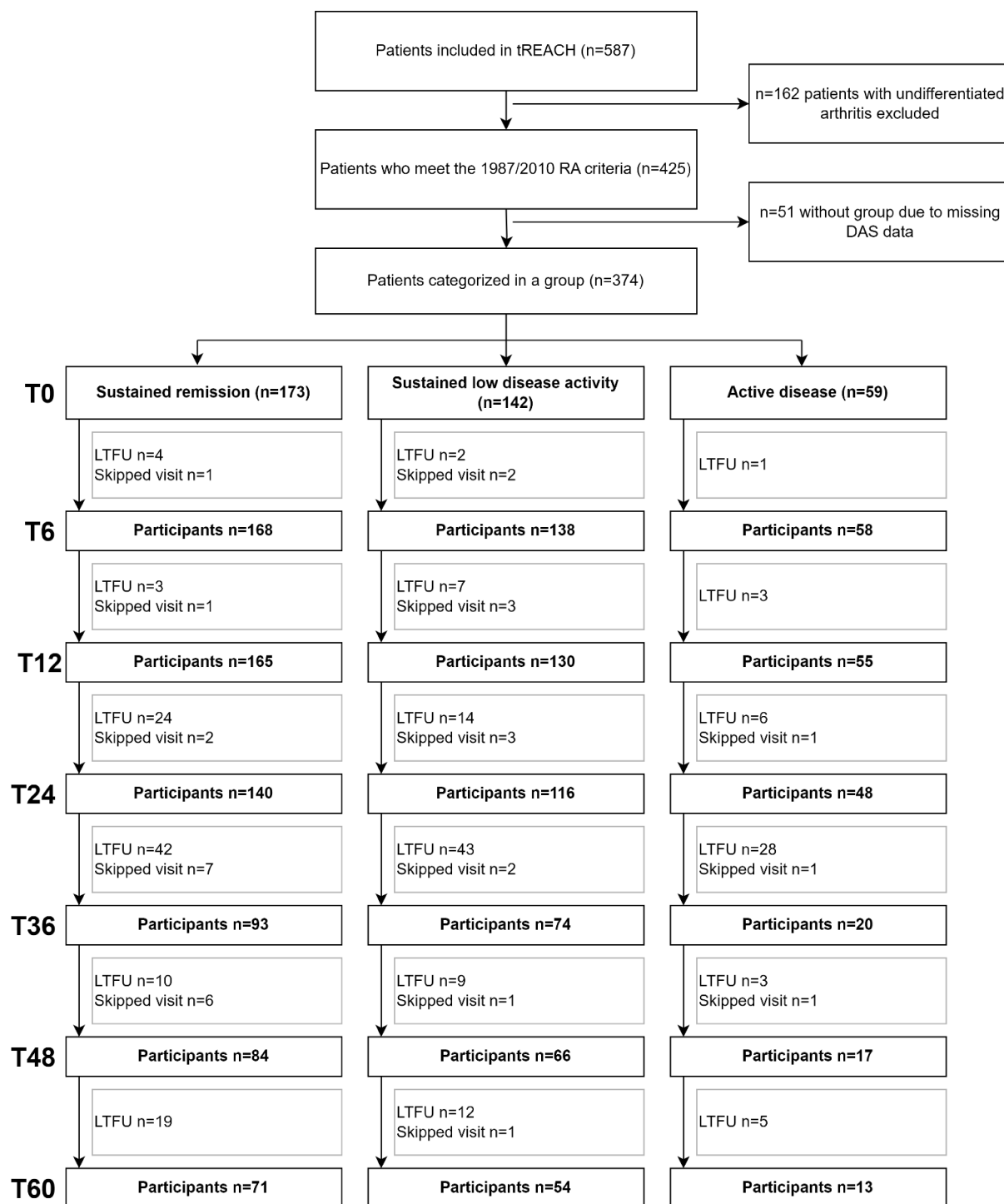


SUPPLEMENTARY MATERIALS



Supplementary Figure S1. Flowchart of disease activity groups
Results are shown as number of patients. *Abbreviation: LTFU, loss to follow-up.*

Supplementary Table S1. Estimated mean differences in patient-reported outcomes during follow-up (1-5 years) for differently defined disease activity groups

	Sustained remission (n=95)	Sustained low disease activity (n=56)		Active disease (n=59)			
		β	(95% CI)	Bonferroni corrected <i>p</i> -value ^a	β	(95% CI)	Bonferroni corrected <i>p</i> -value ^a
Pain (Likert scale 0-10)	Ref	0.37	(-0.13, 0.86)	1	1.49	(0.90, 2.07)	<0.0001
Fatigue (VAS)	Ref	9.43	(2.35, 16.51)	0.063	19.71	(11.77, 27.65)	<0.0001
Functional ability (HAQ-DI)	Ref	0.18	(0.03, 0.32)	0.11	0.60	(0.44, 0.76)	<0.0001
PCS (SF-36)	Ref	-3.05	(-5.85, -0.24)	0.23	-9.05	(-12.22, -5.88)	<0.0001
MCS (SF-36)	Ref	-2.61	(-5.25, 0.03)	0.37	-2.49	(-5.48, 0.51)	0.72
Health status (EQ-5D-3L)	Ref	-0.03	(-0.07, 0.01)	1	-0.07	(-0.12, -0.02)	0.026
Presenteeism (% productivity loss)	Ref	8.53	(1.91, 15.14)	0.080	11.60	(3.55, 19.65)	0.033

Patients were categorized in a disease activity group based on their DAS44/ESR-3 item at 6, 9 and 12 months. Sustained remission includes patients with a DAS44/ESR-3 item <1.6 after 6, 9 and 12 months. Sustained low disease activity includes patients with a DAS44/ESR-3 item 1.6-2.4 after 6 months and a DAS44/ESR-3 item \leq 2.4 after 9 and 12 months. Active disease includes patients with a DAS44/ESR-3 item >2.4 after 6 months and after 9 and/or 12 months.

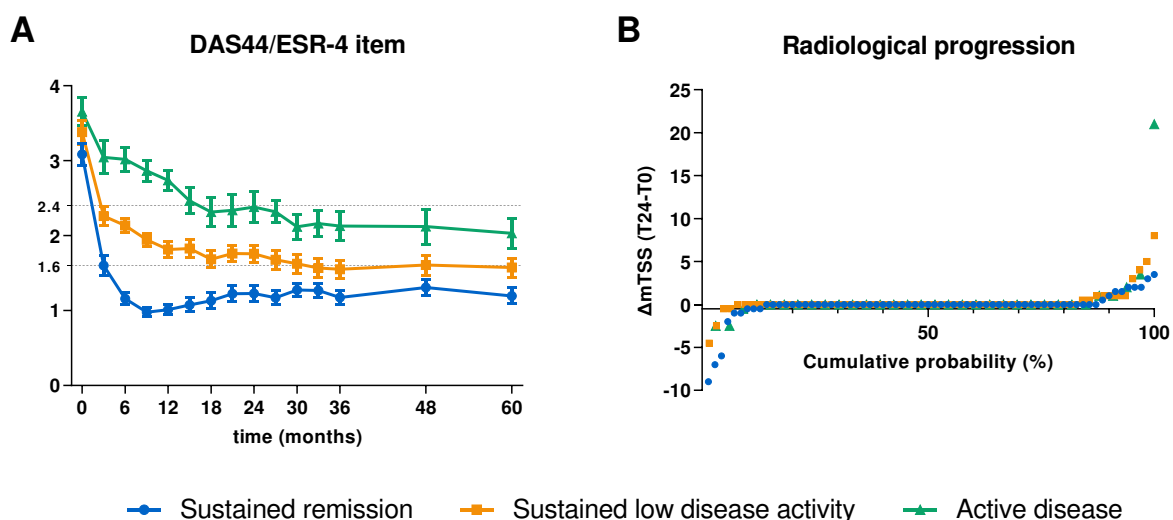
^a n=7. *p* < 0.05 was considered significant and is shown in bold.

β shows the estimated mean difference comparing the sustained remission group with the other two groups over the course of 1-5 years of follow-up. All analyses were adjusted for gender, initial treatment, and DAS44/ESR-3 item.

Abbreviations: EQ-5D-3L, European Quality of life 5-Dimensions 3-Levels; HAQ-DI, Health Assessment Questionnaire–Disability Index; Ref, reference group; SF-36, 36-item Short Form Health Survey (PCS, Physical Component Summary score and MCS, Mental Component Summary score); VAS, Visual Analogue Scale.

Supplementary Figure S2. Disease activity and radiological progression during follow-up for disease activity groups based on the DAS44/ESR-4 item

(A) DAS44/ESR-4 item during follow-up per group, (B) Cumulative probability plots of 2-year radiographic progression scores in 166 RA patients (70 patients in the sustained remission group, 63 patients in the sustained low disease activity group and 33 patients in the active disease group). Cumulative probability was calculated per group.



Supplementary Table S2. Estimated mean differences in patient-reported outcomes during follow-up (1-5 years) for disease activity groups based on the DAS44/ESR-4 item

	Sustained remission (n=171)	Sustained low disease activity (n=125)			Active disease (n=68)		
		β	(95% CI)	Bonferroni corrected <i>p</i> -value ^a	β	(95% CI)	Bonferroni corrected <i>p</i> -value ^a
Pain (Likert scale 0-10)	Ref	0.81	(0.45, 1.16)	<0.0001	1.17	(0.69, 1.64)	<0.0001
Fatigue (VAS)	Ref	12.19	(7.35, 17.02)	<0.0001	16.50	(10.20, 22.81)	<0.0001
Functional ability (HAQ-DI)	Ref	0.27	(0.16, 0.37)	<0.0001	0.56	(0.42, 0.69)	<0.0001
PCS (SF-36)	Ref	-4.38	(-6.34, -2.43)	<0.0001	-8.02	(-10.56, -5.48)	<0.0001
MCS (SF-36)	Ref	-2.74	(-4.69, -0.80)	0.042	-2.15	(-4.68, 0.38)	0.67
Health status (EQ-5D-3L)	Ref	-0.05	(-0.08, -0.02)	0.010	-0.08	(-0.12, -0.05)	0.0002
Presenteeism (% productivity loss)	Ref	6.56	(1.45, 11.66)	0.083	10.38	(3.39, 17.38)	0.025

Patients were categorized in a disease activity group based on their DAS44/ESR-4 item at 6, 9 and 12 months. Sustained remission includes patients with a mean DAS44/ESR-4 item <1.6 between 6 and 12 months and whose DAS44/ESR-4 item was never >2.4. Sustained low disease activity includes patients with a mean DAS44/ESR-4 item between 1.6 and 2.4 between 6 and 12 months. Active disease includes patients with a mean DAS44/ESR-4 item >2.4 between 6 and 12 months and whose DAS44/ESR-4 item was never <1.6.

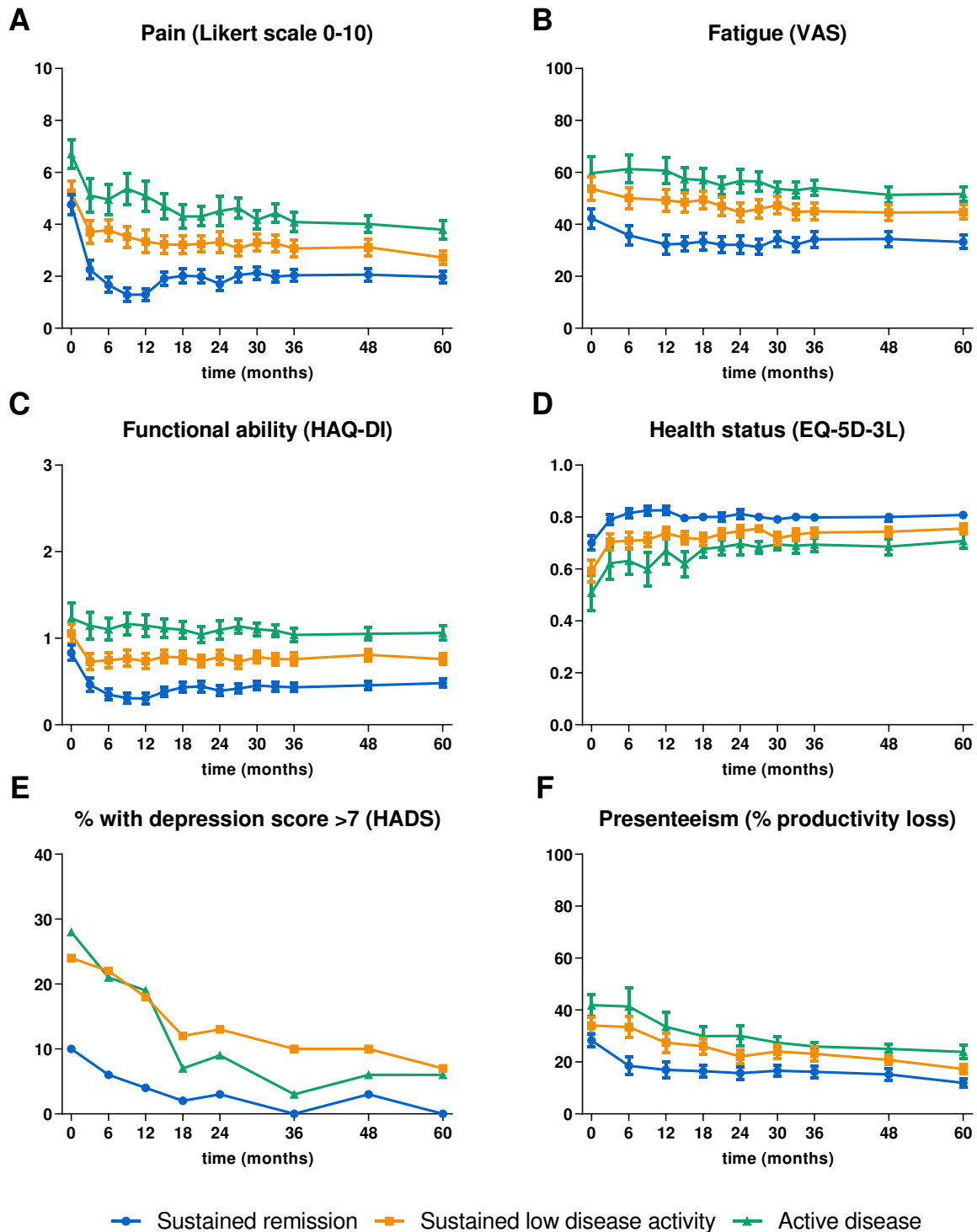
^a n=7. *p* < 0.05 was considered significant and is shown in bold.

β shows the estimated mean difference comparing the sustained remission group with the other two groups over the course of 1-5 years of follow-up. All analyses were adjusted for gender, initial treatment, and DAS44/ESR-4 item.

Abbreviations: EQ-5D-3L, European Quality of life 5-Dimensions 3-Levels; HAQ-DI, Health Assessment Questionnaire–Disability Index; Ref, reference group; SF-36, 36-item Short Form Health Survey (PCS, Physical Component Summary score and MCS, Mental Component Summary score); VAS, Visual Analogue Scale.

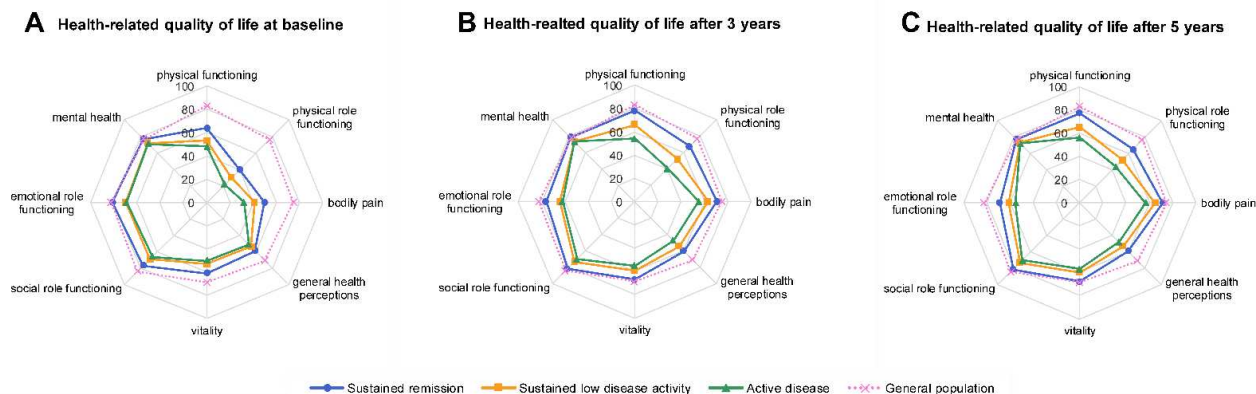
Supplementary Figure S3. Patient-reported outcomes over 5 years of follow-up for disease activity groups based on the DAS44/ESR-4 item

(A) Pain, **(B)** Fatigue, **(C)** Functional ability, **(D)** Health status, **(E)** % of patients with a depression score >7, and **(F)** Presenteeism during follow-up per group. Presenteeism is measured on a 0-100% productivity loss scale, where 0 indicates no impairment and 100 indicates complete impairment. All graphs represent the mean with 95% confidence interval.



Supplementary Figure S4. Health-related quality of life for disease activity groups based on the DAS44/ESR-4 item and the general Dutch population

(A) Mean health-related quality of life scores at baseline, (B) after 3 years, and (C) after 5 years, measured with the short form-36, stratified for disease activity groups based on the DAS44/ESR-4 item and compared with the general Dutch population norms.



Supplementary Table S3. Crude estimates of patient-reported outcomes after 3 and 5 years stratified for disease activity groups based on the DAS44/ESR-3 item

PROs	Time	Sustained remission (n=173)	Sustained low disease activity (n=142)	Active disease (n=59)
Pain (Likert scale 0-10) <i>MCID ≥1</i>	T36	1 (0-2)	2 (1-5)	4 (2-7)
	T60	1 (0-4)	3 (1-5)	4 (2-6)
Fatigue (VAS) <i>MCID ≥10</i>	T36	30.9 (26.9)	44.1 (25.4)	53.3 (19.9)
	T60	32.6 (27.0)	48.3 (24.4)	56.7 (17.2)
Functional ability (HAQ-DI) <i>MCID ≥0.22</i>	T36	0.13 (0.00-0.63)	0.63 (0.25-1.13)	1.31 (1.00-1.50)
	T60	0.25 (0.00-0.75)	0.75 (0.25-1.13)	1.38 (1.25-1.63)
PCS (SF-36) <i>MCID ≥3-5</i>	T36	47.0 (9.1)	41.9 (9.5)	32.9 (10.2)
	T60	46.7 (8.9)	41.1 (9.9)	33.9 (8.2)
MCS (SF-36) <i>MCID ≥3-5</i>	T36	56.7 (6.7)	51.3 (11.5)	57.4 (9.9)
	T60	56.7 (7.1)	52.1 (10.1)	53.7 (9.2)
Health status (EQ-5D-3L) <i>MCID ≥0.04</i>	T36	0.83 (0.10)	0.75 (0.16)	0.76 (0.16)
	T60	0.82 (0.10)	0.73 (0.22)	0.75 (0.17)
Presenteeism (% productivity loss)	T36	13.1 (17.3)	16.8 (21.1)	15.0 (10.0)
	T60	10.3 (16.8)	12.4 (16.1)	30.0 (26.5)

Results are shown as mean (standard deviation) or median (interquartile range).

Abbreviations: EQ-5D-3L: European Quality of life 5-Dimensions 3-Levels; HAQ-DI, Health Assessment Questionnaire–Disability Index; SF-36, 36-item Short Form Health Survey (PCS, Physical Component Summary score and MCS, Mental Component Summary score); VAS: Visual Analogue Scale.

Supplementary Table S4. Residual disease activity for disease activity groups based on the DAS44/ESR-3 item at 1, 3 and 5 years

	1 year			3 years			5 years		
	Sustained remission (n=165)	Sustained low disease activity (n=130)	Active disease (n=55)	Sustained remission (n=93)	Sustained low disease activity (n=74)	Active disease (n=20)	Sustained remission (n=71)	Sustained low disease activity (n=54)	Active disease (n=13)
DAS ≤2.4	165 (100)	113 (87)	21 (38)	87 (94)	64 (86)	9 (45)	64 (90)	40 (74)	9 (69)
DAS <1.6	139 (84)	41 (32)	0 (0)	71 (76)	44 (59)	5 (25)	51 (72)	29 (54)	4 (31)
SJC44 >0	41 (25)	58 (45)	40 (73)	26 (28)	21 (28)	10 (50)	19 (27)	12 (22)	7 (54)
TJC53 >0	46 (28)	98 (75)	55 (100)	28 (30)	44 (59)	17 (85)	26 (37)	30 (56)	13 (100)
ESR elevated	19 (12)	23 (18)	17 (31)	14 (15)	11 (15)	6 (30)	13 (18)	7 (13)	4 (31)

n (%) of patients with residual disease activity. Low disease activity is defined as a DAS44/ESR-3 item ≤2.4, and remission is defined as a DAS44/ESR-3 item <1.6. An ESR of ≥20 (females) or ≥15 (males) was considered elevated in patients ≤50 years, while an ESR of ≥30 (females) or ≥20 (males) was considered elevated in patients >50 years.

Abbreviations: DAS: disease activity score with 3 items (swollen joint count 44 (SJC44), tender joint count 53 (TJC53), erythrocyte sedimentation rate (ESR)).