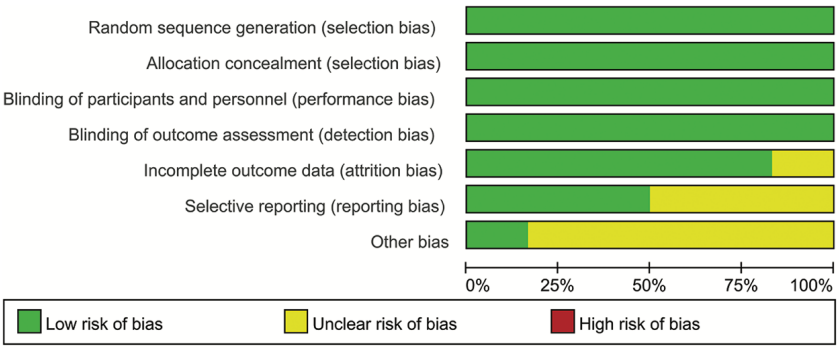
Supplementary Table S1. Characteristics of all the studies included in the meta-analysis.

Author	Year	Recruitment time	Inclusion criteria	Exclusion criteria
Fleischmann R.M.	2019	2015.12 2017.10	Patients ≥18 years. Diagnosis of RA for greater ≥ 3 months. Subjects on MTX therapy ≥3 months and on a stable prescription ≥15 to 25 mg/week (or ≥10 mg/week in subjects intolerant of MTX ≥12.5 mg/week) for ≥4 weeks prior to the first dose of study drug. Subjects take dietary supplements of folic acid or leucovorin during the process. Minimum disease activity criteria ≥ 6 swollen joints (based on 66 joint counts) and ≥ 6 tender joints (based on 68 joint counts) at Screening and Baseline Visits. At least one of the following at Screening: ≥3 bone erosions on x-ray OR ≥1 bone erosion and a positive rheumatoid factor OR ≥1 bone erosion and a positive anti-cyclic citrullinated peptide autoantibodies. Subjects with prior exposure to only one bDMARD (except adalimumab) may be enrolled (up to 20% of total study population) if they have documented evidence of intolerance to the bDMARD or limited exposure (less than 3 months), but required washout periods need to be satisfied. Deactivated csDMARD, except for MTX.	Prior exposure to any JAK (including but not limited to tofacitinib, baricitinib, and filgotinib). Investigators exposed to adalimumab are subjects who have had an inadequate response to bDMARD therapy. History of inflammatory joint disease other than RA. History of secondary Sjogren's syndrome is permitted.
Keystone E.C.	2017	2012.1 2015.3	Have a diagnosis of adult-onset RA as defined by the ACR/EULAR 2010 Criteria for the Classification of RA. Have moderately to severely active RA defined as the presence of at least 6/68 tender joints and at least 6/66 swollen joints. Have a C-reactive protein or high-sensitivity Have a CRP or hsCRP measurement ≥6 mg/L. Have had regular use of MTX for at least the 12 weeks prior to study entry at a dose that is considered acceptable to adequately assess clinical response. Have ≥1 joint erosion in hand, wrist, or foot joints based on radiographic interpretation by the central reader and be rheumatoid factor or anti-CCP antibody positive; or ≥3 joint erosions in hand, wrist, or foot joints based on radiographic interpretation by the central reader regardless of rheumatoid factor or anti-CCP antibody status.	Are currently receiving corticosteroids at doses >10 mg of prednisone per day (or equivalent) or have been receiving an unstable dosing regimen of corticosteroids within 2 weeks of study entry or within 6 weeks of planned randomisation. Have started treatment with NSAIDs or have been receiving an unstable dosing regimen of NSAIDs within 2 weeks of study entry or within 6 weeks of planned randomization. Are currently receiving concomitant treatment with MTX, hydroxychloroquine, and sulfasalazine or cDMARDs. Are currently receiving or have received cDMARDs other than MTX, hydroxychloroquine (up to 400 mg/day), or sulfasalazine (up to 3000 mg/day) within 4 weeks prior to study entry Have received leflunomide in the 12 weeks prior to study entry. Have started a new physiotherapy treatment for RA in the 2 weeks prior to study entry. Have ever received any biologic DMARD. Have received interferon therapy within 4 weeks prior to study entry or are anticipated to require interferon therapy during the study. Have received any parenteral corticosteroid administered by intramuscular or intravenous injection within 2 weeks prior to study entry or within 6 weeks prior to planned randomisation or are anticipated to require parenteral injection of corticosteroids during the study. Have had ≥3 joints injected with intraarticular corticosteroids or hyaluronic acid within 2 weeks prior to study entry or within 6 weeks prior to planned randomisation. Have any condition or contraindication for adalimumab that would preclude the participant from participating in this protocol. Have active fibromyalgia that would make it difficult to appropriately assess RA activity for the purposes of this study. Have a diagnosis of any systemic inflammatory condition other than RA such as, but not limited to, juvenile chronic arthritis, spondyloarthropathy, Crohn's disease, ulcerative colitis, psoriatic arthritis, active vasculitis or gout (participants with secondary Sjögren's syndrome are not excluded). Have a diagnosis of Felty's syndrome. Have had any major surgery within 8 weeks prior to study entry or will require major surgery during

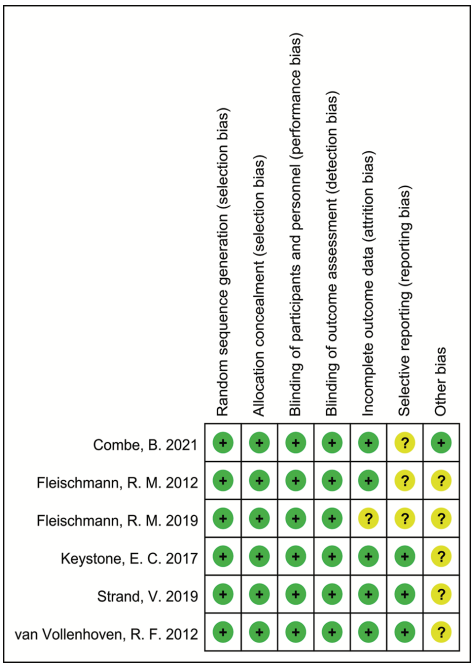
Author	Year	Recruitment time	Inclusion criteria	Exclusion criteria
Keystone E.C.	2017	2012.1 2015.3		the study that, in the opinion of the investigator in consultation with Lilly or its designee, would pose an unacceptable risk to the participant. Have experienced any of the following within 12 weeks of study entry: myocardial infarction, unstable ischemic heart disease, stroke, or New York Heart Association Stage IV heart failure Have a history or presence of cardiovascular, respiratory, hepatic, gastrointestinal, endocrine, haematological, neurological, or neuropsychiatric disorders or any other serious and/or unstable illness that, in the opinion of the investigator, could constitute a risk when taking investigational product or could interfere with the interpretation of data. Are largely or wholly incapacitated permitting little or no self-care, such as being bedridden or confined to a wheelchair. Have a history of, lymphoproliferative disease; or have signs or symptoms suggestive of possible lymphoproliferative disease, including lymphadenopathy or splenomegaly; or have active primary or recurrent malignant disease; or have been in remission from clinically significant malignancy for <5 years. Have been exposed to a live vaccine within 12 weeks prior to planned randomisation or are expected to need/receive a live vaccine during the course of the study (with the exception of herpes zoster vaccination). Have a current or recent clinically serious viral, bacterial, fungal, or parasitic infection. Have had symptomatic herpes zoster infection within 12 weeks prior to study entry Have a history of disseminated/complicated herpes zoster (*e.g*, multidermatomal involvement, ophthalmic zoster, central nervous system involvement, or postherpetic neuralgia). Are immunocompromised and, in the opinion of the investigator, are at an unacceptable risk for participating in the study. Have an HCV, or HIV. Have screening laboratory test values, including TSH, outside the reference range for the population or investigative site that, in the opinion of the investigator, pose an unacceptable risk for the participant's participation in the study. Have screening ECG abnormalities that, in the opinion of the investigator or the sponsor, are clinically significant and indicate an unacceptable risk for the participant's participation in the study Have symptomatic herpes simplex at the time of study enrolment. Have evidence of active or latent TB.
Strand V.	2019	2014.8- 2016.12	Have moderate to severe RA. On MTX but inadequately controlled. Subjects must not have active tuberculosis or an inadequately treated tuberculosis infection. Subjects must use contraception.	Subjects who have been previously treated with adalimumab or Tofacitinib. Subjects with any current malignancy or a history of malignancy, with the exception of adequately treated or excised non metastatic basal cell or squamous cell cancer of the skin or cervical carcinoma in situ. Subjects with specific laboratory test abnormalities Subjects with specific types of infections.
Combe B.	2021	2016.8- 2019.6	Have a diagnosis of RA and are ACR functional class I-III. Have ≥6 swollen joints (from a swollen joint count based on 66 joints) and ≥6 tender joints (from a tender joint count based on 68 joints) at both screening and Day 1. Ongoing treatment with a stable dose of MTX.	Previous treatment with any JAK.

Author	Year	Recruitment time	Inclusion criteria	Exclusion criteria
van Vollenhoven R.F.	2012	2009.5-2011.3	The patient has a diagnosis of RA based upon the ACR 1987 Revised Criteria. The patient must have had an inadequate response to MTX and have active disease, as defined by both: ≥6 joints tender or painful on motion; and ≥6 joints swollen; and fulfills 1 of the following 2 criteria at Screening: 1. ESR (Westergren method) >28 mm in the in the local laboratory. 2. CRP >7 mg/L in the central laboratory. No evidence of active or latent or inadequately treated infection with Mycobacterium tuberculosis. The patient must have been on a stable dose of 7.5 mg to 25 mg weekly of methotrexate and washed out of all other DMARDs.	Blood dyscrasias including con firmed: 1. Haemoglobin <9 g/dL or Haematocrit <30%; 2. White blood cell count <3,000 cu.mm. Absolute neutrophil count <1,200 cu.mm; 4. Platelet count <100,000/L. History of any other autoimmune rheumatic disease other than Sjogren's syndrome No malignancy or history of malignancy. History of infection requiring hospitalisation, parenteral antimicrobial therapy, or as otherwise judged clinically significant by the investigator, within the 6 months prior to the first dose of study drug. Patients who have failed any TNFi for either lack of efficacy or a TNFi mechanism related adverse event. Patients who have previously received adalimum-ab therapy for any reason. Patients who are contraindicated for treatment with adalimumab in accordance with the approved local label. Patients meeting the NYHA Class III and Class IV Congestive Heart failure.
Fleischmann R.M.	2012	2007.9-2009.1	Subjects must have active rheumatoid arthritis. Subjects must have failed at least 1 DMARD. Subjects must not be currently taking any DMARD other than an antimalarial.	Subjects who discontinued any previous TNF inhibitor therapy for either lack of benefit or safety. Subjects who previously received adalimumab therapy for any reason. Subjects with evidence of blood disorders, chronic infections or untreated tuberculosis.

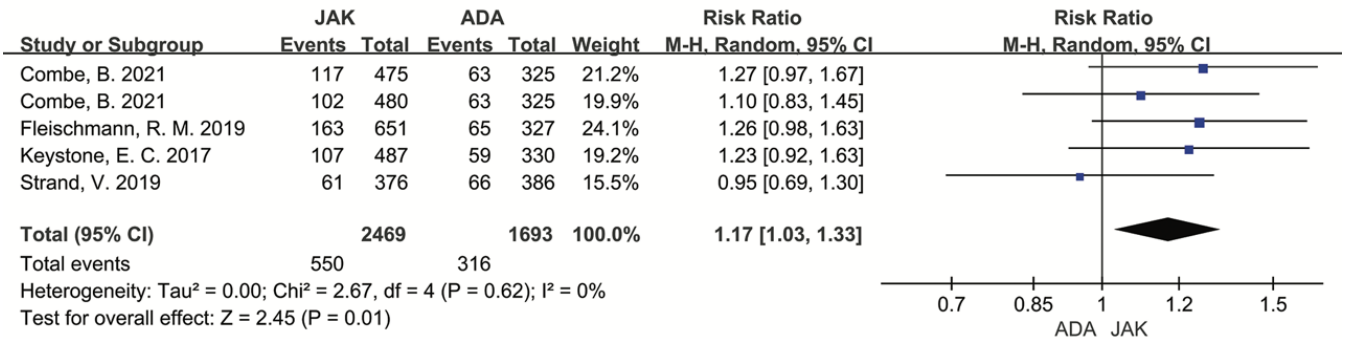
RCT: randomised controlled trial; ABT-494: upadacitinib; MTX: methotrexate; MTX-IR: methotrexate inadequate response; CP 690:550: tofacitinib; CRP: C-reactive protein; RA: rheumatoid arthritis; JAK: Janus kinase inhibitor; ACR/EULAR: American College of Rheumatology/ European League Against Rheumatism; hsCRP: high-sensitivity C-reactive protein; Anti-CCP: anticyclic citrullinated peptide; NSAIDs: non-steroidal anti-inflammatory drugs; cDMARDs: conventional disease-modifying anti-rheumatic drugs; DMARD: disease modifying anti-rheumatic drug; HBV: history of active hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; TSH: thyroid-stimulating hormone; ECG: electrocardiogram; TB: tuberculosis; ESR: erythrocyte sedimentation rate; NYHA: New York Heart Association; TNFi: tumour necrosis factor inhibitors.



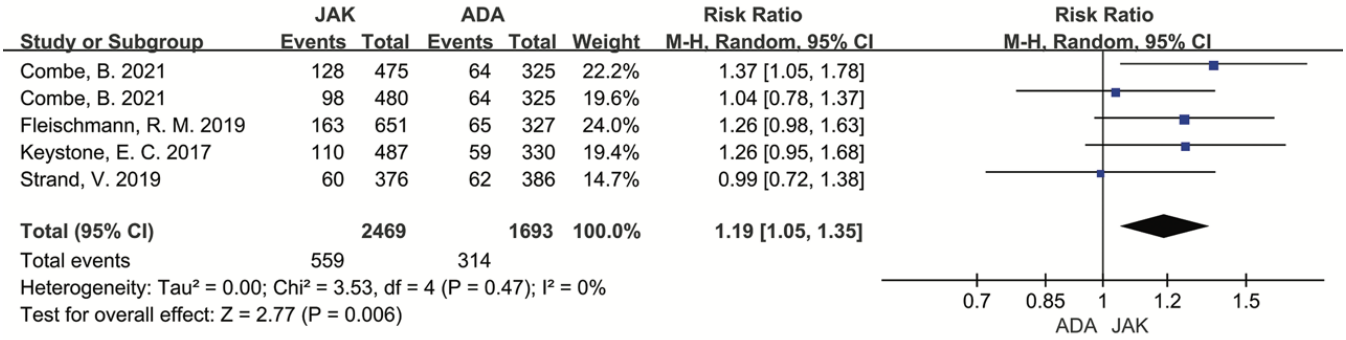
Supplementary Fig. S1. Results of testing for publication bias in a meta-analysis of differences in efficacy between JAKi and ADA for RA.



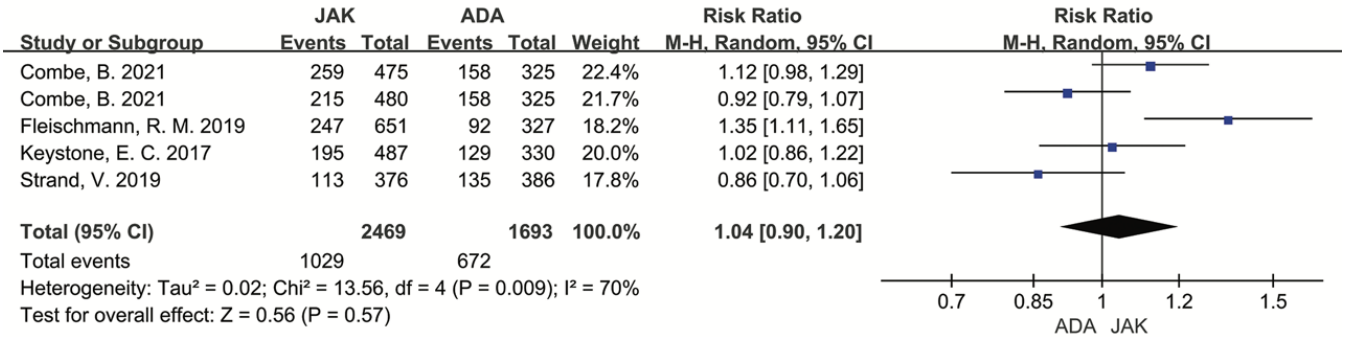
Supplementary Fig. S2. Sensitivity analysis of a meta-analysis of differences in efficacy between JAKi and ADA for RA.



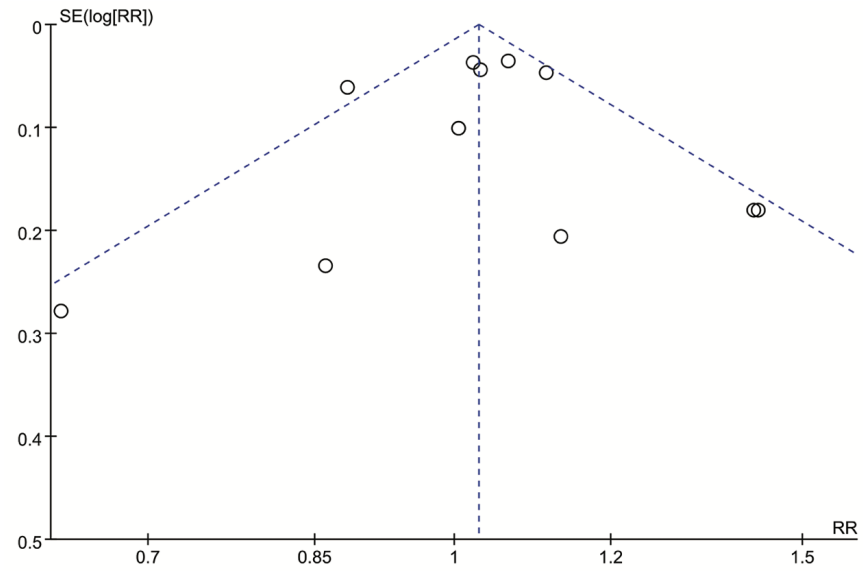
Supplementary Fig. S3. Forest plot of a meta-analysis assessing differences in efficacy of JAKi and ADA in RA using CDAI as an outcome measure.



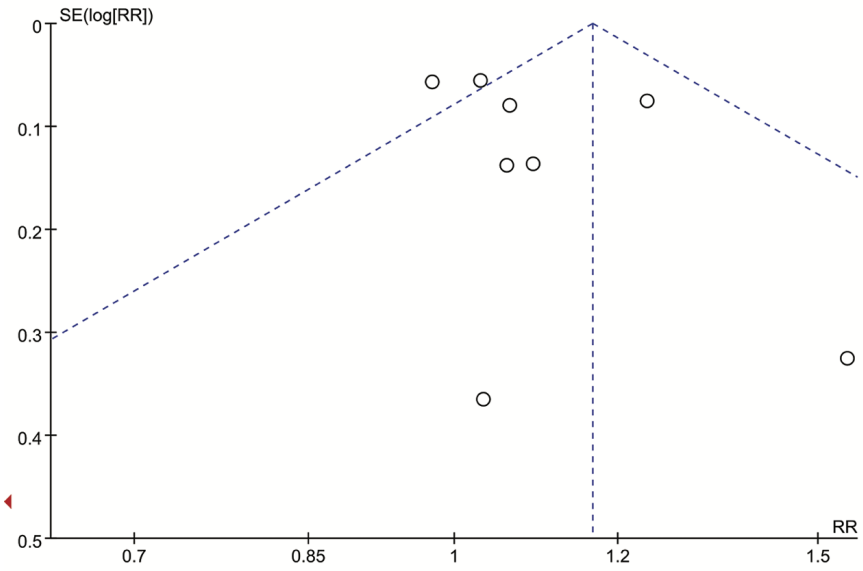
Supplementary Fig. S4. Forest plot of a meta-analysis assessing differences in efficacy of JAKi and ADA in RA using SDAI as an outcome measure.



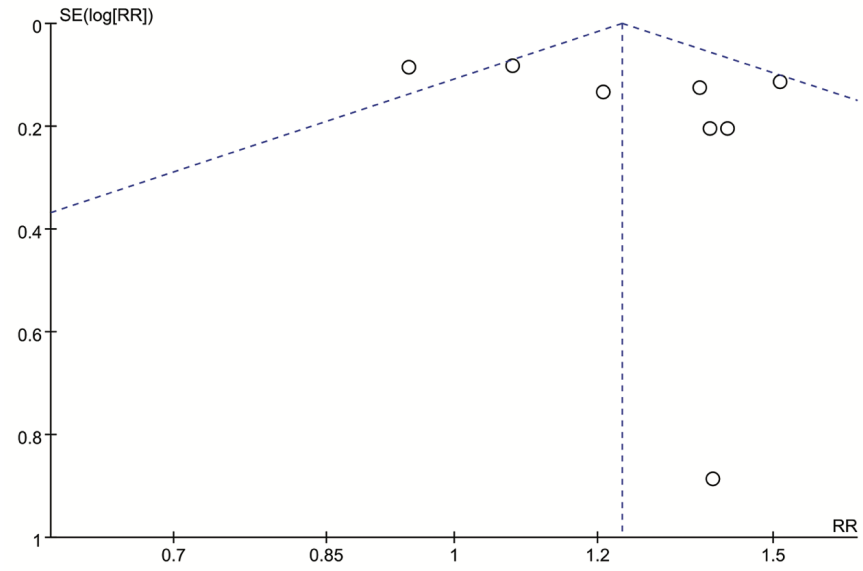
Supplementary Fig. S5. Forest plot of a meta-analysis assessing differences in efficacy of JAKi and ADA in RA using DAS 28-4 (CRP) as an outcome measure.



Supplementary Fig. S6. Funnel plot of the ACR20 in the meta-analysis.



Supplementary Fig. S7. Funnel plot of the ACR50 in the meta-analysis.



Supplementary Fig. S8. Funnel plot of the ACR70 in the meta-analysis.