Supplementary table 3. Summary of studies on therapeutic strategies for RA patients with predominantly non-inflammatory complaints

1st Author, publication year	Study design	Patients (total n)	General description of RA population	Disease duration of RA (mean)	Disease activity at baseline (mean (SD))	Non-inflammatory complaints at baseline HAQ (mean (SD))	VAS-pain (mean (SD))	VAS-fatigue (mean (SD))	EQ-5D (mean (SD))	Other	Intervention group Description	n	Comparator Description	n	Outcome Description	Time point^1	Number and percentage of responders in intervention group	Number and percentage of responders in control group	OR (95% CI)	Risk ratio (95% CI)	Risk Difference (95% CI)	Mean outcome in intervention group (SD)	Mean outcome in control group (SD)	Mean difference (standard error, 95% CI)	p-value	Effect size (cohen's d)	Other	Risk of bias^2	Risk of bias of individual studies included in SLR^3
EXEROSE																												
Function (HAQ)																												
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Joint protection		Alternative intervention/no intervention		Pain and function										Improves function, no difference in pain, high-quality benificial effect		High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.	Low	Moderate-High
											Comprehensive occupation therapy		No intervention		Pain and function										Improves function, no difference in pain, low quality evidence				
											Exercise		No intervention/alternative intervention/different types of exercises		Pain and function										Reduces pain and improves function, no difference in patient global assessment, low quality evidence				
Eversden, 2007	RCT	115	RA patients	9Y	NR	1.38-1.50, range of medians	24-26.5, range of medians	NR	0.69	NA	Hydrotherapy (30min, 1/W)	57	Similar exercises on land (30min, 1/W)	58	HAQ	6W						1.50 (1.06-1.84), median (IQR)	1.44 (0.78-1.84), median (IQR)		ns			High	
Figen, 2011	RCT	60	RA patients with disease duration >1Y	8.5Y	DAS28 5.2	2.8 (intervention 3.9; control 1.5; p=0.001)	NR	NR	NR	NA	Inpatient rehabilitation model (15 sessions during 3W of hospitalisation)	32	Home exercise model (same exercises as intervention group, although at home)	28	HAQ	NR						1 (0.7)	0.7 (0.6)		p=0.001, adjusted for baseline	0.46		High	
Hurkmans, 2009	SLR: RCTs 8	575	RA patients	NR	Low to moderate	NR	NR	NR	NR	NA	Short-term land-based aerobic capacity training and muscle strength training	50 (1 study)	NR		Functional ability (HAQ)							0.54 SDs lower	-0.16				Based on the evidence, aerobic capacity training combined with muscle strength training is recommended as routine practice in patients with RA.	Low	Moderate-High
											Short-term water-based aerobic capacity training		NR		Functional ability and aerobic capacity										Limited evidence for a positive effect				
Lee, 2007	SLR: RCTs 2; Non-RCTs 3	382	RA patients	NR	NR	NR	NR	NR	NR	NA	Tai chi	(2 studies)	Education plus stretching exercises/Usual activity		Functional index										Improvement in RCT; No improvement in non-RCT		Collectively this evidence is not convincing enough to suggest that tai chi is an effective treatment for RA.	Moderate	High
Macedo, 2009	RCT	32	RA patients with medium or high work disability risk on the RA WIS	10Y	DAS28 4.55	1.38	52.69	NR	0.55	NA	Occupational therapy (6-8 sessions of 30-120min)	16	Usual care	16	HAQ-DI	Change from BL until 6M						-0.27 (0.49)	0.17 (0.51)		p=0.02	0.88		High	
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Multicomponent or single exercise/physical activity inteventions	1384 (#2)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Functional disability	NR											Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Siqueira, 2017	RCT	100	Women with RA	8.5Y	NR	0.7	NR	NR	NR	Right knee flexor muscle strength 43,7 Nm; Left knee flexor muscle strengt 42 .5Nm; Right knee extensor muscle strength 88.3Nm; Left knee extensor muscle strength 88.6Nm	Waterbased aerobic exercise (3/W)	33	Usual care	34	HAQ	16W						0.4 (0.4)	1.3 (1.7)		p=0.002	0.73		High	
											Land-based aerobic exercise (3/W)	33	Usual care	34	HAQ	16W						0.8 (0.6)	1.3 (1.7)		p=0.002	0.39			
Pain (VAS-pain)																												
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Joint protection		Alternative intervention/no intervention		Pain and function										Improves function, no difference in pain, high-quality benificial effect		High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.	Low	Moderate-High
											Comprehensive occupation therapy		No intervention		Pain and function										Improves function, no difference in pain, low quality evidence				
											Exercise		No intervention/alternative intervention/different types of exercises		Pain and function										Reduces pain and improves function, no difference in patient global assessment, low quality evidence				
Eversden, 2007	RCT	115	RA patients	9Y	NR	1.38-1.50, range of medians	24-26.5, range of medians	NR	0.69	NA	Hydrotherapy (30min, 1/week)	57	Similar exercises on land (30min, 1/W)	58	VAS-pain	6W						25.5 (11-41), median (IQR)	27.5 (15-58), median (IQR)		ns			High	
Felkthusen, 2016	RCT	70	RA patients with DAS28<3.8, VAS-fatigue >50 (0-100) and disease duration >3Y	10Y	DAS28 3.35	0.7	39.8	68.2	NR	NA	Person-centered physical therapy (a self-care plan was jointly developed and focused on tailoring health-enhancing physical activity, and balancing life activities)	36	Usual physical and social activities	34	VAS-pain	Change from BL until 12W						-4.8 (18.4)	-1.1 (24.6)		p=0.46	0.12		High	
Hurkmans, 2009	SLR: RCTs 8	575	RA patients	NR	low to moderate	NR	NR	NR	NR	NA	Short-term land-based aerobic capacity training		NR		Aerobic capacity											Pooled effect size 0.99 (95%CI 0.29-1.68)	Based on the evidence, aerobic capacity training combined with muscle strength training is recommended as routine practice in patients with RA.	Low	Moderate-High
											Short-term land-based aerobic capacity training and muscle strength training	50 (1 study)	NR		Self-reported pain (VAS 0-10)						0.53 SDs lower	0.9						
Lee, 2007	SLR: RCTs 2; Non-RCTs 3	382	RA patients	NR	NR	NR	NR	NR	NR	NA	Tai chi	(3 studies)	Education plus stretching exercises/Usual activity		Pain										No significant pain reduction in 2 RCTs; significant pain reduction in non-RCT		Collectively this evidence is not convincing enough to suggest that tai chi is an effective treatment for RA.	Moderate	High
Macedo, 2009	RCT	32	RA patients with medium or high work disability risk on the RA WIS	10Y	DAS28 4.55	1.38	52.69	NR	0.55	NA	Occupational therapy (6-8 sessions of 30-120min)	16	Usual care	16	VAS-pain	Change from BL until 6M						-25.31 (24.22)	-1.13 (22.98)		p=0.007	1.02		High	

Manning, 2014	RCT	210	RA patients	20M	DAS28 5.1	NR	45.2	47.2	NR		Group session with education, self-management and global upper extremity exercise training (4 times 2/W), then functional daily home exercise regimen	52	Usual care	56	VAS-pain	Change from BL until 12W	−13.0 (−23.0, −2.9), mean (95% CI)	1.7 (−8.2, 11.6), mean (95% CI)	−14.7 (−26.2, −3.2), mean (95% CI)	p= 0.013				High	
Macfarlane, 2012	SLR: RCTs 11	672	RA patients receiving complementary therapy	NR	NR	NR	NR	NR	NR	NA	Tai chi	10 (1 study)	Stretching and wellness education	10	Pain					ns			No good evidence of efficacy or effectiveness for the practitioner-based complementary therapies considered here.	Moderate	Moderate
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Multicomponent or single exercise/physical activity inteventions	545 (#2)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Pain	NR							Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Williams, 2018	SLR: RCTs 7	841	RA patients	NR	NR	NR	NR	NR	NR	NA	Hand exercises	124 (2 studies)	No exercise		VAS-pain	<3M	95.58	67.6					It is uncertain whether exercise improves hand function or painin the short term. It probably slightly improves function buthas littleor no difference on pain in the medium and long term. It is uncertain whether exercise improves grip and pinch strength in the shortterm, and probably has little or no difference in the medium and long term. The ACR50 response is unknown. People who received exercise with adherence strategies were probably more adherent in the medium term than who did not receive exercise, but with little or no difference in the long term.	Low	High
												445 (1 study)	No exercise		Pain subscale MHQ	3-11M	54.2	51.4						
												437 (1 study)	No exercise		Pain subscale MHQ	≥12M	55.1	51.4						
QoL (EQ-5D)																									
Eversden, 2007	RCT	115	RA patients	9Y	NR	1.38-1.50, range of medians	24-26.5, range of medians	NR	0.69	NA	Hydrotherapy (30min, 1/week)	57	Similar exercises on land (30min, 1/W)	58	EQ-5D	6W	0.69 (0.59-0.78), median (IQR)	0.68 (0.59-0.79), median (IQR)		ns				High	
Lee, 2007	SLR: RCTs 2; Non-RCTs 3	382	RA patients	NR	NR	NR	NR	NR	NR	NA	Tai chi	(1 study)	Education plus stretching exercises		Quality of life					Improvement on vitality subscale of SF36			Collectively this evidence is not convincing enough to suggest that tai chi is an effective treatment for RA.	Moderate	High
Macedo, 2009	RCT	32	RA patients with medium or high work disability risk on the RA WIS	10Y	DAS28 4.55	1.38	52.69	NR	0.55	NA	Occupational therapy (6-8 sessions of 30-120min)	16	Usual care	16	EQ-5D	Change from BL until 6M	0.13 (0.29)	-0.15 (0.33)		p=0.02	0.90			High	
Fatigue (VAS-fatigue)																									
Feldthusen, 2016	RCT	70	RA patients with DAS28<3.8, VAS-fatigue >50 (0-100) and disease duration >3Y	10Y	DAS28 3.35	0.7	39.8	68.2	NR	NA	Person-centered physical therapy (a self-care plan was jointly developed and focused on tailoring health-enhancing physical activity, and balancing life activities)	36	Usual physical and social activities	34	VAS-fatigue	Change from BL until 12W	-23.5 (19.9)	-15.3 (24.6)		p=0.042	0.37			High	
Lee, 2007	SLR: RCTs 2; Non-RCTs 3	382	RA patients	NR	NR	NR	NR	NR	NR	NA	Tai chi	(2 studies)	Usual activity	NR	Fatigue					No improvement in RCT; Suggested effectiveness in non-RCT			Collectively this evidence is not convincing enough to suggest that tai chi is an effective treatment for RA.	Moderate	High
Manning, 2014	RCT	210	RA patients	20M	DAS28 5.1	NR	45.2	47.2	NR	NA	Group session with education, self-management and global upper extremity exercise training (4 times 2/W), then functional daily home exercise regimen	52	Usual care	56	VAS-fatigue	Change from BL until 12W	−7.9 (−18.3, 2.6), mean (95% CI)	1.2 (−9.2, 11.5), mean (95% CI)	−9.0 (−21.0, 2.9), mean (95% CI)	p= 0.136				High	
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Multicomponent or single exercise/physical activity inteventions	628 (#2)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Fatigue	NR							Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Disease activity																									
Feldthusen, 2016	RCT	70	RA patients with DAS28<3.8, VAS-fatigue >50 (0-100) and disease duration >3Y	10Y	DAS28 3.35	0.7	39.8	68.2	NR	NA	Person-centered physical therapy (a self-care plan was jointly developed and focused on tailoring health-enhancing physical activity, and balancing life activities)	36	Usual physical and social activities	34	DAS28	Change from BL until 12W	-0.3 (0.9)	-0.3 (1.0)		p=1.00	0			High	
Figen, 2011	RCT	60	RA patients with disease duration >1Y	8.5Y	DAS28 5.2	2.8 (intervention 3.9; control 1.5; p=0.001)	NR	NR	NR	NA	Inpatient rehabilitation model (15 sessions during 3W of hospitalisation)	32	Home exercise model (same exercises as intervention group, although at home)	28	DAS28	NR	4.1 (1.3)	4.1 (1.2)		p=0.001, adjusted for baseline	0			High	
Macedo, 2009	RCT	32	RA patients with medium or high work disability risk on the RA WIS	10Y	DAS28 4.55	1.38	52.69	NR	0.55	NA	Occupational therapy (6-8 sessions of 30-120min)	16	Usual care	16	DAS28	Change from BL until 6M	-0.94 (1.32)	0.11 (1.21)		p=0.03	0.83			High	
Manning, 2014	RCT	210	RA patients	20M	DAS28 5.1	NR	45.2	47.2	NR	NA	Group session with education, self-management and global upper extremity exercise training (4 times 2/W), then functional daily home exercise regimen	52	Usual care	56	DAS28	Change from BL until 12W	−0.8 (−1.4, −0.2), mean (95% CI)	−0.1 (−0.7, 0.4), mean (95% CI)	0.7 (−1.4, 0.0), mean (95% CI)	p= 0.047				High	
Siqueira, 2017	RCT	100	Women with RA	8.5Y	NR	0.7	NR	NR	NR	Right knee flexor muscle strength 43,7 Nm; Left knee flexor muscle strengt 42. 5Nm; Right knee extensor muscle strength 88.3Nm; Left knee extensor muscle strength 88.6Nm	Waterbased aerobic exercise (3/W)	33	Usual care	34	DAS28	16W	3.1 (1)	4.2 (0.9)		p=0.0001	1.16			High	
											Land-based aerobic exercise (3/W)	33	Usual care	34	DAS28	16W	3.6 (1.2)	4.2 (0.9)		p=0.0001	0.57			High	
Other																									
Hurkmans, 2009	SLR: RCTs 8	575	RA patients	NR	Low to moderate	NR	NR	NR	NR	NA	Short-term land-based aerobic capacity training		NR		Aerobic capacity						Pooled effect size 0.99 (95%CI 0.29-1.68)	Based on the evidence, aerobic capacity training combined with muscle strength training is recommended as routine practice in patients with RA.	Low	Moderate-High
											Short-term land-based aerobic capacity training and muscle strength training		NR		Aerobic capacity and muscle strength					Pooled effect size 0.47 (95%CI 0.0-0.93)				
												74 (2 studies)	NR		Muscle strength		0.47 SDs higher	-2.7 nM							
											Short-term water-based aerobic capacity training		NR		Functional ability and aerobic capacity					Limited evidence for a positive effect				

											Long-term land-based aerobic capacity and muscle strength training			NR			Aerobic capacity and muscle strength						Moderate evidence for a positive effect						
Lau, 2019	RCT	21	RA patients	NR	NR	NR	NR	NR	NR	Weighted RAID 2.99	Neural mobilisation exercises (targeting the median, musculocutaneous, femoral and saphenous nerve, as wel as entire nervous system, 2/D)		11	Control (gentle joint mobilisation exercises targeting the same joints)	10	Weighted RAID	Change from BL until post-treatment		-0.79	-0.15		p=0.65						High		
Lee, 2007	SLR: RCTs 2; Non-RCTs 3	382	RA patients	NR	NR	NR	NR	NR	NR	NA	Tai chi		(2 studies)	Usual activity		Range of motion and joint functions						No improvement		Collectively this evidence is not convincing enough to suggest that tai chi is an effective treatment for RA.				Moderate	High		
													(2 studies)	Education plus stretching exercises/Usual activity		Depression and mood						Improvement of depression and mood							
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Multicomponent or single exercise/physical activity inteventions		586 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Global impact of disease	NR							Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.				Moderate	Moderate		
Siqueira, 2017	RCT	100	Women with RA	8.5Y	NR	0.7	NR	NR	NR	Right knee flexor muscle strength 43,7 Nm; Left knee flexor muscle strengt 42.5Nmh; Right knee extensor muscle strength 88.3Nm; Left knee extensor muscle strength 88.6Nm	Waterbased aerobic exercise (3/W)		33	Usual care	34	Right knee flexor muscle strength	16W		48.8 (11.3)	42.2 (13.1)		p=0.1	0.54						High		
																Left knee flexor muscle strength	16W		44.8 (9.5)	43.1 (13.4)		p=0.64	0.15							
																Right knee extensor muscle strength	16W		95.5 (18.2)	86.0 (29.5)		p=0.2	0.39							
																Left knee extensor muscle strength	16W		88.5 (16.1)	84.7 (24.1)		p=0.8	0.18							
											Land-based aerobic exercise (3/W)		33	Usual care	34	Right knee flexor muscle strength	16W		43.6 (10.3)	42.2 (13.1)		p=0.1	0.12							
																Left knee flexor muscle strength	16W		41.9 (14.9)	43.1 (13.4)		p=0.64	0.01							
																Right knee extensor muscle strength	16W		86.3 (22.4)	86.0 (29.5)		p=0.2	0.01							
																Left knee extensor muscle strength	16W		85.3 (26.1)	84.7 (24.1)		p=0.8	0.02							
Williams, 2018	SLR: RCTs 7	841	RA patients	NR	NR	NR	NR	NR	NR	NA	Hand exercises		11 (1 study)	No exercise	13	Grip function test scale (0-80)	<3M		76.1	75				It is uncertain whether exercise improves hand function or pain in the short term. It probably slightly improves function buthas littleor no difference on pain in the medium and long term. It is uncertain whether exercise improves grip and pinch strength in the shortterm, and probably has little or no difference in the medium and long term. The ACR50 response is unknown. People who received exercise with adherence strategies were probably more adherent in the medium term than who did not receive exercise, but with little or no difference in the long term.				Low	High		
													449 (1 study)	No exercise		MHQ	3-11M		56.6	52.1										
													438 (1 study)	No exercise		MHQ	≥12M		56.4	52.1										
DIET																															
Pain (VAS-pain)																															
Cameron, 2011	SLR: RCTs 22	1278	RA patients	NR	DAS28 40-62 (range)	NR	NR	NR	NR	NA	Gamma linolenic acid (GLA) from evening primrose oil, borage seed oil, or blackcurrent seed oil		11 studies	Placebo		Pain intensity (score 0-100)				-32.83 (-,--56.25-- -9.42)				Moderate evidence that oils containing gamma linolenic acid and tripterygium wilfordii products may offer some benefit in relieving symptoms. Oral use of the latter may be associated with several side effects.				Low	Low-Moderate		
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Herbal therapy (gamma-linolenic acid)			Placebo/alternative herbal intervention								Reduces pain and patient global assessment, moderate quality benificial effect		High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.				Low	Moderate-High		
											Diets			Control/usual diet		Pain						Reduces pain, low quality evidence							
Disease activity																															
Cameron, 2011	SLR: RCTs 22	1278	RA patients	NR	DAS28 40-62 (range)	NR	NR	NR	NR	NA	Tripterygium wilfordii (thunder god vine)		4 studies	Placebo/sulfasalazine		Disease activity						Improvement in some outcomes regarding disease activity; side effects in one study with oral use		Moderate evidence that oils containing gamma linolenic acid and tripterygium wilfordii products may offer some benefit in relieving symptoms. Oral use of the latter may be associated with several side effects.				Low	Low-Moderate		
											Phytodolor		2 studies	Placebo		Efficacy						Poor reporting limited data extraction							
PSYCHOLOGICAL																															
Function (HAQ)																															
Hewlett, 2019	RCT	333	RA patients with fatigue severity of ≥6 (0-10, BRAF-NRS)	10Y, median	DAS28 4.22	mHAQ 0.75	VAS-pain 5.64			Fatigue impact (BRAF-NRS, score 0-10): 7.16	RAFT– Cognitive behaviour fatigue self-management programme delivered to groups of 5–7 RA patients in six 2-hour sessions (weeks 1–6) and a 1-hour consolidation session (week 14) by a pair of local rheumatology nurse specialists and/or occupational therapists		156	Usual care: brief discussion of a RA fatigue self-management booklet with the research nurse.	152	mHAQ	26W		0.70 (0.54)	0.71 (0.51)	Adjusted: 0.02 (-0.06-0.10, p=0.67)		0.02	Adjusted for baseline level and centre				High			

Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Psychosocial interventions	1180 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Functional disability	NR							Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Pain (VAS-pain)																								
Dixon, 2007	SLR: RCTs 27 (18 RA, 7 OA, 2 mixed)	3409	RA and OA patients in whom psychosocial approaches to arthritis pain management and pain-related outcomes were reviewed.	NR	NR	NR	NR	NR	NR	NA	Psychological interventions (Cognitive behavioral therapy (23 studies), stress management (5 studies), psychodynamic intervention (2 studies), biofeedback (1 study), emotional disclosure (1 study), hypnosis (1 study)	NR	Control (usual care (14 studies), education/information control (9 studies), wait-list control (5 studies), attention control (2 studies), receiving only study medication (1 study)	NR	Pain (15 studies)						Effect size 0.177 (95% CI 0.094-0.259), p=0.01, favours treatment; Effect sizes were similar when studies were separated into those conducted with RA vs OA patients.	These findings indicate that psychosocial interventions may have significant effects on pain and other outcomes in arthritis patients. Ample evidence for the additional benefit of such interventions over and above that of standard medical care was found.	Moderate	Low
Ferwerda, 2017	RCT	133	RA patients with elevated levels of distress as measured by heightened scores of the negative mood and anxiety scales of the IRGL	NR	NR	NR	NR	NR	NR	Depressed mood (BDI) 12.49; Negative mood (IRGL) 4.77; Anxiety (IRGL) 21.12; Pain (IRGL) 15.30; Fatigue (CIS) 37.17	Tailored-guided internet-based cognitive-behavioral treatment during 9-65W (depending on individual wishes)	62	Usual care	71	Pain (IRGL)	Post intervention (9-65W)	14.36 (4.68)	15.79 (4.13)		p=0.35	0.32			High	
Hewlett, 2019	RCT	333	RA patients with fatigue severity of ≥6 (0-10, BRAF-NRS)	10Y, median	DAS28 4.22	mHAQ 0.75	VAS-pain 5.64			Fatigue impact (BRAF-NRS, score 0-10): 7.16	RAFT– Cognitive behaviour fatigue self-management programme delivered to groups of 5–7 RA patients in six 2-hour sessions (weeks 1–6) and a 1-hour consolidation session (week 14) by a pair of local rheumatology nurse specialists and/or occupational therapists	156	Usual care: brief discussion of a RA fatigue self-management booklet with the research nurse.	152	VAS-pain	26W	5.47 (2.32)	5.24 (2.41)	Adjusted: 0.16 (-0.33-0.65, p=0.51)		0.10	Adjusted for baseline level and centre	High	
Prothero, 2018	SLR: 9 SLRs	10782	RA patients	NR	NR	NR	NR	NR	NR	NA	Psychological interventions	#5 SLRs, 49 studies	Wait-list/usual care/attention placebo/education	NR	Pain	NR							Riemsma et al. (2003)found that counselling and behaviour change interventionsdid not significantly reduce pain, however, a trend favouring behaviourchange interventions was observed. Using Cohen's classification ofeffect sizes (Cohen, 1977), the reviews byAstin et al. (2002)andKnittleet al. (2010)reported that psychological interventions had small effectson pain reduction post intervention.Astin et al. (2002)tested the effectof psychological interventions on pain at follow-up (averaged 8.5months) which was reduced to non-significance.Cramp et al. (2013)found that 4 out of 6 studies did not show significant effects for pain.Niedermann et al. (2004)found that 2 out of 4 studies showed apositive change both in the short-term (averaged 12.5 weeks) and thelong-term (averaged 10.5 months). One study, which examined theeffectiveness of cognitive behavioral therapy, showed a progressiveworsening of pain at follow-up (6 months) Thefinal study'sfindingswere non-significant post interventions and at 12-month follow-up.; Conclusion: Psychological interventions result in small to moderate improvements in biopsychosocial outcomes for patients with rheumatoid arthritis in addition to those achieved by standard care. Several priorities for futureresearch were identified, including determining the cost effectiveness of non-psychologically trained healthprofessionals delivering psychological interventions.	Low	Low-moderate
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Psychosocial interventions	1316 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Pain	NR							Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Fatigue (FACIT-F/VAS-fatigue)																								
Ferwerda, 2017	RCT	133	RA patients with elevated levels of distress as measured by heightened scores of the negative mood and anxiety scales of the IRGL	NR	NR	NR	NR	NR	NR	Depressed mood (BDI) 12.49; Negative mood (IRGL) 4.77; Anxiety (IRGL) 21.12; Pain (IRGL) 15.30; Fatigue (CIS) 37.17	Tailored-guided internet-based cognitive-behavioral treatment during 9-65W (depending on individual wishes)	62	Usual care	71	Fatigue (CIS)	Post intervention (9-65W)	32.38 (13.42)	34.45 (12.43)		p=0.06	0.16			High	
Hewlett, 2019	RCT	333	RA patients with fatigue severity of ≥6 (0-10, BRAF-NRS)	10Y, median	DAS28 4.22	mHAQ 0.75	VAS-pain 5.64			Fatigue impact (BRAF-NRS, score 0-10): 7.16	RAFT– Cognitive behaviour fatigue self-management programme delivered to groups of 5–7 RA patients in six 2-hour sessions (weeks 1–6) and a 1-hour consolidation session (week 14) by a pair of local rheumatology nurse specialists and/or occupational therapists	156	Usual care: brief discussion of a RA fatigue self-management booklet with the research nurse.	152	Fatigue impact (BRAF-NRS, 0-10)	Change from BL until 26W	-1.36	-0.88	Adjusted: '-0.59 (-1.11--0.06, p=0.03)			Adjusted for baseline level and centre	High	
Prothero, 2018	SLR: 9 SLRs	10782	RA patients	NR	NR	NR	NR	NR	NR	NA	Psychological interventions	#1 SLR, 13 studies	Wait-list/usual care/attention placebo/education	NR	Fatigue	NR							One review (Cramp et al., 2013) reported meta-analysis for fatigue based onfindings from 13 studies. The authorsfound that psychosocial interventions reduced fatigue demonstrating asmall effect. The impact of the psychosocial interventions on fatigue atfollow-up was not measured; Conclusion: Psychological interventions result in small to moderate improvements in biopsychosocial outcomesfor patients with rheumatoid arthritis in addition to those achieved by standard care. Several priorities for futureresearch were identified, including determining the cost effectiveness of non-psychologically trained healthprofessionals delivering psychological interventions.	Low	Low-moderate

Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Psychosocial interventions	1556 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Fatigue	NR						Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Disease activity																							
Prothero, 2018	SLR: 9 SLRs	10782	RA patients	NR	NR	NR	NR	NR	NR	NA	Psychological interventions	#1 SLR, 3 studies	Wait-list/usual care/attention placebo/education	NR	Disease activity	NR						Nyssen et al. (2016) found that expressive writing showed no significant effects postintervention (d =−0.02; 95% CI: =−0.37, 0.32, P = 0.89).Significant effects were, however, observed as follow-up averaged 10weeks (d =−0.61; 95%CI: −−0.96,−0.26, P < 0.001); Conclusion: Psychological interventions result in small to moderate improvements in biopsychosocial outcomesfor patients with rheumatoid arthritis in addition to those achieved by standard care. Several priorities for futureresearch were identified, including determining the cost effectiveness of non-psychologically trained healthprofessionals delivering psychological interventions.	Low	Low-moderate
Other																							
Dissanayake, 2011	SLR: RCTs 34	2021	RA patients in which any type of psychological intervention was used	NR	NR	NR	NR	NR	NR	NA	Disclosure therapy	300	Wait list, standard medical care, active control	NR	Efficacy as defined in individual studies					Consistent supportive evidence		This review shows consistent supportive evidence for the use of disclosure therapy, and CBTwith maintenance therapy as adjunct therapies in patients with RA. It also highlights methodological limitations in the current literature and the need for future research in this area.	Moderate	Low-Moderate
											Cognitive behavioural therapy - maintenance therapy throughout the follow-up period: 5	887							Consistent supportive evidence				
											Cognitive behavioural therapy - long (>6wk): 5	322							Supportive evidence in the short term but conflicting evidence for its long-term efficacy				
											Biofeedback: 2	86							Some supportive evidence				
											Counselling: 3	313							Conflicting evidence				
											Psychotherapy: 2	85							Conflicting evidence				
											Meditation and mindfulness: 2	207							Conflicting evidence				
											Cognitive behavioural therapy - short (<6wk): 6	148							Conflicting evidence				
											Relaxation therapy: 2	114							Limited evidence				
Ferwerda, 2017	RCT	133	RA patients with elevated levels of distress as measured by heightened scores of the negative mood and anxiety scales of the IRGL	NR	NR	NR	NR	NR	NR	Depressed mood (BDI) 12.49; Negative mood (IRGL) 4.77; Anxiety (IRGL) 21.12; Pain (IRGL) 15.30; Fatigue (CIS) 37.17	Tailored-guided internet-based cognitive-behavioral treatment during 9-65W (depending on individual wishes)	62	Usual care	71	Depressed mood (BDI)	Post intervention (9-65W)	8.16 (5.67)	12.27 (5.97)	0.71				High	
															Negative mood (IRGL)	Post intervention (9-65W)	2.93 (3.25)	4.54 (3.71)	0.46	p=0.01; larger improvement in intervention group				
															Anxiety (IRGL)	Post intervention (9-65W)	18.31 (5.44)	20.06 (5.78)	0.31	p<0.001; larger improvement in intervention group				
EDUCATION																							
Function (HAQ)																							
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Patient education		No intervention/usual care/other educational intervention/waiting list controls		Function and patient global assessment					Improves function and patient global assessment, high-quality benifical effect		High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.	Low	Moderate-High
Pain (VAS-pain)																							
Manning, 2014	RCT	210	RA patients	20M	DAS28 5.1	NR	45.2	47.2	NR	NA	Group session with education, self-management and global upper extremity exercise training (4 times 2/W), then functional daily home exercise regimen	52	Usual care	56	VAS-pain	Change from BL until 12W	−13.0 (−23.0, −2.9), mean (95% CI)	1.7 (−8.2, 11.6), mean (95% CI)	−14.7 (−26.2, −3.2), mean (95% CI)	p= 0.013			High	
Fatigue (VAS-fatigue)																							
Manning, 2014	RCT	210	RA patients	20M	DAS28 5.1	NR	45.2	47.2	NR	NA	Group session with education, self-management and global upper extremity exercise training (4 times 2/W), then functional daily home exercise regimen	52	Usual care	56	VAS-fatigue	Change from BL until 12W	−7.9 (−18.3, 2.6), mean (95% CI)	1.2 (−9.2, 11.5), mean (95% CI)	−9.0 (−21.0, 2.9), mean (95% CI)	p= 0.136			High	
Disease activity																							
Manning, 2014	RCT	210	RA patients	20M	DAS28 5.1	NR	45.2	47.2	NR	NA	Group session with education, self-management and global upper extremity exercise training (4 times 2/W), then functional daily home exercise regimen	52	Usual care	56	DAS28	Change from BL until 12W	−0.8 (−1.4, −0.2), mean (95% CI)	−0.1 (−0.7, 0.4), mean (95% CI)	0.7 (−1.4, 0.0), mean (95% CI)	p= 0.047			High	
Other																							
Carandang, 2016	SLR: RCTs 22	2600	RA patients, studies using symptoms of RA as primary outcomes	NR	NR	NR	NR	NR	NR	NA	Disease education, pain management, psychosocial intervention, joint protection and energy conservation, combination of educational techniques		NR		Coping skills for symptoms such as pain and fatigue					Increases		Interventions in which a combination of educational techniques is used may complement pharmacological therapies.	Moderate	Low-High
															Positive affact									
															Most other measured constructs					Increases Limited or no evidence supporting the effectiveness				
SELF-MANAGEMENT INTERVENTIONS (combination of different non-pharmacological interventions)																							
Function (HAQ)																							
Albano, 2010	SLR: 7 SLRs, 10 RCTs, 20 nRCTs	9955	RA patients	NR	NR	NR	NR	NR	NR	NA	Educational programs (aiming at increasing knowledge and improving performance) and psycho-educational programs (combining teaching intervention activities to improve coping and change behaviour)	#5	NR	NR	Functional status							Improvement in all 5 studies; Conclusion: Our study confirms that therapeutic patient education in rheumatology, delivered throughеducational or psycho-educational programs, is effective in terms of acquired knowledge, competencies and psychological improvement, whereas it brings fewer changes in health status and social well-being. The positive results are more frequently observed inshort-term than in long-term.	Moderate	High

Baxter, 2016	RCT	33	RA patients	NR	7.01Y	1.1	NR	NR	15.0	NA	Walking: instructions on a walking route with three loops, to be completed 3-4 times a week	11	Nutrition education session	22	HAQ	Change from BL until 6W	0.0 (0.6)	<0.01 (0.6)	p=0.62	0.0			High	
Hammond, 2004	RCT	328	RA patients	NR	9.5M	1.13	42.16	NR	NR	NA	Occupational therapy: Five sessions: four 1h individual treatments and one 2h group arthritis education program, with additional sessions if needed, within 6-8W.	162	Usual care	164	HAQ	Change from BL until 12M	-0.11 (95%CI -0.18- -0.03)	-0.16 (95%CI -0.25- -0.07)	p=0.39				High	
Iversen, 2010	SLR: 30 RCTs	731 (#5, RA patients)	Patients with RA, OA, fibromyaliga and other types of inflammatory arthritis.	NR	NR	NR	NR	NR	NR	NA	Self-management interventions: educational, behavioural and cognitive approaches to influence health knowledge, attitudes, beliefs and behaviours to promote independence, maintain or adjust life roles, and address the psychological impact of diseases	#5	Same intervention without partner/Usual care/Information booklets/Lifestyle management for arthritis programme/Self-help guide only	NR	Pain, function, fatigue, disease status	NR					Short-term benefits were found in four studies. Three had longer-term follow-up at 12 months, but only two showed benefits; Conclusion: Of the 30 studies identified, only 14 had follow-ups of 12 months or longer, seven of which (two of the same SMART ASMP) led to sustained benefits in pain and/or function. Little is known about benefi ts beyond 12 months as only two had longer-term follow-ups, although both showed some continuing benefits.	Moderate	Low-moderate
Knittle, 2015	RCT	78	RA patients	NR	NR	1.12	NR	NR	NR	NA	Education session plus a motivational interview from a physical therapist and two self-regulation coaching sessions from a rheumatology nurse	38	Group-based education session led by a physical therapist	40	HAQ (post-intervention)	8W	0.99 (0.70)	1.28 (0.58)		0.45	Effect size (Cohen's d): 0.03; p=0.530 (main effects of group × time interaction based on repeated measures mixed ANOVAs adjusted for age, gender, and baseline level of disease activity)		High	
Mollard, 2018	RCT	36	RA patients	NR	NR	0.58	2.78	NR	NR	NA	Usage of the LiveWithArthritis mobile app (supports self-management behaviours with features to monitor and manage the variables associated with RA, e.g. pain, treatment, other lifestyle and environmental data. App can provide reports that might help to identify aspect of patient lifestyle that make their arthritis better or worse and lets patients compare effectiveness of different treatment strategies)	21	Usual care	15	HAQ-II	Change from BL until 6M	0.02	0.05	p=0.83				High	
Srikesavan, 2019	SLR: 6 RCTs	567	RA patients (1 study mixed population with patients with OA and fibromyalgia)	NR	NR	NR	NR	NR	NR	NA	Web-based rehabilitation	#6	Waiting list/usual care	NR	Pain, function and quality of life	NR					Conclusion: The effects of web-based rehabilitation interventions on pain, function, quality of life, self-efficacy, rheumatoid arthritis knowledge, and physical activity are uncertain because of the very-low-quality of evidence mostly from small single trials. Adverse effects were not reported. Large, well-designed trials are needed to evaluate the clinical and cost-effectiveness of web-based rehabilitation interventions in rheumatoid arthritis.	Low	High
Pain (VAS-pain)																								
Albano, 2010	SLR: 7 SLRs, 10 RCTs, 20 nRCTs	9955	RA patients	NR	NR	NR	NR	NR	NR	NA	Educational programs (aiming at increasing knowledge and improving performance) and psycho-educational programs (combining teaching intervention activities to improve coping and change behaviour)	#9	NR	NR	Pain	NR					Improvement in all 9 studies; Conclusion: Our study confirms that therapeutic patient education in rheumatology, delivered througheducational or psycho-educational programs, is effective in terms of acquired knowledge, competencies and psychological improvement, whereas it brings fewer changes in health status and social well-being. The positive results are more frequently observed inshort-term than in long-term.	Moderate	High
Anvar, 2018	RCT	76	Older women with RA	NR	NR	NR	NR	NR	NR	NA	Self-management program: Participants in these classes followed a six week, multidisciplinary, group rehabilitation program as well as a peer education program, consisting of exercise and educational components (six weekly sessions of 1-1.5h).	39	Control: NR	37	VAS-pain (score 0-100, higher score reflects more pain)	6W			p=0.498				High	
DiRenzo, 2018	SLR: 5 RCTs	399	RA patients	NR	NR	NR	NR	NR	NR	NA	Mindfulness/vitality training program	93 (#3)	Wait-list/cognitive behavioural therapy/education	95	VAS-pain	Post-intervention		-0.58 (-1.26-0.10)			>0 favours control; Conclusion: There are few trials evaluating the effect of mindfulness-based interventions on outcomes in patients with RA. Preliminary findings suggest that mindfulness-based interventions may be a useful strategy to improve psychological distress in those with RA.	Low	Moderate-High
El Miedany, 2012	RCT	147	RA patients	NR	11.3Y	NR	9.3	NR	NR	NA	After 6 months of usual care: discussion of treatment goals based on PROMs, education, joint-fitness program (for patients aiming to a) give patients strategies and tools necessary to make daily decisions to cope with their disease; b) educate the patients about how to assess the main arthritis oucome measures regularly for their arthritis; c) help the patients to identify and manage the impact of arthrtis on their personal life; d) show patients how to keep their muscles and joints fit; for health care professionals aiming to a) review the effects of patient education on several outcomes; b) identify the value of PROMs; c) learn how to implement PROMs in management; d) identify the role of patient education as complementary.	74	Usual care	73	VAS-pain	Change from BL until 3M	1.44 (0.9)	1.41 (0.9)	p=0.788	0.03			High	
Feldthusen, 2016	RCT	70	RA patients with DAS28<3.8, VAS-fatigue >50 and disease duration >3Y	DAS28 3.4	12.9Y	NR	39.8	68.2	NR	NA	Tailored health-enhancing physical acitivity and balancing life activities to guide participants in managing their fatigue: starting with individual person-centered meeting during which a self-care plan was developed, then follow-up meetings/phone contacts according to each participant's preferences with a physical therapist, who supported and coached each participant	36	Usual care	34	VAS-pain (post-intervention)	Change from BL until 12W	-4.8 (18.4)	-1.1 (24.6)	p=0.46	0.17			High	
Hammond, 2004	RCT	328	RA patients	NR	9.5M	1.13	42.16	NR	NR	NA	Occupational therapy: Five sessions: four 1h individual treatments and one 2h group arthritis education program, with additional sessions if needed	162	Usual care	164	VAS-pain	Change from BL until 6M	-4.46 (95%CI '8.44- -0.48)	-1.54 (95%CI -6.51-3.44)	p=0.37				High	
Iversen, 2010	SLR: 30 RCTs	731 (#5, RA patients)	Patients with RA, OA, fibromyaliga and other types of inflammatory arthritis.	NR	NR	NR	NR	NR	NR	NA	Self-management interventions: educational, behavioural and cognitive approaches to influence health knowledge, attitudes, beliefs and behaviours to promote independence, maintain or adjust life roles, and address the psychological impact of diseases	#5	Same intervention without partner/Usual care/Information booklets/Lifestyle management for arthritis programme/Self-help guide only	NR	Pain, function, fatigue, disease status	NR					Short-term benefits were found in four studies. Three had longer-term follow-up at 12 months, but only two showed benefits; Conclusion: Of the 30 studies identified, only 14 had follow-ups of 12 months or longer, seven of which (two of the same SMART ASMP) led to sustained benefits in pain and/or function. Little is known about benefi ts beyond 12 months as only two had longer-term follow-ups, although both showed some continuing benefits.	Moderate	Low-moderate
Mollard, 2018	RCT	36	RA patients	NR	NR	0.58	2.78	NR	NR	NA	Usage of the LiveWithArthritis mobile app (supports self-management behaviours with features to monitor and manage the variables associated with RA, e.g. pain, treatment, other lifestyle and environmental data. App can provide reports that might help to identify aspect of patient lifestyle that make their arthritis better or worse and lets patients compare effectiveness of different treatment strategies)	21	Usual care	15	VAS-pain (score 0-10)	Change from BL until 6M	-0.61	0.18	p=0.38				High	

Srikesavan, 2019	SLR: 6 RCTs	567	RA patients (1 study mixed population with patients with OA and fibromyalgia)	NR	NR	NR	NR	NR	NR	NA	Web-based rehabilitation	#6	Waiting list/usual care	NR	Pain, function and quality of life	NR							Conclusion: The effects of web-based rehabilitation interventions on pain, function, quality of life, self-efficacy, rheumatoid arthritis knowledge, and physical activity are uncertain because of the very-low-quality of evidence mostly from small single trials. Adverse effects were not reported. Large, well-designed trials are needed to evaluate the clinical and cost-effectiveness of web-based rehabilitation interventions in rheumatoid arthritis.	Low	High
QoL (EQ-5D)																									
Baxter, 2016	RCT	33	RA patients	NR	7.01Y	1.1	NR	NR	15.0	NA	Walking: instructions on a walking route with three loops, to be completed 3-4 times a week	11	Nutrition education session	22	EQ-5D	Change from BL until 6W	5.0 (4.8)	-0.1 (5.6)		p=0.71	0.98			High	
Srikesavan, 2019	SLR: 6 RCTs	567	RA patients (1 study mixed population with patients with OA and fibromyalgia)	NR	NR	NR	NR	NR	NR	NA	Web-based rehabilitation	#6	Waiting list/usual care	NR	Pain and quality of life	NR							Conclusion: The effects of web-based rehabilitation interventions on pain, function, quality of life, self-efficacy, rheumatoid arthritis knowledge, and physical activity are uncertain because of the very-low-quality of evidence mostly from small single trials. Adverse effects were not reported. Large, well-designed trials are needed to evaluate the clinical and cost-effectiveness of web-based rehabilitation interventions in rheumatoid arthritis.	Low	High
Fatigue (VAS-fatigue)																									
Albano, 2010	SLR: 7 SLRs, 10 RCTs, 20 nRCTs	9955	RA patients	NR	NR	NR	NR	NR	NR	NA	Educational programs (aiming at increasing knowledge and improving performance) and psycho-educational programs (combining teaching intervention activities to improve coping and change behaviour)	#4	NR	NR	Fatigue	NR							Improvement in all 4 studies; Conclusion: Our study confirms that therapeutic patient education in rheumatology, delivered throughеducational or psycho-educational programs, is effective in terms of acquired knowledge, competencies and psychological improvement, whereas it brings fewer changes in health status and social well-being. The positive results are more frequently observed inshort-term than in long-term.	Moderate	High
DiRenzo, 2018	SLR: 5 RCTs	399	RA patients	NR	NR	NR	NR	NR	NR	NA	Mindfulness/vitality training program	(#2)	Wait-list/cognitive behavioural therapy/education	NR	Fatigue	Post-intervention							Significant treatment effect favouring mindfulness/vitality training program; Conclusion: There are few trials evaluating the effect of mindfulness-based interventions on outcomes in patients with RA. Preliminary findings suggest thatmindfulness-based interventions may be a useful strategy to improve psychological distress in those with RA.	Low	Moderate-High
Feldthusen, 2016	RCT	70	RA patients with DAS28<3.8, VAS-fatigue >50 and disease duration >3Y	DAS28 3.4	12.9Y	NR	39.8	68.2	NR	NA	Tailored health-enhancing physical acitivity and balancing life activities to guide participants in managing their fatigue: starting with individual person-centered meeting during which a self-care plan was developed, then follow-up meetings/phone contacts according to each participant's preferences with a physical therapist, who supported and coached each participant	36	Usual care	34	VAS-fatigue (post-intervention)	Change from BL until 12W	-23.5 (19.9)	-15.3 (24.6)		p=0.042	0.37			High	
Iversen, 2010	SLR: 30 RCTs	731 (#5, RA patients)	Patients with RA, OA, fibromyaliga and other types of inflammatory arthritis.	NR	NR	NR	NR	NR	NR	NA	Self-management interventions: educational, behavioural and cognitive approaches to influence health knowledge, attitudes, beliefs and behaviours to promote independence, maintain or adjust life roles, and address the psychological impact of diseases	#5	Same intervention without partner/Usual care/Information booklets/Lifestyle management for arthritis programme/Self-help guide only	NR	Pain, function, fatigue, disease status	NR							Short-term benefits were found in four studies. Three had longer-term follow-up at 12 months, but only two showed benefits; Conclusion: Of the 30 studies identified, only 14 had follow-ups of 12 months or longer, seven of which (two of the same SMART ASMP) led to sustained benefits in pain and/or function. Little is known about benefi ts beyond 12 months as only two had longer-term follow-ups, although both showed some continuing benefits.	Moderate	Low-moderate
Disease activity																									
Albano, 2010	SLR: 7 SLRs, 10 RCTs, 20 nRCTs	9955	RA patients	NR	NR	NR	NR	NR	NR	NA	Educational programs (aiming at increasing knowledge and improving performance) and psycho-educational programs (combining teaching intervention activities to improve coping and change behaviour)	#1	NR	NR	Disease activity score	NR							Improvement in 1 of 1 studies; Conclusion: Our study confirms that therapeutic patient education in rheumatology, delivered throughеducational or psycho-educational programs, is effective in terms of acquired knowledge, competencies and psychological improvement, whereas it brings fewer changes in health status and social well-being. The positive results are more frequently observed inshort-term than in long-term.	Moderate	High
DiRenzo, 2018	SLR: 5 RCTs	399	RA patients	NR	NR	NR	NR	NR	NR	NA	Mindfulness/vitality training program	59 (#2)	Wait-list/cognitive behavioural therapy/education	61	DAS28-CRP	Post-intervention		-0.44 (-0.99-0.12)					>0 favours control; Conclusion: There are few trials evaluating the effect of mindfulness-based interventions on outcomes in patients with RA. Preliminary findings suggest thatmindfulness-based interventions may be a useful strategy to improve psychological distress in those with RA.	Low	Moderate-High
Feldthusen, 2016	RCT	70	RA patients with DAS28<3.8, VAS-fatigue >50 and disease duration >3Y	12.9Y	DAS28 3.4	NR	39.8	68.2	NR	NA	Tailored health-enhancing physical acitivity and balancing life activities to guide participants in managing their fatigue: starting with individual person-centered meeting during which a self-care plan was developed, then follow-up meetings/phone contacts according to each participant's preferences with a physical therapist, who supported and coached each participant	36	Usual care	34	DAS28 (post-intervention)	Change from BL until 12W	-0.3 (0.9)	-0.3 (1.0)		p=1.00	0.0			High	
ALTERNATIVE MEDICNE																									
Pain (VAS-pain)																									
Gok Metin, 2016	RCT	51	RA patients with pain (VAS ≥4) and fatigue (FSS ≥4)	10.7Y	DAS28 2.82 (0.88)	NR	6.02 (0-10)	NR	NR	Fatigue (FSS) 5.60	Aromatherapy (3/W for 3M on both knees, at home)	17	Usual care	17	VAS-pain	6W	1.59 (1.17)	4.29 (2.38)		p=0.001	1.44			High	
											Reflexology (1/W for 40min on both feet, at home)	17	Usual care	17	VAS-pain	6W	0.56 (1.14)	4.29 (2.38)		p=0.001	2.00				
Lee, 2014	SLR: RCTs 1	80	RA patients	7.3-9.2Y	NR	NR	NR	NR	NR	NA	Bee venom acupuncture (ashi points, acupoints near the inflammation point, 2/W)	37	Acupuncture with placebo	37	VAS-pain	2M			-18.10 (-,-23.71 - -12.49)	p<0.05			Low-quality evidence that bee venom acupuncture can significantly reduce pain, morning stiffness, tender joint counts, swollen joint counts and improve QoL.	Low	High
Macfarlane, 2012	SLR: RCTs 11	672	RA patients receiving complementary therapy	NR	NR	NR	NR	NR	NR	NA	Acupuncture (traditional Chinese acupuncture, electrical current acupuncture, single-point acupuncture or undefined acupuncture)	119 (3 studies)	Sham acupuncture	65	Pain reduction					ns			No good evidence of efficacy or effectiveness for the practitioner-based complementary therapies considered here.	Moderate	Moderate
											(Mindfulness) meditation	79 (2 studies)	Waitlist controls or cognitive behavioural therapy for pain education	128	Pain				ns					
											Autogenic training	18 (1 study)	Auricular acupuncture	16	Pain				ns					
											Healing therapy	15 (1 study)	Usual care	14	Pain				ns					
											Progressive muscle relaxation	44 (1 study)	Cognitive behavioural therapy	124	Pain				ns					

											Static magnets	38 (1 study)	Low magnetic strength control	36	Pain					ns							
Fatigue (VAS-fatigue)																												
Gok Metin, 2016	RCT	51	RA patients with pain (VAS ≥4) and fatigue (FSS ≥4)	10.7Y	DAS28 2.82 (0.88)	NR	6.02 (0-10)	NR	NR	Fatigue (FSS) 5.60	Aromatherapy (3/W for 3M on both knees, at home)	17	Usual care	17	Fatigue (FSS)	6W			2.94 (1.13)	4.41 (1.79)	p=0.001	0.98			High			
											Reflexology (1/W for 40min on both feet, at home)	17	Usual care	17	Fatigue (FSS)	6W			1.88 (1.18)	4.41 (1.79)	p=0.001	1.67						
Other																												
Jiang, 2018	RCT	60	RA patients with unilateral elbow stiffness	NR	NR	NR	NR	NR	NR	Maximum angle of active extension position of elbow, mean: 37.2; Maximum angle of active flexion position of elbow, mean: 89.1; Maximum angle of active flexion position of elbow, mean 51.9	Acupotomy loosing (tender point in lateral elbow joint was taken as treatment point, 1/W)	20	Usual care	20	Maximum angle of active extension position of elbow	4W			7.01 (4.85)	32.87 (10.24)	p<0.05	3.23			High			
															Maximum angle of active flexion position of elbow	4W			112.14 (9.14)	90.87 (15.25)	p<0.05	1.69						
															Range of motion	4W			105.13 (15.84)	58.00 (7.45)	p<0.05	3.81						
											Acupotomy loosing (tender point in lateral elbow joint was taken as treatment point, 1/W)	20	Electroacupuncture (Acuepoint of Tianzhu was selected as treatment point, 6/W)	20	Maximum angle of active extension position of elbow	4W			7.01 (4.85)	112.14 (9.14)	p<0.05	14.37						
															Maximum angle of active flexion position of elbow	4W			112.14 (9.14)	98.50 (15.67)	p<0.05	1.06						
															Range of motion	4W			105.13 (15.84)	90.87 (15.25)	p<0.05	0.92						
											Electroacupuncture (Acuepoint of Tianzhu was selected as treatment point, 6/W)	20	Usual care	20	Maximum angle of active extension position of elbow	4W			112.14 (9.14)	32.87 (10.24)	p<0.05	8.17						
															Maximum angle of active flexion position of elbow	4W			98.50 (15.67)	90.87 (15.25)	p<0.05	0.49						
															Range of motion	4W			90.87 (15.25)	58.00 (7.45)	p<0.05	2.74						
Lee, 2014	SLR: RCTs 1	80	RA patients	7.3-9.2Y	NR	NR	NR	NR	NR	NA	Bee venom acupuncture (ashi points, acupoints near the inflammation point, 2/W)	37	Placebo	37	Morning stiffness	2M					-0.70 (-, -2.00 - 0.60)	p<0.05		Low-quality evidence that bee venom acupuncture can significantly reduce pain, morning stiffness, tender joint counts, swollen joint counts and improve QoL.	Low	High	
Macfarlane, 2012	SLR: RCTs 11	672	RA patients receiving complementary therapy	NR	NR	NR	NR	NR	NR	NA	Acupuncture (traditional Chinese acupuncture, electrical current acupuncture, single-point acupuncture or undefined acupuncture)	119 (3 studies)	Sham acupuncture	65	Patient global assessment						Improvement		No good evidence of efficacy or effectiveness for the practitioner-based complementary therapies considered here.	Moderate	Moderate	
											Healing therapy	15 (1 study)	Usual care	14	Patient global assessment						Improvement						
											Static magnets	38 (1 study)	Low magnetic strength control	36	Patient global assessment						Improvement						
CRYOTHERAPY																												
Function (HAQ)																												
Gizinska, 2015	Non-RCT	44	Postmenopauzal women with RA	10.9Y	DAS28 5.14	2.21 (Intervention: 1.82; Control 2.72)	57.00	NR	NR	NA	Whole-body cryotherapy (5/W for 3min)	25	Traditional rehabilitation	19	HAQ	12W			1.64 (1.19)	2.12 (1.30)	p=0.0116	0.39			High			
Jastrząbek, 2013	RCT	40	RA patients	13.55Y	DAS28 6.15	1.2	66.5	63.4	NR	NA	Nitrogen vapour treatment (3 min liquid nitrogen flow treatment, −160 °C, 1/D knee joints and 1/D joints of both hands)	20	Cold air treatment (3 min cool air flow treatment, −30 °C, 1/D knee joints and 1/D joints of both hands)	20	HAQ-DI	10D			0.9 (0.6)	0.9 (0.3)	p= 0.0787	0.0			High			
Pain (VAS-pain)																												
Gizinska, 2015	Non-RCT	44	Postmenopauzal women with RA	10.9Y	DAS28 5.14	2.21 (Intervention: 1.82; Control 2.72)	57.00	NR	NR	NA	Whole-body cryotherapy (5/W for 3min)	25	Traditional rehabilitation	19	VAS-pain	12W			40.80 (17.93)	52.95 (16.36)	p=0.7581	0.71			High			
Jastrząbek, 2013	RCT	40	RA patients	13.55Y	DAS28 6.15	1.2	66.5	63.4	NR	NA	Nitrogen vapour treatment (3 min liquid nitrogen flow treatment, −160 °C, 1/D knee joints and 1/D joints of both hands)	20	Cold air treatment (3 min cool air flow treatment, −30 °C, 1/D knee joints and 1/D joints of both hands)	20	VAS-pain	10D			32.5 (20.3)	40.1 (24.3)	p= 0.4989	0.34			High			
Fatigue (VAS-fatigue)																												
Jastrząbek, 2013	RCT	40	RA patients	13.55Y	DAS28 6.15	1.2	66.5	63.4	NR	NA	Nitrogen vapour treatment (3 min liquid nitrogen flow treatment, −160 °C, 1/D knee joints and 1/D joints of both hands)	20	Cold air treatment (3 min cool air flow treatment, −30 °C, 1/D knee joints and 1/D joints of both hands)	20	VAS-fatigue	10D			36.5 (23.1)	34.4 (22.1)	p= 0.1478	0.09			High			
Disease activity																												
Jastrząbek, 2013	RCT	40	RA patients	13.55Y	DAS28 6.15	1.2	66.5	63.4	NR	NA	Nitrogen vapour treatment (3 min liquid nitrogen flow treatment, −160 °C, 1/D knee joints and 1/D joints of both hands)	20	Cold air treatment (3 min cool air flow treatment, −30 °C, 1/D knee joints and 1/D joints of both hands)	20	DAS28	10D			4.96 (1.07)	5.10 (1.04)	p= 0.6849	0.13			High			
BALNEOTHERAPY																												
Function (HAQ)																												
Annegret, 2016	RCT	98	All RA patients	NR	NR	0.94 (0.57)	5.45	NR	NR	NA	Radon spa therapy (every 2-3D for 20min)	50	Tap water bath (every 2-3D for 20min)	48	HAQ	Change from BL until 26D			0.08 (0.39)	0.10 (0.29)		0.06			High			
Santos, 2016	RCT	44	RA patients	NR	DAS28 4.73 (1.53)	1.42 (0.72)	48.07 (26.48)	56.36 (28.70)	NR	VAS-QoL 47.05 (21.74)	Spa therapy (Sulphur bath treatments, 1/D)	22	Usual care	22	HAQ-DI	21D					+0.37 (0.09-0.64)	p=0.01		Adjusted for baseline	High			
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Hydrotherapy/balneotherapy	998 (#2)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Functional disability	NR								No effect or difference compared to a control treatment ; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate	
Pain (VAS-pain)																												

Allam, 2018	RCT	30	All RA patients	NR	NR	NR	42.1	NR	NR	NA	Siwan therapy (sand bathing and massage with olive oil for 7D)	15	Traditional exercise program (3 sessions a week for 2M) including hot application	15	VAS-pain	NR	37.1 (18.1)	51.1 (13.3)		0.005	0.88			High	
Santos, 2016	RCT	44	RA patients	NR	DAS28 4.73 (1.53)	1.42 (0.72)	48.07 (26.48)	56.36 (28.70)	NR	VAS-QoL 47.05 (21.74)	Spa therapy (Sulphur bath treatments, 1/D)	22	Usual care	22	VAS-pain	21D			+10.19 (-3.47-23.86)	p=0.140		Adjusted for baseline		High	
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Hydrotherapy/balneotherapy	998 (#2)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Pain	NR						No effect or difference compared to a control treatment; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.		Moderate	Moderate
QoL (EQ-5D)																									
Santos, 2016	RCT	44	RA patients	NR	DAS28 4.73 (1.53)	1.42 (0.72)	48.07 (26.48)	56.36 (28.70)	NR	VAS-QoL 47.05 (21.74)	Spa therapy (Sulphur bath treatments, 1/D)	22	Usual care	22	VAS-QoL	21D			+6.53 (-, -9.11-21.18)	p=0.372		Adjusted for baseline		High	
Fatigue (VAS-fatigue)																									
Santos, 2016	RCT	44	RA patients	NR	DAS28 4.73 (1.53)	1.42 (0.72)	48.07 (26.48)	56.36 (28.70)	NR	VAS-QoL 47.05 (21.74)	Spa therapy (Sulphur bath treatments, 1/D)	22	Usual care	22	VAS-fatigue	21D			+2.89 (-, -13.48-19.26)	p=0.723		Adjusted for baseline		High	
Disease activity																									
Santos, 2016	RCT	44	RA patients	NR	DAS28 4.73 (1.53)	1.42 (0.72)	48.07 (26.48)	56.36 (28.70)	NR	VAS-QoL 47.05 (21.74)	Spa therapy (Sulphur bath treatments, 1/D)	22	Usual care	22	DAS28	21D			+0.21 (-, 0.26-0.68)	p=0.368		Adjusted for baseline		High	
Other																									
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Hydrotherapy/balneotherapy	491 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Global impact of disease	NR						No effect or difference compared to a control treatment; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.		Moderate	Moderate
INTENSIFICATION OF PATIENT CARE																									
Function (HAQ)																									
de Thurah, 2018	RCT	294	RA patients with disease duration >2Y	DAS28 2.07	11-12Y, range of medians	NR	NR	NR	NR	NA	Patient-reported outcome based tele-health follow-up carried out by a nurse	88	Conventional outpatient followup by physicians	94	HAQ (ITT analysis)	Change from BL until 52W	0.05 (95%CI -0.02-0.12)	0.08 (95%CI 0.02-0.14)	-0.03 (90%CI -0.13-0.06)	p=0.47				High	
											Patient-reported outcome based tele-health follow-up carried out by a rheumatologist	93	Conventional outpatient followup by physicians	94	HAQ (ITT analysis)	Change from BL until 52W	0.03 (95%CI -0.03-0.09)	0.08 (95%CI 0.02-0.14)	-0.05 (90%CI -0.14-0.04)	p=0.26					
Hewlett, 2005	RCT	209	RA patients	NR	7.0-10.0Y, range of medians	1.30	3.04	NR	NR	NA	Direct access to hospital review (rheumatologist, physiotherapist, occupational therapist) by patients with RA through a nurse-led telephone helpline for 2Y	68	Usual care (review initiated by rheumatologists)	52	HAQ (long-term follow-up)	Change from BL until 6Y	0.19 (-0.125-0.75), median (IQR)	0.25 (0-0.75), median (IQR)		p=0.39				High	
Munoz-Fernandez, 2016	Non-RCT	393 (RA 302)	All RA patients	10.0Y	DAS28 (RA) 2.9	0.8 (RA patients)	NR	NR	0.7	NA	Nursing clinics in rheumatology	181 (RA 142)	No nursing clinic	212 (RA 160)	HAQ (RA)	12M	0.7 (0.7)	0.9 (0.7)		p=0.023	0.29			High	
Tijhuis, 2002	RCT	210	RA patients with increasing difficulty in performing activities of daily living over the previous 6 weeks.	1.9Y	DAS28 5.63 (Nurse specialist patients 5.32; Inpatients 5.72; Day patients 5.85; p<0.05)	1.40 (Nurse specialist patients 1.17; Inpatients 1.49; Day patients 1.54; p<0.01)	NR	NR	NR	NA	Clinical nurse specialist (clinical nurse specialist provided information about RA and prescribed, in consultation with the rheumatologist, joint splints, adaptive equipment, and house adaptations if needed)	71	Inpatient team care (9 treatment days within 2-3W, admitted to the hospital for 12 consecutive days, including the weekend)	71	HAQ	Change from BL until 6W	0.09 (-0.02, 0.20), mean (95% CI)	0.19 (0.08, 0.29), mean (95% CI)		p<0.05, adjusted for age and difference at baseline				High	
													Day patient team care (9 treatment days, 3/W, from 10AM until 4PM with a fixed period of 1.5 hours of bed rest)	71	HAQ	Change from BL until 6W	0.09 (-0.02, 0.20), mean (95% CI)	0.27 (0.16, 0.37), mean (95% CI)		p<0.05, adjusted for age and difference at baseline					
Pain (VAS-pain)																									
Hewlett, 2005	RCT	209	RA patients	7.0-10.0Y, range of medians	NR	1.30	3.04	NR	NR	NA	Direct access to hospital review (rheumatologist, physiotherapist, occupational therapist) by patients with RA through a nurse-led telephone helpline for 2Y	68	Usual care (review initiated by rheumatologists)	52	VAS-pain (long-term follow-up)	Change from BL until 6Y	1.25 (-0.40-3.25), median (IQR)	1.1 (-1.00-3.60), median (IQR)		p=0.91				High	
Wang, 2017	RCT	220	RA patients	8.8Y	DAS28 4.37	NR	NR	43.14	NR	NA	Nurse-led care	110	Rheumatologist-led care	110	VAS-pain	12M	29.21	26.03		p<0.001				High	
QoL (EQ-5D)																									
de Thurah, 2018	RCT	294	RA patients with disease duration >2Y	DAS28 2.07	11-12Y, range of medians	NR	NR	NR	NR	NA	Patient-reported outcome based tele-health follow-up carried out by a nurse	88	Conventional outpatient followup by physicians	94	EQ-5D (ITT analysis)	Change from BL until 52W	-0.02 (95%CI -0.06-0.03)	-0.01 (95%CI -0.06-0.05)	-0.01 (90%CI -0.09-0.05)	p=0.83				High	
											Patient-reported outcome based tele-health follow-up carried out by a rheumatologist	93	Conventional outpatient followup by physicians	94	EQ-5D (ITT analysis)	Change from BL until 52W	-0.02 (95%CI -0.07-0.04)	-0.01 (95%CI -0.06-0.05)	-0.01 (90%CI -0.09-0.07)	p=0.75					
Hewlett, 2005	RCT	209	RA patients	NR	7.0-10.0Y, range of medians	1.30	3.04	NR	NR	NA	Direct access to hospital review (rheumatologist, physiotherapist, occupational therapist) by patients with RA through a nurse-led telephone helpline for 2Y	68	Usual care (review initiated by rheumatologists)	52	QoL (SF-36) (long-term follow-up)	Change from BL until 6Y				ns				High	
Munoz-Fernandez, 2016	Non-RCT	393 (RA 302)	All RA patients	10.0Y	DAS28 (RA) 2.9	0.8 (RA patients)	NR	NR	0.7	NA	Nursing clinics in rheumatology	181 (RA 142)	No nursing clinic	212 (RA 160)	EQ-5D tariff	12M	0.7 (0.2)	0.7 (0.2)		p=0.069	0.0			High	
Fatigue (VAS-fatigue)																									
de Thurah, 2017	SLR: 7 RCTs	548 (#5, only RA patients)	RA patients	NR	NR	NR	NR	NR	NR	NA	Nurse-led follow-up in managing disease control	183	Physician-led follow-up	182	Fatigue	1Y			-4.13 (-9.94-1.68)			>0 favours physician led follow-up; Conclusion: After 1year no difference in disease activity, indicated by DAS-28, were found between embedded nurse-led follow-up compared with conventional physician-led follow-up, in RA patients with low disease activity or remission.		Low	Moderate
Wang, 2017	RCT	220	RA patients	8.8Y	DAS28 4.37	NR	NR	43.14	NR	NA	Nurse-led care	110	Rheumatologist-led care	110	VAS-fatigue	12M	49.41	44.03		p<0.001				High	
Disease activity																									

de Thurah, 2017	SLR: 7 RCTs	548 (#5, only RA patients)	RA patients	NR	NR	NR	NR	NR	NR	NA	Nurse-led follow-up in managing disease control	263	Physician-led follow-up	271	Disease activity	1Y					-0.07 (-0.23-0.09)				>0 favours physician led follow-up; Conclusion: After 1year no difference in disease activity, indicated by DAS-28, were found between embedded nurse-led follow-up compared with conventional physician-led follow-up, in RA patients with low disease activity or remission. No difference was found in patient satisfaction after 1year (standard mean difference (SMD) −0.17 (95 % CI −1.0 to 0.67), whereas a statistical significant difference in favour of nurse-led follow-up was seen after 2years (SMD: 0.6 (95% CI −0.00 to 1.20)).	Low	Moderate
de Thurah, 2018	RCT	294	RA patients with disease duration >2Y	DAS28 2.07	11-12Y, range of medians	NR	NR	NR	NR	NA	Patient-reported outcome based tele-health follow-up carried out by a nurse	88	Conventional outpatient followup by physicians	94	DAS28 (ITT analysis)	Change from BL until 52W				-0.26 (95%CI -0.44- -0.07)	-0.06 (95%CI -0.23-0.12)	-0.19 (90%CI -0.41-0.02)	p=0.15				High	
											Patient-reported outcome based tele-health follow-up carried out by a rheumatologist	93	Conventional outpatient followup by physicians	94	DAS28 (ITT analysis)	Change from BL until 52W				-0.16 (95%CI -0.33-0.03)	-0.06 (95%CI -0.23-0.12)	-0.10 (95%CI -0.30-0.13)	p=0.45					
Munoz-Fernandez, 2016	Non-RCT	393 (RA 302)	All RA patients	10.0Y	DAS28 (RA) 2.9	0.8 (RA patients)	NR	NR	0.7	NA	Nursing clinics in rheumatology	181 (RA 142)	No nursing clinic	212 (RA 160)	DAS28 (RA)	12M				2.7 (1.1)	2.8 (1.1)		p=0.274	0.09			High	
Wang, 2017	RCT	220	RA patients	8.8Y	DAS28 4.37	NR	NR	43.14	NR	NA	Nurse-led care	110	Rheumatologist-led care	110	DAS28	12M				1.02 (1.32)	0.98 (1.06)		p<0.001	0.03			High	
PHARMACOLOGICAL																												
Function (HAQ)																												
Whittle, 2011	SLR: RCTs 11	623	RA patients with pain	NR	NR	NR	NR	NR	NR	NA	Opioids	243 (2 studies)	Placebo		Functional status (HAQ)					0.1 lower (0.33 lower - 0.13 higher)					There is limited evidence that weak oral opioids may be effective analgesics for some patients with RA, but adverse effects are common and may offset the benefits of this class of medications. There is insufficient evidence to draw conclusions regarding the use of weak opioids for longer than six weeks, or the role of strong opioids	Low	High
Pain (VAS-pain)																												
Kawai, 2010	RCT	676	RA patients with systemic disease control but persistent wrist pain	NR	NR	NR	NR	NR	NR	Wrist joint pain (VAS score 0-100): 50.0;	Ketoprofen patch (20mg/D, cutaneous)	338	Placebo	338	VAS-pain of the wrist	Change from BL until 2W				15.7 (16.0)	13.2 (16.4)		p=0.026	0.15			Moderate	
Lee, 2016	RCT	41	RA patients with widespread pain	11.4Y	DAS28-CRP 3.28	NR	NR	NR	NR	Pain intensity (BPI short form) 6.0	Milnacipran (50mg 2/D, oral)	41	Placebo (cross-over after 3W wash-out period)	41	Pain intensity (BPI short form)	Change from BL until 6W						-0.39 (-, -1.27-0.49)	p=0.37; Adjusted by treatment group, study period and sequence				Moderate	
Fidahic, 2017	SLR: RCTs 8	3988	RA patients	9.2Y	NR	NR	NR	NR	NR	NA	Celecoxib	873 (2 studies)	Placebo		VAS-pain	Improvement from BL until 12W						11% (-, 8-14)			Celecoxib may improve clinical symptoms, alleviate pain and contribute to little or no difference in physical function compared to placebo. Celecoxib may slightly improve clinical symptoms compared with tNSAIDs; results for reduced pain and improved physical function were uncertain.	Low	Low-Moderate
Fitzcharles, 2016	SLR: RCTs 4	201 (RA 58)	Patients with RA, OA or fibromyalgia	NR	NR	NR	NR	NR	NR	NA	Cannabinoids (nabiximols, nabilone 0,5-1mg, or PF-04457845 (irreversible fatty acid amide hydrolase-1 inhibitor))	NR	Placebo, amitriptyline or naproxen	NR	Pain	2-8W							Improved in 2 studies		Pain relief and effect on sleep may have some potential therapeutic benefit, but with considerable mild to moderate adverse events. There is currently insufficient evidence to recommend cannabinoid treatment.	Moderate	High
Richards, 2011	SLR: RCTs 8	652	RA patients	NR	NR	NR	NR	NR	NR	NA	Tricyclic antidepressant	30 (1 study)	Control		VAS-pain	<1W				10 higher (worse)	34		No effect		There is currently insufficient evidence to support the routine prescription of antidepressants as analgesics in patients with RA as no reliable conclusions about their efficacy can be drawn from eight placebo RCTs. The use of these agents may be associated with adverse events which are generally mild and do not lead to cessation of treatment	Low	High
												482 (7 studies)			VAS-pain	1-6W							Conflicting results				
												368 (5 studies)			VAS-pain	>6W							Conflicting results				
Whittle, 2011	SLR: RCTs 11	623	RA patients with pain	NR	NR	NR	NR	NR	NR	NA	Codeine (30mg) with paracetamol (500mg)	60 (1 study)	Diclofenac (50mg)		VAS-pain								ns		There is limited evidence that weak oral opioids may be effective analgesics for some patients with RA, but adverse effects are common and may offset the benefits of this class of medications. There is insufficient evidence to draw conclusions regarding the use of weak opioids for longer than six weeks, or the role of strong opioids	Low	High
QoL (EQ-5D)																												
Fidahic, 2017	SLR: RCTs 8	3988	RA patients	9.2Y	NR	NR	NR	NR	NR	NA	Celecoxib	873 (2 studies)	Placebo		HAQ	Improvement from BL until 12W						-0.10 (-, 0.29-0.1)			Celecoxib may improve clinical symptoms, alleviate pain and contribute to little or no difference in physical function compared to placebo. Celecoxib may slightly improve clinical symptoms compared with tNSAIDs; results for reduced pain and improved physical function were uncertain.	Low	Low-Moderate
Fitzcharles, 2016	SLR: RCTs 4	201 (RA 58)	Patients with RA, OA or fibromyalgia	NR	NR	NR	NR	NR	NR	NA	Cannabinoids (nabiximols, nabilone 0,5-1mg, or PF-04457845 (irreversible fatty acid amide hydrolase-1 inhibitor))	NR	Placebo, amitriptyline or naproxen	NR	QoL	2-8W							Improved in 1 study		Pain relief and effect on sleep may have some potential therapeutic benefit, but with considerable mild to moderate adverse events. There is currently insufficient evidence to recommend cannabinoid treatment.	Moderate	High
Disease activity																												
Fidahic, 2017	SLR: RCTs 8	3988	RA patients	9.2Y	NR	NR	NR	NR	NR	NA	Celecoxib	873 (2 studies)	Placebo		ACR20 response	4-12W			1.53 (1.25-1.86, -)			15% (-, 7-25)		Celecoxib may improve clinical symptoms, alleviate pain and contribute to little or no difference in physical function compared to placebo. Celecoxib may slightly improve clinical symptoms compared with tNSAIDs; results for reduced pain and improved physical function were uncertain.	Low	Low-Moderate
											Celecoxib	2930 (7 studies)	tNSAIDs (amtolmetin guacyl, diclofenac, ibuprofen, meloxicam, nabumetone, naproxen, pelubiprofen)		ACR20 response			1.10 (0.99-1.23)			4% (0, 0-8)					
Other																												
Whittle, 2011	SLR: RCTs 11	623	RA patients with pain	NR	NR	NR	NR	NR	NR	NA	Opioids	324 (3 studies)	Placebo		Patient reported global impression of clinical change 'good' or 'very good'	573/1000	398/1000	1.44 (1.03-2.03, -)	18 (1-18,-)						There is limited evidence that weak oral opioids may be effective analgesics for some patients with RA, but adverse effects are common and may offset the benefits of this class of medications. There is insufficient evidence to draw conclusions regarding the use of weak opioids for longer than six weeks, or the role of strong opioids	Low	High
OTHER INTERVENTIONS																												
Custom orthoses																												
Function (HAQ)																												

Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Custom orthoses	340 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Pain	NR				Effective improvement with moderate positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Pain (VAS-pain)																					
Santos, 2019	SLR (8 SLRs)	6740	RA patients	NR	NR	NR	Nr	NR	NR	NR	Custom orthoses	220 (#1)	Usual care/placebo/other non-pharmacological or non-surgical interventions	#8	Functional disability	NR				Effective improvement with small positive effects; Conclusions: Of the included interventions, only multicomponent or single exercise/physical activity interventions,psychosocial interventions and custom orthoses seem to reduce the impact of rheumatoid arthritis.	Moderate	Moderate
Other interventions vs alternative intervention or placebo																					
Function (HAQ)																					
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Low-level laser therapy		Alternative intervention/placebo		Pain and function			Reduces pain and improves function, low quality evidence	High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.	Low	Moderate-High
											Therapeutic ultrasound		Placebo/alternative intervention		Pain and function			Reduces pain and improves function, low quality evidence			
Pain (VAS-pain)																					
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Low-level laser therapy		Alternative intervention/placebo		Pain and function			Reduces pain and improves function, low quality evidence	High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.	Low	Moderate-High
											Therapeutic ultrasound		Alternative intervention/placebo		Pain and function			Reduces pain and improves function, low quality evidence			
Electrical stimulation, hand/foot orthosis, thermotherapy or transcutaneous electrical nerve stimulation vs control																					
Other																					
Christie, 2007	SLR: SLRs 28	NR	RA patients	NR	NR	NR	NR	NR	NR	NA	Other interventions: Acupuncture, balneotherapy, electrical stimulation, occupational therapy (besides joint protection and comprehensive occupation therapy), hand/foot orthosis, thermotherapy, transcutaneous electrical nerve stimulation		All types of controls		Efficacy			Moderate effect and low quality evidence	High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions.	Low	Moderate-High

ACR: American College of Rheumatology; ANOVA: analysis of variance; BDI: Beck Depression Inventory (scale 0-63, higher scores felect higher levels of depression); BL: baseline; BPI: Brief Pain Inventory (scale 0-10); BRAF-NRS: Bristol RheumatoidArthritis Fatigue Numerical Rating Scale (score 0-10, higher scores reflect higher level of symptoms); CGT: cognitive behavioral therapy; CIS: Checklist Individual Strengths (scale 0-56, higher score reflects higher level of fatigue); CI: confidence interval; D: day(s); DAS28: disease activity score assessing 28 joints; EQ-5D: Euro Quality of Life using 5 dimensions; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; FSS: Fatigue Severity Scale (scale 0-7); IRGL: Impact of Rheumatic Diseases on General Health and Lifestyle questionnaire (negative mood scale 0-30, anxiety scale 0-40, pain scale 0-24, higher scores reflect higher levels of symptoms); HAQ: health assessment questionnaire; LSQ: Leeds Satisfaction Questionnaire (scale 1-5, higher scores reflect higher levels of disagreement); mCi: millicurie; mg: milligram; MHQ: Michigan Hand outcome Questionnaire (0-100; higher scores reflect better function); n: number; NA: not applicable; nM: muscular strength assessment; NR: not reported; (n-)RCT: (non-)randomised controlled trial; ns: not significant; NSAIDs: non-steroid anti-inflammatory drug; OA: osteoarthritis; OR: odds ratio; QoL: Quality of Life; RA: rheumatoid arthritis; RAID: Rheumatoid Arthritis Impact of Disease (scale 0-10, higher scores reflect worse disease); VAS: visual analogue scale; SD: standard deviation; SF-36: short form general health questionnaire using 36 items; SLR: systematic literature review; SMD: standardized mean difference; WIS: Work Instability Scale; W: week(s); Y: year(s); ^: abstract; #: number of studies.

1. Latest time point during treatment period that was reported; 2. According to Cochrane Collaboration's tool for individual studies: highest risk of bias as found; According to AMSTAR2 tool for SLRs: Low=zero or one non-critical weakness; Moderate=more than one non-critical weakness; High=one critical flaw with or without non-critical weaknesses; Critically high=more than one critical flaw with or without non-critical weaknesses; 3. Only applicable for SLRs: Summary of RoB of individual studies, as assessed in SLR