Συννοσηρότητες στην ΡΑ: Η επίδρασή τους στην πρόγνωση και θεραπεία της νόσου

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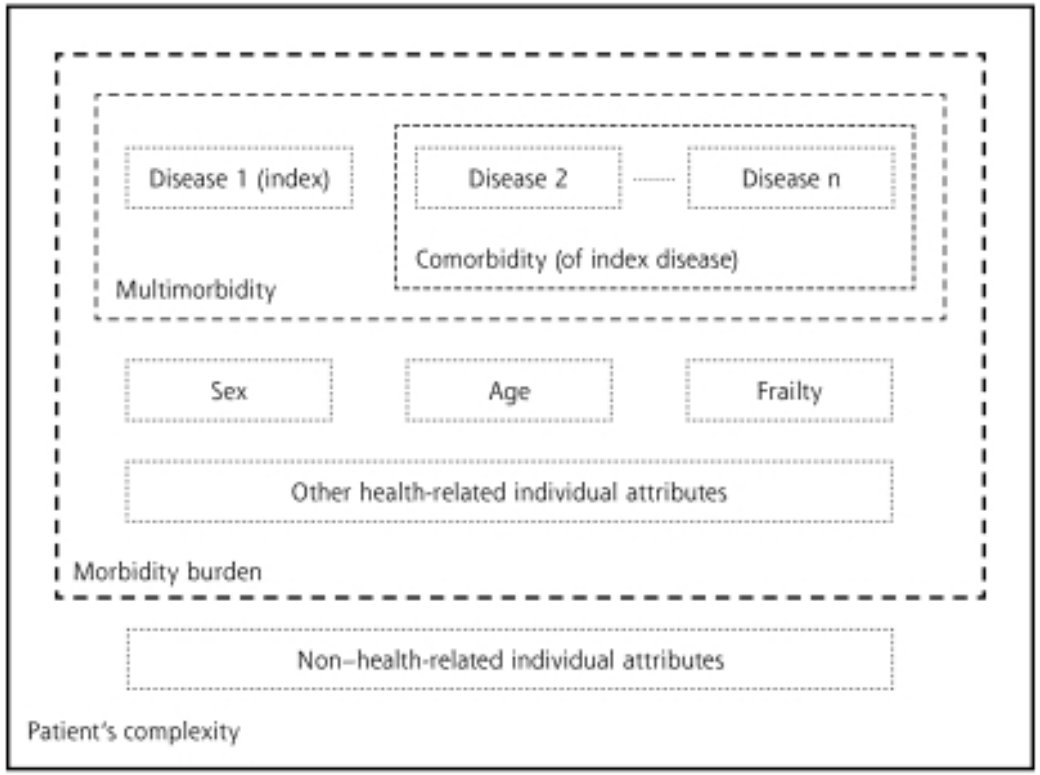
Ρευματολόγος

ΓΝΑ ΄Γ. Γεννηματάς΄

Σύγκρουση συμφερόντων

- Καμία για τη συγκεκριμένη ομιλία

Definition of comorbidity



Comorbidity: presence of additional diseases in relation to an index disease in one individual.

Multimorbidity: presence of multiple diseases in one individual.

Morbidity burden: overall impact of the different diseases in an individual taking into account their severity.

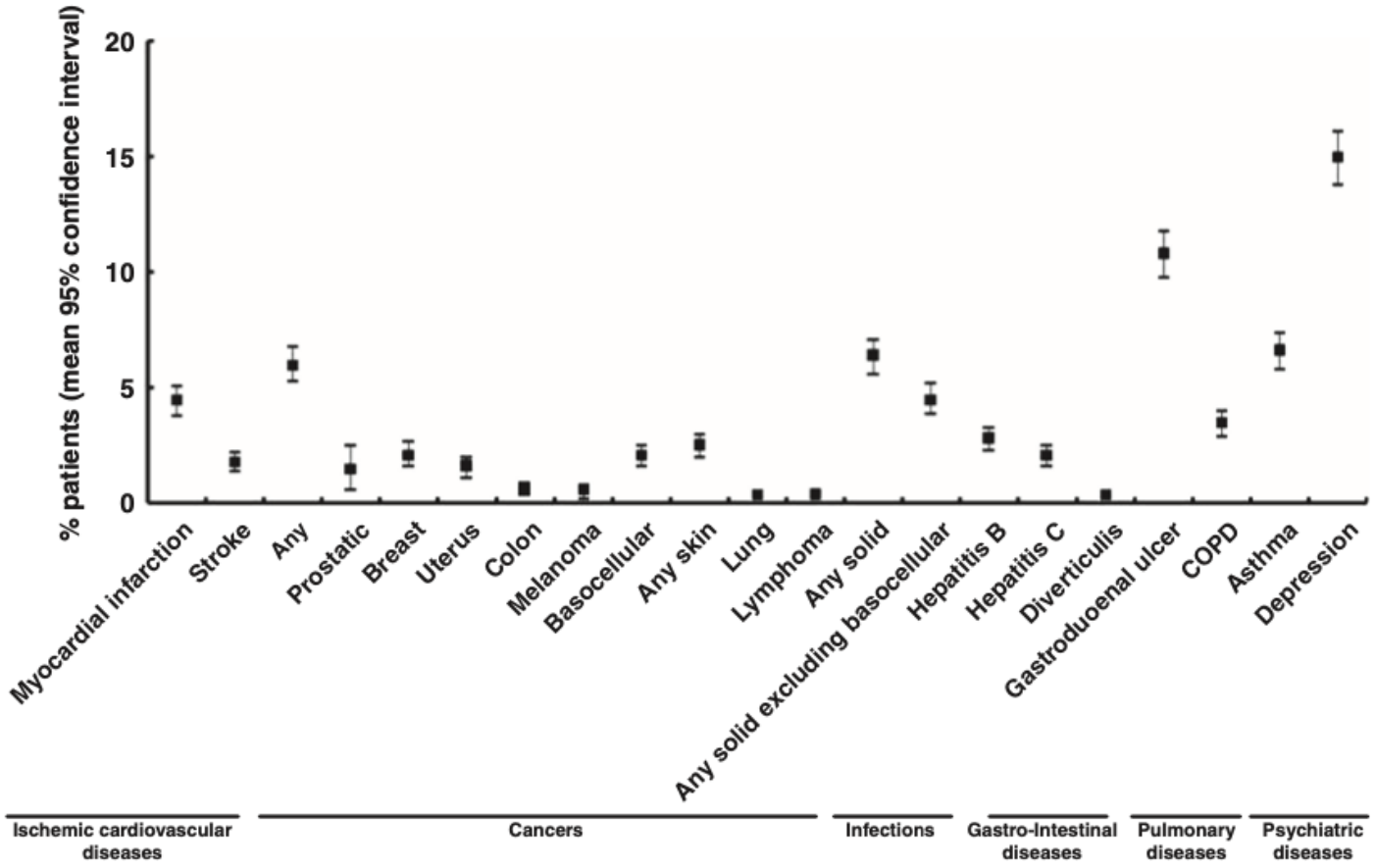
Patient's complexity: overall impact of the different diseases in an individual taking into account their severity and other health-related attributes.

Ann Fam Med 2009;7:357-363. doi:10.1370/afm.983

Prevalence of evaluated comorbidities in the 3920 patients with rheumatoid arthritis (COMORA)

The most commonly observed comorbidities:

- depression (15%)
- asthma (7%)
- cardiovascular (CV) events (myocardial infarction (MI), stroke; 6%)
- solid-organ malignancies (5%)
- chronic obstructive pulmonary disease (4%)



Dougados M, et al. Ann Rheum Dis 2014;73:62–68. doi:10.1136/annrheumdis-2013-204223

Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative

Table 2 Overarching principles and points to consider for reporting or detecting prevalent comorbidities, screening for comorbidity or for risk factors and treatments/vaccination

Overarching principles		Mean (SD) level of agreement
A. Comorbidities such as cardiovascular diseases, malignancies, infections, osteoporosis, peptic ulcer and depression should be carefully assessed and managed in patients with chronic inflammatory rheumatic diseases.		9.8 (0.5)
B. All clinicians including health professionals such as nurses, treating general practitioners and rheumatologists and patients through self-administered questionnaires and self-management programmes play a key role in the screening and detection of comorbidities.		9.5 (0.9)
C. Comorbidities should be subject to a systematic, standardised periodical review (eg, at least every 5 years) for those with a chronic inflammatory rheumatic disease.		9.4 (0.8)
Points to consider	**Level of evidence**	**Mean (SD) level of agreement**
Cardiovascular diseases		
1. History of myocardial infarction, pectoris angina, stent, stroke, transient ischaemic attack, heart failure and lower limb peripheral arterial disease should be documented.	5	9.7 (0.5)
2. Cardiovascular risk factors such as smoking status, body mass index, history of hypertension, hypercholesterolaemia, renal insufficiency and HEART-SCORE index should be documented.	1b	9.5 (0.9)
3. Current cardiovascular treatments such as antihypertensive therapy, antiplatelet therapy, diabetes insulin or non-insulin therapies, lipid-lowering agents and anticoagulants should be documented.	5	9.6 (0.7)
Malignancies		
4. History of malignancies should be documented.	5	9.6 (0.8)
5. Screening procedures for malignancy (including mammography, pap smear, visit to a dermatologist, faecal occult blood test, colonoscopy) and for malignancy risk factors (including family history of breast or colon cancer and personal history of inflammatory bowel disease) should be documented.	1b	8.9 (1.4)
Infections		
6. History of tuberculosis should be documented including prior results of chest X-ray, tuberculin skin test, interferon-γ release assay and BCG vaccination.	2a	9.8 (0.5)
7. History of serious infections, opportunistic infections and chronic viral infections should be documented.	5	9.6 (0.5)
8. Vaccination status for infections including influenza, *Streptococcus pneumoniae*, herpes zoster, human papillomavirus, poliomyelitis, diphtheria, tetanus and hepatitis B should be documented.	1b	9.5 (0.7)
Peptic ulcer		
9. History of gastroscopy-proven peptic ulcer should be documented.	5	9.1 (0.9)
10. Risk factors for peptic ulcer such as age >65 years, proton pump inhibitor intake, personal history of complicated ulcer, *Helicobacter pylori* infection, current use of aspirin, non-steroidal anti-inflammatory drugs, corticosteroids and anticoagulants should be documented	5	9.1 (0.9)
Osteoporosis		
11. History of osteoporotic fracture should be documented.	5	9.5 (0.7)
12. Risk factors for osteoporosis including body mass index <19, physical inactivity, glucocorticoid exposure, alcohol intake, family history of femoral neck fracture, secondary osteoporosis, bone mineral density should be collected and the FRAX global risk should be calculated where applicable.	2b	9.0 (1.2)
13. Current or prior osteoporosis treatments including calcium/vitamin D supplementation, bisphosphonates, strontium ranelate, raloxifene, teriparatide and denosumab should be documented.	5	9.5 (0.7)
Depression		
14. History of depression, current depression and prior screening for depression should be documented.	5	9.0 (1.2)
15. Current treatments for depression should be collected.	5	9.2 (0.9)

BCG, Bacille Calmette Guérin; FRAX, Fracture Risk Assessment Tool.

Baillet A, et al. Ann Rheum Dis 2016;75:965–973

CV Comorbidities in RA

Prevalence of cardiovascular disease in patients with rheumatoid arthritis

- Patients with early RA had a 33% higher CVD risk (composite endpoint of MI, stroke or heart failure) than matched controls without RA [19].
- The increased risk of CVD associated with RA may already be present at an early stage of the disease [19].
- Patients with RA had a risk of CV events (coronary heart disease, cerebral arterial disease or peripheral arterial disease) that was almost double that of the general population [20].
- The increased risk of CVD associated with RA was even higher than that associated with diabetes mellitus [20]

- The incidence of heart failure was almost two-fold higher in patients with RA than in matched controls

- Rheumatoid arthritis patients have higher prevalence and burden of asymptomatic coronary artery disease assessed by coronary computed tomography

Citation	Country	Study Type	Patients (*n*)	CV Event	Prevalence (%)
Daniel 2020 [22]	USA	Systematic review	1,642,402	Atherosclerotic CVD	30%–47%
Panafinda 2013 [23]	Russia	Prospective, observational	200	Ischaemic heart disease MI Coronary artery bypass graft Stroke	19% 1.5% 3.5% 0.5%
Crowson 2017 [24]	International	Prospective, cohort	5638	CVD events *	Men: 20.9% † Women: 11.1% †
Pappas 2018 [25]	International	Registry *CORRONA* International *CORRONA* US	25,987	Any CVD ‡	Latin America: 8.5% Eastern Europe: 21.3% India: 5.6% USA: 8.5%
Dougados 2014 [1]	International	Cross-sectional, observational *COMORA*	4586	MI or stroke	6.0%
Gomes 2017 [26]	Brazil	Cross-sectional, population-based	296	MI	4.4%
Lauper 2018 [27]	Switzerland	Mixed retrospective and prospective cohort	3070	MACE §	2.67 per 1000 person-years ¶
Nikiphorou 2020 [19]	England	Retrospective, case–control	6591	MI, stroke or heart failure	10.62 per 1000 person-years
Agca 2020 [20]	Netherlands	Prospective cohort CARRÉ	326	CV event ‖	32 per 1000 person-years ¶
Solomon 2015 [28]	USA	Registry *CORRONA* US	24,989	MI, stroke or CV death	7.79 per 1000 person-years

1.Taylor PC, J. Clin. Med. **2021**, 10, 509
2. Khalid Y, ESC Heart Failure 2020; 7: 3745-3753
3. Hansen PR, Eur J Intern Med. 2019 Apr;62:72-79

Impact of CV Comorbidities in Patients with RA

Patients with comorbid CVD and RA tend to have worse long-term health outcomes than patients with CVD alone

- In patients undergoing CAG, RA is significantly associated with the 10-year risk of MI, MACE and all-cause mortality regardless of the presence of CAD.
- Patients with RA and CAD carry the largest risk, while the additive risk of RA in patients without CAD is minor.

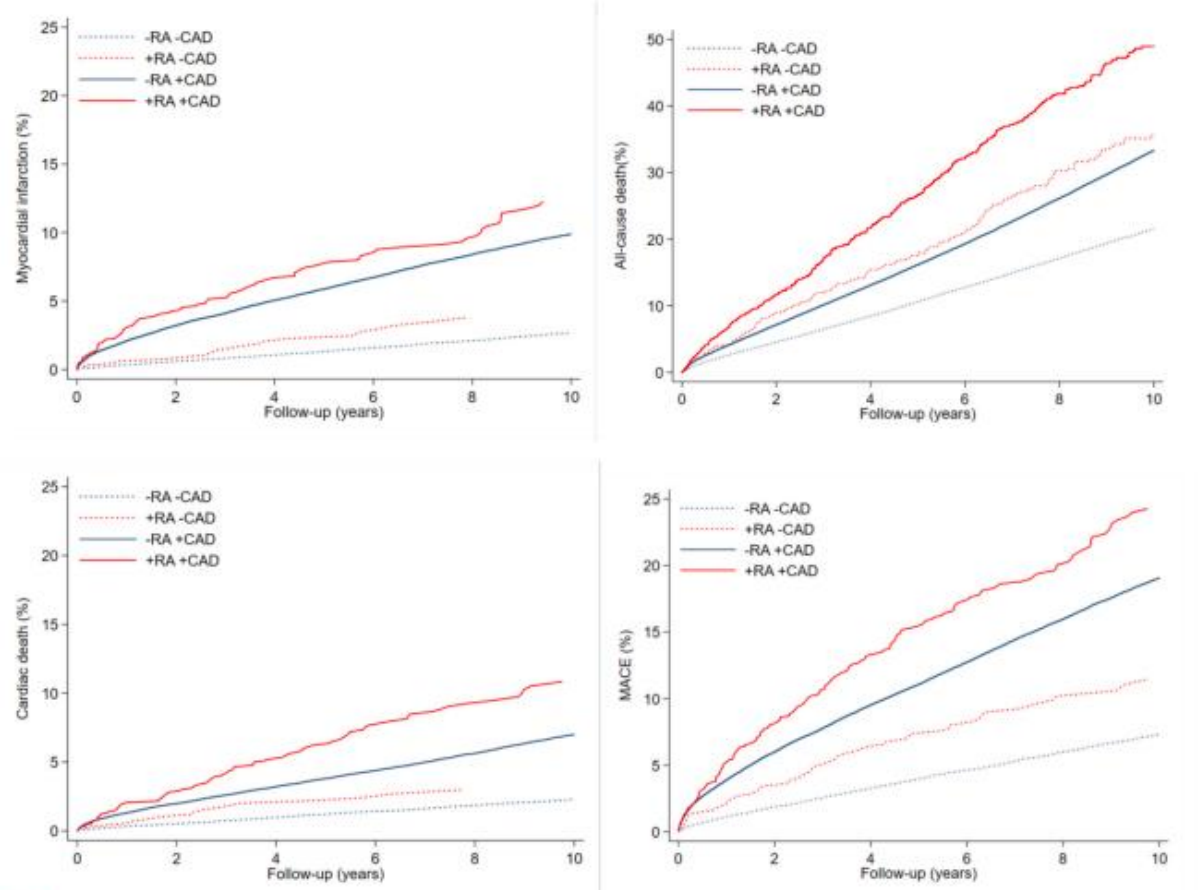
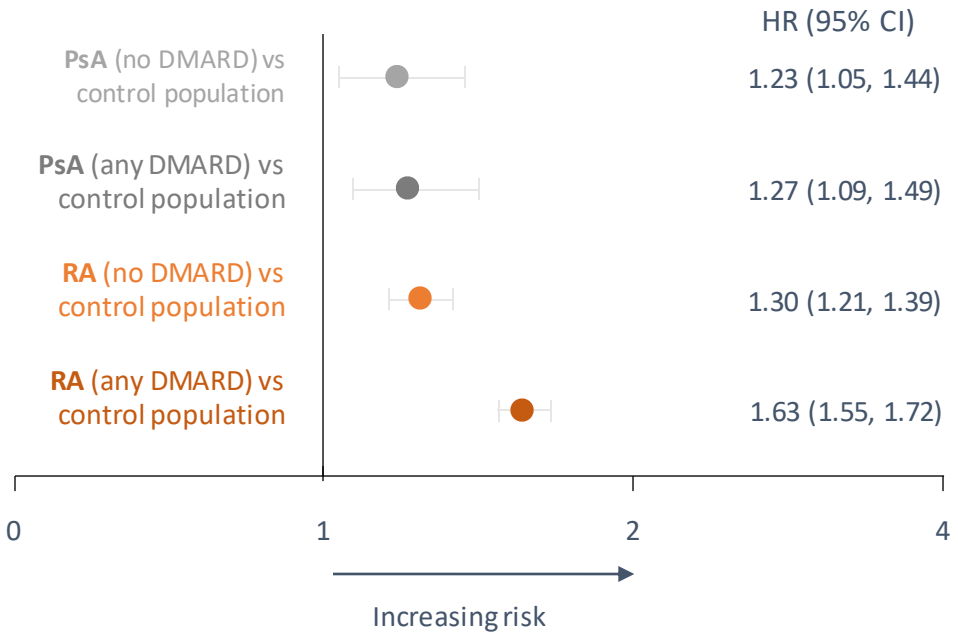


Figure 2 The 10-year cumulative incidence proportion of myocardial infarction, all-cause death, cardiac death and MACE. RA, rheumatoid arthritis; CAD, coronary artery disease; MACE, major adverse cardiovascular events.

Løgstrup B.B, Ann. Rheum. Dis. 2020, 79, 1182–1188

Patients with RMDs have an increased risk of VTEs compared with the general population



Hazard ratios for incidence of VTEs in patients with PsA or RA vs control population

All hazard ratios are age- and sex-adjusted
RMDs (rheumatic and musculoskeletal diseases) refer to inflammatory rheumatic diseases in the context of the presentation
Source: THIN in the UK between 1994 and January 2014. THIN is representative of the UK population in terms of age, sex, geography, and medical conditions. Control population: up to 5 unexposed controls were randomly selected for each patient with psoriasis, PsA, and RA, and were matched on practice and start date within the practice

Ogdie A, et al. Eur Heart J 2018;39:3609–14

Risk Factors for CVD in Patients with RA

- The increased CVD risk observed in patients with RA is likely to be multifactorial reflecting:

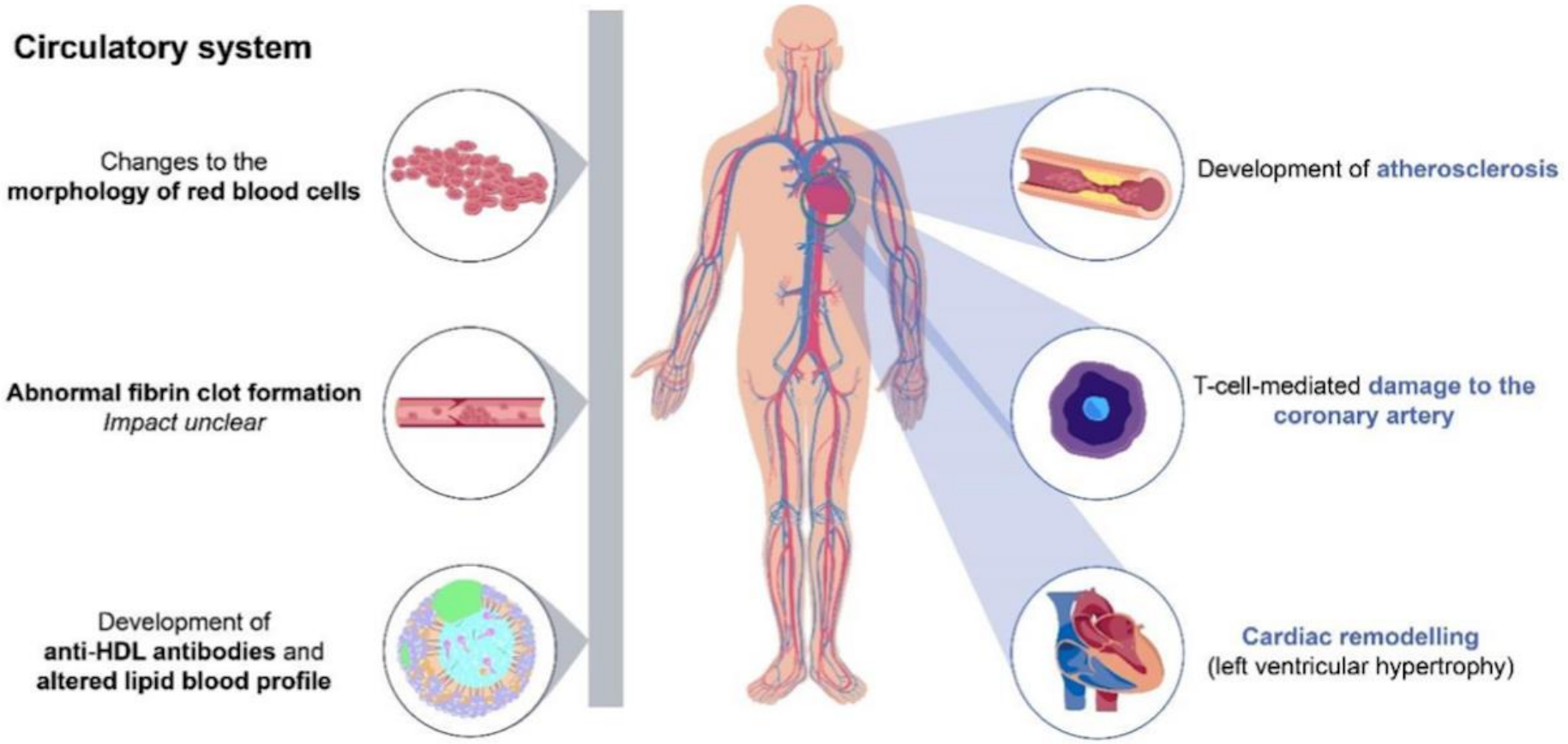
➢ an increased prevalence of traditional CVD risk factors
  - ✓ current tobacco use (19-29%)
  - ✓ hypertension (19-61%)
  - ✓ diabetes mellitus (5-14%)
  - ✓ hyperlipidaemia (10-32%)
  - ✓ high BMI (27-29 kg/m^2)

➢ the impact of systemic inflammation

➢ the potential side effects from medications used to treat RA

Taylor PC, J. Clin. Med. 2021, 10, 509. https://doi.org/10.3390/jcm10030509

Chronic inflammation in rheumatoid arthritis as a risk factor for cardiovascular disease



Taylor PC, J. Clin. Med. **2021**, 10, 509. https://doi.org/10.3390/jcm10030509

Association between rheumatoid arthritis disease activity and risk of cardiovascular disease

Systemic inflammation may, at least in part, explain the remaining risk

Citation	Study Type	Patients (*n*)	CV Event	Disease Activity Parameters with a Significant Impact on Risk of CVD	
				Parameter	Impact on Risk
Crowson 2017 [24]	Prospective, cohort	5638	Fatal or nonfatal CV events *	DAS28 RF/ACPA-positive	PAR: 12.6% PAR: 12.2%
Solomon 2015 [28]	Registry *CORRONA* US	24,989	Composite of MI, stroke or CV death	CDAI	Risk reduced by 21% per 10 pt reduction in time-averaged CDAI
Dalbeni 2020 [39]	Prospective	137	Ultrasound-detected atheromatous plaques	DAS28 (CRP) $\geq$ 2.6	Worsening of atherosclerosis only detected in patients with active disease
Arts 2017 [40]	Prospective, inception cohort	1157	Fatal or nonfatal CV events †	DAS28 $\leq$ 3.2	Reduced risk of CVD (HR: 0.65; 95% CI: 0.43–0.99) ‡
Mantel 2015 [41]	Nested, case–control	138	ACS	Mean DAS28 EULAR $\geq$ 5.2 § ESR > 23/> 22 ¶ SJC > 6/> 4 ¶	OR: 1.32 (95% CI: 1.06–1.64) OR: 2.59 (95% CI: 1.04–6.43) OR: 3.01 (95% CI: 1.54–5.88) OR: 1.32 (95% CI: 1.06–1.64)
Ahlers 2020 [42]	Electronic health record analysis	6161	Heart failure	CRP	OR: 1.29 (95% CI: 1.16–1.44)
Bajraktari 2017 [43]	Cross-sectional	179	Hypertension	CRP, ESR, anti-CCP, DAS28	Significantly higher values reported in hypertensive patients ($p < 0.001$)
Berendsen 2017 [44]	Inception cohort	929	Fatal or nonfatal CV events ‖	RF positivity	HR: 1.52 (95% CI: 1.01–2.30) **

Taylor PC, J. Clin. Med. 2021, 10, 509. https://doi.org/10.3390/jcm10030509

Effect of RA Treatments on CV Risk (1)

- Corticosteroids and NSAIDs, particularly COX-2 inhibitors, are generally associated with an increase in CVD risk in patients with RA
- Nonbiologic DMARDs are associated with an improved CVD risk
- TNF inhibitors and methotrexate significantly reduced the risk of CV events compared with no treatment
- BSRBR-RA demonstrated that treatment with TNF inhibitors significantly reduced the risk of MI compared with csDMARDs, although no differences in MI severity or mortality were observed between treatment groups
- Length of treatment may also have an impact on CV risk
- Cumulative use of 1, 2 or 3 years of anti-TNF therapy is expected to reduce CV risk by 21%, 38% and 51%, respectively, compared with non-use
- The Swedish biologics register: the 1-year risk of ACS for patients with a good EULAR response was approximately half that of patients with no EULAR response

Taylor PC, J. Clin. Med. 2021, 10, 509.

Effect of RA Treatments on CV Risk (2)

- No significant differences between TNF inhibitors and tocilizumab in terms of CV risk
- Abatacept has been associated with modest decreases in the risk of CV events compared with TNF inhibitors and rituximab
- Janus kinase (JAK) inhibitors and, in particular, tofacitinib, have been associated with an increased risk of venous thromboembolisms (VTEs) in postmarketing surveillance studies
- A recent meta-analysis of 26 RCTs, comprising 11,799 patients, indicated that treatment with JAK inhibitors as a class or as individual therapies did not affect the risk of VTEs, CV events or MACE in patients with RA, at least in the short term

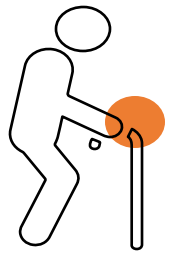
1. Taylor PC, J. Clin. Med. **2021**, 10, 509
2. Xie, W, et alAnn. Rheum. Dis. 2019, 78, 1048–1054

JAK inhibitor consensus statement related to VTE risk

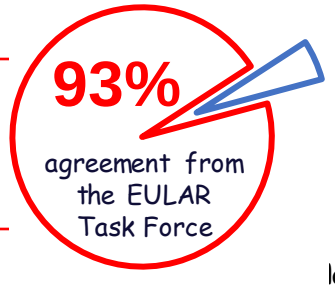
Risk factors for VTEs

- VTE risk factors should be considered by **history** and a **potential clotting abnormality** in patients with a history of VTEs

- Risk is increased in patients:
  - With prior VTEs
  - With increasing age
  - With obesity
  - With prolonged immobility
  - Hereditary (ie, factor V Leiden, prothrombin mutation 20210, and acquired thrombophilia)
  - Treated with Cox 2 inhibitor therapy; prednisolone of ≥7.5 mg/d
  - With major surgical interventions



Contraindications: Recurrent VTE (unless anticoagulated)



lash P, et al. Ann Rheum Dis 2021;80:71-87

EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update

Table 1 Overarching principles and recommendations

	Level of evidence	Strength of recommendation	Level of agreement (SD)
Overarching principles A. Clinicians should be aware of the higher risk for CVD in patients with RA compared with the general population. This may also apply to AS and PsA. B. The rheumatologist is responsible for CVD risk management in patients with RA and other IJD. C. The use of NSAIDs and corticosteroids should be in accordance with treatment-specific recommendations from EULAR and ASAS			
Recommendations			
1. Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA	2b-3	B	9.1 (1.3)
2. CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes in antirheumatic therapy	3–4	C	8.8 (1.1)
3. CVD risk estimation for patients with RA, AS or PsA should be performed according to national guidelines and the SCORE CVD risk prediction model should be used if no national guideline is available	3–4	C–D	8.7 (2.1)
4. TC and HDLc should be used in CVD risk assessment in RA, AS and PsA and lipids should ideally be measured when disease activity is stable or in remission. Non-fasting lipids measurements are also perfectly acceptable	3	C	8.8 (1.2)
5. CVD risk prediction models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the model	3–4	C	7.5 (2.2)
6. Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasound may be considered as part of the CVD risk evaluation in patients with RA	3–4	C–D	5.7 (3.9)
7. Lifestyle recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation for all patients	3	C	9.8 (0.3)
8. CVD risk management should be carried out according to national guidelines in RA, AS or PsA, antihypertensives and statins may be used as in the general population	3–4	C–D	9.2 (1.3)
9. Prescription of NSAIDs in RA and PsA should be with caution, especially for patients with documented CVD or in the presence of CVD risk factors	2a-3	C	8.9 (2.1)
10. Corticosteroids: for prolonged treatment, the glucocorticoid dosage should be kept to a minimum and a glucocorticoid taper should be attempted in case of remission or low disease activity; the reasons to continue glucocorticoid therapy should be regularly checked	3–4	C	9.5 (0.7)

AS, ankylosing spondylitis; ASAS, Assessment of Spondyloarthritis International Society; CVD, cardiovascular disease; EULAR, European League against Rheumatism; HDLc, high-density lipoprotein cholesterol; IJD, inflammatory joint disorder; NSAID, non-steroidal anti-inflammatory drug; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SCORE, Systematic Coronary Risk Evaluation; TC, total cholesterol.

Fortunately, physicians appear to be aware of the need to monitor CVD risk in patients with active RA:

A study of 14,503 patients (SURF-RA) demonstrated that positivity for rheumatoid factor and anticitrullinated protein antibodies, longer disease duration and higher disease activity were associated with a higher likelihood of lipid and blood pressure assessments

1. Agca R, et al. Ann Rheum Dis 2017;76:17–28. doi:10.1136/annrheumdis-2016-209775
2. Myasoedova E, et al [Abstract]. Available online: https://acrabstracts.org/abstract/sex-differences-in-cardiovascular-disease-prevention-in-patients-with-rheumatoid- arthritis-world-wide-data-from-the-surf-ra/ (accessed on 9 November 2020)

Infections in Patients with RA

Prevalence of infections in patients with rheumatoid arthritis

Patients with RA are particularly susceptible to bacterial infections (vs. viral or fungal), and those most frequently reported include respiratory infections, urinary tract infections, mycobacterium tuberculosis infection (TB) and sepsis

Citation	Country	Study Type	Patients (*n*)	Infection Event	Prevalence, *n* (%) *
Doran 2002 [85]	USA	Retrospective, cohort	609	IRH	290 (47.6)
Mehta 2019 [88]	USA	Prospective, cohort	20,361	SI †	1600 (7.9)
Ozen 2019 [89]	USA	Prospective, cohort	11,623	SI	694 (5.9)
Chandrashekara 2019 [90]	India	Cross-sectional	2081	Non-tubercular infection	54 (2.9)
Subesinghe 2016 [91]	UK	Cross-sectional	929	SI ‡	72 (7.8)
Salt 2017 [92]	USA	Retrospective, case–control	55,861	Postoperative joint infections §	1127 (2.0)
Hashimoto 2017 [93]	Japan	Retrospective, single-centre	2688	IRH ¶	274 (10.2)
Rutherford 2018 [94]	UK	Prospective, cohort, registry: *BSRBR-RA*	19,282 ‖	SI **	5.51/100 patient-years
Richter 2016 [95]	Germany	Observational, cohort, registry: *RABBIT*	12,097	SI ††	947 (7.8)

Taylor PC, J. Clin. Med. 2021, 10, 509. https://doi.org/10.3390/jcm10030509

Incidence, risk factors and validation of the RABBIT score for serious infections in a cohort of 1557 patients with rheumatoid arthritis

The incidence of serious infection (SI) was 2.3/100 patient- years. Longer disease duration, history of previous SI, comorbidities and high glucocorticoid dose were independently associated with SI

	Univariate		Multivariate	
Variable	**IRR (95% CI)**	***P***	**IRR (95% CI)**	***P*-value***
Age	1.04 (1.003, 1.087)	0.034	1.007 (0.96, 1.05)	0.72
Disease duration	1.05 (1.01, 1.09)	0.01	**1.05 (1.003, 1.1)**	**0.018**
Baseline HAQ	1.46 (1.07, 2.00)	0.018	1.09 (0.58, 2.08)	0.77
History of serious infection	6.52 (2.75, 15.5)	<0.001	**4.15 (1.70, 10.12)**	**0.002**
Prednisolone ≥10 mg/day *vs* <10 mg/day	3.49 (0.83, 14.65)	0.09	**4.77 (1.47, 15.5)**	**0.009**
bDMARD use	1.10 (0.47, 2.59)	0.81	0.83 (0.32, 2.18)	0.71
Diabetes mellitus	3.67 (1.49, 9.01)	0.005	**2.55 (1.06, 6.14)**	**0.036**
Chronic lung disease	5.87 (2.41, 14.27)	<0.001	**3.13 (1.35, 7.27)**	**0.008**
Cardiovascular disease	4.31 (1.76, 10.58)	0.001	2.06 (0.70, 6.08)	0.19
CKD (stage 3–5 *vs* 0–2)	6.58 (0.98, 44.16)	0.052	3.20 (0.77, 13.31)	0.11

Thomas K, Rheumatology 2021;60:2223–2230 doi:10.1093/rheumatology/keaa557

Disease Activity as a Risk Factor for Infection in Patients with RA

- CORRONA registry: adjusted risk of SI 69% higher in patients with sustained low disease activity compared with those in sustained remission (adjusted IR: 1.7; 95% CI: 1.3–2.2). In patients with moderate-to-high disease activity, the risk of SI was more than double than that observed for patients in sustained remission (IR/100 patient-years: 2.5; 95% CI: 2.2–2.8 vs. IR/100 patient-years: 1.0; 95% CI: 0.9–1.3)
- FORWARD database: compared with patients with noninflammatory rheumatic and musculoskeletal diseases, patients with RA with low disease activity, or in remission, had a similar SI risk; however, patients with moderate and high RA disease activity had a significantly increased SI risk
  - The treatment goal should be to obtain low-grade disease activity or remission as this may result in improved outcomes for patients with SI
- In contradiction, Mehta et al. cautioned that while low disease activity/remission is an attractive target, clinicians should weigh the potential SI risk associated with aggressive treatment strategies in patients with RA while targeting and sustaining remission or low disease activity

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Associations between rheumatoid arthritis treatment regimens and the risk of infection

Citation	Study Type	Patients (*n*) *	Infection Event	Treatments with an Impact on the Risk of Infection	
				Treatment	Impact on Risk
Hashimoto 2017 [93]	Retrospective, single-centre	342	IRH	GC	OR (95% CI): 3.0 (2.1–4.4); $p < 0.0001$ (2 mg/day)
				bDMARD	OR (95% CI): 1.4 (1.0–2.0); $p = 0.033$
				MTX	OR (95% CI): 0.7 (0.6–1.0); $p = 0.034$
Mehta 2019 [88]	Prospective, cohort	20,361	SI	GCs	HR (95% CI) for patients with RA vs. NIRMD: • Excluding GCs: 1.7 (1.5–1.9) • Adjusted for GCs: 1.3 (1.2–1.5)
Richter 2016 [95]	Observational, cohort, registry: *RABBIT*	1017	Sepsis and mortality following SI	GCs	OR (95% CI) for sepsis: • GC 5 to <10 mg/day vs. ref †: 1.3 (0.8–1.9) • GC ≥ 10 mg/day vs. ref †: 1.7 (1.0–2.9) OR (95% CI) for death: • GC 5 to <10 mg/day vs. ref †: 0.9 (0.5–1.8) • GC ≥ 10 mg/day vs. ref †: 2.4 (1.0–5.6)
				TNF inhibitor	OR (95% CI) sepsis vs. ref ‡: 0.6 (0.4–1.0) OR (95% CI) death vs. ref ‡: 0.5 (0.2–1.0)
				Other bDMARD	OR (95% CI) sepsis vs. ref ‡: 0.5 (0.3–0.8) OR (95% CI) death vs. ref ‡: 0.2 (0.1–0.5)
Ozen 2019 [89]	Prospective, cohort	11,623	SI	TNFis	Adjusted HR (95% CI) vs. ref ‡: 1.3 (1.1–1.7)
				Non-TNFi bDMARD	Adjusted HR (95% CI) vs. ref ‡: 1.5 (1.0–2.2)
Strand 2015 [115]	Meta-analysis	66 RCTs; 22 LTS	SI	Tofacitinib 5 mg BID Tofacitinib 10 mg BID Abatacept TNFis Rituximab Tocilizumab	Risk differences (95% CI) vs. placebo §: • 0.4% (−0.2–1.0) • 0.4% (−0.2–1.0) • 0.4% (−0.7–1.5) • 0.9% (0.3–1.6) • −0.4% (−1.6–0.8) • 1.5% (0.7–2.3)
Singh 2015 [116]	Meta-analysis	106 studies (n = 42,330)	SI	bDMARD: low dose; standard dose; high dose	OR (95% CI) vs. ref ‡: 0.9 (0.7–1.3); 1.3 (1.1–1.6); 1.9 (1.5–2.4)
Minozzi 2016 [117]	Meta-analysis	71 RCTs; (n = 22,720); 7 OLE (n = 2236) ¶	SI	TNFis vs. placebo	Fixed-effects model (OR: 1.4; 95% CI: 1.2–1.7) Random-effects model (OR: 1.3; 95% CI: 1.0–1.6)

Taylor PC, J. Clin. Med. 2021, 10, 509

2021 American College of Rheumatology Guidelines for the Treatment of Rheumatoid Arthritis

Recommendations	Certainty of evidence	Based on the evidence report(s) of the following PICO(s)	Evidence table(s), in Supp. App. 2
Nonalcoholic fatty liver disease			
Methotrexate is **conditionally** recommended over alternative DMARDs for DMARD-naive patients with nonalcoholic fatty liver disease, normal liver enzymes and liver function tests, and no evidence of advanced liver fibrosis who have moderate-to high disease activity.	Very low	PICO 87	p. 489
Persistent hypogammaglobulinemia without infection			
In the setting of persistent hypogammaglobulinemia without infection, continuation of rituximab therapy for patients at target is **conditionally** recommended over switching to a different bDMARD or tsDMARD.	Very low	PICO 66	p. 429
Previous serious infection			
Addition of csDMARDs is **conditionally** recommended over addition of a bDMARD or tsDMARD for patients with a serious infection within the previous 12 months who have moderate-to-high disease activity despite csDMARD monotherapy.	Very low	PICO 88	p. 490
Addition of/switching to DMARDs is **conditionally** recommended over initiation/dose escalation of glucocorticoids for patients with a serious infection within the previous 12 months who have moderate-to-high disease activity.	Very low	PICO 90 and PICO 91	p. 496–7
Nontuberculous mycobacterial lung disease			
Use of the lowest possible dose of glucocorticoids (discontinuation if possible) is **conditionally** recommended over continuation of glucocorticoids for patients with nontuberculous mycobacterial lung disease.	Very low	No relevant PICO	
Addition of csDMARDs is **conditionally** recommended over addition of a bDMARD or tsDMARD for patients with nontuberculous mycobacterial lung disease who have moderate-to-high disease activity despite csDMARD monotherapy.	Very low	PICO 92	p. 498
Abatacept is **conditionally** recommended over other bDMARDs and tsDMARDs for patients with nontuberculous mycobacterial lung disease who have moderate-to-high disease activity despite csDMARDs.	Very low	PICO 93	p. 499

Fraenkel L, Arthritis Care & Research , Vol. 73, No. 7, July 2021, pp 924–939

Malignancies in patients with RA

Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis

- Patients with RA are at an increased risk of lung and lymphoma malignancies compared with the general population
- SIR estimates for colorectal and breast cancers continued to show a decrease in risk, whereas cervical cancer, prostate cancer and melanoma appeared to show no consistent trend in risk among patients with RA compared with the general population

Malignant lymphoma

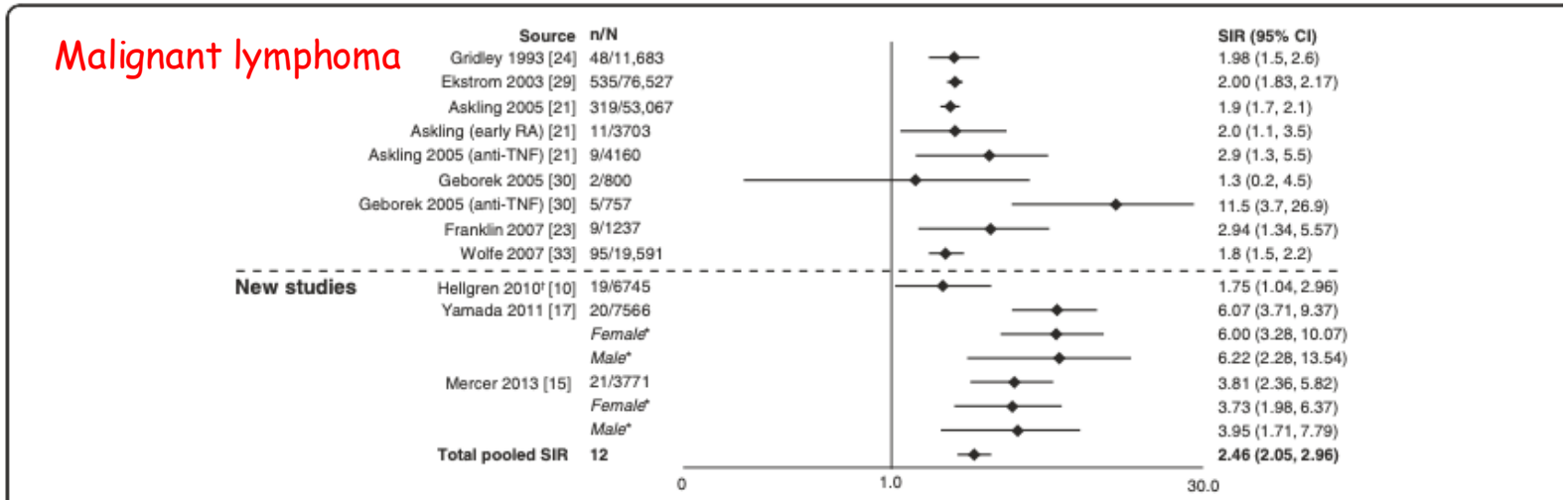


Fig. 3 Relative risk of malignant lymphoma in patients with rheumatoid arthritis (RA) compared with the general population. CI, confidence interval; n, number of malignancies; N, population size; OR, odds ratio; SIR, standardized incidence ratio; TNF, tumor necrosis factor. *SIRs by sex are not included in the total pooled SIR. †Reported as odds ratio

lung cancer

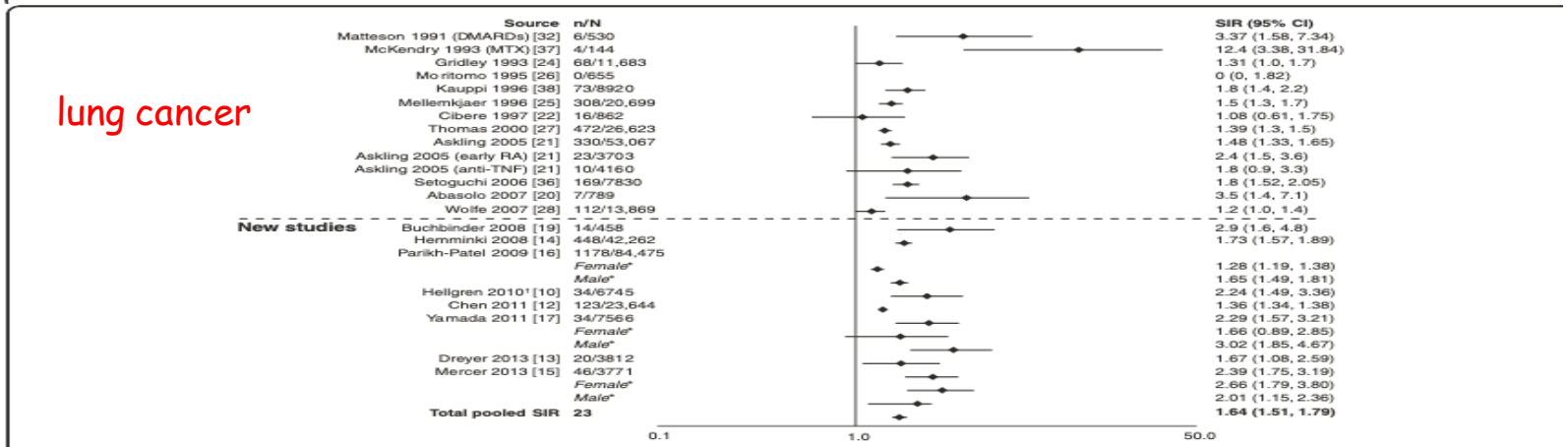


Fig. 6 Relative risk of lung cancer in patients with rheumatoid arthritis (RA) compared with the general population. CI, confidence interval; DMARD, disease-modifying antirheumatic drug; MTX, methotrexate; n, number of malignancies; N, population size; SIR, standardized incidence ratio; TNF, tumor necrosis factor. *SIRs by sex are included in total pooled SIR only if overall SIR was not available. †Reported as odds ratio

Simon TA, Arthritis Research & Therapy (2015) 17:212 DOI 10.1186/

Malignancy and rheumatoid arthritis: Clinical practice points and research agenda (1)

- No strong association between TNFi and cancer occurrence in patients receiving these therapies who have no prior history of cancer
- Most studies have only followed up patients for on average 5 years
- BSRBR-RA database and a Swedish registry reported no impact of TNF inhibitors on the risk of lymphoma
- Increased risk of certain types of cancers such as non-melanoma skin cancer remains less clear
- Patients should be advised on preventative skin care and skin surveillance and should be prompted to report any new persistent skin lesions

1. De Cock D, Best Practice & Research Clinical Rheumatology, https://doi.org/10.1016/ j.berh.2019.03.011
2. Taylor PC, J. Clin. Med. 2021, 10, 509

Malignancy and rheumatoid arthritis: Clinical practice points and research agenda (2)

- Data on the risk of recurrent cancers in patients receiving bDMARDs who have had prior cancer are reassuring
- The data available do not suggest that prior cancer is an absolute contraindication to bDMARDs
- The decision to treat a patient with a prior cancer should be a joint decision between the patient, their rheumatologist and their oncologist, considering the nature of the previous cancer, the treatment received and also the activity of the patient's arthritis and their quality of life, considering what alternative therapies there may be
- Currently unknown whether switching bDMARD class is a better decision than continuing the same bDMARD
- Currently unknown whether bDMARDs increase the risk of cancer in patients with pre-malignant conditions

De Cock D, Best Practice & Research Clinical Rheumatology, https://doi.org/10.1016/ j.berh.2019.03.011

Malignancy and rheumatoid arthritis: Clinical practice points and research agenda (3)

- It remains unknown how physicians should manage anti-rheumatic therapies in patients who develop a cancer while receiving bDMARDs
- The current British guidelines recommend that bDMARD therapy should be stopped but do not offer specific advice on when it is safe to restart
- The American guidelines give specific recommendations on which DMARD to use for the following types of cancer: previously treated or untreated skin cancer, previously treated lymphoproliferative disorders and previously treated solid organ malignancies
- Only one study has reported on clinical decision making with regard to bDMARDs following diagnosis of cancer in patients already receiving TNFi :
  - Among 404 cancers present in more than 12,000 bDMARD-treated patients, over two-thirds of patients who survived at least 6 months following their cancer diagnosis had their TNFi stopped at the point of cancer diagnosis
  - Over the next 4.5 years, over half remained off biologic therapy and for those who did restart, a majority switched class of bDMARD

De Cock D, Best Practice & Research Clinical Rheumatology, https://doi.org/10.1016/ j.berh.2019.03.011

Rheumatoid arthritis: Clinical practice points and research agenda: the jakinibs

- The FDA released an updated boxed warning in September 2021 regarding the increased risk of death, MACEs, malignancies and thrombosis with JAK inhibitors compared with TNF inhibitors
- It also limits all approved uses to certain patients who have not responded to or cannot tolerate one or more TNF blockers
- Although this study only compared tofacitinib with adalimumab, the FDA was concerned about a JAK-inhibitor class effect, and the warning was extended to two other JAK inhibitors approved in the USA for treatment of inflammatory diseases, baricitinib and upadacitinib
- Whether the use of inhibitors with different JAK subtype selectivity or the use of JAK inhibitors in different diseases would improve cardiovascular and carcinogenic risk clearly warrants further investigation

Tanaka Y,Nat Rev Rheumatol. 2022 Mar;18(3):133-145. doi: 10.1038/s41584-021-00726-8. Epub 2022 Jan 5

JAK inhibitor consensus statement: As of date of publication, patient registries and clinical trial data have demonstrated no malignancy signal

Current malignancies as contraindications

- Using a JAK inhibitor should be a shared decision with the patient and should consider timing of past malignancy, presence of uncontrolled malignancy, and any ongoing treatment with chemotherapy or checkpoint inhibitors
- Current malignancy (excluding NMSC and cervical carcinoma in situ undergoing treatment) may be a contraindication for JAK inhibitors; initiating a JAK inhibitor should be a shared decision made with the patient

Patient management

- The Task Force recommends regular skin examinations, especially in countries with increased risk of NMSC, such as Australia

[a]First published online 6 November 2020.
NMSC, non-melanoma skin cancer; JAK, Janus kinase

Nash P, et al. Ann Rheum Dis 2021;80:71–87

2021 American College of Rheumatology Guidelines for the Treatment of Rheumatoid Arthritis

Recommendations	Certainty of evidence	Based on the evidence report(s) of the following PICO(s)	Evidence table(s), in Supp. App. 2
Subcutaneous nodules			
Methotrexate is **conditionally** recommended over alternative DMARDs for patients with subcutaneous nodules who have moderate-to-high disease activity.	Very low	PICO 64	p. 427
Switching to a non-methotrexate DMARD is **conditionally** recommended over continuation of methotrexate for patients taking methotrexate with progressive subcutaneous nodules.	Very low	PICO 65	p. 428
Pulmonary disease			
Methotrexate is **conditionally** recommended over alternative DMARDs for the treatment of inflammatory arthritis for patients with clinically diagnosed mild and stable airway or parenchymal lung disease who have moderate-to-high disease activity.	Very low	PICO 67	p. 430
Heart failure			
Addition of a non–TNF inhibitor bDMARD or tsDMARD is **conditionally** recommended over addition of a TNF inhibitor for patients with NYHA class III or IV heart failure and an inadequate response to csDMARDs.	Very low	PICO 70	p. 435
Switching to a non–TNF inhibitor bDMARD or tsDMARD is **conditionally** recommended over continuation of a TNF inhibitor for patients taking a TNF inhibitor who develop heart failure.	Very low	PICO 71	p. 436
Lymphoproliferative disorder			
Rituximab is **conditionally** recommended over other DMARDs for patients who have a previous lymphoproliferative disorder for which rituximab is an approved treatment and who have moderate-to-high disease activity.	Very low	PICO 75 and PICO 76	p. 446–7
Hepatitis B infection			
Prophylactic antiviral therapy is **strongly** recommended over frequent monitoring alone for patients initiating rituximab who are hepatitis B core antibody positive (regardless of hepatitis B surface antigen status).	Very low	PICO 82	p. 459
Prophylactic antiviral therapy is **strongly** recommended over frequent monitoring alone for patients initiating any bDMARD or tsDMARD who are hepatitis B core antibody positive and hepatitis B surface antigen positive.	Very low	PICO 83	p. 464
Frequent monitoring alone is **conditionally** recommended over prophylactic antiviral therapy for patients initiating a bDMARD other than rituximab or a tsDMARD who are hepatitis B core antibody positive and hepatitis B surface antigen negative.	Very low	PICO 84	p. 471

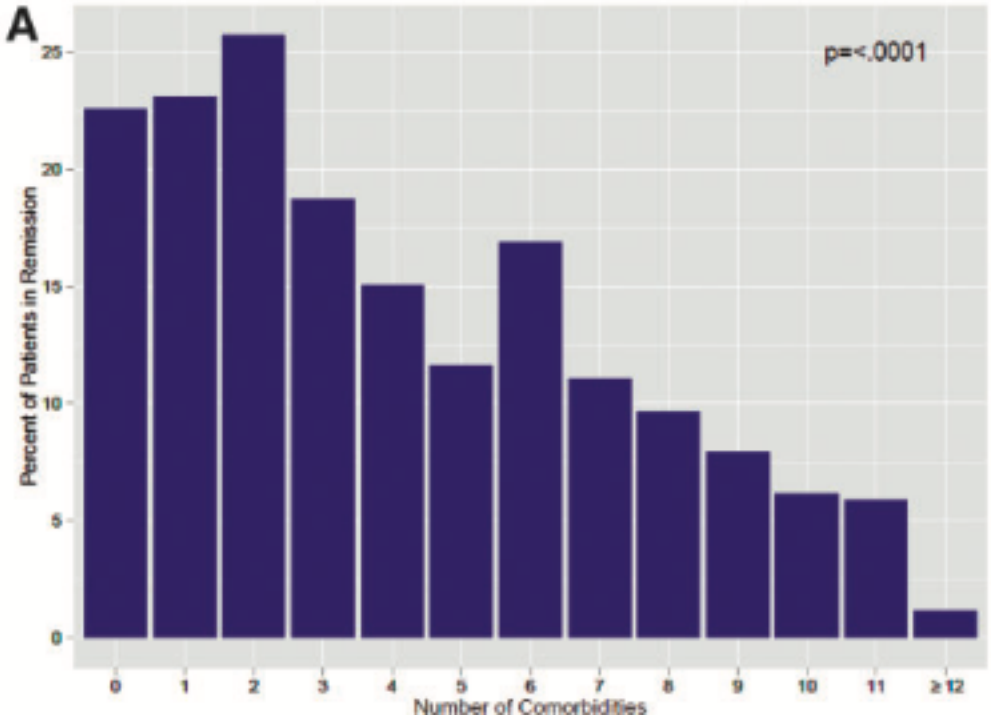
Fraenkel L, Arthritis Care & Research , Vol. 73, No. 7, July 2021, pp 924-939,

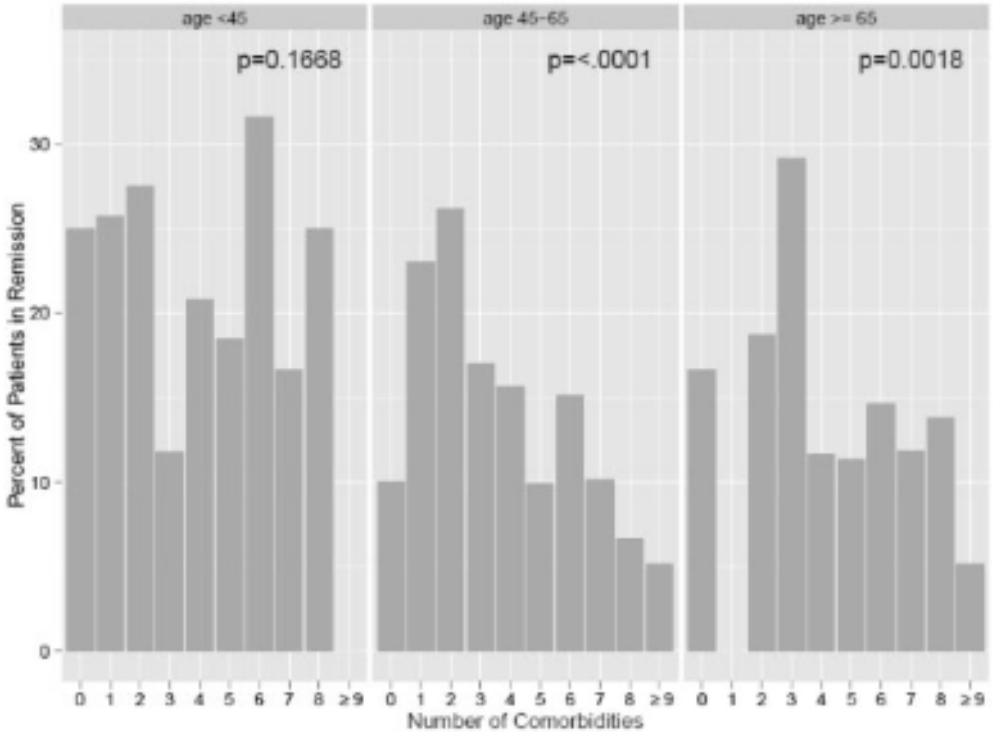
Does treatment of comorbidities improve RA?

- In the randomised, placebo- controlled Trial of Atorvastatin in Rheumatoid Arthritis (TARA), it was found that addition of atorvastatin to standard antirheumatic therapy significantly improved the DAS28 as compared to placebo (treatment group: –0.50, 95 %-CI –0.8 to –0.3; placebo group: +0.03, 95 %- CI –0.2 to 0.3)
- In a cohort study by Schoenfeld et al., it was concluded that statin use was independently associated with a 21 % lower risk of all-cause mortality among patients with RA (HR 0.8, 95 %-CI 0.7- 0.9)
- TRACE RA Consortium : Atorvastatin 40 mg daily is safe and results in a significantly greater reduction of LDL cholesterol level than placebo in patients with RA. The 34% CVE risk reduction is consistent with the Cholesterol Treatment Trialists' Collaboration meta-analysis of statin effects in other populations. Clinically assessed RA disease activity, severity, and quality of life were not significantly different between the 2 groups at the end of the trial. However, levels of CRP were significantly lower, by ~1 mg/liter, in the atorvastatin group than in the placebo group.

1. McCarey, et al, Lancet. 2004;363:2015-21
2. Schoenfeld SR, et al, Ann Rheum Dis 2015. doi: 10.1136/annrheumdis-2015-207714
3. Kitas G, Arthritis & Rheumatology (2019) ;71(9):1437-1449

Comorbidities are associated with poorer outcomes in community patients with rheumatoid arthritis (CORRONA)





Ranganath V, Rheumatology 2013;52:1809-1817

Comorbidities in Patients with Rheumatoid Arthritis and Their Association with Patient-reported Outcomes: Results of Claims Data Linked to Questionnaire Survey

- Compared to controls, all investigated comorbidities were more frequent in persons with RA (mean age 63 yrs, 80% female).
- In addition to cardiovascular risk factors, the most common were osteoarthritis (44% vs 21%), depression (32% vs 20%), and osteoporosis 26% vs 9%).
- Among the survey respondents, 87% of those with 0–1 comorbidity but only 77% of those with ≥ 8 comorbidities were treated by rheumatologists.

Increasing numbers of comorbidities were associated with poorer values for TJC, SJC, function, and WHO-5.

Table 4. Results from multivariable linear regression analyses. Association between comorbidities and patient-reported outcomes in the random sample (n = 2535).

Variables	Estimates (p value)			
	SJC (0–48)	TJC (0–50)	WHO-5	FFbH
Model A: association between no. comorbidities and outcomes				
Comorbidities, per unit	0.37 **(0.0023)**	0.65 **(< 0.0001)**	–1.87 **(< 0.0001)**	–2.30 **(< 0.0001)**
BMI, per 5 units	0.44 (0.1294)	0.45 (0.1701)	–1.43 **(0.0260)**	–2.91 **(< 0.0001)**
Age, per 5 yrs	0.16 (0.1914)	–0.02 (0.8780)	1.46 **(< 0.0001)**	–0.63 **(0.0161)**
Seronegative RA	–0.12 (0.7998)	0.26 (0.6400)	–0.51 (0.6600)	1.93 (0.0679)
Female sex	1.56 **(0.0050)**	1.32 **(0.0265)**	–3.9 **(0.0011)**	–7.34 **(< 0.0001)**
Smoking	1.06 (0.2346)	0.8 (0.4333)	–6.54 **(0.0002)**	–2.44 (0.1055)
Model B: association between specific comorbidities and outcomes				
Cardiac arrhythmia	0.25 (0.7626)	0.56 (0.5472)	0.04 (0.9843)	–1.12 (0.5332)
Coronary heart disease	–0.01 (0.9874)	0.49 (0.6563)	–2.98 (0.1720)	–0.67 (0.7355)
Hypertension	–0.23 (0.7531)	–0.04 (0.9632)	–3.14 **(0.0392)**	–2.06 (0.1493)
Hyperlipidemia	1.05 (0.0982)	1.20 (0.0941)	–0.68 (0.6328)	–0.56 (0.6673)
Hypothyroidism	0.39 (0.6062)	–0.13 (0.8733)	–0.70 (0.6779)	–1.80 (0.2536)
Diabetes	1.25 (0.1509)	1.25 (0.1818)	–2.57 (0.1594)	–3.01 (0.0682)
Osteoporosis	0.33 (0.6352)	1.56 (0.0523)	–0.04 (0.9808)	–5.97 **(< 0.0001)**
Osteoarthritis	1.27 **(0.0292)**	1.43 **(0.0350)**	–2.44 (0.0723)	–4.51 **(0.0002)**
Depression	1.11 (0.0917)	2.66 **(0.0002)**	–12.96 **(< 0.0001)**	–7.24 **(< 0.0001)**
BMI, per 5 units	0.51 (0.0951)	0.63 (0.0618)	–1.45 **(0.0286)**	–3.48 **(< 0.0001)**
Age, per 5 yrs	0.18 (0.1520)	0.00 (0.9819)	1.08 **(0.0004)**	–0.97 **(0.0005)**
Seronegative RA	0.02 (0.9693)	0.25 (0.6690)	0.3 (0.7904)	1.86 (0.0793)
Female sex	1.37 **(0.0126)**	0.72 (0.2805)	–2.61 **(0.0403)**	–5.08 **(< 0.0001)**
Smoking	1.13 (0.2216)	0.71 (0.4643)	–5.63 **(0.0005)**	–2.37 (0.1093)

Values in bold face show statistically significant influence. Only comorbidities with prevalence above 15% were included in the second model. Although obesity had a prevalence above 15%, this comorbidity was not included because of the selection of BMI. SJC: swollen joint count; TJC: tender joint count; WHO-5: World Health Organization 5-item Well-being Index; FFbH: Hannover Functional Ability Questionnaire; RA: rheumatoid arthritis; BMI: body mass index.

Ramos A L, et al, The Journal of Rheumatology 2019; 46:6

Choice and persistence of biologic agents in RA

Role of comorbidities on therapeutic persistence of biological agents in rheumatoid arthritis: results from the RECord-linkage On Rheumatic Disease study on administrative healthcare databases

Comorbidities affect treatment decisions in RA and influence bDMARD failure

- The study included 4657 RA patients
- In the first-line treatment strategy, the Charlson Comorbidity Index (CCI) (RA excluded) was significantly associated with an increased rate of bDMARD failure
- Chronic obstructive pulmonary disease, diabetes, and previous-year bacterial infections were slightly associated with risk of bDMARD failure
- Acute myocardial infarction, mild liver disease and solid tumours were not
- Neoplasms were associated with reduced risk of failure
- Multiple comorbidities were associated with first-line abatacept and rituximab administration

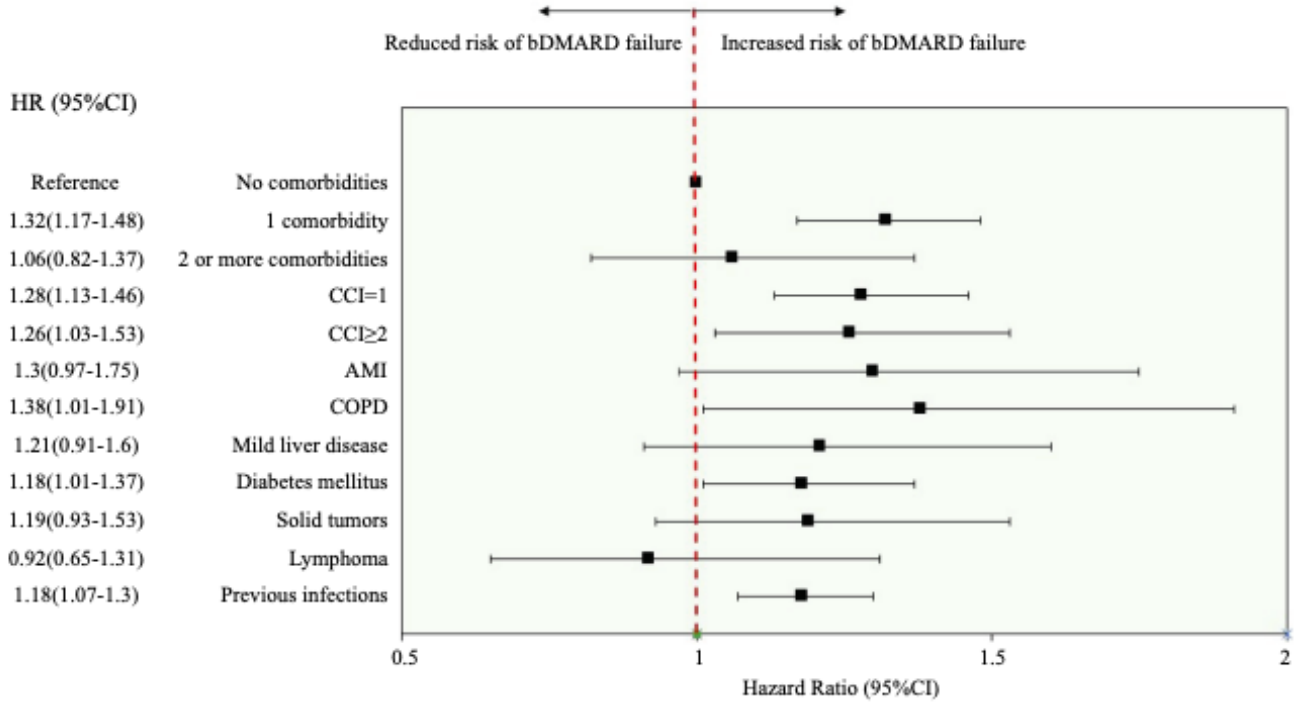


Figure 1. Multivariate analysis of the risk of failure of biological disease-modifying anti-rheumatic drugs (bDMARDs) considering different comorbidities in the first biological treatment line [hazard ratio (HR) adjusted for gender, age, disease duration, average dose of glucocorticoids, concomitant use of non-steroidal anti-inflammatory drug, conventional synthetic disease-modifying anti-rheumatic drugs, and specific bDMARDs]. CCI, Charlson Comorbidity Index; AMI, acute myocardial infarction; COPD, chronic obstructive pulmonary disease; CI, confidence interval.

D' Amico ME, Scand J Rheumatol 2021;00:1–10

Patient characteristics influence the choice of biological drug in RA, and will make non-TNFi biologics appear more harmful than TNFi biologics

- Patients starting non-TNFi were older than those starting TNFi, had lower socioeconomic status, higher disease activity and burden of diseases including malignancy, serious infections and diabetes.
- Differences were most pronounced at first bDMARD initiation.
- These factors were linked to treatment outcome independent of therapy, yielding worse apparent safety and effectiveness for non-TNFi biologics, most extreme for rituximab.
- Standardising to the age/ sex distribution of the TNFi group reduced differences considerably.

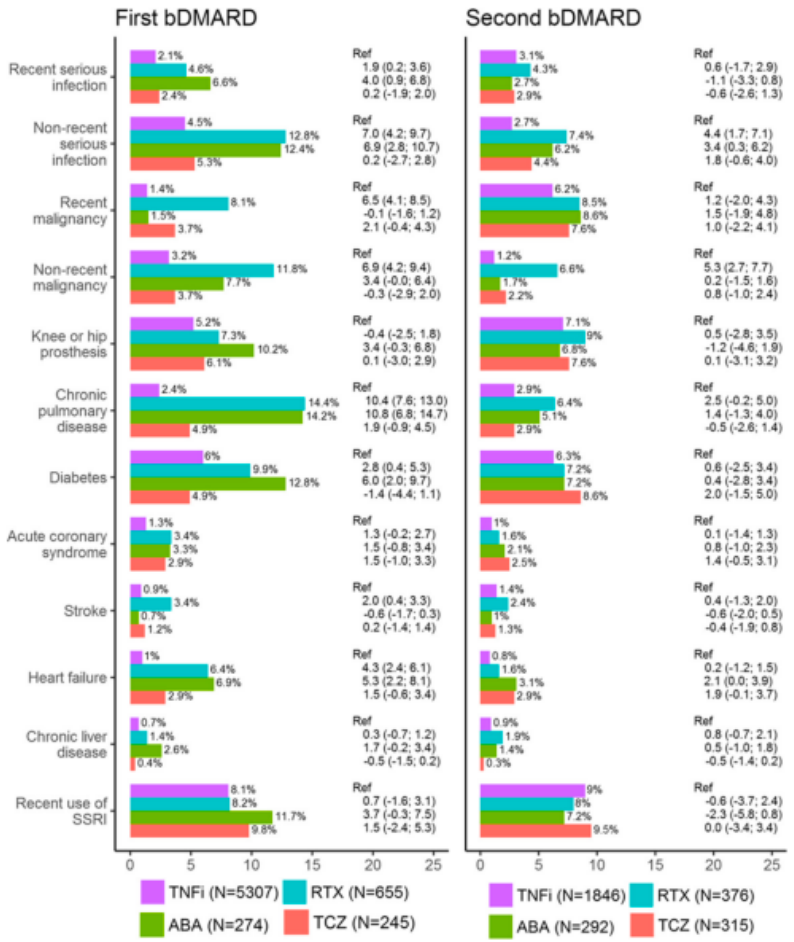


Figure 1 History of disease at treatment start of bDMARD therapy among all patients with rheumatoid arthritis in the SRQ, 2011–2015. Differences in proportion (with 95% CIs) are with reference to TNFi, and adjusted for age, sex and geographical region. bDMARD, biological disease-modifying anti-rheumatic drug; SRQ, Swedish Rheumatology Quality register; SSRI, selective serotonin reuptake inhibitor; TNFi, tumour necrosis factor inhibitor.

Frisell T, et al, Ann Rheum Dis 2018;77:650–657

Conclusions

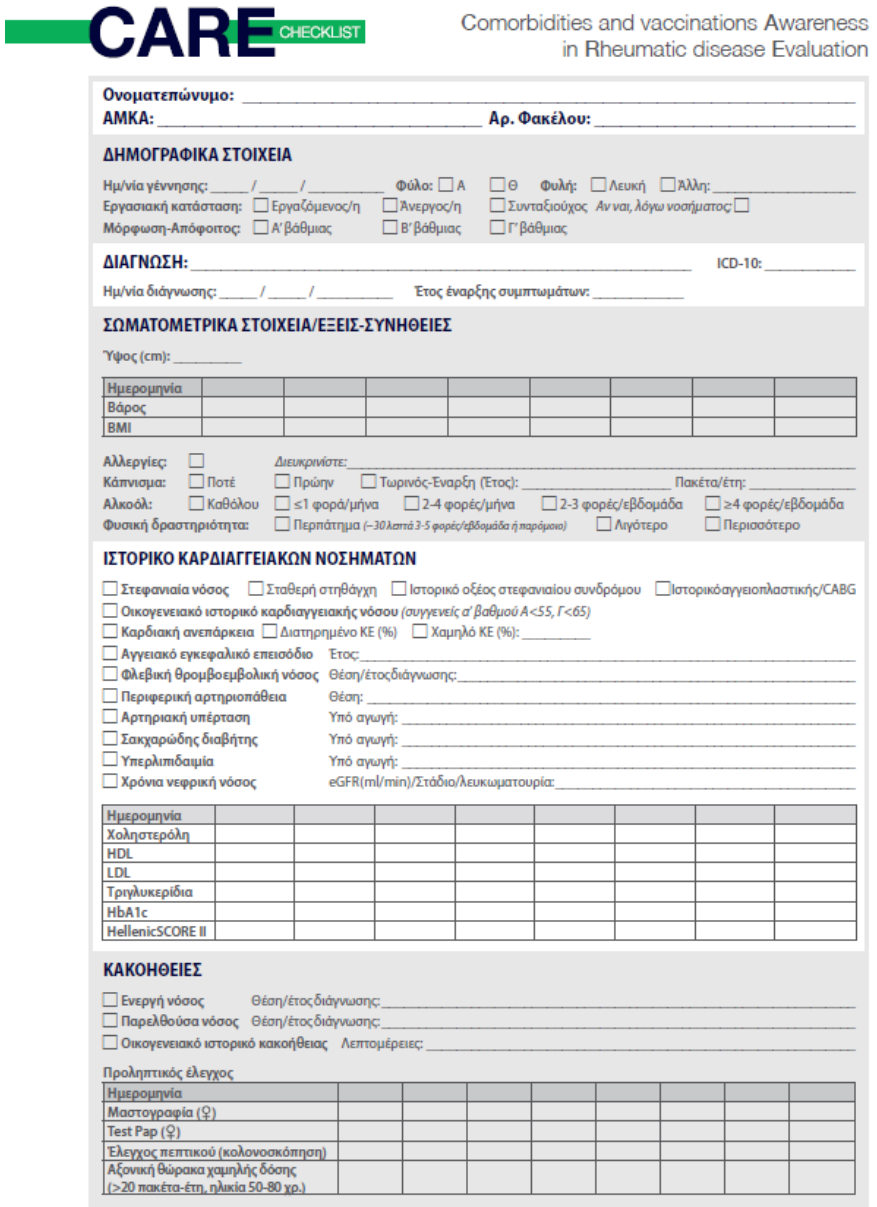
- The relationship between RA and a wide range of comorbid conditions is well known
- The development of comorbidities is associated with poor health outcomes, including decreased function, reduced quality of life, and increased morbidity and mortality
- Treatment decisions should take into account these comorbidities due to known or suspected associations with certain drug classes


Ευχαριστώ πολύ

Τακτική καταγραφή - παρακολούθηση

CARE CHECKLIST

Comorbidities and vaccinations Awareness
in Rheumatic disease Evaluation



CARE CHECKLIST

Comorbidities and vaccinations Awareness in Rheumatic disease Evaluation

Ονοματεπώνυμο: _____

ΑΜΚΑ: _____ **Αρ. Φακέλου:** _____

ΔΗΜΟΓΡΑΦΙΚΑ ΣΤΟΙΧΕΙΑ

Ημ/νία γέννησης: ____ / ____ / ____ Φύλο: ☐ Α ☐ Θ Φυλή: ☐ Λευκή ☐ Άλλη: _____

Εργασιακή κατάσταση: ☐ Εργαζόμενος/η ☐ Άνεργος/η ☐ Συνταξιούχος *Αν ναι, λόγω νοσήματος:* ☐

Μόρφωση-Απόφοιτος: ☐ Α' βάθμιας ☐ Β' βάθμιας ☐ Γ' βάθμιας

ΔΙΑΓΝΩΣΗ: _____ ICD-10: _____

Ημ/νία διάγνωσης: ____ / ____ / ____ Έτος έναρξης συμπτωμάτων: _____

ΣΩΜΑΤΟΜΕΤΡΙΚΑ ΣΤΟΙΧΕΙΑ/ΕΞΕΙΣ-ΣΥΝΗΘΕΙΕΣ

Ύψος (cm): _____

Ημερομηνία								
Βάρος								
BMI								

Αλλεργίες: ☐ *Διευκρινίστε:* _____

Κάπνισμα: ☐ Ποτέ ☐ Πρώην ☐ Τωρινός-Έναρξη (Έτος): _____ Πακέτα/έτη: _____

Αλκοόλ: ☐ Καθόλου ☐ ≤1 φορά/μήνα ☐ 2-4 φορές/μήνα ☐ 2-3 φορές/εβδομάδα ☐ ≥4 φορές/εβδομάδα

Φυσική δραστηριότητα: ☐ Περπάτημα *(~30 λεπτά 3-5 φορές/εβδομάδα ή παρόμοιο)* ☐ Λιγότερο ☐ Περισσότερο

ΙΣΤΟΡΙΚΟ ΚΑΡΔΙΑΓΓΕΙΑΚΩΝ ΝΟΣΗΜΑΤΩΝ

☐ Στεφανιαία νόσος ☐ Σταθερή στηθάγχη ☐ Ιστορικό οξέος στεφανιαίου συνδρόμου ☐ Ιστορικό αγγειοπλαστικής/CABG

☐ Οικογενειακό ιστορικό καρδιαγγειακής νόσου *(συγγενείς α' βαθμού Α<55, Γ<65)*

☐ Καρδιακή ανεπάρκεια ☐ Διατηρημένο ΚΕ (%) ☐ Χαμηλό ΚΕ (%): _____

☐ Αγγειακό εγκεφαλικό επεισόδιο Έτος: _____

☐ Φλεβική θρομβοεμβολική νόσος Θέση/έτος διάγνωσης: _____

☐ Περιφερική αρτηριοπάθεια Θέση: _____

☐ Αρτηριακή υπέρταση Υπό αγωγή: _____

☐ Σακχαρώδης διαβήτης Υπό αγωγή: _____

☐ Υπερλιπιδαιμία Υπό αγωγή: _____

☐ Χρόνια νεφρική νόσος eGFR(ml/min)/Στάδιο/λευκωματουρία: _____

Ημερομηνία								
Χοληστερόλη								
HDL								
LDL								
Τριγλυκερίδια								
HbA1c								
HellenicSCORE II								

ΚΑΚΟΗΘΕΙΕΣ

☐ Ενεργή νόσος Θέση/έτος διάγνωσης: _____

☐ Παρελθούσα νόσος Θέση/έτος διάγνωσης: _____

☐ Οικογενειακό ιστορικό κακοήθειας Λεπτομέρειες: _____

Προληπτικός έλεγχος

Ημερομηνία								
Μαστογραφία (♀)								
Test Pap (♀)								
Έλεγχος πεπτικού (κολονοσκόπηση)								
Αξονική θώρακα χαμηλής δόσης (>20 πακέτα-έτη, ηλικία 50-80 χρ.)								

ΨΥΧΙΚΗ ΥΓΕΙΑ

☐ Κατάθλιψη Υπό αγωγή: _____

☐ Χρόνιος πόνος/ινομυαλγία Υπό αγωγή: _____

☐ Αγχώδης διαταραχή Υπό αγωγή: _____

ΓΑΣΤΡΕΝΤΕΡΙΚΟ

☐ Πεπτικό έλκος ☐ Λήψη ΜΣΑΦ/ακετυλοσαλικυλικού οξέος ☐ Ιστορικό εκκολπωμάτωσης/εκκολπωματίτιδας

ΟΣΤΙΚΗ ΥΓΕΙΑ

☐ Κατάγματα σπονδυλικά ☐ Ιστορικό κατάγματος ισχίου γονέα

☐ Κατάγματα μη σπονδυλικά ☐ Δευτεροπαθής οστεοπόρωση

Ημερομηνία								
BMD ΟΜΣΣ/T-score								
BMD ισχίου/T-score								
FRAX score - Μείζονα οστεοπορωτικά (%)								
FRAX score - Ισχίου (%)								
25(OH) D3								

ΙΣΤΟΡΙΚΟ ΛΟΙΜΩΞΕΩΝ

☐ Σοβαρές (νοσηλεία) ☐ Υποτροπιάζουσες

☐ Βακτηριακές ☐ Ευκαιριακές ☐ Μυκητιασικές ☐ Χαμηλή IgG

☐ Φυματίωση ☐ Ενεργός ☐ Λανθάνουσα ☐ Θεραπεία για λανθάνουσα

☐ TST _____ mm Ημ/νία: ___ / ___ / _____ ☐ IGRA ( ) Ημ/νία: ___ / ___ / _____

☐ Απεικόνιση θώρακα: _____ Ημ/νία: ___ / ___ / _____

☐ VZV λοίμωξη Θέση/έτος: _____

☐ Ηπατίτιδα Β ☐ HBsAg ( ) ☐ anti-HBc ( ) ☐ anti-HBs ( ) Ημ/νία: ___ / ___ / _____

☐ Ηπατίτιδα C ☐ anti-HCV ( ) Ημ/νία: ___ / ___ / _____ *αν (+) HCV-RNA:* _____ ☐ Θεραπεία

ΕΜΒΟΛΙΑΣΜΟΙ

Γρίπη *Σε όλους τους ασθενείς προ της επιδημικής περιόδου* Έτος ☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Πνευμονιόκοκκος

Συζευγμένο (PCV13) *1 δόση εφάπαξ* ☐ ☐

Πολυσακχαριδικό (PPSV23)

<65 ετών *2 δόσεις (ανά 5 έτη)* ☐ ☐ ☐ ☐

≥65 ετών *1 δόση (≥5 έτη από προηγούμενη)* ☐ ☐

Έρπης Ζωστήρας *1 δόση εφάπαξ για ασθενείς ≥50 ετών* ☐ ☐ ★★★ ΠΡΟΣΟΧΗ ΖΩΝ ΕΞΑΣΘΕΝΗΜΕΝΟ ★★★

HPV

18-26 ετών *3 δόσεις* ☐ ☐ ☐

26-45 ετών *2 ή 3 δόσεις (συναπόφαση)*

Ηπατίτιδα Β

Για επίνοσα άτομα που έχουν παράγοντες κινδύνου 3 δόσεις (0, 1 και 6 μήνες) ☐ ☐ ☐

SARS-CoV-2 ☐ ☐

C. Koutsianas