

Appendix A. Searching Strategy

Pubmed. Total articles: 656

1	Ankle
2	Talocrural
3	Talo-crural
4	Talocalcaneal
5	Talo-calcaneal
6	Talofibular
7	Talo-fibular
8	Ligament
9	Lateral Ligament ankle
10	Medial Ligament ankle
11	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10
12	Sprain
13	Strain
14	Ankle injur*
15	Ankle sprain
16	Inversion sprain
17	Eversion sprain
18	12 OR 13 OR 14 OR 15 OR 16 OR 17
19	11 AND 18
20	Conservat* treat*
21	Conservative management
22	Non-surgical treatment
23	CAST
24	Rehabilitation program
25	Myofascial
26	Conservative program
27	Manual Therapy
28	Physiotherapeutic intervention
29	Bandage
30	Plaster
31	Exercise programme

32	Home exercise
33	RICE
34	Taping
35	TENSE
36	Ultrasound
37	20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36
38	19 AND 37

CINAHL. Total articles: 2176

1	Ankle Sprains
2	Inversion Sprain
3	Eversion Sprain
4	Ankle Injury
5	1 OR 2 OR 3 OR 4
6	Conservative treatment
7	Conservative management
8	Rehabilitation programs
9	Bandage
10	Physiotherapeutic
11	6 OR 7 OR 8 OR 9 OR 10
12	5 AND 11

SCOPUS. Total articles: 597

1	TITLE-ABS-KEY (Ankle Sprain)
2	TITLE-ABS-KEY (Inversion Sprain)
3	TITLE-ABS-KEY (Eversion Sprain)
4	TITLE-ABS-KEY (Ankle Injury)
5	1 OR 2 OR 3 OR 4
6	TITLE-ABS-KEY (Conservat* treat*)
7	TITLE-ABS-KEY (Conservative management)
8	TITLE-ABS-KEY (TENSE)

9	TITLE-ABS-KEY (Bandage)
10	TITLE-ABS-KEY (Rehabilitation program)
11	TITLE-ABS-KEY (Physiotherapeutic)
12	6 OR 7 OR 8 OR 9 OR 10 OR 11
13	5 AND 12

SPORTSDiscus via EBSCOHost. Total articles: 5618

1	Ankle Sprains
2	Inversion Sprain
3	Eversion Sprain
4	Ankle injury
5	1 OR 2 OR 3 OR 4
6	Conservative treatment
7	Conservative management
8	Rehabilitation program
9	Physiotherapeutic
10	6 OR 7 OR 8 OR 9 OR 10
11	5 AND 10

PsycINFO. Total articles: 1371

1	Ankle Sprains
2	Inversion Ankle sprain
3	Eversion Ankle sprain
4	1 OR 2 OR 3
5	Conservative treatment
6	Conservative management
7	Rehabilitation program
8	Physiotherapeutic
9	5 OR 6 OR 7 OR 8
10	4 AND 9

PROSPERO. Total articles: 38

1	Ankle Sprains
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Appendix B. Table 1. Characteristics of the studies included in the review

Author Year Country	Patients (n)	Age (years)	Sex		Type of RCT design	Type of sprain	Type of treatment	Follow up	Outcome
			Female	Male					
Pellow JE et al. 2001[24]. South Africa	30	15-50 Total mean age: 24.9 Group 1: 23.7 Group 2: 26.1	11 Group 1: 9 Group 2: 2	19 Group 1: 6 Group 2: 13	Single-blind, comparative, controlled study	Subacute ankle inversion sprains (<48h after initial injury)	Mortise separation adjustment, group 1 (n=15) Detuned ultrasound machine, group 2 (n=15)	28 days	McGill Pain Questionnaire Numerical Pain Rating Scale 101
Kucera et al. 2004 [25]. Prague	203	18-50 Group 1: 27.7 Group 2: 28.3	78 Group 1: 38 Group 2: 40	125 Group 1: 66 Group 2: 59	Randomised, double-blind clinical multicentre parallel study	Acute lateral ankle distortions (24h after the injury)	Verum, Group 1: Cream 10% Reference, Group 2: Cream 1%	14 days	VAS-10
Truyols-Dominguez S. et al. 2013 [26]. Spain	50	28-38 Total mean age: 33	13 Group 1: 6 Group 2: 7	37 Group 1: 19 Group 2: 18	Randomised clinical trial	Acute inversion ankle sprain Grade I and II (Injured <5 days)	Thrust and nonthrust manipulation and exercise intervention, group 1 (n=25) The same protocol plus myofascial manual therapy techniques, group 2 (n=25)	28 days	Numeric pain rating scale Total Functional Score for Assessment of Acute Lateral Ankle Sprains
Bleakley et al. 2006[27]. UK	89	Total mean age: 29.9 Group 1: 29.8 Group 2: 31.2	31 Group 1: 15 Group 2: 16	58 Group1: 28 Group2: 30	Randomised controlled trial, double-blind	Mild/moderate ankle sprain <48h after injury) Grades I and II	Intermittent ice, group 1 (n=43) Standard ice application, group 2 (n=46)	42 days	Binskey's lower extremity functional scale VAS
Cooke et al. 2009 [28]. UK	584	16-72 Total mean age: 30	247 Group 1: 64 Group 2: 54	337 Group 1: 80 Group 2: 88	Multicentred RCT with blinded	Acute severe ankle sprain	Group 1: Tubular bandage (n=144) Group 2: Below-knee cast (n=142) Group 3: Aircast brace (n=149)	270 days	FAOS Functional Limitations Profile

		Group 1: 31 Group 2: 30 Group 3: 29 Group 4: 30	Group 3: 65 Group 4: 64	Group 3: 84 Group 4: 85	assessment of outcome		Group 4: Bledsoe boot (n=149)		SF-12 EQ-5D VAS
Bassett et al. 2007 [11]. New Zealand	47	13-62	19 Group 1: 11 Group 2: 8	28 Group 1: 14 Group 2: 14	Controlled trial	Acute ankle sprain (first-time) Grades I, II and III	Clinical intervention, group 1 (n=25) Home intervention, group 2 (n=22)	14 days	Lower Limb Task Questionnaire Motor Activity Scale
Bleakley et al. 2010 [289]. UK	101	16-65	32 Group1: 17 Group2: 15	69 Group1: 34 Group 2: 35	Randomised controlled trial, blinded outcome assessor	Acute ankle sprain Grade I or II	Standard, group 1 (n=51) Exercise, group 2 (n=50)	112 days	VAS LEFS
Brison et al. 2016 [9]. Canada	504	-	280 Group1: 146 Group2: 134	224 Group 1: 108 Group 2: 116	Randomised controlled trial	Simple Grade I or II ankle sprain.	Physiotherapy, group 1 (n=254) Usual care, group 2 (n=250)	180 days	Foot and Ankle Outcome Score
Cleland et al. 2013 [2930]. USA	74	16-60	36 Group 1: 19 Group 2: 17	38 Group 1: 18 Group 2: 20	Randomised clinical trial, non- blinded	Inversion ankle sprain, acute and subacute	Manual therapy and exercise, group 1 (n=37) Home exercise programme, group 2 (n=37)	180 days	FAAM LEFS Numeric pain rating scale
Coudreuse et al. 2010 [304]. France	233	18-65	86	148	Randomised, double-blind, placebo- controlled study	Lateral ankle sprain (<48 hours after the injury)	Novel plaster with diclofenac, epolamine and heparin, group 1 Placebo plaster, group 2	7 days	VAS

Fotiadis et al. 2011 [312]. Greece	79	Mean age Group 1: 38.21 Group 2: 35.35	35 Group 1: 20 Group 2: 15	44 Group 1: 22 Group 2: 24	Prospective randomised study	Type II and III acute (less than 24h) lateral ankle sprain	Group 1: Micronized purified flavonoid fraction (Daflon 1,000 mg) (n = 42) Group 2: (Control group) Standard treatment (n = 39)	20 days	VAS
Gonzalez de Vega et al. 2013 [10]. Spain	420	18-40	112 Group 1: 39 Group 2: 39 Group3: 34	308 Group 1: 104 Group 2: 101 Group 3: 103	Multicentre, randomised, blinded and active-controlled study	Acute unilateral ankle sprain within the past 24 h. Grades I, II and III	Traumeel ointment (T-O), group 1 (n = 143) Traumeel gel (T-G), group 2 (n = 140) Diclofenac gel, group 3 (n = 137)	42 days	VAS FAAM
Man et al. 2007 [323]. UK	34	Total mean age 30.2 Group 1 34 Group 2 29 Group 3 28	11	23	Randomised trial	Acute ankle sprain injury (within 5 days)	Neuromuscular electrical stimulation treatment, group 1 (n = 11) Submotor ES treatment (control group), group 2 (n=11) Sham ES, group 3 (n=12)	14 days	Adapted Hughston Clinic Subjective Rating Scale for Ankle Disorders score
Kim et al. 2017[334]. South Korea	22	Total mean age: 17.72	0	22	Cross-over randomised design	Grades I and II lateral ankle sprain	Ankle balance taping group 1 Placebo taping group 2 No taping group 3	28 days	VAS
Naeem et al. 2014. [345]. Pakistan	120	Group 1: 28.77 Group 2: 29.83	77 Group 1: 35 Group 2: 42	43 Group 1: 25 Group 2: 18	Level I Randomised controlled trial	Grade I or II lateral ankle sprain	Functional treatment tubigrip, group 1 (n=60) Plaster of Paris, group 2 (n = 60)	42 days	VAS Karlsson score
Sandoval et al. 2010 [356]. Colombia	28	Total mean age: 21 Group 1: 21.3 Group 2: 22.5	10	18	Double-blind, controlled clinical trial	Grade I and II sprain mild or moderate, non-severe	Conventional treatment, group 1 (n=10) HVPC (+) group 2. Conventional treatment and HVPC (positive polarity) (n = 8)	56 days	VAS

		Group 3: 20.3					HVPC (-) group 3. Conventional treatment and HVPC (negative polarity) (n = 10)		
Stasinopoulos et al. 2016 [367]. Greece.	50	18-35 Group 1: 27.92 Group 2: 27.96	15 Group 1: 8 Group 2: 7	35 Group 1: 19 Group 2: 16	Single-centre, parallel group, single-blind, controlled study	Acute ankle sprain Grade II	Group 1: Cryotherapy plus Bioptron light therapy (n = 27) Group 2: Control group, cryotherapy only (n = 23)	5 days	VAS
Sultan et al. 2012 [378]. England	36	Group 1: 30 Group 2: 34	-	-	Single-centre, randomised, single-blinded, clinical trial	Ankle sprains sustained within 72 h. Grade I, II, III.	Tubigrip, group 1 (n=18) Elastic stocking, group 2 (n=18)	56 days	VAS SF12
Tully et al. 2012 [389]. Northern Ireland.	52	16-65 Group 1: 24.1 Group 2: 26.1 Group 3: 21.9	23 Group 1: 6 Group 2: 8 Group 3: 9	29 Group 1: 10 Group 2: 10 Group 3: 9	Randomised controlled trial	Acute ankle sprain (<7 days) Grade I or II	Standard, group 1 (n=16) Exercise, group 2 (n=18) Non-injured control. Group 3 (n=18)	7 days	Lower Extremity Functional Scale VAS
Zhao et al. 2018 [4039]. China.	62	Group 1: 34 Group 2: 30 Group 3: 33	-	-	Randomised controlled trial	Acute ankle sprains identified at 48 hours since the injury. Grades I and II	Standard treatment (RICE), group 1 (n = 19) Standard treatment (RICE) plus acupressure therapy, group 2 (n = 21) Standard treatment plus mock acupressure therapy, group 3 (n = 22)	56 days	VAS American Orthopedic Foot and Ankle Score SF12v2

RCT: Randomised control trial; VAS: Visual Analogue Scale; FAOS: Foot and Ankle Outcome Score; SF-12: Short Form-12; EQ-5D: EuroQol-5D;

LEFS: Lower Extremity Functional Scale; FAAM: Foot and Ankle Ability Measure.

	FAOS ADL	82.3	93.1	-0.1	-0.01	0.1	0.01	0.6	0.05	1.0	0.10	3.0	0.24	1.2	0.12
	FAOS sports	44.7	76.8	-0.3	-0.01	1.0	0.04	0.0	0.00	0.8	0.03	5.0	0.20	2.4	0.10
	FAOS QoL	43.0	64.9	1.9	0.08	4.0	0.15	4.9	0.22	6.1	0.24	5.9	0.26	6.3	0.24
	FLP ambulatory	16.9	6.3	0.1	0.01	-1.5	-0.18	-0.1	0.00	-2.2	-0.26	-3.1	-0.24	-1.7	-0.21
	SF-12 physical	39.2	49.7	-1.3	-0.16	0.2	0.03	-1.4	-0.17	-0.1	-0.01	2.2	0.27	0.3	0.04
	SF-12 mental	43.4	47.7	1.0	0.10	1.4	0.14	0.1	0.01	1.8	0.18	-0.6	-0.05	1.2	0.12
	EQ-5D	0.60	0.73	0.03	0.14	0.06	0.28	0.00	0.02	0.05	0.25	0.06	0.28	0.04	0.18
	VAS pain at rest	19.2	10.1	-0.7	-0.04	0.7	0.05	-0.7	-0.04	-2.9	-0.19	-4.8	-0.27	-0.8	-0.05
Bassett et al.[11]		Clinical intervention group						Home intervention group							
		Pre			Post			Pre			Post				
		LLTQ recreational subscale			12.00±10.10			20.27±12.58			8.18±7.24				
		LLTQ ADL subscale			2.32±3.60			7.18±7.06			1.82±3.58				
	Motor Activity Scale			5.14±1.28			1.77±1.60			5.73±1.08					
Bleakley et al.[289]		Standard						Exercise							
		Score						Score			P-value				
		Pain intensity at rest						1.0±0.16			0.008				
		Pain intensity on activity						3.9±0.28			0.3				
	Subjective function (LEFS)						24.6±1.96			0.38					
Brison et al.[9]		Physiotherapy group				Usual care group									
		1 month		6 months		1 month		6 months		P-value 1 month		P-value 6 months			
		23/180		92/165		33/213		113/174		0.65		0.09			
Cleland et al.[290]		Home Exercise Programme			Manual Therapy and Exercise (MTEx)			Between-Group Differences							
		4 weeks		6 months		4 weeks		6 months		4 weeks		6 months			

	FAAM ADL (0%-100%)	9.6	24.6	21.3	30.8	11.7	6.2
	FAAM sports (0%-100%)	13.8	33.5	27.1	40.7	13.3	7.2
	LEFS (0-80)	5.6	17.3	18.4	25.3	12.8	8.1
	NPRS (0-10)	-1.5	-3.1	-2.7	-3.6	-1.2	-0.47
Coudreuse et al.[340]		DHEP group		Placebo group		P-value	
		Baseline	7 days	Baseline	7 days	Baseline	7 days
	VAS pain (0-100)	73.2±1.0		69.3±1.1		p=0.007	p<0.01
Fotiadis et al.[312]		Daflon group		Control group		P-value	
		2 days	20 days	2 days	20 days	2 days	20 days
	VAS pain (1-10)	2.26 ± 1.86	0.64 ± 1.39	2.0 ± 1.64	0.32 ± 0.57	0.625	0.908
Gonzalez de Vega et al. [10]		Traumeel ointment		Traumeel gel		Diclofenac gel	
		Pre	Post	Pre	Post	Pre	Post
	VAS ankle pain	52.6	3.1	53.1	4.1	55.7	3.1
	FAAM ADL	51.2	41.7	56.0	40.5	51.2	41.7
	FAAM Sports	18.8	50.0	25.0	50.0	18.8	50.0
Man et al.[323]		NMES Group		Submotor ES Group		Sham ES Group	
		Session 1	Session 3	Session 1	Session 3	Session 1	Session 3
	Adapted HCSRSAD	65 (13)	42 (20)	70 (10)	45 (17)	63 (12)	46 (16)
Kim et al.[334]		Aquatic exercise		Land-based Exercise		Interaction Effect	
		Baseline	4 weeks	Baseline	4 weeks		
	VAS for pain	5.70 (0.36)	0.17 (0.16)	5.66 (0.36)	0.73 (0.16)	F = 3.75	P = .033
Naeem et al.[345]		Functional Treatment Tubigrip group		Plaster of Paris (POP) group		P-value	
		At presentation	At 6 weeks	at presentation	at 6 weeks	At presentation	At 6 weeks

	VAS	8.40 ± 0.92	3.88 ± 0.85	8.27 ± 0.94	4.97 ± 0.82	0.434	<0.001				
	Karlsson score	21.17 ± 6.31	76.25 ± 10.67	23.67 ± 5.24	70.10 ± 6.35	0.571	<0.001				
Sandoval et al.[356]		Conventional treatment GC		Conventional treatment EEAV (+)		Conventional treatment EEAV (-)		P value			
		First	Last	First	Last	First	Last	First	Last		
		VAS at rest	1.0±1.6	0.03±0.09	1.6±2.8	0	0.8±1.8	0	0.75	0.29	
		VAS palpation	5.8±2.9	0.7±0.84	5.6±3.3	0.4±0.6	6.9±1.4	0.91±0.91	0.53	0.41	
Stasinopoulos et al.[367]		Cryotherapy and Bioptron Light group			Cryotherapy only group			P-values			
		Pre-treatment		Post-treatment		Before treatment		Post-treatment			
		VAS pain (0-10)		6.66 (6.89–6.46)		4.46 (4.62–4.30)		6.62 (6.79–6.41) 62.88		5.34 (5.48–5.28)	P<0.0005
		Stocking group			Tubigrip						
Sultan et al.[378]		Initial		8 weeks		Initial		8 weeks			
		Total SF-12 score		100 (95–105)		119 (118–121)		100 (94–107)		102 (99–107)	
		VAS score		65 (56–73)		5 (0–11)		66 (59–73)		18 (10–26)	
		Standard group			Exercise group			P Value			
Tully et al.[389]		At baseline		At 1 week		At baseline		1 week		Baseline	1 week
		LEFS		35.31±16.56		54.00±12.61		38.22±19.81		61.63±13.05	
		VAS Pain at rest		26.5 (23.3)		7.1±7.5		19.6 (17.5)		3.3±4.4	
		VAS Pain with activity		53.06±27.7		34.3±22.9		53.3±22.7		25.7±22.1	
Zhao et al.[3940]		STG group		APG group		Mock APG group					
		Baseline		8 weeks		Baseline		8 weeks		Baseline	8 weeks
		VAS pain		5.05		0.26		5.05		0.10	
		AOFAS		39.53		97.47		38.14		99.04	
		Total SF-12 score		107.63		116.21		106.14		119.67	

VAS: Visual Analogue Scale; EQ-5D: EuroQol-5D, LLTQ: Lower Limb Task Questionnaire; NPRS: Numerical Pain Rating Scale; SF-12: Short Form-12;

FAOS: Foot and Ankle Outcome Score; FAAM: Foot and Ankle Ability Measure; LEFS: Lower Extremity Functional Scale.