Treatment and prevention of acute and recurrent ankle sprain: an overview of systematic reviews with meta-analysis

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ABSTRACT

Background Ankle sprains are highly prevalent with high risk of recurrence. Consequently, there are a significant number of research reports examining strategies for treating and preventing acute and recurrent sprains (otherwise known as chronic ankle instability (CAI)), with a coinciding proliferation of review articles summarising these reports.

Objective To provide a systematic overview of the systematic reviews evaluating treatment strategies for acute ankle sprain and CAI.

Design Overview of intervention systematic reviews. Participants Individuals with acute ankle sprain/CAI. Main outcome measurements The primary outcomes were injury/reinjury incidence and function. **Results** 46 papers were included in this systematic review. The reviews had a mean score of 6.5/11 on the AMSTAR quality assessment tool. There was strong evidence for bracing and moderate evidence for neuromuscular training in preventing recurrence of an ankle sprain. For the combined outcomes of pain, swelling and function after an acute sprain, there was strong evidence for non-steroidal anti-inflammatory drugs and early mobilisation, with moderate evidence supporting exercise and manual therapy techniques. There was conflicting evidence regarding the efficacy of surgery and acupuncture for the treatment of acute ankle sprains. There was insufficient evidence to support the use of ultrasound in the treatment of acute ankle sprains.

Conclusions For the treatment of acute ankle sprain, there is strong evidence for non-steroidal antiinflammatory drugs and early mobilisation, with moderate evidence supporting exercise and manual therapy techniques, for pain, swelling and function. Exercise therapy and bracing are supported in the prevention of CAI.

INTRODUCTION

The incidence of ankle sprain is high, posing a significant risk for participants of a wide range of activity types and sports.¹ Ankle sprain is associated with significant socioeconomic cost in addition to the acute debilitating symptoms (which include pain, swelling and impaired function); each year, over two million ankle sprains are treated in emergency departments in the US and UK.^{2–5} The longterm prognosis of acute ankle sprain is poor, with a high proportion of patients (up to 70%) reporting persistent residual symptoms and injury recurrence.^{6 7} 'Chronic ankle instability' (CAI) is the encompassing term used to describe the chronic symptoms that may develop following an acute ankle sprain, with injury recurrence at the epicentre of the chronic paradigm.⁸

There is an abundance of literature evaluating treatment strategies for acute ankle sprains and/or CAI. In accordance with this, a large number of systematic reviews have emerged to combine these studies' findings to synthesise and extract the best evidence for treatment guidelines. However, there are now such a large number of systematic reviews that identification, appraisal and consideration of each individual paper is not feasible for practitioners. This issue is further compounded by the probability that these reviews vary in quality and scope (with several reviews for one prevention/ treatment type) and their inclusion of papers with a high degree of overlap in the injury target (acute ankle sprain/CAI). Thus, there is a need to collate this evidence in a non-biased, systematic manner to ascertain evidence-based recommendations for the treatment of acute ankle sprain and CAI.

The aim of this paper was to provide a systematic overview of the systematic reviews evaluating treatment strategies for acute ankle sprain and CAI. A secondary aim was to identify the current gaps in the literature for researchers, and identify any conflicting evidence between reviews.

METHODOLOGY

Protocol

The study protocol was developed using the framework described by Smith *et al*,⁹ which relates to the methodology of conducting a systematic review of systematic reviews of healthcare interventions. The protocol for the review was not pre-registered prior to its completion.

In January 2016, we undertook a computerised literature search of the following databases from inception: PubMed, PEDro, Scopus, Web of science, EBSCO and the Cochrane library.¹⁰ The database search was further supplemented with a manual search of the reference lists in each review. These processes retrieved a set of systematic reviews closely related to the treatment of ankle sprain injuries and CAI.

The empirical search strategy was developed in accordance with the recommendations outlined by Montori *et al.*¹¹ The search strategy was constructed for MEDLINE and completed in a stepwise manner using the Boolean operators (table 1).

The search strategy was adapted for each database on the basis of previously published recommendations.¹² No restrictions (including language) were applied in any of the databases when the search was completed. One investigator reviewed

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teps	Text string
1)	ankle[Text Word]
2)	sprain OR strain OR rupture OR instability OR unstable OR repeated OR recurrent OR multiple OR functional OR functionally OR chronic OR chronically
;)	intervent*[Title/Abstract] OR rehab*[Title/Abstract] OR prevent*[Title/ Abstract] OR therap*[Title/Abstract]
1)	(#1 AND #2 AND #3)
5)	meta-analysis[Publication Type] OR meta-analysis[Title/Abstract] OR meta-analysis[MeSH Terms] OR review[Publication Type] OR search* [Title/Abstract]
6)	#4 AND #5

all the titles produced by the database searches, and retrieved suitable abstracts. After screening by abstract, full text articles were obtained for review (figure 2).

Inclusion/exclusion criteria

Our inclusion criteria were as follows: (1) the study must be a systematic review, which was defined as a research study that collects and evaluates multiple studies, and that limits inclusion bias of authors by using a clearly defined search strategy; (2) it must evaluate the efficacy of an intervention for the treatment and/or prevention of acute ankle sprain and/or CAI; (3) the efficacy of the intervention must be measured by means of an experimentally quantifiable outcome (detailed later). Patients with CAI were defined by having a history of at least one ankle sprain, a history of the previously injured ankle joint 'giving way' and/or recurrent sprain and/or 'feelings of instability'.⁸ No restrictions were applied with regard to the intervention type or sample population of the studies included in the review papers.

Data extraction

A data extraction form was devised by all the authors. Data extraction was performed by one author. A random sample of studies were selected and doublechecked by a second author, to ensure quality. Data extraction included information related to both the review itself (including study details (author, year of publication and title), the injury type(s), outcome(s), intervention type(s) and main findings), and the individual studies included in the reviews (including study details (author, year of publication and title), design (randomised controlled trial (RCT)/non-RCT), sample population (% males vs females), experimental group N, control group N, injury type(s), intervention type(s), comparison type (s), protocol, outcome(s), findings (number of injuries in the control/experimental groups), conclusions). For studies in which an exercise therapy intervention was administered, the total 'dose' of the intervention (in minutes) was calculated and extracted.

Reviews were divided as to whether they concerned the treatment of acute ankle sprain or CAI (injury type). Owing to the potential overlap of treatment goals, any review that evaluated the efficacy of a prevention strategy for a new or recurrent ankle sprain with sufficient follow-ups (\geq 12 months) was also grouped into the 'CAI treatment' division, as recurrent ankle sprain is considered to be at the centre of the CAI paradigm.⁸ ¹³ No restrictions were placed on the severity or type of ankle sprain sustained (lateral/medial/syndesmotic).

Intervention types were divided into surgical and non-surgical. Non-surgical interventions were further subclassified

into physiotherapeutic (including exercise and manual therapies), external support (including taping, bracing and orthotics), electrophysical (including cryotherapy and any type of electrotherapies), pharmacological (including medications) and complementary (acupuncture; aromatherapy and herbal medicines) agents. These interventions were chosen following a thorough review of the literature and on the basis of the classification system used by Bleakley *et al.*¹⁴

The outcomes of interest were delineated into primary and secondary types. The primary outcomes were (re-) injury incidence/prevalence and/or self-reported function/disability based on a validated questionnaire for ankle joint function.¹³ The secondary outcomes included pain, strength, range of motion (ROM), proprioception and muscle activity in the region of ankle joint, in addition to performance measures (which included biomechanical analyses of static/dynamic postural control, gait or jumping/landing tasks). A schematic depicting the aforementioned classification system is depicted in figure 1.

Risk of bias assessment

The quality of the systematic reviews was independently assessed by two authors (CD and SH) using the AMSTAR tool.¹⁵ Any disagreement between authors was resolved by group consensus. Where reviews provided an overall quality assessment of the included studies (items number 7/8 of the AMSTAR tool), those tools were extracted as potentially valuable research resources.

Analysis

The main conclusions from each systematic review concerning injury and intervention type were extracted. The reviews were categorised as 'high' or 'low' quality based on an arbitrary score of 7/11 on the AMSTAR quality rating. This 'high- quality' threshold was subsequently used to conduct a best evidence synthesis of the reviews. The outcomes, intervention type, main results and conclusions relating to our predefined primary and secondary outcomes (defined in data extraction) from the highquality reviews (ie, rating \geq 7) were compiled in tabular format, and stratified according to intervention type. This best evidence synthesis was conducted in order to provide a reference point for the interventions with the strongest evidence supporting or opposing their use.

Additionally, the individual papers included in each review were identified to determine; if they reported on any of the primary or secondary outcomes. The reference for each individual paper was extracted in such situations. In situations where there were contradictory conclusions from reviews then the individual quality rating of each review was presented (to contextualise a given conclusion to the overall quality of the review that made it); if the conclusions between different reviews were in agreement, the quality range (lowest and highest) of the reviews in question was presented.

Exploratory meta-analyses of the individual studies were performed for the primary outcome of (re-) injury incidence where possible. Only RCTs were included in pooling. Data (experimental group N and injuries after follow-up, control group N and injuries after follow-up; total dose of exercise (where appropriate)) were entered into the Cochrane Collaboration Review Manager (V.4.2) software program. Study effect estimates were calculated using ORs with 95% CIs. Studies were weighted by sample size. Data were assessed for heterogeneity based on the Q test in conjunction with the I² statistic. The significance for χ^2 was set at p<0.1. I² values >50% were considered to represent substantial heterogeneity.¹⁶ In cases where substantial

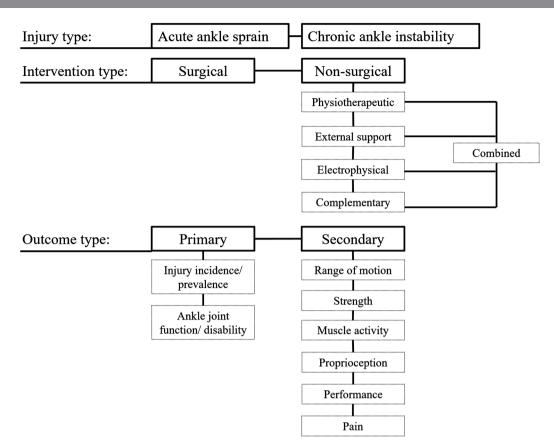


Figure 1 Schematic depicting the injury, intervention and outcome types by which the studies were stratified.

heterogeneity was present, a random-effects model was used. Accordingly, OR values were used to enable several forest plots.

RESULTS

Search results

The initial search strategy produced 2506 articles. A PRISMA diagram of the search strategy is available in figure 2. A total of 46 systematic reviews met the inclusion criteria.¹⁴ ¹⁷⁻⁶¹ The quality of the included reviews is displayed in table 2.

Forty of the reviews performed some kind of quality assessment of their included studies (see online supplementary table S2).

Following the removal of duplicated papers, these reviews collectively included 309 individual reports. Additional information extracted from these studies segregated by injury and intervention is available in the online supplementary information for this article; due to the large volume of extracted information, only information relating to the primary outcomes (injury (re-) incidence/function) has been presented in the main text; all information related to the individual studies included in the reviews/the secondary outcomes is available in the supplemental documents. Please refer to the online supplementary table S1 for the results of the individual studies with respect to the primary and secondary outcomes.

There was a significant amount of overlap between the reviews regarding the injury type of interest, with reviews being classified as 15 investigating treatment both strategies for acute ankle sprain and CAI.¹⁴ ¹⁷ ¹⁹ ²⁴ ²⁸ ³² ³⁴ ³⁷ ⁴¹ ⁴³ ⁴⁵ ⁵⁰ ⁵² ⁵³ ⁶⁰ Twenty reviews investigated treatment strategies for acute ankle sprain specific-ally.¹⁸ 21-23 26 27 29-31 39 40 44 46-49 54 55 58 61 Nine reviews investigated CAI treatment strategies for specifically.²⁰ 33 35 36 42 51 56 57 59 Two reviews investigated treatment strategies for syndesmotic ankle sprain; however, these only included case studies and did not report on either of our primary or secondary outcomes.^{25 38} Eight of the reviews evaluated surgical interventions for the treatment of acute ankle sprain^{20 25 29 31 38-40 51} with 45 evaluating some kind of nonsurgical intervention.¹⁴ ^{17–61} The results and conclusions from the reviews ranking as 'high' quality have been synthesised in a best evidence synthesis table (table 3), stratified by the intervention type.

Acute ankle sprain

Surgical interventions Six reviews^{20 29 31 39 40 51} (quality range=5-10) compared surgical to non-surgical interventions for the treatment of acute ankle sprain. These reviews contained 82 individual (nonduplicate) papers. Of these 82, 33 (32 RCTs, 1 non-RCTs; N=4080; 65% male, 35% female) evaluated a surgical intervention specifically.^{62–9}

None of these reviews reported on the primary outcome of recurrence. Function was determined by the time taken to return to activity/work.^{20 29 31 39 40 51} Of the six reviews, one (quality=6/11) advocated conservative management (including physiotherapeutic and external support interventions) over surgery,³⁹ and two (quality=7/11;⁴⁰ quality= $5/11^{31}$) identified that surgery had better outcomes when compared with conservative management in the treatment of acute ankle sprain.^{31 40} One review (quality=9) found that there was insufficient evidence to determine the relative effectiveness of either surgical or conservative management in the treatment of an acute ankle sprain.²⁹

Despite its projected benefits, several of the reviews identified the propensity for a surgical intervention to have a higher risk **Figure 2** PRISMA flow diagram depicting the search protocol with stepwise article inclusion/exclusion. CAI, chronic ankle instability.

Search process Excluded Total number of hits screened: n = 2,506Medline (PubMed): n = 458Ebsco: n = 859PEDro: n = 0Cochrane Central Register of Controlled Trials: n = 26Scopus: n = 0Web of Science: n = 1,159Articles identified via reference list search: n = 4~ Duplicates: n = 404Articles remaining after 1^{st} screening: n = 2102Based on title: n = 1,906Articles remaining after 2^{nd} screening: n = 196Based on abstract: n = 103Articles remaining after 3rd screening: n = 93 After review of full texts : n = 47• Non-systematic (literature) reviews (21) Unrelated to ankle sprain/CAI (24) No intervention (2)

of complication (which included issues such as wound healing, infection, dystrophy, iatrogenic nerve damage leading to sensory deficit and paraesthesia) compared with a conservative intervention.²⁰ ²⁹ ³¹ ³⁹ ⁴⁰ A surgical intervention was also associated with greater financial cost.²⁹ ⁴⁰

Non-surgical interventions *Physiotherapeutic*

Eighteen systematic reviews evaluated a physiotherapeutic intervention for the treatment of acute ankle sprain¹⁴ ¹⁷ ¹⁹ ²³ ²⁹ ³¹ ³² ³⁹ ⁴¹ ⁴⁴ ⁴⁵ ⁵⁰ ⁵² ⁵³ ⁵⁸ ⁶⁰ ⁶¹ ⁹⁵ (quality range=2–10), which themselves included 118 individual reports were included on removal of papers duplicated between each review. The two main kinds of physiotherapeutic intervention evaluated were exercise therapy and manual therapy.

Exercise therapy

Of the 18 separate systematic reviews, 15^{14} ¹⁷ ²³ ²⁹ ³¹ ³⁹ ⁴¹ ⁴⁴ ⁴⁵ ⁵⁰ ⁵² ⁵³ ⁵⁸ ⁶⁰ ⁶¹ (quality range=2-10) evaluated the effectiveness of exercise therapy for the treatment of acute ankle sprain. Included in these reviews were 41 individual papers (33 RCTs, 8 non-RCTs; N=4680; 68% male, 32% female) where exercise therapy was the primary intervention for the treatment of acute ankle sprain. ⁸² ⁹⁶⁻¹³⁵

The reviews were unanimous in their consensus that exercise therapy improves self-reported function following acute ankle sprain.³ ¹⁴ ¹⁷ ²³ ⁴¹ ⁴⁴ ⁵² ⁵³ ⁶⁰ ⁶¹ Three of the reviews reported

on the primary outcome of recurrence in a sample of individuals with acute ankle sprain.¹⁴ ³⁹ ⁶⁰ All three confirmed the effectiveness of exercise therapy for the prevention of recurrence following an acute ankle sprain.⁴ ¹⁴ ³⁹ ⁶⁰

Manual therapy

Total number of included reviews: n = 46

Of the 18 separate systematic reviews that evaluated a physiotherapeutic intervention, 5^{14} ¹⁹ ³² ⁴⁵ ⁵⁰ (quality range 5–10) evaluated the effectiveness of manual therapy for the treatment of acute ankle sprain. Included in these reviews were $12^{136-147}$ individual papers (all RCTs, N=687) in which some form of manual therapy technique was used in the treatment of acute ankle sprain.⁵

It is unclear whether manual therapy was beneficial for the primary outcomes of self-reported function or injury recurrence. $^{6.7 14}$ 19 32 45 50

Electrophysical agents

Seven systematic reviews evaluated an electrophysical intervention of some kind for the treatment of acute ankle sprain¹⁴ ¹⁸ ⁴⁵ ⁴⁹ ⁵² ⁵³ ⁹⁵ (quality=6.7).² Fifty papers (on removal of duplicates) were included in these reviews. Of these 50 papers, 21 (all RCTs, N=1459; 59% male, 41% female) evaluated the effectiveness of an electrophysical agent in the treatment of acute ankle sprain.⁸ ¹²⁰ ¹²⁴ ¹⁴⁸⁻¹⁶⁶

Applications of ice and compression or the use of elevation do not seem to be effective for improving the primary outcomes

 Table 2
 Quality of the included reviews as rated on the AMSTAR scale

		٨N	/IST/	AR cr	iteri	a							
Author	Year	1	2	3	4	5	6	7	8	9	10	11	Total
Baltaci	2003	0	0	0	1	0	1	0	0	0	0	0	2
Bleakley	2004	1	0	1	0	0	1	1	1	1	0	0	6
Bleakley	2008	1	0	1	0	0	1	1	1	0	0	0	5
Brantingham	2009	1	1	1	1	1	1	1	1	0	1	1	10
de Vries	2006	1	1	1	0	1	1	1	1	1	1	1	10
Dizon and Reyes	2010	1	1	1	1	0	1	1	1	1	0	1	9
Evans	2012	1	0	1	1	0	1	0	0		0	0	4
Feger	2015	0	0	1	0	1	1	1	1	1	0	0	6
Handoll	2001	1	0	1	1	1	1	1	1	1	1	1	10
Jones	2007	0	0	1	1	0	1	0	0	0	0	0	3
Kemler	2011	0	0	1	0	1	1	1	1	1	0	1	7
Kerkhoffs	2001	1	1	1	1	1	1	1	1	1	0	1	10
Kerkhoffs	2003	1	1	1	1	0	1	1	0	1	0	1	8
Kerkhoffs	2007	1	1	1	0	1	1	1	1	1	0	1	9
Kim	2014	1	1	1	1	1	1	1	1	1	0	1	10
Lihua	2012	1	1	0	0	0	1	1	0	0	1	0	5
Loudon	2014	1	0	1	0	0	1	1	1		1	0	6
Loudon	2008	1	0	0	0	0	1	1	1		0	1	5
McGuine	2003	1	0	1	0	0	1	0	0		0	0	3
Mckeon	2008	1	0	1	0	0	1	1	1	0	0	0	5
O'Driscoll	2011	1	0	1	0	0	1	1	1	1	0	1	7
Park	2013	1	1	1	1	0	1	1	1	1	0	1	9
Parlamas	2013	1	1	1	0	0	1	1	0	0	0	0	5
Petersen	2013	1	0	1	0	0	1	1	1		0	1	6
Pijnenburg	2000	1	0	1	0	1	1	1	1	1	0	0	7
Postle	2012	1	1	1	1	1	1	1	0	1	0	0	8
Refshauge	2003	1	0	0	0	0	0	0	0		0	0	1
Schiftan	2015	1	1	1	0	0	1	1	1	1	0	1	8
Seah	2011	0	0	0	0	0	1	1	1		0	0	3
Terada	2013	1	0	1	1	0	1	1	1	0	0	0	6
Thacker	1999	1	0	1	1	0	0	1	1	1	0	0	6
Thacker	2003	1	0	1	1	0	0	1	1	0	0	0	5
van den Bekerom	2012	1	1	1	1	1	1	1	1	1	1	1	11
van den Bekerom	2011	1	0	1	0	0	1	1	1	1	0	0	6
van der Wees	2006	1	1	1	1	1	1	1	1	1	1	0	10
van Ochten	2014	1	0	1	0	0	1	1	1	1	0	0	6
van Os	2005	1	1	1	0	0	1	1	0	1	0	0	6
van Rijn	2010	1	0	1	0	0	1	1	1	1	0	1	7
Verhagen	2000	1	0	1	0	0	1	1	0		0	0	4
Verhagen	2010	1	0	1	0	0	1	1	1		0	0	5
Webster	2010	1	0	1	0	0	1	1	1	0	0	0	5
Wikstrom	2009	1	0	1	0	1	0	1	1	1	1	1	8
Woitzik	2015	1	0	1	0	0	1	1	1	1	0	1	7
Wortmann	2013	1	0	0	0	0	1	0	0		0	0	2
Zech	2009	1	1	1	0	1	1	1	1	1	0	1	9
Zöch	2003	0	0	1	0	1	1	1	1		0	0	5

Items legend: (1) Was an 'a priori' design provided? (2) Was there duplicate study selection and data extraction? (3) Was a comprehensive literature search performed? (4) Was the status of publication (ie, grey literature) used as an inclusion criterion? (5) Was a list of studies (included and excluded) provided? (6) Were the characteristics of the included studies provided? (7) Was the scientific quality of the included studies assessed and documented? (8) Was the scientific quality of the included studies used appropriately in formulating conclusions? (9) Were the methods used to combine the findings of studies appropriate? (10) Was the likelihood of publication bias assessed? (11) Were potential conflicts of interest included?

of self-reported function or recurrence following acute ankle joint sprain compared with no treatment.¹⁸ ⁹⁵ Three reviews concluded that treatment success was achieved on the basis of an exercise therapy intervention that was often combined with a rest/ice/compression/elevation (RICE) protocol.^{52 53 95}

None of the reviews determined any beneficial effect of ultrasound therapy in the treatment of acute ankle sprain.¹⁴ ⁴⁹ However, there are very few trials evaluating the effectiveness of ultrasound therapy for acute ankle sprains,⁴⁹ and fewer still have considered the range of intervention parameters available.¹⁴ ⁴⁹ Similarly, the evidence for the efficacy of laser, electrical stimulation and hyperbaric oxygen therapies is limited due to a lack of related research.¹⁴ ⁴⁵

External support

Six systematic reviews evaluated an external support of some kind for the treatment of acute ankle sprain²⁶ ²⁸ ³⁹ ⁴⁴ ⁵³ ⁶¹ (quality range 3–10). These reviews included 46 individual papers. Twenty-four of these (23 RCTs, 1 non-RCT; N=2141, 66% male, 34% female) evaluated some kind of external support (which included taping, bracing and orthoses⁹) in the treatment of acute ankle sprain. ¹⁰³ ¹⁰⁵ ¹¹⁶ ¹²⁶ ¹³⁵ ^{167–185}

The reviews were unanimous in their consensus that braces and taping are effective in the treatment of acute ankle sprains for the primary outcomes of self-reported function and recurrence.^{10 11 26 28 39 44 53 61}

Complementary

Three systematic reviews evaluated some kind of complementary medicine for the treatment of acute ankle sprain¹⁴ ³⁰ ³⁷ (quality range 5–10). These three reviews included 60 individual papers. There were two papers duplicated between these reviews, leaving 58 individual reports. Of these 58, 35 (all RCTs; N=2358, 67% male, 33% female) evaluated some kind of complementary medicine in the treatment of acute ankle sprain.^{186–220} Acupuncture was the primary focus of the reviews however.¹⁴ ³⁰ ³⁷

Two of the reviews (quality=5/11;¹⁴ $10/11^{30}$) reported that there were insufficient data to determine the relative effectiveness of complementary medicine in the treatment of acute ankle sprain for self-reported function or injury recurrence.¹²

The final review (quality=9/11) concluded that acupuncture was likely to have a therapeutic effect in improving acute symptoms, but acknowledged that the results were likely to be overestimated due to the low quality of the included studies.³⁷

On this basis, the evidence for the efficacy of complementary therapies in the treatment of acute ankle sprain for the primary outcomes of injury recurrence/self-reported function is inconclusive.

Pharmacological

Three systematic reviews evaluated some kind of pharmacological intervention for the treatment of acute ankle sprain^{14 30 44} (quality range 3–10). These reviews included 47 papers (all RCTs; N=6395, 62% male, 38% female). There were no duplicated papers between these reviews. Thirteen papers (N=2423, 47% male, 53% female) evaluated any pharmacological agent (which typically included non-steroidal anti-inflammatory drugs) in the treatment of acute ankle sprain as the primary intervention.^{13 136 186 187 196 199 220–226}

Owing to the short follow-up periods in the individual studies, no conclusions could be made for the primary outcomes of self-reported function or injury recurrence. 6 of 17

Doherty C, et al. Br J Sports Med 2017;51:113-125. doi:10.1136/bjsports-2016-096178

Table 3 Results of the best evidence synthesis from the reviews deemed as 'high' (\geq 7 on the AMSTAR tool) quality. Only outcomes, results and conclusions relating to our predefined primary and secondary outcomes are displayed

Study	AMSTAR	Outcome (s)	Intervention	Results	Review conclusion	Summary
Exercise therapy						
de Vries <i>et al²⁰</i>	10	Functional outcome, subjective stability, recurrent injury, pain, swelling	Any type of treatment for chronic lateral ankle instability was considered	10 included studies; data from 3 out of 4 studies showed a better outcome for neuromuscular training compared with no training	Neuromuscular training alone appears effective in the short term. There is insufficient evidence to support any one surgical intervention over another surgical intervention for CAI but it is likely that there are limitations to the use of dynamic tenodesis.	+
O'Driscoll and Delahunt ³⁶	7	Reinjury, postural stability, strength, self-reported function	Exercise therapy (neuromuscular)	There is limited to moderate evidence to support improvements in dynamic postural stability, and patient perceived functional stability through neuromuscular training in participants with CAI. There is limited evidence of effectiveness for neuromuscular training for improving static postural stability, active and passive joint position sense, isometric strength, and a reduction in injury recurrence rates.	Strong evidence of effectiveness was lacking for all outcome measures. All but one of the studies included in the review were deemed to have a high risk of bias, and most studies were lacking sufficient power. Therefore, in future we recommend conducting higher quality RCTs using appropriate outcomes to assess for the effectiveness of neuromuscular training in overcoming sensorimotor deficits in participants with CAI.	?
Postle <i>et al</i> ⁴¹	8	Reinjury, self-reported function	Exercise therapy (proprioceptive exercise)	The results indicated that there is no statistically significant difference in recurrent injury between the addition of proprioceptive exercises during the rehabilitation of patients following ankle ligament injury ($p<0.68$). The addition of proprioceptive training demonstrated a significant reduction in subjective instability and functional outcomes ($p<0.05$).	Further study is warranted to develop the rigour of the evidence base and to determine the optimal proprioceptive training programme following ankle ligament injury with different populations.	+
Schiftan <i>et al</i> ⁴³	8	Reinjury	Exercise therapy (proprioceptive training)	Results of the meta-analysis combining all participants, irrespective of ankle injury history status, revealed a significant reduction of ankle sprain incidence when proprioceptive training was performed compared with a range of control interventions (RR=0.65, 95% CI 0.55 to 0.77).	Proprioceptive training programmes are effective at reducing the rate of ankle sprains in sporting participants, particularly those with a history of ankle sprain. Current evidence remains inconclusive on the benefits for primary prevention of ankle sprains.	+
van der Wees <i>et al⁵⁰</i>	10	Reinjury, postural stability, ROM	Exercise therapy and manual mobilisation	Exercise therapy was effective in reducing the risk of recurrent sprains after acute ankle sprain: RR 0.37 (95% CI 0.18 to 0.74). No effects of exercise therapy were found on postural sway in patients with functional instability: SMD 0.38 (95% CI -0.15 to 0.91). 4 studies demonstrated an initial positive effect of different modes of manual mobilisation on dorsiflexion ROM.	It is likely that exercise therapy, including the use of a wobble board, is effective in the prevention of recurrent ankle sprains. Manual mobilisation has an (initial) effect on dorsiflexion ROM, but the clinical relevance of these findings for physiotherapy practice may be limited.	+
van Rijn <i>et al⁵³</i>	7	Pain, instability, reinjury	Exercise (additional supervised exercises compared with conventional treatment alone)	There was limited to moderate evidence to suggest that the addition of supervised exercises to conventional treatment leads to faster and better recovery and a faster return to sport at short-term follow-up than conventional treatment alone.	Additional supervised exercises compared with conventional treatment alone have some benefit for recovery and return to sport in patients with ankle sprain, though the evidence is limited or moderate and many studies are subject to bias.	+
Wikstrom <i>et al⁵⁷</i>	8	Postural control	Exercise (balance training)	Balance training improves postural control (ES= -0.857, p<0.0001).	Balance training improves postural control scores after both acute and lateral ankle trauma. However, further research should determine the optimal dosage, intensity, type of training and a risk reduction/ preventative effect associated with balance training after both acute and chronic ankle trauma.	+

Review

Continued

Study	AMSTAR	Outcome (s)	Intervention	Results	Review conclusion	Summar
Woitzik <i>et al⁵⁸</i>	7	Self-reported recovery, pain, instability	Exercise	The evidence suggests that for recent lateral ankle sprain: Rehabilitation exercises initiated immediately postinjury are as effective as a similar programme initiated 1 week postinjury; supervised exercise provides no additional benefit when added to education and advice (including home exercises) compared with education and advice (including home exercises) alone.	For recent lateral ankle sprains, similar outcomes are offered between an accelerated exercise programme and exercises given 1 week postinjury.	+
Zech <i>et al⁶⁰</i>	9	Recurrent sprains and giving way episodes/ postural control/proprioception/muscle reaction time to sudden perturbation/ankle joint functionality scores/muscle strength/ EMG/oedema	Exercise (proprioceptive/ neuromuscular)	Proprioceptive/neuromuscular exercise was effective at increasing functionality as well as at decreasing the incidence of recurrent injuries and 'giving way' episodes after ankle sprains	It can be concluded that proprioceptive and neuromuscular interventions after ankle injuries can be effective for the prevention of recurrent injuries.	+
Conclusions				ce and improving self-reported function. One high-quality e of exercise therapy for improving postural stability (2 rev	review found no evidence for the addition of supervised ex- iews supporting and 1 finding no effect).	ercises to
Manual therapy						
Brantingham et al ¹⁹	10	Self-reported function, ROM, pain, swelling, proprioception, stabilometry	Manual therapy	There is a level of B or fair evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for ankle inversion sprain.	Larger, methodologically improved, and well-funded randomised controlled and clinical trials, as well as observational, clinical, and basic science research, case series, and studies, are both needed and merited.	+
van der Wees et al ⁵⁰	10	Reinjury, postural stability, ROM	Exercise therapy and manual mobilisation	Exercise therapy was effective in reducing the risk of recurrent sprains after acute ankle sprain: RR 0.37 (95% CI 0.18 to 0.74). No effects of exercise therapy were found on postural sway in patients with functional instability: SMD 0.38 (95% CI -0.15 to 0.91). 4 studies demonstrated an initial positive effect of different modes of manual mobilisation on dorsiflexion ROM.	It is likely that exercise therapy, including the use of a wobble board, is effective in the prevention of recurrent ankle sprains. Manual mobilisation has an (initial) effect on dorsiflexion ROM, but the clinical relevance of these findings for physiotherapy practice may be limited.	?
Conclusions				f acute ankle sprain injury. At present, there does not appe I therapy results in any long-term benefits in either acute	ear to be any negative effects of adding manual therapy to ankle sprains or CAI.	an exercise
Surgery						_
de Vries <i>et al</i> ²⁰	10	Primary outcomes: functional outcome, subjective stability Secondary outcomes: recurrent injury, pain, swelling	Any type of treatment for chronic lateral ankle instability was considered	10 included studies; data from 3 out of 4 studies showed a better outcome for neuromuscular training compared with no training.	Neuromuscular training alone appears effective in the short term. There is insufficient evidence to support any one surgical intervention over another surgical intervention for CAI but it is likely that there are limitations to the use of dynamic tenodesis.	?
Kerkhoffs <i>et</i> al ²⁹	9	Reinjury; persistent pain; subjective instability	Surgical compared with conservative interventions	There is insufficient evidence available from RCTs to determine the relative effectiveness of surgical and conservative treatment for acute injuries of the lateral ligament complex of the ankle in adults.	Given the risk of operative complications and the higher costs (including those of hospital admission) associated with surgery, the best available option for most patients would be conservative treatment for acute injuries and close follow-up to identify patients who may remain symptomatic. High-quality RCTs of primary surgical repair vs the best available conservative treatment for well-defined injuries are required.	?

7 of 17

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8 of 17

Table 3 Continued

Study	AMSTAR	Outcome (s)	Intervention	Results	Review conclusion	Summary	
Pijnenburg et af ⁴⁰	7	Pain and self-reported function (giving way)	Any	With respect to giving way, a significant difference was noted between operative treatment and functional treatment (RR 0.23; 95% CI 0.17 to 0.31) in favour of operative treatment and a significant difference was also noted between functional treatment and treatment with a cast for 6 weeks (RR 0.69; 95% CI 0.50 to 0.94) in favour of functional treatment. With respect to residual pain, no significant difference was found between operative and functional treatment and a significant difference was found between functional treatment with a cast for 6 weeks (RR 0.67; 95% CI 0.50 to 0.90).	of the lateral ankle ligaments leads to more residual 0.31) symptoms. Operative treatment leads to better results than functional treatment, and functional treatment leads to better results than cast immobilisation for 6 weeks. ative erence		
Conclusions External support	There is lir	nited evidence supporting surgery for the trea	tment of lateral ankle ruptures comp	ared with no treatment for self-reported function. Howeve	er, there are higher risks of complications with surgical inter	rventions.	
Dizon and Reyes ²¹	9	Reinjury	External ankle supports	The main finding was the reduction of ankle sprain by 69% (OR 0.31, 95% CI 0.18 to 0.51) with the use of ankle brace and reduction of ankle sprain by 71% (OR 0.29, 95% CI 0.14 to 0.57) with the use of ankle tape among previously injured athletes.	No type of ankle support was found to be superior than the other.	+	
Handoll <i>et al²⁴</i>	10	Ankle reinjury, instability	External ankle support; ankle disk training; stretching; health education programme and controlled rehabilitation.	The main finding was a significant reduction in the number of ankle sprains in people allocated external ankle support (RR 0.53, 95% CI 0.40 to 0.69). This reduction was greater for those with a previous history of ankle sprain, but still possible for those without prior sprain. There was limited evidence for reduction in ankle sprain for those with previous ankle sprains who did ankle disk training exercises.	Participants with a history of previous sprain can be advised that wearing such supports may reduce the risk of incurring a future sprain.	+	
Kemler <i>et al²⁶</i>	7	Reinjuries, pain, swelling, instability, and functional outcomes	External support (comparison of different types)	Best evidence syntheses only demonstrated a better treatment result in terms of functional outcome for bracing in comparison to other forms of external support. There were no differences for any other outcomes (eg, reinjuries, residual symptoms).	Further research should focus on economic evaluation and on different types of ankle brace, to examine the strengths and weaknesses of ankle braces for the treatment of acute ankle sprains.	+	
Kerkhoffs et al ²⁸	8	Swelling, instability	External support (comparison of different types)	Persistent swelling at short-term follow-up was less with lace-up ankle support than with semirigid ankle support (RR 4.2 95% Cl 1.3 to 14), an elastic bandage (RR 5.5; 95% Cl 1.7 to 18) and tape (RR 4.1; 95% Cl 1.2 to 14). One trial reported better results for subjective instability using the semirigid ankle support than the elastic bandage (RR 8.0; 95% Cl 1.0 to 62).	We conclude that an elastic bandage is a less effective treatment. Lace-up supports seem better, but the data are insufficient as a basis for definite conclusions.	+	
Conclusions Complementary (a	be superio	r for self-reported function in comparison to t		cing) for reducing reinjury incidence and improving self-re	ported function. There is moderate evidence suggesting bra	icing may	
Kim <i>et al³⁰</i>	10	, Self-reported function, reinjury	Acupuncture	The currently available evidence from a very heterogeneous group of randomised and quasi-RCTs evaluating the effects of acupuncture for the treatment of acute ankle sprains does not provide reliable support for either the effectiveness or safety	Future rigorous randomised clinical trials with larger sample sizes will be necessary to establish robust clinical evidence concerning the effectiveness and safety of acupuncture treatment for acute ankle sprains.	?	

Review

Study	AMSTAR	Outcome (s)	Intervention	Results	Review conclusion	Summary
				of acupuncture treatments, alone or in combination with other non-surgical interventions; or in comparison with other non-surgical intervention.		
Park <i>et al³⁷</i>	9	Pain	Acupuncture	Acupuncture was more effective than various controls in relieving pain, facilitating return to normal activity, and promoting quality of life, but these analyses were based on only a small number of studies. Acupuncture did not appear to be associated with adverse events.	Given methodological shortcomings and the small number of high-quality primary studies, the available evidence is insufficient to recommend acupuncture as an evidence-based treatment option. This calls for further rigorous investigations.	+
Conclusions		nited evidence based primarily on low-quality nd reinjury incidence.	v studies supporting the use of acupu	incture for pain relief in ankle sprain injury. There is limite	d evidence demonstrating no effect of acupuncture on self-	reported
Immobilisation						
Pijnenburg et al ⁴⁰	7	Any	Pain and self-reported function (giving way)	With respect to giving way, a significant difference was noted between operative treatment and functional treatment (RR 0.23; 95% CI 0.17 to 0.31) in favour of operative treatment and a significant difference was also noted between functional treatment and treatment with a cast for 6 weeks (RR 0.69; 95% CI 0.50 to 0.94) in favour of functional treatment. With respect to residual pain, no significant difference was found between operative and functional treatment and a significant difference was found between functional treatment with a cast for 6 weeks (RR 0.69; 95% CI 0.50 to 0.94) in favour of functional treatment. With respect to residual pain, no significant difference was found between functional treatment and a significant difference was found between functional treatment and treatment with a cast for 6 weeks (RR 0.67; 95% CI 0.50 to 0.90).	We concluded that a no-treatment strategy for ruptures of the lateral ankle ligaments leads to more residual symptoms. Operative treatment leads to better results than functional treatment, and functional treatment leads to better results than cast immobilisation for 6 weeks.	-
Kerkhoffs <i>et al²⁷</i>	10	Pain, swelling, subjective and objective instability, recurrent injury	Immobilisation	There is significant evidence to support functional treatment over immobilisation for multiple outcomes. None of the other results were significantly in favour of immobilisation.	Based on our results, functional treatment currently seems a more appropriate treatment and should be encouraged. Concerning effectiveness, immobilisation, if necessary, should be restricted to certain patients and for short time periods.	-
Conclusions	immobilisa	ation in comparison to surgical intervention.	posing the use if immobilisation in th	e treatment of ankle sprain injury, in comparison to funct	ional treatment. There is limited to moderate evidence oppo	osing
Conventional tre	eatment (RICE					
van den Bekerom <i>et al</i> ⁴⁸	11	Pain, swelling, ankle mobility or ROM	RICE therapy	Insufficient evidence is available from RCTs to determine the relative effectiveness of RICE therapy for acute ankle sprains in adults.	Treatment decisions must be made on an individual basis, based on expert opinion and national guidelines.	?
Conclusions	There is no	ot sufficient evidence to draw any conclusions	regarding the effectiveness of RICE	for the treatment of acute ankle sprains. High-quality RCI	s are required before recommendations can be made.	

CAI, chronic ankle instability; EMG, electromyography; ES, effect size; RCT, randomised controlled trial; RICE, rest, ice compression, and elevation; ROM, range of motion; RR, relative risk.

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Review

Chronic ankle instability

None of the included reviews evaluated the efficacy of electrophysical agents, pharmacological interventions or complementary medicine for the treatment of CAI or recurrent ankle sprains.

Surgical interventions: CAI

Two reviews^{20 51} (quality range 6–10) evaluated the efficacy of surgery for the specified treatment of CAI or recurrent ankle sprains.¹⁴ Included in these reviews were 24 individual papers, 8 of which evaluated a surgical intervention for the treatment of CAI or chronic recurrent ankle sprain (all RCTs; N=533; 64% male, 36% female).^{62–64 71 72 94 227 228}

None of the reviews specifically investigated whether a surgical intervention was superior to conservative management for CAI. In the majority of individual studies, a surgical intervention was often implemented provided conservative management had failed.^{62–64} 94 227 228 Furthermore, none of the individual reports had a non-surgical control group,⁵¹ and none of the studies reported on the primary outcome of reinjury incidence.¹⁵ 62–64 71 72 94 227 228

Non-surgical interventions: CAI

Twenty-three reviews evaluated the efficacy of a physiotherapeutic intervention (which included exercise and manual therapies) in the treatment of CAI or recurrent ankle sprain¹⁷ ¹⁹ ²⁰ ²³ ^{32–36} $^{41-43}$ ⁴⁵ ⁴⁶ ⁵⁰ ⁵¹ ^{54–57} ^{59–61} (quality range 1–10). Following the removal of duplicates, these reviews included 122 individual papers (83 RCTs, 39 non-RCTs; N=26349, 82% male, 18% female).

Exercise therapy

Twenty-two of the included reviews evaluated exercise therapy for treating CAI or recurrent ankle sprain¹⁷ ¹⁹ ²⁰ ²³ ^{33–36} ^{41–43} ⁴⁵ ⁴⁶ ⁵⁰ ⁵¹ ^{54–57} ^{59–61} (quality range 1–10). Included in these reviews were 114 individual reports, 61 of these papers evaluated the efficacy of exercise therapy for the treatment of CAI or recurrent ankle sprain specifically (42 RCTs, 19 non-RCTs; N=13963; 70% male, 30% female).⁶⁵ ^{96–99} ^{101–104} ¹⁰⁶ ¹⁰⁷ ^{110–113} ¹¹⁸ ¹¹⁹ ^{121–123} ^{128–135} ^{229–261}

Exercise therapy is generally considered effective in the treatment of CAI for the outcomes of self-reported function²⁰ 23 41 45 51 57 60 and reinjury incidence.^{16–20} $^{33–36}$ 42 43 46 50 51 54 55 60

Manual therapy

Five reviews¹⁹ ³² ⁴⁵ ⁵⁰ ⁵¹ (quality range 6–10) evaluated the effect of ankle joint mobilisation in CAI populations. Of the 122 individual papers included in these reviews, 12 (all RCTs, N=340; insufficient data to calculate male:female ratio) evaluated some kind of manual therapy in the treatment of ankle sprain.^{137–147} ²⁶²

Regarding the primary outcomes of self-reported function or injury recurrence, five of the individual papers included samples with CAI or recurrent ankle sprains¹³⁹ ¹⁴² ¹⁴⁴ ¹⁴⁶ ²⁶² and one reported on the primary outcome of self-reported function with a follow-up period that was not immediately post-treatment.²¹ ¹³⁹

All the reviews identified that manual mobilisation is likely to have a (initial) positive effect on ankle dorsiflexion ROM. $^{19\ 32\ 45\ 50\ 51}$

Nine systematic reviews evaluated the efficacy of an external support intervention for the treatment of CAI²¹ 22 24 34 46 47 54 55 61 (quality range 4–10). These reviews included 115 papers. Of these 115, 63 individual reports were included after removal of papers duplicated between each review. Of the 63 individual reports, 39 (15 RCTs, 24 non-RCTs; N=8734; 90% male, 10% female) evaluated some kind of external support for the treatment of CAI.¹⁰⁸ 173 247-262 The primary outcome in all of the reviews was reinjury incidence.

There was unanimous consensus among the reviews that bracing is effective at preventing a recurrence of an ankle sprain.²¹ ²² ²⁴ ³⁴ ⁴⁶ ⁴⁷ ⁵⁴ ⁵⁵ ⁶¹ With regard to taping, two reviews (quality=5/11;⁴⁶ $4/11^{22}$) concluded that its efficacy could not be supported (and that bracing was superior) whereas three reviews (quality=5/11;⁵⁵ 4/11;⁵⁴ $9/11^{21}$) advocated its value in the prevention of ankle sprain recurrence. It remains unclear whether bracing or taping are effective interventions for the primary prevention of an ankle sprain.²¹ ²⁴ ⁵⁴

The reviews identified that the evidence for modified footwear was inconclusive in the prevention of ankle sprain or its recurrence. $^{23 46 47 54}$

There was a lack of evidence for the value of orthotics in the treatment of CAI or the prevention of ankle sprain recurrence.^{22 24}

Meta-analysis

Exercise interventions significantly decreased the risk of sustaining a recurrent ankle sprain (figure 3; OR=0.59, 95% CI 0.51 to 0.68). An exploratory sensitivity analysis by treatment dose (high dose vs low dose using a median split of 900 min) was performed. Removal of interventions with a lower dose of total exercise (<900 min) improved the odds of the exercise intervention for injury risk (figure 4; OR=0.48, 95% CI 0.37 to 0.63). A summary of the exercise therapy interventions (with overall study quality) presented in the individual papers is presented in online supplementary table S3.

External support interventions were also associated with a significantly decreased risk of sustaining a recurrent ankle sprain (figure 5; OR=0.38, 95% CI 0.30 to 0.47).

DISCUSSION

This systematic review of treatment strategies for acute ankle sprain and CAI found 46 reviews which included 309 individual studies. As the conclusions of each review have been presented, the following topics in the treatment of acute ankle sprain/CAI will be clarified and discussed: surgical interventions; conservative interventions; treatment of specific types of ankle sprain.

Surgical interventions

Treatment strategies in the current review were divided into surgical and non-surgical types. The surgical literature is sparse however, and never were the long-term effects of a surgical intervention on the primary outcome of recurrence investigated. The general consensus of the reviews that investigated a surgical intervention was that a trial of conservative treatment should always be attempted before surgery is undertaken, that surgery should be considered only in patients with persistent symptoms, and that it should be considered on an individual basis.^{29 39 40}

	Exerc	ico	Cont	rol		Odds Ratio		Odds Ratio
Study or Subgroup	Events				Woight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl
Chaiwanichsiri 2005	1	15	2	17	0.4%	0.54 [0.04, 6.58]		
Eils 2010	7	96	21	102	4.2%	0.30 [0.12, 0.75]		
Ekstrand 1983	2	90	11	90	2.4%	0.16 [0.04, 0.76]		
Emery 2005	1	50 66	7	61	1.6%	0.12 [0.04, 0.70]		425 10
Emery 2005	62	426	76	494	13.2%	0.94 [0.65, 1.35]		
Engebretsen 2008	13	102	20	107	3.7%	0.64 [0.30, 1.36]		
Heidt 2000	2	42	20	258	1.2%	0.56 [0.13, 2.50]		
Holme 1999	2	42	13	258 46	2.7%			
						0.18 [0.05, 0.67]		
Hupperets 2009	56	254	89	269	14.8%	0.57 [0.39, 0.85]		and the second sec
McGuine & Keene 2006	12	284	23	299	4.7%	0.53 [0.26, 1.09]	1	Section 2
Mohammadi 2007	1	20	8	20	1.7%	0.08 [0.01, 0.71]	1	1000 C
Nilsson 1983	9	53	9	51	1.7%	0.95 [0.35, 2.64]		
Olsen 2005	31	958	47	879	10.4%	0.59 [0.37, 0.94]		
Pope 1998	11	549	16	544	3.5%	0.67 [0.31, 1.47]		
Pope 2000	19	735	27	803	5.5%	0.76 [0.42, 1.38]		
Soderman 2000	13	121	14	100	3.0%	0.74 [0.33, 1.66]		10 10 10 10 10 10
Stasinopoulos 2004	3	17	6	17	1.1%	0.39 [0.08, 1.94]		
Tropp 1985	7	146	30	171	5.8%	0.24 [0.10, 0.56]		
Van Mechelen 1993	0	159	1	167	0.3%	0.35 [0.01, 8.60]	1	
Van Rijn 2007	13	45	16	47	2.4%	0.79 [0.33, 1.90]		
Verhagen 2004	31	641	38	486	9.0%	0.60 [0.37, 0.98]		
Wedderkopp 1999	6	111	23	126	4.5%	0.26 [0.10, 0.65]		10 10 10 10 10 10 10 10 10 10 10 10 10 1
Wester 1996	6	24	13	24	2.1%	0.28 [0.08, 0.96]		
Total (95% CI)		5000		5178	100.0%	0.57 [0.49, 0.66]		•
Total events	309		531					
Heterogeneity: Chi ² = 31.3		(P = 0)		30%			-	<u></u>
Test for overall effect: Z =		•					0.01	0.1 i 10 100
		0.0000	.,					Favours Exercise Favours Control

Figure 3 Forest plot depicting the results of the meta-analysis for exercise interventions in the treatment of recurrent ankle sprain injury.

	Exerc	ise	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Chaiwanichsiri 2005	1	15	2	17	1.1%	0.54 [0.04, 6.58]	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Eils 2010	7	96	21	102	12.4%	0.30 [0.12, 0.75]	
Ekstrand 1983	2	90	11	90	0.0%	0.16 (0.04, 0.76)	
Emery 2005	1	66	7	61	0.0%	0.12 [0.01, 0.99]	
Emery 2007	62	426	76	494	0.0%	0.94 [0.65, 1.35]	
Engebretsen 2008	13	102	20	107	0.0%	0.64 [0.30, 1.36]	
Heidt 2000	2	42	21	258	3.7%	0.56 [0.13, 2.50]	
Holme 1999	3	46	13	46	0.0%	0.18 (0.05, 0.67)	
Hupperets 2009	56	254	89	269	0.0%	0.57 (0.39, 0.85)	
McGuine & Keene 2006	12	284	23	299	14.0%	0.53 [0.26, 1.09]	
Mohammadi 2007	1	20	8	20	5.0%	0.08 [0.01, 0.71]	· · · · · · · · · · · · · · · · · · ·
Nilsson 1983	9	53	9	51	0.0%	0.95 [0.35, 2.64]	
Olsen 2005	31	958	47	879	0.0%	0.59 [0.37, 0.94]	
Pope 1998	11	549	16	544	0.0%	0.67 [0.31, 1.47]	
Pope 2000	19	735	27	803	0.0%	0.76 [0.42, 1.38]	
Soderman 2000	13	121	14	100	9.0%	0.74 [0.33, 1.66]	
Stasinopoulos 2004	3	17	6	17	0.0%	0.39 [0.08, 1.94]	
Tropp 1985	7	146	30	171	0.0%	0.24 [0.10, 0.56]	
Van Mechelen 1993	0	159	1	167	1.0%	0.35 [0.01, 8.60]	1 x
Van Rijn 2007	13	45	16	47	7.3%	0.79 [0.33, 1.90]	
Verhagen 2004	31	641	38	486	26.9%	0.60 [0.37, 0.98]	
Wedderkopp 1999	6	111	23	126	13.3%	0.26 [0.10, 0.65]	
Wester 1996	6	24	13	24	6.4%	0.28 (0.08, 0.96)	
Total (95% CI)		1558		1646	100.0%	0.48 [0.37, 0.63]	•
Total events	92		180				
Heterogeneity: Chi ² = 9.26	6, df = 10 ((P = 0.5	1); $ ^2 = 0$	Х6			0.01 0.1 1 10 1
Test for overall effect: Z =	5.21 (P <	0.0000	1)				0.01 0.1 1 10 1 Favours Exercise Favours Control

Figure 4 Forest plot depicting the results of the meta-analysis for high-dose exercise interventions only in the treatment of recurrent ankle sprain injury.

Conservative interventions

Meta-analysis

Owing to a significant heterogeneity of outcomes, samples, interventions and follow-up periods, meta-analyses were only undertaken to evaluate the effect of exercise and external support interventions on reinjury in individuals with a history (acute or chronic) of ankle sprain. This analysis elucidated that an exercise intervention can significantly reduce the odds of ankle sprain recurrence, and that this effectiveness is improved if the exercise therapy is given in high (>900 min of exercise therapy training) doses. The other meta-analysis conducted as part of this investigation advocated the use of an external

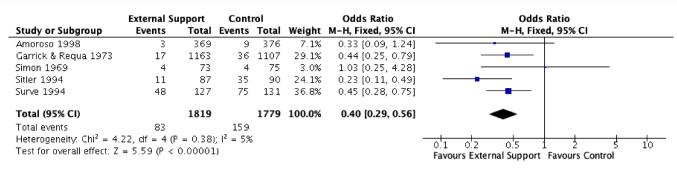


Figure 5 Forest plot depicting the results of the meta-analysis for bracing interventions in the treatment of recurrent ankle sprain injury.

support in reducing the odds of ankle sprain recurrence. The review papers equated the efficacy of taping with bracing⁵⁴, ⁵⁵ (with a similar reinjury risk reduction of 50%, ⁵⁵ while also reducing the severity of the incurred sprain²⁵, ⁵⁴).

Exercise therapy

A number of limitations in the available research were acknowledged in the reviews and as such, the findings of the meta-analysis for exercise therapy should be interpreted with caution. First, many of the authors stated that the studies included in their reviews were very heterogeneous.^{17 20 36 51 60 61} With regard to the statistical pooling performed as part of the current investigation, reflection of the exercise programmes implemented in the individual papers highlights this heterogeneity (see online supplementary table S2). Additionally, information regarding the intervention parameters was not adequately described in most studies. Furthermore, several reviews endorsed the completion of additional high-quality research to identify the specific parameters (such as the dose, intensity, type) of exercise therapy required to improve long-term outcomes.³⁵ ⁴¹ ⁵⁶ ⁵⁷ ⁶⁰ It is also currently unknown as to whether exercise therapies reduce the severity of an ankle reinjury, or increase the number of exposures before an ankle injury occurs.³⁴ Finally, there is a lack of evidence which links improvements in the primary outcomes with improvements in secondary outcomes¹¹¹ (which could elucidate the mechanistic underpinnings of treatment efficacy).

External supports

Generally, the conclusions of the systematic reviews for an external support that included a taping or bracing intervention identified that their benefit could be enhanced with an appropriately designed exercise therapy programme and that the efficacy of these interventions may be 'additive' in the secondary prevention of ankle sprains.⁵⁵ Braces were recommended for all athletes with a previous history of ankle sprain, particularly when engaging in high-risk activities such as indoor/court and field sports.^{22 24} It was recommended that a brace be worn for a minimum of 6 months after an acute ankle sprain to prevent recurrence,^{46 47} and that the benefit of wearing a brace lasts for up to 1 year following the most recent ankle sprain.⁵⁴ Next to the recognised preventive effect, the use of external support was considered to result in less severe ankle sprains.⁵⁴ With regard to the type of external support recommended, Kerkhoffs et al²⁸ and Seah and Mani-Babu⁴⁴ both concluded that lace up ankle supports were superior to semirigid ankle supports.

Manual therapy

Studies on the effect of the physiotherapeutic intervention of manual therapy were limited by short follow-up time frames

Electrophysical agents

No review investigated the efficacy of electrophysical agents in the treatment of CAI. Electrophysical agents were not considered effective treatments for acute ankle sprain. However, the standard practice of applying ice and compression (or the use of elevation) is generally administered concurrently with an exercise therapy intervention.^{52, 53, 95} While it is unknown if a RICE protocol augments the effect of exercise,¹⁸ given the strong empirical evidence base and the popularity of cryotherapy treatment (particularly for the secondary outcome of pain), it may be difficult to randomise a participant to a 'no ice' group.¹⁸ In conjunction with this point, a number of reviews recognised the paucity of high-quality studies evaluating an electrophysical agent in the treatment of acute ankle sprain.¹⁴ 18 53 95

which impeded extrapolation of the long-term benefits of these

techniques for either of the primary outcomes.^{19 32 45 50 51}

Complementary medicine

Similarly, complementary medicine has not been investigated in the treatment of CAI, and is not considered to be effective in the treatment of acute ankle sprain. Both the relevant reviews identified that there seemed to be a short-term benefit of complementary medicine for the secondary outcomes of pain and swelling, but cited that it remains unclear as to whether this is clinically meaningful in the long-term for injury recurrence and self-reported function.^{14 30}

Ankle sprain type

Finally, only two of the reviews evaluated treatment strategies in the management of syndesmotic ankle sprain; the individual papers included in these reviews were all case studies and as such, no meaningful results could be drawn from them. No reviews were identified which sought to investigate treatment strategies for medial ankle sprain. The remaining reviews either did not present a specific definition of the type of ankle sprain (lateral/medial/syndesmotic), or focused on the most prevalent subtype of this injury: a lateral ankle sprain.¹ Future research is required to identify the optimal management strategies for medial and syndesmotic ankle sprains.

Limitations with this review

This review itself is not without limitations. First, due to the inherent nature of this type of study design, the latest literature is unlikely to be included in even the most recently published systematic reviews and is therefore omitted from this article. Additionally, data extraction was conducted by only one author; while all the authors were involved in devising the data extraction form and two performed the quality review, our protocol could have been improved if two authors had independently extracted the data. A sample of the studies was randomly selected to be double checked by a second author, to ensure quality. However, due to the volume of data and time-intensive nature of this, it was unfeasible for a second author to double extract the data.

CONCLUSION

This review summarises the evidence base for a number of interventions designed to treat and prevent acute ankle sprain and CAI. The best evidence synthesis of high-quality reviews indicates there is strong evidence for exercise therapy and bracing in preventing recurrence of an ankle sprain. The efficacy of surgery and acupuncture are controversial in the treatment of acute ankle sprains. There is insufficient evidence examining the effectiveness of ultrasound in the treatment of acute ankle sprains.

What are the findings?

- ► A large number of systematic reviews detail treatment strategies for ankle sprain.
- ▶ This makes appraisal of the literature difficult for clinicians.
- The optimal treatment strategy for acute/recurrent ankle sprain is unclear.
- However the best evidence synthesis indicates there is strong evidence for exercise therapy and bracing in preventing ankle sprain recurrence.

How might it impact on clinical practice in the future?

- ► Exercise therapy and taping/bracing are effective in the management of acute/recurrent ankle sprain.
- There is a lack of evidence for the effectiveness of ultrasound therapy, acupuncture and manual therapy in the treatment of recurrent ankle sprain.
- Surgery for acute/recurrent ankle sprain should only be considered on an individual basis.

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Treatment and prevention of acute and recurrent ankle sprain: an overview of systematic reviews with meta-analysis

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