

ONLINE SUPPLEMENT

Supplementary Table 1. Studies of medication as risk factor for tuberculosis

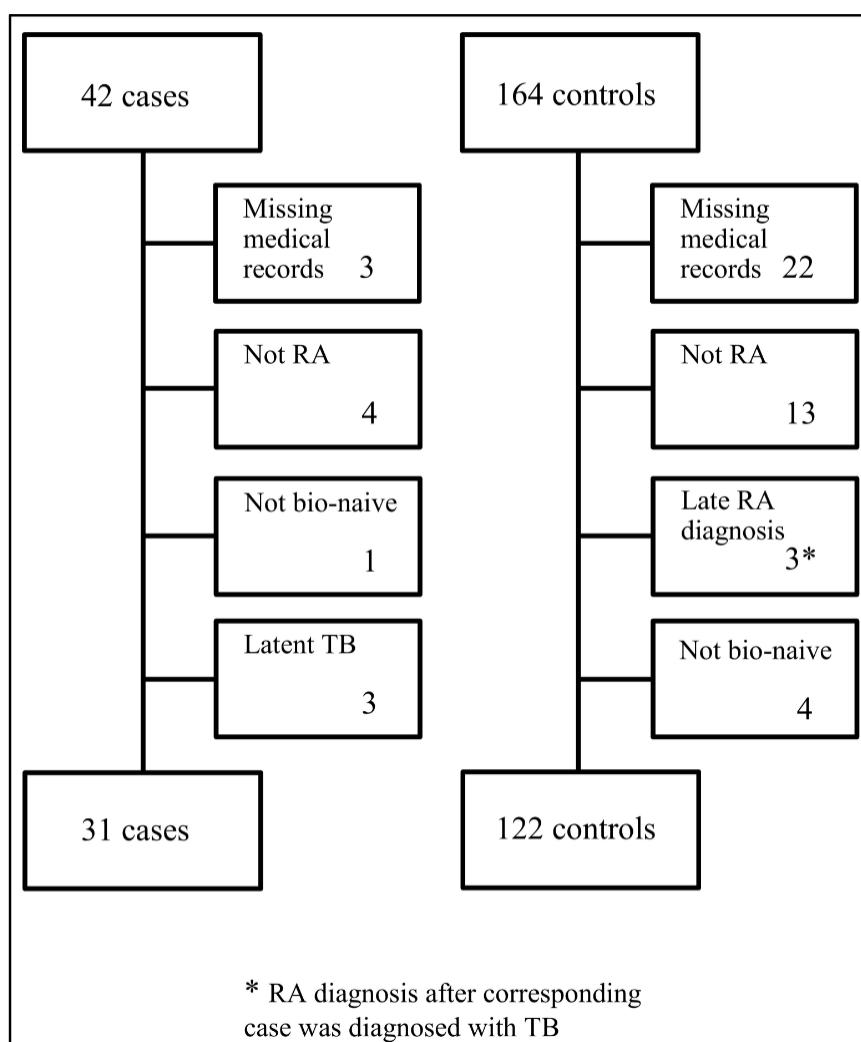
Author Year of publication	Country	Participants	Risk factor /Treated patients	Result ¹
Vadillo Font, 2003 (7)	Spain	3634 patients with auto-immune diseases (RA included)	Methotrexate /NA	Incidence by drugs in RA patients 143/100 000 patient-years for methotrexate
Breedveld, 2006 (8)	Australia, Europe, North America	257 RA patients	Methotrexate /257	No TB cases in 2 years follow up
Brassard, 2009 (9)	Canada	24 282 RA patients (50 TB) ²	Methotrexate /483 24 cases, 254 controls	Association with TB RR 3.4 (1.8-6.4)
Emery, 2010 (10)	Europe	99 RA patients	Methotrexate /99	No TB cases in 2 years follow up
Brode, 2015 (11)	Canada	56 269 RA patients (37 TB) ³	Methotrexate /119 12 cases, 107 controls	No association with TB
Matsuoka , 2018 (12)	Japan	Inflammatory Rheumatological diseases ⁴	Methotrexate /NA	Association with TB OR 4.6 (3.6-5.9)
Brassard, 2006 (13)	Canada	112 300 RA patients (386 TB) ⁵	Traditional DMARDs ⁶ / 17 232 196 cases, 17 036 controls	Association with TB RR 1.2 (1.0-1.5)
Brassard, 2009 (9)	Canada	24 282 RA patients (50 TB) ²	Leflunomide /10 3 cases, 7 controls	Association with TB RR 11.7 (2.1-65.1)
Yoo, 2013 (14)	South Korea	401 RA patients	Leflunomide /401 4 cases	4 patients with TB, 2.9/100 patient-years
Brode, 2015 (11)	Canada	56 269 RA patients (37 TB) ³	Leflunomide /26 6 cases, 20 controls	Association with TB OR 4.02 (1.1-15)
Guiajao-Arrabal, 2016 (15)	Spain	398 lung transplanted patients (6 TB)	Azathioprin and mTOR inhibitors /145	Association with TB 406.3 cases/100 000 patient-years
Kim, 1998 (16)	South Korea	269 rheumatic disease patients (no RA)	Corticosteroids /269 21 cases, 248 controls	Cumulative dose of cs and mean daily dose significantly higher in TB cases $p <0.001$
Jick, 2006 (17)	United Kingdom	497 TB cases, 1966 controls, among cases and controls 17 RA patients ⁷	Corticosteroids /278 Current use: 51 cases, 38 controls Recent use: 10 cases, 10 controls	Association with TB Current use: OR 4.9 (2.9-8.3) Recent use: OR 4.3 (1.6-11.1)

			Past use: 41 cases, 120 controls	Past use: OR 1.4 (0.9-2.1) Use <15 mg/ day: OR 2.8 (1.0-7.9) Use ≥15 mg/ day: OR 7.7 (2.8-21.4)
Agrawal, 2000 (18)	India	77 patients with respiratory diseases on cs, and 80 controls	Corticosteroids /157	5 of the patients with cs developed TB, none of the controls, p <0.05
Brassard, 2006 (13)	Canada	112 300 RA patients (386 TB)	Corticosteroids /4494 73 cases, 4421 controls	Association with TB RR 1.7 (1.3-2.2)
Brassard, 2009 (9)	Canada	24 282 RA patients (50 TB)	Corticosteroids /131 9 cases, 122 controls	Association with TB RR 2.4 (1.1-5.4)
Lai, 2015 (19)	Taiwan	6229 TB cases, 622900 controls ⁸	Corticosteroids/55910	Association with TB Current use: RR 2.8 (2.4-3.1) Recent use: RR 2.0 (1.7-2.3) Ever use: RR 1.6 (1.5-1.7)
Brode, 2015 (11)	Canada	56 269 RA patients (37 TB)	Corticosteroids /143 22 cases, 121 controls	No association with TB
Lai, 2017 (20)	Taiwan	6021 TB cases, 6021 population based controls ⁸ No information about RA comorbidity	Corticosteroids /5562 3230 cases, 2332 controls	Association with TB Ever use: OR 1.9 (1.7-2.1) OR for increasing cumulative dose: 1.03 (1.02-1.03)/mg Use <3 months: OR 1.8 (1.6-2.1) Use >3 months: OR 2.1 (1.9-2.4)

¹ RR and OR are presented as adjusted results with 95% confidence interval, ² Quebec billing and hospitalization databases, ³ Population based case –control study, ⁴ National data base, ⁵ PharMetrics Patient Center Database, ⁶ Treatment with any of the following: methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, auranofin, cyclosporine, penicillamine and cyclophosphamide, ⁷ General Practice Research Database, ⁸ National Health Insurance Data Base

RA= rheumatoid arthritis; TB= tuberculosis; DMARD= disease modifying anti-rheumatic drug; RR=relative risk; OR=odds ratio; cs=corticosteroids

Supplementary Figure 1. Overview of inclusion of patients in the study, identified from Swedish national registers.



RA= rheumatoid arthritis; bio-naïve=biologics-naïve; TB=tuberculosis

Cases= Biological-naïve RA patients with active TB Controls= Biological-naïve RA patients without active TB