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

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Anakinra<br>• JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib)<br>• Proteasome inhibitors (e.g., bortezomib)<br>• Iberdomide<br>• Litifilimab<br>• Low-dose IL-2<br>• Daratumumab<br>• CD19 CAR-T cells<br>• Plasmapheresis<br>• Plasma exchange<br>• Immunoadsorption<br>• 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<br>• Topical agents (glucocorticoids, calcineurin inhibitors)<br>• Glucocorticoids<br>• Hydroxychloroquine, antimalarials<br>• Immunosuppressive agents<br>• Cytotoxic agents<br>• Methotrexate<br>• Leflunomide<br>• Azathioprine<br>• Cyclophosphamide<br>• Mycophenolate<br>• Ciclosporin<br>• Tacrolimus<br>• Retinoids<br>• Dapsone<br>• Thalidomide<br>• Lenalidomide<br>• Biological agents | • Standard of care<br>• Placebo<br>• None | • Disease activity improvement/worsening (SLEDAI, BILAG): mucocutaneous-specific domains<br>• Cutaneous LE Disease Area and Severity Index<br>• Physician Global Assessment<br>• Glucocorticoid sparing<br>• Response (SRI-4, BICLA)<br>• Disease control<br>• Low disease activity (LLDAS)<br>• Remission (various definitions including steroid-free remission)<br>• Relapse, flare, time-to-flare<br>• Treatment failure<br>• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Infection<br>• Hospitalizations |

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Belimumab<br>• Anifrolumab<br>• Rituximab<br>• Obinutuzumab<br>• Ofatumumab<br>• Ocrelizumab<br>• Atacicept<br>• Etanercept<br>• Adalimumab<br>• Abatacept<br>• Tocilizumab<br>• Secukinumab<br>• Ustekinumab<br>• Anakinra<br>• JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib)<br>• Proteasome inhibitors (e.g., bortezomib)<br>• Iberdomide<br>• Litifilimab<br>• Low-dose IL-2<br>• Daratumumab<br>• CD19 CAR-T cells<br>• Intravenous immunoglobulin | | • Death<br>• Toxicity (including retinopathy)<br>• 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<br>• Glucocorticoids<br>• Hydroxychloroquine, antimalarials<br>• Immunosuppressive agents<br>• Cytotoxic agents<br>• Methotrexate<br>• Leflunomide<br>• Azathioprine<br>• Cyclophosphamide<br>• Mycophenolate<br>• Ciclosporin<br>• Tacrolimus<br>• Biological agents | • Standard of care<br>• Placebo<br>• None | • Disease activity improvement/worsening (SLEDAI, BILAG): musculoskeletal-specific domains<br>• Tender joint count<br>• Swollen joint count<br>• Physician Global Assessment<br>• Glucocorticoid sparing<br>• Response (SRI-4, BICLA)<br>• Disease control<br>• Low disease activity (LLDAS)<br>• Remission (various definitions including steroid-free remission)<br>• Relapse, flare, time-to-flare<br>• Treatment failure |

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Belimumab<br>• Anifrolumab<br>• Rituximab<br>• Obinutuzumab<br>• Ofatumumab<br>• Ocrelizumab<br>• Atacicept<br>• Etanercept<br>• Adalimumab<br>• Abatacept<br>• Tocilizumab<br>• Secukinumab<br>• Ustekinumab<br>• Anakinra<br>• JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib)<br>• Proteasome inhibitors (e.g., bortezomib)<br>• Iberdomide<br>• Litifilimab<br>• Low-dose IL-2<br>• Daratumumab<br>• CD19 CAR-T cells | | • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Infection<br>• Hospitalizations<br>• Death<br>• Toxicity (including retinopathy)<br>• 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<br>• Hydroxychloroquine, antimalarials<br>• Immunosuppressive agents<br>• Cytotoxic agents<br>• Methotrexate<br>• Leflunomide<br>• Azathioprine<br>• Cyclophosphamide<br>• Mycophenolate<br>• Ciclosporin<br>• Tacrolimus<br>• Biological agents<br>• Belimumab<br>• Anifrolumab<br>• Rituximab<br>• Obinutuzumab | • Standard of care<br>• Placebo<br>• None | • Disease activity improvement/worsening (SLEDAI, BILAG): neuropsychiatric-specific domains<br>• Neurological deficit (e.g., EDSS)<br>• Neuropsychological tests<br>• Psychiatric scales<br>• Physician Global Assessment<br>• Glucocorticoid sparing<br>• Response (SRI-4, BICLA)<br>• Disease control<br>• Low disease activity (LLDAS)<br>• Remission (various definitions including steroid-free remission)<br>• Relapse, flare, time-to-flare<br>• Treatment failure<br>• Organ damage (including cataract, cognitive dysfunction, osteoporotic |

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Ofatumumab<br>• Ocrelizumab<br>• Atacicept<br>• Etanercept<br>• Adalimumab<br>• Abatacept<br>• Tocilizumab<br>• Secukinumab<br>• Ustekinumab<br>• Anakinra<br>• JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib)<br>• Proteasome inhibitors<br>• Iberdomide<br>• Litifilimab<br>• Low-dose IL-2<br>• Daratumumab<br>• CD19 CAR-T cells<br>• Plasmapheresis<br>• Plasma exchange<br>• Immunoadsorption<br>• Intravenous immunoglobulin | | fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Infection<br>• Hospitalizations<br>• Death<br>• Toxicity (including retinopathy)<br>• 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<br>• Hydroxychloroquine, antimalarials<br>• Immunosuppressive agents<br>• Cytotoxic agents<br>• Methotrexate<br>• Leflunomide<br>• Azathioprine<br>• Cyclophosphamide<br>• Mycophenolate<br>• Ciclosporin | • Standard of care<br>• Placebo<br>• None | • Disease activity improvement/worsening (SLEDAI, BILAG): haematological-specific domains<br>• Complete blood count<br>• Physician Global Assessment<br>• Glucocorticoids sparing<br>• Response (SRI-4, BICLA)<br>• Disease control<br>• Low disease activity (LLDAS)<br>• Remission (various definitions including steroid-free remission) |

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Tacrolimus<br>• Biological agents<br>• Belimumab<br>• Anifrolumab<br>• Rituximab<br>• Obinutuzumab<br>• Ofatumumab<br>• Ocrelizumab<br>• Atacicept<br>• Etanercept<br>• Adalimumab<br>• Abatacept<br>• Tocilizumab<br>• Secukinumab<br>• Ustekinumab<br>• Anakinra<br>• JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib)<br>• Proteasome inhibitors (e.g., bortezomib)<br>• Iberdomide<br>• Litifilimab<br>• Low-dose IL-2<br>• Daratumumab<br>• CD19 CAR-T cells<br>• Plasmapheresis<br>• Plasma exchange<br>• Immunoadsorption<br>• Intravenous immunoglobulin<br>• Thrombopoietin-receptor agonists (romiplostim, eltrombopag) | | • Relapse, flare, time-to-flare<br>• Treatment failure<br>• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Infection<br>• Hospitalizations<br>• Death<br>• Toxicity (including retinopathy)<br>• Cardiovascular disease<br>• 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<br>• Hydroxychloroquine, antimalarials<br>• Immunosuppressive agents | • Standard of care<br>• Mycophenolate<br>• Azathioprine | • Disease activity improvement/worsening (SLEDAI, BILAG): renal-specific domains<br>• Proteinuria improvement/worsening |

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Cytotoxic agents<br>• Methotrexate<br>• Leflunomide<br>• Azathioprine<br>• Cyclophosphamide<br>• Mycophenolate<br>• Ciclosporin<br>• Tacrolimus<br>• Voclosporin<br>• Biological agents<br>• Belimumab<br>• Anifrolumab<br>• Rituximab<br>• Obinutuzumab<br>• Ofatumumab<br>• Ocrelizumab<br>• Atacicept<br>• Telaticept<br>• Dapagliflozin<br>• Etanercept<br>• Adalimumab<br>• Abatacept<br>• Tocilizumab<br>• Secukinumab<br>• Ustekinumab<br>• Anakinra<br>• JAK inhibitors (tofacitinib, baricitinib, upadacitinib, deucravacitinib)<br>• Proteasome inhibitors<br>• Iberdomide<br>• Litifilimab<br>• Low-dose IL-2<br>• Daratumumab<br>• CD19 CAR-T cells<br>• Plasmapheresis<br>• Plasma exchange<br>• Immunoadsorption<br>• Intravenous immunoglobulin<br>• RAAS inhibitors<br>• SGLT2 inhibitors (Dapagliflozin) | • Cyclophosphamide<br>• Ciclosporin<br>• Tacrolimus<br>• Placebo<br>• None | • Kidney function (serum creatinine, eGFR) improvement/worsening<br>• Chronic kidney disease<br>• End-stage kidney disease<br>• Histological improvement/worsening (change in activity/chronicity indices)<br>• Physician Global Assessment<br>• Glucocorticoid dose/tapering<br>• Renal response (e.g., PEER, EULAR-defined endpoints)<br>• Renal remission (complete renal response)<br>• Relapse, flare, time-to-flare<br>• Treatment failure<br>• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Infection<br>• Hospitalizations<br>• Death<br>• Toxicity (including retinopathy)<br>• 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<br>• Lupus Low Disease Activity State (LLDAS)<br>• Remission<br>• Inactive disease<br>• Disease quiescence<br>• Duration of LLDAS/remission | • Active disease<br>• Not in low disease activity or remission or disease quiescence<br>• None | • Relapse, flare, time-to-flare<br>• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Kidney function (serum creatinine, eGFR) improvement/worsening<br>• Chronic kidney disease<br>• End-stage kidney disease<br>• Toxicity<br>• Infection<br>• Hospitalizations<br>• 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<br>• Hydroxychloroquine, antimalarials<br>• Immunosuppressive agents<br>• Cytotoxic agents<br>• Methotrexate<br>• Leflunomide<br>• Azathioprine<br>• Cyclophosphamide<br>• Mycophenolate<br>• Ciclosporin<br>• Tacrolimus<br>• Voclosporin<br>• Biological agents<br>• Belimumab | • Standard of care<br>• Placebo<br>• None | • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Hospitalizations<br>• Death<br>• Toxicity (including bleeding)<br>• Cardiovascular disease<br>• Pregnancy/foetal loss<br>• Live birth<br>• Premature birth<br>• Stillbirth<br>• (Pre-)eclampsia<br>• Vascular thrombosis (venous, arterial) |

| Population(s) | Intervention(s)-exposure(s) | Comparison | Outcome(s) |
|---|---|---|---|
| | • Anifrolumab<br>• Rituximab<br>• Obinutuzumab<br>• Ofatumumab<br>• Ocrelizumab<br>• Atacicept<br>• Complement inhibitors (e.g., eculizumab)<br>• Plasmapheresis<br>• Plasma exchange<br>• Immunoadsorption<br>• Intravenous immunoglobulin<br>• Aspirin<br>• Heparin<br>• Warfarin<br>• Apixaban<br>• Rivaroxaban<br>• 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)<br>• Duration of treatment | • Standard of care<br>• Placebo<br>• None | • Disease activity (SLEDAI, BILAG): global and specific domains<br>• Physician Global Assessment<br>• Glucocorticoid exposure<br>• Disease control<br>• Disease worsening<br>• Treatment re-initiation<br>• Low disease activity (LLDAS)<br>• Remission (including steroid-free remission)<br>• Relapse, flare, time-to-flare<br>• Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes)<br>• Hospitalizations<br>• Death<br>• 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<br>• Vaccination against SARS-CoV2 | • No vaccination<br>• None | • Serological response (protective antibodies)<br>• Herpes zoster infection<br>• SARS-CoV2 infection<br>• COVID-19<br>• Need for hospitalization (e.g., need for oxygen supply, ICU)<br>• Death<br>• Disease activity (SLEDAI, BILAG): global and specific domains<br>• Physician Global Assessment<br>• Glucocorticoid exposure<br>• Disease control<br>• Disease worsening<br>• Relapse, flare, time-to-flare<br>• 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 "vaccinations"[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**

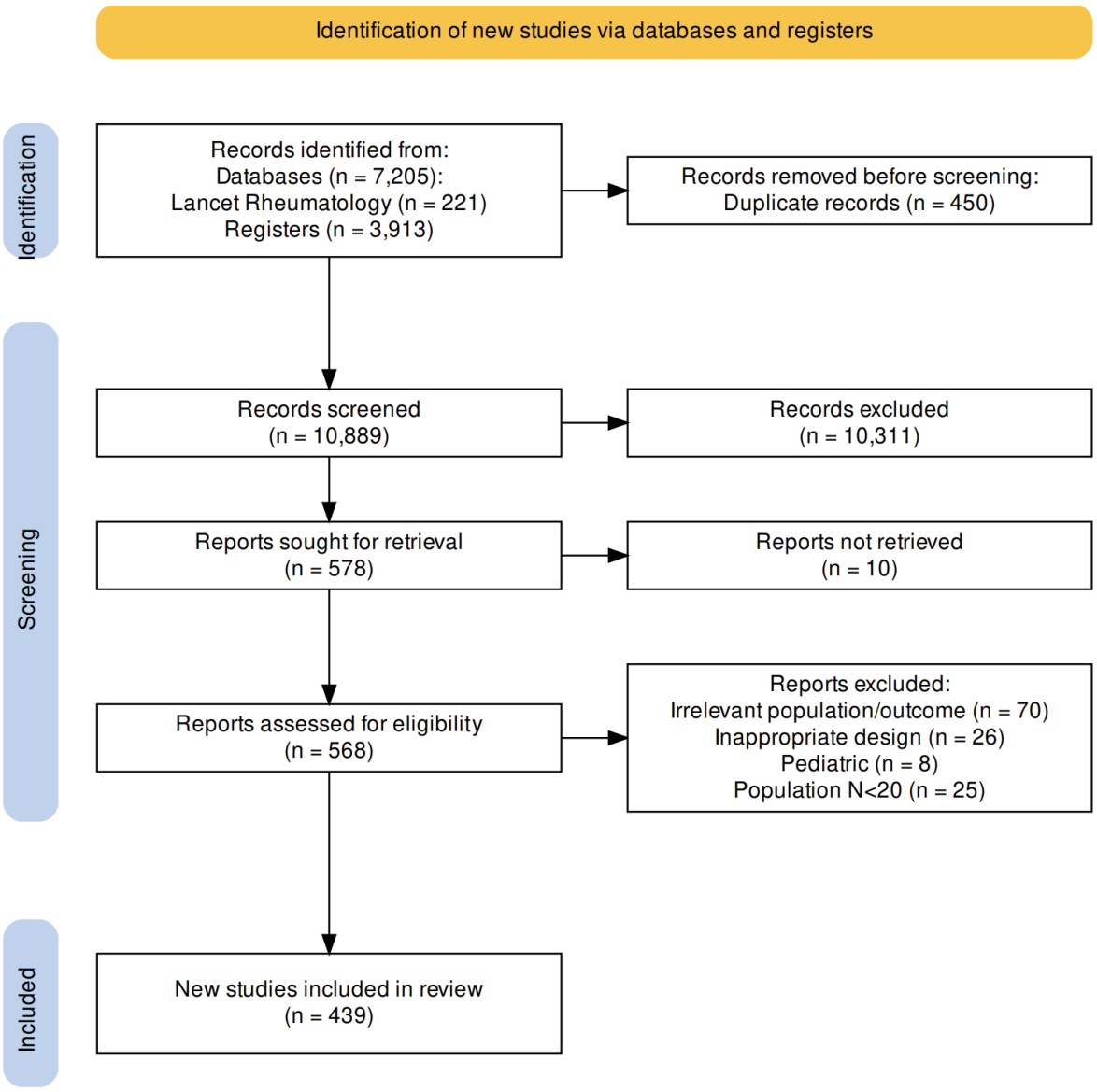
| | |
|---|---|
| ID | Search |
| #1 | MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees |
| #2 | ("systemic lupus erythematosus"):ti,ab,kw (Word variations have been searched) |
| #3 | (lupus):ti,ab,kw (Word variations have been searched) |

#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 |

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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 |
| 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 |

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 |
| 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 |

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 |
| 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 |

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| 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

1. Haddaway N, Page M, Pritchard C, McGuinness L. PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis. Campbell Systematic Reviews. 2022 03/27; 18.
2. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010 Sep; 25(9):603-605.
3. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019; 366:l4898.
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.