Supplementary file Module 4

Scoping question
What is the effectiveness of current treatments for Achilles tendinopathy?

Literature search and selection sub-module 4.1

The search question for sub-module 4.1 was:
Which measurement instruments are best suited for monitoring a treatment effect?

The working group decided not to perform a separate systematic search for this search question. A PICO was not formulated for this question. An exploratory search was performed to consider any relevant reviews on this topic. The results of a currently ongoing international consensus process will be included in the next update of the guideline. This search question was answered based upon expert opinion, taking into account: (1) the results of the national online questionnaire as distributed by the Dutch Patient Federation and the patient panel that was invited for an interview, (2) the results of the International Scientific Tendinopathy Symposium (ISTS) consensus meeting Groningen (the Netherlands) in 2018, (3) the outcome measures used in the randomised controlled trials (RCTs) assessed in sub-module 3, 4 and 5 and (4) any available literature from the exploratory search.

Important outcome measures
The working group considered the outcome measures important if they were deemed important by patients with Achilles tendinopathy, researchers and healthcare providers. These outcomes measures were established as primary outcome measures for sub-module 4.1.

Literature search and selection (methods)
An exploratory search was conducted to consider any relevant reviews on this topic. No predetermined search terms were used for this purpose.

In addition, existing national and international guidelines were searched to answer the question: previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) and (inter)national guideline databases of the Dutch General Practitioners Society (NHG), National Institute for Health and Care Excellence (NICE), National Guidelines Clearinghouse (NGC) and Guidelines International Network (G-I-N). These guidelines and databases were searched for outcome measures for Achilles tendinopathy.

The results of the national online questionnaire as distributed by the Dutch Patient Federation and patient panel interview as part of an already ongoing RCT have been included. The aim was to give patients an important role in determining the most aggravating symptoms due to Achilles tendinopathy. We also asked about their main treatment goals.

The results of the International Scientific Tendinopathy Symposium consensus meeting in 2018 were also included for this search question. The international expert group consisted of patients, researchers and healthcare providers. The results of this consensus meeting therefore contain relevant core domains.

The working group also extracted the outcome measures that were used in the RCTs that were included in sub-modules 3, 4 and 5. We included studies where the full text could be obtained. As the working group chose to include only studies that assessed pre-defined relevant outcome measures in these sub-modules (VISA-A score, patient satisfaction and return to sports), the number of studies included in sub-module 1 is higher than the number of included studies in sub-modules 3, 4 and 5. This was done with the aim to prevent selection bias. The working group decided to present the 10 most frequently used outcome measures. These results reflect which outcome measures are frequently used in scientific research by researchers working in this particular field.

Results
In the exploratory search strategy of existing scientific literature, one suitable review article was found for answering the search question.[1] None of the guidelines assessed discussed the outcome measures to be used in Achilles tendinopathy.

Ninety seven respondents participated in the national online questionnaire as distributed by the Dutch Patient Federation. In addition, 9 patients from an ongoing RCT participated in a patient panel.

The systematic search for the effectiveness of treatment options (sub-modules 3, 4 and 5) yielded a total of 2779 references after removal of duplications. The titles and abstracts of these references were screened. After this preselection, the full-text of 147 articles was reviewed. 86 of these articles were not eligible for inclusion. A flowchart with the reasons for exclusions is provided in Figure 4.1. 61 studies met the criteria and the reported outcome measures were extracted from this. In the 61 RCTs, 85 different outcome measures were used. The 10 outcome measures which were most frequently used in these studies are summarised in Table 4.1.

As no additional scientific literature is available to answer the search question, the working group decided to use the working group's expertise as a basis for answering this question. As a result, the GRADE methodology was not used for answering this search question and no conclusions were formulated.

Literature Summary
Description studies
Not applicable.

Results
Not applicable.

The quality of the evidence
Not applicable.

Conclusion

Midportion and insertional Achilles tendinopathy

- Grade	Due to the choice to use the working group's expertise as a basis for answering the search question of sub-module 4.1, no conclusions were formulated

Considerations
Based on (1) the reported targets of treatment by patients with Achilles tendinopathy, (2) results from a recent review, (3) results from a publication of a recent international consensus meeting and (4) frequently used outcome measures in RCTs on the effectiveness of treatment for Achilles tendinopathy, a number of treatment aims, core domains and measurement instruments are frequently reported.

The most frequently reported symptoms in the patient panel (n=9) were: not being able to perform pain-free (sports) activities (89%), pain during activities of daily living (44%), morning stiffness (33%) and pain as a result of pressure from footwear (33%) (Table 4.2). The treatment aims mentioned in the survey of the Netherlands Patient Federation (n=97) are categorised and ranked as follows: 1) "return to sports " without this being further specified (36%), 2) pain-free return to sports (27%), 3) pain-free functioning during activities of daily living (22%), becoming "pain-free" without further specification (20%) and 5) obtaining a normal function during activities of daily living without further specification (9%) (Table 4.2).

This is in keeping with the results of the international consensus process among 32 patients and 28 international healthcare providers that aimed to identify core domains in the evaluation of

tendinopathy.[2] These included participation in daily activities (day to day, work, sports), pain on activity/loading, function and disability. These emerged as core areas that enable evaluation of the main symptoms, and treatment aims.

The RCTs conducted in this field show that 3 outcome measures are used most frequently: the VISA-A score (46%), the amount of pain on palpation (VAS; 31%) and the amount of pain without any further specification (VAS; 28%) (Table 4.1). A recent review indicates that the validated and disease-specific Victorian Institute of Sport Assessment - Achilles (VISA-A) questionnaire is a suitable outcome measurement tool. This questionnaire was recommended for evaluating symptoms of both midportion and insertional Achilles tendinopathy.[1] The degree of morning stiffness in the Achilles tendon region, function, pain on loading and sports participation are evaluated using this questionnaire. As the evidence for using this outcome measure cannot be expressed to a degree, further research is required into the 'core outcome measures' for Achilles tendinopathy. The working group recommends that the VISA-A questionnaire should be considered for the evaluation of symptoms during treatment.

Other outcome measures that the working group considered important are the return to sports (core domain function and participation) and subjective patient satisfaction (core domain patient overall rating). Both outcome measures can be easily implemented in clinical practice. Returning to sports activities was the most frequently mentioned treatment aim among the patient panel (Table 4.2). Patient satisfaction provides an overview of the subjective evaluation of the patient, including the achieved treatment aims. As the treatment aims are different for each individual, patient satisfaction indicates whether the treatment aims were achieved for this specific individual. Therefore, this is the fourth most commonly used outcome measure in RCTs that assess the effectiveness of treatments in Achilles tendinopathy.

The working group noted that the amount of pain on palpation is a frequently used outcome measure in clinical trials and also pain caused by external pressure (footwear) which was mentioned by a relatively large proportion of patients. This argues for the inclusion of palpation pain as an important outcome measure. However, the working group did not include this outcome measure for a number of reasons. The amount of pain on palpation is difficult to standardize. An algometer could standardise pressure, but especially given that the Achilles tendon is an oval structure where a pressure algometer does not give the same type of pressure as patients experienced with footwear or by external force of the researcher. In addition, the ISTS consensus process has shown that pain provocation tests when performed by a researcher do not belong to the core domains for tendinopathy.[2] Finally, the clinical experience is that palpation pain is not sufficiently responsive to measuring treatment effects. Often patients can already undertake pain-free (sports) activities while there can still be pain on palpation.

In addition to evaluating patient-reported symptoms and pursuing treatment aims, the results of the international consensus meeting also show that there is a need to monitor the recovery process with outcome measures that assess physical functional capacity. A recent review reports 3 clinically applicable tests: the 'heel-rise test', 'hop test' and 'counter movement jump test'.[1] Although these tests have good to excellent reliability, the test properties of the individual tests are moderate. There are also limitations from a practical point of view; it will take approximately 1 hour to perform the full test battery. It is still unclear whether patients who make a good progress, measured with these outcome measures, will also ultimately achieve their personal treatment aims. For this reason, the working group considered that these tests should not be recommended as standard assessment.

The core domain 'structure' is often measured in clinical practice using ultrasound. During the international consensus meeting, structure was not selected as an important core area in monitoring tendinopathy.[2] This is also shown by a cohort of 54 patients with chronic midportion Achilles tendinopathy, where clinical and ultrasound outcomes were collected over a year.[3] The structure of the tendon was quantified using an innovative ultrasound technique (Ultrasound Tissue Characterisation). This study did not show an association between change in structure and

change in symptoms. Also, there was no prognostic value of the initial severity of structural alterations. Based on these data, the working group considered that using imaging as an outcome measure in clinical practice has no added value.

An international working group is currently performing a research project to determine which outcome measurement instruments are best suited to evaluate Achilles tendinopathy. The final outcome is a 'core outcome set' for Achilles tendinopathy with extensive exploration of the literature. The results are expected in 2021 (http://www.comet-initiative.org/studies/details/1323).

Literature search and selection sub-module 4.2
The search question for sub-module 4.2 was:
What is the effect of a wait-and-see policy in Achilles tendinopathy?

A systematic literature analysis was performed to answer this search question, focusing on randomised controlled trials (RCTs) that have investigated the natural course of Achilles tendinopathy.

P: Patients with Achilles tendinopathy;
I: A wait-and-see policy;
C: Change in outcome measure from baseline to follow-up. Another comparison is the difference in change with any other treatment;
O: Outcome measured with patient reported outcome measures (VISA-A score, patient satisfaction, return to sports and subjective recovery)

Important outcome measures
Patient-important outcome measures were determined using information from a survey of 97 patients with Achilles tendinopathy. This was conducted in collaboration with the Dutch Patient Federation. In addition, an in-depth interview was conducted with 9 patients having midportion Achilles tendinopathy. Based on this information, the working group considered the Victorian Institute of Sports Assessment-Achilles (VISA-A) score during the last follow-up measurement of the trial as the primary outcome measure in sub-modules 4.2, 4.3 and 4.4. The validated VISA-A questionnaire consists of 8 questions that cover 3 domains: pain in activities of daily living, pain during functional tests and sports participation.[4] A score of 100 points is optimal and represents an Achilles tendon with a normal function and without symptoms; a score of 0 points represents severe Achilles tendon dysfunction with severe symptoms.
The working group considered patient satisfaction and return to sports as secondary outcome measures. Patient satisfaction and return to sports should be patient-reported; the type of scale was not an exclusion criterion.

Clinically relevant differences for the VISA-A score have been reported in previous studies, with a large variation from 6.5 to 25 points.[5-9] In a recent large prospective study, the minimum clinically important difference of the VISA-A score was 14 points after 3 months of non-surgical treatment.[10] This study used the most accepted anchor-based approach. Based on the above-mentioned results, the working group decided to define the minimum clinically important difference of the VISA-A score at 15 points.
The outcome measures patient satisfaction and return to sports have not been validated and no clinically important differences are known for these outcome measures. These secondary outcome measures are also presented, but without the use of predefined clinically important cut-off points.

Literature search and selection
On 10th January 2019, a search was performed in collaboration with the medical librarian of Erasmus MC, on studies examining the natural course of Achilles tendinopathy (Table 4.3). Relevant literature was searched for in the following databases: Embase, Medline Ovid and Cochrane CENTRAL. Potentially relevant studies were assessed using the following criteria.

Inclusion criteria:

- The study evaluated the effect of a wait-and-see policy or a placebo treatment in Achilles tendinopathy.
- The diagnosis of Achilles tendinopathy was based on clinical findings (local pain and reduced load bearing capacity).
- The study was a randomised controlled trial (RCT).

Exclusion criterion:

- The application of an active treatment by the researchers during the follow-up period in the wait-and-see arm.

In addition, the presence of existing guidelines was sought for the answer to sub-question 1. The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) was consulted. In addition, the (inter)national guideline databases of the Dutch General Practitioners Association (NHG), National Institute for Health and Care Excellence (NICE), National Guidelines Clearinghouse (NGC) and Guidelines International Network (G-I-N) were searched. Systematic reviews on treatment options for Achilles tendinopathy and guidelines on the treatment of Achilles tendinopathy were also screened with the aim of including relevant studies.

Results

The search strategy yielded 157 articles, of which 9 potentially relevant articles were selected based on the title and abstract screening. In addition, in 24 (systematic) reviews and guidelines, the reference list was screened for relevant studies. As a result, 1 potentially relevant article was added. After evaluating the full text of the 10 articles, 1 study was selected for final inclusion.[11] The flowchart depicts the selection process (Figure 4.2).

The assessment of the risk of bias was done by 2 independent reviewers using the Cochrane risk of bias 2.0 tool.[12] In case of inconsistency between the 2 assessors, consensus was sought and a 3rd reviewer was consulted if necessary. For the detailed results of the quality assessment of the studies, we refer to Table 4.4. Two independent reviewers appraised the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[13]

The working group searched in previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007). Two studies were discussed in this guideline in relation to natural course of the disease, both with a focus on the prognosis of Achilles tendinopathy.[14 15] As treatments were given to the patients in both studies, these studies were not considered eligible for answering the current search question. The databases of the NHG, NICE, NGC and G-I-N did not contain existing guidelines on the natural history of Achilles tendinopathy.

Literature Summary

Description of the studies

One RCT was included to answer the search question. The characteristics and most important results of this study can be found in Table 4.5 and are discussed in the results section below.

The quality of the study was evaluated using the Cochrane Risk of Bias assessment Tool 2.0. For the detailed results of the assessment, we refer to Table 4.4.

Results

VISA-A score

Midportion Achilles tendinopathy

Rompe et al.[11] conducted a RCT with 3 study arms in which the effectiveness of shockwave therapy was compared to 1) eccentric exercise therapy and 2) a wait-and-see policy in midportion Achilles tendinopathy. The 25 participants were randomised to the wait-and-see arm and were followed for 16 weeks. Participants in this group had an appointment with an orthopaedic

surgeon. During this consultation, advice on training adjustments, stretching exercises and ergonomic modifications were given. In addition, paracetamol or NSAIDs were advised if necessary. Consequently, a pure 'wait-and-see' policy was not used in this study. Participants were on average 46 years old, 36% male, with a mean symptom duration of 9 months. Seven patients were active in sports (28%), compared to 18 patients who did not participate in any sports (72%). All patients did not undergo any treatment in the 12 weeks prior to the study. However, in their history all patients had been treated with NSAIDs, physiotherapy, inlays, stretching exercises or a corticosteroid injection. The primary outcome measure of this study was the change in VISA-A score (0 to 100 points; a higher score reflects a better improvement) after 16 weeks. This changed non-significantly in the wait-and-see from a mean (SD) of 48 (9) to 55 (13) points after 16 weeks.

Insertional Achilles tendinopathy
No studies have been published that assessed the effect of a wait-and-see policy on the VISA-A score in insertional Achilles tendinopathy.

The quality of the evidence
The certainty of evidence was based on the information from the RCT. This certainty of evidence is provided separately for each predefined outcome measure. As only RCTs could be included, the baseline level of evidence started at 'high' for the GRADE-assessment. The certainty of evidence per outcome measure is shown in Table 4.6. The level of evidence for the outcome measure examined was reduced by 3 levels to a very low certainty of evidence using the GRADE-assessment. The reasons were that there was a very high risk of bias and that there was serious imprecision (Table 4.4).

Outcome measure: patient satisfaction
Midportion and insertional Achilles tendinopathy
No studies have assessed patient satisfaction after a wait-and-see policy in either midportion or insertional Achilles tendinopathy.

Outcome measure: return to sports
Midportion and insertional Achilles tendinopathy
No studies have assessed the return to sports rate after a wait-and-see policy in either midportion or insertional Achilles tendinopathy.

Conclusions

Midportion Achilles tendinopathy

Very low Grade	A wait-and-see policy for 16 weeks does not appear to improve symptoms *Source: Rompe et al.*[11]

Insertional Achilles tendinopathy

- Grade	No studies have been published on the natural course in insertional Achilles tendinopathy.

Considerations
Advantages and disadvantages of the intervention and the quality of the evidence
Only one study assessed the natural course of midportion Achilles tendinopathy using important outcome measures.[11] This results in limitations on the strength of final recommendations that can be made, also because the certainty of the evidence is very low. Another obvious shortcoming of this study is that the healthcare professional did actually advise some active treatments to the patients. It is unclear whether patients actually received an intervention. As a result, it is unclear whether a purely wait-and-see policy was applied. The reporting of this information is only superficial in this study.

No studies have been published on the natural course of insertional Achilles tendinopathy. The results are therefore only applicable to midportion Achilles tendinopathy. However, the working group expected and assumed that the current results could be extrapolated to insertional Achilles tendinopathy and so no distinction was been made between midportion and insertional Achilles tendinopathy in the considerations and recommendations.

The changes on symptom scores of a wait-and-see policy after 16 weeks appear to be negligible to absent. There were no statistically significant or clinically important changes. The included patients had chronic symptoms of Achilles tendinopathy with a minimum symptom duration of 6 months and had undergone other treatments prior to inclusion. It is unknown whether these results can be extrapolated to patients with shorter duration of symptoms where no treatments have been applied. These results can therefore be better translated for second line care than for the first line care.

Values and preferences of patients
It is not known what values and preferences patients have regarding a wait-and-see policy. Many patients are assumed to want to resume or continue their (sports) activities as soon as possible. Discussing temporary adjustment and reduction of (sports) activities (i.e. not a complete cessation of sports) is often well received.[16] However, strictly speaking this is also already an intervention (patient education).

Cost
There are no direct medical costs involved in applying a wait-and-see policy, unlike many of the other possible treatments.

Acceptability for other stakeholders
The main stakeholders who could advise a wait-and-see policy are general practitioners, other primary healthcare providers (physiotherapists, podiatrists) and medical specialists. Due to insufficient availability of high-quality research on this subject, no hard recommendations can be made. Based on the current evidence, it is unclear what should be communicated to the patient about the natural course. In chronic Achilles tendinopathy, the expected change in symptoms seems to be negligible. This will frequently result in patients seeking treatment. The working group considers that the treatment options should be discussed with the individual patient in order to give insight into the different options.

Feasibility and implementation
Not applicable.

Balance between the arguments for and against the intervention
Not applicable.

Literature search and selection sub-module 4.3
The search question for sub-module 4.3 was:
Which non-surgical treatment is most effective for Achilles tendinopathy?

One systematic literature analysis was conducted to answering the search questions of sub-module 3, 4 and 5. We included randomised controlled trials (RCTs) that assessed the effectiveness of treatment options for Achilles tendinopathy. These results have also been published separately in the British Journal of Sports Medicine.[17] The following PICO was formulated to answer this question:

P: Patients with Achilles tendinopathy;
I: Active non-surgical treatment options;
C: A wait-and-see policy, waiting list control group or other active treatment;
O: Perceived symptoms (VISA-A score, patient satisfaction and return to sports).

Important outcome measures

The important outcome measures were determined with information from a survey in 97 patients with Achilles tendinopathy conducted in collaboration with the Dutch Patient Federation. In addition, an in-depth interview was conducted in 9 patients with midportion Achilles tendinopathy. Based on this information, the working group considered the Victorian Institute of Sports Assessment-Achilles (VISA-A) score during the last follow-up measurement of the trial as the primary outcome measure in sub-modules 2, 3 and 4. The validated VISA-A questionnaire consists of 8 questions that cover 3 domains: pain in activities of daily living, pain during functional tests and sports participation.[4] A score of 100 points is optimal and represents an Achilles tendon with a normal function and without symptoms; a score of 0 points represents severe Achilles tendon dysfunction with severe symptoms.

The working group considered patient satisfaction and return to sports as secondary outcome measures. Patient satisfaction and return to sports should be patient-reported; the type of scale was not an exclusion criterion. Side effects and complications of treatment were also considered to assess the safety of the various treatment options.

Clinically important differences for the VISA-A score have been reported in previous studies, with a large variation from 6.5 to 25 points.[5-9] In a recent large prospective study, the minimum clinically important difference of the VISA-A score was 14 points after 3 months of non-surgical treatment.[10] This study used the most accepted anchor-based approach. Based on the above-mentioned results, the working group decided to define the minimum clinically important difference of the VISA-A score at 15 points.

The outcome measures patient satisfaction and return to sports have not been validated and no clinically important differences are known for these outcome measures. These secondary outcome measures are also presented, but without the use of predefined clinically important cut-off points.

Literature search and selection

A search was conducted on 26th February 2019 in collaboration with the Medical Librarian of Erasmus MC. The search was focused on RCTs assessing the effectiveness of a treatment option for Achilles tendinopathy (Table 4.7). Relevant literature was sought in the following databases: Embase, Medline Ovid, Web of Science, Cochrane CENTRAL, CINAHL EBSCOhost, SportDiscuss EBSCOhost and Google Scholar. No language restrictions were applied. Potentially relevant studies were assessed using the following criteria.

Inclusion criteria:

- The study examines the effectiveness of a non-surgical treatment option for Achilles tendinopathy
- The diagnosis of Achilles tendinopathy is based on clinical findings (local pain and reduced load bearing ability).
- The study population was 18 years or older.
- The study was a randomised controlled trial (RCT).

Exclusion criteria:

- 10 or fewer patients per treatment arm.
- No adequate control group (e.g. Achilles tendon on the contralateral side).
- The design is a preclinical study (animal study or in vitro design).

In addition, the presence of existing guidelines was sought for the answer to sub-question 1. The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) was consulted. In addition, the (inter)national guideline databases of the Dutch General Practitioners Association (NHG), National Institute for Health and Care Excellence (NICE), National Guidelines Clearinghouse (NGC) and Guidelines International Network (G-I-N) were searched.

Results
The systematic search for the effectiveness of treatment options yielded a total of 2779 references after removal of duplications. All references were screened based on title and abstract. After this preselection, the full text of 147 articles was reviewed. A total of 118 of these articles did not fulfil the inclusion criteria. A flowchart is included in the appendix (Figure 4.3), including the reasons for exclusion. In the end, 29 studies met the criteria and were included in the literature analysis for the effectiveness of treatment options. Two studies involved a follow-up study of a previously published study.[18-21]

The databases of the NHG, NICE, NGC and G-I-N did not contain existing guidelines on Achilles tendinopathy treatment. The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) described effects of multiple non-surgical treatment options. The NICE database includes 2 guidelines on the use of shockwave therapy and autologous blood injections as treatment for Achilles tendinopathy. These guidelines were also considered by the working group.

Literature Summary
Description of the studies
A total of 29 RCTs were included to answer the search question. The characteristics and main results of these studies can be found in Table 4.8 The majority of studies (25/29 studies) examined the effectiveness of non-surgical treatment in midportion Achilles tendinopathy. The remaining 4 studies evaluated treatment options in insertional Achilles tendinopathy (2 studies) and where the distinction between insertional and midportion was unclear (2 studies). In 2 cases there were 2 publications of 1 study.[18-21]

The population size varied between 28 and 75 participants (median 54) with the rate of 'lost to follow-up' ranging from 0 to 26% (median 10%). The average age was between 40 and 50 years (median 48). The percentage of male participants was higher in 11 studies, compared to 13 studies in which the percentage of female participants was higher (median percentage of male participants 47%). In 2 studies, the male-female ratio was 50% and in 3 studies this ratio was not reported. Twelve studies reported the sports participation of the included population. The percentage of the population active in sport ranged from 31% to 100% (median 72%). The follow-up period of the studies ranged between 6 and 52 weeks (median 25 weeks).

A total of 38 treatment options were examined for midportion Achilles tendinopathy, 2 for insertional Achilles tendinopathy and 4 where the exact location of tendinopathy was not clear. The results are presented for the VISA-A score as a primary outcome measure and for the secondary outcome measures patient satisfaction and return to sports. A network meta-analysis was performed for the primary outcome measure. The secondary outcome measures were presented descriptively.

Assessment of the risk of bias was done by 2 independent reviewers using the Cochrane risk of bias 2.0 tool.[12] In case of inconsistency between the 2 assessors, consensus was sought and a 3rd reviewer was consulted if necessary. Twenty two studies (76%) were at high risk of bias and the other 7 studies (24%) had an unclear risk of bias (Table 4.9). Two independent reviewers appraised the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[13]

Results
The results for this search question are presented descriptively at the level of the treatment categories. The subdivision into treatment categories is shown in Table 4.10. The results of the network meta-analysis (NMA) for the primary outcome measure (VISA-A score) are described at the end of the results section. The level of certainty of the evidence was also taken into account.

Midportion Achilles tendinopathy
Wait-and-see policy

Wait-and-see policy versus exercise therapy: A wait-and-see policy was inferior to eccentric exercise therapy after 16 weeks follow-up. The VISA-A score after 16 weeks of follow-up was 55 (SD 13) in the wait-and-see policy group and 76 (SD 19) in the group performing eccentric exercise therapy ($p<0.001$).[11]

Placebo treatment

Two RCTs consisted of at least 1 treatment arm with only a placebo treatment without co-intervention. There were no statistically significant differences in patient-reported outcome measures after 1 to 12 weeks of follow-up between placebo treatment and ibuprofen or laser therapy.[22 23]

Exercise therapy

In total, 12 RCTs consisted of at least 1 treatment arm with only exercise therapy without co-intervention.

Exercise therapy versus a wait-and-see policy: Eccentric exercise therapy was superior to a wait-and-see policy after 16 weeks follow-up. The VISA-A score after 16 weeks follow-up was 76 (SD 19) in the group performing eccentric exercise therapy and 55 (SD 13) in the wait-and-see policy group ($p<0.001$).[11]

Exercise therapy versus Shockwave therapy: There is conflicting evidence for the effectiveness of shockwave therapy compared to exercise therapy. Eccentric exercise therapy was inferior to shockwave therapy (3 treatment sessions) after 16 weeks follow-up in 1 of the 2 studies included. The VISA-A score after 16 weeks of follow-up was 87 (SD 16) in the group receiving Shockwave therapy and 73 (SD 19) in the group performing eccentric exercise therapy ($p=0.0016$).[24] A previous 3-armed RCT from the same research group showed no significant difference in patient-reported outcome measures between eccentric exercise therapy and Shockwave therapy (3 treatment sessions) after 16 weeks of follow-up. The VISA-A score after 16 weeks follow-up was 70 (SD 16) in the shockwave therapy group and 76 (SD 19) in the eccentric exercise therapy group.[11]

Exercise therapy versus a night splint (in combination with exercise therapy): 2 studies reported no significant differences in patient-reported outcome measures after 12-52 weeks of follow-up between exercise therapy and the use of a night splint in addition to performing exercise therapy.[18 19 25] One of these studies also compared the effectiveness of exercise therapy with a night splint as monotherapy. The return to sports rate was higher in the group performing exercise therapy (63% versus 10%). No statistical tests were performed to assess the significance of the differences.[25]

Exercise therapy versus injection therapy: 2 RCTs compared eccentric exercise therapy without co-intervention with a form of injection therapy. The first study showed that the VISA-A score was significantly higher after 6 to 52 weeks follow-up in the group receiving prolotherapy (4 to 12 injections) in combination with eccentric exercise therapy, compared to eccentric exercise therapy alone ($p<0.01$).[26] The VISA-A score after 52 weeks follow-up was 91 (SD 10) in the prolotherapy group in combination with eccentric exercise therapy and 85 (SD 18) in the group performing eccentric exercise therapy only. There was no significant difference between eccentric exercise therapy only and the application of prolotherapy as monotherapy (4 to 12 treatments, without any form of exercise therapy) at all time points.[26] The second study showed no significant differences in VISA-A score after 6 to 12 weeks of follow-up between eccentric exercise therapy and an injection of autologous blood in combination with eccentric exercise therapy.[27]

Comparison between different types of exercise therapy programs: In 5 studies, 2 types of exercise therapy programs were directly compared with each other. Two studies showed a significant effect of a specific form of exercise therapy. In the first study, patient satisfaction after 12 weeks follow-up was significantly higher in the group performing eccentric exercise therapy

(88% satisfied), compared to the group performing concentric exercise therapy (36% satisfied).[28] In the second study, the VISA-A score was significantly higher after 3 weeks follow-up in the group performing eccentric exercise therapy in a number of daily repetitions that were feasible within the acceptable pain limits (VISA-A score 56, SD 20), compared to the group performing a fixed number of 180 repetitions per day for the same eccentric exercise therapy (41, SD 13, p=0.004). After 6 weeks follow-up, there were no significant between-group differences in VISA-A score. In addition, there was no significant difference in patient satisfaction between the 2 groups after 6 weeks of follow-up.[29]
Three RCTs showed no significant difference in improvement between specific forms of exercise therapy. In the first study, there was no significant difference in VISA-A score and patient satisfaction after 12 to 52 weeks follow-up between eccentric exercise therapy and heavy slow resistance exercise therapy.[30] The second study showed no significant difference in VISA-A score after 6 to 52 weeks follow-up between continuing the sports activities with a pain scale (maximum pain score 5 on a scale of 10) in the first 6 weeks of recovery versus discontinuing Achilles tendon loading activities during this stage. Both groups also performed eccentric exercise therapy.[31] The third study showed no significant difference in return to sports rate after 52 weeks follow-up between isotonic exercise therapy and a gradually progressive exercise therapy program (starting with stretching exercises and progressing to concentric and ultimately eccentric exercises). Both groups also were instructed to perform stretching exercises.[32]

Orthoses
One RCT consisted of a treatment arm with a night splint without co-intervention. No statistical tests were performed on the differences in return to sports rate. The impression was that the return to sports rate was lower if a night splint was used as monotherapy (10%), compared to exercise therapy as monotherapy (63%) versus a combination of exercise therapy and a night splint (38%).[25]

Shockwave therapy
Two RCTs consisted of at least 1 treatment arm with shockwave therapy only without co-interventions. The first study showed that shockwave therapy (3 treatment sessions) was superior to a wait-and-see policy after 16 weeks follow-up. At 16 weeks follow-up, the VISA-A score was 70 (SD 16) in the shockwave therapy group and 55 (SD 13) in the wait-and-see group (p<0.001). There was no significant difference between shockwave therapy and eccentric exercise therapy in this study.[11] In the second study, the VISA-A score after 12 and 26 weeks of follow-up was significantly lower in the shockwave therapy group (VISA-A score after 12 weeks 48 (SD 15), after 26 weeks 52 (SD 15), compared to 2 peritendinous hyaluronic acid injections (VISA-A score after 12 weeks 73(SD 24), after 26 weeks (75 (SD 22)).[33]

Other passive modalities
Two RCTs consisted of at least 1 treatment arm with a passive modality only without co-interventions. In the first study, there were no statistically significant differences in patient-reported outcome measures after 6 to 12 weeks follow-up between Intense Pulsed Light (IPL) and placebo treatment.[23] The second study showed that adding eccentric exercise therapy to passive modalities consisting of massage, therapeutic ultrasound and stretching exercises resulted in better improvement compared to passive modalities only. The VISA-A score was 81 (SD 1) in passive modalities and 98 (SD 2) when adding eccentric exercises to the passive modalities (p=0.01).[34]

Medication
Two RCTs consisted of at least 1 treatment arm with medication only without co-interventions. There were no statistically significant differences in patient-reported outcome measures after 1 to 3 weeks follow-up between placebo treatment and topical Non-steroidal anti-inflammatory drugs (NSAIDs) (1 RCT) or ibuprofen tablets (1 RCT).[22 35]

Acupuncture
One RCT consisted of at least 1 treatment arm with acupuncture treatment only without co-interventions. This study showed that the VISA-A score was significantly higher after 8 to 24 weeks follow-up in a group treated with acupuncture (24 treatment sessions), compared to eccentric exercise therapy (P<0.0001). After 24 weeks follow-up, the VISA-A score in the acupuncture group was 73 (SD 4) and in the group performing eccentric exercise therapy 62 (SD 4).[36]

Injection therapy
Three RCTs consisted of at least 1 treatment arm with injection therapy only without co-interventions. All studies examined a different form of injection therapy. The first study showed that the VISA-A score after 12 and 26 weeks follow-up was significantly higher in the group receiving 2 peritendinous hyaluronic acid injections (VISA-A score after 12 weeks 73 (SD 24), after 26 weeks 75 (SD 22)), compared to shockwave therapy (VISA-A score after 12 weeks 48 (SD 15) and after 26 weeks 52 (SD 15)).[33] The second study showed no significant difference between eccentric exercise therapy and prolotherapy (4 to 12 treatments, without exercise therapy).[26] The third study compared 2 different injection techniques: an injection of Stromal Vascular Fraction (SVF, obtained from fatty tissue) and an intratendinous injection with platelet-rich plasma (PRP). This study showed that the VISA-A score at short term (2 to 4 weeks of follow-up) was significantly higher in the group receiving a SVF injection (VISA-A score after 4 weeks 59 (SD 20), compared to the PRP injection (VISA-A score after 12 weeks 47 (SD 16)). After 4, 9, 17 and 26 weeks, there were no significant between-group differences.[37]

Multimodal treatment options
A total of 11 multimodal treatments (in which 2 or more treatments were applied simultaneously in a treatment arm) have been compared in RCTs. An overview of these multimodal treatments is shown in Table 4.11.

Insertional Achilles tendinopathy
Exercise therapy
Exercise therapy versus Shockwave therapy: Eccentric exercise therapy was inferior to shockwave therapy (3 treatment sessions) after 16 weeks follow-up in 1 RCT. The mean (SD) VISA-A score after 16 weeks follow-up was 79 (10) in the shockwave therapy group and 63 (12) in the eccentric exercise therapy group (p=0.005).[38]

A wait-and-see policy, placebo treatment, orthotics, shockwave therapy, medication, injection therapy or multimodal treatment options
No studies have been conducted that have investigated the effect of a wait-and-see policy, placebo treatment, orthotics, shockwave therapy, medication, injection therapy or multimodal treatment options for insertional Achilles tendinopathy.

Midportion and insertional Achilles tendinopathy (location not specified in study)
Shockwave therapy
One RCT investigated whether there is a difference in patient-reported outcome measures between clinically guided and ultrasound-guided shockwave therapy. There was no significant between-group difference after 12 weeks follow-up.[39]

Injection therapy
One RCT consisted of at least 1 treatment arm with injection therapy only without co-intervention. This study compared the effectiveness of a polidocanol injection with a placebo injection. There was no difference in patient-reported outcome measures between the 2 groups.[40]

A wait-and-see policy, placebo treatment, orthotics, shockwave therapy, medication, injection therapy or multimodal treatment options

No studies have been conducted that investigated the effect of a wait-and-see policy, placebo treatment, orthotics, shockwave therapy, medication, injection therapy or multimodal treatment options.

Network meta-analysis (VISA-A score as outcome measure)

Midportion Achilles tendinopathy

Figure 4.4a-c shows direct comparisons in RCTs for midportion Achilles tendinopathy. Multiple treatment categories have been defined from the broader category of 'multimodal treatment'. This information was used for forming the network meta-analysis (NMA). There were 10 different treatment categories with a total of 180 comparisons to be included in the NMA for midportion Achilles tendinopathy using the VISA-A score.[17] Table 4.12a-b shows the results of the NMA at 3 and 12 months for the treatment categories. This could not be done for the 6-month time point because there were not sufficient studies available to be able to form a network. The results for the equations at the level of the individual treatments are shown in Table 4.13.

VISA-A score at 3 months

At the time point of 3 months, each treatment investigated seemed to be superior to a wait-and-see policy because all active treatments result in an improvement of 15 points or more: exercise therapy+placebo injection therapy (mean difference 19, 95% credible interval -3 to 34), injection therapy (23, 8 to 38), exercise therapy (20, 11 to 30), shockwave therapy (15, 6 to 24), exercise therapy+injection therapy (22, 7 to 36), exercise therapy+shockwave therapy (34, 21 to 47), exercise therapy+night splint (21, 4 to 39), acupuncture (35, 25 to 45) and mucololysaccharide supplements+exercise therapy (28, 14 to 41).

Acupuncture was superior to placebo injection therapy (mean difference 16, credible interval 4 to 30), injection therapy (13, 0 to 25), exercise therapy (15, 11 to 19), shockwave therapy (20, 9 to 31), exercise therapy+injection therapy (13, 2 to 25) and exercise therapy+night splint (14, -1 to 30), but not to exercise therapy+shockwave therapy (1, -9 to 11) and mucopolysaccharide supplements+exercise therapy (7, -3 to 19).

Exercise therapy+shockwave therapy was superior to placebo injection therapy (mean difference 15, credible interval 1 to 31), injection therapy (11, -4 to 26), exercise therapy (14, 5 to 23), shockwave therapy as monotherapy (19, 5 to 32), exercise therapy+injection therapy (12, -2 to 27) and exercise therapy+night splint (13, -4 to 30), but not compared to acupuncture (-1, -11 to 9) and mucolysaccharide supplements+exercise therapy (6 , -7 to 20).

VISA-A score at 12 months

At the 12-month time point, 4 treatment categories could be compared in a network. Exercise therapy (mean difference -5, 95% credible interval -19 to 9), exercise therapy+injection therapy (2, -10 to 13) and exercise therapy+night splint (3, -16 to 22) had a similar outcome as injection therapy.

Insertional Achilles tendinopathy

For insertional Achilles tendinopathy and for non-specified Achilles tendinopathy (studies where the location was not further specified), no networks could be formed because of the small number of studies. Consequently, treatment categories could not be compared.

The quality of the evidence

The certainty of evidence was based on information from the RCTs. This certainty of evidence was provided separately for each predefined outcome measure. As only RCTs could be included, the baseline level of evidence started at 'high' for the GRADE-assessment. All comparisons from the NMA were graded as low-very low, except for exercise therapy+autologous blood injection versus exercise therapy+placebo injection where there was moderate certainty of the

evidence. The main reason for reducing the certainty of evidence were study limitations (n=180 comparisons, 100%) and imprecision (n=158 comparisons, 88%) (Table 4.14).

Network meta-analysis (outcome measures return to sports and patient satisfaction)
Midportion and insertional Achilles tendinopathy
Due to a small number of comparisons in the RCTs reporting the rate of return to sports and patient satisfaction, the working group decided not to perform a network analysis for these outcome measures.

Conclusions

Outcome measure VISA-A score
Midportion Achilles tendinopathy

Very low Grade	The following treatment categories appear to be more effective than a wait-and-see policy after 3 months: exercise therapy, injection therapy, exercise therapy+shockwave therapy, exercise therapy+night splint, acupuncture and mucopolysaccharide supplements+exercise therapy. *Source: van der Vlist et al.*[17]

Very low Grade	Acupuncture may be superior to placebo injection therapy, injection therapy, exercise therapy, shockwave therapy, exercise therapy+injection therapy and exercise therapy+night splint, but not compared to exercise therapy+shockwave therapy and mucopolysaccharide supplements+exercise therapy after 3 months. *Source: van der Vlist et al.*[17]

Very low Grade	Exercise therapy+shockwave therapy may be superior compared to placebo injection therapy, injection therapy, exercise therapy, shockwave therapy, exercise therapy+injection therapy and exercise therapy+night splint, but not compared to acupuncture and mucopolysaccharide supplements+exercise therapy after 3 months. *Source: van der Vlist et al.*[17]

Very low Grade	After 12 months follow up, exercise therapy+injection therapy and exercise therapy+night splint seem to have a similar outcomes to injection therapy. *Source: van der Vlist et al.*[17]

Insertional Achilles tendinopathy

- Grade	There is insufficient evidence of sufficient quality to assess the effectiveness of treatment options in insertional Achilles tendinopathy.

Midportion and insertional Achilles tendinopathy

- Grade	No evidence is available to assess the effectiveness of the following commonly used treatment options: • Patient education • Load management advice • Heel lifts • Percutaneous Needle Electrolysis (PNE) • Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) • Corticosteroid injections

Outcome measure return to sports
Midportion and insertional Achilles tendinopathy

- Grade	There is insufficient evidence of sufficient quality to assess the effectiveness of treatment options for return to sports.

Outcome measure patient satisfaction
Midportion and insertional Achilles tendinopathy

- Grade	There is insufficient evidence of sufficient quality to assess the effectiveness of treatment options for patient satisfaction.

Considerations
This search question was designed to assess the effectiveness of non-surgical treatment options in patients with Achilles tendinopathy.

Advantages and disadvantages of the intervention and the quality of the evidence
The results show that there are many different treatment options available for Achilles tendinopathy. This is especially the case for midportion Achilles tendinopathy. However, the certainty of the evidence for these treatments is low to very low in almost all cases and the estimated treatment effects largely overlap in almost all treatment categories. Where there is no overlap, the results are based on 2 small RCTs (for both acupuncture and exercise therapy+shockwave therapy) both with a high risk of bias.[24 36] This reflects the strong uncertainty in the estimates of treatment effects. This means that no strong recommendations can be made. In addition, the number of RCTs on the effectiveness of treatment options for insertional Achilles tendinopathy is very limited. Consequently, strong recommendations are also not possible for this subtype either. The working group decided that for many treatment categories the advice for midportion Achilles tendinopathy can be extrapolated to insertional tendinopathy. However, the recommended treatment advice will differ for some specific aspects. Where this is the case, this is clearly indicated.

In this consideration, the working group explains why the specific recommendations were ultimately made. The treatment effectiveness, safety, time costs, cost (for the individual patient and/or society), availability, clinical expertise of the healthcare provider and patient preferences are taken into account in these considerations. The working group contemplated that strong consideration should be given to applying the 'shared decision-making' model in order to increase the chances of a successful treatment outcome.[41-43]

Active treatment seems superior to a wait-and-see policy for midportion Achilles tendinopathy. As, in general, there is a clinically important difference between all active treatments and a wait-and-see policy, the working group recommends applying a form of active treatment for Achilles tendinopathy. Although this has not been specifically investigated for insertional Achilles tendinopathy, the working group considers it plausible that these results can be extrapolated to this subtype. Conversely, this means that the working group advised against adopting a wait-and-see policy. This advice is based on studies in patients with chronic Achilles tendinopathy (symptom duration longer than 8 to 12 weeks).

It is debatable whether this can be extrapolated to the subgroup of patients with short symptom duration (reactive tendinopathy). In cases of short symptom duration, a short period of rest (avoiding pain-provoking activities) can be initiated if overload is an obvious risk factor in the history of the individual patient.[44] However, the working group also recommends that these patients should have a follow-up assessment with the aim to apply active treatment to increase the tendon load bearing capacity which could include facilitating a gradual return to (sports) load. The principles in the following sections can also be applied for patients with short duration of symptoms.

The effectiveness of patient education and load management advice have not been studied in RCTs for Achilles tendinopathy. The working group emphasised that other non-surgical

treatments are usually combined with patient education and load management advice in daily clinical practice. The working group decided that patient education contributes to an adequate expectation management and more realistic objectives for patients. The load management advice has the important aim of improving patient's self-awareness and self-efficacy. Based on clinical expertise, the working group recommends considering patient education and load management advice as the basis of the treatment for Achilles tendinopathy.

The term patient education is used to cover the exchange of knowledge between the healthcare provider and patient in an interactive way. The effects of patient education have not been reported separately. It is likely that this education is provided alongside other treatments in trials. Recent research in patients with gluteal tendinopathy shows that patient education in combination with exercise therapy is more effective than a wait-and-see policy or a local corticosteroid injection.[45] According to the working group, patient education for Achilles tendinopathy has 3 elements: explanation about the condition, explanation about the prognosis and pain education. In concrete terms, this means that the degenerative nature of the condition, where longstanding symptoms are normal, is explained. Symptoms may be recurrent, especially if specific provocative (sports) load is continued. Pain education means that healthcare providers share their knowledge about pain. This includes explanations of the neurophysiology of acute and chronic pain (including signs of central sensitisation, if indicated). In the early stage of Achilles tendinopathy, there may still be acute (physiological) pain, whereas in the chronic phase the pain can be pathological (dysfunctional).[46] If there is a lack of a clear relationship between pain and tendon loading activities, dysfunctional pain may be present. Other factors, such as fear for movement and inadequate perceptions about the association between pain and tissue damage, might be present when pain is dysfunctional. Initiating tendon-loading activities regardless of pain could change these perceptions. In these cases, the pain monitoring model might have a less prominent role in the treatment because an important aspect of the treatment of dysfunctional pain is to decrease the focus on pain levels. In addition to physical factors, more attention is being paid to the influence of psychosocial aspects of longstanding pain. Recent research has also shown that these psychosocial factors play an important role in patients with Achilles tendinopathy.[47] Rest (avoiding pain-provoking activities) may be effective to protect the tendon in the early (reactive) phase of the tendinopathy. However, factors such as fear of more damage or a complete rupture and fear of movement can negatively affect recovery. Especially when these factors are present, pain education can be effective in improving experienced health and reducing healthcare consumption. This has been studied mainly in low back pain[48], but not yet in Achilles tendinopathy.

Load management advice consists of temporarily replacing pain-provoking (sports) load with non-provocative (sports) load, gradually increasing (sports) load and the use of a pain scale to monitor and adjust the (sports) load. Although this strategy has also been accepted for patients with tendinopathy, its effect has not been studied in a RCT.[49] Load management advice is closely related to patient education, where it is important to stimulate patients in being and remaining active, but to avoid a too rapid progression of tendon-loading activities resulting in a flare-up of pain. Ultimately, patients should be able to gradually increase the load within the acceptable limits of pain.

The working group also recommends starting with a form of strengthening exercises of the calf muscles and Achilles tendon. This treatment is – together with patient education and load management – the third option that forms the basis of treatment. Exercise therapy is recommended for a period of at least 12 weeks. Within this timeframe, symptom improvement can be expected with adequately performed exercise therapy and this provides a good basis for progressing these exercises. The working group chose to recommend this, because the results of exercise therapy seem comparable to other active non-surgical treatment options. However, there are still unanswered questions regarding exercise therapy and the optimal dose. There are multiple forms of strengthening exercises available including eccentric, concentric, progressive strengthening and heavy-slow resistance exercises. No clear differences have been found in the effectiveness between these forms of exercise therapy. In addition, there is limited or insufficient

knowledge about the influence of different exercise-related factors. These include the variables: training frequency, number of repetitions, the use of external weights and the degree of pain that can be accepted during and after exercises. The results of sub-module 4.5 show that there is very low evidence that there is no influence of (1) the degree of adherence during the exercise program, (2) the addition of extra external weight during exercise therapy and (3) whether the exercises are performed technically correctly. The choice of the form of exercise therapy should therefore be tailored to the individual. Adding extra weight may be considered, especially if the patient's treatment goal requires a high (sports) tendon load. The working group recommends that the degree of pain during and after the exercises should be taken into account when designing an exercise programme for the individual patient.[29] The fact that the exact technique of the exercises seems not to play a prominent role implies that using information leaflets and websites with photo and film material are reasonable options to explain the exercises to patients.

Most research has been performed on the effectiveness of eccentric exercise therapy. As this form is often painful, the level of pain should be taken into account for the individual patient. The working group recommends starting by performing a set of 15 isotonic exercises of the calf muscles. The degree of pain can be evaluated during and after the exercises. If the pain level (score 0 to 10) reaches a score of 5 points or higher, or if the muscle fatigue makes it impossible to perform a single set, the patient should start with isometric exercise forms, which may be less provocative for some individuals.[50] While isometric exercises result in similar levels of pain provocation as isotonic exercises, there are subgroups of patients who respond well to isometric exercises.[50] In that specific group, this step can be useful. Recent research shows that isometric exercises on average have no direct analgesic effect in patients with Achilles tendinopathy.[50 51] If the patient does not experience pain reduction during isometric exercises, the working group recommends moving to less pain-provoking isotonic forms (for example, by temporarily training with 2 legs or by reducing the number of repetitions per set). If the isometric exercises result in pain reduction and the pain score is 5 points or less, then the patient can start with isotonic exercises and progress to using external weights. During the progression of these exercises, the degree of pain during and after the exercises is used to guide progression (a pain score of 5 or less can be accepted). Depending on the desire for (re)starting tendon-loading sports, a phase with plyometric exercises can be performed after completing the isotonic phase. See Figure 4.5 for a schematic diagram of this patient-centred approach, which serves as an example.

Most studies on exercise therapy have been conducted in midportion Achilles tendinopathy. More research should be performed on exercise therapy in insertional Achilles tendinopathy. There is very low level evidence showing that exercise therapy performed on a flat surface is more effective than when exercises are performed past the neutral position into ankle dorsiflexion in insertional Achilles tendinopathy (i.e. on a step or stair) (not included in the results of this search question).[52 53] The hypothesis is that increased ankle dorsiflexion angles result in greater compression force of the calcaneus and retrocalcaneal bursa on the Achilles tendon insertion.[52] This increased pressure can lead to a compression tendinopathy.[54] Removing this compression in the first phase of exercise therapy could be effective. However, high-quality scientific literature for this approach is currently lacking.

Assessment of the kinetic chain and change of this are often performed in daily clinical practice. The concept of the kinetic chain means that the body functions as a whole and the view is that the motion in a single joint is unlikely to fully explain the onset an injury. Limited research has been done on assessing the risk factors in the kinetic chain for the onset of Achilles tendinopathy. In addition, there is no research on the effectiveness of altering elements of the kinetic chain. For this reason, the working group did not include kinetic chain interventions in the recommendations.

There is a very low to low certainty of evidence that acupuncture and exercise therapy+shockwave therapy are the most effective treatment options after 3 months. However, these results are based on 2 small RCTs that both had a high risk of bias.[24 36] In addition, for acupuncture, treatment was only partly described and therefore difficult to reproduce. It is not

clear whether it concerns the classic form of acupuncture and whether intratendinous needling was performed in this study. In addition, the large credible intervals reflect a large uncertainty in the estimates of treatment effects. Both studies only presented results after 3 months, making it impossible to estimate the long-term treatment effects. The results at 12 months of follow-up show that other non-surgical treatments (orthotics and injection therapies) are no more effective than exercise therapy. This effectiveness of the active non-surgical treatment options are discussed below.

A frequently used drug therapy in daily clinical practice is anti-inflammatory drugs (NSAIDs). The effectiveness of a transcutaneous gel and tablet form was studied in 2 RCTs.[22 35] Patients with short living (< 1 month) and longstanding (> 3 months) symptoms were included in these RCTs. NSAIDs were not effective in the short term (1 to 3 weeks follow-up).

The effectiveness of shockwave therapy (radial pressure wave) has been studied in several RCTs.[11 24 33 38 39] Based on the network meta-analysis, it can be concluded that shockwave therapy seems more effective when combined with exercise therapy. If shockwave therapy is considered, the working group recommends using it in addition to strengthening exercises. All RCTs in the network meta-analysis used shockwave therapy in 3 sessions with a weekly interval. There was a variation in number of shocks from 1500 to 2000 pulses per session in which the pulse frequency varied from 4 to 15 Hz and the pressure/energy density was not consistently described. An effect of shockwave therapy should be expected after 3 sessions. There is evidence that targeting the shockwave therapy at the location of the patient's symptoms (clinically guided) is as effective as targeting at the site of ultrasound abnormalities (imaging guided).[39] In the above mentioned studies, radial shockwave therapy and not focused shockwave therapy was used. It is therefore unknown whether these results can be extrapolated to focused shockwave therapy. The effect of shockwave therapy has been studied in both insertional and midportion Achilles tendinopathy. While the results of shockwave therapy for insertional Achilles tendinopathy could not be included in the network meta-analysis, a trend of a positive effect was also found.

Other passive treatments studied include the use of a night splint, inlays, mucopolysaccharide supplements, therapeutic ultrasound, massage, laser therapy and light therapy. The effects of these treatments on the VISA-A score, return to sports and/or patient satisfaction generally appear to be less significant than for shockwave therapy. However, there is a large uncertainty of the estimated treatment effects. A practical problem in testing effectiveness of these passive treatments is the fact that many modifications of the treatments are possible. For example, a night splint can be made in many forms and with different materials and the ankle dorsiflexion angle varies between splints. It should also be mentioned that increased ankle dorsiflexion may result in increased internal compression of the Achilles tendon on the calcaneal bone in patients with insertional Achilles tendinopathy and thereby increased symptoms. Another example is assessing the effectiveness of inlays. These can be prefabricated, but can also be 'custom-made' based on specific patient characteristics (findings on physical examination, static abnormalities and/or a dynamic gait pattern). Developing 'custom-made' inlays requires practical expertise which is not always easy to quantify. Therefore, it will always be difficult to translate the results of an RCT in this area into a widely accepted recommendation for clinical practice.

For injection therapy there are several options. Options that have been studied include polidocanol, lidocaine, autologous blood, platelet-rich plasma, stromal vascular fraction, hyaluronic acid, prolotherapy and high-volume injections. Other treatments using needles include acupuncture and dry needling. There is a large uncertainty around the estimated treatment effects for injections. Based on the analyses that have been done on the comparative effects of the separate injection therapies, no single type of injection appears to be clearly superior. A practical problem in testing effectiveness is the fact that there are many ways to perform the injections. The exact location, use of ultrasound guidance, the volume and dosage of the injected fluid, the application of co-interventions and the number of injections are all factors that may influence the outcome.

A separate entity within the injection therapy treatment category are corticosteroids. These were not included in the network meta-analysis as no RCTs were included that assessed their effectiveness. One small placebo-controlled RCT has been published showing that a peritendinous injection with corticosteroids has no effect in midportion Achilles tendinopathy.[55] The use of corticosteroids in tendinopathies in general is discouraged due to the poor long-term effectiveness.[56]

Side effects or complications due to exercise therapy, orthoses, shockwave therapy, drug therapy, acupuncture and injection therapy are rare (Table 4.8). None of these non-surgical treatment options seems to lead to serious side effects or complications that were reported in the studies included. A temporary increase in symptom severity has been described after initiating exercise therapy, shockwave therapy and injection therapy. In addition, shockwave therapy and injection therapy can lead to irritation and redness of the skin and transient tendon swelling, respectively. Corticosteroid injections have been reported to be associated with an increased risk of tendon rupture. This risk of tendon rupture is higher with an increasing number of injections.[57] Orthotics can lead to minor adverse effects, such as blisters, a feeling of discomfort and local compression neuropathy. Drug treatments are associated with a mild allergic reaction in a low percentage of cases. Side effects were not reported in the study of the effects of acupuncture.

A number of additional non-surgical treatments for Achilles tendinopathy have not been studied in RCTs, but are used in daily clinical practice. Examples include the application of a heel lift insert, myofascial techniques (dry needling) and Percutaneous Needle Electrolysis (PNE). The working group members have the experience that a heel lift insert can lead to a symptom reduction, especially when there are severe symptoms during activities of daily living. The working group does not have experience with myofascial dry needling and PNE. Due this lack of experience, lack of sufficient data on the effectiveness, knowledge on safety and cost aspects, the working group decided not to include these types of treatments in the recommendations.

Values and preferences of patients with Achilles tendinopathy

Information about the practical implementation of exercise therapy is important for patients. However, it is unknown which exact information and knowledge should be given to patients. This has not been sufficiently investigated and is currently unclear. The working group considers that oral information can be well supported by another source, for example an information leaflet or relevant information on reliable internet sources (e.g. for Dutch patients there is a site developed by the Dutch Association of Sports medicine (VSG) www.sportzorg.nl).

When providing information, the distinction between insertional and midportion Achilles tendinopathy should be taken into account. Sports physicians and (sports) physiotherapists are specifically trained for providing patient education (communicating information about tendinopathy), monitoring of symptoms, discussing treatment aims and providing personal guidance. However, other healthcare providers with experience in this field may also be adequately equipped to perform these tasks. Which specific healthcare provider provides information and guidance will depend on the preferences of the individual patient. In addition, a patient group that has a preference for 'self-management' should also be taken into account. According to the working group, it is of paramount importance to ascertain the preferences of the individual patient.

Patients have to invest their time performing exercise therapy if this is advised. This is especially the case with eccentric exercise therapy (180 repetitions per day). In one study, the duration of eccentric exercise therapy was compared to the duration of heavy-slow resistance exercises.[30] The duration of the eccentric exercise program was 308 minutes per week, compared to 107 minutes per week for the heavy-slow resistance exercises. However, this heavy slow resistance exercise therapy is harder to perform as a calf muscle machine or other specific training equipment needs to be used. This could result in additional costs for the individual patient.

In addition, the working group advises involving the patient when designing the exercise therapy program. One study compared the effectiveness of eccentric exercise therapy with a fixed number of repetitions versus exercises within the limits of acceptable pain.[29] The patients who were able to determine the number of repetitions using the pain monitoring model had a similar (on outcome patient satisfaction) or even better (on outcome VISA-A score) outcome in the short term. This pain monitoring model also plays an important role in the progressive exercise therapy as proposed by the working group (Figure 4.5). If patients experience aggravation of symptoms during exercises as a result of their footwear (due to pressure on the Achilles tendon during performing exercises), the working group recommends that the exercises should be performed without footwear.

Cost

No studies have been performed on the (cost) effectiveness of giving patient education, load management advice and guidance during exercise therapy. However, it is expected that the costs for the initial implementation of exercise therapy are low, as these can be carried out with limited supervision or even non-supervised. The working group indicates that it may be considered to perform the patient education, load management advice and instruction of the exercise therapy supervised by a qualified healthcare provider in the first phase. The provision of information can be done verbally, the exercises can be instructed, and there is the possibility for the patients to ask questions. Information via leaflets or via a website can support this and reduce the need for frequent follow-up visits.

The direct costs due to treatment with orthoses, shockwave therapy, medication, acupuncture and injection therapy are expected to be significantly higher than the initial treatment (patient education, load management advice and exercise therapy). This is not addressed in more detail, since this has not been investigated in cost-effectiveness studies and the impact of indirect costs is unknown.

Acceptability for other stakeholders

Providing information and education takes time, whereas time for this is often limited in daily practice. Sufficient time should be made available for this. In addition, patient information platforms should be developed, so that patients with Achilles tendinopathy can find the information and education online. Further research is needed on how best to organise this in clinical practice: such as by whom (doctors, paramedical care provider or a supporting healthcare provider), and in what form (e.g. face-to-face or via an internet platform).

Feasibility and implementation

In the provision of patient education and the instruction and implementation of exercise therapy, it is desirable that there is agreement between healthcare providers. For the Dutch situation, where many disciplines are involved in the treatment of Achilles tendinopathy, further specification of these roles is probably advantageous for effective implementation. This will likely be the case in other countries too.

Balance between the arguments for and against the intervention

Given the similar results between the various non-surgical treatment options, the low risk of complications, feasibility, availability and the expected low cost, the working group recommends starting treatment with patient education, load management advice and progressive calf muscle strengthening exercise therapy.

When considering additional non-surgical treatment, the working group recommends that a number of factors should be taken into account. The working group advises the following considerations for applying additional non-surgical treatments: 1) safety; 2) the patient's time investment; 3) cost and 4) availability.

If patient education, load management advice and an adequately performed calf muscle exercise program do not result in an improvement after 3 months, other additional non-surgical treatment

options may be considered. There is a large uncertainty of the estimated additional effect of other non-surgical treatments, and it is also questionable whether this effect is clinically important, both in the short and long term. This does not necessarily mean that additional treatments should not be considered. However, the working group indicates that communication with the patient about the uncertainty of the added value is necessary. The considerations for applying additional non-surgical treatments should be discussed with the individual patient. Based on this information, additional treatments can be discussed using a shared decision-making model.

Shockwave therapy may be considered in addition to continuing the calf muscle strengthening exercises. Shockwave therapy is safe and sufficiently available in Holland. In most cases, this treatment leads to higher direct costs than the initial treatments (patient education, load management advice and exercise therapy). The working group recommends starting with 3 treatment sessions of shockwave therapy, after which an evaluation can be performed. Shockwave therapy can be discontinued if there is worsening of symptoms, no effect, a limited effect or a full recovery. If there is improvement but no full recovery, the working group recommends considering a maximum of 5 treatment sessions. The working group considers it unlikely that applying more than 5 treatment sessions will result in additional clinically important improvement.
Other additional passive treatments (use of a night splint, inlays, use of mucopolysaccharide supplements, application of therapeutic ultrasound, friction massages, laser therapy and light therapy) can be considered according to the working group. It is important to share with the patient that for some of these treatments the effectiveness is not better than exercise therapy after 1 year of follow-up. The safety of these treatments is sufficiently ensured and in general these treatments are available in Holland. In most cases, however, it leads to higher direct costs than the initial treatments.

The application of injection therapy (injections with polidocanol, lidocaine, autologous blood, platelet-rich plasma, stromal vascular fraction, hyaluronic acid, prolotherapy or a high-volume injection) or acupuncture (intratendinous needling) may be considered. It is important to share with the patient that for some of these treatments it does not have a better effectiveness than exercise therapy after 1 year follow-up. The safety of these treatments is adequately ensured and no serious side effects or complications have been reported in RCTs. With uncontrolled or frequent use, injection therapies may have a larger complication risk (infection and tendon rupture have been reported post-injection).[57 58] The clinical experience of the working group is that injection therapies are often painful. The availability of injection therapies in the Dutch setting is good. In most cases, however, it leads to higher direct costs than the initial treatments (patient education, load management advice and calf muscle exercise therapy). This is partly due to the fact that doctors perform this treatment and because the injected medication leads to higher direct costs. In some cases (injections of platelet-rich plasma and prolotherapy) the potential effectiveness has been evaluated using repeated injections, further increasing direct costs.

The working group advises to be cautious with prescribing a number of additional non-surgical treatments. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have been proven to be ineffective. NSAIDs also have adverse side effects, especially in the elderly. Another potential disadvantage of this medication is the short-term analgesic effect and therefore the interference with load management advice. The use of a pain scale becomes less reliable and this masking effect could lead to patients undertaking more tendon-loading activities than can be tolerated. For these reasons, the working group advises caution with prescribing NSAIDs.

The working group advises avoiding corticosteroid injections. As mentioned above, there is evidence that this treatment is not effective in patients with midportion Achilles tendinopathy, it has a long-term adverse effects, and there are problems with the safety of this treatment (this is particularly true with an increasing number of injections).[55-57] For the above-mentioned reasons, the working group advises caution with prescribing NSAIDs and corticosteroid injections.

Previous national and international guidelines have also made recommendations for the treatment of Achilles tendinopathy. In the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007), the subject 'Treatment' is described as a separate module. The working group of the previous guideline advised that the treatment should initially consist of eccentric exercise therapy. The 2007 guideline recommends not prescribing NSAIDs, corticosteroids or shockwave therapy. Treatment methods such as sclerosing injections or night splints needed to be further investigated. The NICE database contains two guidelines on the use of shockwave therapy and autologous blood injections as treatment for Achilles tendinopathy. These guidelines concluded that there is conflicting evidence of low quality for the use of both shockwave and autologous blood injections, but that there are no significant adverse effects. Therefore, it was recommended to make it clear to the patient before using both therapies that the effectiveness of shockwave therapy and autologous blood injections is unclear. The guideline of the Orthopaedic section of the American Physical Therapy Association considers the following recommendations for patients with midportion Achilles tendinopathy: exercise therapy at least twice a week within the acceptable limits of pain, stretching exercises if there is a limited ankle dorsiflexion angle, neuromuscular exercises for correction of the kinetic chain to reduce eccentric forces on the Achilles tendons, manual therapy to promote range of motion of joints, continuation of (sports) activities within the acceptable limits of pain (no complete rest), patient education, rigid taping to reduce stretch forces on the Achilles tendon, iontophoresis with dexamethasone and dry needling.[59] In this guideline, there was insufficient evidence to advise the following treatments: a heel lift, night splint, orthoses and laser therapy. Treatment with shockwave therapy, corticosteroid injections and platelet-rich plasma injections were outside the scope of this guideline. From the above-mentioned information it can be seen that there are some similarities and differences with the recommendations in existing guidelines. There is a large overlap in the initial treatment advice (patient education, load management advice and calf muscle exercise therapy). This supports the working group in their choice to recommend this initial treatment strategy.

Literature search and selection sub-module 4.4

The search question for sub-module 4.4 was:
Is surgery more effective than non-surgical treatment for Achilles tendinopathy?

For sub-modules 3, 4 and 5, a single systematic literature search was conducted, focusing on randomised studies that assessed the effectiveness of a treatment option for Achilles tendinopathy. The following PICO was drawn up to answer this question:

P: patients with Achilles tendinopathy;
I: surgical treatment;
C: wait-and-see policy, waiting list control or active non-surgical treatment;
O: patient symptoms (VISA-A score, patient satisfaction and return to sports).

Important outcome measures

Important outcome measures were determined using information from a survey in 97 patients with Achilles tendinopathy conducted in collaboration with the Dutch Patient Federation. In addition, an in-depth interview was conducted in 9 patients with midportion Achilles tendinopathy. Based on this information, the working group considered the Victorian Institute of Sports Assessment-Achilles (VISA-A) score during the last follow-up measurement of the trial as the primary outcome measure in sub-modules 2, 3 and 4. The validated VISA-A questionnaire consists of 8 questions that cover 3 domains: pain during activities of daily living, during functional tests and sports participation.[4] A score of 100 points is optimal and represents an Achilles tendon with a normal function and without the presence of symptoms; a score of 0 points represents severe Achilles tendon dysfunction with the presence of severe symptoms. Secondary outcome measures were patient satisfaction and return to sports. Patient satisfaction and return to sports should be patient-reported, where the type of scale used is not an exclusion criterion for this guideline. Side effects and complications of treatment were also considered to assess the safety of the various treatment options.

Clinically important differences for the VISA-A score have been reported in previous studies, with a large variation from 6.5 to 25 points.[5-9] In a recent large prospective study, the minimum clinically important difference of the VISA-A score was 14 points after 3 months of non-surgical treatment.[10] This study used the most accepted anchor-based approach. Based on the above-mentioned results, the working group decided to define the minimum clinically important difference of the VISA-A score at 15 points.
The outcome measures patient satisfaction and return to sports have not been validated and no clinically important differences are known for these outcome measures. These secondary outcome measures are also presented, but without the use of predefined clinically important cut-off points.

Literature search and selection
A search was conducted on 26th February 2019, in collaboration with the Medical Librarian of Erasmus MC. The search was focused on RCTs assessing the effectiveness of a treatment option for Achilles tendinopathy (Table 4.7). Relevant literature was also searched for in the following databases: Embase, Medline Ovid, Web of Science, Cochrane CENTRAL, CINAHL EBSCOhost, SportDiscuss EBSCOhost and Google Scholar. No language restrictions were applied. Potentially relevant studies were assessed using the following criteria.

Inclusion criteria:
- The study examined the effectiveness of surgical treatment for Achilles tendinopathy.
- The diagnosis of Achilles tendinopathy was based on clinical findings (local pain and reduced load bearing capacity).
- The study population was 18 years or older.
- The study was a randomised controlled trial (RCT).

Exclusion criteria:
- 10 or fewer patients per treatment arm.
- No adequate control group (e.g. Achilles tendon contralateral side).
- The design was a preclinical study (animal study or in vitro design).

In addition, the presence of existing guidelines was sought for the answer to sub-question 1. The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) was consulted. In addition, the (inter)national guideline databases of the Dutch General Practitioners Association (NHG), National Institute for Health and Care Excellence (NICE), National Guidelines Clearinghouse (NGC) and Guidelines International Network (G-I-N) were searched.

Results
The systematic search yielded a total of 2779 references after removal of duplications. All references found were judged based on title and abstract. After this preselection, the full text of 147 articles was reviewed. A total of 145 of these articles were excluded. A flowchart is attached (Figure 4.6), including the reasons for exclusion. In the end, 2 studies met the criteria and were included in the literature analysis.

In addition, the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) was also consulted. The databases of the NHG, NICE, NGC and G-I-N did not contain existing guidelines on the surgical treatment of Achilles tendinopathy.

Literature Summary
Description of the studies
Two randomised trials (RCTs) were included to answer the search question. One RCT investigated a surgical treatment option in midportion Achilles tendinopathy, while the other investigated this in insertional Achilles tendinopathy. The working group decided to discuss the

characteristics of both studies separately in the results. The characteristics and main results of these studies can be found in Table 4.15.

Both studies were assessed with the Cochrane Risk of Bias assessment Tool 2.0. The assessment of the risk of bias was done by 2 independent assessors. If they did not agree, consensus was sought and a 3rd assessor was consulted if necessary. Both studies had a high risk of bias. For the detailed results of the assessment of the quality of these studies, see Table 4.16. The level of evidence was determined by 2 independent assessors using the GRADE approach.[13]

Results

As only 2 randomised trials were available, it was not possible to perform a network meta-analysis. The results are discussed descriptively for the VISA-A score, patient satisfaction and return to sports as primary and secondary outcome measures. Since only one study is available for both Achilles tendinopathy subtypes, no subdivision was made for these 3 outcome measures. The characteristics for the individual study are discussed.

Midportion Achilles tendinopathy

One study compared 2 surgical techniques (surgical decompression with excision of degenerative tissue versus radiofrequency microdebridement) in patients with midportion Achilles tendinopathy and concluded that there was no difference between the 2 treatment options.[60] Due to complications that occurred in the radiofrequency microdebridement (wound infections in 10% versus 0% in the surgical decompression group) the use of radiofrequency microdebridement was discouraged by the authors. This study was conducted in 36 patients with midportion Achilles tendinopathy who had not experienced an improvement in symptoms after at least 6 months of non-surgical therapy. The mean age was 48 years (SD not reported) and 42% were male. The follow-up duration was 6 months and at that time there were no patients 'lost to follow-up'.

This study only reported the VISA-A score as an important outcome measure. The mean VISA-A score improved from 31 points at baseline to 60 points after 6 months in the radiofrequency microdebridement group and from 42 to 67 points in the surgical decompression group. There was no significant difference in the VISA-A score between the 2 treatment groups (p=0.57).

Insertional Achilles tendinopathy

One study compared 2 surgical techniques (surgical decompression, osteotomy and transposition of the flexor hallucis longus versus surgical decompression and osteotomy alone) in patients with insertional Achilles tendinopathy and concluded that there is no difference between the 2 treatment options.[61] A transposition was therefore not indicated as an additional surgical treatment technique. This study was conducted in 39 patients with insertional Achilles tendinopathy who showed no improvement after at least 6 months of non-surgical therapy. The mean (SD) age was 61 (7) years and 36% were male. The follow-up duration was 12 months and at that time there were already 10 patients 'lost to follow-up' who were not included in the analyses (original study population 49 patients).

This study only assessed patient satisfaction as an important outcome measure. In the intervention group (surgical decompression, osteotomy and transposition of the flexor hallucis longus), 86% of patients (18/21) were satisfied after 12 months of follow-up, compared to 89% (16/18) in the control group (surgical decompression and osteotomy alone). No statistical analysis was performed. Complications occurred in 38% of patients treated in the surgical decompression, osteotomy and transposition of the flexor hallucis longus group and in 22% of patients treated in the surgical decompression and osteotomy group. These included relatively minor complications such as the receding of the wound edges, blistering, cellulitis, delayed wound healing and the production of wound fluid.

Level of evidence

The level of evidence was determined by comparing the treatment options and is based on results from randomised trials. The level therefore started as high for the GRADE assessment. The level per comparison is shown in Table 4.17. There were 2 comparisons of different surgical techniques. Both were at a high risk of bias, reducing the level by 2 levels. In addition, in both studies there was imprecision, respectively because 1 study showed very broad confidence intervals and the other study did not perform a statistical analysis for the relevant outcome measure. There was no indirect evidence and inconsistency was not applicable due to the absence of studies examining similar treatment options. As a result, in the end there was only a very low level of evidence for both comparisons.

Conclusions

Midportion Achilles tendinopathy

Very low Grade	The effectiveness of surgical decompression with excision of degenerative tissue appears to be similar to radiofrequency microdebridement in patients with midportion Achilles tendinopathy. *Source: Morrison et al.*[60]

Insertional Achilles tendinopathy

Very low Grade	A transposition of the flexor hallucis longus tendon appears to have no added value in surgical decompression and osteotomy for insertional Achilles tendinopathy. *Source: Hunt et al.*[61]

Considerations

Advantages and disadvantages of the intervention and the quality of the evidence

The working group recommends a cautious approach concerning surgical procedures in midportion or insertional Achilles tendinopathy. There is a lack of high quality research available where a surgical technique has been directly compared with a placebo procedure, active non-surgical treatment or a wait-and-see policy. The increase in VISA-A score seen in the current sub-module in patients with midportion Achilles tendinopathy after surgical decompression with excision of degenerative tissue is similar to the effectiveness of active non-surgical treatment such as exercise therapy in a similar group of patients.[11 21] In patients with insertional Achilles tendinopathy, a high patient satisfaction of 86 to 89% was reported after surgery. Patient satisfaction after non-surgical treatment has previously not been studied in an RCT in patients with insertional Achilles tendinopathy. There have also been no randomised studies on the effectiveness of surgical treatment using patient satisfaction as an outcome measure in patients with midportion Achilles tendinopathy.

Multiple surgical techniques have been described for the treatment of Achilles tendinopathy.[62] A distinction is often made between open and minimally invasive procedures. The most frequently used surgical treatments are: an excision of the peritendineum, debridement of the degenerative tendon tissue, longitudinal tenotomies, scraping of neovascularisation, excision of the plantaris tendon, augmentation with an (autologous) donor tendon, excision of the retrocalcaneal bursa and/or Haglund's morphology. The working group considered that the technique used should be adapted depending on both the clinical presentation and the imaging findings in the tendon and surrounding structures.

The complication risk due to surgery appears to be higher than for non-surgical treatments and these also appear to be more serious in nature due to the need for additional treatments (antibiotics in the case of a wound infection and plaster immobilisation in case of a partial rupture).

Patient values and preferences

It is unknown whether patients prefer surgery. Patients who are eligible for surgery often already have long-term symptoms and are therefore more likely to be receptive to more invasive treatments. However, several working group members have the clinical experience that patients are predominantly more receptive to this when the effectiveness is high and the risks are low. A fair representation of the expected effectiveness and possible risks are important to discuss with the patient.

The previously discussed results of the two patient panels showed that the most commonly identified goal of treatment is a pain-free return to (sports) loading. Return to sports has not been assessed as an outcome in the 2 studies on surgical treatment options. Therefore, the working group recommends adding this outcome measure in future research that assess surgical treatment.

Cost

No studies were identified in which the cost-effectiveness of surgical treatment have been assessed. However, we can base our judgement on surgery of the Achilles tendon for completes rupture of the Achilles tendon. Research from the United States shows that the mean cost of day case surgical treatment is $682. If costs for a hospital stay for the night was added, this amount would be $1237.[63] In addition, this calculation does not take into account the out-patient follow up appointments with the orthopaedic surgeon, the possible incapacity for work and the rehabilitation under the supervision of a physiotherapist. The amount mentioned is therefore in addition to the costs that in many cases will also be incurred in the implementation of exercise therapy. However, it is unknown whether the cost of non-surgical treatments will be less high in the long term. Theoretically, the continuation of active non-surgical treatment can lead to increased healthcare consumption and thus to increasing indirect costs. Future cost-effectiveness research in this area is needed in order to obtain more information.

Acceptability for other stakeholders

There is no evidence available for superior effectiveness of surgical treatment compared to exercise therapy and there are potential complications. Surgical treatment should only be considered in a selected group of patients with persistent symptoms without recovery after active non-surgical treatment.

Feasibility and implementation

The working group recommends that full and standardised information be made available on the rationale behind surgical treatment options and the associated effectiveness. It is recommended to describe the advantages and disadvantages of surgical treatment options, so that the patient can make their own decision. The working group considers that it should be made clear to the patient that initial surgical treatment is discouraged due to the unknown effectiveness compared to other active non-surgical treatments, the expected higher costs and the potential complications.

Balance between the arguments for and against the intervention

Given the lack of evidence for effectiveness and potential complications (wound infections 10%) surgery is not recommended and should only be considered in patients who do not recover after extensive implementation of active non-surgical treatment options. The working group recommends a minimum period of 6 months active non-surgical treatment.

The period within which the effect of non-surgical therapy should be expected and after which surgical treatment should be considered, is arbitrary. In a recent systematic review, studies with various tendinopathy sites (including shoulder, elbow, knee and Achilles tendon) were included that investigated the effectiveness of surgical treatments compared to no treatment, placebo treatment or exercise therapy.[64] In this review no difference was found in effectiveness of surgical treatment compared to the control groups. From this finding, it seems more logical to consider surgery only after 12 months of non-surgical therapy. In many cases, 12 months will also be more

realistic, but sometimes a work disability (professional sport or heavy physical labour) may require the patient to consider surgery earlier due to ineffectiveness of non-surgical treatments. It should also be mentioned that this has been particularly investigated in shoulder tendinopathy; there are no randomised trials in Achilles tendinopathy that have directly compared these 2 treatment options. For the above mentioned reasons, the working group felt that a minimum period of 6 months should be maintained.

In the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) Treatment was described as a separate module. The working group of the previous guideline recommended, that, after at least 6 months of non-surgical treatment and persistent severe symptoms and restrictions, surgical treatment could be considered. In the absence of scientific evidence between the various surgical treatment options, the previous working group opted for the least invasive surgery (percutaneous longitudinal tenotomy). The time period given to determine the effect of adequate non-surgical therapy is similar to this guideline. The type of surgery differs however, as the current working group considers that it is unlikely that one type of surgery is suitable for all patients who do not respond to non-surgical treatment. The working group recommends adapting the technique applied based on the clinical presentation and imaging findings of the tendon and surrounding structures.

Literature search and selection sub-module 4.5
The search question for sub-module 4.5 was:
Which factors influence treatment effects in Achilles tendinopathy?

To answer sub-modules 3, 4 and 5, one systematic literature analysis was conducted, focusing on randomised studies that assessed the effectiveness of a treatment option for Achilles tendinopathy. It was decided not to perform a separate search strategy for answering this sub-module, as these factors will be reported in studies examining the effectiveness of a treatment or the prognosis. The following PICO was performed to answer this question:

P: patients with Achilles tendinopathy.
I: presence of factors which may influence the effect of treatment.
C: absence of factors which may influence the effect of treatment.
O: persistence of symptoms (VISA-A score, return to sports, patient satisfaction) during follow-up.

Important outcome measures
Important outcome measures were determined using information from a survey in 97 patients with Achilles tendinopathy conducted in collaboration with the Dutch Patient Federation. In addition, an in-depth interview was conducted in 9 patients with midportion Achilles tendinopathy. Based on this information, the working group considered the Victorian Institute of Sports Assessment-Achilles (VISA-A) score during the last follow-up measurement of the trial as the primary outcome measure in sub-modules 2, 3 and 4. The validated VISA-A questionnaire consists of 8 questions that cover 3 domains: pain during activities of daily living, during functional tests and sports participation.[4] A score of 100 points is optimal and represents an Achilles tendon with a normal function and without the presence of symptoms; a score of 0 points represents severe Achilles tendon dysfunction with the presence of severe symptoms. Secondary outcome measures were patient satisfaction return to sports and subjective recovery. Patient satisfaction, return to sports and subjective recovery should be patient-reported, where the type of scale used is not an exclusion criterion for this guideline.

Literature search and selection
On 26th February 2019, in collaboration with the Medical Librarian of Erasmus MC, a search was conducted for randomised studies assessing the effectiveness of treatment for Achilles tendinopathy (Table 4.7). Relevant literature was searched for in the following databases: Embase, Medline Ovid, Web of Science, Cochrane CENTRAL, CINAHL EBSCOhost,

SportDiscuss EBSCOhost and Google Scholar. Potentially relevant studies were assessed based on the following criteria.

Inclusion criteria:

- The study examines the effectiveness of a non-surgical treatment option for Achilles tendinopathy.
- The diagnosis of Achilles tendinopathy was based on clinical findings (local pain and reduced load bearing capacity).
- The study population was 18 years or older.
- The study was a randomised controlled trial (RCT).
- There is a description of potential prognostic factors on the clinical outcome measure.

Exclusion criteria:

- 10 or fewer patients per treatment arm.
- No adequate control group (e.g. Achilles tendon on contralateral side).
- The design was a preclinical study (animal study or in vitro design).

In addition, the presence of existing guidelines were sought for. The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) was consulted. In addition, the (inter)national guideline databases of the Dutch General Practitioners Association (NHG), National Institute for Health and Care Excellence (NICE), National Guidelines Clearinghouse (NGC) and Guidelines International Network (G-I-N) were searched.

Results

The systematic search for the effectiveness of treatment options yielded a total of 2779 references after removal of duplications. All references found were screened based on title and abstract. After this preselection, the full text of 147 articles were reviewed and143 of these articles were excluded. A flowchart is attached (Figure 4.7), including the reasons for exclusion. In the end, 4 studies met the criteria and were included in the literature analysis.

The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) did not discuss the subject of factors influencing treatment effectiveness. The databases of the NHG, NICE, NGC and G-I-N did not contain existing guidelines on prognostic factors in the treatment of Achilles tendinopathy.

Literature Summary

Description of the studies

A total of 4 randomised trials (RCTs) were included.[16 21 27 65] All studies examined populations with midportion Achilles tendinopathy, no studies were found describing prognostic factors in insertional Achilles tendinopathy. In all studies, a form of exercise therapy was performed. In addition, 3 studies randomised patients to receive an injection of autologous blood or platelet-rich plasma. The population size varied between 24 and 54 participants (median 48) with a 'lost to follow-up' percentage ranging from 0 to 30% (median 7%). The mean age of the included participants was between 46 and 50 years (median 49.5 years) with a percentage of male participants ranging between 38 and 53% (median 51%). The follow-up period of these RCTs ranged between 12 to 52 weeks (median 39 weeks). The characteristics and main results of these studies can be found in Table 4.8.

A total of 11 determinants were investigated as prognostic factor for the course of Achilles tendinopathy symptoms. All studies assessed the effect of the factors on the change in VISA-A score.

All studies were assessed for quality with the Cochrane Risk of Bias assessment Tool 2.0. The assessment of the risk of bias was done by 2 independent assessors. If there was disagreement in

the assessment between the two assessors, consensus was sought and a 3rd assessor was consulted if necessary. Of the 4 studies, 1 study showed a high risk of bias.[27] The other 3 studies had an uncertain risk of bias.[16 21 65] For the detailed results of the assessment of the quality of these studies, see Table 4.9. The "Level of Evidence" assessment was also carried out by two independent assessors using GRADE (Table 4.18).[13]

Results

VISA-A score

Midportion Achilles tendinopathy

Non-modifiable prognostic factors

Baseline VISA-A score: There is a low quality evidence that a lower VISA-A score at baseline results in a greater improvement in the VISA-A score during treatment. Two studies investigated this factor. The first study shows a correlation between the baseline VISA-A score and the VISA-A score after 52 weeks follow-up of r=-0.372 (p=0.03).[21] This means that for each point higher on the baseline VISA-A score the VISA-A score has improved by 0.372 points less at 52 weeks. The second study examined this factor after the same follow-up duration.[16] This study shows a correlation between the baseline VISA-A score and the VISA-A score after 52 weeks of follow-up of r=-0.756 (p<0.05).

Other non-modifiable factors: There is a low quality evidence that there is no association between (1) age, (2) sex, (3) ethnicity, (4) duration of symptoms, (5) degree of structural disorganisation on ultrasound and the effectiveness of treatment in midportion Achilles tendinopathy. There is a very low quality evidence that there is no association between the degree of ultrasound Doppler flow and the effectiveness of treatment in midportion Achilles tendinopathy.[16 21 27 65] Table 4.19 shows an overview of the prognostic factors which have been investigated.

Modifiable prognostic factors

One study investigated modifiable factors that affect the effectiveness of the treatment of midportion Achilles tendinopathy.[65] There is a low quality evidence that there is no association between (1) the degree of physical activity before the onset of symptoms, (2) the degree of adherence to the exercise program, (3) the amount of additional weight with which the exercise therapy was performed and (4) whether the exercises were performed technically correct and the effectiveness of the treatment in midportion Achilles tendinopathy. Table 4.19 shows which studies have investigated the particular factors.

Insertional Achilles tendinopathy

No studies were found that have investigated factors that influence the effectiveness of the treatment of insertional Achilles tendinopathy.

Outcome measure: Return to sports

Midportion and insertional Achilles tendinopathy

No studies were found that investigated factors that influence the effectiveness of the treatment of midportion or insertional Achilles tendinopathy using return to sports as an outcome measure.

Outcome measure: patient satisfaction

Midportion and insertional Achilles tendinopathy

No studies were found that investigated factors that influence the effectiveness of the treatment of midportion or insertional Achilles tendinopathy using patient satisfaction as an outcome measure.

Outcome measure: subjective recovery

Midportion and insertion Achilles tendinopathy

No studies were found that investigated factors that influence the effectiveness of the treatment of midportion or insertional Achilles tendinopathy using subjective recovery as an outcome measure.

Level of evidence of literature

The level of evidence was determined per factor and was based on results using the primary outcome measure from randomised trials. Therefore, the level of evidence started at the high level for the GRADE assessment. The level of evidence per factor is shown in Table 4.19. The level of evidence of the factors was lowered by two levels for all studies because none of the studies had a low risk of bias and all studies did not present confidence intervals for the prognostic factors. In the majority of the studies, there was no inconsistency, indirect evidence or any other form of bias. These factors therefore have a low quality of evidence. The determinant 'degree of ultrasonographic Doppler flow' was studied in only 1 study, where randomisation had been performed at the tendon level (and not a patient level), which can lead to bias. As this can be considered as undesirable for determining prognostic factors, the level of evidence lowered another level to very low quality evidence.

Conclusions

Midportion Achilles tendinopathy

Low Grade	A lower VISA-A baseline score may increase the likelihood of a larger increase in VISA-A score during follow-up. *Source: de Jonge et al.[21] and Silbernagel et al.[16]*

Very low - Low Grade	The following factors do not appear to have prognostic value for the effectiveness of treatment in midportion Achilles tendinopathy measured with the change in VISA-A score: (1) age, (2) sex, (3) ethnicity, (4) duration of symptoms, (5) degree of structural disorganisation on ultrasound examination, (6) ultrasound Doppler flow, (7) the degree of physical activity before the onset of symptoms, (8) compliance with the exercise programme, (9) the amount of additional weight with which the exercise therapy was performed and (10) whether the exercises were performed technically correctly. *Source: Bell et al.[65]; de Jonge et al.[21]; Pearson et al.[27] and Silbernagel et al.[16]*

Insertional Achilles tendinopathy

- Grade	There is no literature available on factors that affect the effectiveness of the treatment of insertional Achilles tendinopathy.

Considerations

The working group concluded that there is insufficient knowledge about factors that may affect the effectiveness of treatment or the natural course of both midportion and insertional Achilles tendinopathy. The lack of knowledge about prognostic factors of specific treatments or the natural course means that good personalised treatment is currently impossible. More research into prognostic factors is needed to make this possible in the future.

The working group members do recognise different types of patient groups with Achilles tendinopathy in clinical practice (e.g. active athletes versus inactive individuals and presence or absence of co-morbidities). The working group believes that these different patients also require personalised treatment. However, the prognosis based on these findings is currently still impossible.

A lower VISA-A score on baseline appears to give a higher chance of a greater increase in VISA-A score during non-surgical treatment. This means that patients who report more symptoms on the VISA-A questionnaire can make more progress in their symptom improvement, measured with the VISA-A questionnaire, during treatment. The working group assumes that this effect mainly has a statistical explanation as a low baseline score gives more room to improve. Someone

with a baseline score of 30 can increase by 70 points, while someone with a score of 70 can only increase by 30 points. In addition, there may be 'regression to the mean', a methodological phenomenon in which low scores at a first measurement tend to change more towards the average score at the next measurement. What is important about this conclusion is that the severity of the symptoms does not have to affect the choice of treatment. Patients with severe symptoms can also have major improvements using non-surgical therapy.

Literature search and selection sub-module 4.6

The search question for sub-module 4.6 was:
What advice (self-management and patient education) should be given to patients with Achilles tendinopathy regarding lifestyle, work and sports loading?

Important outcome measures

The working group chose to answer sub-module 4.6 mainly on the basis of expert opinion of the working group. In addition, any relevant literature from sub-modules 3, 4 and 5 was included to answer sub-module 4.6. The primary outcome for this question is the degree of symptoms after advice regarding lifestyle, work and/or sports load. Outcomes for the experienced symptoms should be patient-reported. Examples include the Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire[4], the percentage of patients returning to sport and patient satisfaction.

Literature search and selection

Relevant studies for the response of sub-module 4.6 were used from the search strategy belonging to sub-module 3, 4 and 5. Therefore, the working group decided not to perform a separate search strategy for sub-module 4.6.

In addition, a search was performed in existing national and international guidelines to answer the question of the current sub-module: the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) and guideline databases of the NHG, NICE, NGC and G-I-N. Existing systematic reviews were also searched for.

Results

The search strategy belonging to sub-module 3, 4 and 5 revealed one relevant article.[16] For the selection process, we refer to Figure 4.8.

The working group found it impossible to answer this question using the GRADE methodology. As it was not possible to formulate a PICO question, no separate search strategy was performed. The search question is mainly answered based on expert opinion.

In addition, the working group relied on the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007). The databases of the NHG, NICE, NGC and G-I-N did not contain guidelines on lifestyle advice, work and/or sports loading in Achilles tendinopathy.

Literature Summary

Description of the studies

One RCT was taken from the search strategy belonging to sub-module 3, 4 and 5. The characteristics and main results of the study can be found in Table 4.8.

Results

Midportion Achilles tendinopathy

One study has been conducted on advice with regard to loading during sports.[16] In this study, there was no significant difference in VISA-A score after 6 to 52 weeks of follow-up between continuing the sports loading with pain (maximum pain score 5 on a scale of 0-10 on a pain scale) in the first 6 weeks of recovery versus discontinuing sports loading at this stage. The pain the next morning had to return to the basic background level of pain (degree of pain that was

present regardless of loading) and if there was no increase in pain and stiffness on a weekly basis (the so-called 'pain monitoring model'). Both groups also performed eccentric exercise therapy.

Insertional Achilles tendinopathy
No studies have been found that have investigated lifestyle, work and/or sports loading advice in insertional Achilles tendinopathy.

Level of evidence of literature
Not applicable.

Conclusions

Midportion Achilles tendinopathy

- **Grade**	If sports loading within acceptable level of pain (maximum VAS 5/10 on a scale of 0 to 10 during exercise, reduction of pain the following morning to baseline pain level and no increase in pain and stiffness on a weekly basis) is advised, then the continuation of sports load seems to have no negative effect on the clinical outcome after 6 to 52 weeks follow-up. There are no studies which have examined lifestyle or work related loading advice in midportion Achilles tendinopathy. *Source: Silbernagel et al.*[16]

Insertional Achilles tendinopathy

- **Grade**	No studies were identified that have examined lifestyle, work related and/or sports loading advice in insertional Achilles tendinopathy. *Source: Silbernagel et al.*[16]

Considerations
The working group recommends a gradual increase of the load (daily activities, physical work and/or sports load) in Achilles tendinopathy. This gradual build-up should be combined with monitoring and controlling pain.

For patients, it can be helpful to express this load build-up quantitatively. In practice, the so-called 'acute to chronic workload ratio' (ACWR) can be used. Studies in professional rugby players, footballers, cricketers and endurance athletes have shown that the risk of injury generally increases when the acute load (e.g. the average distance in a week) is more than 1.5 times higher than the chronic load (e.g. the average distance over the preceding 4 weeks).[66-69] For example: if someone ran an average of 10 km a week over the past 4 weeks, the risk of injury may increase significantly with a load of more than 15 km in the following week. A disadvantage of this approach is that only the amount of training (covered distance) is used and other parameters of external and internal load are not taken into account.

Other parameters that can be measured during sports and may be relevant to monitor are, amongst others: average speed, peak velocity and number of accelerations (external load) and/or average heart rate, heart rate zones and rate of perceived exertion (internal load). For each sport, the degree of importance of each load parameter may vary. In some cases, a combination of internal and external load parameters can be considered (e.g. rate of perceived exertion multiplied by running distance). For less active individuals, this method can also be used. The number of steps taken per day can be recorded (often with an app or smart watch to register) and monitored.
The effect of using this ACWR method on symptoms of Achilles tendinopathy during build-up of (sports) load is not yet known. Based on the expertise and clinical experience of members of

the working group, this advice on gradual increase of tendon load can be an important tool in the management of Achilles tendinopathy.

The working group believes that monitoring and controlling pain are also important tools in the management of Achilles tendinopathy. In the first stage of treatment it is emphasised to perform only loading (ADL and sport) that does not provoke any or minimal pain. This can be monitored by the use of the 'pain monitoring model'. The basis for this is a pain scale, where the (sports) load is ideally performed with a pain score of 0 to 5 on a scale of 0 to 10 (Figure 4.9). On this scale, a score of 0 points represents absence of pain and a score of 10 points represents the worst imaginable pain. In addition, the pain should be significantly less immediately after the (sports) loading and the next morning.[16] If the pain during ADL falls within these acceptable pain limits, then the (sports) load can be gradually increased. Existing running training schedules can be used to gradually increase the load to 5 km in 6 to 8 weeks (the speed of the build-up depends on the pain experienced). On reliable websites in Holland, running training programmes can be found (www.sportzorg.nl). If this level of load tolerance is achieved, then the principle of the 'acute: chronic workload ratio' (ACWR) method described above can be applied. Meanwhile, the endurance capacity/stamina in athletes can be maintained by performing alternative sports that are less stressful for the Achilles tendon and do not cause unacceptable pain provocation. In midportion Achilles tendinopathy these are (sports) loads such as swimming, cycling, exercising on the cross-trainer and walking. In insertional Achilles tendinopathy, swimming and cycling are generally less provocative (sports) loads than exercising on the cross-trainer and walking. This is probably because of the deeper dorsiflexion angles of the ankle that are made during the latter activities. If this adjustment of the load is initiated quickly, a shorter duration of recurrent complaints can be expected.

Lifestyle interventions that are frequently used in healthcare as primary prevention are a healthy diet and optimisation of weight by healthy exercise. This general lifestyle advice applies to each individual. Based on the risk factors and prognostic factors identified for Achilles tendinopathy, there is only very low quality evidence for specific effects of lifestyle advice for this patient group. A strategy to promote healthy exercise is already shown in the paragraph above. With regard to dietary adjustment, the use of alcohol may be limited, as this was a risk factor for Achilles tendinopathy. However, recent data show that alcohol consumption is not a risk factor for the onset of Achilles tendinopathy in runners.[70] For this reason, the working group advises against advising reducing alcohol intake for this specific reason. Although an increased BMI is not a proven risk factor, there are limitations in the studies on the relationship between dyslipidaemia and the onset of Achilles tendinopathy. A recent prospective study shows that Achilles tendinopathy patients with metabolic disorders (hypertension, hypercholesterolemia and diabetes mellitus) recovered less successfully from their injury after a year than patients without these metabolic disorders.[71] Based on these data, the working group suggests that one should consider dietary interventions to optimise weight, in cases of obesity.
There is no scientific literature available which specifically focuses on physical stress during work in patients with Achilles tendinopathy. One can assume that the above elements of lifestyle adjustment also make sense for symptoms of Achilles tendinopathy that have a negative impact on work. Patients with work-related Achilles tendinopathy should receive an advice according to the same principles of patient education, loading advice and exercise therapy treatment as a first step. One should also identify and temporarily adjust provocative factors related to the work.

Figures and Tables supplementary file Module 4

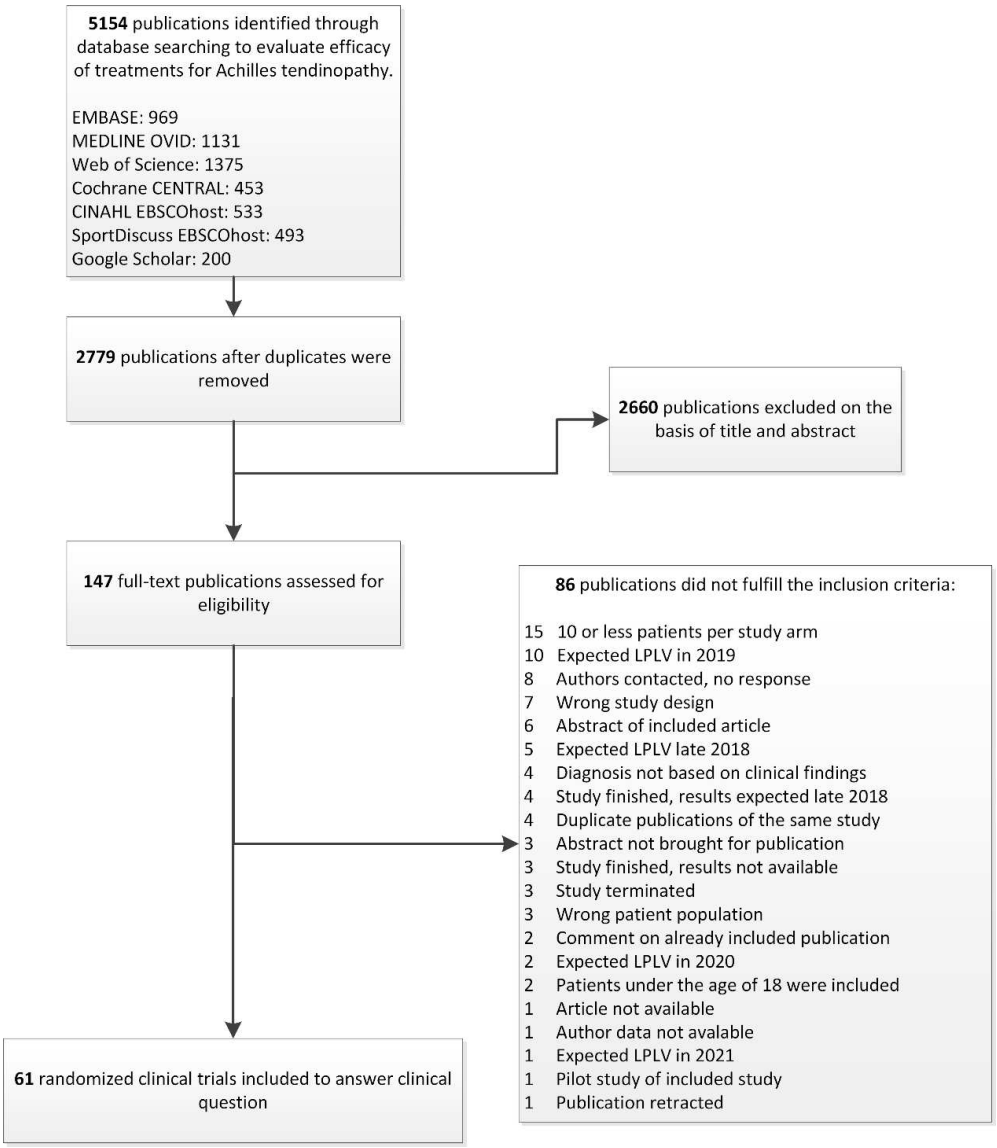


Figure 4.1 – PRISMA flowchart of the selection process used for the module 'Treatment': which treatment is most effective for Achilles tendinopathy? The outcome measures used in the RCTs have been extracted. The number of studies does not correspond to the number of studies included to assess the effectiveness of treatment options (sub-modules 3 and 4), because in these sub-modules a pre-selection was made based on outcome measures which were considered relevant by the working group. Therefore, we included all potentially relevant studies without this pre-selection to prevent selection bias.

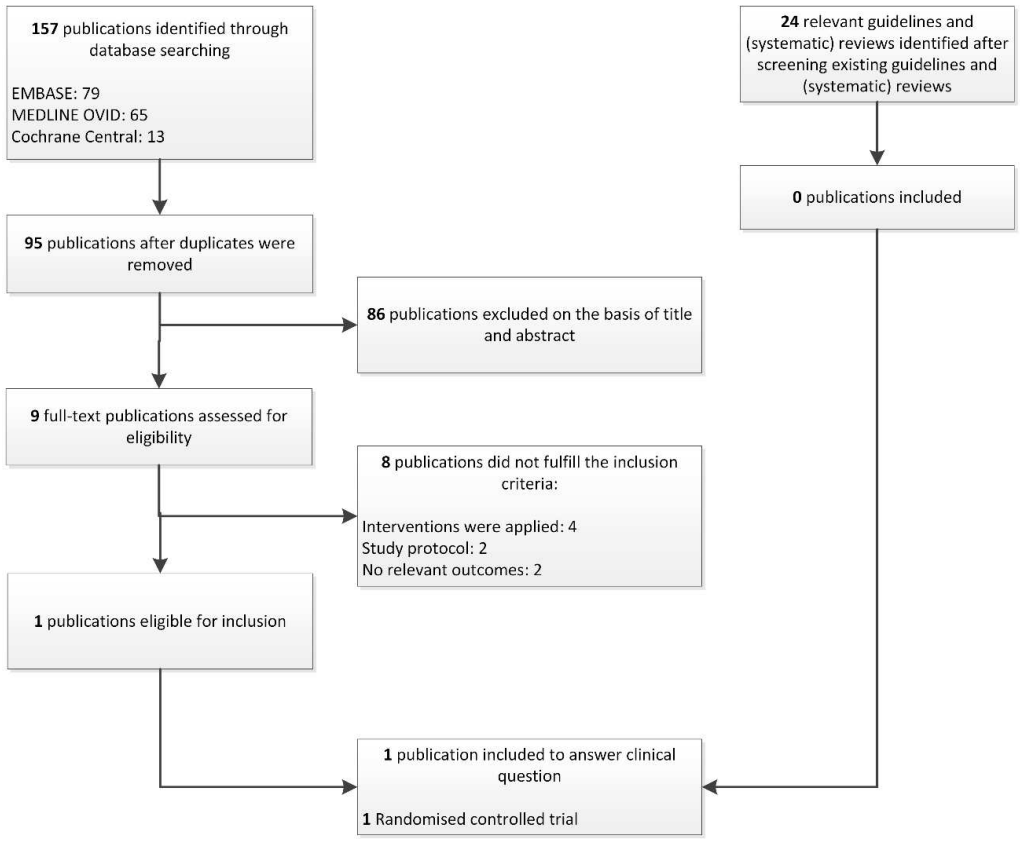


Figure 4.2 – PRISMA flowchart of the selection process used for answering the search question of sub-module 4.2: 'What is the effect of a wait-and-see policy in Achilles tendinopathy?'

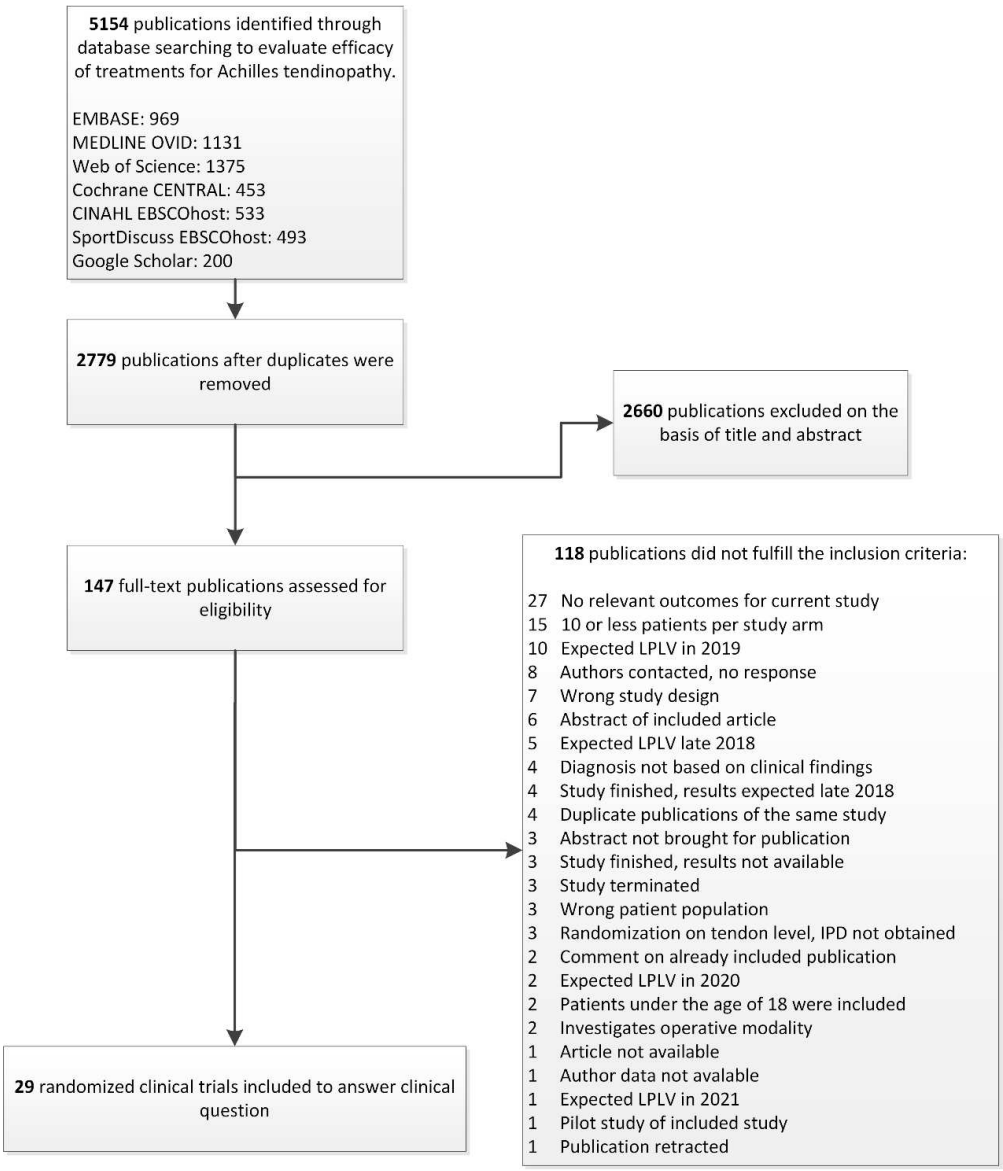


Figure 4.3 – PRISMA flowchart of the selection process for sub-module 3: Which non-surgical treatment is most effective for Achilles tendinopathy?

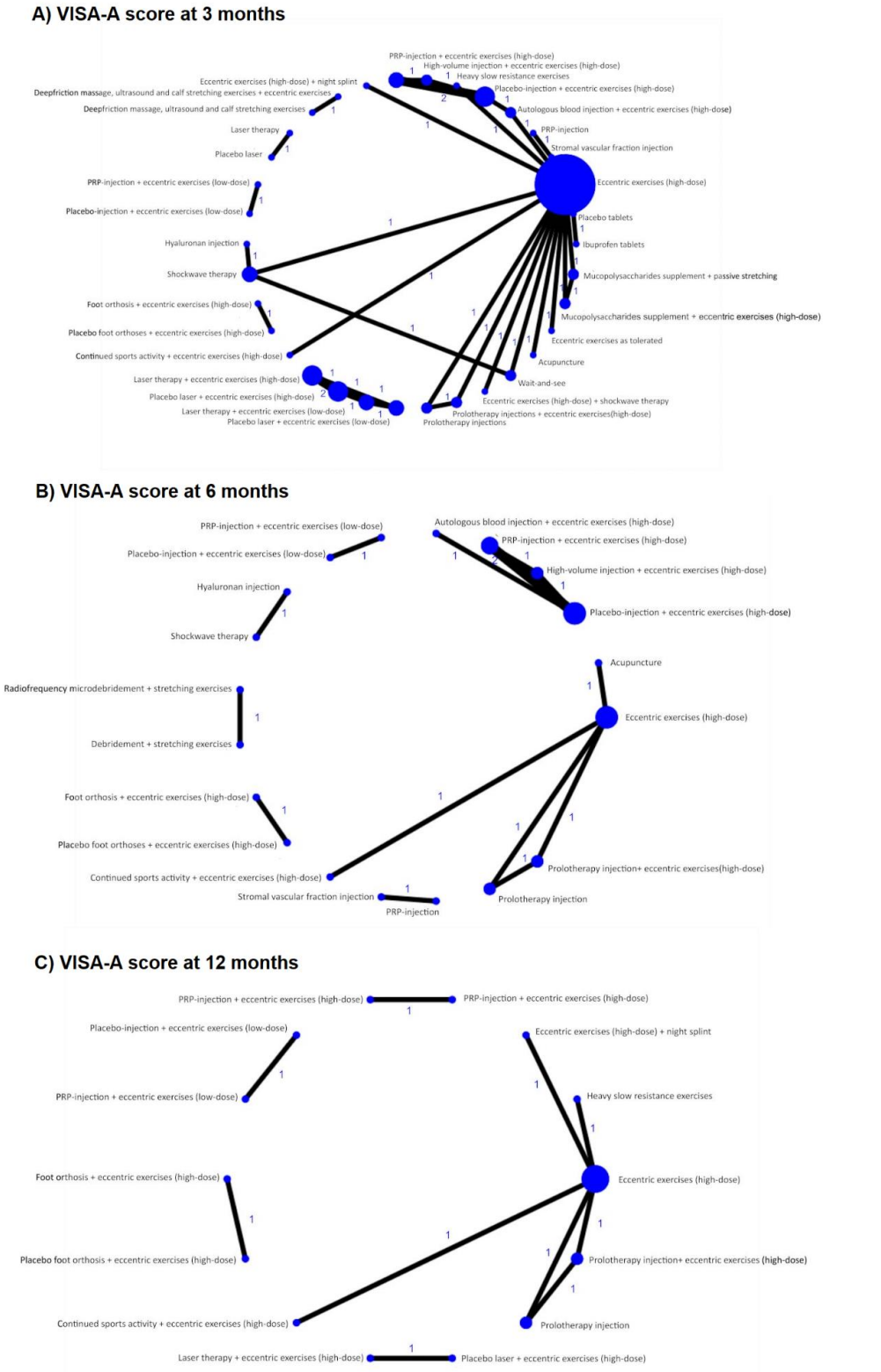


Figure 4.4a-c – Network presentation for the VISA-A score, measured after separate treatments at 3, 6 and 12 months in patients with midportion Achilles tendinopathy. The size of the circle

represents the number of patients who have undergone treatment and the number represents the amount of comparisons. PRP = Platelet-rich plasma, VISA-A = Victorian Institute of Sport Assessment-Achilles.

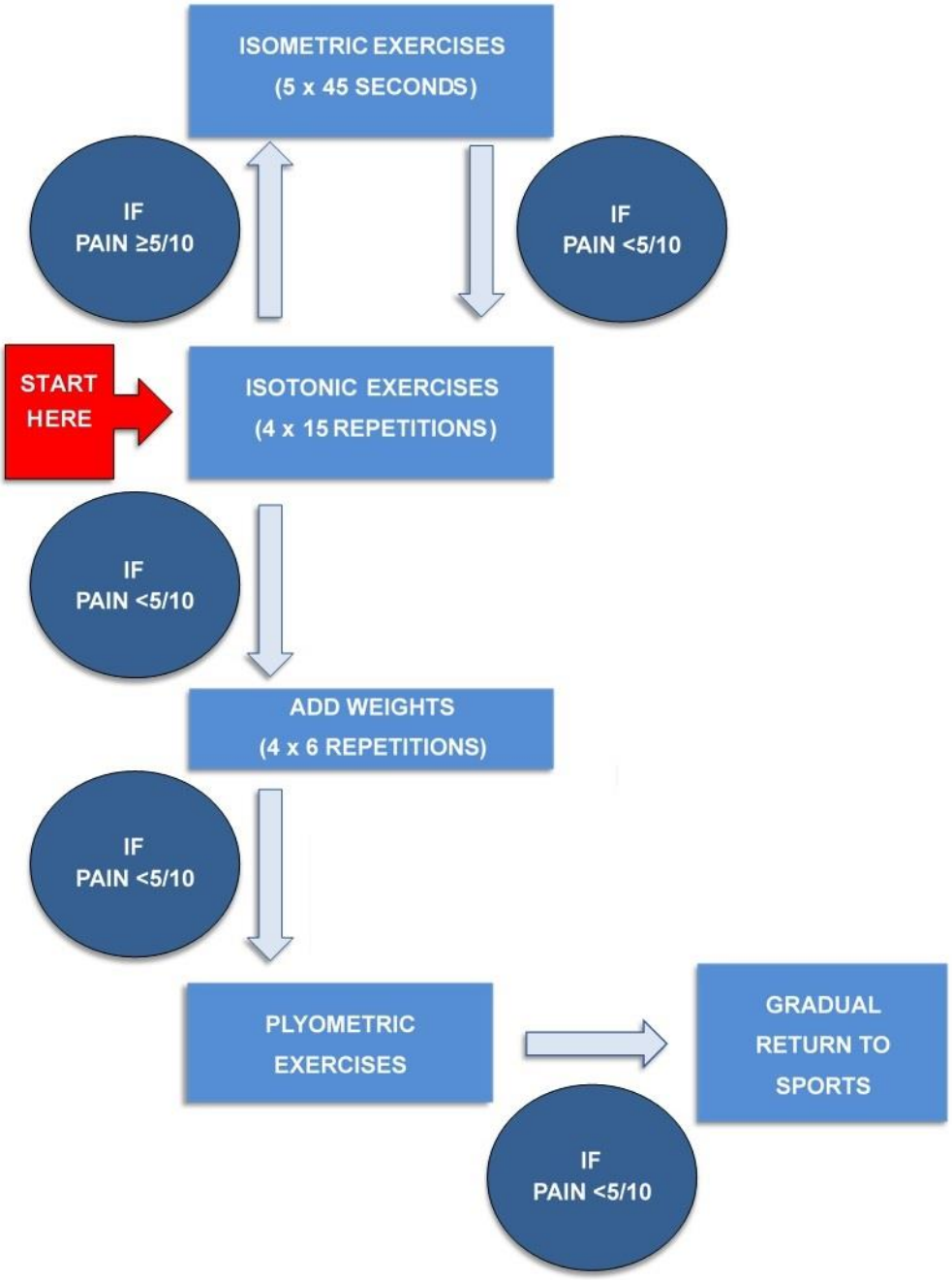


Figure 4.5 – Proposed flow chart for designing the progressive calf muscle strengthening exercises (gastrocnemius and soleus muscles) and plyometric exercises. The degree of pain (measured by VAS score or NRS scale) during and after the exercises and the muscle fatigue are leading for the speed of the progression. Note that for insertional Achilles tendinopathy, exercises are initially advised on a flat surface.

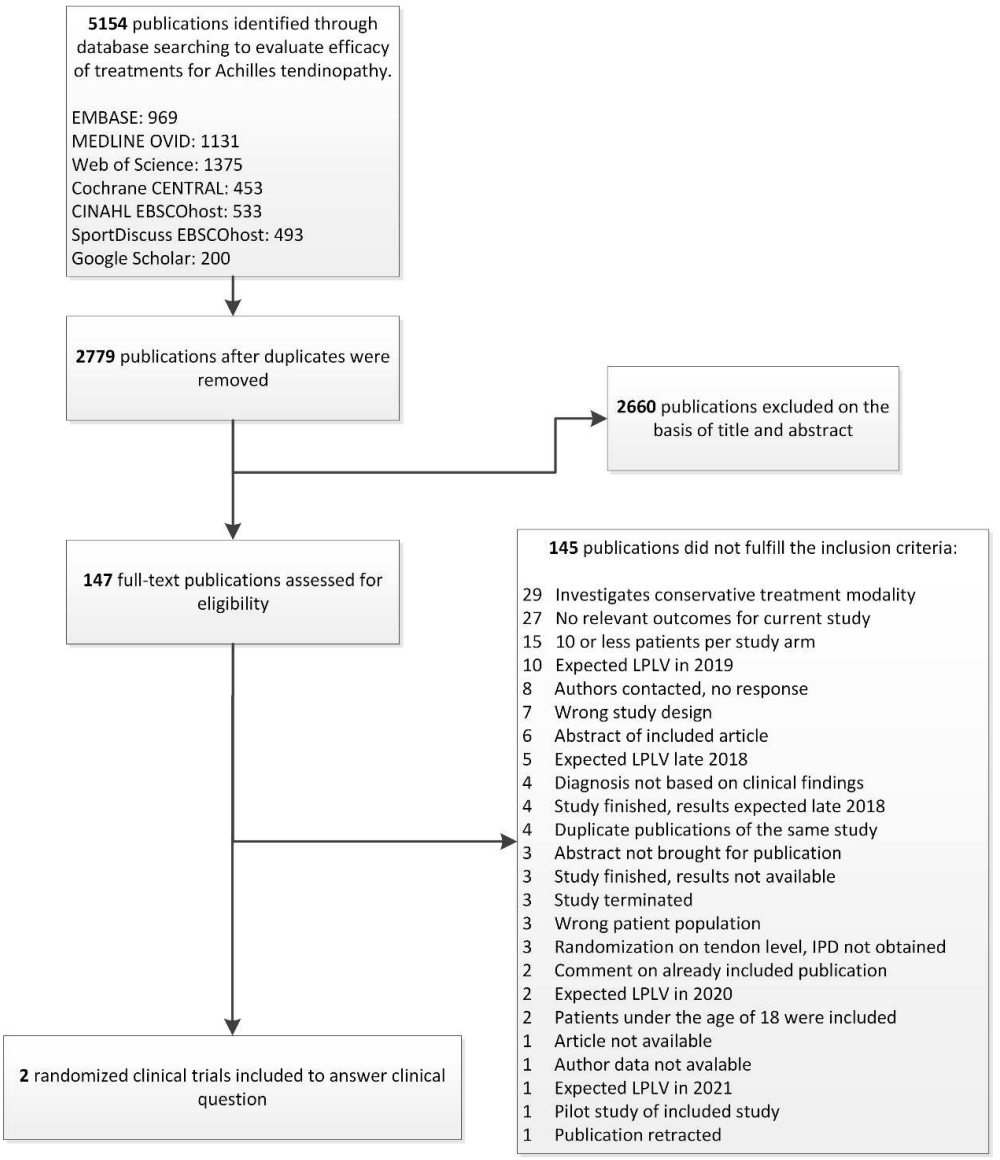


Figure 4.6 – PRISMA flowchart of the selection process for sub-module 4: Is surgery more effective than non-surgical treatment for Achilles tendinopathy?

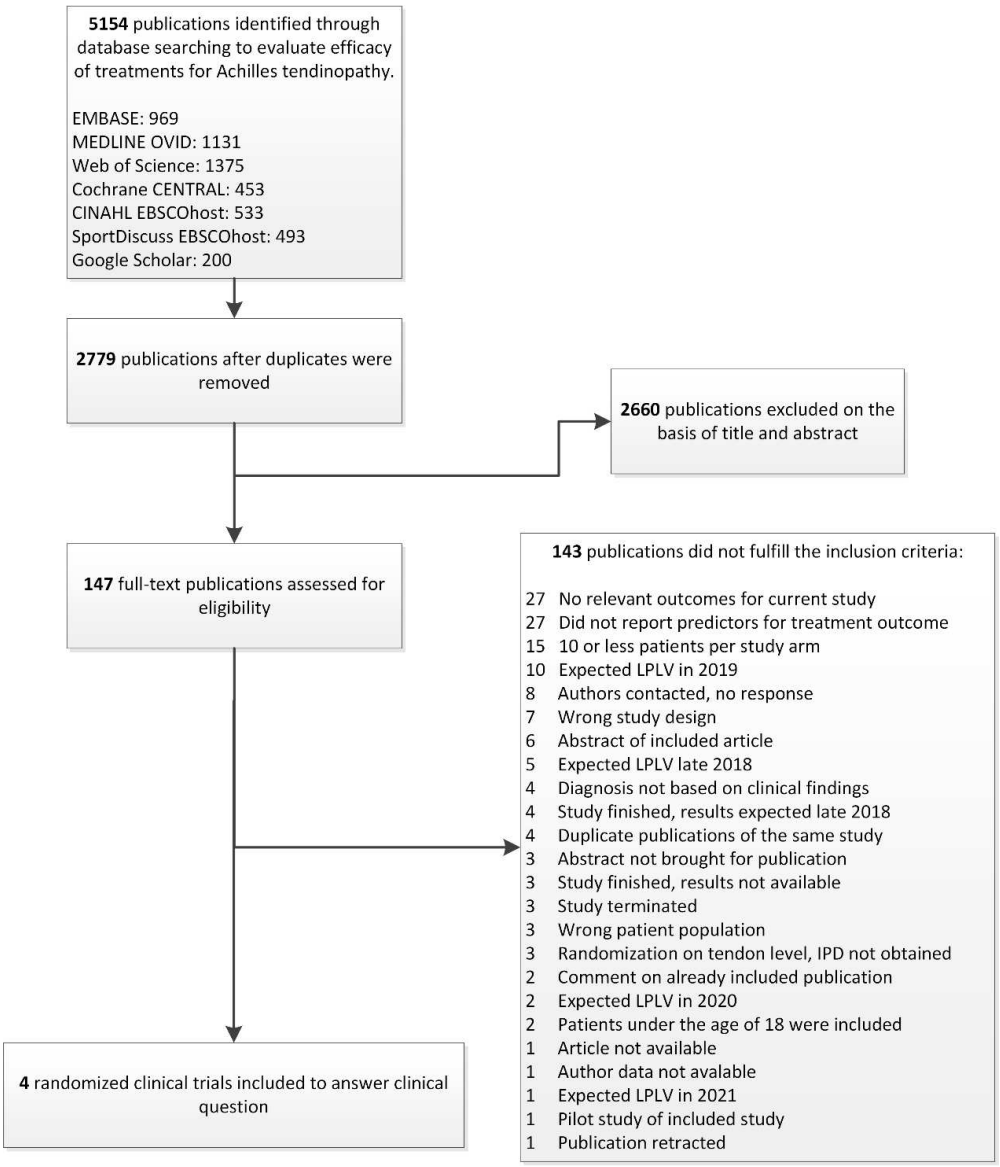


Figure 4.7 – PRISMA flowchart of the selection process for sub-module 4.5: Which factors influence treatment effects in Achilles tendinopathy?

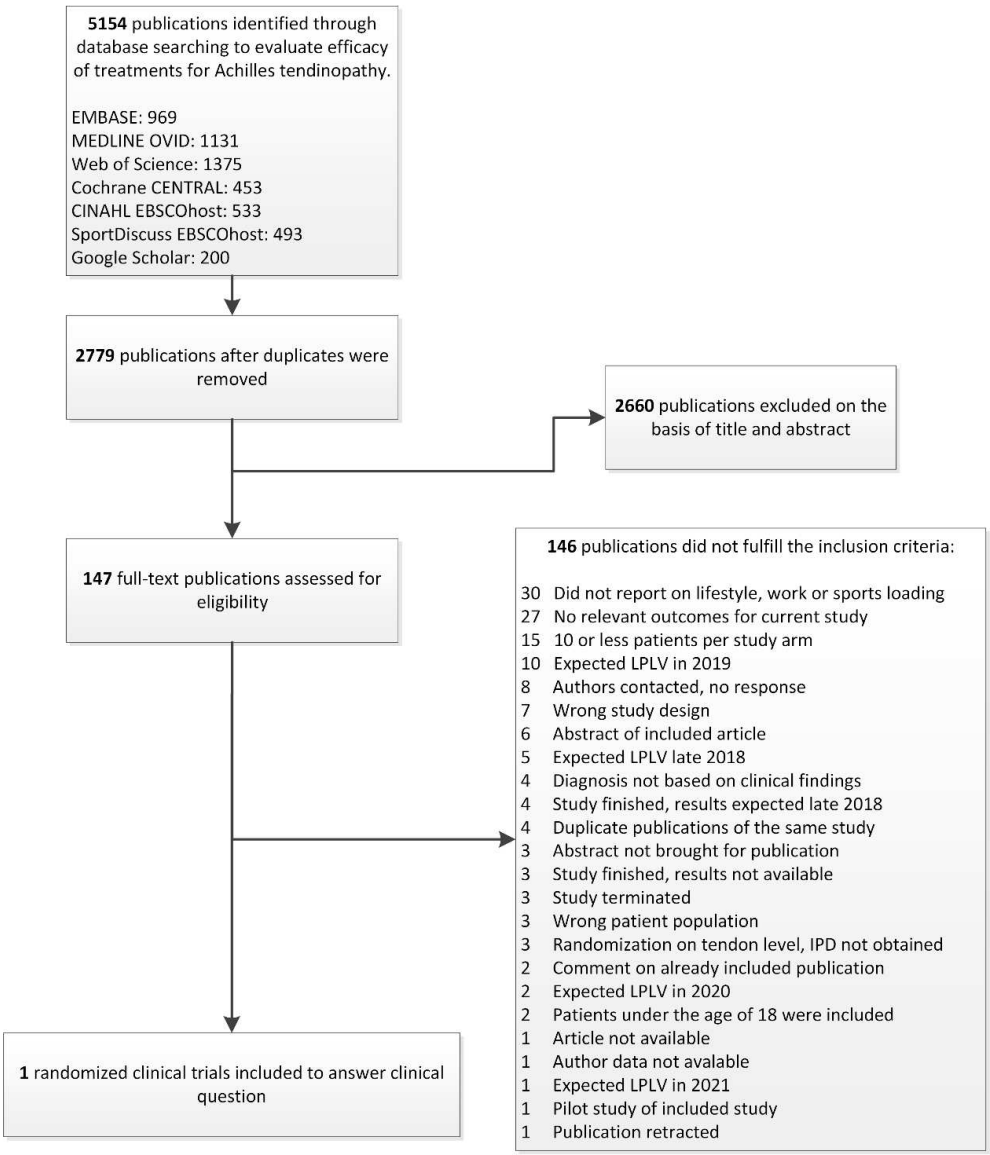


Figure 4.8 – PRISMA flowchart of the selection process for sub-module 4.6: What advice (self-management and patient education) should be given to patients with Achilles tendinopathy regarding lifestyle, workload and sports load?

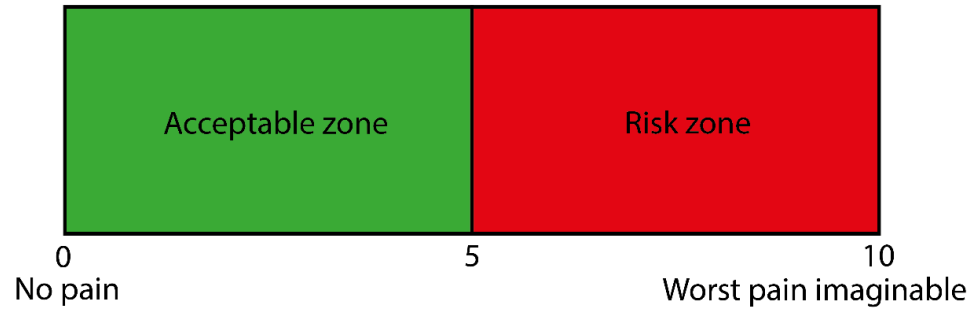


Figure 4.9 – Pain scale that can be used to monitor the symptoms of the Achilles tendon during and immediately after performing exercise therapy. Ideally, the exercises should be performed with a pain score of 0 to 5 on a scale of 0 to 10.

Top 10	**Number of studies (%)**
1. Victorian Institute of Sport Assessment-Achilles (VISA-A) score	28/61 (46%)
2. Pain on palpation (VAS)	19/61 (31%)
3. Pain score (VAS) not further specified	17/61 (28%)
4. Patient satisfaction	13/61 (21%)
5. Pain on activity	10/61 (16%)
6. Pain at rest	8/61 (13%)
7. Range of motion of the ankle	8/61 (13%)
8. American Orthopaedic Foot and Ankle Society (AOFAS) score	7/61 (11%)
9. Return to sports	6/61 (10%)
10. Effectiveness according tot he researcher	6/61 (10%)

Table 4.1 – The 10 most frequently used outcome measures in studies examining the effectiveness of treatment options in Achilles tendinopathy.

An impression of the main treatment goals from the national online questionnaire as distributed by the Dutch Patient Federation (97 respondents)
✓ "Being able to walk as normal as possible"
✓ "Being able to exercise and move pain-free"
✓ "Initially, being able to play sports again at the old level (team sport - ball sports). However, it was clear that this is ambitious. In the meantime, have set the bar is lower and the goal is to be able to run again."
✓ "Perform advice from physiotherapist"
✓ "Less pain and learning how to prevent it from getting worse again"
✓ "That the symptoms reduced/disappear as quickly as possible, allowing me to move pain-free again and thus function properly again at work"
✓ "Being able to walk normally again. Being able to walk further. Less pain and therefore better sleep. Get on and off bike without pain."
Main symptoms (max. 3) prompted among 9 patients with midportion Achilles tendinopathy.
✓ "Pain when driving when accelerating. Not being able to run. Pain that comes on suddenly and unexpectedly which almost stops me walking."
✓ "Not being able to walk pain-free. Pain when touched or with pressure from my shoe on the Achilles tendon."
✓ "Pain during and after cycling. Cycling means riding a normal bike without click pedals. Pain during and after just walking. Stiffness in the morning."
✓ "A few hours after a bike ride, the pain starts to worsen. Not severe, but annoying. When climbing stairs, the pain is always annoying, and also and early in the morning (actually independent of my activities the previous day). With normal walking (walking pace) there is actually a painful feeling with every step (especially on starting to walk and sometimes also halfway)."
✓ "The only complaint is that it is no longer possible to run as used to be possible. This is hard mentally, which makes it very important to be able to run full distances as before."
✓ "Especially complaints of a stiff tendon on starting activities. In addition, some shoes cannot be worn due to discomfort when the shoe presses on the tendon."
✓ "Not being able to run due to pain complaints. Can walk no more than 30-45 minutes. Small distances are pain-free, but longer distances are not possible because of the pain."
✓ "Pain due to pressure from hiking boots. Have done several mountain hiking holidays that could not be done on my own (high) hiking boots. Not being able to run because of the pain."

Table 4.2 – Overview of answers to the question 'which are the main treatment aims?'. These data have been collected by the Dutch Patient Federation (97 respondents) and the main symptoms reported in a panel of 9 patients with midportion Achilles tendinopathy

	Initial search	**After deduplication**
Embase.com	79	79

Medline Ovid	65	11
Cochrane CENTRAL	13	5
Total	**157**	**95**

Database	Search terms
Embase.com	('Achilles tendinitis'/exp OR ((tendinitis/de OR pathology/de) AND 'Achilles tendon'/de) OR (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog*))):ab,ti) NOT ((Conference Abstract)/lim) AND (English)/lim NOT ((animals)/lim NOT (humans)/lim) AND ('watchful waiting'/de OR (((no OR non OR un OR minimal* OR 'not') NEXT/1 (therap* OR treat* OR interv* OR contact* OR operat* OR surg*)) OR ((watchful* OR see OR list*) NEAR/3 wait*) OR ((natural* OR spontaneous) NEAR/6 (course OR development OR history OR remission* OR regress*))):ab,ti)
Medline Ovid	(((Tendinopathy/ OR Pathology/) AND "Achilles tendon"/) OR "Achilles tendon"/pa OR (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog*))).ab,ti.) AND English.lg NOT (exp animals/ NOT humans/) AND (Watchful Waiting/ OR Waiting Lists/ OR (((no OR non OR un OR minimal* OR "not") ADJ (therap* OR treat* OR interv* OR contact* OR operat* OR surg*)) OR ((watchful* OR see OR list*) ADJ3 wait*) OR ((natural* OR spontaneous) ADJ6 (course OR development OR history OR remission* OR regress*))).ab,ti.)
Cochrane CENTRAL	((((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog*))):ab,ti) AND ((((no OR non OR un OR minimal* OR 'not') NEXT/1 (therap* OR treat* OR interv* OR contact* OR operat* OR surg*)) OR ((watchful* OR see OR list*) NEAR/3 wait*) OR ((natural* OR spontaneous) NEAR/6 (course OR development OR history OR remission* OR regress*))):ab,ti)

Table 4.3 – Search strategy for sub-module 4.2 (wait-and-see policy).

Study	Domains						
	Study Participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Other bias
Rompe et al. (2007)	?	+	-	+	-	+	No

Table 4.4 – Risk of bias assessment of the randomised controlled trails evaluating a wait-and-see policy for Achilles tendinopathy.
+ low risk of bias, ? unclear risk of bias, - high risk of bias.

Study	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures	Results wait-and-see therapy
Rompe et al. (2007)	Type of study: RCT Setting: OrthoTrauma Clinic, Orthopaedic Surgery, Gruenstadt, Germany Source of Funding: NR, specific declaration of no conflict of interest	Inclusion criteria: • Unilateral midportion Achilles tendinopathy for ≥6 months • 18-70 years old Exclusion criteria: • Treatment in the last 12 weeks • Other conditions that could contribute to posterior ankle pain • Number of participants (intervention/control): 75 (50/25) • Mean age: 48.6 years • Male subjects: 39%	N=50 Intervention 1: Shock-wave therapy, three sessions with weekly intervals (2000 pulses, energy flux density 0.1 mJ/mm^2). Intervention 2: Eccentric training of the calf muscle both with the knee extended (3x15 repetitions) and flexed (3x15 repetitions) were performed twice a day for 12 weeks.	N=25 Wait-and-see treatment consisting of one visit during the intervention period. Training modifications, implementation of stretching exercises, and ergonomic advice were discussed with the patient. If necessary, paracetamol or NSAIDs were prescribed.	Length of follow-up: 16 weeks Loss to follow-up: Intervention: N=3 (6%) Reasons: Unwilling to come (n=2), discontinued intervention (n=1) Control: N=2 (8%) Reasons: Unwilling to come (n=1),	Primary outcome: • Improvement of VISA-A score from baseline to month 4 Secondary outcomes • General assessment using 6-point Likert scale • Pain assessment (load-induced VAS-score (0-10), pain threshold (kg) and tenderness on 3 kg pressure using algometer (VAS 0-10))	No significant difference was found for improvement of VISA-A score and tendon diameter at 4 months.

		• Important prognostic factors: NR			discontinued intervention (n=1)	• Maximum anteroposterior Achilles tendon thickness	

Table 4.5 – Evidence table of the included randomised trials in which a wait-and-see policy for Achilles tendinopathy was evaluated. Results of the included study are only shown for the wait-and-see arm in case there were multiple study arms in the concerning trial.
Abbreviations: AT, Achilles tendinopathy; NR, not reported; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs; RCT, randomised controlled trial; VAS, Visual Analogue Scale; VISA-A, Victorian Institute of Sports Assessment-Achilles.

Outcome	Number of studies	Mean difference (95% credible interval)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias[c]	Quality of evidence
VISA-A score at 16 weeks	1	7 (NR)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Table 4.6 – GRADE-assessment of a wait-and-see policy in midportion Achilles tendinopathy.

	Initial search	After deduplication
Embase.com	969	944
Medline Ovid	1131	627
Web of science	1375	785
Cochrane CENTRAL	453	90
CINAHL EBSCOhost	533	141
SportDiscuss EBSCOhost	493	72
Google scholar	200	120
Total	**5154**	**2779**

Database	Search terms
Embase.com	('Achilles tendinitis'/exp OR ((tendinitis/de OR pathology/de) AND 'Achilles tendon'/de) OR (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*):ab,ti) AND ('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer*):de,ab,ti)
Medline Ovid	(((Tendinopathy/ OR Pathology/) AND "Achilles tendon"/) OR "Achilles tendon"/pa OR (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*).ab,ti.) AND (Exp Controlled clinical trial/ OR "Double-Blind Method"/ OR "Single-Blind Method"/ OR "Random Allocation"/ OR (random* OR factorial* OR crossover* OR cross over* OR placebo* OR ((doubl* OR singl*) ADJ blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups).ab,ti.) NOT (Animals/ NOT Humans/)
Web of science	TS=(((((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*))) AND TS=(random* OR trial* OR rct)
Cochrane	((((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*))

CENTRAL	OR achillodyn*):ab,ti)
CINAHL EBSCOhost	(((MH Tendinopathy OR MH Pathology) AND MH "Achilles tendon") OR TI (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*) OR AB (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*)) AND (MH Clinical trials OR MH Randomized Controlled Trials OR MH Double-Blind Studies OR MH Single-Blind Studies OR MH Triple-Blind Studies OR MH Random Assignment OR TI (random* OR factorial* OR crossover* OR cross over* OR placebo* OR ((doubl* OR singl*) N1 blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups) OR AB (random* OR factorial* OR crossover* OR cross over* OR placebo* OR ((doubl* OR singl*) N1 blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups)) NOT (MH Animals+ NOT MH Humans+)
SportDiscuss EBSCOhost	(((MH TENDINITIS OR MH TENDINOSIS OR MH Pathology) AND MH "Achilles tendon") OR TI (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*) OR AB (((Achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog* OR pain* OR injur*)) OR achillodyn*)) AND (TI (random* OR factorial* OR crossover* OR cross over* OR placebo* OR ((doubl* OR singl*) N1 blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups) OR AB (random* OR factorial* OR crossover* OR cross over* OR placebo* OR ((doubl* OR singl*) N1 blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups))
Google scholar	"Achilles | calcaneal tendinitis | tendinopathy | tendinosis | tendonitis" intitle:trial | randomized | randomised | rct

Table 4.7 – Search strategy for subm-odule 4.3 (effectiveness non-surgical treatments), sub-module 4.4 (effectiveness surgical treatments), and sub-module 4.5 (factors that affects treatment effectiveness)

Consensus statement

Study	Study characteristics	Patient characteristics	Treatment	Follow-up	Outcome measures	Results	Predictors
Auclair, 1989 [35]	Setting: Eight different centers participated (Army teaching hospital, para commando training center, department of sports medicine, division of Rehabilitation and Sports Medicine, private practices, Medical Emergency division Fire Brigade) in France, Belgium and Germany Source of Funding: NR	Inclusion criteria: - Symptoms lasting less than 1 month - Aged 18 to 50 years Exclusion criteria: - Stage 4 Achilles tendinitis (continual pain at rest) - Symptoms associated with underlying disorders (osteoarthritis, rheumatoid arthritis, gout, hypercholesterolemia) - Skin lesions (wound, eczema, weeping dermatitis) at the gel application site - A history of allergy to anti-inflammatory drugs, active ulcer disease, or severe impairment of renal or hepatic function. • Type of AT: AT (not specified midportion or	Intervention: Local application of niflumic acid percutaneous gel (2.5%) 3 times a day for 7 days. Control: Local application of placebo percutaneous gel (2.5%) 3 times a day for 7 days.	Length of follow-up: 3 weeks Loss to follow-up: 16/243, not reported specifically whether these were exclusions or withdrawals	Primary outcome: - VAS pain on palpation Secondary outcomes: - Resumption of normal sporting activity - Attainment of their previous level of activity - Global efficacy by the researcher - Global efficacy by the patient	Resumption of normal sporting activity: There was no difference in resumption of normal sporting activity (intervention group 78%, control group 76%). Adverse effects: 5/123 (4.1%) in the intervention group and 6/116 (5.2%) of placebo gel group experienced side effects. Most common were cutaneous eruptions. 1 patient in niflumic acid	None investigated

		insertional) • Number of participants: 215 (114/101) • Active participants: 94% • Mean age: 29 years (SD 11) • Male subjects: NR				group stopped treatment after 2 days due to eruptions.	
Balius, 2016 [72]	Setting: Five sports medicine centers in Spain Source of Funding: Commercial funding[1]	Inclusion criteria: - Painful noninsertional Achilles tendinopathy for at least 3 months - Men and nonpregnant women aged 18 to 70 years Exclusion criteria: - Clinical suspicion of insertional tendinopathy, tendon rupture, neural disorder, systemic disease (e.g. gout, spondyloarthropathy, rheumatoid arthritis and sarcoidosis), or pregnancy - Patients which already received a previous treatment with eccentric training or PRP for the studied	Intervention 1: Capsule containing 435 mg mucopolysaccharides, 75 mg collagen type I, and 60 mg vitamin C three times daily for 12 weeks. Additionally, eccentric exercises were performed twice daily for 12 weeks. Intervention 2: Capsule containing 435 mg mucopolysaccharides, 75 mg collagen type I, and 60 mg vitamin C three	Length of follow-up: 12 weeks Loss to follow-up: 3/58; 3 did not attend the inclusion visit (2 in the MCVC+eccentric exercises group and 1 in the MCVC+passive stretching group)	Primary outcome: - VISA-A score Secondary outcomes: - VAS pain at rest - VAS pain during activity - Bilateral thickness (ultrasonographically) - Safety profile	VISA-A score: There was no significant difference at 12 weeks between the 3 treatment groups. The VISA-A score was 88 (SD 16) in intervention group 1, 84 (SD 22) in intervention group 2, and 79 (SD 18) in the control group. Adverse effects: Not reported	None investigated

		injury. • Type of AT: Midportion AT • Number of participants: 55 (17/20/18) • Active participants: NR • Mean age: 41 years (SD 11) • Male subjects: 80%	times daily for 12 weeks. Additionally, stretching exercises were performed daily for 12 weeks. Control: Eccentric exercises were performed twice daily for 12 weeks.				
Bell, 2013 [65]	Setting: Specialist multidisciplinary sports medicine clinic in New Zealand Source of Funding: Specific declaration of no funding	Inclusion criteria: - Aged over 18 - A first episode of midportion Achilles tendinopathy - Symptoms present for at least three months - Diagnosis confirmed by diagnostic ultrasonography Exclusion criteria: - Bilateral Achilles tendon symptoms - Alternative diagnoses such as insertional Achilles tendinopathy - Previous Achilles	Intervention: Unguided peritendinous autologous blood injections (twice; 1 at baseline and 1 after 1 month). Additionally, eccentric exercises were performed twice daily for a minimum of 12 weeks. Control: Unguided peritendinous dry-	Length of follow-up: 26 weeks Loss to follow-up: 2/53; 1 patient per group failed to attend all appointments.	Primary outcome: - VISA-A score Secondary outcomes: - Level of Return to sports - Perceived rehabilitation (Likert scale) - Compliance log	VISA-A score: There was no significant difference at any time point between both treatment groups. At 6 months, VISA-A change from baseline was 18.7 (95% CI: 12.3-25.1) in the intervention group and 19.9 (95% CI: 13.6-26.2) in the	Age, sex, ethnicity, level of physical activity, duration of symptoms, severity on ultrasonography, compliance with eccentric training, additional weight carried during eccentric training, and eccentric exercise technique did not influence the

		tendon rupture or surgery - Previously undergone adjuvant therapies (e.g. any kind of injection, GTN patches, or ESWT). Eccentric training performance was not an exclusion criterion. • Type of AT: Midportion AT • Number of participants: 53 (26/27) • Active participants: 92% • Mean age: 49 years (SD 10) • Male subjects: 53%	needling (twice; 1 at baseline and 1 after 1 month). Additionally, eccentric exercises were performed twice daily for a minimum of 12 weeks.			control group. Return to sports: There was no significant difference at 26 weeks between both treatment groups. At 6 months, 52% of the patients in the intervention group returned to pre-injury level in their desired sport, compared to 36% in the control group. Adverse effects: No complications or adverse events as a result of the injections	magnitude of the effect of treatment on the change in VISA-A score.

Beyer, 2015 [30]	Setting: Institute of Sports Medicine in a general hospital in Denmark Source of Funding: NR	Inclusion criteria: - Recreational athletes with a diagnosed chronic unilateral midportion Achilles tendinopathy Exclusion criteria: - <4 week washout period from any other treatment - Corticosteroid injections in the previous 12 months - Bilateral Achilles tendinopathy - Insertional Achilles tendinopathy - Systemic disease (e.g., rheumatoid arthritis, diabetes) - Any surgery, or any confounding lower limb and ankle injury • Type of AT: Midportion AT • Number of participants: 58 (30/28) • Active participants: NR • Mean age: 48 years (SD	Intervention: Heavy slow resistance (HSR) exercises 3 times per week for 12 weeks using resistance equipment in a fitness center. Control: Eccentric exercises twice daily for 12 weeks.	Length of follow-up: 52 weeks Loss to follow-up: 11/55; 6 withdrew from the intervention group (1 ankle pain, 1 back pain, 2 lack of time, and 2 moved away) and 5 withdrew from the control group (1 ankle pain, 2 back pain, and 2 lack of time)	Primary outcome: - VISA-A score Secondary outcomes: - Patient satisfaction - VAS pain during 5 heel rises - VAS pain during running - Activity level of sporting activities (h/week) - Tendon thickness (ultrasound) - Doppler colour fraction	VISA-A score: There was no significant difference at any time point between both treatment groups. At 12 months, VISA-A score was 89 (SD 2.8) in the intervention group and 84 (SD 3.5) in the control group. Patient satisfaction: There was no significant difference at 12 months between both treatment groups. At 12 months, patient satisfaction was 96% for the intervention	None investigated

		2) • Male subjects: 68%				group and 76% for the control group. Adverse effects: Not reported	
Boesen, 2017 [73]	Setting: Institute of Sports Medicine in a large district hospital in Denmark Source of Funding: Commercial funding[2]	Inclusion criteria: - Healthy males with clinical (thickness and pain) and ultrasonographic (tendon thickness and intratendinous vascularity) features of chronic midportion AT (approximately 2-7 cm proximal to the insertion on the calcaneus). - Aged 18 to 59 years - Symptoms present for at least 3 months. Exclusion criteria: - Clinical suspicion and ultrasonographic indication of other musculoskeletal injuries (e.g., insertional disorders and tendon rupture)	Intervention 1: Ultrasonographic-guided high-volume injection with a mixture of 10 mL 0.5% bupivacaine hydrochloride and approximately 20 mg Depo-Medrol, immediately followed by 10 mL of injectable normal saline 4 times (total volume of 50 mL). Injection was performed once at baseline, but three more placebo injections were given at 2-weekly intervals. Additionally, eccentric exercises	Length of follow-up: 24 weeks Loss to follow-up: 3/60; 1 patient in intervention group 1 could not be contacted, the 2 other patients (1 each in the intervention group 2 and control group) left the trial after 6 weeks due to lack of compliance with the eccentric training regimen.	Primary outcome: - VISA-A score Secondary outcomes: - Patient satisfaction - Return to running - Time frame to return to running VAS pain during activity - Tendon thickness (ultrasound) - Intratendinous vascularity assessed by CD activity - Muscle function measured with the 1-leg heel-rise test	VISA-A score: Improvement in VISA-A score was significantly greater in intervention group 1 (HVI) compared to intervention group 2 (PRP) and the control group at 6 and 12 weeks. At 24 weeks, improvement in VISA-A score was significantly greater in both intervention groups compared to the control group.	None investigated

		- Presence of diabetes or cardiovascular disease - Previous injection with steroids or any kind of blood products (e.g., PRP) or treatment with fluoroquinolones during the last 6 months. • Type of AT: Midportion AT • Number of participants: 60 (20/20/20) • Active participants: 89% • Mean age: 42 years (SD 9) • Male subjects: 100%	were performed twice daily for 24 weeks. Intervention 2: PRP-injections were given at 2-weekly intervals. Additionally, eccentric exercises were performed twice daily for 24 weeks. Control: Peritendinous dry-needling with a few drops of saline at 2-weekly intervals. Additionally, eccentric exercises were performed twice daily for 24 weeks.			Improvement in VISA-A score in intervention group 1 was 27.1 (SD 3.1) at 6 weeks, 28.8 (SD 4.1) at 12 weeks, and 22.2 (SD 4.6) at 24 weeks. Improvement in VISA-A score in intervention group 2 was 13.8 (SD 4.1) at 6 weeks, 14.8 (SD 3.1) at 12 weeks, and 19.6 (SD 4.5) at 24 weeks. Improvement in VISA-A score in the control group was 9.9 (SD 3.3) at 6 weeks, 10.6 (SD 3.0) at 12 weeks, and 8.8 SD (SD 3.3) at	

						24 weeks. <u>Return to running:</u> At 24 weeks, 68% had returned to running in intervention group 1 (HVI), 53% in intervention group 2 (PRP), and 42% in the control group. No statistical tests were performed on this data. <u>Patient satisfaction:</u> Patients in intervention group 1 (HVI) and in intervention group 2 (PRP) are more most	

						frequently satisfied compared to the control group at both 12 and 24 weeks. At 24 weeks, 63% was satisfied in intervention group 1 (HVI), 58% in intervention group 2 (PRP), and 42% in the control group. Adverse effects: No complications (infections, hematomas, or ruptures) were reported after the injection treatments.	
de Jonge, 2010 [19]	Setting: Sports medicine	Inclusion criteria: - aged 18-70 years - Presence of symptoms	Intervention: Night splint worn every night between	Length of follow-up: 52 weeks	Primary outcome: - VISA-A score	VISA-A score: There was no significant	None investigated

	department in a general hospital in the Netherlands Source of Funding: NR	for >2 months of midportion AT - Active participation in sporting activities before the onset of symptoms and the patients' wish to return to their original level of sports. Exclusion criteria: - Previous performance of an intensive programme of heavy-load eccentric exercises - Inability to perform heavy-load exercises - Insertional disorders - Tendon ruptures - Systemic illness • Type of AT: Midportion AT • Number of participants: 56 (28/28) • Active participants: 100% • Mean age: 45 years (SD 8) • Male subjects: 46%	0°and 5°dorsiflexion. Duration of treatment not reported. Additionally, eccentric exercises were performed twice daily for 12 weeks. Control: Eccentric exercises were performed twice daily for 12 weeks.	Loss to follow-up: 8/70 (tendons); 4 did not receive allocated intervention (2 per group), 3 failed to attend, and 1 left to live overseas.	Secondary outcomes: - Patient satisfaction - Neovascularisation score (modified Öhberg score)	difference at any time point between both treatment groups. VISA-A score was 78.2 (SD NR) at 52 weeks for the intervention group, compared to 75.7 (SD NR) for the control group. Patient satisfaction: There was no significant difference at any time point between both treatment groups. Patient satisfaction was 70% in the intervention group, compared to	

						53% in the control group at 52 weeks. Adverse effects: 3/36 (8.3%) in the intervention group, 2/34 (5.9%) in the control group; 2 patients (2 tendons) did not complete the treatment in the eccentric group. 1 patient experienced too much pain and 1 patient developed a subluxation of the peroneal tendon during the study, which prevented him from performing the exercises. In a few cases, the	

						night splint caused minor symptoms, which did not prevent further treatment. 2 patients experienced painful pressure areas and 1 patient could not increase dorsiflexion of the night splint 0° because of paraesthesia of the foot.	
de Jonge, 2011 [21]	Setting: Sports medicine department in a general hospital in the Netherlands Source of Funding: Commercial funding[3]	Inclusion criteria: - Symptoms of chronic midportion Achilles tendinopathy for at least 2 months - Age 18-70 years Exclusion criteria: - Clinical suspicion of other musculoskeletal (insertional disorders and tendon rupture) injuries, inflammatory	Intervention: Ultrasound guided PRP injection in the degenerative area of the body of the tendon once at baseline. Additionally, eccentric exercises were performed twice daily for 12 weeks.	Length of follow-up: 52 weeks Loss to follow-up: 0/54	Primary outcome: - VISA-A score Secondary outcomes: - Patient satisfaction - Return to sports - Neovascularisation score (modified Öhberg score) - UTC imaging	VISA-A score: There was no significant difference at any time point between both treatment groups. VISA-A score was 78.2 (95% CI: 68.0-88.5) at 52 weeks for the	Baseline VISA-A score did influence the magnitude of the effect of treatment on the change in VISA-A score. Duration of symptoms did not influence the magnitude of the

		internal disorders, or use of specific medications that can cause tendinopathy (fluoroquinolones) - Previous performance of a complete heavy load eccentric exercise program or inability to perform it - Previous PRP injection • Type of AT: Midportion AT • Number of participants: 54 (27/27) • Active participants: 85% • Mean age: 50 years (SD 9) • Male subjects: 48%	Control: Ultrasound guided saline injection (2 mL) in the degenerative area of the body of the tendon once at baseline. Additionally, eccentric exercises were performed twice daily for 12 weeks.			intervention group, compared to 77.6 (95% CI: 70.8-84.4) for the control group. Return to previous sports levels: There was no significant difference at 24 and 52 weeks between both treatment groups. At 52 weeks, 57% returned to their previous sports levels in the desired sport in the intervention group, compared to 42% in the control group.	effect of treatment on the change in VISA-A score.

						Patient satisfaction: There was no significant difference at any time point between both treatment groups. Patient satisfaction was 59% in both groups at 52 weeks. Adverse effects: Report there were no complications between 24 weeks and 1-year follow-up.	
Ebbesen, 2018 [40]	Setting: Department of Orthopaedic Surgery in a university hospital in Denmark	Inclusion criteria: - Duration of pain on the Achilles tendon of at least 3 months; - A minimum of 3 months of eccentric exercise	Intervention: Polidocanol (10 mg/mL) injections at the inlet of pathological vessels at the edge of the tendon until	Length of follow-up: 26 weeks Loss to follow-up: 4/48; 1 in the	Primary outcome: - VAS pain during walking Secondary outcomes: - VISA-A score	VISA-A score: There was no significant difference at any time point between both treatment	None investigated

	Source of Funding: Non-commercial funding[4]	- Neovascularisation demonstrated by ultrasonography Exclusion criteria: - Dementia or psychiatric disorders not suited for participation - Contraindication to the use of Polidocanol - Diabetes or hypercholesterolemia - Increased risk of thrombosis - Previous rupture of the Achilles tendon - Pregnancy or breastfeeding - Inability to lie in a prone position - Presence of hypoechoic area in more than 50% of the horizontal cross-sectional area of the tendon identified by ultrasonography, which was considered to increase the risk of tendon rupture. • Type of AT: AT (not	neovascularisation disappeared. After 4 weeks, the procedure was repeated if neovascularisation was still present. Control: Lidocaine (10 mg/mL) injections were performed following the same procedure as the intervention group. After 4 weeks, the procedure was repeated if neovascularisation was still present.	intervention group (reason unknown) and 3 in the intervention group (1 thickening of the ankle, 1 had allergic reactions, and 1 reason unknown)	- Patient satisfaction - Foot and Ankle Outcome Score (FAOS) - Number of injections needed.	groups. VISA-A score was 72.0 (SD 18.1) at 26 weeks for the intervention group, compared to 69.9 (SD 20.0) for the control group. Patient satisfaction: There was no significant difference at 12 and 26 weeks between both treatment groups. Patient satisfaction was 61% in the intervention group and 57% in the control group. Adverse effects: None in the	

		specified midportion or insertional) • Number of participants: 48 (24/24) • Active participants: NR • Mean age: 51 years (SD not provided) • Male subjects: 43%				intervention group, 2/24 (8.3%) in the control group; No serious adverse events were found during this study. 1 patient in the control group developed allergic reaction (most likely to the lidocaine) and 1 patient in the control group had thickening of the ankle (not further specified)	
Heinemeier, 2017 [22]	Setting: Outpatient clinic at Institute of Sports Medicine in	Inclusion criteria: - Experience of pain during Achilles tendon loading for at least 3 months - Clinical signs of	Intervention: Ibuprofen tablets (600 mg) three times/day for 1 week.	Length of follow-up: 1 week Loss to follow-up:	Primary outcome: - Real-time-RT-PCR on a full width tendon biopsy (changes in gene expression)	VISA-A score: There was no significant difference at 1 week follow-up between both	None investigated

	Denmark Source of Funding: Non-commercial funding[5]	midportion Achilles tendinopathy - Ultrasonographic (US) findings of increased Achilles tendon thickness at the midportion, with hypoechoic areas and presence of colour Doppler signal Exclusion criteria: - Currently receiving treatment for their tendinopathy - NSAID use within 6 weeks or corticosteroid injections within 6 months - Severe systemic disease - A BMI >30 or <18 - Smoking or alcohol abuse - Contraindications for ibuprofen treatment - Use of medication that would interfere with the response to ibuprofen. • Type of AT: Midportion AT	Control: Placebo tablets three times/day for 1 week.	NR, most likely no loss to follow-up	Secondary outcomes: - VISA-A score - Ibuprofen content in the blood - VAS tendon pain at rest - VAS tendon pain during activity - Ultrasonographic tendon thickness - Colour Doppler	treatment groups. VISA-A score was 59 (SD 20) at 1 week for the intervention group, compared to 65 (SD 20) for the control group. Adverse effects: Not reported	

		• Number of participants: 26 (13/13) • Active participants: NR • Mean age: 54 years (SD 11) • Male subjects: 62%					
Herrington, 2007 [34]	Setting: Public health service outpatients in the United Kingdom Source of Funding: No funding received	Inclusion criteria: - Aged 20–55 - Duration symptoms >3 months - Diagnosis of non-insertional tendinopathy - Complained of local Achilles pain, stiffness or functional impairment on activity - Negative squeeze test Exclusion criteria: - Rheumatic conditions - Circulatory disorders - Diabetes - History of fracture to foot or ankle - Past surgery to Achilles - History of Achilles tears or rupture - Undergoing any other treatment for their Achilles	Intervention: Eccentric exercises were performed twice daily for 12 weeks. Deep friction massage, ultrasound over the most painful area of the Achilles tendon for 6 weeks by a physiotherapist. A stretching program was advised for 12 weeks. Control: Deep friction massage, ultrasound over the most painful area of the Achilles tendon for 6 weeks by a physiotherapist. A	Length of follow-up: 12 weeks Loss to follow-up: 0/25	Primary outcome: - VISA-A score Secondary outcomes: - None	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group compared the control group at 12 weeks. VISA-A score in the intervention group was 98 (SD 2) at 12 weeks, compared to 81 (SD 1) for the control group (p=0.01). Adverse effects: Not reported	None investigated

		• Type of AT: Midportion AT • Number of participants: 25 (13/12) • Active participants: NR • Mean age: 37 years (SD 8) • Male subjects: NR	stretching program was advised for 12 weeks.				
Hutchison, 2013 [23]	Setting: NR Source of Funding: Commercial funding[6]	Inclusion criteria: - ≥ 3-month history of pain - Tenderness in the Achilles tendon 2-6 cm above the insertion - Hypoechogenic area within the tendon on ultrasound examination and/or an increase in the thickness by > 50% compared with the asymptomatic side (when there were unilateral changes) Exclusion criteria: - Light sensitivity - Fitzpatrick's skin type V/VI - Calcification in the tendon	Intervention: Intense pulsed light (IPL) weekly treatments for a period of 3 weeks. Control: Placebo intense pulsed light weekly treatments for a period of 3 weeks.	Length of follow-up: 12 weeks Loss to follow-up: 4/46; 1 in the intervention group (failed to attend) and 3 in the control group (2 failed to attend and one sustained a fracture of the ankle)	Primary outcome: - VISA-A score Secondary outcomes: - VAS pain (best, average and worst over previous week) - Lower Extremity Functional Scale (LEFS) - Ultrasound anteroposterior thickness and neovessels with Ohberg score	VISA-A score: There was no significant difference at any time point between both treatment groups. VISA-A score was 57.1 (SD 24.5) at 12 weeks for the intervention group, compared to 50.5 (SD 27.0) for the control group. Adverse effects: Reported that	None investigated

		- Rheumatoid arthritis - Autoimmune disorders - Other conditions that could cause pain in heel pain posteriorly • Type of AT: Midportion AT • Number of participants: 47 (23/24) • Active participants: NR • Mean age: 48 years (SD 8) • Male subjects: 64%				there were no adverse events	
Krogh, 2016 [74]	Setting: Public hospital in Denmark Source of Funding: Commercial and non-commercial funding[7]	Inclusion criteria: - Achilles tendinopathy symptoms for > 6 months - Clinical diagnosis of a painful and thickened tendon in relation to activity and on palpation (2-7 cm proximal to insertion on calcaneus) Exclusion criteria: - Age < 18 years - Glucocorticoid injection within the last 6 months	Intervention: Ultrasound guided intratendinous PRP injection once at baseline. Additionally, eccentric exercises, stretching exercises, and coordination exercises were performed (duration and frequency not reported). Control:	Length of follow-up: 52 weeks Loss to follow-up: 16/24 at 52 weeks; 10/12 in PRP group and 6/12 in saline withdrew after 3 months due to "unsatisfactory effects". 0/24 at 3 months.	Primary outcome: - VISA-A score Secondary outcomes: - VAS pain at rest - VAS pain when walking - VAS pain on palpation (NRS 1-4) - Changes in colour Doppler activity - Tendon thickness - Adverse events	VISA-A score: There was no significant difference at 3 months between both treatment groups. VISA-A score was 35.1 (SD NR) at 12 weeks for the intervention group, compared to 41.9 (SD NR) for the control	None investigated

		- Previous Achilles tendon surgery - Known inflammatory diseases (e.g. rheumatoid arthritis, psoriatic arthritis, inflammatory bowel disease) • Type of AT: Midportion AT • Number of participants: 24 (12/12) • Active participants: NR • Mean age: 49 years (SD 9) • Male subjects: 54%	Ultrasound guided intratendinous saline (placebo) injection once at baseline. Additionally, eccentric exercises, stretching exercises, and coordination exercises were performed (duration and frequency not reported).			group. Conclusions are limited to 12 weeks after the treatment due to a large dropout rate. Adverse effects: 1/12 (8.3%) in the intervention group, none in the control group: 1 patient from the PRP group contacted the department within 5 weeks after the initial treatment because of concern about the level of increasing pain (the thickness of the Achilles tendon had increased from 7.9 to 9.2 mm).	

						No events leading to hospitalisation in any of the groups.	
Lynen, 2017 [33]	Setting: Ambulatory care in two hospitals in Germany and Belgium Source of Funding: Commercial funding[8]	Inclusion criteria: - Aged 18-75 years - Painful Achilles midportion tendinopathy for 6 weeks - A pain intensity score of at least 40mm on the visual analogue scale (VAS) Exclusion criteria: - Severe intercurrent illnesses (e.g., uncontrolled diabetes mellitus, peripheral neuropathy) - Contraindications for the test products (e.g., hypersensitivity, recent surgery, local osteomyelitis) - Concomitant diseases (e.g., insertional Achilles tendinopathy) - Other conditions that	Intervention: Two ultrasound guided peritendinous hyaluronan injections at weekly intervals. The performance of excessive sports or physical activities were discouraged during the study. Control: Three sessions extracorporeal shock wave therapy at weekly intervals. The performance of excessive sports or physical activities were discouraged during the study.	Length of follow-up: 26 weeks Loss to follow-up: 4/62; 1 in the intervention group because of several deviations in the selection criteria and 3 in the control group (withdrawal of con-sent before treatment end, loss to follow-up, and lack of efficacy)	Primary outcome: - VAS percent change in pain Secondary outcomes: - VISA-A score - Intensity of clinical parameters (redness, warmth, thickening, tenderness on palpation, crepitus on motion, accumulation of tissue fluid) evaluated on a 5-point ordinal scale (0, none; 1, slight; 2, moderate; 3, severe; 4,extreme), - Patients' and investigators' overall impression of the treatment outcome using a	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group compared to the control group at 12 and 26 weeks ($p<0.01$). The VISA-A scores in the intervention group was 73.0 (SD 24.0) at 12 weeks, and 75.0 (SD 22.0) at 26 weeks. In the control group, VISA-A score was 47.5 (SD 15.0) at 12	None investigated

		were incompatible with study procedures (e.g., concomitant medications potentially interfering with the functional assessments in the study) • Type of AT: Midportion AT • Number of participants: 59 (29/30) • Active participants: NR • Mean age: 45 years (SD 9) • Male subjects: 47%			7-point ordinal scale (1, very much improved; 7, very much worse) - Power Doppler ultrasonography to evaluate the vascularisation stage (grades I-V)	weeks, and 52.0 (SD 15.0) at 26 weeks. Adverse effects: 3 patients (4.8%) in the intervention group (4 adverse events) and 5 patients (8.1%) in the control group (6 adverse events). None of these were considered serious. Eight adverse events were judged as not device or procedure related, and only 2 were thought to have a causal relationship with the study treatments. One participant	

						reported transient, moderate tendon pain after HA injection on day 1, and another participant reported transient, moderate application site pain lasting 2 days after ESWT treatment.	
Mafi, 2001 [28]	Setting: An Orthopaedic Surgery department and Sports Medicine Unit in Sweden Source of Funding: NR	Inclusion criteria: - Severe midportion Achilles tendon pain with diagnosis verified by clinical examination (painful area) and ultrasonography (localised widening of the tendon and hypoechoic areas) Exclusion criteria: - A restricted ankle joint motion due to other	Intervention: Eccentric training regimen on a daily basis for 12 weeks. Control: Concentric training regimen on a daily basis for 12 weeks.	Length of follow-up: 12 weeks Loss to follow-up: 0/44	Primary and secondary outcomes were not specified: - Patient satisfaction - VAS score during activity (0-100 points) - Return to activity level (walking or jogging)	Patient satisfaction: Patient satisfaction was significantly greater at 12 weeks in the intervention group compared to the control group ($p<0.002$). 88%	None investigated

		injuries or diseases • Type of AT: Midportion AT • Number of participants: 44 (22/22) • Active participants: NR • Mean age: 48 years (SD 9) • Male subjects: 55%				of the patients in the intervention group were satisfied, compared to 36% in the control group. Adverse effects: Not reported	
Munteanu, 2015 [75]	Setting: A university clinic and a radiology department of a private hospital in Australia. Source of Funding: Commercial funding[9]	Inclusion criteria: - Age 18-55 years - Symptoms in the mid-portion of one or both Achilles tendons for ≥3 months - Able to complete English VISA-A - Scored <80 on the VISA-A - Regularly used footwear that could accommodate customised foot orthoses - Willing to not receive any physical therapy on the involved Achilles tendon(s) or trial of foot orthoses or	Intervention: Customised foot orthoses in combination with a 12-week eccentric calf muscle training. Control: Sham foot orthoses in combination with a 12-week eccentric calf muscle training.	Length of follow-up: 52 weeks Loss to follow-up: 41/140 at the primary endpoint (12 weeks); 18 patients in the intervention group (13 unable to be contacted, 2 no time, 2 unrelated medical condition, 1	Primary outcome: - VISA-A score Secondary outcomes: - Participant perception of treatment effectiveness (dichotomised from 5-point Likert scale) - Level of physical activity in the previous week (7-day Physical Activity Recall Questionnaire) - Health-related	VISA-A score: There were no significant differences at 1, 3, 6, and 12 months between both treatment groups. VISA-A score was 82.1 (SD 16.3) at 12 months for the intervention group, compared to 79.2 (SD 20.0) for the control group.	None investigated

		bracing during the study period <u>Exclusion criteria:</u> - Previous Achilles tendon surgery or rupture in the symptomatic lower limb(s) - Previous lower limb trauma or osseous abnormality that had caused structural imbalance (e.g. ankle fracture) - Inflammatory arthritis - Metabolic, endocrine, or neurological disorders - Previous breast cancer and/or use of oestrogen inhibitors - Treatment with foot orthoses, heel lifts or eccentric calf muscle exercises within the previous 3 months - Fluoroquinolone usage within the previous 2 years - Injection of local anaesthetic, cortisone		reason not provided) and 23 in the control group (18 unable to be contacted, 1 no time, 2 unrelated medical condition, 2 adverse events, 1 reason not provided). 50/140 at 52 weeks.	quality of life (eight domains of the Short-Form-36 questionnaire - Use of cointerventions (rescue medication, other treatments and footwear changes) - Adverse effects	<u>Adverse effects:</u> 27/54 (50%) in the intervention group, 23/55 (41.8%) in the control group within 1 month. No serious adverse events; 2 participants in sham orthosis group withdrew due to adverse events: 1 knee pain, 1 lower limb stress fracture.	

		or other pharmaceutical agents into the symptomatic Achilles tendon(s) or surrounding area within the previous 3 months - Injury or pathology of the feet, knees, hips and/or back or any condition that may have interfered with participation in the study • Type of AT: Midportion AT • Number of participants: 140 (67/73) • Active participants: NR • Mean age: 44 years (SD 8) • Male subjects: 56%					
Njawaya, 2017 [76]	Setting: University sports medicine clinic in Australia Source of Funding: Commercial	Inclusion criteria: - Pain and impaired function of the Achilles tendon - Proven calcification or spur which was visible on ultrasound Exclusion criteria:	Intervention: Patient-guided radial shock wave therapy at weekly intervals over 3 to 5 weeks Control: Ultrasound-guided shock wave therapy	Length of follow-up: 26-52 weeks Loss to follow-up: 4/31; Reasons for lost to follow-up not	Primary outcomes: - VISA-A score - Pain (VAS) score Secondary outcomes: - Shock Wave Posttreatment Questionnaire	VISA-A score There were no significant differences at 6, 12 and 26 weeks between both treatment groups. VISA-A score was 71.7	None investigated

76 de Vos R-J, et al. Br J Sports Med 2021;0:1–10. doi:10.1136/bjsports-2020-103867

	funding[10]	- Cortisone injection in the area of the Achilles tendon in the previous 3 months - ≤18 years old - Pregnancy - Use of anticoagulant therapy • Type of AT: Insertional AT • Number of participants: 31 (16/15) • Active participants: NR • Mean age: 48 years (SD 13) • Male subjects: 48%	at weekly intervals over 3 to 5 weeks	provided	Analysis consisting of 7 questions asking patients to rate their impression of shock wave	(SD 23.9) at 26 weeks for the intervention group, compared to 69.9 (SD 19.6) for the control group. Adverse effects: Not clearly reported. Less than a fifth of participants reported any pain or side effects of treatment. None of the side effects were serious—they included pain, minor skin damage (rash or bleeding), and tingling. No one required surgery or injectable medications.	

Pearson, 2012 [27]	Setting: Private sports medicine clinic in New Zealand Source of Funding: Commercial funding[11]	Inclusion criteria: - Diagnosis of mid-portion Achilles tendinopathy (activity-related pain of gradual or semiacute onset, postinactivity stiffness, and tenderness, thickening, and nodularity localised to the midtendon) - Duration of symptoms of ≥3 months Exclusion criteria: - Diagnostic uncertainty or concurrent presence of insertional pathology - Anticoagulant therapy - Systemic disease that may contribute to pathology - Being an elite-level sportsperson - Having received any injection therapy for the tendon within the last 3 months. • Type of AT: Midportion AT • Number of participants:	Intervention: A single peritendinous autologous blood injection at baseline in combination with twice daily eccentric-loading exercises for 12 weeks. Control: Twice daily eccentric-loading exercises for 12 weeks.	Length of follow-up: 12 weeks Loss to follow-up: 12/40 tendons; 6 in the intervention group (2 withdrew from the study, 3 did not recover questionnaire, and 1 did not receive treatment) and 6 in the control group (2 withdrew from the study, 3 did not recover questionnaire, and 1 did not receive treatment)	Primary outcome: - VISA-A score Secondary outcomes: - Ratings of perceived discomfort during the injection - Ratings of perceived discomfort over the 48 hours after injection	VISA-A score: There were no significant differences at 6 and 12 weeks between both treatment groups. VISA-A score was 67.1 (SD 21.7) at 12 weeks for the intervention group, compared to 58.9 (SD 20.9) for the control group. Adverse effects: There were no infections and no tendon ruptures.	The degree of neovascularisation did not influence the magnitude of the effect of treatment on the change in VISA-A score.

		24 (11/13) • Active participants: NR • Mean age: 50 years (SD 8) • Male subjects: 38%					
Rompe, 2007 [11]	Setting: Primary care setting in Germany Source of Funding: NR	Inclusion criteria: - Diagnosis of unilateral chronic midportion Achilles tendinopathy for ≥6 months - Failure of nonoperative management - A "wash-out" period of 12 weeks for any nonoperative therapy - Failure of nonoperative treatment (at least one injection of a local anaesthetic/corticosteroid, anti-inflammatory medication, physiotherapy and/or use of orthotics/heel lift) - Age 18-70 years - Ability to complete questionnaires and provide informed consent Exclusion criteria: - Peritendinous	Intervention: Three treatments of radial low-energy shock wave therapy at weekly intervals. It was encouraged to avoid pain-provoking activities. Control group 1: Twice daily eccentric-loading exercises for 12 weeks. It was encouraged to avoid pain-provoking activities. Control group 2: Wait and see treatment. Training modifications, implementation of stretching exercises,	Length of follow-up: 16 weeks Loss to follow-up: 5/75; 1 in the intervention group (unwilling to come), 2 in control group 1 (1 unwilling to come, 1 discontinued intervention), and 2 in control group 2 (1 unwilling to come, 1 discontinued intervention).	Primary outcome: - VISA-A score Secondary outcomes: - General outcome (6-point Likert scale) - Pain assessment (of their main complaint, during the day, and inconvenience) - Maximum anteroposterior diameter of the tendon - Pathologic changes in the tendon - Use of analgesics - All consultations with primary-care physicians, physiotherapists, and other health-	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group and control group 1 (eccentric loading) compared to control group 2 (wait and see policy) at 16 weeks follow-up ($p<0.001$). The VISA-A scores in the intervention group was 70.4 (SD 16.3) at 16 weeks, 75.6 (SD 18.7) in control group 1	None investigated

		injections of a local anaesthetic and/or corticosteroid within the last 4 weeks - Other conditions that could significantly contribute to posterior ankle pain (osteoarthrosis, inflammatory arthritis, radiculopathy, systemic neurologic conditions, etc). - Congenital or acquired deformities of the knee and ankle - Prior surgery to the ankle or the Achilles tendon - Prior Achilles tendon rupture or dislocations or fractures in the area • Type of AT: Midportion AT • Number of participants: 75 (25/25/25) • Active participants: 31% • Mean age: 49 years (SD 11) • Male subjects: 39%	and ergonomic advice were discussed with the patient by an orthopaedic surgeon. It was encouraged to avoid pain-provoking activities.		care providers	(eccentric loading), and 55.0 (SD 12.9) om control group 2 (wait and see policy). Adverse effects: There were no serious complications. In all patients, transient reddening of the skin occurred after low-energy SWT, but no bruising was seen. No device-related complications occurred. Patients reported ache in the calf after eccentric loading, but none had to	

						interrupt the eccentric load training regimen because of this. There were no drug-related complications in group 3. During the study period, no patient sustained a rupture of the Achilles tendon.	
Rompe, 2008 [38]	Setting: Primary care setting in Germany Source of Funding: No funding received	Inclusion criteria: - Age 18-70 years - Ability to complete questionnaires and provide informed consent - Symptoms for ≥6 months - Failure of nonoperative treatment (at least one injection of a local anaesthetic/corticosteroid, anti-inflammatory medication, physiotherapy and/or use of orthotics/heel	Intervention: Three treatments of radial low-energy shock wave therapy at weekly intervals. It was encouraged to await further spontaneous improvement. Control: Twice daily eccentric-loading exercises for 12 weeks.	Length of follow-up: 16 weeks Loss to follow-up: 5/50; 2 in the intervention group (persisting pain) and 3 in the control group (1 refused to attend but still had pain as reported on the	Primary outcome: - VISA-A score Secondary outcomes: - General outcome (6-point Likert scale) - Patients defined success rate - VAS pain during the day - Pain threshold (algometer) - VAS tenderness at 3 kg	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group compared to the control group at 16 weeks follow-up (p=0.005). The VISA-A scores in the intervention	None investigated

		lift) - Clinical diagnosis insertional Achilles tendinopathy Exclusion criteria: - Extensive tendinopathy or paratendinopathy (determined using the Williams arc sign test and the Royal London Hospital test) - Ultrasonographic changes of the midportion of the tendon - Retrocalcaneal bursitis - Haglund deformity with a Fowler-Philip angle of >75°on plain radiographs • Type of AT: Insertional AT • Number of participants: 50 (25/25) • Active participants: 58% • Mean age: 40 years (SD 11) • Male subjects: 40%		telephone, 2 patients refused to attend but they reported by telephone that they were pain-free)	- Use of analgesics - All consultations with primary-care physicians, physiotherapists, and other health-care providers	group was 79.4 (SD 10.4) at 16 weeks, compared to 63.4 (SD 12.0) in the control group. Adverse effects: There were no serious complications. In all patients, transient reddening of the skin occurred after low-energy shock wave treatment, but there was no bruising. No device-related complications occurred. The patients reported aching in the calf after eccentric	

						loading.	
Rompe, 2009 [24]	Setting: Primary care setting in Germany Source of Funding: NR	Inclusion criteria: - Diagnosis of unilateral chronic midportion Achilles tendinopathy for ≥6 months - Failure of nonoperative management - Failure of nonoperative treatment (at least one injection of a local anaesthetic/corticosteroid, anti-inflammatory medication, physiotherapy and/or use of orthotics/heel lift) - Age 18-70 years - Ability to complete questionnaires and provide informed consent Exclusion criteria: - Professional athletes - Peritendinous injections of a local anaesthetic and/or corticosteroid within the last 4 weeks - Other conditions that could significantly	Intervention: Three treatments of radial low-energy shock wave therapy at weekly intervals combined with eccentric-loading exercises twice daily for 12 weeks. It was encouraged to avoid pain-provoking activities. Control: Twice daily eccentric-loading exercises for 12 weeks. It was encouraged to avoid pain-provoking activities.	Length of follow-up: 16 weeks Loss to follow-up: 7/68; 4 in the intervention group (3 unwilling to attend, 1 discontinued intervention) and 3 in the control group (2 unwilling to attend, 1 discontinued intervention)	Primary outcome: - VISA-A score Secondary outcomes: - General outcome (6-point Likert scale) - Pain assessment (of their main complaint, during the day, and inconvenience) - Use of analgesics - All consultations with primary-care physicians, physiotherapists, and other health-care providers	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group compared to the control group at 16 weeks follow-up (p=0.0016). The VISA-A scores in the intervention group was 86.5 (SD 16.0) at 16 weeks, compared to 73.0 (SD 19.0) in the control group. Adverse effects: There were no serious complications. In all patients,	None investigated

		contribute to posterior ankle pain (osteoarthrosis, inflammatory arthritis, radiculopathy, systemic neurologic conditions, etc). - Congenital or acquired deformities of the knee and ankle - Prior surgery to the ankle or the Achilles tendon - Prior Achilles tendon rupture or dislocations or fractures in the area • Type of AT: Midportion AT • Number of participants: 68 (34/34) • Active participants: 31% • Mean age: 50 years (SD 10) • Male subjects: 44%				transient reddening of the skin occurred after low-energy SWT, but no bruising. No device-related complications occurred. Patients reported ache in the calf after eccentric loading, but none had to interrupt the eccentric load training regimen because of this. During the study period, no patient sustained a rupture of the Achilles tendon.	
Roos, 2004 [25]	Setting: NR Source of	Inclusion criteria: - Aged 20–60 years - Patients seeking	Intervention: An anterior night splint worn every	Length of follow-up: 52 weeks	Primary outcome: - Foot and ankle outcome score	Return to sports at pre-injury level:	None investigated

	Funding: Non-commercial funding[12]	medical care within primary care in Helsingborg, Sweden - Insidious onset of Achilles tendinopathy - The activity level prior to the current problems should be at least equivalent to heavy household work, heavy yard work and walking on even ground - At least moderate pain/problems when performing physical activities - Duration of symptoms ≥4 weeks Exclusion criteria: - Insertional Achilles tendinopathy • Type of AT: Midportion AT • Number of participants: 47 (15/13/16) • Active participants: 59% • Mean age: 46 years (SD not provided)	night for 12 weeks in combination with twice daily eccentric-loading exercises for 12 weeks. Control group 1: An anterior night splint worn every night for 12 weeks. Control group 2: Twice daily eccentric-loading exercises for 12 weeks.	Loss to follow-up: 12/47; At 52 weeks 3 in the intervention group (2 did not return questionnaire and 1 had a lumbar hernia), 3 in control group 1 (1 did not return questionnaire, 2 wanted to try other treatment as they were not able to sleep), and 3 in control group 2 (2 did not return questionnaire, 1 could not be reached)	Secondary outcomes: - Return to sports at pre-injury level - Difficulty during sporting activities - Compliance - Side effects	At 12 weeks, 3/8 patients in the intervention group returned to the same activity level, 1/10 in control group 1, and 5/8 in control group 2. No statistical tests were performed. Adverse effects: 33% of patients reported muscle soreness after eccentric exercises; 4 patients had pressure-related problems from the night splint; 2 patients had sleep problems from the night splint.	

		• Male subjects: 48%					
Silbernagel, 2001 [32]	Setting: NR Source of Funding: NR	Inclusion criteria: - Age of ≥18 years - Chronic pain from the Achilles tendon (proximal achillodynia) - Duration of pain ≥3 months Exclusion criteria: - Surgery of the involved foot - History of rheumatoid arthritis, diabetes, or any other illness that was thought to interfere with the study - Participating in any other treatment program for the Achilles tendon disorder • Type of AT: Midportion AT • Number of participants: 49 (27/22) • Active participants: 100% • Mean age: 44 years (SD 12)	Intervention: Gradually progressive calf muscle exercise program combined with stretching exercises 1-3 times per day for 12 weeks. Control: Isotonic calf muscle exercise training program combined with stretching exercises 3 times per day for 12 weeks.	Length of follow-up: 52 weeks Loss to follow-up: 9/49; 3 in the intervention group (stopped at their own request within two weeks of the start of the study) and 6 in the control group (2 decided to have surgery after 6 weeks, 1 patient underwent surgery for bursitis, 1 was not able to attend the evaluation and 2 withdrew without specifying the	Primary and secondary outcomes were not specified: - Return to physical activity - Questionnaire (13 questions, separately analysed) - Success of the treatment - Level of recovery - Ankle dorsiflexion - Ankle plantarflexion - Pain during rest (VAS) - Pain during palpation (VAS) - Jumping test - Toe raise test	Return to physical activity: There was no significant difference in the percentage of patients that returned to the same activity level as before their problems. In the intervention group 11/20 patients returned to the same activity level, compared to 6/17 in the control group (p-value not presented). Adverse effects: Not reported	None investigated

		• Male subjects: 78%		reason)			
Silbernagel, 2007 [16]	Setting: Physical therapy clinic in Göteborg, Sweden with the performance of a home-bases exercise program Source of Funding: Non-commercial funding[13]	Inclusion criteria: - Aged 20-60 years - Achilles tendinopathy with a duration of pain for ≥2 months Exclusion criteria: - Injury to the foot, knee, hip, or back - A history of rheumatoid arthritis or any other illness or injury thought to interfere with the participation in the study - Insertional tendinopathy • Type of AT: Midportion AT • Number of participants: 42 (21/21) • Active participants: NR • Mean age: 46 years (SD 8) • Male subjects: 53%	Intervention: Continued Achilles tendon-loading activity for the first 6 weeks of rehabilitation using a pain monitoring scale (VAS max. 5/10). Both groups performed a progressive Achilles tendon-loading strengthening program once daily for 12 weeks to 6 months. Control: Achilles tendon-loading activity for the first 6 weeks of rehabilitation was discouraged. Both groups performed a progressive Achilles tendon-loading strengthening program once daily	Length of follow-up: 52 weeks Loss to follow-up: 4/42; 2 participants in the intervention group (1 not able to attend any of the evaluations and 1 had pain in the ankle and knee that hindered participation) and 2 participants in the control group (1 because of self-reported noncompliance and one because of illness that did not allow him to start the treatment)	Primary outcome: - VISA-A score Secondary outcomes: - Pain level (VAS) during tendon-loading activity (hopping, countermovement jump, a drop CMJ) - Strength tests (concentric toe raise and an eccentric-concentric toe raise) - Endurance test (standing toe raise test with 10% of the body weight added with a weight belt - Tendon injury on ultrasound	VISA-A score: There were no significant differences at 6, 12, 26, and 52 weeks between both treatment groups. VISA-A score was 85 (SD 12.7) at 52 weeks for the intervention group, compared to 91 (SD 8.2) for the control group. Adverse effects: Not reported	Baseline VISA-A score did influence the magnitude of the effect of treatment on the change in VISA-A score. Duration of symptoms did not influence the magnitude of the effect of treatment on the change in VISA-A score.

			for 12 weeks to 6 months.				
Stevens, 2014 [29]	Setting: Eight clinical sites (2 district hospitals and 6 general practitioner practices) in the United Kingdom Source of Funding: NR	Inclusion criteria: - Aged ≥18 years - Symptoms lasting ≥3 months - Midportion Achilles tenderness (2-7 cm proximal to insertion) on palpation during or after activity Exclusion criteria: - Tendon insertion pain - Fracture of the affected lower limb ≤12 months - Presence of bursitis, rheumatoid arthritis, diabetes, or other systemic disorders - Previous surgical intervention (≤12 months) or steroid injection (in the last month) near the Achilles tendon - Previous experience with eccentric-loading exercises - Sudden onset of symptoms suggesting	Intervention: Twice daily eccentric-loading exercises for 12 weeks with a number of repetitions per day that was tolerable (up to 180). It was encouraged to avoid pain-provoking activities. Control: Twice daily eccentric-loading exercises for 12 weeks with a fixed number of repetitions per day (180). It was encouraged to avoid pain-provoking activities.	Length of follow-up: 6 weeks Loss to follow-up: 6/28; 2 in the intervention group and 4 in the control group. Reasons for lost to follow-up not provided.	Primary outcome: - VISA-A score Secondary outcomes: - Patient satisfaction - VAS pain (not further defined)	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group compared to the control group at 3 weeks follow-up (p=0.004). The VISA-A score in the intervention group was 56.2 (SD 19.7) at 3 weeks, compared to 41.0 (SD 13.0) in the control group. Baseline VISA-A scores were 47.1 (SD 15.6) for the intervention group, and 49.6	None investigated

		partial rupture - Any congenital deformity affecting the lower limb • Type of AT: Midportion AT • Number of participants: 28 (13/15) • Active participants: 46% • Mean age: 49 years (SD 11) • Male subjects: 39%				(SD 10.2) for the control group (indicating worsening of symptoms in the control group).There was no significant difference at 6 weeks between both treatment groups. VISA-A score was 62.5 (SD 12.8) at 6 weeks for the intervention group, compared to 58.7 (SD 13.0) for the control group. Patient satisfaction: There was no significant difference at 6	

						weeks between both treatment groups. Patient satisfaction was excellent/good 69% in the intervention group, and 47% in the control group. Adverse effects: Not reported	
Tumilty, 2012 [77]	Setting: Primary care clinic (not specifically stated where this clinic is located) Source of Funding: Non-commercial funding[14]	Inclusion criteria: - Aged 18-65 - A diagnosis of midportion Achilles tendinopathy - No treatment within the last 3 months Exclusion criteria: - Contraindications to low level laser therapy - Comorbid musculoskeletal or serious conditions that may have confounded treatment - Nonsteroidal anti-	Intervention: Laser therapy (100 mW/cm^2 infrared probe) 3 times per week for 4 weeks. Laser therapy was combined with twice daily eccentric-loading exercises for 12 weeks. Control: Placebo laser therapy 3 times per week for 4 weeks. Placebo laser	Length of follow-up: 52 weeks Loss to follow-up: 7/40; 3 in the intervention group and 4 in the control group. In 3 participants the reason for withdrawal were not ascertained, 2 shift work, 1	Primary outcome: - VISA-A score Secondary outcomes: - Average pain (VAS) of 3 scores (pain now, best pain in the last 24 hours, and worst pain in the last 24 hours) - Compliance to the exercises	VISA-A score: Improvement in VISA-A score was significantly greater in the control group compared to the intervention group at 4 weeks follow-up (p=0.016). The VISA-A score in the control group was 82.8 (SD 8.3) at 4 weeks,	None investigated

		inflammatory drug use - Steroid injections or surgery for the condition - Insertional tendinopathy or bursitis - Neurologic signs - Adverse neural tension affecting the sciatic or sural nerve • Type of AT: Midportion AT • Number of participants: 40 (20/20) • Active participants: NR • Mean age: 46 years (SD 8) • Male subjects: 45%	therapy was combined with twice daily eccentric-loading exercises for 12 weeks.	had travel constraints, and 1 could not be contacted (not mentioned to which group they belonged).		compared to 71.9 (SD 13.5) in the intervention group. There were no significant differences at 12 or 52 weeks between both treatment groups. VISA-A score was 83.0 (SD 14.5) at 52 weeks for the intervention group, compared to 90.9 (SD 10.1) for the control group. Adverse effects: No reports of any adverse reactions from either the low-level laser therapy or the	

						exercise program	
Tumilty, 2016 [78]	Setting: University Physical Therapy Clinic in New Zealand Source of Funding: Non-commercial funding[15]	Inclusion criteria: - Aged 18-65 - A diagnosis of midportion Achilles tendinopathy - Symptoms for ≥3 months - No treatment within the last 3 months - VISA-A score <80 Exclusion criteria: - Contraindications to low level laser therapy - Comorbid musculoskeletal or serious conditions that may have confounded treatment - Nonsteroidal anti-inflammatory drug use - Steroid injections or surgery for the condition - Insertional tendinopathy or bursitis - Neurologic signs - Adverse neural tension	Intervention group 1: Laser therapy (150 J for each part of the tendon) 2 times per week for 4 weeks. Laser therapy was combined with twice daily eccentric-loading exercises for 12 weeks. Intervention group 2: Laser therapy (150 J for each part of the tendon) 2 times per week for 4 weeks. Laser therapy was combined with twice weekly eccentric-loading exercises for 12 weeks. Control group 1: Placebo laser	Length of follow-up: 12 weeks Loss to follow-up: 16/80; 4 in intervention group 1(1 did not start, 3 had no time), 4 in intervention group 2(2 had an unrelated injury, 2 had muscle soreness), 7 in control group 1 (1 did not start, 3 had no time, and 2 had muscle soreness), and 1 in control group 2 (1 unrelated injury).	Primary outcome: - VISA-A score Secondary outcomes: - Numeric Pain Rating Scale (NPRS) - Ultrasonographic tendon thickness	VISA-A score: Improvement in VISA-A score was significantly greater in intervention group 2 compared to the other 3 groups at 12 weeks follow-up ($p<0.01$). There were no significant differences between the other 3 groups. The VISA-A score in intervention group 2 was 99.0 (95% CI 94.4-103.5) at 12 weeks, compared to 88.6 (95% CI 83.9-93.3) in	None investigated

		affecting the sciatic or sural nerve • Type of AT: Midportion AT • Number of participants: 80 (20/20/20/20) • Active participants: NR • Mean age: 47 years (SD 10) • Male subjects: 41%	therapy 2 times per week for 4 weeks. Placebo laser therapy was combined with twice daily eccentric-loading exercises for 12 weeks. Control group 2: Placebo laser therapy 2 times per week for 4 weeks. Placebo laser therapy was combined with twice weekly eccentric-loading exercises for 12 weeks.			intervention group 1, 80.4 (95% CI 75.2-85.7) in control group 1, and 87.6 (95% CI 83.5-91.7) in control group 2. Adverse effects: 6 participants complained of delayed onset muscle soreness (DOMS) within the first week of starting treatment, three of these withdrew from the study; otherwise, no other adverse reactions were reported.	
Usuelli, 2017 [79]	Setting: Foot and Ankle Unit of an orthopaedic	Inclusion criteria: - Unilateral or bilateral chronic Achilles tendinopathy	Intervention: Ultrasound-guided stromal vascular fraction (SVF,	Length of follow-up: 26 weeks	Primary and secondary outcomes were not specified: - VISA-A score	VISA-A score: Improvement in VISA-A score was significantly	None investigated

	department in Italy Source of Funding: NR	- Tendinopathy recalcitrant to non-surgical treatments, including non-steroidal anti-inflammatory drugs, eccentric loading exercises, stretching and biophysical therapy - Symptoms for ≥3 months - Aged 18- 55 - Pain (VAS) at the first visit >5 Exclusion criteria: - Clinical suspicion of other musculoskeletal lesions of the Achilles tendon (insertional disorders, tendon rupture or tears) - Platelet count in whole blood <150×103/µl - Inflammatory disease or other conditions that affected the joints - Immuno-mediated pathology - Any conditions that could increase the interventional risk - Use of tendon-	derived from abdominal subcutaneous tissue) intratendinous injections once at baseline. If pain persisted, the injection procedure was repeated after 2 months. No specific physical therapy was prescribed after the treatment. Control: Ultrasound-guided intratendinous platelet-rich plasma (PRP)-injection once at baseline. If pain persisted, the injection procedure was repeated after 2 months. No specific physical therapy was prescribed after the treatment.	Loss to follow-up: 0/44	- Level of pain using the 0–10 Visual Analog Scale (VAS) - American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score - Short Form Health Survey (SF-36) - Maximum Achilles tendon diameter on MRI as parameter for the lesion size	greater in the intervention group compared to the control group at 15 and 30 days follow-up (p<0.05). At 30 days, the VISA-A score was 59.1 (SD 19.8) in the intervention group, compared to 47.5 (SD 15.9) in the control group. At all other time points (30, 60, 120, and 120 days), there were no significant differences between the 2 groups. The VISA-A score at the final end	

		detrimental drugs (i.e. fluoroquinolones) - Patients who received any previous injective treatment of the target Achilles tendon - Pregnancy or breast-feeding • Type of AT: Midportion AT • Number of participants: 44 (21/23) • Active participants: NR • Mean age: 47 years (SD 5) • Male subjects: 50%				point was 71.1 (SD 19.8) in the intervention group, compared to 70.9 (SD 20.7) in the control group. Adverse effects: Neither serious side effects nor adverse events were observed during the follow-up period. Five patients (25%) of the SVF groups complained for hematoma and cutaneous discomfort at the adipose tissue harvest site for about a week after the procedure.	

Yelland, 2011 [26]	Setting: Five primary care centers in Australia Source of Funding: Non-commercial funding[16]	Inclusion criteria: - Unilateral or bilateral mid-portion Achilles tendinosis (pain 2-7 cm proximal to the calcaneal attachment - Aged >18 years - Activity-related pain for at least 6 weeks - VISA-A score <80 for participants involved in sport and <70 for those not involved in sport Exclusion criteria: - Previous steroid or prolotherapy injections - Surgery to the affected tendon - Previous completion of >50% of the Achilles eccentric loading protocol - Allergies or medical conditions that might limit completion of trial treatments • Type of AT: Midportion AT	Intervention group 1: Intratendinous prolotherapy injection (maximum of 20% glucose/0.1% lignocaine/0.1% ropivacaine solution) weekly for 4-12 treatment sessions. Patients were encouraged to gradually increase their activity levels. Intervention group 2: Intratendinous prolotherapy injection (maximum of 20% glucose/0.1% lignocaine/0.1% ropivacaine solution) weekly for 4-12 treatment sessions. Twice daily eccentric-loading	Length of follow-up: 52 weeks Loss to follow-up: 3/43; 1 in intervention group 1 and 2 in the control group. 1 participant had a heart attack, 1 discontinued because of time restraints and 1 sustained an unrelated injury during the study (not reported which group they belonged to).	Primary outcome: - VISA-A score Secondary outcomes: - Pain (VAS) - Morning stiffness - Limitation of usual activities - Patient global impression of change scale - Achievement of two treatment goals - Direct treatment costs from the preceding 3 months (including GP visits, specialist visits, outpatient visits with allied health professional)	VISA-A score: Improvement in VISA-A score was significantly greater in intervention group 2 compared to the control group at 6 and 52 weeks follow-up (p=0.005/0.007). At 52 weeks, the VISA-A score was 91.4 (SD 9.9) in intervention group 2, compared to 84.9 (SD 18.2) in the control group. Intervention group 1 did not differ between the other 2 groups (VISA-A score at 52	None investigated

		• Number of participants: 43 (14/14/15) • Active participants: 93% • Mean age: 47 years (SD not provided) • Male subjects: NR	exercises were performed for 12 weeks. Patients were encouraged to gradually increase their activity levels. Control: Twice daily eccentric-loading exercises for 12 weeks.			weeks 89.6 (SD 20.1). Adverse effects: None in both intervention groups, 1/15 (6.7%) in the control group; A participant in the control group had a partial calf tear while playing tennis. An independent sports physician did not attribute this to the ELE program.	
Zhang, 2013 [36]	Setting: Two hospitals in a metropolitan city in China Source of Funding: NR	Inclusion criteria: - Chronic Achilles tendinopathy - Aged 18-70 years - Tendon pain located approximately 2-7 cm proximal to the insertion on the calcaneus	Intervention: Acupuncture intratendinous for 30 minutes per session. Sessions were performed 3 times per week for 8 weeks.	Length of follow-up: 24 weeks Loss to follow-up: 4/64; 1 in the intervention group and 3 in	Primary outcomes: - VISA-A score - Pain (VAS) at rest and after activity Secondary outcomes: - Use of painkillers - Working status	VISA-A score: Improvement in VISA-A score was significantly greater in the intervention group compared to the control	None investigated

		- Symptoms present for ≥2 months Exclusion criteria: - Clinical suspicion of other musculoskeletal (insertional disorders and tendon rupture) injuries - Inflammatory internal disorders - Rheumatoid arthritis - Acute condition - Bursitis - Previous surgery - Previous acupuncture treatment - Any other illness or injury thought to interfere with participation in the study • Type of AT: Midportion AT • Number of participants: 64 (32/32) • Active participants: NR • Mean age: 51 years (SD 6) • Male subjects: 38%	Control: Eccentric-loading exercises 2-3 sessions of 15 repetitions. Not reported how many days per week and for how many weeks exercises were performed.	the control group. Reasons for lost to follow-up not provided.		group at 8, 16, and 24 weeks follow-up ($p<0.0001$). At 24 weeks, the VISA-A score was 73.3 (SD 3.6) in the intervention group, compared to 62.4 (SD 4.2) in the control group. Adverse effects: Not reported	

Table 4.8 – Evidence table of the included randomised trials investigating non-surgical treatment options for Achilles tendinopathy.
Abbreviations: AT, Achilles tendinopathy; FHL, flexor hallucis longus; NR, not reported; SD, standard deviation; VAS, visual analogue scale

[1] Bioiberica, SA, Palafolls, Spain (commercial)

[2] Arthrex Denmark A/S

[3] Direct financial support and donation of the platelet-separation kits used in the study were provided by Biomet Biologics LLC, Warsaw, Indiana. Biomet had no role in the design and conduct of the study or the interpretation of the data.

[4] The study was supported by grants from Hans og Nora Buchards Fond, Speciallæge Heinrich Kopps Legat and Region of Northern Denmark.

[5] The Danish Medical Research Council, Lundbeck Foundation, and Novo Nordisk Foundation provided financial support.

[6] This study was sponsored by Cyden Ltd and the Intense Pulsed Light system was provided by Cyden Ltd.

[7] Biomet Biologics provided a Platelet Concentrate Separation Kit and donated an unrestricted grant to the Regional Hospital Silkeborg. The Danish Rheumatism Association supported one of the authors with a 6 month grant. The Health Research Fund of Central Denmark Region supported one of the authors with a 3-month grant.

[8] Ostenil was supplied by TRB Chemedica AG and the ESWT device by PiezoSon 100 plus, Richard Wolf GmbH.

[9] The study was funded by the Prescription Foot Orthotic Laboratory Association (PFOLA). Footwork Podiatric Laboratory Pty Ltd (Melbourne, Australia) donated the customised foot orthoses for this study.

[10] Manufacturers (Sonosite and DJO) provided free use of equipment for the duration of the study.

[11] Pacific Radiology (Wellington, New Zealand) performed the ultrasounds free of charge to the patients.

[12] Study supported by grants from the Swedish National Center for Research in Sports, Zoega Foundation for Medical Research, The Swedish Research Council and Lund University Hospital and Medical Faculty.

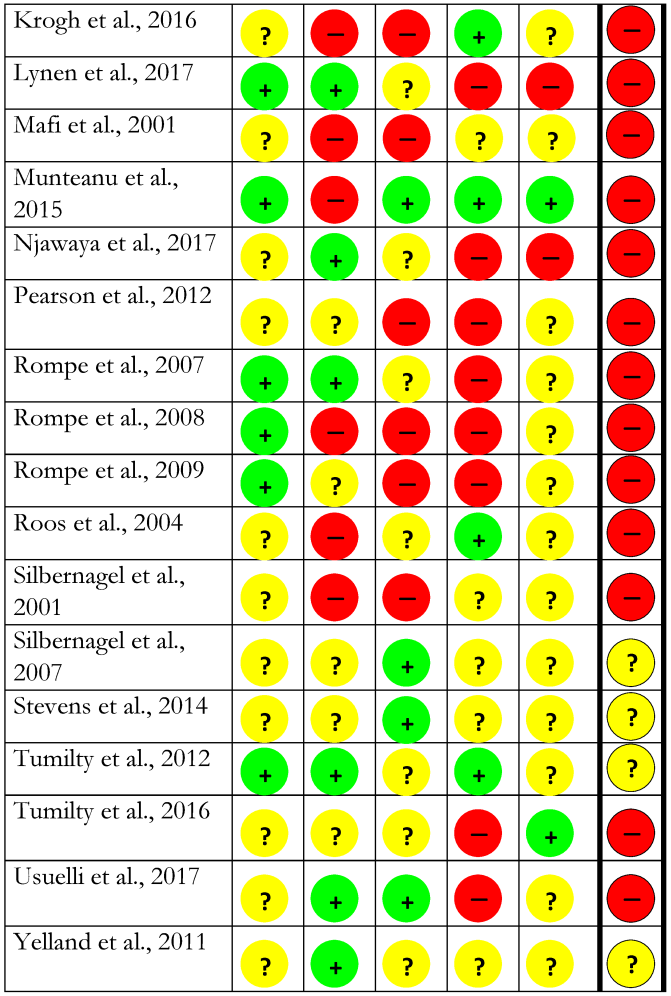
[13] This study was supported by grants from the Swedish National Centre for Research in Sports and the local Research and Development Council of Gothenburg and Southern Bohuslän.

[14] Supported by the University of Otago Dean's Establishment Grant.

[15] This study was funded by the University of Otago Research Grant.

[16] Musculoskeletal Research Foundation of Australia; Australian Podiatry Education and Research Foundation; Griffith University Office of Research.

Trial	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Non-surgical treatments						
Auclair et al., 1989	−	−	−	−	−	−
Balius et al., 2016	−	?	+	−	−	−
Bell et al., 2013	+	+	+	+	?	?
Beyer et al., 2015	?	?	−	−	−	−
Boesen et al., 2017	−	?	+	+	?	−
de Jonge et al., 2010	?	?	+	−	?	−
de Jonge et al., 2011	?	+	+	+	?	?
Ebbesen et al., 2018	−	−	?	+	−	−
Heinemeier et al., 2017	?	+	+	+	?	?
Herrington et al., 2007	?	+	+	−	?	−
Hutchison et al., 2013	−	−	−	+	−	−


Krogh et al., 2016
Lynen et al., 2017
Mafi et al., 2001
Munteanu et al., 2015
Njawaya et al., 2017
Pearson et al., 2012
Rompe et al., 2007
Rompe et al., 2008
Rompe et al., 2009
Roos et al., 2004
Silbernagel et al., 2001
Silbernagel et al., 2007
Stevens et al., 2014
Tumilty et al., 2012
Tumilty et al., 2016
Usuelli et al., 2017
Yelland et al., 2011

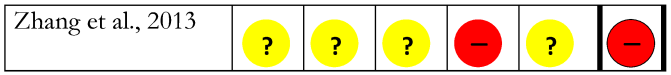


Table 4.9 – Risk of bias assessment of the included randomised studies assessing the effectiveness of non-surgical treatment options. + low ROB, ? unclear ROB, - high ROB.

Treatments	Studies	Classes
Placebo-injection + eccentric exercises (high-dose)	Bell 2013, Boesen 2017, De Jonge 2011	Exercise therapy + placebo injection
Autologous blood injection + eccentric exercises (high-dose)	Bell 2013, Pearson 2012	Exercise + injection therapy
High-volume injection + eccentric exercises (high-dose)	Boesen 2017	Exercise + injection therapy
Platelet-rich plasma (PRP) -injection + eccentric exercises (high-dose)	Boesen 2017, De Jonge 2011	Exercise + injection therapy
Eccentric exercises (high-dose)	Pearson 2012, Beyer 2015, De Jonge 2010, Silbernagel 2007, Yelland 2011, Rompe 2007, Rompe 2009, Zhang 2013, Balius 2016, Stevens 2014, , Roos 2004, Mafi 2001	Exercise therapy
Heavy slow resistance exercises	Beyer 2015	Exercise therapy
Night splint + eccentric exercises (high-dose)	De Jonge 2010, Roos 2004	Exercise + night splint therapy
Continued sports activity + eccentric exercises (high-dose)	Silbernagel 2007	Exercise therapy
Prolotherapy injections	Yelland 2011	Injection therapy
Prolotherapy injections + Eccentric exercises (high-dose)	Yelland 2011	Exercise + injection therapy
Shockwave therapy	Rompe 2007	Shockwave therapy
Wait-and-see	Rompe 2007	Wait-and-see
Shockwave therapy + eccentric exercises (high-dose)	Rompe 2009	Exercise + shockwave therapy

Acupuncture treatment	Zhang 2013	Acupuncture therapy
Mucopolysaccharides supplement + eccentric exercises (high-dose)	Balius 2016	Exercise + mucopolysaccharides supplement therapy
Mucopolysaccharides supplement + passive stretching	Balius 2016	Exercise + mucopolysaccharides supplement therapy
Eccentric exercises as tolerated	Stevens 2014	Exercise therapy

Table 4.10 – Subdivision of treatment options into treatment categories ("classes") of included studies in the network meta-analysis (NMA).

Comparison	Study (first author)
Injection-based multimodal treatment	
Autologous blood injection+eccentric exercises (high-dose) versus. Dry-needling (placebo-injection)+eccentric exercises (high-dose)	Bell =
High-volume injection+eccentric exercises (high-dose) versus. Placebo injection + Eccentric training (high-dose)	Boesen ↑
PRP-injection+eccentric exercises (high-dose) versus. Placebo injection + Eccentric training (high-dose)	Boesen ↑, de Jonge =
PRP-injection+eccentric training (low-dose) versus. placebo injection+eccentric exercises (low-dose)	Krogh =
Medication-based multimodal treatment	
MCVC tablet+eccentric exercises (high-dose) versus. MCVC tablets+passive stretching	Balius =
Orthoses-based multimodal treatment	
Customised foot orthoses+eccentric exercises (high-dose) versus. Sham foot orthoses+eccentric exercises (high-dose)	Munteanu =
Passive modalities-based multimodal treatment	
Continued sports activity+progressive Achilles tendon-loading strengthening program (high-dose) versus. Active rest group+progressive Achilles tendon-loading strengthening program (high-dose)	Silbernagel 2007 =
Low-level laser therapy + eccentric exercise therapy (high-dose) versus. Placebo laser therapy + eccentric exercise therapy (high-dose)	Tumilty 2012 =, Tumilty 2016 =
Low-level laser therapy + eccentric exercise therapy (low-dose) versus. Placebo laser therapy + eccentric exercise therapy (low-dose)	Tumilty 2016 ↑
Low-level laser therapy + eccentric exercise therapy (high-dose) versus. Placebo laser therapy + eccentric exercise therapy (low-dose)	Tumilty 2016 =
Low-level laser therapy + eccentric exercise therapy (low-dose) versus. Placebo laser therapy + eccentric exercise therapy (high-dose)	Tumilty 2016 ↑

Abbreviations: PRP, Platelet-rich plasma; MCVC, mucopolysaccharides, collagen type I, and vitamin C.

Table 4.11 – Overview of randomised trials comparing multimodal treatment options for midportion Achilles tendinopathy. The presence of effective multimodal treatment options is highlighted with a gray bar. For the level of evidence we refer to table 4.15.

A)

Wait-and-see									
19 (-3 to 34)	**Exercise therapy + placebo injection**								
23 (8 to 38)	4 (-11 to 19)	**Injection therapy**							
20 (11 to 30)	1 (-10 to 15)	-2 (-14 to 9)	**Exercise therapy**						
15 (6 to 24)	-4 (-19 to 13)	-8 (-23 to 8)	-5 (-15 to 5)	**Shockwave therapy**					
22 (7 to 36)	4 (-2 to 8)	0 (-13 to 14)	2 (-10 to 13)	7 (-8 to 22)	**Exercise + injection therapy**				
34 (21 to 47)	**15 (1 to 31)**	11 (-4 to 26)	**14 (5 to 23)**	**19 (5 to 32)**	12 (-2 to 27)	**Exercise + shockwave therapy**			
21 (4 to 39)	2 (-18 to 21)	-2 (-21 to 17)	1 (-14 to 15)	6 (-12 to 23)	-1 (-20 to 17)	-13 (-30 to 4)	**Exercise + night splint therapy**		
35 (25 to 45)	**16 (4 to 30)**	13 (0 to 25)	**15 (11 to 19)**	**20 (9 to 31)**	**13 (2 to 25)**	1 (-9 to 11)	14 (-1 to 30)	**Acupuncture therapy**	
28 (14 to 41)	9 (-7 to 25)	5 (-11 to 20)	7 (-3 to 17)	13 (-2 to 26)	6 (-10 to 20)	-6 (-20 to 7)	7 (-11 to 24)	-7 (-19 to 3)	**Exercise + mucopolysaccharides supplement therapy**

B)

Injection therapy			
-5 (-19 to 9)	**Exercise therapy**		
2 (-10 to 13)	7 (-4 to 17)	**Exercise + injection therapy**	
3 (-16 to 22)	8 (-6 to 21)	1 (-16 to 18)	**Exercise + night splint therapy**

Table 4.12 – Comparisons in VISA-A scores between different treatment categories for midportion Achilles tendinopathy at 3 months (A) and 12 months (B) follow-up. Mean differences on the VISA-A score with their 95% credible intervals from the network meta-analysis. For any cell, a negative mean difference favours the upper- left treatment, and a positive mean difference favours the lower-right treatment. Significant comparative treatment class effect differences are shown in bold and are marked grey. VISA-A = Victorian Institute of Sport Assessment-Achilles.

Wait-
and-

see											
26 (-7 to 45)	**Placebo injection + eccentric exercises ***										
28 (-9 to 46)	1 (-8 to 11)	**Autologous blood Injection + eccentric exercises***									
37 (16 to 57)	**11 (4 to 17)**	9 (-2 to 21)	**High volume injection + eccentric exercises**								
27 (6 to 47)	1 (-5 to 7)	-1 (-12 to 10)	**-10 (-17 to -2)**	**PRP injection + eccentric exercises***							
21 (7 to 36)	-5 (-25 to 16)	-6 (-26 to 14)	-16 (-37 to 7)	-6 (-27 to 16)	**Prolo-therapy injection**						
17 (0 to 35)	-9 (-31 to 14)	-10 (-31 to 11)	-19 (-43 to 5)	-10 (-33 to 14)	-4 (-19 to 11)	**Prolo-therapy injection + eccentric exercises***					
20 (11 to 29)	-6 (-23 to 11)	-7 (-23 to 8)	-17 (-35 to 2)	-7 (-24 to 12)	-1 (-13 to 11)	3 (-12 to 18)	**Eccentric exercises***				
24 (15 to 34)	-2 (-19 to 16)	-3 (-19 to 13)	-13 (-31 to 6)	-3 (-20 to 16)	3 (-9 to 15)	7 (-8 to 22)	**4 (2 to 6)**	**Heavy slow resistance exercises***			
20 (5 to 33)	-7 (-27 to 15)	-8 (-27 to 12)	-17 (-39 to 5)	-7 (-28 to 14)	-2 (-18 to 15)	2 (-16 to 21)	-1 (-12 to 11)	-5 (-16 to 7)	**Continued sports activity + eccentric exercises***		
15 (7 to 24)	-11 (-30 to 9)	-12 (-31 to 6)	-22 (-42 to 0)	-12 (-32 to 9)	-6 (-21 to 9)	-2 (-20 to 16)	-5 (-15 to 5)	-9 (-19 to 1**)**	-5 (-20 to 11)	**Shock-wave therapy**	
34 (22 to	8 (-11 to	6 (-11 to 24)	-3 (-23 to	7 (-13 to 27)	13 (-6 to 31)	17 (0 to 33)	**14 (5 to 22)**	**10 (1 to 18)**	14 (0 to 28)	**19 (6 to 31)**	**Eccentric exercises* +**

46)	27)		18)								**shockwave therapy**					
21 (4 to 38)	-6 (-27 to 17)	-7 (-28 to 15)	-16 (-39 to 8)	-6 (-29 to 17)	-1 (-19 to 18)	3 (-17 to 24)	0 (-14 to 15)	-4 (-18 to 11)	1 (-17 to 20)	5 (-12 to 23)	-13 (-30 to 4)	**Eccentric exercises *+ night splint**				
35 (26 to 45)	9 (-8 to 27)	8 (-8 to 24)	-2 (-20 to 17)	8 (-10 to 27)	**14 (2 to 26)**	**18 (3 to 33)**	**15 (12 to 17)**	**11 (8 to 14)**	**15 (4 to 27)**	**20 (10 to 30)**	1 (-7 to 10)	15 (0 to 29)	**Acupuncture**			
24 (11 to 38)	-2 (-21 to 18)	-3 (-22 to 15)	-13 (-33 to 9)	-3 (-23 to 18)	3 (-12 to 18)	7 (-11 to 24)	5 (-6 to 14)	0 (-10 to 10)	4 (-10 to 20)	9 (-5 to 23)	-10 (-22 to 3)	3 (-14 to 21)	**-11 (-21 to -1)**	**Eccentric exercises as tolerated**		
29 (15 to 43)	2 (-17 to 23)	1 (-17 to 20)	-8 (-29 to 14)	2 (-19 to 23)	7 (-8 to 23)	11 (-7 to 30)	8 (-2 to 19)	4 (-6 to 15)	9 (-7 to 25)	13 (-1 to 28)	-5 (-19 to 8)	8 (-10 to 26)	-6 (-17 to 5)	5 (-10 to 19)	**Mucopolysaccharides supplement + eccentric exercises***	
26 (10 to 41)	-1 (-22 to 21)	-2 (-22 to 18)	-11 (-34 to 11)	-1 (-23 to 21)	4 (-13 to 22)	8 (-11 to 28)	5 (-8 to 18)	1 (-12 to 14)	6 (-12 to 23)	10 (-6 to 26)	-8 (-24 to 7)	5 (-15 to 24)	-10 (-23 to 3)	1 (-15 to 17)	-3 (-16 to 10)	**Mucopolysaccharides supplement + passive stretching**

Table 4.13a – Comparative treatment effects expressed with a mean difference for the VISA-A score at 3 months (model 1)
Mean differences on the VISA-A score with their 95% credible intervals from the network meta-analysis in patients with midportion Achilles tendinopathy. For any cell, a negative mean difference favours the upper-left treatment, and a positive mean difference favours the lower-right treatment. Comparative treatment effect differences are shown in bold. * Note that all eccentric exercise regimens were labelled as 'high-dose'. VISA-A = Victorian Institute of Sport Assessment-Achilles; PRP = platelet-rich plasma.

Placebo laser + eccentric exercises (low-dose)	
-4	**Placebo laser + eccentric**

(-12 to 6)	**exercises (high-dose)**		
11 (2 to 21)	**15 (6 to 24)**	**Laser therapy + eccentric exercises (low-dose)**	
-3 (-11 to 6)	**1 (-6 to 8)**	**-14 (-23 to -5)**	**Laser therapy + eccentric exercises (high-dose)**

Table 4.13b – Comparative treatment effects expressed with a mean difference for the VISA-A score at 3 months, model 2
Mean differences on the VISA-A score with their 95% credible intervals from the network meta-analysis in patients with midportion Achilles tendinopathy. For any cell, a negative mean difference favours the upper-left treatment, and a positive mean difference favours the lower-right treatment. Comparative treatment effect differences are shown in bold. VISA-A = Victorian Institute of Sport Assessment.

Prolotherapy Injection				
-10 (-22 to 3)	**Eccentric exercises (high-dose)**			
-12 (-29 to 4)	-2 (-13 to 9)	**Continued sports activity + eccentric exercises (high dose)**		
-5 (-21 to 10)	4 (-11 to 20)	7 (-12 to 26)	**Eccentric exercises (high dose) + prolotherapy injection**	
1 (-12 to 14)	**11 (9 to 13)**	**13 (2 to 25)**	7 (-9 to 22)	**Acupuncture**

Table 4.13c – Comparative treatment effects expressed with a mean difference for the VISA-A score at 6 months, model 1.
Mean differences on the VISA-A score with their 95% credible intervals from the network meta-analysis in patients with midportion Achilles tendinopathy. For any cell, a negative mean difference favours the upper-left treatment, and a positive mean difference favours the lower-right treatment. Comparative treatment effect differences are shown in bold. VISA-A = Victorian Institute of Sport Assessment-Achilles.

Placebo injection + eccentric exercises (high dose)			
0 (-11 to 11)	**Autologous blood injection + eccentric exercises (high dose)**		
5 (-3 to 12)	5 (-8 to 19)	**High volume injection + eccentric exercises (high dose)**	
6 (0 to 13)	6 (-6 to 19)	1 (-6 to 9)	**PRP injection + eccentric exercises (high dose)**

Table 4.13d – Comparative treatment effects expressed with a mean difference for the VISA-A score at 6 months, model 2.
Mean differences on the VISA-A score with their 95% credible intervals from the network meta-analysis in patients with midportion Achilles tendinopathy. For any cell, a negative mean difference favours the upper-left treatment, and a positive mean difference favours the lower-right treatment. Comparative treatment effect differences are shown in bold. VISA-A = Victorian Institute of Sport Assessment-Achilles; PRP = platelet-rich plasma.

Prolotherapy Injection					
-5 (-18 to 9)	**Eccentric exercises (high-dose)**				
-11 (-27 to 4)	-6 (-13 to 1)	**Continued sports activity + eccentric exercises (high dose)**			
0 (-16 to 16)	5 (-4 to 14)	11 (0 to 23)	**Heavy slow resistance exercises**		
2 (-10 to 13)	7 (-4 to 17)	**13 (0 to 26)**	2 (-12 to 15)	**Eccentric exercises (high dose) + prolotherapy injection**	
3 (-17 to 22)	7 (-6 to 20)	14 (-1 to 29)	2 (-14 to 18)	1 (-16 to 17)	**Eccentric exercises (high-dose) + night splint**

Table 4.13e – Comparative treatment effects expressed with a mean difference for VISA-A at 12 months.
Mean differences on the VISA-A score with their 95% credible intervals from the network meta-analysis in patients with midportion Achilles tendinopathy. For any cell, a negative mean difference favours the upper-left treatment, and a positive mean difference favours the lower-right treatment. Comparative treatment effect differences are shown in bold. VISA-A = Victorian Institute of Sport Assessment-Achilles.

Comparison	Mean difference (95% credible interval)	Risk of bias	Inconsistency[a]	Indirectness[b]	Imprecision	Publication bias[c]	Quality of evidence
VISA-A score at 3 months							
Placebo injection + eccentric exercises *v* wait-and-see	26 (-7 to 45)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Autologous blood Injection + eccentric exercises *v* wait-and-see	28 (-9 to 46)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
High volume injection + eccentric exercises *v* wait-and-see	37 (16 to 57)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
PRP injection + eccentric exercises *v* wait-and-see	27 (6 to 47)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy *v* wait-and-see injection	21 (7 to 36)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection + eccentric exercises *v* wait-and-see	17 (0 to 35)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises *v* wait-and-see	20 (11 to 29)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* wait-and-see	24 (15 to 34)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Continued sports activity + eccentric exercises *v* wait-and-see	20 (5 to 33)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* wait-and-see	15 (7 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* wait-and-see	34 (22 to 46)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Eccentric exercises+ night splint *v* wait-and-see	21 (4 to 38)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* wait-and-see	35 (26 to 45)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Eccentric exercises as tolerated *v* wait-and-see	24 (11 to 38)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Mucopolysaccharides supplement + eccentric exercises *v* wait-and-see	29 (15 to 43)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* wait-and-see	26 (10 to 41)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Autologous blood Injection + eccentric exercises *v* Placebo injection + eccentric exercises	1 (-8 to 11)	Serious	NA	No serious indirectness	No serious imprecision	NA	Moderate
High volume injection + eccentric exercises *v* Placebo injection + eccentric exercises	11 (4 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
PRP injection + eccentric exercises *v* Placebo injection + eccentric exercises	1 (-5 to 7)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Prolotherapy injection *v* Placebo injection + eccentric exercises	-5 (-25 to 16)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection + eccentric exercises *v* Placebo injection + eccentric exercises	-9 (-31 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises *v* Placebo injection + eccentric exercises	-6 (-23 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Placebo injection + eccentric exercises	-2 (-19 to 16)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises *v* Placebo injection + eccentric exercises	-7 (-27 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* Placebo injection + eccentric exercises	-11 (-30 to 9)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Placebo injection + eccentric exercises	8 (-11 to 27)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v*	-6 (-27 to 17)	Very serious	NA	No serious	Serious	NA	Very low

Placebo injection + eccentric exercises				indirectness	imprecision		
Acupuncture *v* Placebo injection + eccentric exercises	9 (-8 to 27)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Placebo injection + eccentric exercises	-2 (-21 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Placebo injection + eccentric exercises	2 (-17 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Placebo injection + eccentric exercises	-1 (-22 to 21)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
High volume injection + eccentric exercises *v* Autologous blood Injection + eccentric exercises	9 (-2 to 21)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
PRP injection + eccentric exercises *v* Autologous blood Injection + eccentric exercises	-1 (-12 to 10)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Prolotherapy injection *v* Autologous blood Injection + eccentric exercises	-6 (-26 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection + eccentric exercises *v* Autologous blood Injection + eccentric exercises	-10 (-31 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises *v* Autologous blood Injection + eccentric exercises	-7 (-23 to 8)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Autologous blood Injection + eccentric exercises	-3 (-19 to 13)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity +	-8 (-27 to 12)	Very serious	NA	No serious	Serious	NA	Very low

eccentric exercises *v* Autologous blood Injection + eccentric exercises				indirectness	imprecision		
Shock-wave therapy *v* Autologous blood Injection + eccentric exercises	-12 (-31 to 6)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Autologous blood Injection + eccentric exercises	6 (-11 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Autologous blood Injection + eccentric exercises	-7 (-28 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Autologous blood Injection + eccentric exercises	8 (-8 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Autologous blood Injection + eccentric exercises	-3 (-22 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Autologous blood Injection + eccentric exercises	1 (-17 to 20)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Autologous blood Injection + eccentric exercises	-2 (-22 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
PRP injection + eccentric exercises *v* High volume injection + eccentric exercises	-10 (-17 to -2)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection *v* High volume injection + eccentric exercises	-16 (-37 to 7)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection + eccentric	-19 (-43 to 5)	Very serious	NA	No serious	Serious	NA	Very low

exercises *v* High volume injection + eccentric exercises				indirectness	imprecision		
Eccentric exercises *v* High volume injection + eccentric exercises	-17 (-35 to 2)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* High volume injection + eccentric exercises	-13 (-31 to 6)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises *v* High volume injection + eccentric exercises	-17 (-39 to 5)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* High volume injection + eccentric exercises	-22 (-42 to 0)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* High volume injection + eccentric exercises	-3 (-23 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* High volume injection + eccentric exercises	-16 (-39 to 8)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* High volume injection + eccentric exercises	-2 (-20 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* High volume injection + eccentric exercises	-13 (-33 to 9)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* High volume injection + eccentric exercises	-8 (-29 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* High volume injection + eccentric exercises	-11 (-34 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection *v* PRP injection + eccentric exercises	-6 (-27 to 16)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection + eccentric	-10 (-33 to 14)	Very serious	NA	No serious	Serious	NA	Very low

exercises *v* PRP injection + eccentric exercises				indirectness	imprecision		
Eccentric exercises *v* PRP injection + eccentric exercises	-7 (-24 to 12)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* PRP injection + eccentric exercises	-3 (-20 to 16)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises *v* PRP injection + eccentric exercises	-7 (-28 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* PRP injection + eccentric exercises	-12 (-32 to 9)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* PRP injection + eccentric exercises	7 (-13 to 27)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* PRP injection + eccentric exercises	-6 (-29 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* PRP injection + eccentric exercises	8 (-10 to 27)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* PRP injection + eccentric exercises	-3 (-23 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* PRP injection + eccentric exercises	2 (-19 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* PRP injection + eccentric exercises	-1 (-23 to 21)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Prolotherapy injection + eccentric exercises *v* Prolotherapy injection	-4 (-19 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises *v* Prolotherapy injection	-1 (-13 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Prolotherapy injection	3 (-9 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Continued sports activity + eccentric exercises *v* Prolotherapy injection	-2 (-18 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* Prolotherapy injection	-6 (-21 to 9)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Prolotherapy injection	13 (-6 to 31)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Prolotherapy injection	-1 (-19 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Prolotherapy injection	14 (2 to 26)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Prolotherapy injection	3 (-12 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Prolotherapy injection	7 (-8 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Prolotherapy injection	4 (-13 to 22)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises *v* Prolotherapy injection + eccentric exercises	3 (-12 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Prolotherapy injection + eccentric exercises	7 (-8 to 22)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises *v* Prolotherapy injection + eccentric exercises	2 (-16 to 21)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* Prolotherapy injection + eccentric exercises	-2 (-20 to 16)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Prolotherapy injection + eccentric exercises	17 (0 to 33)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Eccentric exercises + night splint *v* Prolotherapy injection + eccentric exercises	3 (-17 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Prolotherapy injection + eccentric exercises	18 (3 to 33)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Prolotherapy injection + eccentric exercises	7 (-11 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Prolotherapy injection + eccentric exercises	11 (-7 to 30)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Prolotherapy injection + eccentric exercises	8 (-11 to 28)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Eccentric exercises	4 (2 to 6)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Continued sports activity + eccentric exercises *v* Eccentric exercises	-1 (-12 to 11)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Shock-wave therapy *v* Eccentric exercises	-5 (-15 to 5)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Eccentric exercises	14 (5 to 22)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Eccentric exercises	0 (-14 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Eccentric exercises	15 (12 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Eccentric exercises	5 (-6 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Eccentric exercises	8 (-2 to 19)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Mucopolysaccharides supplement + passive stretching *v* Eccentric exercises	5 (-8 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises *v* Heavy slow resistance exercises	-5 (-16 to 7)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* Heavy slow resistance exercises	-9 (-19 to 1)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Heavy slow resistance exercises	10 (1 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Heavy slow resistance exercises	-4 (-18 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Heavy slow resistance exercises	11 (8 to 14)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Eccentric exercises as tolerated *v* Heavy slow resistance exercises	0 (-10 to 10)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Heavy slow resistance exercises	4 (-6 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Heavy slow resistance exercises	1 (-12 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Shock-wave therapy *v* Continued sports activity + eccentric exercises	-5 (-20 to 11)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Continued sports activity + eccentric exercises	14 (0 to 28)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Continued sports activity + eccentric exercises	1 (-17 to 20)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Continued sports	15 (4 to 27)	Very serious	NA	No serious	Serious	NA	Very low

activity + eccentric exercises				indirectness	imprecision		
Eccentric exercises as tolerated *v* Continued sports activity + eccentric exercises	4 (-10 to 20)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Continued sports activity + eccentric exercises	9 (-7 to 25)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Continued sports activity + eccentric exercises	6 (-12 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + shockwave therapy *v* Shock-wave therapy	19 (6 to 31)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Shock-wave therapy	5 (-12 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Shock-wave therapy	20 (10 to 30)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Shock-wave therapy	9 (-5 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Shock-wave therapy	13 (-1 to 28)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Shock-wave therapy	10 (-6 to 26)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Eccentric exercises + shockwave therapy	-13 (-30 to 4)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Eccentric exercises + shockwave therapy	1 (-7 to 10)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Eccentric exercises as tolerated *v* Eccentric exercises + shockwave therapy	-10 (-22 to 3)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Mucopolysaccharides supplement + eccentric exercises *v* Eccentric exercises + shockwave therapy	-5 (-19 to 8)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Eccentric exercises + shockwave therapy	-8 (-24 to 7)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Eccentric exercises + night splint	15 (0 to 29)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Eccentric exercises + night splint	3 (-14 to 21)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Eccentric exercises + night splint	8 (-10 to 26)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Eccentric exercises + night splint	5 (-15 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises as tolerated *v* Acupuncture	-11 (-21 to -1)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Acupuncture	-6 (-17 to 5)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Acupuncture	-10 (-23 to 3)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + eccentric exercises *v* Eccentric exercises as tolerated	5 (-10 to 9)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Eccentric exercises as tolerated	1 (-15 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Mucopolysaccharides supplement + passive stretching *v* Mucopolysaccharides supplement + eccentric exercises	-3 (-16 to 10)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Placebo laser + eccentric exercises (high-dose) *v* Placebo laser + eccentric exercises (low-dose)	-4 (-12 to 6)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Laser therapy + eccentric exercises (low-dose) *v* Placebo laser + eccentric exercises (low-dose)	11 (2 to 21)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Laser therapy + eccentric exercises (high-dose) *v* Placebo laser + eccentric exercises (low-dose)	-3 (-11 to 6)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Laser therapy + eccentric exercises (low-dose) *v* Placebo laser + eccentric exercises (high-dose)	15 (6 to 24)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Laser therapy + eccentric exercises (high-dose) *v* Placebo laser + eccentric exercises (high-dose)	1 (-6 to 8)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Laser therapy + eccentric exercises (high-dose) *v* Laser therapy + eccentric exercises (low-dose)	-14 (-23 to -5)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
VISA-A score at 6 months							
Eccentric exercises (high-dose) *v* Prolotherapy Injection	-10 (-22 to 3)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises (high dose) v Prolotherapy Injection	-12 (-29 to 4)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises (high dose) + prolotherapy injection v Prolotherapy Injection	-5 (-21 to 10)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture v Prolotherapy Injection	1 (-12 to 14)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises (high dose)v Eccentric exercises (high-dose)	-2 (-13 to 9)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low

Eccentric exercises (high dose) + prolotherapy injection *v* Eccentric exercises (high-dose)	4 (-11 to 20)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Eccentric exercises (high-dose)	11 (9 to 13)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Eccentric exercises (high dose) + prolotherapy injection *v* Continued sports activity + eccentric exercises (high dose)	7 (-12 to 26)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Continued sports activity + eccentric exercises (high dose)	13 (2 to 25)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Acupuncture *v* Eccentric exercises (high dose) + prolotherapy injection	7 (-9 to 22)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Autologous blood injection + eccentric exercises (high dose) *v* Placebo injection + eccentric exercises (high dose)	0 (-11 to 11)	Serious	NA	No serious indirectness	No serious imprecision	NA	Moderate
High volume injection + eccentric exercises (high dose) *v* Placebo injection + eccentric exercises (high dose)	5 (-3 to 12)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
PRP injection + eccentric exercises (high dose) *v* Placebo injection + eccentric exercises (high dose)	6 (0 to 13)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
High volume injection + eccentric exercises (high dose) *v* Autologous blood injection + eccentric exercises (high dose)	5 (-8 to 19)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
PRP injection + eccentric exercises (high dose) *v* Autologous blood injection + eccentric exercises (high	6 (-6 to 19)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

dose)							
PRP injection + eccentric exercises (high dose) *v* High volume injection + eccentric exercises (high dose)	1 (-6 to 9)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
VISA-A score at 12 months							
Eccentric exercises (high-dose) *v* Prolotherapy Injection	-5 (-18 to 9)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises (high dose) *v* Prolotherapy Injection	-11 (-27 to 4)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Prolotherapy Injection	0 (-16 to 16)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises (high dose) + prolotherapy injection *v* Prolotherapy Injection	2 (-10 to 13)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Prolotherapy Injection	3 (-17 to 22)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Continued sports activity + eccentric exercises (high dose) *v* Eccentric exercises (high-dose)	-6 (-13 to 1)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Heavy slow resistance exercises *v* Eccentric exercises (high-dose)	5 (-4 to 14)	Very serious	NA	No serious indirectness	No serious imprecision	NA	Low
Eccentric exercises (high dose) + prolotherapy injection *v* Eccentric exercises (high-dose)	7 (-4 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Eccentric exercises (high-dose)	7 (-6 to 20)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Heavy slow resistance exercises *v* Continued sports activity + eccentric exercises (high dose)	11 (0 to 23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises (high dose) + prolotherapy injection *v* Continued	13 (0 to 26)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

sports activity + eccentric exercises (high dose)							
Eccentric exercises + night splint *v* Continued sports activity + eccentric exercises (high dose)	14 (-1 to 29)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises (high dose) + prolotherapy injection *v* Heavy slow resistance exercises	2 (-12 to 15)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Heavy slow resistance exercises	2 (-14 to 18)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
Eccentric exercises + night splint *v* Eccentric exercises (high dose) + prolotherapy injection	1 (-16 to 17)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
	Odds ratio's (95% credible interval)	**Risk of bias**	**Inconsistency**	**Indirectness ss**	**Imprecision**	**Publication bias**	**Quality of evidence**
Return to sports s at 6 months							
Autologous blood injection + eccentric exercises (high dose) *v* Placebo injection + eccentric exercises (high dose)	0.54 (0.15 to 1.88)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
High volume injection + eccentric exercises (high dose) *v* Placebo injection + eccentric exercises (high dose)	3.26 (0.96 to 12.23)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
PRP injection + eccentric exercises (high dose) *v* Placebo injection + eccentric exercises (high dose)	1.68 (0.67 to 4.34)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
High volume injection + eccentric exercises (high dose) *v* Autologous blood injection + eccentric exercises (high dose)	6.03 (1.02 to 37.81)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low
PRP injection + eccentric exercises	3.12 (0.67 to 15.10)	Very serious	NA	No serious	Serious	NA	Very low

(high dose) *v* Autologous blood injection + eccentric exercises (high dose)				indirectness	imprecision		
PRP injection + eccentric exercises (high dose) *v* High volume injection + eccentric exercises (high dose)	0.52 (0.14 to 1.81)	Very serious	NA	No serious indirectness	Serious imprecision	NA	Very low

Table 4.14 – GRADE assessment of individual treatment options for midportion Achilles tendinopathy.
Abbreviations: GRADE = Grading of Recommendations Assessment, Development, and Evaluation; NA = Not applicable; PRP = platelet-rich plasma; VISA-A = Victorian Institute of Sport Assessment-Achilles.
[a] Only 2 treatment comparisons were studied in multiple (i.e. 2) trials. Where this was the case, estimates and credible intervals showed substantial overlap.
[b] Populations, treatments and outcomes measures followed those used in clinical practice, hence there was no indication of indirectness in the evidence.
[c] Publication bias could not be assessed as there were <10 trials available for each of the comparisons.

Study	Study characteristics	Patient characteristics	Treatment	Follow-up	Outcome measures	Results	Predictors
Morrison, 2017 [60]	Setting: Public hospital, control visits at outpatient clinic in the United Kingdom.	Inclusion criteria: - Adult participants (age>16 years) - MRI-proved noninsertional Achilles tendinopathy - No improvement after	Intervention: Radiofrequency microdebridement using the Topaz microdebrider wand. Using this	Length of follow-up: 26 weeks Loss to follow-up:	Primary outcome: - VAS current pain Secondary outcomes: - VISA-A score	VISA-A score: Both groups demonstrated a significant improvement in VISA-A score at 6 months	None investigated

	Source of Funding: Commercial funding[1]	a minimum of 6 months of nonoperative management (including physiotherapy-directed eccentric exercises) Exclusion criteria: - Peripheral neuropathy or vascular disease - Local skin compromise (including ulceration, adherent scars, or inflammatory dermatitis) - Previous Achilles tendon surgery or rupture - Poor compliance with nonoperative treatment • Type of AT: Midportion AT • Number of participants: 36 (20/16) • Active participants: NR • Mean age: 48 years (SD not provided, range 35-65) • Male subjects: 42%	device, automatic timed bursts lasting 1 second at depths varying from 1 to 8 mm and 5 mm apart were applied on the areas of degenerate tendon during surgery. No tissue of the tendon was excised. Control: Traditional surgical decompression with excision of the areas of degenerate tendon.	0/36	- Complications	follow-up (intervention group 31 to 60 points and control group 42 to 67 points; p<0.001). There was no significant difference between both interventions at 6 months follow-up. Adverse effects: 1/20 (5%) in the intervention group, 2/16 (12.5%) in the control group; Two superficial wound infections were noted in the decompression group and were treated successfully with oral antibiotics. One partial Achilles tendon rupture occurred in the Topaz group. All other patients had an uneventful recovery after surgery. No patients required reoperation during the	

						study period.	
Hunt, 2015 [61]	Setting: Not reported Source of Funding: Non-commercial funding[2]	Inclusion criteria: - Patients with a chronic insertional Achilles tendinopathy - Older than 50 years - Failed specific nonoperative treatments (included boot immobilisation and a period of relative rest, an Achilles sleeve device, shoe wear modification, and nonsteroidal anti-inflammatory medications) over at least a 6-month period Exclusion criteria: - Previous ipsilateral Achilles surgery or rupture - Active wound or infection on the ipsilateral leg - Lack of an FHL tendon suitable for transfer • Type of AT: Insertional AT	Intervention: Achilles decompression and ostectomy augmented with a transfer of the flexor hallucis longus (FHL) tendon. Control: Achilles decompression and ostectomy alone.	Length of follow-up: 52 weeks Loss to follow-up: 10/49; 5 patient withdrew from the study before undergoing surgery, and 5 patients were not available for the 1-year follow-up. Not reported to which group these withdrawals were allocated.	Primary and secondary outcomes were not specified: - Patient satisfaction - American Orthopaedic Foot & Ankle Society (AOFAS) ankle/hindfoot score - VAS for pain, - Ankle and hallux plantar flexion strength (measured with MicroFET2 isokinetic dynamometer).	Patient satisfaction: There was no significant difference in patient satisfaction between the two treatment groups. Intervention group: 18/21 patients were satisfied with the outcome. Control group: 16/18 patients were satisfied with the outcome. Adverse effects: 8/21 (38.1%) in the intervention group, 4/18 (22.2%) in the control group; These included minor superficial wound dehiscence (6 patients), skin blistering or cellulitis (2 patients), delayed wound healing (2 patients), and peri-incisional maceration (2 patients). All wounds	None investigated

		• Number of participants: 39 (21/18) • Active participants: NR • Mean age: 61 (SD 7) • Male subjects: 36%				healed without additional surgical intervention. There were no major complications (no neurologic complications and no deep vein thromboses and no patients required additional surgical procedures).	

Table 4.15 – Evidence table of the randomised trials for surgical treatment of Achilles tendinopathy.
Abbreviations: AT, Achilles tendinopathy; FHL, flexor hallucis longus; NR, not reported; SD, standard deviation; VAS, visual analogue scale.
[1] Topaz microdebriders were provided by Arthrocare; Smith & Nephew, Huntingdon, UK.
[2] The study was funded by the OrthoCarolina Research Institute (OCRI), Charlotte, USA.

Trial	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Surgical treatments						
Hunt et al., 2015	?	+	−	+	?	−

Morrison et al., 2017	−	+	+	+	?	−

Table 4.16 – Risk of bias assessment of the included randomised studies assessing the effectiveness of surgical treatment options.
+ low ROB, ? unclear ROB, - high ROB.

Midportion Achilles tendinopathy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Achilles decompression and debridement augmented with FHL transfer	Achilles decompression and debridement alone	Relative (95% CI)	Absolute		
Patient satisfaction (follow-up 52 weeks)												
1	RCT	Very serious	NA	No serious indirectness	Serious[1]	None	21	18	-	86% (18/21) in group 1, 89% (16/18) in group 2.	+000 Very low	Important

[1] **Very wide confidence intervals were presented**

Insertional Achilles tendinopathy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiofrequency microdebridement	Surgical decompression and excision of degenerative tissue	Relative (95% CI)	Absolute		
VISA-A score (follow-up 26 weeks)												
1	RCT	Very serious	NA	No serious indirectness	Serious [1]	None	20	16	-	+24.3 in group 1 (−10 to 61) versus. +28.7 in group 2 (−15 to 66), p=0.569	+000 Very low	Important

Table 4.17 – GRADE assessment per surgical treatment for Achilles tendinopathy.
[1] No statistical analysis was performed.

Predictor of outcome	Numbe r of	Limitations	Inconsistency	Indirectness	Imprecision	Other considerati	Effect size	Dose-response	Effect of confounde	Qualit y

	studies					ons		relationship	rs	
Characteristics (non-modifiable)										
Age	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Sex	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Ethnicity	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Duration of symptoms	3	Unclear risk of bias	No serious inconsistency	No serious indirectness	Unknown[1]	None	-	-	-	Low
Severity of structural disorganisation on ultrasonography	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Degree of ultrasonographic Doppler flow	1	High risk of bias	-	No serious indirectness	Unknown[1]	Yes[2]	-	-	-	Very low
Lower baseline VISA-A score	2	Unclear risk of bias	No serious inconsistency	No serious indirectness	Unknown[1]	None	Small	Not reported	No effect	Low
Characteristics (modifiable)										
Level of physical activity	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Compliance with exercise training	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Additional weight carried during exercise training	1	Unclear risk of bias	-	No serious indirectness	Unknown[1]	None	-	-	-	Low
Technique of exercise	1	Unclear risk	-	No serious	Unknown[1]	None	-	-	-	Low

training of bias indirectness

Table 4.18 – GRADE assessment of the factors that may affect the effectiveness of treatment of midportion Achilles tendinopathy in the included randomised studies. The presence of associations is marked by a grey-coloured bar. All studies assessed the effect of the factors on the change in VISA-A score as an outcome measure.

[1] Confidence intervals of the predictor has not been presented.

[2] Results presented on tendon level, whereas presentation on patient-level would be preferable.

Predictor of outcome	Study (first author and reference number)	Best evidence synthesis
Characteristics (non-modifiable)		
Age	Bell =	Limited evidence for no association
Sex	Bell =	Limited evidence for no association
Ethnicity	Bell =	Limited evidence for no association
Duration of symptoms	Bell =, De Jonge =, Silbernagel =	Limited evidence for no association
Severity of structural disorganisation on ultrasonography	Bell =	Limited evidence for no association
Ultrasonographic Doppler flow	Pearson =	Limited evidence for no association
Lower baseline VISA-A score	De Jonge ↑, Silbernagel ↑	Limited evidence for positive association
Characteristics (modifiable)		
Level of physical activity	Bell =	Limited evidence for no association
Compliance with exercise training	Bell =	Limited evidence for no association
Additional weight carried during exercise training	Bell =	Limited evidence for no association
Technique of exercise training	Bell =	Limited evidence for no association

Table 4.19 – Overview of factors that may affect the effectiveness of the treatment of midportion Achilles tendinopathy in the included randomised studies. The presence of associations is marked by a grey-coloured bar. All studies assessed the effect of the factors on the change in VISA-A score as an outcome measure.

REFERENCES

1. Macdermid JC, Silbernagel KG. Outcome Evaluation in Tendinopathy: Foundations of Assessment and a Summary of Selected Measures. J Orthop Sports Phys Ther. 2015;45(11):950-64.
2. Vicenzino B, de Vos RJ, Alfredson H, et al. ICON 2019-International Scientific Tendinopathy Symposium Consensus: There are nine core health-related domains for tendinopathy (CORE DOMAINS): Delphi study of healthcare professionals and patients. Br J Sports Med. 2020;54(8):444-451.
3. de Jonge S, Tol JL, Weir A, et al. The Tendon Structure Returns to Asymptomatic Values in Nonoperatively Treated Achilles Tendinopathy but Is Not Associated With Symptoms: A Prospective Study. Am J Sports Med. 2015;43(12):2950-58.
4. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. Br J Sports Med. 2001;35(5):335-41.
5. Murphy M, Rio E, Debenham J, et al. Evaluating the progress of mid-portion Achilles tendinopathy during rehabilitation: A review of outcome measures for self-reported pain and function. Int J Sports Phys Ther. 2018;13(2):283-292.
6. Iversen JV, Bartels EM, Langberg H. The victorian institute of sports assessment - achilles questionnaire (VISA-A) - a reliable tool for measuring achilles tendinopathy. Int J Sports Phys Ther. 2012;7(1):76-84.
7. Khan KM, Forster BB, Robinson J, et al. Are ultrasound and magnetic resonance imaging of value in assessment of Achilles tendon disorders? A two year prospective study. Br J Sports Med. 2003;37(2):149-53.
8. McCormack J, Underwood F, Slaven E, et al. The Minimum Clinically Important Difference on the Visa-a and Lefs for Patients with Insertional Achilles Tendinopathy. Int J Sports Phys Ther. 2015;10(5):639-44.
9. Tumilty S, Munn J, Abbott JH, et al. Laser therapy in the treatment of achilles tendinopathy: A pilot study. Photomed Laser Surg. 2008;26(1):25-30.

10. Lagas IF, van der Vlist AC, van Oosterom RF, et al. Victorian Institute of Sport Assessment-Achilles (VISA-A) questionnaire: Minimal clinically important difference for active people with mid-portion Achilles tendinopathy - a prospective cohort study. Accepted for publication in J Orthop Sports Phys Ther. 2021.
11. Rompe JD, Nafe B, Furia JP, et al. Eccentric loading, shock-wave treatment, or a wait- and-see policy for tendinopathy of the main body of tendo Achillis: A randomized controlled trial. Am J Sports Med. 2007;35(3):374-83.
12. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
13. Hultcrantz M, Rind D, Akl EA, et al. The GRADE Working Group clarifies the construct of certainty of evidence. J Clin Epidemiol. 2017;87:4-13.
14. Archambault JM, Wiley JP, Bray RC, et al. Can sonography predict the outcome in patients with achillodynia? J Clin Ultrasound. 1998;26(7):335-9.
15. Paavola M, Kannus P, Paakkala T, et al. Long-term prognosis of patients with achilles tendinopathy. An observational 8-year follow-up study. Am J Sports Med. 2000;28(5):634-42.
16. Silbernagel KG, Thomee R, Eriksson BI, et al. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with Achilles tendinopathy: a randomized controlled study. Am J Sports Med. 2007;35(6):897-906.
17. van der Vlist AC, Winters M, Weir A, et al. Which treatment is most effective for patients with Achilles tendinopathy? A living systematic review with network meta-analysis of 29 randomised controlled trials. Br J Sports Med. 2021;55(5):249-256.
18. de Vos RJ, Weir A, Visser RJ, et al. The additional value of a night splint to eccentric exercises in chronic midportion Achilles tendinopathy: a randomised controlled trial. Br J Sports Med. 2007;41(7):e5.
19. de Jonge S, de Vos RJ, Van Schie HT, et al. One-year follow-up of a randomised controlled trial on added splinting to eccentric exercises in chronic midportion Achilles tendinopathy. Br J Sports Med. 2010;44(9):673-7.
20. de Vos RJ, Weir A, Van Schie HTM, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: A randomized controlled trial. JAMA. 2010;303(2):144-49.
21. de Jonge S, de Vos RJ, Weir A, et al. One-year follow-up of platelet-rich plasma treatment in chronic Achilles tendinopathy: a double-blind randomized placebo-controlled trial. Am J Sports Med. 2011;39(8):1623-29.
22. Heinemeier KM, Øhlenschlæger TF, Mikkelsen UR, et al. Effects of anti-inflammatory (NSAID) treatment on human tendinopathic tissue. J Appl Physiol. 2017;123(5):1397-405.
23. Hutchison AM, Pallister I, Evans RM, et al. Intense pulsed light treatment of chronic midbody Achilles tendinopathy: A double blind randomised placebo-controlled trial. Bone Jt J. 2013;95 B(4):504-09.
24. Rompe JD, Furia J, Maffulli N. Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: A randomized controlled trial. Am J Sports Med. 2009;37(3):463-70.
25. Roos EM, Engström M, Lagerquist A, et al. Clinical improvement after 6 weeks of eccentric exercise in patients with mid-portion Achilles tendinopathy - A randomized trial with 1-year follow-up. Scand J Med Sci Sports. 2004;14(5):286-95.
26. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. Br J Sports Med. 2011;45(5):421-28.
27. Pearson J, Rowlands D, Highet R. Autologous blood injection to treat achilles tendinopathy? A randomized controlled trial. J Sport Rehabil. 2012;21(3):218-24.
28. Mafi N, Lorentzon R, Alfredson H. Superior short-term results with eccentric calf muscle training compared to concentric training in a randomized prospective multicenter study on patients with chronic Achilles tendinosis. Knee Surg Sports Traumatol Arthrosc. 2001;9(1):42-47.
29. Stevens M, Tan CW. Effectiveness of the alfredson protocol compared with a lower repetition-volume protocol for midportion achilles tendinopathy: A randomized controlled trial. J Orthop Sports Phys Ther. 2014;44(2):59-67.
30. Beyer R, Kongsgaard M, Hougs Kjær B, et al. Heavy Slow Resistance Versus Eccentric Training as Treatment for Achilles Tendinopathy: A Randomized Controlled Trial. Am J Sports Med. 2015;43(7):1704-11.

31. Silbernagel KG, Thomeé R, Eriksson BI, et al. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with achilles tendinopathy: A randomized controlled study. Am J Sports Med. 2007;35(6):897-906.
32. Silbernagel KG, Thomeé R, Thomeé P, et al. Eccentric overload training for patients with chronic Achilles tendon pain--a randomised controlled study with reliability testing of the evaluation methods. Scand J Med Sci Sports. 2001;11(4):197-206.
33. Lynen N, De Vroey T, Spiegel I, et al. Comparison of Peritendinous Hyaluronan Injections Versus Extracorporeal Shock Wave Therapy in the Treatment of Painful Achilles' Tendinopathy: A Randomized Clinical Efficacy and Safety Study. Arch Phys Med Rehabil. 2017;98(1):64-71.
34. Herrington L, McCulloch R. The role of eccentric training in the management of Achilles tendinopathy: A pilot study. Phys Ther Sport. 2007;8(4):191-96.
35. Auclair J, Georges M, Grapton X, et al. A double-blind controlled mutlicenter study of percutaneous niflumic acid gel and placebo in the treatment of Achilles heel tendinitis. Current Therapeutic Research, Clinical & Experimental. 1989;46(4):782-88.
36. Zhang BM, Zhong LW, Xu SW, et al. Acupuncture for chronic achilles tendnopathy: A randomized controlled study. Chin J Integr Med. 2013;19(12):900-04.
37. Usuelli FG, Grassi M, Alfieri Montrasio U, et al. Adipose-derived stem cells for the treatment of Achilles tendinopathy: A randomized prospective trial. Foot Ankle Surg. 2016;22(2):20.
38. Rompe JD, Furia J, Maffulli N. Eccentric loading compared with shock wave treatment for chronic insertional achilles tendinopathy: A randomized, controlled trial. J Bone Jt Surg Am. 2008;90(1):52-61.
39. Njawaya MM, Moses B, Martens D, et al. Ultrasound guidance does not improve the results of shock wave for plantar fasciitis or calcific achilles tendinopathy: A randomized control trial. Clin J Sport Med. 2018;28(1):21-27.
40. Ebbesen BH, Mølgaard CM, Olesen JL, et al. No beneficial effect of Polidocanol treatment in Achilles tendinopathy: a randomised controlled trial. Knee Surg Sports Traumatol Arthrosc. 2018;26(7):2038-44.
41. Spinnewijn L, Aarts J, Verschuur S, et al. Knowing what the patient wants: a hospital ethnography studying physician culture in shared decision making in the Netherlands. BMJ Open. 2020;10(3):e032921.
42. Dijkstra HP, Pollock N, Chakraverty R, et al. Return to play in elite sport: a shared decision-making process. Br J Sports Med. 2017;51(5):419-20.
43. Bowen E, Nayfe R, Milburn N, et al. Do Decision Aids Benefit Patients with Chronic Musculoskeletal Pain? A Systematic Review. Pain Med. 2020;21(5):951-69.
44. Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. Br J Sports Med. 2009;43(6):409-16.
45. Mellor R, Bennell K, Grimaldi A, et al. Education plus exercise versus corticosteroid injection use versus a wait and see approach on global outcome and pain from gluteal tendinopathy: prospective, single blinded, randomised clinical trial. BMJ. 2018;361:k1662.
46. Rio E, Moseley L, Purdam C, et al. The pain of tendinopathy: physiological or pathophysiological? Sports Med. 2014;44(1):9-23.
47. Mc Auliffe S, Synott A, Casey H, et al. Beyond the tendon: Experiences and perceptions of people with persistent Achilles tendinopathy. Musculoskelet Sci Pract. 2017;29:108-14.
48. Louw A, Diener I, Landers MR, et al. Preoperative pain neuroscience education for lumbar radiculopathy: a multicenter randomized controlled trial with 1-year follow-up. Spine (Phila Pa 1976). 2014;39(18):1449-57.
49. Davenport TE, Kulig K, Matharu Y, et al. The EdURePmodel for nonsurgical management of tendinopathy. Phys Ther. 2005;85(10):1093-103.
50. van der Vlist AC, van Veldhoven PLJ, van Oosterom RF, et al. Isometric exercises do not provide immediate pain relief in Achilles tendinopathy: A quasi-randomized clinical trial. Scand J Med Sci Sports. 2020;30(9):1712-21.
51. O'Neill S, Radia J, Bird K, et al. Acute sensory and motor response to 45-s heavy isometric holds for the plantar flexors in patients with Achilles tendinopathy. Knee Surg Sports Traumatol Arthrosc. 2019;27(9):2765-73.
52. Fahlstrom M, Jonsson P, Lorentzon R, et al. Chronic Achilles tendon pain treated with eccentric calf-muscle training. Knee Surg Sports Traumatol Arthrosc. 2003;11(5):327-33.

53. Jonsson P, Alfredson H, Sunding K, et al. New regimen for eccentric calf-muscle training in patients with chronic insertional Achilles tendinopathy: results of a pilot study. Br J Sports Med. 2008;42(9):746-9.
54. Cook JL, Purdam C. Is compressive load a factor in the development of tendinopathy? Br J Sports Med. 2012;46(3):163-8.
55. DaCruz DJ, Geeson M, Allen MJ, et al. Achilles paratendonitis: an evaluation of steroid injection. Br J Sports Med. 1988;22(2):64-65.
56. Coombes BK, Bisset L, Vicenzino B. Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: a systematic review of randomised controlled trials. Lancet. 2010;376(9754):1751-67.
57. Seeger JD, West WA, Fife D, et al. Achilles tendon rupture and its association with fluoroquinolone antibiotics and other potential risk factors in a managed care population. Pharmacoepidemiol Drug Saf. 2006;15(11):784-92.
58. Redler A, Proietti L, Mazza D, et al. Rupture of the Patellar Tendon After Platelet-Rich Plasma Treatment: A Case Report. Clin J Sport Med. 2020;30(1):e20-e22.
59. Martin RL, Chimenti R, Cuddeford T, et al. Achilles Pain, Stiffness, and Muscle Power Deficits: Midportion Achilles Tendinopathy Revision 2018. J Orthop Sports Phys Ther. 2018;48(5):A1-A38.
60. Morrison RJM, Brock TM, Reed MR, et al. Radiofrequency Microdebridement Versus Surgical Decompression for Achilles Tendinosis: A Randomized Controlled Trial. J Foot Ankle Surg. 2017;56(4):708-12.
61. Hunt KJ, Cohen BE, Davis WH, et al. Surgical Treatment of Insertional Achilles Tendinopathy with or Without Flexor Hallucis Longus Tendon Transfer. Foot Ankle Int. 2015;36(9):998-1005.
62. Lohrer H, David S, Nauck T. Surgical treatment for achilles tendinopathy - a systematic review Review. BMC Musculoskelet Disord. 2016;17:207.
63. Goel DP, Chan D, Watson K, et al. Safety and hospital costs of Achilles tendon surgery: the serendipitous impact of a randomized clinical trial. Can J Surg. 2009;52(6):467-72.
64. Challoumas D, Clifford C, Kirwan P, et al. How does surgery compare to sham surgery or physiotherapy as a treatment for tendinopathy? A systematic review of randomised trials. BMJ Open Sport Exerc Med. 2019;5(1):e000528.
65. Bell KJ, Fulcher ML, Rowlands DS, et al. Impact of autologous blood injections in treatment of mid-portion Achilles tendinopathy: Double blind randomised controlled trial. BMJ. 2013;346(7908).
66. Bowen L, Gross AS, Gimpel M, et al. Spikes in acute:chronic workload ratio (ACWR) associated with a 5-7 times greater injury rate in English Premier League football players: a comprehensive 3-year study. Br J Sports Med. 2020;54(12):731-738.
67. Hulin BT, Gabbett TJ, Blanch P, et al. Spikes in acute workload are associated with increased injury risk in elite cricket fast bowlers. Br J Sports Med. 2014;48(8):708-12.
68. Hulin BT, Gabbett TJ, Lawson DW, et al. The acute:chronic workload ratio predicts injury: high chronic workload may decrease injury risk in elite rugby league players. Br J Sports Med. 2016;50(4):231-6.
69. Johnston R, Cahalan R, Bonnett L, et al. Training Load and Baseline Characteristics Associated With New Injury/Pain Within an Endurance Sporting Population: A Prospective Study. Int J Sports Physiol Perform. 2019;14(5):590-97.
70. Lagas IF, Fokkema T, Verhaar JAN, et al. Incidence of Achilles tendinopathy and associated risk factors in recreational runners: A large prospective cohort study. J Sci Med Sport. 2020;23(5):448-52.
71. Lagas IF, Fokkema T, Bierma-Zeinstra SMA, et al. How many runners with new-onset Achilles tendinopathy develop persisting symptoms? A large prospective cohort study. Scand J Med Sci Sports. 2020;30(10):1939-1948.
72. Balius R, Álvarez G, Baró F, et al. A 3-Arm Randomized Trial for Achilles Tendinopathy: Eccentric Training, Eccentric Training Plus a Dietary Supplement Containing Mucopolysaccharides, or Passive Stretching Plus a Dietary Supplement Containing Mucopolysaccharides. Curr Ther Res Clin Exp. 2016;78:1-7.
73. Boesen AP, Hansen R, Boesen MI, et al. Effect of High-Volume Injection, Platelet-Rich Plasma, and Sham Treatment in Chronic Midportion Achilles Tendinopathy: A Randomized Double-Blinded Prospective Study. Am J Sports Med. 2017;45(9):2034-43.

74. Krogh TP, Ellingsen T, Christensen R, et al. Ultrasound-Guided Injection Therapy of Achilles Tendinopathy With Platelet-Rich Plasma or Saline: A Randomized, Blinded, Placebo-Controlled Trial. Am J Sports Med. 2016;44(8):1990-97.
75. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. Br J Sports Med. 2015;49(15):989-94.
76. Njawaya MM, Moses B, Martens D, et al. Ultrasound Guidance Does Not Improve the Results of Shock Wave for Plantar Fasciitis or Calcific Achilles Tendinopathy: A Randomized Control Trial. Clin J Sport Med. 2018;28(1):21-27.
77. Tumilty S, McDonough S, Hurley DA, et al. Clinical effectiveness of low-level laser therapy as an adjunct to eccentric exercise for the treatment of Achilles' tendinopathy: A randomized controlled trial. Arch Phys Med Rehabil. 2012;93(5):733-39.
78. Tumilty S, Mani R, Baxter GD. Photobiomodulation and eccentric exercise for Achilles tendinopathy: a randomized controlled trial. Lasers Med Sci. 2016;31(1):127-35.
79. Usuelli FG, Grassi M, Maccario C, et al. Intratendinous adipose-derived stromal vascular fraction (SVF) injection provides a safe, efficacious treatment for Achilles tendinopathy: results of a randomized controlled clinical trial at a 6-month follow-up. Knee Surg Sports Traumatol Arthrosc. 2018;26(7):2000-2010.