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Differences in Recovery of Tendon Health Explained by Midportion Achilles Tendinopathy Subgroups: A 6-Month Follow-up

The persistent symptoms and loss of function[45] accompanying Achilles tendinopathy impair quality of life and interfere with social roles and occupational productivity.[51] Achilles tendinopathy occurs equally in men and women, with highest prevalence in people aged 35 to 56 years.[14] Most cases are associated with overuse, with a lifetime incidence of 50% among runners, although 65% of cases in the general population are not sport related.[14,27] The general health impairments and alterations in tendon structure associated with Achilles tendinopathy can be characterized on a spectrum, with severity ranging widely among patients.[35] Collectively, these impairments can be described across domains of tendon health,[47] consisting of symptoms, tendon structure, lower extremity function, psychological factors, and patient-related factors.

OBJECTIVES: To (1) evaluate whether the defining characteristics of previously reported Achilles tendinopathy subgroups were reproducible in a cohort with midportion Achilles tendinopathy and (2) compare recovery trajectories and outcomes.

DESIGN: Prospective single cohort study.

METHODS: Participants (n = 114; 57 women; age [mean ± standard deviation]: 47 ± 12 years) received the Silbernagel protocol and were evaluated at baseline, and at 8, 16, and 24 weeks. Subgroups were identified using mixture modeling. Main effects of group and time, and interaction effects were evaluated using linear mixed models for 23 outcome measures representing symptoms, lower extremity function, tendon structure, psychological factors, and patient-related factors. Recovery trajectories were reported descriptively to reflect clinically meaningful change for outcomes.

RESULTS: Activity-Dominant (n = 34), Function-Dominant (n = 38), Psychosocial-Dominant (n = 27), and Structure-Dominant (n = 15) subgroups were identified. There were significant effects of group and time for all primary outcome measures, except heel-rise and viscosity limb symmetry indexes. The Activity- and Function-Dominant subgroups achieved functional recovery despite persisting symptoms. The Psychosocial-Dominant subgroup reported the greatest impairments in symptom and foot- and ankle-related quality of life at all time points. The Structure-Dominant subgroup experienced delayed improvement in symptoms and was the only subgroup to not achieve structural recovery. No subgroup met our criteria for complete recovery.

CONCLUSION: The defining characteristics of Achilles tendinopathy subgroups were reproduced in a cohort with midportion Achilles tendinopathy. The Activity- and Function-Dominant subgroups had superior outcomes compared to the Psychosocial- and Structure-Dominant subgroups for symptomatic, functional, and structural recovery. *J Orthop Sports Phys Ther 2023;53(4):217-234. Epub: 23 January 2023. doi:10.2519/jospt.2023.11330*

KEYWORDS: *exercise therapy, mixture modeling, recovery, tendon*

We previously identified 3 specific clinical profiles (subgroups) of people with insertional and midportion Achilles tendinopathy[22]:

- Activity-Dominant: physically active young adults (55% male) experiencing persistent symptoms and minimal-to-no disturbance in all other tendon health domains
- Psychosocial-Dominant: middle-aged individuals (66% female) with severe symptoms, high kinesiophobia (fear of movement), poor quality of life, and minimal-to-no tendon damage
- Structure-Dominant: older individuals (77% male) with substantial tendon damage and severe lower extremity function impairment

It is unclear whether the different subgroups respond to treatment in different ways. Describing recovery trajectories for each tendon health domain can reveal how each subgroup improves or declines over time, and identify delayed recovery. Evaluating differences in recovery (trajectories and outcomes) may inform prognostic factors and future hypotheses about individualized strategies for people with persisting deficits who may benefit from additional treatment.

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A challenge when evaluating recovery is defining what recovery is and when it occurs. Historically, the hallmark of recovery was resolution of symptoms and pain with activity.[20,25,36] However, symptom resolution does not ensure recovery within other domains,[20,54] and alterations in Achilles tendon structural and mechanical properties moderate patient-reported symptoms and function.[11,15] Therefore, addressing each tendon health domain might be vital for recovery.[10,32] Recovery is different for people with midportion and insertional Achilles tendinopathy.[22] Insertional Achilles tendinopathy does not respond as favorably to exercise therapy[4,16] as midportion Achilles tendinopathy and is frequently accompanied by additional pathological findings such as bone defect, bursitis, and enthesophytes.[56]

The purpose of this study was to evaluate (1) whether the defining characteristics of the subgroups were reproducible in a cohort with only midportion Achilles tendinopathy and (2) whether the subgroups recovered differently within the domains of tendon health, when treated with the same treatment protocol.

MATERIALS AND METHODS

This was a prospective cohort study including participants with midportion Achilles tendinopathy. The data were from a larger clinical trial (ClinicalTrials.gov; NCT03523325), providing 1 year of treatment. Data from baseline and at 8, 16, and 24 weeks were analyzed. Data were collected between August 2018 and November 2021. This study received approval by the University of Delaware Institutional Review Board (1063764-12).

Participants

Participants were between 18 and 65 years old, had a chief complaint of pain located within the Achilles tendon midportion (2-6 cm above the calcaneus), had pain with palpation, and experienced pain with loading.[31] Exclusion criteria were previous Achilles tendon rupture, a diagnosis of only insertional Achilles tendinopathy or bursitis, or any other injury that limited the ability to perform exercises on the injured limb. Participants were recruited through flyers, referrals from physician and community physical therapists, and social media. Sixty-one participants with midportion Achilles tendinopathy were included from the previous cohort.[22]

Exercise Therapy Intervention

All participants received the same comprehensive treatment protocol.[49] The Silbernagel protocol and criteria for progression are provided in **APPENDIX A**. Treatment was provided at the University of Delaware Physical Therapy Clinic by physical therapists who were trained to provide the intervention. Clinicians were blinded to outcomes testing and participants' subgroup membership. Frequency of supervised treatment visits and progression was determined at the discretion of the treating clinician. Participants were asked to complete training diaries daily, documenting their exercises, any physical activity, and symptoms/pain level (morning, highest, and lowest).[47,49] Training diaries were reviewed weekly to monitor and progress treatment. The pain-monitoring model (**APPENDIX A**) was used to adjust the exercise load, and physical activity was guided by pain during and after activity.[49,53] Load progression comprised increasing range of motion, repetitions, and adding external load (eg, weight vest or weight machine). At the discretion of the physical therapist, participants were discharged when they met their functional and/or physical activity goals and were independent with managing any remaining symptoms with a maintenance loading program. The number of completed treatment visits was recorded. Participants were encouraged to contact the study team with questions following discharge and could return for treatment if they had a change in status and were unable to self-manage their symptoms.

Outcome Measures

Patient characteristics and medical history were collected at baseline following ICON 2020 recommendations.[40] Recovery (outcomes) at 24 weeks was defined within the domains of tendon health[47] (symptomatic, functional, structural, and psychosocial recovery) represented across 23 outcome measures. All outcome measures, definitions, and recovery criteria are described in **TABLE 1**.

Symptomatic, Functional, Structural, and Psychosocial Outcomes

Symptomatic recovery was assessed with the Victorian Institute of Sport Assessment-Achilles (VISA-A)[41] and self-reported pain with hopping. Participants completed the VISA-A for both limbs. In cases of bilateral symptoms, the most symptomatic limb (lower VISA-A score) was used for data analysis. Participants completed 2 trials of 25 single-leg hops[46] (similar cadence to jumping rope) and immediately rated their Achilles tendon pain.

Functional recovery was assessed using a functional test battery, described in detail by Silbernagel et al.[46] Tests included the countermovement jump, drop countermovement jump, and heel-rise endurance test using a MUSCLELAB™ measurement system (Ergotest Innovation, Porsgrunn, Norway). Physical activity was measured using the Physical Activity Scale (PAS).[21] The PAS is a Likert scale, ranging from (1) hardly any physical activity to (6) hard or very hard physical activity, several times per week.

Structural recovery was assessed by measuring Achilles tendon morphology (B-mode ultrasound) and mechanical properties (continuous shear wave elastography [cSWE]). Ultrasound images were taken using a GE LOGIQ e ultrasound scanner (linear transducer, frequency: 10 MHz, depth: 3.5 cm [General Electric Company, Boston, MA]). Degree of tendon thickening, Achilles tendon thickness and cross-sectional area (CSA) at the thickest portion were measured with the participant lying prone with their feet hanging off the edge of the table.[48,57] Tendon thickening was calculated by subtracting the thickness of healthy

TABLE 1 SUMMARY OF OUTCOME MEASURES

Outcome Variable	Evaluation Method	Definition/Description	Recovery Definition
Symptomatic recovery	VISA-A questionnaire[a]	• Score range of 0 to 100, lower scores indicate more pain and symptoms[41] • MCID of 14 points by 16 weeks[29]	• Score ≥90 points at 24 weeks[50]
	Pain with hopping	• Self-rated Achilles tendon pain with single-leg hopping (25 hops)[46] • Numerical pain-rating scale from 0 to 10 (no pain to worst pain imaginable) • Represents tendon loading tolerance • MCID of 2 points[17]	• ≤2/10 pain with hopping
Functional recovery	Functional test battery consisting of the heel-rise endurance test[a] and 2 jump tests	• The heel-rise test evaluates calf muscle endurance. Total work is expressed in joules (heel-rise height × repetitions × body mass).[46] • Jump tests include the countermovement jump (CMJ) and drop countermovement jump (Drop CMJ). • Average height measured in centimeters from 3 trials for each jump test[46]	• Limb symmetry index (LSI) ≥90% at 24 weeks (most symptomatic limb/least symptomatic limb ×100)[50]
Structural recovery	Tendon morphology: degree of tendon thickening,[a] Achilles tendon thickness, and cross-sectional area (CSA)	• Measured using B-mode ultrasound imaging • Tendon thickening in millimeters describes tendon structural abnormality (difference between healthy tendon thickness and the maximum thickness on the injured tendon). • Two millimeter thickening or more is pathologic.[28] • Maximum Achilles thickness measured in centimeters and CSA measured in square centimeters[48,57]	• LSI values 100 ± 10% at 24 weeks for Achilles thickness, CSA, shear modulus, viscosity
	Tendon mechanical properties: viscosity[a] and shear modulus	• Viscosity measured in Pa·s and shear modulus measured in kilopascals are calculated using continuous Shear Wave Elastography (cSWE)[12,13]	
Psychosocial recovery	FAOS-QoL[a]	• Score range of 0 to 100, with 100 being highest quality of life[42]	• Score ≥90 points at 24 weeks
	TSK-17[a]	• Evaluates fear of movement with score range of 17 to 68. Higher scores mean more fear; scores ≥37 indicate high kinesiophobia.[3,18,30]	• Score <37 points at 24 weeks
	PROMIS-29 subscales	• PROMIS-29 subscales include Social Roles and Activities (PROMIS-SRA), Pain Interference with functioning (PROMIS-PI), Anxiety (PROMIS-ANX). T-scores are calculated for each; higher scores indicate greater presence of the concept being measured.[6]	• T-scores of 50 ± 10 points
	GROC	• Represents change in overall status on a Likert scale ranging from −5 to +5 ("very much worse" to "completely recovered")[34]	• Reported descriptively

Abbreviations: FAOS-QoL, Foot and Ankle Outcome Score-Quality of Life; GROC, global rating of change; MCID, minimally clinically important change; PROMIS-29, Patient-Reported Outcomes Measurement Information Systems-29; TSK-17, Tampa Scale of Kinesiophobia-17 item; VISA-A, Victorian Institute of Sport Assessment-Achilles.
[a]Primary outcome measures.

uniform tendon from the thickest portion of the injured tendon.[11] Continuous shear wave elastography is a valid and stable method for monitoring changes in injured tendon and allows for calculation of 2 tendon mechanical properties: shear modulus (ie, stiffness) and viscosity (ie, rate-dependent stiffness).[12,13] Continuous shear wave elastography data were collected with the participant prone and the ankle positioned at 10 degrees of dorsiflexion using a SonixMDP Q+ ultrasound scanner (Ultrasonix, Vancouver, Canada) with a L14-5/38 probe, a 128-channel data acquisition unit, and an external actuator, which generate shear waves, placed on the posterior lower leg. This method is described in detail by Cortes et al[13] and Corrigan et al.[12]

Psychosocial recovery was assessed using the Foot and Ankle Outcomes Score Quality of Life Subscore (FAOS-QoL),[42] the Tampa Scale of Kinesiophobia-17 item (TSK-17),[3,18,30] select subscales from the Patient-Reported Outcomes Measurement Information Systems-29 (PROMIS-29),[6] and the global rating of change (GROC).[34]

Statistical Analysis

Subgroup membership was determined using mixture modeling from 14 variables[22] representing the domains of tendon health (**APPENDIX B**). Mixture modeling reveals hidden groups among individuals who are assumed to be homogenous.[26,38]

The number of subgroups was determined by comparing model fit between *K*-classes and *K*-1 class. **APPENDIX C** details these model fit statistics[1,5,23,44] and interpretation.[19,23,55] Baseline differences among subgroups were evaluated using 1-way analysis-of-variance or chi-square tests. Significant main effects of group, time, and interaction (group × time) were evaluated using linear mixed models for all outcome measures (primary outcomes: VISA-A, heel-rise work limb symmetry index (LSI), tendon thickening, viscosity LSI, FAOS-QoL, and TSK-17 evaluated at $\alpha = .05$; secondary outcomes at $\alpha = .001$). Pairwise comparisons were tested post hoc using Bonferroni correction. Group, time, and their interaction were included as fixed effects. A compound symmetric covariance matrix was used to model the correlation among residuals. Residuals were tested using Shapiro-Wilk tests to test the assumption of normality and detect outliers. Recovery trajectories for each domain were reported descriptively, and differences were defined by either a statistically significant interaction effect or observed differences in clinically important improvement, decline, or nonchange over time points.

RESULTS

One-hundred fourteen participants were included in this study. The best-fitting mixture model (**APPENDIX C**) identified 4 subgroups: Activity-Dominant (n = 34), Function-Dominant n = 38), Psychosocial-Dominant (n = 27), and Structure-Dominant (n = 15) (**FIGURE 1**). Including 61 participants from the previous cohort did not affect model fit (**APPENDIX E**).

Baseline Characteristics of Subgroups

The characteristics of the subgroups and distinctions among them were akin to the subgroups profiled in the previous study.[22] Baseline characteristics are presented in **TABLE 2**. Activity-Dominant participants were youngest (37 ± 10 years) compared to Function-Dominant (50 ± 10 years), Psychosocial-Dominant (50 ± 11 years), and Structure-Dominant (58 ± 6 years). Majority of Function-Dominant and Activity-Dominant were runners (68% and 68%, respectively) compared to Psychosocial-Dominant (29.6%) and Structure-Dominant (zero runners). Psychosocial-Dominant

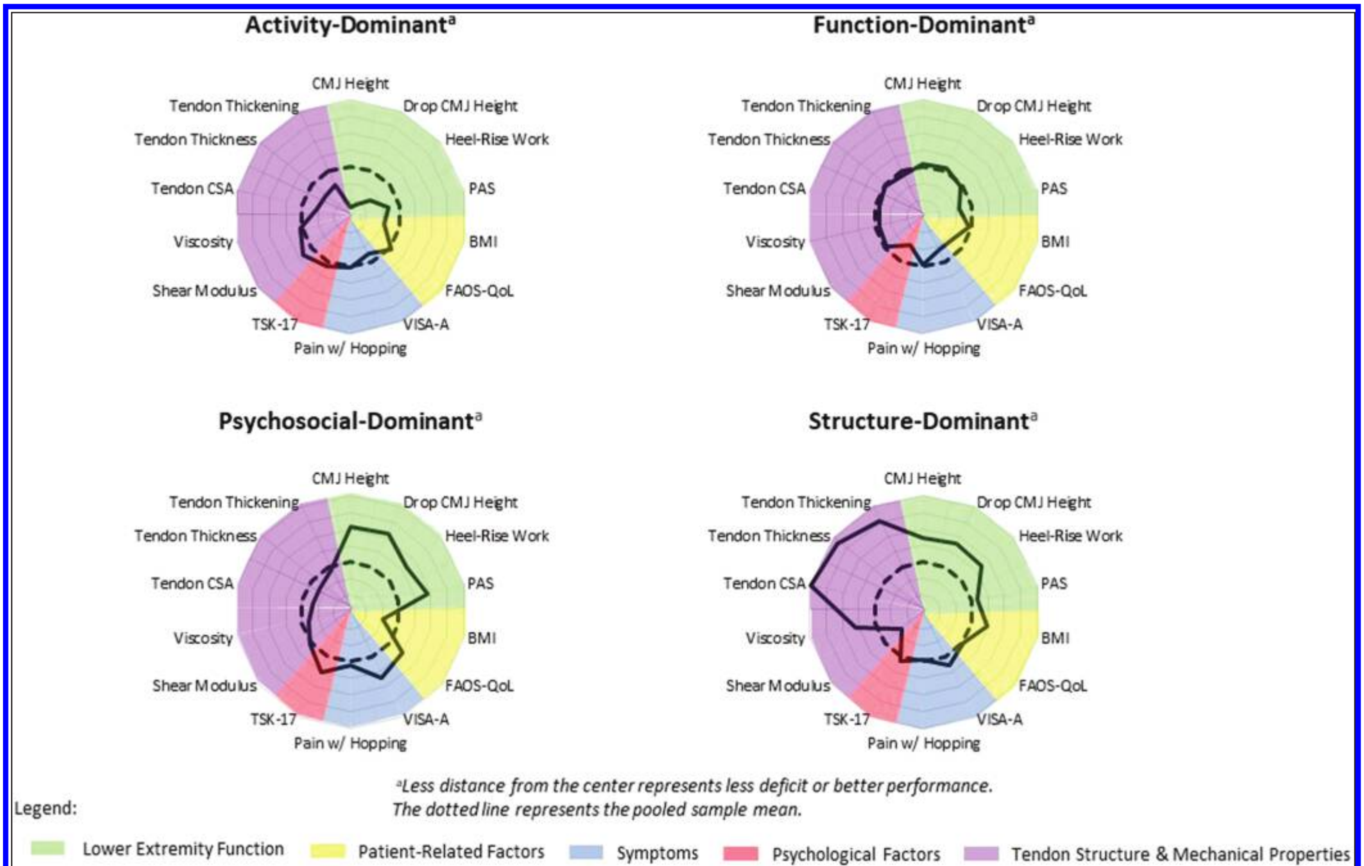


FIGURE 1. Comparison of subgroup baseline characteristics, separated by tendon health domain. Abbreviations: BMI, body mass index; CMJ, countermovement jump; CSA, cross-sectional area; FAOS-QoL, Foot and Ankle Outcomes Score-Quality of Life; PAS, Physical Activity Scale; TSK-17, Tampa Scale of Kinesiophobia-17 item; VISA-A, Victorian Institute of Sport Assessment-Achilles.

TABLE 2 Summary of Subgroup Demographics and Baseline Characteristics

	Pooled Sample (n = 114)	Activity-Dominant (n = 34, 30%)	Function-Dominant (n = 38, 33%)	Psychosocial-Dominant (n = 27, 24%)	Structure-Dominant (n = 15, 13%)	ANOVA P Value	AD vs FD	AD vs PD	AD vs SD	FD vs PD	FD vs SD	PD vs SD
Age, years	47 ± 12 (45-49)	37 ± 10 (33-41)	50 ± 10 (47-53)	50 ± 11 (45-55)	58 ± 6 (54-61)	**<.001**	**<.001**	**<.001**	**<.001**	1.000	.071	.083
Height, cm	171.7 ± 8.6 (170.1-173.3)	174.3 ± 8.2 (171.5-177.2)	170.4 ± 8.5 (167.6-173.2)	167.3 ± 6.4 (164.8-169.9)	176.9 ± 9.0 (171.9-181.9)	**<.001**	.177	**.006**	.722	.420	**.045**	**.002**
Body mass, kg	84.4 ± 19.2 (80.7-88.0)	78.1 ± 11.2 (74.2-82.0)	81.8 ± 24.0 (74.0-89.7)	88.1 ± 16.3 (81.7-94.6)	98.7 ± 17.5 (89.1-108.4)	**<.001**	.822	.150	**.002**	.522	**.015**	.275
BMI	28.6 ± 6.1 (27.4-29.7)	25.7 ± 3.2 (24.6-26.7)	28.0 ± 7.3 (25.6-30.4)	31.6 ± 6.0 (29.2-33.9)	31.5 ± 4.9 (28.6-34.2)	**<.001**	.335	**<.001**	**.007**	.065	.176	1.000
Sex, Female	57 (50%)	9 (26.5%)	20 (52.6%)	23 (85%)	5 (33%)	**<.001**[b]	**.031**	**<.001**	.735	**.008**	.237	**.001**
Symptom duration, months, median [IQR]	10.2 [29.1]	15.2 [42.4]	23.5 [31.1]	7.1 [31.6]	5.5 [16]	.800	.999	.998	.828	.991	.866	.773
Previous history of Achilles tendinopathy, n (%n)	20 (17.5%)	0	8 (21%)	4 (14.8%)	3 (20%)	.857[b]	.551	1.000	.687	.747	1.000	.686
Comorbidities, n (%n)												
Diabetes Mellitus	1 (.8%)	0	0	1 (3.7%)	0	.355[b]	NT	.443	NT	.415	NT	1.000
Rheumatological	2 (1.8%)	0	1 (2.6%)	1 (3.7%)	0	.650[b]	1.000	.443	NT	1.000	1.000	1.000
Thyroid	9 (7.9%)	1 (2.9%)	3 (7.8%)	4 (14.8%)	1 (6.6%)	.398[b]	.617	.161	.523	.437	1.000	.639
Medications, n (%n)												
Fluroquinolones	7 (6.1%)	2 (5.8 %)	1 (2.6%)	3 (11.1%)	1 (6.6%)	.576[b]	.599	.647	1.000	.299	.490	1.000
Steroids	4 (3.5%)	0	1 (2.6%)	3 (11.1%)	0	.091[b]	1.000	.081	NT	.299	1.000	.541
Statins	11 (9.6%)	1 (2.9%)	3 (7.8%)	3 (11.1%)	4 (26.7%)	.074[b]	.617	.313	**.026**	.686	.090	.225
Identify as a runner, n (%n)	57 (50%)	23 (67.6%)	26 (68.4%)	8 (29.6%)	0	**<.001**[b]	1.000	**.009**	**<.001**	**.005**	**<.001**	**.018**
Bilateral symptoms, n (%n)	49 (43%)	17 (50%)	20 (52.6%)	9 (33.3%)	3 (20%)	.060[b]	1.000	.207	.064	.138	**.037**	.485
Physical Activity Scale, median [IQR]	5 [2] (4-5)	5 [1] (5-5)	5 [1] (5-5)	3 [2] (3-4)	5 [2] (4-5)	**<.001**	.982	**<.001**	.982	**<.001**	.153	**.040**
VISA-A	51 ± 18 (47-54)	55 ± 15 (49-60)	58 ± 15 (53-62)	38 ± 17 (31-45)	46 ± 20 (35-56)	**<.001**	.895	**<.001**	.258	**<.001**	.079	.4687
Heel-rise work LSI	91.9 ± 30.2%	102.6 ± 18.0%	94.9 ± 19.8%	85.0 ± 39.5%	71.0 ± 44.1	**.005**	.684	.106	**.005**	.550	**.046**	.464
Tendon thickening, mm	2.38 ± 1.93	1.53 ± 1.21	2.11 ± 1.57	2.16 ± 1.51	5.36 ± 2.09	**<.001**	.376	.398	**<.001**	.999	**<.001**	**<.001**
Viscosity LSI	98.0 ± 34.1%	92.3 ± 23.2%	96.4 ± 90.1%	112.7 ± 49.9%	92.6 ± 30.2%	.158	.965	.152	1.000	.289	.986	.315
FAOS-QoL	40 ± 18 (37-43)	39 ± 18 (33-45)	47 ± 15 (43-52)	31 ± 16 (24-38)	40 ± 22 (37-52)	**.004**	.176	.297	.999	**.002**	.458	.427
TSK-17	38 ± 5 (37-39)	39 ± 5 (37-41)	35 ± 5 (34-37)	41 ± 5 (39-43)	39 ± 5 (36-42)	**<.001**	**.009**	.390	1.000	**<.001**	.064	.581

Abbreviations: AD, Activity-Dominant; BMI, body mass index; FD, Function-Dominant; FAOS-QoL, Foot and Ankle Outcomes Score-Quality of Life; IQR, interquartile range; LSI, limb symmetry index; PD, Psychosocial-Dominant; SD, Structure-Dominant; TSK-17, Tampa Scale of Kinesiophobia-17 item; VISA-A, Victorian Institute of Sport Assessment-Achilles.

[a]*Data are presented as mean ± standard deviation (95% confidence interval) unless otherwise specified.*

[b]*Chi-square test.*

reported the lowest physical activity. Psychosocial- and Structure-Dominant shared similar anthropometrics (body mass index of 31.5 and 31.6, respectively), compared to the Activity-Dominant (25.7) and Function-Dominant (28.0). There was no significant difference in symptom duration among the subgroups. Activity- and Function-Dominant subgroups appeared to have minimal-to-no deficits in tendon structure (**FIGURE 2D, APPENDIX D**).

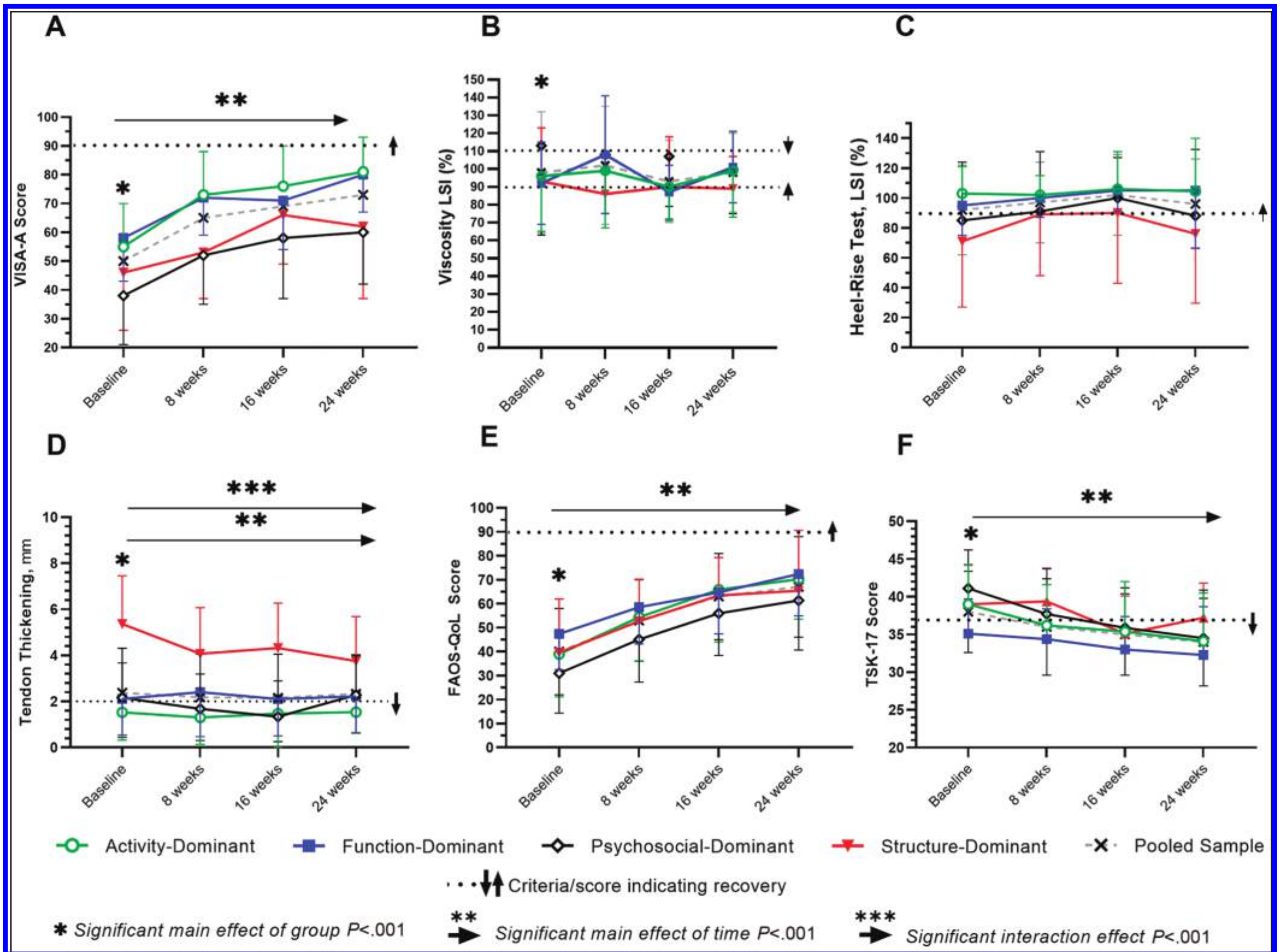


FIGURE 2. Recovery trajectories among subgroups. (A) VISA-A. (B) Viscosity LSI. (C) Heel-rise endurance test LSI. (D) Degree of tendon thickening. (E) FAOS-QoL. (F) Tampa Scale of Kinesiophobia. Abbreviations: FAOS-QoL, Foot and Ankle Outcomes Score-Quality of Life; LSI, limb symmetry index; TSK-17, Tampa Scale of Kinesiophobia-17 item; VISA-A, Victorian Institute of Sport Assessment-Achilles.

Recovery Trajectories Among Subgroups

There were significant effects of group among subgroups for all primary (P<.05) and secondary outcomes (P<.001), apart from heel-rise work LSI (P = .115), and the following secondary outcomes: pain with hopping (P = .112), shear modulus (P = .010), PROMIS Social Roles and Activities (P = .014), and PROMIS Anxiety (P = .756). VISA-A, FAOS-QoL, and TSK-17 (**FIGURE 2A,E,F**) each had significant main effects of time and no significant interaction effects. Marginal means are summarized in **APPENDIX D**.

All subgroups, except Structure-Dominant, met or exceeded the minimal clinically important difference for VISA-A[29] by 8 weeks. Structure-Dominant did not reach the minimal clinically important difference until 16 weeks. Significant effects of time and interaction effect (both P<.001) were observed for tendon thickening (**FIGURE 2D**). Tendon thickening increased for Psychosocial-Dominant (2.16 ± 1.51 mm to 2.28 ± 1.47 mm; P = .032) and Structure-Dominant decreased (5.36 ± 2.09 mm to 3.75 ± 1.94 mm; P<.001) over 24 weeks. Heel-rise work LSI did not change significantly for any subgroup. There was a significant effect of time for heel-rise work (P<.001). Psychosocial recovery trajectories were inconsistent among FAOS-QoL, TSK-17, and GROC scores (**FIGURE 2E,F** and **APPENDIX D**). No significant interaction effects were observed for these measures. TSK-17 scores varied most for Structure-Dominant across time points, whereas Activity- and Psychosocial-Dominant showed consistent improvement. Function-Dominant retained low TSK-17 scores at all time points.

Outcomes at 24 Weeks

The Activity-Dominant and Function-Dominant subgroups approached symptomatic recovery criteria and achieved functional recovery. The Psychosocial-Dominant subgroup reported >2/10 pain with hopping and demonstrated continued deficits on all functional tests. All subgroups, except for Structure-Dominant, reported low kinesiophobia. No subgroup met FAOS-QoL criteria for psychosocial recovery. The structural recovery criterion was met by all subgroups except by Structure-Dominant. **TABLE 3** summarizes recovery status at 24 weeks and attended treatment visits.

DISCUSSION

We identified 4 clinical profiles (subgroups): Activity-Dominant, Function-Dominant, Psychosocial-Dominant, Structural-Dominant) among patients with midportion Achilles tendinopathy. The subgroups mirror the defining attributes of those previously identified,[22] which revealed meaningful differences in baseline tendon health. We identified differences in tendon health recovery trajectories and outcomes among subgroups following 24 weeks of exercise treatment. Identifying latent subgroups and patterns among people is uncommon in musculoskeletal research compared to social and behavioral conditions.[37] Hicks et al[24] recently applied this methodology, which identified subgroups with low back pain with differing outcomes. Likewise, our findings demonstrate the longitudinal benefits and consequences of subgroup membership in patients with midportion Achilles tendinopathy.

Reproducibility of the Subgroups Characteristics

The first study to identify latent subgroups in Achilles tendinopathy[22] included people with insertional (24.8%), midportion (68.9%) Achilles tendinopathy, and both diagnoses (6.2%). Considering distribution was similar among subgroups, excluding insertional Achilles tendinopathy did not impact subgroup enumeration in this cohort. The characteristics of the former Activity-Dominant[22] appear to have been divided into Activity-Dominant and Function-Dominant. The most apparent differences between the 2 subgroups were increased participant age, higher BMI, and the presence of functional deficits observed in the Function-Dominant.

TABLE 3 Recovery Status Within the Domains of Tendon Health at 24-Week Follow-up[a]

	Pooled Sample	Activity-Dominant	Function-Dominant	Psychosocial- Dominant	Structure- Dominant	*P* Value
Treatment						
Attended visits	9 ± 5	9 ± 5	7 ± 5	9 ± 6	9 ± 5	1.00
Compliance	95.6 ± 10.4	94.8 ± 10.5%	95.4 ± 11.8%	94.7 ± 11.1%	98.9 ± 4.3%	.417
Symptomatic Recovery						
VISA-A	72 ± 20 points	81 ± 18 points	80 ± 14 points	60 ± 18 points	62 ± 25 points	**<.001**
	13/71 (18.3%)[b]	4/17 (23.5%)[b]	7/25 (28.0%)[b]	1/16 (6.3%)[b]	1/13 (7.7%)[b]	
Functional Recovery						
Heel-rise work LSI	95.7 ± 29.6%	104.1 ± 20.9%	105 ± 13.8%	87.0 ± 30.0%	76.4 ± 48.1	**.034**
	44/58 (75.9%)[c]	12/15 (80%)[c]	18/19 (94.7%)[c]	8/11 (72.7%)[c]	6/11 (54.5%)[c]	
CMJ height LSI	99.9 ± 32.9%	104.5 ± 21.3%	105.8 ± 25.6%	86.4 ± 49.6%	99.1 ± 40.1%	.478
	35/57 (61.4%)[c]	11/15 (73.3%)[c]	12/19 (63.2%)[c]	6/11 (54.5%)[c]	6/10 (60%)[c]	
Drop CMJ height LSI	88.1 ± 40.6%	104.5 ± 21.3%	105.8 ± 25.6%	86.4 ± 49.7%	99.1 ± 40.1%	.214
	27/54 (47.4%)[c]	11/15 (73.3%)[c]	11/19 (57.9%)[c]	2/9 (22.2%)[c]	3/9 (33.3%)[c]	
Structural Recovery						
Tendon thickening (mm)	2.33 ± 1.70	1.54 ± 0.89	2.22 ± 1.66	2.28 ± 1.47	3.75 ± 1.94	**.025**
Viscosity LSI	97.8 ± 22.7%	99.4 ± 25.6%	99.4 ± 25.6%	102.4 ± 25.9%	87.1 ± 18.3%	.517
	22/53 (41.5%)[d]	5/12 (41.7%)[d]	8/18 (44.4%)[d]	4/12 (33.3%)[d]	5/11 (45.5%)[d]	
Psychosocial Recovery						
TSK-17	34.1 ± 5.6	34.1 ± 6.4	32.3 ± 6.4	34.5 ± 6.4	37.2 ± 4.6	.096
	48/71 (67.6%)[e]	12/18 (66.7%)[e]	20/24 (83.3%)[e]	9/16 (56.3%)[e]	7/13 (53.8%)[e]	
FAOS-QoL	68.0 ± 9.7	70.2 ± 16.6	72.4 ± 17.5	61.3 ± 20.6	65.4 ± 25.2	.389
	13/71 (18.3%)[f]	4/18 (22.2%)[f]	5/24 (20.8%)[f]	1/16 (6.3%)[f]	3/13 (23.1%)[f]	.673
GROC	2.9 ± 1.5	3.8 ± 2.1	3.1 ± 1.3	2.5 ± 1.1	2.9 ± 1.3	

Abbreviations: CMJ, countermovement jump; FAOS-QoL, Foot and Ankle Outcomes Score-Quality of Life; GROC, global rating of change; LSI, limb symmetry index; TSK-17, Tampa Scale of Kinesiophobia-17 item; VISA-A, Victorian Institute of Sport Assessment-Achilles.
[a]*All values are presented as mean ± standard deviation, n individuals who achieved recovery criteria/n (%).*
[b]*VISA-A score ≥90 points.*
[c]*LSI ≥90%.*
[d]*LSI 100 ± 10%.*
[e]*TSK-17 score <37 points.*
[f]*FAOS-QoL score ≥90 points.*

This division also reflects differences in study eligibility criterion. Inclusion age was limited to 65 years in this cohort, compared to no age limit in the previous cohort. The patient characteristics that defined the Psychosocial-Dominant and Structure-Dominant were consistent with the previous study.[22] In both studies, Psychosocial-Dominant reported the worst symptoms and quality of life, highest kinesiophobia, and lowest functional performance of all, and the majority of participants were obese females. Structure-Dominant was again the minority subgroup and the oldest, and the majority of participants were obese males, defined by having the greatest alterations in tendon structure and mechanical properties.

Recovery Trajectories Inform Considerations for Clinical Practice

Similar recovery trajectories were observed for all tendon health domains in Activity- and Function-Dominant. Although both shared minimal tendon health deficits at baseline, a small percentage achieved symptomatic (Activity-Dominant: 23.5%; Function-Dominant: 28%) and psychosocial recovery criteria (22% and 21%, respectively). Having fewer deficits at baseline likely explains the trajectories and outcomes for Activity-Dominant members.[32,52] A chief barrier to recovery for the Activity-Dominant subgroup may be (excessive) physical activity behaviors, which may impede tendon recovery.[33] Unchanged PAS scores observed throughout this study suggests symptom fluctuation, within a tolerable level,[49] is nondetrimental over time, as long as improvements are gained in other domains. Patients often attempt to progress their tendon loading activities swiftly after experiencing a period of asymptomatic status. Therefore, more objective physical activity monitoring, such as wearable technology, may help future research to explore whether physical activity behaviors impede recovery for Activity- and Function-Dominant individuals.

Our findings support kinesiophobia as an important facet to address with patients who have Achilles tendinopathy. The Function-Dominant subgroup had low kinesiophobia, which can manifest as reluctance to acknowledge tendon-overloading behavior as detrimental. The pain monitoring model may be useful in reducing tendon-loading activity, as opposed to promoting increased activity for those with high kinesiophobia. High kinesiophobia may explain persisting deficits in symptoms, function, and psychosocial outcomes in the Psychosocial-Dominant subgroup. This is consistent with recent work[8,9] where greater kinesiophobia was associated with less favorable outcomes. Although the mechanisms for reducing kinesiophobia remain unknown, activity modification using the pain-monitoring model might address kinesiophobia[3] and the observed improvement supports the growing importance of pain education[43] in clinical practice for tendinopathies.

The degree of alteration in tendon structure and mechanical properties, combined with physical deconditioning, and kinesiophobia might explain the outcomes observed for the Structure-Dominant subgroup. Tendon thickening reduced by 30% in the Structure-Dominant subgroup, whereas the other subgroups experienced minimal changes. This finding evokes a debate in the literature as to whether tendon structure can improve with treatment.[2,39] Divergent outcomes (symptoms and tendon structure) between the Structure-Dominant subgroup and the pooled sample highlight potential cause for this debate. In previous treatment studies with stringent inclusion criteria, it is plausible that 1 subgroup was enrolled (eg, a cohort of all-or-no patients with Structure-Dominant characteristics), which could influence results to observe change[39] or no change[2] in tendon structure following treatment. Future research, focused specifically on individual subgroups, is warranted to explore whether other adjunctive interventions might improve outcomes for specific subgroups.

Collectively, our results demonstrate the clinical value of recognizing subgroup membership early. Our results affirm previous findings supporting complete recovery from Achilles tendinopathy may require between 6 months to 1 year.[49] Regardless of subgroup membership, clinicians should anticipate recovery timelines of at least 6 months and should explain this to patients at initial evaluation. Our findings move the field closer toward establishing subgroup-informed tailored treatment strategies to address respective deficits in tendon health that may require adjunctive treatment with exercise therapy.

Limitations

Generalizability of the subgroups is limited by several factors. Our study was limited to individuals aged 18 to 65 years in a general population. Additional subgroups might exist that were underrepresented, such as adolescents and elite athletes. Subgroups were identified from 14 preselected variables representing tendon health. Different tendon health variables might produce different subgroup results. Metabolic factors were not collected in this study, which may have influenced outcomes for subgroup members with comorbidities. Because 61 participants were included in both studies, validation of the subgroups with a new cohort should be performed. Due to the COVID-19 pandemic, we were unable to collect clinical measures for enrolled participants between May and July 2020, although participants completed patient-reported outcome measures online.

Our interpretation of the results might have been different if recovery criteria were defined for each subgroup. Our recovery definitions may not reflect the perspectives of participants. Future research should consider tailoring recovery definitions to each subgroup. For example, the differences in activity/sports participation among the groups predispose different ceiling effects for the VISA-A. In a previous study,[7] the VISA-A was modified (80 points maximum) for sedentary patients by omitting questions related to sports participation and we speculate this could have substantially influenced our results for the Psychosocial- and Structure-Dominant subgroups. GROC scores suggest that 38% of Psychosocial-Dominant participants and 38% of Structure-Dominant participants considered themselves almost or completely recovered (≥ +4) at 24 weeks. Therefore, modified definitions or cutoff scores for recovery and meaningful change may be crucial in future research comparing subgroups.

CONCLUSION

Four midportion Achilles tendinopathy subgroups were identified that are akin to the defining characteristics of the previously established subgroups. Each subgroup had specific deficits at baseline, and recovery trajectories of the subgroups differed across the tendon health domains. The Activity- and Function-Dominant subgroups had the highest proportion of patients who achieved symptomatic recovery. The Psychosocial-Dominant and Structure-Dominant subgroups had remaining functional deficits at 24 weeks. Structural recovery may require more than 24 weeks for the Structure-Dominant subgroup. ◉

KEY POINTS

FINDINGS: Four subgroups were identified in patients with midportion Achilles tendinopathy that are similar to those previously reported. Recovery in terms of symptoms, lower extremity function, tendon structure, and psychosocial factors differed among the subgroups following 24 weeks of exercise therapy and pain-guided activity modification.

IMPLICATIONS: Complete recovery from midportion Achilles tendinopathy may require 24 weeks or longer. Classifying patients into subgroups at baseline may offer valuable prognostic clinical information for each domain of tendon health.

CAUTION: Sixty-one participants were included from the original cohort that first identified Achilles tendinopathy subgroups; additional research is needed for external validation of the subgroup characteristics. Unique recovery trajectories and remaining deficits at 24 weeks warrant future research to determine how to improve treatment for each subgroup.

STUDY DETAILS

AUTHOR CONTRIBUTIONS: All authors planned the study. S.L.H. performed the statistical analyses under the supervision of R.T.P. All authors contributed to the writing of the manuscript. All authors approved the final manuscript.

DATA SHARING: Data are available upon reasonable request to the corresponding author.

PATIENT AND PUBLIC INVOLVEMENT: Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

REFERENCES

1. Akaike H. Factor analysis and AIC. *Psychometrika*. 1987;52:317-332. https://doi.org/10.1007/BF02294359
2. Alfredson H, Zeisig E, Fahlström M. No normalisation of the tendon structure and thickness after intratendinous surgery for chronic painful midportion Achilles tendinosis. *Br J Sports Med*. 2009;43:948-949. https://doi.org/10.1136/bjsm.2008.050955
3. Alghamdi NH, Pohlig RT, Lundberg M, Silbernagel KG. The impact of the degree of kinesiophobia on recovery in patients with Achilles tendinopathy. *Phys Ther*. 2021;101:1-9. https://doi.org/10.1093/ptj/pzab178
4. Bernstein DN, Anderson MR, Baumhauer JF, et al. A comparative analysis of clinical outcomes in noninsertional versus insertional tendinopathy using PROMIS. *Foot Ankle Spec*. 2019;12:350-356. https://doi.org/10.1177/1938640018806662
5. Celeux G, Soromenho G. An entropy criterion for assessing the number of clusters in a mixture model. *J Classif*. 1996;13:195-212. https://doi.org/10.1016/S0167-8655(98)00144-5
6. Cella D, Riley W, Stone A, et al. The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol*. 2010;63:1179-1194. https://doi.org/10.1016/j.jclinepi.2010.04.011
7. Ceravolo ML, Gaida JE, Keegan RJ. Quality-of-life in Achilles tendinopathy: an exploratory study. *Clin J Sport Med*. 2020;30:495-502. https://doi.org/10.1097/JSM.0000000000000636
8. Chimenti RL, Pacha MS, Glass NA, et al. Elevated Kinesiophobia is associated with reduced recovery from lower extremity musculoskeletal injuries in military and civilian cohorts. *Phys Ther*. 2022;102:1-10. https://doi.org/10.1093/ptj/pzab262
9. Chimenti RL, Post AA, Silbernagel KG, et al. Kinesiophobia severity categories and clinically meaningful symptom change in persons with Achilles tendinopathy in a cross-sectional study: implications for assessment and willingness to exercise. *Front Pain Res*. 2021;2:1-14. https://doi.org/10.3389/fpain.2021.739051
10. Corrigan P, Cortes DH, Pohlig RT, Grävare SK. Tendon morphology and mechanical properties are associated with the recovery of symptoms and function in patients with Achilles tendinopathy. *Orthop J Sport Med*. 2020;8:232596712091727. https://doi.org/10.1177/2325967120917271
11. Corrigan P, Cortes DH, Pontiggia L, Silbernagel KG. The degree of tendinosis is related to symptom severity and physical activity levels in patients with midportion Achilles tendinopathy. *Int J Sports Phys Ther*. 2018;13:196-207. https://doi.org/10.26603/ijspt20180196
12. Corrigan P, Zellers JA, Balascio P, Silbernagel KG, Cortes DH. Quantification of mechanical properties in healthy Achilles tendon using continuous shear wave elastography: a reliability and validation study. *Ultrasound Med Biol*. 2019;45:1574-1585. https://doi.org/10.1016/j.ultrasmedbio.2019.03.015
13. Cortes DH, Suydam SM, Silbernagel KG, Buchanan TS, Elliott DM. Continuous shear wave elastography: a new method to measure viscoelastic properties of tendons in vivo. *Ultrasound Med Biol*. 2015;41:1518-1529. https://doi.org/10.1016/j.ultrasmedbio.2015.02.001
14. De Jonge S, Van Den Berg C, De Vos RJ, et al. Incidence of midportion Achilles tendinopathy in the general population. *Br J Sports Med*. 2011;45:1026-1028. https://doi.org/10.1136/bjsports-2011-090342
15. Drew BT, Smith TO, Littlewood C, Sturrock B. Do structural changes (eg, collagen/matrix) explain the response to therapeutic exercises in tendinopathy: a systematic review. *Br J Sports Med*. 2014;48:966-972. https://doi.org/10.1136/bjsports-2012-091285
16. Fahlström M, Jonsson P, Lorentzon R, Alfredson H. Chronic Achilles tendon pain treated with eccentric calf-muscle training. *Knee Surg Sport Traumatol Arthrosc*. 2003;11:327-333. https://doi.org/10.1007/s00167-003-0418-z
17. Farrar JT, Young JP, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*. 2001;94:149-158. https://doi.org/10.1016/S0304-3959(01)00349-9
18. French DJ, France CR, Vigneau F, French JA, Evans TR. Fear of movement/(re)injury in chronic pain: a psychometric assessment of the original English version of the Tampa scale

for kinesiophobia (TSK). *Pain*. 2007;127:42-51. https://doi.org/10.1016/j.pain.2006.07.016

19. Geiser C. Data Analysis With Mplus. Guilford Press; 2013.
20. Grävare Silbernagel K, Malliaras P, de Vos R-J, et al. ICON 2020—International scientific tendinopathy symposium consensus: a systematic review of outcome measures reported in clinical trials of Achilles tendinopathy. *Sport Med*. 2022;613-641. https://doi.org/10.1007/s40279-021-01588-6
21. Grimby G. Physical activity and muscle training in the elderly. *Acta Med Scand*. 1986;220:233-237. https://doi.org/10.1111/j.0954-6820.1986.tb08956.x
22. Hanlon SL, Pohlig RT, Silbernagel KG. Beyond the diagnosis: using patient characteristics and domains of tendon health to identify latent subgroups of Achilles tendinopathy. *J Orthop Sport Phys Ther*. 2021;51:440-448. https://doi.org/10.2519/jospt.2021.10271
23. Henson JM, Reise SP, Kim KH. Detecting mixtures from structural model differences using latent variable mixture modeling: a comparison of relative model fit statistics. *Struct Equ Model*. 2007;14:202-226. https://doi.org/10.1080/10705510709336744
24. Hicks GE, Pohlig RT, Coyle PC, et al. Classification of geriatric low back pain based on hip characteristics with a 12-month longitudinal exploration of clinical outcomes: findings from Delaware spine studies. *Phys Ther*. 2021;101:1-10. https://doi.org/10.1093/ptj/pzab227
25. 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;7:76-84.
26. Koch K-R. Mixed models. In *Bayesian Inference with Geodetic Applications*. Berlin, Germany: Springer; 1990:109-121. *Lecture Notes in Earth Sciences*; vol 31. https://doi.org/10.1007/BFb0048712
27. Kujala UMM, Sarna S, Kaprio J. Cumulative incidence of Achilles tendon rupture and tendinopathy in male former elite athletes. *Clin J Sport Med*. 2005;15:133-135. https://doi.org/10.1097/01.jsm.0000165347.55638.23
28. Kulig K, Chang YJ, Winiarski S, Bashford GR. Ultrasound-based tendon micromorphology predicts mechanical characteristics of degenerated tendons. *Ultrasound Med Biol*. 2016;42:664-673. https://doi.org/10.1016/j.ultrasmedbio.2015.11.013
29. 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 Midportion Achilles tendinopathy: a prospective cohort study. *J Orthop Sport Phys Ther*. 2021;51:510-516. https://doi.org/10.2519/jospt.2021.10040
30. Lundberg M, Styf J. Kinesiophobia among physiological overusers with musculoskeletal pain. *Eur J Pain*. 2009;13:655-659. https://doi.org/10.1016/j.ejpain.2008.08.004
31. Maffulli N, Kenward MG, Testa V, Capasso G, Regine R, King JB. Clinical diagnosis of Achilles tendinopathy with tendinosis. *Clin J Sport Med*. 2003;13:11-15. https://doi.org/10.1097/00042752-200301000-00003
32. Maffulli N, Walley G, Sayana M, Longo UG, Denaro V. Eccentric calf muscle training in athletic patients with Achilles tendinopathy. *Disabil Rehabil*. 2008;30:1677-1684. https://doi.org/10.1080/09638280701786427
33. Magnusson SP, Langberg H, Kjaer M. The pathogenesis of tendinopathy: balancing the response to loading. *Nat Rev Rheumatol*. 2010;6:262-268. https://doi.org/10.1038/nrrheum.2010.43
34. McCormack JR, Underwood FB, Slaven EJ, Cappaert TA. Eccentric exercise versus eccentric exercise and soft tissue treatment (Astym) in the management of insertional Achilles tendinopathy: a randomized controlled trial. *Sports Health*. 2016;8:230-237. https://doi.org/10.1177/1941738116631498
35. Millar NL, Silbernagel KG, Thorborg K, et al. Tendinopathy. *Nat Rev Dis Prim*. 2021;7. https://doi.org/10.1038/s41572-020-00234-1
36. Murphy M, Rio E, Debenham J, Docking S, Travers M, Gibson W. Evaluating the progress of mid-portion Achilles tendinopathy during rehabilitation: a review of outcome measures for muscle structure and function, tendon structure, and neural and pain associated mechanisms. *Int J Sports Phys Ther*. 2018;13:537-551. https://doi.org/10.26603/ijspt20180537
37. Muthén BO, Muthén LK. Integrating person-centered and variable-centered analyses: growth mixture modeling with latent trajectory classes. *Alcohol Clin Exp Res*. 2000;24:882-891. https://doi.org/10.1111/j.1530-0277.2000.tb02070.x
38. Oberski DL. Mixture models: latent profile and latent class analysis. In: *Modern Statistical Methods for HCI*. Cham, Switzerland: Springer; 2016:275-287. https://doi.org/10.1007/978-3-319-26633-6_12
39. Ohberg L. Eccentric training in patients with chronic Achilles tendinosis: normalised tendon structure and decreased thickness at follow up. *Br J Sports Med*. 2004;38:8-11. https://doi.org/10.1136/bjsm.2001.000284
40. Rio EK, Mc Auliffe S, Kuipers I, et al. ICON PART-T 2019–International Scientific Tendinopathy Symposium Consensus: recommended standards for reporting participant characteristics in tendinopathy research (PART-T). *Br J Sports Med*. 2020;54:627-630. https://doi.org/10.1136/bjsports-2019-100957
41. Robinson JM, Cook JL, Purdam C, et al. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Sport Med*. 2001;35:335-341. https://doi.org/10.1136/bjsm.35.5.335
42. Roos EM, Brandsson S, Karlsson J. Validation of the foot and ankle outcome score for ankle ligament reconstruction. *Foot Ankle Int*. 2001;22:788-794. https://doi.org/10.1007/s11420-015-9466-4
43. Sancho I, Morrissey D, Willy RW, Barton C, Malliaras P. Education and exercise supplemented by a pain-guided hopping intervention for male recreational runners with midportion Achilles tendinopathy: a single cohort feasibility study. *Phys Ther Sport*. 2019;40:107-116. https://doi.org/10.1016/j.ptsp.2019.08.007
44. Schwarz G. Estimating the dimension of a model. *Ann Stat*. 1978;6:461-464. https://doi.org/10.1214/aos/1176344136
45. Scott A, Squier K, Alfredson H, et al. ICON 2019: International Scientific Tendinopathy Symposium Consensus: clinical terminology. *Br J Sports Med*. 2020;54:260-262. https://doi.org/10.1136/bjsports-2019-100885
46. Silbernagel KG, Gustavsson A, Thomeé R, Karlsson J. Evaluation of lower leg function in patients with Achilles tendinopathy. *Knee Surg Sport Traumatol Arthrosc*. 2006;14:1207-1217. https://doi.org/10.1007/s00167-006-0150-6
47. Silbernagel KG, Hanlon S, Sprague A. Current clinical concepts: conservative management of Achilles tendinopathy. *J Athl Train*. 2020;55:438-447. https://doi.org/10.4085/1062-6050-356-19
48. Silbernagel KG, Shelley K, Powell S, Varrecchia S. Extended field of view ultrasound imaging to evaluate Achilles tendon length and thickness: a reliability and validity study. *Muscles Ligaments Tendons J*. 2016;6:104-110. https://doi.org/10.11138/mltj/2016.6.1.104
49. Silbernagel KG, Thomeé R, Eriksson BI, Karlsson J. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with Achilles tendinopathy: a randomized controlled study. *Am J Sports Med*. 2007;35:897-906. https://doi.org/10.1177/0363546506298279
50. Silbernagel KG, Thomeé R, Eriksson BI, Karlsson J. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. *Br J Sports Med*. 2007;41:276-280. https://doi.org/10.1136/bjsm.2006.033464
51. Sleeswijk Visser TSO, van der Vlist AC, van Oosterom RF, van Veldhoven P, Verhaar JAN, de Vos R-J. Impact of chronic Achilles tendinopathy on health-related quality of life, work performance, healthcare utilisation and costs. *BMJ Open Sport Exerc Med*. 2021;7: article e001023. https://doi.org/10.1136/bmjsem-2020-001023
52. Stergioulas A, Stergioula M, Aarskog R, Lopes-Martins RAB, Bjordal JM. Effects of low-level laser therapy and eccentric exercises in the treatment of recreational athletes with chronic Achilles tendinopathy. *Am J*

Sports Med. 2008;36:881-887. https://doi.org/10.1177/0363546507312165
53. Thomeé R. A comprehensive treatment approach for patellofemoral pain syndrome in young women. *Phys Ther*. 1997;77:1690-1703. https://doi.org/10.1093/ptj/77.12.1690
54. 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;54:444-451. https://doi.org/10.1136/bjsports-2019-100894
55. Yang CC. Evaluating latent class analysis models in qualitative phenotype identification. *Comput Stat Data Anal*. 2006;50:1090-1104. https://doi.org/10.1016/j.csda.2004.11.004
56. Zellers JA, Bley BC, Pohlig RT, Alghamdi NH, Silbernagel KG. Frequency of pathology on diagnostic ultrasound and relationship to patient demographics in individuals with insertional Achilles tendinopathy. *Int J Sports Phys Ther*. 2019;14:761-769. https://doi.org/10.26603/ijspt201901
57. Zellers JA, Cortes DH, Pohlig RT, Silbernagel KG. Tendon morphology and mechanical properties assessed by ultrasound show change early in recovery and potential prognostic ability for 6-month outcomes. *Knee Surg Sport Traumatol Arthrosc*. 2019;27:2831-2839. https://doi.org/10.1016/j.physbeh.2017.03.040

APPENDIX A

TREATMENT PROTOCOL AND PAIN MONITORING MODEL[49]

Phase	Patient Status	Goals	Treatment Program
Symptom management (weeks 1-2, or longer if needed)	Pain and difficulty with all activities, difficulty performing 10 one-legged heel rises	Start to exercise and understanding nature of the injury and how to use the pain-monitoring model Perform exercise once a day	*Loading Intensity:* Progress loading up to 100% body weight with slow controlled motion. If needed, begin with aquatic therapy, bodyweight support, or isometric plantar flexion. • Pain-monitoring model information and advice on exercise activity • Circulation exercise (moving foot up/down) • Two-legged heel rises standing on the floor (3 × 10-15 repetitions) • One-legged heel rises standing on the floor (3 × 10 repetitions) • Eccentric heel rises standing on the floor (3 × 10 repetitions) • Sitting heel rises (3 × 10 repetitions)
Recovery (weeks 2-5, or longer if needed)	Pain with exercise, morning stiffness, pain when performing heel rises	Start strengthening Perform exercise once a day	*Loading Intensity*: External loading should be introduced once patients can complete the bodyweight treatment program without difficulty.[a] • Two-legged heel rises standing on edge of a step (3 × 15 repetitions) • One-legged heel rises standing on edge of a step (3 × 15 repetitions) • Eccentric heel rises standing on edge of a step (3 × 15 repetitions) • Sitting heel rises (3 × 15 repetitions) • Quick rebounding heel rises (3 × 20 repetitions)
Rebuilding (weeks 3-12, or longer if needed)	Tolerates the recovery phase exercise program well, no pain at the distal tendon insertion, possibly decreased or increased morning stiffness	Heavier strength training, increase or start running or jumping activity Perform exercises every day and with heavier load 2 to 3 times per week	*Loading Intensity*: Continue to progress external resistance and speed of movement based on patient tolerance.[a] • One-legged heel rises standing on edge of step with added weight (3 × 15 repetitions) • Eccentric heel rises standing on edge of step with added weight (3 × 15 repetitions) • Sitting heel rises (3 × 15 repetitions) • Quick rebounding heel rises (3 × 20 repetitions)
Return to sport (months 3-6, or longer if needed)	Minimal symptoms, some but not daily morning stiffness, can participate in sports without difficulty	Maintenance exercise, no symptoms Perform exercises every day and with heavier load 2 to 3 times per week	*Loading Intensity*: Progress from the previous phase to include sport-specific loading speed and movement patterns on high-intensity days. • One-legged heel rises standing on edge of step with added weight (3 × 15 repetitions) • Eccentric heel rises standing on edge of step with added weight (3 × 15 repetitions) • Sitting heel rises (3 × 15 repetitions) • Quick rebounding heel rises (3 × 20 repetitions)

[a]*If pain increases by more than 2 points when exercising while standing on edge of step, then perform exercises on a flat surface.*

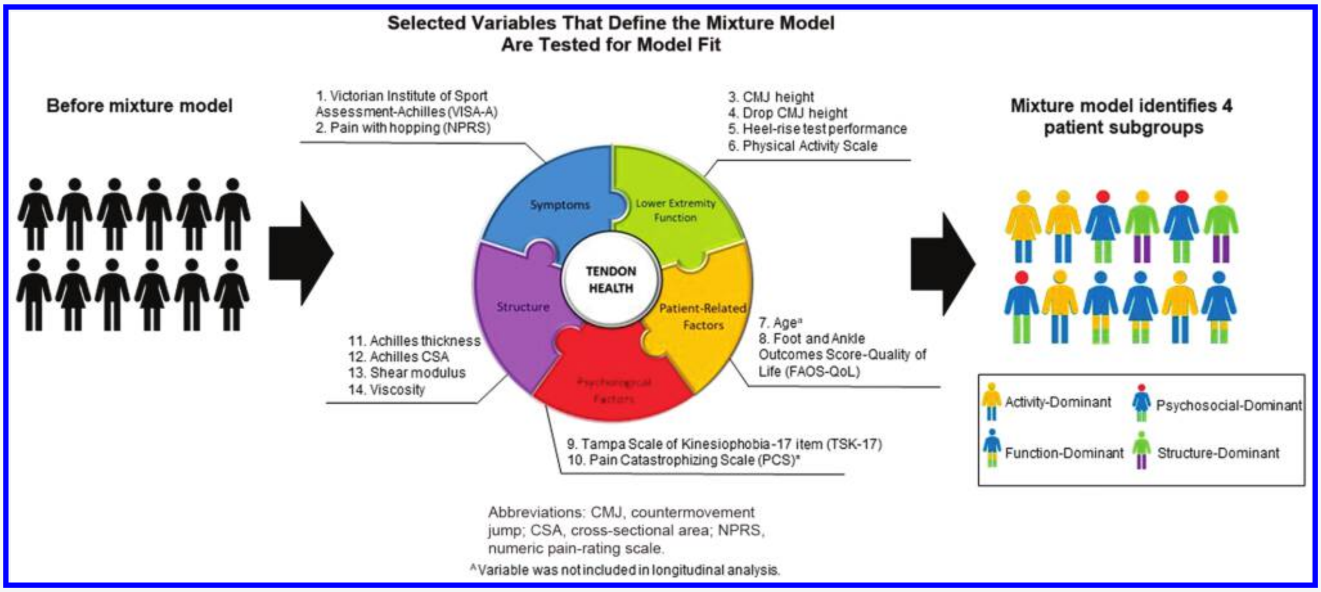
PAIN MONITORING MODEL[49,53] (NPRS)

Safe Zone	Acceptable Zone	High-Risk Zone
0 (No Pain) – 2	2 – 5	5 – 10 (Worst Pain Imaginable)

- Pain is allowed to reach 5 during the activity.
- Pain after the activity is allowed to reach a 5.
- Pain the morning after the activity should not exceed 5.
- Pain and stiffness is not allowed to increase from week to week.

APPENDIX B

MIXTURE MODELING ILLUSTRATED



APPENDIX C

MODEL FIT STATISTICS RESULTS AND INTERPRETATION

Fit Statistic	Two-Subgroup Model	Three-Subgroup Model	Four-Subgroup Model[a]	Five-Subgroup Model[b]
AIC	9824.187	9734.258	9661.881	9616.175
BIC	9941.843	9898.958	9861.624	9856.961
aBIC	9805.935	9709.639	9630.895	9578.822
Entropy	0.874	0.887	0.911	0.931
VLMR test	P = .11	P = .24	P = .86	P = .09
aVLMR test	P = .11	P = .25	P = .86	P = .09
BLR test	P<0.001	P<0.001	P<0.001	P<0.001
Subgroup membership size	1: n = 54 2: n = 60	1: n = 40 2: n = 44 3: n = 30	1: n = 38 2: n = 34 3: n =27 4: n = 15	1: n = 24 2: n = 32 3: n = 15 4: n =38 5: n = 5

Abbreviations: AIC, Akaike Information Criteria; ABIC, sample-adjusted Akaike Bayesian Information Criteria; AVLMR, sample-adjusted Vuong-Lo-Mendell-Rubin; BIC, Bayesian Information Criteria; BLR, bootstrap likelihood ratio; VLMR, Vuong-Lo-Mendell-Rubin.
[a]*A 4-subgroup model was the best-fitting model.*
[b]*Subgroup size must be ≥5% of the total sample to be considered a valid model.*[23]

Model Fit Statistic	Interpretation[19,23,55]
Akaike's Information Criteria (AIC)[1]	Strong indicators for appropriate model fit (number of subgroups) (lowest AIC, BIC, aBIC)
Bayesian Information Criteria (BIC)[44]	
Sample-adjusted BIC (aBIC)[44]	
Entropy[5]	Range of 0 to 1, where closer to 1 indicates strongest separation between and cohesion within subgroups
Vuong-Lo-Mendell-Rubin (VLMR)[23]	Determine statistically significant differences (P =.05) between models (3 vs 2 subgroups)
Sample-adjusted VLMR (aVLMR)[23]	
Bootstrap likelihood ratio (BLR)[23]	

APPENDIX D

SUMMARY OF MARGINAL MEANS AND MAIN EFFECTS[a]

Outcome Measures	Activity-Dominant	Function-Dominant	Psychosocial-Dominant	Structure-Dominant	Group F	Group P	Time F	Time P	Group × Time F	Group × Time P
Primary Outcome Measures										
VISA-A										
Baseline	55 ± 15	58 ± 15	38 ± 17	46 ± 20	14.718	**<.001**	55.090	**<.001**	1.247	.267
8 weeks	73 ± 15	72 ± 13	52 ± 17	53 ± 16						
16 weeks	76 ± 14	71 ± 17	58 ± 20	66 ± 17						
24 weeks	81 ± 12	80 ± 13	60 ± 18	62 ± 25						
Heel-rise work LSI										
Baseline	102.6 ± 18.0	94.9 ± 19.8	85.0 ± 39.5	71.0 ± 44.1	.112	.953	.841	.474	.400	.934
8 weeks	102.2 ± 13.0	100.4 ± 13.0	90.7 ± 39.9	89.1 ± 40.8						
16 weeks	106.2 ± 25.5	104.8 ± 14.3	99.8 ± 26.8	89.7 ± 46.6						
24 weeks	104.0 ± 20.9	105.4 ± 13.8	87.0 ± 30.0	76.4 ± 48.1						
Degree of tendon thickening, mm										
Baseline	1.53 ± 1.21	2.11 ± 1.57	2.16 ± 1.51	5.36 ± 2.09	22.002	**<.001**	6.824	**<.001**	3.224	**.001**
8 weeks	1.30 ± 1.16	2.40 ± 1.92	1.68 ± 1.61	4.07 ± 2.05						
16 weeks	1.47 ± 1.46	2.10 ± 1.60	1.34 ± 1.55	4.32 ± 1.95						
24 weeks	1.54 ± 0.89	2.22 ± 1.66	2.28 ± 1.47	3.75 ± 1.94						
Viscosity LSI										
Baseline	92.3 ± 23.2	96.4 ± 90.1	112.7 ± 49.9	92.6 ± 30.2	3.187	**.027**	.929	.427	.797	.619
8 weeks	108.6 ± 32.9	99.3 ± 108.6	107.6 ± 33.2	85.7 ± 20.5						
16 weeks	87.2 ± 14.3	90.1 ± 18.9	107.3 ± 27.5	85.8 ± 25.2						
24 weeks	101.0 ± 23.0	93.0 ± 20.0	102.4 ± 25.9	87.1 ± 18.3						
FAOS-QoL										
Baseline	39.0 ± 17.9	47.4 ± 14.9	31.0 ± 16.7	39.6 ± 22.4	3.881	**.014**	79.357	**<.001**	.675	.686
8 weeks	54.4 ± 18.2	58.5 ± 15.3	45.1 ± 17.8	52.7 ± 17.5						
16 weeks	65.8 ± 21.7	64.7 ± 17.3	56.0 ± 17.6	63.4 ± 15.9						
24 weeks	70.2 ± 16.6	72.4 ± 17.5	61.3 ± 20.6	65.4 ± 25.2						
TSK-17										
Baseline	39.0 ± 5.3	35.1 ± 4.6	41.1 ± 5.1	39.0 ± 5.2	5.503	**<.001**	22.080	**<.001**	1.739	.081
8 weeks	36.2 ± 5.4	34.4 ± 4.0	37.7 ± 6.0	39.4 ± 4.4						
16 weeks	35.4 ± 6.6	33.0 ± 4.4	35.9 ± 5.3	35.1 ± 5.0						
24 weeks	34.1 ± 6.4	32.3 ± 6.4	34.5 ± 6.4	37.2 ± 4.6						
Secondary Outcome Measures										
Pain with hopping, NPRS										
Baseline	3.1 ± 2.5	2.9 ± 2.4	3.3 ± 2.3	2.8 ± 2.9	2.025	.115	19.443	**<.001**	.923	.506
8 weeks	2.0 ± 2.0	2.0 ± 2.3	2.4 ± 2.0	1.9 ± 2.4						
16 weeks	1.4 ± 1.9	1.4 ± 1.7	1.8 ± 2.1	.5 ± 0.9						
24 weeks	0.7 ± 0.9	0.9 ± 1.4	2.7 ± 2.6	1.4 ± 2.5						
Heel-rise work, J										
Baseline	2260 ± 662	1721 ± 624	1115 ± 675	1057 ± 810	14.477	**<.001**	7.769	**<.001**	1.752	.079
8 weeks	2209 ± 624	1873 ± 552	1382 ± 934	1416 ± 728						
16 weeks	2378 ± 775	2059 ± 643	1375 ± 583	1405 ± 881						
24 weeks	2387 ± 562	1921 ± 562	1254 ± 574	1255 ± 891						
CMJ height, cm										
Baseline	10.9 ± 2.1	6.2 ± 1.5	2.7 ± 1.4	3.8 ± 1.8	106.439	**<.001**	2.525	.059	.941	.491
8 weeks	10.7 ± 2.1	5.6 ± 1.9	3.3 ± 1.8	4.1 ± 2.5						
16 weeks	11.5 ± 2.3	6.1 ± 1.8	3.7 ± 1.7	4.8 ± 2.5						
24 weeks	11.1 ± 2.9	5.7 ± 2.5	2.4 ± 1.5	4.6 ± 3.0						

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APPENDIX D (CONTINUED)

Outcome Measures	Activity-Dominant	Function-Dominant	Psychosocial-Dominant	Structure-Dominant	Group F	Group P	Time F	Time P	Group × Time F	Group × Time P
Drop CMJ height, cm										
Baseline	10.5 ± 2.4	5.7 ± 1.7	1.7 ± 1.7	3.1 ± 2.7	77.831	**<.001**	5.118	.002	1.544	.135
8 weeks	9.9 ± 2.1	5.7 ± 2.5	2.8 ± 2.5	4.0 ± 3.2						
16 weeks	10.5 ± 2.4	6.0 ± 1.9	3.9 ± 2.3	5.6 ± 3.8						
24 weeks	10.1 ± 2.3	5.8 ± 2.5	1.8 ± 1.7	4.6 ± 3.0						
PAS (median [IQR])										
Baseline	5 [1]	5 [1]	3 [2]	5 [2]	16.113	**<.001**	.721	.540	1.384	.196
8 weeks	4 [3]	5 [1]	4 [3]	4 [2]						
16 weeks	5 [2]	5 [1]	4 [1]	4 [2]						
24 weeks	5 [3]	5 [4]	3 [1]	4 [2]						
Achilles thickness, cm										
Baseline	0.62 ± .15	0.74 ± .19	0.66 ± .16	1.19 ± .13	40.083	**<.001**	1.904	.130	.617	.782
8 weeks	0.59 ± .15	0.74 ± .21	0.65 ± .19	1.18 ± .15						
16 weeks	0.62 ± .18	0.72 ± .18	0.64 ± .21	1.19 ± .17						
24 weeks	0.61 ± .14	0.72 ± .21	0.67 ± .18	1.14 ± .16						
Achilles CSA, cm^2										
Baseline	0.72 ± .21	0.85 ± .26	0.77 ± .26	1.72 ± .32	73.051	**<.001**	2.494	.061	.643	.760
8 weeks	0.66 ± .20	0.87 ± .33	0.72 ± .24	1.76 ± .46						
16 weeks	0.73 ± .24	0.92 ± .34	0.79 ± .30	1.90 ± .52						
24 weeks	0.68 ± .21	0.86 ± .30	0.82 ± .27	1.77 ± .38						
Viscosity, kPa·s										
Baseline	50.6 ± 9.4	52.9 ± 9.2	53.5 ± 11.1	45.5 ± 11.3	6.368	**<.001**	.662	.576	.821	.598
8 weeks	56.1 ± 12.0	53.6 ± 12.8	53.7 ± 11.6	43.9 ± 10.8						
16 weeks	53.0 ± 9.2	49.6 ± 7.9	55.6 ± 10.7	42.8 ± 8.9						
24 weeks	54.6 ± 14.7	51.6 ± 9.7	50.0 ± 8.2	39.7 ± 10.0						
Shear modulus, kPa										
Baseline	92.7 ± 22.1	101.0 ± 17.8	99.5 ± 16.8	113.9 ± 22.4	3.972	.010	2.926	.035	.560	.829
8 weeks	98.9 ± 16.6	97.3 ± 19.0	92.0 ± 21.7	107.9 ± 24.2						
16 weeks	106.6 ± 20.1	108.8 ± 22.7	103.1 ± 25.4	115.1 ± 18.4						
24 weeks	95.4 ± 14.0	100.6 ± 21.3	96.4 ± 27.7	114.5 ± 17.6						
PROMIS Social Roles and Activities, t-score										
Baseline	56.0 ± 6.6	57.5 ± 7.7	49.8 ± 8.9	56.0 ± 9.5	3.692	.014	9.814	**<.001**	1.303	.235
8 weeks	57.4 ± 6.4	60.0 ± 7.4	53.0 ± 7.5	57.2 ± 6.9						
16 weeks	59.0 ± 5.7	59.9 ± 5.7	55.2 ± 6.1	58.9 ± 6.1						
24 weeks	61.5 ± 5.3	59.7 ± 6.3	58.1 ± 8.0	58.3 ± 7.0						
PROMIS Pain Interference, t-score										
Baseline	52.7 ± 6.9	51.7 ± 6.6	58.8 ± 6.9	54.3 ± 8.3	10.728	**<.001**	36.803	**<.001**	.232	.990
8 weeks	47.0 ± 5.4	47.0 ± 5.5	52.8 ± 6.0	50.1 ± 6.0						
16 weeks	46.7 ± 5.3	46.7 ± 5.3	52.9 ± 8.1	48.3 ± 7.1						
24 weeks	43.7 ± 4.9	44.4 ± 5.1	51.1 ± 6.8	47.7 ± 7.2						
PROMIS Anxiety, t-score										
Baseline	46.5 ± 7.8	45.6 ± 7.2	48.8 ± 10.3	45.5 ± 7.2	.396	.756	1.456	.227	.669	.737
8 weeks	44.8 ± 6.8	45.5 ± 6.9	46.8 ± 7.9	44.6 ± 6.8						
16 weeks	45.3 ± 6.6	43.7 ± 5.7	46.9 ± 10.9	43.7 ± 6.9						
24 weeks	43.4 ± 6.5	45.0 ± 6.1	44.0 ± 7.3	45.0 ± 8.0						
GROC										
8 weeks	2.0 ± 1.0	1.7 ± 1.3	1.8 ± 1.4	2.3 ± 1.1	1.004	.394	1.780	.153	2.486	.011
16 weeks	2.5 ± 1.6	2.2 ± 1.6	2.1 ± 1.6	1.7 ± 1.5						
24 weeks	3.8 ± 2.1	3.1 ± 1.3	2.5 ± 1.1	2.9 ± 1.3						

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APPENDIX D (CONTINUED)

Outcome Measures	Activity-Dominant	Function-Dominant	Psychosocial-Dominant	Structure-Dominant	Group		Time		Group × Time	
					F	P	F	P	F	P
CMJ height LSI										
Baseline	104.7 ± 16.1	102.4 ± 26.2	88.3 ± 44.0	90.7 ± 43.2	2.342	.077	1.107	.347	1.268	.256
8 weeks	122.4 ± 59.7	102.9 ± 30.3	91.8 ± 38.0	95.0 ± 42.7						
16 weeks	104.0 ± 20.4	102.3 ± 37.1	97.6 ± 36.9	98.6 ± 31.7						
24 weeks	104.6 ± 21.3	105.8 ± 25.6	86.4 ± 49.7	99.1 ± 40.1						
Drop CMJ height LSI										
Baseline	101.9 ± 16.1	87.6 ± 27.1	71.2 ± 83.5	70.7 ± 44.2	3.478	.019	1.075	.361	.667	.729
8 weeks	97.5 ± 30.1	85.5 ± 37.6	76.4 ± 58.7	99.9 ± 98.3						
16 weeks	103.3 ± 27.7	102.3 ± 34.9	93.4 ± 47.6	83.0 ± 44.4						
24 weeks	92.8 ± 35.9	102.4 ± 27.1	70.3 ± 62.4	74.4 ± 42.5						
Shear modulus LSI										
Baseline	98.7 ± 26.1	104.7 ± 25.9	105.8 ± 19.6	113.2 ± 38.9	1.200	.314	2.935	.034	.814	.603
8 weeks	104.0 ± 27.4	97.6 ± 24.9	94.1 ± 25.3	106.2 ± 24.8						
16 weeks	115.7 ± 24.6	108.3 ± 22.9	109.4 ± 32.5	109.2 ± 33.1						
24 weeks	92.6 ± 16.0	97.4 ± 18.4	94.1 ± 16.7	115.7 ± 35.8						
Achilles thickness LSI										
Baseline	106.3 ± 16.4	120.7 ± 33.2	125.0 ± 33.6	175.4 ± 58.8	15.911	**<.001**	2.154	.094	.265	.983
8 weeks	109.7 ± 20.4	120.3 ± 31.3	116.3 ± 26.0	178.2 ± 64.0						
16 weeks	108.1 ± 16.5	121.2 ± 30.8	113.9 ± 34.2	171.9 ± 60.2						
24 weeks	106.0 ± 13.1	116.1 ± 27.0	124.1 ± 33.2	170.8 ± 66.9						
Achilles CSA LSI										
Baseline	109.5 ± 18.7	117.6 ± 33.8	129.9 ± 39.1	209.3 ± 77.1	19.763	**<.001**	2.058	.107	.778	.637
8 weeks	108.3 ± 22.0	125.6 ± 44.6	114.5 ± 40.8	218.7 ± 104.9						
16 weeks	112.3 ± 22.7	133.8 ± 48.0	129.0 ± 41.9	234.1 ± 126.8						
24 weeks	103.3 ± 23.9	123.3 ± 41.0	139.6 ± 47.9	216.1 ± 121.1						

Abbreviations: CSA, cross-sectional area; CMJ, countermovement jump; FAOS-QoL, Foot and Ankle Outcomes Score-Quality of Life; GROC, global rating of change; LSI, Limb Symmetry Index; PAS, Physical Activity Scale; PROMIS, Patient-Reported Outcome Measurement Information System; TSK-17, Tampa Scale of Kinesiophobia-17 item; VISA-A, Victorian Institute of Sport Assessment-Achilles.

[a]*All values are presented as mean ± standard deviation, unless otherwise specified. Primary outcomes were evaluated at P<.05. Secondary outcomes were evaluated at P<.001.*

APPENDIX E

REALLOCATION OF SUBGROUP MEMBERSHIP BETWEEN COHORTS

	Previous Cohort[22] Subgroup Membership (n = 61)	Present Cohort Subgroup Membership			
		Activity-Dominant	Function-Dominant	Psychosocial-Dominant	Structure-Dominant
Activity-Dominant	30	14	16	0	0
Psychosocial-Dominant	24	1	4	16	3
Structure-Dominant	7	0	0	0	7