Supplementary file Module 5

Scoping question

What is the prognosis of individuals with Achilles tendinopathy in the long term?

Literature search and selection

The scoping question was divided into 3 sub-questions:

1. What percentage of patients with Achilles tendinopathy have persistent symptoms for more than 1 year?
2. What percentage of patients with Achilles tendinopathy return to their original level of sport over a period of more than 1 year?
3. What factors affect the long-term prognosis (longer than 1 year) in patients with Achilles tendinopathy?

A systematic literature search was carried out using these sub-questions.

The working group decided not to perform a separate search strategy for answering sub-question 3 (prognostic factors), as these would be contained in studies examining the prognosis of Achilles tendinopathy. For sub-questions 1 and 2, one joint PICO was drawn up:

P: patients with Achilles tendinopathy.
I: outcomes measured using patient-reported outcome measures (PROMs) after long-term follow-up.
C: baseline values of patient-reported outcome measures.
O: persisting symptoms (VISA-A score, patient satisfaction, return to sports and subjective recovery).

The following PICO was drawn up for the answer to *sub-question 3:*

P: patients with Achilles tendinopathy.
I: presence of factors that affect the long-term outcome (1 year and longer) in Achilles tendinopathy.
C: absence of factors that affect the long-term outcome (1 year and longer) in Achilles tendinopathy.
O: persisting symptoms (subjective recovery, VISA-A score, return to sports, patient satisfaction, percentage of patients who develop contralateral symptoms).

Important outcome measures

The working group considered subjective recovery after more than 1 year to be the primary outcome measure for sub-question 1. For subjective recovery, specific questioning about recovery after treatment should be reported by the patient. Subjective recovery was chosen as the primary outcome measure because it gives a representative prognosis for Achilles tendinopathy.

Important secondary outcome measures for sub-question 1 were: the validated Victorian Institute of Sports Assessment-Achilles (VISA-A) score[1], patient satisfaction and percentage of patients who developed contralateral symptoms. There are multiple reasons for these choices. The VISA-A questionnaire is subject to change in (sports) participation over a long period of time that is not related to the injury. The VISA-A questionnaire consists of 8 questions that cover 3 domains: pain, function and sports participation. A score of 100 points is optimal and represents a fully functioning Achilles tendon without pain, a score of 0 points represents a very poorly functioning Achilles tendon with severe symptoms. Patient satisfaction is influenced by the assessment and is not directly linked to successful treatment. Patient satisfaction should be reported by the patient, with a scale but this is not directly relevant to this guideline. The percentage of patients with unilateral symptoms who developed symptoms on the previously asymptomatic side during follow-up was also identified as a secondary outcome measure.

The percentage of patients returning to sports was considered by the working group to be the primary outcome measure for sub-question 2. The particular scale used was not specified. This outcome measure did not take into account the type of sport, the volume and performance level and whether there were symptoms in relation to the return to sports.

The working group considered subjective recovery to be the primary outcome measure for sub-question 3. Important secondary outcome measures for sub-question 3 were: the VISA-A score, return to sports and patient satisfaction.

Literature search and selection

On 10th of January 2019, in collaboration with the Erasmus MC medical librarian, a broad search was conducted for longitudinal studies examining the long-term prognosis of Achilles tendinopathy (Table 5.1). The following databases were searched for relevant literature: Embase and Medline Ovid. Potentially relevant studies were assessed using the following criteria.

Inclusion criteria:

- The study evaluated the prognosis of Achilles tendinopathy with a follow up more than 1 year using important clinical outcome measures.
- At least 20 participants were included in the study.
- The study used a randomised or a prospective longitudinal design (cohort or case-series design).

Exclusion criteria:

- The cohort of patients had a follow-up duration where the range was less than 24 months.
- Retrospective longitudinal design (cohort or case-series design without pre-collected baseline data).

All studies were assessed for quality using the "Quality In Prognosis Studies" (QUIPS) Risk of Bias tool.[2]This tool is recommended by the Cochrane Working Group on studies that examine prognostic factors. This tool assesses 6 domains, where each domain is scored as being at low, medium or high risk of bias. Based on the 6 separate domains, the article was assessed in general, with the following 3 outcomes being possible:

1. High quality: The majority of criteria for a low risk of bias have been met.
2. Acceptable quality: Most of the criteria are met. There are some shortcomings in the study with an associated risk of bias. Conclusions may change in future research.
3. Low quality: Most criteria are not met or there are significant shortcomings of the study. Evidence synthesis was performed by a single assessor using GRADE.[3]

In addition, existing national and international guidelines were reviewed: 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).

Search results

The search strategy yielded a total of 848 articles, of which 27 were potentially relevant after screening the title and abstract. After this preselection, the full text of the remaining 27 articles was reviewed. Seven studies were included in the final analysis.[4-10] A flowchart is attached which shows the selection process (Figure 5.1).

In addition, the working group identified previously described data on prognosis in the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007). This information was also considered. The databases of the NHG, NICE, NGC and G-I-N did not contain existing guidelines on the prognosis of Achilles tendinopathy.

Literature Summary

Sub-question 1 (Percentage of persistent symptoms)

Description studies

One randomised (RCT) and 6 prospective longitudinal studies were included to answer this sub-question. The characteristics and main results of these studies can be found in Table 5.2. More than half of the studies (4/7 studies) examined populations with midportion Achilles tendinopathy, compared to 2 studies in which the location was not further specified. One study reported the presence of long-term symptoms in patients with both midportion and insertional Achilles tendinopathy. The data is presented collectively, but analyses were also carried out to investigate differences in the VISA-A score between the 2 groups. There appears to be no difference in long-term outcomes between midportion and insertional Achilles tendinopathy. All studies involved non-surgical treatments at baseline consisting of: progressive or eccentric exercise therapy, a night splint, shockwave therapy, nitrate patches, (multiple) peritendinous corticosteroid injections, a platelet-rich plasma (PRP) injection and intratendinous needling. The population size varied between 21 and 93 participants at baseline (median 56). The number of patients who completed the last follow-up time ranged between 17 and 77 participants (median 46). As a result, the percentage of patients 'lost to follow-up' ranged from 7% to 21% (median 18%). The mean age of the included participants ranged between 47 and 59 years (median 51) and the percentage of male participants from 43% to 62% (median percentage of male participants 57%). The follow-up time ranged from 2 to 10 years (median 8).

All studies were assessed for quality using the QUIPS Risk of Bias tool. For detailed results of the quality of these studies, we refer to Table 5.3.

Results

Results are shown for subjective recovery as a primary outcome measure for sub-question 1. The VISA-A score, patient satisfaction and the percentage of patients developing contralateral symptoms are shown as secondary outcome measures. A subdivision was created for these 4 outcome measures.

Primary outcome measure: subjective recovery

Midportion Achilles tendinopathy

After 2 to 5 years of follow-up, 23 to 60% of patients with midportion Achilles tendinopathy reported persistent symptoms (Table 5.4). A longer follow-up duration did not show a trend of a decreasing percentage of patients with persistent symptoms. In 1 study of 65 patients (initially randomised design) it was found that 23% of patients had persistent symptoms after 3 years of follow-up.[6] Subjective recovery after treatment (nitrate patch) was significantly better than the control treatment (placebo patch), but given the long time from the last non-surgical treatment, the working group considered it irrelevant to report the difference between the two groups. There are 2 studies that report subjective recovery 5 years after starting a new non-surgical treatment. In the first study, which included 58 patients, 60% had persistent symptoms.[9] At baseline, patients in this RCT were instructed to perform eccentric exercise therapy, in addition to which the intervention group also used a night splint. The second study included 38 patients and reported that 35% had persistent symptoms, 5 years after non-surgical treatment with progressive exercise therapy.[7] The last study had a prospective longitudinal design and included 21 patients of which 53% reported persistent symptoms after 2 years of follow-up.[10] The patients in this study were all treated with minimally invasive techniques (paratenon decompression (injection) and intratendinous dry needling of areas with increased ultrasound Doppler flow.

Insertional Achilles tendinopathy

No studies on subjective long-term recovery have been conducted in insertional Achilles tendinopathy.

Achilles tendinopathy (unspecified midportion or insertional)

The study with the longest follow-up duration (10 years) assessed the long-term course of 77 patients with midportion Achilles tendinopathy (n=63) and insertional Achilles tendinopathy

(n=14).[4] At baseline, patients performed supervised isotonic exercise therapy. If the performance of the exercises was limited by pain, 1 to 3 peritendinous corticosteroid injections were given. After 10 years follow-up, a full functional recovery without physical limitations was reported in 63% of patients. In 27% of patients there was mild functional impairment and in 10% there was a poor functional outcome. The results were reported only for the whole group, but not by subtype (insertional versus midportion).

Secondary outcome measure: VISA-A score

Midportion Achilles tendinopathy

The VISA-A score in midportion Achilles tendinopathy varied in 5 studies with 2 to 10 years follow-up on average between 66 and 99 points. Follow-up values higher than 80 points were found after 3 years, but there was no trend of further increase in the longer term (Table 5.5). Two studies determined the VISA-A score after 5 years follow-up. The first study found a mean (SD) VISA-A score of 90 (11) in 38 patients with midportion Achilles tendinopathy after non-surgical treatment with progressive exercise therapy.[7] This study did not describe the percentage of inactive patients. The second 5-year follow-up study of 58 patients found a mean (SD) VISA-A score of 84 (15).[9] In this study, 9% of patients were inactive. At baseline, patients in this RCT were instructed to perform eccentric exercise therapy, in addition to which the intervention group also used a night splint. The study with the longest follow-up duration of 10 years assessed the long-term outcome of 63 patients with midportion Achilles tendinopathy.[4] After 10 years of follow-up, a mean (SD) VISA-A score of 80 (21) was reported. In this study some (9%) of the included patients were inactive. At baseline, patients performed supervised eccentric/concentric exercise therapy with the addition of 1 to 3 peritendinous corticosteroid injections if exercises were limited by pain. The final 2 studies determined the VISA-A score after 2 and 3 years respectively. The first study was an RCT (nitrate patch versus placebo patch) in 65 patients.[6] After 3 years follow-up, a mean VISA-A score of 95 (SD not explicitly stated) and 99 (SD not explicitly stated) were found in both groups. Additionally, there was no reporting of what percentage of patients were inactive. The second study was a prospective longitudinal study involving 36 patients who had undergone 3 shockwave therapy at baseline.[8] After 2 years of follow-up, the mean VISA-A score was 66 (range 18 to 94) for patients with midportion Achilles tendinopathy. The percentage of inactive patients was not reported. The workgroup found it important to consider if inactive patients were included because this can affect the VISA-A score (the maximum VISA-A score for inactive patients being 60/100 points).

Insertional Achilles tendinopathy

Long-term outcome assessment was examined in 2 prospective longitudinal studies. In the first study, 20 patients underwent 3 sessions of shockwave therapy and at 2 years follow-up they had a mean VISA-A score of 70 points (range 52 to 97).[8] There was no reporting of whether patients were inactive. In the second study (n=14), the long-term course was assessed after 10 years.[4] In this study, a mean (SD) VISA-A score of 90 (10) was reported. In this study, some of the included patients were inactive (9%), which may have affected the VISA-A score. At baseline, patients performed supervised eccentric/concentric exercise therapy with the addition of 1 to 3 peritendinous corticosteroid injections if the exercises were limited due to pain.

Secondary outcome measure: patient satisfaction

Midportion Achilles tendinopathy

The patient satisfaction in midportion Achilles tendinopathy varied between 50% and 76% after 2 to 5 years follow-up. There is no trend towards a higher patient satisfaction with longer follow-up duration.

In the largest prospective longitudinal study of 58 patients, 50% reported a good to excellent patient satisfaction after 5 years follow-up.[9] Of these, 41% reported good and 9% excellent patient satisfaction after treatment with eccentric exercise therapy with or without a night splint. A prospective longitudinal study of 21 patients reported high to very high patient satisfaction in 76% of patients.[10] These patients were all treated with minimally invasive injection therapy. The last study involved a prospective longitudinal study of 36 patients with midportion Achilles

tendinopathy that measured patient satisfaction after 3 sessions of shockwave therapy as an average on a five-point Likert scale.[8] On average, "much improved" was reported by patients after 2 years of follow-up (on average 2.2 points, SD not reported). As the results were presented only as an average Likert score (1 point "completely recovered", 6 points "worse"), they cannot be further specified or categorised.

Insertional Achilles tendinopathy
In a prospective longitudinal study of 20 patients with insertional Achilles tendinopathy, patient satisfaction after 3 sessions of shockwave therapy was expressed as an average of a five-point Likert scale after 2 years of follow-up.[8] On average, "somewhat improved" was reported by patients (on average 2.7 points, SD not reported). As the results were only presented as an average Likert score (1 point "completely recovered", 6 points "worse"), they cannot be further specified.

Achilles tendinopathy (unspecified if midportion or insertional)
One study rated patient satisfaction after a follow-up duration of 2 years in insertional or midportion Achilles tendinopathy without performing subgroup analyses. In this prospective longitudinal study of 30 patients, 93% reported that they were satisfied with the result of treatment after an injection of platelet-rich plasma followed by eccentric exercise therapy.[5]

Secondary outcome measure: percentage of patients who develop Achilles tendinopathy on the contralateral side
Midportion Achilles tendinopathy
The percentage of patients who develop contralateral symptoms of midportion Achilles tendinopathy at 5 years follow up varied between 9% and 43%.

Two studies examined the percentage of patients who developed contralateral symptoms. Both studies used a follow-up duration of 5 years. The first study (n=34 with unilateral midportion Achilles tendinopathy) reported pain symptoms from the previously asymptomatic side during follow-up in 43% of patients.[9] At baseline, patients in this originally randomised study were instructed in the execution of eccentric exercise therapy, in addition the intervention group also used a night splint. In the second study, 34 patients with unilateral midportion Achilles tendinopathy were included and performed progressive exercise therapy.[7] Nine percent of the patients developed symptoms of the asymptomatic side.

Insertional Achilles tendinopathy
No studies have been conducted for insertional Achilles tendinopathy about the development of symptoms of the asymptomatic side.

The quality of the evidence
The quality of the evidence was determined per outcome measure and is based on results from prospective longitudinal studies (cohort study or case series). The quality of evidence starts at a high level for prognostic factors according to the GRADE assessment in this type of design. The quality of evidence per outcome measure is shown in Table 5.6. The level was not increased for any outcome measure during the GRADE assessment, it was reduced by 2 to 3 levels for all outcome measures to low or very low. This was done due to imprecision in all outcome measures, a high risk of bias in all the studies and inconsistency in 2 outcome measures.

Sub-question 2 (Percentage returning to sport)
Description of studies
One case series was included to answer this sub-question.[10] The characteristics and most important results of this study can be found in Table 5.1. As there is only 1 study, the characteristics are described below.

The study was assessed using the QUIPS Risk of Bias tool. For the detailed results of the assessment of the quality of this study, we refer to Table 5.3.

Results
The results are shown for return to sports as the primary outcome measure for sub-question 2.

Midportion Achilles tendinopathy
One study examined a population with midportion Achilles tendinopathy, all of whom were treated with minimally invasive injection therapy.[10] The population size was 21 at baseline and 17 completed the last follow-up. The mean age was 55 years (43% male). The percentage of patients who returned to their desired sport 2 years after treatment was at least 85%. All 17 patients who could be contacted at follow-up had returned to their desired sport. The remaining 4 patients were not available to report this outcome measure. The same study found that 8/17 patients had a full recovery from symptoms, which shows that patients without full recovery of symptoms could also return to sports. The amount of pain during sport was not reported. It is also unclear at what level and intensity sport they participated in after 2 years.

Insertional Achilles tendinopathy
No studies have been conducted that have assessed the long-term return to sports in insertional Achilles tendinopathy.

Quality of evidence
The quality of the evidence is determined per outcome measure and is based on results from prospective longitudinal studies (cohort study or case series). The quality of evidence starts at a high level for prognostic factors according to the GRADE assessment in this type of design. The quality of evidence per outcome measure is shown in Table 5.6. The level for the return to sports outcome measure was reduced by 2 levels. This was due to imprecision and a high risk of bias in the study included.

Sub-question 3 (Prognostic factors)
Description of studies
To answer this sub-question, 1 prospective longitudinal study with a multivariate model and 3 studies with a univariate model were taken into account. The prospective longitudinal study, which incorporated a multivariate model, included a population of 58 patients with midportion Achilles tendinopathy.[9] Treatment consisting of eccentric exercise therapy with or without a night splint. The mean age was 51 years (range 36 to 64) and 59% of the patients were male. Forty-six patients completed the last follow-up, meaning that 21% were lost to follow-up. The follow-up duration was 5 years. The characteristics and main results of the 3 studies with univariate analyses can be found in Table 5.2.

All studies were assessed with the QUIPS Risk of Bias tool. For detailed results of the assessment, we refer to Table 5.3. Due to the limited number of studies that examined prognostic factors with a multivariate analysis, studies with a univariate analysis are also briefly described in the results and in Table 5.2. We did not perform a GRADE assessment for the studies with univariate analyses, because of the uncertainty of the evidence.

Results
For the answer to sub-question 3, the prognostic value of baseline variables, we used the primary outcome measure subjective recovery. The VISA-A score, patient satisfaction and return to sports were secondary outcome measures.

Studies with multivariate analysis
VISA-A score
Midportion Achilles tendinopathy
In the only prospective longitudinal study in which a multivariate analysis was performed in 58 patients, no prognostic factors were found that were associated with the prognosis of Achilles tendinopathy after treatment with eccentric exercise therapy with or without the addition of a night splint.[9] The following factors were investigated: age, gender, BMI, duration of symptoms at

baseline, thickness of the Achilles tendon on ultrasound and amount of ultrasonographic Doppler flow. No factors were associated with the final VISA-A score.

Subjective recovery
No studies were found on prognostic factors for subjective recovery.

Patient satisfaction
No studies were found on prognostic factors for patient satisfaction.

Return to sports
No studies were found on prognostic factors for return to sports.

Studies with univariate analysis
Midportion Achilles tendinopathy
A prospective longitudinal study in 38 patients showed a relationship between persistent symptoms 12 months after starting progressive exercise therapy and the VISA-A score after 5 years.[7] The asymptomatic group at 12 months after starting this treatment had a mean (SD) VISA-A score of 91 (10) after 5 years. The group that had persistent symptoms 12 months after starting treatment had a mean (SD) VISA-A score of 79 (7) after 5 years. The two groups differed significantly from each other (p=0.023). Other outcome measures examined were found to have no prognostic value for the degree of symptoms after 5 years of follow-up: age, sex and degree of kinesiophobia.

Insertional Achilles tendinopathy
No studies have been conducted on prognostic factors for insertional Achilles tendinopathy in the long term.

Achilles tendinopathy (unspecified midportion or insertional)
Two studies examined prognostic factors using a univariate model in a population with unspecified Achilles tendinopathy. In the largest study, 93 patients with Achilles tendinopathy were included and supervised for 6 months preforming eccentric and/or concentric exercise therapy with the addition of 1 to 3 injections of peritendinous corticosteroids if exercises were limited by pain.[4] After 10 years follow-up, the following factors were found to have no prognostic value for the degree of symptoms for insertional or midportion Achilles tendinopathy: an abnormal ultrasound structure of the Achilles tendon and the amount of ultrasonographic Doppler flow. In addition, the number of peritendinous injections with corticosteroids did not affect the outcome after 10 years. No factors were identified that were associated with symptoms in this group.
The second study was a prospective longitudinal study in which 56 patients with insertional or midportion Achilles tendinopathy were included and underwent 3 sessions of shockwave therapy at baseline.[8] After 2 years of follow-up, the following factors were found to have no prognostic value for the degree of symptoms: age and duration of symptoms at baseline. No prognostic factors were identified in this group.

Quality of evidence
The quality of the evidence is reported per prognostic factor and is based on the results from prospective longitudinal studies (cohort study or case series). Therefore, the quality starts at the high level for the GRADE-assessment. The level of evidence is shown per determinant in Table 5.7. The level was reduced by 2 levels for all determinants to low. The only study for answering the current sub-question was of low quality and imprecision could not be assessed due to the lack of confidence intervals.

Conclusions

Sub-question 1. What percentage of patients with Achilles tendinopathy have persistent symptoms for more than 1 year?

Midportion Achilles tendinopathy

Very low Grade	From 23 to 60% of patients with midportion Achilles tendinopathy have persistent symptoms after 2 to 5 years follow-up despite various non-surgical treatments. There may be a trend where less patients have persisting symptoms with longer follow-up. *Source: Paoloni et al.[6]; Silbernagel et al.[7]; van der Plas et al.[9] and Yeo et al.[10]*

Low Grade	After 2 to 10 years follow-up the VISA-A score in patients with midportion Achilles tendinopathy varies between 66 and 99 points, despite various non-surgical treatments. *Source: Johannsen et al.[4]; Paoloni et al.[6]; Silbernagel et al.[7] and van der Plas et al.[9]*

Low Grade	Patient satisfaction after 2 to 5 years seems to vary between 50 to 76% in midportion Achilles tendinopathy after various non-surgical treatments. There does not appear to be a higher patient satisfaction with a longer follow-up duration. *Source: van der Plas et al.[9] and Yeo et al.[10]*

Very low Grade	In patients with unilateral midportion Achilles tendinopathy, 9 to 43% developed symptoms on the asymptomatic side during 5 years of follow-up. *Source: Silbernagel et al.[7] and van der Plas et al.[9]*

Insertional Achilles tendinopathy

Low Grade	The VISA-A score in insertional Achilles tendinopathy is around 70 points, 2 years after undergoing non-surgical treatment. *Source: Taylor et al.[8]*

Low Grade	Patients with insertional Achilles tendinopathy report being on average, "somewhat improved" 2 years after non-surgical treatment. *Source: Taylor et al.[8]*

Achilles tendinopathy (unspecified midportion or insertional)

Low Grade	37% of patients have persistent symptoms of midportion or insertional Achilles tendinopathy at 10 years follow-up, despite several non-surgical treatments. *Source: Johannsen et al.[4]*

Low Grade	Patient satisfaction is around 93% in patients with midportion or insertional Achilles tendinopathy 2 years after non-surgical treatment. *Source: Monto et al.[5]*

Sub-question 2. What percentage of patients with Achilles tendinopathy return to their original level of sport over a period of more than 1 year?

Midportion Achilles tendinopathy

Low Grade	At least 85% of patients with midportion Achilles tendinopathy appear to return to their original level of sports after non-surgical treatment. *Source: Yeo et al.*[10]

Insertional Achilles tendinopathy

- Grade	Due to the lack of studies no conclusions can be drawn in insertional Achilles tendinopathy.

Sub-question 3. What factors affect the long-term prognosis (longer than 1 year) in patients with Achilles tendinopathy?

Midportion Achilles tendinopathy

Very low Grade	The following factors may not have prognostic value for midportion Achilles tendinopathy: age, gender, BMI, duration of symptoms at baseline, ultrasound tendon thickening and amount of ultrasonographic Doppler flow. *Source: van der Plas et al.*[9]

Insertional Achilles tendinopathy

- Grade	Due to the lack of studies, no conclusion can be drawn on possible prognostic factors for insertional Achilles tendinopathy.

Considerations

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

This module attempts to answer the question of what the long term prognosis for patients with Achilles tendinopathy is, and which factors affect it. Most studies with long-term follow-up were done in patients with midportion Achilles tendinopathy and to a limited extent in insertional Achilles tendinopathy.[4-10] Based on the available data comparing these two entities, there does not appear to be an obvious difference in prognosis. For this reason, the working group considered it plausible that the results of the studies in midportion Achilles tendinopathy can be extrapolated to insertional Achilles tendinopathy and in the considerations and recommendations they are discussed as one.

The starting point of sub-question 1 was to answer which percentage of patients experience persistent symptoms of Achilles tendinopathy after more than a year. According to the current literature, this rate appears to be between 23% and 60% after 2 to 5 years.[6 7 9 10] There is limited evidence that there is a lower percentage of patients with persistent symptoms as the follow up lengthens. Based on this, the workgroup acknowledged the existence of a reasonably large subgroup of patients who have persistent long term symptoms. The study with the longest follow-up duration (10 years), included both insertional and midportion Achilles tendinopathy. In this study, 37% of patients still had some degree of pain and functional impairment.[4] This was also found in a recently published abstract of a prospective cohort study in 43 of the 54 patients (80% follow-up) with midportion Achilles tendinopathy.[11] In this cohort, after 10 years, the rate of persistent complaints was 23%. As these results have not yet been published and were therefore not identified in the search strategy, this study can only be taken into account in these considerations. Figure 5.2 provides an overview of all studies with long-term follow-up in Achilles tendinopathy (insertional and midportion Achilles tendinopathy combined). The working group noted that the prognosis for those with short-living symptoms is largely unknown and may be more favourable. In a recently published prospective cohort study, new information about this subgroup has become available.[12] In this study, 100 runners with new onset Achilles tendon pain were included. After 1 year, 32% had persistent symptoms. Therefore, although a

substantial percentage of patients had persistent symptoms, the prognosis appears better than in patients with chronic (> 2 months) symptoms at the start of the study.

A more favourable prognosis is found when the VISA-A score is used as an outcome measure. According to the literature, the VISA-A score in midportion Achilles tendinopathy appears to vary between 66 and 99 points after 2 to 10 years.[4 6 7 9] As the VISA-A score is a continuous outcome measure, the interpretation is more difficult. Recent research shows that a score of 60 points or higher is rated by athletes as an acceptable level (PASS - Patient Acceptable Symptom State).[13] From that point of view, these averages can be interpreted as an acceptable outcome. What is striking, however, is that the distribution of VISA-A scores is very large (an SD mostly between 10 and 20 points). This possibly reflects the subgroup of patients who have a poor long-term outcome. Another potential disadvantage of the VISA-A score is that it does not directly inform whether an individual has achieved their goals. For example, an inactive person can score up to 60 points and be very satisfied with that outcome, while an athlete with a score of 60 points (maximum 100 points can be achieved for an athlete) is probably not satisfied.[14] This shows that the VISA-A score is more suited for use within a homogenous sporting population. However, a validation process is currently underway to develop a VISA-A questionnaire for inactive patients.[15] As a result, better distinction can be made in populations in the future and therefore more targeted research can be done. In addition, there may be a subgroup of people who are not fully recovered, but who participate in sports again. They have improved load bearing capacity (people score better on the VISA-A questionnaire), but are not completely free of symptoms.

Physical activity and sport can play an important role in Achilles tendinopathy. Johannsen et al.[4] report that 68 out of 93 patients included (73%) were active in sport prior to their Achilles tendon symptoms. Another study showed that 84% were injured during sports[7], and in another study, 42 out of 46 patients (91%) were active in sports prior to their injury.[9] These studies did not specify whether these were sports where the Achilles tendon is more heavily loaded and of the frequency of sports participation. Yeo et al.[10] reported that all patients undertook some form of regular physical activities (walking, running, cycling, golf, soccer and tennis). Taylor et al.[8] and Paoloni et al.[6] did not mention whether patients participated in sport. This indicates that the interpretation of the VISA-A score depends heavily on the patient's interpretation and on the instructions of the healthcare providers. This means that comparing VISA-A scores between different studies should be done with caution.

Patient satisfaction seems to vary between 50% and 76% after 2 to 5 years of follow-up.[9 10] Although this is an easily accessible outcome measure and can be explained quite understandably to patients, the disadvantage is that satisfaction can be determined by many factors. A patient may be satisfied with the quality of care provided and express this as a good patient satisfaction outcome, but this is not necessarily linked to a successful treatment.

There seems to be an increased risk of Achilles tendinopathy on the asymptomatic contralateral side within 5 years. Two studies specifically looked at this and found the probability was between 9 and 43%.[7 9] This phenomenon seems to be a regular occurrence; however it should be mentioned that there is a large spread of the data and methodological shortcomings of the studies included.

There are no studies in which the percentage of patients with persisting insertional Achilles tendinopathy symptoms is reported over a period of longer than 1 year. Only outcome measures using the VISA-A score and patient satisfaction have been examined in 1 study of low methodologically quality. The VISA-A score in patients with an insertional Achilles tendinopathy was 70 points, 2 years after shockwave therapy and the patients were on average "somewhat improved".[8]

Sub-question 2 focused on one of the main limitations for patients, the impairment of ability to tolerate (sports) loading. The working group was interested in the percentage of patients who could return to their original level of sports in the long term (> 1 year). A study in patients with

midportion Achilles tendinopathy described that more than 85% of patients returned to their previous sport.[10] This should be interpreted with caution because this conclusion is based on a study with low methodological quality. In the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) a retrospective study discussed a return to sports rate of 80% after 8 years.[16] Due to the very wide distribution of the follow-up moment (average 8 years, standard deviation 2 years) the results of this study cannot be translated into practice and was found not to be suitable for answering the research question. There are no studies that have described long-term return to sports in insertional Achilles tendinopathy. The working group wanted to stress that this outcome measure should be used more precisely in future research. It is important to know the following aspects of return to sports: do patients return to their desired sport? Do patients return to their previous level of sports? Do patients return to their previous level of performance? Do patients experience symptoms during their sports? These components have been identified as knowledge gaps.

Sub-question 3 focused on which factors affect the long-term prognosis (longer than 1 year after treatment). The following factors do not appear to have prognostic value: age, gender, BMI, duration of symptoms at baseline, ultrasound thickening of the Achilles tendon and amount of ultrasonographic Doppler flow. However, this is based on low quality evidence. These factors were also not predictive of the onset of Achilles tendinopathy (module 1 risk factors). It is important that health care professionals realise that these factors do not cause a poor long-term prognosis. The previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) reported that ultrasound grading of Achilles tendinopathy had prognostic value. This was based on the results of a study with a very wide range of follow-up (average 25 months, range 5 to 52 months) and was found unsuitable for answering the research question by our working group.[17] In addition, more recent data with an advanced ultrasound technique (Ultrasound Tissue Characterisation) shows that the degree of structural abnormalities is not a prognostic factor.[18] For this reason, the working group considered it plausible that clinically measurable ultrasound findings are not predictive for the long-term prognosis. There have been no studies investigating prognostic factors in insertional Achilles tendinopathy.

Patient values and preferences

A survey by the Netherlands Patient Federation showed that 63% of patients had a main objective of returning to sports (with or without residual symptoms). In particular, this module examines the long-term prognosis, with only one study reporting return to sports in patients with midportion Achilles tendinopathy. In this study that was at least 85%. This could mean that most patients can achieve their long-term goal. However, it is unknown whether their return to sports was at their previous level. The average VISA-A score of 66-99 points with a large variation implies that at some patients still had pain, most likely during and/or after sports.

Cost

It is likely that the cost of care will increase as a result of continued utilisation by patients who have persistent symptoms. The search for a solution is reflected by trying different treatments over time with different healthcare providers. This can potentially be overcome by a care coordinator who creates a realistic expectation pattern, helps decision making and motivates the patient in these often long journeys. The individual patient's coping strategy can affect the frequency of treatment. A study in the UK showed that if a specific guideline for Achilles tendinopathy was implemented within an orthopaedic department, the cost of care was reduced by 51% (from £13,340 to £5,660 per group, 46 patients per group).[19] In particular, savings were made on physiotherapy sessions, imaging and a reduction in repeated consultations. Recognition and counselling of this patient group is therefore also important in light of healthcare consumption and its financial consequences.

Acceptability for other stakeholders

As described earlier, there is a relatively large group of patients who continue to have complaints after more than year. Put into perspective of absolute numbers, this is even more impressive. The incidence of Achilles tendinopathy in Dutch general practice is approximately 2.35/1,000

registered adult patients.[20 21] With a total of 5,028 GP practices and an average of 2,095 enrolled people per practice, this equates to an absolute number of nearly 25,000 new patients with Achilles tendinopathy annually. Based on this, the subgroup who continue to have long-term symptoms would be around 6,000 people. Healthcare providers who treat these patients will have to deal with patients who have very longstanding and may be dissatisfied. These healthcare providers have a task to provide the right information and advice, focusing in particular on the long-term prognosis of Achilles tendinopathy. Important topics and treatment goals could be expectation management, influencing coping style, improving self-reliance, coaching and stimulating motivation.[22]

Feasibility and implementation
Not applicable

Balance between the arguments for and against the intervention
Not applicable

Figures and Tables supplementary Module 5

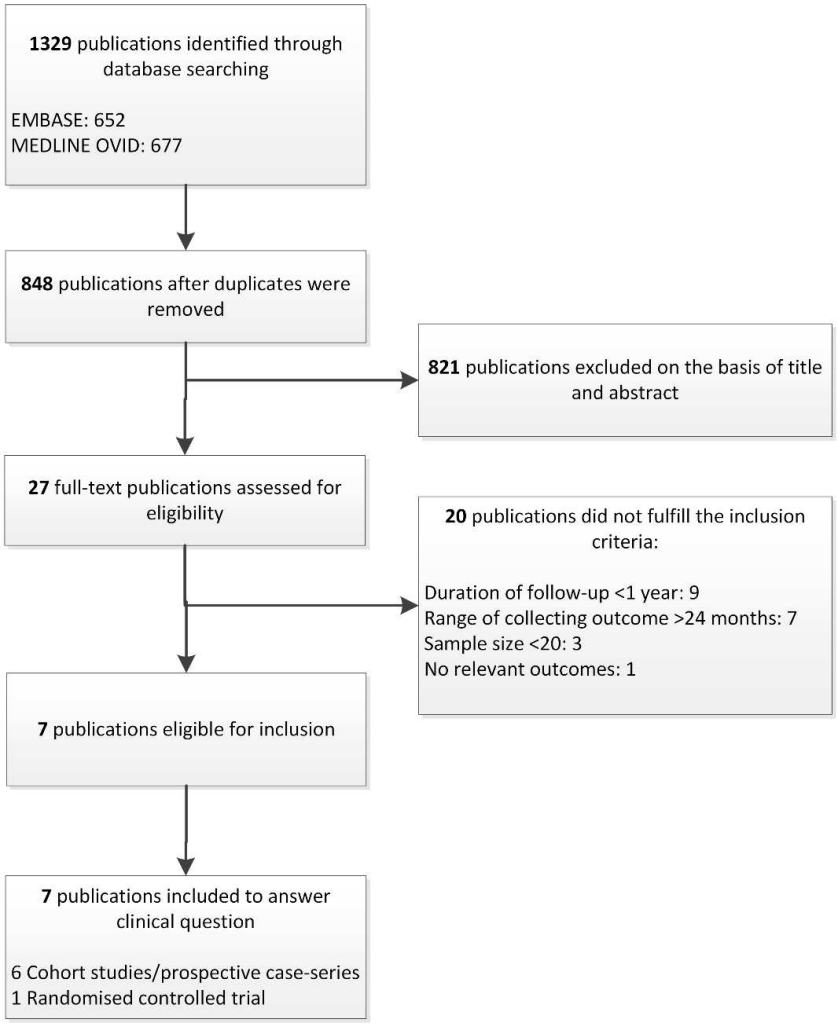

Figure 5.1 – PRISMA Flowchart of the study selection process: Module 5.

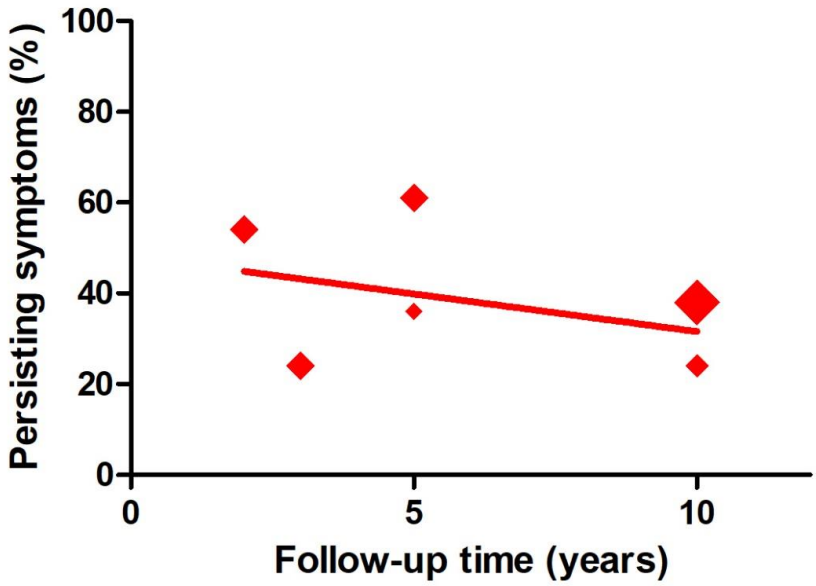

Figure 5.2 – An overview of subjective recovery over time for patients with Achilles tendinopathy. The diamonds represent individual studies which evaluated subjective recovery on the long term (>1 year). The size of the diamond represents the study size. The trendline shows the correlation between the different studies and shows a mild decrease of the percentage of persisting symptoms in time. In this figure we used the most recent data.

	Initial search	After deduplication
Embase.com	652	637
Medline ovid	677	211
Total	**1329**	**848**

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 ('cohort analysis'/exp OR 'longitudinal study'/de OR 'retrospective study'/exp OR 'prospective study'/exp OR 'follow up'/exp OR (cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR 'follow up*' OR followup*):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 (exp cohort studies/ OR (cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR follow up* OR followup*).ab,ti.)

Table 5.1 – Search strategy for Module 5 (prognosis of Achilles tendinopathy).

Study	Study characteristics	Patient characteristics	Treatment	Follow-up	Outcome measures	Results	Predictors
Johannsen et al. (2018)	Type of study: Prospective longitudinal study Setting: Outpatient rheumatology clinics around Copenhagen (Brønshøj and Farum), Denmark. Source of Funding: Non-commercial funding[1]	Inclusion criteria: • Local tenderness at palpation of the tendon, tenosynovium or tendon insertion impairing the daily activities of the patient. • ≥18 years old Exclusion criteria: • Arthritis • Type of AT: Insertional AT (n=18) and midportion AT (n=75) • Number of participants: 93 • Active participants: 91% • Mean age: 58.6 years (SD not reported for whole group) • Male subjects: 54%	Until 6 months of follow-up: Reduced running and jumping activities, concentric/eccentric exercises, calf stretching, and if training was impossible due to too severe pain supplemented with one to three ultrasound-guided CS injections (1 mL Lidocaine 10 mg/mL and 1 mL methylprednisolone acetate 40 mg/mL) in order to continue the training. After this period, patients were free to receive other treatments. 16% underwent surgery.	Length of follow-up: 10 years Loss to follow-up: 16/93; 5 deceased, 6 no contact possible, 1 moved abroad and 4 were not motivated	Primary and secondary outcomes were not specified: • Global assessment of function on a 4-grade scale • Tendon ruptures • Sought for other treatments • VISA-A score • VAS during 20 one-legged heel rises, pain at palpation and morning pain.	Excellent physical function was reported in 63% and a good physical function in 27%. VISA-A score was mean 84 (SD 19). The VISA-A score for midportion AT was 80 (SD 21) and for insertional AT 90 (SD 10).	Ultrasonographic heterogeneity and an increased blood flow at entry did not predict a poor outcome. No differences in outcomes of insertional and midportion Achilles tendinopathy. Analysis: Univariate

Monto et al. (2012)	Type of study: Prospective longitudinal study Setting: Not reported Source of Funding: Commercial funding[2]	Inclusion criteria: • Chronic unilateral Achilles tendinosis who had failed extensive traditional nonoperative management (rest, physical therapy, silicone heel lifts, CAM walker bracing, cast immobilisation, night splinting, and non-steroidal medication) for at least 6 months. Exclusion criteria: • None • Type of AT: Insertional AT and midportion AT • Number of participants: 30 • Active participants: 87% • Mean age: 47 years (range 33-	Platelet-rich Plasma injection (4 cc) followed by a standard home eccentric exercise program. No other treatment modalities were used during the study.	Length of follow-up: 2 years Loss to follow-up: 2/30; both had persisting pain	Primary and secondary outcomes were not specified: • AOFAS hindfoot score • Working status • MRI or ultrasound findings of chronic tendinitis (thickening, calcifications and/or tendon tears) • Satisfaction rate	28 of 30 patients were satisfied with the results of the PRP treatment at final 24-month follow-up.	None investigated

		66) • Male subjects: 57%					
Paoloni et al. (2007)	Type of study: Prospective longitudinal study (original study RCT) Setting: Orthopaedic Research Institute, St. George Hospital, New South Wales, Australia Source of Funding: Commercial funding[3]	Inclusion criteria: • Noninsertional Achilles tendinopathy (based on a history of an insidious onset, a tender nodule 2-6 cm from the calcaneal insertion, and an ultrasound examination excluding a frank tendon tear) • ≥18 years old Exclusion criteria: • Symptoms less than 3 months • Current pregnancy • Previous operation or dislocation of the affected ankle • Distal neurological signs • Local	Intervention: Active glyceril trinitrate patch, which delivered 1.25 mg of glyceril trinitrate every 24 hours. Patches were replaced daily and applied at the site of maximal tenderness for 6 months. Control: Placebo transdermal patch. Patches were replaced daily and applied at the site of maximal tenderness for 6 months. Co-interventions: All participants were instructed to perform a tendon rehabilitation program consisting of 1) rest from aggravating activities, 2) the use of 1-1.5 cm heel-raise wedges, 3) daily static stretching of the calf muscles, and 4) eccentric calf muscle-	Length of follow-up: 3 years Loss to follow-up: Intervention group: 8/32; 3 had to discontinue treatment because of side effects, 1 had relocated overseas, 1 suffered a recent Weber A fibular fracture, 1 had a posterior tibial tendon repair after acute tendon rupture, and 2 gave no reason Control group: 5/33; 1 had to discontinue treatment because of side	Primary and secondary outcomes were not specified: • Degree of Achilles tendon tenderness on a four-point scale • Patient rated pain score after the single-leg stationary 10 hop test (0-10) • VISA-A score • Recovery from initial injury (dichotomised VISA-A score)	88% of the patients in the intervention group were asymptomatic (VISA-A score of 100) after 3 years, compared to 67% in the control group (p=0.03). Combined outcome 77%. Total VISA-A scores at 3 years 98.9 (SD 3.6) for the intervention group and 94.6 (SD 2.9) for the control group. VISA-A score not determined at baseline. Return to previous level of activity not significantly different between both groups. Not	None investigated

		corticosteroid injection during the last 3 months • Type of AT: Midportion AT • Number of participants: 65 • Active participants: NR • Median age: 49 years (range 36-77) • Male subjects: 61.5%	strengthening program.	effects, 1 had relocated interstate, 1 had a lower limb reconstructive surgery after a motorbike accident, 1 had a operative correction of a hallux valgus, and 1 gave no reason		investigated whether trends of a decrease in time were significantly different. Raw data not presented.	
Silbernagel et al. (2011)	Type of study: Prospective longitudinal study (original study RCT) Setting: SportRehab physical therapy clinic, Göteborg, Sweden Source of Funding: Non-commercial funding[4]	Inclusion criteria: • Achilles tendinopathy (combination of Achilles tendon pain, thickening, and impaired performance) for more than 2 months. • 20-60 years Exclusion criteria: • injury to the foot, knee, hip, or back and/or history of rheumatoid arthritis or any	Intervention: Continued Achilles tendon-loading activity for the first 6 weeks using a pain-monitoring model (pain allowed to reach level 5 on the VAS-scale, running from 0-10). Control group: Active rest with restriction of physical activity that caused the symptoms for the first 6 weeks. Co-interventions: Progressive Achilles	Length of follow-up: 5 years Loss to follow-up: 4/38; 1 declined because of other illnesses, 3 did not return questionnaires	Primary and secondary outcomes were not specified: • Recovery from initial injury • Current symptoms • Other treatments • Satisfaction with treatment • VISA-A score • Physical activity score (6-point scale) • Tampa scale for Kinesiophobia • Test battery: Jump	VISA-A score was 90 (SD 11) at 5 year follow-up. 22 out of 34 (65%) patients were fully recovered at 5 year follow-up. 3 out of 34 (8.8%) patients developed symptoms on the previously uninjured side.	If there are continued symptoms at 12-month evaluation, VISA-A score at 5 year follow-up is significantly lower compared to asymptomatic patients (79±7 versus. 91±10). Age, sex, level of kinesiophobia, VISA-A score at baseline, 3 months, and 6 months do not

		other illness or injury thought to interfere with the participation in the study. • Patients with insertional tendinopathy • Type of AT: Midportion AT • Number of participants: 38 • Active participants: NR, mean Physical activity level scale moderate exercise 1-2 h/wk to moderate exercise >3 h/wk. • Mean age: 51 years (SD 8.2) • Male subjects: 52.9%	tendon-loading strengthening program for 12 weeks to 6 months. Exercises were performed once a day.		tests (countermovement jump, a drop CMJ, and hopping), 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 and tendon injury on ultrasound.		predict long-term outcome. Analysis: Univariate
Taylor et al. (2016)	Type of study: Prospective longitudinal study Setting: Not reported	Inclusion criteria: • A history, clinical and ultrasonographic features suggestive of refractory AT	Extracorporeal shockwave therapy. Three session with 2500 pulses per treatment were administered at weekly intervals. Frequency and pressure	Length of follow-up: 2 years Loss to follow-up: 10/56; Reasons	Primary and secondary outcomes were not specified: • VAS at rest and on activity • VISA-A score • Likert satisfaction	Midportion AT: VISA-A improved from 40 (range 9-94) at baseline to 66 (range 18-94) at 2 years ($p<0.0001$).	Age and duration of symptoms does not predict the VISA-A score at 2 years. Analysis: Univariate

	Source of Funding: Not reported	(>3 months duration) • Initially failed treatment by non-surgical means with eccentric exercises, heel inserts and/or non-steroidal anti-inflammatory drugs (NSAIDs) Exclusion criteria: • None • Type of AT: Insertional AT (n=20) and midportion AT (n=36) • Number of participants: 56 • Active participants: NR • Mean age: 54 years (range 38-80) • Male subjects: 58.7%	ranged from 10 Hz and 1.5 Bar respectively for the first 500 pulses increasing to a pressure of2.5 Bar for the remaining 2000 pulses, largely dictated by patient comfort.	not provided	scores (6 point scale)	Likert satisfactions scores were on average much improved. Insertional AT: VISA-A improved from 43 (range 7-72) at baseline to 70 (range 52-97) at 2 years (p=0.0006). Likert satisfactions scores were on average somewhat improved.	

Van der Plas et al. (2012)	Type of study: Prospective longitudinal study (original study RCT) Setting: Sports Medicine Department, The Hague Medical Centre, Leidschendam, The Netherlands Source of Funding: Not reported	Inclusion criteria: • Chronic midportion AT • Presence of symptoms for more than 2 months • Participation in sporting activities and the wish to return • 18-70 years Exclusion criteria: • Previous performance of an intensive program of heavy-load eccentric exercises • Inability to perform heavy-load exercises. • Tendon ruptures • Systemic illness • Type of AT: Midportion AT • Number of participants: 58 • Active	Intervention: Night splint. Patients had to maintain a neutral position (0°) for the first 4 weeks, and after this period a dorsiflexed position of at least 5° was used. Control: None besides co-interventions. Co-interventions: Eccentric calf muscle exercises 180 repetitions per day. Patients should ignore the pain and if exercises could be performed without any discomfort, load was increased using a backpack. All patients were instructed to avoid weight-bearing sporting activities for the first 4 weeks. After 4 weeks, gradual Return to sports s activities was encouraged if the pain allowed.	Length of follow-up: 5 years Loss to follow-up: 12/58; 6 patients were not reachable for follow-up, 5 patients refused to participate, and 1 had a direct trauma to the Achilles tendon 2 days before follow-up.	Primary outcome: • VISA-A score Secondary outcomes: • Pain status (pain-free, not pain-free) • Condition of the uninvolved tendon (affected, not affected) • Subjective patient satisfaction • Received alternative treatments • Continuation of the eccentric exercises (continued, stopped after the heel-drop program)	The VISA-A score improved from 49.2 (SD 20.1) at baseline to 83.6 (SD 14.9) at 5-year follow-up ($p<0.001$). 39.7% reported to be completely pain-free at 5-year follow-up. Of the patients with unilateral AT, 43.3% developed some degree of pain in the contralateral tendon during the 5-year follow-up. 50% of the patients reported a excellent or good patient satisfaction and 50% a moderate or poor satisfaction at 5-year follow-up (8.6% excellent, 41.1% good).	Age, sex, BMI, duration of symptoms at baseline, degree of neovascularisation at baseline, and sagittal tendon thickness at baseline do not influence the VISA-A score at 5-year follow-up or the difference in VISA-A score between baseline and 5-year follow-up. Analysis: Multivariate

		participants: 91% • Mean age: 50.9 years (range 36-64) • Male subjects: 58.7%					
Yeo et al. (2016)	Type of study: Prospective longitudinal study Setting: Tertiary unit, not further specified Source of Funding: Not reported	Inclusion criteria: • Non-insertional Achilles tendinopathy confirmed on ultrasound • Presence of symptoms for more than 3 months • ≥18 years Exclusion criteria: • Partial or complete tendon rupture as diagnosed on ultrasound • Not able to comply with our rehabilitation protocols (e.g. learning disability) • Phobia of needles • Coexisting causes of lower leg pain	Ultrasound-guided intratendinous needling of neovascular areas and small-volume hydrostatic paratenon decompression was performed 6-weekly. All patients then underwent a standardised physiotherapy regime for 4 weeks concentrating on eccentric exercises. There were no restrictions with regard to Return to sports activities. This procedure was repeated at 6-weekly intervals if there was sonographic evidence of persistent paratenon adhesion and neovascularity until symptomatic resolution or no improvement was evident.	Length of follow-up: 2 years Loss to follow-up: 4/21; Reasons not provided	Primary outcome: • VAS at rest and during activity Secondary outcomes: • Return to sports • Satisfaction level • Anteroposterior diameter of the tendon • Neovascularity score	76 % (16 tendons) of patients had very high or high satisfaction level with 8/17 (47%) patients having complete resolution of symptoms. All 17 patients were able to continue their sporting interests.	None investigated

		(e.g. sciatica) • Type of AT: Midportion AT • Number of participants: 21 • Active participants: 100% • Mean age: 55.3 years (range 39-76) • Male subjects: 42.9%					

Table 5.2 – Evidence table of included prospective studies (randomised, cohort and case-series) which investigated the long term prognosis (> 1 year) of Achilles tendinopathy.
Abbreviations: AT, Achilles tendinopathy; RCT, Randomised controlled trial; SD, Standard deviation; VAS, Visual analogue scale; VISA-A, Victorian Institute of Sport Assessment – Achilles.
[1] The study was funded by 'Fonden for Faglig udvikling I Speciallægepraksis' governmental support.
[2] Lead author has received benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article. Not further specified who the sponsor was.
[3] Lead author received a one-time monetary payment to fund the pretrial pilot study from Schering-Plough Australia.
[4] Swedish National Centre for Research in Sports and the local Research and Development Council of Gothenburg and Southern Bohuslän.

Study	**Domains**							
	Study Participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Other bias	Overall quality
Johannsen et al. (2018)	+	?	-	+	?	NA[1]	No	+
Monto et al. (2012)	?	+	NA[2]	?	?	NA[1]	No	+

Paoloni et al. (2007)	?	?	NA[2]	+	?	-	No	+
Silbernagel et al. (2011)	?	?	+	+	?	+	No	+
Taylor et al. (2016)	?	?	-	+	?	NA[1]	No	+
Van der Plas et al. (2012)	+	?	?	+	?	+	No	++
Yeo et al. (2016)	+	?	NA[2]	?/+[3]	?	?	No	+

Table 5.3 – Risk of bias of the included prospective longitudinal studies which investigated the long term prognosis (> 1 year) of Achilles tendinopathy.
For individual domains: + low risk of bias, ? unclear risk of bias, - high risk of bias.
For overall quality: +++ high quality, ++ acceptable quality, + low quality.
Abbreviations: NA, Not applicable
1 Only descriptive reporting of the data.
2 No prognostic factors were investigated.
3 Low risk of bias for outcome continued sporting activities, unclear risk of bias for outcome patient satisfaction

Study	Duration follow-up	Percentage of persistent complaints during follow-up
Yeo, 2016 [10]	2 years	53%
Paoloni, 2007 [6]	3 years	23%[1]
Silbernagel, 2011 [7]	5 years	35%
van der Plas, 2012 [23]	5 years	60%

Table 5.4 – Overview of studies with more than 1 year follow-up that assessed the percentage of patients with persistent symptoms. All studies were conducted in midportion Achilles tendinopathy.
[1] Based on the dichotomised VISA-A score, where a score of 100 corresponds to asymptomatic and a score of ≤ 99 with symptomatic.

Study	Duration follow-up	VISA-A score during follow-up (including measures of dispersal)
Taylor, 2016 [8]	2 years	66 (range 18-94)
Paoloni, 2007 [6]	3 years	95– 99 (SD not explicitly stated) [1]
van der Plas, 2012 [23]	5 years	84 (SD 15)
Silbernagel, 2011 [7]	5 years	90 (SD 11)
Johannsen, 2018 [4]	10 years	80 (SD 21)
[1] Presented as the combined results of a randomised trial. See main text for details		

Table 5.5 – Overview of studies with more than 1 year of follow-up that assessed the VISA-A score. All studies included patients with midportion Achilles tendinopathy.

Outcome measure	Number of studies	Inconsistency	Indirectness	Imprecision	Other considerations	Effect size	Dose-response relationship	Effect of confounders	Study quality (QUIPS Risk of Bias tool)	Quality of evidence
Midportion Achilles tendinopathy										
VISA-A score	4	No serious inconsistency	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low
Subjective recovery	4	Serious inconsistency	No serious indirectness	Serious imprecision	None	-	-	-	Low	Very low
Patient satisfaction	2	No serious inconsistency	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low
Symptoms contralateral side	2	Serious inconsistency	No serious indirectness	Serious imprecision	None	-	-	-	Low	Very low
Return to sports s	1	-	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low
Insertional Achilles tendinopathy										
VISA-A score	1	-	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low
Subjective recovery	1	-	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low
Achilles tendinopathy (location not specified)										
Subjective recovery	1	-	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low
Patient satisfaction	1	-	No serious indirectness	Serious imprecision	None	-	-	-	Low	Low

Table 5.6 – GRADE-assessment for the prognosis of Achilles tendinopathy.

Potential prognostic factors	Number of studies	Study limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Effect size	Dose-response relationship	Effect of confounders	Study quality (QUIPS Risk of Bias tool)
Patient characteristics (non-modifiable)										
Age	1	Acceptable quality	-	No serious indirectness	Precision not reported	None	-	-	-	Low
Sex	1	Acceptable quality	-	No serious indirectness	Precision not reported	None	-	-	-	Low
BMI	1	Acceptable quality	-	No serious indirectness	Precision not reported	None	-	-	-	Low
Duration of symptoms	1	Acceptable quality	-	No serious indirectness	Precision not reported	None	-	-	-	Low
Tendon thickness (AP) measured on ultrasound	1	Acceptable quality	-	No serious indirectness	Precision not reported	None	-	-	-	Low
Intratendinous and/or peritendinous Doppler flow on ultrasound	1	Acceptable quality	-	No serious indirectness	Precision not reported	None	-	-	-	Low

Table 5.7 – GRADE-assessment of prognostic factors for Achilles tendinopathy.

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