123]) have been shown to lower cardiovascular outcomes in randomised controlled trials for secondary prevention of cardiovascular disease in the general population and other trials are ongoing (eg, hydroxychloroquine[124]) but further evidence is needed on the cardiovascular outcomes and safety of such immunoregulatory agents in RMDs. Although the role of hydroxychloroquine in APS, and of non-steroidal anti-inflammatory drugs (NSAIDs) in SLE, was examined in our SLR (Supplementary SLR report, section II), the panel agreed that any statement on the use of these medications should be deferred until more robust evidence is available. More evidence is needed about the effect of glucocorticoids, NSAIDs and IL-1 antagonists, the dosage and duration of colchicine treatment, and the risk and benefits of the concomitant use of colchicine and statins in patients with gout.

Most of the recommendations of established low-cost clinical interventions may apply to both high-resource and low-resource countries worldwide. Implementation strategies for promoting

CVR management in RMDs include interactive educational workshops involving health professionals, patients and stakeholders with the support of healthcare professional societies and patient associations, social media dissemination and strategies customised to local and national policies such as academic detailing, audits and feedback techniques.

The panel believes that these recommendations will enable healthcare providers and patients to mutually engage in a long-term care pathway tailored to patients' needs and expectations for improving cardiovascular health in RMDs. As new data accumulate, this first set of 'best available' evidence on cardiovascular prevention in gout, vasculitis, SSc, myositis, MCTD, SS, SLE and APS will be timely updated.

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EULAR recommendations for cardiovascular risk management in Rheumatic and Musculoskeletal Diseases, including Systemic Lupus Erythematosus and Antiphospholipid Syndrome

Systematic literature review (SLR) report

SLR for Gout, Vasculitis, and other Rheumatic and Musculoskeletal diseases: Daisy Vedder, Eline Houben, Laura Boekel, Chetan Mukhtyar, Gary J. MacFarlane, Michael T. Nurmohamed

SLR for Systemic Lupus Erythematosus and Antiphospholipid Syndrome: George C. Drosos, Michael M. Ward, Maria G. Tektonidou

Drosos GC, *et al. Ann Rheum Dis* 2022;0:1–12. doi: 10.1136/annrheumdis-2021-221733

IV. Abbreviations

AA	aortic aneurysm
AAV	ANCA-associated vasculitis
ACC	American College of Cardiology
ACEI	angiotensin-converting enzyme inhibitors
aGAPSS	adjusted Global Antiphospholipid Syndrome Score
AHA	American Heart Association
AP	angina pectoris
APS	antiphospholipid syndrome
ARB	angiotensin receptor blockers
AUC	area under the curve
CAD	coronary artery disease
CCB	calcium channel blockers
CHD	coronary heart disease
CI	confidence interval
CVA	cerebrovascular accident
CVD	cardiovascular disease
CYC	cyclophosphamide
DOI	digital object identifier
EUVAS	European Vasculitis Society
FRS	Framingham risk score
GCA	giant cell arteritis
HCQ	hydroxychloroquine
HF	heart failure
HR	hazards ratio
IHD	ischemic heart disease
MCTD	mixed connective tissue disease
MI	myocardial infarction
MTX	methotrexate
NA	not available
NSAID	non-steroidal anti-inflammatory drug
O/P	observed/predicted
OR	odds ratio
PAD	peripheral arterial disease
PICO	patient; intervention; comparator; outcome
py	patient-years
RCT	randomized clinical trial
RR	risk ratio
SCORE	Systematic Coronary Risk Evaluation
SLAM	Systemic Lupus Activity Measure
SLE	systemic lupus erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
SLICC	Systemic Lupus Erythematosus International Collaborating Clinics
SLR	systematic literature review
SS	Sjögren's syndrome
SSc	systemic sclerosis
SUA	serum uric acid
TE	thrombotic event
TIA	transient ischemic attack
ULT	urate lowering therapy
yrs	years

I. Methods

A. Search strategies

1. Exclusion criteria

- Non-English language publications
- Animal studies
- Basic science studies
- Non-adult population studies
- Narrative review
- Case reports, case series
- Conference abstracts
- Not related to PICO questions (unrelated topic/outcome)
- Same cohort publications
- Other (study design, guidelines, updates from public health authorities, letters, comments)

2. Search terms

a. Gout

1) Gout (patient population)

Medline/PubMed:
"Gout"[Mesh] OR "Hyperuricemia"[Mesh] OR gout[tiab] OR "Arthritis, Gouty"[Mesh] OR gouty[tiab] OR hyperuricem*[tiab] OR hyper-uricem*[tiab] OR hyperuricaem*[tiab] OR hyper-uricaem*[tiab] OR hyperuricacid*[tiab]

Embase:
'gout'/exp OR 'hyperuricemia'/exp OR gout: ti,ab,kw OR gouty:ti,ab,kw OR hyperuricem*:ti,ab,kw OR ‘hyper uricem*’:ti,ab,kw OR hyperuricaem*:ti,ab,kw OR ‘hyper uricaem*’:ti,ab,kw OR hyperuricacid*:ti,ab,kw

Cochrane:
((gout OR gouty OR hyperuricem* OR “hyper uricem*” OR hyperuricaem* OR “hyper uricaem*” OR hyperuricacid*)

2) *C*ardiovascular disease (outcome)

Medline/PubMed:
"Arteriosclerosis"[Mesh] OR "Cardiovascular Diseases"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Stroke"[Mesh] OR angina pectoris[tiab] OR arrhythmi*[tiab] OR arrythmi*[tiab] OR dysrhythmi*[tiab] OR arteriosclero*[tiab] OR atherosclero*[tiab] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR cardio-vascular event*[tiab] OR cerebrovascular disease*[tiab] OR coronary disease*[tiab] OR cvd[tiab] OR cvds[tiab] OR heart disease*[tiab] OR heart failure*[tiab] OR peripheral arterial disease*[tiab] OR peripheral artery disease*[tiab] OR peripheral vascular disease*[tiab] OR stroke*[tiab]

Embase:
'cardiovascular disease'/exp OR 'angina pectoris':ti,ab,kw OR 'arrhythmi*':ti,ab,kw OR 'arrythmi*':ti,ab,kw OR 'dysrhythmi*':ti,ab,kw OR 'arteriosclero*':ti,ab,kw OR 'atherosclero*':ti,ab,kw OR 'cardiovascular disease*':ti,ab,kw OR 'cardiovascular event*':ti,ab,kw OR 'cardio-vascular event*':ti,ab,kw OR 'cerebrovascular disease*':ti,ab,kw OR 'coronary disease*':ti,ab,kw OR 'cvd':ti,ab,kw OR 'cvds':ti,ab,kw OR 'heart disease*':ti,ab,kw OR 'heart failure*':ti,ab,kw OR 'peripheral arterial disease*':ti,ab,kw OR 'peripheral artery disease*':ti,ab,kw OR 'peripheral vascular disease*':ti,ab,kw OR 'stroke*':ti,ab,kw

Cochrane:
("angina pectoris" OR "arrhythmi*" OR "arrythmi*" OR "dysrhythmi*" OR "arteriosclero*" OR "atherosclero*" OR "cardiovascular disease*" OR "cardiovascular event*" OR "cardio-vascular event*" OR "cerebrovascular disease*" OR "coronary disease*" OR "cvd" OR "cvds" OR "heart disease*" OR "heart failure*" OR "peripheral arterial disease*" OR "peripheral artery disease*" OR "peripheral vascular disease*" OR "stroke*"):ti,ab,kw

3) cardiovascular risk prediction tools

Medline/PubMed:
"framingham" [tiab] OR "Systematic Coronary Risk Evaluation"[tiab] OR "QRISK"[tiab] OR "Pooled Cohort Risk Equation"[tiab] OR "ASCVD"[tiab] OR "Reynolds Risk Score"[tiab] OR "RRS"[tiab] OR "Prospective Cardiovascular Münster Study"[tiab] OR "PROCAM"[tiab]

Embase:
'Framingham risk score'/exp OR 'framingham':ti,ab,kw OR 'Systematic Coronary Risk Evaluation'/exp OR 'Systematic Coronary Risk Evaluation':ti,ab,kw OR 'QRISK':ti,ab,kw OR 'Pooled Cohort Risk Equation':ti,ab,kw OR 'ASCVD':ti,ab,kw OR 'Reynolds risk score'/exp OR 'Reynolds Risk Score':ti,ab,kw OR 'RRS':ti,ab,kw OR 'Prospective Cardiovascular Münster Study':ti,ab,kw OR 'PROCAM':ti,ab,kw

Cochrane:
("framingham" OR "Systematic Coronary Risk Evaluation" OR "QRISK" OR "Pooled Cohort Risk Equation" OR "ASCVD" OR "Reynolds Risk Score" OR "RRS" OR "Prospective Cardiovascular Münster Study" OR "PROCAM")):ti,ab,kw

4) antihypertensives
Medline/PubMed:
"Antihypertensive Agents"[Mesh:NoExp] OR "Antihypertensive Agents" [Pharmacological Action] OR "Calcium Channel Blockers"[Mesh:NoExp] OR "Calcium Channel Blockers" [Pharmacological Action] OR "Spironolactone"[Mesh] OR "Eplerenone"[Mesh] OR "Clonidine"[Mesh] OR "Diuretics"[Mesh:NoExp] OR "Diuretics" [Pharmacological Action] OR "Methyldopa"[Mesh] OR "Hydralazine"[Mesh] OR "aliskiren" [Supplementary Concept] OR antihypertensiv*[tiab] OR anti-hypertensiv*[tiab] OR blood pressure lowering drug*[tiab] OR blood pressure lowering agent*[tiab] OR blood pressure medicat*[tiab] OR angiotensin-converting enzyme inhibitor*[tiab] OR ACE inhibit*[tiab] OR angiotensin receptor

block*[tiab] OR angiotensin receptor antagon*[tiab] OR calcium channel block*[tiab] OR calcium channel antagon*[tiab] OR beta block*[tiab] OR alpha block*[tiab] OR diuretic*[tiab] OR spironolacton*[tiab] OR eplerenon*[tiab] OR clonidin*[tiab] OR methyldopa[tiab] OR hydralazin*[tiab] OR aliskiren*[tiab]

Embase:
'antihypertensive agent'/de OR 'dipeptidyl carboxypeptidase inhibitor'/de OR 'calcium channel blocking agent'/de OR 'spironolactone'/exp OR 'eplerenone'/exp OR 'clonidine'/exp OR 'diuretic agent'/de OR 'methyldopa'/exp OR 'hydralazine'/exp OR 'aliskiren'/exp OR 'antihypertensiv*':ti,ab,kw OR 'anti-hypertensiv*':ti,ab,kw OR 'blood pressure lowering drug*':ti,ab,kw OR 'blood pressure lowering agent*':ti,ab,kw OR 'blood pressure medicat*':ti,ab,kw OR 'angiotensin-converting enzyme inhibitor*':ti,ab,kw OR 'ACE inhibit*':ti,ab,kw OR 'angiotensin receptor block*':ti,ab,kw OR 'angiotensin receptor antagon*':ti,ab,kw OR 'calcium channel block*':ti,ab,kw OR 'calcium channel antagon*':ti,ab,kw OR 'beta block*':ti,ab,kw OR 'alpha block*':ti,ab,kw OR 'diuretic*':ti,ab,kw OR 'spironolacton*':ti,ab,kw OR 'eplerenon*':ti,ab,kw OR 'clonidin*':ti,ab,kw OR 'methyldopa':ti,ab,kw OR 'hydralazin*':ti,ab,kw OR 'aliskiren*':ti,ab,kw

Cochrane:
("antihypertensiv*" OR "anti-hypertensiv*" OR "blood pressure lowering drug*" OR "blood pressure lowering agent*" OR "blood pressure medicat*" OR "angiotensin-converting enzyme inhibitor*" OR "ACE inhibit*" OR "angiotensin receptor block*" OR "angiotensin receptor antagon*" OR "calcium channel block*" OR "calcium channel antagon*" OR "beta block*" OR "alpha block*" OR "diuretic*" OR "spironolacton*" OR "eplerenon*" OR "clonidin*" OR "methyldopa" OR "hydralazin*" OR "aliskiren*"):ti,ab,kw

5) Lipid lowering medication

Medline/PubMed:
"Hypolipidemic Agents"[Mesh:NoExp] OR "Hypolipidemic Agents" [Pharmacological Action] OR "Angiotensin-Converting Enzyme Inhibitors"[Mesh:NoExp] OR "Angiotensin-Converting Enzyme Inhibitors" [Pharmacological Action] OR "Ezetimibe"[Mesh] OR lipid lowering[tiab] OR statin*[tiab] OR ezetimibe[tiab] OR PCSK9[tiab]

Embase:
'antilipemic agent'/de OR 'hydroxymethylglutaryl coenzyme A reductase inhibitor'/exp OR 'ezetimibe'/exp OR 'lipid lowering':ti,ab,kw OR 'statin*':ti,ab,kw OR 'ezetimibe':ti,ab,kw OR 'PCSK9':ti,ab,kw

Cochrane:
("lipid lowering" OR "statin*" OR "ezetimibe" OR "PCSK9"):ti,ab,kw

6) Antiplatelet therapy

Medline/PubMed:

"Platelet Aggregation Inhibitors"[Mesh] OR "Salicylates"[Mesh] OR anti-platelet*[tiab] OR antiplatelet*[tiab] OR antithrombocytic*[tiab] OR anti thrombocytic*[tiab] OR aspirin[tiab] OR ascal[tiab] OR platelet aggregation inhibit*[tiab]

Embase:
'antithrombocytic agent'/de OR 'salicylic acid derivative'/exp OR 'anti-platelet*':ti,ab,kw OR 'antiplatelet*':ti,ab,kw OR 'antithrombocytic*':ti,ab,kw OR 'anti thrombocytic*':ti,ab,kw OR 'aspirin':ti,ab,kw OR 'ascal':ti,ab,kw OR 'platelet aggregation inhibit*':ti,ab,kw

Cochrane:
("anti-platelet*" OR "antiplatelet*" OR "antithrombocytic*" OR "anti thrombocytic*" OR "aspirin" OR "ascal" OR "platelet aggregation inhibit*"):ti,ab,kw

7) Disease activity (*Medline/PubMed:*
"Chronic Disease"[Mesh] OR "Recurrence"[Mesh] OR "Disease Progression"[Mesh] OR "Uric Acid/blood"[Mesh] OR (disease*[ti] AND (aggravati*[ti] OR progressi*[ti] OR exacerbati*[ti] OR chronic[ti] OR durati*[ti] OR recurren*[ti] OR periodic*[ti] OR relaps*[ti] OR flare*[ti])) OR "blood urate"[ti] OR "blood uric acid"[ti] OR "plasma urate"[ti] OR "plasma uric acid"[ti] OR "serum urate"[ti] OR "serum uric acid"[ti] OR "urate blood level"[ti] OR acute polyarthriti*[ti] OR hamarthriti*[ti] OR holarthriti*[ti] OR polyarthropath*[ti] OR polyarthros*[ti] OR progressive chronic polyarthriti*[ti] OR polyarticular*[ti] OR tophus[ti] OR tophi[ti] OR tophaceous*[ti] OR (disease*[ot] AND (aggravati*[ot] OR progressi*[ot] OR exacerbati*[ot] OR chronic[ot] OR durati*[ot] OR recurren*[ot] OR periodic*[ot] OR relaps*[ot] OR flare*[ot])) OR "blood urate"[ot] OR "blood uric acid"[ot] OR "plasma urate"[ot] OR "plasma uric acid"[ot] OR "serum urate"[ot] OR "serum uric acid"[ot] OR "urate blood level"[ot] OR acute polyarthriti*[ot] OR hamarthriti*[ot] OR holarthriti*[ot] OR polyarthropath*[ot] OR polyarthros*[ot] OR progressive chronic polyarthriti*[ot] OR polyarticular*[ot] OR tophus[ot] OR tophi[ot] OR tophaceous*[ot]

Embase:
'disease activity'/mj OR 'chronic disease'/exp/mj OR 'disease duration'/exp/mj OR 'recurrent disease'/exp/mj OR 'disease exacerbation'/exp/mj OR 'uric acid blood level'/exp/mj OR 'tophus'/exp/mj OR 'tophaceous gout'/exp/mj OR 'polyarthritis'/exp/mj OR ((disease* AND (aggravati* OR progressi* OR exacerbati* OR chronic OR durati* OR recurren* OR periodic* OR relaps* OR flare*)) OR 'blood urate' OR 'blood uric acid' OR 'plasma urate' OR 'plasma uric acid' OR 'serum urate' OR 'serum uric acid' OR 'urate blood level' OR 'acute polyarthriti*' OR hamarthriti* OR holarthriti* OR polyarthropath* OR polyarthros* OR 'progressive chronic polyarthriti*' OR polyarticular* OR tophus OR tophi OR tophaceous*):ti,kw

Cochrane:
((disease* AND (aggravati* OR progressi* OR exacerbati* OR chronic OR durati* OR recurren* OR periodic* OR relaps* OR flare*)) OR "blood urate" OR "blood uric acid" OR "plasma urate" OR "plasma uric acid" OR "serum urate" OR "serum uric acid" OR "urate blood level" OR "acute polyarthriti*" OR hamarthriti* OR holarthriti* OR polyarthropath* OR polyarthros* OR "progressive chronic polyarthriti*" OR polyarticular* OR tophus OR tophi OR tophaceous*):ti,ab,kw

8) Disease specific medication

Medline/PubMed:

"Adrenal Cortex Hormones"[Mesh] OR "Glucocorticoids"[Mesh] OR "Glucocorticoids" [Pharmacological Action] OR "Methylprednisolone"[Mesh:NoExp] OR "Prednisolone"[Mesh:NoExp] OR "Prednisone"[Mesh] OR "Dexamethasone"[Mesh:NoExp] OR "Allopurinol"[Mesh] OR "Colchicine"[Mesh:NoExp] OR "Diclofenac"[Mesh] OR "Febuxostat"[Mesh] OR "Naproxen"[Mesh] OR "Pegloticase" [Supplementary Concept] OR "Uricosuric Agents"[Mesh] OR "Uricosuric Agents" [Pharmacological Action] OR "Benzbromarone"[Mesh] OR "Anti-Inflammatory Agents, Non-Steroidal"[Mesh] OR "Anti-Inflammatory Agents, Non-Steroidal" [Pharmacological Action] OR "Celecoxib"[Mesh] OR "Etoricoxib"[Mesh] OR "Ibuprofen"[Mesh] OR "Interleukin-1"[Mesh] OR "Interleukin 1 Receptor Antagonist Protein"[Mesh] OR "canakinumab" [Supplementary Concept] OR "Urate Oxidase"[Mesh] OR "rasburicase" [Supplementary Concept] OR “adrenal cortex hormone”[ti] OR “adrenal cortical hormone”[ti] OR adrenal cortical steroid*[ti] OR adrenal steroid*[ti] OR adreno cortical steroid*[ti] OR adreno corticosteroid*[ti] OR adrenocortical hormone*[ti] OR adrenocortical steroid*[ti] OR adrenocorticosteroid*[ti] OR cortical steroid*[ti] OR cortico steroid*[ti] OR corticoid*[ti] OR corticosteroid*[ti] OR glucocorticoid*[ti] OR glucocorticoidsteroid*[ti] OR glucocortoid*[ti] OR glycocorticoid*[ti] OR glycocorticosteroid*[ti] OR methylprednisolon*[ti] OR prednisolon*[ti] OR prednison*[ti] OR dexamethason*[ti] OR colchicin*[ti] OR colchin*[ti] OR diclofen*[ti] OR diclophen*[ti] OR febuxostat[ti] OR naproxen[ti] OR pegloticase[ti] OR uricosuric*[ti] OR benzbroma*[ti] OR nsaid*[ti] OR “non steroidal anti inflammatory”[ti] OR “nonsteroidal anti inflammatory”[ti] OR “non steroidal antiinflammatory”[ti] OR “nonsteroidal antiinflammatory”[ti] OR celecoxib[ti] OR etoricoxib[ti] OR ibuprofen[ti] OR “interleukin 1”[ti] OR “il 1”[ti] OR anakinra[ti] OR canakinumab[ti] OR xanthine oxidase inhibit*[ti] OR “urate oxydase”[ti] OR “urate oxygen oxidoreductase”[ti] OR “urate o2 oxidoreductase”[ti] OR “urate oxygen oxidoreductase”[ti] OR uratoxidase[ti] OR uricase[ti] OR rasburicase[ti] OR pegloticase[ti] OR “adrenal cortex hormone”[ot] OR “adrenal cortical hormone”[ot] OR adrenal cortical steroid*[ot] OR adrenal steroid*[ot] OR adreno cortical steroid*[ot] OR adreno corticosteroid*[ot] OR adrenocortical hormone*[ot] OR adrenocortical steroid*[ot] OR adrenocorticosteroid*[ot] OR cortical steroid*[ot] OR cortico steroid*[ot] OR corticoid*[ot] OR corticosteroid*[ot] OR glucocorticoid*[ot] OR glucocorticoidsteroid*[ot] OR glucocortoid*[ot] OR glycocorticoid*[ot] OR glycocorticosteroid*[ot] OR methylprednisolon*[ot] OR prednisolon*[ot] OR prednison*[ot] OR dexamethason*[ot] OR colchicin*[ot] OR colchin*[ot] OR diclofen*[ot] OR diclophen*[ot] OR febuxostat[ot] OR naproxen[ot] OR pegloticase[ot] OR uricosuric*[ot] OR benzbroma*[ot] OR nsaid*[ot] OR “non steroidal anti inflammatory”[ot] OR “nonsteroidal anti inflammatory”[ot] OR “non steroidal antiinflammatory”[ot] OR “nonsteroidal antiinflammatory”[ot] OR celecoxib[ot] OR etoricoxib[ot] OR ibuprofen[ot] OR “interleukin 1”[ot] OR “il 1”[ot] OR anakinra[ot] OR canakinumab[ot] OR xanthine oxidase inhibit*[ot] OR “urate oxydase”[ot] OR “urate oxygen oxidoreductase”[ot] OR “urate o2 oxidoreductase”[ot] OR “urate oxygen oxidoreductase”[ot] OR uratoxidase[ot] OR uricase[ot] OR rasburicase[ot] OR pegloticase[ot]

Embase:

'corticosteroid'/mj OR 'glucocorticoid'/mj OR 'methylprednisolone'/exp/mj OR 'prednisolone'/exp/mj OR 'prednisone'/exp/mj OR 'dexamethasone'/exp/mj OR

'allopurinol'/exp/mj OR 'colchicine'/exp/mj OR 'diclofenac'/exp/mj OR 'febuxostat'/exp/mj OR 'naproxen'/exp/mj OR 'pegloticase'/exp/mj OR 'uricosuric agent'/mj OR 'benzbromarone'/exp/mj OR 'nonsteroid antiinflammatory agent'/mj OR 'celecoxib'/exp/mj OR 'etoricoxib'/exp/mj OR 'ibuprofen'/exp/mj OR 'interleukin 1'/exp/mj OR 'anakinra'/exp/mj OR 'canakinumab'/exp/mj OR 'interleukin 1 inhibitor'/exp/mj OR 'xanthine oxidase inhibitor'/mj OR 'urate oxidase'/exp/mj OR 'rasburicase'/exp/mj OR 'pegloticase'/exp/mj OR (‘adrenal cortex hormone’ OR ‘adrenal cortical hormone’ OR ‘adrenal cortical steroid*’ OR ‘adrenal steroid*’ OR ‘adreno cortical steroid*’ OR ‘adreno corticosteroid*’ OR ‘adrenocortical hormone*’ OR ‘adrenocortical steroid*’ OR adrenocorticosteroid* OR ‘cortical steroid*’ OR ‘cortico steroid*’ OR corticoid* OR corticosteroid* OR glucocorticoid* OR glucocorticoidsteroid* OR glucocortoid* OR glycocorticoid* OR glycocorticosteroid* OR methylprednisolon* OR prednisolon* OR prednison* OR dexamethason* OR colchicin* OR colchin* OR diclofen* OR diclophen* OR febuxostat OR naproxen OR pegloticase OR uricosuric* OR benzbroma* OR nsaid* OR ‘non steroid* anti inflammatory’ OR ‘nonsteroid* anti inflammatory’ OR ‘non steroid* antiinflammatory’ OR ‘nonsteroid* antiinflammatory’ OR celecoxib OR etoricoxib OR ibuprofen OR 'interleukin 1’ OR ‘il 1’ OR anakinra OR canakinumab OR 'xanthine oxidase inhibit*' OR ‘urate oxydase’ OR ‘urate oxygen oxidoreductase’ OR ‘urate o2 oxidoreductase’ OR ‘urate oxygen oxidoreductase’ OR uratoxidase OR uricase OR rasburicase OR pegloticase):ti,kw

Cochrane:
(“adrenal cortex hormone” OR “adrenal cortical hormone” OR “adrenal cortical steroid*” OR “adrenal steroid*” OR “adreno cortical steroid*” OR “adreno corticosteroid*” OR “adrenocortical hormone*” OR “adrenocortical steroid*” OR adrenocorticosteroid* OR “cortical steroid*” OR “cortico steroid*” OR corticoid* OR corticosteroid* OR glucocorticoid* OR glucocorticoidsteroid* OR glucocortoid* OR glycocorticoid* OR glycocorticosteroid* OR methylprednisolon* OR prednisolon* OR prednison* OR dexamethason* OR colchicin* OR colchin* OR diclofen* OR diclophen* OR febuxostat OR naproxen OR pegloticase OR uricosuric* OR benzbroma* OR nsaid* OR (“non steroid*” AND “anti inflammatory”) OR (nonsteroid* AND “anti inflammatory”) OR (“non steroid*” AND antiinflammatory) OR (nonsteroid* AND antiinflammatory) OR celecoxib OR etoricoxib OR ibuprofen OR “interleukin 1” OR “il 1” OR anakinra OR canakinumab OR “xanthine oxidase inhibit*” OR “urate oxydase” OR “urate oxygen oxidoreductase” OR “urate o2 oxidoreductase” OR “urate oxygen oxidoreductase” OR uratoxidase OR uricase OR rasburicase OR pegloticase):ti,ab,kw

9) Prevalence cardiovascular disease
Medline/PubMed
"Morbidity"[Mesh:NoExp] OR "Incidence"[Mesh] OR "Prevalence"[Mesh] OR "epidemiology" [Subheading:NoExp] OR "Mortality"[Mesh] OR "mortality" [Subheading] OR frequenc*[ti] OR morbidit*[ti] OR occurenc*[ti] OR prevalenc*[ti] OR incidenc*[ti] OR frequenc*[ot] OR morbidit*[ot] OR occurenc*[ot] OR prevalenc*[ot] OR incidenc*[ot]

Embase
'morbidity'/mj OR 'incidence'/exp/mj OR 'prevalence'/mj OR 'epidemiology'/mj OR 'mortality'/exp/mj OR 'epidemiology'/lnk OR frequenc*:ti,kw OR morbidit*:ti,kw OR

occurenc*:ti,kw OR prevalenc*:ti,kw OR incidenc*:ti,kw

Cochrane
(frequenc* OR morbidit* OR occurenc* OR prevalenc* OR incidenc*):ab,ti,kw

b. Vasculitis, systemic sclerosis, mixed connective tissue disease, myositis and Sjögren's syndrome

1) ANCA-associated vasculitis (patient population)

Medline/PubMed:
(vasculiti*[tiab] AND ANCA [tiab]) OR antineutrophil [tiab] OR pauci [tiab] OR churg strauss syndrome [tiab] OR "Churg-Strauss Syndrome"[Mesh] OR Churg-Strauss Vasculitis [tiab] OR Wegener [tiab] OR polyangiiti*[tiab] OR polyarteriti*[tiab] OR "Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis"[Mesh] OR Granulomatosis [tiab] OR "Granulomatosis with Polyangiitis" [Mesh]

Embase:
('vasculiti*':ti,ab,kw AND 'ANCA':ti,ab,kw) OR 'antineutrophil':ti,ab,kw OR 'pauci':ti,ab,kw OR 'churg strauss syndrome':ti,ab,kw OR 'Churg Strauss syndrome'/exp OR 'Churg-Strauss Vasculitis':ti,ab,kw OR 'Wegener':ti,ab,kw OR polyangiiti*:ti,ab,kw OR polyarteriti*:ti,ab,kw OR 'ANCA associated vasculitis'/exp OR Granulomatosis:ti,ab,kw OR 'Wegener granulomatosis'/exp OR 'anti neutrophil cytoplasmic antibody associated vasculitis':ti,ab,kw OR 'granulomatosis with polyangiitis':ti,ab,kw

Cochrane:
(('vasculiti*' AND 'ANCA') OR 'antineutrophil' OR 'pauci' OR 'churg strauss syndrome' OR 'Churg-Strauss Vasculitis' OR 'Wegener' OR polyangiiti* OR polyarteriti* OR 'ANCA associated vasculitis' OR Granulomatosis OR 'Wegener granulomatosis' OR 'anti neutrophil cytoplasmic antibody associated vasculitis' OR 'granulomatosis with polyangiitis')

2) Giant cell arteritis (patient population)

Medline/PubMed:
"Giant Cell Arteritis"[Mesh] OR Giant Cell Arteritid* [tiab] OR Horton's Giant Cell Arteritis [tiab] OR Horton's Disease [tiab] OR Temporal Arterit* [tiab] OR Giant Cell Aortit* [tiab] OR Cranial Arterit* [tiab]

Embase:
'giant cell arteritis'/exp OR 'Giant Cell Arteritid*':ti,ab,kw OR 'Horton* Giant Cell Arteritis':ti,ab,kw OR 'Horton* Disease':ti,ab,kw OR 'Temporal Arterit*':ti,ab,kw OR 'Giant Cell Aortit*':ti,ab,kw OR 'Cranial Arterit*':ti,ab,kw OR 'giant cell arteriitis':ti,ab,kw

Cochrane:
(('giant cell arteritis' OR 'Giant Cell Arteritid*' OR 'Horton* Giant Cell Arteritis' OR 'Horton* Disease' OR 'Temporal Arterit*' OR 'Giant Cell Aortit*' OR 'Cranial Arterit*' OR 'giant cell

arteriitis')

3) Systemic sclerosis (patient population)

Medline/PubMed:
"Scleroderma, Systemic"[Mesh] OR Systemic Sclerosis [tiab] OR Systemic Scleroderma [tiab] OR "Scleroderma, Diffuse"[Mesh] OR Progressive Scleroderma [tiab] OR Sudden Onset Scleroderma [tiab] OR Systemic Scleroses [tiab] OR Diffuse Scleroderma [tiab] OR Progressive Systemic Sclerosis [tiab]

Embase:
'systemic sclerosis'/exp OR 'Systemic Sclerosis':ti,ab,kw OR 'Systemic Scleroderm*':ti,ab,kw OR 'diffuse scleroderma'/exp OR 'Progressive Scleroderm*':ti,ab,kw OR 'Sudden Onset Scleroderm*':ti,ab,kw OR 'Systemic Scleroses':ti,ab,kw OR 'Diffuse Scleroderm*':ti,ab,kw OR 'Progressive Systemic Sclerosis':ti,ab,kw

Cochrane:
(('Systemic Sclerosis' OR 'Systemic Scleroderm*' OR 'Progressive Scleroderm*' OR 'Sudden Onset Scleroderm*' OR 'Systemic Scleroses' OR 'Diffuse Scleroderm*' OR 'Progressive Systemic Sclerosis')

4) Mixed connective tissue disease (patient population)

Medline/PubMed:
"Mixed Connective Tissue Disease"[Mesh] OR "Mixed Connective Tissue Disease" [tiab] OR Sharp Syndrome [tiab] OR MCTD [tiab] OR (mixed [tiab] AND connective[tiab] AND tissue[tiab] AND disease[tiab])

Embase:
'mixed connective tissue disease'/exp OR 'Mixed Connective Tissue Disease':ti,ab,kw OR 'Sharp Syndrome':ti,ab,kw OR MCTD:ti,ab,kw OR 'mixed collagen disease':ti,ab,kw

Cochrane:
(('Mixed Connective Tissue Disease' OR 'Sharp Syndrome' OR MCTD OR 'mixed collagen disease')

5) Sjogren Syndrome (patient population)

Medline/PubMed:
"Sjogren's Syndrome"[Mesh] OR Sjogrens Syndrome [tiab] OR Sjogren's syndrome [tiab]OR Sjogren Syndrome [tiab] OR Sicca Syndrome [tiab]

Embase:
'Sjoegren syndrome'/exp OR 'sjoegren disease':ti,ab,kw OR 'sjogren disease':ti,ab,kw OR 'sjogren disease':ti,ab,kw OR 'sjogren syndrome':ti,ab,kw OR 'sjogrens syndrome':ti,ab,kw OR 'sicca syndrome':ti,ab,kw

Cochrane:
((Sjoegren syndrome' OR 'sjoegren disease' OR 'sjogren disease' OR 'sjogren disease' OR 'sjogren syndrome' OR 'sjogrens syndrome' OR 'sicca syndrome')

6) Myositis (patient population)

Medline/PubMed:
"Polymyositis"[Mesh] OR Polymyosit* [tiab] OR Multiple Myosit* [tiab] OR Idiopathic Polymyosit* [tiab] OR Polymyositis Ossificans [tiab] OR "Dermatomyositis"[Mesh] OR Dermatomyositis [tiab] OR Dermatopolymyositis [tiab] OR (Polymyositis [tiab] AND Dermatomyositis [tiab]) OR Adult Type Dermatomyositis [tiab]

Embase:
'polymyositis'/exp OR 'Polymyosit*':ti,ab,kw OR 'Multiple Myosit*':ti,ab,kw OR 'Idiopathic Polymyosit*':ti,ab,kw OR 'Polymyositis Ossificans':ti,ab,kw OR 'dermatomyositis'/exp OR 'Dermatomyositis':ti,ab,kw OR 'Dermatopolymyositis':ti,ab,kw OR ('Polymyositis':ti,ab,kw AND 'Dermatomyositis':ti,ab,kw) OR 'Adult Type Dermatomyositis':ti,ab,kw

Cochrane:
(('Polymyosit*' OR 'Multiple Myosit*' OR 'Idiopathic Polymyosit*' OR 'Polymyositis Ossificans' OR 'Dermatomyositis' OR 'Dermatopolymyositis' OR ('Polymyositis' AND 'Dermatomyositis') OR 'Adult Type Dermatomyositis')

7) Cardiovascular disease (outcome all PICO's)

Medline/PubMed:
"Arteriosclerosis"[Mesh] OR "Cardiovascular Diseases"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Stroke"[Mesh] OR angina pectoris[tiab] OR arrhythmi*[tiab] OR arrythmi*[tiab] OR dysrhythmi*[tiab] OR arteriosclero*[tiab] OR atherosclero*[tiab] OR blood pressure[tiab] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR cardio-vascular event*[tiab] OR cerebrovascular disease*[tiab] OR coronary disease*[tiab] OR cvd[tiab] OR cvds[tiab] OR heart disease*[tiab] OR heart failure*[tiab] OR peripheral arterial disease*[tiab] OR peripheral artery disease*[tiab] OR peripheral vascular disease*[tiab] OR stroke*[tiab]

Embase
'cardiovascular disease'/exp OR 'angina pectoris':ti,ab,kw OR 'arrhythmi*':ti,ab,kw OR 'arrythmi*':ti,ab,kw OR 'dysrhythmi*':ti,ab,kw OR 'arteriosclero*':ti,ab,kw OR 'atherosclero*':ti,ab,kw OR 'blood pressure':ti,ab,kw OR 'cardiovascular disease*':ti,ab,kw OR 'cardiovascular event*':ti,ab,kw OR 'cardio-vascular event*':ti,ab,kw OR 'cerebrovascular disease*':ti,ab,kw OR 'coronary disease*':ti,ab,kw OR 'cvd':ti,ab,kw OR 'cvds':ti,ab,kw OR 'heart disease*':ti,ab,kw OR 'heart failure*':ti,ab,kw OR 'peripheral arterial disease*':ti,ab,kw OR 'peripheral artery disease*':ti,ab,kw OR 'peripheral vascular disease*':ti,ab,kw OR 'stroke*':ti,ab,kw

Cochrane
"Arteriosclerosis" OR "Cardiovascular Diseases" OR "Myocardial Ischemia" OR "Stroke" OR "angina pectoris" OR arrhythmi* OR arrythmi* OR dysrhythmi* OR arteriosclero* OR

atherosclero* OR blood pressure OR cardiovascular disease* OR cardiovascular event* OR cardio-vascular event* OR cerebrovascular disease* OR coronary disease* OR cvd OR cvds OR heart disease* OR heart failure* OR peripheral arterial disease* OR peripheral artery disease* OR peripheral vascular disease* OR stroke*

8) Cardiovascular risk prediction tools
Medline/PubMed:
"framingham" [tiab] OR "Systematic Coronary Risk Evaluation"[tiab] OR "QRISK"[tiab] OR "Pooled Cohort Risk Equation"[tiab] OR "ASCVD"[tiab] OR "Reynolds Risk Score"[tiab] OR "RRS"[tiab] OR "Prospective Cardiovascular Münster Study"[tiab] OR "PROCAM"[tiab]

Embase
'Framingham risk score'/exp OR 'framingham':ti,ab,kw OR 'Systematic Coronary Risk Evaluation'/exp OR 'Systematic Coronary Risk Evaluation':ti,ab,kw OR 'QRISK':ti,ab,kw OR 'Pooled Cohort Risk Equation':ti,ab,kw OR 'ASCVD':ti,ab,kw OR 'Reynolds risk score'/exp OR 'Reynolds Risk Score':ti,ab,kw OR 'RRS':ti,ab,kw OR 'Prospective Cardiovascular Münster Study':ti,ab,kw OR 'PROCAM':ti,ab,kw

Cochrane
("framingham" OR "Systematic Coronary Risk Evaluation" OR "QRISK" OR "Pooled Cohort Risk Equation" OR "ASCVD" OR "Reynolds Risk Score" OR "RRS" OR "Prospective Cardiovascular Münster Study" OR "PROCAM"))

9) Antihypertensives *Medline/PubMed:*
"Antihypertensive Agents"[Mesh:NoExp] OR "Antihypertensive Agents" [Pharmacological Action] OR "Calcium Channel Blockers"[Mesh:NoExp] OR "Calcium Channel Blockers" [Pharmacological Action] OR "Spironolactone"[Mesh] OR "Eplerenone"[Mesh] OR "Clonidine"[Mesh] OR "Diuretics"[Mesh:NoExp] OR "Diuretics" [Pharmacological Action] OR "Methyldopa"[Mesh] OR "Hydralazine"[Mesh] OR "aliskiren" [Supplementary Concept] OR antihypertensiv*[tiab] OR anti-hypertensiv*[tiab] OR blood pressure lowering drug*[tiab] OR blood pressure lowering agent*[tiab] OR blood pressure medicat*[tiab] OR angiotensin-converting enzyme inhibitor*[tiab] OR ACE inhibit*[tiab] OR angiotensin receptor block*[tiab] OR angiotensin receptor antagon*[tiab] OR calcium channel block*[tiab] OR calcium channel antagon*[tiab] OR beta block*[tiab] OR alpha block*[tiab] OR diuretic*[tiab] OR spironolacton*[tiab] OR eplerenon*[tiab] OR clonidin*[tiab] OR methyldopa[tiab] OR hydralazin*[tiab] OR aliskiren*[tiab]

Embase
antihypertensive agent'/de OR 'dipeptidyl carboxypeptidase inhibitor'/de OR 'calcium channel blocking agent'/de OR 'spironolactone'/exp OR 'eplerenone'/exp OR 'clonidine'/exp OR 'diuretic agent'/de OR 'methyldopa'/exp OR 'hydralazine'/exp OR 'aliskiren'/exp OR 'antihypertensiv*':ti,ab,kw OR 'anti-hypertensiv*':ti,ab,kw OR 'blood pressure lowering drug*':ti,ab,kw OR 'blood pressure lowering agent*':ti,ab,kw OR 'blood pressure medicat*':ti,ab,kw OR 'angiotensin-converting enzyme inhibitor*':ti,ab,kw OR 'ACE inhibit*':ti,ab,kw OR 'angiotensin receptor block*':ti,ab,kw OR 'angiotensin receptor antagon*':ti,ab,kw OR 'calcium channel block*':ti,ab,kw OR 'calcium channel antagon*':ti,ab,kw OR 'beta block*':ti,ab,kw OR 'alpha block*':ti,ab,kw OR 'diuretic*':ti,ab,kw OR 'spironolacton*':ti,ab,kw OR 'eplerenon*':ti,ab,kw OR 'clonidin*':ti,ab,kw OR 'methyldopa':ti,ab,kw OR 'hydralazin*':ti,ab,kw OR

‘aliskiren*’:ti,ab,kw

Cochrane
"Antihypertensive Agents" OR "Antihypertensive Agents" OR "Calcium Channel Blockers" OR "Calcium Channel Blockers" OR "Spironolactone" OR "Eplerenone" OR "Clonidine" OR "Diuretics" OR "Diuretics" OR "Methyldopa" OR "Hydralazine" OR "aliskiren" OR antihypertensiv* OR anti-hypertensiv* OR blood pressure lowering drug* OR blood pressure lowering agent* OR blood pressure medicat* OR angiotensin-converting enzyme inhibitor* OR ACE inhibit* OR angiotensin receptor block* OR angiotensin receptor antagon* OR calcium channel block* OR calcium channel antagon* OR beta block* OR alpha block* OR diuretic* OR spironolacton* OR eplerenon* OR clonidin* OR methyldopa OR hydralazin* OR aliskiren*

10) Lipid lowering medication *Medline/PubMed:*
"Hypolipidemic Agents"[Mesh:NoExp] OR "Hypolipidemic Agents" [Pharmacological Action] OR "Angiotensin-Converting Enzyme Inhibitors"[Mesh:NoExp] OR "Angiotensin-Converting Enzyme Inhibitors" [Pharmacological Action] OR "Ezetimibe"[Mesh] OR lipid lowering[tiab] OR statin*[tiab] OR ezetimibe[tiab] OR PCSK9[tiab]

Embase
'antilipemic agent'/de OR 'hydroxymethylglutaryl coenzyme A reductase inhibitor'/exp OR 'ezetimibe'/exp OR ‘lipid lowering’:ti,ab,kw OR ‘statin*’:ti,ab,kw OR ‘ezetimibe’:ti,ab,kw OR ‘PCSK9’:ti,ab,kw

Cochrane
"Hypolipidemic Agents" OR "Hypolipidemic Agents" OR "Angiotensin-Converting Enzyme Inhibitors" OR "Angiotensin-Converting Enzyme Inhibitors" OR "Ezetimibe" OR lipid lowering OR statin* OR ezetimibe OR PCSK9

11) antiplalet therapy
Medline/PubMed:
"Platelet Aggregation Inhibitors"[Mesh] OR "Salicylates"[Mesh] OR anti-platelet*[tiab] OR antiplatelet*[tiab] OR antithrombocytic*[tiab] OR anti thrombocytic*[tiab] OR aspirin[tiab] OR ascal[tiab] OR platelet aggregation inhibit*[tiab]

Embase
'antithrombocytic agent'/de OR 'salicylic acid derivative'/exp OR ‘anti-platelet*’:ti,ab,kw OR ‘antiplatelet*’:ti,ab,kw OR ‘antithrombocytic*’:ti,ab,kw OR ‘anti thrombocytic*’:ti,ab,kw OR ‘aspirin’:ti,ab,kw OR ‘ascal’:ti,ab,kw OR ‘platelet aggregation inhibit*’:ti,ab,kw

Cochrane
"Platelet Aggregation Inhibitors" OR "Salicylates" OR anti-platelet* OR antiplatelet* OR antithrombocytic* OR anti thrombocytic* OR aspirin OR ascal OR platelet aggregation inhibit*

12) Disease related risk factors
Medline/PubMed:
"disease activity" [tiab] OR "disease activity score" [tiab] OR "disease duration" [tiab] OR

"clinical course" [tiab] OR "Birmingham vasculitis activity score" [tiab] OR BVAS [tiab]

Embase

a. 'disease activity'/exp OR 'disease course'/exp OR 'disease activity score'/exp OR 'disease activity':ti,ab,kw OR 'disease course':ti,ab,kw OR 'disease activity score':ti,ab,kw OR 'Birmingham vasculitis activity score':ti,ab,kw OR 'BVAS':ti,ab,kw

b. 'disease activity'/exp OR 'disease course'/exp OR 'disease activity score'/exp OR 'disease activity':ti,ab,kw OR 'disease course':ti,ab,kw OR 'disease activity score':ti,ab,kw OR 'Birmingham vasculitis activity score':ti,ab,kw OR 'BVAS':ti,ab,kw

c. 'disease activity'/exp OR 'disease course'/exp OR 'disease activity score'/exp OR 'disease activity':ti,ab,kw OR 'disease course':ti,ab,kw OR 'disease activity score':ti,ab,kw OR 'European Scleroderma Study Group (EScSG) activity index':ti,ab,kw OR 'EScSG activity index':ti,ab,kw OR '12-point DAI':ti,ab,kw OR 'Combined Response Index for Systemic Sclerosis':ti,ab,kw OR 'CRISS':ti,ab,kw

d. 'disease activity'/exp OR 'disease course'/exp OR 'disease activity score'/exp OR 'disease activity':ti,ab,kw OR 'disease course':ti,ab,kw OR 'disease activity score':ti,ab,kw

e. 'disease activity'/exp OR 'disease course'/exp OR 'disease activity score'/exp OR 'disease activity':ti,ab,kw OR 'disease course':ti,ab,kw OR 'disease activity score':ti,ab,kw OR 'EULAR Sjögren's syndrome (SS) disease activity index':ti,ab,kw OR 'ESSDAI':ti,ab,kw OR 'EULAR SS Disease Activity Index':ti,ab,kw

f. 'disease activity'/exp OR 'disease course'/exp OR 'disease activity score'/exp OR 'disease activity':ti,ab,kw OR 'disease course':ti,ab,kw OR 'disease activity score':ti,ab,kw OR 'Myositis disease activity assessment tool':tiabkw OR 'mdaat':ti,ab,kw

Cochrane

"disease activity" OR "disease activity score" OR "disease duration" OR "clinical course" OR "Birmingham vasculitis activity score" OR BVAS

13) Disease related medication

Medline/PubMed:

"Glucocorticoids" [Mesh] OR prednisone* [tiab] OR methylprednisone [tiab] OR glucocorticoid* [tiab] OR corticosteroid* [tiab] OR "methotrexate" [Mesh] OR methotrexate [tiab] OR "mycophenolic acid" [Mesh] OR mycophenolate mofetil [tiab] OR cellcept [tiab] OR mycophenolic acid [tiab] OR "azathioprine" [Mesh] OR azathioprine [tiab] or Imuran [tiab] OR immuran [tiab] OR "cyclophosphamide" [Mesh] OR cyclophosphamide [tiab] OR endoxan [tiab] OR "rituximab" [Mesh] OR rituximab [tiab] OR CD20 Antibody [tiab] OR "cyclosporin" [Mesh] OR cyclosporin [tiab] OR neoral [tiab] OR "hydroxychloroquine" [Mesh] OR hydroxychloroquine [tiab] OR plaquenil [tiab*]*

Embase

'glucocorticoid'/mj OR prednisone*:ti,ab,kw OR methylprednisone:ti,ab,kw OR glucocorticoid*:ti,ab,kw OR corticosteroid*:ti,ab,kw OR 'methotrexate'/mj OR methotrexate:ti,ab,kw OR 'mycophenolic acid'/mj OR mycophenolate mofetil:ti,ab,kw OR

cellcept:ti,ab,kw OR mycophenolic acid:ti,ab,kw OR 'azathioprine'/mj OR azathioprine:ti,ab,kw or Imuran:ti,ab,kw OR immuran:ti,ab,kw OR 'cyclophosphamide'/mj OR cyclophosphamide:ti,ab,kw OR endoxan:ti,ab,kw OR 'rituximab'/mj OR rituximab:ti,ab,kw OR CD20 Antibody:ti,ab,kw OR 'cyclosporine'/mj OR cyclosporin:ti,ab,kw OR cyclosporine:ti,ab,kw OR neoral:ti,ab,kw OR 'hydroxychloroquine'/mj OR hydroxychloroquine:ti,ab,kw OR plaquenil:ti,ab,kw

Cochrane
glucocorticoid OR prednisone* OR methylprednisone OR glucocorticoid* OR corticosteroid* OR methotrexate OR mycophenolic NEXT acid OR mycophenolate NEXT mofetil OR cellcept OR azathioprine OR Imuran OR immuran OR cyclophosphamide OR endoxan OR rituximab OR CD20 NEXT Antibody OR cyclosporine OR cyclosporin OR neoral OR hydroxychloroquine OR plaquenil:ti,ab,kw

14) Prevalence cardiovascular disease *Medline/PubMed*
"Morbidity"[Mesh:NoExp] OR "Incidence"[Mesh] OR "Prevalence"[Mesh] OR "epidemiology" [Subheading:NoExp] OR "Mortality"[Mesh] OR "mortality" [Subheading] OR frequenc*[ti] OR morbidit*[ti] OR occurenc*[ti] OR prevalenc*[ti] OR incidenc*[ti] OR frequenc*[ot] OR morbidit*[ot] OR occurenc*[ot] OR prevalenc*[ot] OR incidenc*[ot]

Embase
'morbidity'/mj OR 'incidence'/exp/mj OR 'prevalence'/mj OR 'epidemiology'/mj OR 'mortality'/exp/mj OR 'epidemiology'/lnk OR frequenc*:ti,kw OR morbidit*:ti,kw OR occurenc*:ti,kw OR prevalenc*:ti,kw OR incidenc*:ti,kw

Cochrane
(frequenc* OR morbidit* OR occurenc* OR prevalenc* OR incidenc*):ab,ti,kw

c. Systemic lupus erythematosus and the antiphospholipid syndrome

1) Cardiovascular risk prediction tools

Medline/PubMed:

((((systemic lupus erythematosus[MeSH Terms]) OR "systemic lupus erythematosus"[Title/Abstract])) AND (("framingham" [tiab] OR "Systematic Coronary Risk Evaluation"[tiab] OR "QRISK"[tiab] OR "Pooled Cohort Risk Equation"[tiab] OR "ASCVD"[tiab] OR "Reynolds Risk Score"[tiab] OR "RRS"[tiab] OR "Prospective Cardiovascular Münster Study"[tiab] OR "PROCAM"[tiab])))
(((((antiphospholipid syndrome[MeSH Terms]) OR "antiphospholipid syndrome"[Title/Abstract])) AND (("framingham" [tiab] OR "Systematic Coronary Risk Evaluation"[tiab] OR "QRISK"[tiab] OR "Pooled Cohort Risk Equation"[tiab] OR "ASCVD"[tiab] OR "Reynolds Risk Score"[tiab] OR "RRS"[tiab] OR "Prospective Cardiovascular Münster Study"[tiab] OR "PROCAM"[tiab]))))

Embase:

'systemic lupus erythematosus'/exp
'systemic lupus erythematosus*':ab,ti,kw
'antiphospholipid syndrome'/exp
'antiphospholipid syndrome*':ab,ti,kw
'framingham risk score' 'framingham' 'systematic coronary risk evaluation' 'systematic coronary risk evaluation' 'qrisk' 'pooled cohort risk equation' 'ascvd' 'reynolds risk score' 'reynolds risk score' 'rrs' 'prospective cardiovascular münster study':ti,ab,kw OR :ti,ab,kw

Cochrane:

("systemic lupus erythematosus"):ab,ti,kw
MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
'antiphospholipid syndrome*':ab,ti,kw
MeSH descriptor: [Antiphospholipid Syndrome] explode all trees
("framingham" OR "Systematic Coronary Risk Evaluation" OR "QRISK" OR "Pooled Cohort Risk Equation" OR "ASCVD" OR "Reynolds Risk Score" OR "RRS" OR "Prospective Cardiovascular Münster Study" OR "PROCAM"):ti,ab,kw

2) Antihypertensives

Medline/PubMed:

(systemic lupus erythematosus[MeSH Terms]) OR "systemic lupus erythematosus"[Title/Abstract]
(antiphospholipid syndrome[MeSH Terms]) OR "antiphospholipid syndrome"[Title/Abstract]
("Antihypertensive Agents"[Mesh:NoExp] OR "Antihypertensive Agents" [Pharmacological Action] OR "Calcium Channel Blockers"[Mesh:NoExp] OR "Calcium Channel Blockers" [Pharmacological Action] OR "Spironolactone"[Mesh] OR "Eplerenone"[Mesh] OR "Clonidine"[Mesh] OR "Diuretics"[Mesh:NoExp] OR "Diuretics" [Pharmacological Action] OR "Methyldopa"[Mesh] OR "Hydralazine"[Mesh] OR "aliskiren" [Supplementary Concept] OR antihypertensiv*[tiab] OR anti-hypertensiv*[tiab] OR blood pressure lowering drug*[tiab] OR blood pressure lowering agent*[tiab] OR blood pressure medicat*[tiab] OR angiotensin-converting enzyme inhibitor*[tiab] OR ACE inhibit*[tiab] OR angiotensin receptor block*[tiab] OR angiotensin receptor antagon*[tiab] OR calcium channel block*[tiab] OR calcium channel antagon*[tiab] OR beta block*[tiab] OR alpha block*[tiab] OR diuretic*[tiab] OR

spironolacton*[tiab] OR eplerenon*[tiab] OR clonidin*[tiab] OR methyldopa[tiab] OR hydralazin*[tiab] OR aliskiren*[tiab])
("Arteriosclerosis"[Mesh] OR "Cardiovascular Diseases"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Stroke"[Mesh] OR angina pectoris[tiab] OR arrhythmi*[tiab] OR arrythmi*[tiab] OR dysrhythmi*[tiab] OR arteriosclero*[tiab] OR atherosclero*[tiab] OR blood pressure[tiab] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR cardio-vascular event*[tiab] OR cerebrovascular disease*[tiab] OR coronary disease*[tiab] OR cvd[tiab] OR cvds[tiab] OR heart disease*[tiab] OR heart failure*[tiab] OR peripheral arterial disease*[tiab] OR peripheral artery disease*[tiab] OR peripheral vascular disease*[tiab] OR stroke*[tiab])

"lupus nephritis"[tiab] OR lupus nephritis[mh] OR "lupus glomerulonephritis"tiab] OR "lupoid nephritis"[tiab] OR ((lupus erythematosus, systemic[mh] OR SLE[tiab] OR "systemic lupus erythematosus"[tiab] OR "lupus erythematosus"[tiab] OR "libman sacks"[tiab] OR "lupus vasculitis"[tiab]) AND (kidney diseases[mh] OR "kidney disease*"[tiab] OR "kidney failure"[tiab] OR "renal failure"[tiab] OR "renal insufficiency"[tiab] OR "kidney insufficiency"[tiab] OR "kidney damage"[tiab] OR "renal damage"[tiab] OR "kidney impairment[tiab] OR "renal impairment"[tiab]))
Antihypertensive Agents[mh] OR antihypertensive*[tiab] OR anti-hypertensive*[tiab] OR adrenergic beta-antagonists[mh] OR adrenergic alpha antagonists[mh] OR angiotensin converting enzyme inhibitors[mh] OR ace inhibitor*[tiab] OR calcium channel blockers[mh] OR ganglionic blockers[mh] OR diuretics[mh] OR blood pressure lowering drug[tiab] OR blood pressure medicat*[tiab] OR angiotensin coverting enzyme inhibitor*[tiab] OR angiotensin receptor antagonist*[tiab] OR calcium channel blocker*[tiab] OR calcium channel antagonist*[tiab] OR beta blocker*[tiab] OR alpha blocker*[tiab] OR diuretic*[tiab] OR spironolactone[tiab] OR eplirone[tiab] OR clonidine[tiab] OR thiazide[tiab] OR methyldopa[tiab] OR hydralazine[tiab] OR aliskiren[tiab] OR antihypertensive agents[pa]

Embase:

'systemic lupus erythematosus'/exp OR 'systemic lupus erythematosus':ti,ab,kw 'antiphospholipid syndrome'/exp OR 'antiphospholipid syndrome':ti,ab,kw 'antihypertensive agent'/de OR 'dipeptidyl carboxypeptidase inhibitor'/de OR 'calcium channel blocking agent'/de OR 'spironolactone'/exp OR 'eplerenone'/exp OR 'clonidine'/exp OR 'diuretic agent'/de OR 'methyldopa'/exp OR 'hydralazine'/exp OR 'aliskiren'/exp OR 'antihypertensiv*':ti,ab,kw OR 'anti-hypertensiv*':ti,ab,kw OR 'blood pressure lowering drug*':ti,ab,kw OR 'blood pressure lowering agent*':ti,ab,kw OR 'blood pressure medicat*':ti,ab,kw OR 'angiotensin-converting enzyme inhibitor*':ti,ab,kw OR 'ace inhibit*':ti,ab,kw OR 'angiotensin receptor block*':ti,ab,kw OR 'angiotensin receptor antagon*':ti,ab,kw OR 'calcium channel block*':ti,ab,kw OR 'calcium channel antagon*':ti,ab,kw OR 'beta block*':ti,ab,kw OR 'alpha block*':ti,ab,kw OR 'diuretic*':ti,ab,kw OR 'spironolacton*':ti,ab,kw OR 'eplerenon*':ti,ab,kw OR 'clonidin*':ti,ab,kw OR 'methyldopa':ti,ab,kw OR 'hydralazin*':ti,ab,kw OR 'aliskiren*':ti,ab,kw 'cardiovascular disease'/exp OR 'angina pectoris':ti,ab,kw OR 'arrhythmi*':ti,ab,kw OR 'arrythmi*':ti,ab,kw OR 'dysrhythmi*':ti,ab,kw OR 'arteriosclero*':ti,ab,kw OR 'atherosclero*':ti,ab,kw OR 'blood pressure':ti,ab,kw OR 'cardiovascular disease*':ti,ab,kw OR 'cardiovascular event*':ti,ab,kw OR 'cardio-vascular event*':ti,ab,kw OR 'cerebrovascular disease*':ti,ab,kw OR 'coronary disease*':ti,ab,kw OR 'cvd':ti,ab,kw OR 'cvds':ti,ab,kw OR 'heart disease*':ti,ab,kw OR 'heart failure*':ti,ab,kw OR 'peripheral arterial disease*':ti,ab,kw OR 'peripheral artery disease*':ti,ab,kw OR 'peripheral vascular disease*':ti,ab,kw OR 'stroke*':ti,ab,kw

'lupus erythematosus nephritis'/exp OR 'lupus nephritis':ti,ab OR 'lupoid nephritis':ti,ab OR 'lupus nephropathy':ti,ab OR 'lupus glomerulonephritis':ti,ab OR ('systemic lupus erythematosus'/exp/mj OR 'systematic lupus erythematosus':ti,ab OR 'systemic lupus':ti,ab OR 'lupus erythematosus'/de OR 'lupus erythematosus':ti,ab OR 'disseminated lupus':ti,ab OR 'libman sacks':ti,ab OR 'lupus vasculitis':ti,ab) AND 'kidney disease'/exp/mj OR (((kidney* OR renal) NEAR/4 (failure OR damage* OR insufficiency OR impairment OR disease*)):ti,ab)
'antihypertensive agent'/exp OR 'beta adrenergic receptor blocking agent'/exp OR 'alpha adrenergic receptor blocking agent'/exp OR 'dipeptidyl carboxypeptidase inhibitor'/exp OR 'calcium channel blocking agent'/exp OR 'ganglion blocking agent'/exp OR 'diuretic agent'/exp OR 'anti hypertensive*':ti,ab OR 'ace inhibitor*':ti,ab OR 'blood pressure lowering drug*':ti,ab OR 'blood pressure medicat*':ti,ab OR 'angiotensin coverting enzyme inhibitor*':ti,ab OR 'angiotensin receptor antagonist*':ti,ab OR 'calcium channel blocker*':ti,ab OR 'calcium channel antagonist*':ti,ab OR 'beta blocker*':ti,ab OR 'alpha blocker*':ti,ab OR diuretic*:ti,ab OR spironolactone:ti,ab OR eplirone:ti,ab OR clonidine:ti,ab OR thiazide:ti,ab OR methyldopa:ti,ab OR hydralazine:ti,ab OR aliskiren:ti,ab
'hypertension'/exp/dm_dt,dm_th OR 'hypertension'/exp/mj OR 'blood pressure':ti,ab OR hypertens*:ti

Cochrane:

("systemic lupus erythematosus"):ti,ab,kw
("antiphospholipid syndrome"):ti,ab,kw
(“antihypertensiv*” OR “anti-hypertensiv*” OR “blood pressure lowering drug*” OR “blood pressure lowering agent*” OR “blood pressure medicat*” OR “angiotensin-converting enzyme inhibitor*” OR “ACE inhibit*” OR “angiotensin receptor block*” OR “angiotensin receptor antagon*” OR “calcium channel block*” OR “calcium channel antagon*” OR “beta block*” OR “alpha block*” OR “diuretic*” OR “spironolacton*” OR “eplerenon*” OR “clonidin*” OR “methyldopa” OR “hydralazin*” OR “aliskiren*”):ti,ab,kw
(“angina pectoris” OR “arrhythmi*” OR “arrythmi*” OR “dysrhythmi*” OR “arteriosclero*” OR “atherosclero*” OR “blood pressure” OR “cardiovascular disease*” OR “cardiovascular event*” OR “cardio-vascular event*” OR “cerebrovascular disease*” OR “coronary disease*” OR “cvd” OR “cvds” OR “heart disease*” OR “heart failure*” OR “peripheral arterial disease*” OR “peripheral artery disease*” OR “peripheral vascular disease*” OR “stroke*”):ti,ab,kw

[mh "lupus nephritis"] OR "lupus nephritis" OR "lupus glomerulonephritis" OR "lupoid nephritis" OR "lupus nephropathy" OR ([mh "lupus erythematosus, systemic"] OR "systemic lupus erythematosus" OR "lupus erythematosus" OR "libman sacks" OR "lupus vasculitis") AND ([mh "kidney diseases] OR ((kidney OR renal) NEAR/4 (damage OR insufficiency OR failure OR disease)))
[mh "Antihypertensive Agents"] OR anti-hypertensive* OR antihypertensive* OR [mh "adrenergic beta-antagonists"] OR [mh "adrenergic alpha antagonists"] OR [mh "angiotensin converting enzyme inhibitors"] OR "ace inhibitor*" OR [mh "calcium channel blockers"] OR [mh "ganglionic blockers"] OR [mh "diuretics"] OR "pressure lowering drug*" OR "blood pressure medicat*" OR "angiotensin coverting enzyme inhibitor*" OR "angiotensin receptor antagonist"ti,ab OR "calcium channel blocker*" OR "calcium channel antagonist*" OR "beta blocker*" OR "alpha blocker*" OR diuretic* OR spironolactone OR eplirone OR clonidine OR thiazide OR methyldopa

3) Lipid-lowering medications

Medline/PubMed:

(systemic lupus erythematosus[MeSH Terms]) OR "systemic lupus erythematosus"[Title/Abstract]
(antiphospholipid syndrome[MeSH Terms]) OR "antiphospholipid syndrome"[Title/Abstract]
("Hypolipidemic Agents"[Mesh:NoExp] OR "Hypolipidemic Agents" [Pharmacological Action] OR "Angiotensin-Converting Enzyme Inhibitors"[Mesh:NoExp] OR "Angiotensin-Converting Enzyme Inhibitors" [Pharmacological Action] OR "Ezetimibe"[Mesh] OR lipid lowering[tiab] OR statin*[tiab] OR ezetimibe[tiab] OR PCSK9[tiab])
("Arteriosclerosis"[Mesh] OR "Cardiovascular Diseases"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Stroke"[Mesh] OR angina pectoris[tiab] OR arrhythmi*[tiab] OR arrythmi*[tiab] OR dysrhythmi*[tiab] OR arteriosclero*[tiab] OR atherosclero*[tiab] OR blood pressure[tiab] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR cardio-vascular event*[tiab] OR cerebrovascular disease*[tiab] OR coronary disease*[tiab] OR cvd[tiab] OR cvds[tiab] OR heart disease*[tiab] OR heart failure*[tiab] OR peripheral arterial disease*[tiab] OR peripheral artery disease*[tiab] OR peripheral vascular disease*[tiab] OR stroke*[tiab])

Embase:

'systemic lupus erythematosus'/exp OR 'systemic lupus erythematosus':ti,ab,kw
'antiphospholipid syndrome'/exp OR 'antiphospholipid syndrome':ti,ab,kw
'antilipemic agent'/de OR 'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp OR 'ezetimibe'/exp OR 'lipid lowering':ti,ab,kw OR 'statin*':ti,ab,kw OR 'ezetimibe':ti,ab,kw OR 'pcsk9':ti,ab,kw
'cardiovascular disease'/exp OR 'angina pectoris':ti,ab,kw OR 'arrhythmi*':ti,ab,kw OR 'arrythmi*':ti,ab,kw OR 'dysrhythmi*':ti,ab,kw OR 'arteriosclero*':ti,ab,kw OR 'atherosclero*':ti,ab,kw OR 'blood pressure':ti,ab,kw OR 'cardiovascular disease*':ti,ab,kw OR 'cardiovascular event*':ti,ab,kw OR 'cardio-vascular event*':ti,ab,kw OR 'cerebrovascular disease*':ti,ab,kw OR 'coronary disease*':ti,ab,kw OR 'cvd':ti,ab,kw OR 'cvds':ti,ab,kw OR 'heart disease*':ti,ab,kw OR 'heart failure*':ti,ab,kw OR 'peripheral arterial disease*':ti,ab,kw OR 'peripheral artery disease*':ti,ab,kw OR 'peripheral vascular disease*':ti,ab,kw OR 'stroke*':ti,ab,kw

Cochrane:

("systemic lupus erythematosus"):ti,ab,kw
("antiphospholipid syndrome"):ti,ab,kw
(“lipid lowering” OR “statin*” OR “ezetimibe” OR “PCSK9”):ti,ab,kw
(“angina pectoris” OR “arrhythmi*” OR “arrythmi*” OR “dysrhythmi*” OR “arteriosclero*” OR “atherosclero*” OR “blood pressure” OR “cardiovascular disease*” OR “cardiovascular event*” OR “cardio-vascular event*” OR “cerebrovascular disease*” OR “coronary disease*” OR “cvd” OR “cvds” OR “heart disease*” OR “heart failure*” OR “peripheral arterial disease*” OR “peripheral artery disease*” OR “peripheral vascular disease*” OR “stroke*”):ti,ab,kw

4) Disease activity

Medline/PubMed:

(lupus erythematosus, systemic[mh] OR SLE[tiab] OR "systemic lupus erythematosus"[tiab] OR "lupus erythematosus"[tiab] OR "libman sacks"[tiab] OR "lupus nephritis"[tiab] OR "lupus vasculitis"[tiab] OR "lupus glomerulonephritis"[tiab])
("disease activity"[tiab] OR "lupus activity"[tiab] OR sle disease activity index*[tiab] OR "systemic lupus erythematosus disease activity"[tiab] OR "systemic lupus erythematosus

activity"[tiab] OR SLEDAI[tiab] OR "SLEDAI 2K"[tiab] OR "SELENA SLEDAI"[tiab] OR british isles lupus assessment*[tiab] OR BILAG[tiab] OR ECLAM[tiab] OR "European consensus lupus activity"[tiab] OR systemic lupus activity measure*[tiab] OR SLAM[tiab] OR systemic lupus activity questionnaire*[tiab])
(cardiovascular diseases[mh] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR CVD[tiab] OR coronary[tiab] OR cardiovascular[tiab] OR cardiac[tiab] OR heart*[tiab] OR heart disease*[tiab] OR cardiac disease*[tiab] OR "heart failure"[tiab] OR CHF[tiab] OR ((cardiac[tiab] OR heart[tiab] OR atrial[tiab] OR ventricular[tiab] OR sinus[tiab]) AND (arrhythmia*[tiab] OR flutter[tiab] OR block[tiab] OR tachycard*[tiab] OR fibrillat*[tiab] OR bradycard*[tiab] OR premature complex*[tiab])) OR myocardial infarct*[tiab] OR angina*[tiab] OR acute coronary syndrome*[tiab] OR coronary artery disease*[tiab] OR coronary stenos*[tiab] OR coronary thrombos*[tiab] OR (ischem*[tiab] AND (heart[tiab] OR coronary[tiab])) OR "coronary vasospasm"[tiab] OR coronary artery spasm*[tiab] OR myocardial stun*[tiab] OR stroke[mh] OR stroke[tiab] OR CVA[tiab] OR cerebrovascular accident*[tiab] OR brain ischemia[mh] OR brain ischemia*[tiab] OR brain infarct*[tiab] OR "transient ischemic attack"[tiab] OR TIA[tiab] OR atherosclerosis[tiab] OR peripheral 3 arterial disease*[tiab] OR coronary artery obstruction*[tiab] OR coronary artery thrombos*[tiab] OR peripheral occlusive artery disease*[tiab] OR "Coronary Stenosis"[Mesh] OR "Myocardial Stunning"[Mesh] OR "Coronary Vasospasm"[Mesh] OR "Atherosclerosis"[Mesh] OR "Peripheral Arterial Disease"[Mesh] OR "Coronary Thrombosis"[Mesh] OR "Brain Infarction"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Heart Diseases"[Mesh] OR "Myocardial Infarction"[Mesh])

Embase:

('systemic lupus erythematosus'/exp OR SLE:ti,ab OR "systemic lupus erythematosus":ti,ab OR "lupus erythematosus":ti,ab OR "libman sacks":ti,ab OR "lupus nephritis":ti,ab OR "lupus vasculitis":ti,ab OR "lupus glomerulonephritis":ti,ab)
('disease activity'/exp OR 'disease activity index'/exp OR 'disease activity score'/exp OR 'SLEDAI'/exp OR 'british isles lupus assessment group index'/exp OR 'european consensus lupus activity measurement'/exp OR 'systemic lupus activity measure'/exp OR 'systemic lupus activity questionnaire'/exp OR "disease activity":ti,ab OR "lupus activity":ti,ab OR “sle disease activity index”:ti,ab OR “sle disease activity indexes”:ti,ab OR "systemic lupus erythematosus disease activity":ti,ab OR "systemic lupus erythematosus activity":ti,ab OR SLEDAI:ti,ab OR "SLEDAI 2K":ti,ab OR "SELENA SLEDAI":ti,ab OR “british isles lupus assessment”:ti,ab OR “british isles lupus assessments”:ti,ab OR BILAG:ti,ab OR ECLAM:ti,ab OR "European consensus lupus activity":ti,ab OR “systemic lupus activity measure”:ti,ab OR “systemic lupus activity measures”:ti,ab OR “systemic lupus activity measurement”:ti,ab OR “systemic lupus activity measurements”:ti,ab OR SLAM:ti,ab OR “systemic lupus activity questionnaire”:ti,ab OR “systemic lupus activity questionnaires”:ti,ab)
('cardiovascular disease'/exp OR “cardiovascular disease”:ti,ab OR “cardiovascular diseases”:ti,ab OR “cardiovascular event”:ti,ab OR “cardiovascular events”:ti,ab OR CVD:ti,ab OR coronary:ti,ab OR cardiovascular:ti,ab OR cardiac:ti,ab OR heart*:ti,ab OR “heart disease”:ti,ab OR 'heart disease'/exp 5 OR “heart diseases”:ti,ab OR “cardiac disease”:ti,ab OR “cardiac diseases”:ti,ab OR "heart failure":ti,ab OR "heart failures":ti,ab OR CHF:ti,ab OR ((cardiac:ti,ab OR heart:ti,ab OR atrial:ti,ab OR ventricular:ti,ab OR sinus:ti,ab) AND (arrhythmia*:ti,ab OR flutter:ti,ab OR block:ti,ab OR tachycard*:ti,ab OR fibrillat*:ti,ab OR bradycard*:ti,ab OR “premature complex”:ti,ab OR “premature complexes”:ti,ab)) OR “myocardial infarct”:ti,ab OR “myocardial infarcts”:ti,ab OR “myocardial infarction”:ti,ab OR “myocardial infarctions”:ti,ab OR 'angina pectoris'/exp OR angina*:ti,ab OR “acute coronary syndrome”:ti,ab OR “acute coronary syndromes”:ti,ab OR 'acute coronary syndrome'/exp OR “coronary artery disease”:ti,ab OR “coronary artery diseases”:ti,ab OR 'coronary artery disease'/exp OR 'coronary artery obstruction'/exp OR “coronary stenosis”:ti,ab OR “coronary

stenoses":ti,ab OR "coronary thrombosis":ti,ab OR "coronary thromboses":ti,ab OR 'coronary artery thrombosis'/exp OR (ischem*:ti,ab AND (heart:ti,ab OR coronary:ti,ab)) OR "coronary vasospasm":ti,ab OR "coronary vasospasms":ti,ab OR 'coronary artery spasm'/exp OR "myocardial stunning":ti,ab OR stroke:ti,ab OR CVA:ti,ab OR 'cerebrovascular accident'/exp OR "cerebrovascular accident":ti,ab OR "cerebrovascular accidents":ti,ab OR "brain ischemia":ti,ab OR 'brain ischemia'/exp OR "brain infarct":ti,ab OR "brain infarcts":ti,ab OR "brain infarction":ti,ab OR "brain infarctions":ti,ab OR 'transient ischemic attack'/exp OR "transient ischemic attack":ti,ab OR "transient ischemic attacks":ti,ab OR TIA:ti,ab OR 'atherosclerosis'/exp OR atherosclerosis:ti,ab OR "peripheral arterial disease":ti,ab OR "peripheral arterial diseases":ti,ab OR 'peripheral occlusive artery disease'/exp)

Cochrane:

[mh "lupus erythematosus, systemic"]
(SLE OR "systemic lupus erythematosus" OR "lupus erythematosus" OR "libman sacks" OR "lupus nephritis" OR "lupus vasculitis" OR "lupus glomerulonephritis"):ti,ab,kw
("disease activity" OR "lupus activity" OR "sle disease activity index" OR "sle disease activity indexes" OR "systemic lupus erythematosus disease activity" OR "systemic lupus erythematosus activity" OR SLEDAI OR "SLEDAI 2K" OR "SELENA SLEDAI" OR "british isles lupus assessment" OR "british isles lupus assessments" OR BILAG OR ECLAM OR "European consensus lupus activity" OR "systemic lupus activity measure" OR "systemic lupus activity measures" OR "systemic lupus activity measurement" OR "systemic lupus activity measurements" OR SLAM OR "systemic lupus activity questionnaire" OR "systemic lupus activity questionnaires"):ti,ab,kw
("cardiovascular diseases" OR "cardiovascular disease" OR "cardiovascular event" OR "cardiovascular events" OR CVD OR coronary OR cardiovascular OR cardiac OR heart* OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "heart failure" OR CHF OR ((cardiac OR heart OR atrial OR ventricular OR sinus) AND (arrhythmia* OR flutter OR block OR tachycard* OR fibrillat* OR bradycard* OR premature complex*)) OR "myocardial infarct" OR "myocardial infarcts" OR "myocardial infarction" OR "myocardial infarctions" OR angina* OR "acute coronary syndrome" OR "acute coronary syndromes" OR "coronary artery disease" OR "coronary artery diseases" OR "coronary stenosis" OR "coronary 7 stenoses" OR "coronary thrombosis" OR "coronary thromboses" OR (ischem* AND (heart OR coronary)) OR "coronary vasospasm" OR "coronary vasospasms" OR "coronary artery spasm" OR "coronary artery spasms" OR "myocardial stunning" OR stroke OR CVA OR "cerebrovascular accident" OR "cerebrovascular accidents" OR "brain ischemia" OR "brain ischemias" OR "brain infarct" OR "brain infarcts" OR "brain infarction" OR "brain infarctions" OR "transient ischemic attack" OR TIA OR atherosclerosis OR "peripheral arterial disease" OR "peripheral arterial diseases" OR "coronary artery obstruction" OR "coronary artery obstructions" OR "coronary artery thrombosis" OR "coronary artery thromboses" OR "peripheral occlusive artery disease" OR "peripheral occlusive artery diseases"):ti,ab,kw
([mh stroke] OR [mh "cardiovascular diseases"] OR [mh "Coronary Stenosis"] OR [mh "Myocardial Stunning"] OR [mh "Coronary Vasospasm"] OR [mh "Atherosclerosis"] OR [mh "Peripheral Arterial Disease"] OR [mh "Coronary Thrombosis"] OR [mh "Brain Infarction"] OR [mh "Acute Coronary Syndrome"] OR [mh "Heart Diseases"] OR [mh "Myocardial Infarction"] OR [mh "brain ischemia"])

5) Glucocorticoids

Medline/PubMed:

(lupus erythematosus, systemic[mh] OR SLE[tiab] OR "systemic lupus erythematosus"[tiab] OR "lupus erythematosus"[tiab] OR "libman sacks"[tiab] OR "lupus nephritis"[tiab] OR "lupus vasculitis"[tiab] OR "lupus glomerulonephritis"[tiab])
(((low[tiab] OR lower*[tiab] OR daily[tiab] OR mean[tiab] OR average[tiab] OR cumulative[tiab]) AND (dose*[tiab] OR dosing[tiab] OR dosage*[tiab] OR use*[tiab])) AND (corticosteroid[tw] OR corticosteroids[tw] OR glucocorticoid[tw] OR glucocorticoids[tw] OR prednisone[tw] OR prednisolone[tw] OR methylprednisolone[tw] OR Metipred[tw] OR Urbason[tw] OR Medrol[tw] OR Predate[tw] OR Predonine[tw] OR Dehydrocortisone[tw] OR delta-Cortisone[tw] OR Rectodelt[tw] OR Prednison Hexal[tw] OR Sterapred[tw] OR Ultracorten[tw] OR Winpred[tw] OR Apo-Prednisone[tw] OR Cortan[tw] OR Cortancyl[tw] OR Panafcort[tw] OR Decortin[tw] OR Dacortin[tw] OR Decortisyl[tw] OR Deltasone[tw] OR Encortone[tw] OR Encorton[tw] OR “Liquid Pred”[tw] OR Meticorten[tw] OR Orasone[tw] OR Panasol[tw] OR Prednidib[tw] OR Pronisone[tw] OR Sone[tw] OR "Adrenal Cortex Hormones"[Mesh] OR "Glucocorticoids"[Mesh] OR "Prednisone"[Mesh] OR "Glucocorticoids" [Pharmacological Action] OR "Prednisolone"[Mesh] OR "Methylprednisolone"[Mesh])
(cumulative corticosteroid use*[tiab] OR cumulative corticosteroid dos*[tiab] OR cumulative corticosteroid exposure*[tiab] OR cumulative glucocorticoid use*[tiab] OR cumulative glucocorticoid dos*[tiab] OR cumulative glucocorticoid exposure*[tiab] OR daily corticosteroid dose*[tiab] OR daily glucocorticoid dos*[tiab] OR mean corticosteroid dos*[tiab] OR mean glucocorticoid dos*[tiab])
(cardiovascular diseases[mh] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR CVD[tiab] OR coronary[tiab] OR cardiovascular[tiab] OR cardiac[tiab] OR heart*[tiab] OR heart disease*[tiab] OR cardiac disease*[tiab] OR "heart failure"[tiab] OR CHF[tiab] OR ((cardiac[tiab] OR heart[tiab] OR atrial[tiab] OR ventricular[tiab] OR sinus[tiab]) AND (arrhythmia*[tiab] OR flutter[tiab] OR block[tiab] OR tachycard*[tiab] OR fibrillat*[tiab] OR bradycard*[tiab] OR premature complex*[tiab])) OR myocardial infarct*[tiab] OR angina*[tiab] OR acute coronary syndrome*[tiab] OR coronary artery disease*[tiab] OR coronary stenos*[tiab] OR coronary thrombos*[tiab] OR (ischem*[tiab] AND (heart[tiab] OR coronary[tiab])) OR "coronary vasospasm"[tiab] OR coronary artery spasm*[tiab] OR myocardial stun*[tiab] OR stroke[mh] OR stroke[tiab] OR CVA[tiab] OR cerebrovascular accident*[tiab] OR brain ischemia[mh] OR brain ischemia*[tiab] OR brain infarct*[tiab] OR "transient ischemic attack"[tiab] OR TIA[tiab] OR atherosclerosis[tiab] OR peripheral arterial disease*[tiab] OR coronary artery obstruction*[tiab] OR coronary artery thrombos*[tiab] OR peripheral occlusive artery disease*[tiab] OR "Coronary Stenosis"[Mesh] OR "Myocardial Stunning"[Mesh] OR "Coronary Vasospasm"[Mesh] OR "Atherosclerosis"[Mesh] OR "Peripheral Arterial Disease"[Mesh] OR "Coronary Thrombosis"[Mesh] OR "Brain Infarction"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Heart Diseases"[Mesh] OR "Myocardial Infarction"[Mesh])

Embase:

('systemic lupus erythematosus'/exp OR SLE:ti,ab OR "systemic lupus erythematosus":ti,ab OR "lupus erythematosus":ti,ab OR "libman sacks":ti,ab OR "lupus nephritis":ti,ab OR "lupus vasculitis":ti,ab OR "lupus glomerulonephritis":ti,ab)
((low:ti,ab OR lower*:ti,ab OR daily:ti,ab OR mean:ti,ab OR average:ti,ab OR cumulative:ti,ab) AND (dose*:ti,ab OR dosing:ti,ab OR dosage*:ti,ab OR use*:ti,ab) AND (corticosteroid:ti,ab OR corticosteroids:ti,ab OR glucocorticoid:ti,ab OR glucocorticoids:ti,ab OR prednisone:ti,ab OR prednisolone:ti,ab OR methylprednisolone:ti,ab OR Metipred:ti,ab OR Urbason:ti,ab OR Medrol:ti,ab OR Predate:ti,ab OR Predonine:ti,ab OR Dehydrocortisone:ti,ab OR delta-Cortisone:ti,ab OR Rectodelt:ti,ab OR “Prednison Hexal”:ti,ab OR Sterapred:ti,ab OR Ultracorten:ti,ab OR Winpred:ti,ab OR “Apo-Prednisone”:ti,ab OR Cortan:ti,ab OR Cortancyl:ti,ab OR Panafcort:ti,ab OR Decortin:ti,ab OR Dacortin:ti,ab OR Decortisyl:ti,ab OR Deltasone:ti,ab OR Encortone:ti,ab OR Encorton:ti,ab OR “Liquid Pred”:ti,ab OR

Meticorten:ti,ab OR Orasone:ti,ab OR Panasol:ti,ab OR Prednidib:ti,ab OR 6 Pronisone:ti,ab OR Sone:ti,ab OR 'glucocorticoid'/exp OR 'corticosteroid'/exp OR 'prednisone'/exp OR 'prednisolone'/exp OR 'methylprednisolone'/exp))
(“cumulative corticosteroid use”:ti,ab OR “cumulative corticosteroid uses”:ti,ab OR “cumulative corticosteroid dose”:ti,ab OR “cumulative corticosteroid doses”:ti,ab OR “cumulative corticosteroid exposure”:ti,ab OR “cumulative corticosteroid exposures”:ti,ab OR “cumulative glucocorticoid use”:ti,ab OR “cumulative glucocorticoid uses”:ti,ab OR “cumulative glucocorticoid dose”:ti,ab OR “cumulative glucocorticoid doses”:ti,ab OR “cumulative glucocorticoid exposure”:ti,ab OR “cumulative glucocorticoid exposures”:ti,ab OR “daily corticosteroid dose”:ti,ab OR “daily corticosteroid doses”:ti,ab OR “daily glucocorticoid dose”:ti,ab OR “daily glucocorticoid doses”:ti,ab OR “mean corticosteroid dose”:ti,ab OR “mean corticosteroid doses”:ti,ab OR “mean glucocorticoid dose”:ti,ab OR “mean glucocorticoid doses”:ti,ab)
('cardiovascular disease'/exp OR “cardiovascular disease”:ti,ab OR “cardiovascular diseases”:ti,ab OR “cardiovascular event”:ti,ab OR “cardiovascular events”:ti,ab OR CVD:ti,ab OR coronary:ti,ab OR cardiovascular:ti,ab OR cardiac:ti,ab OR heart*:ti,ab OR “heart disease”:ti,ab OR 'heart disease'/exp OR “heart diseases”:ti,ab OR “cardiac disease”:ti,ab OR “cardiac diseases”:ti,ab OR "heart failure":ti,ab OR "heart failures":ti,ab OR CHF:ti,ab OR ((cardiac:ti,ab OR heart:ti,ab OR atrial:ti,ab OR ventricular:ti,ab OR sinus:ti,ab) AND (arrhythmia*:ti,ab OR flutter:ti,ab OR block:ti,ab OR tachycard*:ti,ab OR fibrillat*:ti,ab OR bradycard*:ti,ab OR “premature complex”:ti,ab OR “premature complexes”:ti,ab)) OR “myocardial infarct”:ti,ab OR “myocardial infarcts”:ti,ab OR “myocardial infarction”:ti,ab OR “myocardial infarctions”:ti,ab OR 'angina pectoris'/exp OR angina*:ti,ab OR “acute coronary syndrome”:ti,ab OR “acute coronary syndromes”:ti,ab OR 'acute coronary syndrome'/exp OR “coronary artery disease”:ti,ab OR “coronary artery diseases”:ti,ab OR 'coronary artery disease'/exp OR 'coronary artery obstruction'/exp OR “coronary stenosis”:ti,ab OR “coronary stenoses”:ti,ab OR “coronary thrombosis”:ti,ab OR “coronary thromboses”:ti,ab OR 'coronary artery thrombosis'/exp OR (ischem*:ti,ab AND (heart:ti,ab OR coronary:ti,ab)) OR "coronary vasospasm":ti,ab OR "coronary vasospasms":ti,ab OR 'coronary artery spasm'/exp OR “myocardial stunning”:ti,ab OR stroke:ti,ab OR CVA:ti,ab OR 'cerebrovascular accident'/exp OR “cerebrovascular accident”:ti,ab OR “cerebrovascular accidents”:ti,ab OR “brain ischemia”:ti,ab OR 'brain ischemia'/exp OR “brain infarct”:ti,ab OR “brain infarcts”:ti,ab OR “brain infarction”:ti,ab OR “brain infarctions”:ti,ab OR 'transient ischemic attack'/exp OR "transient ischemic attack":ti,ab OR "transient ischemic attacks":ti,ab OR TIA:ti,ab OR 'atherosclerosis'/exp OR atherosclerosis:ti,ab OR “peripheral arterial disease”:ti,ab OR “peripheral arterial diseases”:ti,ab OR 'peripheral occlusive artery disease'/exp)

Cochrane:

[mh “lupus erythematosus, systemic”]
(SLE OR "systemic lupus erythematosus" OR "lupus erythematosus" OR "libman sacks" OR "lupus nephritis" OR "lupus vasculitis" OR "lupus glomerulonephritis"):ti,ab,kw
((low OR lower* OR daily OR mean OR average OR cumulative) AND (dose* OR dosing OR dosage* OR use*) AND (corticosteroid OR corticosteroids OR glucocorticoid OR glucocorticoids OR prednisone OR prednisolone OR methylprednisolone)):ti,ab,kw
(Metipred OR Urbason OR Medrol OR Predate OR Predonine OR Dehydrocortisone OR deltaCortisone OR Rectodelt OR “Prednison Hexal” OR Sterapred OR Ultracorten OR Winpred OR Apo-Prednisone OR Cortan OR Cortancyl OR Panafcort OR Decortin OR Dacortin OR Decortisyl OR Deltasone OR Encortone OR Encorton OR “Liquid Pred” OR Meticorten OR Orasone OR Panasol OR Prednidib OR Pronisone OR Sone):ti,ab,kw
([mh "Adrenal Cortex Hormones"] OR [mh "Glucocorticoids"] OR [mh "Prednisone"] OR [mh "Prednisolone"] OR [mh "Methylprednisolone"])

("cumulative corticosteroid use" OR "cumulative corticosteroid uses" OR "cumulative corticosteroid dose" OR "cumulative corticosteroid doses" OR "cumulative corticosteroid exposure" OR "cumulative corticosteroid exposures" OR "cumulative glucocorticoid use" OR "cumulative glucocorticoid uses" OR "cumulative glucocorticoid dose" OR "cumulative glucocorticoid doses" OR "cumulative glucocorticoid exposure" OR "cumulative glucocorticoid exposures" OR "daily corticosteroid dose" OR "daily corticosteroid doses" OR "daily glucocorticoid dose" OR "daily glucocorticoid doses" OR "mean corticosteroid dose" OR "mean corticosteroid doses" OR "mean glucocorticoid dose" OR "mean glucocorticoid doses"):ti,ab,kw
("cardiovascular diseases" OR "cardiovascular disease" OR "cardiovascular event" OR "cardiovascular events" OR CVD OR coronary OR cardiovascular OR cardiac OR heart* OR "heart disease" OR "heart diseases" OR "cardiac disease" OR "cardiac diseases" OR "heart 9 failure" OR CHF OR ((cardiac OR heart OR atrial OR ventricular OR sinus) AND (arrhythmia* OR flutter OR block OR tachycard* OR fibrillat* OR bradycard* OR premature complex*)) OR "myocardial infarct" OR "myocardial infarcts" OR "myocardial infarction" OR "myocardial infarctions" OR angina* OR "acute coronary syndrome" OR "acute coronary syndromes" OR "coronary artery disease" OR "coronary artery diseases" OR "coronary stenosis" OR "coronary stenoses" OR "coronary thrombosis" OR "coronary thromboses" OR (ischem* AND (heart OR coronary)) OR "coronary vasospasm" OR "coronary vasospasms" OR "coronary artery spasm" OR "coronary artery spasms" OR "myocardial stunning" OR stroke OR CVA OR "cerebrovascular accident" OR "cerebrovascular accidents" OR "brain ischemia" OR "brain ischemias" OR "brain infarct" OR "brain infarcts" OR "brain infarction" OR "brain infarctions" OR "transient ischemic attack" OR TIA OR atherosclerosis OR "peripheral arterial disease" OR "peripheral arterial diseases" OR "coronary artery obstruction" OR "coronary artery obstructions" OR "coronary artery thrombosis" OR "coronary artery thromboses" OR "peripheral occlusive artery disease" OR "peripheral occlusive artery diseases"):ti,ab,kw
([mh stroke] OR [mh "cardiovascular diseases"] OR [mh "Coronary Stenosis"] OR [mh "Myocardial Stunning"] OR [mh "Coronary Vasospasm"] OR [mh "Atherosclerosis"] OR [mh "Peripheral Arterial Disease"] OR [mh "Coronary Thrombosis"] OR [mh "Brain Infarction"] OR [mh "Acute Coronary Syndrome"] OR [mh "Heart Diseases"] OR [mh "Myocardial Infarction"] OR [mh "brain ischemia"])

6) Immunosuppressives

Medline/PubMed:

(lupus erythematosus, systemic[mh] OR SLE[tiab] OR "systemic lupus erythematosus"[tiab] OR "lupus erythematosus"[tiab] OR "libman sacks"[tiab] OR "lupus nephritis"[tiab] OR "lupus vasculitis"[tiab] OR "lupus glomerulonephritis"[tiab])
(antirheumatic drug*[tiab] OR antirheumatic agent*[tiab] OR anti rheumatic drug*[tiab] OR anti rheumatic agent*[tiab] OR immunosuppressant*[tw] OR immunosuppressive*[tiab] OR azathioprine[tw] OR Azothioprine[tw] OR Imurel[tw] OR Imuran[tw] OR Immuran[tw] OR methotrexate[tw] OR Amethopterin[tw] OR mycophenolate acid*[tiab] OR "Mycophenolate Mofetil"[tw] OR Cellcept[tw] OR Myfortic[tw] OR "Mycophenolate Sodium"[tw] OR cyclophosphamide*[tw] OR Sendoxan[tw] OR "Cyclophosphamide Anhydrous"[tw] OR Cytophosphane[tw] OR "Cyclophosphamide Monohydrate"[tw] OR Cytophosphan[tw] OR Cytoxan[tw] OR Endoxan[tw] OR Neosar[tw] OR Procytox[tw] OR Cyclophosphane[tw] OR cyclosporine[tiab] OR Ciclosporin[tw] OR Cyclosporin[tw] OR Neoral[tw] OR Sandimmune[tw] OR Sandimmun[tw] OR rituximab[tiab] OR Rituxan[tw] OR Mabthera[tw] OR belimumab[tiab] OR Benlysta[tw] OR LymphoStat-B[tw] OR monoclonal antibod*[tiab] OR "Antirheumatic Agents"[Mesh] OR "Immunosuppressive Agents"[Mesh] OR "Immunosuppressive Agents"[Pharmacological Action] OR "Azathioprine"[Mesh] OR "Methotrexate"[Mesh] OR

"Mycophenolic Acid"[Mesh] OR "Cyclophosphamide"[Mesh] OR "Cyclosporine"[Mesh] OR "Rituximab"[Mesh] OR "belimumab" [Supplementary Concept] OR "Antibodies, Monoclonal"[Mesh])
(cardiovascular diseases[mh] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR CVD[tiab] OR coronary[tiab] OR cardiovascular[tiab] OR cardiac[tiab] OR heart*[tiab] OR heart disease*[tiab] OR cardiac disease*[tiab] OR "heart failure"[tiab] OR CHF[tiab] OR ((cardiac[tiab] OR heart[tiab] OR atrial[tiab] OR ventricular[tiab] OR sinus[tiab]) AND (arrhythmia*[tiab] OR flutter[tiab] OR block[tiab] OR tachycard*[tiab] OR fibrillat*[tiab] OR bradycard*[tiab] OR premature complex*[tiab])) OR myocardial infarct*[tiab] OR angina*[tiab] OR acute coronary syndrome*[tiab] OR coronary artery disease*[tiab] OR coronary stenos*[tiab] OR coronary thrombos*[tiab] OR (ischem*[tiab] AND (heart[tiab] OR coronary[tiab])) OR "coronary vasospasm"[tiab] OR coronary artery spasm*[tiab] OR myocardial stun*[tiab] OR stroke[mh] OR stroke[tiab] OR CVA[tiab] OR cerebrovascular accident*[tiab] OR brain ischemia[mh] OR brain ischemia*[tiab] OR brain infarct*[tiab] OR "transient ischemic attack"[tiab] OR TIA[tiab] OR atherosclerosis[tiab] OR peripheral arterial disease*[tiab] OR coronary artery obstruction*[tiab] OR coronary artery thrombos*[tiab] OR peripheral occlusive artery disease*[tiab] OR "Coronary Stenosis"[Mesh] OR "Myocardial Stunning"[Mesh] OR "Coronary Vasospasm"[Mesh] OR "Atherosclerosis"[Mesh] OR "Peripheral Arterial Disease"[Mesh] OR "Coronary Thrombosis"[Mesh] OR "Brain Infarction"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Heart Diseases"[Mesh] OR "Myocardial Infarction"[Mesh])

Embase:

('systemic lupus erythematosus'/exp OR SLE:ti,ab OR "systemic lupus erythematosus":ti,ab OR "lupus erythematosus":ti,ab OR "libman sacks":ti,ab OR "lupus nephritis":ti,ab OR "lupus vasculitis":ti,ab OR "lupus glomerulonephritis":ti,ab)
('antirheumatic agent'/exp OR 'immunosuppressive agent'/exp OR 'azathioprine'/exp OR 'methotrexate'/exp OR 'mycophenolic acid'/exp OR 'cyclophosphamide'/exp OR 'cyclosporine'/exp OR 'rituximab'/exp OR 'mycophenolate mofetil'/exp OR 'belimumab'/exp OR 'monoclonal antibody'/exp OR “antirheumatic drug”:ti,ab OR “antirheumatic drugs”:ti,ab OR “antirheumatic agent”:ti,ab OR “antirheumatic agents”:ti,ab OR “anti rheumatic drug”:ti,ab OR “anti rheumatic drugs”:ti,ab OR “anti rheumatic agent”:ti,ab OR “anti rheumatic agents”:ti,ab OR immunosuppressant*:ti,ab OR immunosuppressive*:ti,ab OR azathioprine:ti,ab OR Azothioprine:ti,ab OR Imurel:ti,ab OR Imuran:ti,ab OR Immuran:ti,ab OR methotrexate:ti,ab OR Amethopterin:ti,ab OR “mycophenolate acid”:ti,ab OR “mycophenolate acids”:ti,ab OR “Mycophenolate Mofetil”:ti,ab OR Cellcept:ti,ab OR Myfortic:ti,ab OR “Mycophenolate Sodium”:ti,ab OR cyclophosphamide*:ti,ab OR Sendoxan:ti,ab OR “Cyclophosphamide Anhydrous”:ti,ab OR Cytophosphane:ti,ab OR “Cyclophosphamide Monohydrate”:ti,ab OR Cytophosphan:ti,ab OR Cytoxan:ti,ab OR Endoxan:ti,ab OR Neosar:ti,ab OR Procytox:ti,ab OR Cyclophosphane:ti,ab OR cyclosporine:ti,ab OR Ciclosporin:ti,ab OR Cyclosporin:ti,ab OR Neoral:ti,ab OR Sandimmune:ti,ab OR Sandimmun:ti,ab OR rituximab:ti,ab OR Rituxan:ti,ab OR Mabthera:ti,ab OR belimumab:ti,ab OR Benlysta:ti,ab OR LymphoStat-B:ti,ab OR “monoclonal antibody”:ti,ab OR “monoclonal antibodies”:ti,ab)
('cardiovascular disease'/exp OR “cardiovascular disease”:ti,ab OR “cardiovascular diseases”:ti,ab OR “cardiovascular event”:ti,ab OR “cardiovascular events”:ti,ab OR CVD:ti,ab OR coronary:ti,ab OR cardiovascular:ti,ab OR cardiac:ti,ab OR heart*:ti,ab OR “heart disease”:ti,ab OR 'heart disease'/exp OR “heart diseases”:ti,ab OR “cardiac disease”:ti,ab OR “cardiac diseases”:ti,ab OR "heart failure":ti,ab OR "heart failures":ti,ab OR CHF:ti,ab OR ((cardiac:ti,ab OR heart:ti,ab OR atrial:ti,ab OR ventricular:ti,ab OR sinus:ti,ab) AND (arrhythmia*:ti,ab OR flutter:ti,ab OR block:ti,ab OR tachycard*:ti,ab OR fibrillat*:ti,ab OR bradycard*:ti,ab OR “premature complex”:ti,ab OR “premature complexes”:ti,ab)) OR

“myocardial infarct”:ti,ab OR “myocardial infarcts”:ti,ab OR “myocardial infarction”:ti,ab OR “myocardial infarctions”:ti,ab OR 'angina pectoris'/exp OR angina*:ti,ab OR “acute coronary syndrome”:ti,ab OR “acute coronary syndromes”:ti,ab OR 'acute coronary syndrome'/exp OR “coronary artery disease”:ti,ab OR “coronary artery diseases”:ti,ab OR 'coronary artery disease'/exp OR 'coronary artery obstruction'/exp OR “coronary stenosis”:ti,ab OR “coronary stenoses”:ti,ab OR “coronary thrombosis”:ti,ab OR “coronary thromboses”:ti,ab OR 'coronary artery thrombosis'/exp OR (ischem*:ti,ab AND (heart:ti,ab OR coronary:ti,ab)) OR "coronary vasospasm":ti,ab OR "coronary vasospasms":ti,ab OR 'coronary artery spasm'/exp OR “myocardial stunning”:ti,ab OR stroke:ti,ab OR CVA:ti,ab OR 'cerebrovascular accident'/exp OR “cerebrovascular accident”:ti,ab OR “cerebrovascular accidents”:ti,ab OR “brain ischemia”:ti,ab OR 'brain ischemia'/exp OR “brain infarct”:ti,ab OR “brain infarcts”:ti,ab OR “brain infarction”:ti,ab OR “brain infarctions”:ti,ab OR 'transient ischemic attack'/exp OR "transient ischemic attack":ti,ab OR "transient ischemic attacks":ti,ab OR TIA:ti,ab OR 'atherosclerosis'/exp OR atherosclerosis:ti,ab OR “peripheral arterial disease”:ti,ab OR “peripheral arterial diseases”:ti,ab OR 'peripheral occlusive artery disease'/exp)

Cochrane:

[mh “lupus erythematosus, systemic”]
(SLE OR "systemic lupus erythematosus" OR "lupus erythematosus" OR "libman sacks" OR "lupus nephritis" OR "lupus vasculitis" OR "lupus glomerulonephritis"):ti,ab,kw
(“antirheumatic drug” OR “antirheumatic drugs” OR “antirheumatic agent” OR “antirheumatic agents” OR “anti rheumatic drug” OR “anti rheumatic drugs” OR “anti rheumatic agent” OR “anti rheumatic agents” OR immunosuppressant* OR immunosuppressive* OR azathioprine OR Azothioprine OR Imurel OR Imuran OR Immuran OR methotrexate OR Amethopterin OR “mycophenolate acid” OR “mycophenolate acids” OR “Mycophenolate Mofetil” OR Cellcept OR Myfortic OR “Mycophenolate Sodium” OR cyclophosphamide* OR Sendoxan OR “Cyclophosphamide Anhydrous” OR Cytophosphane OR “Cyclophosphamide Monohydrate” OR Cytophosphan OR Cytoxan OR Endoxan OR Neosar OR Procytox OR Cyclophosphane OR cyclosporine OR Ciclosporin OR Cyclosporin OR Neoral OR Sandimmune OR Sandimmun OR rituximab OR Rituxan OR Mabthera OR belimumab OR Benlysta OR LymphoStat-B OR “monoclonal antibody” OR “monoclonal antibodies”):ti,ab,kw
([mh "Antirheumatic Agents"] OR [mh "Immunosuppressive Agents"] OR [mh "Azathioprine"] OR [mh "Methotrexate"] OR [mh "Mycophenolic Acid"] OR [mh "Cyclophosphamide"] OR [mh "Cyclosporine"] OR [mh "Rituximab"] OR [mh "Antibodies, Monoclonal"])
(“cardiovascular diseases” OR “cardiovascular disease” OR “cardiovascular event” OR “cardiovascular events” OR CVD OR coronary OR cardiovascular OR cardiac OR heart* OR “heart disease” OR “heart diseases” OR “cardiac disease” OR “cardiac diseases” OR “heart failure” OR CHF OR ((cardiac OR heart OR atrial OR ventricular OR sinus) AND (arrhythmia* OR flutter OR block OR tachycard* OR fibrillat* OR bradycard* OR premature complex*)) OR “myocardial infarct” OR “myocardial infarcts” OR “myocardial infarction” OR “myocardial infarctions” OR angina* OR “acute coronary syndrome” OR “acute coronary syndromes” OR “coronary artery disease” OR “coronary artery diseases” OR “coronary stenosis” OR “coronary stenoses” OR “coronary thrombosis” OR “coronary thromboses” OR (ischem* AND (heart OR coronary)) OR “coronary vasospasm” OR “coronary vasospasms” OR “coronary artery spasm” OR “coronary artery spasms” OR “myocardial stunning” OR stroke OR CVA OR “cerebrovascular accident” OR “cerebrovascular accidents” OR “brain ischemia” OR “brain ischemias” OR “brain infarct” OR “brain infarcts” OR “brain infarction” OR “brain infarctions” OR "transient ischemic attack" OR TIA OR atherosclerosis OR “peripheral arterial disease” OR “peripheral arterial diseases” OR “coronary artery obstruction” OR “coronary artery obstructions” OR “coronary artery thrombosis” OR “coronary artery thromboses” OR “peripheral occlusive artery disease” OR “peripheral occlusive artery diseases”):ti,ab,kw

([mh stroke] OR [mh “cardiovascular diseases”] OR [mh "Coronary Stenosis"] OR [mh "Myocardial Stunning"] OR [mh "Coronary Vasospasm"] OR [mh "Atherosclerosis"] OR [mh "Peripheral Arterial Disease"] OR [mh "Coronary Thrombosis"] OR [mh "Brain Infarction"] OR [mh "Acute Coronary Syndrome"] OR [mh "Heart Diseases"] OR [mh "Myocardial Infarction"] OR [mh “brain ischemia”])

7) Antimalarials

Medline/PubMed:

(lupus erythematosus, systemic[mh] OR SLE[tiab] OR "systemic lupus erythematosus"[tiab] OR "lupus erythematosus"[tiab] OR "libman sacks"[tiab] OR "lupus nephritis"[tiab] OR "lupus vasculitis"[tiab] OR "lupus glomerulonephritis"[tiab])
(Antiphospholipid syndrome[mh] OR antibodies, antiphospholipid[mh] OR “hughes syndrome”[tiab] OR “antiphospholipid antibody syndrome”[tiab] OR “anti-phospholipid syndrome”[tiab] OR “antiphospholipid antibody syndrome”[tiab] OR antiphospholipid antibod*[tiab])
("Antimalarials"[Mesh] OR "Antimalarials"[Pharmacological Action] OR "Chloroquine"[Mesh] OR "Hydroxychloroquine"[Mesh] OR "Artemisinins"[Mesh] OR "artemisinine"[Supplementary Concept] OR antimalarial[tiab] OR “anti malarial”[tiab] OR antimalarials[tiab] OR “anti malarials”[tw] OR “Antimalarial Agents”[tiab] OR “antimalarial agent”[tiab] OR “anti malarial agents”[tiab] OR “anti malarial agent”[tiab] OR “Antimalarial Drugs”[tiab] OR “antimalarial drug”[tiab] OR “anti malarial drug”[tiab] OR “anti malarial drugs”[tiab] OR Chlorochin[tw] OR Chingamin[tw] OR Khingamin[tw] OR Nivaquine[tw] OR “Chloroquine Sulfate”[tw] OR Aralen[tw] OR Arechine[tw] OR Oxychloroquine[tw] OR Plaquenil[tw] OR “Hydroxychloroquine Sulfate”[tw] OR chloroquine[tiab] OR hydroxychloroquine[tiab] OR artemisinins[tiab] OR artemisinine[tw])
(cardiovascular diseases[mh] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR CVD[tiab] OR coronary[tiab] OR cardiovascular[tiab] OR cardiac[tiab] OR heart*[tiab] OR heart disease*[tiab] OR cardiac disease*[tiab] OR "heart failure"[tiab] OR CHF[tiab] OR ((cardiac[tiab] OR heart[tiab] OR atrial[tiab] OR ventricular[tiab] OR sinus[tiab]) AND (arrhythmia*[tiab] OR flutter[tiab] OR block[tiab] OR tachycard*[tiab] OR fibrillat*[tiab] OR bradycard*[tiab] OR premature complex*[tiab])) OR myocardial infarct*[tiab] OR angina*[tiab] OR acute coronary syndrome*[tiab] OR coronary artery disease*[tiab] OR coronary stenos*[tiab] OR coronary thrombos*[tiab] OR (ischem*[tiab] AND (heart[tiab] OR coronary[tiab])) OR "coronary vasospasm"[tiab] OR coronary 3 artery spasm*[tiab] OR myocardial stun*[tiab] OR stroke[mh] OR stroke[tiab] OR CVA[tiab] OR cerebrovascular accident*[tiab] OR brain ischemia[mh] OR brain ischemia*[tiab] OR brain infarct*[tiab] OR "transient ischemic attack"[tiab] OR TIA[tiab] OR atherosclerosis[tiab] OR peripheral arterial disease*[tiab] OR coronary artery obstruction*[tiab] OR coronary artery thrombos*[tiab] OR peripheral occlusive artery disease*[tiab] OR "Coronary Stenosis"[Mesh] OR "Myocardial Stunning"[Mesh] OR "Coronary Vasospasm"[Mesh] OR "Atherosclerosis"[Mesh] OR "Peripheral Arterial Disease"[Mesh] OR "Coronary Thrombosis"[Mesh] OR "Brain Infarction"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Heart Diseases"[Mesh] OR "Myocardial Infarction"[Mesh])

Embase:

('systemic lupus erythematosus'/exp OR SLE:ti,ab OR "systemic lupus erythematosus":ti,ab OR "lupus erythematosus":ti,ab OR "libman sacks":ti,ab OR "lupus nephritis":ti,ab OR "lupus vasculitis":ti,ab OR "lupus glomerulonephritis":ti,ab)

('antiphospholipid syndrome'/exp OR 'phospholipid antibody'/exp OR 'antiphospholipid antibody syndrome'/exp OR “Antiphospholipid syndrome”:ti,ab OR “hughes syndrome”:ti,ab OR “antiphospholipid antibody syndrome”:ti,ab OR “anti-phospholipid syndrome”:ti,ab OR “antiphospholipid antibody syndrome”:ti,ab OR “antiphospholipid antibody”:ti,ab OR “antiphospholipid antibodies”:ti,ab OR “phospholipid antibody”:ti,ab OR “phospholipid antibodies”:ti,ab)
('antimalarial agent'/exp OR 'chloroquine'/exp OR 'hydroxychloroquine'/exp OR 'artemisinin'/exp OR antimalarial:ti,ab OR “anti malarial”:ti,ab OR antimalarials:ti,ab OR “anti malarials”:ti,ab OR “Antimalarial Agents”:ti,ab OR “antimalarial agent”:ti,ab OR “anti malarial agents”:ti,ab OR “anti malarial agent”:ti,ab OR “Antimalarial Drugs”:ti,ab OR “antimalarial drug”:ti,ab OR “anti malarial drug”:ti,ab OR “anti malarial drugs”:ti,ab OR Chlorochin:ti,ab OR Chingamin:ti,ab OR Khingamin:ti,ab OR Nivaquine:ti,ab OR “Chloroquine Sulfate”:ti,ab OR Aralen:ti,ab OR Arequin:ti,ab OR Arechine:ti,ab OR Oxychlorochin:ti,ab OR Oxychloroquine:ti,ab OR Hydroxychlorochin:ti,ab OR Plaquenil:ti,ab OR “Hydroxychloroquine Sulfate”:ti,ab OR chloroquine:ti,ab OR hydroxychloroquine:ti,ab OR artemisinins:ti,ab OR artemisinine:ti,ab)
('cardiovascular disease'/exp OR “cardiovascular disease”:ti,ab OR “cardiovascular diseases”:ti,ab OR “cardiovascular event”:ti,ab OR “cardiovascular events”:ti,ab OR CVD:ti,ab OR coronary:ti,ab OR cardiovascular:ti,ab OR cardiac:ti,ab OR heart*:ti,ab OR “heart disease”:ti,ab OR 'heart disease'/exp OR “heart diseases”:ti,ab OR “cardiac disease”:ti,ab OR “cardiac diseases”:ti,ab OR "heart 5 failure":ti,ab OR "heart failures":ti,ab OR CHF:ti,ab OR ((cardiac:ti,ab OR heart:ti,ab OR atrial:ti,ab OR ventricular:ti,ab OR sinus:ti,ab) AND (arrhythmia*:ti,ab OR flutter:ti,ab OR block:ti,ab OR tachycard*:ti,ab OR fibrillat*:ti,ab OR bradycard*:ti,ab OR “premature complex”:ti,ab OR “premature complexes”:ti,ab)) OR “myocardial infarct”:ti,ab OR “myocardial infarcts”:ti,ab OR “myocardial infarction”:ti,ab OR “myocardial infarctions”:ti,ab OR 'angina pectoris'/exp OR angina*:ti,ab OR “acute coronary syndrome”:ti,ab OR “acute coronary syndromes”:ti,ab OR 'acute coronary syndrome'/exp OR “coronary artery disease”:ti,ab OR “coronary artery diseases”:ti,ab OR 'coronary artery disease'/exp OR 'coronary artery obstruction'/exp OR “coronary stenosis”:ti,ab OR “coronary stenoses”:ti,ab OR “coronary thrombosis”:ti,ab OR “coronary thromboses”:ti,ab OR 'coronary artery thrombosis'/exp OR (ischem*:ti,ab AND (heart:ti,ab OR coronary:ti,ab)) OR "coronary vasospasm":ti,ab OR "coronary vasospasms":ti,ab OR 'coronary artery spasm'/exp OR “myocardial stunning”:ti,ab OR stroke:ti,ab OR CVA:ti,ab OR 'cerebrovascular accident'/exp OR “cerebrovascular accident”:ti,ab OR “cerebrovascular accidents”:ti,ab OR “brain ischemia”:ti,ab OR 'brain ischemia'/exp OR “brain infarct”:ti,ab OR “brain infarcts”:ti,ab OR “brain infarction”:ti,ab OR “brain infarctions”:ti,ab OR 'transient ischemic attack'/exp OR "transient ischemic attack":ti,ab OR "transient ischemic attacks":ti,ab OR TIA:ti,ab OR 'atherosclerosis'/exp OR atherosclerosis:ti,ab OR “peripheral arterial disease”:ti,ab OR “peripheral arterial diseases”:ti,ab OR 'peripheral occlusive artery disease'/exp)

Cochrane:

[mh “lupus erythematosus, systemic”]
(SLE OR "systemic lupus erythematosus" OR "lupus erythematosus" OR "libman sacks" OR "lupus nephritis" OR "lupus vasculitis" OR "lupus glomerulonephritis"):ti,ab,kw
([mh “Antiphospholipid syndrome”] OR [mh “antibodies, antiphospholipid”])
(“hughes syndrome” OR “antiphospholipid antibody syndrome” OR “anti-phospholipid syndrome” OR “anti-phospholipid antibody syndrome” OR “antiphospholipid antibody” OR “antiphospholipid antibodies”):ti,ab,kw
(Arequin OR Oxychlorochin OR Hydroxychlorochin OR antimalarial OR “anti malarial” OR antimalarials OR “anti malarials” OR “Antimalarial Agents” OR “antimalarial agent” OR “anti malarial agents” OR “anti malarial agent” OR “Antimalarial Drugs” OR “antimalarial drug” OR “anti malarial drug” OR “anti malarial drugs” OR Chlorochin OR Chingamin OR Khingamin OR

Nivaquine OR “Chloroquine Sulfate” OR Aralen OR Arechine OR Oxychloroquine OR Plaquenil OR “Hydroxychloroquine Sulfate” OR chloroquine OR hydroxychloroquine OR artemisinins OR artemisinine):ti,ab,kw
([mh "Antimalarials"] OR [mh "Chloroquine"] OR [mh "Hydroxychloroquine"] OR [mh "Artemisinins"])
(“cardiovascular diseases” OR “cardiovascular disease” OR “cardiovascular event” OR “cardiovascular events” OR CVD OR coronary OR cardiovascular OR cardiac OR heart* OR “heart disease” OR “heart diseases” OR “cardiac disease” OR “cardiac diseases” OR “heart failure” OR CHF OR ((cardiac OR heart OR atrial OR ventricular OR sinus) AND (arrhythmia* OR flutter OR block OR tachycard* OR fibrillat* OR bradycard* OR premature complex*)) OR 7 “myocardial infarct” OR “myocardial infarcts” OR “myocardial infarction” OR “myocardial infarctions” OR angina* OR “acute coronary syndrome” OR “acute coronary syndromes” OR “coronary artery disease” OR “coronary artery diseases” OR “coronary stenosis” OR “coronary stenoses” OR “coronary thrombosis” OR “coronary thromboses” OR (ischem* AND (heart OR coronary)) OR “coronary vasospasm” OR “coronary vasospasms” OR “coronary artery spasm” OR “coronary artery spasms” OR “myocardial stunning” OR stroke OR CVA OR “cerebrovascular accident” OR “cerebrovascular accidents” OR “brain ischemia” OR “brain ischemias” OR “brain infarct” OR “brain infarcts” OR “brain infarction” OR “brain infarctions” OR "transient ischemic attack" OR TIA OR atherosclerosis OR “peripheral arterial disease” OR “peripheral arterial diseases” OR “coronary artery obstruction” OR “coronary artery obstructions” OR “coronary artery thrombosis” OR “coronary artery thromboses” OR “peripheral occlusive artery disease” OR “peripheral occlusive artery diseases”):ti,ab,kw
([mh stroke] OR [mh “cardiovascular diseases”] OR [mh "Coronary Stenosis"] OR [mh "Myocardial Stunning"] OR [mh "Coronary Vasospasm"] OR [mh "Atherosclerosis"] OR [mh "Peripheral Arterial Disease"] OR [mh "Coronary Thrombosis"] OR [mh "Brain Infarction"] OR [mh "Acute Coronary Syndrome"] OR [mh "Heart Diseases"] OR [mh "Myocardial Infarction"] OR [mh “brain ischemia”])

8) NSAIDs

Medline/PubMed:

(lupus erythematosus, systemic[mh] OR SLE[tiab] OR "systemic lupus erythematosus"[tiab] OR "lupus erythematosus"[tiab] OR "libman sacks"[tiab] OR "lupus nephritis"[tiab] OR "lupus vasculitis"[tiab] OR "lupus glomerulonephritis"[tiab])
("Anti-Inflammatory Agents, Non-Steroidal"[Mesh] OR "Anti-Inflammatory Agents, Non-Steroidal" [Pharmacological Action] OR “Anti-Inflammatory Analgesics”[tiab] OR “Anti-Inflammatory Analgesic”[tiab] OR “Non Steroidal Anti Inflammatory Agents”[tiab] OR “non steroidal anti inflammatory agent”[tiab] OR “non steroidal anti inflammatory drug”[tiab] OR “non steroidal anti inflammatory drugs”[tiab] OR “non steroidal anti inflammatory analgesic”[tiab] OR “non steroidal anti inflammatory analgesics”[tiab] OR “non steroidal antiinflammatory agent”[tiab] OR “non steroidal antiinflammatory agents”[tiab] OR “non steroidal antiinflammatory drug”[tiab] OR “non steroidal antiinflammatory drugs”[tiab] OR “non steroidal antiinflammatory analgesic”[tiab] OR “non steroidal antiinflammatory analgesics”[tiab] OR “nonsteroidal antiinflammatory agents”[tiab] OR “nonsteroidal antiinflammatory agent”[tiab] OR “nonsteroidal antiinflammatory drug”[tiab] OR “nonsteroidal antiinflammatory drugs”[tiab] OR “nonsteroidal antiinflammatory analgesic”[tiab] OR “nonsteroidal antiinflammatory analgesics”[tiab] OR “Nonsteroidal Anti-Inflammatory Agents”[tiab] OR “Nonsteroidal Anti-Inflammatory Agent”[tiab] OR “nonsteroidal anti inflammatory drug”[tiab] OR “nonsteroidal anti inflammatory drugs”[tiab] OR “nonsteroidal anti inflammatory analgesic”[tiab] OR “nonsteroidal anti inflammatory analgesics”[tiab] OR NSAIDs[tiab] OR ibuprofen[tw] OR naproxen[tw] OR Anaprox[tw] OR

Aleve[tw] OR Proxen[tw] OR Synflex[tw] OR Naprosin[tw] OR Naprosyn[tw] OR diclofenac[tw] OR voltaren[tw] OR Feloran[tw] OR Voltarol[tw] OR Novapirina[tw] OR Orthofen[tw] OR Ortofen[tw] OR Orthophen[tw] OR celecoxib[tw] OR Celebrex[tw] OR meloxicam[tw] OR Miloxicam[tw] OR Mobic[tw] OR Mobicox[tw] OR Mobec[tw] OR Movalis[tw] OR indomethacin[tw] OR Indometacin[tw] OR Osmosin[tw] OR Indocid[tw] OR Metindol[tw] OR Amuno[tw] OR Indocin[tw] OR ketoprofen[tw] OR Profenid[tw] OR Alrheumum[tw] OR Orudis[tw] OR Alrheumat[tw] OR nabumetone[tw] OR 3 Nabumeton[tw] OR Relifex[tw] OR Relif[tw] OR Mebutan[tw] OR Listran[tw] OR Relafen[tw] OR oxaprozin[tw] OR Daypro[tw] OR piroxicam[tw] OR feldene[tw] OR sulindac[tw] OR Clinoril[tw] OR Arthrocine[tw] OR Klinoril[tw] OR Chibret[tw] OR Aclin[tw] OR Copal[tw] OR salsalate[tw] OR “salicylsalicylic acid”[tw] OR Disalcid[tw] OR “salicyl salicylate”[tw] OR Saloxium[tw] OR tolmetin[tw] OR Tolectin[tw] OR diflunisal[tw] OR Dolobid[tw] OR Dolobis[tw] OR etoricoxib[tw] OR Arcoxia[tw] OR ketorolac[tw] OR flurbiprofen[tw] OR Flubiprofen[tw] OR Ocufen[tw] OR Strefen[tw] OR Flugalin[tw] OR Froben[tw] OR Ansaid[tw] OR "Froben SR"[tw] OR Ocuflur[tw] OR etodolac[tw] OR “Etodolic Acid”[tw] OR Ultradol[tw] OR Lodine[tw] OR Ramodar[tw] OR "Ibuprofen"[Mesh] OR "Naproxen"[Mesh] OR "Diclofenac"[Mesh] OR "Celecoxib"[Mesh] OR "Meloxicam"[Mesh] OR "Indomethacin"[Mesh] OR "Ketoprofen"[Mesh] OR "Nabumetone"[Mesh] OR "Oxaprozin"[Mesh] OR "Piroxicam"[Mesh] OR "Sulindac"[Mesh] OR "salicylsalicylic acid" [Supplementary Concept] OR "Tolmetin"[Mesh] OR "Diflunisal"[Mesh] OR "Etoricoxib"[Mesh] OR "Ketorolac"[Mesh] OR "Flurbiprofen"[Mesh] OR "Etodolac"[Mesh]) (cardiovascular diseases[mh] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR CVD[tiab] OR coronary[tiab] OR cardiovascular[tiab] OR cardiac[tiab] OR heart*[tiab] OR heart disease*[tiab] OR cardiac disease*[tiab] OR "heart failure"[tiab] OR CHF[tiab] OR ((cardiac[tiab] OR heart[tiab] OR atrial[tiab] OR ventricular[tiab] OR sinus[tiab]) AND (arrhythmia*[tiab] OR flutter[tiab] OR block[tiab] OR tachycard*[tiab] OR fibrillat*[tiab] OR bradycard*[tiab] OR premature complex*[tiab])) OR myocardial infarct*[tiab] OR angina*[tiab] OR acute coronary syndrome*[tiab] OR coronary artery disease*[tiab] OR coronary stenos*[tiab] OR coronary thrombos*[tiab] OR (ischem*[tiab] AND (heart[tiab] OR coronary[tiab])) OR "coronary vasospasm"[tiab] OR coronary artery spasm*[tiab] OR myocardial stun*[tiab] OR stroke[mh] OR stroke[tiab] OR CVA[tiab] OR cerebrovascular accident*[tiab] OR brain ischemia[mh] OR brain ischemia*[tiab] OR brain infarct*[tiab] OR "transient ischemic attack"[tiab] OR TIA[tiab] OR atherosclerosis[tiab] OR peripheral arterial disease*[tiab] OR coronary artery obstruction*[tiab] OR coronary artery thrombos*[tiab] OR peripheral occlusive artery disease*[tiab] OR "Coronary Stenosis"[Mesh] OR "Myocardial Stunning"[Mesh] OR "Coronary Vasospasm"[Mesh] OR "Atherosclerosis"[Mesh] OR "Peripheral Arterial Disease"[Mesh] OR "Coronary Thrombosis"[Mesh] OR "Brain Infarction"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Heart Diseases"[Mesh] OR "Myocardial Infarction"[Mesh]

Embase:

('systemic lupus erythematosus'/exp OR SLE:ti,ab OR "systemic lupus erythematosus":ti,ab OR "lupus erythematosus":ti,ab OR "libman sacks":ti,ab OR "lupus nephritis":ti,ab OR "lupus vasculitis":ti,ab OR "lupus glomerulonephritis":ti,ab)
('nonsteroid antiinflammatory agent'/exp OR 'ibuprofen'/exp OR 'naproxen'/exp OR 'diclofenac'/exp OR 'celecoxib'/exp OR 'meloxicam'/exp OR 'indometacin'/exp OR 'ketoprofen'/exp OR 'nabumetone'/exp OR 'oxaprozin'/exp OR 'piroxicam'/exp OR 'sulindac'/exp OR 'salsalate'/exp OR 'tolmetin'/exp OR 'diflunisal'/exp OR 'etoricoxib'/exp OR 'ketorolac'/exp OR 'flurbiprofen'/exp OR 'etodolac'/exp OR “Anti-Inflammatory Analgesics”:ti,ab OR “Anti-Inflammatory Analgesic”:ti,ab OR “Non Steroidal Anti Inflammatory Agents”:ti,ab OR “non steroidal anti inflammatory agent”:ti,ab OR “non steroidal anti inflammatory drug”:ti,ab OR “non steroidal anti inflammatory drugs”:ti,ab OR “non steroidal anti inflammatory analgesic”:ti,ab OR “non steroidal anti inflammatory analgesics”:ti,ab OR

"non steroidal antiinflammatory agent":ti,ab OR "non steroidal antiinflammatory agents":ti,ab OR "non steroidal antiinflammatory drug":ti,ab OR "non steroidal antiinflammatory drugs":ti,ab OR "non steroidal antiinflammatory analgesic":ti,ab OR "non steroidal antiinflammatory analgesics":ti,ab OR "nonsteroidal antiinflammatory agents":ti,ab OR "nonsteroidal antiinflammatory agent":ti,ab OR "nonsteroidal antiinflammatory drug":ti,ab OR "nonsteroidal antiinflammatory drugs":ti,ab OR "nonsteroidal antiinflammatory analgesic":ti,ab OR "nonsteroidal antiinflammatory analgesics":ti,ab OR "Nonsteroidal Anti-Inflammatory Agents":ti,ab OR "Nonsteroidal Anti-Inflammatory Agent":ti,ab OR "nonsteroidal anti inflammatory drug":ti,ab OR "nonsteroidal anti inflammatory drugs":ti,ab OR "nonsteroidal anti inflammatory analgesic":ti,ab OR "nonsteroidal anti inflammatory analgesics":ti,ab OR NSAIDs:ti,ab OR ibuprofen:ti,ab OR naproxen:ti,ab OR Anaprox:ti,ab OR Aleve:ti,ab OR Proxen:ti,ab OR Synflex:ti,ab OR Naprosin:ti,ab OR Naprosyn:ti,ab OR diclofenac:ti,ab OR 6 voltaren:ti,ab OR Feloran:ti,ab OR Voltarol:ti,ab OR Novapirina:ti,ab OR Orthofen:ti,ab OR Ortofen:ti,ab OR Orthophen:ti,ab OR celecoxib:ti,ab OR Celebrex:ti,ab OR meloxicam:ti,ab OR Miloxicam:ti,ab OR Mobic:ti,ab OR Mobicox:ti,ab OR Mobec:ti,ab OR Movalis:ti,ab OR indomethacin:ti,ab OR Indometacin:ti,ab OR Osmosin:ti,ab OR Indocid:ti,ab OR Metindol:ti,ab OR Amuno:ti,ab OR Indocin:ti,ab OR ketoprofen:ti,ab OR Profenid:ti,ab OR Alrheumum:ti,ab OR Orudis:ti,ab OR Alrheumat:ti,ab OR nabumetone:ti,ab OR Nabumeton:ti,ab OR Relifex:ti,ab OR Relif:ti,ab OR Mebutan:ti,ab OR Listran:ti,ab OR Relafen:ti,ab OR oxaprozin:ti,ab OR Daypro:ti,ab OR piroxicam:ti,ab OR feldene:ti,ab OR sulindac:ti,ab OR Clinoril:ti,ab OR Arthrocine:ti,ab OR Klinoril:ti,ab OR Chibret:ti,ab OR Aclin:ti,ab OR Copal:ti,ab OR salsalate:ti,ab OR "salicylsalicylic acid":ti,ab OR Disalcid:ti,ab OR "salicyl salicylate":ti,ab OR Saloxium:ti,ab OR tolmetin:ti,ab OR Tolectin:ti,ab OR diflunisal:ti,ab OR Dolobid:ti,ab OR Dolobis:ti,ab OR etoricoxib:ti,ab OR Arcoxia:ti,ab OR ketorolac:ti,ab OR flurbiprofen:ti,ab OR Flubiprofen:ti,ab OR Ocufen:ti,ab OR Strefen:ti,ab OR Flugalin:ti,ab OR Froben:ti,ab OR Ansaid:ti,ab OR "Froben SR":ti,ab OR Ocuflur:ti,ab OR etodolac:ti,ab OR "Etodolic Acid":ti,ab OR Ultradol:ti,ab OR Lodine:ti,ab OR Ramodar:ti,ab) ('cardiovascular disease'/exp OR "cardiovascular disease":ti,ab OR "cardiovascular diseases":ti,ab OR "cardiovascular event":ti,ab OR "cardiovascular events":ti,ab OR CVD:ti,ab OR coronary:ti,ab OR cardiovascular:ti,ab OR cardiac:ti,ab OR heart*:ti,ab OR "heart disease":ti,ab OR 'heart disease'/exp OR "heart diseases":ti,ab OR "cardiac disease":ti,ab OR "cardiac diseases":ti,ab OR "heart failure":ti,ab OR "heart failures":ti,ab OR CHF:ti,ab OR ((cardiac:ti,ab OR heart:ti,ab OR atrial:ti,ab OR ventricular:ti,ab OR sinus:ti,ab) AND (arrhythmia*:ti,ab OR flutter:ti,ab OR block:ti,ab OR tachycard*:ti,ab OR fibrillat*:ti,ab OR bradycard*:ti,ab OR "premature complex":ti,ab OR "premature complexes":ti,ab)) OR "myocardial infarct":ti,ab OR "myocardial infarcts":ti,ab OR "myocardial infarction":ti,ab OR "myocardial infarctions":ti,ab OR 'angina pectoris'/exp OR angina*:ti,ab OR "acute coronary syndrome":ti,ab OR "acute coronary syndromes":ti,ab OR 'acute coronary syndrome'/exp OR "coronary artery disease":ti,ab OR "coronary artery diseases":ti,ab OR 'coronary artery disease'/exp OR 'coronary artery obstruction'/exp OR "coronary stenosis":ti,ab OR "coronary stenoses":ti,ab OR "coronary thrombosis":ti,ab OR "coronary thromboses":ti,ab OR 'coronary artery thrombosis'/exp OR (ischem*:ti,ab AND (heart:ti,ab OR coronary:ti,ab)) OR "coronary vasospasm":ti,ab OR "coronary vasospasms":ti,ab OR 'coronary artery spasm'/exp OR "myocardial stunning":ti,ab OR stroke:ti,ab OR CVA:ti,ab OR 'cerebrovascular accident'/exp OR "cerebrovascular accident":ti,ab OR "cerebrovascular accidents":ti,ab OR "brain ischemia":ti,ab OR 'brain ischemia'/exp OR "brain infarct":ti,ab OR "brain infarcts":ti,ab OR "brain infarction":ti,ab OR "brain infarctions":ti,ab OR 'transient ischemic attack'/exp OR "transient ischemic attack":ti,ab OR "transient ischemic attacks":ti,ab OR TIA:ti,ab OR 'atherosclerosis'/exp OR atherosclerosis:ti,ab OR "peripheral arterial disease":ti,ab OR "peripheral arterial diseases":ti,ab OR 'peripheral occlusive artery disease'/exp)

Cochrane:

[mh “lupus erythematosus, systemic”]
(SLE OR "systemic lupus erythematosus" OR "lupus erythematosus" OR "libman sacks" OR "lupus nephritis" OR "lupus vasculitis" OR "lupus glomerulonephritis"):ti,ab,kw
(“Anti-Inflammatory Analgesics” OR “Anti-Inflammatory Analgesic” OR “Non Steroidal Anti Inflammatory Agents” OR “non steroidal anti inflammatory agent” OR “non steroidal anti inflammatory drug” OR “non steroidal anti inflammatory drugs” OR “non steroidal anti inflammatory analgesic” OR “non steroidal anti inflammatory analgesics” OR “non steroidal antiinflammatory agent” OR “non steroidal antiinflammatory agents” OR “non steroidal antiinflammatory drug” OR “non steroidal antiinflammatory drugs” OR “non steroidal antiinflammatory analgesic” OR “non steroidal antiinflammatory analgesics” OR “nonsteroidal antiinflammatory agents” OR “nonsteroidal antiinflammatory agent” OR “nonsteroidal antiinflammatory drug” OR “nonsteroidal antiinflammatory drugs” OR “nonsteroidal antiinflammatory analgesic” OR “nonsteroidal antiinflammatory analgesics” OR “Nonsteroidal Anti-Inflammatory Agents” OR “Nonsteroidal Anti-Inflammatory Agent” OR “nonsteroidal anti inflammatory drug” OR “nonsteroidal anti inflammatory drugs” OR “nonsteroidal anti inflammatory analgesic” OR “nonsteroidal anti inflammatory analgesics” OR NSAIDs OR ibuprofen OR naproxen OR Anaprox OR Aleve OR Proxen OR Synflex OR Naprosin OR Naprosyn OR diclofenac OR voltaren OR Feloran OR Voltarol OR Novapirina OR Orthofen OR Ortofen OR Orthophen OR celecoxib OR Celebrex OR meloxicam OR Miloxicam OR Mobic OR Mobicox OR Mobec OR Movalis OR indomethacin OR Indometacin OR Osmosin OR Indocid OR Metindol OR Amuno OR Indocin OR ketoprofen OR Profenid OR Alrheumum OR Orudis OR Alrheumat OR nabumetone OR Nabumeton OR Relifex OR Relif OR Mebutan OR Listran OR Relafen OR oxaprozin OR Daypro OR piroxicam OR feldene OR sulindac OR Clinoril OR Arthrocine OR Klinoril OR Chibret OR Aclin OR Copal OR salsalate OR “salicylsalicylic acid” OR Disalcid OR “salicyl salicylate” OR Saloxium OR tolmetin OR Tolectin 9 OR diflunisal OR Dolobid OR Dolobis OR etoricoxib OR Arcoxia OR ketorolac OR flurbiprofen OR Flubiprofen OR Ocufen OR Strefen OR Flugalin OR Froben OR Ansaid OR "Froben SR" OR Ocuflur OR etodolac OR “Etodolic Acid” OR Ultradol OR Lodine OR Ramodar):ti,ab,kw
([mh "Anti-Inflammatory Agents, Non-Steroidal"] OR [mh "Ibuprofen"] OR [mh "Naproxen"] OR [mh "Diclofenac"] OR [mh "Celecoxib"] OR [mh "Meloxicam"] OR [mh "Indomethacin"] OR [mh "Ketoprofen"] OR [mh "Nabumetone"] OR [mh "Oxaprozin"] OR [mh "Piroxicam"] OR [mh "Sulindac"] OR [mh "salicylsalicylic acid"] OR [mh "Tolmetin"] OR [mh "Diflunisal"] OR [mh "Etoricoxib"] OR [mh "Ketorolac"] OR [mh "Flurbiprofen"] OR [mh "Etodolac"])
(“cardiovascular diseases” OR “cardiovascular disease” OR “cardiovascular event” OR “cardiovascular events” OR CVD OR coronary OR cardiovascular OR cardiac OR heart* OR “heart disease” OR “heart diseases” OR “cardiac disease” OR “cardiac diseases” OR “heart failure” OR CHF OR ((cardiac OR heart OR atrial OR ventricular OR sinus) AND (arrhythmia* OR flutter OR block OR tachycard* OR fibrillat* OR bradycard* OR premature complex*)) OR “myocardial infarct” OR “myocardial infarcts” OR “myocardial infarction” OR “myocardial infarctions” OR angina* OR “acute coronary syndrome” OR “acute coronary syndromes” OR “coronary artery disease” OR “coronary artery diseases” OR “coronary stenosis” OR “coronary stenoses” OR “coronary thrombosis” OR “coronary thromboses” OR (ischem* AND (heart OR coronary)) OR “coronary vasospasm” OR “coronary vasospasms” OR “coronary artery spasm” OR “coronary artery spasms” OR “myocardial stunning” OR stroke OR CVA OR “cerebrovascular accident” OR “cerebrovascular accidents” OR “brain ischemia” OR “brain ischemias” OR “brain infarct” OR “brain infarcts” OR “brain infarction” OR “brain infarctions” OR "transient ischemic attack" OR TIA OR atherosclerosis OR “peripheral arterial disease” OR “peripheral arterial diseases” OR “coronary artery obstruction” OR “coronary artery obstructions” OR “coronary artery thrombosis” OR “coronary artery thromboses” OR “peripheral occlusive artery disease” OR “peripheral occlusive artery diseases”):ti,ab,kw
([mh stroke] OR [mh “cardiovascular diseases”] OR [mh "Coronary Stenosis"] OR [mh "Myocardial Stunning"] OR [mh "Coronary Vasospasm"] OR [mh "Atherosclerosis"] OR [mh "Peripheral Arterial Disease"] OR [mh "Coronary Thrombosis"] OR [mh "Brain Infarction"] OR

[mh "Acute Coronary Syndrome"] OR [mh "Heart Diseases"] OR [mh "Myocardial Infarction"] OR [mh “brain ischemia”])

B. Data abstraction

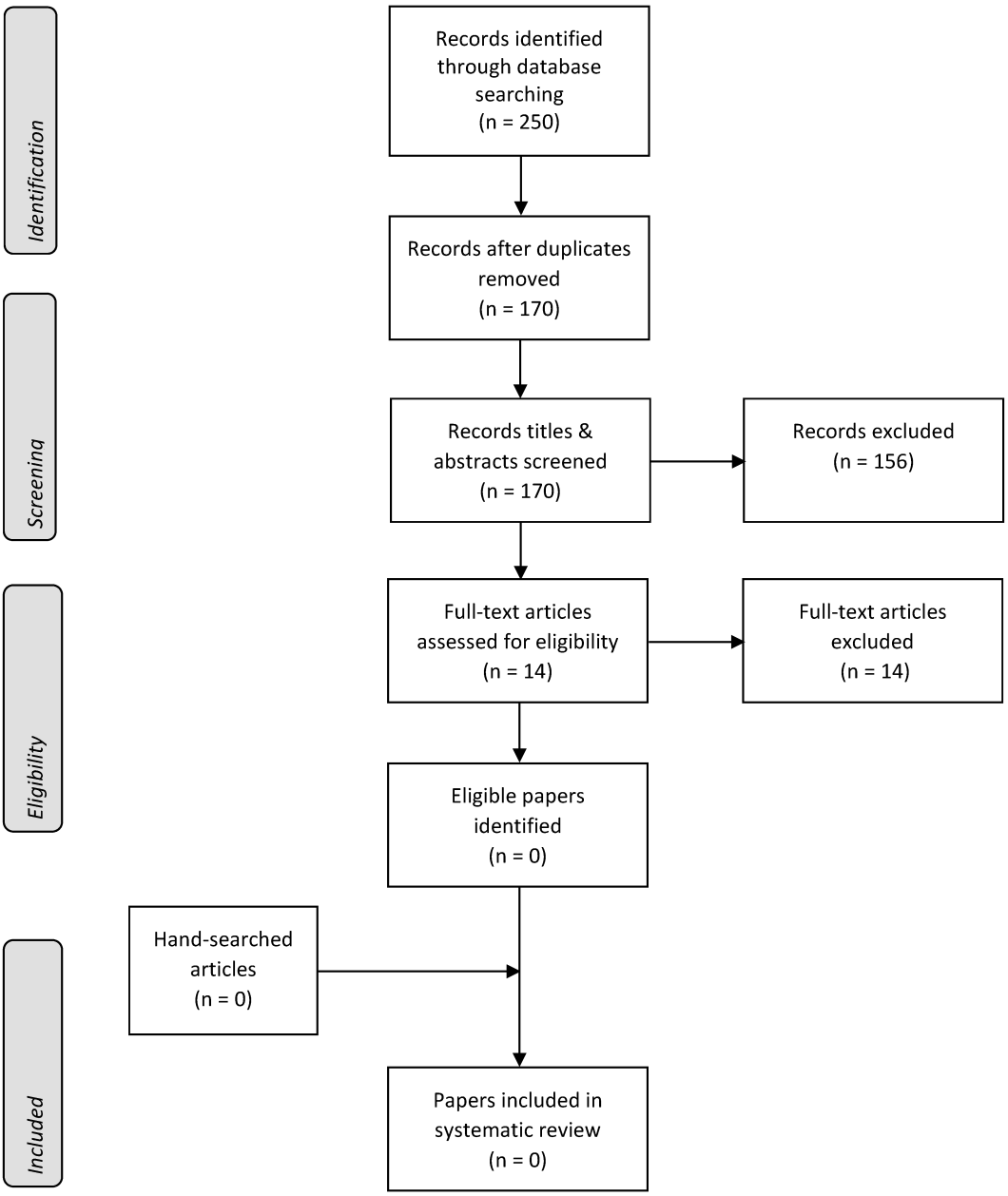
Data were abstracted from published reports. Authors were not contacted for other data or clarifications.
When hazard ratios were provided, we used these values as the measure of effect.
For cohort studies, we used relative risks when these were reported. If relative risks were not reported but data were reported that permitted relative risks to be calculated, we did so. When data were reported for cohort studies as odds ratios, and the report did not allow calculation of relative risks, we included the odds ratio.
For case-control studies, we reported the odds ratio as the measure of effect.
I^2 is a measure of heterogeneity of effects among studies, with a range of 0% (no heterogeneity) to 100% (high heterogeneity).
For multiple published studies of the same clinical cohort, we describe all relevant studies.
Quality of randomized controlled trials was assessed with the Cochrane risk-of-bias tool.
Quality of observational studies was assessed with the Newcastle-Ottawa scale; studies were classified as of low, intermediate or high quality based on a rating system of 0–3, 4–6, and 7–9 stars, respectively.

II. Results

A. Gout

1. Cardiovascular risk prediction tools

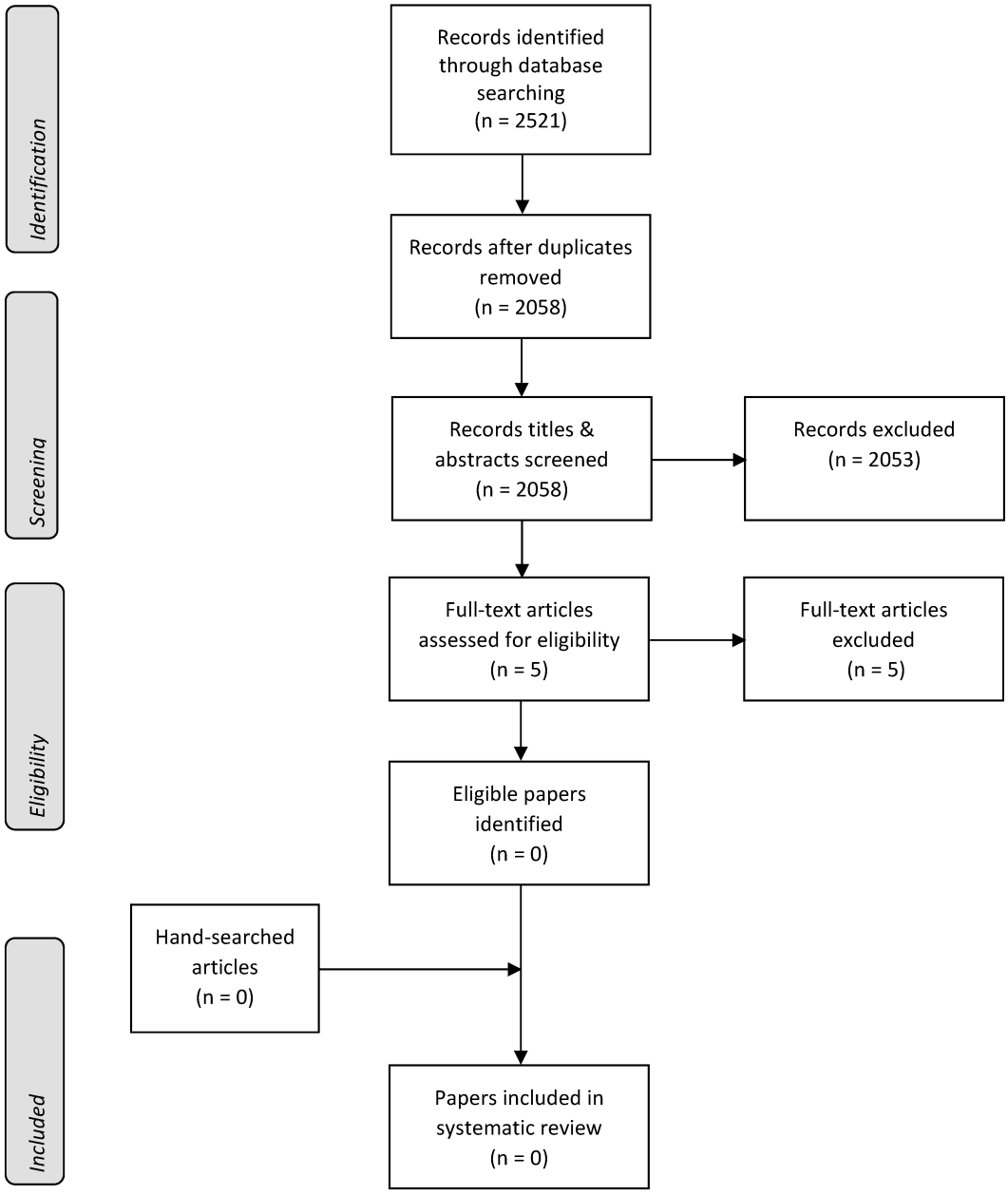
PICO: '*In patients with gout, what is the performance of risk prediction tools to predict cardiovascular risk?*'



2. Interventions targeting traditional cardiovascular risk factors

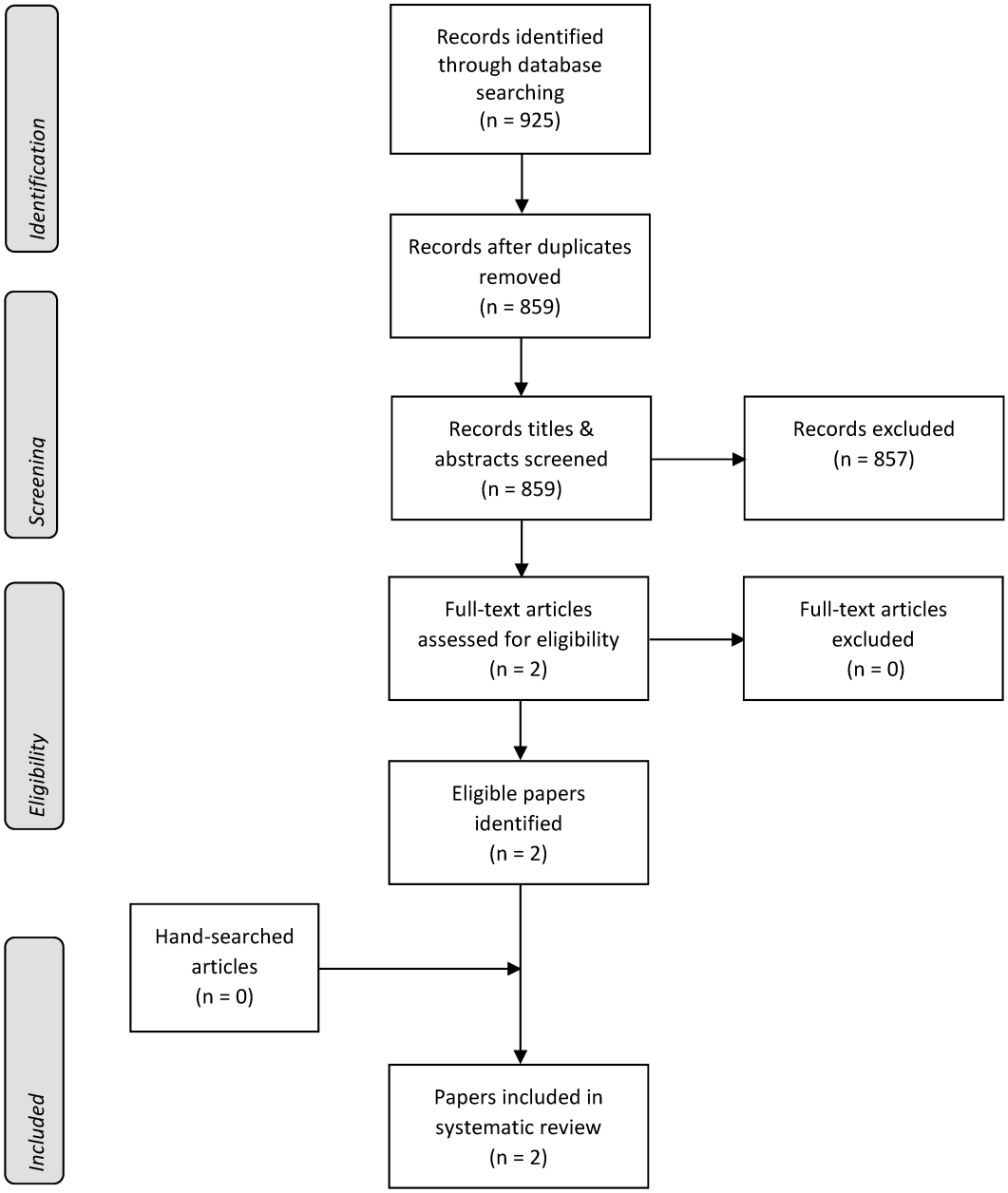
   a. Antihypertensives

   PICO: *'In patients with gout, what is the effect of antihypertensives on cardiovascular outcomes, in comparison with the general population?'*



b. Lipid-lowering agents

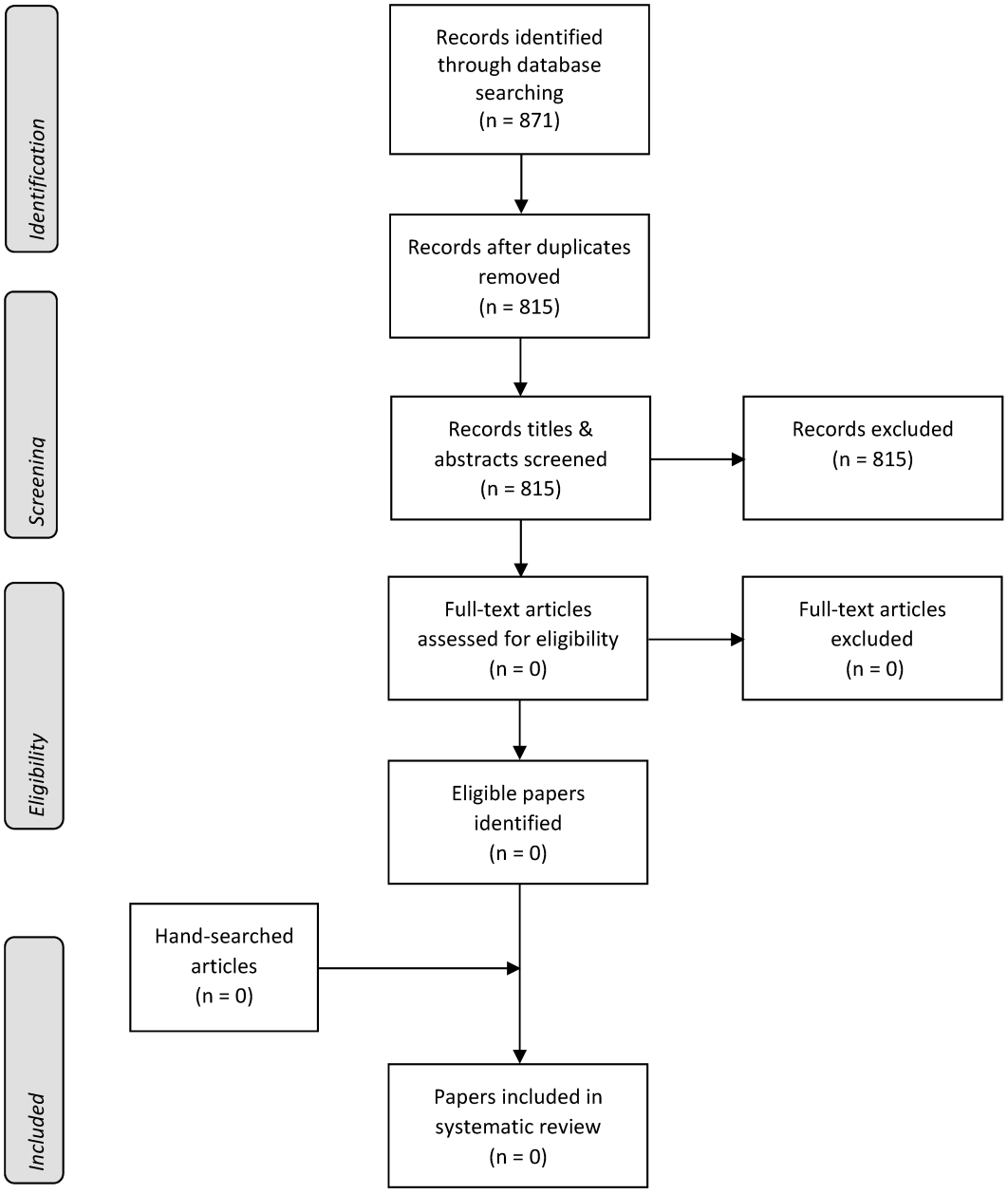
PICO: *'In patients with gout, what is the effect of lipid lowering agents on cardiovascular outcomes, in comparison with the general population?'*



Reference	Design	Intervention	Comparison	Follow-up	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
	Coronary heart disease									
Garcia-Gill, 2019	Retrospective cohort	Statin use	No treatment	9,8 years	736	7782	2025	2503	HR 0.84 (0.60, 1,19)	High
	Cerebrovascular disease (ischemic stroke)									
Garcia-Gill, 2019	Retrospective cohort	Statin use	No treatment	9,8 years	736	7782	30	349	HR 0.68 (0.44, 1,05)	High
	All cause mortality									
Garcia-Gill, 2019	Retrospective cohort	Statin use	No treatment	9,8 years	736	7782	86	825	HR 0.87 (0.67-1.12)	High
Keller, 2019	Retrospective cohort	Statin use	No treatment	5.0/4.6 years	18007	18007	2025	2503	HR 0.84 (0.79-0.89)	High

c. Antiplatelets

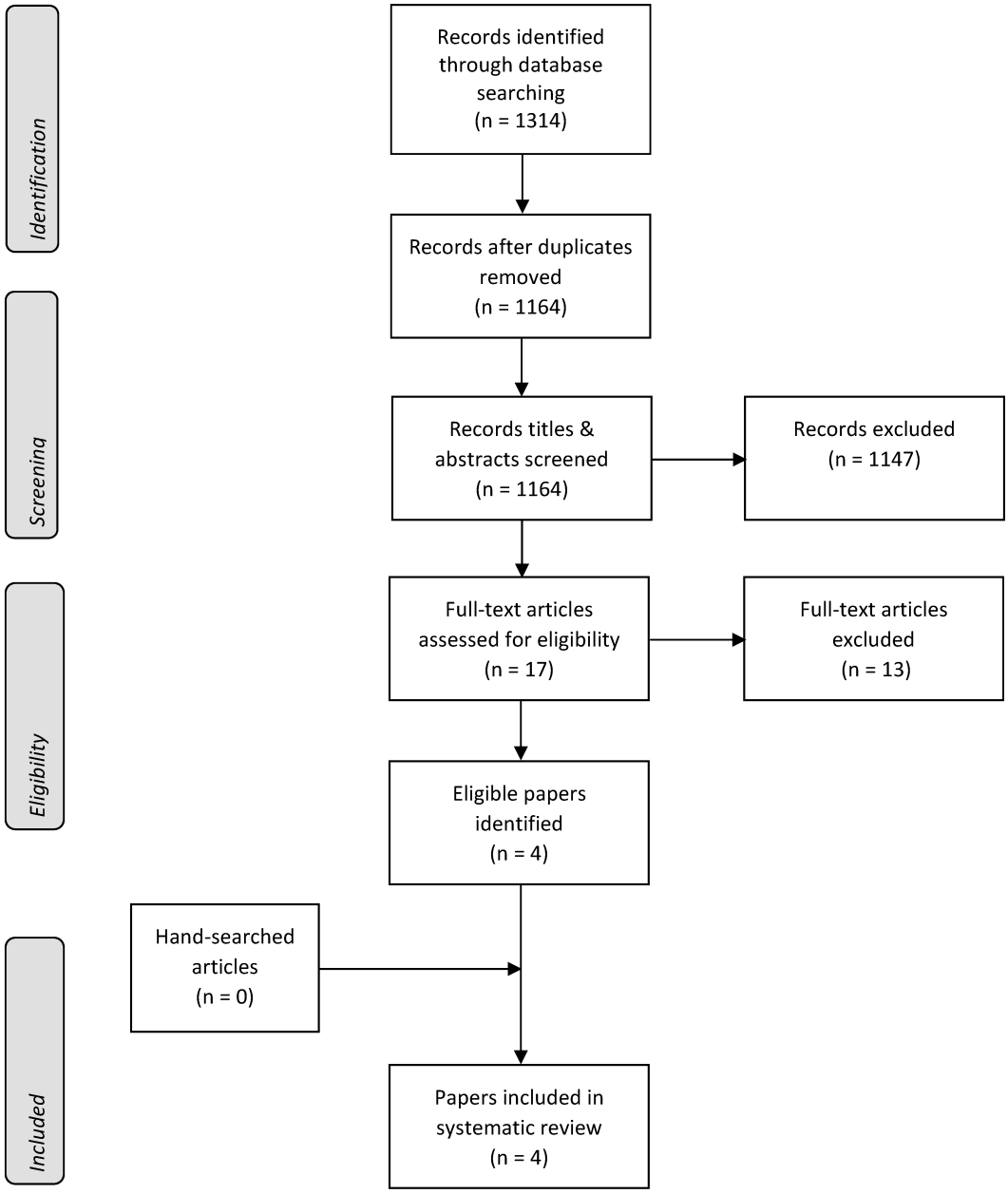
PICO: *'In patients with gout, what is the effect of antiplatelets on cardiovascular outcomes, in comparison with the general population?'*



3. Interventions targeting disease-related cardiovascular risk factors

   a. Serum uric acid

      PICO: '*In gout patients, what Is the effect of high disease activity on the risk of CVD?*'

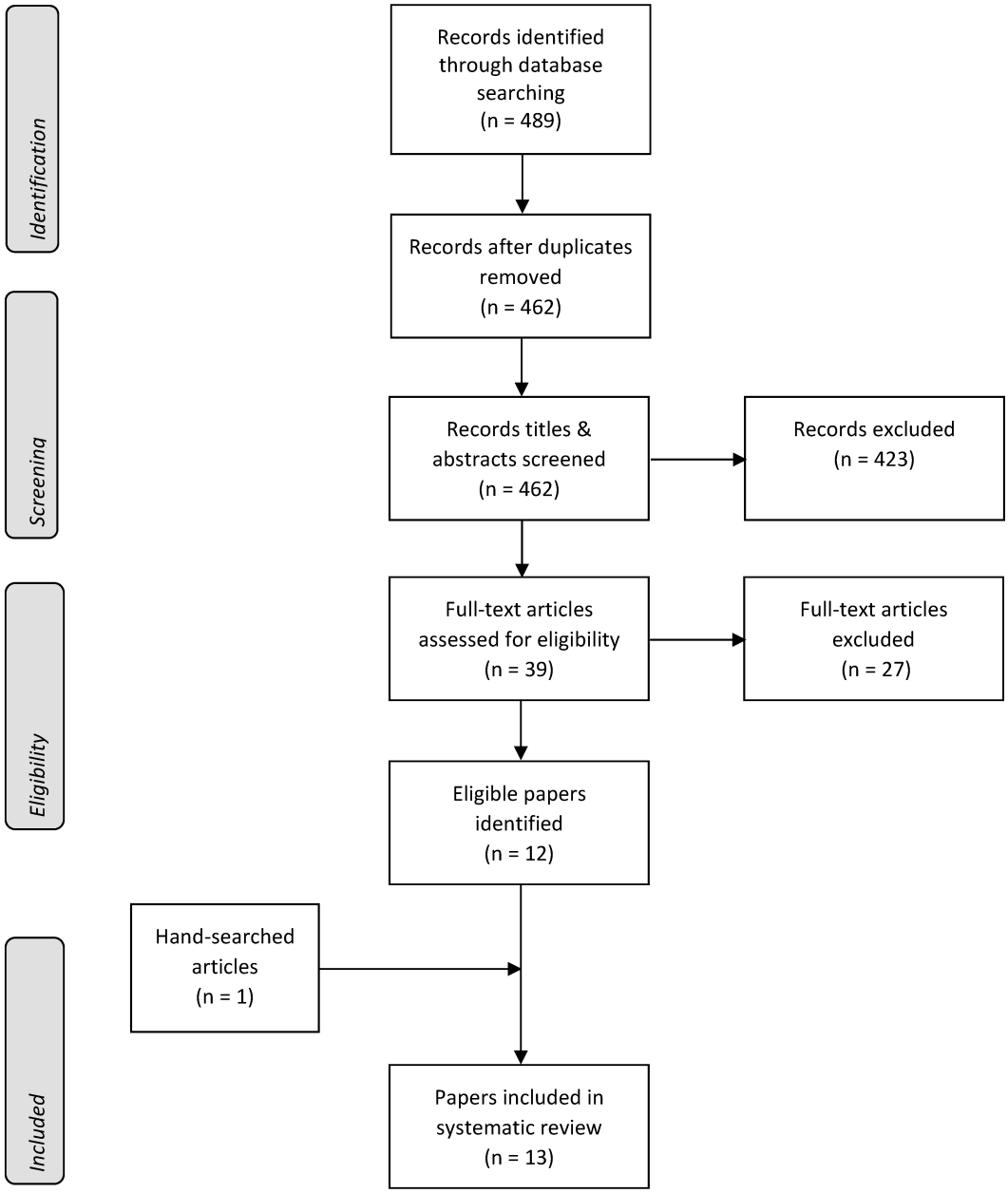


Reference	Design	Exposure	Control	Follow-up (years)	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
	Acute coronary syndrome									
Noyes Essex, 2017	Retrospective cohort	SUA 6.0-8.0 mg/dL SUA>8.0 mg/dL	SUA <6.0/>8.0 mg/dL SUA<8.0 mg/dL	1	23242 15531	40999 48710	385 347	733 771	HR 1.18 (1.03, 1,36) HR 1.59 (1.38, 1.84)	High
	Coronary artery disease									
Noyes Essex, 2017	Retrospective cohort	SUA >8.0mg/dL	SUA<8.0 mg/dL	1	12841	40464	1605	4155	HR1.41 (1.33, 1.51)	High
	Chronic heart failure									
Noyes Essex, 2017	Retrospective cohort	SUA >8.0mg/dL	SUA<8.0 mg/dL	1	13880	45434	1208	2327	HR2.01 (1.86, 2.18)	High
	(Cardiovascular) Mortality									
Disveld, 2019	Prospective cohort	SUA>9,33mg/dl) Tophaceous gout	SUA≦ 9.33mg/dl No tophi	5	NA NA	NA NA	32 NA	34 NA	OR 2.17 (1.20, 3.89) OR 1.96 (1.11, 3.47)	High
Stack, 2013	Retrospective cohort	SUA 5,2-6,25mg/dl SUA >6,25 mg/dl	SUA <4,3mg/dl SUA<4,3 mg/dl	10	4190 4093	3838 3838	725 985	432 432	HR1.33 (1.04, 1.70) HR1.54 (1.17, 2.04)	High
Perez-Ruiz, 2014	Prospective cohort	SUA per 1mg/dl increase Tophaceous gout	NA No tophi		706 215	NA 491	NA NA	NA NA	HR1.16 (1.03-1.32) HR2.05 (1.29-3.28)	Intermediate

		≧4 flares/year	<4 flares		191	515	NA	NA	HR1.05 (0.95-1.15)	
		Polyarticular gout	Mono articular		244	462	NA	NA	HR3.36 (0.44-4.66)	

b. Urate lowering therapy

PICO: '*In gout patients, what Is the effect of the use disease related medication on the risk of CVD?*'



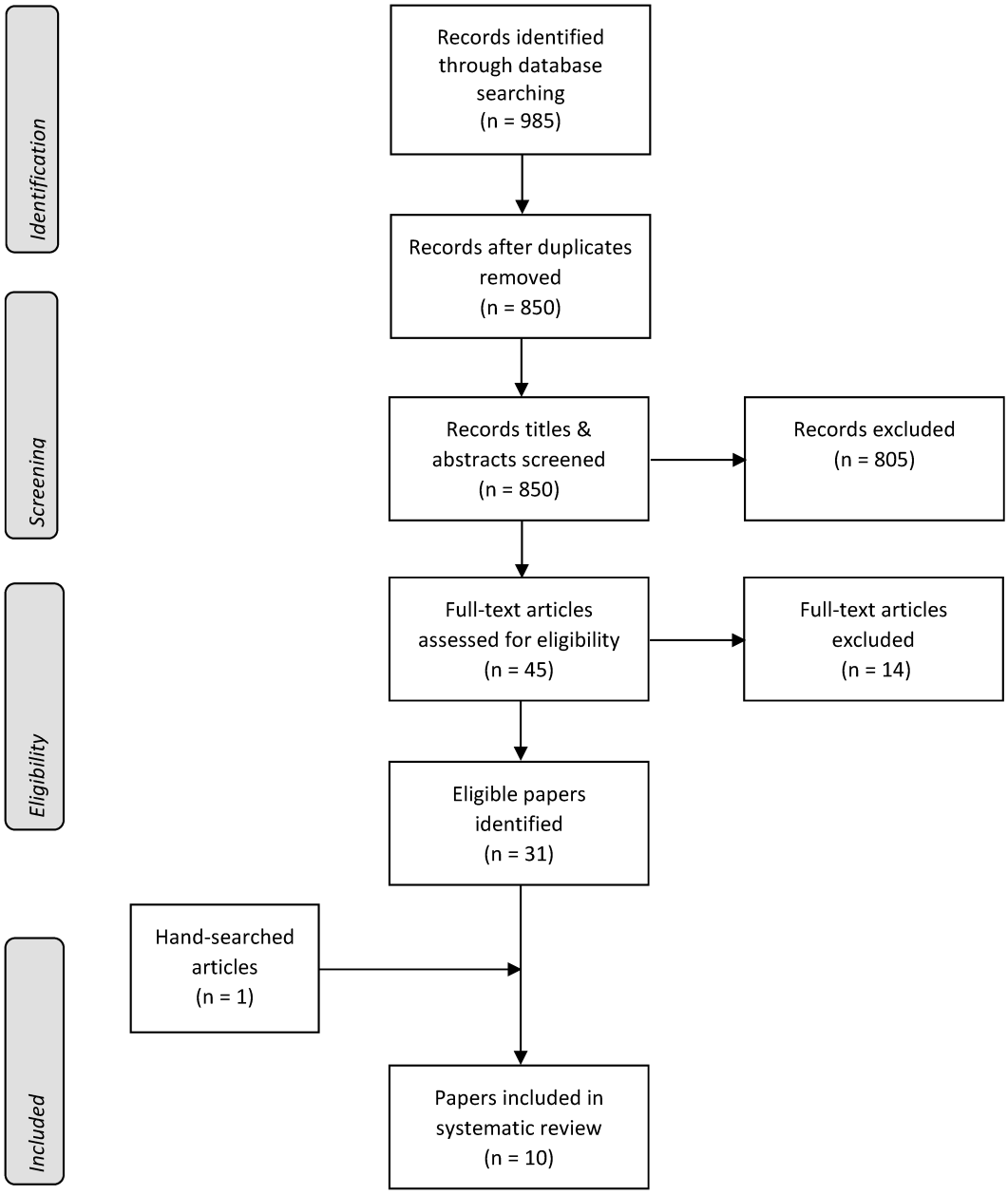
Reference	Design	Therapy	Control	Follow-up (mean)	Number of patients, exposed	Number of patients, control	Event	Events (N=) exposed/control	Relative effect (95% CI)	Study quality
Cardiovascular events										
Crittenden, 2012	Cross sectional	colchicine	No colchicine	NA	576	712	MI	7 / 18	RR0.46	Intermediate
Solomon, 2015	Retrospective cohort	Colchicine	No colchicine	1,5 years	501	501	Composite: MI, CVA/TIA All-cause mortality	28 / 82 43 / 103	HR0.51 (0.30-0.88) HR0.27 (0.17-0.43)	Intermediate

Reference	Design	Therapy	Control	Follow-up (mean)	Number of patients, exposed	Number of patients, control	Event	Events (N=) exposed/control	Relative effect (95% CI)	Study quality
Cardiovascular events (composite endpoints)										
Foody, 2017	Retrospective cohort	Febuxostat 40-60mg	Allopurinol Median: 150mg	0,75 years	370 (gout +CKD 3-4_)	2056 (gout + CKD3-4)	Major event: (CAD, CVA, PAD)	14 / 138	HR0.52 (0.30-0.91)	Intermediate
Kang, 2019	Retrospective cohort	Allopurinol <300mg	Febuxostat <80mg	0,8 years	39640	9910	CVD: MI, TIA, cor. Revasc.	648 / 125	HR1.09 (0.90-1.32)	Intermediate
Zhang, 2018	Retrospective cohort study	Febuxostat >40mg.	Allopurinol 300mg	1,15 years	24936	74808	CV event: MI, CVA.	935 / 3105	HR1.01 (0.94-1.08)	Intermediate
White, 2018	RCT	Febuxostat 40-80mg	Allopurinol 200-600mg	2,6 years	3098	3092	CV death, MI, CVA, revasc	335 / 321	HR1.03 (0.87-1.23)	*High* *Low level of bias (RCT)*
Joo, 2014	Retrospective cohort	>3 years ULT SUA<6mg/dL	>3 years ULT, SUA>6.0mg/dL	7.6 years	53	147	CVD: MI, HF, CVA, angina	3 / 9	NA.	Intermediate

Kim, 2015	Retrospective cohort	XOI (allopurinol / febuxostat)	No XOI, SUA>6.8mg/dL	1.3-1.4 years.	32505PY	29305PY	CVD: MI, CVA, HF, revasc.	788/628	HR1.16 (0.99-1.34)	Intermediate
Lin, 2017	Retrospective cohort	Allopurinol Benzbromaron A+B	No ULT therapy	NA	1422 4141 2484	1422 4141 2484	CAD	196/151 507/387 304/204	HR1.07 (0.86-1.33) HR1.05 (0.92-1.21) HR0.94 (0.71-1.03)	High
Kim, 2018	Retrospective cohort	Probenecid 500-1000mg	Allopurinol 100-300mg	1 year	8611PY	41816PY	MI, CVA	203/1182	HR0.80 (0.69-0.93)	Intermediate
Kok, 2014	Retrospective cohort	Allopurinol Median: 100mg.	Non-allopurinol (69% uricosuric)	5 years	2483	2483	CV event: CHD, HHD, HF, CVA, 'other CVD'	566/470	HR1.25 (1.10-1.41)	High
Mackenzie, 2020	RCT	Allopurinol mean: 278 mg	Febuxostat Mean: 274 mg	4 years	3065	3063	CVD: CVD mortality, non-fatal MI, ACS, stroke	241/ 222	HR0.85 (0.70-1.03)	*High (low risk of bias, RCT)*
Mortality										
Chen, 2015	Prospective cohort	ULT (allopurinol /benzbromaron)	no ULT	6,5 years	764	764	CVD mortality	5 / 21	HR0.29 (0.11-0.80)	Intermediate
Kang, 2019	Retrospective cohort	Allopurinol <300mg	Febuxostat <80mg	0,8 years	39640	9910	All-cause mortality	545 / 135	HR0.96 (0.79-1.16)	Intermediate
Kim, 2018	Retrospective cohort	Probenecid 500-1000mg	Allopurinol 100-300mg	1 year	8753PY	42719PY	All-cause mortality	255 / 1387	HR0.87 (0.76-1.00)	Intermediate
Kok, 2012	Retrospective cohort	Allopurinol ≥300mg.	Allopurinol 100mg.	5 years	395	1262	CVD Mortality	NA	HR0.75 (0.59-0.94)	High

Zhang, 2018	Retrospective cohort study	Febuxostat	Allopurinol	1,15 years	24936	74808	All cause mortality	1144/ 4022	HR0.95 (0.89-1.02)	Intermediate
White, 2018	RCT	Febuxostat 40-80mg	Allopurinol 200-600mg	2,6 years	3098	3092	CVD mortality	134 / 100	HR1.34 (1.03-1.73)	*High (low level of bias, RCT)*
Mackenzie, 2020	RCT	Allopurinol mean: 278 mg	Febuxostat Mean: 274 mg	4 years	3065	3063	CVD mortality	82 / 62	HR0.91 (0.66-1.27)	

4. Prevalence and incidence of cardiovascular disease

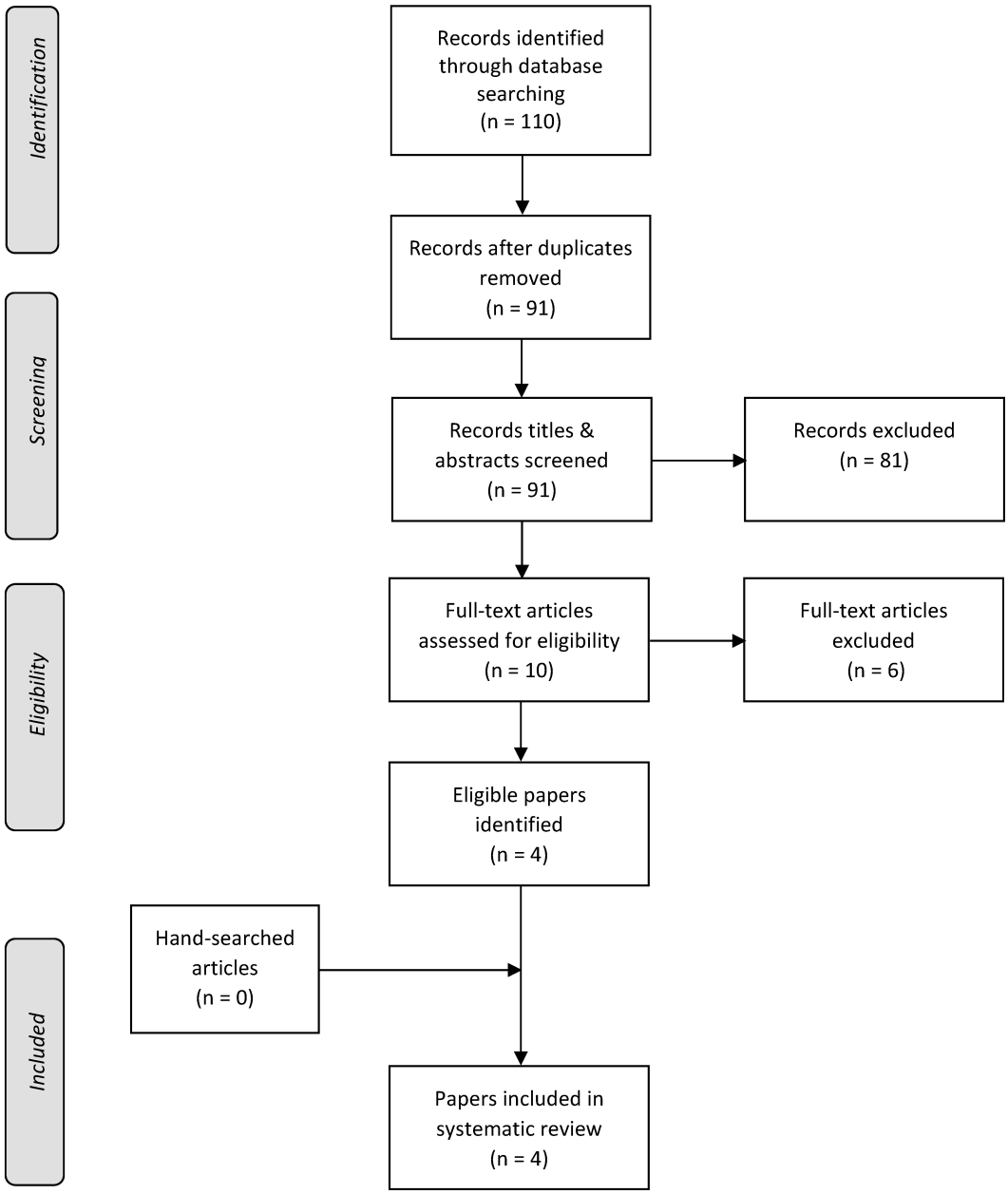


Reference	Cohort	Number of patients	Follow up (years)	Event	Relative effect (95% CI)
CVD					
Abbott, 1988	Framingham Study	5209	32	Coronary heart disease	RR 1.60 (1.1-2.5)
DeVera, 2010	British Columbia linked Health Database	57852	7	Acute MI men: Acute MI women:	RR 1.11 (0.99-1.23) RR 1.39 (1.20-1.61)
Clarson, 2015	UK Clinical Practice Research Datalink	48152	10	Vascular event men: Vascular event women:	RR 1.06 (1.01-1.12) RR 1.25 (1.12-1.25)
Janssens, 2016	General practitioner database Netherlands	1859	2,5	CVD composite (AP, MI, HF, TIA/CVA, PAD, AA)	HR 1.44 (1.18-1.76)
Kuo, 2013	Taiwan National Health Insurance Research	26556	8	Myocardial infarction	HR 1.23 (1.11-1.36)
Seminog, 2013	England National Health service database	202033	3,8	Myocardial infarction Stroke	RR 1.82 (1.78-1.85) RR 1.71 (1.68-1.75)
Singh, 2018	Medicare database >65 years.	94809	6	Myocardial infarction	HR2.08 (1.95-2.21)
CVD Mortality					
Krishnan, 2008	MRFIT	9105	17	HR1.35 (1.06-1.72)	
Choi, 2007	Health Professionals Follow up	51297	12	HR1.38 (1.15-1.66)	
Teng, 2012	Singapore Chinese Health Study	47035	10	HR1.23 (0.97-1.56)	

B. Vasculitis, systemic sclerosis (SSc), mixed connective tissue disease (MCTD), myositis and Sjögren's syndrome (SS)

1. Cardiovascular risk prediction tools

PICO: '*In patients with vasculitis, SSc, MCTD, myositis and SS, what's the performance of risk prediction tools to predict cardiovascular risk?*'

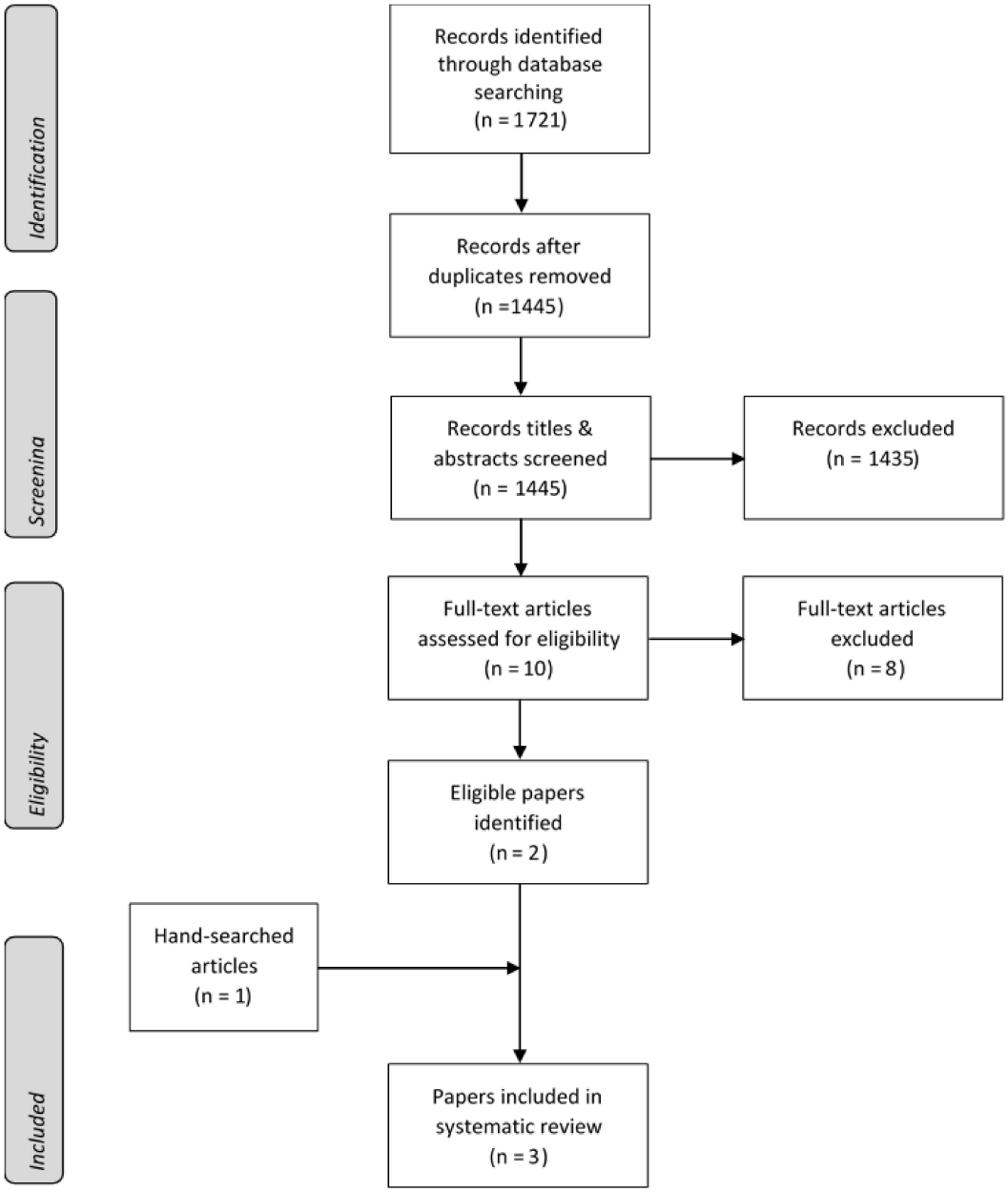


Reference	Design	Risk tool	Follow-up	Performance	Study quality score
Berti 2018	Retrospective cohort	Office based Framingham	10 yrs	10yr Framingham: 20% Observed 10yr incidence: 40%	intermediate
Terrier 2013	Prospective cohort	Framingham (type unknown)	7.1 yrs	10yr Framingham: 9% Observed events 5 and 10 yr: 10% and 27%.	intermediate
Suppiah 2011	Prospective cohort	Office based Framingham	5 yrs	AUC EUVAS Model: 0,73 AUC Framingham: 0,65	intermediate
Udayakumar 2015	Retrospective cohort	Office based Framingham	10 yrs	10yr Framingham: 30% (all CV events) Observed 10yr incidence: 8% (only CHD)	intermediate

2. Interventions targeting traditional cardiovascular risk factors

   a. Antihypertensives

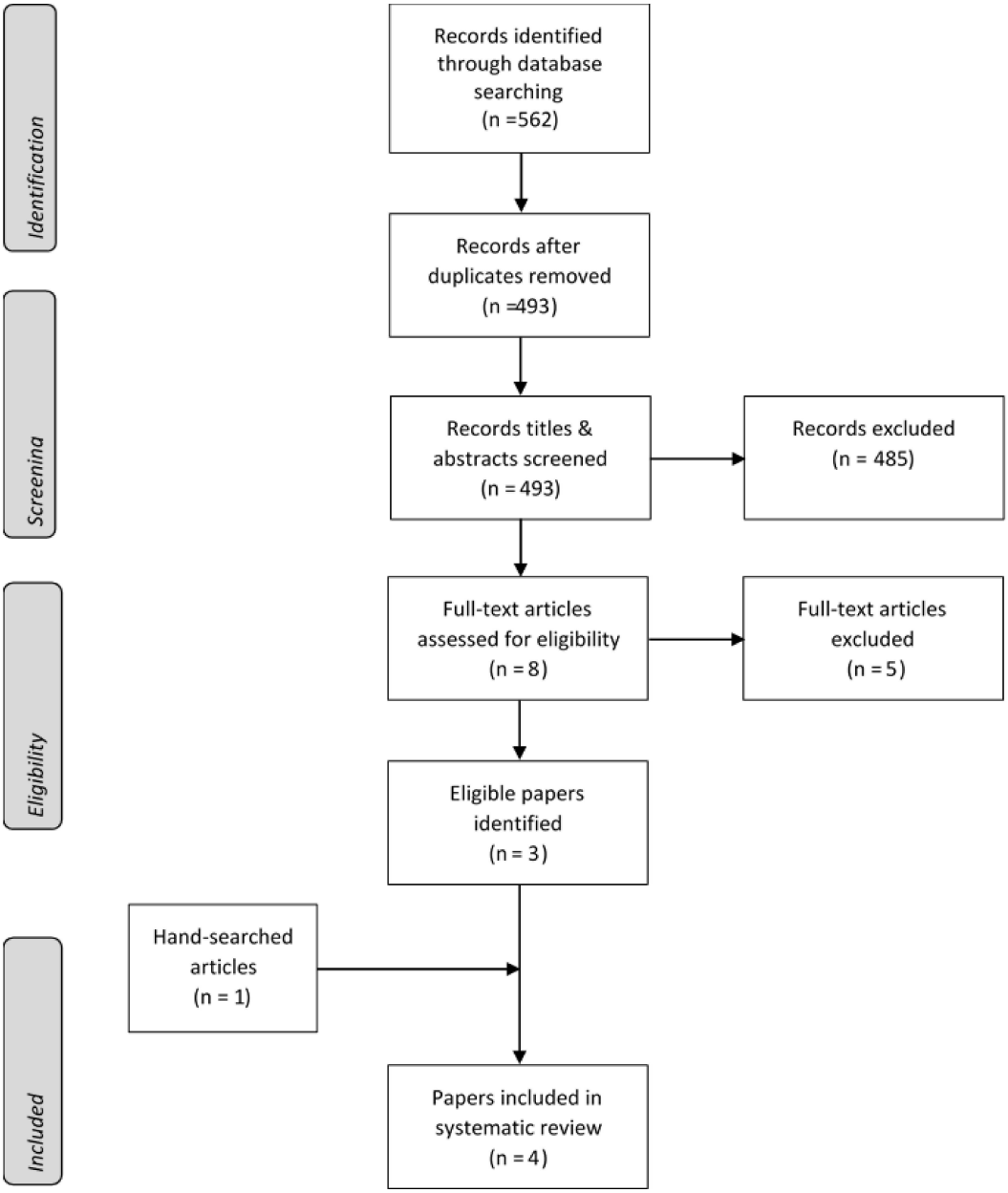
   PICO: *'In patients with vasculitis, SSc, MCTD, myositis and SS, does treatment with antihypertensives result in better cardiovascular outcomes than no treatment with antihypertensives?'*



Reference	Design	Intervention	Control	Number of patients, intervention	Number of patients control	Events, intervention	Events, control	Relative effect (95% CI)	Quality score
Alba 2014	Prospective cohort	ACE/ARB	No ACE/ARB	27 GCA	79 GCA	1 TIA	5 strokes/TIA.	RR 0.59 (0.07 – 4.79)	intermediate
Grossman 2017	Retrospective cohort	Beta blockers	No beta blockers	23 GCA	60 GCA	11 (48%) cranial ischemic events	12 (20%)	RR 4.35 (1.33–14.2)	intermediate
Valentini 2019	Prospective cohort	CCB/ACEi/ARB	No CCB/ACE/ARB	448 SSc	153 SSC	7 Ventricular arrhitmyas (2%)	5 ventricular arrhitmyas (5%)	HR 0.28 (0.09 to 0.90)	intermediate

b. Lipid-lowering agents

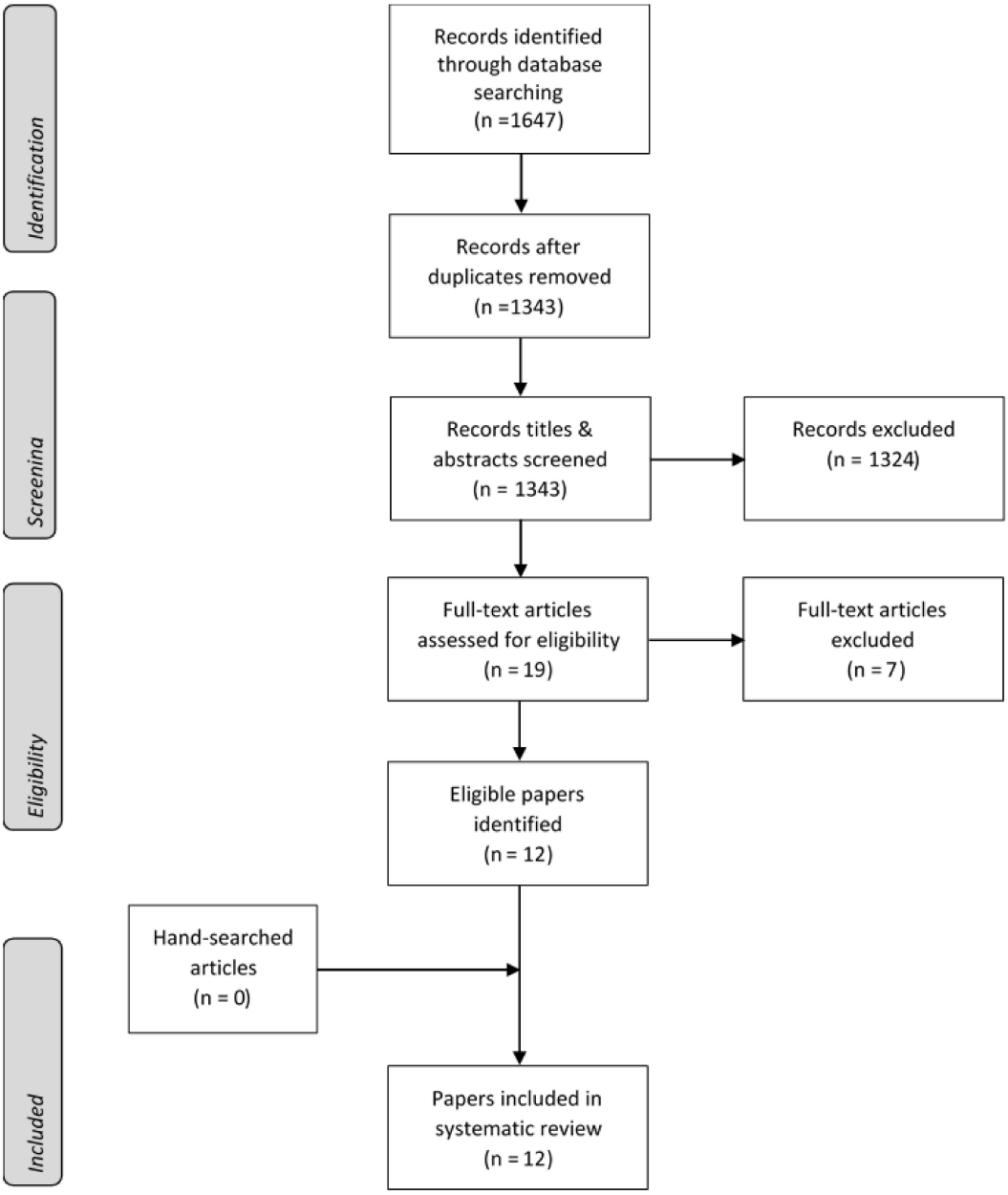
PICO: '*In patients with vasculitis, SSc, MCTD, myositis and SS, does treatment with lipid lowering-medications result in better cardiovascular outcomes than no treatment with these medications?*'



Reference	Design	intervention	Control	Number of patients, intervention	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Study quality score
Grossman 2017	Retrospective cohort	Statins	No statins	21 GCA	62 GCA	5 (24%)	19 (31%)	RR 0.78 (0.33 – 1.82)	Inter mediate
Pugnet 2016	Retrospective cohort	Statins	No statins	28 GCA	75 GCA	unknown	unknown	HR 0.993 (0.986–0.999) Statins in cumulative DDD Per year: HR 0.48 (CI 0.33- 0.69)	Inter mediate
Navraez 2007	Retrospective cohort	Statins	No statins	30 GCA	91 GCA	CVA 2 (7%) IHD 1 (3%) PAD 0 (0%)	CVA 3 (3%) IHD 1 (1%) PAD 5 (5%)	P = 0.60 P = 0.43 P = 0.19	Inter mediate
Pariente 2019	Retrospective cohort	Statins	No statins	21 GCA	108 GCA	5 (24%)	13 (12%)	RR 1.98 (0.79 – 4.96)	Inter mediate

c. Antiplatelets

PICO: *'In patients with vasculitis, SSc, MCTD, myositis and SS, does treatment with antiplatelets result in better cardiovascular outcomes than no treatment with antiplatelets?'*



Reference	Design	Intervention	Control	Number of patients, intervention	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Quality score
Grossman 2017	Retrospective cohort	Platelet inhibitors	No platelet inhibitors	24 GCA	59 no GCA	7 (29%)	17 (29%)	1.01 (0.48 – 2.12)	intermediate
Pariente 2019	Retrospective cohort	Platelet inhibitors	No platelet inhibitors	31 GCA	98 GCA	9 (29%)	9 (9%)	3.16 (1.34 – 7.26)	intermediate
Pugnet 2016	Retrospective cohort	Platelet inhibitors	No platelet inhibitors	16 GCA	87 GCA	0 (0%)	18 (21%)	NA	intermediate
Valentini 2019	Prospective cohort	Platelet inhibitors	No platelet inhibitors	161 SSc	182	17 (10%)	29 (16%)	0.41 (1.98 16.56) Frailty analysis: 0.53 (0.26–1.08)	intermediate

For GCA, the panel agreed to update the SLR of the 2018 EULAR recommendation for the management of large vessel vasculitis*. Therefore, only articles that were published after 2015 are included in the table.

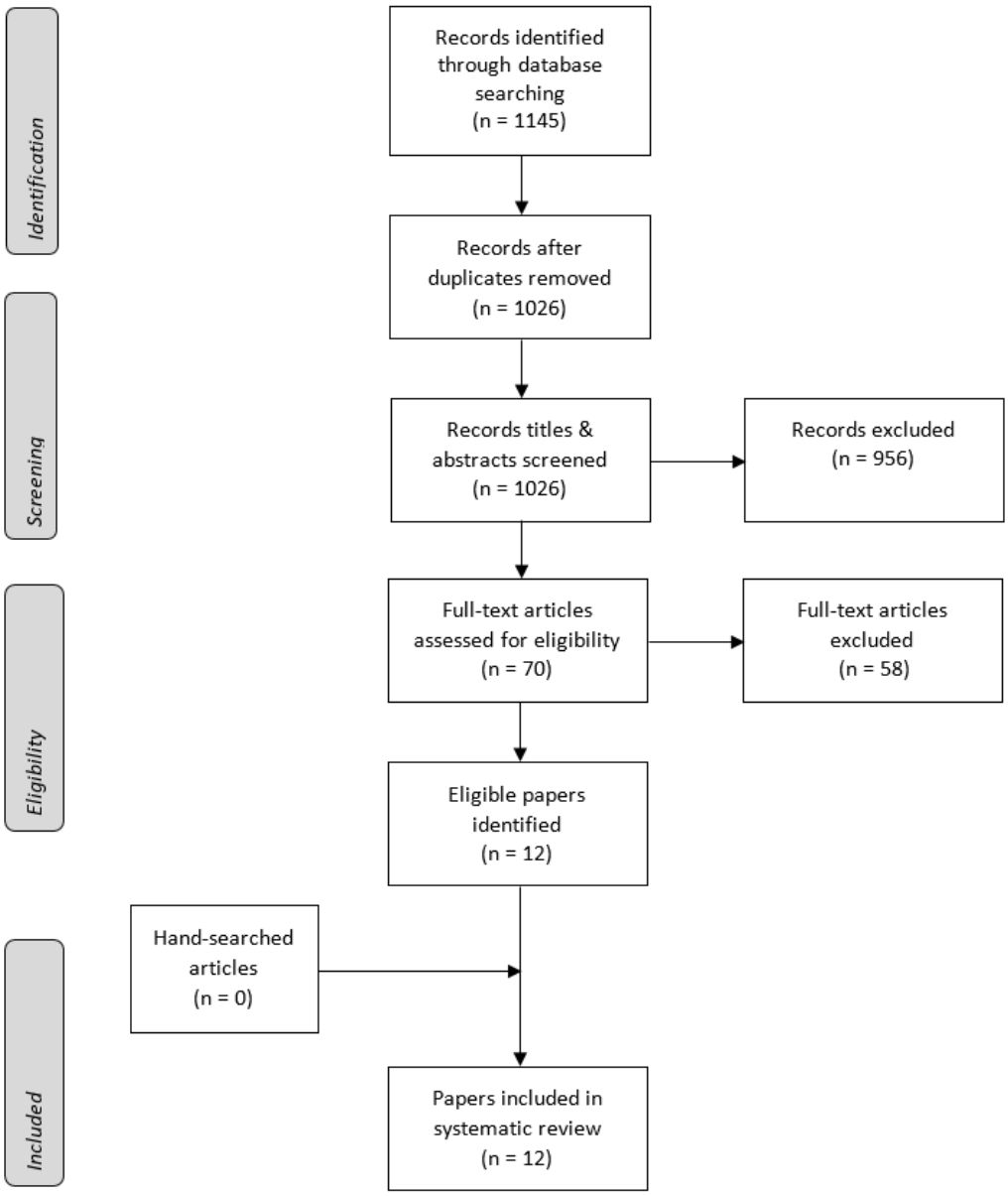
*Hellmich B., Agueda A., Monti S. et. al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis, Ann Rheum Dis. 2020 Jan;79(1):19-30. doi: 10.1136/annrheumdis-2019-215672.

3. Interventions targeting disease-related cardiovascular risk factors

   a. Disease features

      PICO: '*What is the effect of high disease activity on the risk of CVD?*'

      i. Disease activity
      ii. Disease duration



Reference	Design	Exposure	Control	Number of patients, exposed	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Quality score
Disease activity									
Houben E. et al. 2020	Prospective cohort study	Disease activity: BVAS	-	231 GPA, 105 EGPA (newly diagnosed)	-	20 non-fatal, 3 fatal CV events	-	Higher BVAS (per point) HR: 1.09 (1.03-1.16) Adjusted HR: 1.09 (1.02-1.16)	High
Bai et al. 2018	Retrospective cohort study	Disease activity: BVAS	-	349 MPA, 119 GPA, 36 RLV (newly diagnosed)	-	CVE: 117 MI: 77 (65.8%) Stroke: 40 (34.2%)	CVE: 117 MI: 77 (65.8%) Stroke: 40 (34.2%)	Predictive value BVAS for CVE: HR 1.039 (1.011 – 1.067) Predictive value of BVAS for CVD-related mortality: HR: 1.064 (1.018 – 1.113) Predictive value of BVAS for CVE after 2 years since diagnosis: HR: 1.067 (1.021-1.115) Predictive value of BVAS for CVD-related mortality after 2 years of diagnosis: HR: 1.104 (1.033 – 1.180)	High
Robson et al. 2014	Prospective cohort study	Disease activity: BVAS	-	535 patients MPA, n = 254 GPA, n = 281	-	ACS, iCVA, MI, no numbers mentioned	-	Significant relationship between iCVA and entry BVAS: adjusted OR: 1.77 (1.01 – 3.10) No significant relationship between entry BVAS and other CVD.	High

Suppiah et al. 2015	Prospective cohort study	Disease activity: BVAS	-	427 patients WG, n = 237 MPA, n = 190	-	CV event: 78 CV deaths: 32 Non-fatal MI: 42 Non-fatal stroke: 25	-	BVAS score was not associated with cardiovascular events.	High
Disease duration									
Albrecht et al. 2017	Prospective cohort study	Disease duration	-	1858 patients (1420 PMR, 177 GCA, 261 PMR & GCA)	-	No longitudinal data on frequency of outcome variable described (only cross-sectional at baseline)	-	The frequency of cardiac disease was not increased in patients with longstanding disease, even in patients with more active disease.	Intermediate
Amiri et al. 2015	Prosspective cohort study	Disease duration	Healthy age and sex matched subjects	809 GCA patients	8577	MI: 83 Stroke: 60 Both: 123		Risk of CV events highest in first year after diagnosis; risk decreases in subsequent years but remains statistically significant for over the first 5 years. HR < 1y MI: 4.76 (3.29-6.88) HR < 1y Stroke: 3.20 (2.11-4.87) HR < 1y Both: 3.92 (3.91-5.28)	High
Bartoloni et al.	Restrospective cohort study	Disease duration	-	408 pSS patients	-	HF: 8 TIA: 6 Stroke: 4 Angina: 4	-	Cardiac events and peripheral obliterive arteriopathy appear to	Intermediate

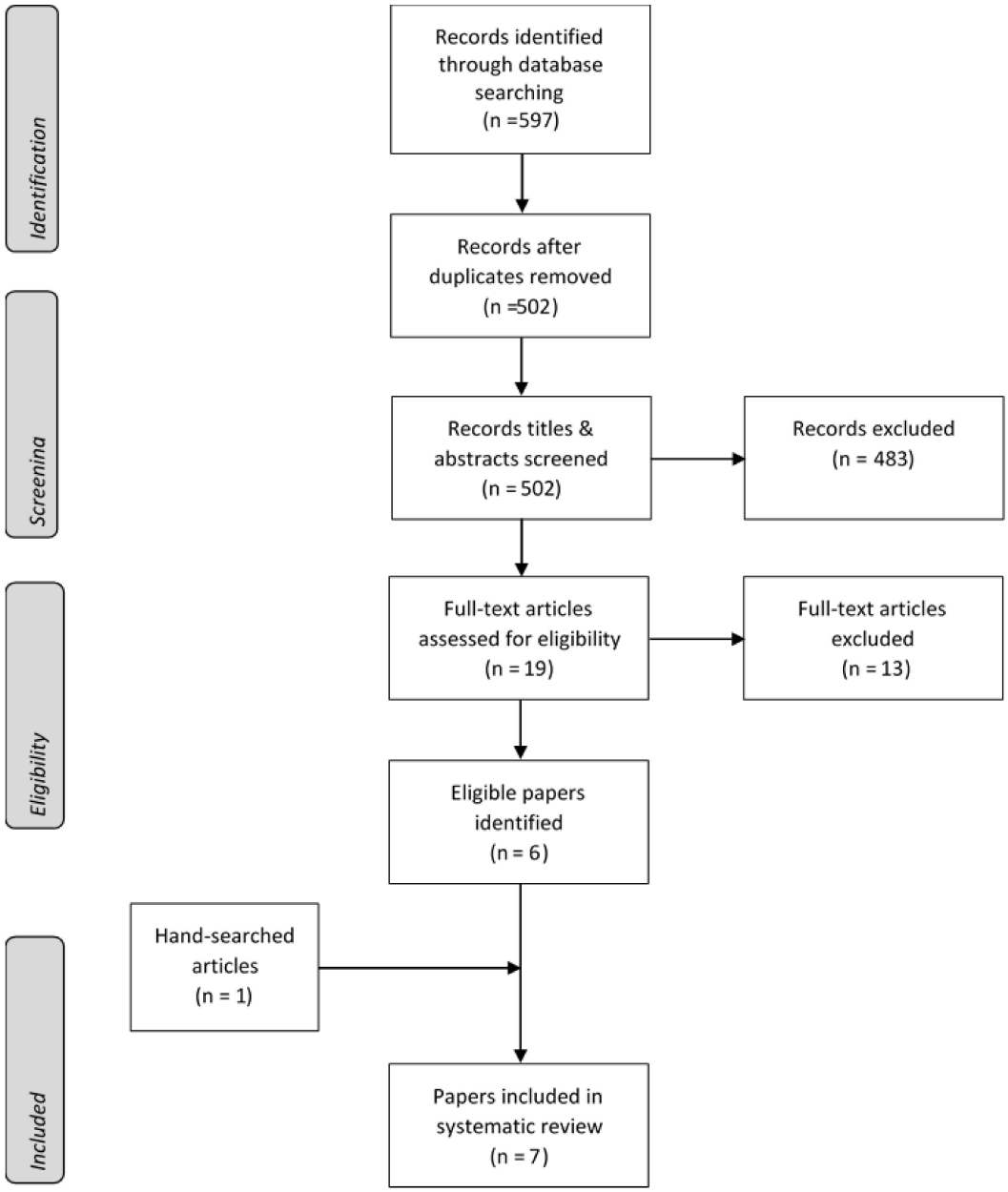
						MI: 3 Obliterative arteriopathy: 2		be associated with longer disease duration.	
Mofors et al. 2019	Prospective cohort study	Disease duration	Sex, age and region of residency matched controls	960 pSS patients	9600	MI: 53 CI: 34 VTE: 50	-	MI: First 5 years after diagnosis: HR 0.9, (0.4-1.8) 5-10 years after diagnosis: HR 1.8 (1.1-2.9 and >10 years after diagnosis: HR 1.9 (1.3-3.0) Cerebral infarction: No increased risk for CI first 5 and 5-10 years after diagnosis. I10 years after diagnosis: HR 1.6 (1.0-2.7) Thromboembolism: 1st 5 years (HR: 2.1, CI 1.2-3.5) 5-10y: HR: 2.8 (1.6-4.) >10y: HR: 1.8 (1.1-2.9)	High
Lescoat et al. 2019	Observational cross-sectional study	Disease duration	-	204 SSc patients	-	Unilateral UAO: 76 Bilateral UAO: 49	-	Unilateral, bilateral or both UOA: Unadjusted OR: 1.66 (1.23-2.24) Adjusted OR not significant, but no values described	Intermediate

b. Medications

PICO: *'In patients with vasculitis, SSc, MCTD, myositis and SS, is the use of immunosuppressive treatment related to cardiovascular outcome?*'

Immunosuppressives:

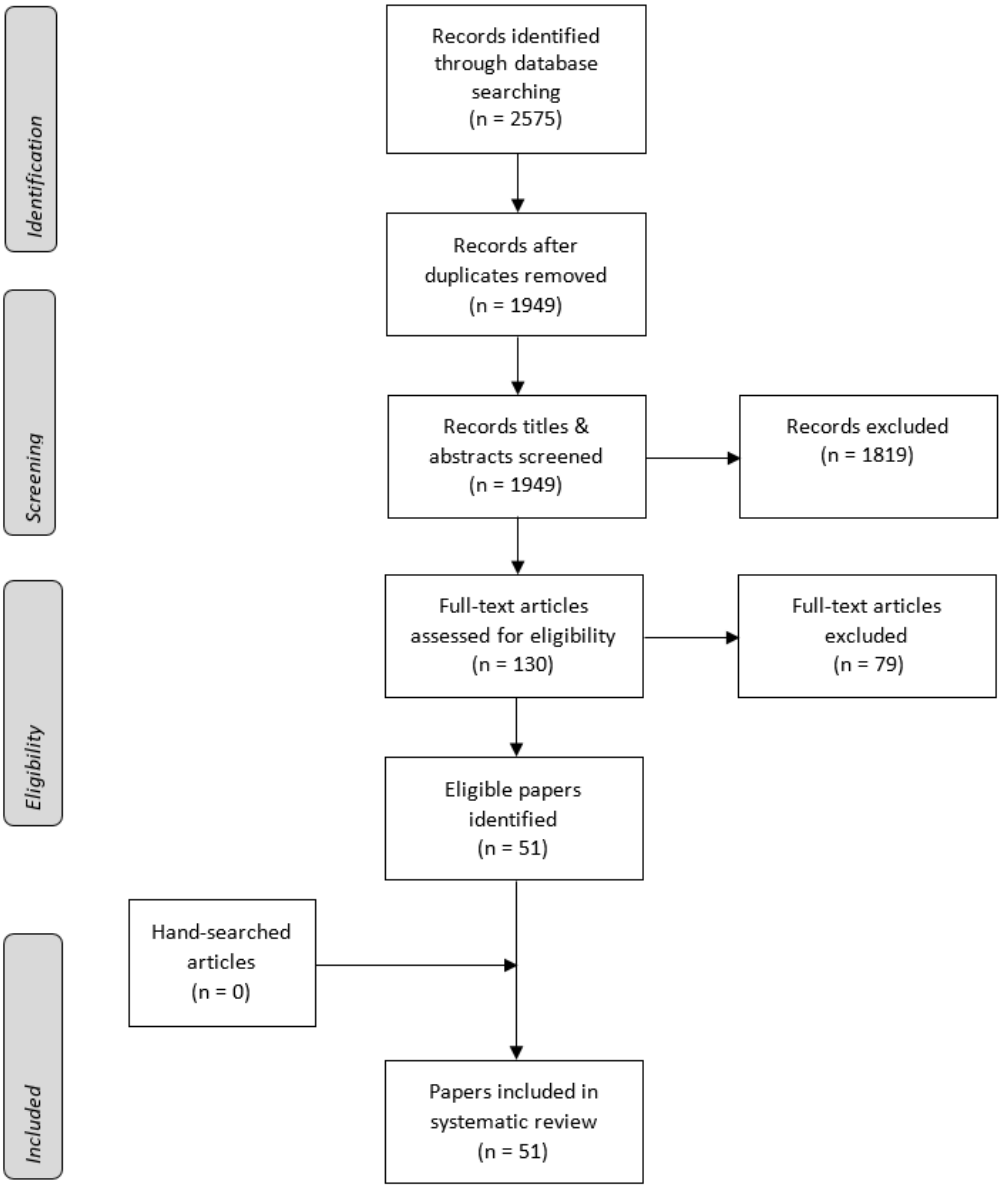
- *Glucocorticoids*
- *Methotrexate*
- *Mycophenolate mofetil*
- *Azathioprine*
- *Cyclophosphamide*
- *Rituximab*
- *Cyclosporin*
- *Hydroxychloroquine*


Identification
Screenina
Eligibility
Included
Records identified through database searching (n =597)
Records after duplicates removed (n =502)
Records titles & abstracts screened (n = 502)
Records excluded (n = 483)
Full-text articles assessed for eligibility (n = 19)
Full-text articles excluded (n = 13)
Eligible papers identified (n = 6)
Hand-searched articles (n = 1)
Papers included in systematic review (n = 7)

Reference	Design	intervention	Control	Number of patients, intervention	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Quality score
Albrecht 2018	Retrospective cohort	Glucocorticoids	No glucocorticoids	286 GCA	152 GCA	unknown	unknown	NA	Intermediate
Boysson 2019	Retrospective cohort	Glucocorticoids Other: MTX, tocilizumab, dapsone, a-TNF-alfa, anakinra	No glucocorticoids No other immunosuppressors	GCA, GC unknown Other: 73	GCA, GC unknown Other: 215	unknown	unknown	Glucocorticoid: 1.57 (0.03–12.95), month Other: 0.44 (0.29–0.66)	Intermediate
Gale 2018	Retrospective cohort	Risk per 1 gram increase in cumulative glucocorticoid dose over 52 weeks	Lowest glucocorticoid dose	GCA NA	GCA NA	NA	NA	CVA USA cohort 1.01 (0.98, 1.04) UK 1.00 (0.99, 1.02) IHD USA 1.01 (0.99, 1.04) UK 1.01 (0.99, 1.03)	High

Faurshou 2009	Prospective cohort	CYC	No CYC	AAV 129 (44%) 1-36 g 76 (26%) >36 g	No CYC 41 (14%) Unknown 47 (16%) → excluded	18 (14%) in 1-36g 23 (30%) in >36g	8 (20%) no CYC	No CYC RR 1.8 (0.8 – 3.6) CYC 1-36 RR 1.4 (0.8 – 2.2) CYC > 36 RR 2.0 (1.3 p 3.0)	High
Tisseverasinghe 2009	Prospective cohort	Glucocorticoids, NSAIDS, non steroidal immunomodulator (MTX, AZA, antimalarial agents,CYC)	NO Glucocorticoids, NSAIDS, immunomodulators,	Dermatomyositis/polymyositis Immunomodulators: 154 AZA: 83	Dermatomyositis/polymyositis No immunomodulators: 275 No AZA: 328	Immunomodulators: 24 (16%) AZA 9 (11%)	No immunomodulators: 56 (20%) AZA 71 (22%)	Immunomodulators RR of 0.5 (0.2 - 1.0) AZA RR 03 (0.1-0.8) No relation between events and other medication	Intermediate
Wu 2018	Retrospective cohort	Glucocorticoids NSAIDS DMARDs (HCQ, MTX, Sulfasalazine)	No glucocorticoids NSAIDS DMARDs	pSS unknown	pSS unknown	unknown	unknown	Glucocorticoids RR 1.45 (1.07–1.97) NSAID RR 1.31 (1.05–1.65) DMARDs RR 0.92(0.66–1.27)	High
Chu 2013	Prospective cohort	Glucocorticoids Other immunosuppressors: AZA, MTX, CYC, Cyclosporin	No glucocorticoids No other immunosuppressors	Frequent users: 325 SSc 171 SSc	1019 SSc 1173 SSc	9 (3%) 2 (1%)	22 (2%) 29 (2%)	Glucocorticoids (HR 1.41 (0.64-3.09) other immunosuppressors HR 0.83 (0.33-2.11)	High

4. Prevalence and incidence of cardiovascular disease



a. Mixed connective tissue disease

	Cohort	Number of patients	Follow up	Event	Relative effect (95% CI)
CVD					
Alenghat et al. 2016	USA	African Americans: 202 isolated UCTD/MCTD White Americans: 457 isolated UCTD/MCTD	N.A.	ASCVD (Atherosclerotic cardiovascular disease)	African Americans: Prevalence ratio: 2.3 (1.7-2.9) White Americans: Prevalence ratio: 1.0 (0.7-1.3)

b. Sjögren's syndrome

	Cohort	Number of patients	Follow up	Event	Relative effect (95% CI)
CVD					
Alenghat et al. 2016	USA	African Americans: 424 White Americans: 699	N.A.	ASCVD (Atherosclerotic cardiovascular disease)	African Americans: Isolated Sjögren; Prevalence ratio: 1.7 (1.1-2.5) All Sjögren: Prevalence ratio: 2.9 (2.5-3.4) White Americans: Isolated Sjögren; Prevalence ratio: 0.5 (0.3-0.9) All Sjögren: Prevalence ratio: 1.5 (1.3-1.9)
Luni et al 2017	United States	13086 Sjögren		IHD	Adjusted HR: 0.898 (0.844-0.955)

Wu et al. 2018	China	365 pSS patients	Observation period: 256883 person-months for patents, 1043101 person-months for controls	CHD (coronary heart disease)	All patients: HR: 1.24 (CI: 1.10-1.40) Low risk patients: HR: 1.52 (1.21 – 1.92)
Yong et al. 2018	Systematic review and meta-analysis	9 studies included	N.A.	CVD + CVA, CVD, CVA	Pooled OR CVD + CVA: 1.28 (0.11-1.46) CVA: 1.31 (0.96 – 1.79) CVD: 1.30 (1.09-1.55)
Zöller 2012	Sweden	-	-	Stroke	hCVA: Standardized IR: 0.81 (0.26 – 1.90) iCVA: Standardized IR: 1.31 (1.02 – 1.67)
Zöller 2012	Sweden	-	-	CHD	Standardized IR: 1.63 (1.42 – 1.87)

c. Systemic sclerosis

	Cohort	Number of patients	Follow up	Event	Relative effect (95% CI)
CVD					

Alenghat et al. 2016	USA	African Americans: 391 White Americans: 451	N.A.	ASCVD (Atherosclerotic cardiovascular disease)	African Americans: Isolated SSc; Prevalence ratio: 2.7 (2.1-3.6) All SSc: Prevalence ratio: 3.8 (3.3-4.3) White Americans: Isolated Ssc; Prevalence ratio: 2.2 (1.7-2.9) All SSc: Prevalence ratio: 2.6 (2.1-3.1)
Ali et al. 2015	Systematic review	5 included studies with control group and RR/OR/HR reported effect	-	CAD (coronary artery disease)	RR 1.7 (0.8-3.7) OR: 3.2 (2.3-4.5) HR: 1.8 (1.1-3.1) OR 3.3 (1.1-10.6) HR: 2.5 (1.6-3.8)
Chiang et al. 2013	Taiwan	1238	Median 4.7y, max 10y	ischemic stroke	Unadjusted HR: 1.44 (CI: 1.15-1.80) Adjusted HR: 1.43 (CI: 1.12-1.83)
Hu et al. 2018	Canada	78	Mean 9.8 years (9.2y for controls)	Any CV, CAD, MI, Angina, PVD, CHF	Any CV: HR: 2.38 (CI: 1.28 – 4.43) Adjusted HR: 2.66 (1.39 – 5.11) CAD: (MI + angina) HR: 2.35 (CI: 1.17 – 4.71) HR adjusted: 2.60 (1.25 – 5.41) MI: HR: 3.14 (CI: 0.97 – 10.14) Adjusted HR: 4.88 (CI: 1.21 – 19.72) Angina: HR: 2.37 (0.97 – 7.10) Adjusted HR: 2.11 (0.68 – 6.56) PVD (PAD + AAA) HR: 3.88 (CI: 0.91-16.33) CHF HR 2.10 (CI: 0,90 – 4,89) Adjusted HR: 1.92 (0.69 – 5.32)

Zöller 2012	Sweden	-	-	Stroke	hCVA: Standardized IR: 2.87 (1.48 – 5.03) iCVA: Standardized IR: 1.21 (0.9 – 1.58)
Zöller 2012	Sweden	-	-	CHD	Standardized IR: 1.46 (1.37 – 1.55)

d. ANCA-associated vasculitis

	Cohort	Number of patients	Follow up	Event	Relative effect (95% CI)
CVD					
Berti et al. 2018	Canada	Newly diagnosed AAV: 58	N.A.	CAD = AF, HF, CVA, PVD (incl. VTE, DVT and PE)	Any CVD: HR 3.15 (1.51-6.57) CAD: HR 0.87 (0.29-2.60) CHF: HR 2.62 (1.05-6.51) AF: HR 1.65 (0.78-3.48) CAD, HF or AF: HR 2.96 (1.42-6.15) CVA: HR 8.49 (2.54-28.30) PVD: HR 0.70 (0.08-6.40) VTE: HR 3.26 (0.84-12.60) PE: HR 1.33 (0.23-7.54)
Houben et al. 2017	Meta-analysis	7 included studies	N.A.	total CVE, IHD and CV	Pooled RR for total CVE: 1.65 (1.23-2.22) Pooled RR for IHD: 1.60 (1.39 – 1.84) Pooled RR for CVA: 1.20 (0.98 0 1.48)
Li et al. 2017	UK	570 newly diagnosed GPA	N.A.	Stroke/Tia, PVD, VTE, HF, IHD	IHD: HR: 0.91 (0.60-1.38) Stroke/TIA: HR: 1.08 (0.70-1.67) PVD: HR: 0.96 (0.45 – 2.09) HF: HR: 1.46 (0.93-2.30) HRs stratified for follow-up length: VTE: >=3y: 2.56 (1.44-4.54) <3y: 5.24 (2.83-9.71)

Mourguet et al. 2019	France	99 GPA, 26 MPA	Mean: 88.4 +- 78.3 months	CAD, Stroke (only CVA)	CAD: Incidence rate (age adjusted): 8.5 per 1000ptY Cumulative event incidence at 1, 5 and 10y: 2% (CI 1-4) 8% (5-10) 12% (CI 8-18) Stroke: Incidence rate (age adjusted): 10.2 per 1000ptY Cumulative event incidence at 1, 5 and 10y: 2% (CI 1-4) 3% (2-5) 11% (CI 6-15)
Wallace et al. 2019	USA	Newly diagnosed AAV patients 313 MPO+ 171 PR3+	Mean and SD: 7.0 +- 4.1y	CVD	Cumulative incidence for CVD: 0.8% (CI: 0.3 – 2.0) Increased cumulative incidence of death for CVD by 5 and 10 years after treatment initiation: 3.4% (CI: 2.0-5.4) 7.1% (CI: 4.5-10.4) Standardized mortality ratio: 2.3 (1.9-2.8)
Romeu et al. 2014	French REIN registry from 2002 to 2011	425 AAV on dialysis 259 GPA 166 MPA	Median follow-up of 23 months (IQR: 8-44)	CVA, PVD	Prevalence in AAV vs. non-AAV: CVA: 11% vs. 5.0% ($p < 0.0001$) PVD: 5% vs. 14% ($p < 0.0001$)

For AAV, the panel agreed to update the SLR of a 2016 meta-analysis.* Therefore, only articles that were published after janurary 2016 are included in the table.

* Houben E, Penne EL, Voskuyl AE, van der Heijden JW, Otten RHJ, Boers M, et al. Cardiovascular events in anti-neutrophil cytoplasmic antibody-associated vasculitis: a meta-analysis of observational studies. *Rheumatology (Oxford)* 2018;57:555-562.

e. Giant Cell Arteritis

	Cohort	Number of patients	Follow up	Event	Relative effect (95% CI)
CVD					
Amiri N et al 2016	Canada	809 GCA	N.A.	MI or stroke event	MI HR: 2.75 (2.16-3.5) Adjusted HR: 1.77 (1.29-2.43) Stroke HR: 2.21 (1.68-2.91) Adjusted: 2.04 (1.43-2.93)
Aouba et al. 2018	France	6313 GCA	N.A.	IHD and CVD	Standardized Mortality Odds Ratio (SMOR) IHD:1.45 (1.35-1.64) CVD: 1.23 (1.09-1.39)
Chazal et al 2018	France	4628 GCA	N.A.	CVA and IHD	SMOR: GCA as UCD (65-85y) CVA: 1.2 (0.8—1.8) IHD: 1.7 (1.3-2.3) SMOR: GCA as NUCD (65-85y) CVA: 2.4 (2.0—2.8) IHD: 0.9 (0.7-1.1)
Gonzalez-Gay et al 2005	Spain	210 GCA	January 1981 to December 2001	IHD	Standardized Mortality Ratio (SMR): 1.62 (0.7-3.2)

			prevalent diagnosis		
Kermani T et al. 2013	USA	204 GCA	Median 8.8 years	Cause specific mortality (CHD)	RR: 1.3 (0.95, 1.8)
Lee YH et al. 2018	Meta-analysis	7 studies; but only 4 had cardiovascular specific information	N.A.	CVD	SMR 1.312 (1.136-1.516)
Li L et al. 2017	UK	6796 GCA	N.A.	MI, AP, IHD, Stroke/TIA, PVD, HF	MI: HR: 1.65 (1.43-1.89) Adjusted HR: 1.57 (1.36-1.82) AP: HR: 1.39 (1.21-1.61) Adjusted HR: 1.36 (1.17-1.58) IHD: HR: 1.41 (1.22-1.62) Adjusted HR: 1.37 (1.18-1.59) Stroke/TIA: HR: 1.43 (1.31-1.57) Adjusted HR: 1.41 (1.29-1.55) PVD: HR: 1.98 (1.70-2.31) Adjusted: 1.75 (1.49-2.06) HF: HR: 1.45 (1.29-1.63) Adjusted: 1.46 (1.29-1.65)
Lo Gullo et al 2016	Olmsted County, MN, USA	244 GCA	N.A.	Stroke (iCVA, hCVA, TIA, amourosis fugax) or any CV	No significant differences in incidence of Stroke or any CV event between patients and controls
Mohammed A et al 2017	Skane Healthcare Register – Sweden	768 GCA	N.A.	First IHD or CVA	CVA: RR: 1.40 (1.12–1.74) IHD: RR: 1.20 (1.00–1.44)
Pugnet, G et al 2016	France	103 GCA	N.A.	Any CV hospitalization, CAD, HF	Any CV: IR: 3.3 (1.9-6.2) CAD: IR: 5.0 (1.3-26.7) HF: IR: 2.4 (0.9-6.0)

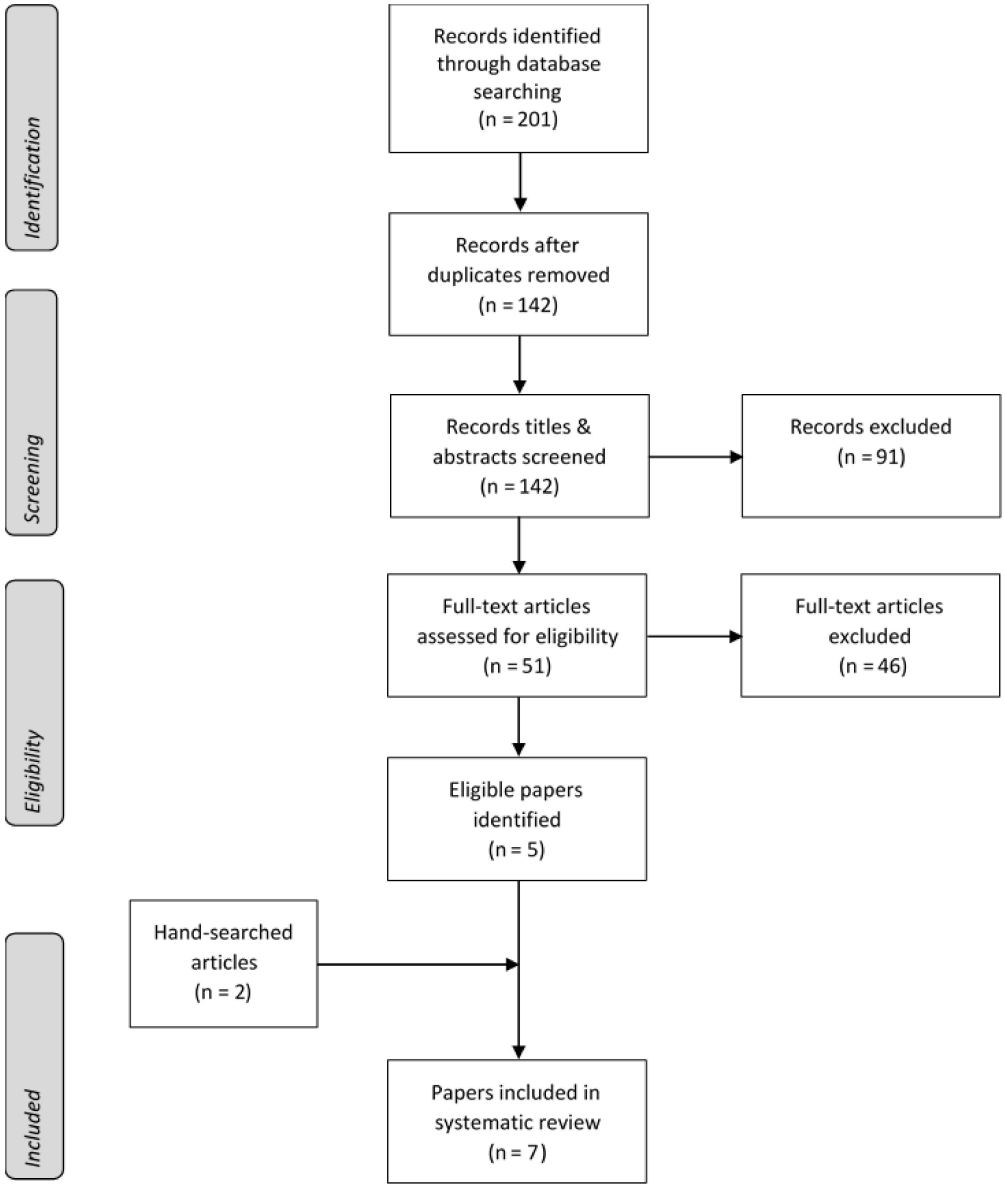
Ungprasert et al 2015	Meta-analysis	6 included studies - GCA	N.A.	CAD	Pooled RR : 1.51 (0.88-2.61)
Ungprasert et al 2016	Meta-analysis	4 included studies - GCA	N.A.	PVD	Pooled RR : 1,88 (1.04-3.41)
Ungprasert et al 2018	Meta-analysis	7 included studies - GCA	N.A.	CVA	Pooled RR: 1.4 (1.27, 1.56)
Alenghat et al. 2016	USA	African Americans: 340 White Americans: 265	N.A.	ASCVD (Atherosclerotic cardiovascular disease)	African Americans: Isolated DM/DP Prevalence ratio: 3.2 (2.6-4.1) All DM/DP Prevalence ratio: 3.5 (3.0-4.0) White Americans: Isolated DM/DP Prevalence ratio: 1.8 (1.2-2.6) All DM/DP Prevalence ratio: 2.2 (1.7-2.8)
De Moraes et al. 2013	Brazil	84 DM 105 Healthy controls	N.A.	MI and Stroke	Chi-square test: MI: p 0.112 Stroke: p 0.024
Lin et al. 2015	Taiwan	2029 with DM/PM 81166 controls	N.A.	newly diagnosed ACS	HR after adjusting for age, sex and comorbidities to develop ACS: 1.98 (1.17-3.35) RR after 5 year follow-up period: 4.35 (1.78-10.6) RR shorter than 5y follow up: 1.30 (0.66-2.58)
Rai et al. 2016	Canada	424 PM, 350 DM	N.A.	MI and Stroke	MI: PM: HR: 3.89 (2.28-6.65) DM: HR: 2.92 (0.54 – 3.331) Stroke: PM: HR: 1.76 (0.91 – 3.40) DM: HR: 1.33 (0.54 – 3.31)
Tisseverasinghe et al. 2009	Canada	607 inflammatory myopathy patients	Mean and SD: 4 +- 3.7y	MI	RR 1.95 (1.35 – 2.72)
Ungprasert et al. 2015	Systematic review & meta-analysis	3 included studies	-	Ischemic Stroke	Pooled Risk Ratio: 1.61 (CI: 1.28-2.02) PM/DM vs. controls

Ungprasert et al. 2014	Systematic review & meta-analysis	4 included studies	-	CAD	Pooled risk ratio: 2.24 (CI: 1.02-4.92) After excluding the only case-control study: 2.99 (CI: 1.80-4.97)
Zöller 2012	Sweden	-	-	Stroke	hCVA: Standardized IR: 1.85 (0.66 – 4.04) iCVA: Standardized IR: 1.52 (1.05 – 2.13)
Zöller 2012	Sweden	-	-	CHD	Standardized IR: 1.92 (1.67 – 2.19)

B. Systemic lupus erythematosus and the antiphospholipid syndrome

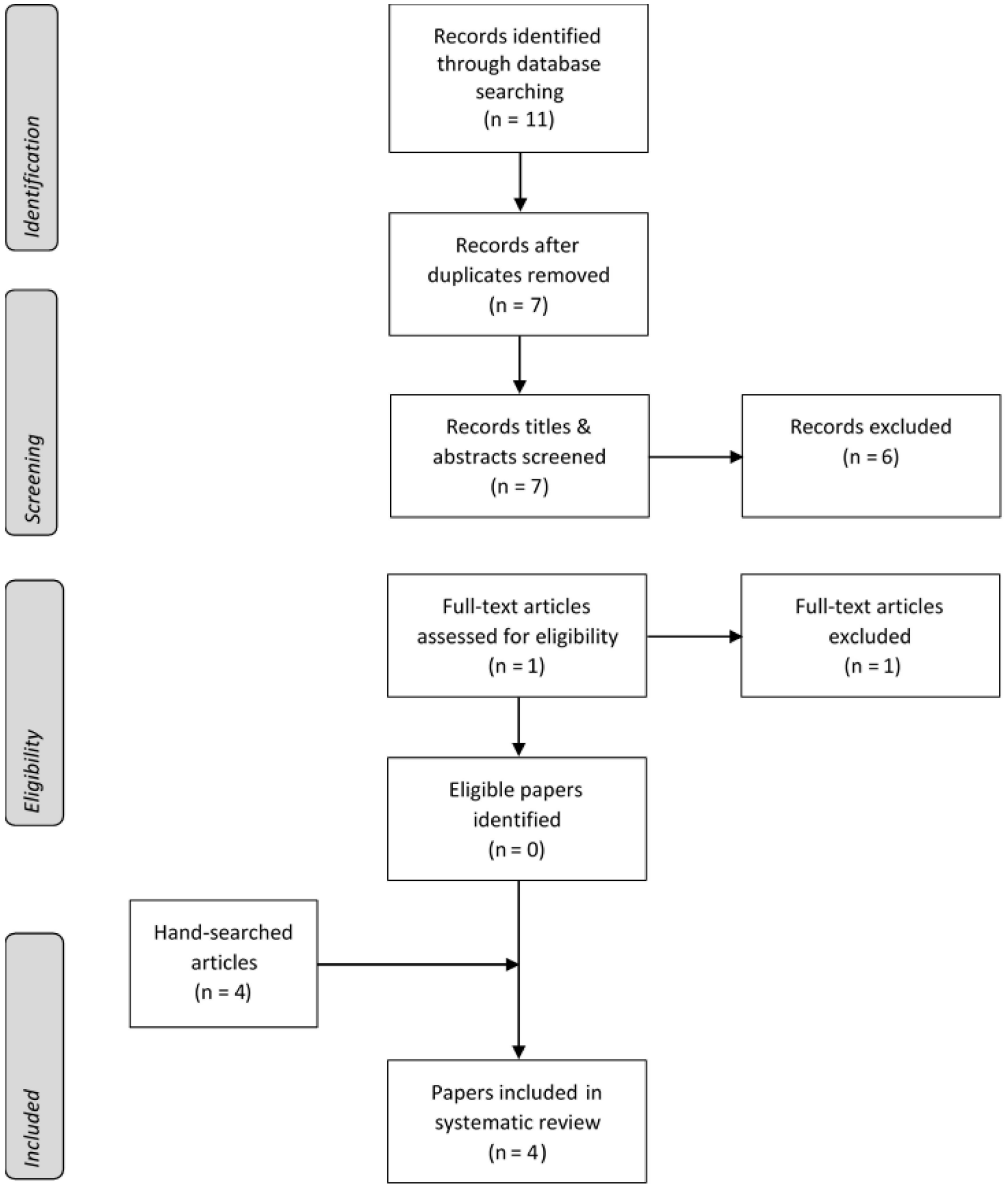
1. Cardiovascular risk prediction tools

PICO: '*In patients with SLE, what's the performance of risk prediction tools to predict cardiovascular risk?*'



Reference	Design	Risk tool	Population	Follow-up	Performance	Study quality
General risk prediction tools						
Esdaile, 2001	Prospective cohort	Framingham risk score	263	8.6 yrs	MI – observed/predicted 17/1.7; O/P ratio 10.1 (5.8-15.6) Stroke – observed/predicted 16/2; O/P ratio 7.9 (4.0-13.6)	Intermediate
Bessant, 2004	Prospective cohort	Framingham risk score	47	10 yrs	CHD events – observed/predicted 8.5%/1.4% Stroke – observed/predicted 10.6%/0.6%	Intermediate
Magder, 2012	Prospective cohort	Framingham risk score	1179	9500 p-y	CVD events – observed/predicted 109/41; O/P ratio 2.66 (2.16-3.16) Stroke – observed/predicted 62/10; RR 6.2 Cardiac events – observed/predicted 51/29; RR 1.8	Intermediate
Haque, 2018	Prospective cohort	Framingham risk score	112	5.8 yrs	CVD events – observed/predicted 8/1	Intermediate
Gustafsson, 2012	Prospective cohort	SCORE	124	10 yrs	CVD deaths – observed/predicted 9/4	High
Modified general risk prediction tools						
Urowitz, 2016	Retrospective cohort	Modified Framingham risk score	1013	6.7 yrs	CVD events N=95 Original FRS – Sensititvity/Specificity 0.13/0.98 Modified FRS – Sensititvity/Specificity 0.31/0.809	Intermediate
Disease-specific risk prediction tools						
Petri, 2019	Prospective cohort	SLE cardiovascular risk equation	1721 [Overall CVD events]; 1777 ['Hard' CVD events]	66% >5 yrs	[1] Overall CVD events formula: - CVD events N=168 - AUC: 0.78 - Estimated risk higher than FRS[a,b] [2] 'Hard' CVD events formula: - CVD events N=121 - AUC: 0.77 - Estimated risk higher than ACC/AHA score[a] [a]Except patients with moderately high risk from traditional CVD risk factors and [b]no SLE-related risk factors	High

PICO: '*In patients with APS, what's the performance of risk prediction tools to predict cardiovascular risk?*'

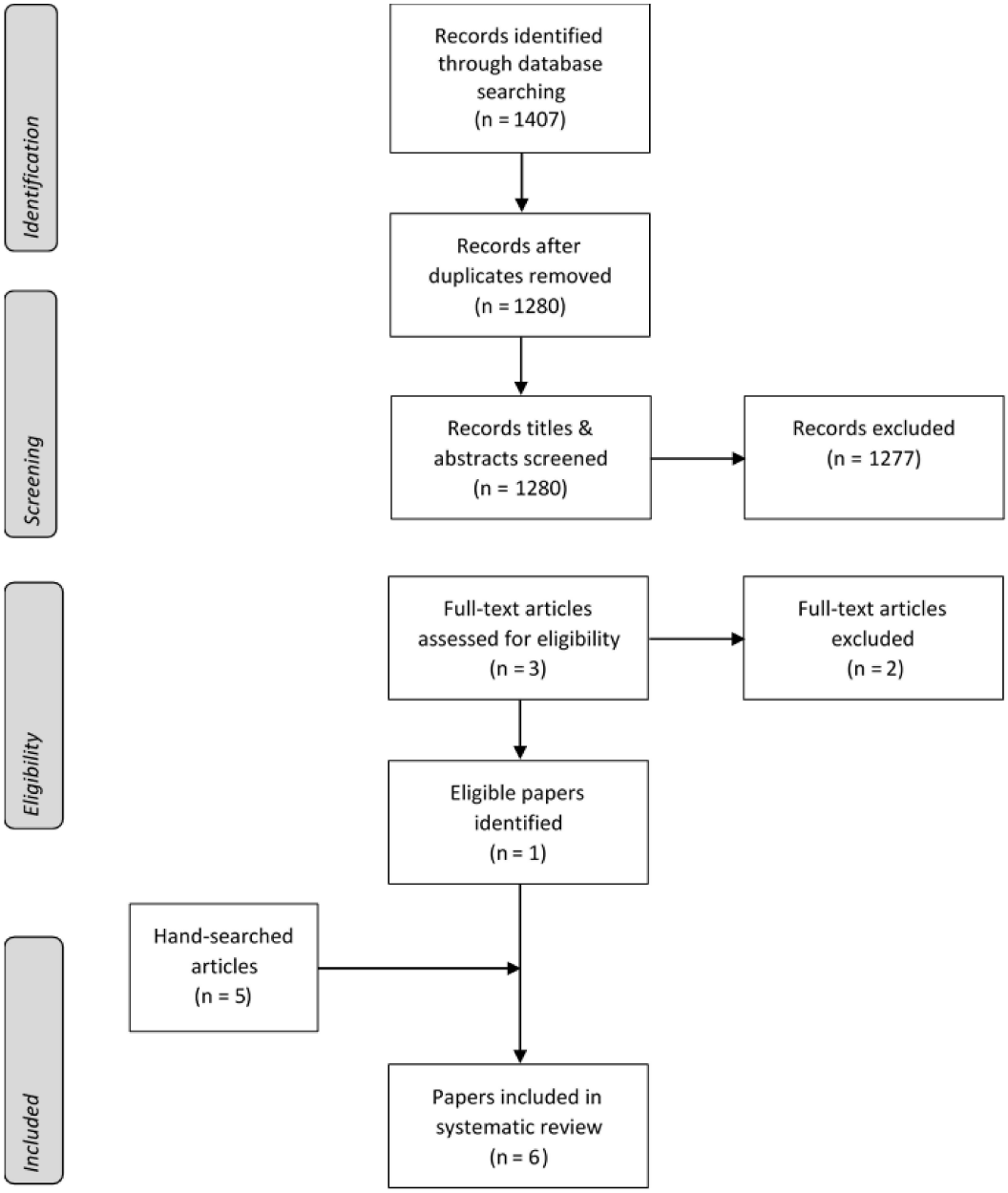


Reference	Design	Risk tool	Population	Follow-up	Performance	Study quality
Disease-specific risk prediction tools						
Di Minno, 2018	Retrospective cohort	aGAPSS; $aGAPSS_{CVD}$	192 aPL+	na	Events (CAD, stroke) N=52 [1] aGAPSS: - AUC: 0.58 - Sensititvity/Specificity 0.52/0.67[a] - Positive predictive value 0.369[a] [2] $aGAPSS_{CVD}$: - AUC: 0.65 - Sensitivity/Specificity 0.67/0.72[a] - Positive predictive value 0.479[a] [a]High-risk cutoff ≥11	Intermediate
Radin, 2019	Retrospective cohort	aGAPSS	397	na	Events (recurrent arterial and/or venous thrombosis) N=111 Risk cut-off ≥7: - Sensititvity/Specificity 0.51/0.50 - Positive predictive value 0.38	Intermediate

2. Interventions targeting traditional cardiovascular risk factors

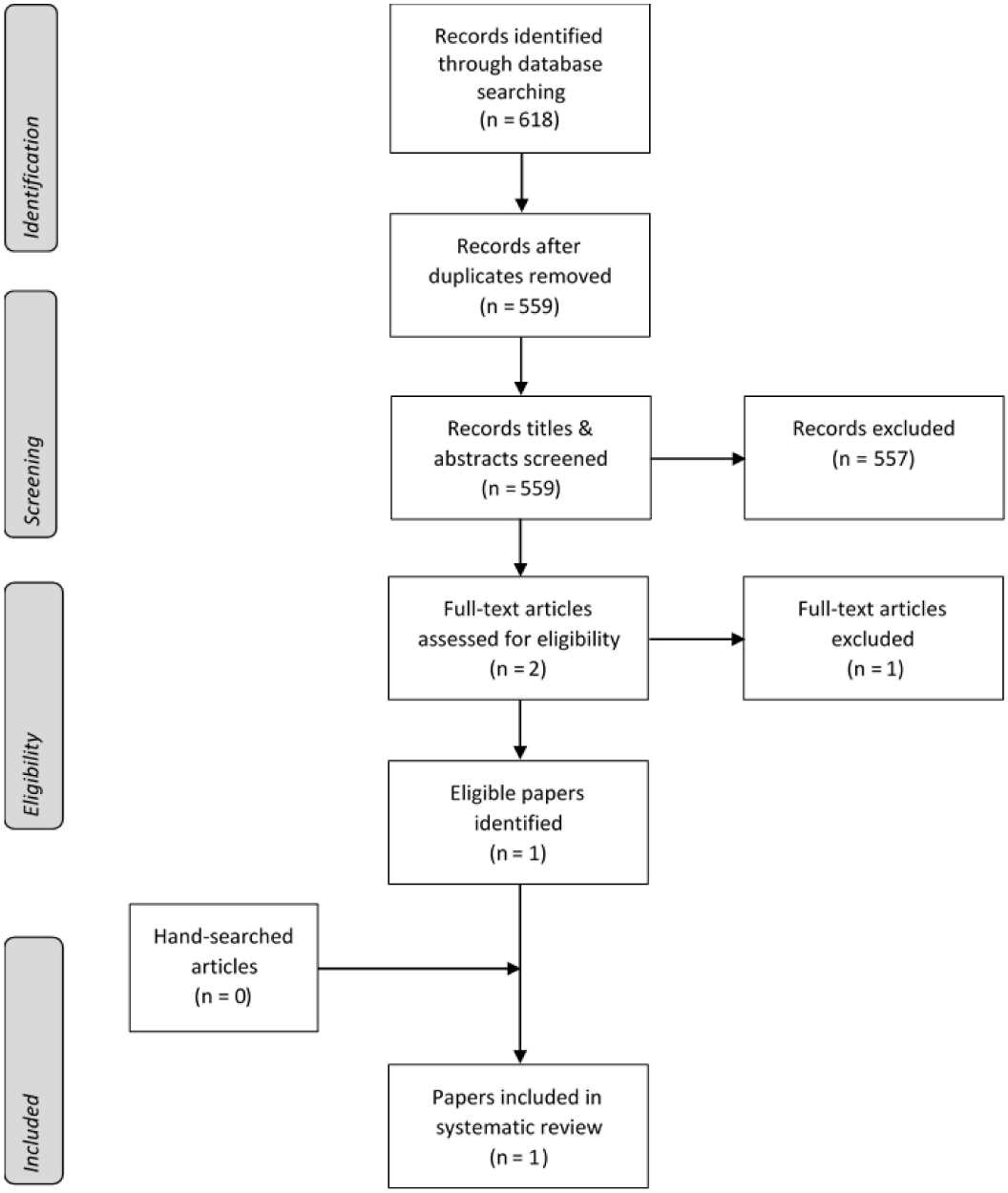
   a. Antihypertensives

   PICO: '*In patients with SLE, does treatment with antihypertensives result in better cardiovascular outcomes than no treatment with antihypertensives?*'



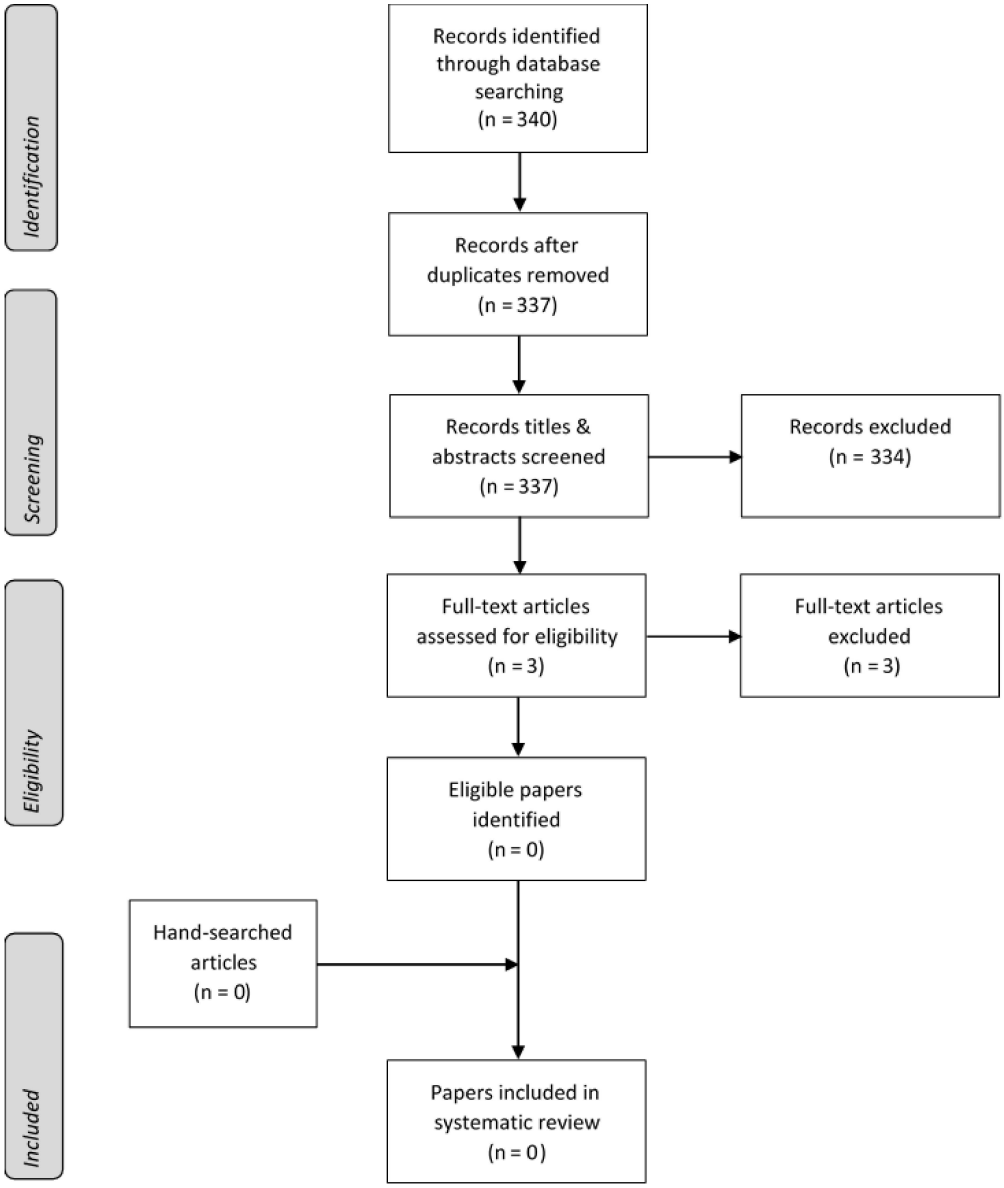
Reference	Design	Intervention	Control	Number of patients, intervention	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Study quality
Vascular events									
Becker-Merok, 2009	Prospective cohort	Antihypertensives	NA	NA	NA	41 (25.9%)	NA	OR 0.19 (0.06, 0.67)	High
Atherothrombotic events									
Becker-Merok, 2009	Prospective cohort	Antihypertensives	NA	158	NA	30 (19%)	NA	OR 0.21 (0.05, 0.94)	High
Coronary artery disease									
Nikpour, 2011	Prospective cohort	Systolic BP, per mmHg	NA	991	NA	94	NA	HR 1.02 (1.01, 1.04)	High
		Diastolic BP, per mmHg	NA	991	NA	94	NA	HR 1.04 (1.01, 1.07)	
CVD events									
Stojan, 2020	Prospective cohort	SBP ≥ 132 mmHg	SBP < 114 mmHg	2156 py	1969 py	26/1000 py	4.6/1000 py	RR 2.5 (1.1, 5.5), p = .03	High
		SBP 122-131 mmHg	SBP < 114 mmHg	2144 py	1969 py	12.6/1000 py	4.6/1000 py	RR 1.6 (0.7, 3.8)	
		SBP 114-121 mmHg	SBP < 114 mmHg	2021 py	1969 py	6.4/1000 py	4.6/1000 py	RR 1.2 (0.5, 2.9)	
Tselios, 2020	Prospective cohort	BP > 140/90	Normotensive	155	1061	18.9/1000 py	4.5/1000 py	HR 1.65 (1.01, 2.69)	High
		BP 130-139/80-89	Normotensive	316	1061	11.5/1000 py	4.5/1000 py	HR 1.73 (1.13, 2.65)	

PICO: '*In patients with lupus nephritis, does treatment with antihypertensives result in better cardiovascular outcomes than no treatment with antihypertensives?*'



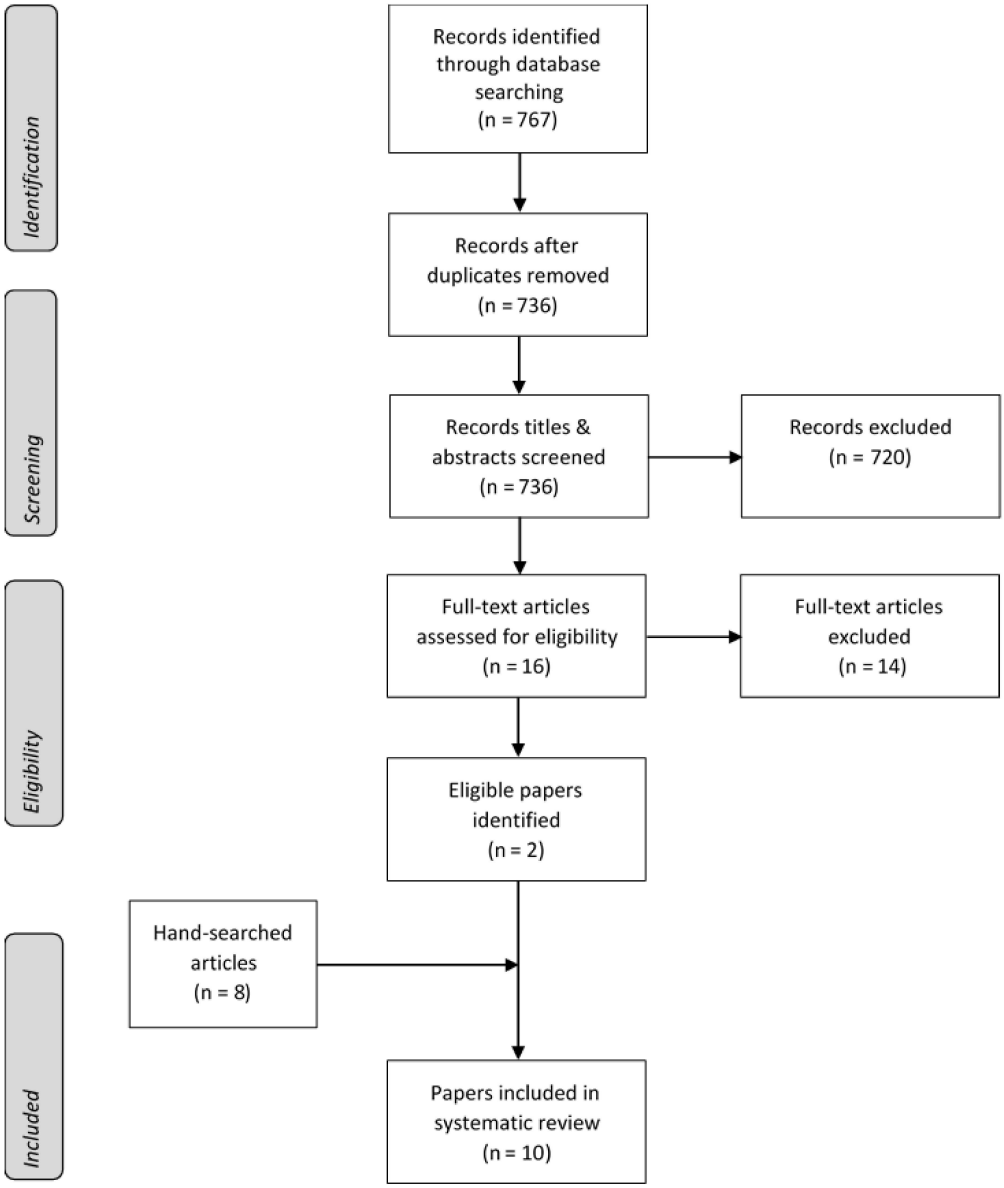
Reference	Design	Intervention	Control	Number of patients, intervention	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Study quality
CVD events									
Tselios, 2016	Prospective cohort	ACEI/ARB	No ACEI/ARB	144	301	14 (9.7%)	26 (8.6%)	HR 0.94 (0.48, 1.79)	Intermediate

PICO: '*In patients with APS, does treatment with antihypertensives result in better cardiovascular outcomes than no treatment with antihypertensives?*'



b. Lipid-lowering agents

PICO: '*In patients with SLE, does treatment with lipid lowering-medications result in better cardiovascular outcomes than no treatment with these medications?*'

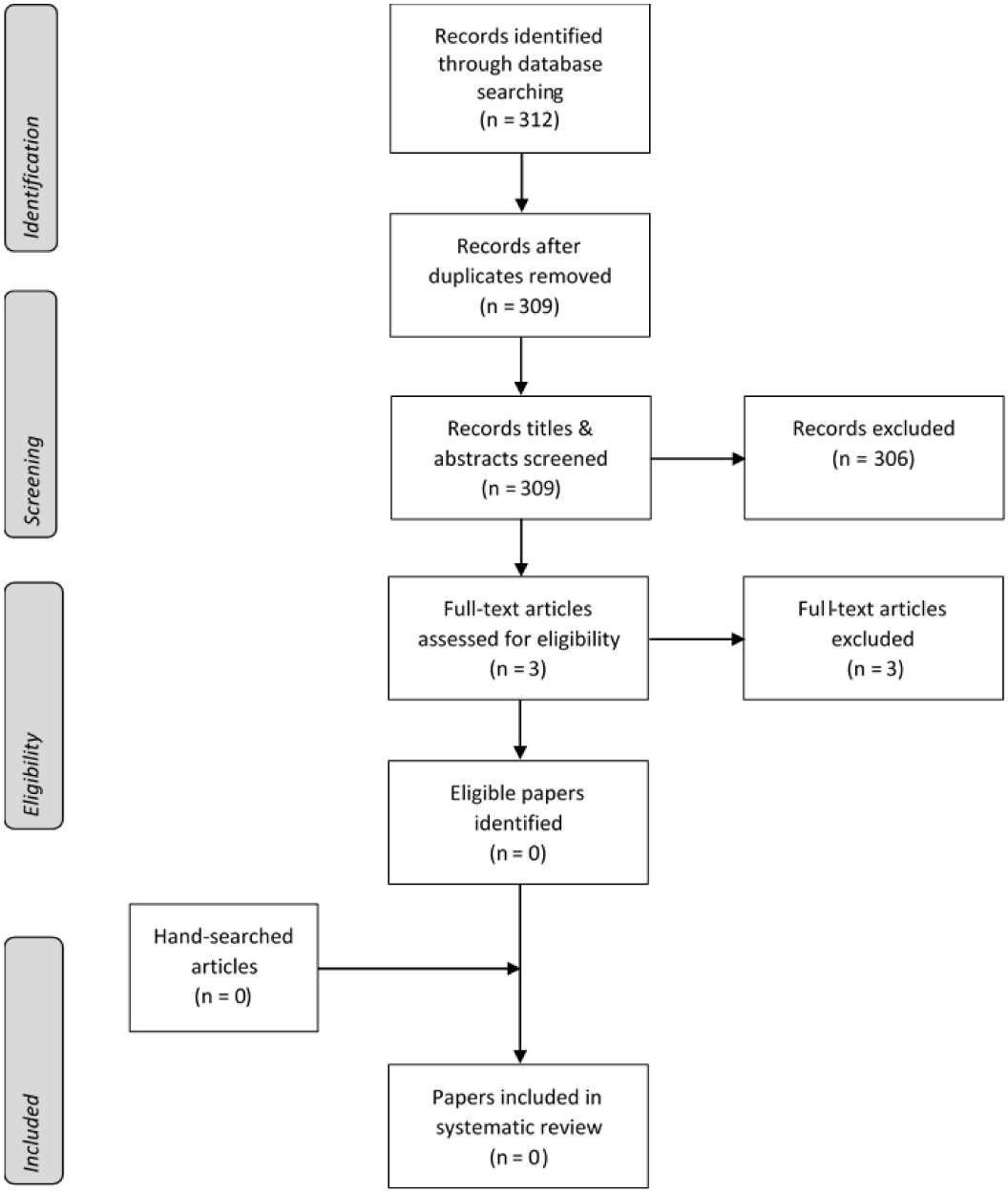


Reference	Design	Intervention	Comparison	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
CAD events									
Yu, 2015	Retrospective cohort	Long duration statin	No treatment	777	1317	27	192	HR 0.20 (0.13, 0.31)	Intermediate
		Short duration statin	No treatment	1673	1317	107	192	HR 0.41 (0.32, 0.53)	
		Lipid lowering treatment other than statin	No treatment	328	1317	35	192	HR 0.57 (0.39, 0.82)	
Cerebrovascular disease									
Yu, 2015	Retrospective cohort	Long duration statin	No treatment	777	1317	13	105	HR 0.14 (0.08, 0.25)	Intermediate
		Short duration statin	No treatment	1673	1317	44	105	HR 0.27 (0.19, 0.39)	
		Lipid lowering treatment other than statin	No treatment	328	1317	23	105	HR 0.67 (0.42, 1.06)	
Mikdashi, 2007	Prospective cohort	Total cholesterol increase 10 mg/dL	NA	232	NA	44	NA	HR 1.09 (1.02, 1.16)	High
CVD events									
Kao, 2013	Prospective cohort	Lipid lowering medication	No lipid lowering medication	18	370	3 (17%)	15 (4%)	HR 3.70 (1.01, 13.54)	High
Iudici, 2016	Prospective cohort	Statin	No statin	NA	NA	NA	NA	HR 2.09 (0.43, 10.02)	High
Fernandez-Nebro, 2015	Retrospective cohort	Statin ever	No statin ever	843	2806	149 (17.6%)	120 (4.3%)	RR 4.13 (3.29, 5.19)	Intermediate
Haque, 2018	Prospective cohort	Statin	No statin	NA	NA	NA	NA	OR 1.83 (0.52, 6.48)	Intermediate
Petri, 2019	Prospective cohort	Total cholesterol increase 25 mg/dL	NA	1777	NA	121	NA	HR 1.08 (0.99, 1.16)	High

CVD damage									
Pons-Estel, 2009	Prospective cohort	Statin	No statin	43	594	12 (27.9%)	83 (14%)	RR 1.99 (1.18, 3.36)	High

Reference	Design	Case	Control	Number of patients, cases	Number of patients, controls	Exposed, cases	Exposed, controls	Relative effect (95% CI)	Study quality
Statin Use									
Smrzova, 2014	Case control	SLE with CAD	SLE without CAD	21	42	9 (42.3%)	4 (9.5%)	OR 7.12 (1.85, 27.34)	Low
LDL > 3.2 mmol/L									
Nikpour, 2013	Case control	SLE with CAD	SLE without CAD	21	363	12 (57%)	119 (32.8%)	OR 2.73 (1.12, 6.66)	Intermediate
Trigylcerides > 2.0 mmol/L									
Nikpour, 2013	Case control	SLE with CAD	SLE without CAD	21	363	8 (38%)	98 (27%)	OR 1.66 (0.66, 4.13)	Intermediate

PICO: '*In patients with APS, does treatment with lipid lowering-medications result in better cardiovascular outcomes than no treatment with these medications?*'



c. Antiplatelets

No separate SLR was performed because the task force panel agreed that current EULAR recommendations about the use of antiplatelets in SLE* and APS† should be included in the recommendations for cardiovascular risk management of these diseases.

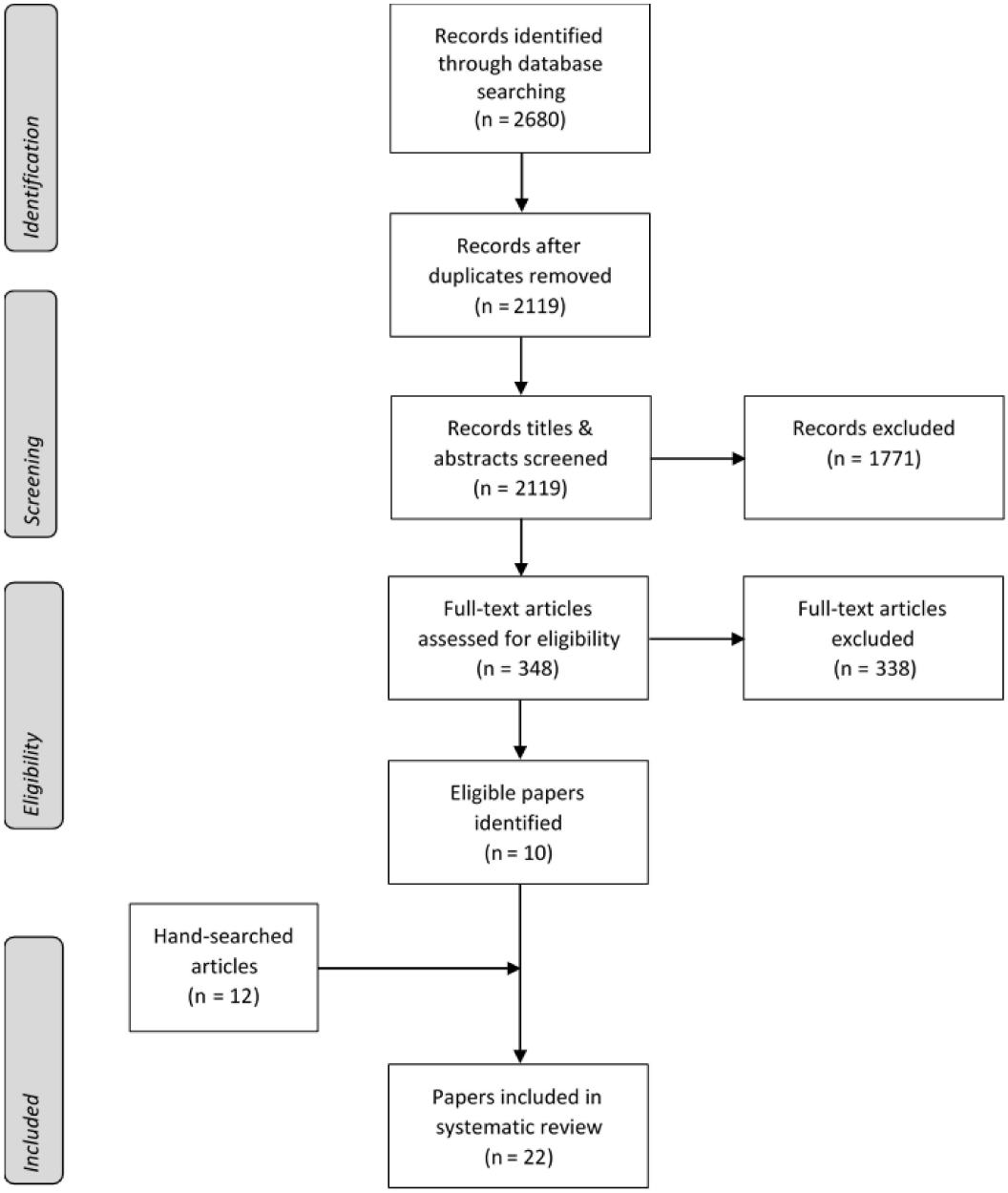
*Fanouriakis A, Kostopoulou M, Alunno A, et al. *Ann Rheum Dis* 2019;78:7367-7345. DOI: 10.1136/annrheumdis-2019-215089

†Tektonidou MG, Andreoli L, Limper M, et al. *Ann Rheum Dis* 2019;78:1296-1304. DOI: 10.1136/annrheumdis-2019-215213

3. Interventions targeting disease-related cardiovascular risk factors

   a. Disease activity

   PICO: '*In patients with SLE, is a history of less disease activity associated with better cardiovascular outcomes than more disease activity?*'



Reference	Design	Exposure	Control	Number of patients, exposed	Number of patients, control	Events, intervention	Events, control	Relative effect (95% CI)	Study quality
Vascular events (arterial and venous)									
Becker-Merok, 2009	Prospective cohort	Weighted average SLEDAI > 3	Weighted average SLEDAI ≤ 3	NA	NA	NA	NA	OR 2.67 (1.19, 6.02)	High
Atherothrombotic events									
Bengtsson, 2012	Prospective cohort	SLEDAI, per unit increase	NA	NA	269	NA	25	HR 1.06 (0.97, 1.15)	Intermediate
Fasano 2018	Prospective cohort	SLEDAI, per unit increase	NA	NA	507	NA	37	HR 1.05 (0.99, 1.12)	High
Magder, 2012	Prospective cohort	SLEDAI, per unit increase	NA	NA	1874	NA	135	RR 1.05 (1.00, 1.11)	Intermediate
		Mean SLEDAI ≥ 5	Mean SLEDAI 0-1	1393 py	2125 py	19.4/1000 py	10.8/1000 py	RR 2.78 (1.57, 4.91)	
		Mean SLEDAI 2.5-5	Mean SLEDAI 0-1	3091 py	2125 py	15,9/1000 py	10.8/1000 py	RR 1.79 (1.09, 2.94)	
		Mean SLEDAI 1-2.5	Mean SLEDAI 0-1	2875 py	2125 py	12.2/1000 py	10.8/1000 py	RR 1.23 (0.72, 2.09)	
Romero-Diaz, 2008	Retrospective cohort	SLEDAI, per unit increase	NA	NA	241	NA	24	HR 1.1 (1.0, 1.2)	Intermediate
Rivest, 2000	Retrospective cohort	SLAM per unit increase	NA	NA	200	NA	23	No association in multivariable analysis	Intermediate
Gustafsson, 2009	Retrospective cohort	SLAM > 6 at baseline	SLAM ≤ 6 at baseline	82	100	12 (14.6%)	12 (12%)	RR 1.22 (0.57, 2.57)	Intermediate
Iudici, 2016	Prospective cohort	Mean SLEDAI over time, per unit increase	NA	NA	167	NA	9	HR 1.04 (0.78, 1.26)	High
Nikpour, 2011	Prospective cohort	Time-varying SLEDAI, per unit increase	NA	NA	991	NA	94	HR 1.09 (1.05, 1.13)	High

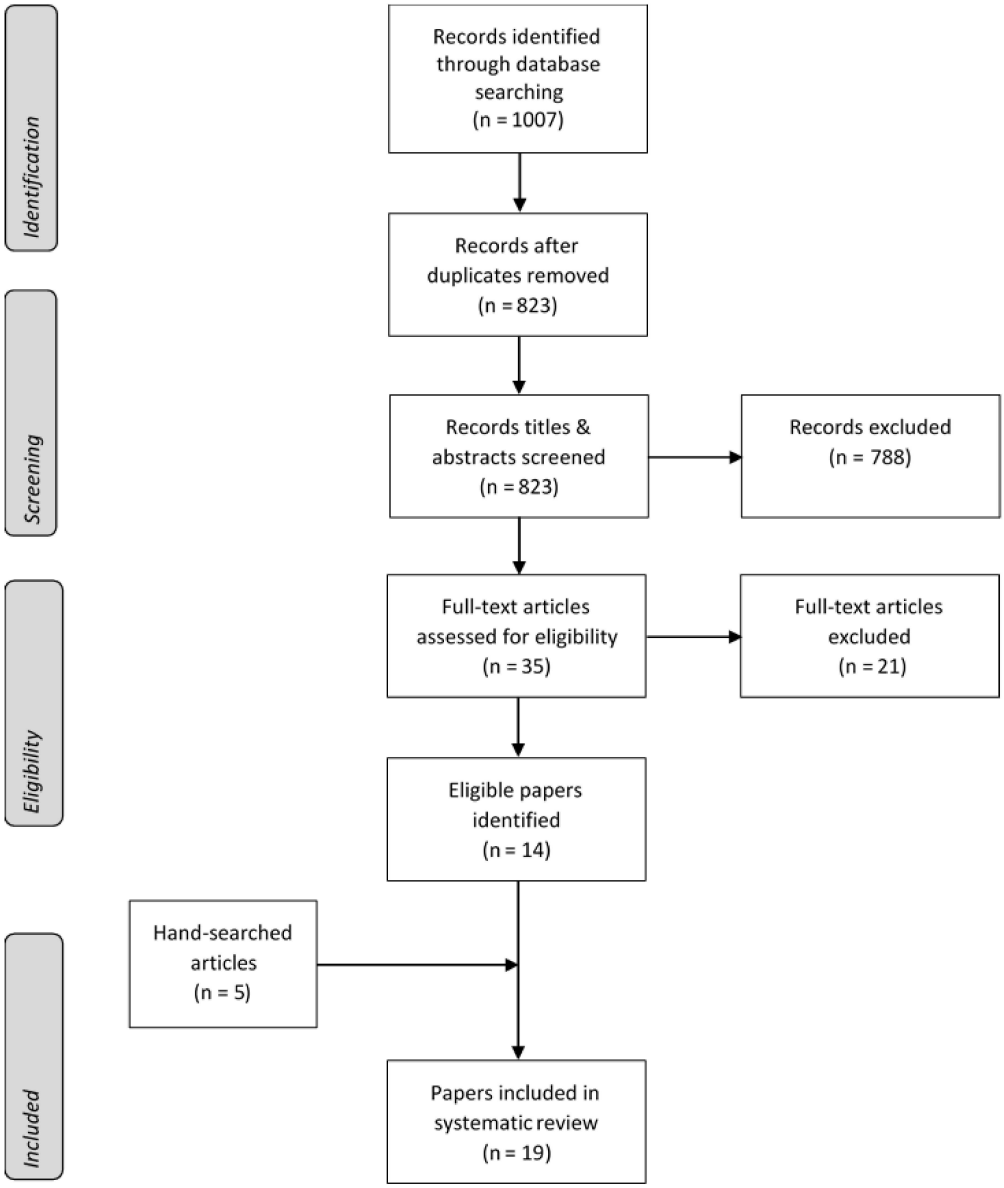
Ibanez, 2005	Prospective cohort	Time-varying mean SLEDAI, per unit increase	NA	NA	575	NA	55	HR 1.08 (1.00, 1.16)	High
Haque, 2018	Prospective cohort	SLEDAI at baseline, per unit increase	NA	NA	124	NA	12	OR 1.77 (1.15, 2.62)	Intermediate
Ischemic stroke									
Mikdashi, 2007	Prospective cohort	SLEDAI ≥ 16	Unclear	NA	NA	NA	NA	HR 1.31 (0.40, 4.31)	High
		SLEDAI 6-15	Unclear	NA	NA	NA	NA	HR 1.36 (0.45, 4.13)	
		SLEDAI < 6	Unclear	NA	NA	NA	NA	HR 1.77 (0.79, 3.97)	
CVD damage									
Pons-Estel, 2009	Prospective cohort	SLAM at baseline	NA	NA	637	NA	43	OR 1.01 (0.94, 1.09)	High

Reference	Design	Case	Control	Number of patients, cases	Number of patients, controls	Exposed, cases	Exposed, controls	Relative effect (95% CI)	Study quality
"SLEDAI Activity" (undefined)									
Pullmann, 2004	Case control	SLE with CAD	SLE without CAD	74	71	NA	NA	OR 2.57 (1.3, 5.09)	Low
SLEDAI									
Goldberg, 2009	Case control	SLE with CAD	SLE without CAD	17	224	6.0 (median)	4.0 (median)	P = .19	Intermediate
Tselios, 2017	Prospective cohort	SLE with CVD event	SLE without CVD event	41	169	3.98 ± 4.16	4.04 ± 4.21	P = .93	High
Urowtiz, 2007	Case control	SLE with CVD event	SLE without CVD event	118	118	6.2 ± 3.6	5.5 ± 3.8	P = .12	Intermediate
Hinojosa-Azaola, 2016	Prospective cohort	SLE with arterial thrombosis	SLE without thrombosis	8	184	5.4 (median of longitudinal values)	4.2 (median of longitudinal values)	P = .53	Intermediate

SLAM									
Kao, 2013	Prospective cohort	SLE with CVD events	SLE without CVD events	17	375	6.3 ± 4.0 (mean, SD)	6.5 ± 3.6 (mean, SD)	P = .63	High

b. Glucocorticoids

PICO: '*In patients with SLE, is use of lower doses of glucocorticoids associated with better cardiovascular outcomes than use of higher doses?*'



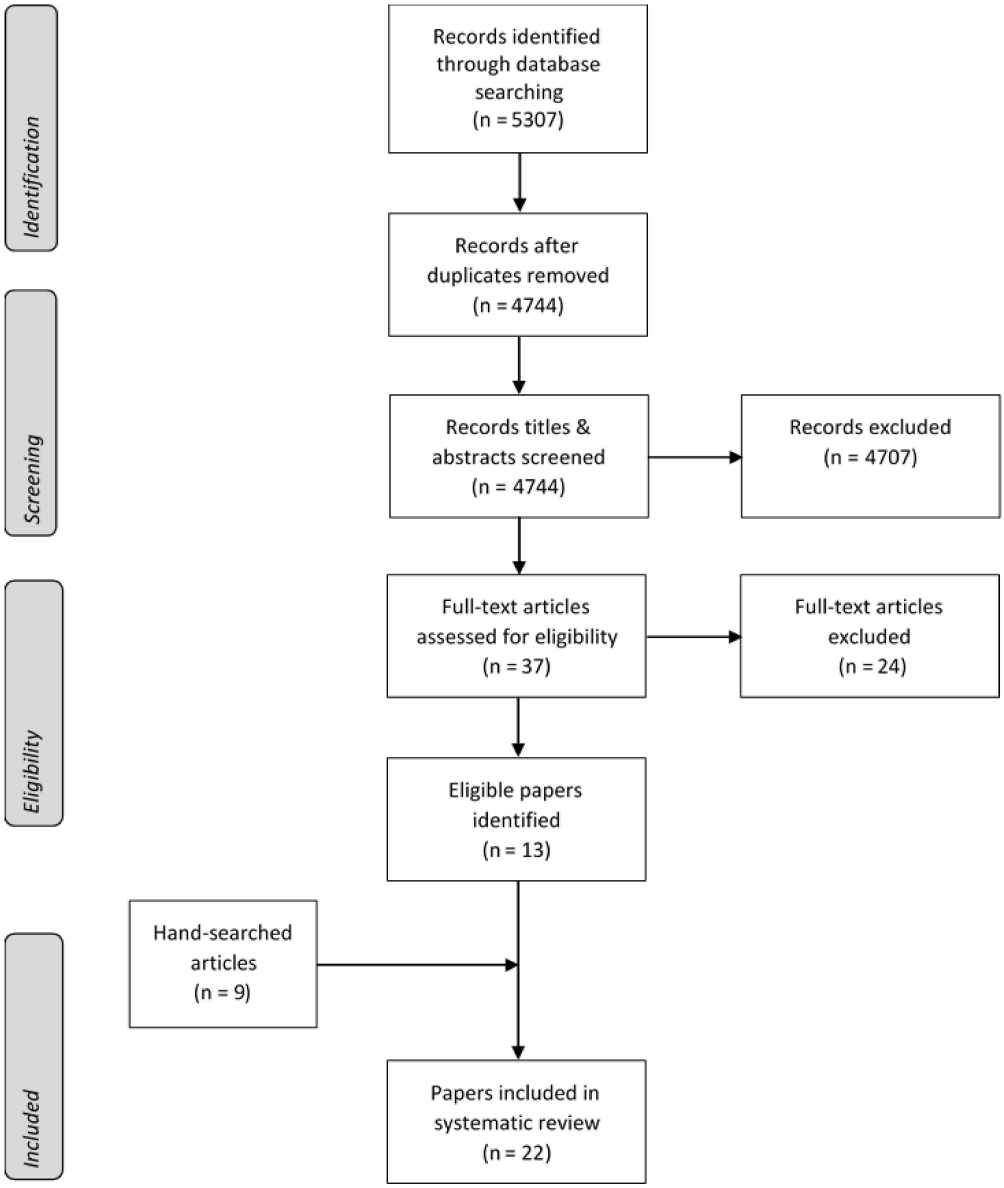
Reference	Design	Intervention	Comparison	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
CVD damage (SLICC damage index)									
Al Sawah, 2015	Prospective cohort	Mean prednisone ≥ 7.5 mg/d	Mean prednisone < 7.5 mg/d	884	1315	NA	NA	HR 1.54 (1.01, 2.34)	High
Ruiz-Arruza, 2018	Retrospective cohort	Corticosteroid minimization group	Usual care group	74	213	4 (5.4%)	21 (9.8%)	HR 0.28 (0.08, 0.95)	High
Vascular events									
Becker-Merok, 2009	Prospective cohort	Prednisolone dose (continuous)	NA	158	NA	41 (25.9%)	NA	OR 0.38 (0.17, 0.84)	High
Atherothrombotic events									
Becker-Merok, 2009	Prospective cohort	Prednisolone dose (continuous)	NA	158	NA	30 (19%)	NA	OR 0.30 (0.12, 0.75)	High
Fasano, 2019	Prospective cohort	Cumulative corticosteroids ≥ 40 g	Cumulative corticosteroids < 40 g	131	163	NA	NA	HR 1.89 (0.80, 4.47)	High
Magder, 2012	Prospective cohort	Current prednisone dose ≥ 20 mg/d	No prednisone	707 py	4640 py	35.4/100 py	9.9/100 py	RR 5.1 (3.1, 8.3)	Intermediate
		Current prednisone dose 10-19 mg/d	No prednisone	1538 py	4640 py	20.2/100 py	9.9/100 py	RR 2.4 (1.5, 3.8)	
		Current prednisone dose 1-9 mg/d	No prednisone	2600 py	4640 py	12.3/100 py	9.9/100 py	RR 1.3 (0.8, 2.0)	
Fernandez-Nebro, 2005	Retrospective cohort	Prednisone> 30 mg/d ever	Never prednisone > 30 mg/d	794	2855	108 (13.6%)	161 (5.6%)	RR 2.41 (1.91, 3.04)	Intermediate
Haque, 2018	Prospective cohort	Mean steroid dose (continuous)	NA	124	NA	12 (10%)	NA	HR 1.14 (1.03, 1.26)	Intermediate

Ischemic heart disease									
Chen, 2017	Retrospective cohort	Prednisone ≤ 10mg/d, intermittent	No corticosteroid	NA	NA	NA	NA	HR 0.97 (0.59, 1.61)	Intermediate
		Prednisone ≤ 10 mg/d, continuous	No corticosteroid	NA	NA	NA	NA	HR 0.87 (0.54, 1.39)	
		Prednisone > 10 md/d, intermittent	No corticosteroid	NA	NA	NA	NA	HR 1.74 (1.15, 2.64)	
		Prednisone > 10 mg/d, continuous	No corticosteroid	NA	NA	NA	NA	HR 2.09 (1.26, 3.48)	
Zonana-Nacach, 2000	Retrospective cohort	Cumulative prednisone ≥ 36.5 g	No corticosteroid	NA	NA	NA	NA	RR 1.7 (1.2, 2.3)	Intermediate
Stroke									
Chen, 2017	Retrospective cohort	Prednisone ≤ 10mg/d, intermittent	No corticosteroid	NA	NA	NA	NA	HR 2.10 (1.37, 3.22)	Intermediate
		Prednisone ≤ 10 mg/d, continuous	No corticosteroid	NA	NA	NA	NA	HR 1.48 (0.93, 2.34)	
		Prednisone > 10 md/d, intermittent	No corticosteroid	NA	NA	NA	NA	HR 3.36 (2.26, 5.00)	
		Prednisone > 10 mg/d, continuous	No corticosteroid	NA	NA	NA	NA	HR 5.48 (3.46, 8.65)	
Zonana-Nacach, 2000	Retrospective cohort	Cumulative prednisone dose ≥ 36.5 g	No corticosteroid	NA	NA	NA	NA	RR 1.3 (0.9, 1.8)	Intermediate
Hanly, 2018	Prospective cohort	Corticosteroid	NA	NA	NA	NA	NA	HR Not significant	Intermediate

Reference	Design	Case	Control	Number of patients, cases	Number of patients, controls	Exposed, cases	Exposed, controls	Relative effect (95% CI)	Study quality
Prednisone > 7.5mg/d									
Bessant, 2006	Case control	SLE with CVD event	SLE without CVD event	28	29	11 (39.3%)	4 (13.8%)	OR 8.0 (1.07, 355)	Intermediate
Cumulative prednisone dose									
Hinojosa-Azaola, 2016	Prospective cohort	SLE with CVD event	SLE without CVD event	8	184	17.3 g	11.8 g	P = .04	Intermediate
Svenungsson, 2001	Case control	SLE with CVD event	SLE without CVD event	26	26	38.2 g	25.6 g	P = .05	Intermediate
Urowitz, 2007	Case control	SLE with arterial event	SLE without arterial event	118	118	39.9 g	34.8 g	P = .34	Intermediate
Tselios, 2017	Prospective cohort	SLE with CVD event	SLE without CVD event	41	169	43.0 g	28.4 g	P = .10	High
Mean daily prednisone dose									
Siricheepchaiyan, 2016	Case control	SLE with event	SLE without event	10	149	13 mg/d	8.5 mg/d	P = 0.04	Intermediate
Urowitz, 1976	Prospective cohort	SLE with AMI	Entire SLE cohort	6	81	10.4 mg/d	18.1 mg/d	NA	Low
Tselios, 2017	Prospective cohort	SLE with CVD event	SLE without CVD event	41	169	9.7 mg/d	11.7 mg/d	0.33	High

c. Immunosuppressives

PICO: '*In patients with SLE, is use of immunosuppressive medications associated with better cardiovascular outcomes than no use of immunosuppressive medications?*'



Reference	Design	Intervention	Comparison	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
Vascular events (arterial and venous)									
Becker-Merok, 2009	Prospective cohort	Immunosuppressive	NA	NA	NA	NA	NA	OR 0.44 (0.20, 0.94)	High
Atherothrombotic events									
Becker-Merok, 2009	Prospective cohort	Immunosuppressive	NA	NA	NA	NA	NA	OR 0.39 (0.15, 0.99)	High
Fernandez-Nebro, 2015	Retrospective cohort	Methotrexate ever	No methotrexate	576	3073	46 (8%)	530 (15.6%)	RR 1.10 (0.81, 1.50)	Intermediate
		Azathioprine ever	No azathioprine	1139	2510	124 (10.8%)	145 (5.7%)	RR 1.88 (1.49, 2.37)	
		Cyclophosphamide ever	No cyclophosphamide	775	2874	86 (11.1%)	183 (6.3%)	RR 1.74 (1.36, 2.23)	
		Mycophenolate Ever	No mycophenolate	522	3127	58 (11.1%)	211 (6.7%)	RR 1.60 (1.21, 2.12)	
		Rituximab ever	No rituximab	226	3423	26 (11.5%)	243 (7.1%)	RR 1.62 (1.10, 2.38)	
Haque, 2018	Prospective cohort	Cyclophosphamide ever	No cyclophosphamide	12	112	NA	NA	OR 4.2 (1.77, 35)	Intermediate
		Azathioprine ever	No azathioprine	NA	NA	NA	NA	OR 3.3 (0.94, 11.58)	
Tselios, 2017	Prospective cohort	Immunosuppressive ever	No immunosuppressive	64	146	16 (25%)	25 (17.1%)	RR 1.46 (0.83, 2.54)	High
Wang, 2012	Retrospective cohort	Cyclophosphamide ever	No cyclophosphamide	678	394	43 (6.3%)	28 (7.1%)	RR 0.89 (0.56, 1.41)	Intermediate
		Other immunesuppressives	No other immunosuppressives	543	529	30 (5.5%)	41 (7.7%)	RR 0.71 (0.45, 1.12)	
Kao, 2013	Prospective cohort	Immunosuppressives	No immunosuppressives	82	310	2 (2.4%)	15 (4.8%)	RR 0.50 (0.11, 2.16)	High

Magder, 2012	Prospective cohort	Immunosuppressive use	No immunosuppressive use	4535 py	4646 py	16/1/1000 py	12.1/1000 py	RR 1.43 (1.01, 2.03)	Intermediate
Bertoli, 2009	Prospective cohort	Azathioprine use	No azathioprine use	335	979	47 (14%)	75 (7.6%)	HR 1.53 (1.07, 2.20)	Intermediate
		Methotrexate use	No methotrexate use	249	1105	23 (9.2)	95 (8.6%)	HR 1.31 (0.90, 1.97)	
		Cyclophosphamide use	No cyclophosphamide use	273	1041	35 (12.8%)	87 (8.3%)	HR 1.33 (0.97, 1.97)	
		Mycophenolate mofetil use	No mycophenolate use	249	1065	23 (9.2%)	99 (9.3%)	HR 0.87 (0.55, 1.39)	
Gustafsson, 2009	Retrospecitve cohort	Azathioprine use	No azathioprine use	69	113	1 (1.4%)	23 (20%)	HR 0.51 (0.03, 2.47)	Intermediate
		Cyclophosphamide use	No cyclophosphamide use	27	155	2 (7.4%)	22 (14.2%)	HR 0.60 (0.01, 2.03)	
Mok, 2007	Retrospective cohort	Cyclophosphamide use > 3 months	No cyclophosphamide use > 3 months	78	84	NA	NA	HR 0.81 (0.39, 1.68)	High
		Azathioprine use > 3 months	No azathioprine use > 3 months	121	41	NA	NA	HR 0.95 (0.50, 1.82)	
		Mycophenolate use > 3 months	No mycophenolate use > 3 months	32	130	NA	NA	HR 0.59 (0.21, 1.67)	
		Calcineurin inhibitor use > 3 months	No calcineurin inhibitor use > 3 months	32	130	NA	NA	HR 0.86 (0.38, 1.98)	
Ischemic heart disease									
Ibanez, 2005	Prospective cohort	Immunosuppressives ever	No immunesuppressives	278	297	31 (10.8%)	24 (8.1%)	HR 1.93 (1.05, 3.56)	High
Cardiovascular damage									
Pons-Estel, 2009	Prospective cohort	Cyclophosphamide ever	No cyclophosphamide	168	469	14 (8.3)	29 (6.2%)	RR 1.34 (0.73, 2.49)	Intermediate
		Azathioprine ever	No azathioprine	191	446	16 (8.3)	27 (6.0%)	RR 1.38 (0.76, 2.51)	

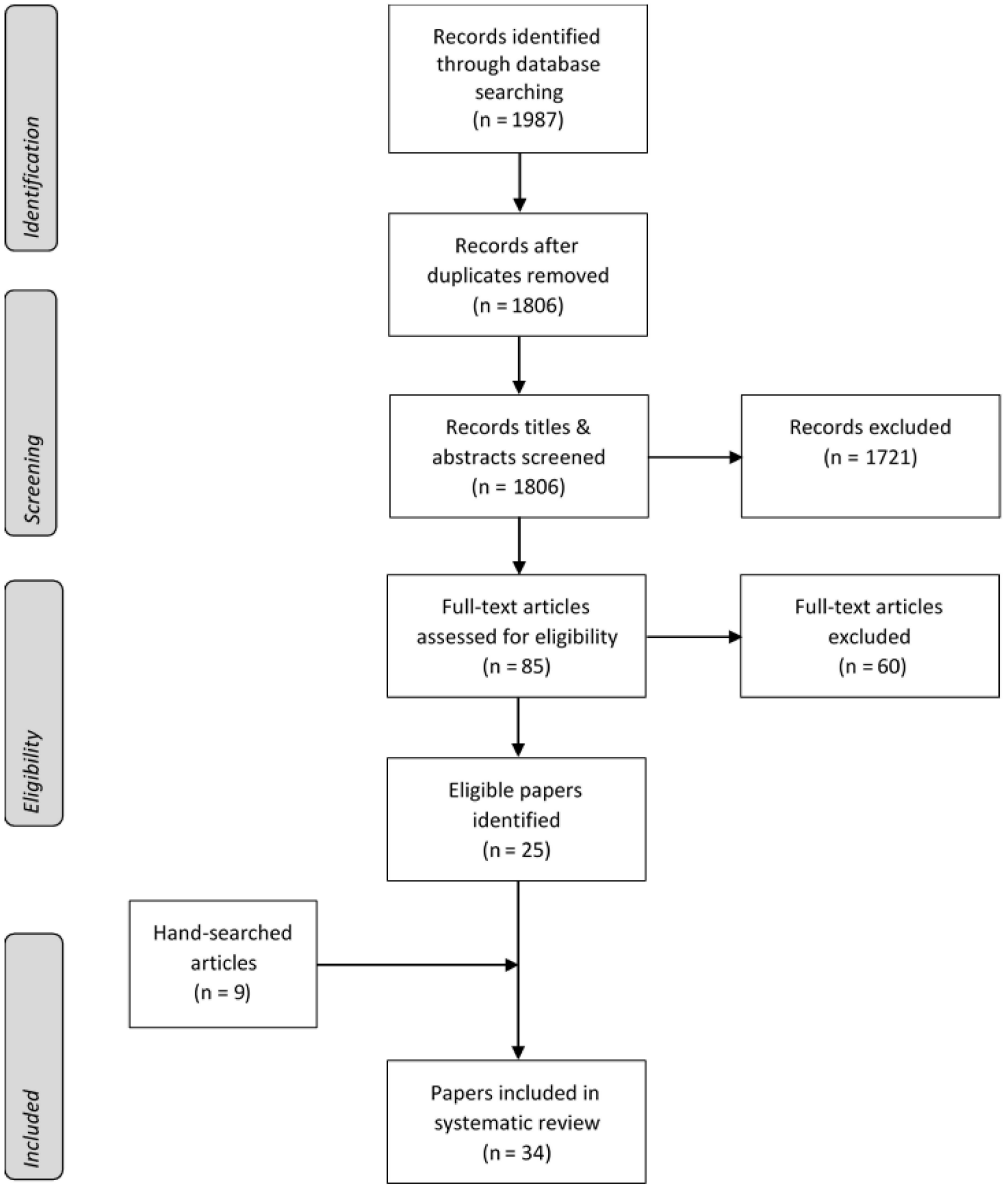
		Mycophenolate mofetil ever	No mycophenolate	66	571	2 (3.0%)	41 (7.2%)	RR 0.42 (0.10, 1.71)	
Stroke									
Hanly, 2018	Prospective cohort	Immunosuppressive use	No immunosuppressive use	732	1094	NA	NA	"no association"	Intermediate

Reference	Design	Case	Control	Number of patients, cases	Number of patients, controls	Exposed, cases	Exposed, controls	Relative effect (95% CI)	Study quality
Azathioprine									
Haque, 2010	Case control	SLE with MI or angina	SLE without CAD	53	96	NA	NA	OR 2.33 (1.16, 4.67)	Intermediate
Hinojosa-Azaola, 2016	Prospective cohort	SLE with CVD event	SLE without CVD event	8	184	8 (100%)	135 (73%)	OR 6.2 (0.3, 109.6)	Intermediate
Bessant, 2006	Case control	SLE with CVD event	SLE without CVD event	29	29	NA	NA	"Not significant"	Intermediate
Smrzova, 2014	Case control	SLE with MI, stroke or TE	SLE without MI, stroke or TE	21	42	50.3 g	44.0 g	"Not significant"	Low
Siricheepchaiyan, 2016	Case control	SLE with CVD event	SLE without CVD event	10	149	1 (10%)	37 (24.8%)	OR 0.32 (0.04, 2.68)	Intermediate
Methotrexate									
Haque, 2010	Case control	SLE with MI or angina	SLE without CAD	53	96	NA	NA	OR 1.35 (0.51, 3.62)	Intermediate
Hinojosa-Azaola, 2016	Prospective cohort	SLE with CVD event	SLE without CVD event	8	184	1 (13%)	22 (12%)	OR 1.05 (0.12, 8.96)	Intermediate
Siricheepchaiyan, 2016	Case control	SLE with CVD event	SLE without CVD event	10	149	1 (10%)	15 (10.1%)	OR 1.00 (0.11, 8.39)	Intermediate
Cyclophosphamide									
Haque, 2010	Case control	SLE with MI or angina	SLE without CAD	53	96	NA	NA	OR 0.92 (0.30, 2.87)	Intermediate
Hinojosa-Azaola, 2016	Prospective cohort	SLE with CVD event	SLE without CVD event	8	184	4 (50%)	50 (37.3%)	OR 2.68 (0.6, 11.1)	Intermediate
Bessant, 2006	Case control	SLE with CVD event	SLE without CVD event	29	29	NA	NA	"Not significant"	Intermediate

Demir, 2016	Case control	SLE with CVD event	SLE without CVD event	49	257	29 (59.2%)	112 (43.6%)	OR 1.88 (1.01, 3.49)	Intermediate
Smrzova, 2014	Case control	SLE with MI, stroke or TE	SLE without MI, stroke or TE	21	42	3.6 g	1.76 g	P = .03	Low
Siricheepchaiyan, 2016	Case control	SLE with CVD event	SLE without CVD event	10	149	4 (40%)	20 (13.4%)	OR 4.30 (1.11, 16.59)	Intermediate
Cyclosporine									
Haque, 2010	Case control	SLE with MI or angina	SLE without CAD	53	96	NA	NA	OR 0.75 (0.19, 3.05)	Intermediate
Smrzova, 2014	Case control	SLE with MI, stroke or TE	SLE without MI, stroke or TE	21	42	76.6 g	75.2 g	“Not significant”	Low
Mycophenolate									
Hinojosa-Azaola, 2016	Prospective cohort	SLE with CVD event	SLE without CVD event	8	184	0	18 (9..8%)	OR 0	Intermediate
Smrzova, 2014	Case control	SLE with MI, stroke or TE	SLE without MI, stroke or TE	21	42	122.8 g	28.7 g	“Not significant”	Low
Siricheepchaiyan, 2016	Case control	SLE with CVD event	SLE without CVD event	10	149	3 (30%)	32 (21.5%)	OR 1.56 (0.38, 6.41)	Intermediate
Immunosuppressives									
Szalai, 2005	Case control	SLE with arterial event	SLE without arterial event	25	32	7 (28%)	6 (19%)	OR 1.68 (0.48, 5.83)	Intermediate
Urowitz, 2007	Case control	SLE with CVD event	SLE without CVD event	118	118	55 (46.6%)	35 (29.6%)	OR 2.07 (1.21, 3.53)	High
Goldberg, 2009	Case control	SLE with CAD	SLE without CAD	17	224	4 (23.5%)	70 (31.4%)	OR 0.68 (0.21, 2.15)	Intermediate

d. Antimalarials

PICO: '*In patients with SLE, is use of antimalarials associated with better cardiovascular outcomes than no use of antimalarials?*'



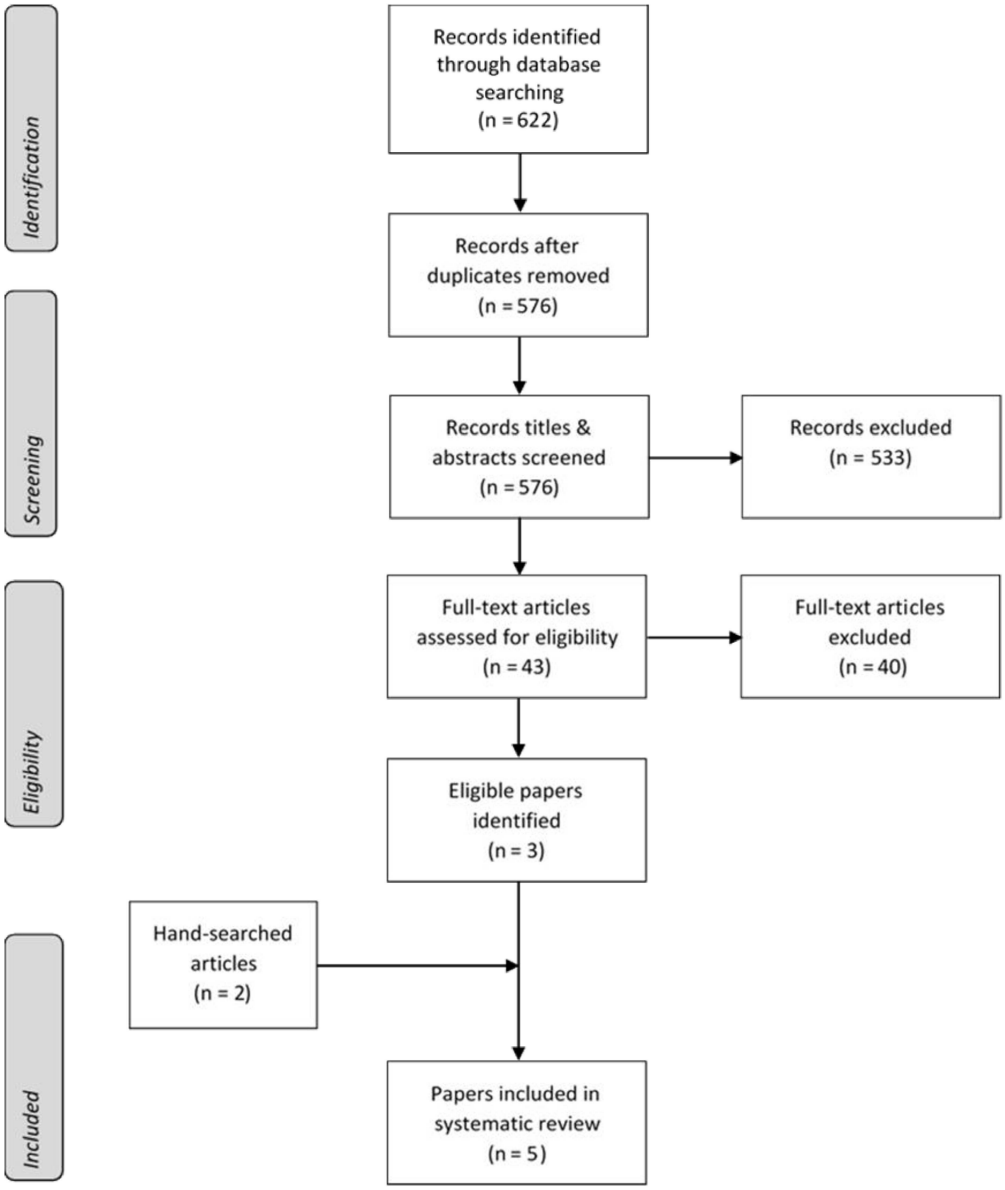
Reference	Design	Intervention	Comparison	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
Vascular events (arterial or venous)									
Becker-Merok, 2009	Prospective cohort	HCQ	No HCQ	NA	NA	NA	NA	OR 0.20 (0.09, 0.43)	High
Choojitrom, 2008	Retrospective cohort	Antimalarials	No Antimalarials	24	43	4 (16.7%)	22 (51.1%)	RR 0.32 (0.12, 0.83)	Intermediate
Kaiser, 2009	Retrospective cohort	HCQ	No HCQ	1534	396	NA	NA	OR 0.63 (0.48, 0.83)	Intermediate
Atherothrombotic events									
Becker-Merok, 2009	Prospective cohort	HCQ	No HCQ	158	NA	NA	NA	OR 0.19 (0.08, 0.47)	High
Fasano, 2018	Retrospective cohort	HCQ	No HCQ	431	76	26 (6.0%)	11 14.4%)	HR 0.32 (0.16, 0.66)	High
Hinojosa-Azaola, 2016	Prospective cohort	HCQ	No HCQ	128	64	5 (3.9%)	3 (4.7%)	RR 0.83 (0.20, 3.38)	Intermediate
Kao, 2013	Prospective cohort	HCQ	No HCQ	228	164	7 (3%)	10 (6.1%)	RR 0.50 (0.19, 1.30)	High
Martinez-Berriotxoa, 2007	Prospective cohort	Antimalarials	No antimalarials	165	74	15 (9.1%)	15 (20.2%)	RR 0.44 (0.23, 0.87)	High
Mok, 2005	Prospective cohort	HCQ ever	No HCQ	418	207	32 (7.6%)	16 (7.7%)	RR 0.99 (0.55, 1.77)	Intermediate
Romero-Diaz, 2009	Retrospective cohort	Chloroquine ever	No Chloroquine	66	150	3 (4.5%)	21 (14%)	RR 0.33 (0.10, 1.05)	Intermediate
Siso, 2008	Retrospective cohort	Antimalarial use prior to nephritis	No antimalarial use prior to nephritis	56	150	5 (9%)	23 (15.3%)	RR 0.61 (0.24, 1.51)	Intermediate
Tselios, 2017	Prospective cohort	Antimalarial use	No antimalarial use	113	97	23 (20.3%)	18 (18.5%)	RR 1.09 (0.63, 1.91)	High
Magder, 2012	Prospective cohort	Current HCQ use ≥ 6 consecutive months	No HCQ	5104 py	2570 py	10.6/1000 py	17.9/1000 py	RR 0.54 (0.36, 0.79)	Intermediate

		Current HCQ use < 6 months	No HCQ	827 py	2570 py	16.9/1000 py	17.9/1000 py	RR 1.02 (0.56, 1.86)	
		Past HCQ use	No HCQ	984 py	2570 py	20.3/1000 py	17.9/1000 py	RR 1.13 (0.67, 1.91)	
Bertoli, 2009	Prospective cohort	HCQ use ever	No HCQ use	1111	203	106 (9.5%)	16 (7.9%)	HR 0.96 (0.57, 1.62)	Intermediate
Mok, 2007	Retrospective cohort	HCQ use > 3 months	No HCQ use > 3 months	59	93	NA	NA	HR 1.08 (0.47, 2.46)	High
Gustafsson, 2009	Retrospective cohort	Antimalarial use at study entry	No antimalarial use at study entry	52	130	5 (9.6%)	19 (14.6%)	HR 1.01 (0.32, 2.67)	Intermediate
Fernandez-Nebro, 2015	Retrospective cohort	Antimalarial use ever	No antimalarial use	2878	771	195 (6.8%)	74 (9.6%)	RR 0.70 (0.54, 0.92)	Intermediate
Haque, 2018	Prospective cohort	Antimalarial use ever	No antimalarial use	107	17	12 (11.2%)	0	RR undefined	Intermediate
Coronary artery disease									
Hochman, 2009	Prospective cohort	Antimalarials ever	No antimalarials	NA	NA	NA	NA	HR 1.30 (0.64, 2.66)	Intermediate
Nikpour, 2011	Prospective cohort	HCQ ever	No HCQ	673	318	51 (7.5%)	43 (13.5%)	HR 0.50 (0.31, 0.79)	High
Ibanez, 2005	Prospective cohort	Antimalarials ever	No antimalarials	385	176	36 (9.3%)	19 (10.8%)	RR 0.87 (0.51, 1.47)	High
Petri, 1992	Prospective cohort	HCQ	No HCQ	104	125	6 (5.7%)	13 (10.4%)	RR 0.55 (0.21, 1.41)	Intermediate
Acute coronary events									
Hsu, 2017	Retrospective cohort	Antimalarial use (high adherence)	No antimalarial use	1946	1946	0.9/1000 py	1.5/1000 py	RR 0.58 (0.29, 1.15)	High
Coronary artery disease or heart failure									
Pons-Estel, 2009	Prospective cohort	HCQ ever	No HCQ	545	92	38 (7.0%)	5 (5.4%)	RR 1.28 (0.51, 3.18)	Intermediate
Stroke									
Hsu, 2017	Retrospective cohort	Antimalarial use (high adherence)	No antimalarial use	1946	1946	4.5/1000 py	4.4/1000 py	RR 1.03 (0.73, 1.45)	High

Hanly, 2018	Prospective cohort	Antimalarial use	No antimalarial use	1231	595	NA	NA	"no association"	Intermediate
CVD Damage (SLICC damage index)									
Al Sawah 2015	Prospective cohort	Antimalarial use	No antimalarial use	NA	NA	NA	NA	HR 0.90 (0.60, 1.34)	Intermediate

Reference	Design	Case	Control	Number of patients, cases	Number of patients, controls	Exposed, cases	Exposed, controls	Relative effect (95% CI)	Study quality
HCQ									
Bessant, 2006	Case control	SLE with CVD event	SLE without CVD event	29	29	6 (20.7%)	13 (44.8%)	OR 0.36 (0.08, 1.23)	Intermediate
Demir 2016	Case control	SLE with CVD	SLE without CVD	49	257	35 (73.5%)	229 (89.1%)	OR 0.30 (0.14, 0.64)	Intermediate
Haque 2010	Case control	SLE with CVD event	SLE without CVD event	53	96	NA	NA	OR 1.13 (0.54, 2.39)	Intermediate
Jung 2010	Case control	SLE with arterial event	SLE without arterial event	32	64	NA	NA	OR 0.34 (0.12, 0.99)	Intermediate
Urowitz, 2007	Case control	SLE with CVD event	SLE without CVD event	118	118	79 (66.9%)	64 (54.2%)	OR 1.70 (1.00, 2.90)	Intermediate
Antimalarial									
Siricheepchaiyan 2016	Case control	SLE with CVD	SLE without CVD	10	141	7 (70%)	114 (76.5%)	OR 0.56 (0.13, 2.28)	Intermediate
Goldberg, 2009	Case control	SLE with CVD event	SLE without CVD event	17	224	11 (64.7%)	119 (53.4%)	OR 1.21 (0.47, 3.13)	Intermediate

PICO: '*In patients with APS, is use of antimalarials associated with better cardiovascular outcomes than no use of antimalarials?*'*



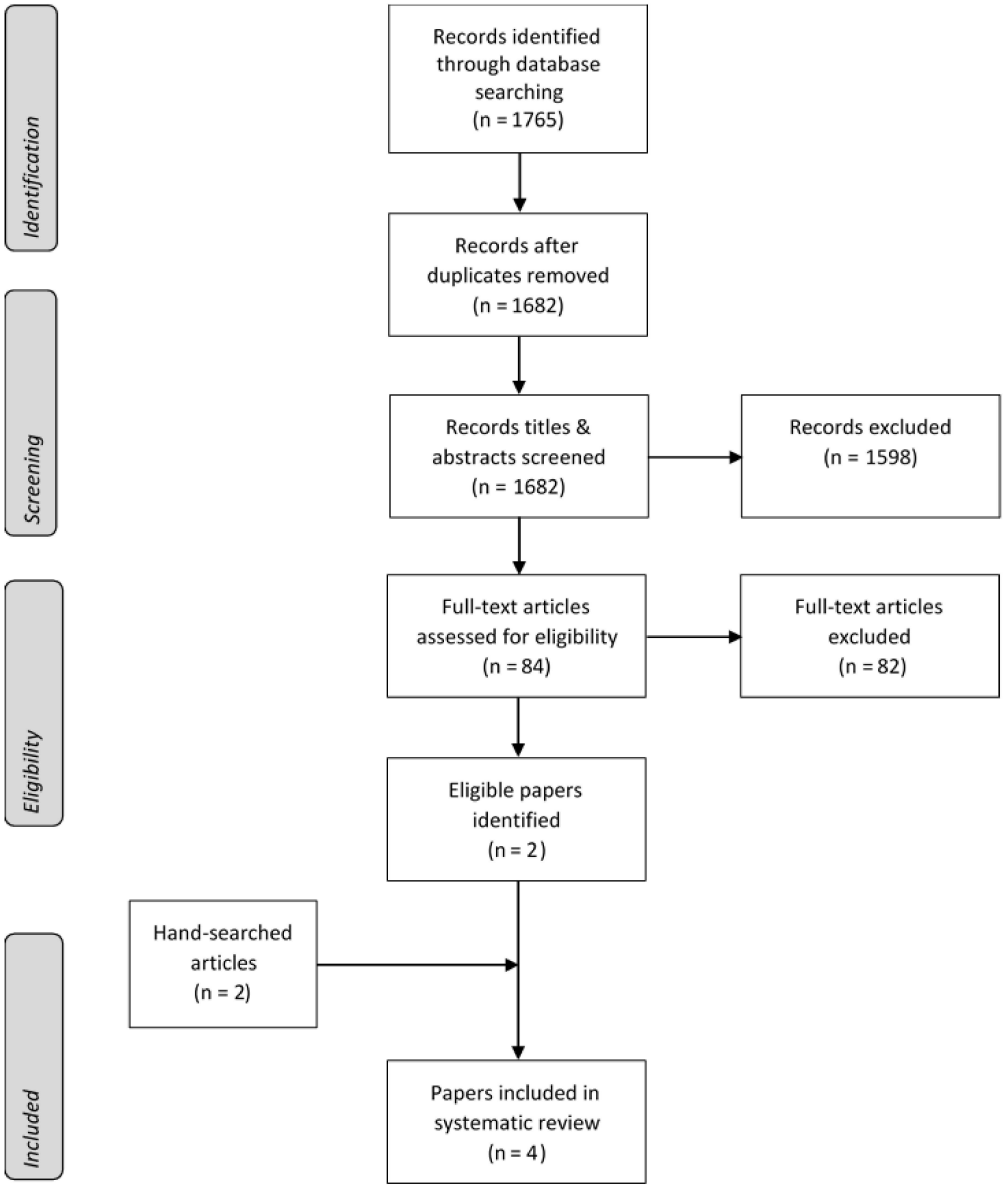
Reference	Design	Intervention	Comparison	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
Recurrent thrombosis									
Kravvariti 2020	Randomized trial	HCQ 200-400 mg/d + standard care	Standard care	25	25	1 (4%)	6 (24%)	HR 0.09 (0.01, 1.26)	Unclear risk-of-bias
Mustonen, 2014	Retrospective cohort	HCQ	No HCQ	26	46	3 (11.5%)	6 (13%)	RR 0.88 (0.24, 3.25)	Intermediate
Nuri 2016	Retrospective cohort	HCQ	No HCQ	57	57	7 (12.2%)	7 (12.2%)	RR 1.00	High

Reference	Design	Case	Control	Number of patients, cases	Number of patients, controls	Exposed, cases	Exposed, controls	Relative effect (95% CI)	Study quality
Antimalarials									
Erkan, 2002	Case control	Thrombotic APS	APL without thrombosis	77	56	4 (5.2%)	21 (37.5%)	OR 0.09 (0.02, 0.29)	Intermediate

*Evidence was inconclusive and, therefore, the task force panel judged no statement can be offered about the use of these medications.

e. Non-steroidal anti-inflammatory drugs

PICO: '*In patients with SLE, is use of NSAIDs associated with worse cardiovascular outcomes than no use of NSAIDs?*'*



Reference	Design	Intervention	Comparison	Number of patients, intervention	Number of patients, comparison	Events, intervention	Events, comparison	Relative effect (95% CI)	Study quality
CVD events									
Kao, 2013	Prospective cohort	NSAID	No NSAID	137	258	8 (5.8%)	9 (3.5%)	RR 1.67 (0.66, 4.24)	High
Fernandez-Nebro, 2015	Retrospective cohort	NSAIDs ever	No NSAIDs ever	2460	1159	176 (7.1%)	93 (8.0%)	RR 0.91 (0.71, 1.17)	Intermediate
Magder, 2012	Prospective cohort	Current NSAID use	No NSAID use	2616 py	4106 py	13.8/1000 py	12.7/1000 py	RR 0.94 (0.70, 1.60)	Intermediate
		Past NSAID use	No NSAID use	2761 py	4106 py	16.7/1000 py	12.7/1000 py	RR 1.17 (0.69, 1.56)	

*Evidence was inconclusive and, therefore, the task force panel judged no statement can be offered about the use of these medications.

4. Prevalence and incidence of cardiovascular disease

a. Systemic lupus erythematosus

No separate SLR was performed about the incidence and prevalence of CVD events in SLE relative to the general population because we used the results of a very recent systematic review and meta-analysis* of high methodological quality on this question.
Evidence supporting publication bias was present for ischemic stroke, but not for composite stroke or myocardial infarction. Subgroup analysis suggested effect modification by age in the risk of stroke, with much higher relative risks in SLE at younger ages, and no increased risk of stroke in SLE among the elderly. Data did not allow for a similar analysis for myocardial infarction.

Risk of cardiovascular events in systemic lupus erythematosus			
Outcome	Number of studies	Pooled Relative Risk (95% CI)	I^2
Composite stroke	11	2.13 (1.73, 2.61)	88%
Ischemic stroke	5	2.18 (1.78, 2.67)	75.4%
Myocardial infarction	8	2.99 (2.34, 3.82)	85.7%

*Yazdany J, Pooley N, Langham J, *et al*. *RMD Open* 2020;6. DOI: 10.1136/rmdopen-2020-001247

b. Antiphospholipid syndrome

No studies were identified that directly addressed incidence and prevalence of CVD events in APS relative to the general population, likely because thrombotic events including stroke and myocardial infarction comprise part of the definition of APS. We compared data about the incidence and prevalence of stroke and myocardial infarction in APS from the Euro-Phospholipid cohort* with those in the general population, using data from the UK statistics about similar age and gender populations and the same time period.†

Risk of cardiovascular events in the antiphospholipid syndrome		
Outcome	Euro-Phospholipid cohort	UK statistics
	Incidence	
Myocardial infarction	1.8/1000 py	NA
Stroke	4.8/1000 py	NA
	Prevalence	
Myocardial infarction	5.5%	0.29%
Stroke	19.8%	0.79%

*Cervera R, Serrano R, Pons-Estel GJ, et al. *Ann Rheum Dis* 2015;74:1011-1018. DOI: 10.1136/annrheumdis-2013-204838

†Bhatnagar P, Wickramasinghe K, Williams J, Rayner M, Townsend N. *Heart* 2015;101:1182-1189. DOI: 10.1136/heartjnl-2015-307516

III. Articles included in the systematic literature review

A. Gout

Abbott RD, Br, FN, Kannel WB, Castelli WP. Gout and coronary heart disease: the Framingham Study. J Clin Epidemiol. 1988;41(3):237-42. [Incidence/Prevalence CVD]

Chen JH, Lan JL, Cheng CF, Liang WM, Lin HY, Tsay GJ, et al. Effect of urate-lowering therapy on the risk of cardiovascular disease and all-cause mortality in patients with gout: A Case-matched Cohort Study. Journal of Rheumatology. 2015;42(9):1694-701. [Disease Medication]

Chen SY, Chen CL, Shen ML. Severity of gouty arthritis is associated with Q-wave myocardial infarction: a large-scale, cross-sectional study. Clin Rheumatol. 2007;26(3):308-13. [Disease activity]

Choi HK, Curhan G. Independent impact of gout on mortality and risk for coronary heart disease. Circulation. 2007;116(8):894-900. [Incidence/Prevalence CVD]

Clarson LE, Hider SL, Belcher J, Heneghan C, Roddy E, Mallen CD. Increased risk of vascular disease associated with gout: a retrospective, matched cohort study in the UK clinical practice research datalink. Ann Rheum Dis. 2015;74(4):642-7. [Incidence/Prevalence CVD]

Crittenden DB, Lehmann RA, Schneck L, Keenan RT, Shah B, Greenberg JD, et al. Colchicine use is associated with decreased prevalence of myocardial infarction in patients with gout. Journal of Rheumatology. 2012;39(7):1458-64. [Disease Medication]

De Vera MA, Rahman MM, Bhole V, Kopec JA, Choi HK. Independent impact of gout on the risk of acute myocardial infarction among elderly women: a population-based study. Ann Rheum Dis. 2010;69(6):1162-4. [Incidence/Prevalence CVD]

Disveld IJM, Zoakman S, Jansen TLTA, Rongen GA, Kienhorst LBE, Janssens HJEM, et al. Crystal-proven gout patients have an increased mortality due to cardiovascular diseases, cancer, and infectious diseases especially when having tophi and/or high serum uric acid levels: a prospective cohort study. Clinical Rheumatology. 2019. [Disease activity]

Essex MN, Hopps M, Bienen EJ, Udall M, Mardekian J, Makinson GT. Evaluation of the Relationship between Serum Uric Acid Levels and Cardiovascular Events in Patients with Gout: A Retrospective Analysis Using Electronic Medical Record Data. Journal of Clinical Rheumatology. 2017;23(3):160-6. [Disease activity]

Foody J, Turpin RS, Tidwell BA, Lawrence D, Schulman KL. Major cardiovascular events in patients with gout and associated cardiovascular disease or heart failure and chronic kidney disease initiating a xanthine oxidase inhibitor. American Health and Drug Benefits. 2017;10(8):393-400. [Disease Medication]

Garcia-Gil M, Comas-Cufí M, Ramos R, Martí R, Alves-Cabratosa L, Parramon D, et al. Effectiveness of Statins as Primary Prevention in People With Gout: A Population-Based Cohort Study. Journal of Cardiovascular Pharmacology and Therapeutics. 2019. [Lipid-lowering agents]

Janssens HJ, Arts PG, Schalk BW, Biermans MC. Gout and rheumatoid arthritis, both to keep in mind in cardiovascular risk management: A primary care retrospective cohort study. Joint Bone Spine. 2017;84(1):59-64. [Incidence/Prevalence CVD]

Joo K, Kwon SR, Lim MJ, Jung KH, Joo H, Park W. Prevention of comorbidity and acute attack of gout by uric acid lowering therapy. J Korean Med Sci. 2014;29(5):657-61. [Disease Medication]

Kang EH, Choi HK, Shin A, Lee YJ, Lee EB, Song YW, et al. Comparative cardiovascular risk of allopurinol versus febuxostat in patients with gout: a nation-wide cohort study. Rheumatology (Oxford, England). 2019. [Disease Medication]

Keller SF, Rai SK, Lu N, Oza A, Jorge AM, Zhang Y, et al. Statin use and mortality in gout: A general population-based cohort study. Seminars in Arthritis and Rheumatism. 2018;48(3):449-55. [Lipid-lowering agents]

Kim SC, Neogi T, Kang EH, Liu J, Desai RJ, Zhang M, et al. Cardiovascular Risks of Probenecid Versus Allopurinol in Older Patients With Gout. Journal of the American College of Cardiology. 2018;71(9):994-1004. [Disease Medication]

Kim SC, Schneeweiss S, Choudhry N, Liu J, Glynn RJ, Solomon DH. Effects of xanthine oxidase inhibitors on cardiovascular disease in patients with gout: A cohort study. American Journal of Medicine. 2015;128(6):653.e7-.e16. [Disease Medication]

Kok VC, Horng JT, Chang WS, Hong YF, Chang TH. Allopurinol therapy in gout patients does not associate with beneficial cardiovascular outcomes: a population-based matched-cohort study. PLoS One. 2014;9(6):e99102. [Disease Medication]

Krishnan E, Svendsen K, Neaton JD, Grandits G, Kuller LH, Group MR. Long-term cardiovascular mortality among middle-aged men with gout. Arch Intern Med. 2008;168(10):1104-10. [Incidence/Prevalence CVD]

Kuo CF, Yu KH, See LC, Chou IJ, Ko YS, Chang HC, et al. Risk of myocardial infarction among patients with gout: a nationwide population-based study. Rheumatology (Oxford). 2013;52(1):111-7. [Incidence/Prevalence CVD]

Lin HC, Daimon M, Wang CH, Ho Y, Uang YS, Chiang SJ, et al. Allopurinol, benzbromarone and risk of coronary heart disease in gout patients: A population-based study. International Journal of Cardiology. 2017;233:85-90. [Disease Medication]

Mackenzie IS, Ford I, Nuki G, Hallas J, Hawkey CJ, Webster J, et al. Long-term cardiovascular safety of febuxostat compared with allopurinol in patients with gout (FAST): a multicentre, prospective, randomised, open-label, non-inferiority trial. Lancet. 2020;396(10264):1745-57. [Disease Medication]

Perez-Ruiz F, Martinez-Indart L, Carmona L, Herrero-Beites AM, Pijoan JI, Krishnan E. Tophaceous gout and high level of hyperuricaemia are both associated with increased risk of mortality in patients with gout. Ann Rheum Dis. 2014;73(1):177-82. [Disease activity]

Seminog OO, Goldacre MJ. Gout as a risk factor for myocardial infarction and stroke in England: evidence from record linkage studies. Rheumatology (Oxford). 2013;52(12):2251-9. [Incidence/Prevalence CVD]

Singh JA, Cleveland JD. Gout and the risk of myocardial infarction in older adults: a study of Medicare recipients. Arthritis Res Ther. 2018;20(1):109. [Incidence/Prevalence CVD]

Solomon DH, Liu CC, Kuo IH, Zak A, Kim SC. Effects of colchicine on risk of cardiovascular events and mortality among patients with gout: A cohort study using electronic medical records linked with Medicare claims. Annals of the Rheumatic Diseases. 2016;75(9):1674-9. [Disease Medication]

Stack AG, Hanley A, Casserly LF, Cronin CJ, Abdalla AA, Kiernan TJ, et al. Independent and conjoint associations of gout and hyperuricaemia with total and cardiovascular mortality. Qjm. 2013;106(7):647-58. [Disease activity]

Teng GG, Ang LW, Saag KG, Yu MC, Yuan JM, Koh WP. Mortality due to coronary heart disease and kidney disease among middle-aged and elderly men and women with gout in the Singapore Chinese Health Study. Ann Rheum Dis. 2012;71(6):924-8. [Incidence/Prevalence CVD]

White WB, Saag KG, Becker MA, Borer JS, Gorelick PB, Whelton A, et al. Cardiovascular safety of febuxostat or allopurinol in patients with gout. New England Journal of Medicine. 2018;378(13):1200-10. [Disease Medication]

Zhang M, Solomon DH, Desai RJ, Kang EH, Liu J, Neogi T, et al. Assessment of Cardiovascular Risk in Older Patients With Gout Initiating Febuxostat Versus Allopurinol. Circulation. 2018;138(11):1116-26. [Disease Medication]

Zhang T, Pope JE. Cardiovascular effects of urate-lowering therapies in patients with chronic gout: A systematic review and meta-analysis. Rheumatology (United Kingdom). 2017;56(7):1144-53. [Disease Medication]

B. Vasculitis, systemic sclerosis, mixed connective tissue disease, myositis and Sjögren's syndrome

Alba MA, Garcia-Martinez A, Prieto-Gonzalez S, Espigol-Frigole G, Butjosa M, Tavera-Bahillo I, et al. Treatment with angiotensin II receptor blockers is associated with prolonged relapse-free survival, lower relapse rate, and corticosteroid-sparing effect in patients with giant cell arteritis. Semin Arthritis Rheum. 2014;43(6):772-7. [Antihypertensives]

Albrecht K, Huscher D, Buttgereit F, Aringer M, Hoese G, Ochs W, et al. Long-term glucocorticoid treatment in patients with polymyalgia rheumatica, giant cell arteritis, or both diseases: results from a national rheumatology database. Rheumatol Int. 2018;38(4):569-77. [Disease activity] [Disease medication]

Alenghat FJ. The Prevalence of Atherosclerosis in Those with Inflammatory Connective Tissue Disease by Race, Age, and Traditional Risk Factors. Sci Rep. 2016;6:20303. [Incidence/Prevalence CVD]

Ali H, Ng KR, Low AH. A qualitative systematic review of the prevalence of coronary artery disease in systemic sclerosis. Int J Rheum Dis. 2015;18(3):276-86. [Incidence/Prevalence CVD]

Amiri N, De Vera M, Choi HK, Sayre EC, Avina-Zubieta JA. Increased risk of cardiovascular disease in giant cell arteritis: a general population-based study. Rheumatology (Oxford). 2016;55(1):33-40. [Disease activity] [Incidence/Prevalence CVD]

Aouba A, Gonzalez Chiappe S, Eb M, Delmas C, de Boysson H, Bienvenu B, et al. Mortality causes and trends associated with giant cell arteritis: analysis of the French national death certificate database (1980-2011). Rheumatology (Oxford). 2018;57(6):1047-55. [Incidence/Prevalence CVD]

Bai YH, Li ZY, Chang DY, Chen M, Kallenberg CG, Zhao MH. The BVAS is an independent predictor of cardiovascular events and cardiovascular disease-related mortality in patients with ANCA-associated vasculitis: A study of 504 cases in a single Chinese center. Semin Arthritis Rheum. 2018;47(4):524-9. [Disease activity]

Bartoloni E, Baldini C, Schillaci G, Quartuccio L, Priori R, Carubbi F, et al. Cardiovascular disease risk burden in primary Sjogren's syndrome: results of a population-based multicentre cohort study. J Intern Med. 2015;278(2):185-92. [Disease activity]

Berger CT, Wolbers M, Meyer P, Daikeler T, Hess C. High incidence of severe ischaemic complications in patients with giant cell arteritis irrespective of platelet count and size, and platelet inhibition. Rheumatology (Oxford). 2009;48(3):258-61. [Antiplatelet Therapy]

Berti A, Matteson EL, Crowson CS, Specks U, Cornec D. Risk of Cardiovascular Disease and Venous Thromboembolism Among Patients With Incident ANCA-Associated Vasculitis: A 20-Year Population-Based Cohort Study. Mayo Clin Proc. 2018;93(5):597-606. [Prediction Tools] [Incidence/Prevalence CVD]

Caramaschi P, Biasi D, Caimmi C, Barausse G, Sabbagh D, Tinazzi I, et al. Digital amputation in systemic sclerosis: prevalence and clinical associations. A retrospective longitudinal study. J Rheumatol. 2012;39(8):1648-53. [Disease activity]

Chazal T, Lhote R, Rey G, Haroche J, Eb M, Amoura Z, et al. Giant-cell arteritis-related mortality in France: A multiple-cause-of-death analysis. Autoimmun Rev. 2018;17(12):1219-24. [Incidence/Prevalence CVD]

Chiang CH, Liu CJ, Chen PJ, Huang CC, Hsu CY, Chan WL, et al. Primary Sjogren's syndrome and risk of ischemic stroke: a nationwide study. Clin Rheumatol. 2014;33(7):931-7. [Incidence/Prevalence CVD]

Chu SY, Chen YJ, Liu CJ, Tseng WC, Lin MW, Hwang CY, et al. Increased risk of acute myocardial infarction in systemic sclerosis: a nationwide population-based study. Am J Med. 2013;126(11):982-8. [Disease medication]

de Boysson H, Liozon E, Espitia O, Daumas A, Vautier M, Lambert M, et al. Different patterns and specific outcomes of large-vessel involvements in giant cell arteritis. J Autoimmun. 2019;103:102283. [Disease medication]

de Moraes MT, de Souza FH, de Barros TB, Shinjo SK. Analysis of metabolic syndrome in adult dermatomyositis with a focus on cardiovascular disease. Arthritis Care Res (Hoboken). 2013;65(5):793-9. [Incidence/Prevalence CVD]

Faurschou M, Mellemkjaer L, Sorensen IJ, Svalgaard Thomsen B, Dreyer L, Baslund B. Increased morbidity from ischemic heart disease in patients with Wegener's granulomatosis. Arthritis Rheum. 2009;60(4):1187-92. [Disease medication]

Gale S, Wilson JC, Chia J, Trinh H, Tuckwell K, Collinson N, et al. Risk Associated with Cumulative Oral Glucocorticoid Use in Patients with Giant Cell Arteritis in Real-World Databases from the USA and UK. Rheumatol Ther. 2018;5(2):327-40. [Disease medication]

Gonzalez-Gay MA, Pineiro A, Gomez-Gigirey A, Garcia-Porrua C, Pego-Reigosa R, Dierssen-Sotos T, et al. Influence of traditional risk factors of atherosclerosis in the development of severe ischemic complications in giant cell arteritis. Medicine (Baltimore). 2004;83(6):342-7. [Incidence/Prevalence CVD]

Grossman C, Barshack I, Koren-Morag N, Ben-Zvi I, Bornstein G. Risk factors for severe cranial ischaemic events in patients with giant cell arteritis. Clin Exp Rheumatol. 2017;35 Suppl 103(1):88-93. [Antihypertensives] [Lipid lowering agents] [Antiplatelet Therapy]

Houben E, Mendel A, Carette S, Voskuyl AE, Penne EL, Pagnoux C. Predictors of fatal and non-fatal cardiovascular events in ANCA-associated vasculitis: Data from the Toronto CanVasc cohort. Joint Bone Spine. 2020;87(3):221-4. [Disease activity]

Houben E, Penne EL, Voskuyl AE, van der Heijden JW, Otten RHJ, Boers M, et al. Cardiovascular events in anti-neutrophil cytoplasmic antibody-associated vasculitis: a meta-analysis of observational studies. Rheumatology (Oxford). 2018;57(3):555-62. [Incidence/Prevalence CVD]

Kermani TA, Warrington KJ, Crowson CS, Ytterberg SR, Hunder GG, Gabriel SE, et al. Large-vessel involvement in giant cell arteritis: a population-based cohort study of the incidence-trends and prognosis. Ann Rheum Dis. 2013;72(12):1989-94. [Incidence/Prevalence CVD]

Kurmann RD, Sandhu AS, Crowson CS, Matteson EL, Osborn TG, Warrington KJ, et al. Cardiovascular Risk Factors and Atherosclerotic Cardiovascular Events Among Incident Cases of Systemic Sclerosis: Results From a Population-Based Cohort (1980-2016). Mayo Clin Proc. 2020;95(7):1369-78. [Incidence/Prevalence CVD]

Lee MS, Smith SD, Galor A, Hoffman GS. Antiplatelet and anticoagulant therapy in patients with giant cell arteritis. Arthritis Rheum. 2006;54(10):3306-9. [Antiplatelet therapy]

Lee YH, Song GG. Overall and cause-specific mortality in giant cell arteritis : A meta-analysis. Z Rheumatol. 2018;77(10):946-51. [Incidence/Prevalence CVD]

Li L, Neogi T, Jick S. Giant cell arteritis and vascular disease-risk factors and outcomes: a cohort study using UK Clinical Practice Research Datalink. Rheumatology (Oxford). 2017;56(5):753-62. [Incidence/Prevalence CVD]

Li L, Neogi T, Jick S. A cohort study of comorbidity in patients with granulomatosis with polyangiitis. Rheumatology (Oxford). 2018;57(2):291-9. [Incidence/Prevalence CVD]

Lin YN, Lin CL, Chang KC, Kao CH. Increased subsequent risk of acute coronary syndrome for patients with dermatomyositis/polymyositis: a nationwide population-based retrospective cohort study. Scand J Rheumatol. 2015;44(1):42-7. [Incidence/Prevalence CVD]

Lo Gullo A, Koster MJ, Crowson CS, Makol A, Ytterberg SR, Saitta A, et al. Venous Thromboembolism and Cerebrovascular Events in Patients with Giant Cell Arteritis: A Population-Based Retrospective Cohort Study. PLoS One. 2016;11(2):e0149579. [Incidence/Prevalence CVD]

Luni FK, Malik SA, Khan AR, Riaz H, Singh H, Federman D, et al. Risk of Ischemic Heart Disease in Patients With Sjogren's Syndrome. Am J Med Sci. 2017;354(4):395-8. [Incidence/Prevalence CVD]

Martinez-Taboada VM, Lopez-Hoyos M, Narvaez J, Munoz-Cacho P. Effect of antiplatelet/anticoagulant therapy on severe ischemic complications in patients with giant cell arteritis: a cumulative meta-analysis. Autoimmun Rev. 2014;13(8):788-94. [Antiplatelet therapy]

Mofors J, Holmqvist M, Westermark L, Bjork A, Kvarnstrom M, Forsblad-d'Elia H, et al. Concomitant Ro/SSA and La/SSB antibodies are biomarkers for the risk of venous thromboembolism and cerebral infarction in primary Sjogren's syndrome. J Intern Med. 2019;286(4):458-68. [Disease activity]

Mohammad AJ, Bakoush O, Sturfelt G, Segelmark M. The extent and pattern of organ damage in small vessel vasculitis measured by the Vasculitis Damage Index (VDI). Scand J Rheumatol. 2009;38(4):268-75. [Disease activity]

Mohammad AJ, Englund M, Turesson C, Tomasson G, Merkel PA. Rate of Comorbidities in Giant Cell Arteritis: A Population-based Study. J Rheumatol. 2017;44(1):84-90. [Incidence/Prevalence CVD]

Mollan SP, Sharrack N, Burdon MA, Denniston AK. Aspirin as adjunctive treatment for giant cell arteritis. Cochrane Database Syst Rev. 2014(8):CD010453. [Antiplatelet Therapy]

Mourguet M, Chauveau D, Faguer S, Ruidavets JB, Bejot Y, Ribes D, et al. Increased ischemic stroke, acute coronary artery disease and mortality in patients with granulomatosis with polyangiitis and microscopic polyangiitis. J Autoimmun. 2019;96:134-41. [Incidence/Prevalence CVD]

Narvaez J, Bernad B, Nolla JM, Valverde J. Statin therapy does not seem to benefit giant cell arteritis. Semin Arthritis Rheum. 2007;36(5):322-7. [Lipid lowering agents]

Narvaez J, Bernad B, Gomez-Vaquero C, Garcia-Gomez C, Roig-Vilaseca D, Juanola X, et al. Impact of antiplatelet therapy in the development of severe ischemic complications and in the outcome of patients with giant cell arteritis. Clin Exp Rheumatol. 2008;26(3 Suppl 49):S57-62. [Antiplatelet Therapy]

Nesher G, Berkun Y, Mates M, Baras M, Rubinow A, Sonnenblick M. Low-dose aspirin and prevention of cranial ischemic complications in giant cell arteritis. Arthritis Rheum. 2004;50(4):1332-7. {Antiplatelet Therapy]

Pariente A, Guedon A, Alamowitch S, Thietart S, Carrat F, Delorme S, et al. Ischemic stroke in giant-cell arteritis: French retrospective study. J Autoimmun. 2019;99:48-51. [Lipid lowering agents] [Antiplatelet Therapy]

Pugnet G, Sailler L, Fournier JP, Bourrel R, Montastruc JL, Lapeyre-Mestre M. Predictors of Cardiovascular Hospitalization in Giant Cell Arteritis: Effect of Statin Exposure. A French Population-based Study. J Rheumatol. 2016;43(12):2162-70. [Lipid lowering agents] [Antiplatelet Therapy] [Incidence/Prevalence CVD]

Rai SK, Choi HK, Sayre EC, Avina-Zubieta JA. Risk of myocardial infarction and ischaemic stroke in adults with polymyositis and dermatomyositis: a general population-based study. Rheumatology (Oxford). 2016;55(3):461-9. [Incidence/Prevalence CVD]

Robson J, Doll H, Suppiah R, Flossmann O, Harper L, Hoglund P, et al. Damage in the anca-associated vasculitides: long-term data from the European vasculitis study group (EUVAS) therapeutic trials. Ann Rheum Dis. 2015;74(1):177-84. [Disease activity]

Robson J, Doll H, Suppiah R, Flossmann O, Harper L, Hoglund P, et al. Glucocorticoid treatment and damage in the anti-neutrophil cytoplasm antibody-associated vasculitides: long-term data from the European Vasculitis Study Group trials. Rheumatology (Oxford). 2015;54(3):471-81. [Disease activity]

Robson J, Doll H, Suppiah R, Flossmann O, Harper L, Hoglund P, et al. Damage in the anca-associated vasculitides: long-term data from the European vasculitis study group (EUVAS) therapeutic trials. Ann Rheum Dis. 2015;74(1):177-84. [Disease activity]

Romeu M, Couchoud C, Delaroziere JC, Burtey S, Chiche L, Harle JR, et al. Survival of patients with ANCA-associated vasculitis on chronic dialysis: data from the French REIN registry from 2002 to 2011. QJM. 2014;107(7):545-55. [Incidence/Prevalence CVD]

Salvarani C, Casali B, Farnetti E, Pipitone N, Formisano D, Nicoli D, et al. PlA1/A2 polymorphism of the platelet glycoprotein receptor IIIA and risk of cranial ischemic complications in giant cell arteritis. Arthritis Rheum. 2007;56(10):3502-8. [Antiplatelet Therapy]

Salvarani C, Della Bella C, Cimino L, Macchioni P, Formisano D, Bajocchi G, et al. Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis. Rheumatology (Oxford). 2009;48(3):250-3. [Antiplatelet Therapy]

Suppiah R, Judge A, Batra R, Flossmann O, Harper L, Hoglund P, et al. A model to predict cardiovascular events in patients with newly diagnosed Wegener's granulomatosis and microscopic polyangiitis. Arthritis Care Res (Hoboken). 2011;63(4):588-96. [Disease activity] [Prediction Tools]

Szamosi S, Csiki Z, Szomjak E, Szolnoki E, Szoke G, Szekanecz Z, et al. Plasma homocysteine levels, the prevalence of methylenetetrahydrofolate reductase gene C677T polymorphism and macrovascular disorders in systemic sclerosis: risk factors for accelerated macrovascular damage? Clin Rev Allergy Immunol. 2009;36(2-3):145-9. [Disease activity]

Terrier B, Chironi G, Pagnoux C, Cohen P, Puechal X, Simon A, et al. Factors associated with major cardiovascular events in patients with systemic necrotizing vasculitides: results of a longterm followup study. J Rheumatol. 2014;41(4):723-9. [Prediction Tools]

Tisseverasinghe A, Bernatsky S, Pineau CA. Arterial events in persons with dermatomyositis and polymyositis. J Rheumatol. 2009;36(9):1943-6. [Disease medication] [Incidence/Prevalence CVD]

Udayakumar PD, Chandran AK, Crowson CS, Warrington KJ, Matteson EL. Cardiovascular risk and acute coronary syndrome in giant cell arteritis: a population-based retrospective cohort study. Arthritis Care Res (Hoboken). 2015;67(3):396-402. [Prediction Tools]

Ungprasert P, Cheungpasitporn W, Wijarnpreecha K, Ahuja W, Ratanasrimetha P, Thongprayoon C. Risk of ischemic stroke in patients with polymyositis and dermatomyositis: a systematic review and meta-analysis. Rheumatol Int. 2015;35(5):905-9. [Incidence/Prevalence CVD]

Ungprasert P, Koster MJ, Warrington KJ. Coronary artery disease in giant cell arteritis: a systematic review and meta-analysis. Semin Arthritis Rheum. 2015;44(5):586-91. [Incidence/Prevalence CVD]

Ungprasert P, Suksaranjit P, Spanuchart I, Leeaphorn N, Permpalung N. Risk of coronary artery disease in patients with idiopathic inflammatory myopathies: a systematic review and meta-analysis of observational studies. Semin Arthritis Rheum. 2014;44(1):63-7. [Incidence/Prevalence CVD]

Ungprasert P, Thongprayoon C, Kittanamongkolchai W, Srivali N, Cheungpasitporn W. Peripheral arterial disease in patients with giant cell arteritis: a meta-analysis. Int J Rheum Dis. 2016;19(8):819-25. [Incidence/Prevalence CVD]

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Studies that were included in the SLR for the use of NSAIDs in SLE (*) and antimalarials in APS (†). Evidence was inconclusive and, therefore, the task force panel judged no statement can be offered about the use of these medications.