Remission is NOT a realistic goal in RA

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EDITOR'S CHOICE

2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative

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Ann Rheum Dis 2010;69:1580-8

Table 3 The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA

	Score
Target population (Who should be tested?): Patients who	
1) have at least 1 joint with definite clinical synovitis (swelling)*	
2) with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A-D; a score of ≥6/10 is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)**	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)††	5
B. Serology (at least 1 test result is needed for classification)‡‡	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)§§	
Normal CRP *and* normal ESR 0	0
Abnormal CRP *or* normal ESR 1	1
D. Duration of symptoms¶¶	
<6 weeks	0
≥6 weeks	1

Aletaha et al Ann Rheum Dis 2010(9);69:1580-8

Treatment strategy

Initiation of treatment is based on

- Diagnosis
- Prognostic indicators
- Current status (which parameters?)

Follow-up of treatment (disease monitoring)

- Which parameters?
- Identification of treatment goal(s)
  - Improvement
  - Achievement of a pre-defined state
- When to stop or change treatment

EDITOR'S CHOICE

Treating rheumatoid arthritis to target: recommendations of an international task force

Josef S Smolen,[1,2] Daniel Aletaha,[1] Johannes W J Bijlsma,[3] Ferdinand C Breedveld,[4] Dimitrios Boumpas,[5] Gerd Burmester,[6] Bernard Combe,[7] Maurizio Cutolo,[8] Maarten de Wit,[9] Maxime Dougados,[10] Paul Emery,[11] Alan Gibofsky,[12] Juan Jesus Gomez-Reino,[13] Boulos Haraoui,[14] Joachim Kalden,[15] Edw[16] [17]
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Desirée van der Heijde,[4] for the T2T Expert Comm

ARD 2010
69:631-37

ARD 2010
69:629-30

'Treat to target': moving targets from hypertension, hyperlipidaemia and diabetes to rheumatoid arthritis

Dan Atar,[1,2] Kåre Inge Birkeland,[2,3] Till Uhlig[4]

Evidence for treating rheumatoid arthritis to target: results of a systematic literature search

Monika Schoels,[1] Rachel Knevel,[2] Daniel Aletaha,[3] Johannes W J Bijlsma,[4] Ferdinand C Breedveld,[2] Dimitrios T Boumpas,[5] Gerd Burmester,[6] Bernard Combe,[7] Maurizio Cutolo,[8] Maxime Dougados,[9] Paul Emery,[10] Desirée van der Heijde,[2] Tom W J Huizinga,[2] Joachim Kalden,[11] Edward C Keystone,[12] Tore K Kvien,[13] Emilio Martin-Mola,[14] Carlomaurizio Montecucco,[15] Maarten de Wit,[16] Josef S Smolen[1,3]

ARD 2010
69:638-43

Editorial

It's Good to Feel Better But It's Better to Feel Good

Revised Definition of Outcomes in RA*

	DAS28	SDAI	CDAI
Remission	<2.6	≤3.3	≤2.8
Near Remission (Low Dz activity)	≤3.2	≤11	≤10
High disease activity	>5.1	>26	>22

*adapted from Aletaha D, Smolen J. SDAI and CDAI. Clin Exp Rheum 23 (Suppl 3g): S100-8, 2005

Criteria

EDITOR'S CHOICE

American College of Rheumatology/European League Against Rheumatism Provisional Definition of Remission in Rheumatoid Arthritis for Clinical Trials

David T Felson,[1,2] Josef S Smolen,[3] George Wells,[4] Bin Zhang,[5] Lilian H D van Tuyl,[1] Julia Funovits,[6] Daniel Aletaha,[6] Cornelia F Allaart,[7] Joan Bathon,[8*] Stefano Bombardieri,[9] Peter Brooks,[10] Andrew Brown,[11] Marco Matucci-Cerinic,[12] Hyon Choi,[4] Bernard Combe,[13] Maarten de Wit,[14] Maxime Dougados,[15] Paul Emery,[16] Daniel Furst,[17] Juan Gomez-Reino,[18] Gillian Hawker,[19] Edward Keystone,[20] Dinesh Khanna,[17] John Kirwan,[21] Tore K. Kvien,[22] Robert Landewé,[23] Joachim Listing,[24] Kaleb Michaud,[25] Emilio Martin-Mola,[26] Pamela Montie,[27] Theodore Pincus,[28] Pamela Richards,[29] Jeffrey N Siegel,[30†] Lee S Simon,[31] Tuulikki Sokka,[32] Vibeke Strand,[33] Peter Tugwell,[3] Alan Tyndall,[34] Desirée van der Heijde,[7] Suzan Verstappen,[35] Barbara White,[36] Frederick Wolfe,[37,38] Angela Zink,[24] and Maarten Boers[5]

Published online in ARD and A&R

Table 6 American College of Rheumatology/European League Against Rheumatism definitions of remission in rheumatoid arthritis clinical trials*

Boolean-based definition

At any time point, patient must satisfy all of the following:
Tender joint count ≤1†
Swollen joint count ≤1†
C reactive protein ≤1 mg/dl
Patient global assessment ≤1 (on a 0–10 scale)‡

Index-based definition

At any time point, patient must have a Simplified Disease Activity Index score of ≤3.3§

Published online in ARD and A&R

Extended report

Evidence for treating rheumatoid arthritis to target: results of a systematic literature search

Monika Schoels,[1] Rachel Knevel,[2] Daniel Aletaha,[3] Johannes W J Bijlsma,[4] Ferdinand C Breedveld,[2] Dimitrios T Boumpas,[5] Gerd Burmester,[6] Bernard Combe,[7] Maurizio Cutolo,[8] Maxime Dougados,[9] Paul Emery,[10] Desirée van der Heijde,[2] Tom W J Huizinga,[2] Joachim Kalden,[11] Edward C Keystone,[12] Tore K Kvien,[13] Emilio Martin-Mola,[14] Carlomaurizio Montecucco,[15] Maarten de Wit,[16] Josef S Smolen[1,3]

ARD 2010;69:638-43

Papers retrieved and selection process

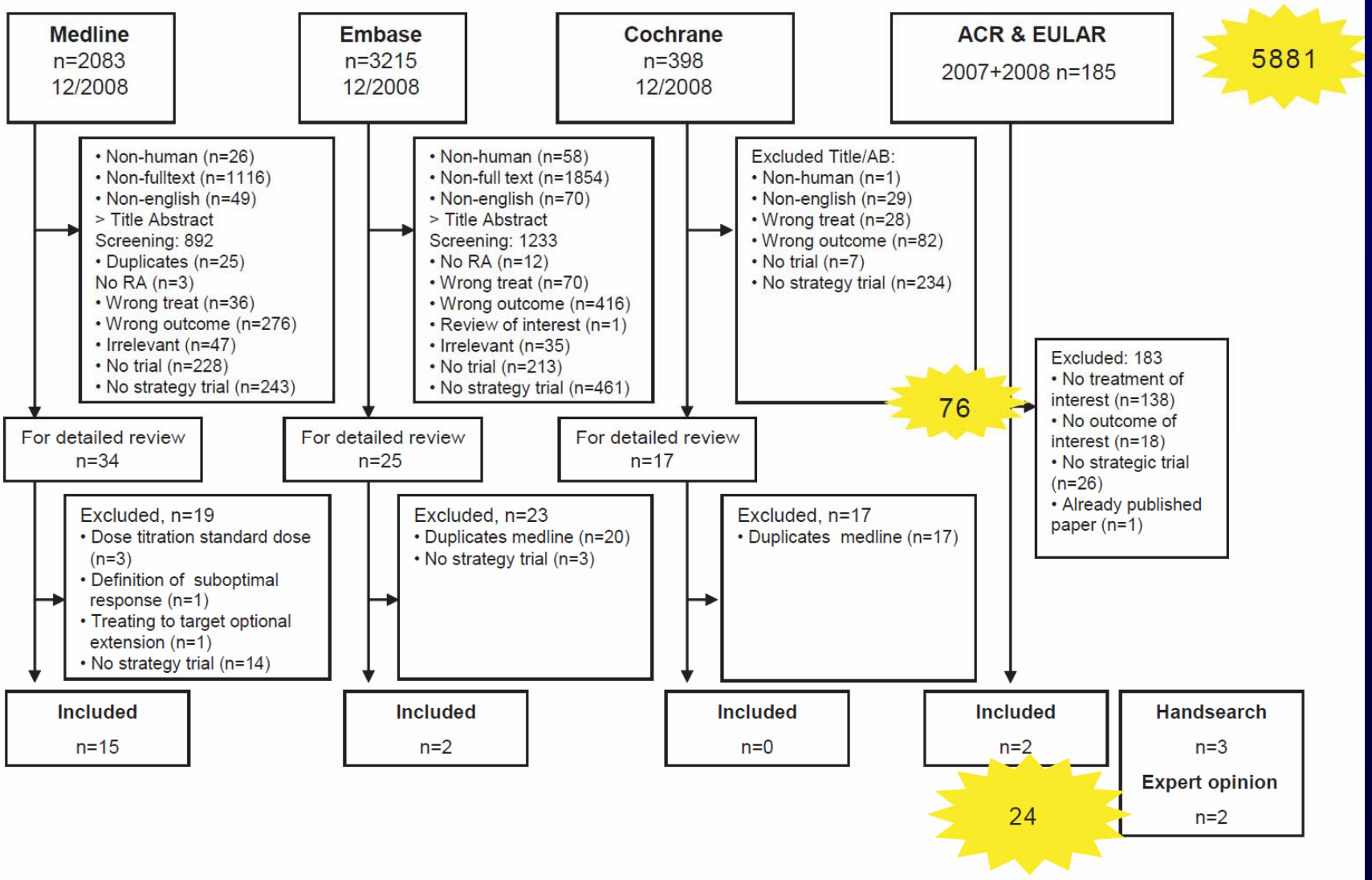


Figure 1 Flow chart of the systematic literature search. Illustrated are the results of the initial search and the selection process of abstract screening, full text review and hand search. AB, abstract; ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; RA, rheumatoid arthritis.

Trial	Groups	Target
(A) TICORA study; Grigor *et al*, 2004[25]	**Targeted**	DAS<2.4 LDA
	Routine	'Opinion of treating rheumatologist' ; synovitis, 'lack of efficacy'
(B) CAMERA study; Verstappen *et al*, 2007[27]	Targeted	Response criteria: >20 % improvement compared to previous visit of SJC and 2 out of 3: ESR, TJC, PGA ≤50% improvement compared to baseline of SJC and 2 out of 3: ESR, TJC, PGA (inadequate response)
	Routine	SJC + 'opinion of treating rheumatologist'
(C) Fransen *et al*, 2005[28]	Intensive	DAS28≤3.2 LDA
	Routine	'opinion of treating rheumatologist'
(D) Symmons *et al*, 2005[29]	Targeted	suppressing clinical and laboratory evidence of joint inflammati on: SJC & TJC = 0, CRP less than twice the upper limit of the normal range.
	Routine	'symptom control'
(E) Edmonds *et al*, (abstract) 2007[31]	Targeted I	CRP normal range
	Targeted II	SJC<3
(F) van Tuyl *et al*, 2008[30]	Targeted I	DAS28≤3.2 LDA
	Targeted II	Cartilage degradation (CTX-II≤150 in ELISA)
(G) Stenger *et al*, 1998[32]	Targeted	CRP decrease≤50%
	Routine	'opinion of treating rheumatologist'

Summary SLR

- Most of the core trials used a **state as the target**; mostly this state was **low disease activity**
- Time frame for assessment of targets varied from **1 to 4 months**
- Most T2T studies were done in **early RA**
- All studies that compared T2T with routine approaches **showed significant clinical benefits of T2T**
- The effect of T2T on functional and radiographic outcomes needs further investigation
- More studies are needed in established/late RA

SLR Schoels et al ARD 2010;69:638-40

From discussion

Five[26–28 30 32] studies investigated early disease (using different definitions of 'early' – see supplementary table S3). Only one trial[29] focused explicitly on late disease (duration: >5 years) and found no advantage of tight control on functional outcomes. Thus, patients with established RA seem to be underinvestigated regarding the value of treating to a target. Since longer disease duration impairs treatment outcomes,[33] extending results from early RA to the general patient population could be misleading. Furthermore, just focusing on HAQ might also be misguiding, since with increasing disease duration responsiveness of physical function to therapeutic interventions decreases (even to placebo levels).[34]

SLR Schoels et al ARD 2010;69:638-40

Table S3 Baseline characteristics

Author	SJC applied	HAQ	DAS	APR CRP [mg/L] ESR [mm/h]	Radiogr. Status: Score employed	Follow-up	Dis. duration defined per incl.-criteria*; and at baseline**
Grigor[38]	SJC44 12±4§	2.0±0.8§	DAS 4.9±0.9§	CRP 44±53§ ESR 45±31§	TSS 28±23§	18 mo	<5 yrs* 19±16 mo§**
Verstappen[39]	SJC38 14±6§	1.2±0.7§		ESR 36±27§	Radiographic damage score: 1.6±4.2§	1 yr / 2yrs	<1yr*
Fransen[40]	n.r.	n.r.	DAS28 4.6±1.2§	ESR 20 (10-32)$	Joint damage 65%	24 we	6 (3-14) yrs$$**
Symmons[41]	3 (1,5.5)$$	1.25 (0.88,1.88)$$	n.r.	CRP 8 (3,19)$$ ESR 21 (10,32)$$	Larsen 67 (39,97)$$ Eroded joint count 11 (5,19)$$	3 yrs	>5 yrs* 12.5±6.8 yrs§**
Edmonds[42]	3 groups: 12±5§ 11.6±5§ 11.84±5§	n.r.	DAS28 5.1±1.2 4.9±1.3 5.07±1.5	CRP 12±11§ 20.7±28§ 17.7±25§	n.r.	2 yrs	7.2±6.6 yrs§**
Van Tuyl[43]	SJC28 10±6§	0.93±0.74§	DAS28 5.37±0.98§	ESR 36±29§	TSS 6.8±11.8§ Erosions: 56%	40 we	2±2 mo§**
Stenger[44]	14 (2-36)$	n.r.	n.r.	CRP 53 (8-186)$	Radiogr. score: 4(0-28)$	2 yrs	6.5±3.2 yrs§**

SLR Schoels et al ARD 2010;69:638-40

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

Josef S Smolen,[1,2] Robert Landewé,[3] Ferdinand C Breedveld,[4] Maxime Dougados,[5] Paul Emery,[6] Cecile Gaujoux-Viala,[5,7] Simone Gorter,[3] Rachel Knevel,[4] Jackie Nam,[6] Monika Schoels,[2] Daniel Aletaha,[1] Maya Buch,[6] Laure Gossec,[5] Tom Huizinga,[4] Johannes W J W Bijlsma,[8] Gerd Burmester,[9] Bernard Combe,[10] Maurizio Cutolo,[11] Cem Gabay,[12] Juan Gomez-Reino,[13] Marios Kouloumas,[14] Tore K Kvien,[15] Emilio Martin-Mola,[16] Iain McInnes,[17] Karel Pavelka,[18] Piet van Riel,[19] Marieke Scholte,[14] David L Scott,[20] Tuulikki Sokka,[21] Guido Valesini,[22] Ronald van Vollenhoven,[23] Kevin L Winthrop,[24] John Wong,[25] Angela Zink,[26] Désirée van der Heijde[4]

Ann Rheum Dis 2010;69:964-75

Outcome

- 15 recommendations were formulated
- The key statements are supported by data review (5 papers with systematic literature review)* and expert opinion

* Synthetic DMARDs (inc. combination) without glucocorticoid (GC)

GC inc. DMARD combination

Biological DMARDs

Treatment strategies

Economic implication

Final set of 15 recommendations on the management of RA	
1.	Therapy with synthetic DMARDs should be started as soon as the diagnosis of RA is made
2.	Treatment should be aimed at reaching a target of remission or low disease activity as soon as possible in every patient; as long as the target has not been reached, adjustment of the treatment should be done by frequent (every 1-3 months) and strict monitoring
3.	MTX should be part of the first treatment strategy in patients with active RA
4.	In case of MTX contraindications (or intolerance), the following DMARDs should be considered as part of the (first) treatment strategy: leflunomide, sulfasalazine or injectable gold
5.	In DMARD naïve patients, irrespective of the addition of glucocorticoids, synthetic DMARD monotherapy rather than combination therapy of synthetic DMARDs may be applied
6.	Glucocorticoids added at low to moderately high doses to synthetic DMARD monotherapy (or combinations of synthetic DMARDs) provide benefit as initial short term treatment, but should be tapered as rapidly as clinically feasible
7.	If the treatment target is not achieved with the first DMARD strategy, addition of a biological DMARD should be considered in case of presence of poor prognostic factors; in the absence of poor prognostic factors, switch to another synthetic DMARD strategy should be considered
8.	In patients responding insufficiently to MTX and/or other synthetic DMARDs with or without glucocorticoids, biological DMARDs should be commenced*; current practice would be to start a TNF inhibitor (adalimumab, certolizumab, etancercept, golimumab, infliximab)** which should be combined with methotrexate*
9.	Patients with RA who have failed a first TNF inhibitor therapy, should receive another TNF inhibitor, abatacept, rituximab or tocilizumab
10.	In case of refractory severe RA or contraindications to biological agents or the previously mentioned synthetic DMARDs, the following synthetic DMARDs might be also considered, as monotherapy or in combination with some of the above: azathioprine, cyclosporine A (or exceptionally cyclophosphamide)
11.	Intensive medication strategies should be considered in every patient, although patients with poor prognostic factors have more to gain
12.	If a patient is in persistent remission, after having tapered glucocorticoids, one can consider tapering[#] biological DMARDs[§], especially if this treatment is combined with a synthetic DMARD
13.	In case of sustained long-term remission, cautious titration of synthetic DMARD dose could be considered, as a shared decision between patient and physician
14.	DMARD naïve patients with poor prognostic markers might be considered for combination therapy of methotrexate plus a biological[$$]
15.	When adjusting therapy, factors apart from disease activity, such as progression of structural damage, co-morbidities and safety issues should be taken into account

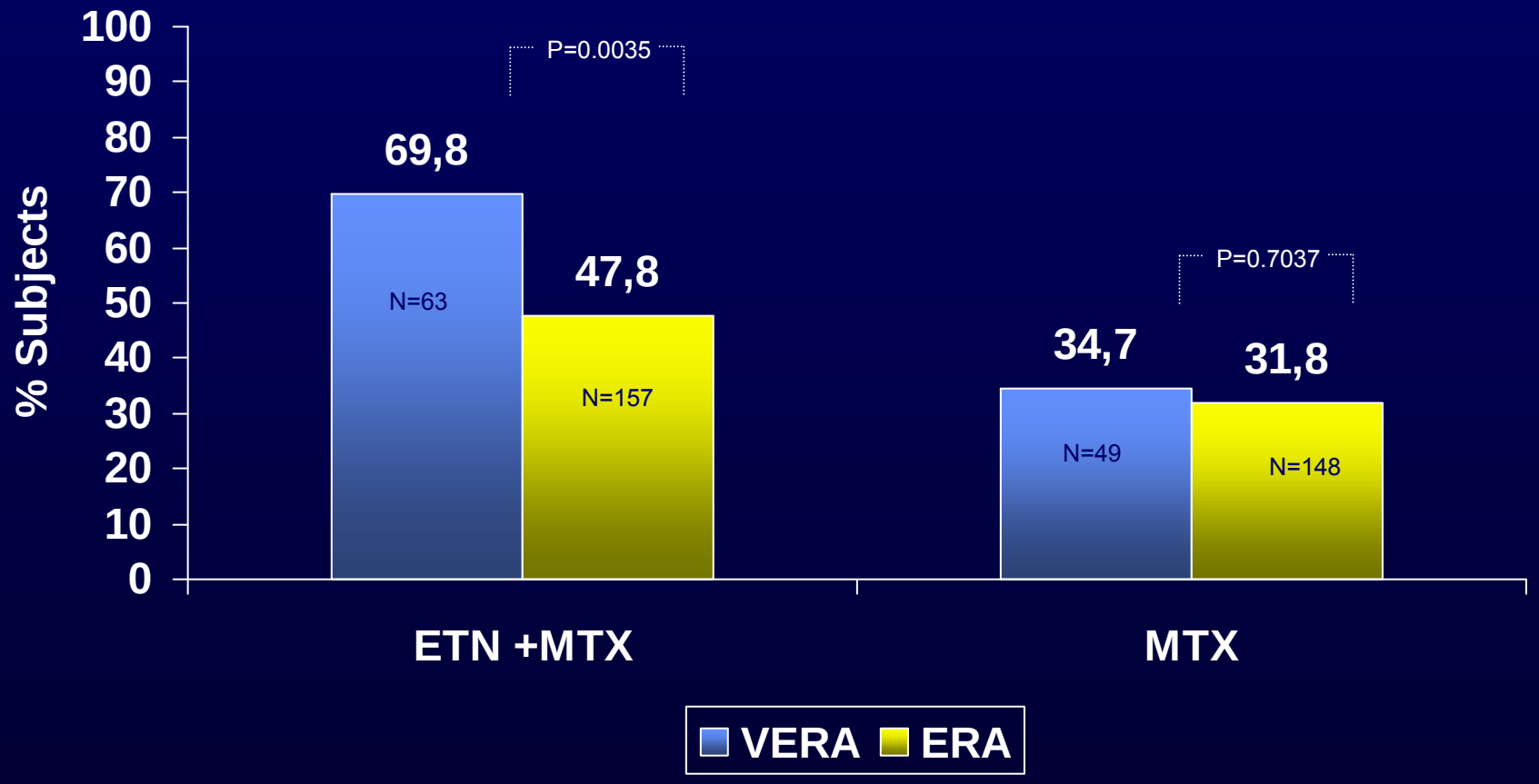
How frequently is remission achieved in RCT and in real life?

Objective: explorative analyses from the COMET study, presented at EULAR 2010

- To determine whether treatment intervention very early (VERA; ≤4 mos) improves remission (DAS28<2.6) and low disease activity (DAS28<3.2) rates at 52 weeks compared with early RA (ERA: >4 mos to 2 yrs)

Emery et al. Presented at EULAR 2010.LB0001

COMET: Remission (DAS 28<2.6) at Week 52



Emery et al. Presented at EULAR 2010.LB0001

The Problem of Rheumatoid Arthritis Disease Act and Remission in Clinical Practice

TIMOTHY S. SHAVER, JAMES D. ANDERSON, DAVID N. WEIDENSAUL, SHADI S. SHAHOURI, RUTH E. BUSCH, TED R. MIKULS, KALEB MICHAUD, and FREDERICK WOLFE

ABSTRACT. ***Objective.*** To investigate the results and feasibility of available scales to measure minimal disease activity (MDA) and remission in rheumatoid arthritis (RA) in the clinic.

Methods. We studied 849 consecutive patients with RA seen in a community rheumatology practice for routine RA care by 4 rheumatologists, beginning in March 2007 and ending in August 2007. Patients and physicians completed a simple form at each visit. We calculated the Disease Activity Score 28 (DAS28), Clinical Disease Activity Index (CDAI), physician assessment of global activity, and the Patient Activity Scale (PAS-II). From these we calculated remission and MDA prevalence in this community practice.

Results. The DAS28 could not be determined in more than 50% of patients because of referring physician and insurance company restrictions. Remission prevalences differed by assessment method: DAS28 28.5%, CDAI 6.5%–8.1%, physician global 12.5%, PAS 13.7%. MDA was 26.9% using the American College of Rheumatology core set variables, 34.7% using the DAS28, and 26.8% using the PAS-II. The kappa statistic was only fair (0.2 to 0.4) for most comparisons between assessment methods. No significant differences were noted for remission and MDA according to biologic therapy.

Conclusion. The CDAI and/or physician global and PAS-II are simple acceptable ways to measure RA activity in the clinic, but results differ strikingly according to method. Further standardization appears to be required for full implementation of the CDAI. Caution is urged before using these methods for regulatory purposes. (First Release April 15 2008; J Rheumatol 2008;35:1015–22)

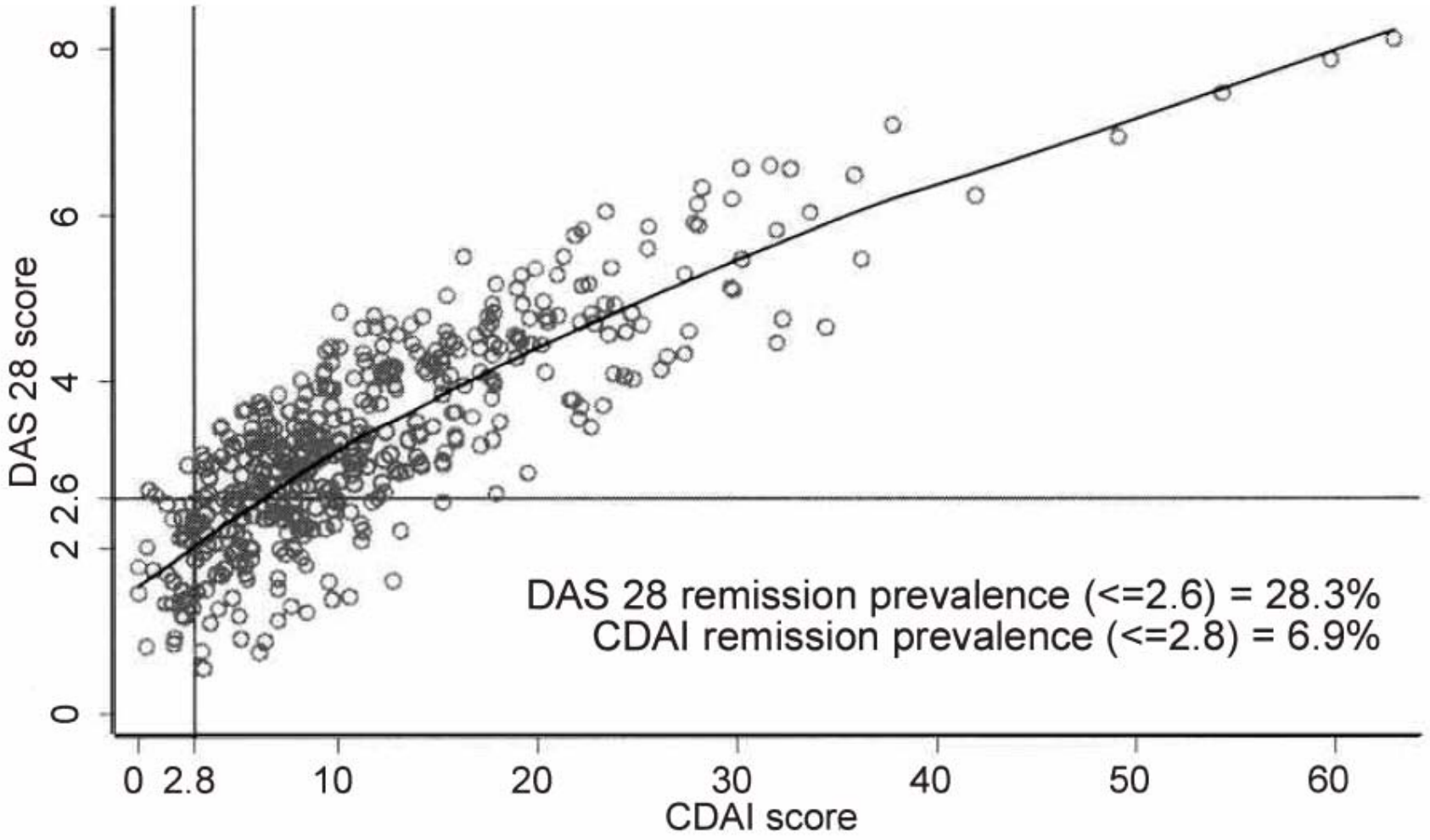


Figure 1. Plot of DAS28 values against CDAI values (n = 435). The line is determined by Lowess regression. Circles below the horizontal line at 2.6 represent patients in DAS28 remission. Circles to the left of the vertical line at 2.8 represent patients in CDAI remission. Kappa for the DAS28 and CDAI scales was fair, 0.253[26].

Shaver TS et al J Rheumatol 2008;35:1015-22

Table 1. Remission, minimal disease activity, and clinical variables in 849 patients with RA.

Variable	All Data			Complete Data (n = 408)
	n	% Missing	%*	%
Remission indices				
DAS28 ≤ 2.6	435	48.8	28.5	28.2
CDAI ≤ 2.8	795	6.6	6.5	6.9
CDAI ≤ 3	795	6.6	8.1	8.8
MD global ≤ 1	816	4.9	12.5	14.5
PAS-II ≤ 1.25	822	3.2	13.7	13.5
Swollen, tender joints = 0	847	1.4	23.7	24.3
Swollen, tender joints = 0, ESR < 10	453	46.8	9.5	8.1
Minimal disease activity				
DAS28 criteria (DAS28 ≤ 2.85)	435	48.8	34.7	34.3
Core criteria	424	50.1	26.9	26.0
PAS-II ≤ 2.2	822	3.2	26.8	25.5

Shaver TS et al J Rheumatol 2008;35:1015-22

Remission in Early Rheumatoid Arthritis

MARGARET H.Y. MA, IAN C. SCOTT, GABRIELLE H. KINGSLEY, and DAVID L. SCOTT

ABSTRACT. ***Objective.*** We systematically reviewed remission as an outcome measure in observational studies and randomized controlled trials (RCT) in early rheumatoid arthritis (RA). Our objectives were to identify its frequency using different criteria, to determine the influence of different treatment strategies on remission, and to review the effects of remission on radiological outcomes.

Methods. Pubmed, Medline and Embase were searched using the following terms: Early Rheumatoid Arthritis or Early RA combined with Remission, Treatment, anti-Tumor Necrosis Factor (TNF) or Disease-modifying Antirheumatic Drugs (DMARD). Remissions were reported using American College of Rheumatology (ACR) criteria and Disease Activity Score (DAS) criteria.

Results. Seventeen observational studies (4762 patients) reported remission in 27% of patients, 17% by ACR criteria and 33% by DAS criteria. Twenty RCT (4 comparing DMARD monotherapies, 13 comparing monotherapy with combination therapies, 3 comparing combination therapies) enrolled 4290 patients. ACR remissions occurred in 16% receiving DMARD monotherapy and 24% combination therapies (random effects OR 1.69, 95% CI 1.12–2.36). DAS remissions occurred in 26% and 42%, respectively (OR 2.01, 95% CI 1.46–2.78). Observational studies showed continuing radiological progression despite remission. RCT showed less radiological progression in remission when treated with combination therapy compared to monotherapies.

Conclusion. Remission is a realistic treatment goal in early RA. Combination therapies using DMARD with or without TNF inhibitors increase remissions. Radiological progression occurred in remission but is reduced by combination therapies. ACR and DAS remission criteria are not directly comparable and standardization is needed. (First Release June 1 2010; J Rheumatol 2010; 37:1444–53; doi:10.3899/jrheum.091131)

Remission rates in observationsl studies varied between 12 and 54%

Table 1. Remissions in observational studies * remission over 6 months at any point. Results are mean values unless denoted "i" indicating median data; "ii", DAS.

Study	Year	Remission	Disease Duration, mo	Age, yrs	Female, %	RF+, %	ESR	DAS28	Followup, mo	DMARD	Number at Entry	Number at Followup	Remission, at Study End (%)
Prevoo[9]	1996	ACR	< 12	55[i]	63	78	—	—	72	Monotherapy	227	49	15 (31)
Eberhardt[38]	1998	ACR	< 24	—	63	75	29	—	60	Monotherapy	183	176	37 (20)**
Young[39]	2000	ACR	8	—	66	63	—	—	60	Monotherapy	941	732	94 (13)
Makinen[40]	2005	ACR	5	56	61	54	—	—	60	Monotherapy	127	111	19 (17)
Möttönen[41]	1996	ACR	< 24	46	75	63	30[i]	—	72	Combination included	142	142	45 (32)
Lindqvist[42]	2002	ACR	< 24	—	63	75	—	—	120	Combination included	183	163	30 (18)
Sanmarti[43]	2003	ACR	< 24	52	78	—	45	5.8	12	Combination included	65	60	12 (20)
Fransen[30]	2004	ACR	< 12	55	66	76	—	—	72	Combination included	424	77	9 (12)
Cantagrel[17]	1999	DAS	< 12	—	—	71	—	—	24	Not stated	108	108	15 (14)
Tengstrand[44]	2004	DAS	< 12	57	64	58	—	5.1	24	Monotherapy	844	844	279 (33)
Vázquez[45]	2007	DAS	< 24	55	81	74	40	5.7	24	Monotherapy	115	105	34 (32)
Khanna[46]	2007	DAS	< 14	51	—	100	43	5.5	24	Monotherapy	200	101	33 (33)
Gossec[47]	2004	DAS	< 12	51	73	81	40	4.1[ii]	60	Combination included	191	165	38 (23)
Forslind[48]	2007	DAS	≤ 12	58	64	60	—	5.3	60	Combination included	698	608	234 (39)
Proudman[23]	2007	DAS	< 24	56	76	61	42	5.3	36	Combination included	61	52	28 (54)
Sanmarti[49]	2007	DAS	< 24	55	81	74	40	5.7	24	Combination included	115	105	34 (32)
Machold[21]	2007	DAS	≤ 3	51	75	—	—	—	36	Combination included	138	55	16 (29)

Ma MHY et al J Rheumatol 2010;37:1444-53

Remission rates in RCTs varied between 9 and 56%

Table 2B. Remission in clinical trials (cases at end of followup).

Study	Year	Disease Duration, mo	Followup, mo	Remission	Control Cases	Control Treatment	Control Remission (%)	Treatment Cases	Treatment Treatment	Treatment Remission (%)
Monotherapy										
Eberhardt[50]	1996	24	24	ACR derivative	22	Placebo	5 (12)	21	D-Penicillamine	4 (12)
Rau[51]	1997	16	12	ACR derivative	87	MTX	10 (12)	87	GSTM	21 (24)
Van Jaarsveld[52]	2000	< 12	24	ACR derivative	107	HCQ	29 (27)	105	MTX (short lag)	25 (24)
Choy[18]	2002	< 12	12	DAS28	55	Diclofenac	0	62	SSZ	0
Monotherapy vs combination therapy										
Boers[1]	1997	< 24	12	ACR	76	SSZ	19 (24)*	79	SSZ/MTX/Pred	24 (32)*
Möttönen[7]	1999	< 24	24	ACR	98	SSZ or MTX	18 (18)	97	MTX/SSZ/HCQ/Pred	36 (37)
Proudman[53]	2000	< 12	12	ACR	42	SSZ	4 (10)	40	MTX/CSA/1A Methylpred	5 (13)
Ferraccioli[54]	2002	16	36	ACR	42	SSZ	3 (7)	42	MTX/CsA	4 (9)
Gerards[55]	2003	< 36	12	ACR	60	CsA	4 (7)	60	CsA/MTX	6 (10)
Wassenberg[56]	2005	< 24	24	ACR	86	DMARD	8 (9)	80	DMARD/Pred	13 (16)
St. Clair[57]	2004	< 36	12	DAS28	245	MTX	37 (15)	325	MTX/Infliximab	101 (31)
Svensson[24]	2005	< 12	24	DAS28	126	DMARD	42 (33)	116	DMARD/Pred	65 (56)
Allaart[3]	2006	< 12	24	DAS44	126	DMARD	58 (46)	128	MTX/Infliximab	54 (42)
Breedveld[6]	2006	< 36	24	DAS28	257	MTX	64 (25)	268	MTX/Adalimumab	131 (49)
Choy[2]	2008	< 24	24	DAS28	117	MTX	21 (18)	116	MTX/CsA/Pred	32 (28)
Emery[4]	2008	< 24	12	DAS28	263	MTX	73 (28)	265	MTX/Etanercept	132 (50)
Hetland[19]	2006	< 6	12	1. DAS28 2. ACR	68	MTX/IA Steroids	1. 23 (34) 2. 19 (28)	69	MTX/CsA/IA steroids	1.30 (43) 2.24 (35)
Combination vs combination therapy										
Verstappen[58]	2007	< 12	24	ACR derivative	148	Conventional MTX +/– CsA	55 (37)	151	Intensive MTX +/– CsA	76 (50)
Saunders[59]	2008	Mean 11.5†	12	DAS28	44	Step up	21 (45)	47	Parallel	16 (33)
Verschueren[20]**	2008	< 12	12	DAS28	17	Step up	No values	46	Step down	No values

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Real life data from NOR-DMARD

(intervention study/register with all DMARD regimens)

	All		Dis duration < 3 years	
	MTX N=2150	MTX+ TNFi N=1041	MTX N=1364	MTX+ TNFi N=260
Mean age	56.4	51.8	55.7	46.1
Mean disease duration	5.4	10.6	0.4	1.4
% females	71.4	72.9	69.1	69.9
% RF positive	63.6	75.2	62.0	68.8
DAS28	4.9	5.2	4.9	5.2

Proportion of RA patients in remission after DMARD treatment (NOR-DMARD)

	3 months		6 months		12 months	
	MTX N=1828	MTX+ TNFi N=858	MTX N=1554	MTX+ TNFi N=726	MTX N=1267	MTX+ TNFi N=595
ACR/EULAR	7	7	9	9	11	11
SDAI≤3.3	9	9	13	12	16	14
DAS28<2.6	23	20	28	26	34	29

Proportion of RA patients with disease duration <3 years in remission after DMARD treatment (NOR-DMARD)

	3 months		6 months		12 months	
	MTX N=1169	MTX+ TNFi N=219	MTX N=1005	MTX+ TNFi N=177	MTX N=842	MTX+ TNFi N=145
ACR/EULAR	9	10	11	8	14	13
SDAI≤3.3	12	12	15	15	19	20
DAS28<2.6	26	23	31	32	39	38

Proportion of RA patients achieving components of ACR/EULAR remission criteria after DMARD treatment (NOR-DMARD)

	3 months		6 months		12 months	
	MTX N=1828	MTX+ TNFi N=858	MTX N=1554	MTX+ TNFi N=726	MTX N=1267	MTX+ TNFi N=595
SJC≤1	37	36	46	46	54	51
TJC≤1	35	34	41	41	48	42
PG≤1	17	15	19	17	18	18
CRP≤1	69	68	73	71	76	72

Proportion of RA patients with disease duration <3 years achieving components of ACR/EULAR remission criteria after DMARD treatment (NOR-DMARD)

	3 months		6 months		12 months	
	MTX N=1169	MTX+ TNFi N=219	MTX N=1005	MTX+ TNFi N=177	MTX N=842	MTX+ TNFi N=145
SJC≤1	40	34	50	48	59	56
TJC≤1	38	30	42	42	50	47
PAG≤1	19	21	22	17	21	20
CRP≤1	73	67	77	76	79	76

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Remission and Rheumatoid Arthritis

Data on Patients Receiving Usual Care in Twenty-Four Countries

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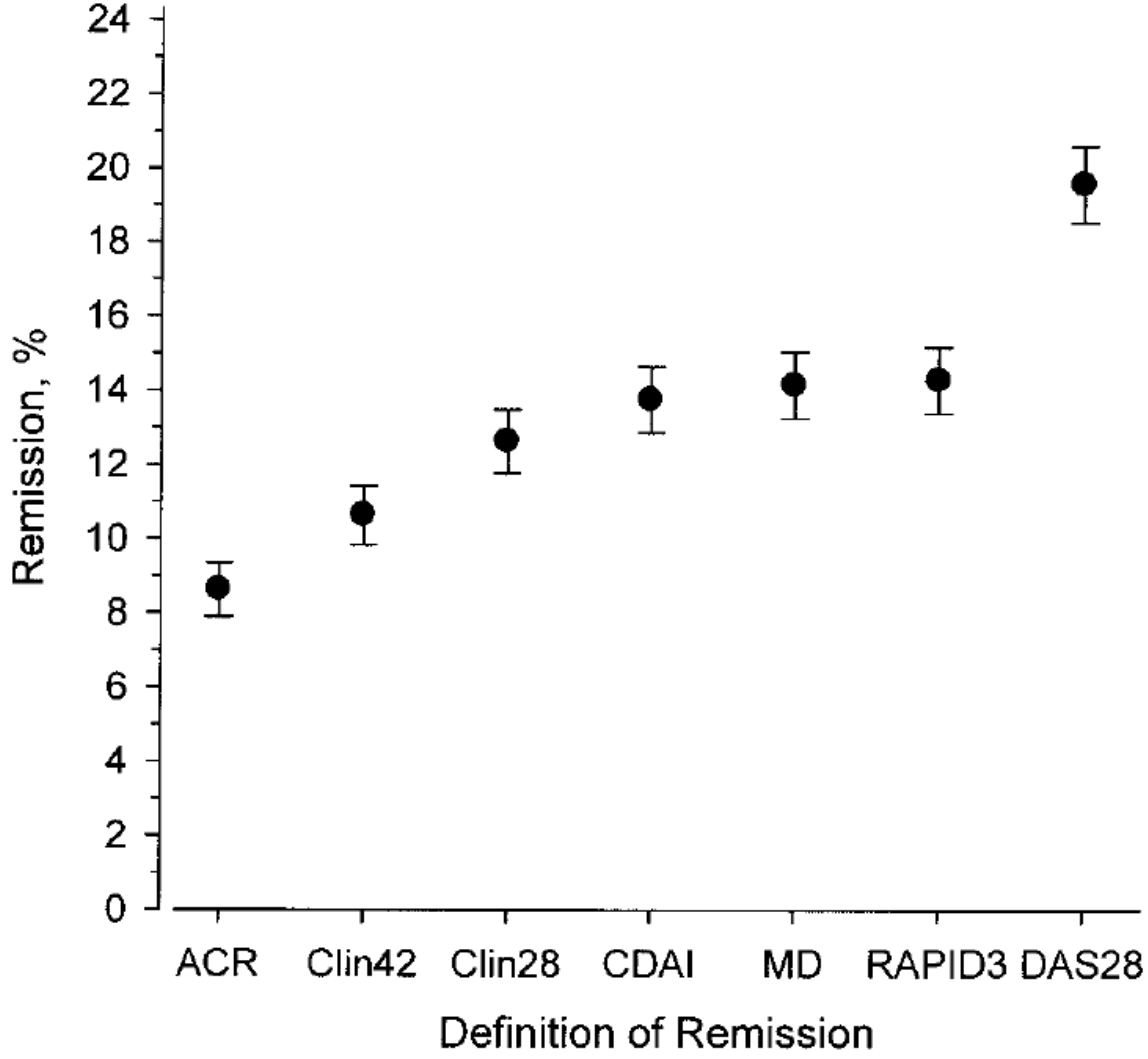

Sokka et al A&R 2008;58:2642-51

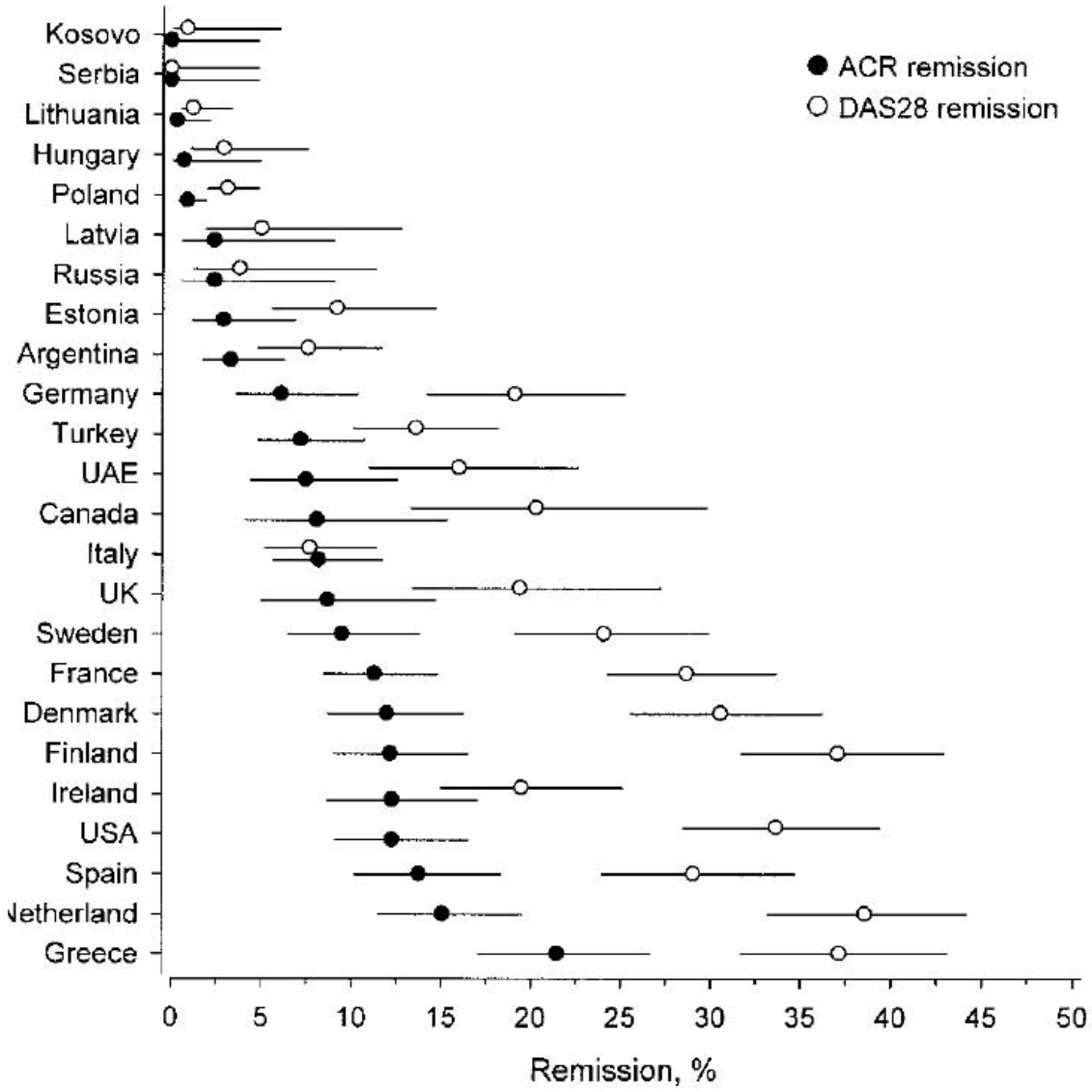

Figure 2. Sex-, age, and disease duration–adjusted rates of remission by country in the QUEST-RA (Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis) study, according to the ACR and DAS28 definitions of remission. Bars show the 95% confidence intervals. See Figure 1 for definitions.

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Main points

- Remission (as linked to no progression of bone damage and functional disability) is an ideal but not realistic goal
  - No agreement on remission criteria – large variation in proportions achieving remission between the criteria
  - Different proportions achieving remission between short versus established disease – and between cohorts studied in RCTs and real life
  - Differences across countries
- The treatment target should be individualized (could for example be zero or maximum one swollen joint)!

Final set of 10 recommendations on treating rheumatoid arthritis to target based on both evidence and expert opinion Part 1 (recommendation 1-5)

1. The primary target for treatment of rheumatoid arthritis should be a state of **clinical remission**.
2. Clinical remission is defined as the **absence** of signs and symptoms **of significant inflammatory disease activity**.
3. While remission should be a clear target, based on available evidence **low disease activity may be an acceptable alternative** therapeutic goal, particularly in established, long-standing disease.
4. Until the desired treatment target is reached, drug **therapy should be adjusted** at least every 3 months.
5. Measures of disease activity must be obtained and documented regularly, as frequently as monthly for patients with high/moderate disease activity or less frequently (such as every 3 to 6 months) for patients in sustained low disease activity or remission.

Final set of 10 recommendations on treating rheumatoid arthritis to target based on both evidence and expert opinion Part 2 (recommendation 6-10)

6. The use of **validated composite measures** of disease activity, which include joint assessments, is needed in routine clinical practice to guide treatment decisions.
7. Structural changes and functional impairment should be considered when making clinical decisions, in addition to assessing composite measures of disease activity.
8. The desired **treatment target should be maintained** throughout the remaining course of the disease.
9. The choice of the (composite) measure of disease activity and the level of the target value may be influenced by **considerations of co-morbidities, patient factors and drug related risks**.
10. The **patient has to be appropriately informed** about the treatment target and the strategy planned to reach this target under the supervision of the rheumatologist.

2010 treatment strategy of RA

- early diagnosis
- early use of synthetic disease modifying therapies (MTX)
- identify an INDIVIDUALIZED treatment target (ideally remission)
- monitor (tight control) and adjust disease-modifying therapy according to the target
- add biological DMARD if target is not achieved
- continue to monitor and adjust therapy as long as the target is not achieved