

Supplemental figure S1: search performed in OVID (MEDLINE database) on 01-06-2022

<input type="checkbox"/>	# ▲ Searches	Results	Type	Actions	Annotations
<input type="checkbox"/>	1 (T2T or "treatment target\$1" or (treat\$ adj3 target) or "targeted treatment" or ("treating rheumatoid arthritis" adj3 target) or "target oriented approach" or ("disease activity" or DAS or DAS28 or remission or DFR or CDAI or SDAI or RADAI or RAPID3) adj2 (steered or driven or guided)) or "objectively steered" or "intensive management" or "intensive outpatient management" or "intensive disease management" or "step up" or (tight adj3 control\$) or "tight\$2 controlled" or (aggressive adj (care or treatment or therapy)) or "goal directed therapy" or "goal steered treatment" or ((systematic or standardized or standardised) adj monitoring) or (target\$ adj3 (remission or "low disease activity" or LDA)) or ((aiming at" or "aiming for" or "aimed at" or "aim of treatment") adj2 (remission or "disease activity" or DAS)).ab,ti.	80015	Advanced	Display Results More ▾	
<input type="checkbox"/>	2 rheumatoid arthritis.ab,kf,ti.	115858	Advanced	Display Results More ▾	
<input type="checkbox"/>	3 *Arthritis, Rheumatoid/	87058	Advanced	Display Results More ▾	
<input type="checkbox"/>	4 ("randomized controlled trial" or "randomised controlled trial" or RCT or "cohort study" or "clinical trial" or "systematic review" or "meta-analysis").ab,ti.	847747	Advanced	Display Results More ▾	
<input type="checkbox"/>	5 exp Clinical Trials as Topic/	374453	Advanced	Display Results More ▾	
<input type="checkbox"/>	6 exp Random Allocation/	106851	Advanced	Display Results More ▾	
<input type="checkbox"/>	7 exp Therapeutics/	4995109	Advanced	Display Results More ▾	
<input type="checkbox"/>	8 exp Drug Therapy/	1467895	Advanced	Display Results More ▾	
<input type="checkbox"/>	9 exp Cohort Studies/	2354530	Advanced	Display Results More ▾	
<input type="checkbox"/>	10 ("clinical trial" or review or "systematic review" or "meta-analysis" or "randomized controlled trial" or "randomised controlled trial" or "controlled clinical trial" or "clinical study").pt.	4044413	Advanced	Display Results More ▾	
<input type="checkbox"/>	11 4 or 5 or 6 or 7 or 8 or 9 or 10	9638122	Advanced	Display Results More ▾	
<input type="checkbox"/>	12 2 or 3	133885	Advanced	Display Results More ▾	
<input type="checkbox"/>	13 exp Animals/	25530668	Advanced	Display Results More ▾	
<input type="checkbox"/>	14 exp Humans/	20517682	Advanced	Display Results More ▾	
<input type="checkbox"/>	15 13 not 14	5012986	Advanced	Display Results More ▾	
<input type="checkbox"/>	16 1 and 11 and 12	1392	Advanced	Display Results More ▾	
<input type="checkbox"/>	17 16 not 15	1381	Advanced	Display Results More ▾	
<input type="checkbox"/>	18 16 not 15	1381	Advanced	Display Results More ▾	
<input type="checkbox"/>	19 limit 18 to (english language and yr="2003 -Current")	1176	Advanced	Display Results More ▾	

Supplemental figure S2: search performed in Embase on 01-06-2022

<input type="checkbox"/>	#	Search term	Count
<input type="checkbox"/>	#11	#1 AND #6 AND #9 NOT #7 AND [english]/lim AND [2003-2022]/py	1,740
<input type="checkbox"/>	#10	#1 AND #6 AND #9	1,911
<input type="checkbox"/>	#9	#2 OR #8	202,191
<input type="checkbox"/>	#8	'rheumatoid arthritis'/mj	133,487
<input type="checkbox"/>	#7	'animal'/exp NOT 'human'/exp	5,792,476
<input type="checkbox"/>	#6	#3 OR #4 OR #5	5,711,787
<input type="checkbox"/>	#5	review:it OR 'clinical trial':it OR 'systematic review':it OR 'meta-analysis':it OR 'randomized controlled trial':it OR 'randomised controlled trial':it OR 'controlled clinical trial':it OR 'clinical study':it	2,935,445
<input type="checkbox"/>	#4	'randomized controlled trial':exp OR 'randomization':exp OR 'clinical trial':exp OR 'cohort analysis':exp OR 'systematic review':exp OR 'meta analysis':exp	2,899,190
<input type="checkbox"/>	#3	'randomized controlled trial':ab,ti OR 'randomised controlled trial':ab,ti OR rct:ab,ti OR 'cohort study':ab,ti OR 'clinical trial':ab,ti OR 'systematic review':ab,ti OR 'meta analysis':ab,ti	1,161,022
<input type="checkbox"/>	#2	'rheumatoid arthritis':ti,ab,kw	178,895
<input type="checkbox"/>	#1	t2t:ab,ti OR 'treatment target':ab,ti OR ((treat* NEAR/3 target):ab,ti) OR 'targeted treatment':ab,ti OR ((treating rheumatoid arthritis' NEAR/3 target):ab,ti) OR 'target oriented approach':ab,ti OR (((disease activity' OR das28 OR das OR remission OR dfr OR cdai OR sdaI OR radai OR rapid3) NEAR/2 (steered OR driven OR guided)):ab,ti) OR 'objectively steered':ab,ti OR 'intensive management':ab,ti OR 'intensive outpatient management':ab,ti OR 'intensive disease management':ab,ti OR 'step up':ab,ti OR ((tight NEAR/3 control*):ab,ti) OR 'tight* controlled':ab,ti OR ((aggressive NEXT/1 (care OR treatment OR therapy)):ab,ti) OR 'goal directed therapy':ab,ti OR 'goal steered treatment':ab,ti OR (((systematic OR standardized OR standardised) NEXT/1 monitoring):ab,ti) OR ((target* NEAR/3 (remission OR 'low disease activity' OR Ida)):ab,ti) OR (((aiming at' OR 'aiming for' 'aimed at' OR 'aim of treatment') NEAR/2 (remission OR 'disease activity' OR das)):ab,ti)	120,745

Supplemental figure S3: search performed in Cochrane database on 01-06-2022

ID	Search Hits
#1	((T2T OR "treatment target*" OR (treat* NEAR/2 target) OR "targeted treatment" OR ("treating rheumatoid arthritis" NEAR/3 target) OR "target oriented approach" OR ("disease activity" OR DAS OR DAS28 OR remission OR DFR OF CDAI OR SDAI OR RADAI OR RAPID3) NEAR/2 (steered OR driven OR guided)) OR "objectively steered" OR "intensive management" OR "intensive outpatient management" OR "intensive disease management" OR "step up" OR (tight NEAR/3 control*) OR (tight* NEXT controlled) OR (aggressive NEXT (care OR treatment OR therapy)) OR "goal directed therapy" OR "goal steered treatment" OR ((systematic OR standardized OR standardised) NEXT monitoring) OR (target* NEAR/3 (remission OR "low disease activity" OR LDA)) OR ((aiming at" OR "aiming for" OR "aimed at" OR "aim of treatment") NEAR/2 (remission OR "disease activity" OR DAS))):ti,ab,kw (Word variations have been searched) 17800
#2	("rheumatoid arthritis"):ti,ab,kw (Word variations have been searched) 16699
#3	MeSH descriptor: [Arthritis, Rheumatoid] this term only 6150
#4	MeSH descriptor: [Clinical Trials as Topic] explode all trees 48676
#5	MeSH descriptor: [Random Allocation] explode all trees 20677
#6	MeSH descriptor: [Therapeutics] explode all trees 327999
#7	MeSH descriptor: [Drug Therapy] explode all trees 147897
#8	MeSH descriptor: [Cohort Studies] explode all trees 159921
#9	(("clinical trial" OR "systematic review" OR "meta-analysis" OR "randomized controlled trial" OR "randomised controlled trial" OR "controlled clinical trial" OR "clinical study")):pt (Word variations have been searched) 640747
#10	MeSH descriptor: [Animals] explode all trees 647954
#11	(("randomized controlled trial" OR "randomised controlled trial" OR RCT OR "cohort study" OR "clinical trial" OR "systematic review" OR "meta analysis")):ti,ab,kw (Word variations have been searched) 775820
#12	MeSH descriptor: [Humans] explode all trees 647921
#13	#2 OR #3 17332
#14	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #11 1143210
#15	#10 NOT #12 33
#16	#1 AND #13 AND #14 664
#17	#16 NOT #15 664

Supplemental figure S4: search performed in preMEDLINE database on 01-06-2022

#13	...	>	Search: #11 AND #12	113	07:24:38
#12	...	>	Search: "pubstatus:aheadofprint"[All Fields] OR "publisher"[Filter] OR "pubmednotmedline"[Filter]	4,707,474	07:23:47
#11	...	>	Search: #10 NOT #7	1,759	07:23:16
#10	...	>	Search: #1 AND #8 AND #9	1,767	07:23:00
#9	...	>	Search: #4 OR #5 OR #6	9,669,394	07:22:43
#8	...	>	Search: #2 OR #3	159,576	07:22:20
#7	...	>	Search: "animals"[MeSH Terms] NOT "humans"[MeSH Terms]	5,010,889	07:16:38
#6	...	>	Search: "clinical trial"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Publication Type] OR "meta analysis"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "clinical study"[Publication Type]	4,205,976	07:16:27
#5	...	>	Search: "clinical trials as topic"[MeSH Terms] OR "random allocation"[MeSH Terms] OR "therapeutics"[MeSH Terms] OR "drug therapy"[MeSH Terms] OR "cohort studies"[MeSH Terms]	6,789,890	07:16:14
#4	...	>	Search: "randomized controlled trial"[Title/Abstract] OR "randomised controlled trial"[Title/Abstract] OR RCT[Title/Abstract] OR "cohort study"[Title/Abstract] OR "clinical trial"[Title/Abstract] OR "systematic review"[Title/Abstract] OR "meta analysis"[Title/Abstract]	866,551	07:16:04
#3	...	>	Search: rheumatoid arthritis[MeSH Terms]	121,464	07:15:52
#2	...	>	Search: "rheumatoid arthritis"[Title/Abstract]	115,887	07:15:43
#1	...	>	Search: T2T[Title/Abstract] OR "treatment target*[Title/Abstract] OR "treat to target*[Title/Abstract] OR "treating to target*[Title/Abstract] OR "targeted treatment*[Title/Abstract] OR "target oriented approach*[Title/Abstract] OR ((disease activity*[Title/Abstract] OR DAS[Title/Abstract] OR DAS28[Title/Abstract] OR remission[Title/Abstract] OR DFR[Title/Abstract] OR CDAI[Title/Abstract] OR SDAI[Title/Abstract] OR RADAII[Title/Abstract] OR RAPID3[Title/Abstract])) AND (steered[Title/Abstract] OR driven[Title/Abstract] OR guided[Title/Abstract])) OR "intensive management*[Title/Abstract] OR "intensive outpatient management*[Title/Abstract] OR "intensive disease management*[Title/Abstract] OR "step up*[Title/Abstract] OR "tight control*[Title/Abstract] OR "tightly controlled*[Title/Abstract] OR "aggressive care*[Title/Abstract] OR "aggressive therapy*[Title/Abstract] OR "aggressive treatment*[Title/Abstract] OR "goal directed therapy*[Title/Abstract] OR "systematic monitoring*[Title/Abstract] OR "standardized monitoring*[Title/Abstract] OR "standardised monitoring*[Title/Abstract] OR (target*[Title/Abstract] AND (remission[Title/Abstract] OR "low disease activity*[Title/Abstract] OR LDA[Title/Abstract]))) OR ((aiming[Title/Abstract] OR "aimed at*[Title/Abstract] OR "aim of treatment*[Title/Abstract] AND (remission[Title/Abstract] OR "disease activity*[Title/Abstract] OR DAS[Title/Abstract]))	56,934	07:15:21

Supplemental Table S1

Author/trial	Year	Cohort /RCT	Treatment arms extracted	Target	Early RA, Formal treatment protocol, bDMARD available	Risk of Bias	Used in analyses
de Cock et al.[27]	2014	Cohort	1. Initial monotherapy (n=42) 2. Initial combination therapy (n=32)	DAS28-CRP<3.2	Yes, No, Yes	Low	DAS-remission, mean DAS, HAQ and SHS year 1 and 2-3
T-4 study [28]	2012	RCT	DAS-driven arm (n=56)	DAS28-ESR<2.6	Yes, Yes, Yes	Some concerns	DAS- and SCB-remission, mean DAS, HAQ and SHS year 1
Bosello et al.[29]	2011	Cohort	DAS-driven (n=121)	DAS44ESR ≤2.4	Yes, Yes, Yes	Low	DAS- and SCB-remission, mean DAS and HAQ year 1
Brenol et al. [30]	2015	Cohort	All patients (n=241)	DAS28ESR < 3.2	No, No, No	Some concerns	DAS- and SCB-remission, mean HAQ, SDAI/CDAI and DAS year 1
GUEPARD [31]	2013	RCT	GUEPARD arm (n=65)	DAS28-ESR<3.2	Yes, Yes, Yes	Some concerns	Mean DAS, HAQ and SDAI/CDAI year 1
GUEPARD [32]	2011	RCT	GUEPARD arm (n=65)	DAS28-ESR<3.2	Yes, Yes, Yes	Some concerns	Mean SHS year 1
NOR-VEAC [33]	2019	Cohort	T2T cohort (n=293)	DAS28-ESR<2.6	Yes, No, Yes	Some concerns	DAS-remission, mean SDAI/CDAI and DAS at year 1, SCB remission and mean DAS at year 2-3
NOR-VEAC [34]	2020	Cohort	NOR-VEAC (n=330)	DAS28-ESR<2.6	Yes, No, Yes	Some concerns	DAS-remission year 2-3, SCB-remission year 1 and 2-3
tREACH[35]	2016	Cohort	1. Initial triple therapy (n=281) 2. Initial monotherapy (n=281)	DAS44-ESR≤2.4	Yes, Yes, Yes	Low	DAS-remission year 2-3
Wabe et al.[36]	2016	Cohort	All patients (n=198 at year 1 and n=149 at year 3)	DAS28-ESR<2.6	Yes, Yes, No	Some concerns	DAS- and SCB-remission, mean HAQ and mean SHS year 1 and year 2
BIODAM[37]	2019	Cohort	All patients (n=571)	DAS44-ESR<1.6	No, No, Yes	Some concerns	DAS-remission at year 2-3 Mean DAS, HAQ at years 1 and 2-3
BIODAM[38]	2020	Cohort	All patients (n=571)	DAS44-ESR<1.6	No, No, Yes	Some concerns	DAS remission year 1, SCB remission year 1 and 2-3
Harrold et al. [39]	2018	RCT	Treat-to-target (n=246)	CDAI≤10	No, No, Yes	High	Mean HAQ year 1
Hodkinson et al. [40]	2015	RCT	1. SDAI-target (n=42) 2. CDAI-target (n=60)	1. SDAI≤11 2. CDAI≤10	Yes, Yes, No	Some concerns	DAS-remission, mean DAS and HAQ year 1
BeSt [41]	2018	RCT	Initial combination therapy with prednisone (arm 3 of BeSt) (n=133)	DAS44-ESR ≤2.4	Yes, Yes, Yes	Low	DAS- and SCB-remission and mean DAS year 1
BeSt [42]	2006	RCT	1. Sequential monotherapy (n=126) 2. Step up combination therapy (n=121) 3. Initial combination therapy with prednisone (n=133)	DAS44-ESR ≤2.4	Yes, Yes, Yes	Low	Mean HAQ and SHS year 2-3

			4. Initial combination therapy with infliximab (n=128)				
BeSt [90]	2005	RCT	1. Sequential monotherapy (n=126) 2. Step up combination therapy (n=121) 3. Initial combination therapy with tapered high-dose prednisone (n=133) 4. Initial combination therapy with infliximab (n=128)	DAS44-ESR ≤2.4	Yes, Yes, Yes	Low	Mean HAQ and SHS year 1
BeSt [43]	2009	RCT	1. Sequential monotherapy + Step up combination therapy (group 1+2 BeSt), (n=234)	DAS44-ESR ≤2.4	Yes, Yes, Yes	Low	DAS-remission and mean DAS year 1
BeSt [44]	2015	RCT	1. Sequential monotherapy (n=115) 2. Step up combination therapy (n=101) 3. Initial combination therapy with prednisone (n=119) 4. Initial combination therapy with infliximab (n=119)	DAS44ESR ≤2.4	Yes, Yes, Yes	Low	DAS-remission 4-6 years
U-Act-Early [45]	2016	RCT	1. Tocilizumab + methotrexate (n=106) 2. Tocilizumab + placebo methotrexate (n=103) 3. Methotrexate + placebo tocilizumab (n=108)	DAS28-ESR<2.6	Yes, Yes, Yes	Low	Mean HAQ and SHS year 1 and 2-3
IDEA [46]	2013	RCT	1. Methotrexate + methylprednisolone (n=57) 2. Methotrexate + infliximab (n=55)	DAS44-ESR ≤2.4	Yes, Yes, Yes	Low	DAS- and SCB remission, mean HAQ and SHS year 1
CIMESTRA and OPERA [47]	2018	RCT	1. CIMESTRA (n=150) 2. OPERA (all patients) (n=180)	1. (SJC 0) 2. DAS28CRP ≤3.2	1. Yes, Yes, No 2. Yes, Yes, Yes	1. Some concerns 2. Low	SCB remission year 2-3
OPERA [48]	2013	RCT	1. Adalimumab + methotrexate (n=89) 2. Methotrexate + placebo adalimumab (n=91)	DAS28CRP ≤3.2	Yes, Yes, Yes	Low	DAS- and SCB-remission year 1 and mean DAS, HAQ, SDAI/CDAI year 1
OPERA [49]	2015	RCT	1. Adalimumab + methotrexate (n=89) 2. Methotrexate + placebo adalimumab (n=91)	DAS28-CRP ≤3.2	Yes, Yes, Yes	Low	DAS-remission and mean DAS, HAQ and SHS year 2-3
TICORA [50]	2004	RCT	Intensive group (n=55)	DAS28-ESR<3.2	Yes, Yes, No	Low	SCB remission, mean DAS, HAQ and SHS year 1
Saunders et al. [51]	2008	RCT	1. Step-up therapy (n=47) 2. Triple therapy (n=49)	DAS28-ESR<3.2	Yes, Yes, Yes	Some concerns	SCB remission, mean DAS, HAQ and SHS year 1
ARCTIC [52]	2016	RCT	Conventional tight control (n=112)	DAS44-ESR<1.6	Yes, Yes, Yes	Low	DAS- and SCB-remission, mean DAS and SHS years 1 and 2-3 Mean SDAI/CDAI year 1

DREAM [53]	2016	Cohort	1. Step-up therapy (n=128) 2. Initial combination therapy (n=128)	DAS28-ESR<2.6	Yes, Yes, Yes	Some concerns	DAS remission year 1
DREAM [54]	2019	Cohort	All patients (n=229)	DAS28-ESR<2.6	Yes, Yes, Yes	Some concerns	Mean DAS year 2-3
DREAM [55]	2011	Cohort	All patients (n=534)	DAS28-ESR<2.6	Yes, Yes, Yes	Some concerns	Mean SHS year 1
DREAM [91]	2013	Cohort	All patients (n=342)	DAS28-ESR<2.6	Yes, Yes, Yes	Some concerns	SCB-remission year 1 and 2-3 DAS-remission, mean HAQ and SHS year 2-3
DREAM [56]	2017	Cohort	All patients (n=229)	DAS28-ESR<2.6	Yes, Yes, Yes	Some concerns	DAS-remission year 4-6, mean HAQ and DAS year 1
CareRA [57]	2021	RCT	1. COBRA Classic (n=69) 2. COBRA Slim, high risk (n=75) 3. COBRA Avant-Garde (n=59) 4. COBRA Slim, low risk (n=23) 5. Methotrexate tight step-up (n=26)	DAS28-CRP≤3.2	Yes, Yes, No	Some concerns	DAS remission years 1, 2-3 and 4-6, SCB remission year 1
CareRA [58]	2019	RCT	1. COBRA Classic (n=98) 2. COBRA Slim, high risk (n=98) 3. COBRA Avant-Garde (n=93) 4. COBRA Slim, low risk (n=43) 5. Methotrexate tight step-up (n=47)	DAS28-CRP≤3.2	Yes, Yes, No	Some concerns	SCB remission, mean SHS and HAQ year 2-3
CareRA [59]	2016	RCT	1. COBRA Classic (n=98) 2. COBRA Slim, high risk (n=98) 3. COBRA Avant-Garde (n=93) 4. COBRA Slim, low risk (n=43) 5. Methotrexate tight step-up (n=47)	DAS28-CRP≤3.2	Yes, Yes, No	Some concerns	Mean DAS, HAQ and SHS year 1
IMAGINE-RA [60]	2019	RCT	Conventional treat-to-target (n=100)	DAS28-CRP≤3.2	No, Yes, Yes	Low	DAS- and SCB-remission, mean DAS, HAQ and SHS year 2-3
COBRA-light [61]	2014	RCT	1. COBRA (n=81) 2. COBRA-light (n=81)	DAS44-ESR<1.6	Yes, Yes, Yes	Low	DAS- and SCB-remission, mean DAS, HAQ and SHS year 1
Brown et al. [62]	2019	Cohort	All patients (n=300)	DAS28-ESR<2.6	Yes, Yes, Yes	Low	DAS-remission year 1
El Miedany et al. [63]	2015	Cohort	1. Biological DMARD + conventional DMARD (n=192) 2. Conventional DMARD (n=288)	DAS28-ESR≤3.2	Yes, No, Yes(arm1) No(arm2)	Low	Mean DAS and HAQ year 1
Fedele et al. [64]	2018	Cohort	ERA-patients (n=408)	DAS44-ESR≤2.4	Yes, Yes, Yes	Some concerns	DAS- and SCB-remission year 1
Montecucco et al. [65]	2012	RCT	1. Methotrexate (n=110) 2. Methotrexate + low dose prednisone (n=110)	DAS28-ESR≤3.2	Yes, Yes, Yes	Some concerns	DAS- and SCB-remission and mean DAS year 1
Pope et al. [66]	2013	RCT	1. DAS-group (n=100) 2. SJC-group (n=99)	1. DAS28-ESR<2.6 2. (SJC 0)	No, No, Yes	Low	DAS-remission, mean DAS and HAQ year 1

Song et al. [67]	2018	Cohort	1. Remission-steered (n=163) 2. (LDA or remission – steered, n=163))	1. DAS28-ESR<2.6 (2. DAS28-ESR < 2.6 or <3.2)	Yes, No, Yes	High	DAS-remission year 1
Tam et al. [68]	2018	RCT	1. SDAI-steered (n=57) 2. DAS-steered (n=60)	1. SDAI≤3.3 2. DAS28-CRP<2.6	Yes, Yes, Yes	Some concerns	DAS- and SCB remission year 1, mean DAS, HAQ, and SDAI/CDAI year 1
Teh et al. [69]	2011	Cohort	All patients (n=142)	DAS28-ESR<2.6	No, No, Yes	Some concerns	DAS-remission and mean DAS year 1
Verschueren et al. [70]	2008	Cohort	Step-up therapy (n=52)	DAS28-CRP<3.2	Yes, No, No	Low	DAS-remission and mean DAS year 1
Zhao et al. [71]	2020	RCT	Tight control arm (n=54)	DAS28-CRP≤3.2	No, Yes, Yes	Some concerns	DAS-remission, mean DAS and SDAI/CDAI year 1
Bugatti et al. [72]	2012	Cohort	All patients (n=161)	DAS44-ESR≤2.4	Yes, Yes, No	Low	DAS- and SCB-remision year 1
Horton et al. [73]	2016	Cohort	All patients (n=105)	DAS28-CRP < 2.6	Yes, No, Yes	Some concerns	DAS- and SCB-remission year 1
CRANE [74]	2014	Cohort	All patients (n=145)	DAS28-ESR < 3.2	Yes, Yes, Yes	Some concerns	Mean HAQ year 1
CRANE [75]	2021	Cohort	All patients (n=197)	DAS28-ESR < 3.2	Yes, Yes, Yes	Some concerns	DAS- and SCB-remission year 1 and 2-3
Huang et al. [76]	2022	Cohort	1. TARRA cohort (n=389 at year 1, n=283 at year 2) 2. CENTRA cohort (n=111 at year 1, n=67 at year 2)	SDAI <= 11	No, No, Yes	1. Some concerns 2. Some concerns	DAS- and SCB-remission and mean DAS year 1 and 2-3. SDAI-CDAI year 1.

(b)DMARD: (biological) disease modifying antirheumatic drug, CDAI: Clinical Disease Activity Index, DAS(28/44): Disease activity score (based on a 28/44-joint count), CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, HAQ: Health assessment questionnaire, ITS: intention to study analysis, ITT: intention to treat analysis, LDA: low disease activity, NM:not mentioned, PP: per protocol analysis, RA: rheumatoid arthritis, SCB-remission: SDAI/CDAI/Boolean remission, SDAI: Simplified Disease Activity Index, RCT: Randomized Controlled Trial, SHS: Sharp van der Heijde Score, T2T: treat-to-target..

Articles that met the inclusion criteria but were not used in the meta-regression analyses, and the reason not to use them

Author/trial	Year	Cohort /RCT	Treatment arms extracted	Target	Risk of Bias	Outcome measures reported	Reason not used in analysis
de Andrade et al.[77]	2017	Cohort	All patients (n=229)	DAS28-ESR<2.6	Some concerns	Mean DAS, CDAI and HAQ at year 7	Not enough arms at this time-point (7years) for analysis
BeSt [78]	2007	RCT	Sequential monotherapy group and Step up combination therapy group (arms 1 and 2 of BeSt) (n=247)	DAS44-ESR ≤2.4	Low	Mean change in DAS, HAQ, and SHS at year 1	Duplicate results with other extracted BeST papers
BeSt [92]	2017	RCT	1. Sequential monotherapy (n=109) 2. Step up combination therapy (n=104) 3. Initial combination therapy with prednisone (n=109) 4. Initial combination therapy with infliximab (n=107)	DAS44-ESR ≤2.4	Low	Mean change in SHS at year 10	Not enough arms at this time-point for analysis
BeSt [79]	2014	RCT	1. Sequential monotherapy (n=111) 2. Step up combination therapy (n=94) 3. Initial combination therapy with prednisone (n=113) 4. Initial combination therapy with infliximab (n=116)	DAS44-ESR ≤2.4	Low	Mean change in SHS at year 5	Not enough arms at this time-point for analysis
BeSt [80]	2016	RCT	1. Sequential monotherapy (n=126) 2. Step up combination therapy (n=121) 3. Initial combination therapy with prednisone (n=133) 4. Initial combination therapy with infliximab (n=128)	DAS44-ESR ≤2.4	Low	DAS44ESR-remission, mean HAQ and SHS at year 10	Not enough arms at this time-point for analysis
BeSt [81]	2012	RCT	1. Sequential monotherapy (n=126) 2. Step up combination therapy (n=121) 3. Initial combination therapy with prednisone (n=133) 4. Initial combination therapy with infliximab (n=128)	DAS44-ESR ≤2.4	Low	Drug free remission at year 7	Not enough arms for analysis for this outcome measure and this time-point
BeSt [82]	2009	RCT	1. Sequential monotherapy (n=126) 2. Step up combination therapy (n=121) 3. Initial combination therapy with prednisone (n=133) 4. Initial combination therapy with infliximab (n=128)	DAS44-ESR ≤2.4	Low	Patient Reported Outcomes	Not enough arms for analysis of patient reported outcomes
BeSt [83]	2012	RCT	All arms of BeSt, DAS-driven therapy (n=508)	DAS44ESR ≤2.4	Low	Drug free remission at year 5	Not enough arms for analysis of drug free remission

U-Act-Early [84]	2017	RCT	1. Tocilizumab + methotrexate (n=106) 2. Tocilizumab + placebo methotrexate (n=103) 3. Methotrexate + placebo tocilizumab (n=108)	DAS28-ESR<2.6	Low	Mean change SHS years 1 and 2	Duplicate results with other extracted publication
U-Act-Early [85]	2020	RCT	1. Tocilizumab + methotrexate (n=106) 2. Tocilizumab + placebo methotrexate (n=103) 3. Methotrexate + placebo tocilizumab (n=108)	DAS28-ESR<2.6	Low	Median change in SHS at year 5	Duplicate results with other extracted publication
DREAM [86]	2015	Cohort	Tight control (n=126)	DAS28-ESR<2.6	Some concerns	DAS-remission, mean change in DAS and HAQ at year 1	Duplicate results with other extracted publication
DREAM [87]	2021	Cohort	All patients (n=219)	DAS28-ESR<2.6	Some concerns	Median SHS at years 1, 3 and 6	Duplicate results with other extracted publication
Gullick et al. [88]	2019	Cohort	All patients (n=1693)	DAS28-ESR<2.6	Some concerns	DAS-remission, mean DAS at year 10	Not enough arms for analysis at this time-point
Ebrahimian et al. [89]	2021	Cohort	1. Very early treatment (n=196) 2. Early treatment (n=275) 3. Late treatment (n=138)	ACR-EULAR Boolean remission	Some concerns	Mean DAS, Boolean remission at years 5-7	Not enough arms for analysis at this time-point

DAS(28/44): Disease activity score (based on a 28/44-joint count), CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, HAQ: Health assessment questionnaire, LDA: low disease activity, RA: rheumatoid arthritis, RCT: Randomized Controlled Trial, SHS: Sharp van der Heijde Score.

Supplemental table S2: effect of treatment target on clinical and radiographic outcome measures after 1 year of T2T with 95% CI, based on parsimonious models

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Improvement mean DAS28-ESR	0.27 (-0.18 - 0.72)	0.43 (-0.26 - 1.13)	0.16 (-0.58 - 0.91)
Proportion DAS-remission	0.09 (-0.02 - 0.21)	0.21 (0.01 - 0.40)	0.11 (-0.08 - 0.31)
<i>DAS28-ESR subgroup*</i>	0.08 (-0.03 - 0.20)	0.22 (0.05 - 0.39)	0.14 (-0.03 - 0.30)
<i>DAS44-ESR subgroup*</i>	0.38 (0.21 - 0.55)	NA	NA
<i>DAS28-CRP subgroup*</i>	-0.18 (-0.38 - 0.02)	NA	NA
Proportion SDAI/CDAI/Boolean remission	-0.01 (-0.15 - 0.12)	0.40 (0.07 - 0.73)	0.41 (0.08 - 0.74)
<i>SDAI/CDAI subgroup*</i>	-0.01 (-0.19 - 0.16)	0.34 (0.00 - 0.68)	0.35 (0.03 - 0.68)
<i>Boolean remission subgroup*</i>	0.03 (-0.13 - 0.19)	NA	NA
Improvement mean SDAI/CDAI	-3.05 (-6.22 - 0.12)	2.03 (-1.31 - 5.37)	5.08 (0.61 - 9.55)
Improvement mean HAQ	0.00 (-0.10 - 0.10)	-0.03 (-0.18 - 0.13)	-0.03 (-0.19 - 0.14)
Improvement in progression mean SHS per year (log transformed)	-0.09 (-0.49 - 0.31)	NA	NA

*The subgroups refer to the type of reported outcome measure. ACR: American College of Rheumatology, CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index, SHS: Sharp/van der Heijde score. Dark green=statistically significant improvement ($p<0.05$), light green= statistically non-significant improvement ($p\geq0.05$), orange= statistically non-significant deterioration ($p\geq0.05$).

Supplemental table S3: effect of treatment target on clinical and radiographic outcome measures after 2-3 years of T2T with 95% CI, based on parsimonious models.

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Improvement mean DAS28-ESR	0.67 (-0.17 - 1.50)	0.31 (-1.05 - 1.66)	-0.36 (-1.72 - 1.01)
Proportion DAS-remission	0.21 (0.02 - 0.40)	0.29 (0.02 - 0.57)	0.08 (p=0.48)
<i>DAS-ESR subgroup (28 or 44)*</i>	0.14 (-0.87 - 1.14)	0.01 (-1.55 - 1.58)	-0.12 (-1.31 - 1.06)
Proportion SDAI/CDAI/Boolean remission	-0.05 (-0.15 - 0.04)	0.31 (0.15 - 0.47)	0.36 (0.21 - 0.52)
<i>CDAI/SDAI subgroup*</i>	-0.05 (-0.16 - 0.06)	0.30 (0.12 - 0.47)	0.34 (0.21 - 0.48)
Improvement mean HAQ	0.02 (-0.28 - 0.32)	NA	NA
Improvement in progression mean SHS per year (log transformed)	-0.20 (-0.54 - 0.15)	NA	NA

*The subgroups refer to the type of reported outcome measure. CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index, SHS: Sharp/van der Heijde score. Dark green=statistically significant improvement ($p<0.05$), light green= statistically non-significant improvement ($p\geq0.05$), orange= statistically non-significant deterioration ($p\geq0.05$).

Supplemental table S4: effect of treatment target on clinical and radiographic outcome measures after 4-6 years of T2T with 95% CI, based on parsimonious models.

Target Outcome	DAS-remission vs. DAS-LDA	CDAI/SDAI LDA vs. DAS-LDA	CDAI-SDAI LDA vs. DAS-remission
Proportion DAS-remission	0.10 (-0.22 - 0.43)	NA	NA

*According to any of the DAS-variants (e.g. 28/44 joints, ESR/CRP). The parsimonious model has been corrected for the DAS-variant.. CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, LDA: low disease activity, SDAI: simplified disease activity index. Light green= statistically non-significant improvement ($p \geq 0.05$).

Supplemental table S5: effect of treatment target on clinical and radiographic outcome measures after 1 year of T2T with 95% CI, based on full models.

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Improvement mean DAS28-ESR	0.28 (-0.19 - 0.75)	0.41 (-0.32 - 1.15)	0.13 (-0.67 - 0.94)
Proportion DAS-remission	0.09 (-0.03 - 0.21)	0.21 (0.00 - 0.41)	0.12 (-0.08 - 0.31)
<i>DAS28-ESR subgroup*</i>	0.10 (-0.03 - 0.23)	0.23 (0.05 - 0.40)	0.13 (-0.05 - 0.30)
<i>DAS44-ESR subgroup*</i>	0.37 (0.19 - 0.55)	NA	NA
<i>DAS28-CRP subgroup*</i>	-0.20 (-0.55 - 0.15)	NA	NA
Proportion SDAI/CDAI/Boolean remission	-0.01 (-0.16 - 0.13)	0.40 (0.04 - 0.75)	0.41 (0.06 - 0.76)
<i>SDAI/CDAI subgroup*</i>	-0.01 (-0.19 - 0.16)	0.34 (0.00 - 0.68)	0.35 (0.03 - 0.68)
<i>Boolean remission subgroup*</i>	0.03 (-0.13 - 0.19)	NA	NA
Improvement mean SDAI/CDAI	-3.05 (-6.22 - 0.12)	2.03 (-1.31 - 5.37)	5.08 (0.61 - 9.55)
Improvement mean HAQ	-0.02 (-0.11 - 0.08)	-0.04 (-0.19 - 0.11)	-0.02 (-0.19 - 0.14)
Improvement in progression mean SHS per year (log transformed)	-0.09 (-0.49 - 0.31)	NA	NA

*The subgroups refer to the type of reported outcome measure. ACR: American College of Rheumatology, CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index, SHS: Sharp/ van der Heijde score. Dark green=statistically significant improvement ($p < 0.05$), light green= statistically non-significant improvement ($p \geq 0.05$), orange= statistically non-significant deterioration ($p \geq 0.05$).

Supplemental table S6: effect of treatment target on clinical and radiographic outcome measures after 2-3 years of T2T with 95% CI, based on full models.

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/SDAI LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Improvement mean DAS28-ESR	0.66 (-0.32 - 1.64)	0.31 (-1.37 - 1.98)	-0.36 (-1.99 - 1.28)
Proportion DAS-remission	0.21 (-0.08 - 0.51)	0.27 (-0.23 - 0.76)	0.05 (-0.35 - 0.45)
<i>DAS-ESR subgroup (28 or 44)*</i>	0.14 (-0.87 - 1.14)	0.01 (-1.55 - 1.58)	-0.12 (-1.31 - 1.06)
Proportion SDAI/CDAI/Boolean remission	-0.05 (-0.15 - 0.05)	0.32 (0.14 - 0.50)	0.37 (0.20 - 0.54)

<i>CDAI/SDAI subgroup*</i>	-0.05 (-0.17 - 0.06)	0.29 (0.10 - 0.48)	0.34 (0.20 - 0.49)
Improvement mean HAQ	0.03 (-0.32 - 0.39)	NA	NA
Improvement in progression mean SHS per year (log transformed)	-0.18 (-0.54 - 0.17)	NA	NA

*The subgroups refer to the type of reported outcome measure. CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index, SHS: Sharp/ van der Heijde score. Dark green=statistically significant improvement ($p<0.05$), light green=statistically non-significant improvement ($p\geq0.05$), orange= statistically non-significant deterioration ($p\geq0.05$).

Supplemental table S7: effect of treatment target on clinical and radiographic outcome measures after 4-6 years of T2T with 95% CI, based on full models.

Target Outcome	DAS-remission vs. DAS-LDA	CDAI/SDAI LDA vs. DAS-LDA	CDAI-SDAI LDA vs. DAS-remission
Proportion DAS-remission*	0.10 (-0.23 - 0.44)	NA	NA

*According to any of the DAS-variants (e.g. 28/44 joints, ESR/CRP). The full model has been corrected for the DAS-variant.. CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, LDA: low disease activity, SDAI: simplified disease activity index. Light green= statistically non-significant improvement ($p\geq0.05$).

Supplemental table S8: effect of treatment target on clinical and radiographic outcome measures after 1 year of T2T with 95% CI, based on univariate models.

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Improvement mean DAS28-ESR	0.42 (-0.12 - 0.96)	0.29 (-0.60 - 1.18)	-0.13 (-1.06 - 0.79)
Proportion DAS-remission	0.02 (-0.10 - 0.13)	0.06 (-0.15 - 0.27)	0.04 (-0.17 - 0.25)
<i>DAS28-ESR subgroup*</i>	0.10 (-0.06 - 0.26)	0.16 (-0.07 - 0.39)	0.06 (-0.16 - 0.28)
<i>DAS44-ESR subgroup*</i>	0.08 (-0.13 - 0.28)	NA	NA
<i>DAS28-CRP subgroup*</i>	-0.08 (-0.30 - 0.14)	NA	NA
Proportion SDAI/CDAI/Boolean remission	-0.03 (-0.15 - 0.09)	0.28 (0.02 - 0.54)	0.31 (0.04 - 0.58)
<i>SDAI/CDAI subgroup*</i>	0.01 (-0.15 - 0.16)	0.27 (0.03 - 0.52)	0.27 (0.02 - 0.52)
<i>Boolean remission subgroup*</i>	-0.08 (-0.31 - 0.14)	NA	NA
Improvement mean SDAI/CDAI	1.42 (-4.29 - 7.14)	3.97 (-4.04 - 11.99)	2.55 (-5.84 - 10.94)
Improvement mean HAQ	0.18 (-0.05 - 0.42)	-0.18 (-0.56 - 0.21)	-0.36 (-0.76 - 0.04)
Improvement in progression in mean SHS per year (log transformed)	-0.34 (-0.80 - 0.11)	NA	NA

*The subgroups refer to the type of reported outcome measure. ACR: American College of Rheumatology, CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index, SHS: Sharp/ van der Heijde score.

Supplemental table S9: effect of treatment target on clinical and radiographic outcome measures after 2-3 years of T2T with 95% CI, based on univariate models.

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Improvement mean DAS28-ESR	0.40 (-0.45 - 1.24)	0.71 (-0.55 - 1.97)	0.32 (-0.91 - 1.54)
Proportion DAS-remission	-0.03 (-0.22 - 0.16)	0.11 (-0.22 - 0.43)	0.14 (-0.20 - 0.47)
<i>DAS-ESR subgroup (28 or 44)*</i>	0.12 (-0.08 - 0.32)	0.27 (0.00 - 0.53)	0.15 (-0.09 - 0.40)
Proportion SDAI/CDAI/Boolean remission	0.02 (p=0.66)	0.31 (p<0.0001)	0.29 (0.15 - 0.43)
<i>CDAI/SDAI subgroup *</i>	0.03 (-0.07 - 0.13)	0.31 (0.16 - 0.45)	0.28 (0.15 - 0.41)
Improvement mean HAQ	0.03 (-0.31 - 0.37)	NA	NA
Improvement in progression in mean SHS per year (log transformed)	-0.33 (-0.62 - 0.06)	NA	NA

*The subgroups refer to the type of reported outcome measure. CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index, SHS: Sharp/ van der Heijde score.

Supplemental table S10: effect of treatment target on clinical and radiographic outcome measures after 4-6 years of T2T with 95% CI, based on univariate models.

Target Outcome	DAS-remission vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-LDA	SDAI/CDAI-LDA vs. DAS-remission
Proportion DAS-remission*	0.06 (-0.43 - 0.55)	NA	NA

*According to any of the DAS-variants (e.g. 28/44 joints, ESR/CRP). CDAI: clinical disease activity index, CI: confidence interval, CRP: C-reactive protein, DAS: disease activity score, based on either a 28- or 44 joint count and either on CRP or ESR, ESR: erythrocyte sedimentation rate, LDA: low disease activity, SDAI: simplified disease activity index.

Supplemental table S11: subgroup analyses of cohort studies vs. RCT showing the effect of treatment target on clinical outcome measures with 95% CI, based on parsimonious models.

Target Outcome	Target (compared to DAS-LDA)	Cohort studies	RCTs
Improvement mean DAS28-ESR, year 1	DAS-remission	0.40 (-0.17 - 0.97)	0.27 (-0.37 - 0.91)
	SDAI/CDAI LDA	0.58 (-0.42 - 1.57)	-0.34 (-1.48 - 0.81)
Proportion DAS-remission, year 1	DAS-remission	0.15 (-0.02 - 0.31)	0.10 (-0.10 - 0.30)
	SDAI/CDAI LDA	0.41 (0.10 - 0.71)	-0.06 (-0.41 - 0.30)
Proportion DAS-remission, year 2-3	DAS-remission	0.12 (-0.18 - 0.42)	-0.11 (-0.89 - 0.68)
	SDAI/CDAI LDA	0.20 (-0.15 - 0.54)	NA
Improvement mean HAQ, year 1	DAS-remission	0.14 (-0.15 - 0.43)	-0.06 (-0.15 - 0.04)
	SDAI/CDAI LDA	NA	-0.11 (-0.27 - 0.04)
Improvement mean HAQ, year 2-3	DAS-remission	0.13 (-0.08 - 0.34)	-0.11 (-0.78 - 0.57)
	SDAI/CDAI LDA	NA	NA

Proportion SDAI/CDAI/Boolean remission, year 1	DAS-remission	-0.02 (0.89)	0.04 (-0.21 – 0.28)
	SDAI/CDAI LDA	0.38 (0.07 – 0.68)	NA
Proportion SDAI/CDAI/Boolean remission, year 2-3	DAS-remission	-0.28 (-0.42 – -0.14)	0.10 (-0.01 – 0.20)
	SDAI/CDAI LDA	0.05 (-0.10 – 0.20)	-0.05 (-0.15 – 0.05)

CDAI: Clinical Disease Activity Index, CI: confidence interval, DAS: Disease Activity Score, ESR: erythrocyte sedimentation rate, HAQ: Health Assessment Questionnaire, LDA: low disease activity, RCT: randomized controlled trial, SDAI: Simplified Disease Activity Index

Supplemental table S12: sensitivity ‘leave-one-out’ analyses using parsimonious models.

Outcome [target vs. DAS-LDA]	Original coefficient parsimonious model	Minimum coefficient leave-one- out analysis	Maximum coefficient leave-one-out analysis
Improvement in mean DAS28-ESR year 1 [DAS remission]	0.27 (p=0.24)	0.14 (p=0.58)	0.40 (p=0.09)
Improvement in mean DAS28-ESR year 1 [SDAI/CDAI LDA]	0.43 (p=0.22)	0.34 (p=0.31)	0.57* (p=0.03)
Improvement in mean DAS28-ESR year 2-3 [DAS remission]	0.67 (p=0.12)	0.50 (p=0.41)	0.81 (p=0.06)
Improvement in mean DAS28-ESR year 2-3 [SDAI/CDAI LDA]	0.31 (p=0.66)	-0.03 (p=0.98)	0.55 (p=0.55)
Increase in % DAS-remission year 1 [DAS remission]	0.09 (p=0.11)	0.08 (p=0.19)	0.12 (p=0.05)
Increase in % DAS-remission year 1 [SDAI/CDAI LDA]	0.21* (p=0.04)	0.16 (p=0.11)	0.23* (p=0.03)
Increase in % DAS-remission year 2-3 [DAS remission]	0.21* (p=0.03)	0.17* (p=0.003)	0.37* (p=0.03)
Increase in % DAS-remission year 2-3 [SDAI/CDAI LDA]	0.29* (p=0.04)	0.21* (p=0.009)	0.38* (p=0.02)
Increase in % DAS-remission year 4-6 [DAS-remission]	0.10 (p=0.53)	0.00 (p=0.99)	0.21 (p=0.20)
Improvement in mean SDAI/CDAI year 1 [DAS remission]	-3.05 (p=0.06)	-4.72* (p=0.04)	1.12 (p=0.87)
Improvement in mean SDAI/CDAI year 1 [SDAI/CDAI LDA]	2.03 (p=0.23)	-2.80 (p=0.72)	5.56* (p<0.0001)
Increase in % SDAI/CDAI/Boolean remission year 1 [DAS remission]	-0.01 (p=0.85)	-0.04 (p=0.60)	0.02 (p=0.78)
Increase in % SDAI/CDAI/Boolean remission year 1 [SDAI/CDAI LDA]	0.40* (p=0.02)	0.29 (p=0.10)	0.52* (p=0.005)
SDAI/CDAI Boolean rem year 2-3 [DAS-remission]	-0.05 (p=0.26)	-0.08 (p=0.19)	-0.01 (p=0.79)
SDAI/CDAI Boolean rem year 2-3 [SDAI/CDAI LDA]	0.31* (p=0.0002)	0.26* (p=0.02)	0.40* (p=0.006)
Mean HAQ year 1 [DAS-remission]	0.00 (p=0.99)	-0.02 (p=0.66)	0.03 (p=0.60)
Mean HAQ year 1 [SDAI/CDAI LDA]	-0.03 (p=0.73)	-0.09 (p=0.24)	-0.01 (p=0.90)
Mean HAQ year 2-3 [DAS-remission]	0.02 (p=0.87)	-0.03 (p=0.85)	0.07 (p=0.71)

In the leave-one-out analyses, each analysis is performed numerous times, excluding one arm at each analysis to assess the influence of individual arms. Leave-one-out analyses for the outcome improvement in yearly SHS progression could not be performed as the model could not achieve convergence in this analysis.

CDAI: clinical disease activity index, DAS: disease activity score based on 28/44 joints, ESR: erythrocyte sedimentation rate, HAQ: health assessment questionnaire, LDA: low disease activity, SDAI: simplified disease activity index