Τι νεότερο στη Ρευματοειδή Αρθρίτιδα;

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ΙΑΤΡΙΚΗ ΣΧΟΛΗ

Περίγραμμα

- Επιδημιολογία - Πρόγνωση
- Στεροειδή - Βιολογικά: νέα γνώση
- Βιοδείκτες Πρόγνωσης

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Incidence

EPIDEMIOLOGICAL SCIENCE

Is the epidemiology of rheumatoid arthritis changing? Results from a population-based incidence study, 1985–2014

Elena Myasoedova [1], John Davis,[1] Eric L Matteson,[1] Cynthia S Crowson [1,2]

- **What it is known**

✓ Variability in the incidence of RA in different populations:

- **Declines** in RA occurrence have been reported in several populations in the USA, Western Europe and Japan during the second half 20th century
- **Increase** in the incidence of RA in the late 1990s to early 2000s, particularly in females, has been reported in Olmsted County, Minnesota and in Denmark.

- **Aim of the study:**

To examine trends in the incidence of RA from 2005 to 2014

✓ Overall

✓ By serological status

✓ Compared with 1995–2004 and 1985–1994

Myasoedova E, et al. Ann Rheum Dis 2020;0:1–5. doi:10.1136/annrheumdis-2019-216694

Incidence

Main findings:

- ✓ Overall, the incidence of RA overall **was stable** during 2005–2014 compared with the previous decade.
- ✓ **Decreasing incidence of (RF)-positive** RA and increasing incidence of RF-negative RA in 2005–2014 as compared with the previous decades.

Table 2 Incidence rates of RA by 1987 ACR criteria per 100 000 population (95% CI)

Group	Decade of RA incidence	Female	Male	Total
Overall	1985–1994	48 (41 to 56)	32 (25 to 40)	40 (35 to 46)
	1995–2004	55 (48 to 63)	30 (24 to 36)	43 (38 to 48)
	2005–2014	53 (47 to 59)	29 (24 to 34)	41 (37 to 45)
RF positive	1985–1994	33 (27 to 40)	23 (17 to 30)	28 (24 to 33)
	1995–2004	39 (33 to 45)	19 (15 to 24)	30 (26 to 33)
	2005–2014	26 (22 to 30)	15 (12 to 19)	21 (18 to 24)
RF negative	1985–1994	15 (11 to 19)	9 (5 to 12)	12 (9 to 15)
	1995–2004	16 (13 to 20)	10 (7 to 14)	13 (11 to 16)
	2005–2014	26 (22 to 31)	14 (11 to 18)	20 (18 to 23)

Incidence

Table 1 Patient characteristics by decade of RA incidence

Characteristics*	Decade of RA incidence 1985–1994 (n=240)	1995–2004 (n=344)	2005–2014 (n=427)	P value
Age at RA incidence (years)	56.6 (16.6)	56.0 (15.5)	55.4 (15.4)	0.73
Female sex	160 (67%)	240 (70%)	291 (68%)	0.73
Smoking at RA incidence				
Never smoker	97 (40%)	161 (47%)	242 (57%)	
Current smoker	51 (21%)	62 (18%)	64 (15%)	
Former smoker	91 (38%)	121 (35%)	121 (28%)	
BMI at RA incidence (kg/m^2)	27.0 (5.5)	28.1 (6.1)	29.6 (6.8)	<0.001
Obesity (BMI ≥30 kg/m^2) at RA incidence	57 (24%)	114 (33%)	175 (41%)	<0.001
History of obesity at or before RA incidence	77 (32%)	147 (43%)	210 (49%)	<0.001
RF positive	166 (69%)	238 (69%)	216 (51%)	<0.001
Anti-CCP positive Not tested	33 (73%) 195	86 (49%) 170	197 (50%) 30	0.009
Erosion in the first year after RA incidence	33 (17%)	65 (21%)	96 (25%)	0.048
RF positive	27 (19%)	50 (23%)	49 (25%)	0.47
RF negative	6 (10%)	15 (16%)	47 (25%)	0.017

How might this impact on clinical practice or future developments?

- ✓ Rising incidence of RF-negative RA suggests the **need for increased awareness** and timely recognition of RF-negative RA by physicians.
- ✓ The changing **prevalence of environmental factors, such as smoking, obesity and others, may have contributed to decreasing incidence of RF-positive** RA and increasing incidence of RF-negative RA in 2005–2014.

Myasoedova E, et al. Ann Rheum Dis 2020;0:1–5. doi:10.1136/annrheumdis-2019-216694

Mortality

Normal mortality of the COBRA early rheumatoid arthritis trial cohort after 23 years of follow-up

Pomme BM Poppelaars,[1] Lilian H D van Tuyl,[1] Maarten Boers[1,2]

- Mortality in patients with rheumatoid arthritis (RA) **is higher** than in the general population.

- A **meta-analysis of studies on incident RA** diagnosed from 1953 to 2007Q
  - **failed to demonstrate any obvious decrease** in the excess mortality, at least in relative terms,
  - **although a decreasing mortality rate was observed** (but during the same time period, mortality rates have decreased also in the general population).

Poppelaars PBM, et al. Ann Rheum Dis. 2019 May;78(5):586

Mortality

- Questions in the study:
  - ✓ Mortality in the **COBRA-trial cohort after 23 years** follow-up, compared with a reference sample
  - ✓ Explores associations between mortality and well-known prognostic factors.

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Mortality

- Questions in the study:
  - ✓ Mortality in the **COBRA-trial cohort after 23 years** follow-up, compared with a reference sample
  - ✓ Explores associations between mortality and well-known prognostic factors.

- Duration of follow-up in patients alive was mean 23 (range 22–24) years.
- SMR
  - Total SMR=0.80 [95% CI 0.59 - 1.06])
  - COBRA patients SMR 0.75 [0.47 - 1.14]
  - SSZ patients SMR 0.85 [0.56 - 1.25]); p=0.61)

- Factors significantly associated with increased mortality hazard:
  - damage progression at 28 weeks
  - high HAQ score
  - absence of HLA-DR 2 or 3
  - disease duration from start of treatment

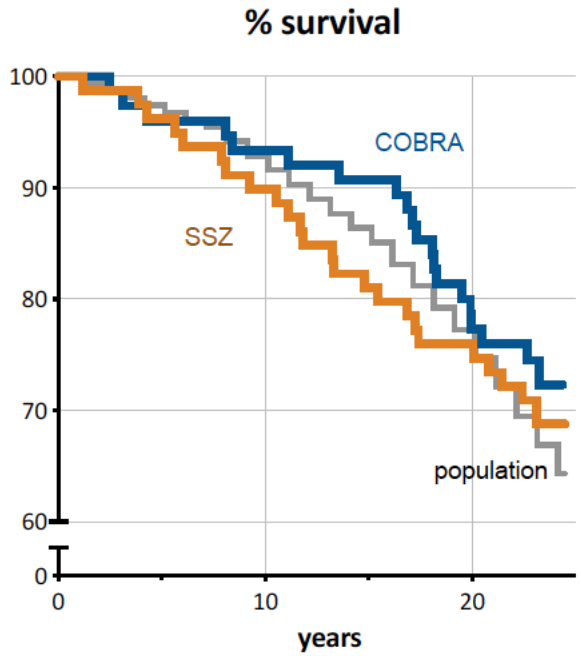


Figure 1 Survival curves of the COBRA trial cohort by treatment. COBRA, n=75 (1 patient missing); SSZ, n=79. Survival of the reference cohort from the general population in grey. Note that all living patients have now been followed for 22–24 years, so the proportion of survivors equals the proportion at risk.

Poppelaars PBM, et al. Ann Rheum Dis. 2019 May;78(5):586

Mortality

What does this study add?

- This prospective cohort study in patients with early RA is one of the first to show a **normalisation** of RA mortality after 23 years of follow-up.
- Several well-known prognostic factors were related to mortality.

How might this impact on clinical practice or future developments?

- The study confirms that early and intensive treatment of RA has long-term benefits and suggests that treating to target is especially important for patients with poor prognosis.

Poppelaars PBM, et al. Ann Rheum Dis. 2019 May;78(5):586

Mortality following new-onset Rheumatoid Arthritis: has modern Rheumatology had an impact?

Marie Holmqvist,[1] Lotta Ljung,[2] Johan Askling[1]

The aim of this study

- Assess overall mortality in a clinical inception cohort of patients with RA compared with the general population
- Emphasis on the development of absolute risk and RR of death as a function of **both disease duration and calendar period of RA**

Methods

- Nationwide population-based cohort study of patients with newly diagnosed RA with individually matched general population comparator subjects, based on prospectively recorded register data.
- We further set out to investigate mortality risks with different RA phenotypes

Holmqvist M, et al. Ann Rheum Dis 2017; doi:10.1136/annrheumdis-2017-212131

Mortality

Clinical characteristics of patients with new-onset RA at inclusion

Table 2 Clinical characteristics of patients with new-onset RA at inclusion in the Swedish Rheumatology Quality Register, including data on treatments initiated within 1 year of inclusion, by calendar period of RA diagnosis

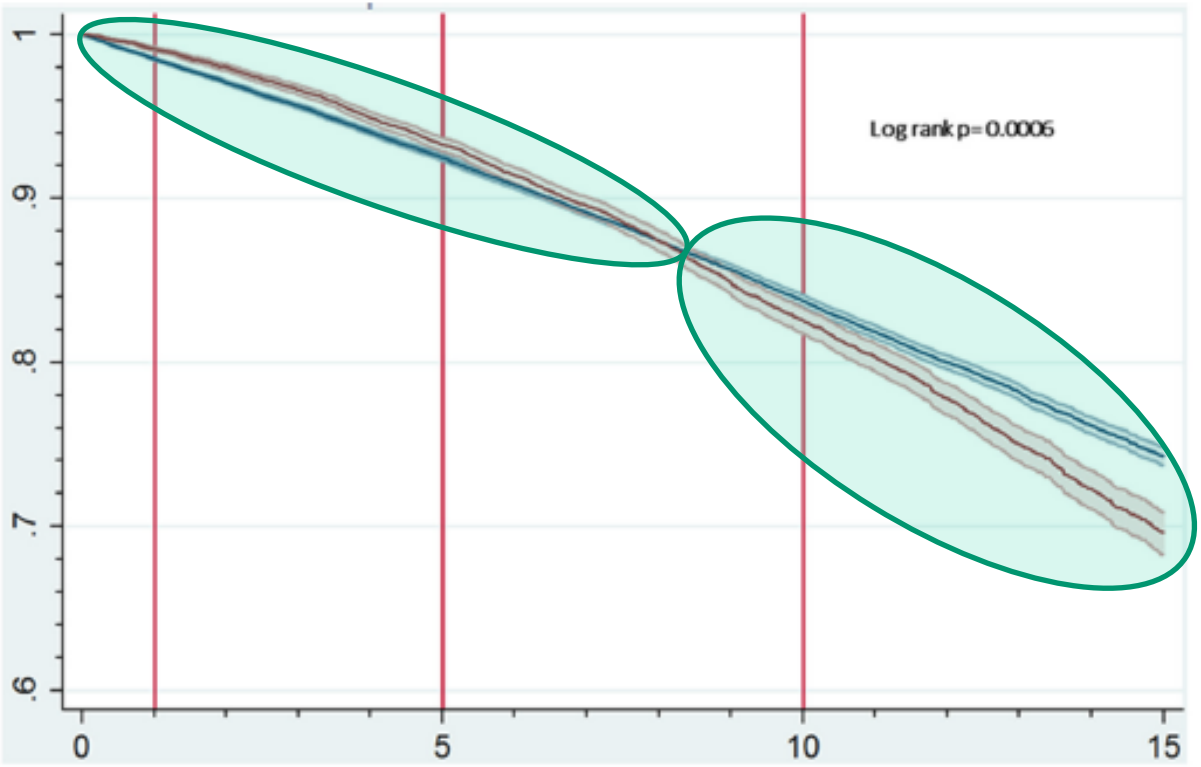
Year of RA diagnosis	All n=17512	1997–2001 n=2766	2002–2006 n=3960	2007–2011 n=5513	2012–2015 n=5273
DAS28 at inclusion*	4.9 (1.4)	5.1 (1.3)	5.3 (1.3)	4.9 (1.5)	4.6 (1.5)
DAS28 at 3–6 months*†	3.2 (1.4)	3.5 (1.4)	3.4 (1.4)	3.1 (1.3)	3.0 (1.3)
Symptom duration at index date, weeks*	25 (16.7)	27 (20.0)	26 (18.3)	24 (15.9)	24 (14.4)
Oral glucocorticoids‡	10348 (59.1)	1313 (47.5)	1882 (47.5)	3742 (67.9)	3411 (64.7)
DMARD, any‡	16223 (92.6)	2503 (90.5)	3788 (95.7)	5131 (93.1)	4801 (91)
DMARD, Mtx‡	14353 (82.0)	1771 (64.0)	3327 (84.0)	4754 (86.2)	4501 (85.4)
Biological drugs‡	2229 (12.7)	187 (6.8)	502 (12.7)	751 (13.6)	789 (15.0)

Holmqvist M, et al. Ann Rheum Dis 2017; doi:10.1136/annrheumdis-2017-212131

Mortality

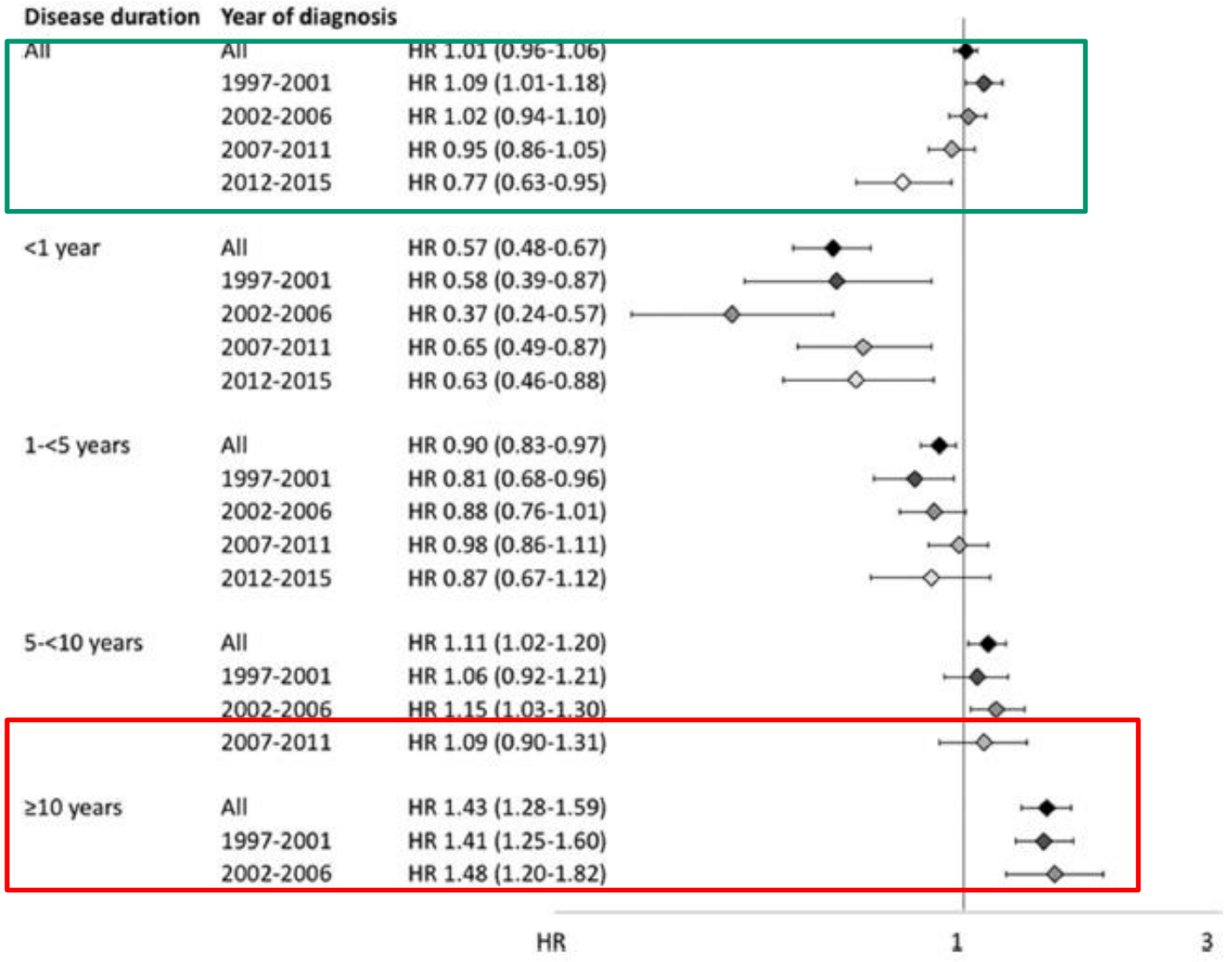
Across all calendar periods of RA diagnosis, an initial mortality ‘deficit’ turned into an **excess mortality 5–10 years after RA diagnosis.**

Kaplan-Meier survival curve comparing patients with new-onset rheumatoid arthritis (RA, red line) with the general population (blue line).



At risk at start of period	17512/78847	16062/71657	10282/45474	4737/21270	RA/
N deaths during period	146/1127	777/3630	869/3182	489/1592	General
Cumulative mortality	0.8%/1.4%	5%/6%	10%/10%	13%/12%	population

The relative risk of death among patients with rheumatoid arthritis (RA), overall and by calendar period of RA diagnosis compared with the general population



Holmqvist M, et al. Ann Rheum Dis 2017; doi:10.1136/annrheumdis-2017-212131

What does this study add?

- In conclusion, despite a decreasing absolute mortality rate, the excess risk of mortality in RA compared with the general population remains

How might this impact on clinical practice or future developments?

- To close this gap, increased efforts to prevent disease progression and comorbidity, from disease onset throughout the disease course, are needed.

Holmqvist M, et al. Ann Rheum Dis 2017; doi:10.1136/annrheumdis-2017-212131

Mortality in RA

- ✓ Altogether it appears that in the long term the increase in longevity seen in the general population is matched and perhaps surpassed by increases seen in the RA population
- ✓ But a detrimental difference remains
- ✓ It is likely that the improved prognosis is the sum of earlier detection and treatment, more aggressive treatment, and better handling of (especially cardiovascular) comorbidity.

Poppelaars PBM, et al. Ann Rheum Dis. 2019 May;78(5):586

Περίγραμμα

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- Στεροειδή - Βιολογικά: νέα γνώση
- Βιοδείκτες Πρόγνωσης

Immunosuppression and the risk of readmission and mortality in patients with rheumatoid arthritis undergoing hip fracture, abdominopelvic and cardiac surgery

Michael D George ,[1] Joshua F Baker,[1,2] Kevin L Winthrop ,[3] Seth D Goldstein,[4,5] E Alemao,[6] Lang Chen,[7] Qufei Wu,[1] Fenglong Xie,[7] Jeffrey R Curtis[7]

- **What is already known:**
- ✓ Studies of the risk of immunosuppression in patients undergoing surgery most commonly involve patients undergoing **elective arthroplasty**, but few studies have evaluated other major surgery.

- **Aim of the study:**
- ✓ To evaluate the impact of biologics and glucocorticoids on outcomes after other major surgeries.

ARD 2020 May;79(5):573

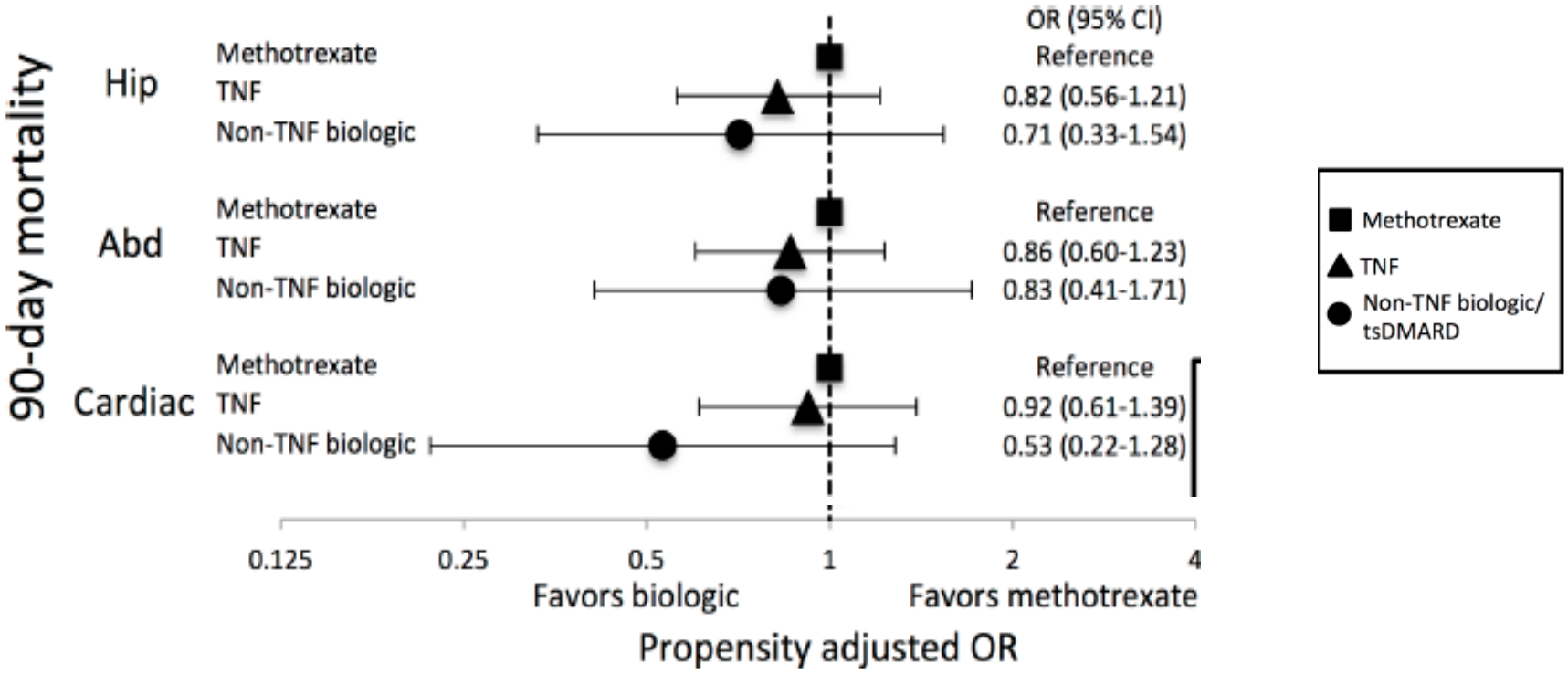
Design

- Retrospective cohort study
  - Medicare data 2006–2015
- RA patients undergoing
  - hip fracture repair,
  - abdominopelvic surgery
  - cardiac surgery
- Compared
  - 90-day mortality and
  - 30-day readmission

- **Treatments**
  - Methotrexate
  - TNFi or a non-TNFi biologic/tsDMARD <8 weeks before surgery
  - Glucocorticoids

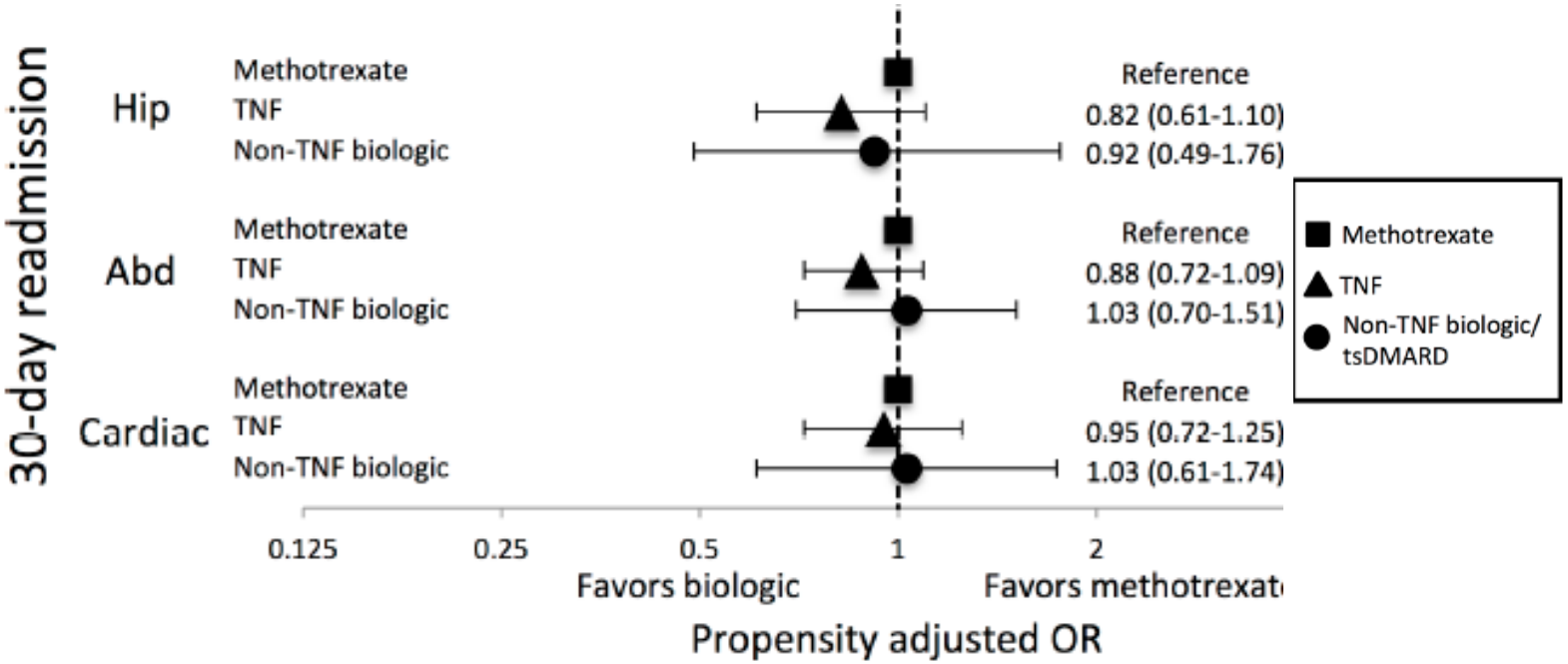
Comparable risk for **mortality** between MTX & bDMARDs treated patients

Associations of biologic use with mortality and readmission by surgery type. OR from inverse probability-weighted logistic regression models.



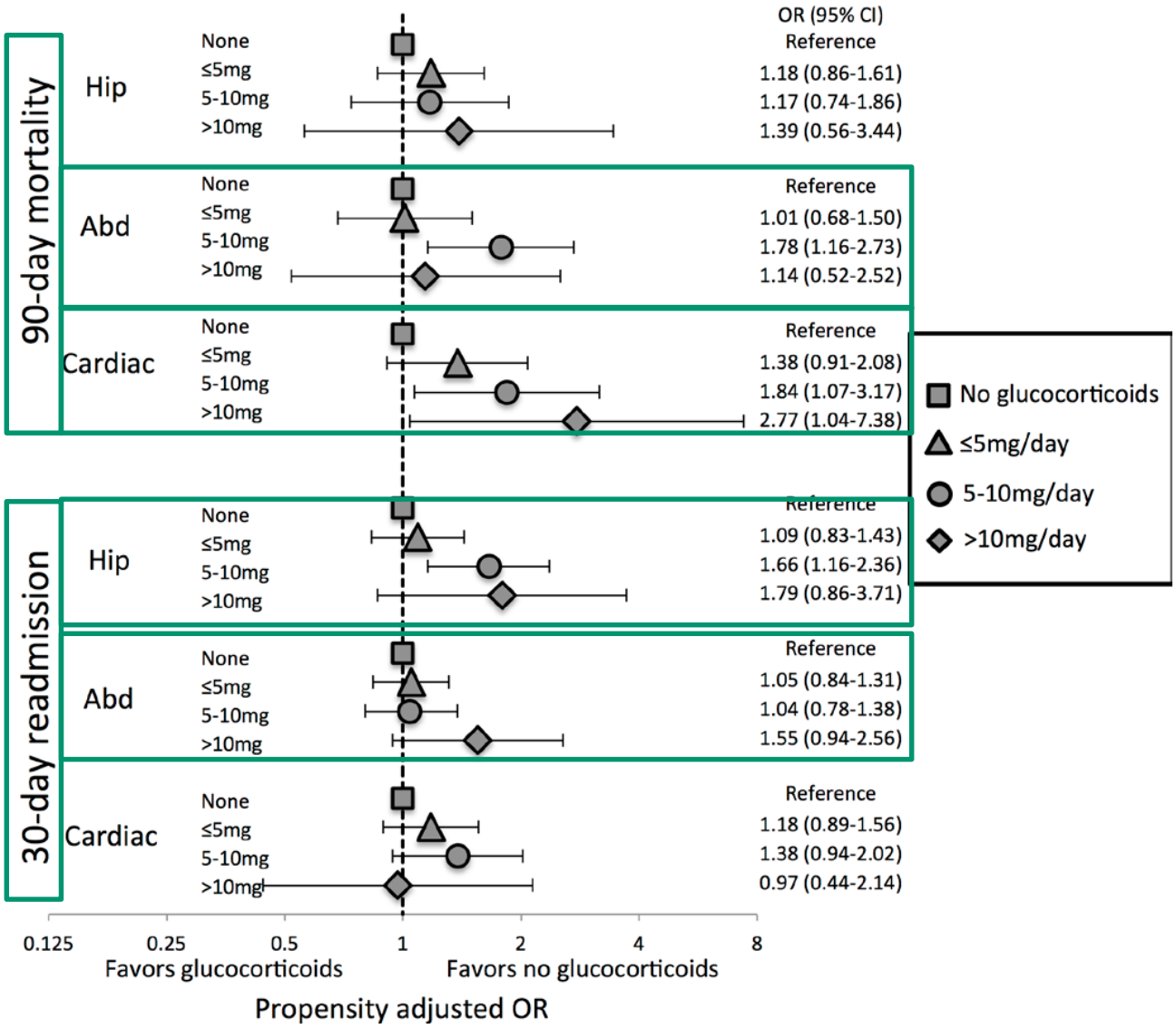
ARD 2020 May;79(5):573

Comparable risk for **readmission** between MTX & bDMARDs treated patients



ARD 2020 May;79(5):573

STEROIDS: >5 but mostly >10mg/d →higher mortality among patients undergoing cardiac surgery, trend for increased readmissions



ARD 2020 May;79(5):573

What does this study add?

- RA patients on bDMARDs did not have a greater risk of postoperative infections vs patients receiving MTX
- Glucocorticoids were associated with a dose-dependent increase in the risk of postoperative infection.

How might this impact clinical practice:

- Prolonged interruptions in biologics before major surgery is likely not required,
- Minimising glucocorticoids before surgery should be a focus of perioperative management.

ARD 2020 May;79(5):573

Continuing versus tapering glucocorticoids after achievement of low disease activity or remission in rheumatoid arthritis (SEMIRA): a double-blind, multicentre, randomised controlled trial

Gerd R Burmester, Frank Buttgereit*, Corrado Bernasconi, Jose M Álvaro-Gracia, Nidia Castro, Maxime Dougados, Cem Gabay, Jacob M van Laar, Jan Michael Nebesky, Attila Pethoe-Schramm, Carlo Salvarani, Marc Y Donath, Markus R John, on behalf of the SEMIRA collaborators*

Current EULAR Recommendations:

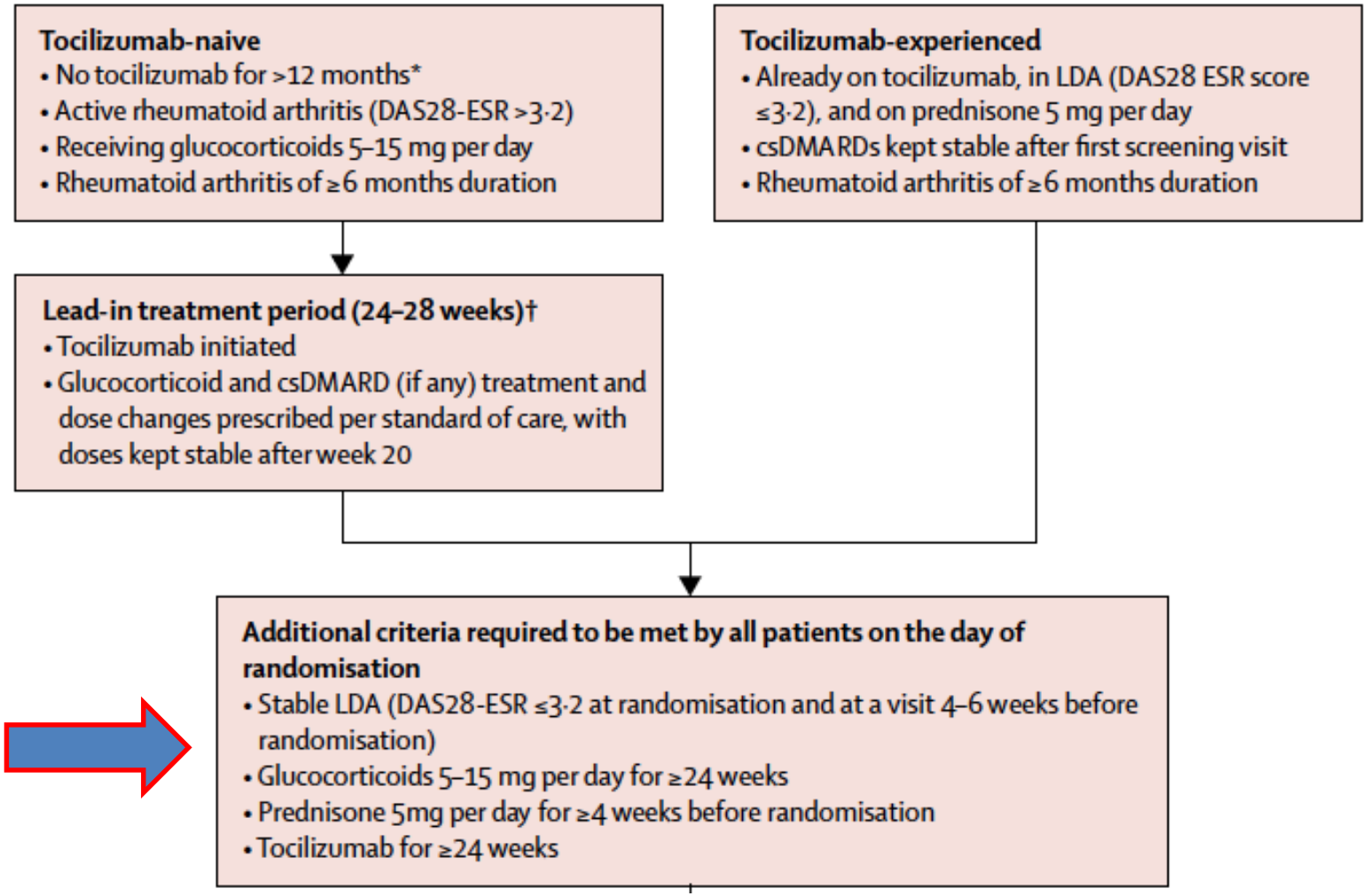
- "Short-term GC should be considered when initiating or changing csDMARDs, in different dose regimens and routes of administration, but should be tapered as rapidly as clinically feasible"

Aim of the study:

- To investigate the **efficacy and safety of a scheme for tapering oral glucocorticoids** compared with **continuing** low- dose oral glucocorticoids in patients with rheumatoid arthritis and stable disease.

Lancet. 2020 Jul 25;396(10246):267

Design



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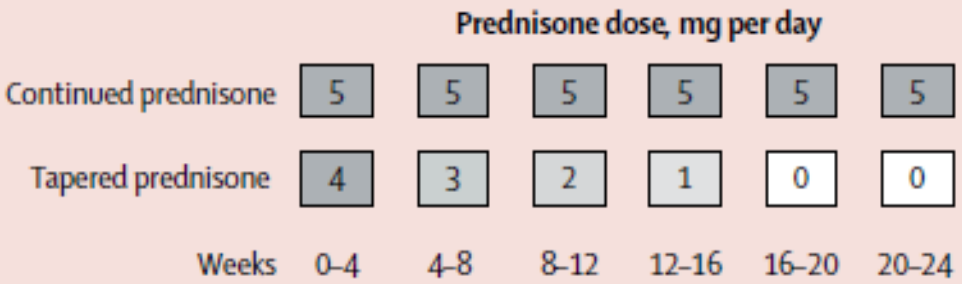
Steroids protocol

A minimum of 226 patients had to meet the criteria and would be randomly assigned 1:1 to the 24-week double-blind treatment groups



- Tocilizumab and csDMARDs (if any) maintained at stable doses throughout the 24-week period
- Patients who had a rheumatoid arthritis flare‡ were treated with a 2-week course of prednisone 5 mg per day, while blinded treatment was continued. Flare rescue treatment was extended for a second 2-week course if the patient was still flaring after completing the first course. Patients were withdrawn if still flaring after 4 sequential weeks of flare treatment.

Flare was defined as DAS28-ESR >3·2 and an increase in DAS28-ESR >0·6 from the randomisation visit value.

Outcomes

- ***Primary outcome:***

  Difference in mean DAS28-ESR change from baseline to week 24

  (0,6 defined as clinically relevant)

- ***Secondary outcomes:***

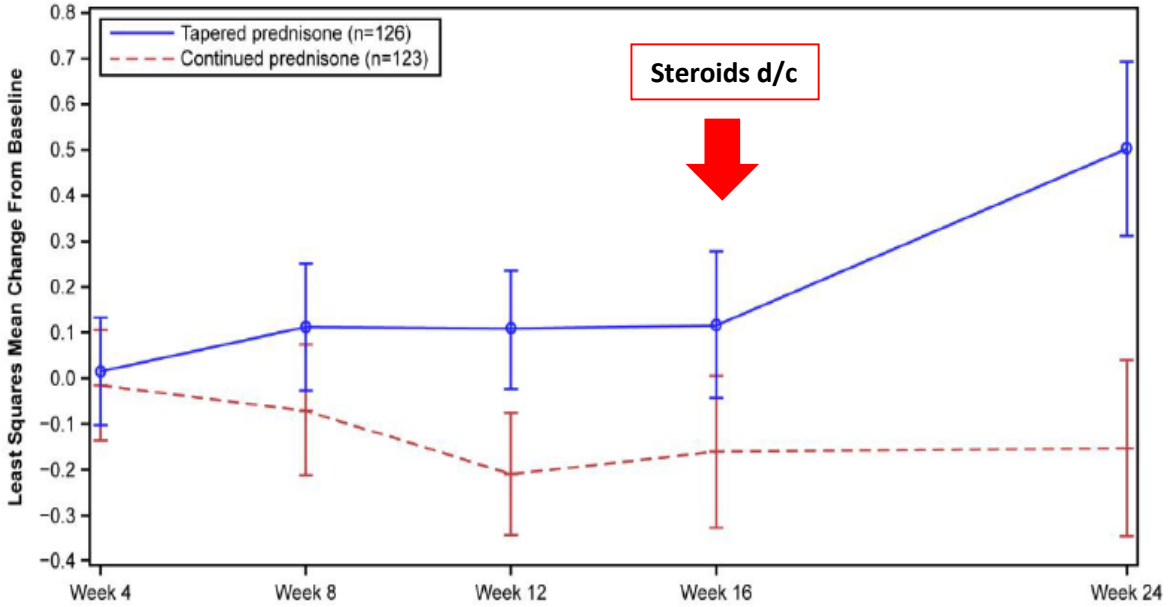
- ***Treatment success*** (low disease activity at week 24 & absence of flare for 24 weeks & no confirmed adrenal insufficiency necessitating replacement therapy)

- Others:
  - change in CDAI, rheumatoid arthritis flare rate, patient-reported outcomes (rheumatoid arthritis impact of disease, HAQ-DI, work productivity and activity impairment questionnaire: rheumatoid arthritis)
  - Safety: adverse events, serious adverse events, adverse events of special interest and adrenal insufficiency necessitating replacement therapy

Results

Primary endpoint

	Tapered prednisone (n=131)	Continued prednisone (n=128)	Difference (taper – continuation)
Primary endpoint			
DAS28-ESR change from baseline to week 24	0·538 (0·097; 0·346 to 0·729)	−0·075 (0·099; −0·271 to 0·121)	0·613 (0·135; 0·346 to 0·879) p<0·0001*
LOCF analysis	0·412 (0·090; 0·235 to 0·590)	−0·120 (0·092; −0·301 to 0·062)	0·532 (0·125; 0·285 to 0·779) p<0·0001*
MMRM analysis	0·504 (0·097; 0·313 to 0·696)†	−0·154 (0·099; −0·350 to 0·042)‡	0·658 (0·138; 0·386 to 0·930) p<0·0001*



Lancet. 2020 Jul 25;396(10246):267

Result

Secondary endpoint: treatment success

Pts with *low disease activity by week 24*, *no flare* and *no confirmed adrenal insufficiency* necessitating replacement therapy:

77% in the continued group

65% in the tapered group

} Relative risk 0.83[95% CI 0.71–0.97]

Conclusion

Continuing prednisone *at a dose of 5 mg per day over 24 weeks was* ***safe*** *and* ***better for maintaining disease control*** *than tapering prednisone from 5 mg per day to 0 mg per day in patients who had RA with a low disease activity treated with TCZ and who historically received at least 24 weeks of concomitant low-dose GC treatment.*

BUT

The ***65% treatment success*** *rate of prednisone tapering might be an important consideration for shared decision making!*

Lancet. 2020 Jul 25;396(10246):267

EULAR definition of difficult-to-treat rheumatoid arthritis

Nagy G, et al. Ann Rheum Dis. doi:10.1136/annrheumdis-2020--217344

EULAR definition of difficult-to-treat rheumatoid arthritis

1. Treatment according to EULAR recommendation and failure of ≥2 b/tsDMARDs (**with different mechanisms of action**) after failing csDMARD.

Nagy G, et al. Ann Rheum Dis. doi:10.1136/annrheumdis-2020--217344

EULAR definition of difficult-to-treat rheumatoid arthritis

1. Treatment according to EULAR recommendation and failure of ≥2 b/tsDMARDs (**with different mechanisms of action**) after failing csDMARD.

2. Signs suggestive of active/progressive disease, **defined as ≥1 of**:
   a. At least **moderate disease activity** (DAS28-ESR>3.2 or CDAI>10).
   b. **Signs** (including APR and imaging) and/ or **symptoms** suggestive of active disease (joint related or other).
   c. Inability to taper **glucocorticoid** treatment (below 7.5 mg/day prednisone or equivalent).
   d. **Rapid radiographic progression** (with or without signs of active disease).
   e. Well-controlled disease according to above standards, but still having RA symptoms that are **causing a reduction in quality of life**.

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3. The management of signs and/or symptoms is perceived as problematic by the rheumatologist and/or the patient.

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All three criteria need to be present in D2T RA

Nagy G, et al. Ann Rheum Dis. doi:10.1136/annrheumdis-2020--217344

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- Επιδημιολογία - Πρόγνωση
- Στεροειδή - Βιολογικά: νέα γνώση
- Βιοδείκτες Πρόγνωσης

Multi-omics and machine learning accurately predicts clinical response to Adalimumab and Etanercept therapy in patients with rheumatoid arthritis

Arthritis & Rheumatology, 2020

Authors: Weiyang Tao[1,2], Arno N. Concepcion[2], Marieke Vianen[2], Anne C.A. Marijnissen[3], Floris P.G.J. Lafeber[3], Timothy R.D.J. Radstake[1,2,*,#], Aridaman Pandit[1,2,*,#]

- Potential predictors to response to TNFi
  - age, sex, disease duration, disease activity, smoking status, concomitant methotrexate therapy
  - "Matrix" of response to golimumab based on clinical parameters

- Limitations:
  - did not illustrate the **biological mechanisms** that underlie this differential response to the TNFi
  - did not embark on potential treatment responses to **individual TNFi.**

Multi-omics and machine learning accurately predicts clinical response to Adalimumab and Etanercept therapy in patients with rheumatoid arthritis

AR, 2020

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RA is characterized by the chronic infiltration of immune cells in the synovial membrane and activation of immune cells in the BM and peripheral blood.

Arthritis Rheumatol. 2020 Sep 10. doi: 10.1002/art.41516.

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RA is characterized by the chronic infiltration of immune cells in the synovial membrane and activation of immune cells in the BM and peripheral blood.

- Several **transcriptomic and epigenetic studies** have been conducted on synovium and blood of patients with RA. To understand biological processes associated with disease and anti-TNF response
- These studies have demonstrated that transcriptomic and epigenetic profiling **has the potential to predict response to anti-TNF** therapies before treatment

- Limitations:
  - Clinical predictors:
    - low clinical value
  - Molecular
    - Differential responses to **individual TNFi**
    - **Bulk peripheral blood and cell-specific**

Arthritis Rheumatol. 2020 Sep 10. doi: 10.1002/art.41516.

Aim

- To generate cell-specific profiles that can predict response to two TNFi, **ADA and ETN**, prior to treatment initiation

Method

- **Transcriptomics and epigenetic profiling** of immune cell types and whole PBMCs along with deep clinical profiling of RA patients

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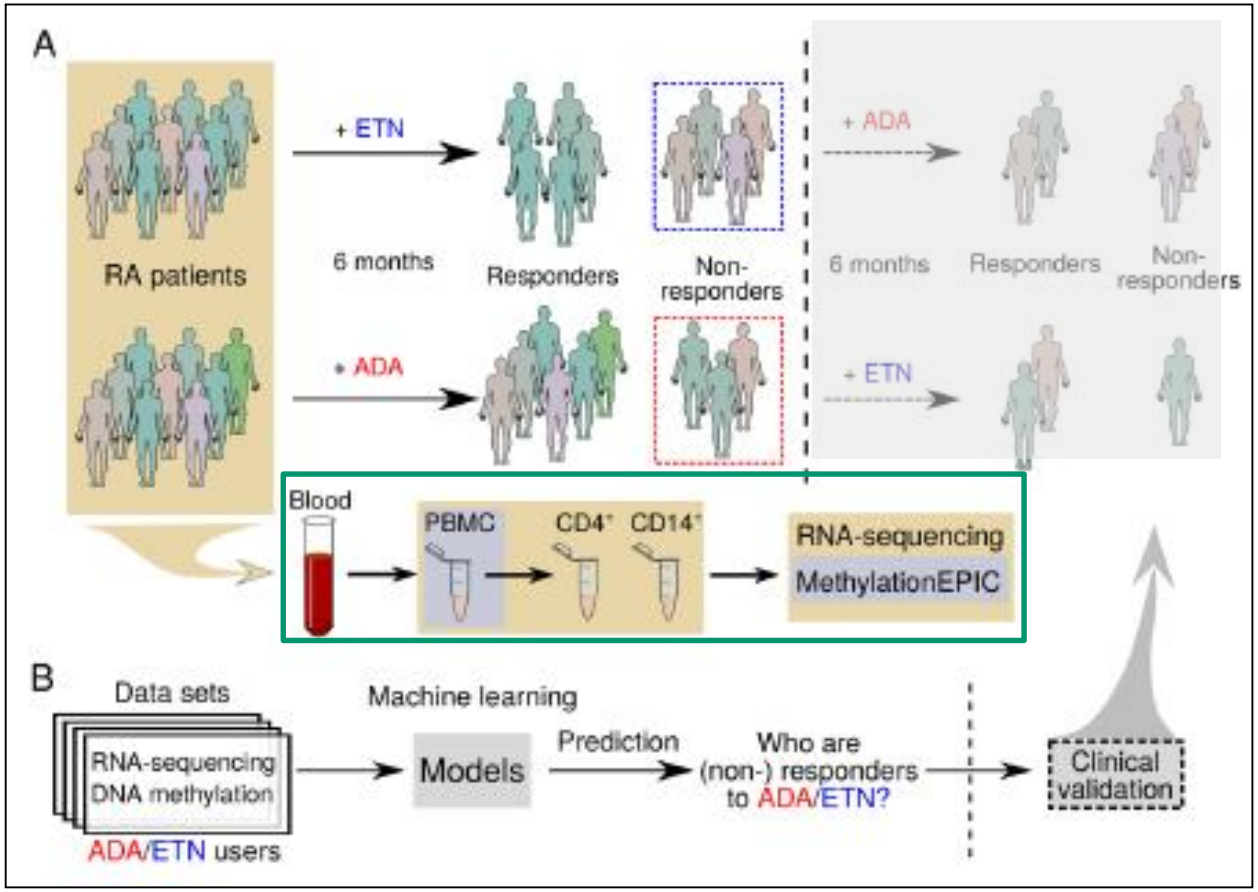
Method

- **Transcriptomics and epigenetic profiling** of immune cell types and whole PBMCs along with deep clinical profiling of RA patients



Arthritis Rheumatol. 2020 Sep 10. doi: 10.1002/art.41516.

PBMCs

- ✓ Approximately 50% response (Good & moderate) to ADA or ETN.

Table S1. Demographics and baseline characteristics of patients in ADA and ETN cohorts.

	Note	ADA	ETN	p-value
Sample size (N)		38	42	-
Response (6 months)	Good	11	11	0.8361
	Moderate	9	8	
	No	18	23	

- ✓ No clinical variable at baseline could predict response

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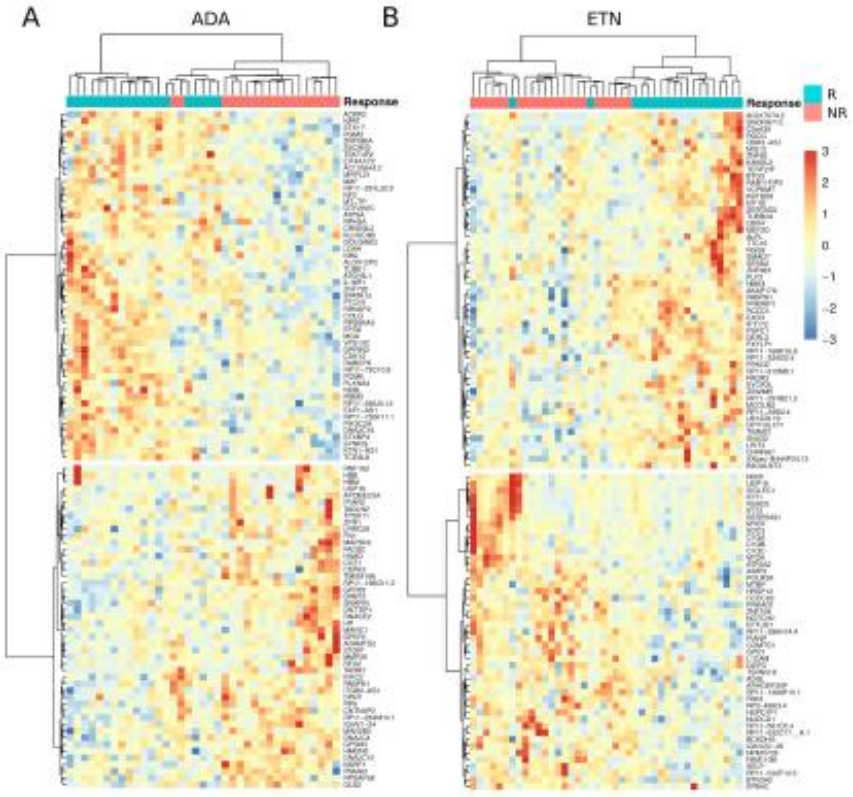
- PBMCs RNAseq (molecular signature)

✓ 549 differentially expressed genes (DEGs, nominal p-value<0.05) between ADA responders and nonresponders

✓ 460 DEGs between ETN responders and non-responders



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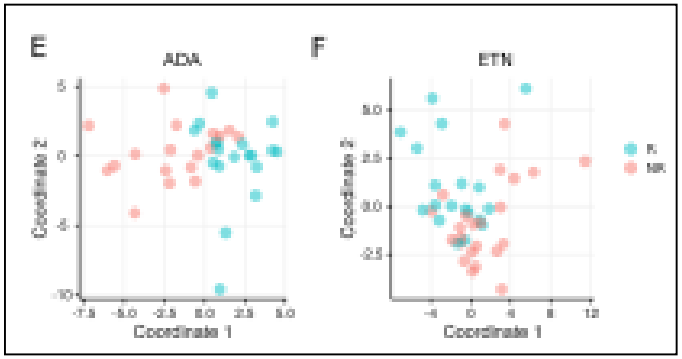
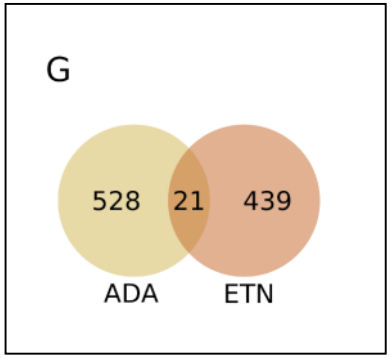
- ✓ **PBMCs RNAseq may predict response to ADA or ETN**
- ✓ **Distinct RNA expression profiles between responders in the 2 TNFis**

- **The expression of TNF was not associated (p>0.05) with the response to either ADA or ETN !!!**

- Multidimensional scaling analysis performed using DEGs shows that we can differentiate between responders and non-responders in each cohort

- **Only 2% of genes differentially expressed overlapped in the 2 cohorts!!!**

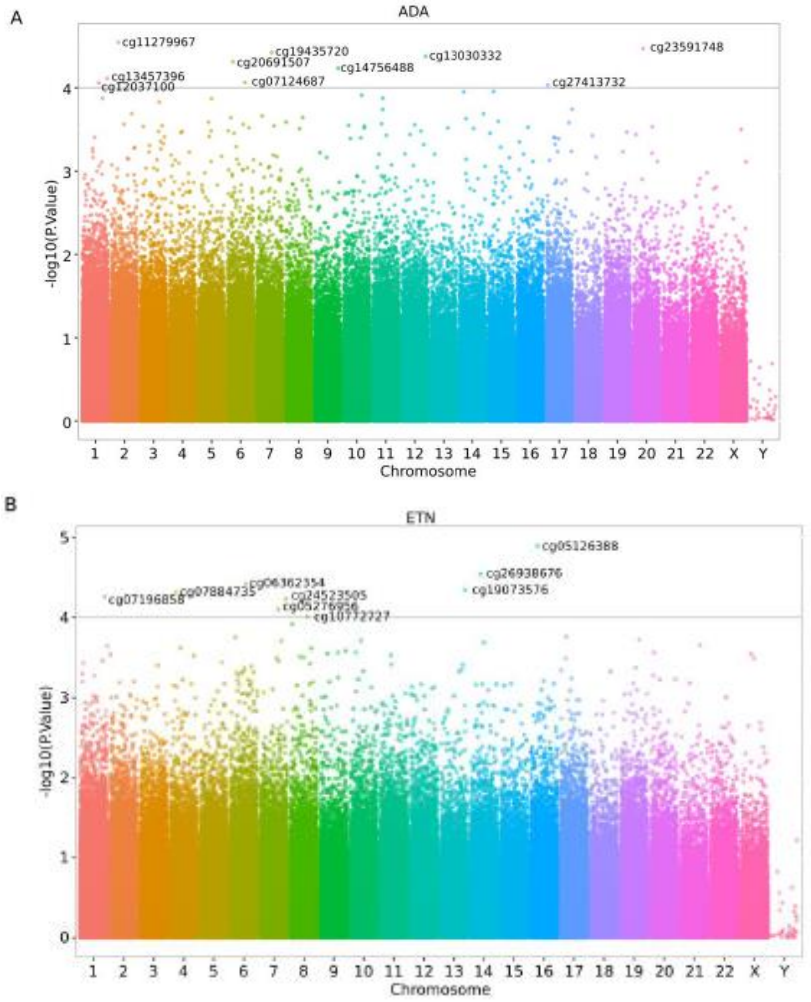




PBMCs

✓ Distinct hypermethylation pattern between ADA and ETN responders

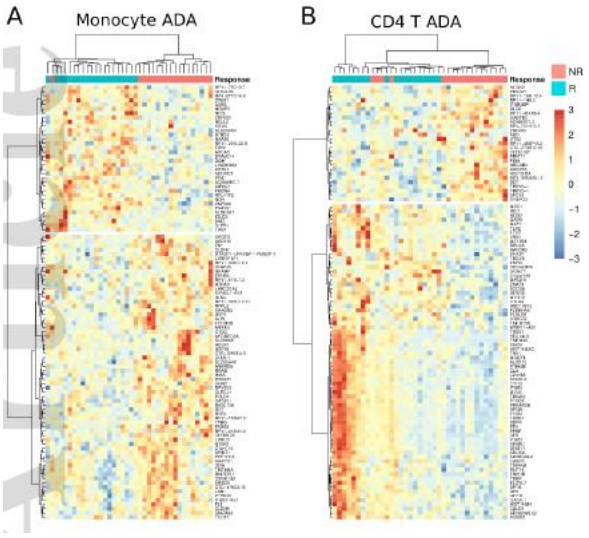
- Genome-wide DNA methylation analysis of PBMCs showed
  - DMPs are distributed 7,719 and 7,850 genes, for ADA cohort and ETN cohort, respectively.
  - Approximately 46% (7424) of DMPs were hypermethylated in ADA responders, while a drastically higher fraction of DMPs (76.3%, 12994) were hypermethylated in ETN responders.

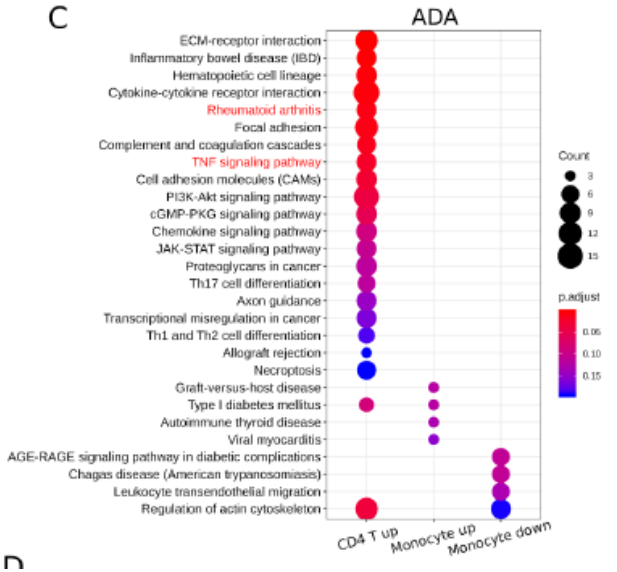


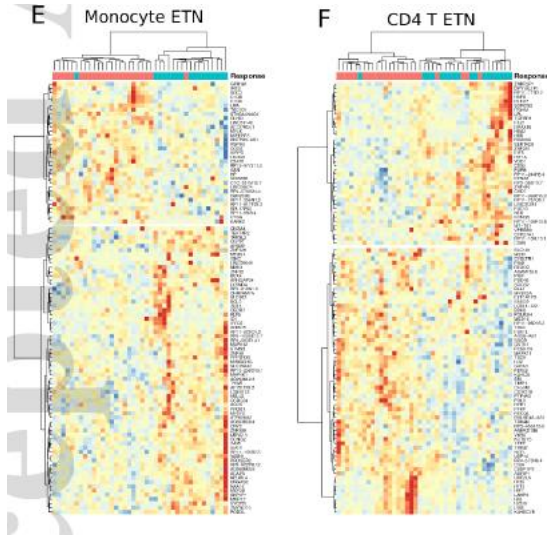
CD4 / CD14

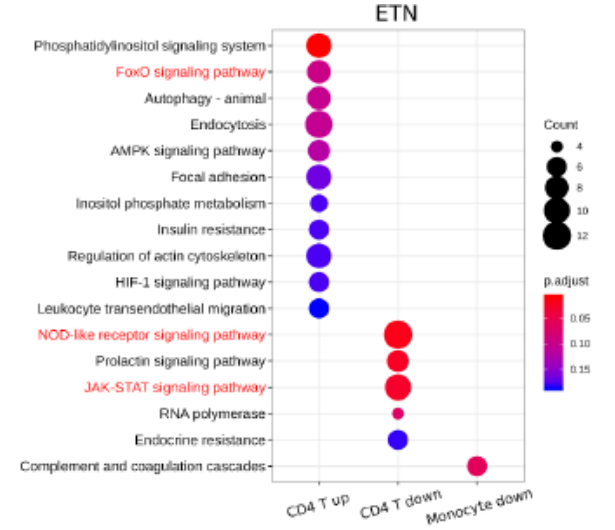
"CD4+ T cells showed clearer molecular "**TNF signaling**" signatures associated with response to ADA compared to monocytes.

- ✓ Differential gene expression analyses identified:
  - ✓ 444 and 635 DEGs between responders and non-responders to **ADA** in monocytes and CD4+ T cells, respectively
  - ✓ 599 and 769 DEGs were associated with response to **ETN** in monocytes and CD4+ T cells, respective







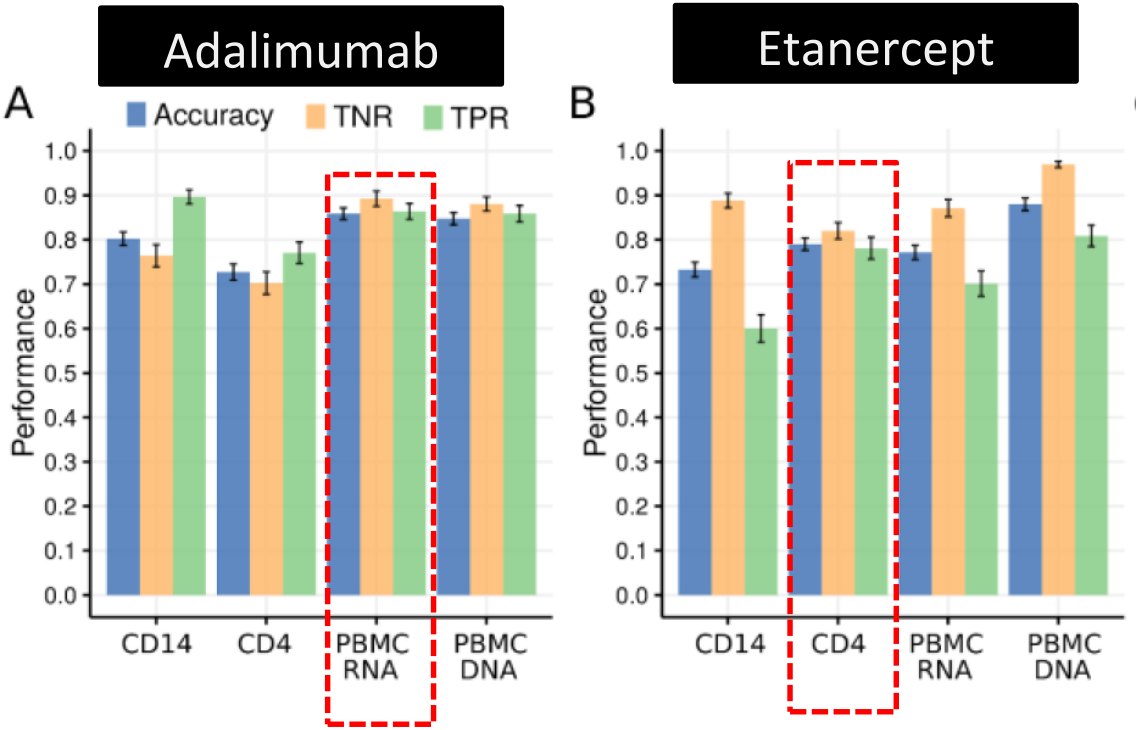


Algorithms

- ✓ Machine learning models accurately predict clinical response
- ✓ The prediction accuracy of these molecular signatures differs between cell types and treatments
- ✓ Need to study more than one drug, cell type or epigenetic layers.

Built machine learning models to predict response exploiting the:

- Transcriptomic signatures from monocytes, CD4+ T and PBMCs,
- Methylation signatures from PBMC



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Conclusion:

Machine learning models based on molecular signatures could accurately predict response before ADA and ETN treatment, paving the path towards personalized treatment strategies with TNFi.

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Dynamics of circulating TNF during adalimumab treatment using a drug-tolerant TNF assay

Lea C. Berkhout[1]*, Merel J. I'Ami[2]*, Jill Ruwaard[2], Margreet H. Hart[1], Pleuni Ooijevaar-de Heer[1], Karien Bloem[1], Michael T. Nurmohamed[2,3], Ronald F. van Vollenhoven[2,3,4], Maarten Boers[3,5], Daniel F. Alvarez[6], Catherine H. Smith[7], Gerrit J. Wolbink[1,2], Theo Rispens[1†]

Aim

- To investigate the correlation between TNF concentrations and clinical response to TNFi
- To assess whether TNF levels may define responders who may d/c TNFi

Methods

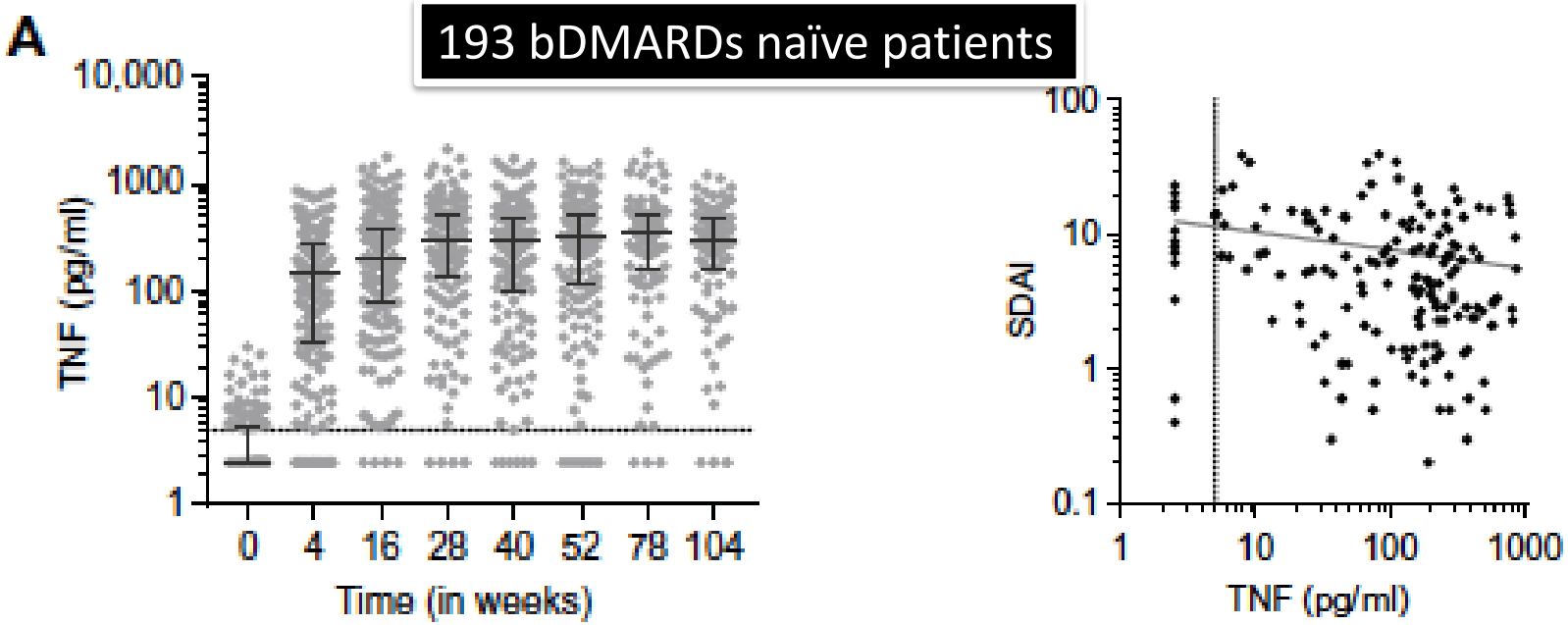
- To quantify TNF, independent of the presence of large amounts of adalimumab, we developed a drug-tolerant competition enzyme-linked immunosorbent assay

Sci Transl Med. 2019 Jan 30;11(477):eaat3356

TNFα serum levels increase over time in adalimumab treated patients (X50 times!)

Week correlation to early TNFα levels and clinical responses

- Week correlation of TNFα @4wk to response @52wk

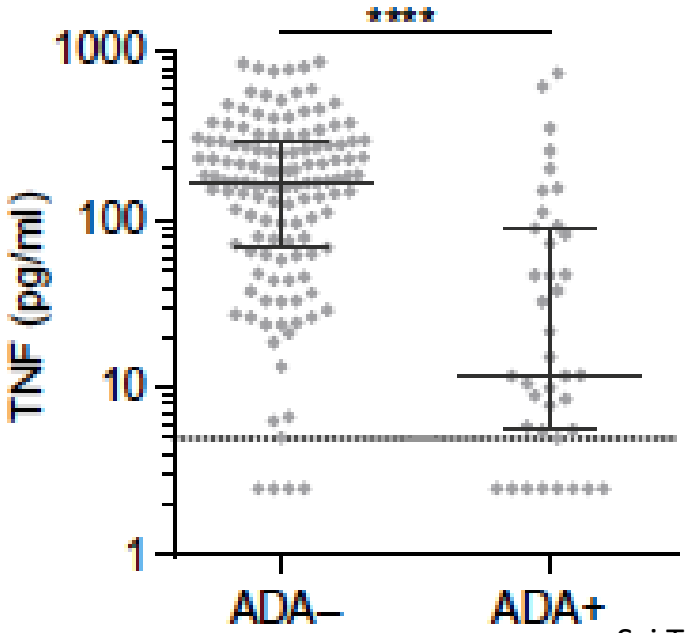


Sci Transl Med. 2019 Jan 30;11(477):eaat3356

Correlation of early TNFα levels to anti-drug antibodies (ADA)

43 (22%) patients developed detectable ADAs during 52 weeks of follow-up.

TNF concentrations @ 4wks are associated to ADA detection during 52 weeks of follow-up.



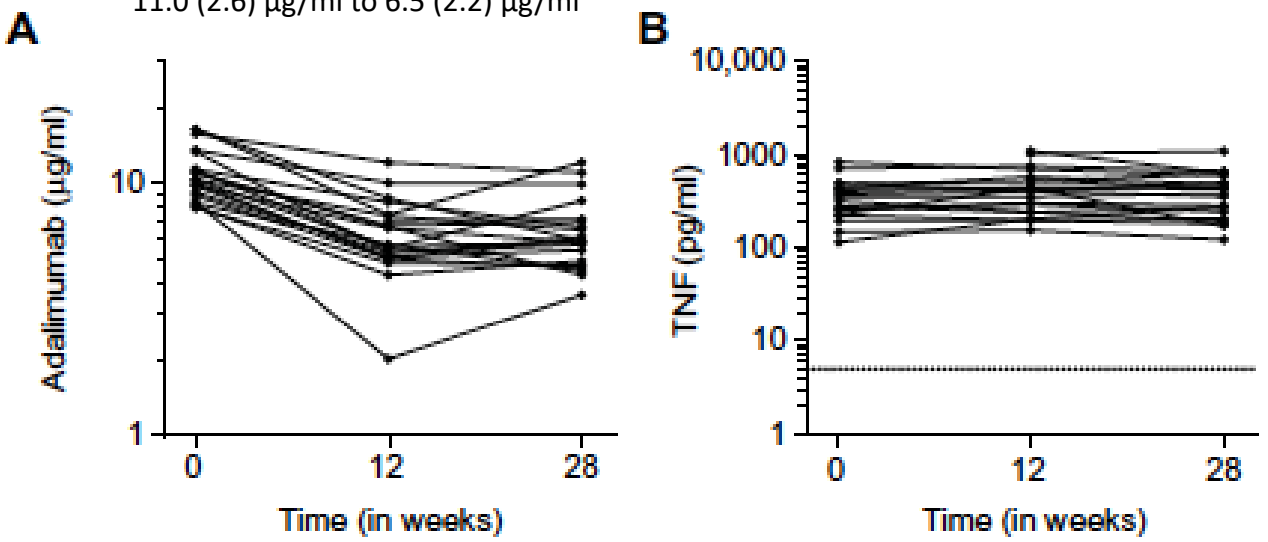
Sci Transl Med. 2019 Jan 30;11(477):eaat3356

No correlation between adalimumab levels and TNFα serum levels

21 patients who prolonged dose intervals (Q2 to Q3wks)

Adalimumab levels dropped while TNFα remained stable

11.0 (2.6) µg/ml to 6.5 (2.2) µg/ml



Adalimumab concentration around as low as 0.1 µg/ml is sufficient for near quantitative in vivo capture of TNF.

Conclusions

- ✓ Early low TNF is strongly associated with ADA formation and may be used as timely predictor of nonresponse toward adalimumab treatment.
- ✓ TNF cannot be used as a biomarker for treatment discontinuation.

Sci Transl Med. 2019 Jan 30;11(477):eaat3356