Systematic Literature Review

Supplementary material

Contents

Systematic Literature Review

Supplementary file 1: Research questions and PICOs

PICO 1 – Therapeutic interventions

PICO 1a – Active SLE

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?

Table S1.1

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• Patients with active SLE	• Sun protection • NSAIDs • Glucocorticoids • Hydroxychloroquine, antimalarials	• Standard of care • Azathioprine • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): global and specific domains • Cutaneous LE Disease Area and Severity Index

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
	• 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 • 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		• 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

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; NSAIDs: Nonsteroidal anti-inflammatory drug; JAK: Janus kinase; IL-2: Interleukin-2; CAR-T: Chimeric antigen receptor T-cell, SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; LE: Lupus erythematosus; SRI: SLE responder index; BICLA: British Isles lupus assessment group-based composite lupus assessment; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events

PICO 1b – Active mucocutaneous involvement

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?

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Table S1.2

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 • 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	• 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 • Death • Toxicity (including retinopathy) • Thrombosis

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; JAK: Janus kinase; IL-2: Interleukin-2; CAR-T: Chimeric antigen receptor T-cell, SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; LE: Lupus erythematosus; SRI: SLE responder index; BICLA: British Isles lupus assessment group-based composite lupus assessment; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events

PICO 1c – Active musculoskeletal involvement

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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?

Table S1.3

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 • 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	• 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 • Organ damage (including cataract, cognitive dysfunction, osteoporotic fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Toxicity (including retinopathy) • Thrombosis

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; NSAIDs: Nonsteroidal anti-inflammatory drug; JAK: Janus kinase; IL-2: Interleukin-2; CAR-T: Chimeric antigen receptor T-cell, SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; LE: Lupus erythematosus; SRI: SLE responder index; BICLA: British Isles lupus assessment group-based composite lupus assessment; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events

PICO 1d – Active neuropsychiatric involvement

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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?

Table S1.4

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 • 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	• 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 fracture, osteonecrosis, stroke, cardiovascular disease/MACEs, malignancy, diabetes) • Infection • Hospitalizations • Death • Toxicity (including retinopathy) • Thrombosis

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; JAK: Janus kinase; IL-2: Interleukin-2; CAR-T: Chimeric antigen receptor T-cell, SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; EDSS: Expanded disability status scale; SRI: SLE responder index; BICLA: British Isles lupus assessment group-based composite lupus assessment; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events

PICO 1e – Active haematological involvement

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?

Table S1.5

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 • 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)	• 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) • 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

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; JAK: Janus kinase; IL-2: Interleukin-2; CAR-T: Chimeric antigen receptor T-cell, SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; SRI: SLE responder index; BICLA: British Isles lupus assessment group-based composite lupus assessment; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events

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PICO 1f – Active kidney involvement

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?

Table S1.6

Population(s)	Intervention(s)-exposure(s)	Comparison	Outcome(s)
• SLE patients with active kidney involvement	• Glucocorticoids • Hydroxychloroquine, antimalarials • Immunosuppressive agents • 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)	• Standard of care • Mycophenolate • Azathioprine • Cyclophosphamide • Ciclosporin • Tacrolimus • Placebo • None	• Disease activity improvement/worsening (SLEDAI, BILAG): renal-specific domains • Proteinuria improvement/worsening • 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

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; JAK: Janus kinase; IL-2: Interleukin-2; CAR-T: Chimeric antigen receptor T-cell, RAAS: Renin angiotensin aldosterone system; SGLT: Sodium-glucose transport proteins; SLEDAI:

Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; eGFR: Estimated glomerular filtration rate; PERR: Primary efficacy renal response; MACEs: Major adverse cardiovascular events

PICO 2 – Targets of treatment

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?

Table S1.7

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

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events; eGFR: Estimated glomerular filtration rate

PICO 3 – SLE and antiphospholipid syndrome

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?

Table S1.8

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

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; MACEs: Major adverse cardiovascular events

PICO 4 – Tapering/withdrawal of treatment in SLE

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?

Table S1.9

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)

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group; LLDAS: Lupus low disease activity state; MACEs: Major adverse cardiovascular events

PICO 5 – Vaccination against herpes zoster (HZ) and SARS-CoV2 viruses

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?

Table S1.10

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

PICO: Population intervention comparison outcome; SLE: Systemic lupus erythematosus; SARS-CoV2: Severe acute respiratory syndrome coronavirus 2; COVID: Coronavirus disease; ICU: Intensive care unit; SLEDAI: Systemic lupus erythematosus activity index; BILAG: British Isles lupus assessment group

Supplementary file 2: Search strings

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

Cochrane Library 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)

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#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)

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#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

Cochrane Library search string for PICO 2:

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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

Cochrane Library 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)

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#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)

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#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)

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#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

Cochrane Library 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

Cochrane Library 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

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Supplementary file 3: Risk of bias

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 [1]. 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

Table S 3.1

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

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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
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
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

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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
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
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

Systematic Literature Review

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
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
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

Systematic Literature Review

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
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
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

Systematic Literature Review

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
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
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

Systematic Literature Review

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
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

Table S3.2

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

Systematic Literature Review

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
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 [2]. 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.

Table S3.3

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

Systematic Literature Review

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 [3]. 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.

Table S3.4

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

Systematic Literature Review

Supplementary file 4: Data synthesis

Supplementary Tables

S4.1. **Studies evaluating beneficial effects of hydroxychloroquine in SLE**

Outcome	**N of studies**	**Magnitude of effect (HR, RR, OR)**	**Best LoE**	**References**
Mortality	10	RR 0.20-0.68 (pooled 0.46)	Meta-analysis	[4-13]
Flares	12	0.03-0.72	Prospective Cohort	[14-25]
Belimumab discontinuation	1	OR 0.33	Retrospective Cohort	[26]
Congestive heart failure	1	OR 0.28	Cross-sectional	[27]
Thrombosis (combined/MI/stroke/VTE)	4	OR 0.67-0.86/0.88/0.20-0.87/0.74	Prospective Cohort	[11, 28-30]
Coronary artery disease	1	OR 0.31	Retrospective Cohort	[30]
Infections	2	0.99	Meta-analysis	[31, 32]
Serious/Bacterial infection	2	HR 0.18/0.49	Retrospective Cohort	[31, 33]
Osteonecrosis	2	HR 0.25-0.38	Retrospective Cohort	[34, 35]
Pneumocystis jirovecii pneumonia	1	HR 0.51	Retrospective Cohort	[36]
Renal damage	1	0.54	Prospective Cohort	[10]
Hospitalized infection	1	No association	Retrospective Cohort	[37]
Preeclampsia	1	OR 0.16	Retrospective Cohort	[38]
Atrial fibrillation	1	OR 0.12	Retrospective Cohort	[39]
Damage	1	OR 0.71	Retrospective Cohort	[40]
Infection-related death	1	OR 9.26 for non-users	Retrospective Cohort	[13]
Non-melanoma skin cancer	2	0.23 and 1 negative study (adj. OR 2.7)	Prospective Cohort	[41, 42]
Cancer (general)	1	0.43	Case-Control	[43]
Recovery of renal function in LN	1	3.89	Prospective Cohort	[44]

HR: Hazard ratio; RR: Risk ratio; OR: Odds ratio; LE: Lupus erythematosus; MI: Myocardial infarction; VTE: Venous thromboembolism; LN: Lupus nephritis.

S4.2. **Studies related to specific GC doses and risk for infections**

Study	Design - N	Dose (Pz equivalent)	Type of infection and association	Risk of bias
Prata, Clin Rheumatol, 2022 [33]	Cohort - 259	Mean ≥ 7.5 mg/day Mean ≥ 10 mg//day	**Infection of any type** Pz ≥ 7.5 mg/day: HR = 1.95, 95%CI 1.26–3.03 **Non-serious infection** Pz≥ 7.5 mg/day:HR = 1.89, 95%CI 1.21–2.96) **Serious infection** Pz ≥ 10 mg/day: HR = 4.32, 95%CI 1.39–13.40)	Poor
Yates, Lupus Sci Med, 2020 [45]	Cohort - 173	Linear	**Serious infection** (aHR 1.21;95% CI 1.07-1.37)	Fair
Wang, Arthritis Care Res, 2022 [36]	Case control - 24367	Mean > 7.5 mg/day	***Pneumocystis jirovecii* pneumonia** (HR 4.83, P < 0.001)	Good
Wang, Lupus, 2020 [46]	Case control - 159	> 7.5 mg/day (mean?)	**Bloodstream infection** (aOR 3.74, 95% CI 1.19-11.71	Fair
Abe, Arthritis Res Ther, 2022 [47]	Cohort - 509	Mean 2.6-5.0 mg/day Mean 5.1-7.5 mg/day Mean 7.6-15.0 mg/day	**Hospitalized infection** (vs. mean 0-2.5 mg/day) • 2.6–5.0 mg/day: HR 2.69 (95% CI 0.90–7.99) • 5.1-7.5 mg/day: HR 6.80 (95% CI 2.17–21.27) • 7.6-15.0 mg/day: HR 7.68 (95% CI 2.38–24.85)	Good
Sakai, Lupus, 2020 [37]	Cohort - 2190	1) Linear; 2) IV pulse	**Hospitalized infection** (1) HR 1.03, 95% CI 1.02–1.04; 2) HR 3.45, 95% CI 1.40-8.51	Poor
Wu, Front Immunol, 2022 [48]	Meta-analysis	Mean ≥ 20 mg/day	**Tuberculosis** (pooled prevalence 3.06% vs. 1.48% in < 20 mg/day)	Low quality
Kwan, Lupus Sci Med, 2022 [49]	Cross-sectional - 149	Linear	**Herpes zoster** (HR 1.01 95%CI 1.00 to 1.02)	Fair
Su, Ther Adv Musculoskel Dis, 2021 [50]	Retro cohort – 24,541	Pulse IV MP in previous 60 days Mean > 5 mg/day	**Invasive fungal infections** Pulse IV MP: HR 29.11, 95% CI: 23.30–36.37 Mean > 5 mg/day: HR 1.26, 95% CI: 1.01–1.58	Good

GC: Glucocorticoids; Pz: Prednisone; HR: Hazard ratio; CI: Confidence interval; aHR: Adjusted hazard ratio; aOR: Adjusted odds ratio; IV: Intravenous; MP: Methyl-prednisone

S4.3. **Studies related to specific GC doses and adverse outcomes other than infections**

Study	Design - N	Dose (Pz equivalent)	Outcome and association	Risk of bias
Park, Sci Rep, 2021 [51]	Cohort - 259	Mean > 5 mg/day	**Thrombotic events** (HR 3.67, 95% CI: 1.32-10.20)	Good
Miyawaki, Arthritis Res Ther, 2021 [52]	Cross-sectional - 175	Linear	**Worse emotional health** (β - 2.54 (95%CI -4.48 to -0.60)	Not applicable
			Damage	
Apostolopoulos, Lancet Rheumatol, 2019 [53]	Cohort – 1707	Time-adjusted mean	HR 1.14, [95% CI 1.03–1.26)	Good
Frontini, Clin Exp Rheumatol, 2021 [12]	Cohort - 187	Mean > 5 mg/day	HR: 3.38, CI:1.98-5.75	Poor
Danza, Lupus, 2022 [54]	Retro cohort - 48	Mean 32.6 mg/day at 1st month Mean 7.38 mg/day at 1st year	**Damage at 5 years** (ROC)	Fair
Davidson, Lupus Sci Med, 2018 [55]	Case control - 407 cases	Cumulative dose • 0 g (no exposure) • >0 and <3.65 g (<10 mg/day • for a year) • ≥3.65 g and <18.25 g (1–5 years at 10 mg/day) • ≥18.25 g (>5 years at 10 mg/day)	**Damage items** • A one-category increase in cumulative GC dose associated with risk of cataract (OR (95% CI) 1.855 (1.190 - 2.892 and osteoporosis (OR (95% CI) 1.604 (1.067 - 2.412)) • ORs for avascular necrosis, diabetes and hypertension not significant	Poor
Ugarte-Gil, Ann Rheum Dis, 2022 [56]	Retro - 1606	• Mean 1-5 mg/day • Mean 6-9 mg/day • Mean ≥10 mg/day	**Severe COVID outcomes** • 1–5 mg/day: HR 1.86, 95% CI 1.20 to 2.66 • 6–9 mg/day: HR 2.47, 95% CI 1.24 to 4.86	Good

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			• ≥10 mg/day: HR 1.95, 95% CI 1.27 to 2.99	
			Osteonecrosis	
Long, Lupus, 2021 [34]	Cohort – 1158	• 1 mg/kg/day at initial Dx	• HR 2.20, p 0.008	Poor
Chen, Ther Adv Muscul Dis, 2021 [57]	Cohort – 449	• Linear; 2) IV pulse	• aOR 1) 1.1, 95% CI 1.0–1.1; 2) 4.4, 95% CI 1.9–10.1	Good
Shararir, PLOS One, 2021 [35]	Cohort – 390	• 30 mg/day for 4 wks	• OR 3.84, 95%CI 1.81-8.11	Fair
Kallas, Arthritis Care Res, 2022 [58]	Cohort - 2428	• ≥ 40 mg/day 2) IV pulse or IM	• 1) aHR 3.54, 95% CI 1.49-8.37; 2) None	Fair
Kandane-Rathnayake, Lancet Rheumatol, 2022 [59]	Cohort - 3811	Cumulative (linear)	**Mortality** (aHR 1.36, 95%CI 1.01–1.85)	Good

GC: Glucocorticoids; Pz: Prednisone; HR: Hazard ratio; CI: Confidence interval; OR: Odds ratio; aOR: Adjusted odds ratio; aHR: Adjusted hazard ratio

S4.4. **Association of attainment of remission or LLDAS with risk for disease flares**

Study	Design	Target	Association	Risk of bias
Golder, Lancet Rheumatol, 2019 (APLC) [60]	Cohort	Remission (various DORIS definitions)-50; LLDAS-50	Remission: aHR 0.26-0.54 LLDAS: aHR 0.41	Good
Golder, Lancet Rheumatol, 2019 (APLC) [60]	Cohort	LLDAS-50	HR 0.65, 95% CI 0·56–0·75	Good
Gerosa, J Clin Med, 2022 [61]	Retro	LLDAS; Remission (DORIS)	LLDAS: HR 0.487, 95% CI 0.305-0.778 DORIS remission: HR 0.611, 95% CI 0.338-0.963	Fair
Sun, Lupus Sci Med, 2022 [62]	Cohort	LLDAS; Remission (DORIS)	LLDAS (not in remission): HR 0.58, 95% CI 0.38-0.88 Remission: HR 0.46, 95% CI 0.30-0.69	Good
Hao, Lupus Sci Med, 2022 (APLC) [63]	Cohort	LLDAS; DORIS remission	Lower flare rate after achievement of LLDAS, clinical remission, and complete remission on-Tx	Good
Kikuchi, Rheumatology, 2022 [64]	Cohort	LLDAS within 12 months	No association with flares	Poor
Hao, Clin Rheumatol, 2022 [65]	Retro	LLDAS-50	Lowest flare rate in LLDAS ≥ 50% group (p 0.000)	Fair
Kang, Rheumatology, 2021 [66]	Retro	LLDAS, MDA, LDA (Toronto)	LLDAS associated with reduced flare (OR 0.09, 95% CI: 0.03, 0.24) – MDA and LDA (Toronto) showed no association	Good
Tselios, Arthritis Care Res, 2019 [67]	Cohort	Remission; LDA (Clinical SLEDAI ≤2)	Comparable for remission and LDA	Poor

LLDAS: Lupus low disease activity state; aHR: Adjusted hazard ratio; HR: Hazard ratio; CI: Confidence interval; Tx: Treatment; OR: Odds ratio; MDA: Minimal disease activity; LDA: Low disease activity; SLEDAI: Systemic lupus erythematosus disease activity index

S4.5. **Associations of remission at different timepoints with long-term outcomes in lupus nephritis**

Study	Design	Target	Outcome	Association	Risk of bias
Teh, Clin Kidney J, 2018 [68]	Retro cohort	CR at 1 year	Mortality	No CR at 1 year: aHR 2.99 (95% CI 1.35- 6.65)	Good
Ichinose, Lupus, 2019 [69]	Retro	CR at 1 year	Renal flare	aHR 0.06 (95% CI 0.00– 0.45)	Poor
Davidson, J Rheumatol, 2018 [70]	Retro	Remission (mALMS, mBLISS-LN) at 2 years	ESKD/Death	mBLISS-LN: HR 0.25 (95% CI 0.08-0.780 mALMS: HR 0.23 (95%CI 0.06-0.83)	Poor
Yadav, Lupus, 2022 [71]	Retro	CR at 2 years	CKD	No CR at 2 years: HR 6.27 (95% CI 1.57–25.09)	Fair
Medina-Rosas, Semin Arthritis Rheum, 2018 [72]	Retro cohort	Complete UPR recovery at 2 years (vs partial)	eGFR ≤ 15 m/min; ESKD; composite	Low eGFR: CR at 2 years aHR 0.11 (95% I 0.03-0.32) vs. NR and 0.24 (0.09-0.65) vs. PR; PR vs NR not significant Similar results for ESKD and composite	Good
Cooper Blenkinsopp, Lupus Sci Med, 2022 [73]	Cohort	Modified PERR at 2 years	CKD; ESKD; Death	ESKD/death: aHR 0.33 (95% CI 0.13-0.87) CKD: aHR 0.26 (95% CI 0.14-0.47)	Good
Frontini, Clin Exp Rheumatol, 2022 [12]	Retro	CR	SDI; Mortality	SDI: aHR:0.993, 95%CI:0.987–0.999 Mortality: Only in univariate analysis	Poor
Pirson, Lupus Sci Med, 2021 [74]	Retro	CR (any time point)	CKD; ESKD	Never remission: CKD 48% (vs 16%) – ESKD: 20% (vs 2%) Early remission (≤ 1 year): significantly higher eGFR at last follow-up vs. late remitters	Poor
Enfrein, RMD Open, 2022 [75]	Retro	Remission (absence)	CKD	aHR 70.60, 95% CI 14.18 to 351.45	Poor
Du, Clin Rheumatol, 2022 [76]	Cohort	PR within 6 months	Renal response at 2 years	OR 8.09, 95% CI 2.06–31.73	Fair

CR: Complete remission; aHR: Adjusted hazard ratio; ESKD: End stage kidney disease; HR: Hazard ratio; CI: Confidence interval; UPR: Urine protein; eGFR: Estimated glomerular filtration rate; NR: No response; PR: Partial remission; CKD: Chronic kidney disease; SDI: SLICC Damage ndex

S4.6. **Immunogenicity and safety of vaccines against SARS-CoV2 in patients with SLE**

Study	Design	N - Vaccine	COVID-19	Humoral Immunogenicity	AE	SLE flares	Risk of bias
Naveen, Rheumatology, 2022 [77]	Cross-sectional	583 – 54% mRNA	NA	NA	Minor: 83.0%; Major: 2.6%, Hospitalization: 0.2	NA	Not applicable
Mok, Vaccine, 2022 [78]	Retro	449 (+465 unvacc.) – 61.5% mRNA	NA	NA	NA	8.2% vs. 6.2% in unvaccinated – OR 1.40 [0.81–2.43]	Poor
Zavala-Flores, Clin Rheumatol, 2022 [79]	Prospective	100 - mRNA	NA	NA	90-92% (severe NR)	9% after 1st – 20% after 2nd dose (2% severe)	Poor
Boedecker-Lips, Rheumatology, 2022 [80]	Cross-sectional	50 (30 BEL, 20 no BEL)	NA	80% after 2, 90% after 3 vaccinations	NA	NA	Not applicable
Gerosa, Vaccines, 2022 [81]	Retro	452 – 98% mRNA	17%	NA	26.3%	4% (1% severe)	Fair
Wang, Biomed Pharmacother, 2022 [82]	Cross-sectional	60 (+ 70 RA, 35 HC) - Sinovac	NA	50%	25% (0% severe)	NA	Not applicable
So, Ther Adv Musculoskelet Dis, 2022 [83]	Prospective	65 (+ 50 HC) – 59%mRNA – 41% inactivated	0%	NA	82% (0% severe)	No change in SLEDAI – 0% flares	Fair
Yuki, Arthritis Care Res, 2022 [84]	Prospective	232 (+ 58 non-SLE controls) - Sinovac	4%	62-70%	59% (0% severe)	No change in SLEDAI	Fair
Moyon, Ann Rheum Dis, 2022 [85]	Prospective	126 - mRNA	NA	57% (0% severe)	0% severe	2% (0% severe) - No change in SLEDAI or BILAG	Good
Izmirly, Arthritis Rheumatol, 2022 [86]	Prospective	90 (+ 20 controls) – 94.5% mRNA	NA	71%	NA	11% (1% severe)	Poor
Ammitzbøl, ACR Open Rheumatol, 2021 [87]	Prospective	61 (+ 73 RA) - mRNA	NA	89%	NA	NA	Fair

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Study	Design	N - Vaccine	COVID-19	Humoral Immunogenicity	AE	SLE flares	Risk of bias
Mormile, Vaccines, 2022 [88]	Prospective	41 - mRNA	NA	100%	0% severe	No change in mean SLEDAI (24% increased SLEDAI)	Poor
Yoshida, Lupus Sci Med, 2022 [89]	Prospective	150 - mRNA	NA	NA	NA	No increased risk of flares	Good
Larsen, Clin Exp Rheumatol, 2023 [90]	Prospective	123 - 93.5% mRNA	31.7% (all mild)	83% after 2nd dose – 93.5% after 3rd	91% (0% severe)	No change in SLAQ and SDI	Fair
Assawasaksakul, Lupus Sci Med, 2022	Prospective	71	0%	97%	91% (0% severe)	7% after 4th dose	Poor
Assawasaksakul, Vaccines, 2022 [91]	Prospective	64	NA	81%	86%	0%	Poor
Tang, Clin Exp Med, 2022 [92]	Cross-sectional	188 (+ 190 HC) - Sinovac	NA	NA	44% (0% severe)	1%	Not applicable
Barbhaiya, Clin Rheumatol 2022, [93]	Cross-sectional	136 – 97% mRNA	NA		61-71% (0% severe)	1st dose: 6% (1% severe) 2nd dose: 3% (0% severe)	Not applicable
Bartels, Clin Rheumatol 2022 [94]	Cross-sectional	128 - mRNA	NA	NA	98%	0% severe flares	Not applicable
Rider, Rheumatology, 2022 [95]	Cross-sectional	763 – 74% mRNA			44% (self-reported)	7% self-reported (severity not reported)	Not applicable
Ferri, J Autoimmun, 2022 [96]	Prospective	38 - mRNA	NA	87%	45%	5% (0% severe)	Poor
Fornaro, J Rheumatol, 2022 [97]	Prospective	68 - mRNA	NA	NA	53% after 1st dose 67% after 2nd dose Severity not reported	No change in mean SLEDAI	Poor
Felten, Lancet Rheumatol, 2022 [98]	Cross-sectional	696 – 66% mRNA, 23% inactivated	0%	NA	45% after 1st dose 53% after 2nd dose (17% severe)	3% (2% severe)	Not applicable

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SARS-CoV2: Severe acute respiratory syndrome coronavirus 2; SLE: Systemic lupus erythematosus; AE: Adverse events; NA: Not available; OR: Odds ratio; BEL: Belimumab; RA: Rheumatoid arthritis; HC: Healthy controls; SLEDAI: Systemic lupus erythematosus disease activity index; BILAG: British Isles lupus assessment group index; SLAQ: Systemic lupus erythematosus activity questionnaire; SDI: Systemic damage index

S4.7. **Administered therapies and response to SARS-CoV2 vaccination in SLE patients**

Study	Design	N - Vaccine	Therapy received and associations	Risk of bias
Garcia-Cirera, Sci Rep, 2022 [99]	Cross-sectional	39 – Not specified	GC (75% decrease) and RTX (89% decrease) associated with reduced neutralizing antibody levels within 3-6 months (multi)	Poor
So, Ther Adv Musculoskelet Dis, 2022 [83]	Prospective	65 (+ 50 HC) – 59%mRNA – 41% inactivated	MMF significantly associated with lower levels of neutralizing antibody (β = -15.2, 95% CI -24.4 - -6.0, p 0.002); Dose of GC significantly associated with lower levels of neutralizing antibody (β = -2.01, 95% CI -3.66 - -0.37, p = 0.018) (multi)	Fair
Yuki, Arthritis Care Res, 2022 [84]	Prospective	232 (+ 58 non-SLE controls) - Sinovac	GC and MMF use independently associated with lower seroconversion (P < 0.001) and NAb positivity (P < 0.001) (multi)	Fair
Moyon, Ann Rheum Dis, 2022 [85]	Prospective	126 - mRNA	Use of MMF or MTX is associated with reduced vaccine efficacy; Use of GC, HCQ, belimumab not associated	Good
Izmirly, Arthritis Rheumatol, 2022 [86]	Prospective	90 (+ 20 controls) – 94.5% mRNA	Use of any immunosuppressant or Pz prior to vaccination associated with decreased vaccine responses	Poor
Ammitzbøl, ACR Open Rheumatol, 2021 [87]	Prospective	61 (+ 73 RA) - mRNA	Only 4/17 pts (24%) receiving RTX mounted Ab response against SARS-CoV2 (15 RA - 2 SLE) (OR 0.07; 95% CI, 0.02-0.26) (multi)	Fair

SARS-CoV2: Severe acute respiratory syndrome coronavirus 2; SLE: Systemic lupus erythematosus; GC: Glucocorticoids; RTX: Rituximab; HC: Healthy controls; MMF: Mycophenolate mofetil; CI: Confidence interval; NAb: neutralizing antibodies; MTX: Methotrexate; HCQ: Hydroxychloroquine; Pz: Prednisone; OR: Odds ratio

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