Systematic Literature Review (SLR) report for the 2023 update of the EULAR recommendations for the management of SLE

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Research questions and PICOs

For this update the research questions focused on five different domains: 1) the benefit/harm of SLE treatments (including lupus nephritis, neuropsychiatric, mucocutaneous, musculoskeletal and haematological lupus), 2) the benefits from the attainment of remission/low disease activity, 3) the risk/benefit from treatment tapering/withdrawal, 4) the management of SLE with aPL/APS and 5) the safety/toxicity of immunizations against zoster and SARS-Cov2.

Given the diversity of SLE populations, interventions, and outcomes different PICOS were developed for each individual question. As a first step a draft of the PICOs was circulated among the Task Force members who were encouraged to propose additional treatments or outcomes. The final version of PICOs was used as basis for the formulation of the respective search queries. Points-to consider for special areas/topics of interest were also included after each research question. The research questions with the respective PICOs, and points to consider are listed below.

PICO 1 – Therapeutic interventions

PICO 1a. In patients with active SLE, what is the evidence for the benefits and harms of therapeutic interventions including antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents, plasma exchange/immunoadsorption?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• Patients with active SLE	• Sun protection • NSAIDs • Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin • Tacrolimus • Biological agents • Belimumab • Anifrolumab • Rituximab • Obinutuzumab • Ofatumumab • Ocrelizumab • Atacicept • Etanercept • Adalimumab • Abatacept • Adalimumab • Tocilizumab • Secukinumab • Ustekinumab	• Standard of care • Azathioprine • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): global and specific domains • Cutaneous LE Disease Area and Severity Index • Tender joint count • Swollen joint count • Physician Global Assessment • Glucocorticoid sparing • Response (SRI-4, BICLA) • Disease control • Low disease activity (LLDAS) • Remission (various definitions including steroid-free remission) • Relapse, flare, time-to-flare • Treatment failure • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Adverse events/toxicity (including retinopathy) • Thrombosis

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Anakinra • JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib) • Proteasome inhibitors (e.g., bortezomib) • Iberdomide • Litifilimab • Low-dose IL-2 • Daratumumab • CD19 CAR-T cells • Plasmapheresis • Plasma exchange • Immunoadsorption • Intravenous immunoglobulin		

Points to consider (for the SLR and/or data extraction):

- Stratification according to: patient age, ancestry/race, disease duration, prior treatments, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Glucocorticoids: capture dosage details such as the use of pulse methylprednisolone, initial dose, average dosage, tapering scheme
- Evidence on the efficacy of treatments in relapsing and refractory disease
- Collect data on global disease activity indices and activity from individual domains (e.g., serositis)
- Collect data on relevant safety outcomes: retinopathy, infections (including HZV, opportunistic), MACEs, hospitalizations, death

PICO 1b. In patients with SLE and active mucocutaneous involvement, what is the evidence for the benefits and harms of therapeutic interventions including sun protection, topical agents, antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with active mucocutaneous involvement	• Sun protection • Topical agents (glucocorticoids, calcineurin inhibitors) • Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin • Tacrolimus • Retinoids • Dapsone • Thalidomide • Lenalidomide • Biological agents	• Standard of care • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): mucocutaneous-specific domains • Cutaneous LE Disease Area and Severity Index • Physician Global Assessment • Glucocorticoid sparing • Response (SRI-4, BICLA) • Disease control • Low disease activity (LLDAS) • Remission (various definitions including steroid-free remission) • Relapse, flare, time-to-flare • Treatment failure • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Belimumab • Anifrolumab • Rituximab • Obinutuzumab • Ofatumumab • Ocrelizumab • Atacicept • Etanercept • Adalimumab • Abatacept • Tocilizumab • Secukinumab • Ustekinumab • Anakinra • JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib) • Proteasome inhibitors (e.g., bortezomib) • Iberdomide • Litifilimab • Low-dose IL-2 • Daratumumab • CD19 CAR-T cells • Intravenous immunoglobulin		• Death • Toxicity (including retinopathy) • Thrombosis

Points to consider (for the SLR and/or data extraction):

- Stratification according to subtype: ACLE, SCLE, DLE and other forms of CCLE; patient age, ancestry/race, disease duration, prior treatments, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Glucocorticoids: capture dosage details such as the use of pulse methylprednisolone, initial/cumulative dose, tapering scheme
- Evidence on the efficacy of treatments in relapsing and refractory disease

PICO 1c. In patients with SLE and active musculoskeletal involvement, what is the evidence for the benefits and harms of therapeutic interventions including antimalarials, glucocorticoids, immunosuppressive and biological/targeted agents?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with active musculoskeletal involvement	• NSAIDs • Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin • Tacrolimus • Biological agents	• Standard of care • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): musculoskeletal-specific domains • Tender joint count • Swollen joint count • Physician Global Assessment • Glucocorticoid sparing • Response (SRI-4, BICLA) • Disease control • Low disease activity (LLDAS) • Remission (various definitions including steroid-free remission) • Relapse, flare, time-to-flare • Treatment failure

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Belimumab • Anifrolumab • Rituximab • Obinutuzumab • Ofatumumab • Ocrelizumab • Atacicept • Etanercept • Adalimumab • Abatacept • Tocilizumab • Secukinumab • Ustekinumab • Anakinra • JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib) • Proteasome inhibitors (e.g., bortezomib) • Iberdomide • Litifilimab • Low-dose IL-2 • Daratumumab • CD19 CAR-T cells		• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Toxicity (including retinopathy) • Thrombosis

Points to consider (for the SLR and/or data extraction):

- Stratification according to arthritis phenotype (e.g., RA-like), patient age, ancestry/race, disease duration, prior treatments, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Glucocorticoids: capture dosage details such as the use of pulse methylprednisolone, initial dose, average dosage, tapering scheme
- Evidence on the efficacy of treatments in relapsing and refractory disease

PICO 1d. In patients with SLE and active neuropsychiatric involvement, what is the evidence for the benefits and harms of therapeutic interventions including antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents, plasma exchange/immunoadsorption?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with active neuropsychiatric involvement	• Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin • Tacrolimus • Biological agents • Belimumab • Anifrolumab • Rituximab • Obinutuzumab	• Standard of care • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): neuropsychiatric-specific domains • Neurological deficit (e.g., EDSS) • Neuropsychological tests • Psychiatric scales • Physician Global Assessment • Glucocorticoid sparing • Response (SRI-4, BICLA) • Disease control • Low disease activity (LLDAS) • Remission (various definitions including steroid-free remission) • Relapse, flare, time-to-flare • Treatment failure • Organ damage (including cataract, cognitive dysfunction, osteoporotic

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Ofatumumab • Ocrelizumab • Atacicept • Etanercept • Adalimumab • Abatacept • Tocilizumab • Secukinumab • Ustekinumab • Anakinra • JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib) • Proteasome inhibitors • Iberdomide • Litifilimab • Low-dose IL-2 • Daratumumab • CD19 CAR-T cells • Plasmapheresis • Plasma exchange • Immunoadsorption • Intravenous immunoglobulin		fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Toxicity (including retinopathy) • Thrombosis

Points to consider (for the SLR and/or data extraction):

- Neuropsychiatric lupus as a single entity and according to individual manifestations (ACR nomenclature; 19 syndromes)
- Stratification according to: patient age, ancestry/race, disease duration, prior treatments, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Glucocorticoids: capture dosage details such as the use of pulse methylprednisolone, initial dose, average dosage, tapering scheme
- Evidence on the efficacy of treatments in relapsing and refractory disease
- Relevant safety outcomes: infections (including HZV, opportunistic), hospitalizations, death

PICO 1e. In patients with SLE and active haematological involvement, what is the evidence for the benefits and harms of therapeutic interventions including antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents, plasma exchange/immunoadsorption?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with active haematological involvement	• Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin	• Standard of care • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): haematological-specific domains • Complete blood count • Physician Global Assessment • Glucocorticoids sparing • Response (SRI-4, BICLA) • Disease control • Low disease activity (LLDAS) • Remission (various definitions including steroid-free remission)

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Tacrolimus • Biological agents • Belimumab • Anifrolumab • Rituximab • Obinutuzumab • Ofatumumab • Ocrelizumab • Atacicept • Etanercept • Adalimumab • Abatacept • Tocilizumab • Secukinumab • Ustekinumab • Anakinra • JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib) • Proteasome inhibitors (e.g., bortezomib) • Iberdomide • Litifilimab • Low-dose IL-2 • Daratumumab • CD19 CAR-T cells • Plasmapheresis • Plasma exchange • Immunoadsorption • Intravenous immunoglobulin • Thrombopoietin-receptor agonists (romiplostim, eltrombopag)		• Relapse, flare, time-to-flare • Treatment failure • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Toxicity (including retinopathy) • Cardiovascular disease • Thrombosis

Points to consider (for the SLR and/or data extraction):

- Stratification according to patient age, ancestry/race, disease duration, prior treatments, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Glucocorticoids: capture dosage details such as the use of pulse methylprednisolone, initial dose, average dosage, tapering scheme
- Evidence on the efficacy of treatments in relapsing and refractory disease
- Relevant safety outcomes: infections (including HZV, opportunistic), hospitalizations, death

PICO 1f. In patients with SLE and active kidney involvement, what is the evidence for the benefits and harms of therapeutic interventions including antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents, plasma exchange/immunoadsorption?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with active kidney involvement	• Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents	• Standard of care • Mycophenolate • Azathioprine	• Disease activity improvement/worsening (SLEDAI, BILAG): renal-specific domains • Proteinuria improvement/worsening

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin • Tacrolimus • Voclosporin • Biological agents • Belimumab • Anifrolumab • Rituximab • Obinutuzumab • Ofatumumab • Ocrelizumab • Atacicept • Telaticept • Dapagliflozin • Etanercept • Adalimumab • Abatacept • Tocilizumab • Secukinumab • Ustekinumab • Anakinra • JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib) • Proteasome inhibitors • Iberdomide • Litifilimab • Low-dose IL-2 • Daratumumab • CD19 CAR-T cells • Plasmapheresis • Plasma exchange • Immunoadsorption • Intravenous immunoglobulin • RAAS inhibitors • SGLT2 inhibitors (Dapagliflozin)	• Cyclophosphamide • Ciclosporin • Tacrolimus • Placebo • None	• Kidney function (serum creatinine, eGFR) improvement/worsening • Chronic kidney disease • End-stage kidney disease • Histological improvement/worsening (change in activity/chronicity indices) • Physician Global Assessment • Glucocorticoid dose/tapering • Renal response (e.g., PEER, EULAR-defined endpoints) • Renal remission (complete renal response) • Relapse, flare, time-to-flare • Treatment failure • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Toxicity (including retinopathy) • Thrombosis

Points to consider (for the SLR and/or data extraction):

- Stratification according to kidney histology: proliferative, mixed proliferative and membranous, pure membranous (class V) lupus nephritis; presence of thrombotic microangiopathy (or other features of APS nephropathy); presence of crescents; activity and chronicity index; presence of IF/TA – limitations of current approaches to histologic classification, use of activity and chronicity scores
- Stratification according to: patient age, ancestry/race, disease duration, prior treatments, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Glucocorticoids: dosage details such as the use of pulse methylprednisolone, initial dose, average dosage, tapering scheme
- Evidence on the efficacy of treatments in relapsing and refractory disease
- Relevant safety outcomes: infections (including HZV, opportunistic), hospitalizations, death

PICO 2. In patients with SLE, what is the evidence that attainment of low disease activity and remission are associated with improved patient and disease outcomes?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients	• Low disease activity • Lupus Low Disease Activity State (LLDAS) • Remission • Inactive disease • Disease quiescence • Duration of LLDAS/remission	• Active disease • Not in low disease activity or remission or disease quiescence • None	• Relapse, flare, time-to-flare • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Kidney function (serum creatinine, eGFR) improvement/worsening • Chronic kidney disease • End-stage kidney disease • Toxicity • Infection • Hospitalizations • Death

Points to consider (for the SLR and/or data extraction):

- Evidence on the prognostic value of various existing definitions and their modification, treated as binary variables (attainment or not) or (percentage of) time spent under the state
- Stratification according to: general SLE, lupus nephritis
- Stratification according to: patient age, ancestry/race, disease duration, selected biomarkers (serological activity, serum complements, anti-dsDNA, IFN-signature)

PICO 3. In patients with SLE and antiphospholipid syndrome (including thrombotic microangiopathy), what is the evidence for the benefits and harms of therapeutic interventions including antiplatelets, anticoagulants, antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents, plasma exchange/immunoadsorption?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with antiphospholipid syndrome	• Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • Cytotoxic agents • Methotrexate • Leflunomide • Azathioprine • Cyclophosphamide • Mycophenolate • Ciclosporin • Tacrolimus • Voclosporin • Biological agents • Belimumab	• Standard of care • Placebo • None	• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Hospitalizations • Death • Toxicity (including bleeding) • Cardiovascular disease • Pregnancy/foetal loss • Live birth • Premature birth • Stillbirth • (Pre-)eclampsia • Vascular thrombosis (venous, arterial)

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• Anifrolumab • Rituximab • Obinutuzumab • Ofatumumab • Ocrelizumab • Atacicept • Complement inhibitors (e.g., eculizumab) • Plasmapheresis • Plasma exchange • Immunoadsorption • Intravenous immunoglobulin • Aspirin • Heparin • Warfarin • Apixaban • Rivaroxaban • Eculizumab		

Points to consider (for the SLR and/or data extraction):

- Stratification according to: APS phenotype (obstetric APS, thrombotic APS, catastrophic APS), patient age, ancestry/race, selected biomarkers (serum complements, anti-dsDNA, IFN-signature)
- Evidence on the efficacy of treatments in relapsing and refractory disease

PICO 4. In patients with SLE and quiescent disease, what is the evidence for the benefits and harms of tapering and/or withdrawal of treatment including antimalarials, glucocorticoids, immunosuppressive, biological/targeted agents?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with quiescent disease (low disease activity or remission)	• Treatment withdrawal, discontinuation, tapering (including glucocorticoids, hydroxychloroquine, antimalarials, immunosuppressive agents, biological agents) • Duration of treatment	• Standard of care • Placebo • None	• Disease activity (SLEDAI, BILAG): global and specific domains • Physician Global Assessment • Glucocorticoid exposure • Disease control • Disease worsening • Treatment re-initiation • Low disease activity (LLDAS) • Remission (including steroid-free remission) • Relapse, flare, time-to-flare • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Hospitalizations • Death • Toxicity (including bleeding)

Points to consider (for the SLR and/or data extraction):

- Data stratification according to: patient age, ancestry/race, selected biomarkers (serum complements, anti-dsDNA, IFN-signature), disease duration, type of disease (SLE, lupus nephritis), tapering/withdrawal of glucocorticoids versus other therapeutic agents

PICO 5. In patients with SLE, what is the evidence for the benefits and harms of vaccination against infectious pathogens including herpes zoster and SARS-CoV2 viruses?

Detailed PICO – see also 'Points to consider'

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients	• Vaccination against zoster • Vaccination against SARS-CoV2	• No vaccination • None	• Serological response (protective antibodies) • Herpes zoster infection • SARS-CoV2 infection • COVID-19 • Need for hospitalization (e.g., need for oxygen supply, ICU) • Death • Disease activity (SLEDAI, BILAG): global and specific domains • Physician Global Assessment • Glucocorticoid exposure • Disease control • Disease worsening • Relapse, flare, time-to-flare • Toxicity

Points to consider (for the SLR and/or data extraction):

- Stratification according to: patient age, ancestry/race, disease status (active, inactive), type of disease (SLE, lupus nephritis), concomitant treatments (dose of glucocorticoids, immunosuppressives, biologics), major comorbidities (diabetes mellitus, cardiovascular disease, chronic respiratory disorders)
- Stratification according to type of vaccine (e.g., attenuated, recombinant, mRNA), number of booster vaccinations

Inclusion and exclusion criteria:

Inclusion criteria:

SLE adult population
Studies reporting data regarding efficacy/safety of treatments/withdrawal of treatments.
Studies reporting data regarding efficacy/safety of immunization against herpes or SARS-CoV2
Studies reporting outcomes associated with attainment of low disease activity or remission.
Eligible trial designs:

- Meta-analyses
- RCTs, quasi-RCTs
- Cohort studies (prospective and retrospective)
- Case-control studies
- Cross sectional-studies

Exclusion criteria:

Reviews
Case series
Case reports
Conference abstracts
Animal studies
Non-English language
Trials with population <20
Trials on paediatric populations

Search strategy

In line with the EULAR standardised operating procedures, the SLR included two databases (MEDLINE and the Cochrane Library - CENTRAL database) and one additional journal not indexed in PubMed (Lancet Rheumatology). Eligible studies had to be published between December 2017 and December 2022. The search queries for MEDLINE and CENTRAL were as follows:

Medline Search string for PICO 1 (PICOs 1a–1f)

("SLE"[Title] OR "lupus"[Title]) AND ("glucocorticoid*"[All Fields] OR "glucocorticoids"[MeSH Terms] OR "steroid*"[All Fields] OR "steroids"[MeSH Terms] OR "corticosteroid*"[All Fields] OR "anti inflammatory agents, non steroidal"[MeSH Terms] OR "non-steroidal anti-inflammatory agents"[Title] OR "nsaid"[Title] OR "nsaids"[Title] OR "nsaid s"[Title] OR ("hydroxychloroquine"[MeSH Terms] OR "hydroxychloroquine"[All Fields]) OR "antimalarial*"[All Fields] OR ("quinacrine"[MeSH Terms] OR "quinacrine"[All Fields]) OR ("methotrexate"[MeSH Terms] OR "methotrexate"[All Fields] OR "methotrexate s"[All Fields] OR "methotrexates"[All Fields]) OR ("leflunomid"[All Fields] OR "leflunomide"[MeSH Terms] OR "leflunomide"[All Fields] OR "leflunomide s"[All Fields]) OR ("calcineurin"[MeSH Terms] OR "calcineurin"[All Fields] OR "calcineurin s"[All Fields] OR "calcineurine"[All Fields] OR "calcineurins"[All Fields]) OR ("cyclosporine"[MeSH Terms] OR "cyclosporine"[All Fields] OR "ciclosporin"[All Fields] OR "ciclosporine"[All Fields] OR "cyclosporin"[All Fields] OR "cyclosporine s"[All Fields] OR "cyclosporins"[MeSH Terms] OR "cyclosporins"[All Fields] OR "cyclosporines"[All Fields]) OR ("tacrolimus"[MeSH Terms] OR "tacrolimus"[All Fields]) OR ("voclosporin"[Supplementary Concept] OR "voclosporin"[All Fields]) OR ("azathioprin"[All Fields] OR "azathioprine"[MeSH Terms] OR "azathioprine"[All Fields]) OR ("mycophenolate"[All Fields] OR "mycophenolates"[All Fields] OR "mycophenolic"[All Fields]) OR ("mycophenolate"[All Fields] OR "mycophenolates"[All Fields] OR "mycophenolic"[All Fields]) OR ("cyclophosphamide"[MeSH Terms] OR "cyclophosphamide"[All Fields] OR "cyclophosphamid"[All Fields] OR "cyclophosphamide s"[All Fields] OR "cyclophosphamides"[All Fields]) OR ("rituximab"[MeSH Terms] OR "rituximab"[All Fields] OR "rituximab s"[All Fields]) OR ("belimumab"[Supplementary Concept] OR "belimumab"[All Fields]) OR ("abatacept"[MeSH Terms] OR "abatacept"[All Fields]) OR "biologic*"[All Fields] OR "intravenous immunoglobulin"[All Fields] OR "plasma exchange"[All Fields] OR ("plasmapheresis"[MeSH Terms] OR "plasmapheresis"[All Fields] OR "plasmaphereses"[All Fields]) OR ("immunoadsorption"[All Fields] OR "immunoadsorptions"[All Fields]) OR ("anifrolumab"[Supplementary Concept] OR "anifrolumab"[All Fields]) OR ("obinutuzumab"[Supplementary Concept] OR "obinutuzumab"[All Fields]) OR ("ofatumumab"[Supplementary Concept] OR "ofatumumab"[All Fields]) OR ("ocrelizumab"[Supplementary Concept] OR "ocrelizumab"[All Fields]) OR ("taci receptor igg fc fragment fusion protein"[Supplementary Concept] OR "taci receptor igg fc fragment fusion protein"[All Fields] OR "atacicept"[All Fields]) OR ("etanercept"[MeSH Terms] OR "etanercept"[All Fields]) OR ("adalimumab"[MeSH Terms] OR "adalimumab"[All Fields]) OR ("tocilizumab"[Supplementary Concept] OR "tocilizumab"[All Fields]) OR ("secukinumab"[Supplementary Concept] OR "secukinumab"[All Fields]) OR ("ustekinumab"[MeSH Terms] OR "ustekinumab"[All Fields]) OR ("interleukin 1 receptor antagonist protein"[MeSH Terms] OR "interleukin 1 receptor antagonist protein"[All Fields] OR "anakinra"[All Fields]) OR

("tofacitinib"[Supplementary Concept] OR "tofacitinib"[All Fields] OR "tofacitinib s"[All Fields]) OR ("baricitinib"[Supplementary Concept] OR "baricitinib"[All Fields]) OR ("upadacitinib"[Supplementary Concept] OR "upadacitinib"[All Fields]) OR ("deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[All Fields]) OR ("proteasome inhibitors"[MeSH Terms] OR "proteasome inhibitors"[All Fields]) OR ("bortezomib"[MeSH Terms] OR "bortezomib"[All Fields]) OR ("iberdomide"[Supplementary Concept] OR "iberdomide"[All Fields]) OR "Litifilimab"[All Fields] OR ("interleukin 2"[MeSH Terms] OR "interleukin 2"[All Fields] OR "IL-2"[All Fields]) OR ("daratumumab"[Supplementary Concept] OR "daratumumab"[All Fields]) OR "CAR-T cells"[All Fields] OR ("receptors"[All Fields] AND "thrombopoietin"[All Fields]) OR ("receptors, thrombopoietin"[MeSH Terms] OR "thrombopoietin receptors"[All Fields]) OR ("romiplostim"[Supplementary Concept] OR "romiplostim"[All Fields]) OR ("eltrombopag"[Supplementary Concept] OR "eltrombopag"[All Fields]) OR ("sodium glucose transporter 2 inhibitors"[MeSH Terms] OR "sodium glucose transporter 2 inhibitors"[All Fields] OR ("sglt2"[All Fields] AND "inhibitor"[All Fields])) OR ("dapagliflozin"[Supplementary Concept] OR "dapagliflozin"[All Fields] OR "dapagliflozin s"[All Fields]) OR (("renin"[MeSH Terms] OR "renin"[All Fields]) AND ("angiotensin s"[All Fields] OR "angiotensin"[All Fields] OR "angiotensins"[MeSH Terms] OR "angiotensins"[All Fields] OR "angiotensin"[All Fields]) AND "inhibitors"[All Fields]))

Hits: 3,755

CENTRAL search string for PICO 1**:**

https://www.cochranelibrary.com/advanced-search/search-manager?search=7138193

ID	Search
#1	MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
#2	("systemic lupus erythematosus"):ti,ab,kw (Word variations have been searched)
#3	(lupus):ti,ab,kw (Word variations have been searched)
#4	("glucocorticoid") (Word variations have been searched)
#5	MeSH descriptor: [Glucocorticoids] explode all trees
#6	MeSH descriptor: [Steroids] explode all trees
#7	(steroid) (Word variations have been searched)
#8	(corticosteroid) (Word variations have been searched)
#9	MeSH descriptor: [Anti-Inflammatory Agents, Non-Steroidal] explode all trees
#10	("non-steroidal anti-inflammatory agents"):ti (Word variations have been searched)
#11	(nsaids):ti (Word variations have been searched)
#12	MeSH descriptor: [Hydroxychloroquine] explode all trees
#13	("hydroxychloroquine") (Word variations have been searched)
#14	("antimalarial") (Word variations have been searched)
#15	MeSH descriptor: [Quinacrine] explode all trees
#16	("quinacrine") (Word variations have been searched)

#17 MeSH descriptor: [Methotrexate] explode all trees
#18 ("methotrexate") (Word variations have been searched)
#19 MeSH descriptor: [Leflunomide] explode all trees
#20 ("leflunomide") (Word variations have been searched)
#21 MeSH descriptor: [Calcineurin] explode all trees
#22 ("calcineurin") (Word variations have been searched)
#23 MeSH descriptor: [Cyclosporine] explode all trees
#24 ("ciclosporin") (Word variations have been searched)
#25 MeSH descriptor: [Tacrolimus] explode all trees
#26 ("tacrolimus") (Word variations have been searched)
#27 (voclosporin) (Word variations have been searched)
#28 MeSH descriptor: [Azathioprine] explode all trees
#29 ("azathioprin") (Word variations have been searched)
#30 ("azathioprine") (Word variations have been searched)
#31 MeSH descriptor: [Mycophenolic Acid] explode all trees
#32 ("mycophenolate") (Word variations have been searched)
#33 ("mycophenolic") (Word variations have been searched)
#34 MeSH descriptor: [Cyclophosphamide] explode all trees
#35 ("cyclophosphamide") (Word variations have been searched)
#36 MeSH descriptor: [Rituximab] explode all trees
#37 ("rituximab") (Word variations have been searched)
#38 (belimumab) (Word variations have been searched)
#39 MeSH descriptor: [Abatacept] explode all trees
#40 ("abatacept") (Word variations have been searched)
#41 ("biologic") (Word variations have been searched)
#42 ("intravenous immunoglobulin") (Word variations have been searched)
#43 ("plasma exchange") (Word variations have been searched)
#44 MeSH descriptor: [Plasmapheresis] explode all trees
#45 ("plasmapheresis") (Word variations have been searched)
#46 (anifrolumab) (Word variations have been searched)
#47 (obinutuzumab) (Word variations have been searched)
#48 (ofatumumab) (Word variations have been searched)

#49 (ocrelizumab) (Word variations have been searched)
#50 (atacicept) (Word variations have been searched)
#51 MeSH descriptor: [Etanercept] explode all trees
#52 ("etanercept") (Word variations have been searched)
#53 MeSH descriptor: [Adalimumab] explode all trees
#54 ("adalimumab") (Word variations have been searched)
#55 (tocilizumab) (Word variations have been searched)
#56 (secukinumab) (Word variations have been searched)
#57 (ustekinumab) (Word variations have been searched)
#58 MeSH descriptor: [Ustekinumab] explode all trees
#59 MeSH descriptor: [Interleukin 1 Receptor Antagonist Protein] explode all trees
#60 (interleukin 1 receptor antagonist) (Word variations have been searched)
#61 (anakinra) (Word variations have been searched)
#62 (tofacitinib) (Word variations have been searched)
#63 (baricitinib) (Word variations have been searched)
#64 (upadacitinib) (Word variations have been searched)
#65 (deucravacitinib) (Word variations have been searched)
#66 MeSH descriptor: [Proteasome Inhibitors] explode all trees
#67 ("protease inhibitor") (Word variations have been searched)
#68 MeSH descriptor: [Bortezomib] explode all trees
#69 ("bortezomib") (Word variations have been searched)
#70 (iberdomide) (Word variations have been searched)
#71 (litifilimab) (Word variations have been searched)
#72 MeSH descriptor: [Interleukin-2] explode all trees
#73 (interleukin 2) (Word variations have been searched)
#74 ("IL 2") (Word variations have been searched)
#75 (daratumumab) (Word variations have been searched)
#76 (CAR-T cells) (Word variations have been searched)
#77 MeSH descriptor: [Receptors, Thrombopoietin] explode all trees
#78 (romiplostim) (Word variations have been searched)
#79 (eltrombopag) (Word variations have been searched)
#80 MeSH descriptor: [Sodium-Glucose Transporter 2 Inhibitors] explode all trees

#81 (sodium glucose transporter 2 inhibitors) (Word variations have been searched)

#82 (sglt2) (Word variations have been searched)

#83 (dapagliflozin) (Word variations have been searched)

#84 MeSH descriptor: [Renin] explode all trees

#85 (renin) (Word variations have been searched)

#86 MeSH descriptor: [Angiotensins] explode all trees

#87 ("angiotensin") (Word variations have been searched)

#88 (inhibitors) (Word variations have been searched)

#89 #1 OR #2 OR #3

#90 #84 OR #85

#91 #86 OR #87

#92 #90 AND #91 AND #88

#93 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #92

#94 #89 AND #93

Hits: 2347

Medline search string for PICO 2**:**

(("SLE"[Title] OR "lupus"[Title]) AND ("remission"[All Fields] OR "remissions"[All Fields] OR "low disease activity"[All Fields] OR "LLDAS"[All Fields] OR "inactive disease"[All Fields] OR "quiescent disease"[All Fields] OR "disease quiescence"[All Fields] OR "treat to target"[All Fields]))

Hits: 929

CENTRAL search string for PICO 2**:**

https://www.cochranelibrary.com/advanced-search/search-manager?search=7138194

ID Search
#1 MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
#2 ("systemic lupus erythematosus"):ti,ab,kw (Word variations have been searched)
#3 (lupus):ti,ab,kw (Word variations have been searched)
#4 (remission) (Word variations have been searched)
#5 (low disease activity) (Word variations have been searched)

#6 (LLDAS) (Word variations have been searched)
#7 (inactive disease) (Word variations have been searched)
#8 (quiescent disease) (Word variations have been searched)
#9 (disease quiescence) (Word variations have been searched)
#10 (treat to target) (Word variations have been searched)
#11 #1 OR #2 OR #3
#12 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
#13 #11 AND #12

Hits: 911

Medline search string for PICO 3**:**

(("SLE"[Title] OR "lupus"[Title]) AND ("anti b2*"[All Fields] OR "anti beta*"[All Fields] OR "anti beta2*"[All Fields] OR "anti cardiolipin*"[All Fields] OR "anticardiolipin*"[All Fields] OR "lupus anticoagulant"[All Fields] OR "LAC"[All Fields] OR "aPL"[All Fields] OR "antiphospolipid"[All Fields] OR ("syndrom"[All Fields] OR "syndromal"[All Fields] OR "syndromally"[All Fields] OR "syndrome"[MeSH Terms] OR "syndrome"[All Fields] OR "syndromes"[All Fields] OR "syndrome s"[All Fields] OR "syndromic"[All Fields] OR "syndroms"[All Fields]) OR ("arch plast surg"[Journal] OR "adv psychol study"[Journal] OR "acta pharmacol sin"[Journal] OR "aps"[All Fields])) AND ("manage"[All Fields] OR "managed"[All Fields] OR "management s"[All Fields] OR "managements"[All Fields] OR "manager"[All Fields] OR "manager s"[All Fields] OR "managers"[All Fields] OR "manages"[All Fields] OR "managing"[All Fields] OR "managment"[All Fields] OR "organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields] OR ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields]) OR ("therapeutical"[All Fields] OR "therapeutically"[All Fields] OR "therapeuticals"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapeutic"[All Fields]) OR ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "treatments"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "treatment s"[All Fields]) OR "anticoagul*"[All Fields] OR "antiplatelet*"[All Fields] OR "anti platelet*"[All Fields] OR ("aspirin"[MeSH Terms] OR "aspirin"[All Fields] OR "aspirins"[All Fields] OR "aspirin s"[All Fields] OR "aspirine"[All Fields]) OR ("heparin"[MeSH Terms] OR "heparin"[All Fields] OR "heparine"[All Fields] OR "heparins"[All Fields] OR "heparin s"[All Fields] OR "heparinate"[All Fields] OR "heparinated"[All Fields] OR "heparines"[All Fields] OR "heparinic"[All Fields] OR "heparinisation"[All Fields] OR "heparinised"[All Fields] OR "heparinization"[All Fields] OR "heparinize"[All Fields] OR "heparinized"[All Fields] OR "heparinizing"[All Fields]) OR ("warfarin"[MeSH Terms] OR "warfarin"[All Fields] OR "warfarin s"[All Fields] OR "warfarinization"[All Fields] OR "warfarinized"[All Fields] OR "warfarins"[All Fields]) OR ("apixaban"[Supplementary Concept] OR "apixaban"[All Fields] OR "apixaban s"[All Fields]) OR ("rivaroxaban"[MeSH Terms] OR "rivaroxaban"[All Fields]) OR "glucocorticoid*"[All Fields] OR "glucocorticoids"[MeSH Terms] OR "steroid*"[All Fields] OR "steroids"[MeSH Terms] OR "corticosteroid*"[All Fields] OR "anti inflammatory agents, non steroidal"[MeSH Terms] OR "non-steroidal anti-inflammatory agents"[Title] OR "nsaid"[Title] OR "nsaids"[Title] OR "nsaid s"[Title] OR ("hydroxychloroquine"[MeSH Terms] OR "hydroxychloroquine"[All Fields]) OR "antimalarial*"[All Fields] OR ("quinacrine"[MeSH Terms] OR "quinacrine"[All Fields]) OR ("methotrexate"[MeSH Terms] OR "methotrexate"[All Fields] OR "methotrexate s"[All Fields] OR "methotrexates"[All Fields]) OR ("leflunomid"[All Fields] OR "leflunomide"[MeSH Terms] OR "leflunomide"[All Fields] OR "leflunomide s"[All Fields]) OR ("calcineurin"[MeSH Terms] OR "calcineurin"[All Fields] OR "calcineurin s"[All Fields] OR "calcineurine"[All Fields] OR "calcineurins"[All Fields]) OR ("cyclosporine"[MeSH Terms] OR "cyclosporine"[All Fields] OR "ciclosporin"[All Fields] OR "ciclosporine"[All Fields] OR "cyclosporin"[All Fields] OR "cyclosporine s"[All Fields] OR "cyclosporins"[MeSH Terms] OR "cyclosporins"[All Fields] OR "cyclosporines"[All Fields]) OR ("tacrolimus"[MeSH Terms] OR "tacrolimus"[All Fields]) OR ("voclosporin"[Supplementary Concept] OR "voclosporin"[All Fields]) OR ("azathioprin"[All Fields] OR "azathioprine"[MeSH Terms] OR "azathioprine"[All Fields]) OR ("mycophenolate"[All Fields] OR

"mycophenolates"[All Fields] OR "mycophenolic"[All Fields]) OR ("mycophenolate"[All Fields] OR "mycophenolates"[All Fields] OR "mycophenolic"[All Fields]) OR ("cyclophosphamide"[MeSH Terms] OR "cyclophosphamide"[All Fields] OR "cyclophosphamid"[All Fields] OR "cyclophosphamide s"[All Fields] OR "cyclophosphamides"[All Fields]) OR ("rituximab"[MeSH Terms] OR "rituximab"[All Fields] OR "rituximab s"[All Fields]) OR ("belimumab"[Supplementary Concept] OR "belimumab"[All Fields]) OR ("abatacept"[MeSH Terms] OR "abatacept"[All Fields]) OR "biologic*"[All Fields] OR "intravenous immunoglobulin"[All Fields] OR "plasma exchange"[All Fields] OR ("plasmapheresis"[MeSH Terms] OR "plasmapheresis"[All Fields] OR "plasmaphereses"[All Fields]) OR ("immunoadsorption"[All Fields] OR "immunoadsorptions"[All Fields]) OR ("anifrolumab"[Supplementary Concept] OR "anifrolumab"[All Fields]) OR ("obinutuzumab"[Supplementary Concept] OR "obinutuzumab"[All Fields]) OR ("ofatumumab"[Supplementary Concept] OR "ofatumumab"[All Fields]) OR ("ocrelizumab"[Supplementary Concept] OR "ocrelizumab"[All Fields]) OR ("taci receptor igg fc fragment fusion protein"[Supplementary Concept] OR "taci receptor igg fc fragment fusion protein"[All Fields] OR "atacicept"[All Fields]) OR "complement inactivating agents"[MeSH Terms] OR (("complement"[All Fields] AND "inactivating"[All Fields] AND "agents"[All Fields]) OR "complement inactivating agents"[All Fields] OR ("complement"[All Fields] AND "inhibitor"[All Fields]) OR "complement inhibitor"[All Fields]) OR ("thrombo*"[All Fields] OR "pregnan*"[All Fields] OR ("blood vessels"[MeSH Terms] OR ("blood"[All Fields] AND "vessels"[All Fields]) OR "blood vessels"[All Fields] OR "vascular"[All Fields] OR "neovascularization, pathologic"[MeSH Terms] OR ("neovascularization"[All Fields] AND "pathologic"[All Fields]) OR "pathologic neovascularization"[All Fields] OR "vascularisation"[All Fields] OR "vascularization"[All Fields] OR "vascularisations"[All Fields] OR "vascularise"[All Fields] OR "vascularised"[All Fields] OR "vascularities"[All Fields] OR "vascularitis"[All Fields] OR "vascularity"[All Fields] OR "vascularizations"[All Fields] OR "vascularize"[All Fields] OR "vascularized"[All Fields] OR "vascularizes"[All Fields] OR "vascularizing"[All Fields] OR "vasculars"[All Fields]) OR "obstetric*"[All Fields])))

Hits: 1359

CENTRAL search string for PICO 3**:**

https://www.cochranelibrary.com/advanced-search/search-manager?search=7138190

ID	Search
#1	MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
#2	("systemic lupus erythematosus"):ti,ab,kw (Word variations have been searched)
#3	(lupus):ti,ab,kw (Word variations have been searched)
#4	(anti b2) (Word variations have been searched)
#5	(anti beta) (Word variations have been searched)
#6	("anti-cardiolipin") (Word variations have been searched)
#7	(anti cardiolipin) (Word variations have been searched)
#8	("lupus anticoagulant") (Word variations have been searched)
#9	(LAC) (Word variations have been searched)
#10	(aPL) (Word variations have been searched)
#11	(antiphospholipid) (Word variations have been searched)
#12	(management) (Word variations have been searched)

#13 (therapeutics) (Word variations have been searched)
#14 MeSH descriptor: [Therapeutics] explode all trees
#15 MeSH descriptor: [Disease Management] explode all trees
#16 (treatment) (Word variations have been searched)
#17 ("anticoagulant") (Word variations have been searched)
#18 ("antiplatelet") (Word variations have been searched)
#19 ("aspirin") (Word variations have been searched)
#20 MeSH descriptor: [Aspirin] explode all trees
#21 ("heparin") (Word variations have been searched)
#22 MeSH descriptor: [Heparin] explode all trees
#23 MeSH descriptor: [Warfarin] explode all trees
#24 ("Warfarin") (Word variations have been searched)
#25 ("warfarin") (Word variations have been searched)
#26 (apixaban) (Word variations have been searched)
#27 MeSH descriptor: [Rivaroxaban] explode all trees
#28 ("rivaroxaban") (Word variations have been searched)
#29 ("glucocorticoid") (Word variations have been searched)
#30 MeSH descriptor: [Glucocorticoids] explode all trees
#31 MeSH descriptor: [Steroids] explode all trees
#32 (steroid) (Word variations have been searched)
#33 (corticosteroid) (Word variations have been searched)
#34 MeSH descriptor: [Anti-Inflammatory Agents, Non-Steroidal] explode all trees
#35 ("non-steroidal anti-inflammatory agents"):ti (Word variations have been searched)
#36 (nsaids):ti (Word variations have been searched)
#37 MeSH descriptor: [Hydroxychloroquine] explode all trees
#38 ("hydroxychloroquine") (Word variations have been searched)
#39 ("antimalarial") (Word variations have been searched)
#40 MeSH descriptor: [Quinacrine] explode all trees
#41 ("quinacrine") (Word variations have been searched)
#42 MeSH descriptor: [Methotrexate] explode all trees
#43 ("methotrexate") (Word variations have been searched)
#44 MeSH descriptor: [Leflunomide] explode all trees

#45 ("leflunomide") (Word variations have been searched)
#46 MeSH descriptor: [Calcineurin] explode all trees
#47 ("calcineurin") (Word variations have been searched)
#48 MeSH descriptor: [Cyclosporine] explode all trees
#49 ("ciclosporin") (Word variations have been searched)
#50 MeSH descriptor: [Tacrolimus] explode all trees
#51 ("tacrolimus") (Word variations have been searched)
#52 (voclosporin) (Word variations have been searched)
#53 MeSH descriptor: [Azathioprine] explode all trees
#54 ("azathioprin") (Word variations have been searched)
#55 ("azathioprine") (Word variations have been searched)
#56 MeSH descriptor: [Mycophenolic Acid] explode all trees
#57 ("mycophenolate") (Word variations have been searched)
#58 ("mycophenolic") (Word variations have been searched)
#59 MeSH descriptor: [Cyclophosphamide] explode all trees
#60 ("cyclophosphamide") (Word variations have been searched)
#61 MeSH descriptor: [Rituximab] explode all trees
#62 ("rituximab") (Word variations have been searched)
#63 (belimumab) (Word variations have been searched)
#64 MeSH descriptor: [Abatacept] explode all trees
#65 ("abatacept") (Word variations have been searched)
#66 ("biologic") (Word variations have been searched)
#67 ("intravenous immunoglobulin") (Word variations have been searched)
#68 ("plasma exchange") (Word variations have been searched)
#69 MeSH descriptor: [Plasmapheresis] explode all trees
#70 ("plasmapheresis") (Word variations have been searched)
#71 (anifrolumab) (Word variations have been searched)
#72 (obinutuzumab) (Word variations have been searched)
#73 (ofatumumab) (Word variations have been searched)
#74 (ocrelizumab) (Word variations have been searched)
#75 (atacicept) (Word variations have been searched)
#76 MeSH descriptor: [Complement Inactivating Agents] explode all trees

#77 (complement inactivating factors) (Word variations have been searched)

#78 (complement inhibitor) (Word variations have been searched)

#79 ("thrombose") (Word variations have been searched)

#80 ("thrombosis") (Word variations have been searched)

#81 ("pregnancy") (Word variations have been searched)

#82 MeSH descriptor: [Blood Vessels] explode all trees

#83 (vascular) (Word variations have been searched)

#84 (obstetric) (Word variations have been searched)

#85 #1 OR #2 OR #3

#86 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

#87 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84

#88 #85 AND #86 AND #87

Hits: 249

Medline search for PICO 4:

(("SLE"[Title] OR "lupus"[Title]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "treatments"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "treatment s"[All Fields] OR ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapies"[All Fields]) OR ("manage"[All Fields] OR "managed"[All Fields] OR "management s"[All Fields] OR "managements"[All Fields] OR "manager"[All Fields] OR "manager s"[All Fields] OR "managers"[All Fields] OR "manages"[All Fields] OR "managing"[All Fields] OR "management"[All Fields] OR "organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields])) AND ("stop*"[All Fields] OR "withdraw*"[All Fields] OR "discontin*"[All Fields] OR "taper*"[All Fields] OR ("duration"[All Fields] OR "durations"[All Fields])))

Hits: 829

CENTRAL search string for PICO 4**:**

https://www.cochranelibrary.com/advanced-search/search-manager?search=7138188

ID Search

#1	MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
#2	("systemic lupus erythematosus"):ti,ab,kw (Word variations have been searched)
#3	(lupus):ti,ab,kw (Word variations have been searched)
#4	MeSH descriptor: [Therapeutics] explode all trees
#5	(therapeutics) (Word variations have been searched)
#6	(stop) (Word variations have been searched)
#7	("withdrawal") (Word variations have been searched)
#8	("discontinuation") (Word variations have been searched)
#9	(taper) (Word variations have been searched)
#10	("duration") (Word variations have been searched)
#11	#1 OR #2 OR #3
#12	#4 OR #5
#13	#6 OR #7 OR #8 OR #9 OR #10
#14	#11 AND #12 AND #13

Hits: 375

Medline search string for PICO 5**:**

(("SLE"[Title] OR "lupus"[Title]) AND ((("vaccination"[MeSH Terms] OR "vaccination"[All Fields] OR "vaccinable"[All Fields] OR "vaccinal"[All Fields] OR "vaccinate"[All Fields] OR "vaccinated"[All Fields] OR "vaccinates"[All Fields] OR "vaccinating"[All Fields] OR "vaccinations"[All Fields] OR "vaccination s"[All Fields] OR "vaccines"[MeSH Terms] OR "vaccines"[All Fields] OR "vaccine"[All Fields] OR "vaccins"[All Fields]) AND ("herpes zoster"[MeSH Terms] OR ("herpes"[All Fields] AND "zoster"[All Fields]) OR "herpes zoster"[All Fields])) OR ("sars cov 2"[MeSH Terms] OR "sars cov 2"[All Fields] OR "covid"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19"[All Fields])))

Hits: 333

CENTRAL search string for PICO 5**:**

https://www.cochranelibrary.com/advanced-search/search-manager?search=7138094

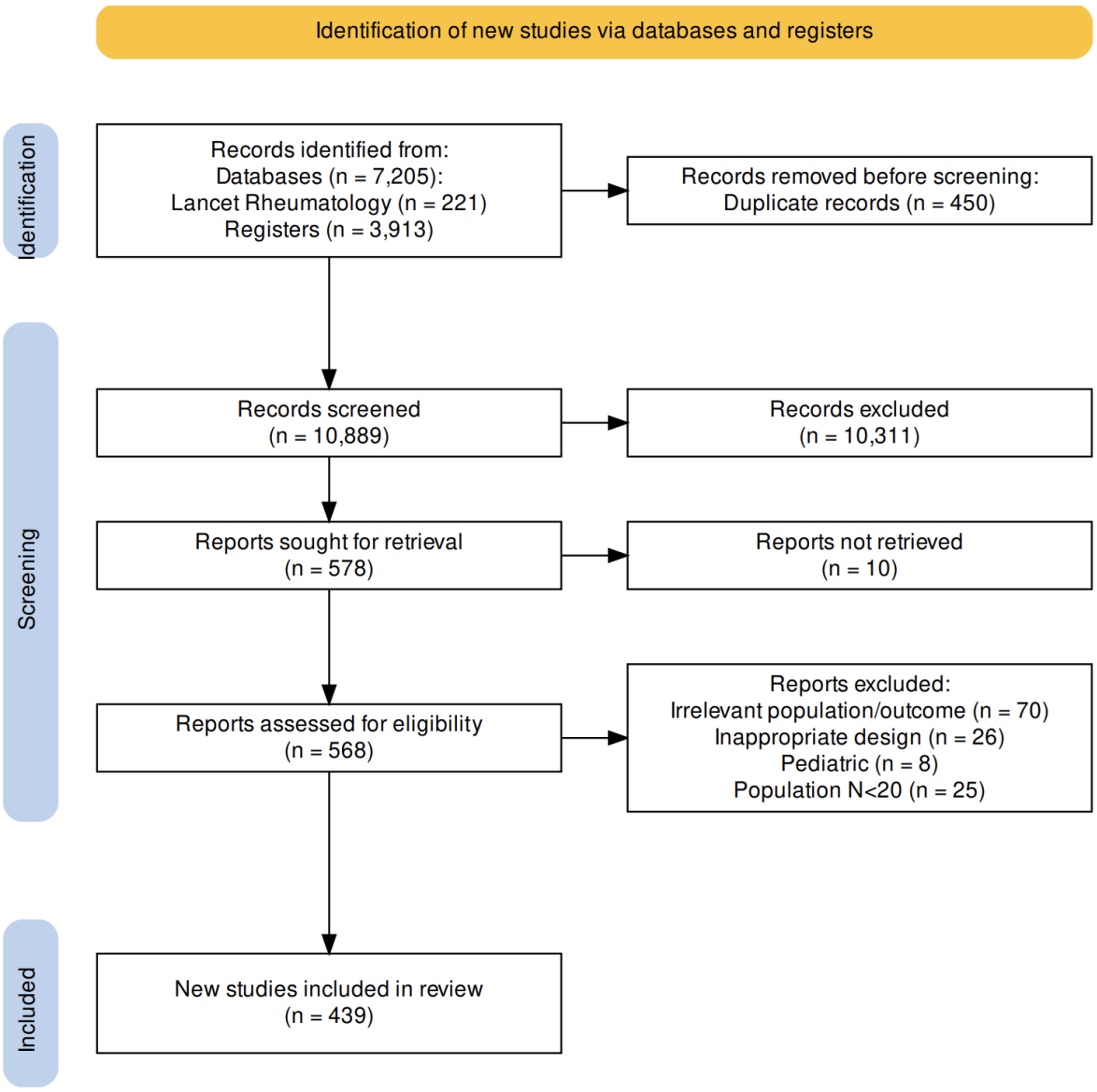
ID	Search
#1	MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
#2	("systemic lupus erythematosus"):ti,ab,kw (Word variations have been searched)
#3	(lupus):ti,ab,kw (Word variations have been searched)

#4 MeSH descriptor: [Vaccines] explode all trees
#5 (vaccine) (Word variations have been searched)
#6 (vaccination) (Word variations have been searched)
#7 MeSH descriptor: [Herpes Zoster] explode all trees
#8 ("herpes zoster virus") (Word variations have been searched)
#9 ("herpes virus") (Word variations have been searched)
#10 (zoster) (Word variations have been searched)
#11 MeSH descriptor: [COVID-19] explode all trees
#12 MeSH descriptor: [COVID-19 Vaccines] explode all trees
#13 ("SARS CoV") (Word variations have been searched)
#14 (covid 19) (Word variations have been searched)
#15 (covid) (Word variations have been searched)
#16 #1 OR #2 OR #3
#17 #4 OR #5 OR #6
#18 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
#19 #17 AND #18
#20 #16 AND #19

Hits: 31

Flowchart

Prisma flowchart with the use of the package DiagrammeR R [1]



Summary fact sheets for all included studies

All relevant data are presented in a separate Excel file.

Risk of bias assessment

A risk of bias assessment was performed for all eligible studies using the appropriate tools based on their design. The Newcastle-Ottawa scale (NOS) was used to assess cohort and case-control studies, RoB2 was used for RCTs and quasi RCTs and AMSTAR2 was used to assess meta-analyses.

Risk of bias assessment of cohort studies and case-control studies using NOS

The NOS scale is a risk of bias tool for the assessment of cohorts and case control studies based on their performance in three grouping items namely the selection of population, the comparability and the outcomes/exposures of the respective study [2]. Each cohort or case-control study is graded with a maximum of one star for each numbered item within the Selection and Outcome categories while Comparability can be graded with a maximum of two stars. For cohort studies, the number of stars and their distribution determines whether the study is of good, fair, or poor quality according to AHRQ (Agency for Healthcare Research and Quality) standards:
Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Newcastle Ottawa scale	Risk domain								
	Selection				Comparability	Outcomes			
Cohort study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality of study
Rathoon, Indian J Nephrol, 2022	0	0	0	1	0	0	1	0	Poor
Nikoloudaki, Front Immunol, 2023	1	0	1	1	0	1	0	1	Poor
Zhang, Front Immunol 2022	1	1	1	0	1	1	0	1	Good
Floris RMD Open, 2022	0	1	1	1	1	1	1	1	Good
Aloub, Open Access Rheumatol, 2022	0	0	1	0	0	0	0	0	Poor
Hurst, AM J Med, 2022	1	1	1	1	0	1	1	1	Poor
Hunnicutt, Lupus Sci Med, 2022	0	0	1	1	0	1	1	0	Poor
Carter, Arthritis Rheumatol, 2022	1	0	1	1	0	1	0	0	Poor
Kagawa, Acta Med Okayama, 2022	0	0	1	0	0	1	1	1	Poor
Enfrein, RMD Open, 2022	0	0	1	1	0	1	1	0	Poor
Kao, J Ocul Phrmacol Ther, 2022	0	0	0	0	0	1	1	1	Poor
Ko, Semin Arthritis Rheum, 2022	1	1	0	1	2	1	1	1	Good
Dobrowolski, Rheumatology, 2022	1	1	1	1	1	1	0	1	Good
Connelly, Arthritis Rheumatol, 2022	0	0	1	1	2	1	1	1	Good

Systematic Literature Review - Report

Newcastle Ottawa scale	Risk domain								
	Selection				Comparability	Outcomes			
Cohort study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality of study
Mok, Vaccine, 2022	1	1	0	0	1	1	0	1	Fair
Hoque, Arthritis Rheumatol, 2022	1	1	0	1	2	1	1	1	Good
Wang, Lupus Sci Med, 2022	1	1	0	1	1	0	0	1	Poor
Chen, J Int Med Res, 2022	0	1	0	1	1	0	0	0	Poor
Ugarte-Gil, Ann Rheum Dis, 2022	1	1	1	1	1	1	1	1	Good
Nakai, Clin Rheumatol, 2022	0	0	1	1	0	1	1	0	Poor
Li, Pak J Med Sci, 2022	0	0	0	1	0	0	1	0	Poor
Nakai, Lupus Sci Med, 2022	0	0	1	1	1	1	0	0	Poor
Kapsia, Front Med, 2022	0	0	1	0	0	1	1	0	Poor
Khattab, Lupus, 2022	1	1	1	1	1	1	0	1	Good
Hussenbocus, Clin Rheumatol, 2022	1	1	0	1	0	1	0	1	Poor
Miyazaki, Rheumatology, 2022	1	1	1	1	2	1	1	1	Good
Almeida-Brasil, Ann Rheum Dis, 2022	1	1	0	1	2	1	0	1	Good
Ohkubo, Mod Rheumatol, 2022	0	0	1	1	1	1	1	0	Fair
Ayano, Mod Rheumatol, 2022	0	0	1	0	1	1	0	0	Poor
Yuki, Arthritis Care Res, 2022	1	0	1	0	2	1	1	0	Fair
Keyes, J Am Acad Dermatol, 2022	0	0	0	1	1	0	1	0	Poor
Simard, Lupus Sci Med, 2022	1	1	1	1	2	1	1	1	Good
Liao, J Clin Rheumatol, 2022	0	0	1	1	1	1	0	0	Poor
Izmirly, Arthritis Rheumatol, 2022	1	0	1	1	0	1	1	1	Poor
Sonigo, J Am Acad dermatol, 2021	0	0	1	0	0	1	1	0	Poor
Ruiz-Irastorza, Autoimmun Rev, 2021	0	0	1	1	1	1	0	1	Fair
Chen, Lupus, 2021	1	1	0	1	0	1	1	1	Poor
Tselios, ACR Open Rheumatol, 2021	1	1	1	1	1	1	1	1	Good
Olivieri, Joint Bone Spine, 2021	1	0	1	1	0	1	0	0	Poor
Piranavan, Clin Immunol, 2021	0	0	0	1	0	0	0	1	Poor
Abdelbaky, Egypt J Intern Med, 2021	1	0	1	0	0	1	0	0	Poor
Yoshida, Lupus, 2021	0	0	0	1	0	1	1	0	Poor
Fasano, Clin Exp Rheumatol, 2021	0	1	1	1	2	1	1	1	Good
Ugarte, Rheumatology, 2021	1	1	1	1	2	1	1	1	Good
Hill, Lupus Sci Med, 2021	1	0	0	1	2	2	1	1	Fair
Chen, Ther Adv Musculoskelet Dis, 2021	1	1	1	1	2	1	0	1	Good
Lobbes, Rheumatology, 2022	0	0	0	1	0	1	1	0	Poor
Zen, Rheumatology, 2022	1	0	1	1	2	1	1	0	Good

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Newcastle Ottawa scale	Risk domain								
	Selection				Comparability	Outcomes			
Cohort study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality of study
Roccatello, Kidney Int Rep, 2021	0	1	1	1	1	1	0	1	Good
Tselios, Arthritis Care Res, 2022	1	1	1	1	1	1	1	1	Good
Wang, Arthritis Care Res, 2021	1	1	1	1	2	1	0	1	Good
Abe, Biomed Res Int, 2021	1	0	0	1	0	1	0	0	Poor
Hoque, Arthritis Care Res, 2021	1	1	0	1	2	1	0	1	Good
Petri, Arthritis Rheumatol, 2021	1	0	1	1	2	1	0	1	Good
Choi, Rheumatology, 2021	0	1	0	1	2	1	0	1	Fair
Zickert, Rheumatology, 2021	0	0	1	1	0	1	0	1	Poor
Birt, Lupus Sci Med, 2020	1	0	1	0	0	0	1	1	Poor
Almeida-Brasil, Arthritis Care Res, 2022	1	1	0	1	2	0	1	1	Good
Haugaard, J Am Acad Dermatol, 2021	1	1	0	1	1	1	1	1	Good
Reátegui-Sokolova, RMD Open, 2021	0	0	0	1	2	1	0	5	Poor
Ceccarelli, Isr Med Assoc J, 2020	0	0	1	1	0	1	1	0	Poor
Collins, Rheumatol Ther, 2020	1	0	1	0	0	0	0	1	Poor
Sogayise, Int J Nephrol, 2020	1	1	1	1	0	1	1	0	Poor
Jin, Rheumatology, 2021	1	1	0	1	2	1	0	1	Good
Gupta, Arthritis Care Res, 2021	1	1	1	1	2	1	0	1	Good
Urowitz, Lupus Sci Med, 2020	1	1	1	1	2	1	1	1	Good
Sakai, Lupus, 2020	1	1	0	1	2	1	0	0	Fair
Nikfar, Int J Clin Pract, 2021	1	1	1	1	2	1	1	0	Good
Jakez-Ocampo, Clin Rheumatol, 2020	1	1	0	1	1	1	1	0	Good
Kang, Rheumatology, 2021	1	1	1	0	2	1	1	1	Good
Kandane-Rathnayake, Lancet Rheumatol, 2022	1	1	1	1	2	1	0	1	Good
Golder, Lancet Rheumatol, 2019	1	1	1	1	2	1	0	1	Good
28528869 Silva-Fernández et al	1	1	1	1	1	1	1	0	Good
28566017 Li et al	0	0	1	1	0	1	0	1	Poor
28704598 Ruiz-Arruza et al	0	0	1	0	0	0	1	0	Poor
28753077 Sheikholeslami et al	1	0	1	1	0	1	0	0	Poor
28856466 Sun et al	0	0	1	1	0	1	0	0	Poor
28862513 Emamikia et al	1	1	1	1	0	1	1	1	Good
28901731 Kasitanon et al	0	0	1	1	1	1	0	0	Fair
28935492 Iaccarino et al	1	0	1	1	1	1	1	0	Good
28970217 Zen et al	1	1	1	1	1	1	1	0	Good
29061479 Chasset et al	0	0	1	1	0	0	1	0	Poor
29087260 Mok et al	1	1	1	1	1	1	1	1	Good

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Newcastle Ottawa scale	Risk domain								
	Selection				Comparability	Outcomes			
Cohort study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality of study
29142034 Chen et al	1	0	1	1	1	1	0	0	Poor
29142038 Pakchotanon et al	1	0	0	1	2	1	1	0	Fair
29157178 Lee et al	1	0	1	1	2	1	0	0	Poor
29186572 Cunha et al	1	0	1	1	0	1	1	0	Poor
29216396 McCarthy et al	1	0	1	1	0	1	0	0	Poor
29222972 Deguchi et al	1	0	1	1	2	1	1	0	Good
29247540 Serris et al	1	0	1	1	0	1	1	0	Poor
29320974 Ganapati et al	1	1	1	1	0	1	0	0	Poor
29308726 Iwata et al	1	0	1	1	0	1	1	1	Poor
29409143 Furie et al	1	0	1	1	0	1	1	1	Poor
29420200 Morand et al	1	1	1	1	2	1	1	0	Good
29448881 Choi et al	0	0	1	1	0	1	1	0	Poor
29449503 Yue et al	0	0	1	1	2	1	1	0	Fair
29531772 Tani et al	1	0	1	1	2	1	1	0	Good
29515299 Sahay et al	1	1	1	1	0	1	0	0	Poor
29509932 Yap et al	1	1	1	1	0	1	1	0	Poor
29496892 Davidson et al	1	1	1	1	2	1	0	0	Poor
29460699 Furie et al	1	1	1	1	1	1	0	1	Fair
29561474 Goswami et al	1	0	1	1	2	1	0	0	Poor
29555348 Fanouriakis et al	1	0	1	1	0	1	1	1	Poor
29611341 Joo et al	1	1	1	1	0	1	1	0	Poor
29631512 Liu et al	1	0	1	1	2	1	1	0	Good
29635998 Ugarte et al	1	0	1	1	0	1	1	0	Poor
29657872 Soyuöz et al	0	0	1	1	0	1	0	0	Poor
29720229 Hanaoka et al	0	0	1	1	0	1	0	0	Poor
29792370 Tanaka et al	1	0	1	1	0	1	1	0	Poor
29806142 Petri et al	1	1	1	1	2	1	1	0	Good
29807477 Doria et al	1	0	1	1	0	1	0	1	Poor
29854814 Su et al	0	0	1	1	0	1	0	0	Poor
29855561 Burt et al	0	0	1	1	0	1	1	1	Poor
29931367 Hsu et al	1	1	1	1	1	1	1	0	Fair
29950160 Kwon et al	1	1	1	0	2	0	1	0	Poor
29954281 Spinelli et al	0	0	1	1	1	1	1	1	Fair
29987550 Monzavi et al	0	0	1	1	0	1	0	0	Poor
29998829 Park et al	1	0	1	1	0	1	0	0	Poor
30008461 Garnier et al	0	0	1	1	0	1	0	0	Poor
30055090 Tselios et al	1	1	1	1	0	1	1	0	Poor
30194649 Fasano et al	1	1	1	1	2	1	1	0	Good

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Newcastle Ottawa scale	Risk domain								
	Selection				Comparability	Outcomes			
Cohort study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality of study
30203113 Karasawa et al	0	0	1	1	0	1	1	0	Poor
30284580 Alsuwaida et al	0	0	1	1	0	1	0	0	Poor
30338639 Miyagawa et al	0	0	1	1	0	1	0	0	Poor
30451641 Gonzalez-Echavarri et al	0	0	1	1	2	1	0	0	Poor
30487482 Hossain et al	0	0	1	1	0	1	0	0	Poor
30538815 Tani et al	0	0	0	1	0	1	0	0	Poor
30523554 Goswami et al	1	0	1	1	2	1	1	0	Good
30552172 Sciascia et al	1	0	1	1	2	1	0	0	Poor
30557058 Okabayashi et al	1	0	1	1	2	1	0	0	Poor
30588322 Merrill et al	1	1	1	1	1	1	1	0	Good
30588323 van Vollenhoven et al	1	1	1	1	0	1	0	0	Poor
30626831 Hanaoka et al	0	0	1	1	0	1	0	0	Poor
30678605 Alarcon et al	1	1	1	1	0	1	0	0	Poor
30700214 Ichinose et al	1	1	1	1	0	1	0	0	Poor
30719729 Ototake et al	0	0	1	1	0	1	1	0	Poor
30755141 Martin-Iglesias et al	1	0	1	1	0	1	1	0	Poor
30771238 Wallace et al	1	0	1	1	0	1	1	1	Poor
30778862 Kawazoe et al	0	0	1	1	0	1	0	0	Poor
30852830 von Kempis et al	1	0	1	1	0	1	0	0	Poor
30937637 Sumethkul et al	0	0	1	1	0	1	0	0	Poor
30941559 Rebelo et al	1	0	1	1	0	1	1	0	Poor
30979713 Huang et al	1	0	1	1	0	1	1	0	Poor
31031386 Sharma et al	0	0	1	1	0	1	0	0	Poor
31074727 Tseng et al	1	0	1	1	0	1	1	0	Poor
31102498 Cassia et al	1	0	1	1	0	1	1	0	Poor
31122136 Geraldino-Pardilla et al	1	0	1	1	2	1	0	0	Poor
31175481 Hanaoka et al	1	0	1	1	0	1	1	0	Poor
31195632 Yang et al	1	0	1	1	2	1	1	0	Good
31199180 Tanaka et al	0	0	1	1	0	1	1	1	Poor
31264525 Anjo et al	0	0	1	1	0	1	1	0	Poor
31275608 Tani et al	0	`	1	1	2	1	1	0	Poor
31293110 Jung et al	1	0	1	1	0	1	0	0	Poor
31302695 van Vollenhoven et al	1	0	1	1	0	1	1	1	Poor
31464233 Al Hamzi et al	1	0	1	1	0	1	1	0	Good
31551028 Reategui-Sokolova et al	1	1	1	1	2	1	1	0	Good
31583978 Won et al	0	0	1	1	2	1	1	0	Poor
31600023 Floris et al	0	0	1	1	2	1	1	0	Poor

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Newcastle Ottawa scale	Risk domain								
	Selection				Comparability	Outcomes			
Cohort study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality of study
31653191 Nieto-Aristizabal et al	0	0	1	1	0	1	0	0	Poor
31769212 van Vollenhoven et al	1	1	1	1	0	1	0	1	Poor
31777844 Aouhab et al	0	0	1	1	0	1	0	0	Poor
31793379 Lee et al	1	0	1	1	2	1	1	0	Good
32020727 Miyagawa et al	1	1	1	1	0	1	0	0	Poor
32192398 Pedrosa et al	0	0	1	1	0	1	0	0	Poor
32238515 Takeuchi et al	1	0	1	1	0	1	1	0	Poor
32275125 Gatto et al	1	0	1	1	2	1	1	0	good
32321345 Sun et al	1	0	1	1	2	1	1	0	Good
32321721 Saccon et al	1	0	1	1	0	1	1	0	Poor
32434863 Vázquez-Otero et al	1	0	1	1	0	1	0	0	Poor
32437258 Prasad et al	1	1	1	1	0	1	1	0	Poor
32448782 Mok et al	1	1	1	1	2	1	1	1	Good
32452167 Padiyar et al	0	0	1	1	0	1	0	0	Poor
32462476 Argolini et al	0	0	1	1	2	1	1	1	Fair
32493152 Saleh et al	1	1	1	1	2	1	0	0	Poor
32522920 Wakiya et al	0	0	1	1	0	1	0	0	Poor
32791930 Babini et al	1	0	1	1	0	1	1	0	Poor
32813314 Bernatsky et al	1	1	1	1	2	1	1	0	Good
28857717 Pakchotanon et al	1	1	1	1	2	1	1	0	Good
28888363 Medina-Rosas et al	1	1	1	1	2	1	1	0	Good
29423203 Lay The et al	0	0	1	1	2	1	1	0	Fair
29478901 Wang et al	1	0	1	1	0	1	1	1	Poor
30045812 De Rosa et al	1	0	1	1	2	1	1	1	Good
30406967 Hanaoka et al	0	0	1	1	0	1	0	0	Poor
30755146 Ichinose et al	0	0	1	1	2	1	0	0	Poor
30821926 Sharma et al	0	0	1	1	1	1	1	0	Fair
31642908 Zen et al	0	0	1	1	2	1	1	0	Fair
31685314 Malvar et al	1	0	1	1	0	1	1	1	Poor
28659045 Watanabe et al	1	1	1	1	2	1	1	0	Good
29130759 Mecacci et al	0	0	1	1	0	1	0	0	Poor
29723256 Hanaoka et al	0	0	1	1	0	1	1	1	Poor
30837214 Gebhart et al	0	0	1	1	2	1	1	0	Fair
31905492 Dogan et al	0	0	1	1	0	1	0	0	poor
29667100 The et al	0	0	1	1	2	1	1	0	Fair
34121836 Abdelbaky et al	0	0	1	1	0	1	0	0	Poor

Newcastle-Ottawa scale	Risk domain								
	Selection				Comparability	Exposure			
Case control study	Adequacy of case definition	Representativeness of cases	Selection of controls	Definition of controls	Comparability of the cases and controls on the basis of design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate	Total number of stars
Su, Front Immunol, 2022	1	0	1	1	1	1	1	0	5/9
Sada, Lupus Sci Med, 2022	1	0	0	1	1	0	1	0	4/9
Jorge, JAMA 2022	1	1	1	1	2	1	1	1	9/9
Damara, Cureus, 2022	1	0	0	0	0	1	1	0	3/9
Mancuso, Clin Exp Rheumatol, 2022	1	1	1	0	1	1	1	0	6/9
Rua-Figeroa, Semin Arthritis Rheum, 2022	0	0	1	1	0	0	1	0	3/9
Kwan, Lupus Sci Med, 2022	1	1	1	1	1	0	1	0	6/9
Jorge, Arthritis Care Res, 2022	1	1	1	1	2	1	1	1	9/9
Long, Lupus, 2021	0	1	1	1	0	0	1	1	5/9
Lo, PLOS One, 2021	1	1	1	1	2	0	1	1	8/9
Garelick, Rheumatology, 2021	0	0	1	1	1	1	1	0	5/9
Wang, Lupus, 2020	1	1	1	1	1	1	1	0	7/9
Papachristos, Semin Arthritis Rheum, 2022	1	1	1	1	2	1	1	0	8/9
29765616 Davidson et al	0	0	0	1	1	1	1	0	4/9
30103646 Yang et al	1	1	1	1	2	1	1	1	9/9
30367020 Gadakchi et al	1	0	1	0	1	1	1	0	5/9
31066646 Dall'Era	1	0	0	0	0	1	1	0	3/9
31474597 Mukwikwi et al	1	1	1	1	1	1	1	1	8/9
32407570 Jorge et al	1	1	1	1	1	1	1	0	7/9
32442312 Lenfant et al	1	1	0	1	0	1	1	0	5/9
32586407 Guo et al	1	1	1	1	1	1	1	0	7/9
32653901 Bultink et al	1	1	1	1	1	1	1	0	7/9
32807233 Fernandez-Ruiz et al	1	0	0	1	2	1	1	0	6/9
28857715 Ugarte-Gil et al	1	1	1	1	2	1	1	0	8/9

Risk of bias assessment for RCTs and quasi-RCTs using RoB2

RoB2 is a Cochrane risk-of-bias tool for randomized trials [3]. Risk of bias is assessed in 5 different domains including bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. The tool uses algorithms to determine the individual risk of bias for each domain. The domain-level ratings determine the overall risk of bias of a study. In brief, a trial is of low overall risk of bias if all domains are of low risk of bias, a study is considered to raise some concerns if there are concerns in at least one domain but no high risk of bias in any domain and, a study is of high risk of bias if at least one domain is of high risk of bias or multiple domains raise some concerns.

RoB2	**Risk domain**					
RCT	Risk of bias arising from the randomization process	Risk of bias due to deviations from the intended interventions	Missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	**Overall risk of bias**
Zhang, Drugs R&D, 2022	High	Some concerns	Low	Low	Low	High
Morand, Arthritis Rheumatol, 2022	Low	Low	Low	Low	Low	Low
Wang, RMD Open,	High	Low	Low	Some concerns	Low	High
Zheng, Mod Rheumatol, 2022	Low	Low	Low	Low	Low	Low
Wallace, Lupus, 2022	Low	Low	Low	Low	Low	Low
Furie, N Engl J Med, 2022	Low	Low	Low	Low	Low	Low
Yu, Am J Kidney Dis, 2022	Low	Low	Low	Low	Low	Low
Arriens, Arthritis Rheumatol, 2022	Low	Low	Low	Low	Low	Low
Van Vollenhoven, Ann Rheum Dis, 2022	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns
Fu, Ann Rheum Dis, 2022	Some concerns	Low	Some concerns	Low	Low	Some concerns
Jourde-Chiche, Ann Rheum Dis, 2022						Some concerns
Lipsky, Ann Rheum Dis, 2022	Low	Low	Low	Low	Low	Low
Zhang, RMD Open, 2022	Low	Some concerns	Some concerns	Low	Low	Some concerns
Zheng, JAMA Netw Open, 2022	Low	Low	Low	Low	Low	Low
Vital, Ann Rheum Dis, 2022	Low	Low	Low	Low	Low	Low
Zhang, Front Med, 2022	Some concerns	Low	Some concerns	Low	Low	Some concerns
Merrill, N Engl J Med, 2022	Low	Low	Low	Low	Low	Low

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RoB2	Risk domain					
RCT	Risk of bias arising from the randomization process	Risk of bias due to deviations from the intended interventions	Missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	**Overall risk of bias**
Ye, Am J Transl Res, 2022	Some concerns	Low	Some concerns	High	High	High
Furie, Lupus Sci Med, 2022	Low	Some concerns	Some concerns	Low	Low	Some concerns
Jayne, Ann Rheum Dis, 2022	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns
Jiang, Lupus Sci Med, 2022	Low	Low	Low	Some concerns	Low	Some concerns
Bandhan, Int J Rheum Dis, 2022	High	Some concerns	Low	Low	Low	High
Furie, Ann Rheum Dis, 2022	Low	Low	Low	Low	Low	Low
Rovin, Kidney Int, 2022	Low	Low	Low	Low	Low	Low
Tanaka, RMD Open, 2022	Low	Low	Some concerns	Low	Low	Low
Rovin, Lancet, 2021	Low	Low	Low	Low	Low	Low
Ginzler, Arthritis Rheumatol, 2022	Low	Low	Low	Low	Low	Low
Hasni, Nat Communicat, 2021	Some concerns	Low	Low	Low	Some concerns	Some concerns
Isenberg, Arthritis Rheumatol, 2021	Low	Low	Low	Low	Low	Low
Furie, Rheumatology, 2021	Low	Low	Low	Low	Low	Low
Wallace, Rheumatology, 2021	Low	Low	High	Low	Low	High
Maslen, Lupus Sci Med, 2021	Low	Low	Low	Low	Low	Low
Tummala, Lupus Sci Med, 2021	Low	Low	Low	Low	Low	Low
Barua, Dermatol Ther, 2021	Some concerns	Low	Low	Low	Low	Some concerns
Chatham, Arthritis Rheumatol, 2021	Low	Low	High	Low	Low	High
Furie, N Engl J Med, 2020	Low	Low	Low	Low	Low	Low
Bruce, Lancet Rheumatol, 2021	Low	Low	Some concerns	Low	Low	Some concerns
Morand, Lancet Rheumatol, 2022	Low	Low	Low	Low	Low	Low
Sheikh, Lancet Rheumatol, 2021	Low	Low	Low	Low	Low	Low
29073347 Merrill et al	Some concerns	Some concerns	Low risk	Some concerns	Low risk	Some concerns
29105558 Kamanamool et al	Some concerns	Some concerns	Low risk	Some concerns	Low risk	Some concerns

RoB2	Risk domain					
RCT	Risk of bias arising from the randomization process	Risk of bias due to deviations from the intended interventions	Missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	**Overall risk of bias**
29295825 Zhang et al	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
29450636 Mehra et al	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
29671280 Doria et al	Some concerns	Some concerns	Some concerns	Some concerns	Low risk	High risk of bias
29996800 Sedhain et al	High risk	High risk	Some concerns	Low risk	Low risk	High risk of bias
30043749 Wallace et al	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
30249507 van Vollenhoven et al	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
30420324 Rovin et al	Low risk	Low risk	Some concerns	Low risk	Low risk	Some concerns
30426311 Zhang et al	Low risk	Some concerns	Some concerns	Low risk	Low risk	Some concerns
30488367 An et al	High risk	High risk	Low risk	Low risk	Some concerns	High risk of bias
31537547 He et al	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
31571750 Bharati et al	High risk	High risk	Low risk	Some concerns	Some concerns	High risk of bias
31851795 Morand et al	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
31852672 Mathian et al	High risk	High risk	Low risk	Low risk	Low risk	High risk of bias
32755035 Atisha-Fregoso et al	Some concerns	Some concerns	Low risk	Some concerns	Low risk	Some concerns
31530556 Mok et al	Some concerns	Low risk	Low risk		Low risk	Some concerns

Risk of bias assessment for meta-analyses

The AMSTAR2 (A MeaSurement Tool to Assess systematic Reviews) tool was used to assess the risk of bias of meta-analyses of RCTs and quasi-RCTs [4]. Meta-analyses of cohort studies and network meta-analyses were not considered for evaluation. Each eligible study was assessed using a checklist of sixteen items (https://amstar.ca/Amstar_Checklist.php) including seven critical domains (registration of a predefined protocol, adequacy of literature search, justification for excluding individual studies, risk of bias from individual studies, appropriateness of meta-analytical methods, consideration of risk of bias when interpreting the results of the review, and assessment of presence of publication bias). Based on the ratings a study is of high, moderate, low, or critically low quality.

Meta-analysis	Quality of study based on AMSTAR2
Oon, Semin Arthritis Rheum, 2018	Critically Low
Tunnicliffe, Cochrane Database Syst Rev, 2018	High
Alshaiki, Eur J Rheumatol, 2018	Critically Low
Deng, Turk J Med Sci, 2018	Critically Low
Thong, Lupus, 2019	Critically Low
Zhong, Drug Des Devel Ther , 2019	Critically Low
Zhou, Drug Des Devel Ther, 2019	Critically Low
Liu, Clin Rheumatol, 2019	Critically Low
Zhou, J Pharm Pharm Sci, 2019	Critically Low
Yang, Clin Rheumatol, 2020	Critically Low
Chasset, J Am Acad Dermatol, 2018	Critically Low
Gu, Arch Osteoporos, 2019	Critically Low
Kneeland, Arthritis Care Res, 2022	Critically Low
Liu, Front Immunol, 2022	Critically Low
Lee, Lupus, 2022	Critically Low
Wu, Front Immunol, 2022	Critically Low
Chen, J Clin Rheumatol, 2022	Critically Low
Chiang, Lupus, 2022	Critically Low
Teng, Int J Rheum Dis, 2022	Critically Low
Xie, Lupus Sci Med, 2021	Low
Lee, Z Rheumatol, 2021	Critically Low
Zhang, Medicine, 2020	Low
Koh, Lupus, 2020	Critically Low
Jiang, Medicine, 2020	Critically Low
Ji, Lupus Sci Med, 2022	Critically Low

References

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4. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017; 358:j4008.