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Living with rheumatic disease in the pandemic

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Inflammation, immunosuppression and infection

"Not surprised you got pneumonia – you're taking methotrexate"

Inflammation, immunosuppression and infection

"Not surprised you got pneumonia – you're taking methotrexate"

- May be true for some treatments – corticosteroids, cancer chemotherapy
- Evidence from pre-COVID-19 studies did not support it

Inflammation, immunosuppression and infection

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TABLE 2. Crude and adjusted RR, by drug exposure, 1 January 1980 to 31 December 2003

	All infections requiring hospitalization (ICD 9 codes 001–139, 480–486)				
	Cases ($n = 1970$)	Controls ($n = 19\ 700$)	Crude	Adjusted[a]	
Drug exposure[b]	Number exposed	Number exposed	RR	RR	(95% CI[c])
Methotrexate	697	5937	1.29	1.10	(0.98–1.23)
Azathioprine	87	364	2.46	1.52	(1.18–1.97)
Cyclophosphamide	73	116	6.75	3.26	(2.28–4.67)
Anti-malarial agents[d]	542	5350	1.02	1.06	(0.94–1.19)
Anti-TNF agents[e]	5	24	2.14	1.93	(0.70–5.34)
All other DMARDs[f]	347	3403	1.03	0.92	(0.80–1.05)
Glucocorticoids	1344	8150	3.20	2.56	(2.29–2.85)
	Pneumonia only (ICD-9 codes 480–486)				
	Cases ($n = 1315$)	Control (13 150)	Crude	Adjusted	
Drug exposure	Number exposed	Number exposed	RR	RR	(95% CI)
Methotrexate	477	3856	1.41	1.16	(1.02–1.33)
Azathioprine	52	259	2.06	1.30	(0.94–1.79)
Cyclophosphamide	31	66	4.87	2.64	(1.60–4.36)
Anti-malarial agents	368	3551	1.06	1.06	(0.92–1.22)
Anti-TNF agents	3	20	1.54	1.29	(0.36–4.67)
All other DMARDs	230	2180	1.07	0.99	(0.84–1.16)
Glucocorticoids	906	5529	3.22	2.07	(2.37–3.08)

[a]Cases and controls are age- and gender-matched. All variables are adjusted for each other and for number of physician visits. [b]Drug exposure is the prescription within the 45 days prior to the index date; includes both oral and parenteral exposures, where applicable. [c]CI, confidence interval. [d]Anti-malarial agents include hydroxychloroquine and chloroquine. [e]TNF tumour necrosis factor; these were first listed on the population provincial formulary only in 2002. [f]DMARD, disease-modifying anti-rheumatic drug. All other DMARDs: sulphasalazine, leflunomide, cyclosporine, gold compounds, minocycline, penicillamine.

Bernatsky S. *et al*. Anti-rheumatic drug use and risk of serious infections in rheumatoid arthritis. Rheumatology 2007;46;1157–1160

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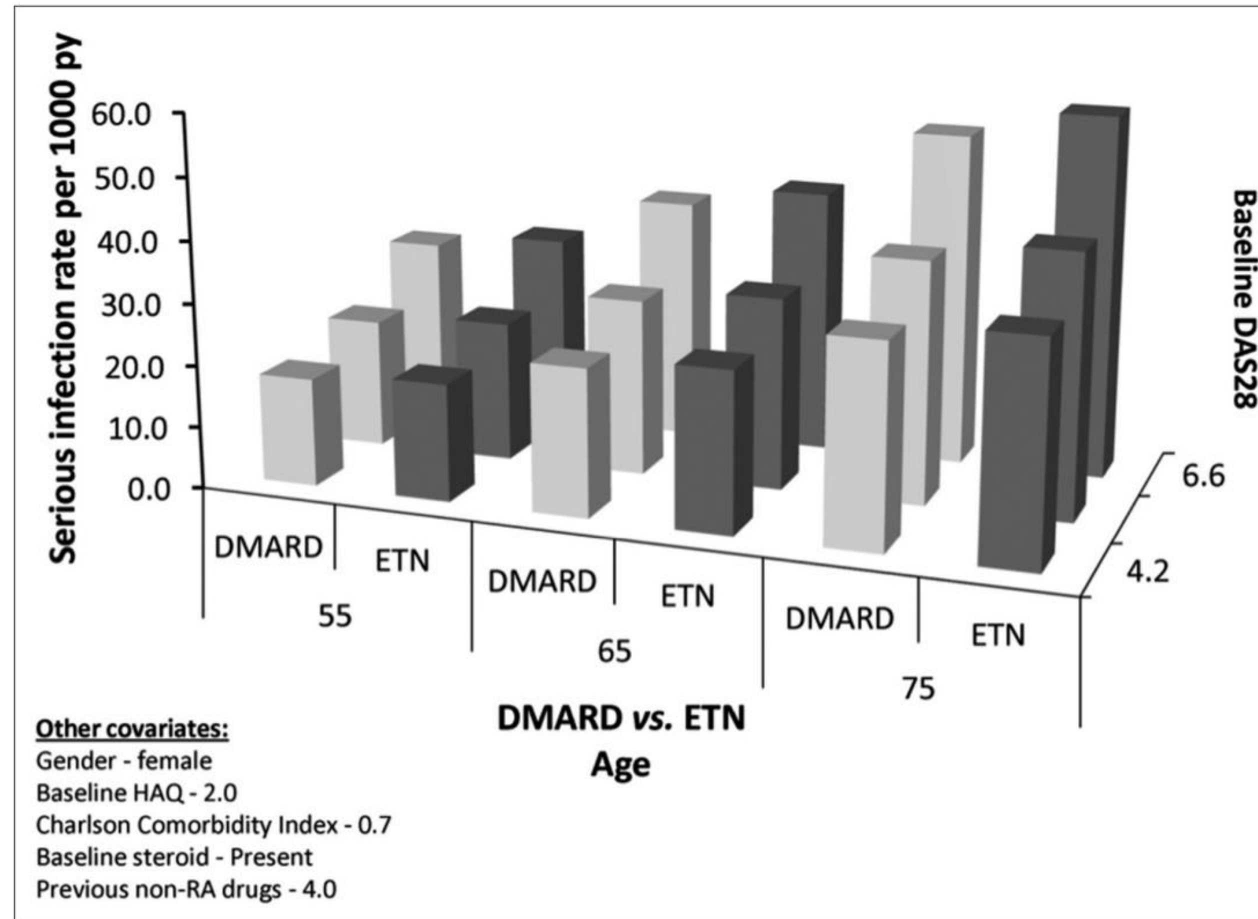
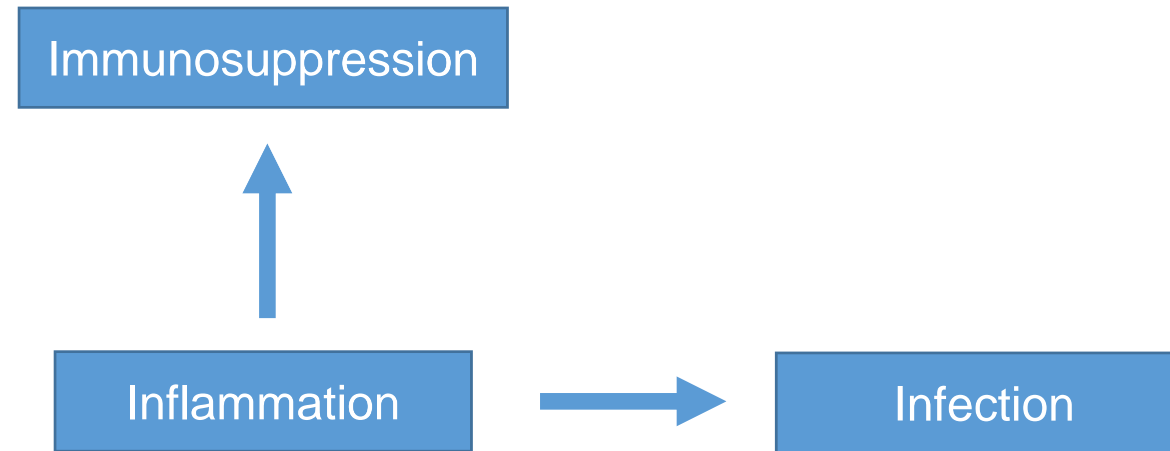


Fig. 2. Serious infection risk per 1000 py for patients treated with ETN *versus* DMARDs by age and DAS28 score.
The data presented are based on predictions generated from a parametric model.

Emery *et al.* Clinical and Experimental Rheumatology 2014; 32: 653-660.

Inflammation, immunosuppression and infection



- Infection risk conferred by underlying disease more than treatment

March 2020

The COVID-19 pandemic

"On those drugs, if you catch COVID-19, you will DIE!"

The COVID-19 pandemic

Factors to consider:

- Little was known about SARS-CoV2 and DMARD use
- DMARDs like MTX, SSZ, LEF and TNFi biologics have minimal effect on infection risk
- Corticosteroids, cyclophosphamide and azathioprine might increase risk
- OTOH a robust immune system might not be much help in naïve patients…
- …and might be harmful

The COVID-19 pandemic

Factors to consider:

- Risk of exposure to SARS-CoV2 was low during lockdown
- Stopping DMARDs would result in flares that might increase infection risk
- High disease activity increases infection risk
- Flares treated with corticosteroids
- Breaking lockdown to seek treatment
- ***Patients therefore advised to continue treatment and minimize CS use***

The COVID-19 pandemic

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Table 3 Unadjusted and adjusted logistic regression models examining the association between demographic and clinical characteristics and COVID-19 hospitalisation status

	No. hospitalised/ No. cases (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	P value*
Female	185/423 (44)	0.72 (0.51 to 1.02)	0.83 (0.54 to 1.28)	0.39
Age >65 years	119/170 (70)	4.02 (2.74 to 5.89)	2.56 (1.62 to 4.04)	<0.01
Rheumatic disease diagnosis†				
Rheumatoid arthritis	104/225 (46)	*Ref*	*Ref*	--
Systemic lupus erythematosus	48/85 (56)	1.51 (0.91 to 2.49)	1.80 (0.99 to 3.29)	0.06
Psoriatic arthritis	22/74 (30)	0.49 (0.28 to 0.86)	0.94 (0.48 to 1.83)	0.85
Axial spondyloarthritis or other spondyloarthritis	16/48 (33)	0.58 (0.30 to 1.12)	1.11 (0.50 to 2.42)	0.80
Vasculitis	24/39 (62)	1.86 (0.93 to 3.73)	1.56 (0.66 to 3.68)	0.31
Other	63/129 (49)	1.11 (0.72 to 1.71)	0.94 (0.55 to 1.62)	0.82
Comorbidities (present vs not)				
Hypertension or cardiovascular disease	136/218 (62)	2.83 (1.01 to 4.00)	1.86 (1.23 to 2.81)	<0.01
Lung disease‡	83/127 (65)	2.71 (1.80 to 4.08)	2.48 (1.55 to 3.98)	<0.01
Diabetes	48/69 (70)	3.01 (1.76 to 5.18)	2.61 (1.39 to 4.88)	<0.01
Chronic renal insufficiency/end-stage renal disease	33/40 (83)	6.11 (2.66 to 14.04)	3.02 (1.21 to 7.54)	0.02
Ever smoker (vs never smoker)	68/129 (53)	1.41 (1.13 to 1.77)	1.18 (0.90 to 1.53)	0.23
Rheumatic disease medication prior to COVID-19 diagnosis§				
No DMARD	52/97 (54)	*Ref*	*Ref*	--
csDMARD only	149/272 (55)	1.05 (0.66 to 1.67)	1.23 (0.70 to 2.17)	0.48
b/tsDMARDs only	31/107 (29)	0.35 (0.20 to 0.63)	0.46 (0.22 to 0.93)	0.03
csDMARD+b/tsDMARD combination therapy	45/124 (36)	0.49 (0.29 to 0.85)	0.74 (0.37 to 1.46)	0.38
NSAIDs	39/111 (35)	0.55 (0.35 to 0.84)	0.64 (0.39 to 1.06)	0.08
Prednisone-equivalent glucocorticoids				
None	162/403 (40)	*Ref*	*Ref*	--
1–9 mg/day	67/125 (54)	1.72 (1.15 to 2.57)	1.03 (0.64 to 1.66)	0.91
≥10 mg/day	43/64 (67)	3.05 (1.74 to 5.32)	2.05 (1.06 to 3.96)	0.03

Gianfrancesco M, et al. Ann Rheum Dis 2020;79:859–866. doi:10.1136/annrheumdis-2020-217871

2021
The year of the vaccine

2021: The year of the vaccine

"Can I have the COVID vaccine?"

- 2 Feb 2021 MAAC approved the Pfizer vaccine
- The NZ government has now secured 10 million doses
- Rheumatology patients are being vaccinated in the global roll-out
- A study of the Pfizer vaccine is being conducted in RA patients – results Oct 2021
- It is not a live vaccine – there is no reason not to give it to RD patients
- No official announcement on whether RD patients will be in "Group 3"

In Summary

What have we learned?

- Inflammation (high disease activity) is a major risk factor for infection
- csDMARDs and bDMARDs have minimal impact on infection risk
- Corticosteroids increase risk of infection
- Powerful inflammation suppressing regimens may protect against risk of adverse COVID-19 outcome
- Rheumatic disease patients can and should receive COVID-19 vaccines

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For more information
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