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Which treatments are most effective for common tendinopathies? A systematic review and network meta-analysis protocol.

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Conflicts of interest

The authors declare no conflict of interest.

1.0 Introduction

Tendinopathy is a common musculoskeletal condition associated with degenerative changes within a tendon affecting both athletic and non-athletic populations.¹ The condition is characterized by a combination of pain,¹ and impaired movement² and function³, requiring extended periods for recovery.^{2,4,5} Tendinopathy can affect any muscle-tendon unit in the body,⁶ however, it is most frequently reported in the Achilles, patellar, lateral elbow, rotator cuff, and hip tendons.⁶ Surveys of prevalence of lower extremity tendinopathy in the general population have reported rates of 11.8 and 10.5 per 1000 person-years,⁷ whilst prevalence for upper limb tendinopathies have been estimated between 1.3% to 21.0%.⁸⁻¹⁰ Tendinopathies can affect children, adolescents, and adults of all ages, and many tendinopathies have a chronic or recurrent course.⁶ Costs to the individual, the health service and economy (due to absenteeism and loss of productivity) are substantial such that identifying effective interventions is a priority. Musculoskeletal conditions including tendinopathies also have a substantive influence on primary and secondary healthcare use.¹¹ By identifying effective interventions across a range of tendinopathies, General Practitioners and other first-contact practitioners (e.g. physiotherapists) can be confident in delivering effective evidence-based practice. With an ageing population, and increasing pressure and demands on healthcare services, the need for clear guidance for evidence-based practice has never been more important.

The clinical management of symptomatic tendinopathy requires complex clinical reasoning with reference to the pathoanatomical diagnosis. Rehabilitation strategies can vary substantively depending on the site, stage of the tendinopathy, functional baseline, contributing issues within the kinetic chain, and patient factors including activity level, comorbidities, and coexisting presentations.¹² Current research supports the role of appropriate loading in strength training as the primary treatment of tendinopathy.¹³ Different principles of loading such as eccentric loading, combined loading, and heavy, slow resistance training (HSRT) have each been recommended with similar goals to initiate tendon adaptations and restore function. However, observable structural change does not always correlate with positive therapeutic outcomes. Most tendinopathies have associated movement dysfunction which may require movement retraining or motor control-based exercises to retrain normal patterns of muscle recruitment. There is also evidence to suggest the role of potential corticospinal involvement or central sensitisation resulting from persistent pain particularly in chronic tendinopathy. Given the complexities involved, treatments may comprise multiple therapy modes with exercise frequently used as an adjunct with ultrasound, extracorporeal shockwave, laser therapy, or following regenerative or ortho-biologic procedures such as prolotherapy, platelet-rich plasma or stem-cell therapies.¹⁴ Additionally, for those with refractory symptoms, surgical interventions may be indicated.

Currently, the best therapy for tendinopathy remains uncertain. Previous systematic reviews have generally focused on single tendinopathies and resorted to qualitative syntheses of evidence due to concerns of both statistical and clinical heterogeneity. Where, meta-analyses have been conducted, these have generally focussed on small numbers of homogenous studies employing conventional pairwise approaches that do not offer comparative effectiveness of the wide range of treatments, leading to a lack of established hierarchy in tendinopathy interventions. More recent perspectives in evidence synthesis highlight that with complex

interventions statistical heterogeneity should be expected and as is the case with primary data, variance presents opportunities for informative explanatory analyses.¹⁵ Currently a range of approaches have been developed to best synthesise complex and heterogenous data, with statistical approaches including the use of network meta-analyses (NMA) that can potentially be combined with meta-regression.¹⁵ Recent NMAs investigating tendinopathy treatments have focused on localised site-specific tendons with pain relief and function as the predominant outcomes.¹⁶⁻²⁰ Four NMAs have investigated comparative effectiveness of treatments in upper extremity tendinopathies, three of which studied injection therapies in the shoulder¹⁷ or elbow^{18,19} while one other focused on non-surgical treatments for chronic calcific tendinitis of the shoulder.¹⁶ In a NMA of non-surgical treatments for patellar tendinopathy of 11 trials, Chen et al.²⁰ concluded that platelet-rich plasma has the greatest improvements in pain and function compared with other treatment options. However, the review excluded studies that compared different types of exercise therapy from their analysis. Two recent NMAs assessing the effectiveness of evidence-based treatment for adults with Achilles tendinopathy reported somewhat conflicting findings. The review of 29 RCTs by van der Vlist et al.²¹ concluded there was strong evidence that all active treatments were superior to wait-and-see, but no one active treatment could be recommended over another. In contrast, Rhim et al.²² suggested that high-volume injection with corticosteroid and extracorporeal shockwave therapy may be combined with eccentric exercise to produce sustained benefits in Achilles tendinopathy. However, these latter results were based on a small sample size of two pooled studies. All previous NMAs investigating tendinopathy treatments have reported substantive statistical heterogeneity but have not included sufficient data to explore the variance and thereby generate additional relevant clinical findings. Therefore, the purpose of the present systematic review and NMA is to compare the effectiveness of different treatment classes across a range of tendinopathies and outcomes to better establish a treatment hierarchy. Where sufficient data are obtained, the potential for covariates including patient demographics and condition specifics (e.g. symptom severity) to explain statistical heterogeneity will be explored.

2.0 Inclusion criteria

This review is part of a project funded by the National Institute for Health Research (NIHR); Health Technology Assessment (HTA) 129388 Exercise therapy for the treatment of tendinopathies. The inclusion criteria are influenced by the project aims, the results of our initial scoping review mapping the exercise and tendinopathy literature¹⁴ as well as stakeholder workshops.

Participants

This review will include people of any age or gender with a diagnosis of tendinopathy of any severity or duration and at any anatomical location. Studies that include participants with tendinopathy in the absence of full thickness or large tears, will be included. Groups where the tear size cannot be determined will also be excluded as these require different management approaches. We will accept trial authors' diagnoses where a clearly verifiable group of clinical features is reported including: pathognomonic location of pain; a symptom altering response to applied load and/or stretch, with there being a specific test for most tendinopathies; strategies to rule out differential diagnoses; ultrasound or magnetic resonance imaging confirmation of structural change. Studies with mixed Swinton, Shim, Pavlova, Moss, Maclean, Greig, Parkinson, Morrissey, Alexander, Cooper (2021)

groups will have data included where there is clear reporting of the tendinopathic group, or they make up > 90% of the investigated cohort. Our definition of tendinopathy therefore includes tendinopathies such as PTSD (posterior tibial tendon dysfunction), tibialis posterior tendinopathy, peroneal tendinopathy, and GTPS (greater trochanteric pain syndrome). However, it excludes plantar heel pain as this condition may respond differently to exercise therapy and could potentially confound the review findings.

Intervention

The primary health technology being assessed is exercise therapy for the treatment of any tendinopathy. Exercise therapies considered for inclusion will comprise five treatment classes: 1) resistance; 2) plyometric; 3) vibration; 4) flexibility and 5) movement pattern retraining modalities (see appendix I for definitions). Exercise therapy may be delivered in a range of settings (e.g. primary care, secondary care, community, people's homes) by a range of health or exercise professionals (e.g. physiotherapists, strength & conditioning coaches, personal trainers) or support workers, and may be supervised or unsupervised (i.e. self-management). No restrictions will be placed on these factors for inclusion.

To be included in the review, studies are required to report sufficient information regarding the exercise intervention to enable appropriate identification of treatment class and quantification of exercise dose. In clinical settings it has been recommended that exercise dose is determined by duration, frequency, and intensity; where duration reflects the amount of time accrued in a single exercise session, frequency captures the number of exercise sessions over periods such as a week, and exercise intensity is defined either in absolute terms (such as the metabolic cost of an exercise session), or in relative terms (such as the performance of a given activity as a function of some percentage of measurable maximum capacity). To be included in the review, studies are required to provide sufficient information to describe at least two of the three parameters describing exercise dose. Where sufficient information is not presented in the main text of a study, a search will be made of the publishers' website to check for supplementary files that may include relevant information.

Comparator

The review will include studies that compare exercise therapies with non-active therapies (placebo or no intervention), other conservative therapies or surgery. Definitions of broad and specific treatment classes for the different therapy types are provided in appendix I.

Outcomes

Based on the results of our initial scoping review and subsequent stake holder workshops we will include outcomes that assess ten domains: 1) Disability; 2) Physical function capacity; 3) Pain on loading/activity; 4) Pain over a specified time; 5) Pain without further specification 6) Participant/patient rating overall condition; 7) Participation; 8) Quality of life; 9) Adverse effects/events; and 10) Range of motion (for studies investigating rotator cuff tendinopathy only). Definitions for each domain and example measurement tools are presented in appendix II.

Types of studies

We will include randomized controlled trials and non-randomized controlled trials.

Swinton, Shim, Pavlova, Moss, Maclean, Greig, Parkinson, Morrissey, Alexander, Cooper (2021)

Context

The context will include primary care, secondary care or community locations in any developed nation (defined as the top 62 countries in the Human Development Index at the time of protocol development)²³ for the findings to be relevant to the UK context.

3.0 Exclusion criteria

We will exclude self-described pilot studies and non-intervention studies where the purpose of the research is to investigate the acute effects of exercise on physiological or biomechanical variables such as pain, collagen turnover or mechanical properties of tendons.

4.0 Methods

The review will be conducted according to the PRISMA extension statement for reporting of systematic reviews incorporating NMAs of health care interventions²⁴ and the recent GRADE approach to drawing conclusions from NMA using a minimally contextualised framework.²⁵

Search strategy

The search strategy used for this study was part of a larger search conducted to scope the entire tendinopathy and exercise therapy research base. The search comprised three steps; Firstly, a limited search of MEDLINE and CINAHL using initial keywords (MH tendinopathy OR TX tendin* OR TX tendon*) AND (MH exercise OR TX exercis*) was conducted with analysis of the text words in the titles/abstracts and those used to describe articles to develop a full search strategy. Secondly, the full search strategy was adapted to each database and applied systematically to: MEDLINE, CINAHL, AMED, EMBase, SPORTDiscus, Cochrane library (Controlled trials, Systematic reviews), JBI Evidence Synthesis, PEDRO, and Epistemonikos (a full search strategy for MEDLINE is presented in appendix III). The following trial registries were also searched: ClinicalTrials.gov, ISRCTN Registry, The Research Registry, EU-CTR (European Union Clinical trials Registry), ANZCTR (Australia and New Zealand Clinical trials Registry). Finally, the third step involved conducting a search of cited and citing articles using Scopus and hand-searching a total of 130 systematic reviews that were identified to include information relevant to exercise therapy and tendinopathy. No limit was placed on language, with research studies published in languages other than English translated via Google Translate or via international collaborations of the review team members. Searches were initiated from 1998 as (i) the heavy load eccentric calf-training protocol for Achilles tendinosis by Alfredsson et al²⁶ was published in 1998 and may be considered seminal work in the field of tendinopathy, and (ii) there has been a proliferation of research on exercise interventions for tendinopathies post 1998.

Study selection

Swinton, Shim, Pavlova, Moss, Maclean, Greig, Parkinson, Morrissey, Alexander, Cooper (2021)

Proquest® Refworks will be used to manage references and remove duplicates, before importing to Covidence (Melbourne, Australia) to facilitate screening. Two levels of screening will be conducted. First all titles/abstracts will be reviewed, independently, by two members of the research team. Conflicts will be resolved by discussion or by input from a third reviewer. Full-text copies of all studies included at title/abstract screening stage will be retrieved and these will also be screened independently by two members of the research team with conflicts resolved in the same way.

Data extraction

Data will be extracted independently by 8 members of the review team (PS/KC/LA/RM/LG/EP/JS/AP) into pre-piloted excel sheets. Data will be independently coded as described in the accompanying codebook (appendix IV). To quantify reliability, 10% of studies will be selected at random and extraction completed in duplicate. Reliability will be quantified using Cohens K statistic ²⁷ for categorical variables and percentage agreement for continuous variables.

Risk of bias assessment

We will use the Cochrane Collaboration's Risk of Bias tool ²⁸ and all five domains: 1) selection bias; 2) performance bias; 3) detection bias; 4) attrition bias; and 5) reporting bias, to assess risk of bias for all included RCTs. For non-random designs, we will use the ROBINS-I tool ²⁹ and all seven domains: 1) bias due to confounding; 2) bias in selection of participants into the study; 3) bias in classification of interventions; 4) bias due to deviations from intended interventions; and 5) bias due to missing data; 6) bias in measurement of outcomes; and 7) bias in selection of the reported. An overall risk of bias judgement will be made for each outcome and time point as either 'low risk', 'some concerns' or 'high risk' of bias. A single assessment will be made by a reviewer from the team with comments saved to justify selection for each signalling question. To quantify reliability, 10% of studies will be selected at random and extraction completed in duplicate.

Statistical analysis

We will fit treatment class (broad and specific) Bayesian models. Pairwise effect sizes will be calculated with standardised mean differences (SMD_{pre}) for continuous outcomes and proportional odds models used for binary outcomes. Initially, direct pair-wise comparisons will be estimated. We will then combine direct and indirect comparisons using NMA and hierarchical NMA if possible.³⁰ Outcomes will be analysed separately according to short (≤ 12 weeks), medium (13-52 weeks) and long (> 52) time frames. Following the GRADE approach for presentation and interpretation of results, we will select a reference intervention defined as the most connected node in the network. To maintain a minimally contextualised framework, we will select a no effect threshold and move any treatment or treatment class above or below the reference if 95% credible intervals do not span the threshold. Second classifications will then be made based on comparisons with treatment classes moved relative to the reference. In each of the classifications, treatment classes will be separated into: 1) moderate to high certainty; and 2) low to very low certainty based on risk of bias, inconsistency and indirectness.³¹ Inconsistency will be assessed using model-based methods and comparison of residual deviance and the deviance information criterion).³² Finally, consistency of the treatment and treatment class hierarchies created in previous steps will be

assessed by examining pairwise comparisons not previously used. Sources of statistical heterogeneity will only be explored in cases where there are 10 or more trials available per comparison.²¹

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Appendix I: Definitions use to define broad and specific treatment classes.

Broad Treatment Class	Definition	Specific Treatment Class	Definition
Exercise	Exercise therapy is defined as a regimen or program of physical activities specifically designed and prescribed to correct impairments, restore musculoskeletal function, and/or maintain a state of wellbeing.	Resistance	Exercise designed primarily to increase strength of muscles by causing them to produce substantive force against an applied resistance which can take several forms including the mass of the body or its segments, isoinertial resistance, elastic resistance, or strength training equipment such as isokinetic devices. In tendinopathy, the stimulus may also be intended to provoke tendon remodelling, reduce pain and improve function.
		Flexibility	Exercise designed to increase joint range of motion and extensibility of muscles and/or associated tissues. Also referred to as range-of-motion exercises or stretching.
		Proprioception	Exercise designed to enhance the sensation of the joint relative to body position and movement, sense of force, and to encourage muscular stabilisation of the joint in the absence of external stabilising devices e.g. ankle brace.
		Plyometric	Exercise where a resistance is overcome by a muscle rapidly stretching then shortening
		Vibration	Exercise where body segments are held stationary or actively displaced as per definitions for other treatment classes whilst applying a rapid oscillating resistance
Non-active (placebo, sham, wait and see)	Includes any appropriate inactive treatment such as waiting list control, sham shockwave, sham laser, sham taping or true placebo.	Non-active (placebo, sham, wait and see)	Includes any appropriate inactive treatment such as waiting list control, sham shockwave, sham laser, sham taping or true placebo.
Electro-therapy	Modality that delivers therapeutic levels of physical energy into a biologic system e.g. soft tissue.	Shockwave	Extracorporeal shockwave therapy (radial or focussed)
		Laser	Low level laser therapy

		Other	Other less common electro-therapies such as ultrasound, radar and diadynamic current.
Biomechanics	Treatment using external devices that alters the kinematics/kinetics of the limb.	Immobilisation	Any intervention that prevents specific features of joint movement e.g. splinting
		Altered loading	Any intervention aimed at altering tendon loading e.g. taping, tennis elbow clasp/brace and orthotics.
Manual Therapy	Manual therapy is the skilled application of “hands-on” techniques to treat soft tissues and joint structures for the purpose of improving pain, increasing range of motion, stimulating tissue repair response, and/or improving function.	Manual Therapy	Manual therapy is the skilled application of “hands-on” techniques to treat soft tissues and joint structures for the purpose of improving pain, increasing range of motion, stimulating tissue repair response, and/or improving function.
Injection Therapy	Injection therapy for tendinopathy typically involves direct administration of a pharmacologically active drug, or combination of drugs using a syringe and needle or equivalent. It may or may not be image-guided.	Autologous	An autologous injection is an injection of a substance drawn from the patient to whom it is then given, usually at the tendinopathy site after content manipulation with the purpose of stimulating tissue healing.
		Drug	An injection of a classified drug, often mixed with another drug (e.g. corticosteroid with local anaesthetic) for the purpose of reducing pain and stimulating tissue healing.
		Volumetric	An injection deliberately constructed to administer a large volume of fluid to exert a mechanical, as well as pharmacological, effect on the tissues to reduce pain, promote tissue healing and mobilise adherent tissue.
Surgery	Any relevant surgical intervention for tendinopathy	Minimally invasive peritendinous	Minimally invasive procedure with small portals and insertion of surgical tools in the peritendinous area.
		Open intra-tendinous	A more traditional open approach where the tendon is exposed and the peri-tendinous and intra-tendinous areas surgically treated.

Appendix II: Outcome domains and example outcomes included in review.

Domain	ICON Definition	Example Tools
Disability	Composite scores of a mix of patient-rated pain & disability due to the pain, usually relating to tendon-specific activities/tasks	VISA scales; DASH; quick DASH; SPADI; Patient-rated tennis-elbow evaluation questionnaire; Constant Murley Score; WORC (Western Ontario Rotator Cuff Index); AOFAS (American Orthopaedic Foot & Ankle Society); Roles and Maudsley score; ASES (American Shoulder & Elbow Surgeons Index); Tegner activity score; Lysholm knee scale; Pain free function questionnaire; Ankle activity score; Subjective elbow Value (SEV); Placzek score; Shoulder disability questionnaire; International Knee Documentation Committee form (IKDC); Penn Shoulder score (university of Pennsylvania shoulder score) (PSS); Brief pain inventory (BPI); UCLA Shoulder Rating Scale; FILLA - functional index of leg and lower limb; Neer Shoulder Score; Nirschl phase rating scale; American Shoulder and Elbow Surgeon's (MASES) questionnaire; Mayo Elbow Performance Score (MEPS); Shoulder rating questionnaire (SRQ)
Pain on loading/activity	Patient reported intensity of pain performing a task that loads the tendon	VAS; NRS; Pain experience scale
Pain over a specified time	Patient-reported pain intensity over period of time e.g. morning/night/24-hours/1-week	VAS; NRS Painful days in 3 months
Pain without further specification	Patient asked about pain levels without reference to activity or timeframe	VAS; NRS; Borg CR10 Scale; Pain status
Physical function capacity	Quantitative measures of physical tasks (e.g. hops, times walk, single leg squat) includes muscle strength	Counter movement jump; One-leg triple hop; Single-leg decline squat; Muscle strength measured by dynamometry (hand-held, isokinetic); Repetition maximum; Manual muscle testing.
Patient rating overall condition	Single-assessment numerical evaluation of symptom status	Global impression/rating of change; patient-acceptable symptom status/state
Participation	Patient rating of the level of participation/engagement across areas of their life	Sport participation; return to sport; work ability; return to work; sick leave
Quality of Life	General wellbeing	EQ5D; EQ3D; SF-36 or SF-12; Assessment of Quality of Life (AQoL); Nottingham Health Profile; Gothenburg QoL Instrument
Adverse effects/events	Unwanted unintended effects of treatments	Adverse event reporting
Range of Motion (Shoulder only)	Active or passive range of motion in specified plane, measured in degrees.	Hand-held goniometer; inclinometer

Appendix III: Search strategy

MEDLINE (EBSCOHost)

Search conducted on 27 April, 2020

Search	Query	Records retrieved
#1	MH exercise OR AB exercis* OR MH “isometric contraction” OR MH rehabilitation OR TX eccentric OR TX concentric OR TX “heavy slow resistance” OR TX isokinetic	362,722
#2	MH tendinopathy OR MH “shoulder injuries” OR MH tendons OR MH “tendon injuries” OR TX tendin* OR TX tendon* OR MH bursitis OR AB bursitis OR MH “posterior tibial tendon dysfunction” OR MH “shoulder impingement syndrome” OR AB “greater trochanteric pain syndrome”	96,490
#3	#1 AND #2	4,363
Limited to 1998 to present		

Appendix IV: Extraction codebook

Column	Heading	Description	
Study Details	A	Initials Reviewer	Identification of individual extracting information
	B	Covidence Identifier	Reference number for Covidence
	C	Author	First author surname <i>et al.</i> ,
	D	Year	Year of publication
	E	Title	Study title
	F	Country	Country where study was conducted
	G	Journal	Journal name
	H	Aims/Purpose	Study aims/purpose
	I	Tendinopathy type	1=Achilles; 2= Lateral elbow (tennis); 3 = Patellar; 4 = Rotator cuff (SI)
	J	Study Design	RCT = 1; Quasi-experimental = 2
	K	Age Mean	Mean age of study sample as a whole
	L	Age SD	Standard deviation age of study sample as a whole
	M	Baseline Total N	Total sample across all interventions measured at baseline
	N	Training Status Description	Brief description of training status of study sample as a whole
	O	Training Status Code	1 = Performance; 2 = Sporting; 3 = Other
	P	Sex	Percentage female of study sample as a whole
	Q	BMI Mean	Mean BMI of study sample as a whole
	R	BMI SD	Standard deviation of BMI of study sample as a whole
	S	Symptom Severity Mean	Mean severity measure at baseline of study sample as a whole
T	Symptom Severity SD	Standard deviation of severity measure at baseline of study sample as a whole	
U	Symptom Duration Mean (Months)	Mean symptom duration reported in months	
V	Symptom Duration SD (Months)	Standard deviation symptom duration reported in months	
W	Population Comments	Any additional information relevant to the participants investigated including diagnostic criteria	
Outcomes	X	Outcome Category	1 = Disability; 2 = Pain on loading/activity; 3 = Pain over a specified time; 4 = Pain without further specification; 5 = Physical function capacity; 6 = Patient rating overall condition; 7) Participation; 8) Quality of life; 9) Adverse effects/events; 10) Range of motion
	Y	Outcome Tool	Description of outcome tool
	Z	Reflection	1 = Increase in outcome indicates positive treatment; -1 = Decrease in outcome indicates positive treatment
	AA	Measurement Time (Weeks)	Time of measurement in weeks
Intervention	AB	Dominant Broad Treatment Class	Only one dominant theme to be selected 1 = Exercise; 2 = Non-active; 3 = Electro-therapy; 4 = Biomechanics; 5 = Manual Therapy; 6 = Injection Therapy; 7 = Surgery
	AC	Total Broad Treatment class	Multiple themes to be selected as required 1 = Exercise; 2 = Non-active; 3 = Electro-therapy; 4 = Biomechanics; 5 = Manual Therapy; 6 = Injection Therapy; 7 = Surgery
	AD	Dominant Specific Treatment Class	Only one dominant theme to be selected 1 = Resistance; 2 = Plyometric; 3 = Vibration; 4 = Flexibility; 5 = Proprioception; 6 = Non-active; 7 = Shockwave; 8 = Laser; 9 = Electro-therapy Other; 10 = Immobilisation; 11 = Altered loading; 12 = Manual Therapy; 13 = Autologous; 14 = Drug; 15 = Volumetric; 16 = Minimally invasive; 17 = Open intra-tendinous
	AE	Total Specific Treatment Class	Multiple themes to be selected as required 1 = Resistance; 2 = Plyometric; 3 = Vibration; 4 = Flexibility; 5 = Proprioception; 6 = Non-active; 7 = Shockwave; 8 = Laser; 9 = Electro-therapy Other; 10 = Immobilisation; 11 = Altered loading; 12 = Manual Therapy; 13 = Autologous; 14 = Drug; 15 = Volumetric; 16 = Minimally invasive; 17 = Open intra-tendinous
	AF	Intervention N	Intervention sample size at specified time
	AG	Intervention Total Duration	Total duration of exercise intervention in weeks

	AH	Intervention Adherence %	Reporting of adherence to exercise (reported as a percentage) if applicable
	AI	Intervention Location	Location exercise was performed 1 = Home; 2 = Clinic; 3 = Fitness facility; 4 = NR; 5 = NA
	AJ	Intervention Volume	Numerical value describing volume
	AK	Intervention Volume Category	1 = Duration of session (mins); 2 = sets * repetitions; 3 = number of repetitions; 4 = number of sets
	AL	Intervention Volume Comments	Any additional information relevant.
	AM	Intervention Intensity	Numerical value describing intensity
	AN	Intervention Intensity Category	1 = Absolute; 2 = Relative
	AO	Intervention Frequency	Number of sessions per week. Where there is progression, average value is to be entered.
	AP	Intervention Frequency Comments	Any additional information relevant.
	AQ	Intervention Progression	Multiple themes to be selected as required 1 = No progression; 2 = NR; 3 = Progression volume; 4 = Progression intensity; 5 = Progression frequency; 6 = Progression specificity; 7 = Progression capacity; 8 = Other
	AR	Intervention Progression Comments	Any additional information relevant.
Data	AS	Intervention Baseline Mean	Baseline mean for exercise therapy
	AT	Intervention Baseline SD	Baseline standard deviation for exercise therapy
	AU	Intervention Measurement Mean	Mean of outcome for exercise therapy at stated time point
	AV	Intervention Measurement SD	Standard deviation of outcome for exercise therapy at stated time point
	AW	Control Baseline Mean	Baseline mean for control
	AX	Control Baseline SD	Baseline standard deviation for control
	AY	Control Measurement Mean	Mean of outcome for control at stated time point
	AZ	Control Measurement SD	Standard deviation of outcome for control at stated time point
	BA	Measurement Comments	State if a different value has been entered for means (e.g. median), a different value for standard deviations (e.g. standard error, IQR, percentiles, distance from mean to upper bound). Provide the relevant statistic (width of CI's, width of percentiles). Also state if data has extracted by digitization

* Outcome Specific