Appendix 1. Mycobacterial specimen culture methods.

Specimens were processed and analyzed as described by Hanna *et al*.(1) Cultures were set-up in liquid media using the BACTEC MGIT 960 system (Becton Dickinson, Franklin Lakes, NJ) and on solid Lowenstein-Jensen media. Speciation was performed using DNA probes (AccuProbe, Gen-Probe, San Diego, California, USA) for *M. avium* complex (MAC) and *M. gordonae*, and by high performance liquid chromatography (HPLC) for all other species until 2008, and thereafter by commercial line-probe assay (GenoType, Hain Lifescience, Germany). The mycobacteria database included personal identifiers, specimen collection date, anatomic source of the specimen, and organ identified. We excluded *M. gordonae* from the NTM outcomes because it is usually a contaminant and is infrequently associated with significant disease.(2)

References

1. Hanna BA, Ebrahimzadeh A, Elliott LB, et al. Multicenter evaluation of the BACTEC MGIT 960 system for recovery of mycobacteria. J Clin Microbiol 1999;37:748-52.
2. Arnow, P.M., et al., Endemic contamination of clinical specimens by *Mycobacterium gordonae*. Clinical Infectious Diseases, 2000. **31**(2): p. 472-6.

Appendix 2. NTM isolation data.

NTM isolation (NTMi) was defined as any culture positive for NTM from any body site.

Table 1. Baseline characteristics on the index date for NTM isolation cases and controls*

Characteristic	NTMi cases N = 338	NTMi controls N = 3319	SDM†
Female	220 (65)	2170 (65)	0.01
Age, mean +/- SD	76.8 +/- 6.1	76.7 +/- 6.0	0.02
RA duration (yrs), mean +/- SD	8.9 +/- 5.4	8.9 +/- 5.3	0.01
High income	193 (57)	1955 (59)	0.04
Rural residency	20 (6)	507 (15)	0.27
Extra-articular RA: Lung Skin Other	70 (21) 42 (12) 7 (2)	246 (7) 331 (10) 46 (1)	0.48 0.08 0.06
ADGs, mean +/- SD	11.1 +/- 3.4	8.8 +/- 3.6	0.65
Asthma	131 (39)	623 (19)	0.50
COPD	214 (63)	1040 (31)	0.69
GERD	99 (29)	806 (24)	0.12
CKD	45 (13)	374 (11)	0.06
Diabetes	83 (25)	861 (26)	0.03

* Values are the number of patients (%) unless otherwise indicated. †SDM = standardized difference of the mean; >0.1 (10%) implies a meaningful imbalance between groups (1). Abbreviations: NTMi = nontuberculous mycobacterial isolation, SDM = standardized difference of the mean, RA = rheumatoid arthritis, SD = standardized deviation, ADGs = aggregated diagnostic groups, COPD = chronic obstructive pulmonary disease, GERD = gastro-esophageal reflux disease, CKD = chronic kidney disease.

Table 2. Odds ratios (ORs) for NTM isolation according to anti-rheumatic medication use

Exposure	Crude OR (95% CI)	p-value	Adjusted OR* (95% CI)	p-value
Anti-TNF use				
No use	1.0 (ref)		1.0 (ref)	
Past use	**3.20 (1.04-9.81)**	0.04	2.6 (0.63-10.46)	0.18
Current use	**1.91 (1.15-3.18)**	0.01	**1.88 (1.07-3.32)**	0.03
Oral corticosteroids				
Non-current use	1.0 (ref)		1.0 (ref)	
Low dose	1.24 (0.91-1.71)	0.18	0.89 (0.63-1.25)	0.50
Mod dose	**3.06 (2.12-4.41)**	<0.001	**1.99 (1.33-2.97)**	<0.001
High dose	**3.90 (2.86-5.32)**	<0.001	**2.55 (1.81-3.59)**	<0.001
Methotrexate				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	**1.31 (1.04-1.67)**	0.02	**1.39 (1.06-1.81)**	0.02
Leflunomide				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	**2.27 (1.56-3.30)**	<0.001	**1.85 (1.22-2.81)**	0.004
Sulfasalazine				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	0.83 (0.49-1.41)	0.49	0.79 (0.44-1.41)	0.43
Hydroxychloroquine				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	**1.31 (1.01-1.70)**	0.04	1.24 (0.94-1.65)	0.13
High risk DMARD†				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	**2.74 (1.57-4.78)**	<0.001	1.81 (0.91-3.60)	0.09
Low risk DMARD∞				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	1.34 (0.60-3.02)	0.48	1.83 (0.74-4.52)	0.19
NSAID				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	0.92 (0.73-1.16)	0.49	1.06 (0.81-1.37)	0.68
PPI				
Non-current use	1.0 (ref)		1.0 (ref)	
Current use	**1.33 (1.06-1.67)**	0.01	0.91 (0.70-1.17)	0.46

Bolded odds ratio values are statistically significantly different than reference group. *Adjusted for income, rurality, presence of extra-articular RA, other anti-rheumatic medication use, ADGs (aggregated diagnostic groups), and comorbidities (asthma, chronic obstructive pulmonary disease, and gastro-esophageal reflux disease). †High risk DMARDs include cyclophosphamide, azathioprine, cyclosporine, mycophenolate, and chlorambucil. ∞Low risk DMARDs include gold and penicillamine. Abbreviations: NTMi = nontuberculous

mycobacteria isolation, OR = odds ratio, CI = confidence interval, anti-TNF = anti-tumor necrosis factor, DMARD = disease modifying anti-rheumatic drug, NSAID = non-steroidal anti-inflammatory, PPI = proton pump inhibitor.

Reference

1. Austin PC, Grootendorst P, Anderson GM. A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. *Statistics in Medicine* 2007; 26(4): 734-53.

Appendix 3. NTM species data

Table 1. NTM species causing disease among RA patients, by number of cases and percent

Site	NTM species	Number of cases	Percent
Any site	MAC	116	55
	M. xenopi	55	26
	RGM	21	10
	Other	19	9
Pulmonary	MAC	110	60
	M. xenopi	55	30
	RGM	9	5
	Other	10	5
Non-pulmonary	MAC	6	22
	M. xenopi	0	0
	RGM	12	44
	Other	9	33

MAC = *Mycobacterium avium* complex, RGM = Rapid growing mycobacteria - includes *M. abscessus, M. chelonae, and M. fortuitum*

Table 2. NTM species causing disease among RA patients by anti-TNF usage

	All cases		Current anti-TNF		Non-current anti-TNF*	
	N	%	N	%	N	%
MAC	116	55	6	40	110	56
All others	95	45	9	60	86	44

MAC = *Mycobacterium avium* complex, anti-TNF = anti-tumor necrosis factor.
 *Non-current anti-TNF use includes past anti-TNF use and no anti-TNF use. These two categories were grouped together because there were too few individuals with prior use to allow us to report NTM species in this group (in accordance with data use restrictions, cells containing fewer than six individuals cannot be reported).