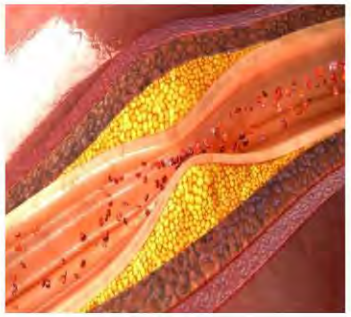
# ΚΑΡΔΙΑΓΓΕΙΑΚΗ ΝΟΣΗΡΟΤΗΤΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΡΕΥΜΑΤΙΚΑ ΝΟΣΗΜΑΤΑ

ΔΗΜΗΤΡΟΥΛΑΣ ΘΕΟΔΩΡΟΣ

Δ’ ΠΑΘΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ ΑΠΘ

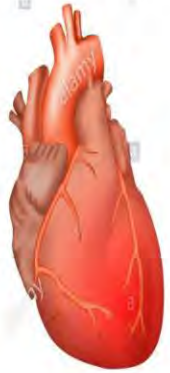
# CARDIOVASCULAR RISK/DISEASE IN SYSTEMIC DISEASES

## Vasculature



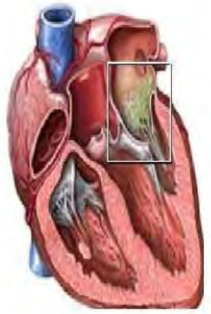
Accelerated Atherosclerosis
Coronary Microvascular Dysfunction
Vasospasm
APLS
Vasculitis
Pulmonary Hypertension

## Pericardial Disease



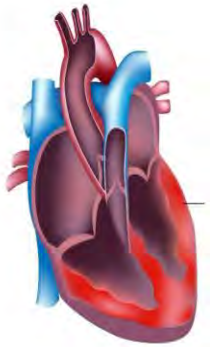
Pericarditis
Tamponade
Constrictive Pericarditis

## Valvular Disease



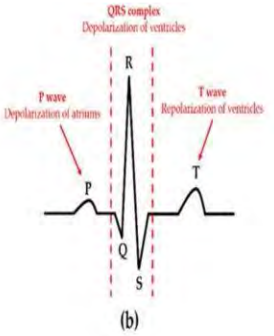
Endocarditis
Valve thrombosis
Valvular Regurgitation
Valvular Stenosis

## Myocardial



Myocarditis
Heart Failure
Cardiomyopathy
HCQ-CMP

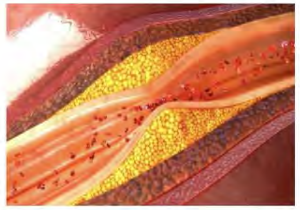
## Electrical




Atrial fibrillation
SVT
Conduction Disease
Prolonged QT
Ventricular Arrythmias

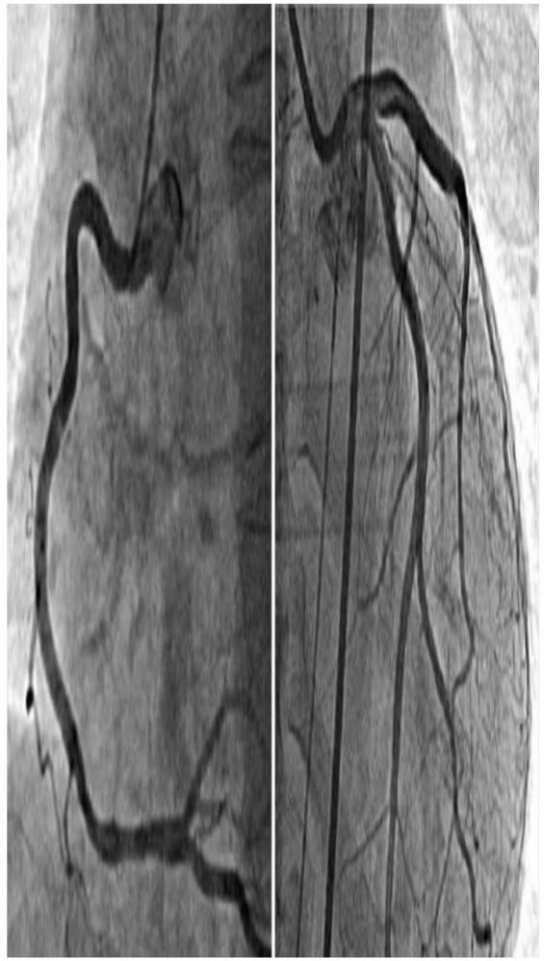
# CARDIOVASCULAR RISK/DISEASE IN SYSTEMIC DISEASES

**Vasculature**

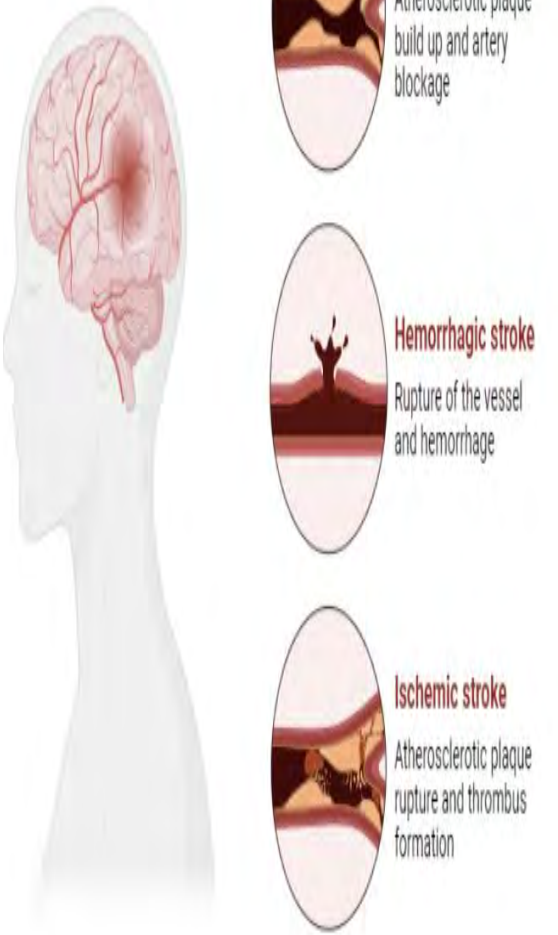


Accelerated Atherosclerosis
Coronary Microvascular Dysfunction
Vasospasm
APLS
Vasculitis
Pulmonary Hypertension

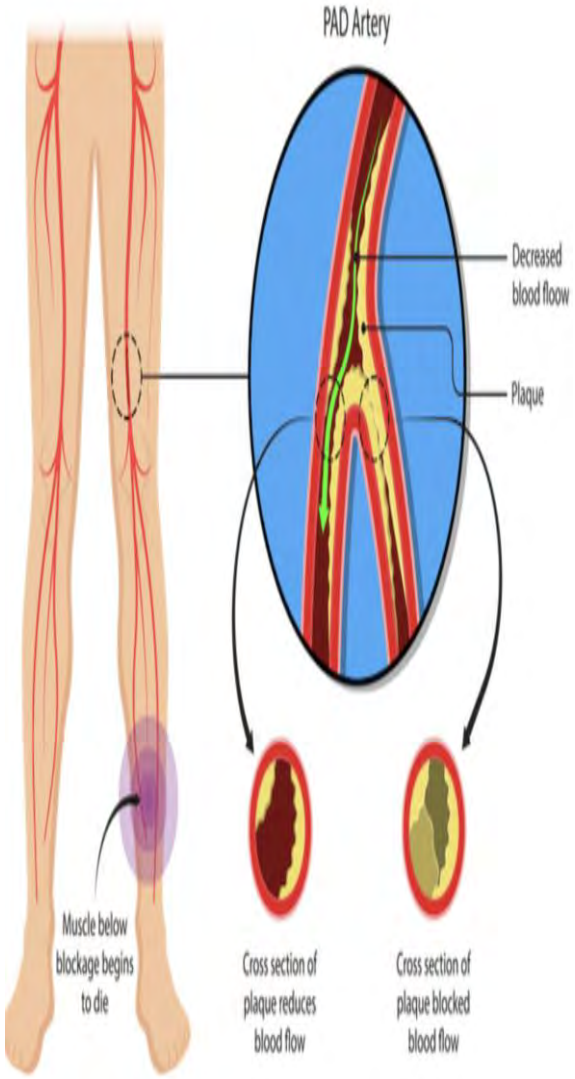
Coronary



Cerebrovascular




Peripheral

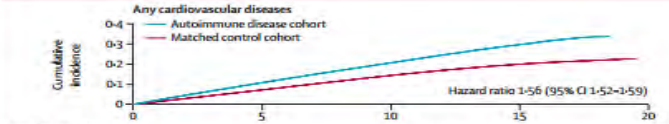


THE LANCET

# Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK

*Nathalie Conrad, Geert Verbeke, Geert Molenberghs, Laura Goetschalckx, Thomas Callender, Geraldine Cambridge, Justin C Mason, Kazem Rahimi, John J V McMurray, Jan Y Verbakel*

| | Cohort | | Events | | Hazard ratio (95% CI) |
|---|---|---|---|---|---|
| | Autoimmune disease | Matched controls | Autoimmune disease | Matched controls | |
| Any autoimmune disease | 446449 | 2102830 | 68413 | 231410 | 1·56 (1·52–1·59) |
| Number of autoimmune diseases | | | | | |
| 1 | 404547 | 1902682 | 55301 | 198769 | 1·41 (1·37–1·45) |
| 2 | 37226 | 177676 | 11005 | 28570 | 2·63 (2·49–2·78) |
| ≥3 | 4676 | 22472 | 2107 | 4071 | 3·79 (3·36–4·27) |
| Connective tissue diseases | 160217 | 761918 | 36846 | 118391 | 1·68 (1·63–1·74) |
| Ankylosing spondylitis | 9864 | 46121 | 1423 | 3822 | 1·97 (1·85–2·35) |
| Polymyalgia rheumatica | 48102 | 231802 | 15390 | 55870 | 1·47 (1·40–1·54) |
| Rheumatoid arthritis | 66796 | 318456 | 15520 | 46594 | 1·83 (1·74–1·92) |
| Sjögren's syndrome | 9933 | 47330 | 2327 | 6139 | 2·08 (1·81–2·39) |
| Systemic lupus erythematosus | 10483 | 49402 | 2204 | 4227 | 2·82 (2·38–3·33) |
| Systemic sclerosis | 2159 | 10310 | 752 | 1320 | 3·59 (2·81–4·59) |
| Vasculitis | 37940 | 178494 | 7839 | 22658 | 1·87 (1·73–2·01) |
| Organ-specific diseases | 407078 | 1909992 | 53706 | 175205 | 1·60 (1·56–1·64) |
| Addison's disease | 2548 | 12055 | 604 | 1218 | 2·83 (1·96–4·09) |
| Coeliac disease | 24895 | 115692 | 2507 | 8618 | 1·50 (1·33–1·69) |
| Type 1 diabetes | 50264 | 235540 | 9697 | 23568 | 2·36 (2·21–2·52) |
| Inflammatory bowel disease | 49214 | 230236 | 6470 | 19532 | 1·71 (1·59–1·85) |
| Graves' disease | 44001 | 207508 | 6409 | 20535 | 1·61 (1·49–1·74) |
| Hashimoto's thyroiditis | 7630 | 35650 | 822 | 2364 | 1·76 (1·41–2·19) |
| Multiple sclerosis | 12006 | 56523 | 1356 | 3876 | 1·85 (1·56–2·20) |
| Myasthenia gravis | 2171 | 10319 | 544 | 1812 | 1·61 (1·21–2·15) |
| Pernicious anaemia | 32910 | 156887 | 8228 | 27099 | 1·61 (1·50–1·73) |
| Psoriasis | 185178 | 869184 | 21197 | 73465 | 1·47 (1·41–1·53) |
| Primary biliary cirrhosis | 4612 | 21973 | 1086 | 3060 | 2·00 (1·66–2·41) |
| Vitiligo | 23709 | 109914 | 1791 | 6526 | 1·38 (1·19–1·60) |





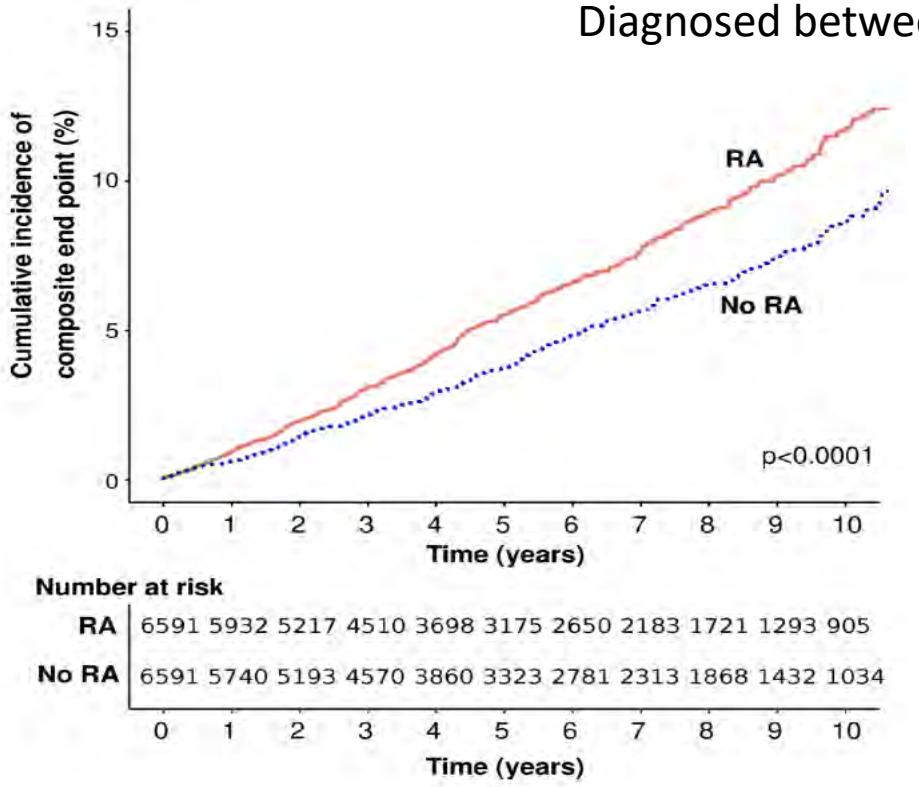


Conrad N et al, Lancet 2022

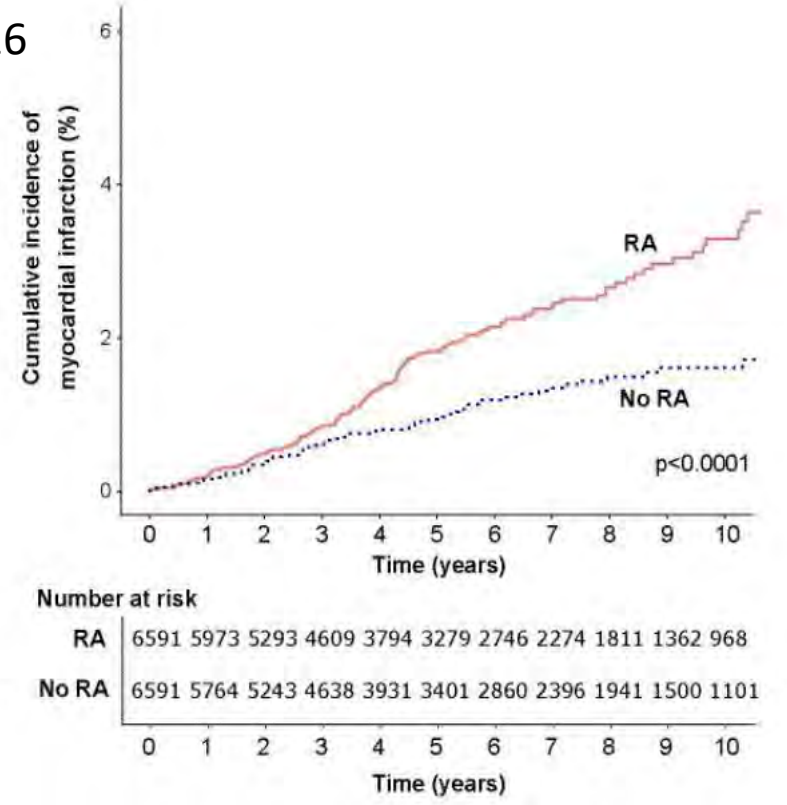
BMJ Journals
Heart

# Cardiovascular risk factors and outcomes in early rheumatoid arthritis: a population-based study

Diagnosed between 2004 and 2016



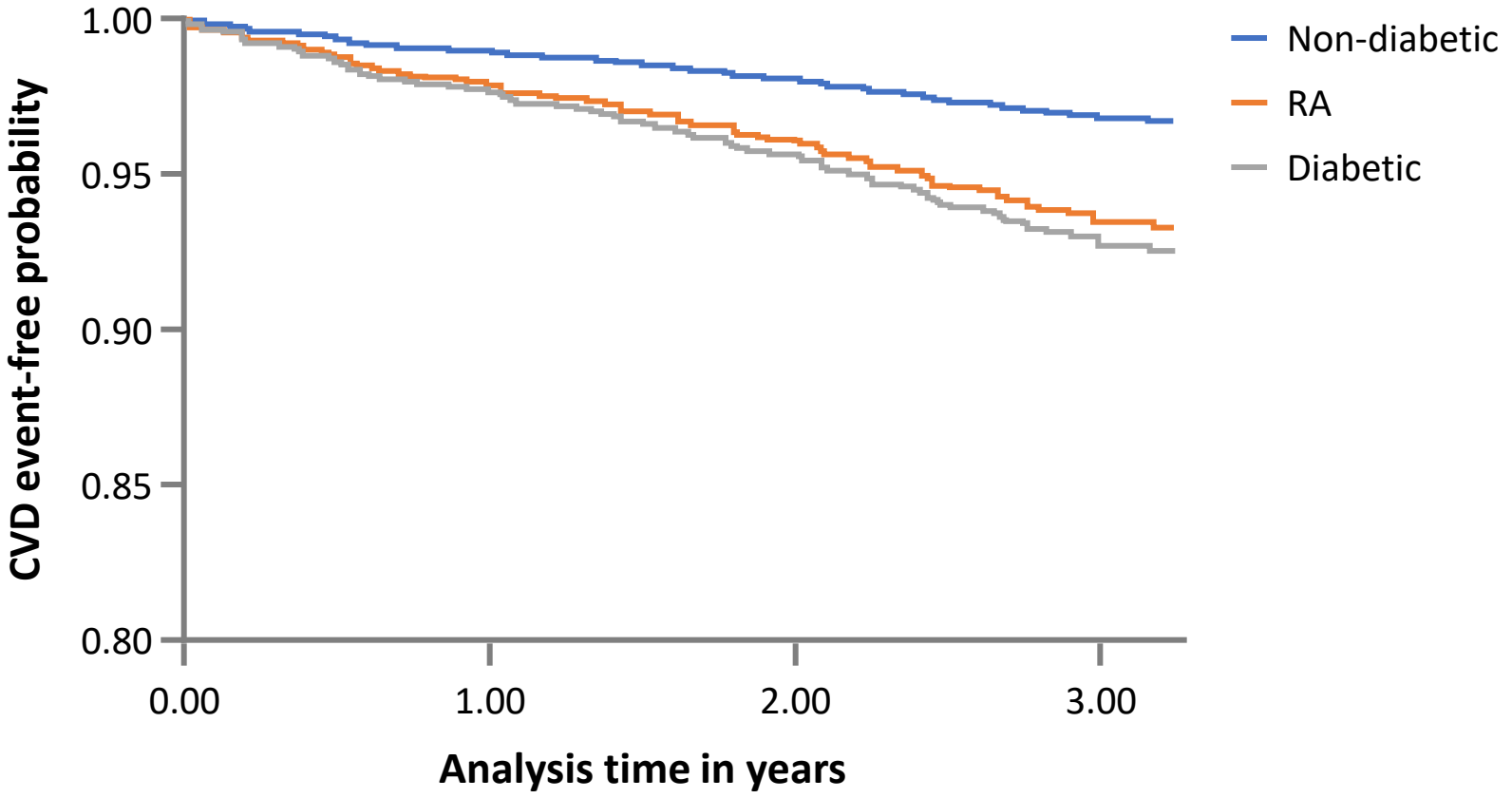

Cumulative incidence of the composite endpoint (myocardial infarction, stroke or heart failure) in people with rheumatoid arthritis (RA) and matched controls without RA.




Cumulative incidence of myocardial infarction in people with rheumatoid arthritis (RA) and matched controls without RA.

Nikiphorou E, et al. *Heart*. 2020;106(20):1566-1572.

# Rheumatoid arthritis: CVD risk magnitude comparable to that of diabetes mellitus



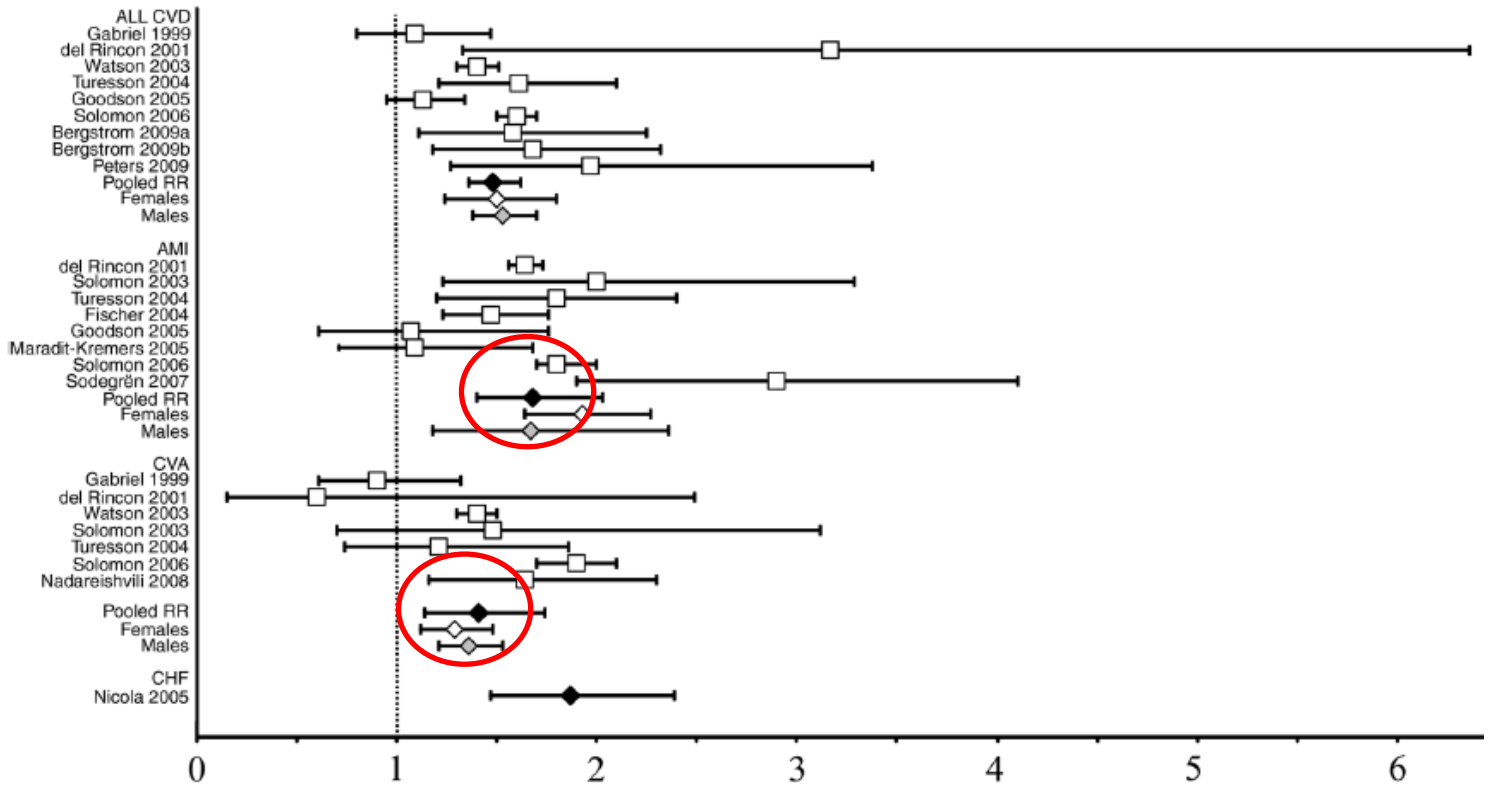

Nurmohamed & Kitas Ann Rheum Dis 2011;70(6):881–883
John et al. Curr Opin Cardiol 2011;26(4):327 333
Stamatelopoulos et al. Arterioscler Thromb Vasc Biol 2009 ;29(10):1702–1708
Linhardsen et al. Ann Rheum Dis 2011;70(6):929–934

Figure: adapted from Peters et al. Arthritis Rheum. 2009 ;61(11):1571–1579

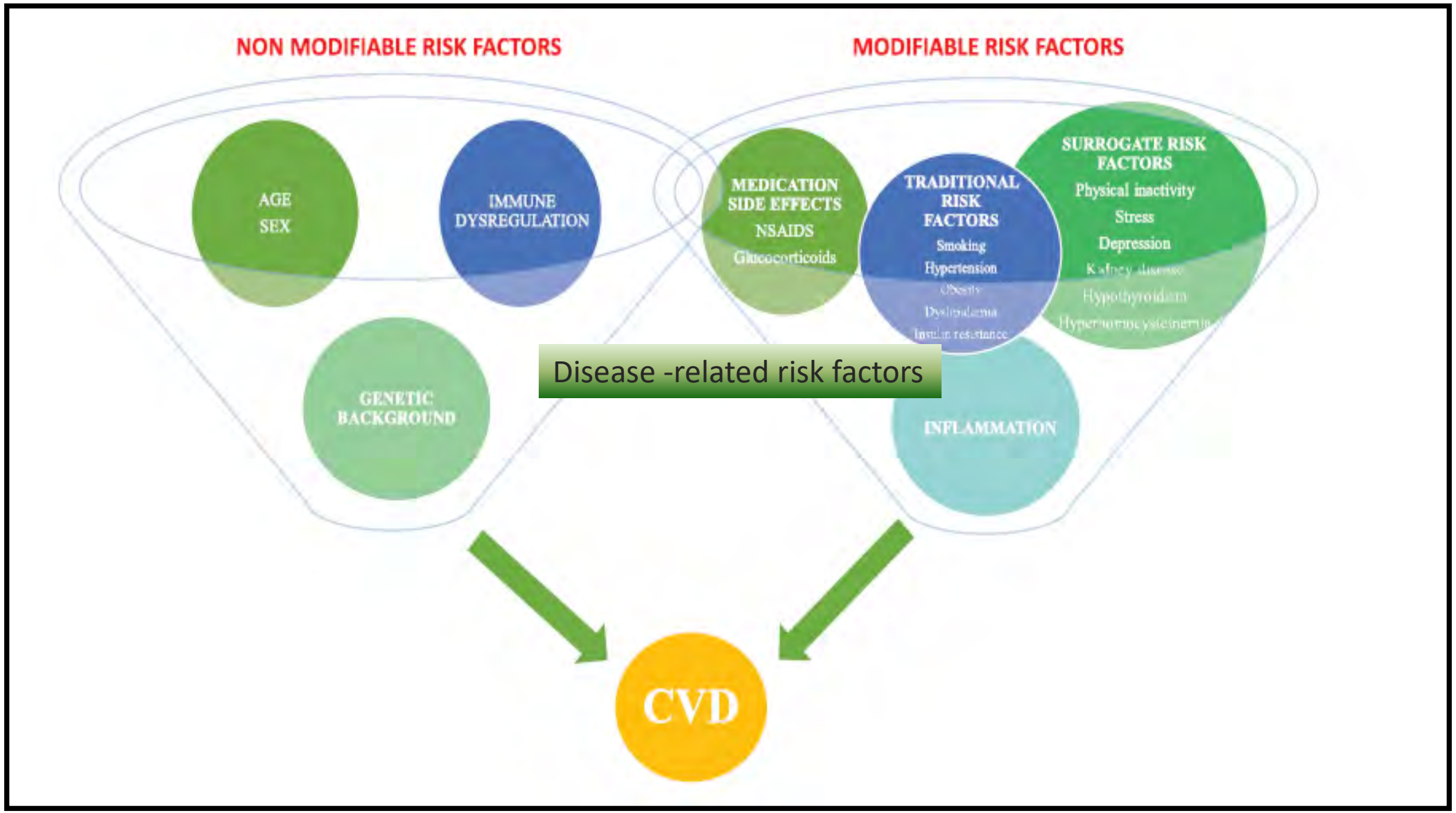
# RA and CVD risk
# Epidemiology & outcomes

The risk of incident CVD is increased by 48% in patients with RA compared to the general population

- Meta-analysis for RA
  - 14 studies comprising 41 490 patients
  - 48% ⇧ risk of incident CVD in RA (RR 1.48 (95% CI 1.36 to 1.62)
  - 68% ⇧ risk of MI and 41% CVA
  - CHF risk was assessed in only one study (RR 1.87 (95% CI 1.47 to



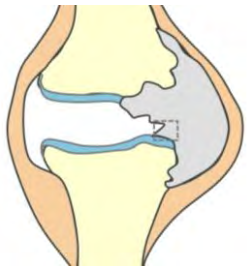

Avina-Zubieta JA et al Ann Rheum Dis 2012




Zegkos et al, Ther Adv Musculoskelet Dis 2016

# RA poor prognostic factors contribute to overall increased CVD

Data from a combination of 13 cohorts from patients with RA from 10 countries 5638 patients mean follow-up 5,8 years



**Disease activity DAS> 3,2**

Accounts for 13% of the risk


**Seropositivity**

Accounts for 12 % of the risk

**ESR and CRP**

Each account for about 5% of the risk


Up to 30% of CVD risk in RA patients is attributed to RA-related characteristics

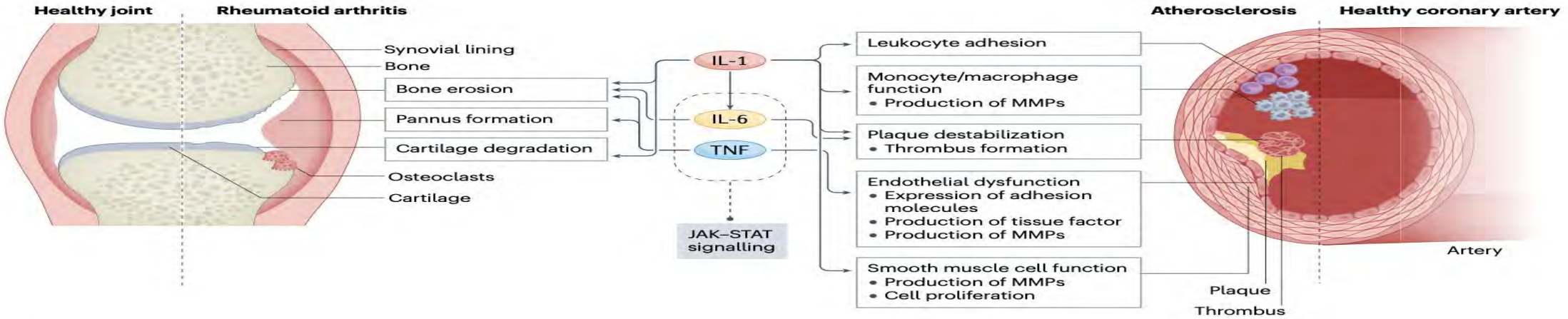
Effective disease control is fundamental for the reduction of CV risk

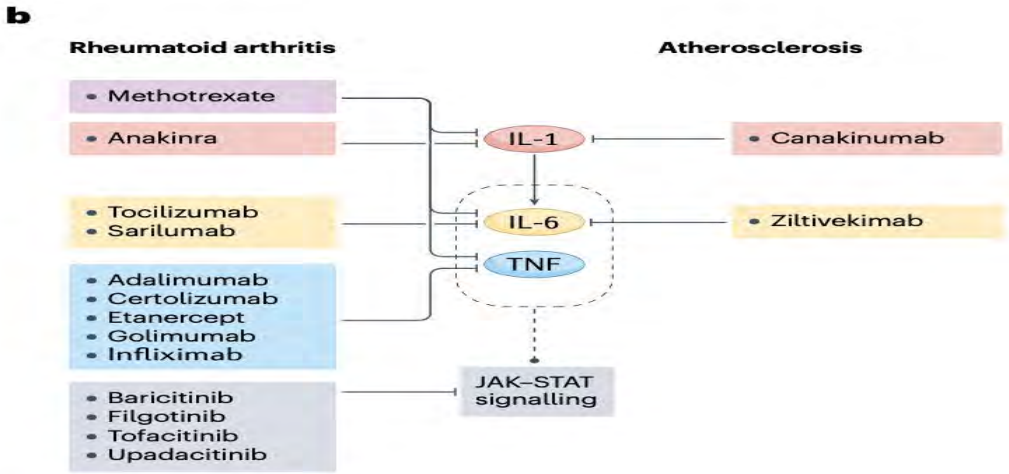
Cynthia S Crowson et al, Ann Rheum Dis 2018

nature REVIEWS RHEUMATOLOGY

# Shared inflammatory pathways of rheumatoid arthritis and atherosclerotic cardiovascular disease

Brittany N. Weber[1], Jon T. Giles[2] & Katherine P. Liao[3,4]

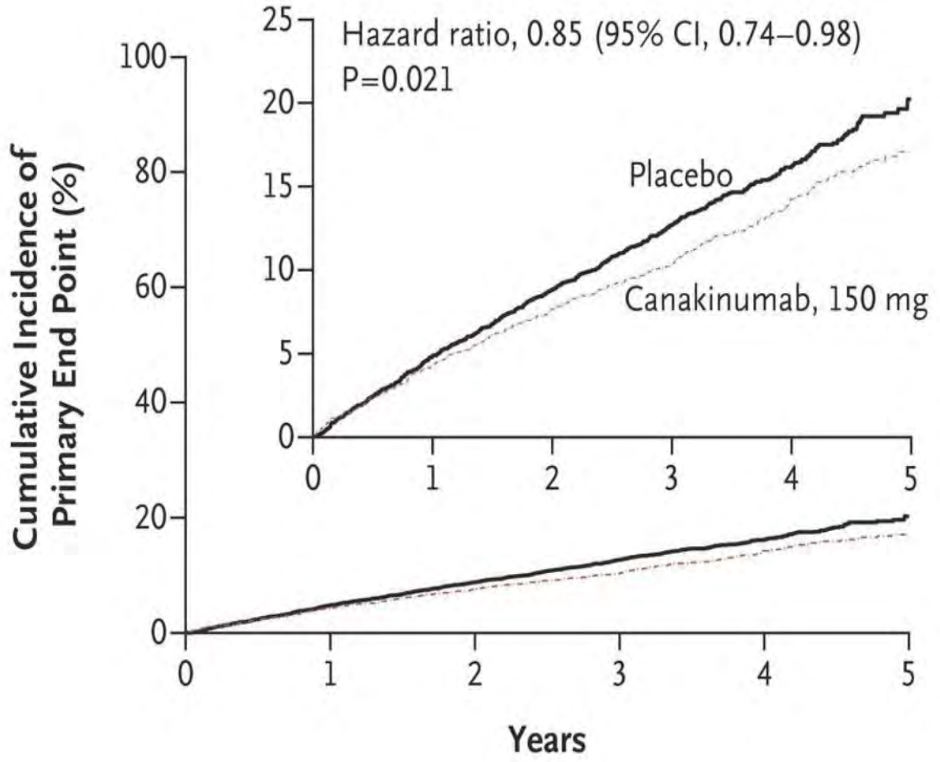



Waber B et al, Nat Rev Rheumatol 2023

## CANTOS Trial

### CANAKINUMAB 150 mg vs PLACEBO

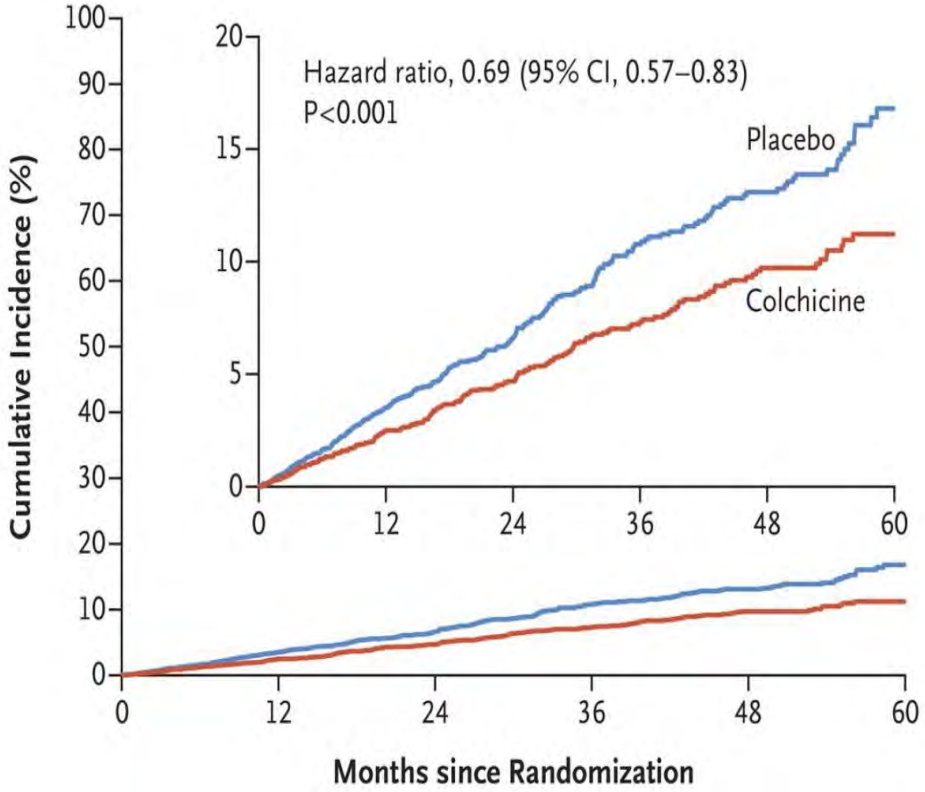



| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 3344 | 3141 | 2973 | 2632 | 1266 | 210 |
| Canakinumab | 2284 | 2151 | 2057 | 1849 | 907 | 207 |

Ridker P, et al. N Engl J Med 2017;377;1119-1131.

## LoDoCo2 Trial

### Colchicine vs Placebo




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 2760 | 2655 | 1703 | 821 | 590 | 161 |
| Colchicine | 2762 | 2685 | 1761 | 890 | 629 | 166 |

Nidorf S, et al. N Engl J Med 2020;383;1838-1847.

# Atherosclerosis and CVD in SLE – an important clinical problem and scientifically of interest

## Increased atherosclerosis in SLE

**TABLE 2. Ultrasound Measurements of Common Carotid Artery Atherosclerosis**

| | SLE Cases | SLE Controls | Population Controls |
|---|---|---|---|
| IMT, mm | 0.66±0.15*† | 0.60±0.14 | 0.59±0.12 |
| | (0.66) | (0.57) | (0.58) |
| Plaque occurrence | 17/26‡§ | 10/26‖ | 3/26 |

Values are given as mean±SD (median).
*$P$=0.03 vs SLE controls.
†$P$=0.001 vs population controls.
‡$P$=0.07 vs SLE controls.
§$P$=0.002 vs population controls.
‖$P$=0.02 vs population controls.

Svenungsson E, Jensen-Urstad K, Heimburger M, Silveira A, Hamsten A, de Faire U, Witztum JL and Frostegard J. Risk factors for cardiovascular disease in systemic lupus erythematosus. *Circulation*. 2001;104:1887-93.

## Atherosclerotic plaques more frequent in SLE

**Table 2 Cardiovascular measurements in SLE-patients and controls**

| | Cases | Controls | *P*-level |
|---|---|---|---|
| IMT R, mm | 0.60 ± 0.13 | 0.62 ± 0.13 | 0.27 |
| IMT L, mm | 0.59 (0.50 to 0.71) | 0.60 (0.52 to 0.70) | 0.62 |
| Plaque,% (no.) | 42.98% ($n$ = 49) | 30.32% ($n$ = 37) | 0.029 |
| clMarea R, mm$^2$ | 11.39 (9.60 to 14.34) | 11.90 (9.9.93 to 14.01) | 0.51 |
| clMarea L, mm$^2$ | 11.81 (9.41 to 13.43) | 11.64 (9.88 to 13.83) | 0.78 |
| **Low-echogenic plaques (grade 1) left and right carotid artery** | **44** | **31** | **0.0962** |
| Low-echogenic plaques (grade 1) left carotid artery | 25 | 13 | 0.016 |
| Low-echogenic plaques (grade 1) right carotid artery | 19 | 18 | 0.62 |
| Plaque distribution* | Plaque 0 = 62 (54.38%) | Plaque 0 = 85 (69.67%) | 0.015 |
| | Plaque 1 = 20 (17.54%) | Plaque 1 = 20 (16.39%) | 0.74 |
| | Plaque 2 = 29 (25.43%) | Plaque 2 = 17 (13.93%) | 0.019 |
| History of cerebrovascular events | 7.89% ($n$ = 9) | 0.81% ($n$ = 1) | 0.007 |
| History of AMI | 4.38% ($n$ = 5) | 0 | 0.025 |
| History of CABG | 2.63% ($n$ = 3) | 0 | - |
| History of heart valve prothesis/impairmeant | 9.64% ($n$ = 11) | 0.81% ($n$ = 1) | 0.002 |
| History of peripheral arterial surgery | 1.75% ($n$ = 2) | 0 | - |
| Claudication | 8.77% ($n$ = 10) | 0.81% ($n$ = 1) | 0.003 |
| CVD** | 21.92% ($n$ = 25) | 2.45% ($n$ = 3) | < 0.001 |

*Plaque 0, no plaque; Plaque 1, plaque on one side; Plaque 2, plaque on both sides.
**Either of history of: cerebrovascular events, AMI, CABG, heart valve prothesis/impairment, peripheral arterial surgery, claudication.
AMI, acute myocardial infarction; CABG, coronary artery by-pass graft; clMa, calculated intima-media area; CVD cardiovascular disease; IMT, common carotid intima-media thickness.

Anania C, Gustafsson T, Hua X, Su J, Vikstrom M, de Faire U, Heimburger M, Jogestrand T and Frostegård J. Increased prevalence of vulnerable atherosclerotic plaques and low levels of natural IgM antibodies against phosphorylcholine in patients with systemic lupus erythematosus. *Arthritis Res Ther*. 2010;12:R214.

# Progression of subclinical atherosclerosis in systemic lupus erythematosus versus rheumatoid arthritis: the impact of low disease activity

TABLE 2 Baseline characteristics and atherosclerotic plaque prevalence in SLE patients, according to LDA status

| Parameter | SLE | | | RA | | |
|---|---|---|---|---|---|---|
| | LDA ($n$ = 89) | Active ($n$ = 12) | *P*-value | LDA ($n$ = 63) | Active ($n$ = 22) | *P*-value |
| Age, mean (S.D.), years | 45 (12) | 38 (12) | 0.069 | 48 (11) | 48 (9) | 0.865 |
| Female, % | 92 | 92 | 0.955 | 92 | 82 | 0.179 |
| Disease duration | 8.7 (7.5) | 8.5 (7.9) | 0.724 | 9.2 (10.6) | 11.7 (8.5) | 0.026* |
| SCORE, mean (S.D.) | 0.4 (0.8) | 0.2 (0.4) | 0.528* | 0.5 (1.1) | 0.4 (0.7) | 0.990 |
| HCQ at baseline, % | 70 | 33 | 0.013 | 3 | 9 | 0.259 |
| HCQ at follow-up, % | 80 | 92 | 0.322 | 11 | 9 | 0.791 |
| Corticosteroids at baseline, % | 58 | 83 | 0.096 | 64 | 68 | 0.692 |
| Prednisone daily dose (mg) at baseline, mean (S.D.) | 4.7 (6.4) | 22.7 (19.1) | <0.001* | 4.0 (3.5) | 4.5 (3.4) | 0.533* |
| Cumulative prednisone dose (g) from diagnosis to baseline, mean (S.D.) | 8.8 (11.6) | 15.5 (15.6) | 0.143* | 8.8 (19.4) | 5.3 (6.3) | 0.910* |
| Cumulative prednisone during follow-up, mean (S.D.) | 3.2 (3.9) | 13.3 (7.9) | <0.001* | 3.6 (3.5) | 5.4 (4.1) | 0.052* |
| Immunosuppressants at baseline, % | 36 | 67 | 0.041 | 65 | 41 | 0.047 |
| Immunosuppressants at follow-up, % | 30 | 67 | 0.013 | 46 | 27 | 0.124 |

*P*-values derived from chi-squared tests for qualitative and Student's test for quantitative variables, except when marked with *, in which case the Mann-Whitney test was used due to deviation from normality. LDA was defined as fulfilment of the following criteria for at least 75% of the follow-up time: DAS28-ESR ⩽ 2.8 in RA, and as SLEDAI-2K ⩽ 4 and PGA (0-3) ⩽1 without new disease activity or major organ activity, prednisone ⩽7.5 mg/day and/or well-tolerated immunosuppressant dosages in SLE. SCORE: Systemic Coronary Risk Evaluation; LDA: low disease activity; PGA: physician global assessment.

Kravvariti E, Konstantonis G, Sfikakis PP, Tektonidou MG. Progression of subclinical atherosclerosis in systemic lupus erythematosus versus rheumatoid arthritis: the impact of low disease activity. Rheumatology (Oxford). 2018;57:2158-2166

RESEARCH Open Access

# Prevalence of comorbidities in systemic sclerosis versus rheumatoid arthritis: a comparative, multicenter, matched-cohort study

Stylianos Panopoulos[1], Maria Tektonidou[1], Alexandros A. Drosos[2], Stamatis-Nick Liossis[3], Theodoros Dimitroulas[4], Alexandros Garyfallos[4], Lazaros Sakkas[5], Dimitrios Boumpas[6], Paraskevi V. Voulgari[2], Dimitrios Daoussis[3], Konstantinos Thomas[7], Georgios Georgiopoulos[7], Georgios Vosvotekas[8], Dimitrios Vassilopoulos[7*] and Petros P. Sfikakis[1]

DM (p=0.007), Dyslipidemia(p=0.001), BMI (p=0.001) more common in RA

**Table 2** Prevalence of comorbidities in systemic sclerosis (SSc) and rheumatoid arthritis (RA) matched cohorts

| Comorbidity | SSc | RA | Crude OR | Adjusted OR |
|---|---|---|---|---|
| Diabetes mellitus | 23 (5.6) | 48 (11.8) | 0.45 (0.27–0.75) | - |
| Dyslipidemia | 72 (17.7) | 123 (30.2) | 0.50 (0.36–0.69) | - |
| Arterial hypertension | 131 (32.1) | 125 (30.6) | 1.07 (0.80–1.44) | - |
| Coronary event | 11 (2.7) | 15 (3.7) | 0.73 (0.33–1.60) | 0.74 (0.34–1.62)* |
| Stroke | 8 (1.9) | 14 (3.4) | 0.56 (0.23–1.35) | 0.55 (0.21–1.32)* |
| Ischemic stroke | 5 (1.2) | 12 (2.9) | 0.40 (0.14–1.17) | 0.39 (0.14–1.15) |
| Hemorrhagic stroke | 3 (0.7) | 2 (0.5) | 1.5 (0.25–9.04) | 1.48 (0.23–8.96) |
| Neoplasia | 17 (4.2) | 19 (4.7) | 0.89 (0.46–1.74) | - |
| Chronic obstructive pulmonary disease | 21 (5.2) | 15 (3.7) | 1.42 (0.72–2.80) | 1.46 (0.74–2.90)** |
| Osteoporosis | 98 (24.0) | 92 (22.6) | 1.09 (0.79–1.50) | 1.08 (0.78–1.49)*** |
| Depression | 90 (22.1) | 49 (12) | 2.07 (1.42–3.03) | - |

All data are shown as number (percentage)
*OR* odds ratio
*Adjusted for smoking, corticosteroid treatment, arterial hypertension, dyslipidemia
**Adjusted for smoking
***Adjusted for corticosteroid treatment

RHEUMATOLOGY
Original article
Rheumatology 2021;60:170–178
doi:10.1093/rheumatology/keaa321
Advance Access publication 29 June 2020

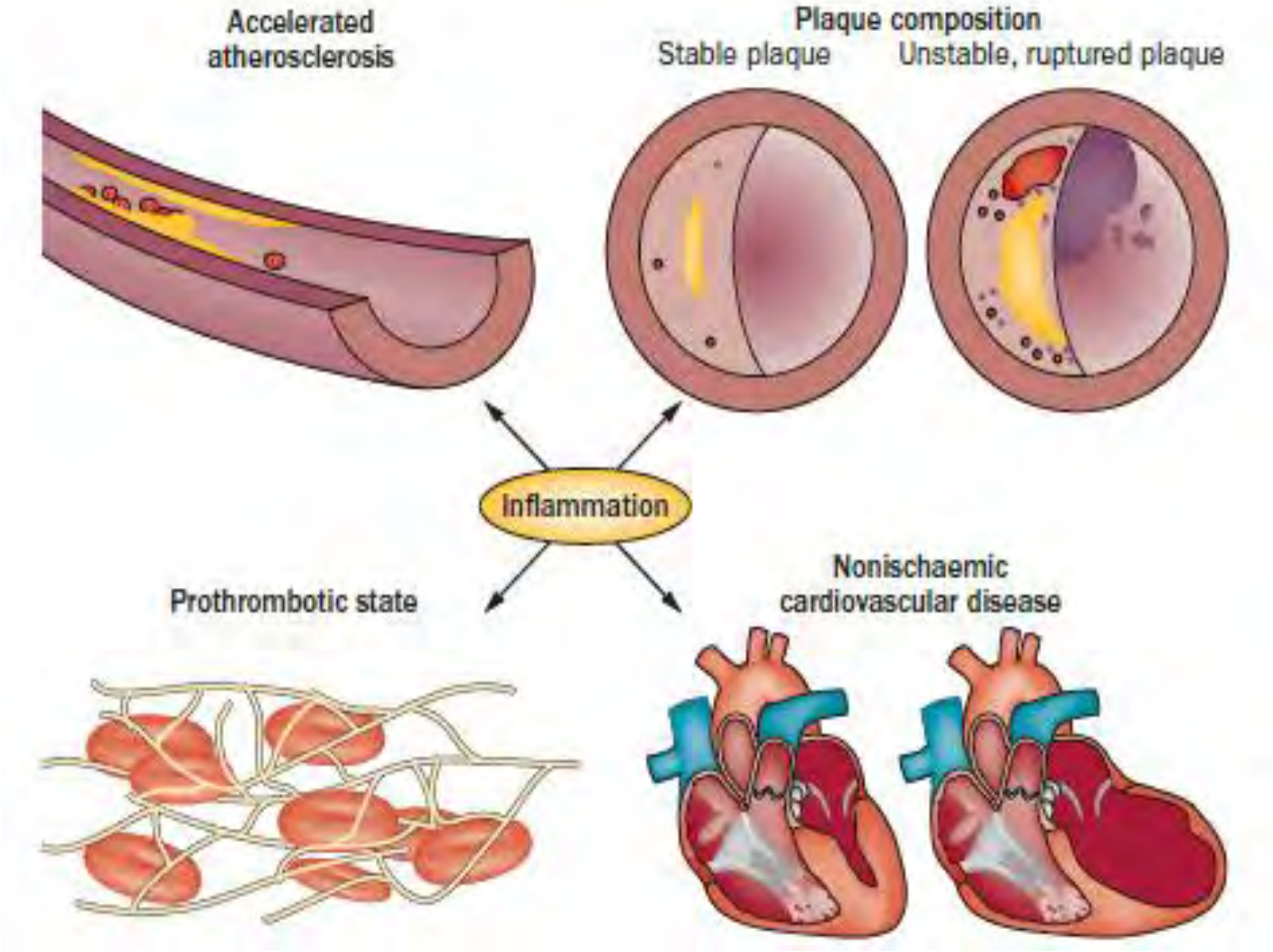
# Comparable or higher prevalence of comorbidities in antiphospholipid syndrome *vs* rheumatoid arthritis: a multicenter, case-control study

Stylianos Panopoulos[1], Konstantinos Thomas[1], Georgios Georgiopoulos[1], Dimitrios Boumpas[1], Christina Katsiari[2], George Bertsias[3], Alexandros A. Drosos[4], Kyriaki Boki[5], Theodoros Dimitroulas[6], Alexandros Garyfallos[6], Charalampos Papagoras[7], Pelagia Katsimbri[1], Apostolos Tziortziotis[2], Christina Adamichou[3], Evripidis Kaltsonoudis[4], Evangelia Argyriou[5], Georgios Vosvotekas[8], Petros P. Sfikakis[1], Dimitrios Vassilopoulos[1], and Maria G. Tektonidou[1]

| | APS (*n* = 326) | RA (*n* = 652) | Crude OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| Arterial hypertension | 97 (29.8%) | 136 (20.9%) | 1.61 (1.19, 2.18) | 1.87 (1.33, 2.64) |
| Smoking (ever) | 175 (53.7%) | 264 (40.5%) | 1.70 (1.30, 2.22) | 1.75 (1.33, 2.30) |
| Hyperlipidaemia | 79 (24.2%) | 135 (20.7%) | 1.23 (0.89, 1.68) | 1.29 (0.92, 1.81) |
| Obesity | 48 (21.0%) | 105 (19.6%) | 1.09 (0.74, 1.59) | 1.07 (0.73, 1.58) |
| Stroke | 66 (20.3%) | 9 (1.4%) | 18.1 (8.91, 36.9) | 13.7 (6.5, 29.1)[a] |
| Coronary artery disease (CAD) | 16 (4.9%) | 13 (2.0%) | 2.54 (1.21, 5.34) | – |
| Major cardiovascular events (combined stroke and CAD) | 79 (24.2%) | 22 (3.4%) | 9.16 (5.58, 15.02) | 9.97 (5.44, 18.28)[a] |
| Osteoporosis | 66 (20.3%) | 92 (14.1%) | 1.55 (1.09, 2.19) | 1.61 (1.09, 2.40)[b] |
| Diabetes mellitus | 18 (5.5%) | 58 (8.9%) | 0.60 (0.35, 1.03) | 0.58 (0.33, 1.02)[b] |
| Chronic obstructive pulmonary disease | 11 (3.4%) | 14 (2.2%) | 1.59 (0.71, 3.55) | 1.22 (0.53, 2.83)[c] |
| Depression | 53 (16.3%) | 66 (10.1%) | 1.72 (1.17, 2.54) | 1.73 (1.16, 2.59)[d] |
| Neoplasms | 14 (4.3%) | 27 (4.1%) | 1.04 (0.54, 2.01) | 1.01 (0.51, 1.99)[e] |

# SYSTEMIC INFLAMMATION AND MECHANISMS OF EXCESS CARDIOVASCULAR RISK

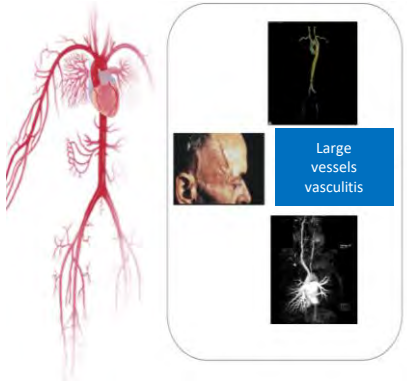
Treatments required for disease control - particularly chronic corticosteroids and immunosuppressives



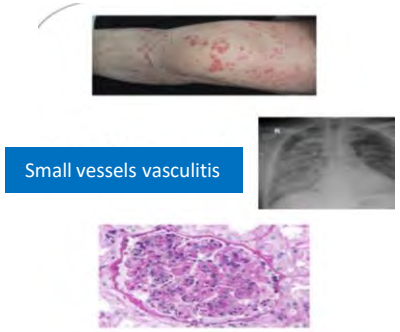

Nurmohamed et al, Nat Rev Rheumatol 2015

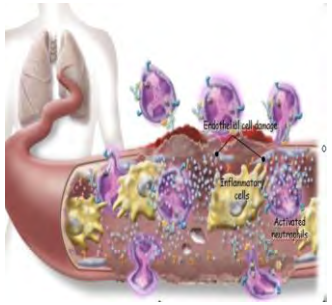
# DISEASE SPECIFIC MECHANISMS OF EXCESS CARDIOVASCULAR RISK



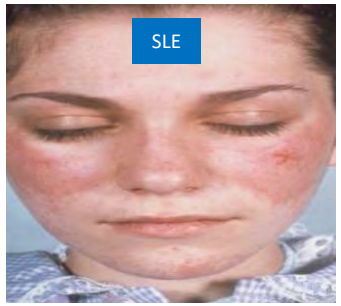


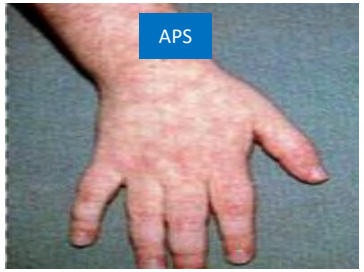


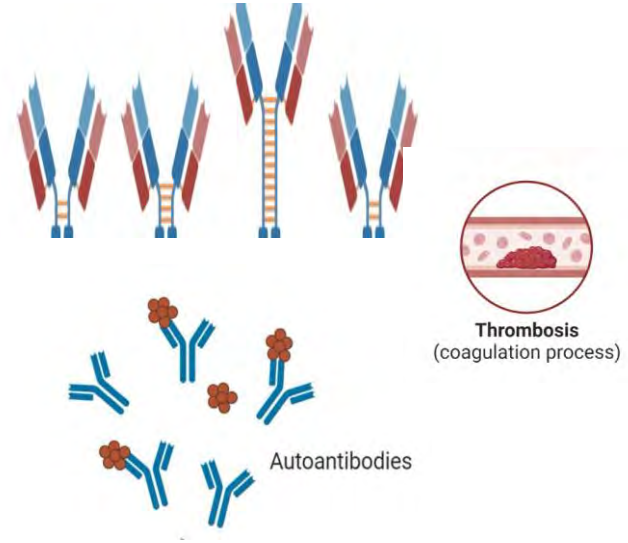


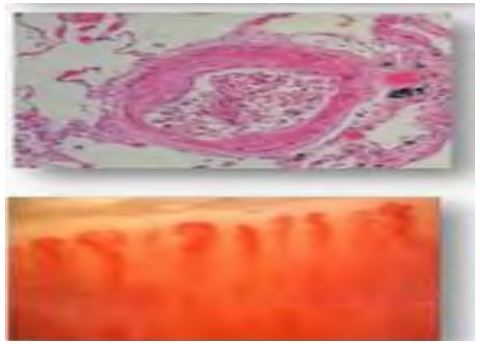




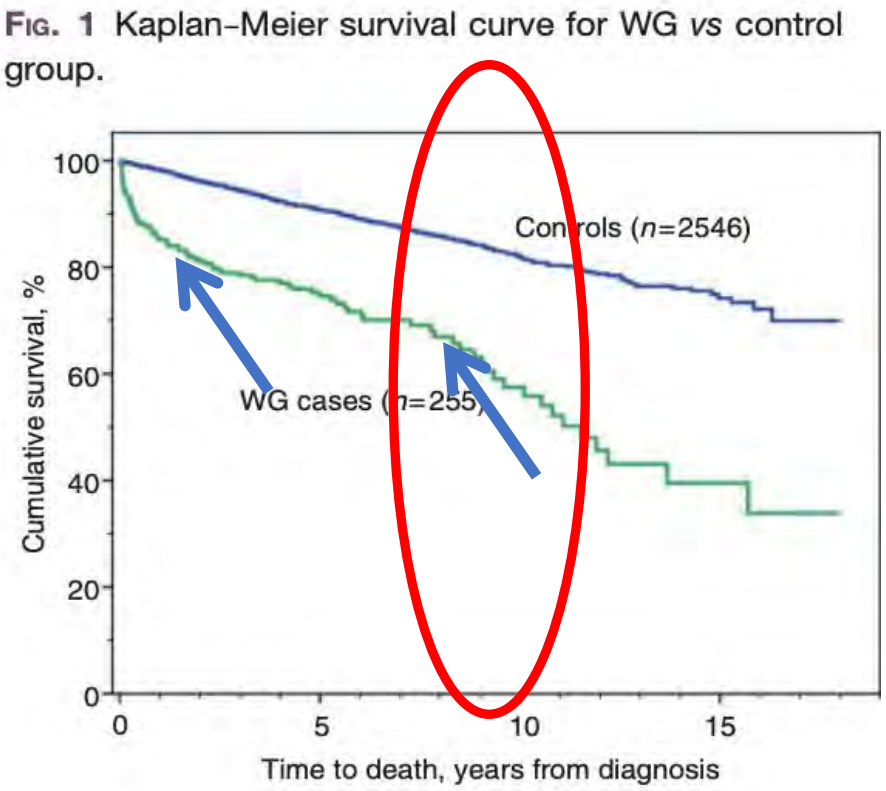



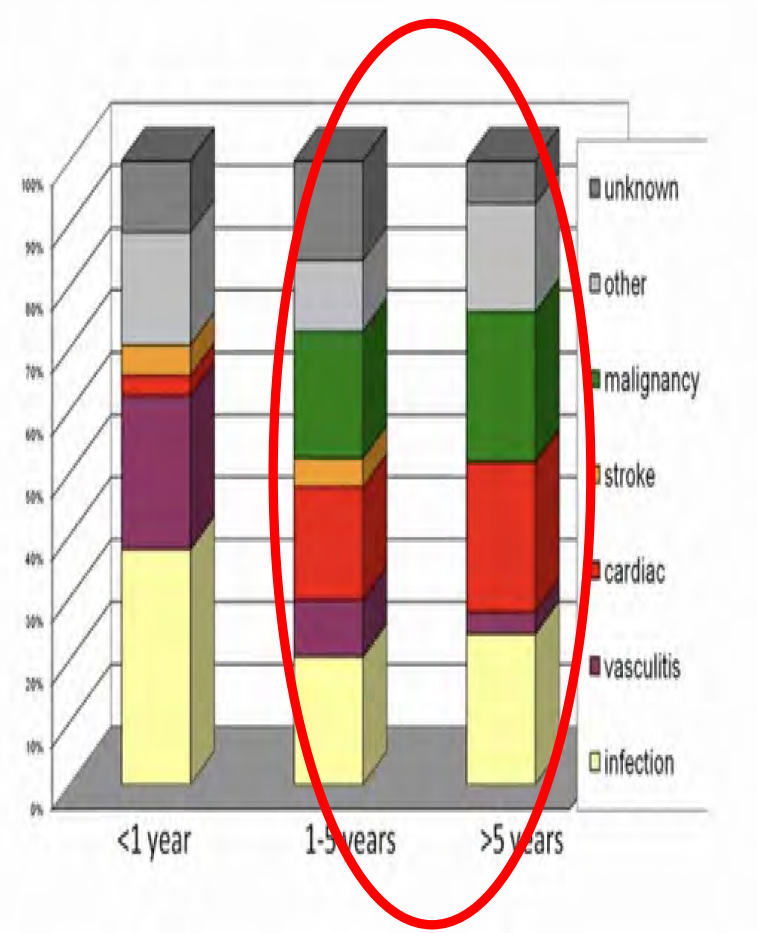







# BIMODAL PATERN OF MORTALITY RATE IN ANCA VASCULITIS


*Luqmani R, et al, Rheumatology 2011*

*Flossman et al, Ann Rheum Dis 2011*

# “The most important information”

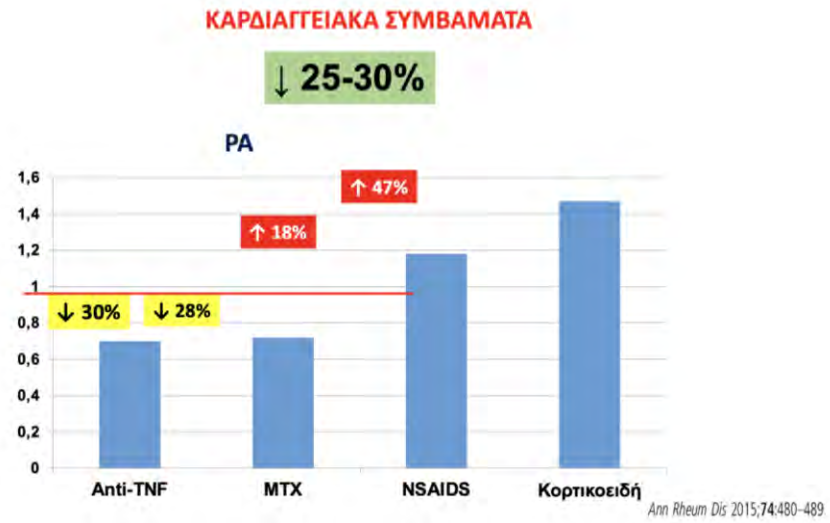
“… the most important information to be gathered from clinical trials in RA is not necessarily comparison of agents, but rather **the strategy of tight control**, aiming for remission.”

**1/ set treatment target**
**2/ assess disease activity**
**3/ adjust treatment strategy**

*Sokka et al. Lancet 2009; 374:430–431*

# The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis

Camille Roubille,[1] Vincent Richer,[2] Tara Starnino,[3] Collette McCourt,[4] Alexandra McFarlane,[5] Patrick Fleming,[6] Stephanie Siu,[7] John Kraft,[8] Charles Lynde,[8] Janet Pope,[7] Wayne Gulliver,[9] Stephanie Keeling,[5] Jan Dutz,[4] Louis Bessette,[10] Robert Bissonnette,[11] Boulos Haraoui[12]




Ann Rheum Dis 2015;17:480-489

# Relationship between exposure to tumour necrosis factor inhibitor therapy and incidence and severity of myocardial infarction in patients with rheumatoid arthritis

Audrey S L Low,[1] Deborah P M Symmons,[1,2] Mark Lunt,[1] Louise K Mercer,[1] Chris P Gale,[3,4] Kath D Watson,[1] William G Dixon,[1] Kimme L Hyrich,[1] on behalf of the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA) and the BSRBR Control Centre Consortium

**Table 2** Risk of MI compared between sDMARD and TNFi cohorts

| | sDMARD; n=3058 | TNFi; n=11 200 |
|---|---|---|
| Median duration of follow-up per patient, years (IQR) | 3.5 (1.8, 4.9) | 5.3 (3.6, 6.4) |
| Total person-years of exposure, pyrs | 10 337 | 55 636 |
| Primary drug exposure model: on-TNFi+90 days | | |
| Number of verified first MIs | 58 | 194 |
| Crude incidence rate of verified first MI per 10 000 pyrs (95% CI) | 56 (43 to 73) | 35 (30 to 40) |
| Unadjusted HR (95% CI) | Referent | 0.78 (0.58 to 1.05) |
| HR adjusted for age and gender (95% CI) | | 1.19 (0.89 to 1.59) |
| HR after adjusting for PD* (95% CI) | | 0.61 (0.41 to 0.89) |
| Sensitivity analyses | | |
| In subjects ever exposed to TNFi; PD-adjusted HR (95% CI) | | 0.67 (0.46 to 0.96) |
| Trimming the PD at 5%; PD-adjusted HR (95% CI) | | 0.56 (0.34 to 0.93) |

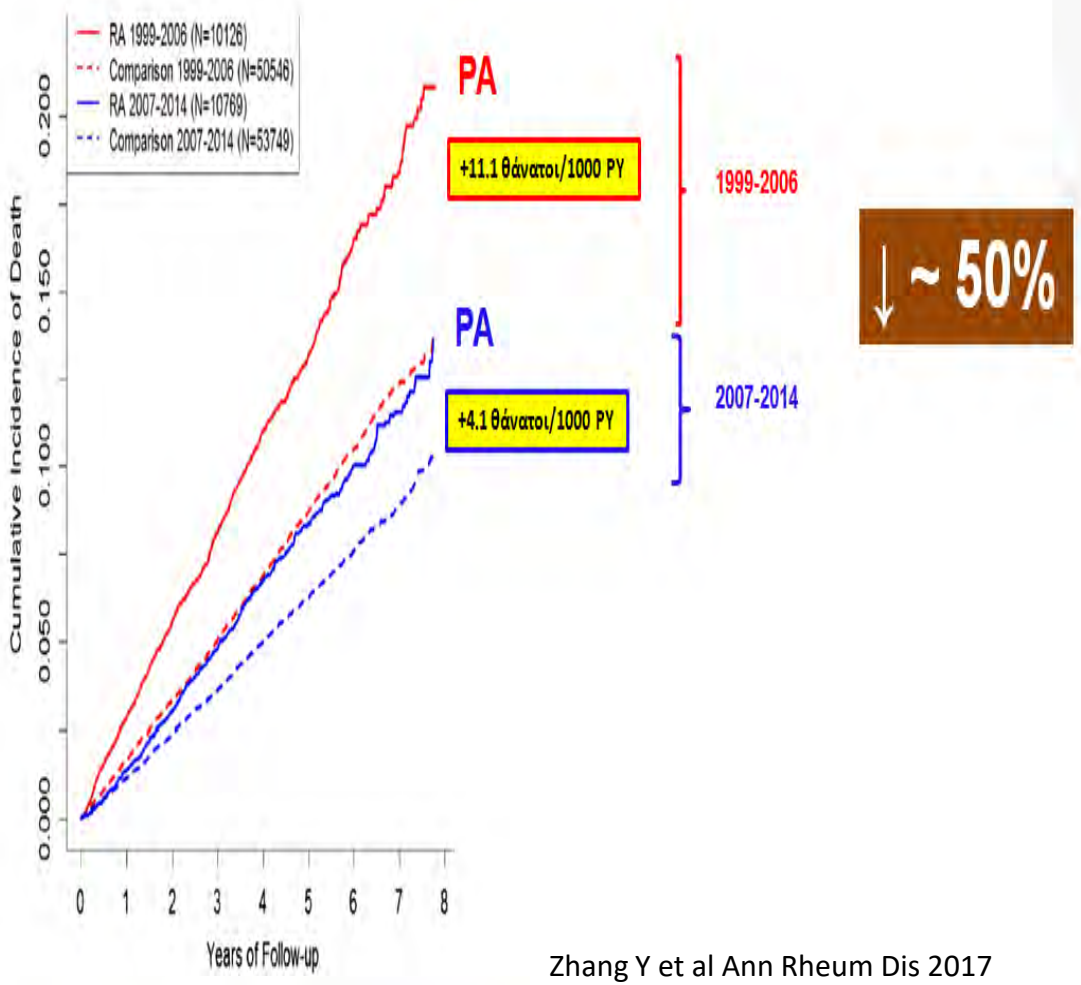
*Deciles of propensity score (PD). The PD included age, gender, DAS28, disease duration, health assessment questionnaire score, whether the patients used four or more sDMARDs prior to study registration (yes/no), whether the patients were recruited to the register before or after 30 June 2004, hypertension, diabetes, chronic lung disease, smoking (ever/never), antiplatelet therapy, NSAID/COX-2 inhibitor use, glucocorticoid use and statin use.

Ann Rheum Dis 2017 Apr;76(4):654-660

BMJ Journals
Annals of the Rheumatic Diseases

Clinical and epidemiological research
Extended report

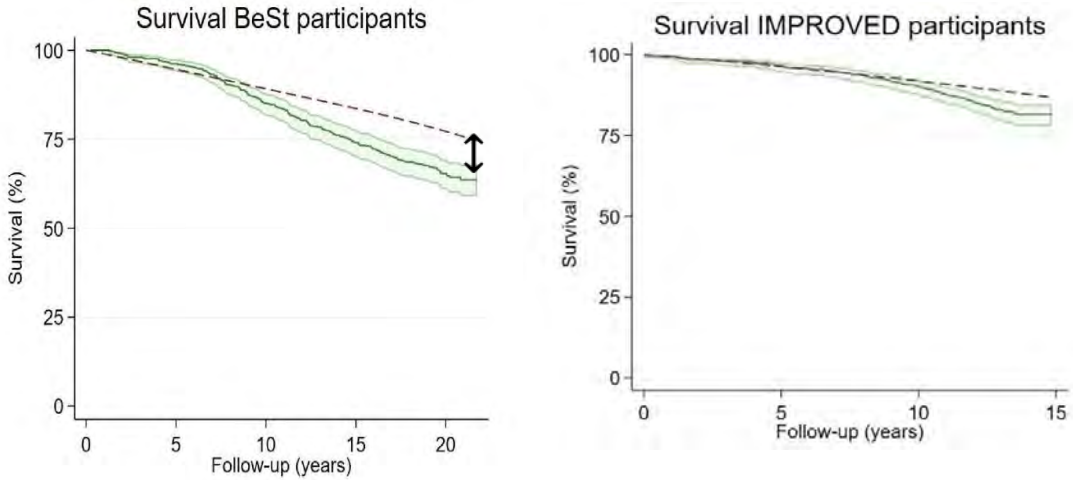
# Improved survival in rheumatoid arthritis: a general population-based cohort study

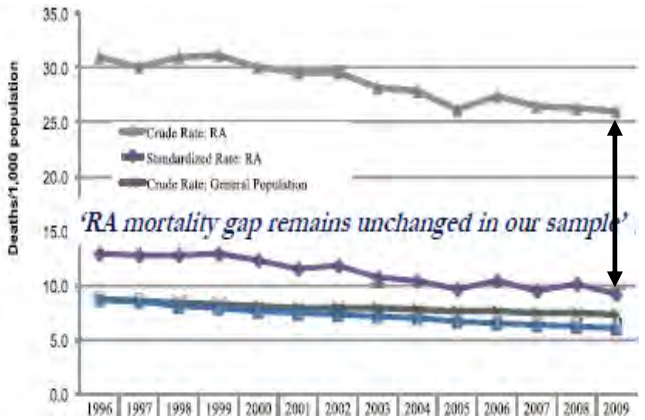



Zhang Y et al Ann Rheum Dis 2017

CLINICAL SCIENCE

# Long-term mortality in treated-to-target RA and UA: results of the BeSt and IMPROVED cohort




Widdifield, Arthritis Care & Research 2015

Heckett SL et all, Ann Rheum Dis 2023

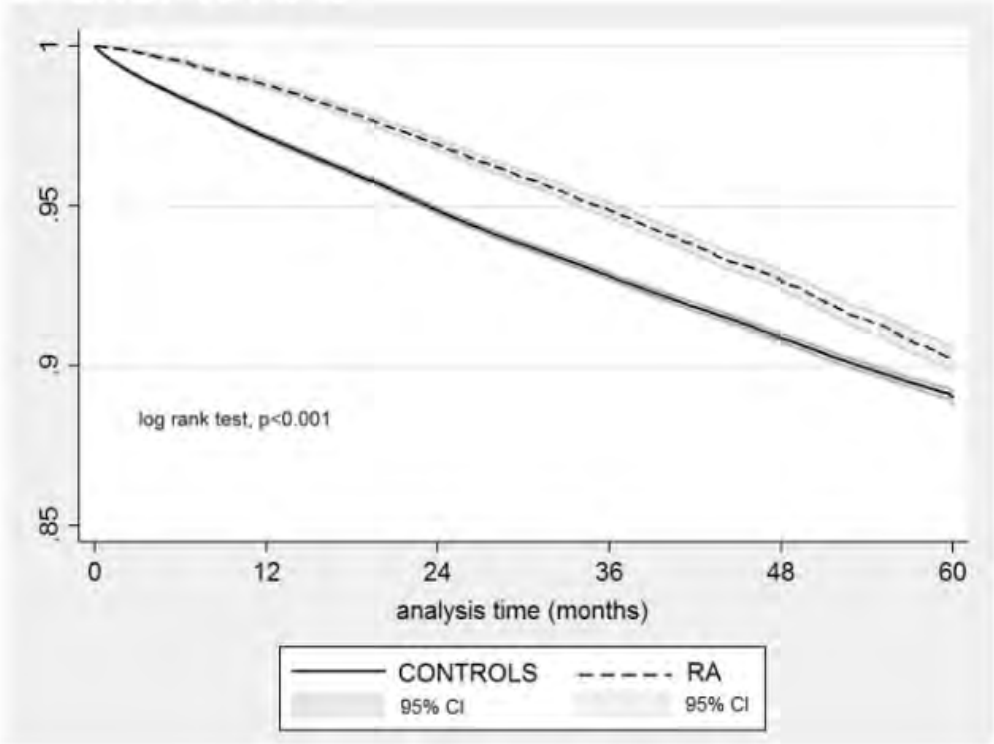
RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

# All-cause mortality in systemic rheumatic diseases under treatment compared with the general population, 2015–2019

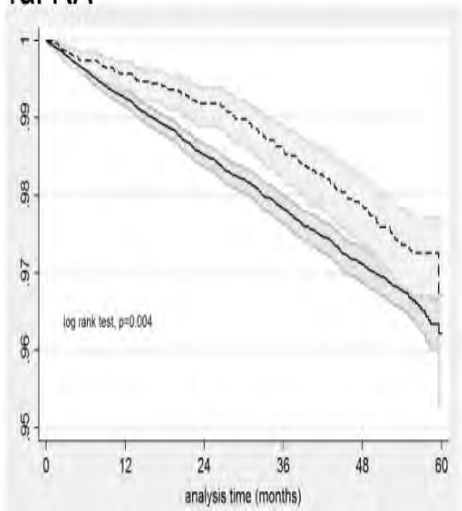
Vasiliki-Kalliopi Bournia ,[1] George E Fragoulis ,[1] Panagiota Mitrou,[2] Konstantinos Mathioudakis,[3] Anastasios Tsolakidis,[3] George Konstantonis,[1] Georgia Vourli,[4] Dimitrios Paraskevis,[4] Maria G Tektonidou ,[1] Petros P Sfikakis[1]

Panel 1. RA



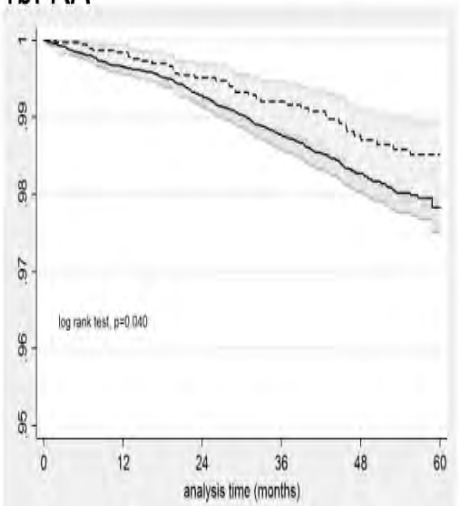

a. Males

1a. RA




b. Females

1b. RA



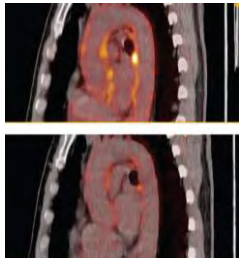

Bournia et al, RMD Open 2021

CLINICAL SCIENCE

# Reducing cardiovascular risk with immunomodulators: a randomised active comparator trial among patients with rheumatoid arthritis

Daniel H Solomon ,[1] Jon T Giles,[2] Katherine P Liao,[1] Paul M Ridker,[1] Pamela M Rist,[1] Robert J Glynn,[1] Rachel Broderick,[2] Fengxin Lu,[1] Meredith T Murray,[1] Kathleen Vanni,[1] Leah M Santacroce,[1] Shady Abohashem,[3] Philip M Robson,[4] Zahi Fayad,[4] Venkatesh Mani,[4] Ahmed Tawakol,[3] Joan Bathon,[2] TARGET Trial Consortium

115 patients with active RA on MTX received were randomly assigned to receive TNF inhibitor or HCQ + SLS (triple therapy)



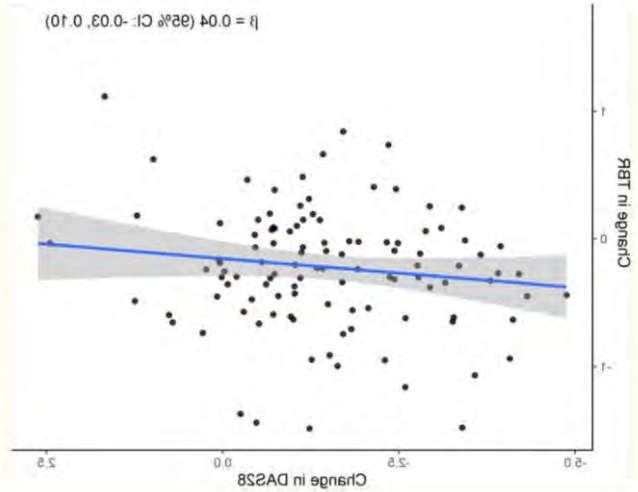
Baseline and follow-up 18F- fluorodeoxyglucose-positron emission tomography/CT scans were assessed for change in arterial inflammation, measured as an arterial target-to-background ratio (TBR) in the carotid arteries and aorta.

**Table 2** Results of FDG-PET/CT scans target to background ratio comparing subjects randomised to TNF inhibitors versus triple therapy

| | Baseline | | Follow-up | | Differences (Δ=baseline to follow-up) | | | |
|---|---|---|---|---|---|---|---|---|
| | TNFi | Triple therapy | TNFi | Triple therapy | ΔTNFi | ΔTriple therapy | TNFi versus triple therapy | |
| Arterial location assessed | Mean (SD) | | | | | | β (95% CI) | P value |
| Primary outcome | | | | | | | | |
| MDS of index vessel* | 2.72 (0.75) | 2.62 (0.51) | 2.47 (0.68) | 2.43 (0.51) | −0.24 (0.51) | −0.19 (0.51) | −0.02 (−0.19 to 0.15) | 0.79 |
| Secondary outcomes† | | | | | | | | |
| MDS of aorta | 2.67 (0.79) | 2.64 (0.50) | 2.50 (0.69) | 2.47 (0.42) | −0.17 (0.52) | −0.17 (0.39) | 0.01 (−0.14 to 0.17) | 0.87 |
| Aorta | 2.46 (0.66) | 2.48 (0.43) | 2.45 (0.74) | 2.42 (0.38) | −0.02 (0.43) | −0.06 (0.34) | 0.03 (−0.11 to 0.18) | 0.64 |
| Bilateral carotids | 2.13 (0.36) | 2.21 (0.44) | 2.07 (0.51) | 2.11 (0.46) | −0.06 (0.48) | −0.10 (0.51) | −0.003 (−0.20 to 0.19) | 0.98 |
| Index vessel | 2.51 (0.62) | 2.45 (0.45) | 2.43 (0.74) | 2.38 (0.47) | −0.09 (0.43) | −0.07 (0.47) | −0.01 (−0.17 to 0.16) | 0.94 |

Follow-up value is at study conclusion (approximately 24 weeks). Triple therapy refers to the use of weekly methotrexate, sulfasalazine 1000 mg two times per day, and hydroxychloroquine 200–400 mg per day. Counts of the number of individuals included in each analysis: TBR MDS—TNFi=58, triple therapy=57; aorta—TNFi=56, triple therapy=52; left carotid—TNFi=44, triple therapy=41; right carotid—TNFi=43, triple therapy=42; average carotid—TNFi=45, triple therapy=43.
*When vessel is not specified, the measurement refers to the index vessel with the most diseased segment.
†P values for the secondary outcomes are nominal and not corrected for multiple testing. All β estimates and p values are from ANCOVA models that estimate the change in TBR as a function of the baseline TBR, treatment group and the randomisation strata.
ANCOVA, analysis of covariance; FDG-PET/CT, 18F-fluorodeoxyglucose positron emission tomography/CT scan; MDS, most disease segment examining right and left carotid arteries and aorta; TBR, target to background ratio; TNFi, TNF inhibitor.

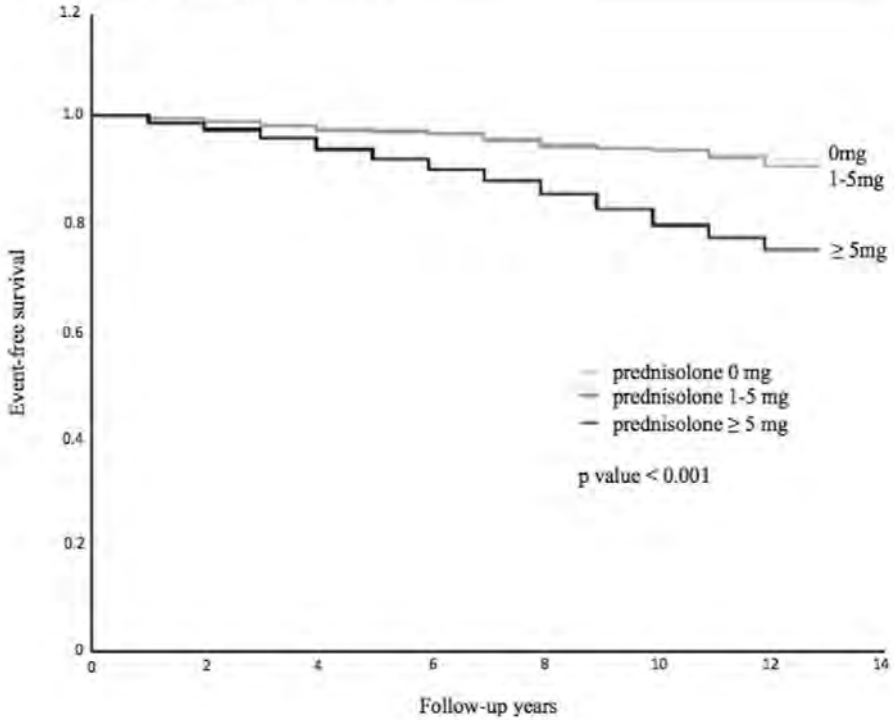
8% decrease in vascular inflammation overall (in the most diseased vessel – carotid or aorta), p=0.001



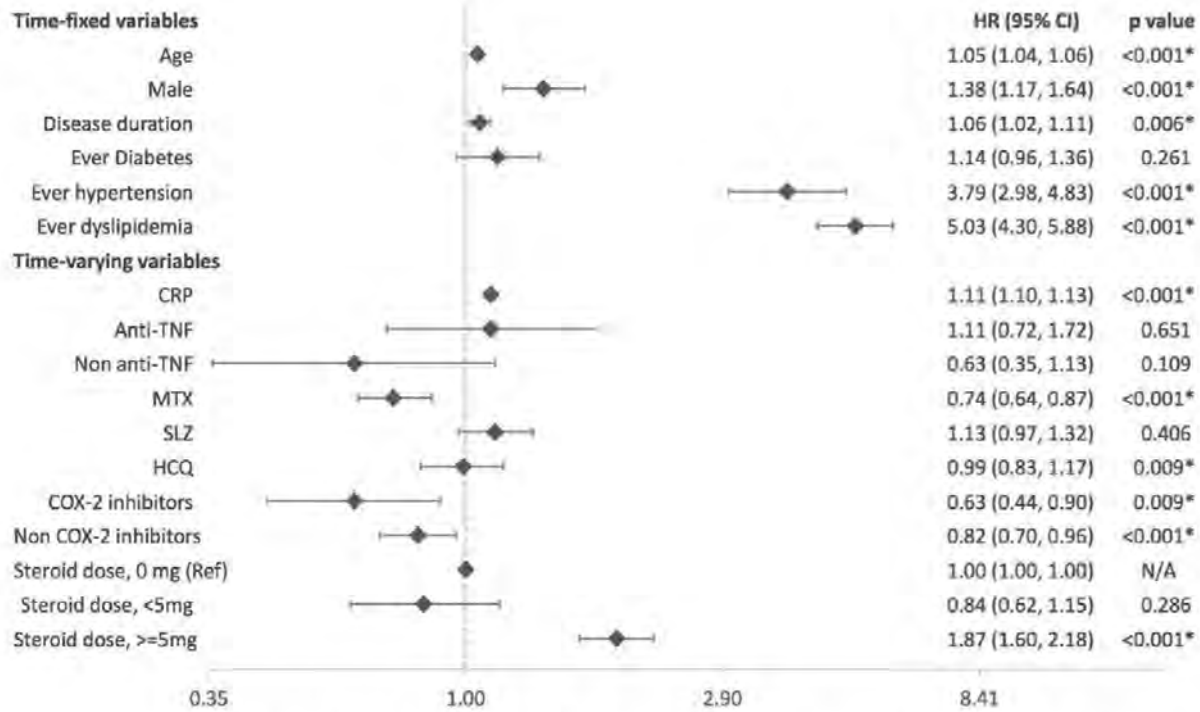

Solomon D et al, Ann Rheum Dis 2023

# Higher doses (≥ 5 mg) of prednisone increase the risk of cardiovascular disease

Major adverse CV event-free Survival of RA in varying GC doses




Forest plot for predictors of MACE in RA Cohort




Multivariate Cox Regression Model using time-varying covariates (age sex, disease duration, diabetes, hypertension, dyslipidemia)

So H, *et al*. *Ann Rheum Dis* 2023;**82**:1387–1393.

Randomized Controlled Trial > Arthritis Rheumatol. 2020 Jan;72(1):31-40.
doi: 10.1002/art.41095.

## Cardiovascular Safety of Tocilizumab Versus Etanercept in Rheumatoid Arthritis: A Randomized Controlled Trial

Jon T Giles [1], Naveed Sattar [2], Sherine Gabriel [3], Paul M Ridker [4], Steffen Gay [5], Charles Warne [6], David Musselman [7], Laura Brockwell [6], Emma Shittu [6], Micki Klearman [7], Thomas R Fleming [8]

Comparative Study > Semin Arthritis Rheum. 2018 Dec;48(3):399-405.
doi: 10.1016/j.semarthrit.2018.03.012. Epub 2018 Mar 22.

## No difference in cardiovascular risk of tocilizumab versus abatacept for rheumatoid arthritis: A multi- database cohort study

Seoyoung C Kim [1], Daniel H Solomon [2], James R Rogers [3], Sara Gale [4], Micki Klearman [4], Khaled Sarsour [4], Sebastian Schneeweiss [3]

Observational Study > J Am Heart Assoc. 2018 Jan 24;7(3):e007393.
doi: 10.1161/JAHA.117.007393.

## Comparative Cardiovascular Risk of Abatacept and Tumor Necrosis Factor Inhibitors in Patients With Rheumatoid Arthritis With and Without Diabetes Mellitus: A Multidatabase Cohort Study

Eun Ha Kang [1 2], Yinzhu Jin [1], Gregory Brill [1], Jennifer Lewey [1 3], Elisabetta Patorno [1], Rishi J Desai [1], Seoyoung C Kim [4 5]

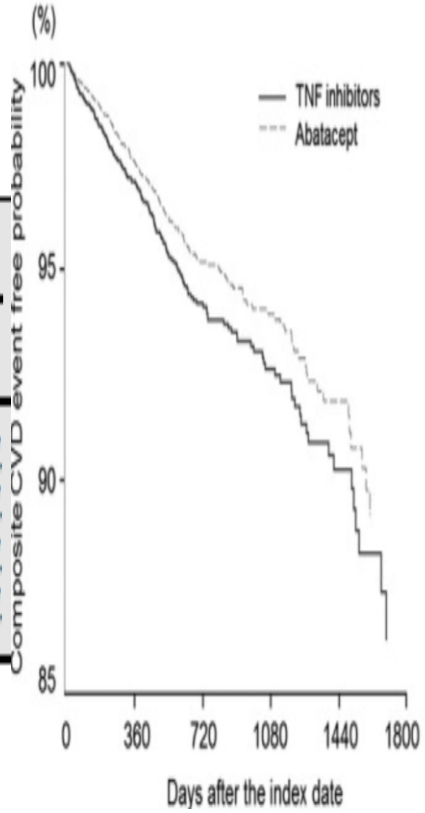
- **HR for MACE tocilizumab vs. etanercept**
  - **1.05 (95% CI 0.77, 1.43) for intention to treat population**
    - MACE rate 1.82/100 patient years for tocilizumab group
    - MACE rate 1.70/100 patient-years for etanercept group
  - **1.11 (95% CI 0.78, 1.62) for on-treatment population**

Table 3

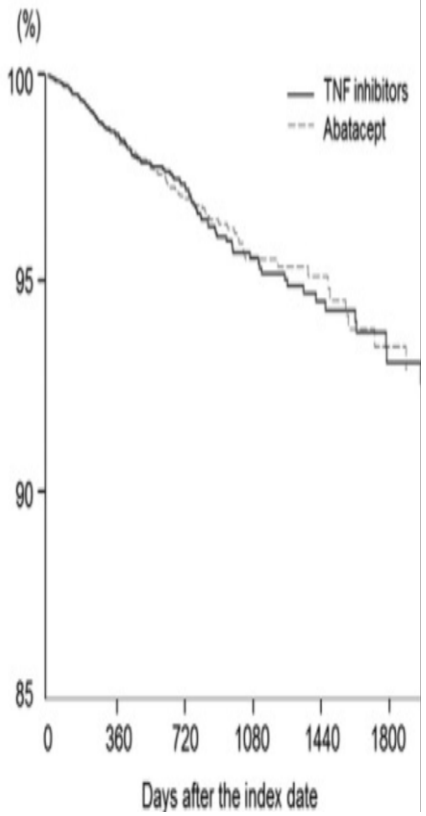
Incidence rate and hazard ratio of the composite cardiovascular endpoint in tocilizumab users versus abatacept: propensity score-matched with a 1:3 variable ratio

| | Tocilizumab | | | | | Abatacept | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. of subjects | Events | Person-years | IR[a] (95% CI) | HR | No. of subjects | Events | Person-years | IR[a] (95% CI) | HR |
| Medicare | 1516 | 18 | 1097 | 1.64 (1.01-2.54) | 0.96 (0.56-1.63) | 4075 | 59 | 3497 | 1.69 (1.30-2.16) | Ref. |
| PharMetrics | 1735 | 5 | 1336 | 0.37 (0.14-0.82) | 0.67 (0.25-1.84) | 3840 | 18 | 3061 | 0.59 (0.36-0.91) | Ref. |
| MarketScan | 2986 | 9 | 2163 | 0.42 (0.21-0.76) | 0.68 (0.32-1.42) | 6770 | 35 | 5126 | 0.68 (0.48-0.94) | Ref. |
| Combined | 6237 | 32 | 4596 | 0.70 (0.49-0.97) | 0.82[b] (0.55-1.22) | 14,685 | 112 | 11,684 | 0.96 (0.79-1.15) | Ref. |

A. Medicare

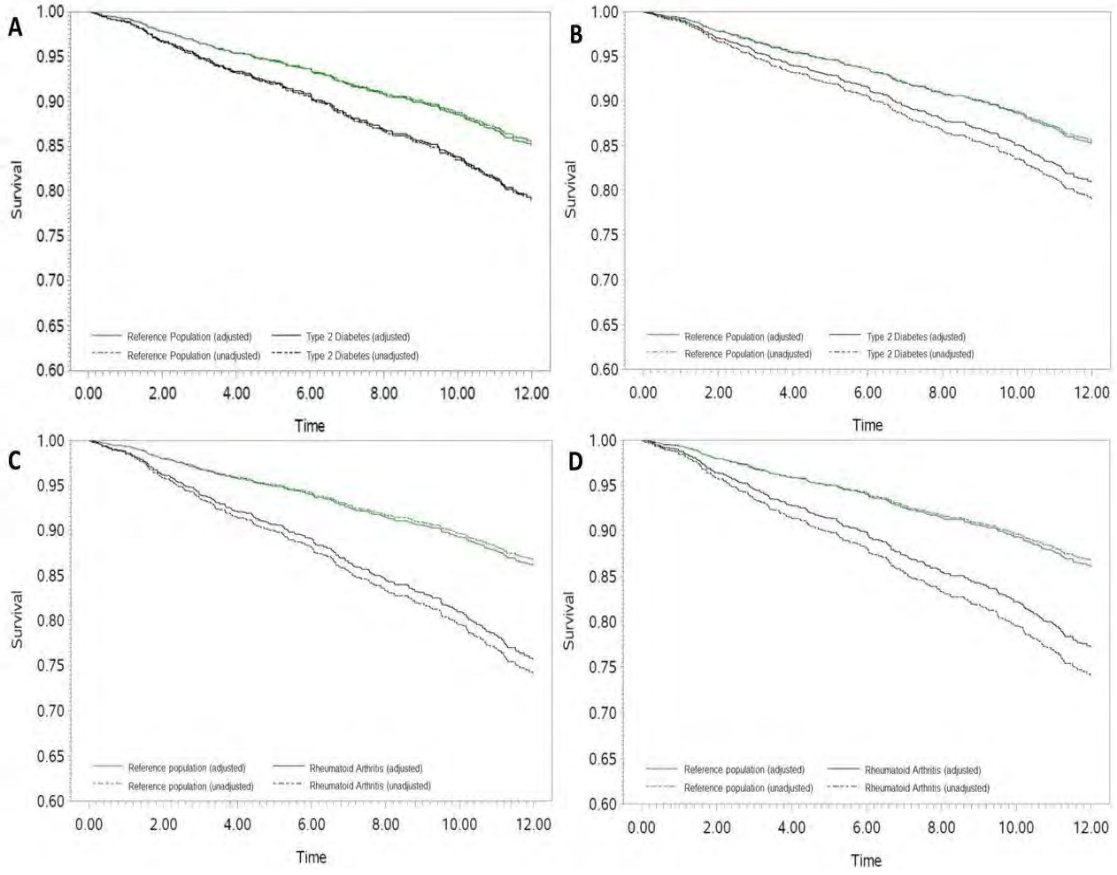



B. Market Scan



# Cardiovascular Event Risk in Rheumatoid Arthritis Compared with Type 2 Diabetes: A 15-year Longitudinal Study

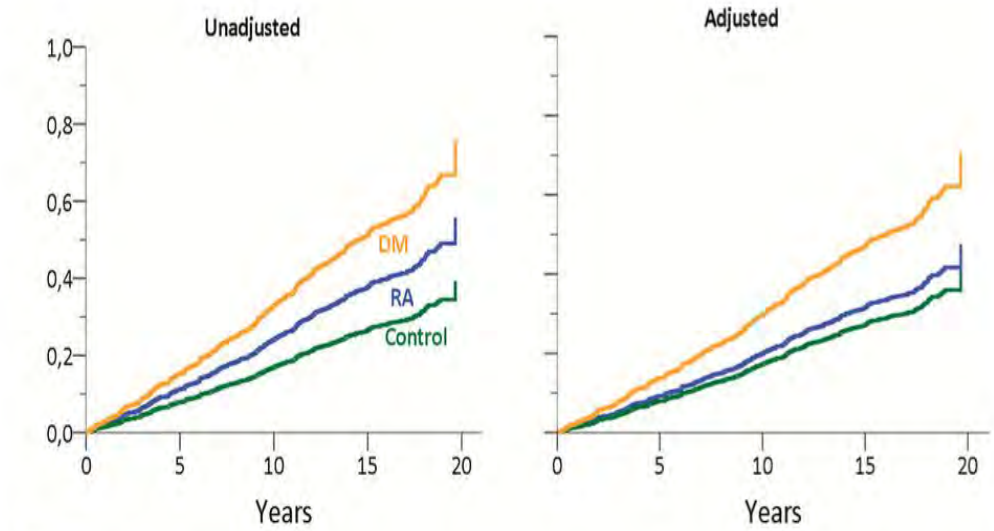
Rabia Agca, Luuk H.G.A. Hopman, Koen J.C. Laan, Vokko P. van Halm, Mike J.L. Peters, Yvo M. Smulders, Jacqueline M. Dekker, Giel Nijpels, Coen D.A. Stehouwer, Alexandre E. Voskuyl, Maarten Boers, Willem F. Lems and Michael T. Nurmohamed




Rabia Agca et al. J Rheumatol 2020

# In RA patients without prevalent CVD, incident CVD is mainly associated with traditional risk factors: A 20-year follow-up in the CARRÉ cohort study

R. Raadsen [a,*], R. Agca [a,b], M. Boers [a,b,c], V.P. van Halm [d], M.J.L. Peters [e], Y. Smulders [f], J.W.J. Beulens [c], M.T. Blom [c], C.D.A. Stehouwer [g,h], A.E. Voskuyl [a,b], W.F. Lems [a,b], M. T. Nurmohamed [a,b]




| Patients at risk | | | | |
|---|---|---|---|---|
| RA | 192 | 144 | 94 | 1 |
| DM | 80 | 59 | 38 | 0 |
| Controls | 1147 | 968 | 802 | 4 |

Raadsen R et al, Semin Arthritis Rheum 2023

# THE RISK OF ACUTE CORONARY SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ATTAINED REMISSION WITH METHOTREXATE OR A TUMOR NECROSIS FACTOR INHIBITOR.

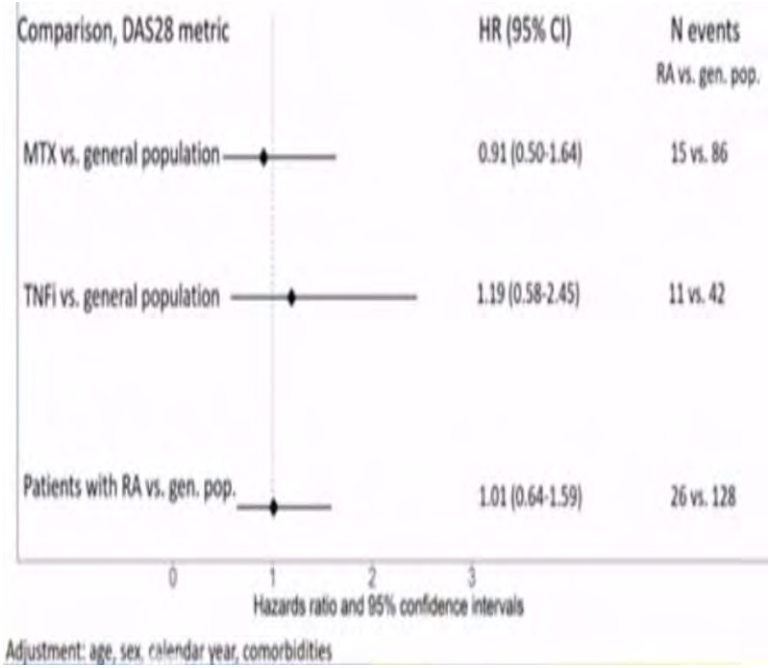
B. Delcoigne[1], L. Ljung[1], S. Aarrestad Provan[2], E. Kristianslund[2], J. Askling[1]

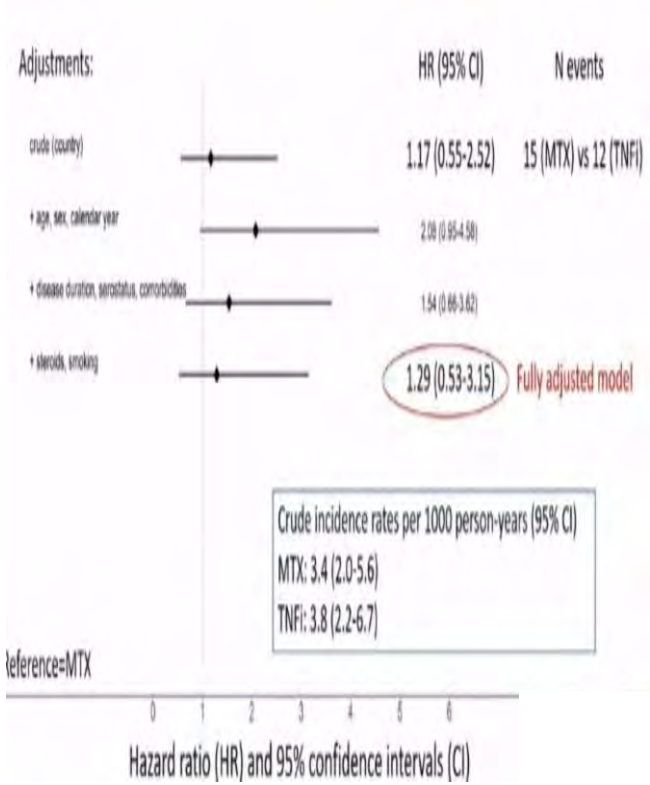
[1]Karolinska Institutet, Department of Medicine Solna - Clinical Epidemiology Division, Stockholm, Sweden

[2]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway

4,488 treatment courses with MTX and 13,056 with TNFi. Everyone had started MTX or a TNFi between 2012 and 2021 AND were followed for 1 year from the first date at which remission was recorded (40% and 32% of MTX- and TNFi).

15 ACS in MTX vs 12 in TNFi group




*Patients with RA who reach remission on MTX have a similar ACS risk as those reaching remission on TNFi. The incidence rates of ACS in patients in remission were comparable to the incidence rate in the general population.*

EULAR 2023 Abstract: OP0038

# Monitor individual risk factors
## e.g. Hypertension in RA

- Of the total RA population in secondary care, 70% are hypertensive…

**30%**

- Of those with hypertension, ~40% remain undiagnosed...

**39%** **61%**

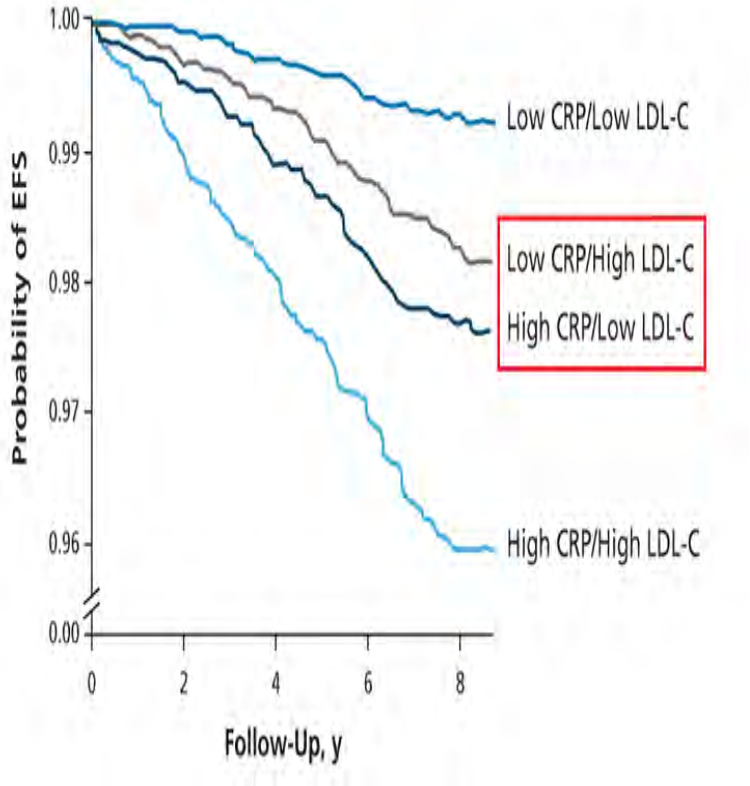
- Of those diagnosed, ~80% are sub-optimally controlled…

**22%**

**78%**

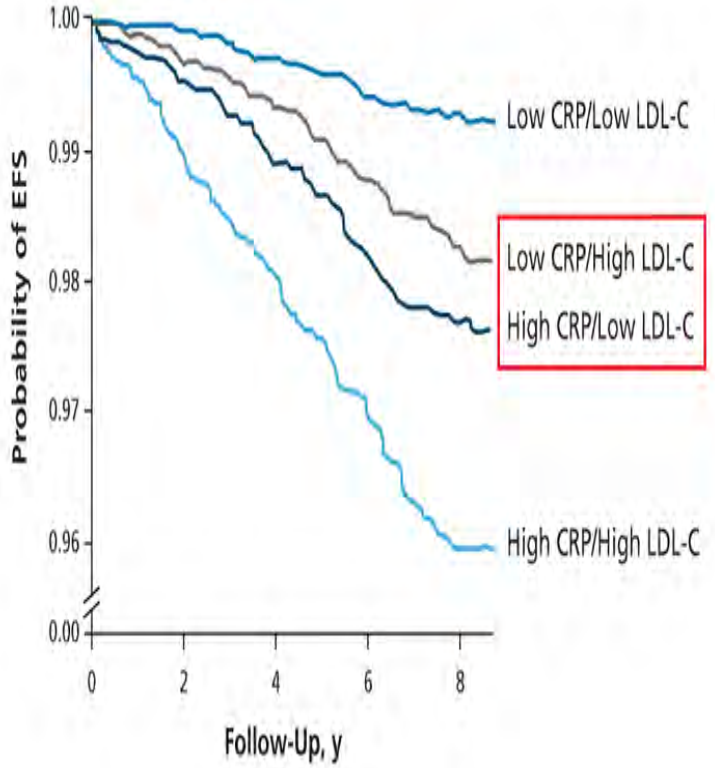
Panoulas et al. *Rheumatology* 2007;46:1477–82.

# LIPID PARADOX IN RA




*Reference(s):* 1. Choy E, Sattar N. *Ann Rheum Dis*. 2009;68:460-469.
2. Popa C et al. *Mediators Inflamm*. 2012;2012:785946.
3. Georgiadis A et al. *Arthritis Res Ther*. 2006;8:R82.

# LIPID PARADOX IN RA





*Reference(s):* 1. Choy E, Sattar N. *Ann Rheum Dis*. 2009;68:460-469.
2. Popa C et al. *Mediators Inflamm*. 2012;2012:785946.
3. Georgiadis A et al. *Arthritis Res Ther*. 2006;8:R82.

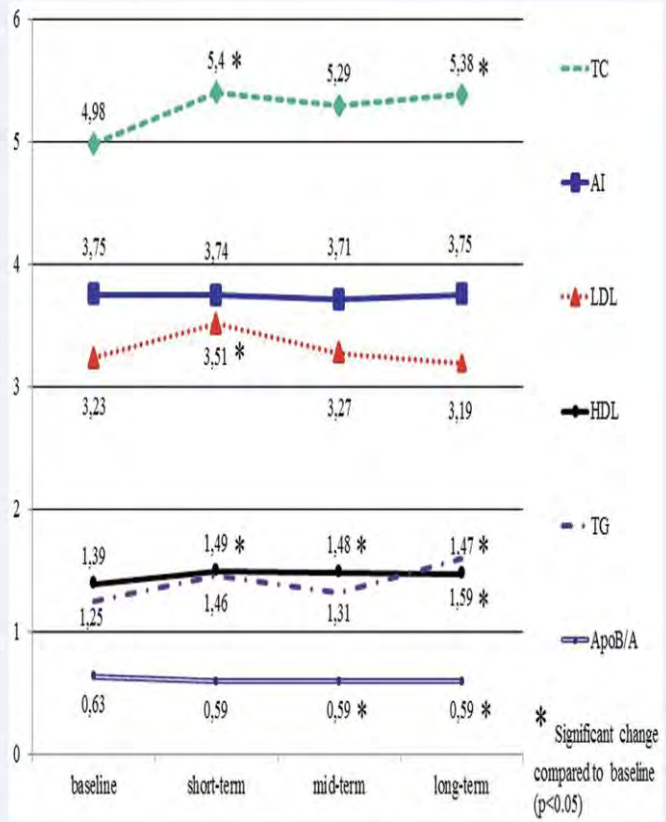


BMJ Journals
Annals of the Rheumatic Diseases


EXTENDED REPORT

## Effect of TNF inhibitors on lipid profile in rheumatoid arthritis: a systematic review with meta-analysis


Claire Immediato Daïen,[1] Yohan Duny,[2] Thomas Barnetche,[3] Jean-Pierre Daurès,[2] Bernard Combe,[1] Jacques Morel[1]

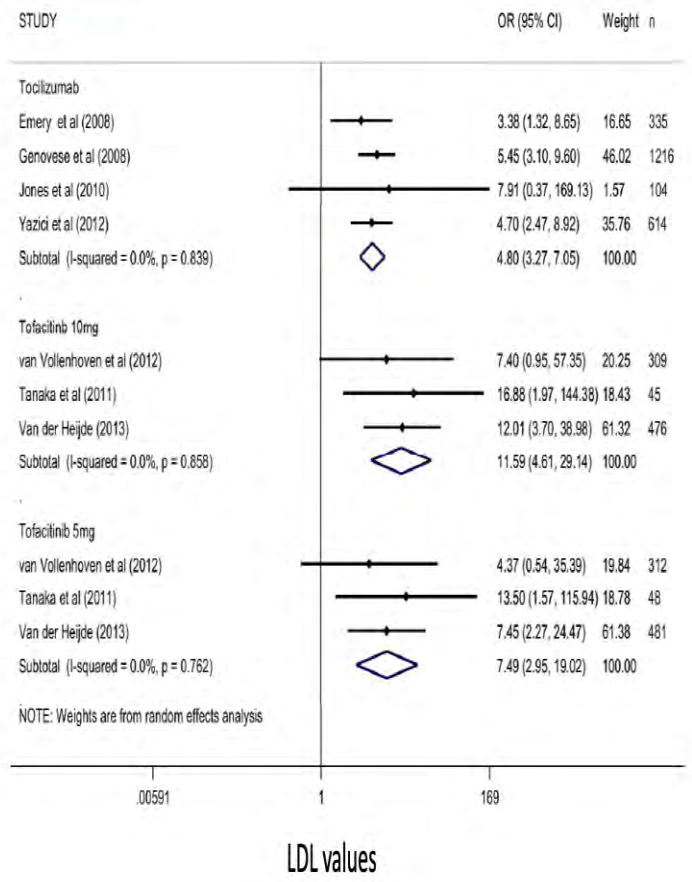





Arthritis & Rheumatology


## Lipid Profile Changes in Patients With Chronic Inflammatory Arthritis Treated With Biologic Agents and Tofacitinib in Randomized Clinical Trials: A Systematic Review and Meta-Analysis


Alejandro Souto ✉, Eva Salgado, José Ramón Maneiro, Antonio Mera, Loreto Carmona, Juan J. Gómez-Reino

Arthritis & Rheumatology

AN OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

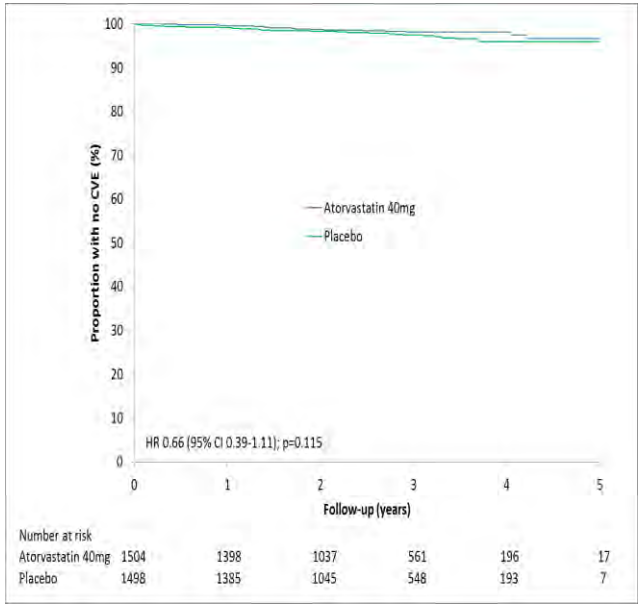
AMERICAN COLLEGE of RHEUMATOLOGY

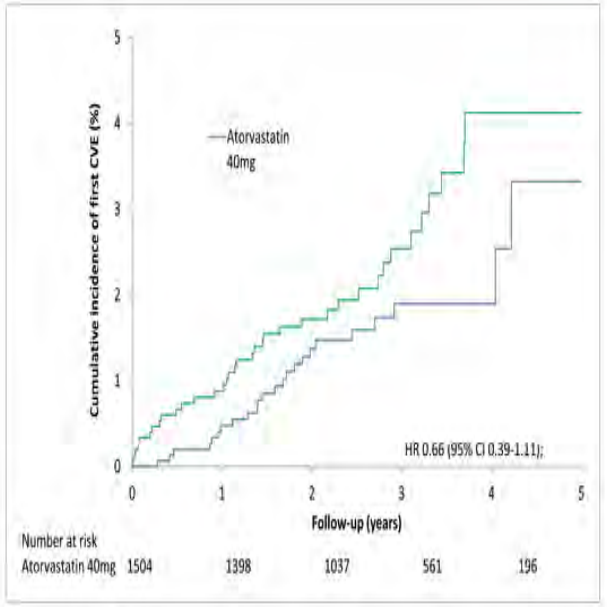
Original Article | Open Access

# A Multicenter, Randomized, Placebo-Controlled Trial of Atorvastatin for the Primary Prevention of Cardiovascular Events in Patients With Rheumatoid Arthritis

George D. Kitas MD, PhD, FRCP, Peter Nightingale PhD, Jane Armitage FRCP, FFPH, Naveed Sattar FMedSci, Jill J. F. Belch MD, FRCP, Deborah P. M. Symmons MD, FRCP on behalf of ... See all authors

| | Atorvastatin 40mg (n=1504) | | Placebo (n=1498) | |
|---|---|---|---|---|
| Type of adverse event (ICD10 chapter) | Number of patients | % (of group) | Number of patients | % (of group) |
| Infectious and parasitic disease | 16 | 1·1 | 15 | 1·0 |
| Neoplasms | 28 | 1·9 | 30 | 2·0 |
| Blood and blood forming organs and immune system diseases | 5 | 0·3 | 2 | 0·1 |
| Endocrine, nutritional and metabolic disease | 1 | 0·1 | 1 | 0·1 |
| Mental & behavioural disorder | 2 | 0·1 | 1 | 0·1 |
| Nervous system | 4 | 0·3 | 10 | 0·7 |
| Eye & adnexa | 8 | 0·5 | 5 | 0·3 |
| Ear and mastoid disease | 2 | 0·1 | 0 | 0·0 |
| Circulatory disease | 40 | 2·7 | 45 | 3·0 |
| Respiratory disease | 33 | 2·2 | 38 | 2·5 |
| Digestive system disease | 37 | 2·5 | 28 | 1·9 |
| Skin and subcutaneous system disease | 12 | 0·8 | 8 | 0·5 |
| Musculoskeletal and connective tissue disease | 20 | 1·3 | 22 | 1·5 |
| Genitourinary system disease | 13 | 0·9 | 11 | 0·7 |
| Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified | 8 | 0·5 | 10 | 0·7 |
| Injury, poisoning | 18 | 1·2 | 16 | 1·1 |
| External causes morbidity and mortality | 23 | 1·5 | 19 | 1·3 |
| None | 111 | 7·4 | 97 | 6·5 |
| Missing | 14 | 0·9 | 14 | 0·9 |
| Any adverse event | 298 | 19·8 | 292 | 19·5 |

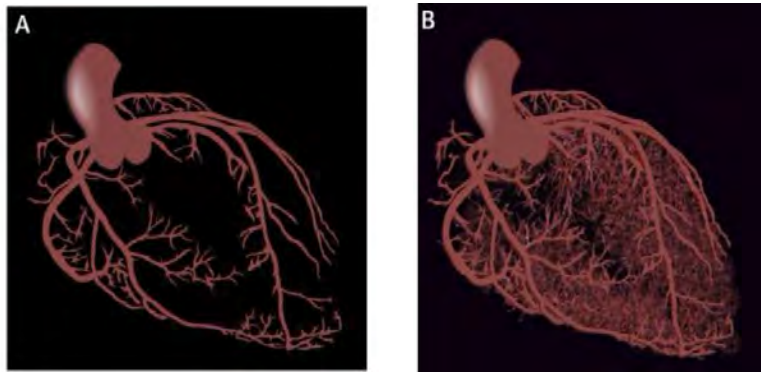


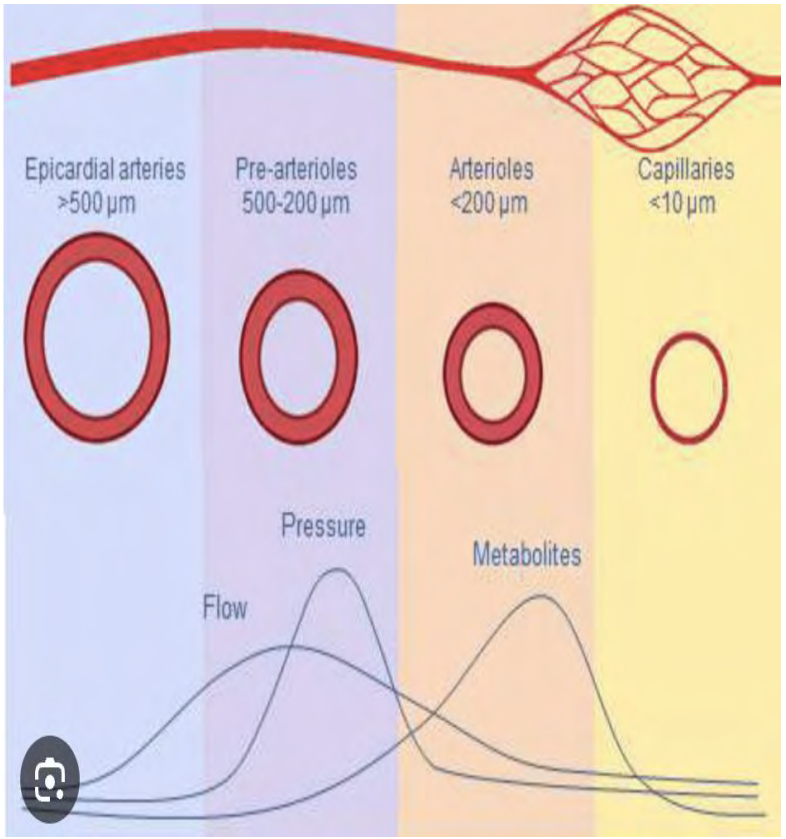




Atorvastatin was safe, with no excess reports of muscle pain or other significant symptoms among those allocated atorvastatin compared to those receiving placebo.

Kitas et al, Arthritis & Rheumatology 2019

# Microvascular coronary artery disease



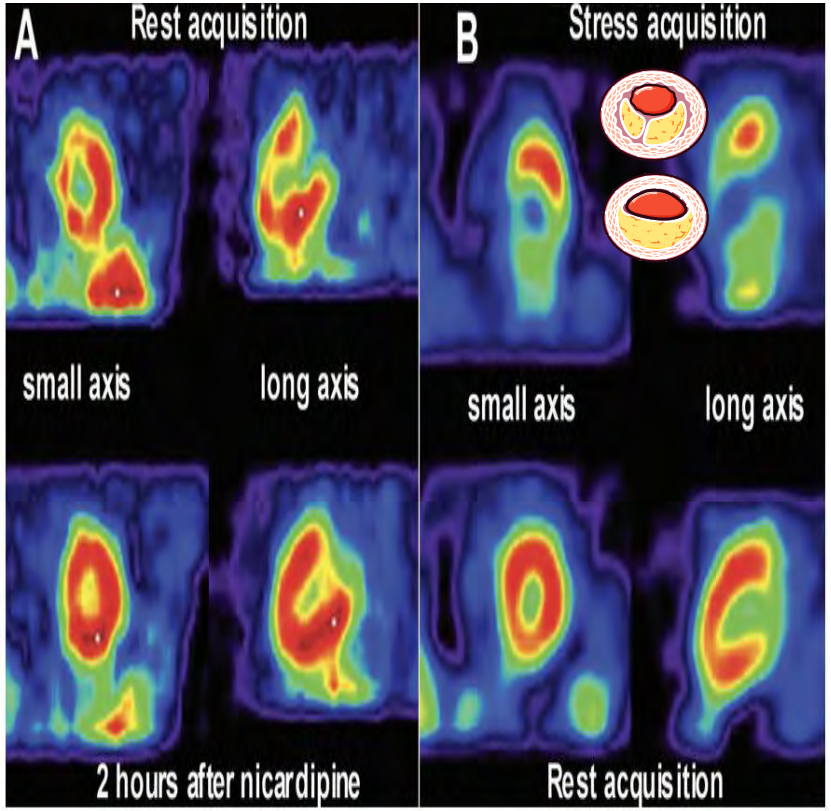




Vancheri F et al J Clin Med 2020

SPECT μυοκαρδίου με θάλλιο προ και μετά στρες με αδενοσίνη

Σκληρόδερμα

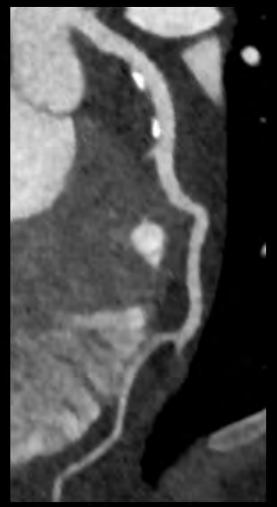
Αθήρωμα

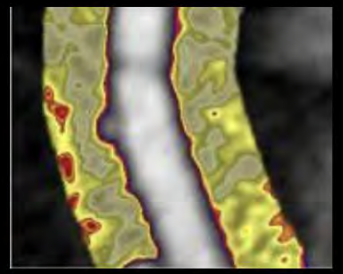


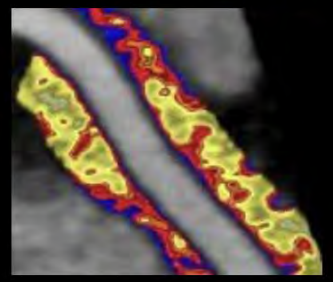

Allanore et al, Clin Exp Rheumatol 2010

# Expansion of Cardiovascular Imaging Tools

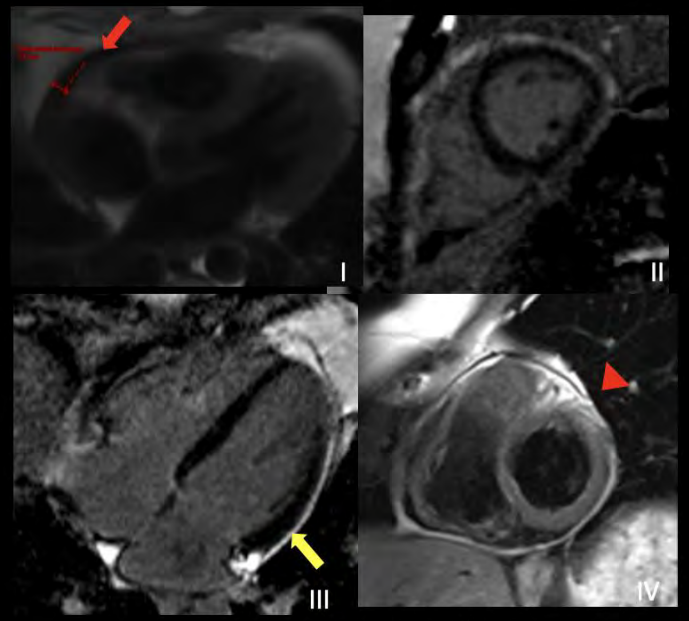
## Coronary CTA

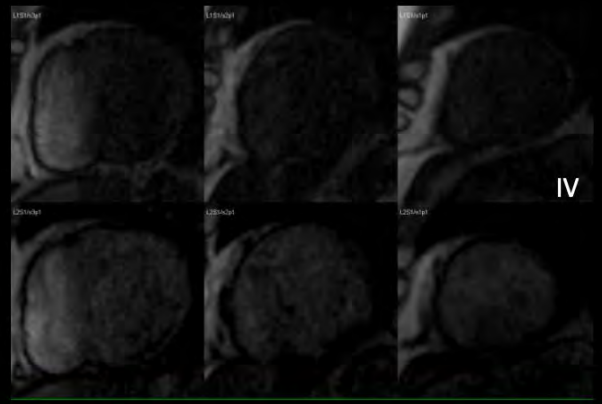






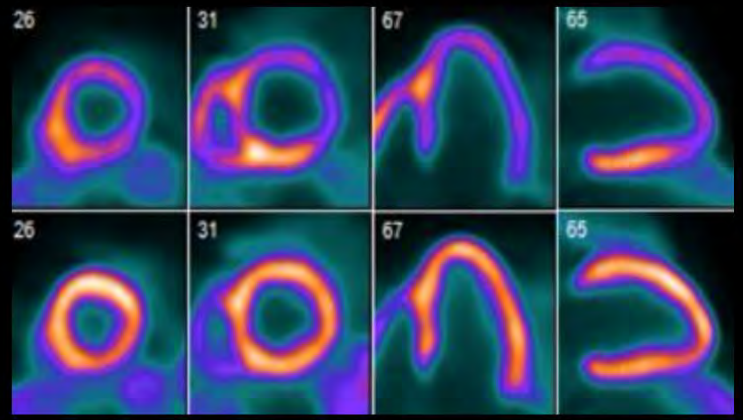
## Stress CMR

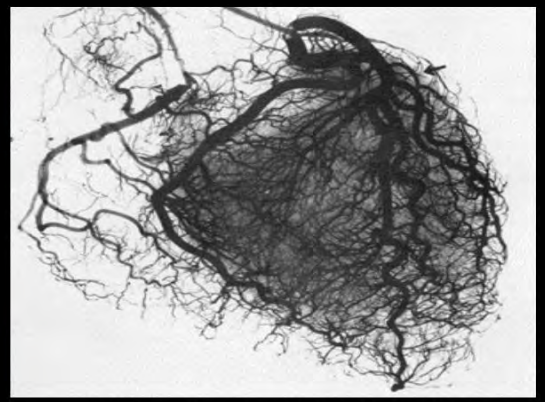



Lupus pericarditis

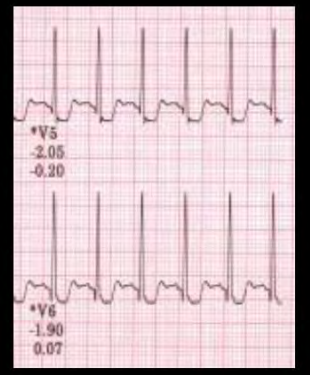
## Stress PET



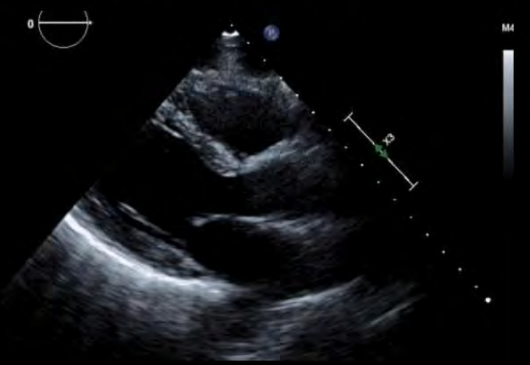



Microvascular Function

## Exercise ECG




## Echocardiography

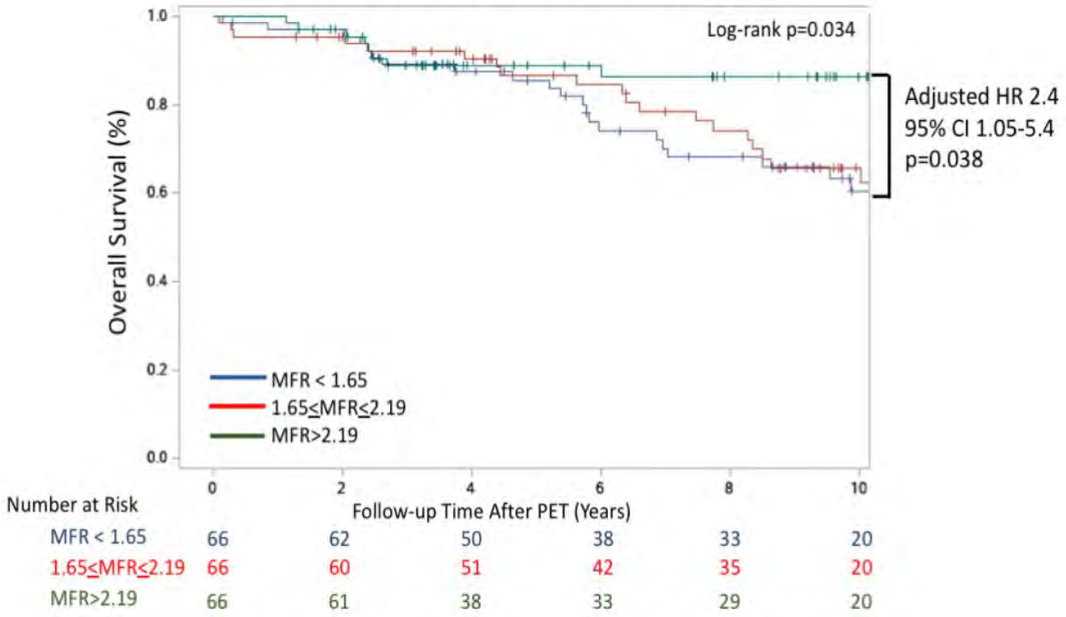


**Journal of the American Heart Association**
Volume 10, Issue 13, 6 July 2021
https://doi.org/10.1161/JAHA.120.018555

ORIGINAL RESEARCH

# Coronary Microvascular Dysfunction in Systemic Lupus Erythematosus

## All-cause Mortality



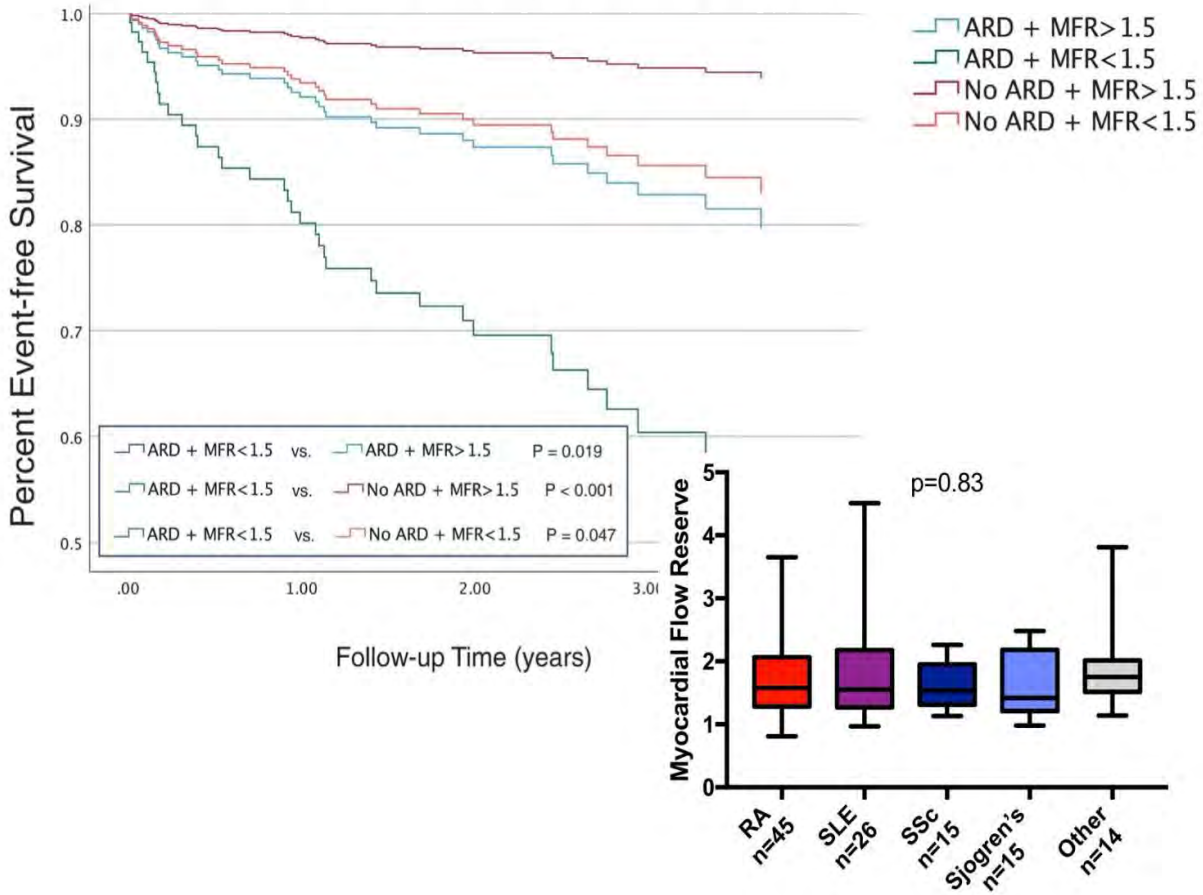

Weber BN et al, DiCarli MF. *J Am Coll Cardiol Img*. 2021.

**Circulation: Cardiovascular Imaging**
Volume 14, Issue 9, September 2021; Page e012208
https://doi.org/10.1161/CIRCIMAGING.120.012208

ORIGINAL ARTICLE

# Association Between Impaired Myocardial Flow Reserve on $^{82}$Rubidium Positron Emission Tomography Imaging and Adverse Events in Patients With Autoimmune Rheumatic Disease

## Adjusted Event-free Survival for Combined End Point of Death, MI or HF Admission



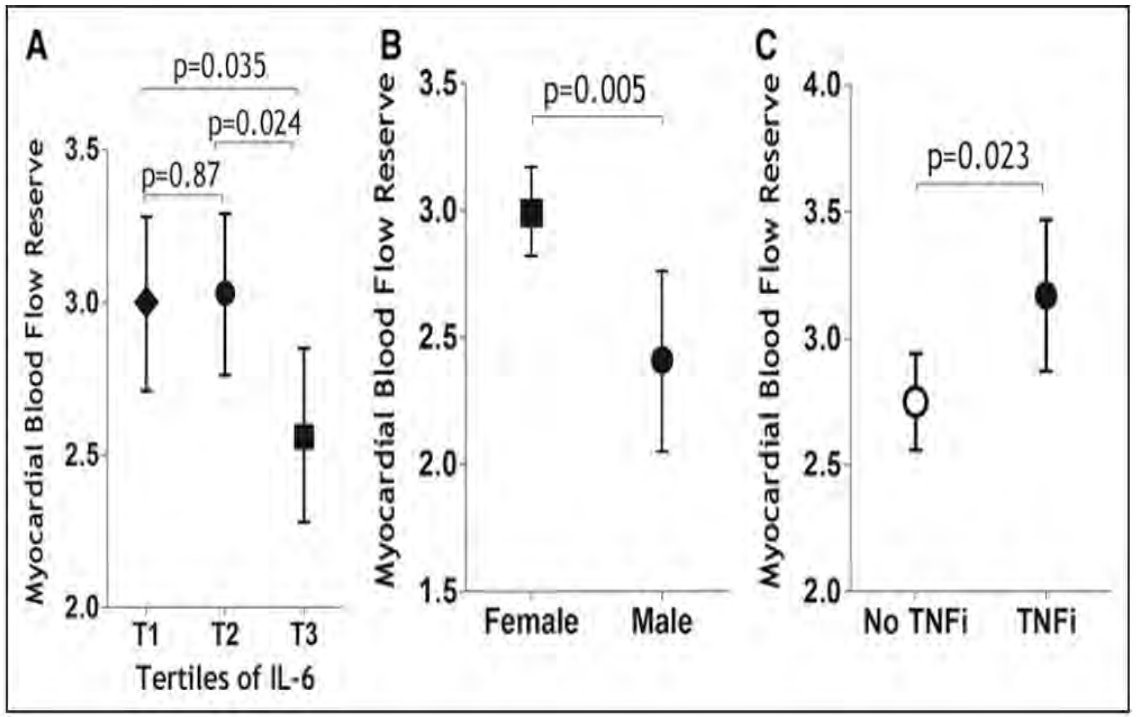

Feher et al. *Circ. Cardiovasc Imaging* 2021

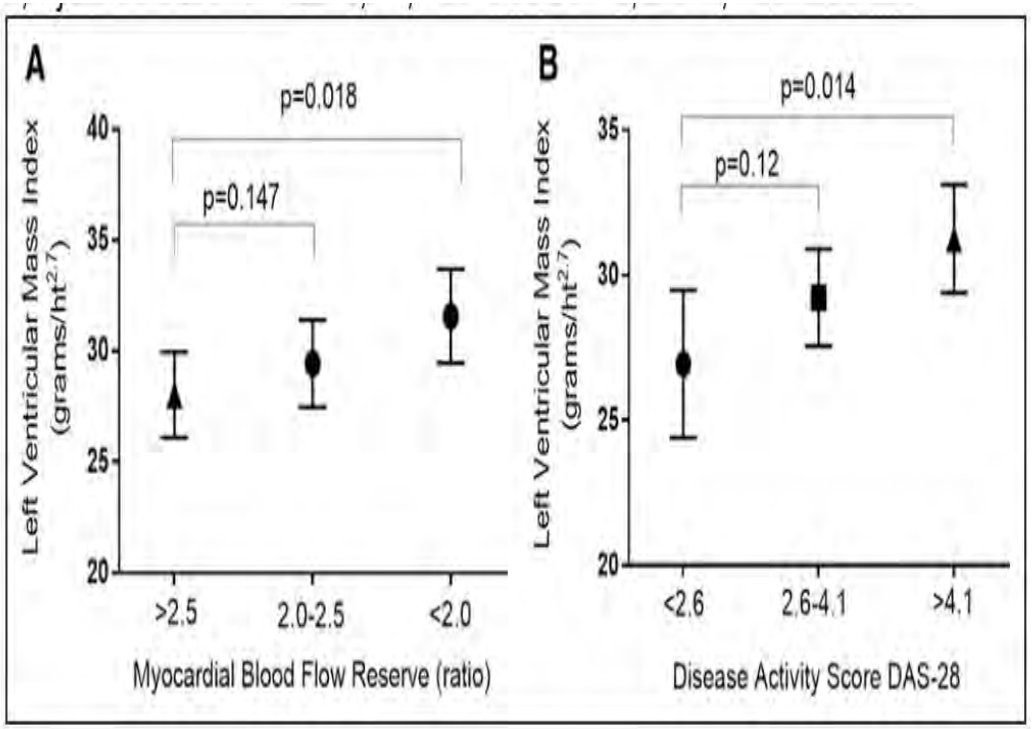
Circulation: Cardiovascular Imaging
Volume 12, Issue 1, January 2019
https://doi.org/10.1161/CIRCIMAGING.117.007495

ORIGINAL ARTICLE

# Myocardial Microvascular Dysfunction in Rheumatoid Arthritis

## Quantitation by $^{13}$N-Ammonia Positron Emission Tomography/Computed Tomography




Amigues I et al, Circ Cardiovasc Imag 2019

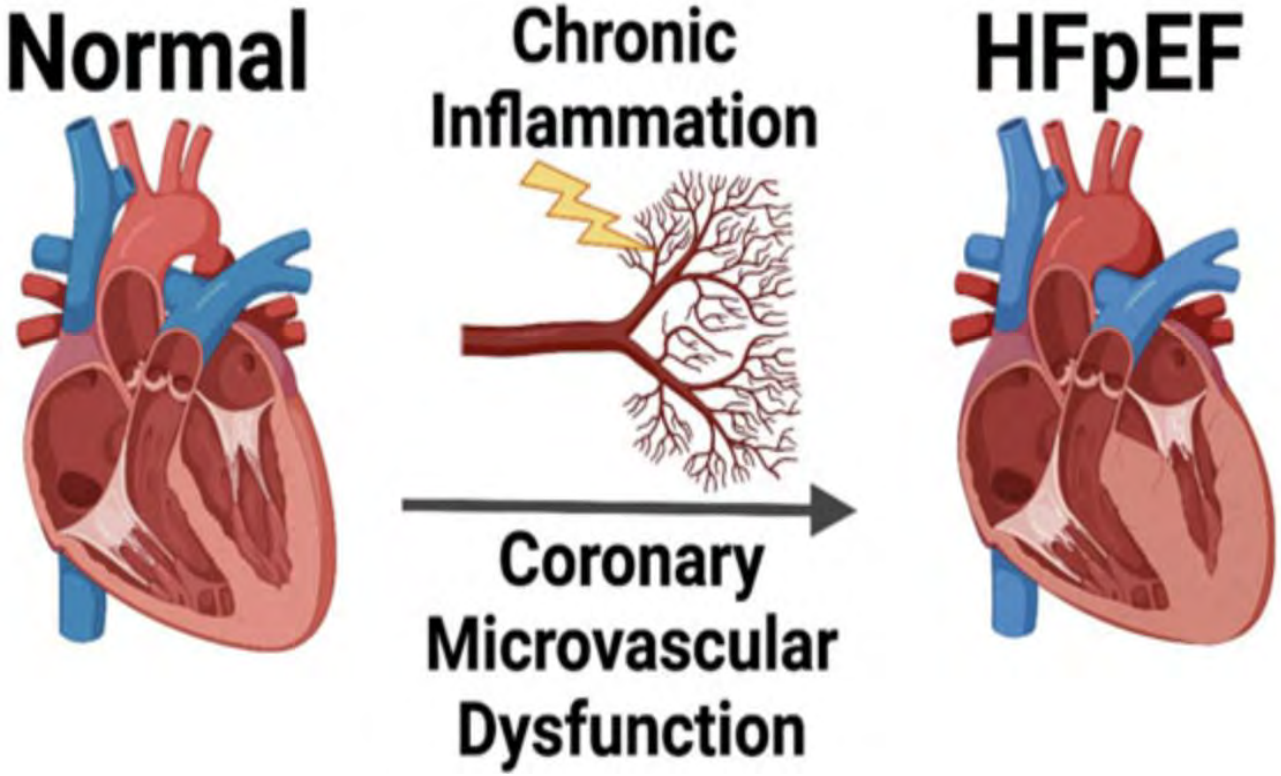
*Current Cardiology Reviews*, 2022, *18*, e310821195986

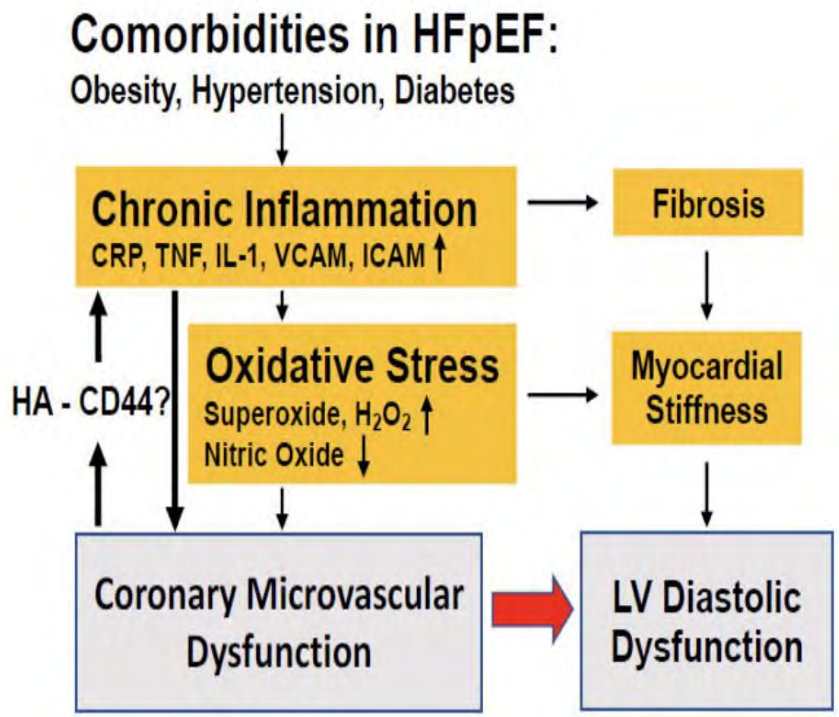
MINI-REVIEW ARTICLE

# Coronary Microvascular Dysfunction and Heart Failure with Preserved Ejection Fraction – implications for Chronic Inflammatory Mechanisms

Katie Anne Fopiano[1], Sawan Jalnapurkar[2], Alec C. Davila[1], Vishal Arora[2,*] and Zsolt Bagi[1,*]

[1]*Department of Physiology, Medical College of Georgia, Augusta University, Augusta, GA 30912, USA;* [2]*Division of Cardiology, Department of Medicine, Medical College of Georgia, Augusta University Augusta, GA 30912, USA*



# Left Ventricular Diastolic Dysfunction Predicts Mortality in Patients With Systemic Sclerosis

Anders H. Tennøe, MD,[a,b] Klaus Murbræch, MD, PhD,[c] Johanna C. Andreassen, BSc,[c] Håvard Fretheim, MD,[a] Torhild Garen, MSc,[a] Einar Gude, MD, PhD,[c] Arne Andreassen, MD, PhD,[c] Svend Aakhus, MD, PhD,[d,e] Øyvind Molberg, MD, PhD,[a,b] Anna-Maria Hoffmann-Vold, MD, PhD[a,b]

275 SSc patients assessed with echo and 186 f/up (median 3,4 years)

46/275 (17%) DD

54/189 (29%)DD

57% of patients with DD at baseline died, compared with 13% without DD

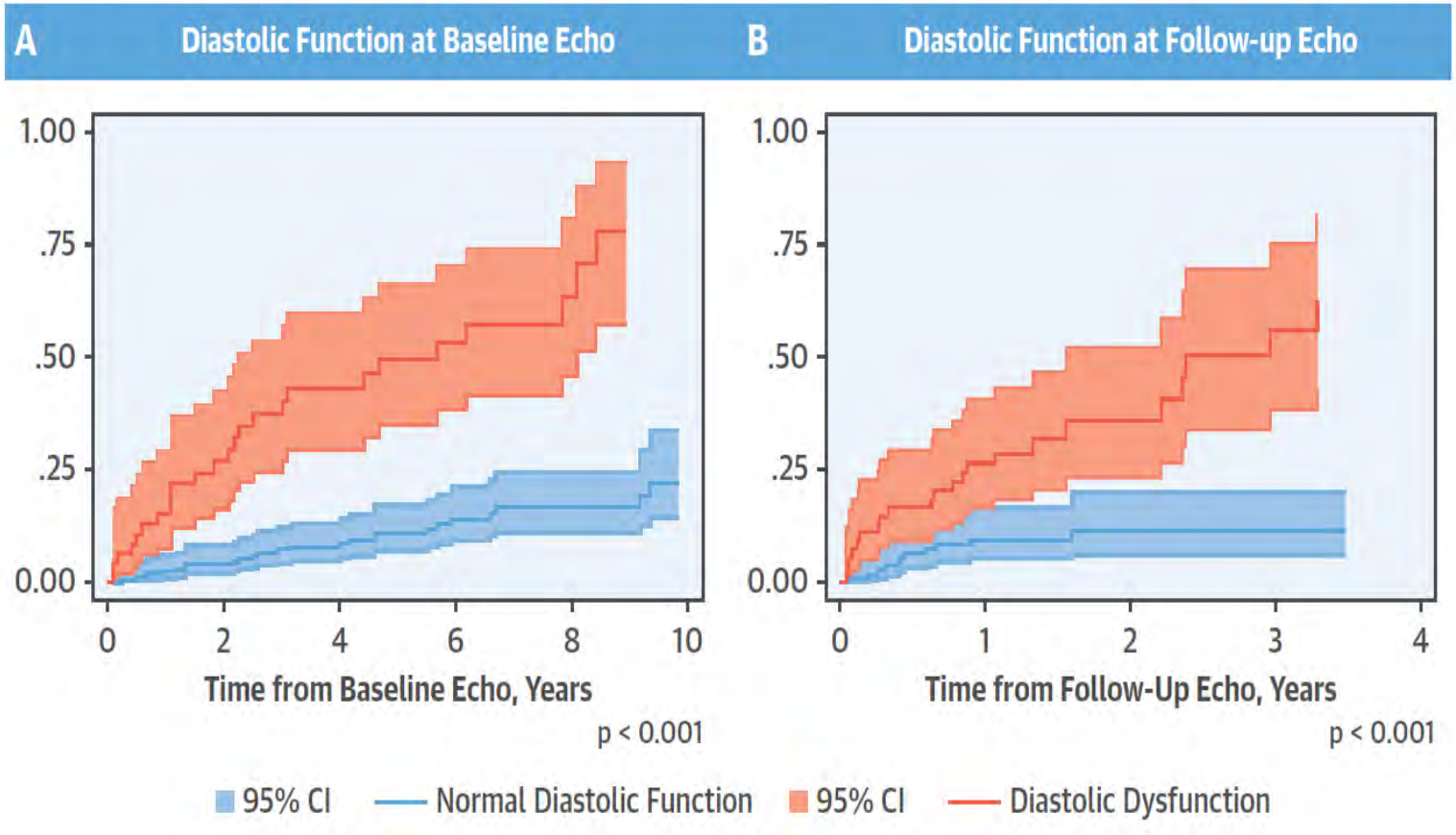


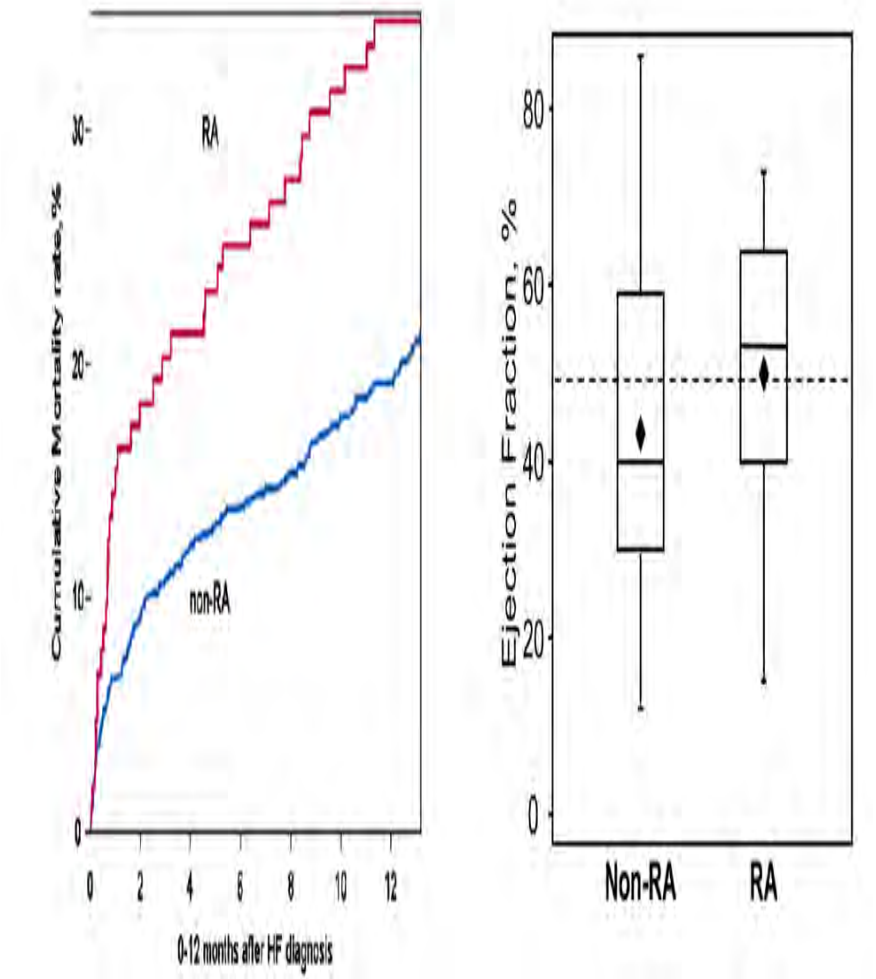

**TABLE 3** Prediction of Mortality by Multivariable Cox Regression

| | Multivariable Cox Regression on Mortality | | |
|---|---|---|---|
| | HR | 95% CI | p Value |
| DD | 3.71 | 1.69-8.14 | 0.001 |
| DLCO, % | 0.96 | 0.94-0.98 | 0.001 |
| Age | 1.05 | 1.02-1.09 | 0.003 |
| Male | 1.23 | 0.54-2.80 | 0.624 |
| mRSS | 1.06 | 1.03-1.09 | <0.001 |
| TAPSE | 0.35 | 0.17-0.73 | 0.005 |
| NT-proBNP | 1.01 | 1.01-1.01 | 0.014 |
| C-index | | 0.89 | |

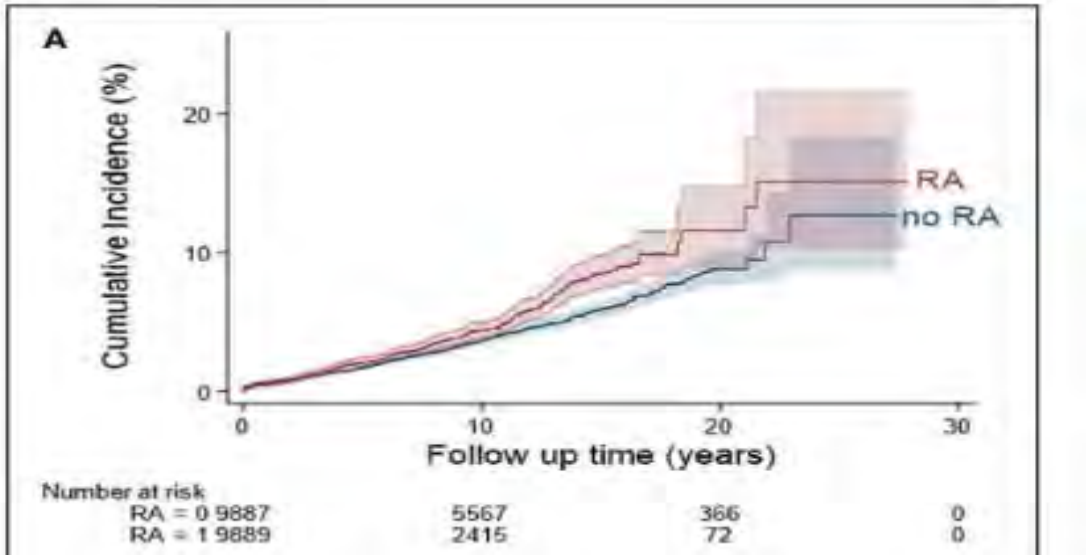
CI = confidence interval; DD = diastolic dysfunction; DLCO = diffusion capacity of the lung for carbon monoxide; HR = hazard ratio; mRSS = modified Rodnan skin score; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; TAPSE = tricuspid annular plane systolic excursion.

J Am Coll Cardiol. 2018 Oct 9;72(15):1804-1813.

# NON-ISHEMIC HEART FAILURE IN RHUEMATOID ARTHRITIS




9889 patients with RA and 9889 control patients without autoimmune disease matched for age, sex, and race.




✓RA was associated with an increased risk of HF, with the majority of cases (60%) being HFpEF

✓ among patients with RA, higher levels of CRP were associated with greater risk for HF while methotrexate use was associated with lower risk of HFpEF

✓ the pattern of comorbidities and their relative strengths of association differed between patients with RA who developed HFpEF and HFrEF ((hypertension, obesity, chronic kidney disease, DM)

Sherine G. Ann Rheum Dis 2008

Ahlers MJ, et al. J Am Heart Assoc 2020 May 18;9(10):e014661.

BMJ Journals
Annals of the Rheumatic Diseases

CLINICAL SCIENCE

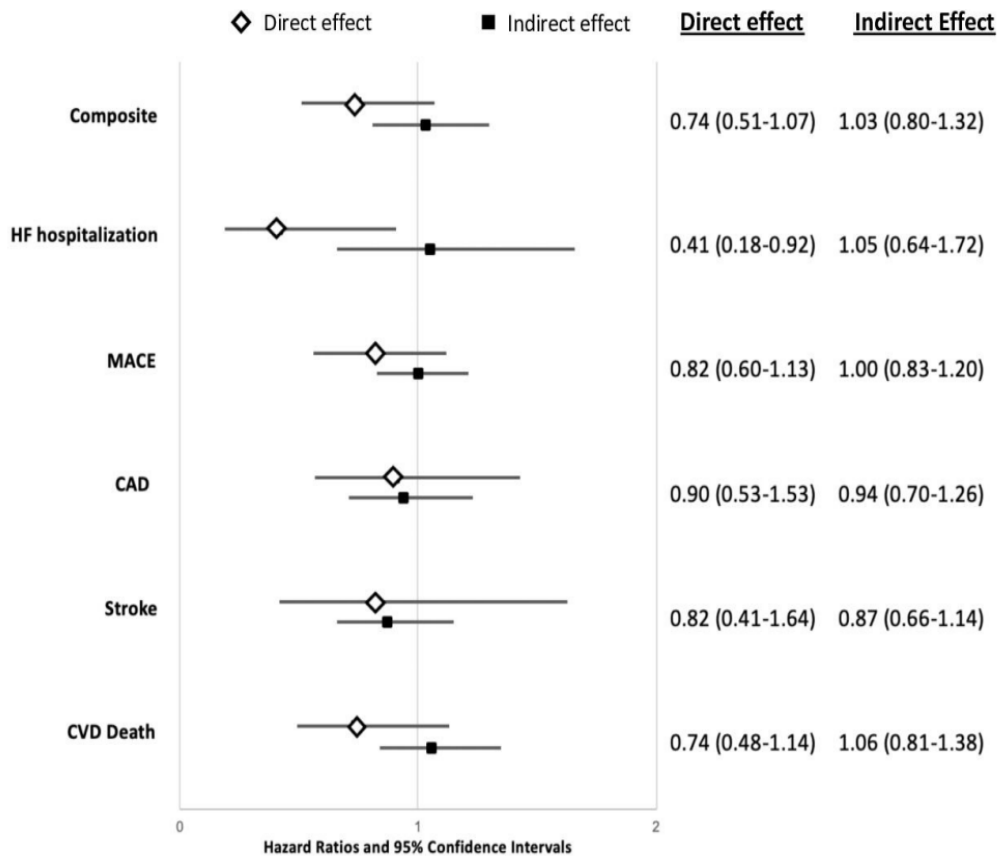
# Investigating changes in disease activity as a mediator of cardiovascular risk reduction with methotrexate use in rheumatoid arthritis

Tate M Johnson ,[1,2] Harlan R Sayles,[1,3] Joshua F Baker,[4,5] Michael D George,[4,5] Punyasha Roul,[1] Cheng Zheng,[3] Brian Sauer,[6,7] Katherine P Liao,[8] Daniel R Anderson,[9] Ted R Mikuls ,[1,2] Bryant R England [1,2]

Among 2044 RA patients (90% male, mean age 63.9 years, baseline DAS28-CRP 3.6), there were 378 incident CVD events. Using MSM, MTX use was associated with a24% reduced risk of composite CVD events (HR 0.76, 95% CI 0.58 to 0.99) including a 57% reduction in HF hospitalisations (HR 0.43, 95% CI 0.24 to 0.77)

**Table 3** Association of methotrexate use with cardiovascular disease events in veterans with rheumatoid arthritis*

| Event category† | HR (95% CI) | P value |
|---|---|---|
| Composite | **0.76 (0.58 to 0.99)** | **0.04** |
| HF hospitalisation | **0.43 (0.24 to 0.77)** | **0.005** |
| MACE | 0.82 (0.63 to 1.06) | 0.12 |
| CAD | 0.84 (0.55 to 1.28) | 0.42 |
| Stroke | 0.72 (0.34 to 1.53) | 0.39 |
| CVD Death | 0.79 (0.55 to 1.13) | 0.19 |

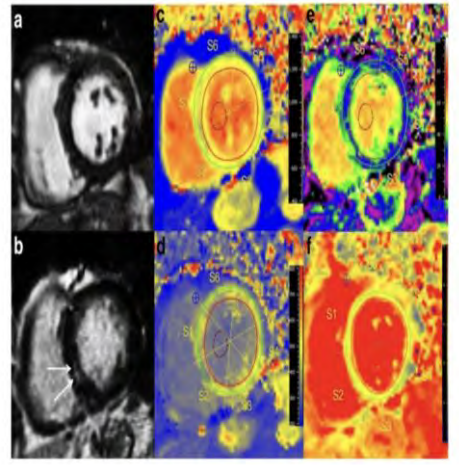


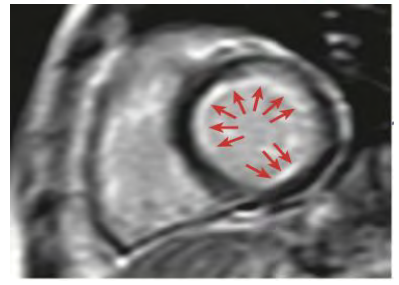

Johnson TM, et al. Ann Rheum Dis 2021;80:1385–1392.

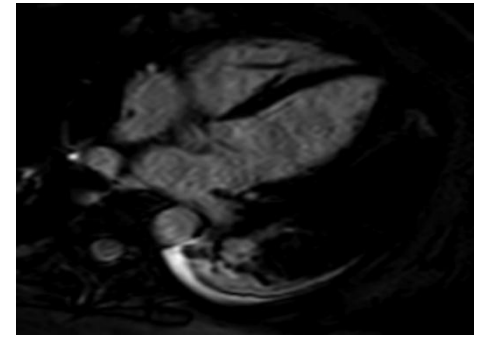
# MYOCARDIAL INFLAMMATION IN THE ACUTE PHASE OF SYSTEMIC DIEASES (..when the heart is burning… )

| |
|---|
| Myocarditis (myocardial oedema) |
| Diffuse subendocardial vasculitis (coronary microvascular disease) |
| Cardiomyopathy (myocardial fibrosis) |
| Coronary arteritis |

- Subtle clinical signs which may be overlooked due to the coexistence of systemic features of the disease
- Absence of specific manifestations
- EGC, Echo lack sensitivity
- Endomyocardial biopsy difficult to perform







# How we can assess cardiac involvement in systemic rheumatic diseases

**Acknowledgment of the increased risk of cardiovascular disease/myocardial disease**

- Clinical examination/evaluation
- Assessment of traditional CVD risk factors
- Risk stratification based on the symptoms, type of disease
  - -chest pain at rest or on exertion
  - - dyspnea at rest or on exertion
  - - palpitations
  - - unexplained fatigue
- ECG/24 h Holter monitoring
- Echocardiography
- Biochemical markers (troponin, NT-proBNP)

} low threshold for CV investigations



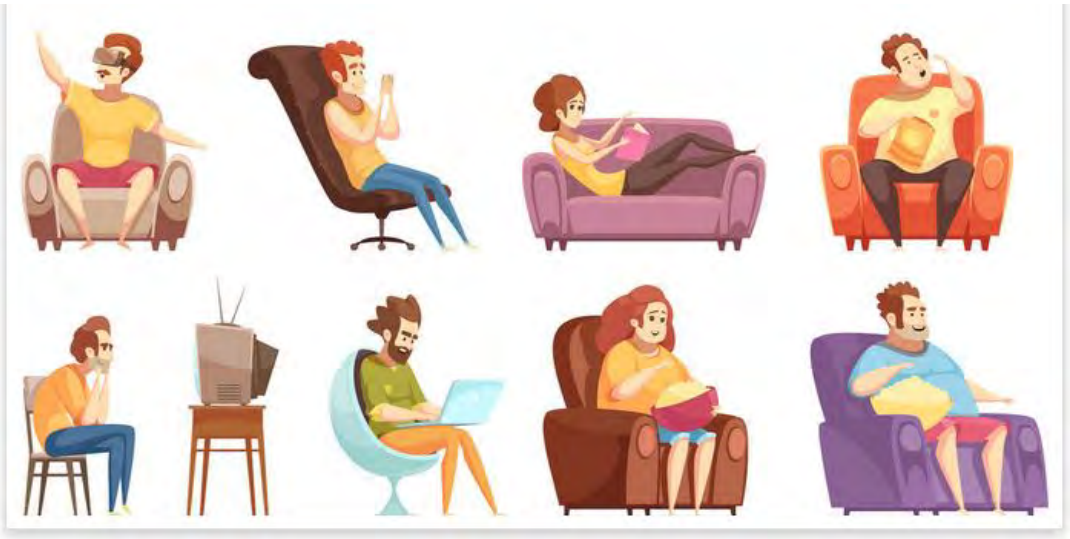

# HEART DISEASE IN RHEUMATIC DISEASEAS

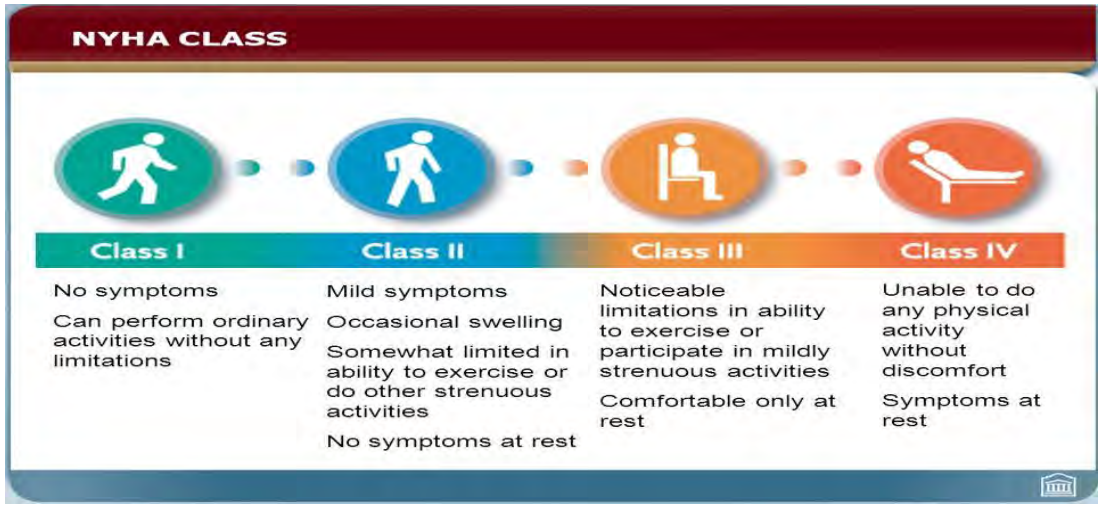


✓*different constellation of clinical signs which makes the clinical evaluation complex*

✓*sedentary style of life*

✓*ankle swelling and reduced functional capacity can be misinterpreted as signs of RA rather than progressing HF*

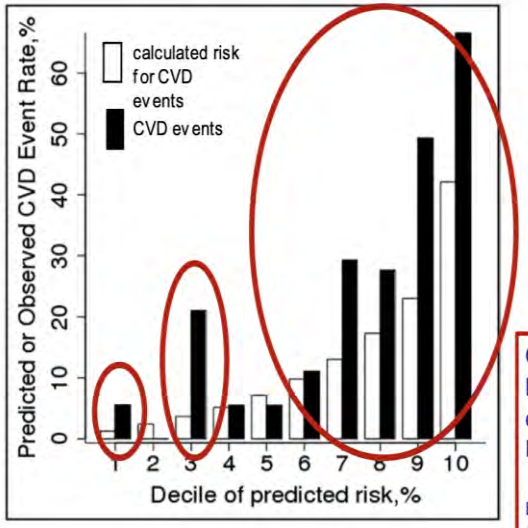




## Usefulness of Risk Scores to Estimate the Risk of Cardiovascular Disease in Patients With Rheumatoid Arthritis

Cynthia S. Crowson, MS[a,b,*], Eric L. Matteson, MD, MPH[a,b], Veronique L. Roger, MD, MPH[a,c], Terry M. Therneau, PhD[a], and Sherine E. Gabriel, MD, MSc[a,b]

Am J Cardiol 2012;110:420–424




CVD risk prediction of CVD events in RA patients from US is generally inaccurate by the Framingham and Reynolds CVD risk calculators

Comparable inaccuracies have been reported using 4 risk calculators in European RA patients

by E Arts *et al*
Ann Rheum Dis. 2015 Apr;74(4):668-74

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

## Cardiovascular risk assessment in patients with antiphospholipid syndrome: a cross-sectional performance analysis of nine clinical risk prediction tools

George C Drosos,[1] George Konstantonis,[1] Petros P Sfikakis,[1,2] Maria G Tektonidou [1,2]

RMD Open 2023;**9**:e003601

Table 3 Performance measures of cardiovascular risk prediction tools to identify high ASCVR in patients with APS (N=121)

| | Spiegelhalter's z-test p value | AUC (95% CI) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | MCC | Highest Youden index | Optimal high-risk cut-off |
|---|---|---|---|---|---|---|---|
| First CVD event risk prediction tools | | | | | | | |
| SCORE | 0.47 | 0.60 (0.49 to 0.71) | 17.1 (7.2 to 32.1) | 90.2 (76.9 to 97.3) | 0.11 | 0.15 | 0.2% |
| mSCORE | 0.47 | 0.59 (0.47 to 0.70) | 22 (10.6 to 37.6) | 85.4 (70.8 to 94.4) | 0.10 | 0.20 | 1% |
| FRS | 0.48 | 0.72 (0.63 to 0.81) | 9.8 (2.7 to 23.1) | 95.3 (86.9 to 99) | 0.10 | 0.36 | 3.2% |
| PCRE | 0.49 | 0.68 (0.57 to 0.78) | 26.8 (14.2 to 42.9) | 90.2 (76.9 to 97.3) | 0.22 | 0.29 | 5.3% |
| Globorisk | 0.57 | 0.70 (0.59 to 0.80) | 41.5 (26.3 to 57.9) | 82.9 (67.9 to 92.8) | 0.27 | 0.27 | 3% |
| PROCAM | 0.50 | 0.75 (0.66 to 0.83) | 9.5 (2.7 to 22.6) | 96.1 (88.9 to 99.2) | 0.11 | 0.41 | 1.7% |
| Recurrent CVD event risk prediction tools | | | | | | | |
| SMART* | 0.47 | 0.64 (0.50 to 0.76) | 50 (31.3 to 68.7) | 77.8 (57.7 to 91.4) | 0.29 | 0.35 | 20.3% |
| SMART† | 0.49 | 0.66 (0.51 to 0.79) | 56 (34.9 to 75.6) | 76.2 (52.8 to 91.8) | 0.33 | 0.42 | 20.3% |
| aGAPSS* | 0.50 | 0.59 (0.46 to 0.72) | 58.1 (39.1 to 75.5) | 34.5 (17.9 to 54.3) | 0.08 | 0.29 | 14 points |
| aGAPSS† | 0.50 | 0.56 (0.41 to 0.71) | 60 (38.7 to 78.9) | 40.9 (20.7 to 63.6) | 0.01 | 0.24 | 14 points |
| $aGAPSS_{CVD}$* | 0.50 | 0.57 (0.44 to 0.70) | 67.7 (48.6 to 83.3) | 34.5 (17.9 to 54.3) | 0.02 | 0.25 | 16 points |
| $aGAPSS_{CVD}$† | 0.50 | 0.56 (0.41 to 0.70) | 68.0 (46.5 to 85.1) | 36.4 (17.2 to 59.3) | 0.05 | 0.24 | 16 points |
| Patients without triple aPL positivity | | | | | | | |
| aGAPSS* | 0.49 | 0.60 (0.42 to 0.76) | 38.1 (18.1 to 61.6) | 76.9 (46.2 to 95) | 0.16 | 0.22 | 9 points |
| aGAPSS† | 0.49 | 0.62 (0.42 to 0.79) | 44.4 (21.5 to 69.2) | 72.7 (39 to 94) | 0.17 | 0.25 | 9 points |
| $aGAPSS_{CVD}$* | 0.52 | 0.69 (0.50 to 0.83) | 52.4 (29.8 to 74.3) | 76.9 (46.2 to 95) | 0.29 | 0.36 | 10 points |
| $aGAPSS_{CVD}$† | 0.51 | 0.68 (0.48 to 0.84) | 55.6 (30.8 to 78.5) | 72.7 (39.0 to 94) | 0.28 | 0.36 | 10 points |

Results about Spiegelhalter's z-test, AUC, sensitivity, specificity and MCC computed according to established high-risk cut-offs for each risk prediction model.
*Patients with arterial with or without venous events.
†Patients with isolated arterial events.
aGAPSS, adjusted Global Antiphospholipid Syndrome Score; $aGAPSS_{CVD}$, aGAPSS for CVD; aPL, antiphospholipid antibodies; APS, antiphospholipid syndrome; ASCVR, atherosclerotic cardiovascular risk; AUC, area under the curve; CVD, cardiovascular disease; FRS, Framingham Risk Score; MCC, Matthews' correlation coefficient; mSCORE, modified SCORE; PCRE, Pooled Cohorts Risk Equation; PROCAM, Prospective Cardiovascular Muncher Study calculator; SCORE, Systematic Coronary Risk Evaluation; SMART, Secondary Manifestations of Arterial Disease risk score.

# Assess composite CVD risk in RA

| Exclusions | FRS[1] Age >75, CVD/Diabetes | NCEP[2] Age >80, CVD/Diabetes | SCORE[3] Age >65,CVD / Diabetes / TC ≥8 /LDL ≥6 / BP ≥180/110 | RRS[4] Age >80, CVD/Diabetes | QRISK2[5] Age ≥75, CVD/Diabetes |
|---|---|---|---|---|---|
| Age/gender | ✓ | ✓ | ✓ | ✓ | ✓ |
| Postcode | | | | | ✓ |
| Ethnicity | | | | | ✓ |
| BMI | | | | | ✓ |
| Smoking | ✓ | ✓ | ✓ | ✓ | ✓ |
| FHx CVD | | ✓ | | ✓ | ✓ |
| Diastolic BP | ✓ | ✓ | | | |
| Systolic BP | ✓ | ✓ | ✓ | ✓ | ✓ |
| TC | ✓ | ✓ | ✓ | ✓ | ✓ |
| HDL | ✓ | ✓ | ✓ | ✓ | ✓ |
| BP treated? | ✓ | ✓ | | | ✓ |
| RA | | | | | ✓ |
| AF | | | x 1.5 per EULAR recommendations | | ✓ |
| CKD | | | | | ✓ |
| hs-CRP | | | | ✓ | |


1. Schnabel, et al. *Lancet* 2009;373:739-45.
2. NCEP. *JAMA* 2001;285:2486-97.
3. SCORE. *Eur Heart J* 2012 May. Epub.
4. Ridker, et al. *JAMA* 2007;297:611-9.
5. Hippisley-Cox, et al. *BMJ* 2008;336:1475-82.


AF = atrial fibrillation; CKD = chronic kidney disease; FHx = family history; FRS = Framingham Risk Score; NCEP = National Cholesterol Education Program; RRS = Reynolds Risk Score

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

R Agca,[1] S C Heslinga,[1] S Rollefstad,[2] M Heslinga,[1] I B McInnes,[3] M J L Peters,[4] T K Kvien,[5] M Dougados,[6] H Radner,[7] F Atzeni,[8] J Primdahl,[9,10,11] A Södergren,[12] S Wallberg Jonsson,[12] J van Rompay,[13] C Zabalan,[14] T R Pedersen,[15] L Jacobsson,[16,17] K de Vlam,[18] M A Gonzalez-Gay,[19] A G Semb,[20] G D Kitas,[21] Y M Smulders,[4] Z Szekanecz,[22] N Sattar,[23] D P M Symmons,[24] M T Nurmohamed[25]

Agca R, et al. Ann Rheum Dis 2017;76:17–28.

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

# EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome

George C Drosos ,[1] Daisy Vedder ,[2] Eline Houben,[3] Laura Boekel ,[2] Fabiola Atzeni,[4] Sara Badreh,[5] Dimitrios T Boumpas ,[6,7] Nina Brodin,[8,9] Ian N Bruce,[10,11] Miguel Ángel González-Gay ,[12] Søren Jacobsen ,[13,14] György Kerekes,[15] Francesca Marchiori,[16] Chetan Mukhtyar ,[17] Manuel Ramos-Casals,[18] Naveed Sattar,[19] Karen Schreiber,[20] Savino Sciascia ,[21] Elisabet Svenungsson ,[22] Zoltan Szekanecz ,[23] Anne-Kathrin Tausche,[24] Alan Tyndall,[25] Vokko van Halm,[26] Alexandre Voskuyl,[27] Gary J Macfarlane ,[28] Michael M Ward ,[29] Michael T Nurmohamed,[2,30] Maria G Tektonidou [1,7]

Drosos GC, *et al*. *Ann Rheum Dis* 2022;81:768–779.

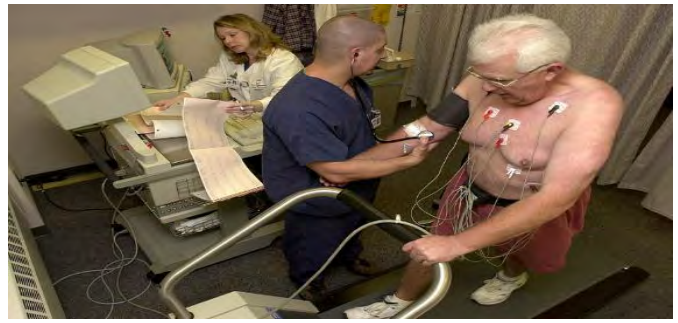
| Overarching principles | LoA* (SD) |
|---|---|
| A. Clinicians should be aware of increased CVR in patients with RMDs including gout, vasculitis, SSc, myositis, MCTD, SS, SLE and APS. For all RMDs, reduction of disease activity is likely to lessen CVR. | 9.92 (0.39) |
| B. Rheumatologists are responsible for CVR assessment and management in collaboration with primary care providers, internists or cardiologists and other healthcare providers. | 9.55 (1.12) |
| C. CVR factor screening should be performed regularly in all individuals with RMDs. Risk management should include screening for and strict control of CVR factors (smoking cessation, management of blood pressure, lipids and diabetes). CVR assessment is recommended within 6 months of diagnosis and repeated based on individual patient characteristics and risk levels. | 9.55 (0.84) |
| D. Patient education and counselling on CVR, treatment adherence and lifestyle modifications, such as healthy diet and regular physical activity, are important in the management of CVR in these patients. | 9.88 (0.42) |

- ✓ Sufficient control of disease activity
- ✓ Management of traditional CVD risk factors (as per general population)
- ✓ Life style changes (smoking, diet, exercise)
- ✓ Minimization/discontinuation of steroid use
- ✓ Disease specific CVD manifestaions

# MANAGING CVD RISK IN SYSTEMIC RHEUMATIC DISEASES

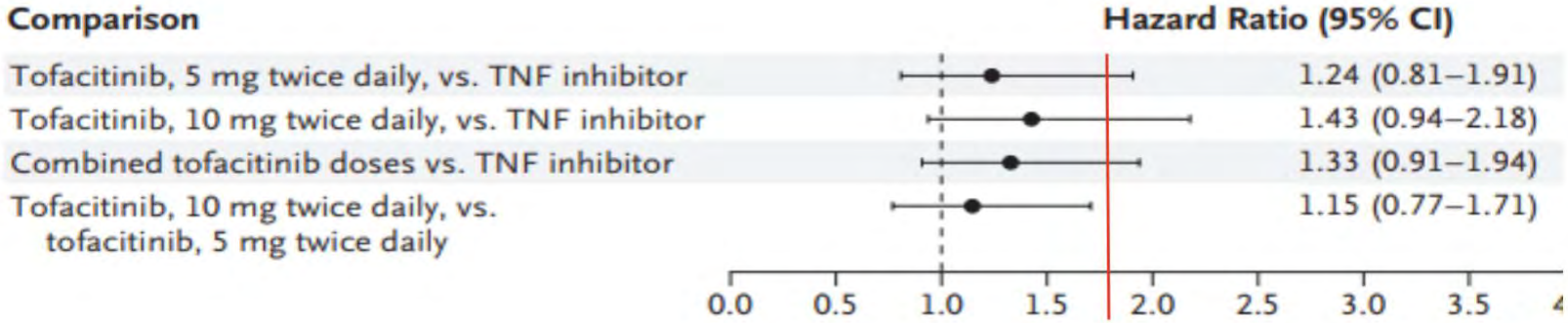
Management of CVD risk factors (hypertension, dyslipidaemia and glucose intolerance irrespective of whether they are the result of the disease or its treatment )

Lifestyle modifications (smoking, exercise, weight loss, diet)

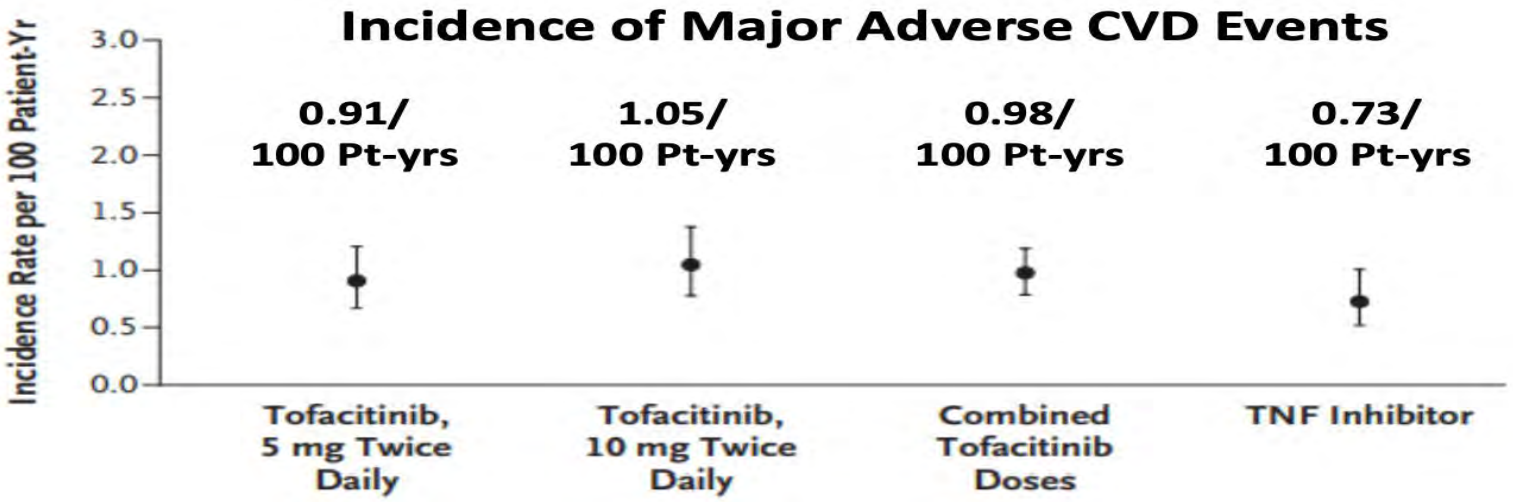



# ORAL Surveillance Safety Trial: Tofacitinib vs. TNF Inhibitors

Tofacitinib was **not non-inferior** to TNF inhibitors for cardiovascular events




The incidence of MACE was higher with the combined tofacitinib doses (3.4%; 98 patients) than with a TNF inhibitor (2.5%; 37 patients).




| | | | | |
|---|---|---|---|---|
| No. of Patients with First Event/Total No. (%) | 47/1455 (3.2) | 51/1456 (3.5) | 98/2911 (3.4) | 37/1451 (2.5) |
| No. of Patient-Yr | 5166.32 | 4871.96 | 10,038.28 | 5045.27 |
| Incidence Rate per 100 Patient-Yr (95% CI) | 0.91 (0.67–1.21) | 1.05 (0.78–1.38) | 0.98 (0.79–1.19) | 0.73 (0.52–1.01) |
| NNH (patient-yr) vs. TNF Inhibitor | 567 | 319 | — | — |
| NNH (over 5-yr period) vs. TNF Inhibitor | 113 | 64 | — | — |

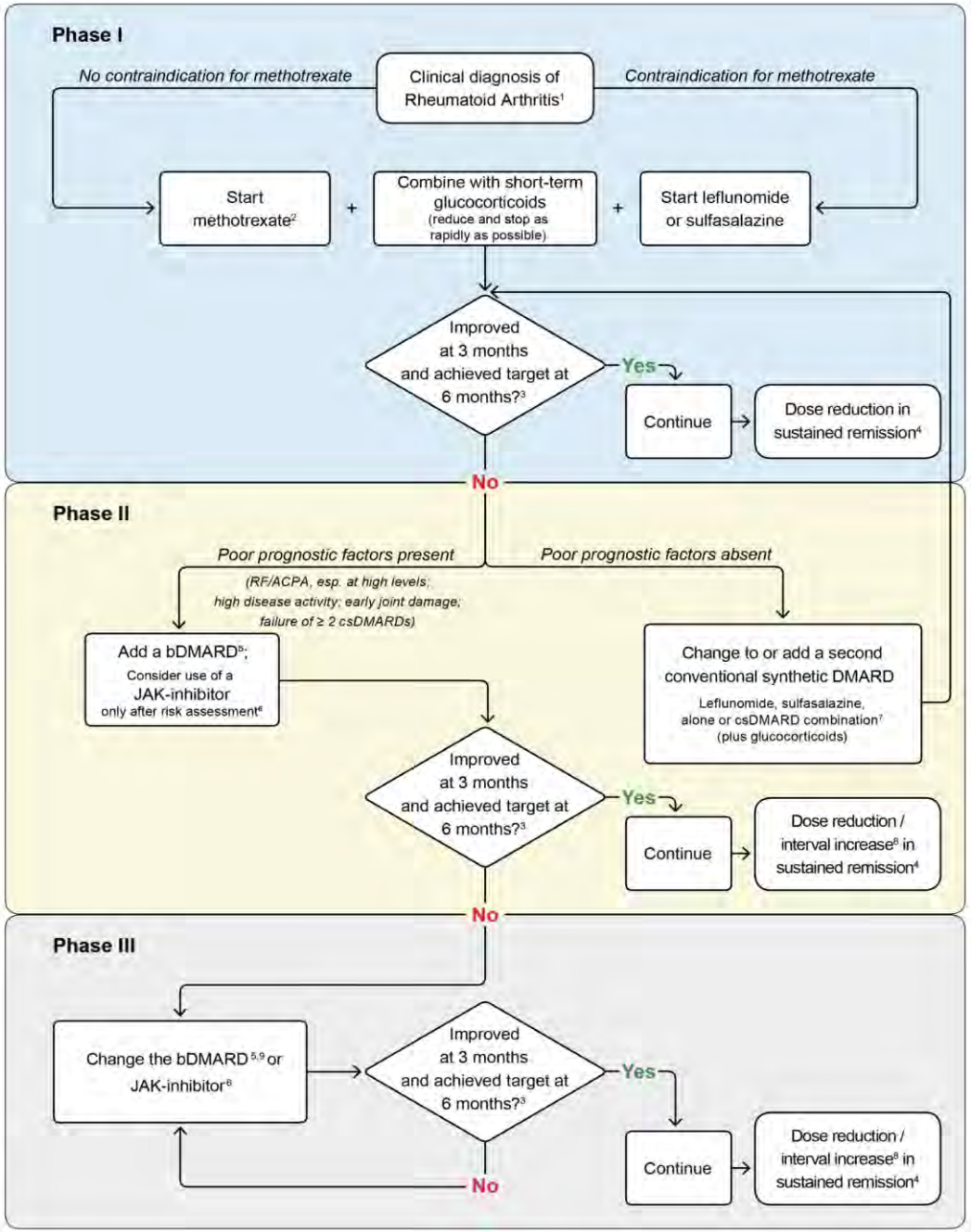
Ytterberg SR et al. N Engl J Med. 2022 Jan 27;386(4):316-326

Recommendation

# EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update

## Risk factors

Age>65
History of CVD/MI/thromboembolic event
History of current or past smoking
CVD risk factors (hypertension, DM, obesity)
Risk factors for clots (blood clotting disorders, hormone replacement therapy, major surgery or immobile)

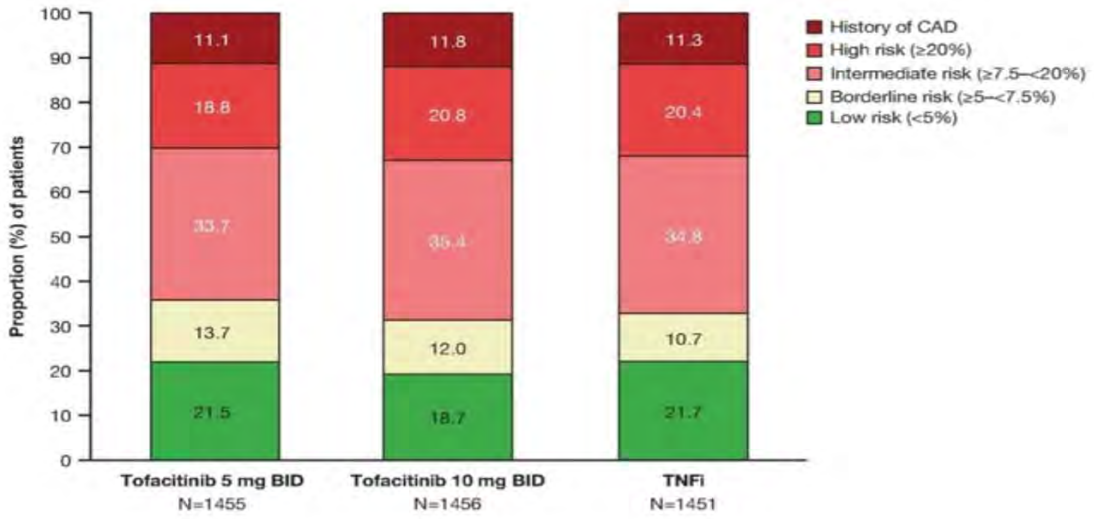


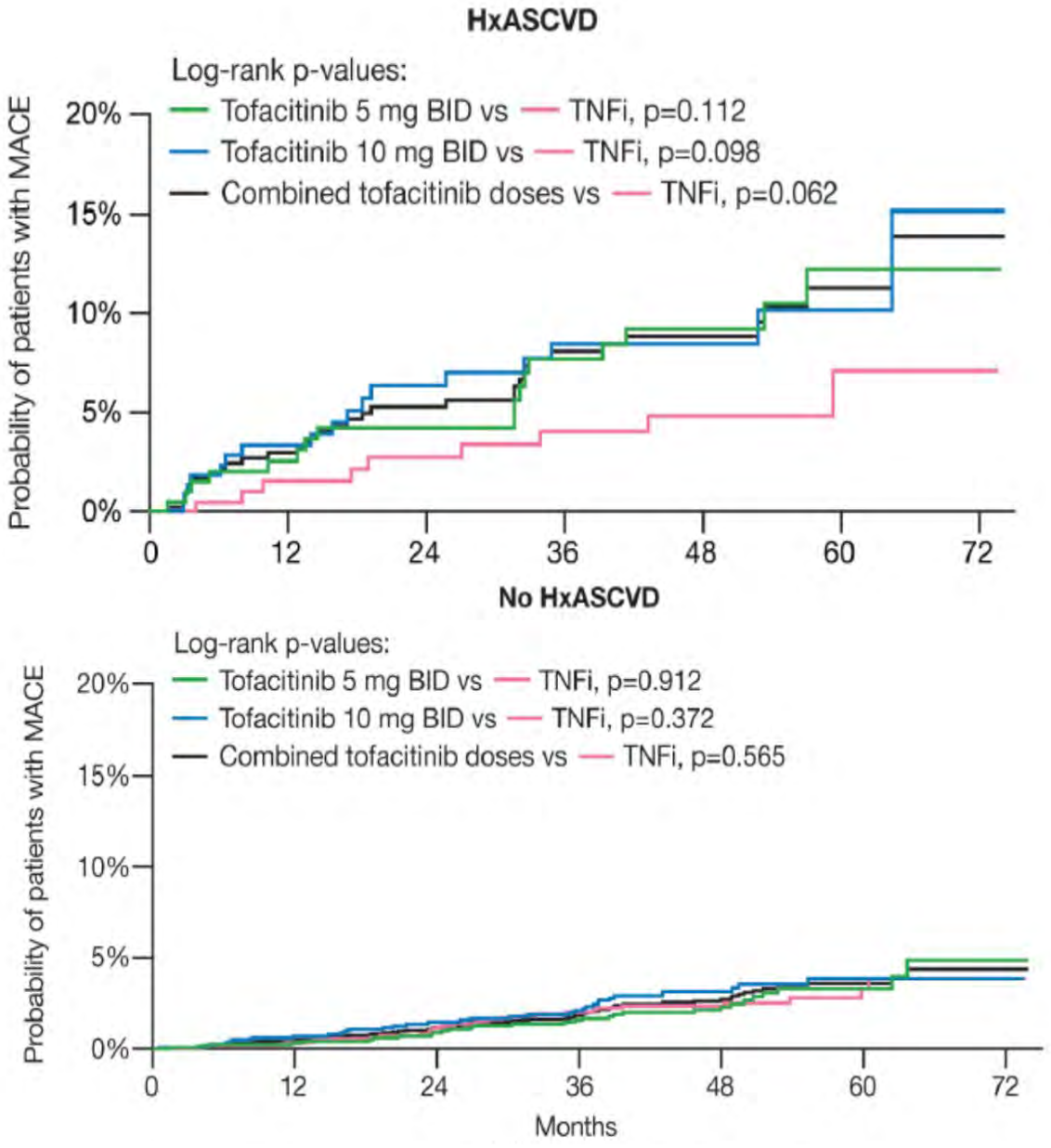
CLINICAL SCIENCE

# Risk of major adverse cardiovascular events with tofacitinib versus tumour necrosis factor inhibitors in patients with rheumatoid arthritis with or without a history of atherosclerotic cardiovascular disease: a post hoc analysis from ORAL Surveillance

Christina Charles-Schoeman ,[1] Maya H Buch ,[2,3] Maxime Dougados ,[4,5] Deepak L Bhatt ,[6] Jon T Giles,[7] Steven R Ytterberg,[8] Gary G Koch,[9] Ivana Vranic,[10] Joseph Wu,[11] Cunshan Wang,[11] Kenneth Kwok,[12] Sujatha Menon,[11] Jose L Rivas,[13] Arne Yndestad,[14] Carol A Connell,[11] Zoltan Szekanecz [15]

- CVD events and differential effect vs. TNFi concentrated in those with a history of coronary disease and those with the highest aggregate CVD risk



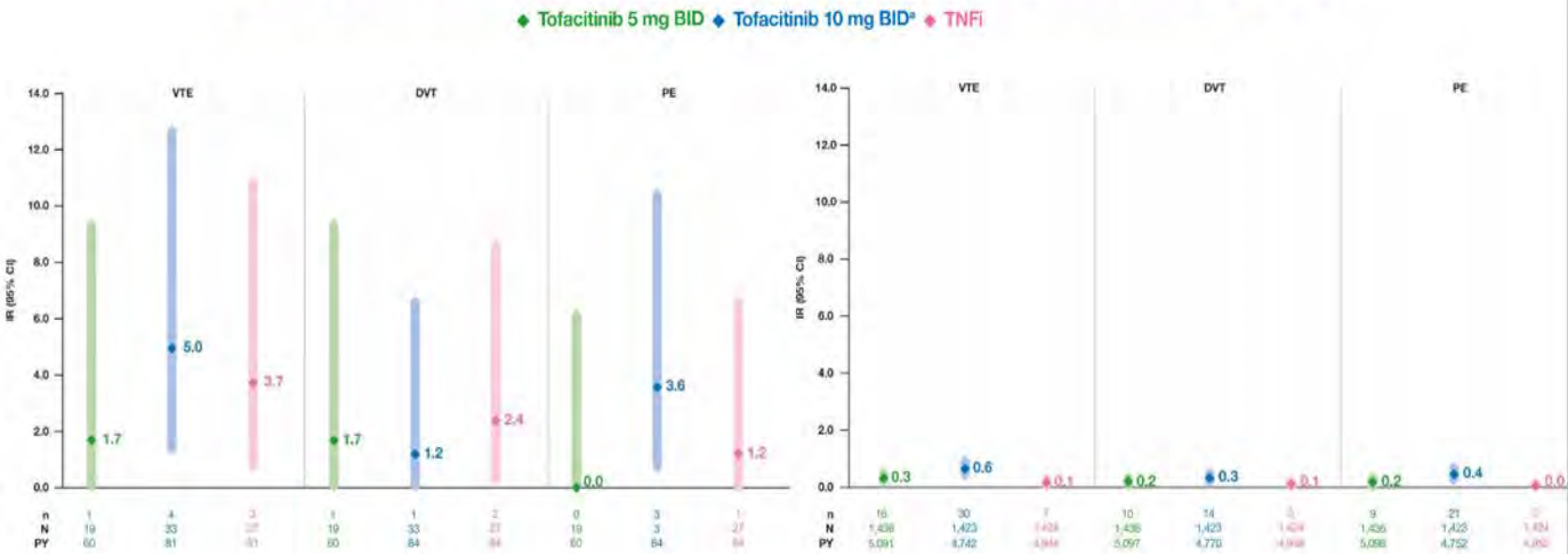




Charles-Schoeman C, et al Ann Rheum Dis 2023 Jan;82(1):119-129.

# Incidence Rates for VTE, DVT, and PE in Patients With and Without a History of VTE

## Patients with History of VTE

## Patients without History of VTE



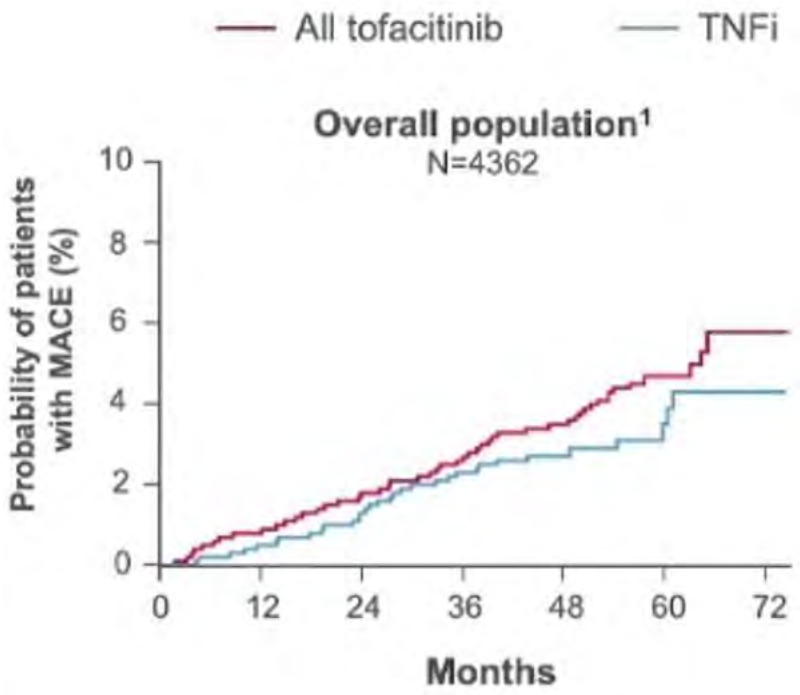

[a]The tofacitinib 10 mg BID treatment group included patients who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019. BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate; PE, pulmonary embolism; PY, patient-years; TNFi, tumor necrosis factor inhibitor; VTE, venous thromboembolism

Charles-Schoeman C, et al. The Risk of Venous Thromboembolic Events in Patients with RA Aged ≥ 50 Years with ≥ 1 Cardiovascular Risk Factor: Results from a Phase 3b/4 Randomized Safety Study of Tofacitinib vs TNF Inhibitors | *Arthritis Rheumatol.* 2021; 73 (suppl 10).

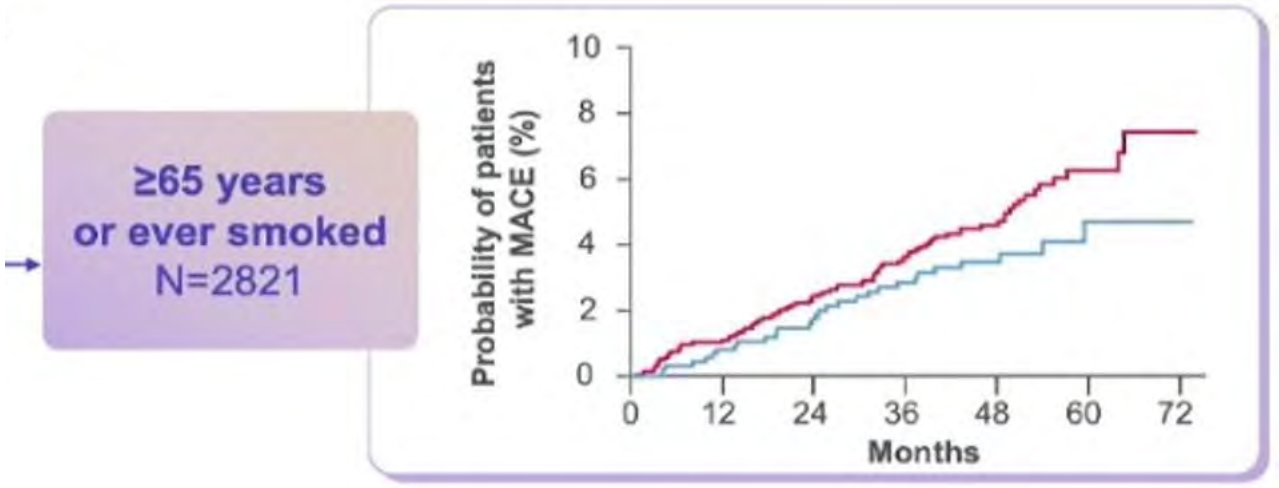
CLINICAL SCIENCE

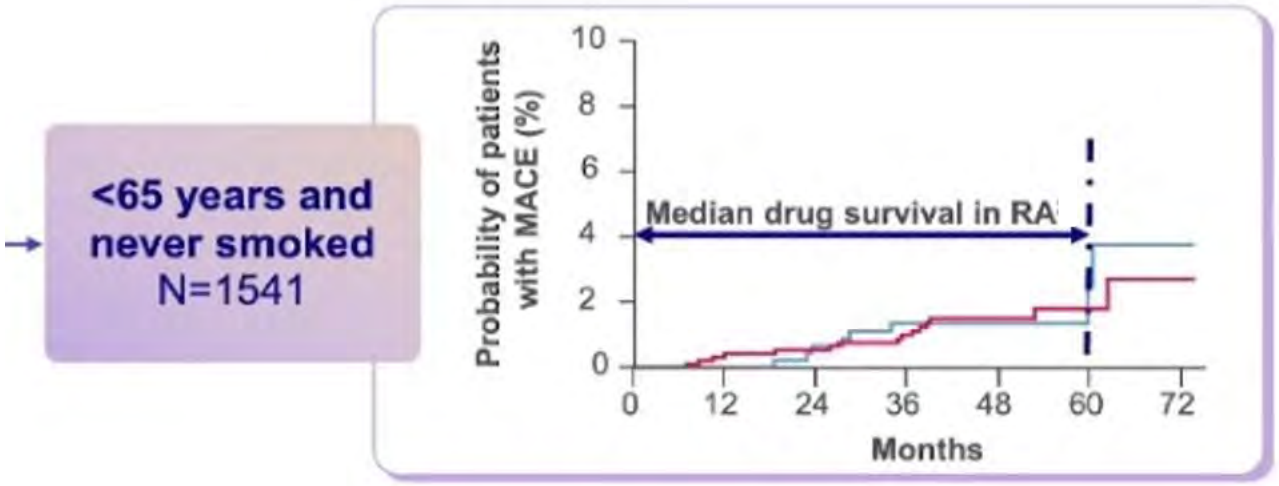
# Identification of two tofacitinib subpopulations with different relative risk versus TNF inhibitors: an analysis of the open label, randomised controlled study ORAL Surveillance

Lars Erik Kristensen,[1] Silvio Danese,[2] Arne Yndestad,[3] Cunshan Wang,[4] Edward Nagy,[5] Irene Modesto,[6] Jose Rivas,[6] Birgitta Benda[7]




Patients < 65 year old and never smoked (low risk population) showed no detectable increase risk for MACE for TOFA compared to TNFi



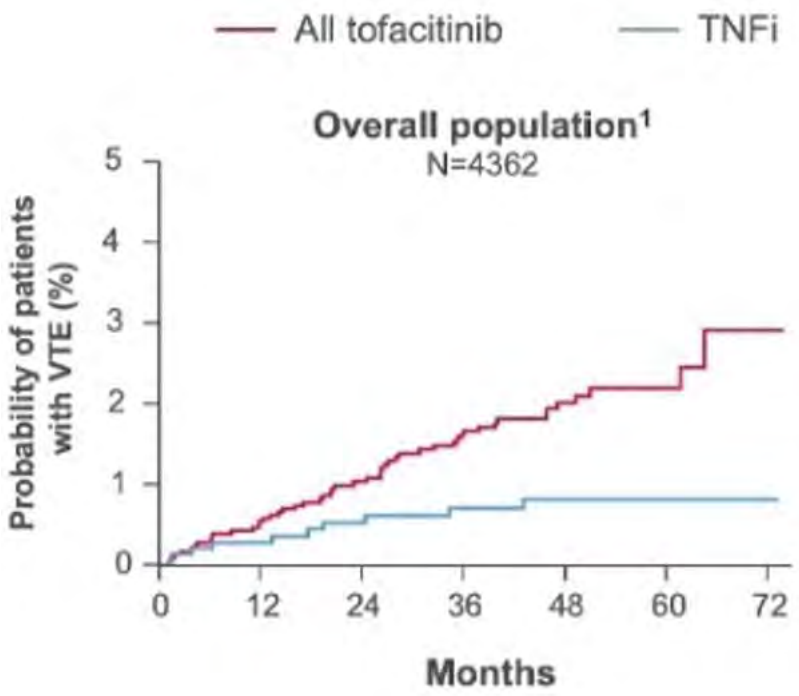

Kristensen L, et al Ann Rheum Dis 2023

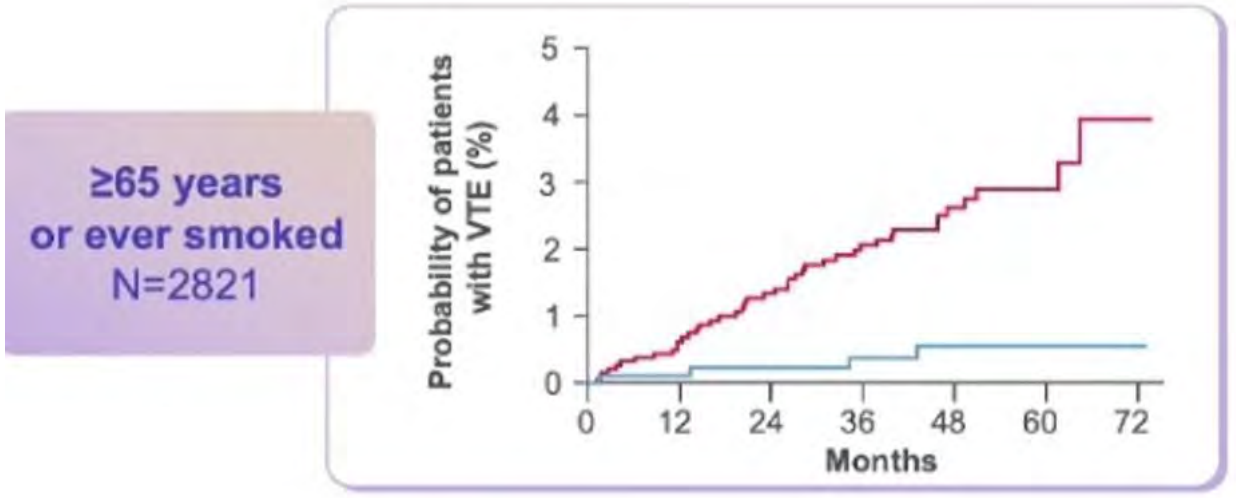
CLINICAL SCIENCE

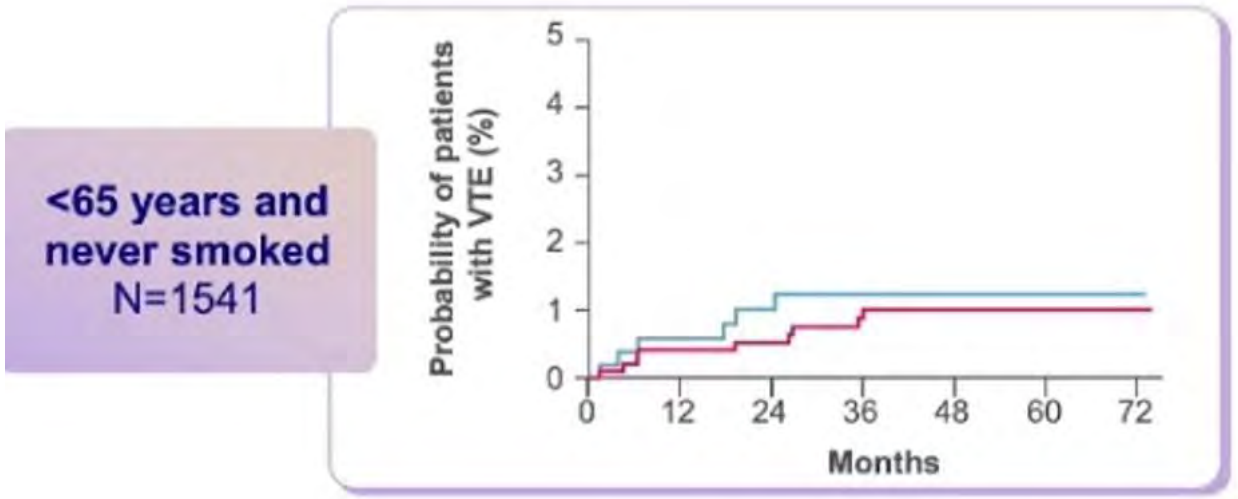
# Identification of two tofacitinib subpopulations with different relative risk versus TNF inhibitors: an analysis of the open label, randomised controlled study ORAL Surveillance

Lars Erik Kristensen,[1] Silvio Danese,[2] Arne Yndestad,[3] Cunshan Wang,[4] Edward Nagy,[5] Irene Modesto,[6] Jose Rivas,[6] Birgitta Benda[7]

Patients < 65 year old and never smoked (low risk population) showed no detectable increase risk for VTE for TOFA compared to TNFi




Kristensen L, et al Ann Rheum Dis 2023

EPIDEMIOLOGICAL SCIENCE

# Venous thromboembolism with JAK inhibitors and other immune-modulatory drugs: a Swedish comparative safety study among patients with rheumatoid arthritis

Viktor Molander ,[1,2] Hannah Bower ,[1] Thomas Frisell ,[1] Benedicte Delcoigne ,[1] Daniela Di Giuseppe,[1] Johan Askling ,[1,2] The ARTIS study group

- The Swedish Rheumatology Quality Register was linked to national health registers

  to identify treatment cohorts (exposure) of initiators of a JAKi (TOFA/BARI), a TNFi, or a non-TNFi bDMARD (n=32 737 treatment initiations).
- We also identified a general population cohort matched 1:5, n=92 108), an 'overall RA' comparator cohort (n=85 722)

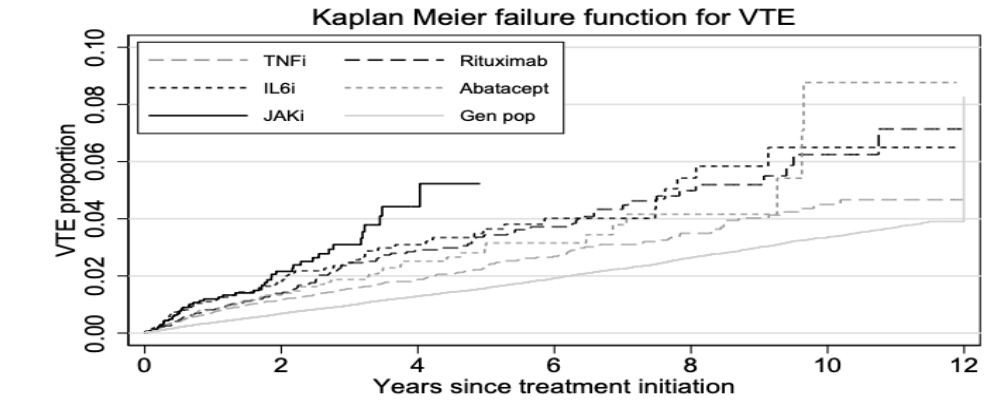
**Table 2** Number of treatment initiations, person-years at risk, VTE events, age- and sex-standardised incidence rates, and HRs for VTE in Swedish patients with RA (by treatment b/tsDMARD cohort and overall) and matched individuals from the general population between 2010 and 2020

| | Obs. | PYs at risk | VTE events | Standardised IR/1000 PYs (95% CI) | Unadjusted HR (95% CI) | HR (95% CI) Model 1* | HR (95% CI) Model 2† | HR (95% CI) Model 3‡ |
|---|---|---|---|---|---|---|---|---|
| Cohort | | | | | | | | |
| TNFi | 19 950 | 55 765 | 287 | 5.15 (4.58 to 5.78) | 1 (ref) | 1 (ref) | 1 (ref) | 1 (ref) |
| Rituximab | 4032 | 14 871 | 102 | 6.05 (4.98 to 7.34) | 1.35 (1.08 to 1.70) | 1.09 (0.86 to 1.38) | 0.97 (0.76 to 1.23) | 0.94 (0.74 to 1.20) |
| IL6i | 3019 | 8 354 | 66 | 7.54 (5.92 to 9.59) | 1.54 (1.18 to 2.01) | 1.44 (1.09 to 1.92) | 1.30 (0.97 to 1.73) | 1.25 (0.94 to 1.67) |
| Abatacept | 3382 | 8 651 | 56 | 5.69 (4.38 to 7.40) | 1.25 (0.94 to 1.67) | 1.10 (0.81 to 1.49) | 0.89 (0.65 to 1.20) | 0.89 (0.66 to 1.21) |
| JAKi | 2354 | 4 184 | 48 | 11.33 (8.54 to 15.04) | 2.16 (1.59 to 2.93) | 1.94 (1.40 to 2.70) | 1.63 (1.17 to 2.28) | 1.73 (1.24 to 2.42) |
| Baricitinib§ | 1825 | 3 412 | 41 | 11.35 (8.35 to 15.41) | 2.27 (1.64 to 3.15) | 2.00 (1.41 to 2.83) | 1.69 (1.19 to 2.40) | 1.79 (1.25 to 2.55) |
| Tofacitinib§ | 424 | 667 | 7 | 11.30 (5.39 to 23.70) | 1.96 (0.92 to 4.15) | 1.91 (0.89 to 4.11) | 1.56 (0.72 to 3.35) | 1.66 (0.77 to 3.59) |
| Overall RA cohort | 85 722 | 633 871 | 4476 | 5.86 (5.69 to 6.04) | n/a | n/a | n/a | n/a |
| Gen pop | 92 180 | 597 854 | 2001 | 3.28 (3.14 to 3.43) | 0.67 (0.59 to 0.76) | 0.66 (0.57 to 0.76) | n/a | n/a |

*Model 1 adjusted for age, sex and line of therapy. Overall RA cohort excluded from model.
†Model 2 additionally adjusted for comorbidities and socioeconomic variables. Overall RA cohort and general population excluded from model.
‡Model 3 additionally adjusted for RA disease variables, civil status and smoking, using an indicator for missing variables. Overall RA cohort and general population excluded from model.
§Estimates obtained from a separate model where JAKi cohort is split into baricitinib and tofacitinib.
b/tsDMARD, biologic/targeted synthetic disease modifying anti-rheumatic drug; Gen pop, general population; IL6i, interleukin 6 inhibitor; IR, incidence rate; JAKi, Janus kinase inhibitor; n/a, not applicable; PY, person years; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor; VTE, venous thromboembolism.

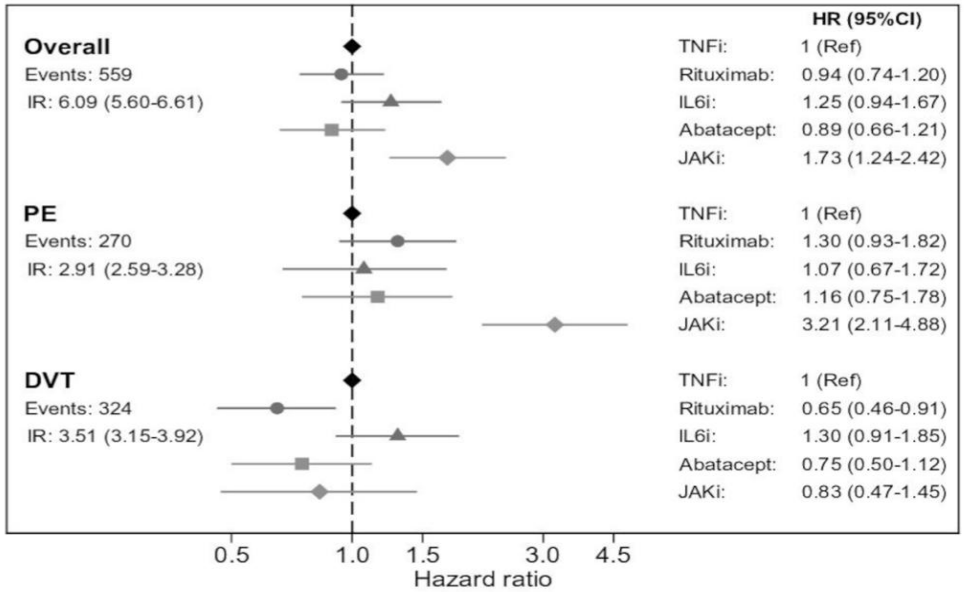
Selection bias – no information on disease activity

# Real world data: Swedish registry




At-risk table

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| TNFi | 19950 | 9100 | 5077 | 2814 | 1505 | 626 | 0 |
| Rituximab | 4032 | 2467 | 1553 | 877 | 466 | 176 | 0 |
| IL6i | 3019 | 1291 | 801 | 453 | 233 | 88 | 0 |
| Abatacept | 3382 | 1436 | 775 | 396 | 172 | 45 | 0 |
| JAKi | 2354 | 927 | 122 | 0 | 0 | 0 | 0 |
| Gen pop | 92180 | 83377 | 65726 | 49348 | 33757 | 18431 | 0 |




Molander V, et al. Ann Rheum Dis 2022

Rheumatoid arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

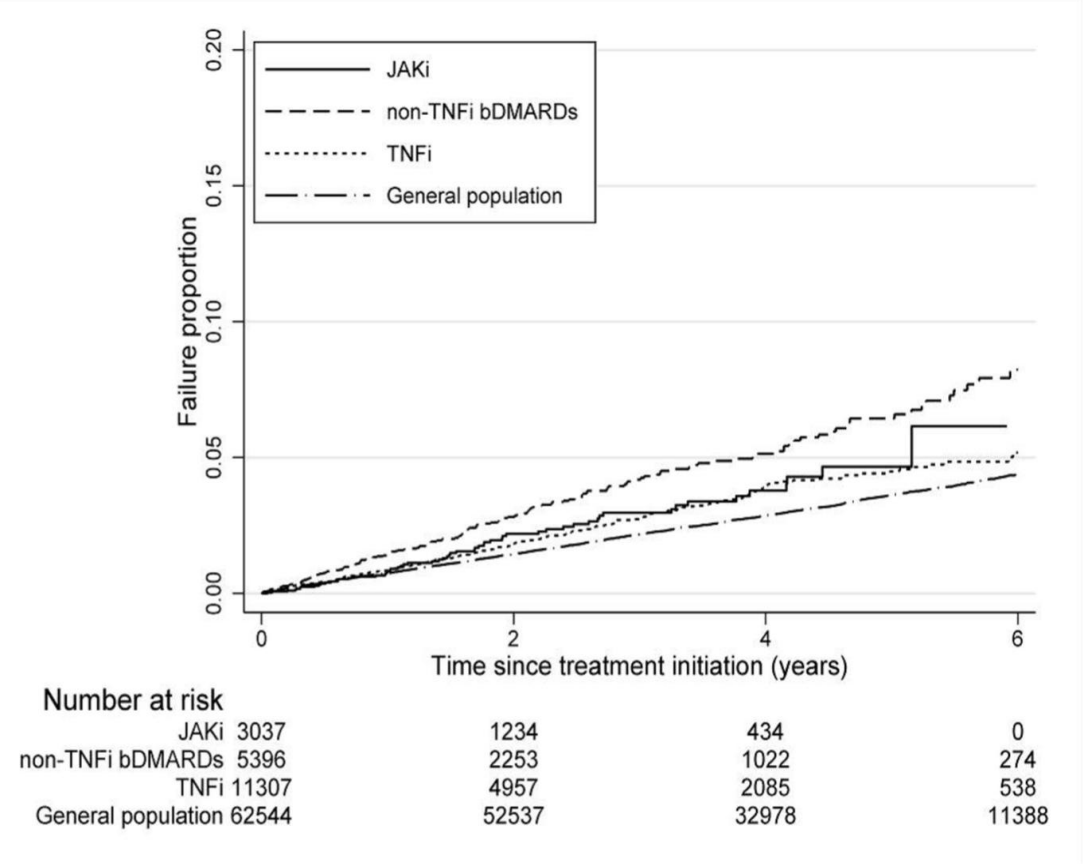
ORIGINAL RESEARCH

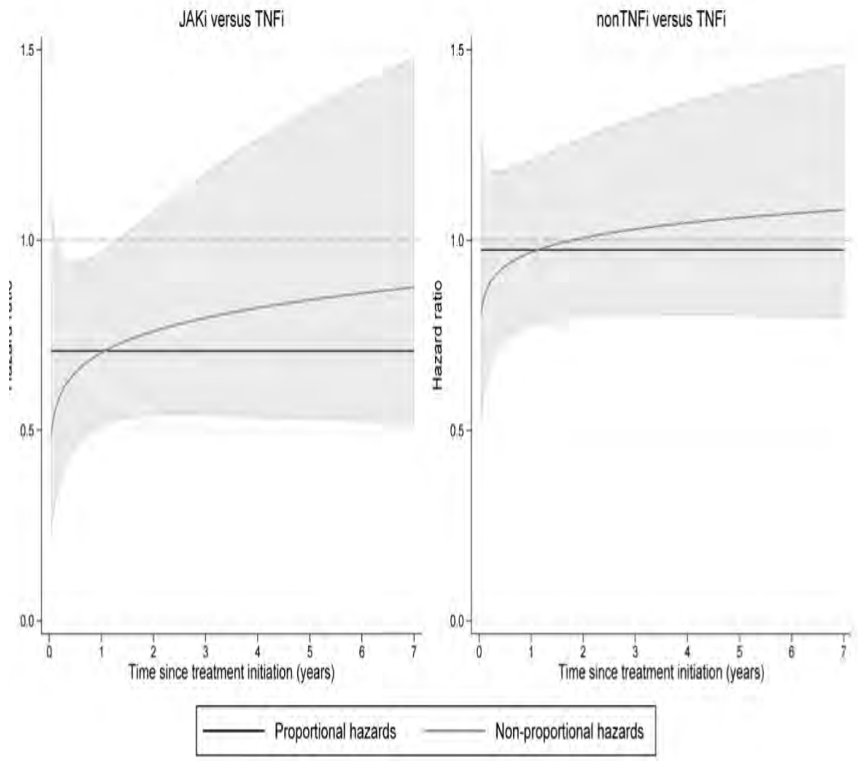
# Comparative cardiovascular safety with janus kinase inhibitors and biological disease-modifying antirheumatic drugs as used in clinical practice: an observational cohort study from Sweden in patients with rheumatoid arthritis

Hannah Bower ,[1] Thomas Frisell ,[1] Daniela di Giuseppe ,[1] Benedicte Delcoigne ,[1] Johan Askling [1,2]

13492 patients with RA initiating a JAKi, non-TNFi bDMARD or TNFi treatment (Swedish Rheumatology Quality Register between 2016 and 2021).

MACE: myocardial infarction, stroke and fatal CV events




Bower H, et al. RMD Open 2023;**9**:e003630.

# INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JAK-INHIBITORS COMPARED TO BDMARDS: DATA FROM AN INTERNATIONAL COLLABORATION OF REGISTRIES (THE "JAK-POT" STUDY)

R. Aymon[1], D. Mongin[1], S. A. Bergstra[2], D. Choquette[3], C. Codreanu[4], R. L. Cordtz[5], D. C. Diederik[6], L. Dreyer[5], O. Elkayam[7], D. Huschek[8], K. Hyrich[9], F. Iannone[10], N. Inanc[11], L. Kearsley-Fleet[9], T. K. Kvien[12], B. Leeb[13], G. Lukina[14], D. Nordström[15], F. Onen[16], K. Pavelka[17], M. Pombo-Suarez[18], S. Aarrestad Provan[12], A. M. Rodrigues[19], Z. Rotar[20], A. Strangfeld[6], P. Verschueren[6], J. Zavada[17], D. Courvoisier[1], A. Finckh[1], K. Lauper[1]

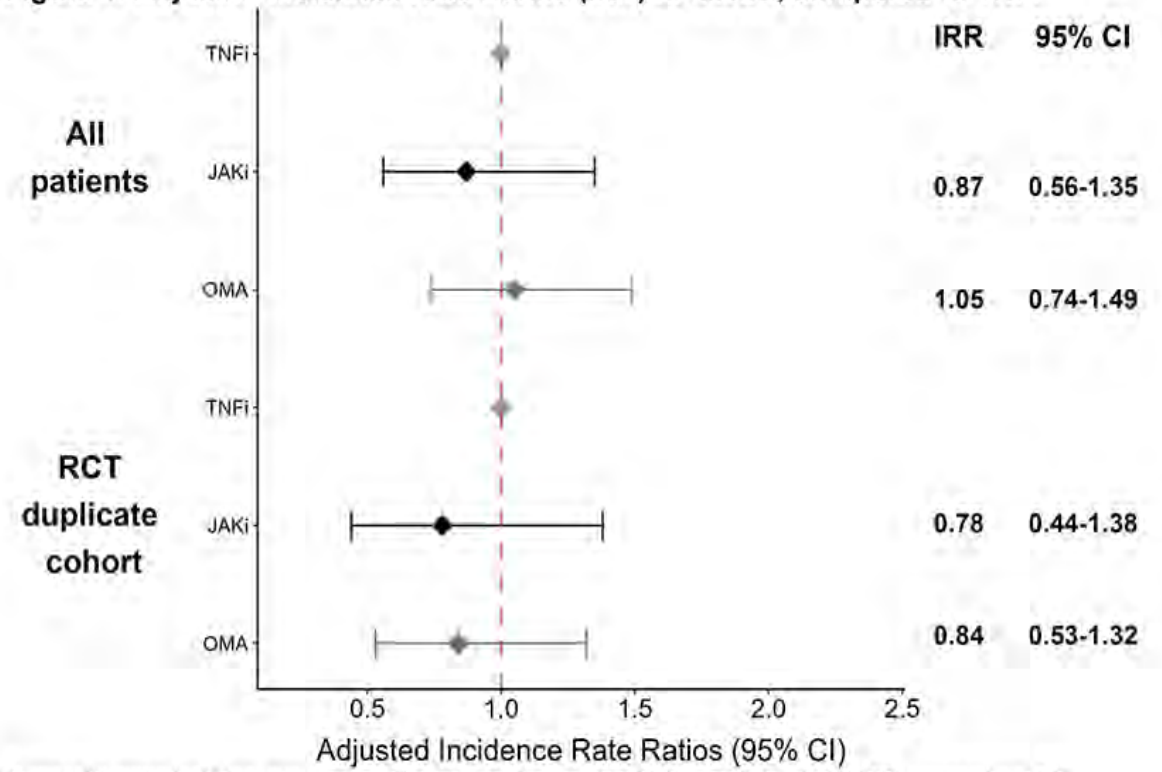
MACE: myocardial infarction, stroke and fatal CV events

Real world data from registries of 16 countries

Over n= 50,325 treatment courses initiations

there were 182 incident MACE reported

**Figure 1: Adjusted Incidence Rate Ratios (IRR) of MACE, compared to TNFi**




**Propensity score includes: age, gender, disease duration, seropositivity, previous b/tsDMARD, concomitant GC, concomitant csDMARD, DAS28, HAQ, Rheumatic Disease Comorbidity Index**

EULAR 2023 Abstract: OP0219

# What is next - CV risk assessment

JAK inhibitors are here to stay
(great efficacy, novel indications)

RA disease control is protective against CVD outcomes

Screening patients for various risk factors prior to therapy selection "high risk population" (age, smoking, history of ASCVD, VTE, PE)

Continue to weight CVD risk and benefit

Individualize therapy for patients with RA taking into account risk factors, co-morbidities and concomitant medications.

More data for well-design longitudinal studies

Reduce risk
Maximize benefit

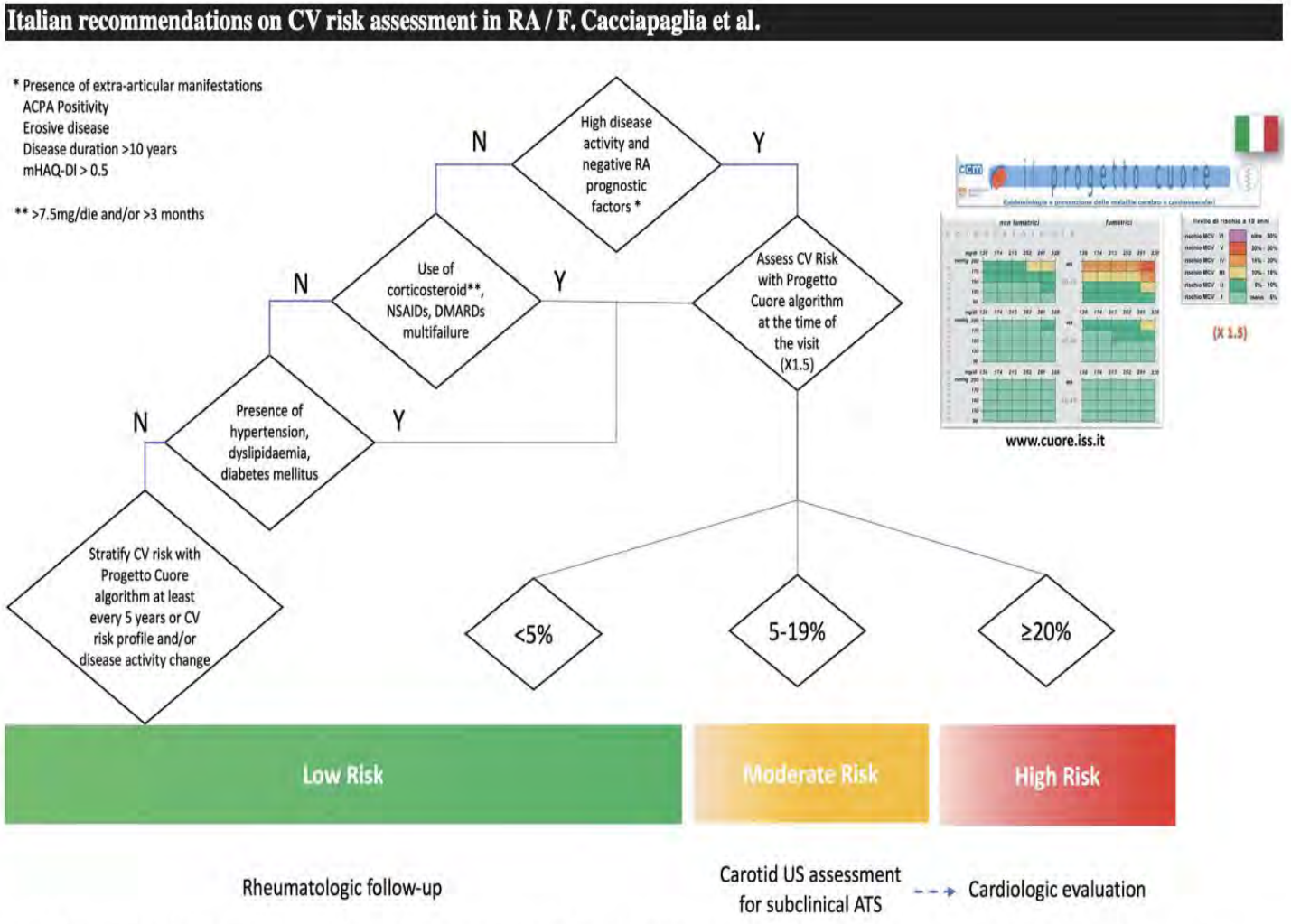




**Fig. 1.** Recommended algorithm as flowchart for the evaluation of CV risk in RA patients in clinical practice.
ACPA: anti-citrullinated peptides antibodies; CV: cardiovascular; DMARDs: disease-modifying anti-rheumatic drugs; mHAQ-DI: modified Health Assessment Questionnaire Disability Index; NSAIDs: non-steroidal anti-inflammatory drugs; RA: rheumatoid arthritis.

Cacciapaglia et al, Clin Exp Rheumatol. 2023

# ΣΥΜΠΕΡΑΣΜΑΤΑ

- Στα συστηματικά ρευματικά νοσήματα η καρδιαγγειακή νοσηρότητα αποτελεί έναν από τους σημαντικότερους παράγοντες πρόωρης θνητότητας

- Οι κλασσικοί και οι νεότεροι παράγοντες κινδύνου είναι ΕΞΙΣΟΥ σημαντικοί για την ανάπτυξη καρδιαγγειακής νόσου και θα πρέπει να παρακολουθούνται σε τακτική βάση

- Η πολυπλοκότητα των μηχανισμών που εμπλέκονται στην ανάπτυξη καρδιαγγειακής νόσου στα φλεγμονώδη νοσήματα κάνουν το σχεδιασμό και την καθιέρωση στρατηγικών πρόληψης ιδιαίτερα δυσχερή.

- Συμβατικά και βιολογικά DMARDS μπορεί να έχουν βλαπτική επίδραση στο μυοκάρδιο, αλλά ταυτόχρονα είναι δυνατόν να μειώσουν τον κίνδυνο καρδιαγγειακής νόσου ελέγχοντας τη συσσωρευτική δράση του συστηματικού φλεγμονώδους φορτίου συνολικά στο καρδιοαγγειακό σύστημα