OUTCOME PREDICTORS FOR PATELLAR TENDINOPATHY IN JUMPING ATHLETES

Submitted in part fulfilment of the requirements of the degree of Doctor of Philosophy

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Statement of originality

I, Abdulhamit Tayfur, confirm that the research included within this thesis is my own work or that where it has been carried out in collaboration with, or supported by others, that this is duly acknowledged below and my contribution indicated. Previously published material is also acknowledged below.

I attest that I have exercised reasonable care to ensure that the work is original, and does not to the best of my knowledge break any UK law, infringe any third party's copyright or other Intellectual Property Right, or contain any confidential material.

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Acknowledgements

Dedication

I dedicate this PhD to my dear parents;

My mother *İnayet Tayfur* and my father *Mığdat Tayfur*

who showed me love, support and encouragement my entire life. Thank you for your understanding and patience for my absence from all important family moments during my PhD. I feel so lucky to have such a great parents.

Bu doktora araştırmasını hayatım boyunca benden sevgisini ve desteğini esirgemeyen sevgili ebeveynlerime;

Canım annem İnayet Tayfur ve canım babam Mığdat Tayfur'a

ithaf ediyorum. Doktora eğitimim sırasında tüm önemli aile anlarından uzak kalmama rağmen gösterdiğiniz anlayış ve sabır için sonsuz teşekkür ederim. Böyle harika bir anne babaya sahip olduğum için kendimi çok şanslı hissediyorum.

Abstract

Introduction

Patellar Tendinopathy (PT) is poorly understood with the absence of statistical models considering combinations of various associated factors potentially obscuring understanding of how jumping athletes with PT present and progress. I developed and conducted an international prospective cohort of jumping athletes with a one year follow-up to determine the outcome predictors for PT recovery in order to understand who gets better, why and when.

Aims

The overarching aim of this thesis was to build statistical models that explain how PT presents in jumping athletes, predict PT outcome and are clinically useful.

Methods

This PhD consisted of four studies: Systematic review, feasibility study, case-control study and cohort study. I assessed quality, risk of bias and evidence levels of the current literature with the systematic review and provided an evidence gap map for the associations between landing biomechanics and PT. In preparation for the cohort study, I tested feasibility, validity and reliability of measurements. Online questionnaire battery yielded data from an international cohort of jumping athletes with a one year follow-up. I conducted multivariable regression analysis with self-reported variables to explain how jumping athletes with PT present in the case-control study and to predict recovery of PT in the cohort study.

Results

The systematic review with evidence gap map and meta-analysis identified that landing biomechanics might be associated with PT, but the level of evidence was typically limited or very limited with a high risk of bias. I have therefore focused on non-biomechanical factors in the prospective cohort study. The tested questionnaires were valid and reliable for online use, and the cohort study plan was feasible. The case-control study showed that self-reported sports specific and bio-psycho-social factors partially distinguish PT from other knee problems (n=221) with acceptable accuracy (AUC=0.76), specificity (70.8%) and sensitivity (70.5%), and partially explain both the variance of PT severity (n=132, R^2=0.44) and compromised participation with acceptable accuracy (AUC=0.72). 128 jumping athletes with PT provided 25,284 days total analysis time at risk (198±141 days) in the cohort study survival analysis. Recovery rate was 45%, mainly occurring around 6 months. The final multivariable cox proportional-hazards model partially predicted PT recovery with acceptable model performance and internal validation (optimism-corrected Harrell's C

discrimination=0.77 and Calibration Slope=0.86). The model showed PT recovery was associated with a higher KOOS-PF score (lower severity), a shorter time-off from sport, feeling more rested after sleep, not having concurrent tendon problems, higher training duration and symptoms which are modified by movement.

Conclusion

This is the first research project investigating outcome prediction for PT in a large international cohort of elite and non-elite jumping athletes. The developmental statistical causal model showed that the combination of sports specific and biomedical variables were potentially predictive of PT recovery. Demographic or psychosocial variables did not contribute to the model. These findings could support clinical decision making by helping to clarify who gets better, why they get better and when they get better. Our exploratory recovery model is readily applicable in clinical practice and could help researchers and clinicians to better understand the prognosis of PT.

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Thesis at a glance

Studies	Systematic Review Chapter 3	Feasibility Chapter 5	Case-control Chapter 6	Prospective Cohort Chapter 7
Aim(s)	To investigate whether landing biomechanics among jumping athletes are associated with PT and can predict onset.	To assess feasibility, validity and reliability by testing data collection procedures for a cohort study.	To determine what combinations of self-reported factors distinguish PT from other knee problems, and explain the variance of PT severity.	To determine what combination of self-reported factors predicts recovery of jumping athletes with PT.
Participants	17 studies including 116 JPTs, 14 with previous PT, 45 with asymptomatic PT abnormality and 202 controls.	36 jumping athletes equally spread between those with PT, other knee problems and controls.	132 jumping athletes with PT and 89 with other knee problems.	128 jumping athletes with PT.
Methods	We searched three databases from inception to May 2021. We assessed quality, risk of bias, evidence levels and provided an evidence gap map.	Combination of remote contact, assessment in clinic and biomechanical evaluation.	A previously validated, reliable online questionnaire battery yielded data from an international sample.	A previously validated, reliable online questionnaire battery yielded data from an international sample with a one year follow-up.
Conclusions	Landing biomechanics may be associated with PT, but the level of evidence was limited with high risk of bias high. Need high quality prospective studies to investigate causal relations.	The cohort study plan is feasible with the online questionnaire battery performing equivalently to traditional administration.	Sports specific, biomedical and psychological factors partially distinguish PT from other knee problems. Availability is mainly explained by sports specific factors, while psychosocial factors impact on severity.	The statistical causal model showed that the combination of sports specific and biomedical variables were potentially predictive of PT recovery. Demographic or psychosocial variables did not contribute to the model.

Keys: PT, patellar tendinopathy; JPTs, jumping athletes with PT.

Personal development

Key transferable skills were presented in . Please see the Appendix 1 for the full version of the completed Skill Point Database.

Mr A Tayfur (170630090)

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Points Summary

⊞ Show Yearly Totals

Year	Type	Pts: A	B	C	D	Total	Cap: A	B	C	D	Total
Total	Conference Attendance (One day)	6,0	4,0	0,0	0,0	10,0					
	Conference Attendance (Three days)	45,0	30,0	0,0	0,0	75,0					
	Conference Attendance (Two days)	12,0	8,0	0,0	0,0	20,0					
	Conference attendance sub-total	18,0	12,0	0,0	0,0	30,0		18.0	12.0			30.0
	Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)	120,0	0,0	0,0	0,0	120,0	120.0				120.0
	Doctoral College event/course	0,0	7,0	4,0	5,0	16,0					
	Education & Learning Course (Queen Mary Academy)	0,0	2,0	0,0	2,0	4,0					
	Other CPD course	0,0	0,0	6,5	0,0	6,5					
	Other course/event attendance	40,0	6,0	0,0	5,0	51,0					
	Researcher Development Course	32,0	24,0	14,0	16,0	86,0					
	School/Institute Induction < or = 3 hours	1,0	1,0	1,0	1,0	4,0		3.0	3.0	3.0	9.0
	Course/event/seminar attendance sub-total	193,0	40,0	25,5	29,0	287,5					
	Ethical Approval (NHS)	5,0	0,0	15,0	5,0	25,0	5.0		15.0	5.0	25.0
	Ethical Approval (standard, not fast-track)	3,0	0,0	9,0	3,0	15,0	3.0		9.0	3.0	15.0
	Ethical approval sub-total	8,0	0,0	24,0	8,0	40,0					
	Conference Presentation (Oral)	9,0	9,0	0,0	12,0	30,0	9.0	9.0		12.0	30.0
	Conference Presentation (Poster)	9,0	9,0	0,0	12,0	30,0	9.0	9.0		12.0	30.0
	Internal Presentation (< or =30 mins)	3,0	3,0	0,0	6,0	12,0	3.0	3.0		6.0	12.0
	Giving presentations sub-total	21,0	21,0	0,0	30,0	72,0					
	Journal Club/Reading Group/lab meeting/mentoring group - attendance	15,0	0,0	0,0	0,0	15,0	30.0				30.0
	Meeting/club/reading group attendance sub-total	15,0	0,0	0,0	0,0	15,0					
	Mentoring/supervising of Project Student	8,0	4,0	0,0	8,0	20,0	8.0	4.0		8.0	20.0
	Teaching/demonstrating/marking/preparation	0,0	2,5	0,0	2,5	5,0		15.0		15.0	30.0
	Teaching sub-total	8,0	6,5	0,0	10,5	25,0					
	Refereed Publication (Journal Paper, Book chapter, not abstract) acceptance	2,0	0,0	0,0	8,0	10,0	4.0			16.0	20.0
	Written publications sub-total	2,0	0,0	0,0	8,0	10,0					
	Total (with caps applied)	265,0	79,5	49,5	85,5	479,5					
	Target	60.0	20.0	15.0	30.0	210.0					

Key:
A: Knowledge and intellectual abilities, B: Personal effectiveness.
C: Research governance and organisation, D: Engagement, influence and impact
If you have any queries, please contact: Skills Points Database Support at spdsupport@qmul.ac.uk
This application is maintained by the Software Development Team, IT Services.

Figure 1: Points summary In Skill Point Database

Academic activities

I attended several academic activities during my PhD. For instance, I mentored one iBSc (Mr Arman Haque, 2017-2018) and one MSc (Mr Michael Harrison, 2018-2019) student project as a second supervisor. Both students graduated with distinction. I did 15 hours theoretical and practical teaching in Biomechanics and Rehabilitation Module (2019-2020) in Sports and Exercise Medicine Department (SEM). Marking iBSc and MSc exams and projects, being viva examiner and interviewer for the iBSc Program in SEM, and helping conference organization of the annual meetings of SEM were other academic activities I had.

I became an Honorary Physiotherapist of the Tendon Clinic in Barts NHS Trust (03.02.19 - 02.02.22) to be able to work with NHS outpatients related to my project. I also conducted other research related activities such as peer review in SCI journals (e.g. Journal of Sport Rehabilitation) and being a member of the site team for 1-year follow-up data collection of more than 70 patients for Achilles Team Trial (another project of Prof Morrissey).

Trainings

I attended numerous trainings during my PhD to be able to conduct my studies. For instance, I attended to 'Introduction to Good Clinical Practice eLearning (Primary Care)' provided by National Institute of Health Research (28.10.2017) and 'Good Clinical Practice for Interventional Studies' by Joint Research Management Office of QMUL (17.01.2018) as it is a practical guide to ethical and scientific quality standards in clinical research, and I needed for my ethics approvals in the UK. To be able to collect US imaging data, I attended to 'Introduction to MSK Ultrasound Imaging Course in Sports Medicine' on 29-30 September 2017 and 'Advanced Lower Limb Muscle Tendon Injury Masterclass' on 14-15 September 2019 provided by Sports Medicine Ultrasound Group. To be able to collect biomechanical data, I attended two trainings organised by Codamotion Group including 'The basics of the Coda technology and how to use it' (03.01.2018) and 'Odin/Gate 3D Analysis system, Kistler Force Plates and Delsys EMG integration' (10.01.2018).

I also attended numerous data analysis related trainings including 'Systematic review and meta-analysis' and 'Fundamentals of Data Visualisation' courses via QMUL Researcher Development Course or several online courses via Coursera or Udemy regarding epidemiology and related statistical analysis methodologies. For instance, I attended to 6-week online course labelled 'Epidemiology: The Basic Science of Public Health' on Coursera (19 February - 19 March 2018) to understand more about the observational studies I planned to use in my PhD project. I learned

sophisticated data and statistical analysis software such as MATLAB, R and STATA and necessary coding knowledge. MATLAB helped me to analyse the biomechanical data for the feasibility study, while R helped for data visualisation. STATA helped case-control and cohort study analyses. These analyses required learning linear regression and logistic regression for case-control study and survival analysis for cohort study. Lastly, I attended to 'Statistical Methods for Risk Prediction and Prognostic Models' online statistical course by Keele University (19-21 May 2021) in order to learn advance statistical analyses such as testing model performance, model validation and optimisation.

After completing my PhD, I will continue my career as an academic in Turkey which mostly requires conducting research, giving theoretical lectures and practice in clinic. Therefore, developing strong academic skills in research, teaching and clinic was essential for me.

Publications and presentations related to PhD work

Published

1. **Tayfur A**, Haque A, Salles JI, Malliaras P, Screen H, Morrissey D. Are landing patterns in jumping athletes associated with patellar tendinopathy? A systematic review with evidence gap map and meta-analysis. Sport Med. 2021; 52:123-37. DOI: https://doi.org/10.1007/s40279-021-01550-6

2. **Tayfur A**, Salles JI, Miller SC, Screen H, Morrissey D. Patellar tendinopathy outcome predictors in jumping athletes: feasibility of measures for a cohort study. Physical Therapy in Sport. 2020; 44: 75-84. DOI: https://doi.org/10.1016/j.ptsp.2020.05.004

3. **Tayfur A,** Şendil A, Karakaya J, Ergun N. Cross-cultural adaptation, validity, and reliability of Turkish version of Identification of Functional Ankle Instability (IdFAI) scale. Acta Orthop Traumatol Turc. 2020; 54(3): 300-4. DOI: https://doi.org/10.5152/j.aott.2020.03.256.

Under review

4. **Tayfur A**, Şendil A, Sezik AÇ, Kaux J-F, Sancho I, Le Sant G, Dönmez G, Duman M, Tayfur B, Pawson J, Uzlaşır S, Miller SC, Screen H, Morrissey, D. Self-reported bio-psycho-social factors partially distinguish patellar tendinopathy from other knee problems and explain patellar tendinopathy severity in jumping athletes: A case-control study.

5. Sancho I, Morrissey D, Willy RW, **Tayfur A**, Lascurain-Aguirrebeña I, Barton C, Malliaras P. Recreational runners with Achilles tendinopathy have clinically detectable impairments: a case-control study.

In preparation

6. **Tayfur A**, …, Zenner D, Screen H, Morrissey D. Outcome predictors for recovery of patellar tendinopathy in jumping athletes: an international prospective cohort study.

Presentations

1. LASEM Sports Medicine Student Showcase, Outcome predictors for recovery of patellar tendinopathy in jumping athletes: A cohort study, **Oral Presentation,** October 27, 2020, Online, La Trobe University, Australia.

2. 21st Annual Conference in Sport & Exercise Medicine, Reliability and validity of a graded loaded challenge for patellar tendinopathy: A laboratory study, **Oral Presentation,** September 13, 2019, QMUL, London, UK.

3. Scandinavian Sports Medicine Congress, Are jump landing patterns associated with patellar tendinopathy in competitive athletes? - A systematic review, **Poster Presentation,** January 31, 2019, Copenhagen, Denmark.

4. 5th International Scientific Tendinopathy Symposium, Patellar tendinopathy outcome predictors in competitive athletes: Feasibility for a cohort study, **Poster Presentation**, September 28, 2018, University Medical Center Groningen, Holland.

5. 5th International Scientific Tendinopathy Symposium, Are jump landing patterns associated with patellar tendinopathy in competitive athletes? - A systematic review, **Poster Presentation**, September 28, 2018, University Medical Center Groningen, Holland.

6. Sports Traumatology and Rehabilitation Congress, Rehabilitation of isolated MCL injuries, **Invited Speaker,** March 30, 2018, Uskudar University, Istanbul, Turkey.

7. 9th International Sports Physiotherapists Congress, Sports specific performance tests: Volleyball, **Invited Speaker,** November 11, 2017, Ankara, Turkey.

Awards

1. The Queen Mary, University of London Postgraduate Research Fund has been granted (12.11.2020) successfully for the 3-day statistical analysis course labelled '*Statistical methods for risk prediction and prognostic models*'. **Award: £550.**

2. **Best Presentation** in Young Investigators Category in 21st Annual Conference in Sports & Exercise Medicine, Reliability and validity of a graded loaded challenge for patellar tendinopathy: A laboratory study, **Oral Presentation,** September 13, 2019, QMUL, London, UK. **Award: £500.**

Project collaborators external to direct thesis supervision

Chapter 3

Assoc Prof Peter Malliaras: Department of Physiotherapy, Monash University, Australia

Dr Jose Incaio Salles: Visitor research fellow at Queen Mary University of London

Dr Arman Haque: iBSc student at Queen Mary University of London

Chapter 5

Dr Jose Incaio Salles: Visitor research fellow at Queen Mary University of London

Dr Stuart Charles Miller: Lecturer at Queen Mary University of London

Chapter 6

Dr Ateş Şendil: School of Physical Education & Sports, Cyprus Health and Social Sciences University

Mr Atilla Çağatay Sezik: Department of Physiotherapy and Rehabilitation, Yuksek Ihtisas University, Turkey

Prof Kaux Jean-François: Physical Medicine & Sport Traumatology Department, University and University Hospital of Liège, Belgium

Mr Igor Sancho: PhD student at Queen Mary University of London

Dr Guillaume Le Sant: Movement, Interactions, Performance, University of Nantes, France

Dr Gürhan Dönmez: Sports Medicine, Hacettepe University, Turkey

Mr Mehmet Duman: Republic of Turkey Ministry of Youth and Sports

Ms Beyza Tayfur: PhD student at Queen Mary University of London

Ms Jessica Pawson: Research physiotherapist at Barts Health NHS Trust, London, UK

Mr Serkan Uzlaşır: School of Sports Science & Technology, Nevşehir Hacı Bektaş Veli University, Turkey

Stuart Charles Miller: Lecturer at Queen Mary University of London

Chapter 7

Dr Dominik Zenner: Senior clinical lecturer at Queen Mary University of London

List of abbreviations

ACL	Anterior cruciate ligament injury
ACWR	Acute: chronic workload ratio
AL	Acute load
AU	Arbitrary units
AUC	Area under the ROC curve
BMI	Body mass index
CL	Chronic load
CONOSRT-PF	Consolidated Standards of Reporting Trials - Pilot and Feasibility trials
CSA	Cross-sectional area
eCRF	electronic Case Record Form
eHEALS	eHealth Literacy Scale
EPV	Event per variable
EQ5D5L	Health-related Quality of Life
ESWT	Extracorporeal shockwave therapy
EWMA	Exponentially Weighted Moving Average Model
FA	Full Availability
FSWT	Focused shockwave therapy
GPS	Global Positioning Systems
GRF	Ground reaction force
GRoC	Global Rating of Change Scale
GSE	General Self Efficacy Scale
IC	Initial contact
ICC	Intraclass Correlation Coefficient
ICF	Informed consent form
JPTs	Jumping athletes with PT
KOOS	Knee Injury and Osteoarthritis outcome score
LR	Loading rate
MRI	Magnetic resonance imaging
NA	Not applicable
NHS	National Health Service
NP	Navigate Pain
NREM	Non-rapid eye movement
OP	Other knee problems
PASS	Patient Acceptable Symptom State
PCS	Pain Catastrophizing Scale
PFP	Patellofemoral pain
PIS	Patient information sheet
PROBAST	Prediction model Risk Of Bias ASsessment Tool
PROMs	Patient reported outcome measures
PT	Patellar tendinopathy
PTF	Patellar tendon force
RA	Rolling Average Model
RCT	Randomised controlled trial
ROC	Receiver operating characteristic
ROM	Range of motion
RPE	Rating of perceived exertion

RSWT	Radial shockwave therapy
SANE	Single Assessment Numeric Evaluation
SEM	Sports and Exercise Medicine Department
sRPE	sessional RPE
ST	Smart Trial
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TSK	Tampa Scale for Kinesiophobia
US	Ultrasound
VAS	Visual Analogue Scale
vGRF	Vertical GRF
VISA-P	Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon

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1   Introduction

This PhD project is about outcome predictors for patellar tendinopathy (PT) in jumping athletes. PT is a common, painful, repetitive-use condition in athletes who participate in sports that require a lot of jumping, landing and sprinting (1,2). A recent randomised controlled study (RCT) (3) reported that 82% of the participants in their sample underwent prior treatment for PT but did not fully recover. Overall, recovery rates are unsatisfactory, with observational studies showing resolution in around 65% at six months irrespective of intervention (4,5). The condition causes more than four weeks off sport in up to 60% of athletes (5,6), is difficult to manage, with at least 25% suffering recurrence (6). Furthermore, PT symptoms may last for years, affect sports and work participation, and even be a reason to end a sports career in up to 50% of affected jumping athletes (4,7). Intriguingly, causal explanation of PT non-recovery and recurrence remain elusive (8), despite its high prevalence in well-defined, accessible populations and many research studies. Therefore, PT is a huge burden for the jumping athletes and if it does not recover fully, may become a disabling problem.

1.1   Anatomy of patellar tendon

Tendons are anatomic structures between muscles and bones making joint movement possible by transmitting the force created in the muscle to the bone. Bright white in colour, fibro-elastic in tissue, and being resistance to mechanical loads are main properties of a healthy tendon. The patellar tendon is the extension of the quadriceps femoris muscle tendon and extends from the inferior patellar pole to the tibial tuberosity (Figure 2). Width and thickness of the patellar tendon are approximately 3 to 3.5 cm and 4 to 5 mm, respectively (9,10). Patellar tendon length changes from 5 to 7.5 cm based on the attachment on the patella and tibial tuberosity (11). Cross-sectional area (CSA) of patellar tendon is around 1.5 cm^2 (12), and it increases distally (13).
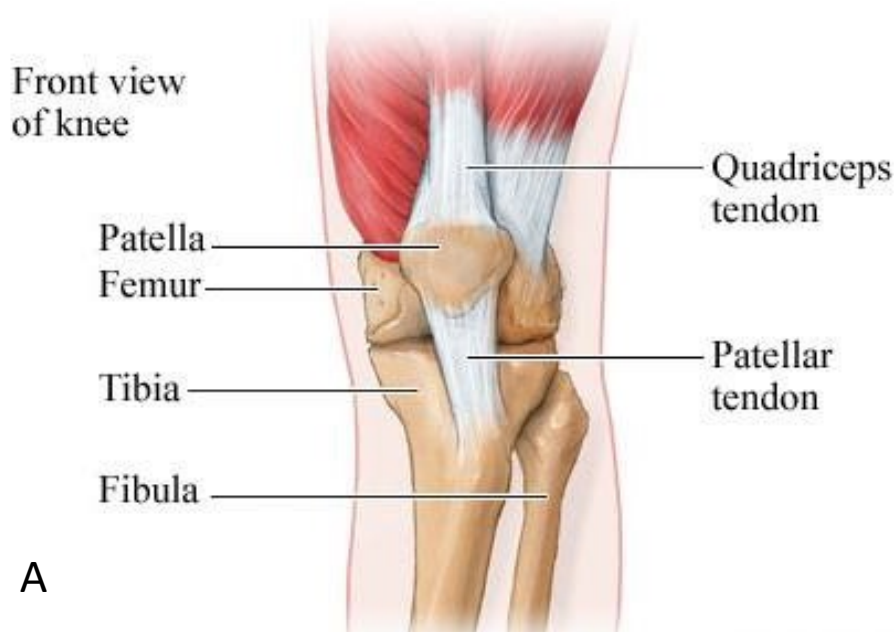
Figure 2: Anatomy of patellar tendon, A: Anterior aspect of the knee, B: US imaging of proximal patellar tendon, C: US imaging of distal patellar tendon

1.2 Tendon biomechanics and properties

Tendon is a multi-unit hierarchical structure that consist of collagen molecules, fibrils, fibril bundles, fascicles and tendon units that run parallel to the geometrical axis (14,15) (Figure 3). The parallel arrangement of fibre bundles is very efficient for tendons to transfer high muscle force to the skeleton for movement, although tendons have a low resistance to shear forces (16). Thus, tendons are designed to transfer forces with minimal deformation or energy loss (16). Typical parameters describing the tendon mechanical properties were described by Heinemeier and Kjaer (17). Typical the relationship between tendon extension and the force required to achieve this extension is reported in a force-extension curve. The gradient of this curve is the stiffness, with steeper gradients defining a stiffer tendon. These measurements offer a useful baseline and identify the overall forces a tendon can withstand. However, they are referred to as 'sample properties', as they are specific to the individual tendon under exploration. In order to acquire more general understanding of the

material properties of tendon, it is necessary to normalise these parameters to the size of the tendon sample under investigation. This is carried out by converting to a stress-strain curve (Figure 4). Stress reports the force normalised to the tendon cross sectional area, whilst strain reported the extension normalised to original sample length. The gradient of this curve is the modulus, or the normalised stiffness. Modulus varies throughout the stress-strain curve, but is usually a maximum somewhere in the middle of the linear region, termed the yield point (Figure 4). If a tendon is stretched beyond this point irrecoverable damage is initiated.

Both force and stress are often reported when exploring tendon strength, as strength is not only related to the tendon CSA but also the structure and composition of the specific tendon, impacted by variables such as intrafibrillar cross links and collagen type distribution (16,18). The material properties of tendon vary widely, with rough ranges provide in Figure 4.
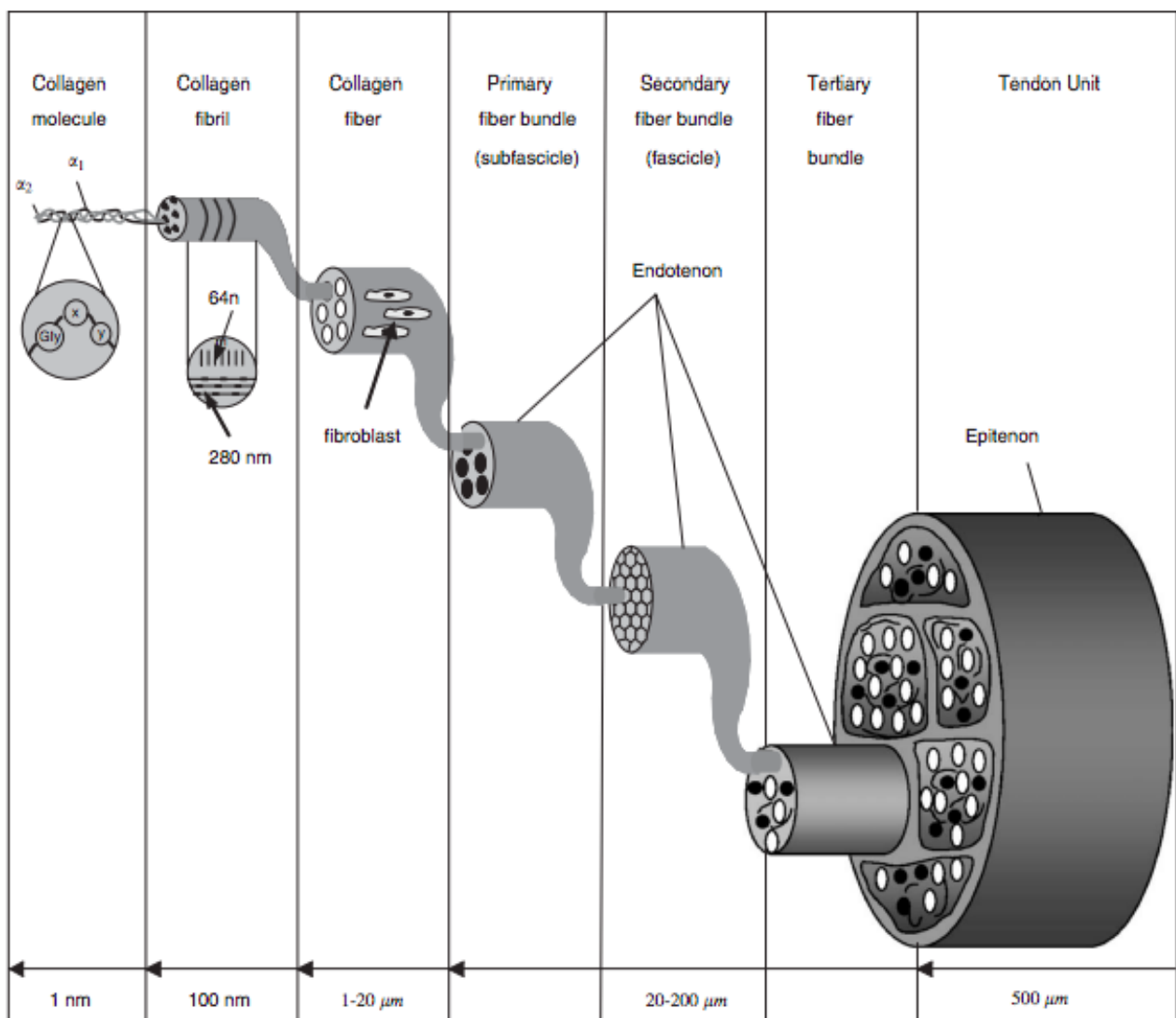
Figure 3: A schematic of a multi-unit hierarchical structure of the tendon. This figure is used without permission (14,15), for the thesis only.
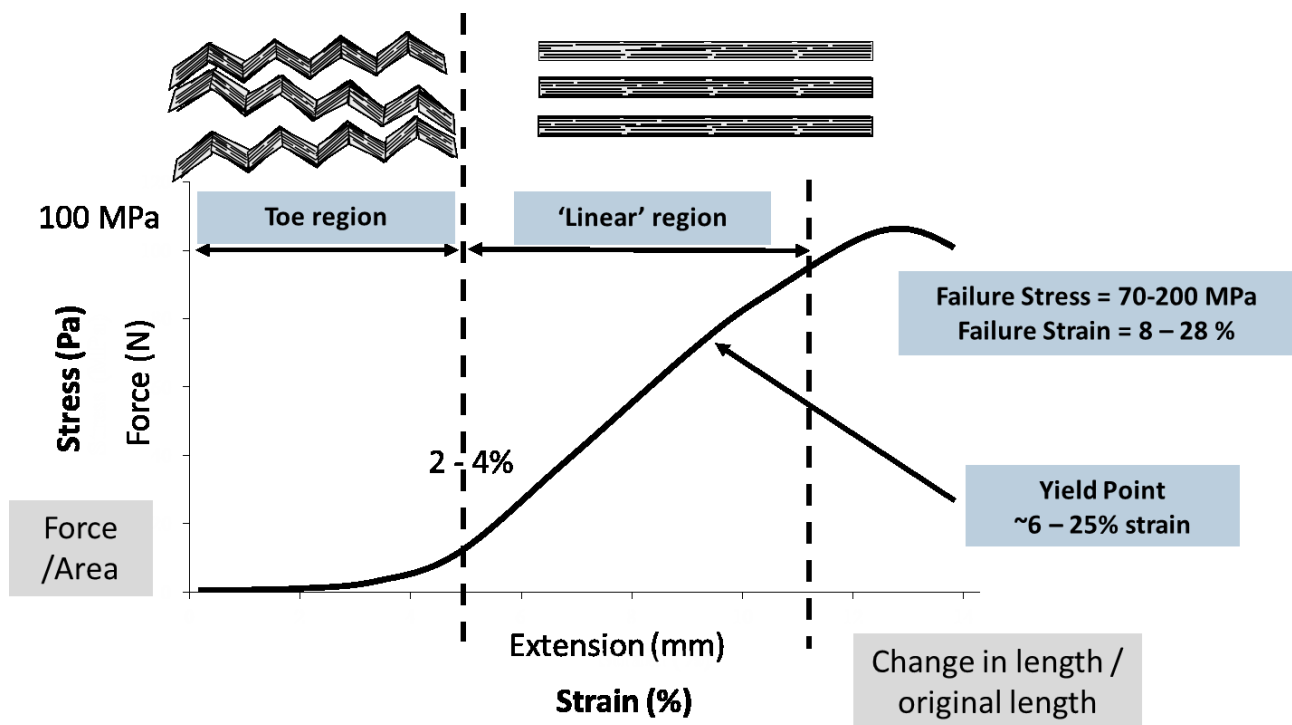
Figure 4: Tendon stress-strain curve. This figure is adapted from Prof Hazel Screen's lecture notes, 2021.

1.3 Pathophysiology and differential diagnosis

The key pathophysiologic features of PT are being a degenerative disease, especially located in the posterior aspect of the proximal part of patellar tendon adjacent to the inferior patellar pole and being non-inflammatory disorder (19). For tendon pain, light microscopy reveals collagen separation such as thin, frayed, and fragile tendon fibrils, separated from each other lengthwise and disrupted in cross section (19,20). An increased number of tenocytes with myofibroblastic differentiation (tendon repair cells) can be observed instead of classic inflammatory cells (20). This matches with tendinosis (21) and it is not just a result of tendinitis in long term. Tendinosis presents without inflammatory cells in acute tendon injury in animals (22). Therefore, the main pathophysiologic phenomenon is tendinosis instead of tendinitis for PT.

Patellar tendinopathy would be diagnosed clinically based on load dependent (1,23,24) localised pain to the inferior patella pole (25,26) by palpation or simply asking to patients. Ultrasound (US) or magnetic resonance imaging (MRI) would be used to support the diagnosis of PT (9,27,28). Pain with prolonged sitting, squatting, and stairs, may present as other signs of PT (29). However, the source of these symptoms could be other potential knee pathologies. Therefore, differential diagnosis between PT and other knee pathologies is important.

Tendinopathy in the knee can also occur at the quadriceps tendon or insertion of the patellar tendon at the tibial tuberosity (29). Quadriceps tendinopathy localises to its insertion on the superior patella pole (30) and is often related to activities requiring deep knee flexion (31). Distal patellar tendon pain is localised to its insertion and frequently seen in distance runners (32). Infrapatellar bursa irritation frequently coexists with distal patellar tendinopathy as it is adjacent to the distal patellar tendon attachment (29,33). Mid- or whole-tendon patellar tendinopathy generally occurs after a direct blow (34); however, same injury mechanism may also cause bursa, fat pad and patellofemoral joint problems (29).

The contribution of Hoffa's (infrapatellar) fat pad to anterior knee pain is not understood fully. However, the fat pad is known to have vascular (35) and fascial (36) connections to the patellar tendon. Fat-pad injury often related to repetitive end-range knee extension and also would be associated with a tibiofemoral hyperextension overstrain (37). A relation has been described between infrapatellar fat-pad hypertrophy with PT (38). The localisation of pain is the main difference between these two conditions. Fat-pad pain is a more diffuse pain in the anterior inferior knee, and it occurs especially during end-range extension or with palpation applied directly to the fat pad during Hoffa test (37). The patellofemoral joint would be another cause of anterior knee pain among jumping athletes. Patellofemoral associated pain is usually diffusely around the patella (39) instead of localising inferior patella pole. Diagnosis of patellofemoral pain (PFP) would be based on exclusion of other pathologies as there are no clear sensitive and specific clinical tests (40,41).

Athletes with PFP often report symptoms during activities that have lower load on tendon, such as walking, running, or cycling (24), which should result in a higher suspicion for a diagnosis other than PT. Additionally, reduction of pain when using patellofemoral taping, with provocative manoeuvres, such as lunge or squat (40), and patellofemoral joint mobility examination would also be helpful in the differential diagnosis of PFP (29). Plica (42) and chondral surface pathologies would also cause anterior knee pain. Palpation of the plica, a history of a snapping sensation, and MRI often assist in the diagnosis of a plica. The clinical presentation of osteochondral lesions localised to the inferior part of the patella or of the trochlea may sometimes mimic PT. Clinically, joint effusion is usually a sign of intra-articular pathology and does not present in PT (29). Age could be an important factor in the differential diagnosis as both PT and isolated fat-pad irritation are common in adolescents (24). Additionally, Osgood-Schlatter syndrome at the tibial tuberosity (common) or Sinding-Larsen-Johansson syndrome at the inferior patella pole (rare) would be potential source of anterior knee pain in this age group (43).

1.4   Definitions

The following terminologies are defined in this PhD project based on the literature:

Tendinopathy is a condition characterized by a combination of tendon pain and tenderness to palpation verified by US or MRI findings demonstrating structural changes in the affected area (9,27,28).

Patellar tendinopathy is defined as a lesion associated with load dependent pain and tenderness at the inferior pole of the patella (9,27).

Persistent pain is defined by condition as one or more current pain symptoms present on most days over a period of 6 months or more (44).

Recovery is defined by an authoritative consensus statement for use in epidemiological studies in athletes as the return to training and competitions with full availability (45) at any time point.

If an athlete is not fully available for training and competitions it is considered as a *non-recovery*.

To our knowledge, there is no definition or a valid and reliable question for full availability. Therefore, if an athlete is able to train and compete without restriction it is considered as *full availability*.

Recovery is being collected as a main outcome with the Global Rating of Change Scale (GRoC) (46). If an athlete states top two categories of GRoC (Figure 5) at any time point it is considered that they recovered.

Full availability (FA) is being collected with binary questions (Figure 5) for training and competitions separately to ensure about recovery based on definition.

Recurrence is defined by an authoritative consensus statement about epidemiological conditions in sport as an incident of the same type and at the same site linked to an index incident and which occurs after an athlete's return to full function and participation ("full recovery") from the index recordable incident (45).

With respect to your knee pain, how satisfied are you with your condition?

- ◉ Better
- ○ No change
- ○ Worse

How much better?

- ○ Slightly better
- ○ Somewhat better
- ○ Moderately better
- ◉ Much better
- ○ Very much better

Are you currently fully available* for training?

- ◉ Yes
- ○ No

*Full availability means that you are able to train/compete without restriction.

Are you currently fully available* for competition?

- ○ Yes
- ◉ No

Figure 5: Global Rating of Change (GRoC) scale and binary questions for 'Full Availability'. Circle refers the top two categories of GRoC. In this figure, the participant is not fully recovered due to being unavailable for the competition.

1.5 Injury prevalence

Injuries of the lower extremity account for more than 50% of reported injuries in all levels of sports (47), and the mostly injured joints are knee and ankle (47–49). Approximately, 30-50% of all sports related injuries are reported as tendinopathy (50) with clinical symptoms such as load-related pain,

tenderness, localised swelling and disability (51). Tendinopathy is frequently reported within the upper and lower limb (52) and 6% of all knee injuries over 6 months are diagnosed with PT (53).

PT is a common painful repetitive condition in athletes who participate in sports that require a lot of jumping, landing and sprinting (1,2). The overall prevalence of PT is 14% and 8.5% among elite and non-elite athletes of different sports, respectively (1,2). The highest prevalence of PT is found in volleyball (44.6% elite; 14.4% non-elite) and basketball (31.9% elite; 11.8% non-elite), both sports have a high impact loading on the knee (1,2). PT prevalence is higher in male athletes (13.5% elite; 10.2% non-elite) compare to females (5.6% elite; 6.4% non-elite) (1,2).

PT causes significant time off sport, is difficult to manage, and is prone to recurrence, estimated to be between 12% and 27% (6). Furthermore, symptoms of PT may last for a prolong period (around 30 months elite; 18 months non-elite), affect sports and work participation, and even be career-ending for up to 50% of athletes with PT (4,7). As a result, PT is a common recurrent repetitive-use condition, especially in jumping athletes, and takes time to recover.

1.6   Recovery rate

Recovery rates are around 50% for knee conditions (54,55). Only 25% recovery after 3 months, increasing to 44% after 12 months was reported in patients with a new episode of knee complaints (54). More specifically people with PFP, another chronic knee pain condition, have a recovery rate of 55% and 40% at 3 and 12 months, respectively (55). PT also has similar recovery rates, with the highest reported being 65% (Table 1) (4,5). Higher recovery rates of PT were reported in soccer players (6,56). Definition of recovery could be the reason of higher rates as it was based on time loss from training or match play. When standard methods of injury registration, typically relying on a "time-loss", are used in epidemiological studies, overuse injuries are difficult to record (57). PT symptoms such as pain or functional limitation generally appear gradually and may be transient in nature. Thus, it is likely that athletes continue to train and compete despite the presence of overuse injuries, hence non-recovery, at least in the early phase (58). While improvements have been reported for different treatments in RCTs, full-recovery was not achieved in terms of Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon (VISA-P) or Visual Analogue Scale (VAS) scores in either short or long-term (59–61). Therefore, PT is a huge burden for the jumping athletes and if it does not recover fully, may become a very disabling impairment.

Table 1: Recovery rates of PT. Keys: NA, Not applicable; US, ultrasound; ESWT, Extracorporeal shockwave therapy; FSWT, Focused ESWT; RSWT, Radial ESWT; RCT, Randomised controlled trial.

Study	Sample size	Study groups	Follow up time	Follow up frequency	Recovery definition	Prevalence & Incidence	% Recovery	% Recurrence
Hagglund et al., 2011, Cohort (6)	2229 soccer players	NA	8 years between 2002-2009	Weekly & Monthly	Followed consensus document (62,63). Time loss: an injury that occurred during a scheduled training session or match that caused absence from the next training session or match. Tissue injury: an injury is recorded regardless of whether or not it causes subsequent absence from training or match play.	For each season: 2.4% (season prevalence) with an incidence of 0.12 injuries/1000 hours	61% absence < 1 week, 10% absence > 4 weeks from training & match play. The median absence was 5 days, with 75% of players (out of 137 players with PT) returning within 12 days.	12%-27%
Kettunen et al., 2002, Case Control (4)	32 male athletes	18 athletes with PT 14 control	15 years between 1984-1999	15 years (baseline and at the end)	Occurrence of knee pain during the previous year was investigated, and those who reported having pain in the knee at least once per month were classified as having monthly knee pain.	NA	53% of athletes (9 out of 17) with PT reported that they had quit their sports career, compared with 7% of the control (1 out of 14). 33% of athletes with PT (6 of 18) and 14% of the control subjects (2 of 14) reported monthly knee pain.	NA
Fredberg et al., 2008, RCT (56)	209 Danish professional soccer players (Only symptoms directly related to the Achilles and patellar tendons were included.)	Half the teams were randomized to an intervention group with prophylactic eccentric training and stretching of the Achilles and patellar tendons during the season	Over 12 months with use of US & injury registration	A year (baseline and at the end) + players with Achilles and patellar tendon injuries during the season were examined	Followed consensus document (62). An injury: any physical complaint sustained by a player resulting from a soccer match or training, irrespective of the need for medical attention or time loss from soccer activities. An injury requiring medical attention was referred to as a "medical-attention" injury or preventing a player from being able to take a full part in future soccer activities was a "time-loss" injury. A re-injury: an injury of the same type and at the same site as an index injury and occurring after a player's return to full participation after the index injury. Injuries were classified into 3 severity categories: 1. medical attention and according to the length of absence from soccer activities (time loss), 2. "minor" (1-28 days, including the day of injury), and 3. "major" (>28 days, including the day of injury). A player was defined as injured until the club medical staff cleared him for participation in full training or match play. A player who performed alternative training or participated in only a part of the training session (e.g. during rehabilitation after an injury, or due to a pain syndrome) was considered injured.	2.1 injuries per player (14.4 injuries/1000 hours of soccer)	The majority of injuries were medical-attention or minor, resulting in an absence <7 days. Players with major injuries that necessitated rest for >28 days, re-injuries were responsible in only 7% of players with PT.	21%
Zwerver et al., 2011, RCT (59)	57 volleyball, 1 handball and 4 basketball players (non-elite) 57 completed the study intervention	Effectiveness of patient-guided focused ESWT treatment (compared to placebo ESWT) on pain reduction and recovery of function in athletes with PT	22 weeks	1, 12 and 22 weeks after the final ESWT or placebo treatment	Recovery was followed based on VISA-P score. A 15-point difference in the VISA-P score between the treatment and placebo is considered to be clinically relevant.	NA	Mean VISA-P Scores / ESWT / Placebo — Before 59.4±11.7 / 62.4±13.4; After 1-week 66.8±16.2 / 66.3±19.0; After 12-week 66.7±17.5 / 68.9±20.3; After 22-week 70.5±18.9 / 72.7±8.0	NA
Van der Worp et al., 2014, RCT (60)	43 athletes with PT (57 patellar tendons)	Patients undergo three sessions of either FSWT or RSWT at 1-week intervals, both in combination with eccentric decline squat training	14 weeks	1, 4, 7 and 14 weeks after the final treatment	Recovery was followed based on VISA-P score. A difference in the VISA-P score of 15 points at the end of the study (12 weeks) is considered to be clinically relevant.	NA	Mean VISA-P Scores / FSWT / RSWT — Baseline 48.6 ± 18.7 / 48.8 ± 17.2; 1-week 53.7 ± 17.2 / 53.9 ± 16.0; 4-week 54.1 ± 16.3 / 58.1 ± 18.2; 7-week 59.6 ± 16.9 / 53.5 ± 21.5; 14-week 63.6 ± 24.2 / 58.4 ± 22.1	NA
Willberg et al., 2011, RCT (61)	45 athletes with PT (52 patellar tendons)	Group A: Treatment with US and colour Doppler-guided sclerosing polidocanol injections. Group B: US and colour Doppler-guided arthroscopic shaving	12 months	Group A: 6-8 weeks after each treatment Group B: 2 weeks and 6-8 weeks post-operatively. Further follow-ups at 6 and 12 months after treatment.	Recovery was followed based on the clinical effect of the treatment by having the patients to score the level of patellar tendon pain (a difference of 50 mm in VAS between the groups) during their specific sport or recreational activity, and at rest, and evaluate patient satisfaction with the results of the treatment.	NA	Mean VAS Scores / Group A / Group B — Baseline at rest 37.8 ± 24.9 / 44.6 ± 28.4; Baseline at activity 69.0 ± 17.3 / 76.5 ± 13.6; Follow up at rest 19.2 ± 23.2 / 5.0 ± 8.3; Follow up at activity 41.1 ± 28.5 / 12.8 ± 19.3; Satisfaction with result, 0–100% 52.9 ± 32.6 / 86.8 ± 20.8	NA
Cook et al., 1997, Cross Sectional (5)	100 athletes with PT	NA	A 9-year period (retrospectively)	NA	Recovery was followed based on sports participation.	NA	67% of athletes were prevented from playing or training for > 4-week, or both. 34% of athletes were unable to play for > 6-month, with 19% of this group side-lined for > 12-month. 51 athletes entered the study with their 1st episode of PT; 32 athletes: 2nd or 3rd episode, 17 athletes: at least 4th episode. 3 athletes reported having symptoms for 10 or more years. Thus, virtually half of the cases were athletes with recurrence of PT.	%49

1.7 Potential variables explaining patellar tendinopathy onset or prognosis

There are several previously identified intrinsic and extrinsic risk factors increasing the onset of PT in athletes. Age, height, weight, sex, genetics, alignment of lower limb, flexibility, jump height are the main intrinsic factors (2,64). Extrinsic factors include practicing a jumping sport characterized by high demands on speed and power for the leg extensors, the number of training hours (elite athletes > non-elite), amount of training, playing surface, number of jumps performed, playing position and the high frequency and intensity of training and competition (2,64–67). It therefore seems plausible that the higher the mechanical overload on the tendon, the greater the risk for developing a PT (2).

1.7.1 Intrinsic factors

1.7.1.1 Age

Non-elite athletes with PT were significantly younger than those without PT (2), although there was no significant difference in elite athletes (1). Being younger would be associated with the aetiology of PT in elite and non-elite jumping athletes (68), in contrast with the later study, which found no association (69). However, because of changes in tendon structure and mechanical properties, it has been suggested that the risk for tendinopathy increases with an age over 30 (70–72). The reason of this conflict could be the studies which found younger age as a risk factor have not recruited athletes over 35 years old. Another reason could be that athletes with PT stop playing their sports more often than athletes without injury. A third reason could be that younger athletes may increase the volume and intensity of training load very quickly. On the other hand, there was no association between age and PT in five studies (73–77) investigated in a systematic review (78). However, some of these studies (74,75) only recruited students and elite level players. This led to a smaller age range, making it hard to find an association between age and PT. Therefore, the results for age are still inconclusive in terms of onset of PT and there is no available data for the prognosis of PT.

1.7.1.2 Sex

PT is more prevalent in male athletes, elite and non-elite, compare to females (1,2). Being male is a risk factor for PT in elite and non-elite jumping athletes (68,69). Being female has been reported as a protective factor for PT, and there was no significant difference in PT status of females in terms of menopausal status (79). Reduced tendon thickening and pathology has been reported among females taking hormone replacement therapy (80). This would indicate that hormones (e.g. oestrogen) may explain the protective effect of sex. Hormone concentrations may also affect

susceptibility to tendinopathy as oestrogen has a direct effect on fibroblast proliferation and collagen synthesis (81). This sex difference could also be caused by the difference in the force-generating capacity of the quadriceps between male and female athletes (1). Puberty could be another reason as female athletes may potentially have more mature tendon compare to males as they generally enter puberty earlier and grow earlier. Number of jumps in young elite volleyball players could affect the difference in sex indirectly as male athletes jumped (35.7 jumps/hour in training, 62.2 jumps/hour in competition) more than females (13.7 jumps/hour in training, 41.9 jumps/hour in competition) (82). In contrast, there was no differences between male and female athletes in the risk of PT (77,83). There were also no differences in menstrual history (age of menarche, number of cycles in the past 12 months and use of oral contraceptives) between female athletes with and without PT (76). In conclusion, there is some evidence that sex is associated with the onset of PT, but there is no available data for the prognosis of PT.

1.7.1.3   Height, weight and body mass index

Jumping athletes with PT were significantly taller, and weighed more than those without PT (1,2,68,69), and body mass index (BMI) did not differ between athletes with and without PT (2,68). There was no association between height and PT in six studies (73–76,84,85) investigated in a systematic review (78). On the other hand, weight would be associated with the aetiology of PT (75,83,85). In contrast, there was no association between weight and PT in other studies, although athletes with PT were on average heavier than those without PT (73,74,76,84,86). A higher BMI has been identified associated with PT in jumping athletes (83), and other studies found similar results only for male volleyball players (85) or only for basketball players (69). Being heavier and having higher BMI may cause tendinopathy through higher load on the patellar tendon. In conclusion, there are some evidence for weight and BMI in terms of developing PT, and very limited evidence for height. However, there is no available data for the prognosis of PT.

1.7.1.4   Anthropometrics and alignment of lower limb

There is some evidence that waist-to-hip ratio, leg-length difference and foot arch height are risk factors for developing PT. Waist girth and hip girth (only in males with bilateral PT) were associated with PT for male volleyball players (85), but not in another study that only included elite female basketball players (76). A waist-girth score (>83 cm) increased having signs of PT on imaging by 74% (85), and treatment could be less effective in people with high adiposity levels (87). An association has been reported between a higher waist-to-hip ratio and PT in female athletes with unilateral PT (76) and in males with bilateral PT (85). This indicates a larger abdominal fat distribution relative to

gluteofemoral fat deposits (88). Fat distribution in human is controlled by a complex interaction of hormones and is specifically influenced by the female sex hormones (oestrogen and progesterone), but the mechanisms whereby hormones control this fat distribution are unclear (89). Van der Worp et al. also reported higher odds ratio for waist-to-hip ratio in elite and non-elite jumping athletes, but it was not independently associated with PT when accounting for other related variables such as sex (68). The influence of a higher waist-to-hip ratio could be purely mechanical as in the case of weight, or non-mechanical such as an increase of free fatty acids and pro-inflammatory cytokines resulting from elevated abdominal adiposity may negatively influence tendon health (85,90). There was no difference in skinfolds between elite junior basketball players with and without PT (84).

Relation between leg-length difference and PT has been investigated by several studies. Greater leg-length difference has been reported in jumping athletes with PT compared to controls, the symptomatic leg on average being the longer one (83). A larger leg-length difference in athletes with PT was also reported by Kujala et al. (86,91), in contrast with another study, which found no association (74). Moreover, a longer tibia length relative to height was found in elite female basketball players with unilateral PT (76). Crossley et al. and Kujala et al. suggested that the possible association for leg-length difference could be the fact that the longer leg is the preferred take-off leg in jumping more often (83,86). Crossley et al. also stated that the leg-length differences were too small to be considered functionally important (83). It was even smaller in the study of Kujala et al. (86). Thus, although there is some difference in leg-length, whether this link is clinically relevant remains a question. There was no association between PT and Q-angle, Q-angle displacement or medial tibial intercondylar distance (74,86).

Jumping athletes with PT had a lower foot arch height compare to those without PT (83), in contrast with a study which found no association (79). However, Morton et al. used an online survey to investigate the relation in arch height (79). It has been reported that runners with lower foot arch height were more likely to develop knee and soft tissue injuries than runners with higher arch height who were more likely to develop ankle and bone injuries (92). They found a greater peak knee flexion angle in runners with a lower arch, and postulate that greater quadriceps muscle force is needed to prevent further knee flexion. This could be the case during jump-landing, hence in athletes with PT. As a result, there are some evidence that anthropometrics may cause PT, but no data are available for the prognosis of PT.

1.7.1.5 Strength and flexibility

There is some evidence that quadriceps and hamstring flexibility, and quadriceps strength are risk factors for developing PT (78). It was hypothesized that lower quadriceps strength could cause PT, yet it could also be caused by atrophy as a result of inactivity brought about by PT (78). There was a significant difference between athletes with and without PT in quadriceps and hamstring flexibility, and athletes with PT had a lower flexibility compared to those without PT (74). The reason for flexibility could be that less flexibility increases tendon strain during joint movements, and thus, might lead to tendon overload (74). Morton et al. found similar results by using online survey for hamstring flexibility, but not for quadriceps flexibility and ankle dorsiflexion range (79). Using online survey for these variables could be the reason of conflicting results. On the other hand, there was no differences in hamstring flexibility in another study (83). Sit-and-reach test has been investigated by several studies as a measure of hamstring and low back flexibility. Sit-and-reach scores were significantly lower in female basketball players with unilateral PT and in male basketball players with bilateral PT compared to their controls (84). Other studies found no differences in sit-and-reach test scores (76,83,93).

Reduced ankle dorsiflexion range is identified as a risk factor for PT in jumping athletes (93,94), but there was no association in another study (83). Normalised peak knee extensor moment was lower in jumping athletes with unilateral PT compared to controls, but it was not for athletes with bilateral PT (83). There were no differences between groups in knee flexion and extension torques (86), concentric and eccentric strength (76,95), hamstring and quadriceps strength (74), or ankle plantar flexion strength (93), calf endurance (83), speed, endurance and agility (84) and the hamstring-quadriceps quotient, which describes the imbalance between knee flexors and extensors (95). As a result, there are some evidence that strength and flexibility may cause PT, but no data are available for the prognosis of PT.

1.7.1.6 Jump performance

There is some evidence that vertical jump performance is a risk factor for developing PT. Female basketball players with PT jumped higher than those without PT, but there was no difference in males (84). It has been reported that volleyball players with PT had also a better performance on jump tasks (73,75). However, there were no differences in jump height (76,93), in a speed and distance hop test (83) between groups. In conclusion, there is some evidence that jump performance is associated with the onset of PT, but it is still inconclusive in terms of prognosis of PT.

1.7.1.7 Jump and landing biomechanics

The knee is responsible for transferring load and dissipating mechanical energy during jump-landings. A portion of this load is transferred through the patellar tendon (96). Overload as a result of high eccentric loads during repeated jumping is thought to be the main cause of PT (97,98). However, in a systematic review it was found that a stiff landing might also pose a threat for developing PT, as PT was associated with factors related to horizontal landing more than take-off (99). The increased vertical ground reaction force during the take-off phase of spike and block jumps was associated with an increased risk of patellar tendon pain, as well as increased knee flexion during landing from jump and a greater external tibial torsion moment during take-off (100). Similar results have been shown in a later study that large external tibial torsional moments combined with deep knee flexion angles during a jump and landing increases the risk of PT (101). Differences in lower extremity landing kinematics have been noted between volleyball players with a history of PT when compared to those without a history concluding that a stiff landing pattern with limited knee motion at landing and a short landing time is associated with development of PT (102,103). In my systematic review (Chapter 3), I concluded that landing biomechanics may be associated with PT presence, but the level of evidence for the majority of variables was limited or very limited, and risk of bias high despite good applicability.

1.7.1.8 Genetics

Involvement of genetics in tendon injury was originally proposed because of an association between the blood group O and chronic Achilles tendinopathy or Achilles tendon ruptures (104–106). The gene for ABO on chromosome 9q34 encodes for transferases which, apart from verifying the structure of glycoprotein antigens on red blood cells, might also determine the structure of some proteins of the extracellular matrix of tendons (104). Sequence variants within genes (e.g. variants within the TNC, COL1A1, COL5A1 and MMP3) that encode for several tendon and/or ligament extracellular matrix proteins have been shown that there was an association with specific musculoskeletal soft tissues injuries such as chronic Achilles tendinopathy, Achilles tendon ruptures, cruciate ligament ruptures and/or shoulder dislocations (107–109). The COL5A1 gene, which is in close proximity to the ABO genes on chromosome 9q34, encodes for a structural component of type V collagen (110). This collagen type forms heterotypic fibres with type I collagen in tendons and possibly plays an important role in regulating fibrillogenesis and, thus, tendon strength (14,111). However, it is still not clear whether COL5A1 and TNC genes are the ideal markers of tendinopathy (112).

Recent studies have been investigated relation between other genes and tendinopathy. A significant association between BMP4 rs2761884 and tendinopathies (patellar, Achilles, shoulder, and hip abductors) has been reported (71). Athletes with a polymorphic genotype had 2.4 times more susceptibility to tendinopathy (71). Another association between disease and haplotype TTGGA in BMP4 was observed, and the FGF3 TGGTA and FGF10 rs900379 haplotypes demonstrated a tendency of association with tendinopathy (71). These findings suggest that haplotypes in BMP4 and FGF3 genes might contribute to the tendon disease process in elite volleyball players. Relation between tendinopathy and VEGF and KDR genes has also been investigated in volleyball athletes (72). KDR 1192 GA and GA + AA genotypes and the KDR (-604C>T, 1192G>A and 1719T>A) haplotypes CGA and CAT were associated with lower risk of tendinopathies (patellar, shoulder and Achilles) (72). VEGF and KDR polymorphisms were not associated with clinical symptoms complaints such as pain, traumatic lesion and being away from training due to injury (72). These results provide that the KDR polymorphisms were associated with tendinopathy and may contribute to predict tendinopathy outcome. In contrast, there was no difference in genotype or minor allele frequencies in elite volleyball players with and without PT (113). However, the low-frequency homozygous T/T genotype of the COL1A1 gene (rs1800012) was absent in PT group (113). In conclusion, there is a limited evidence that genetics are associated with tendinopathy, and further studies are needed especially on PT prognosis.

1.7.1.9   Ultrasound changes

Athletes with PT reveal some pathological abnormalities when examined by ultrasound. However, relation between structural tendon changes and pain remains unclear. Current knowledge is not clear whether the presence of ultrasound changes in asymptomatic tendons predicts outcome of tendon problems. There is some conflicting evidence on patellar tendon. It has been reported that a hypoechoic area was a risk factor for developing PT in elite junior basketball players, but also that structural changes were not necessarily associated with symptoms (114). Similar results have been reported for professional soccer players (115). However, the same research group also reported that ultrasound changes did not predict future tendon problems in adult athletes (116). Hypoechoic changes were observed in asymptomatic tendons by 10-30%, and hypoechoic areas can resolve, remain unchanged, or expand (10,114,115,117). Neovascularisation, increase of blood flow and perfusion, was reported in chronic painful Achilles tendons (118). Moreover, neovascularisation has been observed in the area with tendon changes (localised widening of the tendon with focal hypoechoic areas) in all painful tendons, but not in any of the normal pain-free tendons (118). Later

studies have shown similar findings for the patellar tendon as well (119–122). As a result, presence of ultrasound findings in the tendon may be predictor of PT outcome.

1.7.1.10 Relation with other diseases and family history

A positive family history of tendon disorders has been identified as a risk factor (79,123). Genetic association should also be considered in addition to family history if there are genes that may be inherited and put athletes at greater risk of non-recovery. Family history of rheumatoid arthritis, psoriasis, ankylosing spondylitis may also be associated with PT as tendinopathies are reported in inflammatory and autoimmune conditions (124). There was an association between tendon health and high cholesterol, and familial hypercholesterolemia was associated with tendon disease and rupture (90). Achilles tendon was significantly thicker in female patients with type 2 diabetes compared to nondiabetic matched controls (125). Tendinopathy symptoms associated with the use of statins have been reported (126). Prevalence of lower limb tendinopathy increases in active post-menopausal women who were not taking hormone replacement therapy (80). Loss of oestrogen is thought to result in poorer tendon health (90). An indirect association between smoking and Achilles tendinopathy has been shown (123) potentially due to lifestyle. A trend toward significance has been reported between PT and current or previous low back pain (79). There is not so much literature on relation with PT and low back pain. Thus, it is unknown whether PT leads to low back pain or vice versa. Similar approach could be applied for the relation between PT and previous knee injuries. PT group had experienced a previous knee injury that had kept them out of sport for more than 6 weeks with a higher significant odds ratio (79). In conclusion, potential contribution of other diseases should also be considered for the prognosis of PT.

1.7.2 Extrinsic factors

1.7.2.1 Playing surface

The incidence of PT is higher in volleyball players who play on concrete compared to those who play on parquet or linoleum (77). Similarly, higher odds ratio for playing on concrete in athletes has been reported (68). For the elite beach volleyball players, who jump and land in soft sand, a prevalence of 9% has been reported, which is much lower than the rate for indoor volleyball players (66). It was suggested that a softer playing surface reduces the risk of PT (66). In contrast, there was no association between PT and the percentages of running on hard surfaces (95), but type of activity was different. There is some evidence that playing surface is associated with the onset of PT, but it is still inconclusive in terms of prognosis of PT.

1.7.2.2 Number of jumps

Volume of jumping, especially maximal and horizontal stop jumps, might increase the load on PT (75,127,128), hence the type of training could influence on the risk of PT (79). There was no difference in jump frequency between young elite volleyball players with and without PT, although it differed between male and female athletes. Number of jumps in male volleyball players (35.7 jumps/hour in training, 62.2 jumps/hour in competition) was higher than females (13.7 jumps/hour in training, 41.9 jumps/hour in competition) (82). Jump frequency has substantial inter-individual and sex differences during training and competition in volleyball players (82). Total jump volume may represent an important predictor for PT outcome prediction alongside the training load.

1.7.2.3 Amount of training/competition, numbers of years playing and type of training

Many studies evaluated the influence of the sports related factors on the development of PT. The volume of training and competitions should also be considered in addition to the mechanical loading imposed by jumps and landings. There are five studies reported an association with the amount of training/competition and numbers of years playing in volleyball and basketball players (71–73,76,77) and another three studies with no association with developing PT in volleyball players (75,93) and female runners (95). The relationship between training time and PT incidence has been found in volleyball and basketball players (127,129). As hours of training (>20 hours a week) increased the association with PT became stronger and had a very significant higher odds ratio (79). Similarly, training and playing volleyball or basketball (>12 hours a week) and/or in combination with weight training (>5 hours a week) is associated with an increased risk of PT (130). More strength training was associated with PT (75), in contrast with other studies which found no association (73,77). There was no association between PT and the amount of jump training (73,75), warm-up time and stretching time (73), or stretching time during warm-up and after training (75).

Hours of training per week, type of sport (volleyball > basketball) and playing level (national level > regional) showed increased odds ratios for PT (68). Associated with amount of training, number of semi-professional or professional athletes has been reported higher in PT group (79). A comparison of injury rates between basketball and volleyball players who participate at various competitive levels revealed that the rate of injury increases in accordance with the competition levels (1,47,131). Playing higher level of sport is likely to increase training time and is therefore likely to explain increasing risk of PT. Another reason for this could be that athletes at the higher level have more muscle power and jump higher, hence place heavier load on the knee (75). The reason for type of sport (volleyball > basketball) is not clear. It could be differences in terms of number of jumps or

jump style/performance. It has been reported that elite volleyball players jump higher than elite basketball players in a drop jump task (132), and basketball and volleyball players use different jumping techniques, adapted to the demands of their sport (133). On the other hand, a trend was reported for years playing volleyball and basketball, but no significant difference in hours of training per week, playing level, and sports participation of athletes with and without PT (69). The reason of this conflict could be that this study (69) is the second part of their previous study (68), and athletes who were diagnosed with PT in the first study were not invited for the second survey. This caused the less national level athlete relative to previous study. The found trend for years of playing volleyball or basketball seems to be a coincidence (69) as results were conflicting, shorter sports participation for volleyball while longer for basketball. Total years playing sports, current number of training and match hours did not differ between non-elite athletes with and without PT, although they differed in terms of demographics (e.g. sex) (2). In elite athletes, with and without PT, there was no significant difference in number of years of participation in organized training and number of hours with sport-specific training (1). However, athletes with PT did significantly more weight and jump training (1). Basketball players with PT did significantly more sport-specific training than those without PT, while male handball players did significantly more plyometric training (1). Playing position was also associated with PT in volleyball as it has been reported that middle blockers tend to suffer from PT more than players in other positions (66) and playing as outside hitters or middle blockers was a risk for PT compared to playing as setters (68,75). This is probably because of the different demands of these playing positions. Outside hitters, opposites and middle blockers jumped more during a game than setters (134). They did not include libero players because of their specific defensive role, it was thought that they jump less than players in other positions.

Young volleyball players who developed PT had greater total training volume and greater exposure in relation to players who were asymptomatic (135). It has been hypothesized that a sudden change and increase in training volume when young, promising players are promoted from the junior to the senior level could increase the risk of PT (136). Therefore, degenerative changes of the tendon may take place with accumulated training volume (79), and athletes, who increase their training volume the most, may have the highest risk of developing PT (75,136).

In conclusion, there is some evidence that sports-related factors are associated with the onset of PT, but no data are available for the prognosis of PT. Specifically, we are interested whether acute: chronic workload ratio (ACWR) could be another predictor variable as it is associated with injury risk

(137), plus training loads is found an associated factor for the onset of PT, and ACWR has never been investigated for PT outcome prediction.

1.8   Training load monitoring

Elite athletes are exposed to high training-load, intense competition calendars, and very short periods of rest and recovery (138). It is known that game congestion is related to increased injury rates (139). Because of the importance of player availability, there has been a surge in training-load and monitoring research recently (140). Evidence suggests that inadequate training-load management is a major risk factor for injury (138). Therefore, most of the training-load related injuries are preventable, and thus, sport science and sports medicine practitioners should address these issues by applying monitoring protocols (137). For these reasons, monitoring of training- and game-load is very important to prevent injuries and to improve the management of present injuries.

Heart rate monitoring and micro technology, including global positioning systems (GPS) and accelerometers are commonly used to quantify training-load in team sports (141). The GPS devices are used to measure distance travelled, running speeds, and repeated-sprint efforts of athletes (142). On the other hand, accelerometers provide further information on the impacts tolerated by the athletes, giving feedback on the overall body load these impacts generate (142). Accelerometers have acceptable level of technical reliability both within and between devices for measuring physical activity, providing increased practical application within team sports (143).

All methods might have their own inherent strengths and weaknesses (Table 2) usually depend on the context of the program they are applied and the objectives to be achieved (140). Acceptable validity and reliability provide an essential criterion, but the resources available will then affect the level of tolerance to issues related to expense, precision, ease of use, and staffing. While standards for implementation should be similar to those expected in research, the choice of method may be affected by the logistics of implementation. For instance, GPS time–motion analysis is only possible in an outdoor environment, requires hardware and software, and is restricted to locomotor movements and position tracking. It is, however, easily interpretable and can be used to prescribe training. Accelerometers, often integrated with other sensors in wearable devices, are similar in cost, hardware and software requirements. Accelerometers have the advantage of being independent of location and activity yet possess limitations in data interpretation and direct use to prescribe training. In contrast, sessional-rating of perceived exertion scale (sRPE) is a low-cost method that has the advantage of being able to quantify load irrespective of mode or location.

However, both methods, GPS and accelerometers, have a strong reliance on technology and technical expertise, and a high risk of data loss. Additionally, they might be quite expensive and difficult to apply with large groups of athletes (144–146). Therefore, alternative methods that are low-cost and easy to apply within large groups may be more effective and appropriate.

Table 2: Features of training load monitoring methods. This table is adapted from Bourdon et al. (140). Keys: RPE, rating of perceived exertion; sRPE, session rating of perceived exertion; ACWR, acute: chronic workload ratio; GPS, global positioning systems; L, low; M, medium; H, high; Y, yes; N, no; AU, arbitrary units; AL, acute load; CL, chronic load.

Methods	Cost	Hardware needed	Software needed	Ease of use	Valid	Reliable	Used to prescribe	Variables
RPE	L	N	Y/N	H	M-H	M-H	Y	Single variable in AU (time dependent)
sRPE	L	N	Y/N	H	M-H	M-H	Y	Single variable in AU (time dependent)
ACWR	L-M	Y/N	Y	M	M-H	M-H	Y	Size of AL relative to CL
GPS	M	Y	Y	M	M-H	M	Y	Velocity, distance, acceleration, time in zones, location
Accelerometer	M	Y	Y	L-M	M-H	M	N	x-y-z g force

A low-cost method of training-load monitoring which has gained popularity in the last few years is the acute: chronic workload ratio (ACWR). ACWR (137) measures the relationship between acute load (current week load) and chronic load (last 4-weeks average load) based on the difference between 'fatigue' and 'fitness' from Banister's model (147). Monitoring ACWR helps to keep player's workload in the 'high-load, low-risk zone' (ACWR= 0.8-1.3). If ACWR is too low (less than 0.8) or too high (1.5 or more), injury risk increases, and workload may be adjusted (Figure 6) (137,148). ACWR allows practitioners to view a snapshot of an athlete's training-load history including competitions; thus, allowing practitioners to assess the availability of their athletes for competitions, to improve load management, to track performance, and act as a daily marking value for injury risk.

Measuring training-load basically requires multiplying intensity by duration (149). Athletes provide their intensity with sRPE (Figure 7) and the duration in minutes (150). The units also could be 'kg' lifted weight, 'km' distance for running or swimming, and number of repetitions (140). The overall training- and game-load may be affected by; the level of opponents, time available for recovery between sessions, and location of competitions (149).
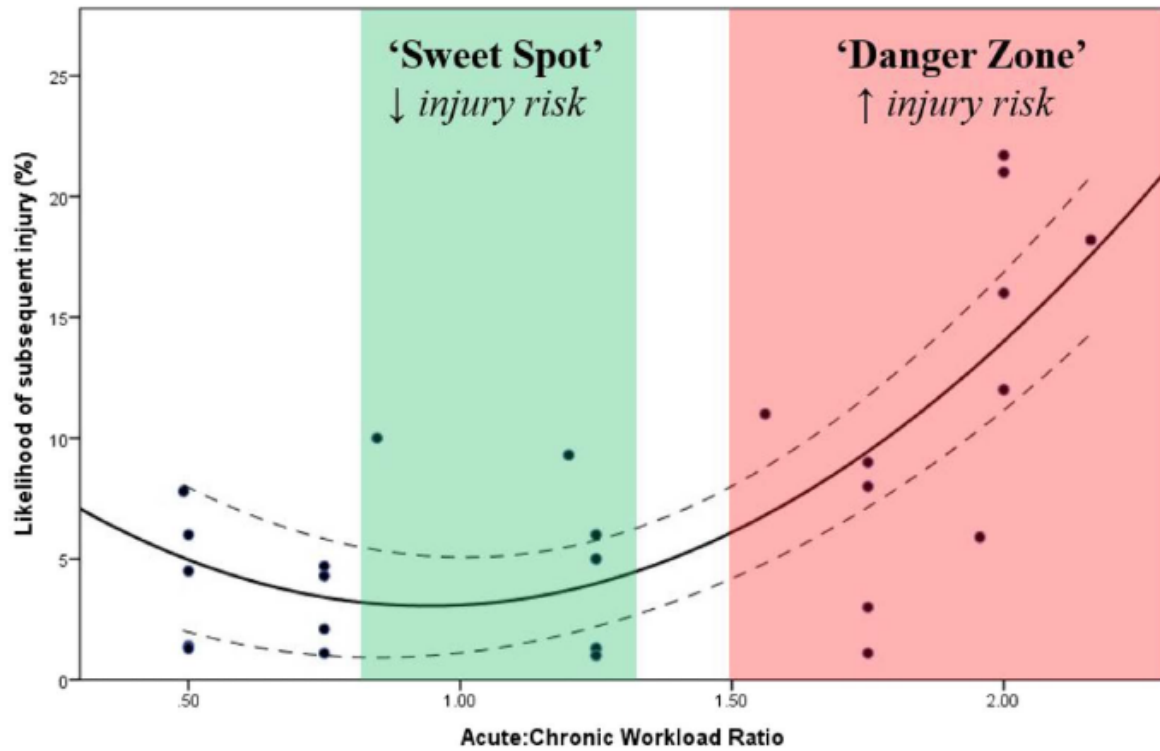
Figure 6: Guide to interpreting and applying ACWR data. The green area (sweet spot) shows ACWRs where injury risk is low. The red area (danger zone) represents ACWRs where injury risk is high. To minimise injury risk, practitioners should aim to maintain ACWR within a range of approximately 0.8–1.3. This figure is used without permission (137,148), for the thesis only.

Figure 7: Rating of Perceived Exertion (RPE) Scale.

The Acute Load (AL) represents the cumulative load of the current week (151). AL gives information about training- and match-load over the last 7-day period. It represents the 'fatigue' aspect of the ACWR. The chronic workload (CL) is the average weekly load, typically over the previous 4 weeks (28-day) (151). CL provides a clear indication of what athletes have done leading up to the present training or game day. It is commonly viewed as a sign of an athlete's 'fitness'. For instance, an athlete has a weekly average workload as below:

- Week 1=800
- Week 2=1000
- Week 3=700
- Week 4=1300

In this case, AL (week 1) is 800, CL is the average of these four workloads [(800+1000+700+1300)/4=950], and ACWR is provided as 0.84 by AL/CL (800/950). This process would need to be replicated for each athlete, and for every session. The final AL value, the exact calculation of the CL, and interpretation of the data will vary according to the type of ACWR model the practitioner wishes to use. There are two models named The Rolling Average Model (RA) or the Exponentially Weighted Moving Average Model (EWMA) (152). The RA model uses absolute (i.e. total) workload performed in 1-week AL relative to the 4-week CL as in the previous example (152). The EWMA model places a greater emphasis on the most recent workload an athlete has performed by assigning a decreasing weighting for each older workload value (152).

ACWR approach was reported to identify injury risk in a variety of athletes (151,153,154). However, while interesting for monitoring injury risk, the validity of the ACWR has recently been questioned (155,156) as the rolling average fails to account for the decaying nature of fatigue and fitness effects over time, and therefore it may not accurately represent variations in the manner in which loads are accumulated. An alternative method is to use an exponentially weighted moving average (157) for the calculation of acute and chronic loads, which assigns a decreasing weighting to compensate for the latency effects of loads (156). Further research is, however, required to determine if this new model provides a superior approach for predicting performance and/or injury.

There is no report for the reliability of the ACWR according to our knowledge. However, Scott et al reported the validity and reliability of the sRPE method which is one of the components of the ACWR (142). They reported that the sRPE may not be sensitive to detect small changes in exercise intensity during short intermittent running sessions because of the poor levels of reliability. However, the

sRPE still is a valid method that has reported strong associations between heart rate based and RPE-based methods to quantify training-load in high-intensity, intermittent team sport (142,144).

In this PhD, I designed a 1-year prospective cohort to determine outcome predictors for PT in jumping athletes. I aimed to recruit participants with the online survey and follow them up for a year. ACWR is a valid, easy to apply, and a low-cost method to identify the relation between training-load and outcome prediction of PT. However, ACWR is difficult to manage for a large group with an online based method for a long time period, as it should be collected daily after each session. I conducted a feasibility study (Chapter 5) to test the main cohort study procedures including ACWR method. I aimed to see if I can collect daily ACWR retrospectively for the last 6-week period at a time. The feasibility study showed that training load recall percentage decreased until week-3 with only the 20% maintaining a training diary completing the full 6 weeks. Additionally, participants reported that entering daily training load data for 6-week period was very long. Therefore, weekly training load data was collected every three weeks via online survey.

1.9   Literature gap

To our knowledge no data are available that describe a single variable or model (combination of variables) that predicts recovery of PT. It has been shown that a multivariable model predicts non-recovery better than a single variable in the case of shoulder pain (158). Therefore, using a model could enable clinicians to improve decisions on the prognosis of jumping athletes with PT (JPTs) and to manage patients' expectations accordingly. It may also provide evidence-based indications for testable exercise programs, rehabilitation strategies and training volume management.

As discussed earlier, exact pathophysiology of tendinopathy is not clear. PT is a common condition with a poor recovery. Although there is some evidence on factors associated with onset of PT, there is no evidence for the prognosis. It was reported the number and overall methodological quality of the studies was low (78), and studies allowing causal inference are scarce due to the lack of prospective studies. It was also suggested that including recreational athletes to make the results more generalizable for future studies as many studies used elite-level athletes (78). Moreover, results were often conflicting, and many studies used univariate statistical techniques to test differences between groups, even without correction for multivariable testing (78). Using more sophisticated statistical procedures such as multivariable statistical techniques has been suggested (78) to identify outcome predictors while accounting for other pertinent variables. Prospective cohort study design is widely preferred for epidemiological studies to develop a prediction model

and to identify causal relationships between exposures and health outcome (159). PT is likely to have a multifactorial aetiology (78), therefore identifying outcome predictors for prognosis could be more challenging.

In conclusion, there is a clear need for a high-quality prospective cohort study which uses sophisticated statistical methods in order to build statistical models to explain how PT presents in jumping athletes, and what the outcome predictors of recovery are. To achieve this, I needed to prepare the methods for, and undertake, collection of epidemiological data from a large number of participants then follow them up for one year to determine causal relationships between how athletes present and how they recover. This model will inform delivery of a tool to predict outcome, in subsequent research.

2 Aims, objectives, impacts and hypotheses

The overarching aim of this thesis was to build statistical models that explain how PT presents in jumping athletes, predict PT outcome and are potentially suitable to be used in clinical practice.

The impact of success should be providing an approach that improves clinicians and researchers understanding of the condition prognosis, hence better management of jumping athletes with PT (JPTs). In other words, the outputs from this project should allow medical professionals to improve their clinical decision making by addressing who gets better, why they get better and when they get better.

2.1 Specific aims, objectives, impacts and hypotheses

The purpose of the introduction chapter was to clarify the gap in the existing literature by providing an overview of current knowledge about PT, epidemiology of PT, reported associated factors for PT, and to orientate the reader to the following chapters.

To achieve the overarching aim, this thesis consisted of four studies with the following specific aims, objectives, impacts and hypotheses:

2.1.1 The systematic review and meta-analysis

I introduced a variety of potential associated factors with PT onset and prognosis in the introduction chapter. These were mainly demographics, anthropometrics, sports specific and biomedical factors. Intriguingly, despite PT high prevalence and many research studies, very little known specific to relation between landing biomechanics and PT, hence a causal explanation for PT presence remains elusive. Therefore, a review of the association between landing biomechanics of PT are presented in chapter 3.

The aim of the systematic review was to determine whether jump-landing biomechanics are altered among JPTs and can predict onset.

The impact of success should be synthesising evidence regarding the role of jump-landing biomechanics in PT for professionals attempting to manage and prevent PT in jumping athletes by using biomechanical strategies and to guide future research.

The alternative hypothesis was that there is a strong level of evidence with low risk of bias showing an association between jump-landing biomechanics and PT in jumping athletes.

2.1.2 Study development

In the introduction and systematic review chapters, I concluded that there is a clear need for a high-quality prospective cohort study to better understand presentation and prognosis of PT in jumping athletes. Thus, I planned an international prospective cohort study with a variety of measurements including online questionnaire, physical assessment, ultrasound imaging and biomechanical tests to collect potential factors related to PT.

The purpose of the study development chapter was to demonstrate the progress of the measurement development for the cohort study.

2.1.3 The feasibility study

I presented the progress of the online questionnaire, clinical and ultrasound assessments and biomechanical tests of the planned cohort study in the study development chapter. I conducted a feasibility study to assess these data collection procedures. Therefore, feasibility, validity and reliability of the planned cohort study measurements are presented in chapter 5.

The main aim was to assess feasibility, by testing data collection procedures in order to optimise the success of a planned international prospective cohort study. The secondary aim was to test the validity and reliability of selected measurements.

The impact of success should include useful information about data collection procedures and guide the necessary amendments to optimise the planned cohort study.

The alternative hypothesis was that data collection procedures of the planned cohort study were feasible, valid and reliable.

2.1.4 The case control analysis of the cohort study

I concluded that the cohort study plan is feasible in the feasibility study chapter. In chapter 6, I specifically focused on how jumping athletes with PT (JPTs) present and differ from athletes with other knee problems. We also lack a clear understanding of why some athletes present with worse severity than others. Therefore, the findings from the baseline surveys of the cohort study are presented in chapter 6 as a case-control study.

The main aim was to improve our understanding of JPTs by determining what combination of self-reported factors distinguishes JPTs from athletes with other knee problems. The secondary aim was to investigate the variance of PT severity as defined either by condition severity or sporting availability.

The primary impact of success would be a better understanding of the condition by comparing to other knee problems. The secondary impact of success should be providing deeper explanation of the variance in PT severity, hence better management of the condition.

The alternative hypothesis was that multivariable statistical regression models distinguish PT from other knee problems and explain both the variance of condition severity and compromised participation in jumping athletes.

2.1.5   The prospective cohort study

I presented how JPTs present and differ from athletes with other knee problems in the case-control study chapter. Specifically, PT severity and compromised participation were partially explained by the exploratory multivariable models. In chapter 7, I focused on outcome predictors for recovery of PT. Therefore, findings from the follow-up surveys of the cohort study are presented in chapter 7.

The aim of the cohort study was to improve our understanding of prognosis in JPTs by determining what combination of self-reported factors predicts PT recovery.

The impact of success would be a better understanding of PT prognosis and management of JPTs by providing an explanation of PT recovery.

The alternative hypothesis was that multivariable statistical survival model predicts outcome for PT in jumping athletes.

3 Are landing patterns in jumping athletes associated with patellar tendinopathy? A systematic review with evidence gap map and meta-analysis

In the introduction chapter, I introduced a variety of potential associated factors with PT onset and prognosis. These were mainly demographics, anthropometrics, sports specific and biomedical factors. Intriguingly, despite PT high prevalence and many research studies, very little known specific to relation between landing biomechanics and PT, hence a causal explanation for PT presence remains elusive. Therefore, a review of the association between landing biomechanics of PT are presented in this chapter.

Preliminary results of this systematic review were presented at the 2018 5th International Scientific Tendinopathy Symposium in Netherlands and the 2019 Scandinavian Sports Medicine Congress in Denmark. This review has been accepted for publication by Sports Medicine (Impact Factor=11.136, https://doi.org/10.1007/s40279-021-01550-6) after three rounds of comprehensive peer review and has been adapted for the thesis.

3.1 Introduction

The knee has a major role in transferring load and dissipating mechanical energy during landing (96). A high proportion of this load is transmitted through the patellar tendon (96) helping the lower limb joints to distribute kinetic energy (160) which has been proposed as one of the causal biomechanical factors for PT onset. Increased vertical jump performance (height) has previously been found to be a possible associated factor for PT in volleyball players, but only limited evidence exists (78). The mechanism is likely to be higher knee loads during higher jumps (78) which highlights the potential importance of landing patterns in jumping athletes. An association between altered landing kinematics and PT onset was previously reported (99). Thus, landing biomechanics including kinematics (e.g. initial contact angles of joints, peak joint angles or angular velocities) and kinetics (e.g. joint moments, ground reaction forces, tendon forces or lower limb muscle activation patterns) are plausible factors that may influence PT onset or become impaired following PT onset. Therefore, synthesising study results concerning landing biomechanics is necessary.

Van der Worp et al. (2014) (99) conducted a systematic review with six studies reporting horizontal landing kinematics potentially linked to PT onset. Harris et al. (2020) (161) published an updated systematic review of 15 studies finding 37 biomechanical variables to be associated with PT and

asymptomatic patellar tendon abnormality (PTA), however there was no grading of evidence level or pooling of data therefore limiting data interpretation. De Bleecker et al. (2020) (162) published a systematic review with meta-analysis investigating jump-landing kinematics for a range of lower extremity overuse injuries, including nine reports specific to PT, which concluded that the kinematic associations with PT are poorly understood. No recent comprehensive review has scoped the literature to demonstrate evidence gaps (as per established approaches (163,164)), graded the evidence, assessed the risk of bias and pooled data of a comprehensive search of the literature. An updated review that addresses these deficits would help make sense of the literature for professionals attempting to manage and prevent PT.

The aim of this review was to determine whether jump-landing biomechanics are altered among jumping athletes with PT (JPTs) and can predict onset. A secondary aim was to quantify research quality and identify gaps in the literature to synthesise evidence regarding the role of jump-landing biomechanics in PT and guide future research. The alternative hypothesis was that there is a strong level of evidence with low risk of bias showing an association between jump-landing biomechanics and PT in jumping athletes.

3.2   Materials and methods

The PRISMA Statement guided the design and reporting of this systematic review (165) (Appendix 2). We could not register this review to PROSPERO due to starting the data extraction before November 2019 when PROSPERO rules changed.

3.2.1   Search strategy

PubMed, Web of Science and the Cochrane Library databases were searched from inception to May 2021. We used two domains in the search strategy with the following terms: patellar tendinopathy OR tendinitis OR tenosynovitis OR tendinosis OR other relevant synonyms for the condition domain AND jumping OR landing OR biomechanics for the task and measurements domain. Detailed search terms used can be found in Appendix 3. No limits such as 'time' or 'human studies' were applied to the search.

3.2.2   Inclusion and exclusion criteria

Interventional, cross-sectional, case-control and prospective cohort studies in the English language investigating the association between three-dimensional landing biomechanics and PT were

considered for inclusion. Case report, case series, meetings, letters, editorials, reviews, pilot studies, abstracts and animal studies were excluded. We included studies in jumping athletes (any sport) with history of patellar tendinopathy (or synonyms; tendinitis/ tenosynovitis/ tendinosis) and/or patellar tendinopathy diagnosed clinically, and/or asymptomatic patellar tendon abnormalities assessed on ultrasound imaging and/or healthy controls with or without assessment of tendon morphology. Studies of asymptomatic athletes with PT abnormality were considered eligible for this review as this abnormality has been shown to be a risk factor for PT development (115,166), hence potentially improving understanding for the associations with landing biomechanics. Measures of interest included kinematic variables such as initial contact angles of joints (hip, knee, ankle) or segments (i.e. trunk), range of motion and peak angles in the same joints or segments, and joint angular velocities; and kinetic variables such as joint moments, peak ground reaction forces (GRF) in both horizontal and vertical planes, peak patellar tendon force and lower limb muscle activation patterns.

3.2.3 Study selection

All studies identified by the search strategy were downloaded by two independent authors (AT and AH) into Mendeley Desktop (version 1.19.5, Mendeley Ltd., London, UK). After removing duplications, two authors independently screened all titles and abstracts and retained the papers according to inclusion criteria. The full-text of the retained papers from the titles and abstracts alone were obtained and evaluated for the final inclusion, and any disagreements resolved at a consensus meeting with a third author (DM). Reference lists and citing articles of retained manuscripts were checked.

3.2.4 Quality assessment

The methodological quality of the included studies was assessed by two authors (AT and AH) using a sixteen-part adapted Downs and Black checklist (Table 3) that has a maximum score of 17 available, with questions suited to intervention trials excluded, as has previously been utilised (167). Scores of ≥13 (>75%), 11-12 (60–74%) and ≤10 (<60%) were taken to indicate high, moderate and low quality, respectively (168,169). For prospective studies, item 9 and 26 were retained as they concern follow-up. Thus, we used an eighteen-part checklist with corresponding scores to assess prospective cohort studies only (Table 3). Additionally, for item 5 we considered age, sex, activity levels, height and mass or body mass index as a confounding factor for scoring.

3.2.5 Risk of bias assessment

Two authors (AT and AH) assessed the risk of bias for each included study using Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) (170) tool. QUADAS-2 is strongly recommended for risk of bias assessment (171), utilizing diagnostic accuracy study criteria (170). This approach was taken as the main aim of the included studies was to distinguish the people with and without the condition. QUADAS-2 consists of four key domains covering 'patient selection', 'flow and timing', 'index test' and 'reference standard' (three-dimensional biomechanical tests and clinical diagnosis in this instance). Domains are assessed in terms of risk of bias and applicability yielding two judgements. These are stringently judged, with a study judged "high" or "unclear" on at least one domain being designated 'at risk of bias' or as having 'concerns regarding applicability' (170).

3.2.6 Data extraction

Descriptive information was extracted from all included studies by two independent authors (AT and AH). This included publication details (author, year, study design), sample sizes, participant characteristics, the jumping task and biomechanical outcomes (i.e. kinematics, kinetics and muscle activation patterns) (Table 4). The biomechanical data for each outcome required to calculate effect sizes (mean and standard deviation) were extracted and corresponding authors contacted for additional data when needed. Additionally, we used WebPlotDigitizer (https://automeris.io/WebPlotDigitizer/) to extract data when only presented in graphs.

3.2.7 Data analysis

Quantitative analysis was conducted if the pooled data were methodologically homogeneous using random effects models. Heterogeneity was further analysed with I^2 and was considered as low (>25-50%), moderate (>50-75%), or high (>75%) (172). The Cochrane Review Manager software (Version 5.3. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014) were used for the meta-analysis.

3.2.8 Levels of evidence

Based on the quality assessment, each variable of interest was assigned a level of evidence according to recommendations made by van Tulder et al. (173):

(1) Strong evidence provided by pooled results derived from three or more studies, including a minimum of two high-quality studies that were statistically homogenous (I^2 not significant at 0.05); may be associated with a statistically significant or non-significant pooled result;

(2) Moderate evidence provided by statistically significant pooled results derived from multiple studies that were statistically heterogeneous (p<0.05), including at least one high-quality study; or from multiple moderate or low-quality studies which were statistically homogenous (p>0.05);

(3) Limited evidence provided by results from one high-quality study or multiple moderate or low-quality studies that are statistically heterogeneous (p<0.05);

(4) Very limited evidence provided by results from one moderate or low-quality study; and

(5) Conflicting evidence provided by pooled results that are not significant and derived from multiple studies, regardless of quality, which are statistically heterogeneous (p<0.05, i.e., inconsistent).

3.3 Results

Search results and study selection process are shown in Figure 8. One prospective cohort (64), one cross-sectional (174) and 14 case-control (100,101,103,175–185) studies, 16 in total, were included into qualitative analysis. Studies included 104 JPTs, 14 with previous PT, 45 with asymptomatic PT abnormality and 190 controls. We were only able to conduct limited quantitative analysis due to methodological and outcome heterogeneity. After quality assessment, we identified four high (179–182), nine moderate (64,103,174–177,183–185) and three low quality (100,101,178) studies. Quality assessment results and the characteristics of the included studies are shown in Table 3 and Table 4, respectively. Risk of bias assessment and applicability results are contained in Table 3. All studies had high risk of bias, but low concerns regarding applicability. Specifically, only one study (64) was at low risk of bias for the 'patient selection' domain. All studies were at low risk of bias for the 'reference standard' domain, while only three studies (100,101,179) had low risk of bias for the 'index test' domain. For the 'flow and timing' domain only one study (100) had low risk of bias and the remainder had high risk of bias.

Identification

Records identified through database searching:
PubMed=1608
Web of Science=2122
Cochrane Library=999
(n=4729)

Additional records identified through other sources (n=0)

Screening

Records after duplicates removed
(n=3756)

Records screened
(n=3756)

Records excluded
(n=3641)

Eligibility

Full-text articles assessed for eligibility
(n=115)

Full-text articles excluded, with reasons (n=99)
•Not reporting associations between landing and PT (n=52)
•Non jump-landing cohorts/tasks (n=25)
•Kinematic/ kinetic measurements not made (n=13)
•Conference abstracts (n=3)
•Protocol registration (n=2)
•Pilot study (n=2)
•Two dimensional biomechanics (n=1)
•Animal (n=1)

Included

Studies included in qualitative synthesis
(n=16)

Studies included in quantitative synthesis
(n=6)

Figure 8: PRISMA flow diagram

| Study | Modified Downs and Black checklist items[a] | | | | | | | | | | | | | | | | | | QUADAS-2 | | | | | | |
| | 1 | 2 | 3 | 5 | 6 | 7 | 10 | 11 | 12 | 15 | 16 | 18 | 20 | 21 | 22 | 25 | Total (x/17) | Quality | Risk of Bias | | | | Applicability | | |
																			PS	IT	RS	FT	PS	IT	RS
Harris et al. (179)	1	1	1	2	1	1	1	0	0	1	1	1	1	1	1	0	**14**	**H**	red	green	green	red	green	green	green
Scattone et al. (180)	1	1	1	2	1	1	1	0	0	0	1	1	1	1	0	1	**13**	**H**	red	red	green	red	green	green	green
Sorenson et al. (181)	1	1	1	2	1	1	1	0	0	0	1	1	1	1	0	1	**13**	**H**	red	green	green	red	green	green	green
Souza et al. (182)	1	1	1	2	1	1	1	0	0	0	1	1	1	1	0	1	**13**	**H**	red	green	green	red	green	green	green
Bisseling et al. (183)	1	1	1	2	1	1	1	0	0	0	1	1	1	0	1	0	**12**	**M**	red	green	green	red	green	green	green
Bisseling et al. (103)	1	1	1	2	1	1	1	0	0	0	1	1	1	0	1	0	**12**	**M**	red	green	green	red	green	green	green
Edwards et al. (184)	1	1	1	1	1	1	1	0	0	0	1	1	1	0	0	1	**11**	**M**	red	green	green	red	green	green	green
Edwards et al. (174)	1	1	1	1	1	1	1	0	0	0	1	1	1	0	0	1	**11**	**M**	red	green	green	red	green	green	green
Fietzer et al. (185)	1	1	1	2	1	1	1	0	0	0	1	1	1	0	0	1	**12**	**M**	red	green	green	red	green	green	green
Kulig et al. (175)	1	1	1	2	1	1	1	0	0	0	1	1	1	0	0	1	**12**	**M**	red	green	green	red	green	green	green
Pietrosimone et al. (176)	1	1	1	2	1	1	0	0	0	0	1	1	1	1	0	1	**12**	**M**	red	green	green	red	green	green	green
Rosen et al. (177)	1	1	1	1	1	1	1	0	0	0	1	1	1	1	0	1	**12**	**M**	red	green	green	red	green	green	green
van der Worp et al. (64)	1	1	1	2	1	0	0	0	0	0	1	0	1	1	1	1	**13**[b]	**M**	green	green	green	red	green	green	green
Mann et al. (178)	1	1	0	1	1	1	0	0	0	0	1	1	1	1	0	1	**10**	**L**	red	green	green	green	green	green	green
Richards et al. (100)	0	1	1	0	1	0	1	0	0	1	1	1	1	1	0	1	**10**	**L**	red	green	green	green	green	green	green
Richards et al. (101)	1	1	1	0	1	0	1	0	0	1	1	1	1	1	0	0	**10**	**L**	red	green	red	green	green	green	green

Keys for abbreviations: H, high; M, moderate; L, low; PS, patient selection; IT, index text; RS, reference standard; FT, flow and timing.

Keys for colors: High risk, Unclear risk, Low risk

For modified Downs and Black checklist items; 1-3, 6, 7, 10-12, 15, 16, 18, 20, 21, 22 and 25: 0=No or unable to determine, 1=Yes. For item 5: 0=No, 1=Partially, 2=Yes.

[a]Items: 1, Clear aim; 2, Outcome measures described; 3, Participant characteristics described; 5, Confounding variables described; 6, Main findings described; 7, Measures of random variability provided; 10, Actual probability values reported; 11, Participants are representative of the population; 12, Confounders comparable between study groups and the source population; 15, Blinding assessors; 16, Analyses performed were planned; 18, Appropriate statistics; 20, Valid and reliable outcome measures; 21, Appropriate case-control matching (same population); 22, Participants recruited over the same time period; 25, Adjustment made for confounding factors.

[b]Items used for prospective studies only: 9, characteristics of patients lost to follow-up; 26, numbers of patients lost to follow-up: 0=No or unable to determine, 1=Yes. van der Worp et al. (64): Item-9=1 and item-26=1, 13 out of 19 in total which is moderate.

Study	Population (n)	Demographics	Tasks implemented	Kinetic & kinematic measurements
Harris et al., 2020, Case-control (179)	19 Junior basketball players (male: 9, female: 10), PT (8), C (11)	PT:16.5±0.6 yrs; 191.4±14.4 cm; 78.7±15.1 kg, 1.4±1.1 h/w C:15.9±0.7 yrs; 183.7±10.9 cm; 73.9±9.7 kg, 2.4±1.0 h/w Sporting level: elite	Stop-jump horizontal landing phase	Peak PTF & GRFs/ LR of PTF & vGRF/ peak force timing/ peak net internal joint moments/ impulses/ peak joint angles & RoM (ankle, knee, hip, L5-S1 (lumbopelvis), & T12-L1 (thoracolumbar))
Scattone et al., 2017, Case-control (180)	21 Male volleyball & basketball players, PT (7), PTA (7), C (7)	PT:18.0±1.2 yrs; 189±5 cm; 80.2±7.9 kg, 14.4±7.3 h/w PTA:21.0±5.2 yrs; 194±11 cm; 90.8±13.7 kg, 11.0±6.5 h/w C:16.3±1.4 yrs; 196±10 cm, 82.3±10.9 kg, 15.3±6.9 h/w Sporting level: elite	Bipedal drop landings from a 50-cm bench in 3 different trunk positions: self-selected, extended & flexed	Ankle DF, knee, hip, and trunk flexion angles (at IC & peak angles)/ peak vGRF & PTF/ peak ankle PF and peak knee & hip extensor moments/ forward head projection/ knee pain.
Sorenson et al., 2010, Case-control (181)	13 Male volleyball players, PT (6), C (7)	PT:29.3±4.1 yrs; 196±5 cm; 92.8±4.0 kg C:24.3±8.0 yrs; 197±11 cm; 91.8±5.8 kg Sporting level: elite	Maximum-effort volleyball approach jumps	Peak, average & time-integrated vGRF/ knee RoM, net joint work & average net joint power/ peak & average net joint moment/ joint angular velocity.
Souza et al., 2010, Case-control (182)	14 Male volleyball players, PT (7), C (7)	PT:28.9±4.5 yrs; 197±11 cm; 91.7±5.9 kg C:24.9±7.8 yrs; 197±14 cm; 94.4±6.4 kg Sporting level: elite	20 successive continuously hop on the dominant side. Only stance phase of task were used for analysis.	Sagittal plane net joint moments (ankle, knee, hip)/ total support moment (sum of the averaged hip & knee extensor and ankle plantar flexor net joint moments)/ joint contributions to the total support moment
Bisseling et al., 2007, Case-control (183)	24 Male volleyball players, Previous PT (7), Recent PT (9), C (8)	Previous:22.4±2.6 yrs; 189±7 cm; 79.5±5.6 kg Recent:24.1±3.3 yrs; 192±6 cm; 85.0±10.1 kg C:23.6±2.5 yrs; 189±8 cm; 84.5±13.2 kg All training ≥3 times a week and being competitive ≥5 yrs	Drop landings with various high platforms (30-50-70cm)	Peak & loading rate vGRF/ joint flexion angles, angular velocity, peak moments/ LR of ankle & knee moments/ joint power & work.
Bisseling et al., 2008, Case-control (103)	15 Male volleyball players, Previous PT (7), C (8)	Previous:22.4±2.6 yrs; 189±7 cm; 79.5±5.6 kg, 7.9±4.0 h/w C:23.6±2.5 yrs; 189±8 cm; 84.5±13.2 kg, 7.7±2.7 h/w Sporting level: elite & non-elite	Spike jump dominant foot landing	Joint maximum angle, RoM touchdown till peak vGRF, angles at IC & peak vGRF/ joint velocities/ ankle & knee moments/ LR of knee extensor moment & vGRF.
Edwards et al., 2010, Case-control (184)	14 Male athletes from team sports, PTA (7), C (7)	PTA:25.2±4.7 yrs; 183.4±7.2 cm; 83.2±9.0 kg C:22.3±2.4 yrs; 185.9±8.1 cm; 82.0±12.6 kg Sporting/ training level not reported	5 stop-jumps, involving a simultaneous two-foot horizontal & vertical landing	Peak PTF & vGRF/ LR of PTF & vGRF/ joint kinematics/ time of onset & peak muscle activity relative to peak PTF time.
Edwards et al., 2017, Cross-sectional (174)	7 players with PTA, Volleyball (1), Basketball (4), Soccer (2)	25.2±4.7 yrs; 183.4±7.2 cm; 83.2±9.0 kg Sex and sporting/ training level not reported	5 stop-jump task trials before and after a fatigue protocol	Peak vGRF & anterior-posterior GRF/ lower limb kinematics/ net peak PTF/ net internal peak knee moment/ LR of PTF & vGRF.
Fietzer et al., 2012, Case-control (185)	18 Dancers (male: 9, female: 9), PT (6), C (12)	PT:18.8±0.8 yrs; 172±11 cm; 66.9±7.3 kg C:18.9±1.2 yrs; 168±8 cm; 59.2±9.1 kg Pre-professional training programme (elite)	Eight saut de chat landing	Ground reaction forces/ joint landing angles & velocity.
Kulig et al., 2015, Case-control (175)	18 Male volleyball players, PT (9), C (9)	PT:25.9±6.2 yrs; 195±5 cm; 89.7±6.6 kg C:23.1±7.3 yrs; 197±10 cm; 94.1±7.3 kg Sporting level: elite	3 successful spike jump landings	GRFs & impulses / Sagittal plane joint angles (ankle, knee, hip) at IC & during the maximal knee flexion / The lower extremity contact angle (novel)

Study	Participants	Demographics	Task	Outcomes
Pietrosimone et al., 2020, Case-control (176)	41 Male young athletes, PT (13), PTA (14), C (14)	PT:19.6±1.6 yrs; 182±5 cm; 83.5±5.1 kg; 8.0±1.0 Tegner scale PTA:21.0±2.0 yrs; 184±7 cm; 81.6±13.0 kg; 8.0±1.0 Tegner scale C:19.6+1.6 yrs; 184±9 cm; 79.9±13.0 kg; 8.0±0.9 Tegner scale	5 trials of a double leg jump-landing task from a 30 cm box	PTF & GRF / knee & hip joint moments / PTF impulse / internal knee extension moment impulse / knee power & work
Rosen et al., 2015, Case-control (177)	60 Volleyball players, PT (30, male: 15, female: 15), C (30, male: 15, female: 15)	PT:21.3±3.2 yrs; 174.5±9.4 cm; 72.8±12.4 kg C:21.5±3.0 yrs; 174.9±10.5 cm; 72.0±14.7 kg All recreational ≥90 minutes of physical activity per week at ≥4 on Tegner scale	5 trials of a 40-cm, 2-legged drop landing, followed immediately by a 50% maximum vertical jump	Joint angles at IC/ peak joint angles/ maximum angular displacement.
van der Worp et al., 2016, Prospective Cohort (64)	49 Basketball, volleyball, korfball players, PT (3, male: 2, female: 1), C (46, male:30, female:16)	Male:21.8±3.5 yrs; 196±7 cm; 86.2±10.4 kg Female:21.6±2.7 yrs; 178±7 cm; 68.3±10.7 kg All teams played at ≥3rd highest national level (elite & sub-elite)	A jump-landing-rebound task from a 30-cm high box at the start of each season (follow up for 2 seasons (n=18) & 1 season (n=31))	At baseline and at end: joint angles/ angle between foot and ground for IC phase between landing from horizontal jump and take-off of the vertical jump/ leg stiffness.
Mann et al., 2013, Case-control (178)	20 Male junior basketball players, PTA (10), C (10)	For 22 athletes: 17.7+1.5 yrs; 183+10 cm; 78.0+14.7 kg. Unknown for groups, but reported matched Sporting level: pre-elite	5 successful stop-jumps	Sagittal plane knee & hip joints and trunk segment kinematics at IC and at the maximal knee flexion, plus hip flexion RoM.
Richards et al., 1996, Case-control (100)	10 Male volleyball players, PT (3), C (7)	23.2±0.8 yrs; 197.6±1.9 cm; 91.9±1.2 kg Sporting level: elite	Block jump-landing phases with 1 step approach. Spike jump-landing with only 1 foot hitting force plate.	Maximal vGRF/ knee moments & kinematics/ knee (flexion, adduction, abduction) & tibial (IR & ER) angles.
Richards et al., 2002, Case-control (101)	10 Male volleyball players, PT (3), C (7)	23.2±0.8 yrs; 197.6±1.9 cm; 91.9±1.2 kg Sporting level: elite	A series of spike jump-landing	Ankle DF, PF, inversion & eversion angles and moments/ tibial IR & ER angles and moments.

Keys: PT, patellar tendinopathy; PTA, asymptomatic patellar tendon abnormality; C, control; F, female; M, male; vGRF, vertical ground reaction force; LR, loading rate; DF, dorsiflexion; PF, plantarflexion; IR, internal rotation; ER, external rotation; RoM, range of motion; IC, initial contact; PTF, patellar tendon force; RCT, randomised controlled trial; h/w, training hours per week.

Kinematic Variables			Patellar Tendinopathy		PTA
			Previous	Current	
Angles at IC	Ankle	Plantarflexion	↓		
	Ankle	Angles at IC		↔	
	Knee	Flexion	↓		↑
	Knee	Angles at IC		↔	
	Hip	Flexion			↑
	Hip	External rotation in fatigue			↓
	Hip	Angles at IC		↔	
Velocities at IC	Knee	Flexion			↓
	Hip	Extension			↑
Range of Motion	Ankle	Sagittal plane kinematics (Dorsiflexion)	↔	↓	↔
	Ankle	Inversion at peak PTF			↑
	Knee	Flexion		↓ ↑	↓
	Knee	Internal rotation at peak vGRF			↑
	Knee	Sagittal plane kinematics		↔	
	Hip	Sagittal plane kinematics (Flexion)		↔ ↑ ↓	↓
	Hip	Adduction at peak vGRF			↑
	Hip	External rotation at peak vGRF in fatigue			↓
		Lower extremity contact angle		↓	
		Common landing technique or kinematic patterns		↔	
		Joint positions from IC to peak PTF in fatigue			↔
Trunk Position		Pain with greater trunk flexion		↓	
		Trunk kinematics		↔	↔
		Forward head projection		↔	↔
Joint angular velocities, acceleration, & angular displacement	Ankle	Angular velocities	↑		
	Knee	Angular velocities	↑	↔	
	Knee	Flexion velocity at peak PTF			↓
	Knee & Hip	Max angular displacement in sagittal plane		↓	
	Hip	Velocity - Flexion at peak vGRF & ER at peak PTF			↑
		Ankle, knee & hip angular velocities (IC to peak PTF) in fatigue			↔
		Landing velocity		↔	

Keys for directions: ↓ = lower, smaller, slower; ↑ = higher, greater, faster; ↔ = no relation; Empty = no direction.
Keys for colors: No evidence, Very limited, Limited, Moderate, Strong.

Figure 9: Evidence gap map for kinematics. Arrows show the direction of the variables associated with the condition. Keys: ER, external rotation; IC, initial contact; max, maximum; min, minimum; PTA, asymptomatic Patellar Tendinopathy abnormality; PTF, Patellar tendon force; vGRF, vertical ground reaction force.

Kinetic Variables			Patellar Tendinopathy — Previous	Patellar Tendinopathy — Current	PTA
Peak PTF & its Loading Rate		Peak PTF		↔ (Limited) ↓ (Very limited)	↔ (Very limited)
		Peak PTF vs PTA		↓ (Limited)	
		PTF in flexed trunk position vs self-selected or extended		↓ (Limited)	↓ (Limited)
		LR of PTF		↓ (Limited)	↔ (Very limited)
		PTF impulse		↓ (Limited)	↔ (Very limited)
		PTF impulse vs PTA		↓ (Very limited)	
		Duration from IC to peak PTF			↔ (Very limited)
		Landing technique or net PTF in fatigue state			↔ (Very limited)
Ground Reaction Forces & its Loading Rate		Peak vGRF		↔ (Strong) ↓ (Limited) ↑ (Very limited)	↔ (Moderate)
		Average vGRF		↔ (Limited)	
		Peak braking GRF		↑ ↔ (Very limited)	
		Peak vGRF in flexed trunk position vs extended		↓ (Limited)	↓ (Limited)
		In fatigue - Peak anterior-posterior GRF & LR of vGRF			↑ (Very limited)
		LR of vGRF during horizontal landing		↓ (Limited)	
		LR of vGRF during vertical landing	↑ (Very limited)		↓ (Very limited)
		vGRF impulse		↔ (Strong) ↑ (Very limited)	
		Braking impulse		↑ ↔ (Very limited)	
		Peak propulsive GRF and its impulse		↔ (Limited)	
		In horizontal landing, duration from IC to 1st & 2nd peak vGRF		↑ (Limited)	
		In horizontal landing, LR of vGRF & duration from IC to peak vGRF			↔ (Very limited)
Joint moments	Foot	Inversion moment		(Very limited)	
	Ankle	LR of moment development	↑ (Very limited)	↔ (Limited)	
		Contribution to the total support moment		↔ (Limited)	
	Knee	Peak moment in sagittal plane vs controls		↔ (Strong) ↓ (Very limited)	↑ (Limited)
		Peak moment in sagittal plane vs PTA		↓ (Limited)	
		Average moment in sagittal plane		↔ (Limited)	
		LR of moment development	↑ (Limited)	↔ (Very limited)	
		ER or peak tibial ER moments		(Very limited)	
		Contribution to the total support moment		↓ (Limited)	
		Extensor moment impulse		↓ (Very limited)	↔ (Very limited)
		Extensor moment impulse vs PTA		↓ (Limited)	
	Ankle & Hip	Peak moment in sagittal plane		↔ (Moderate)	
		Average moment in sagittal plane		↔ (Limited)	
	Hip	Contribution to the total support moment		↑ (Limited)	
		Total support moment		↔ (Limited)	
		Sagittal plane trunk joint moments		↔ (Limited)	
Joint energetics	Knee	Power	↑ (Very limited)	↓ (Moderate) ↔ (Very limited)	↔ (Very limited)
		Negative joint work		↓ (Moderate)	↔ (Very limited)
		Positive joint work		↔ (Limited)	
	Ankle & Hip	Power & Work	↔ (Very limited)	↔ (Limited)	
Leg stiffness		Leg stiffness	↑ (Very limited)	↑ (Very limited)	
EMG		Different muscle recruitment order			(Very limited)
		Onset time or peak muscle burst activity relative to peak PTF			↔ (Very limited)

Keys for directions: ↓ = lower, smaller, slower; ↑ = higher, greater, faster; ↔ = no relation; Empty = no direction.
Keys for colors: No evidence, Very limited, Limited, Moderate, Strong.

Figure 10: Evidence gap map for kinetics. Arrows show the direction of the variables associated with the condition. Keys: ER, external rotation; IC, initial contact; LR, loading rate; PTA, asymptomatic Patellar Tendinopathy abnormality; PTF, Patellar tendon force; vGRF, vertical ground reaction force.

3.3.1 Levels of evidence

Findings and gaps in the literature were presented in Figure 9 and Appendix 4 for kinematics and Figure 10 and Appendix 5 for kinetics with their relation to PT or asymptomatic PT abnormality alongside their level of evidence.

3.3.1.1 Kinematics

Strong evidence suggests no relation between PT and sagittal plane knee (175,179–181) and hip (175,179,180) kinematics in peak joint angles or RoM nor any relation between angle at peak vGRF and patellar tendon force (PTF). Moderate evidence shows no relation between PT and hip, knee or ankle joint angles at IC (175,177,179,185), trunk kinematics (peak or angles at IC) (179,180) and knee angular velocities (181,183). These variables were measured during drop landings (177,180,183), volleyball approach jump-landings (181), spike jump (175), stop-jump horizontal landing (179) and saut de chat landing (185).

We conducted a meta-analysis for ankle dorsiflexion range of motion (Figure 11) throughout the landing task, and moderate evidence indicated an association of lower peak dorsiflexion angle with PT (I^2=40%, effect size=-0.73 (95%CI -1.42 to -0.04), p=0.04) (64,175,180,183) in adult athletes during multiple vertical jump-landing tasks consisting of spike and drop landings. When we pooled data for the drop landing task only, the association between smaller peak dorsiflexion angle with PT (I^2=0%, effect size=-1.11 (95%CI -1.76 to -0.46), p=0.001) (64,180,183) was consistent. However, adding young athletes (179) (stop-jump horizontal landing phase) into the analysis increased the heterogeneity and eliminated the association with PT (I^2=61%, effect size=-0.46 (95%CI -1.21 to 0.28), p=0.22) (64,175,179,180,183). Therefore, there was moderate evidence of smaller peak ankle dorsiflexion angle being associated with PT during multiple vertical jump-landing tasks in adult athletes (Figure 11).

Limited evidence suggests a relation between higher knee angular velocity (mean difference range:-0.7 to -0.6) (103,183) and previous PT. There is a relation between PTA and greater knee flexion angle at IC (mean difference range:7.8°-14.1°) (178,184), slower knee flexion velocities at IC (mean difference:183 °/s) (184) and fatigue state (mean difference:70 °/s) (174) with limited evidence. Limited evidence shows a relation between PT and lower knee flexion range of motion (mean difference range:7.7°-8.6°) (64,177) and greater hip flexion range of motion (mean difference:11.3°) (64). Additionally, limited evidence suggests a relation between trunk position and knee pain during drop landing in JPTs as landing with greater trunk flexion decreased the pain immediately (180). These variables were measured during drop landings (64,177,180,183), spike jump (103) and stop-jump horizontal or vertical landing phases (174,178,184). Limited evidence shows no relation between PT and forward head projection (180) during drop landing or no relation between PTA and sagittal plane ankle kinematics (180) during drop landing.

Very limited evidence suggests an association between previous PT and smaller ankle plantarflexion (103) and knee flexion (103) at IC and higher LR of ankle angular velocities (103), or no association with sagittal plane ankle kinematics (183). Very limited evidence shows a relation between PTA and greater ankle inversion (184) at peak PTF, greater knee internal rotation (184) at peak vGRF, smaller knee flexion angle (184) from IC to peak PTF, slower knee flexion velocity at peak PTF (184), greater hip flexion angle (184) and faster hip extension velocity (184) at IC, smaller hip external rotation in fatigue state (174) at IC and at peak vGRF, lower hip flexion RoM (178), greater hip adduction (184) at peak vGRF, faster hip external rotation velocity at peak PTF (184) and faster hip flexion velocity at peak vGRF (184), or no association with ankle, knee and hip joint positions and angular velocities from IC to peak PTF during both fatigue states (174). Very limited evidences shows a relation between PT and deeper knee flexion (100), less Lower Extremity Contact Angle (175), more hip flexion (64), lower peak hip flexion angles (177), lower maximum angular displacement in sagittal plane at knee (177) and at hip (177), or no association with landing technique (64), kinematic patterns (64) and landing velocity in any plane or the calculated resultant value (185). These variables were measured during drop landings (64,177,183), stop-jump horizontal or vertical landing phases (174,178,184), saut de chat landing (185), spike (100,103,175) or block jumps (100).
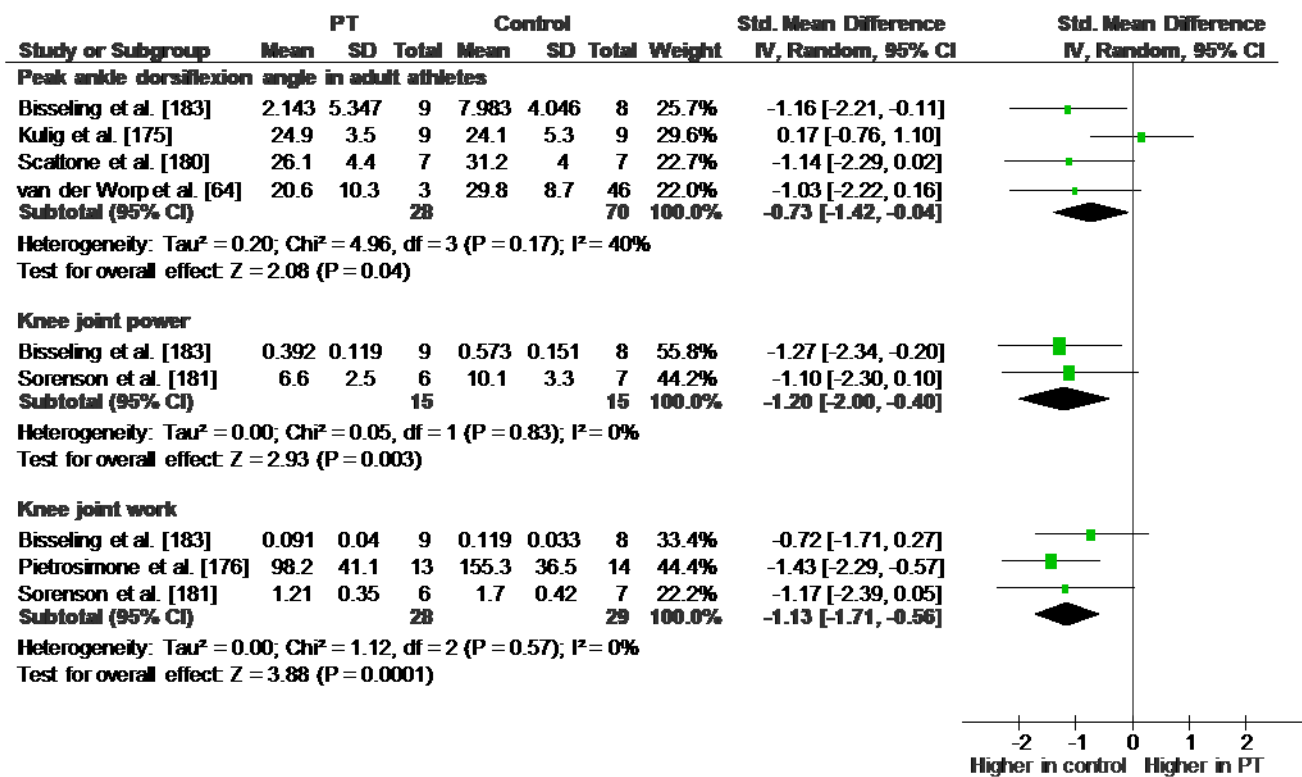
Figure 11: Meta-analysis for ankle dorsiflexion angle in adult athletes, knee joint power and knee joint work in jumping athletes with current patellar tendinopathy symptoms compared to healthy controls. Keys: PT, patellar tendinopathy; SD, standard deviation; Std, standard; IV, inverse variance; CI, confidence interval.

3.3.1.2 Kinetics

Strong evidence indicates no relation between PT and peak vGRF (175,179,180,183), vGRF impulse (175,179,181) and peak sagittal plane knee moments (179–181). Moderate evidence shows no relation between PT and sagittal plane hip (179,180) and ankle (179,180) joint moments, and no relation between PTA and peak vGRF (180,184). These variables were measured during drop landings (180,183), volleyball approach jump-landings (181), spike jump (175), and stop-jump horizontal landing (179,184).

In meta-analysis, moderate evidence indicates reduced knee joint power (I^2=0%, effect size=-1.20 (95%CI -2.00 to -0.40), p=0.003) (181,183) and work (I^2=0%, effect size=-1.13 (95%CI -1.71 to -0.56), p<0.001) (176,181,183) in JPTs with current symptoms only vs healthy controls (Figure 11) during volleyball approach (181) or drop landings (176,183).

Limited evidence indicates a relation between previous PT and higher loading rate (LR) of knee moment (mean difference range:-0.83 to 0.82) (103,183). Limited evidence also indicates associations between PT and lower LR of PTF (mean difference:16.3 BW·s-1) (179), lower LR of vGRF (mean difference:29.8 BW·s-1) (179), longer stance durations from IC to first and second peak vGRF (mean difference range:18.9-55.3) (179), smaller sagittal plane knee extensor moments compare to PTA (mean difference:0.07 N·m·N-1, p=0.03, d=1.77) (180), and greater hip (mean difference:8%) (182) and less knee (mean difference:8.4%) (182) contribution to the total support moment. Conflicting findings were detected as limited evidence shows both greater (100,185) (36%, p<0.001) (185) or lower (181) (22%, p=0.003) (181) peak vGRF in JPTs. Furthermore, limited evidence indicates that PTF may be related to both PT and trunk positions. There was a main effect of group (p=0.048; η^2=0.29) and of trunk position (p<0.001; η^2=0.56) in peak PTF (180). Regardless of trunk position, JPTs had smaller peak PTF than asymptomatic athletes with PTA (p=0.045; d=0.98) (180), and landing with greater trunk flexion decreased the PTF immediately in symptomatic athletes (180). Additionally, limited evidence suggests a relation between peak vGRF and trunk position as smaller peak vGRF was reported in landing with a flexed trunk position than extended (p=0.043; d=0.44) (180). These variables were measured during drop landings (180,183), volleyball approach jump-landings (181), spike (100,103) or block jumps (100), stop-jump horizontal landing (179), hopping (182), and saut de chat landing (185).

Limited evidence shows no relation between PT and peak PTF (179), average vGRF (181), average net ankle, knee and hip joints moments (182), total support moment (182) or individual contributions of the ankle to the total support moment (182), sagittal plane lumbo-pelvic and

thoraco-lumbar peak internal joint moments (179). These variables were measured during volleyball approach jump-landings (181), hopping (182), and stop-jump horizontal landing (179).

One of the key findings with very limited evidence was that athletes with previous (183) or current PT (64) present with increased landing stiffness measured during drop landings. Additionally, very limited evidence suggests an association between previous PT and higher LR of vGRF (183) and higher LR of ankle moment development (183), or no association with ankle and hip joints power and work (183). Very limited evidence suggests a relation between PTA and different muscle recruitment order (184), greater peak anterior-posterior GRF in fatigue state (174), lower LR of vGRF (184) during vertical landing, higher LR of vGRF in fatigue state (174), or no association with PTF (176,184), LR of PTF (184), PTF impulse (176), duration from IC to peak PTF (184), landing technique or patellar tendon loading in fatigue state (174), LR of vGRF and duration from IC to peak vGRF during horizontal landing phase (184), knee extension moment impulse (176), knee joint power and work (176), onset time or peak muscle burst activity relative to peak PTF (184). Very limited evidence shows a relation between PT and less PTF and PTF impulse (176), greater peak braking GRF (185), greater vertical and braking impulses (185), foot inversion moment (101), smaller sagittal plane knee moments (183), external rotation moment at the knee (100) or peak tibial external rotation moment (100), less knee extension moment impulse (176), or no association with peak braking GRF and braking impulse (175), peak propulsive GRF and propulsive impulse (185), ankle and hip joints power and work (183). These variables were measured during drop landings (176,183), stop-jump horizontal or vertical landing phases (174,184), saut de chat landing (185), spike (100,101,175) or block jumps (100).

3.4   Discussion

We conducted this systematic review to determine whether jump-landing biomechanics are altered among jumping athletes with PT (JPTs) and can predict onset in order to provide clinically applicable evidence-based information for professionals seeking to prevent and manage PT in jumping athletes. What can be taken forward are five strong (all non-associated), 10 moderate (three associated and suitable for meta-analysis, seven non-associated) and 93 tentative (58 associated, 35 non-associated) findings. It is notable how few robust relevant positive findings were found in part because the existing literature is low quality and heterogeneous both in terms of methodology and outcomes to make useful clinical conclusions. However, a strength of our review is that we have

highlighted evidence gaps in the available literature, with a lack of adequately powered prospective studies that enable assessment of multi-factorial models being notable.

Moderate evidence indicates an association between smaller ankle dorsiflexion range and current PT during vertical jump-landing (64,175,180,183). Reduced ankle dorsiflexion angle has also been clinically identified as a risk factor for PT onset (93,94). Ankle dorsiflexion has been shown to be a key shock absorbing feature during landing (186). During impact and throughout landing from a jump, eccentric calf muscle contraction accounts from 37% to 50% of the total kinetic energy absorbed by the muscular system (160). Thus, a limitation in the dorsiflexion range might reflect altered landing biomechanics that impact on PT presence. Harris et al. (179) reported contradictory findings for ankle dorsiflexion range in junior athletes who performed stop-jump horizontal landings. Previous literature (99,178,184) showed that athletes presented with different landing strategies during horizontal and vertical landing tasks. This suggests that investigating the landing biomechanics in both horizontal and vertical phases of different sports specific tasks are warranted. It is also plausible that landing patterns might differ in young athletes compared to adults, as young athletes are still growing and learning or improving the necessary techniques required for their sports. Therefore, we should also take into account age alongside different type of tasks. However, it seems that findings from adults may not be readily applied to skeletally immature young athletes.

If knee flexion angles are greater at initial contact, the available range of motion (further flexion) during landing is restricted, which will lead to decreased displacement of the centre of mass after initial contact and increased landing stiffness (99,187). It was suggested that increased landing stiffness may cause increased loading rates or forces on the patellar tendon (99). Although findings with very limited evidence (64,183) from this systematic review supported previous literature, showing athletes with previous or current PT present with increased landing stiffness, limited evidence showed that JPTs present with lower patellar tendon loading rates (179). We also detected no association between PT and knee sagittal plane range of motion (175,179–181) with strong evidence, and knee angles at initial contact (175,177,179,185) with moderate evidence. Overall, landing stiffness might be a factor contributing to PT, but the current evidence contradicts the potential explanations of observed stiffness. Therefore, future research investigating landing stiffness is needed in order to elucidate the association with PT.

Jumping athletes with PT had lower knee forces, resulting in reduced knee joint power (176,181,183) and work (181,183) with moderate evidence, and sagittal plane knee moments (180,183) and patellar tendon loads (176,180) with limited or very limited evidence. JPTs may

modify their landing patterns to avoid higher patellar tendon loads and reduce their pain by minimising those knee forces. This should not be taken to be a causal relationship, as it may represent reverse causality. A posited explanation is that athletes may load their contralateral side to protect the injured side and to avoid higher forces, as lower limb movement asymmetry has been shown during landing in male athletes with healthy patellar tendons (188). On the other hand, training athletes using softer landing patterns could be one of the modifications. There are studies investigating leg stiffness by comparison of a hard landing (stiff) vs a soft landing vs normal landing (160,189). Although the stiffness measures were indirect, small decreases were found in knee moments but larger increases in knee angles during soft landings compared to hard landings (160,189). This indicates softer landings lead to lower knee joint stiffness and reduced forces (187). However, we found no association between PT and sagittal plane knee moments (179–181) (strong evidence) and patellar tendon loads (179) (limited evidence).

Trunk position may be related to PT indirectly as limited evidence indicates that JPTs used landing techniques with greater truncal flexion which decreased pain and tendon forces during drop landing (180), although trunk flexion did not differ compared to controls (180). Furthermore, greater truncal-flexion increased peak knee and hip flexion angles during drop landing, despite decreased peak ankle dorsiflexion angle (180). Relative to self-selected or extended trunk positions, a flexed trunk position also resulted in less vGRF and patellar tendon forces (180). Therefore, flexed trunk position may help decrease stiffness in knee and hip joints, hence might be a strategy for a soft-landing pattern.

3.4.1   Limitations

The quality of existing literature to explore the associations between jump-landing activities and PT was problematic, as 75% of the included papers were moderate or low quality and risk of bias was high for all papers. Thus, the data does not provide strong evidence for the biomechanical factors of interest, and causal relationships remained unclear due to the lack of prospective studies. Variability of the existing literature is also high, in terms of differences in the tasks implemented, population or variable of interest measured. Therefore, we were limited in our ability to pool data for a meta-analysis of many parameters due to high heterogeneity. Findings from this review were especially limited for the female population as 11 of 16 studies only recruited males. We did not specify whether healthy control groups had to have had ultrasound assessment, so it is possible that some control participants in 11 of 16 studies might have had asymptomatic patellar tendon abnormalities. While these would not alter the clinical diagnosis, it is plausible that they would have

pre-clinical alterations in landing mechanics. However, we performed a sensitivity analysis for peak ankle dorsiflexion angle without any resultant change of findings. For completeness, we recommend future studies include ultrasound imaging. Additionally, in 13 out of the 16 included studies, small sample sizes reduced the methodological quality as they failed to provide the minimum requirement of 10 'events per variable' of interest (190).

3.4.2   Future directions

It is clear that definitive, adequately powered, well-designed prospective studies with high quality measurements and adequate follow up are required to determine whether jump-landing biomechanical factors play a part in the development, presentation and/or prognosis of PT, alongside non-biomechanical factors. Additionally, high quality prospective studies could also establish multi-factorial causality models to inform planned interventions, while RCTs could investigate the effects of movement strategies on risk reduction.

Many studies (175,177,179–181,183,185) have identified factors which have a theoretically plausible relationship to PT but were not found to be associated. Strong or moderate evidence indicated that there was no relation between PT and sagittal plane peak knee and hip kinematics, lower limb joint angles at initial contact, trunk kinematics, knee angular velocities, peak vGRF and vGRF impulse, and peak sagittal plane lower limb joint moments. This systematic review showed that studies allowing causal inference are scarce as most of the existing literature consists of case-control studies, there being only one prospective cohort (64), and that with a problematically small sample size of JPTs.

There were five studies including a PTA group (two comparing to PT and controls (176,180), two comparing to controls (178,184) and one including only PTA (174)), while only two studies included previous PT (one comparing to PT and controls (183), and one comparing to controls (103)). Based on the available evidence, these groups presented different biomechanical features compared to PT or controls in ankle and knee angles at IC, ankle dorsiflexion angle, knee angular velocity, knee joint power and work, while they presented similar features in trunk kinematics, leg stiffness, and ankle and hip joint power and work. We also note that no study has simultaneously investigated participants with asymptomatic PTA, current PT and previous PT which could provide explanations for causal relationships, as this would take into consideration the time periods before, during and after the condition. Nor have investigations of joint angular velocities at initial contact, ankle and hip angular velocities after touchdown, leg stiffness, loading rate of forces and muscle activation in

PT population been performed. These would be useful areas to explore causal relationships with high quality large prospective cohort studies.

Existing literature mainly focused on ground reaction forces (GRF) which represents total load on the lower limb. 11 out of 16 included studies investigated GRF (nine studies in PT (100,103,175,176,179–181,183,185) and four in PTA (174,176,180,184)), while this number was lower for studies exploring knee moment (five studies in PT (100,103,180,181,183) and two in PTA (174,180)) and patellar tendon force (three studies in PT (176,179,180) and four in PTA (174,176,180,184)). We suggest that GRF might not be the ideal variable for JPTs due to the limitations of inverse dynamic modelling. There is a particular lack of study on tendon forces, which could provide improved understanding about force distribution and its relationship with PT. Therefore, we still need to know more about forces acting on the knee, and especially patellar tendon force, as we know a high load is transmitted across the knee and it is a primary shock absorber (96).

Future work should also consider non-biomechanical factors alongside biomechanical variables to identify co-variates and interactions. There are several previously identified intrinsic and extrinsic non-biomechanical risk factors increasing the onset of PT in athletes. Age, height, weight, sex, genetics, alignment of lower limb, flexibility, and increased jump height were the main intrinsic factors reported (2,64). Extrinsic factors include practicing a jumping sport characterized by high demands on speed and power for the leg extensors, the number of training hours (elite athletes > non-elite), amount of training, playing surface, number of jumps performed, playing position and the high frequency and intensity of training and competition (2,64–67). It seems plausible that the higher the mechanical overload on the tendon, the greater the risk for developing a PT (2) irrespective of the landing biomechanics. Therefore, future high-quality prospective studies simultaneously measuring plausible biomechanical and non-biomechanical variables – such as workload, clinical examination findings and psychosocial factors - would be the key approach required to determine what part jump-landing biomechanical factors play in the development or management of PT.

3.4.3   Clinical implications

At present, only limited guidance can be provided for clinicians. Evidence is only moderate or limited, but from this, we have identified biomechanical variables which are clinically modifiable, to inform professionals managing and trying to prevent PT. Clinicians could initially focus on increasing

ankle sagittal plane range of motion in order to improve the absorption of the reaction forces from landing, potentially decreasing the load on the patellar tendon. Another approach would be increasing truncal-flexion during landing as it may help reduce pain and tendon forces (180). Lastly, working on soft landing patterns may be beneficial as it helps decreasing landing stiffness, by reducing knee joint moments and increasing knee range of motions (160,189). The risk of such strategies in terms of performance reduction need to be considered, so an alternative approach would be to enhance the athletes' capacity to deal with such forces during a session and maximise recovery strategies.

3.5   Conclusion

Landing biomechanics may be associated with PT, but the level of evidence for the majority of variables was limited or very limited, and risk of bias high despite good applicability. At present, only limited guidance for clinicians and coaches is warranted with three recommendations that can be summarised around making landings less stiff, at least initially. Specifically, these are: improving ankle dorsiflexion-plantarflexion range; optimising truncal-flexion strategies and using soft landing patterns. The literature quality is currently insufficient for robust recommendations, with high-quality prospective studies now essential in order to determine whether jump-landing biomechanics play a part in the development, presentation and/or prognosis of PT, alongside non-biomechanical factors. Further prospective studies could also establish multi-factorial causality while RCTs could investigate the effects of movement strategies on risk reduction and recovery.

4 Study development

In the introduction and systematic review chapters, I concluded that there is a clear need for a high-quality prospective cohort study to better understand presentation and prognosis of PT in jumping athletes. Thus, I planned an international prospective cohort study with a variety of measurements including online questionnaire, physical assessment, ultrasound imaging and biomechanical tests to collect potential factors related to PT.

The purpose of this chapter was to demonstrate the progress of the measurement development for the cohort study. Therefore, I will present the development of the online questionnaire, clinical and ultrasound assessments and biomechanical tests in this chapter including amendments from the feasibility study findings (Chapter 5).

I designed a 1-year prospective international cohort study to achieve project aims. This study was planned to be completed in three levels as shown below.

1. High numbers low levels of measurement (online web survey and questionnaires)
2. Medium numbers medium level of measurement (as above plus some clinical & US imaging assessment)
3. Small numbers high level of measurement (as above plus laboratory-based biomechanics analyses)

The cohort study plan was to collect information from a large number of jumping athletes via online survey and questionnaires in two main groups (athletes with PT and those with other knee problems), more detailed information on a medium number, and highly detailed information on a small number of people. The first data set was planned to be collected via an electronic data capture tool in multiple countries. Then, I followed the participants for a year with 3-weekly follow-up surveys, based on retrospective training load monitoring, in order to determine causal relationships between how athletes present and how they recover.

4.1 Changes for online questionnaire battery

4.1.1 Smart Trial

Online survey which was hosted on Survey Monkey and tested in the feasibility study (Chapter 5) was applied into another software called Smart Trial (ST) to decrease the problems and restriction and to improve the data collection process and security of the data. ST is a registered online

electronic Case Record Form (eCRF), developed according to three different ISO quality standards and hosted in a secure environment supported by Microsoft Azure. They have a complete set of tools and procedures to ensure both stable work environment, and secure data storage.

Amendments for the online survey were applied based on feasibility study results. These amendments included to avoid repetitions in survey, to improve logics between questions, to improve or add instructions, and to reduce time burden. Clinical and US imaging assessment forms were also applied into ST in order to store the data in one place and to give access to collaborators for entering their data.

Applying everything in a new software required a huge amount of time. Training was done to learn ST system. Then, online survey with amendments was established in ST. Steps were;

- Creating forms for each questionnaire with instructions and logics (Figure 12),
- Creating pathways for each study group (Figure 13),
- Creating baseline and follow up events for each pathway (Figure 14),
- Preparing e-mail and SMS content for each event (Figure 15).
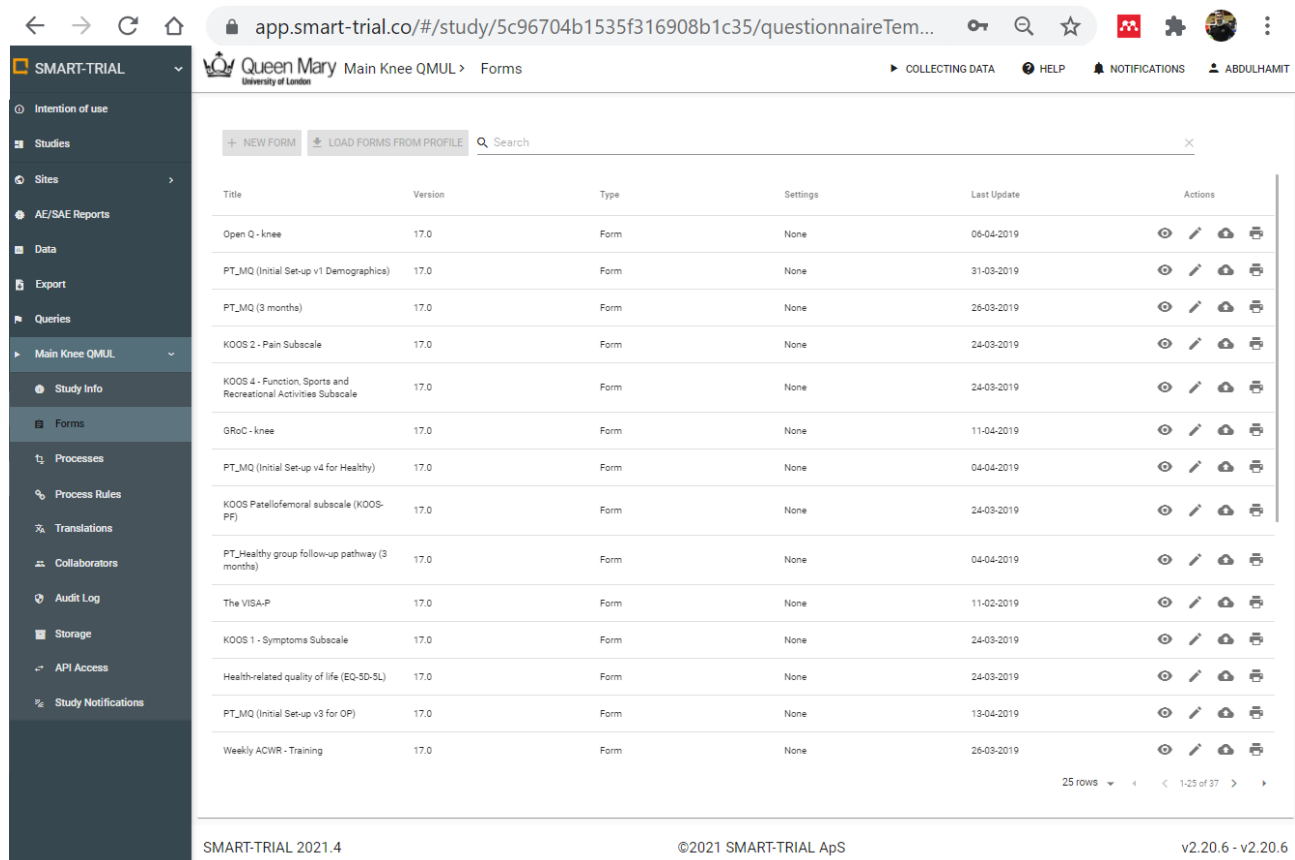
Figure 12: Creating forms for each questionnaire in ST

Figure 13: Creating pathways for each study group in ST

Figure 14: Creating baseline and follow up events for each pathway in ST
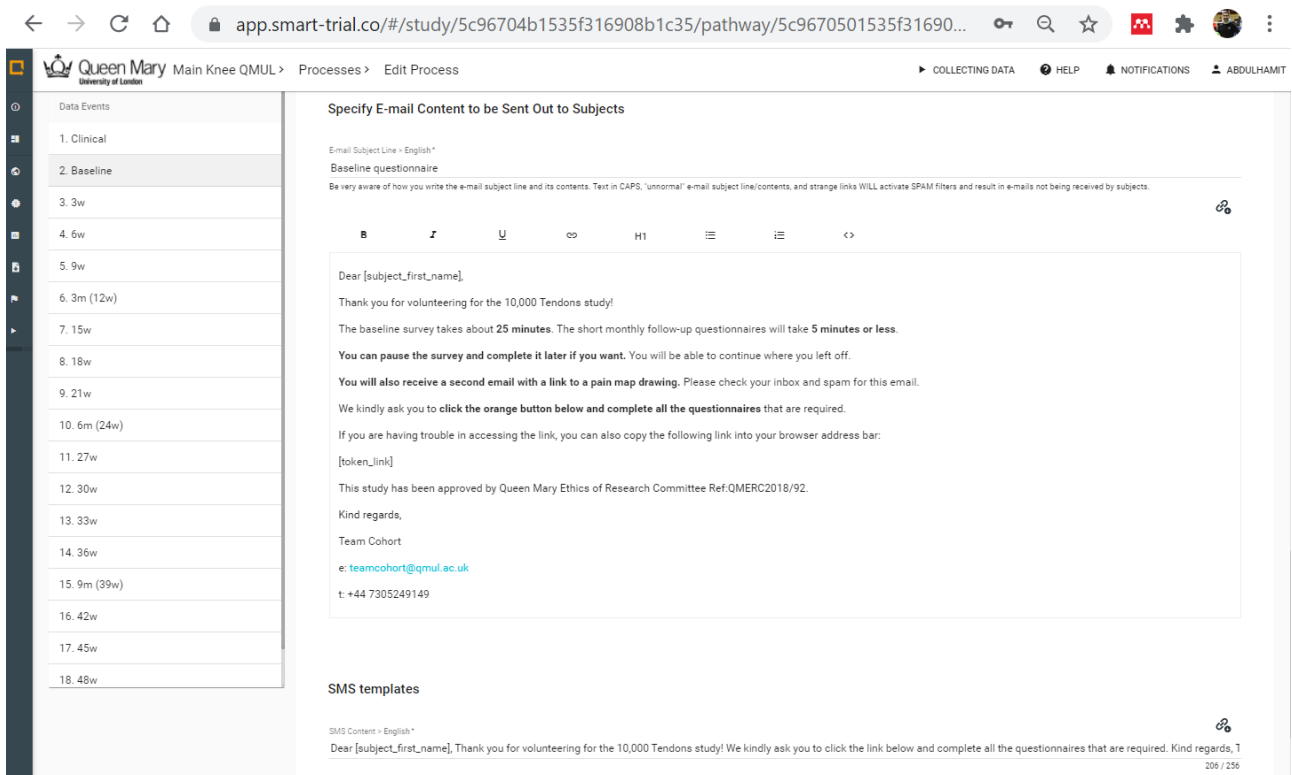
Figure 15: Preparing e-mail and SMS content for each event in ST

After establishing everything in ST, stress tests were applied to make sure whether online survey was working properly. Stress tests included i) device and browser check to see question types work with different screen sizes and software, ii) to check whether all answer areas are suitable for their question's types, iii) to check logics between questions, and iv) to test the limits of answers such as answers with only number, decimal numbers or only text, and upper or lower limits for certain values like height and weight.

Character limitation was also tested for free text questions. 6022 words (13 pages in a Word document) were entered for a single free text question. Then data was exported and checked. There were 4805 words (10 pages) in a single excel cell and the rest came with a separate cell. This caused the rest of other data broken by separating them into another row and they were under the unrelated questions. However, typing this amount of words was rarely expected. Furthermore, I entered wrong or correct answers to check export function. Then, inputs were compared with outputs to make sure that they were completely same (Figure 16). Lastly, grammar and spelling was checked. For the survey established in ST, please see the documents here:

https://www.dropbox.com/sh/hd7152qgun781gi/AADNF5zgMVzzrsqZ-wvZ8sEPa?dl=0.

	A	B	C	AB	AC	GQ
1	Input					Form 2
2				Height (cm)	Weight (kg)	Please describe your main knee problems in your own words?
3				Number	Number	Free text
4	id	status	patientId	E1_F23_Q2	E1_F23_Q3	E2_F9_Q1
5	5ca0c1b0a8309d15a8ee3976	ONGOING	InOut1	181	97	I have problems when I do jumping, landing, running and kneeling. Very painful and I had to modif
6						
7	Output					
8				Height (cm)	Weight (kg)	Please describe your main knee problems in your own words?
9				Number	Number	Free text
10	id	status	patientId	E1_F23_Q2	E1_F23_Q3	E2_F9_Q1
11	5ca0c1b0a8309d15a8ee3976	ONGOING	InOut1	181	97	I have problems when I do jumping, landing, running and kneeling. Very painful and I had to modif
12						

Figure 16: Survey input comparison with their export from ST in excel.

4.1.2   Navigate Pain

Improving pain map was one of the outputs from the feasibility study (Chapter 5). Basically, participants answered the pain map question by choosing numbers located in grid lines in the pain map picture, only anterior aspect of the knee (Figure 17). It was aimed to use a drawable pain map including all aspects of the knee with more professional picture and having features to obtain pain type, severity and duration.

First, pain map picture was improved to make it more professional (Figure 18). Then, whole body chart was decided to be used in order to capture all painful areas of athletes which could give more reasonable data (e.g. relation between low back pain and leg pain).
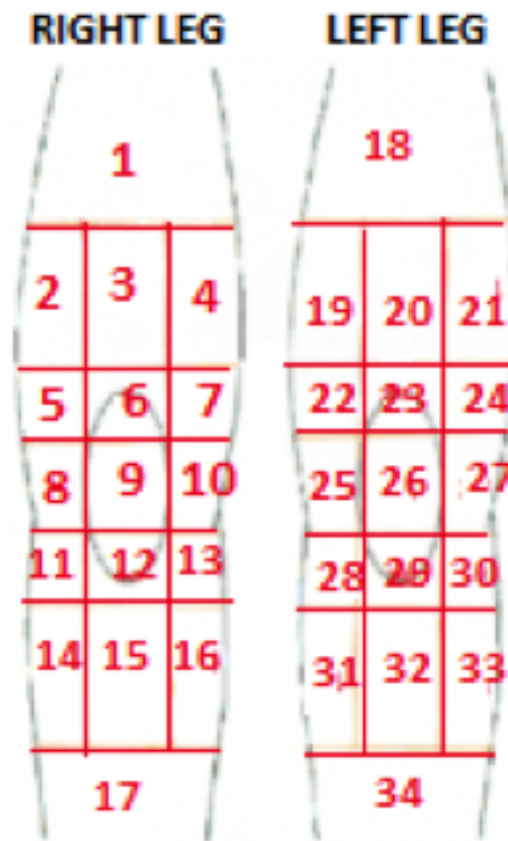
Figure 17: Pain map with grid lines, only anterior aspect of the knee, was used in the feasibility study (Chapter 5) with permission of Prof Morrissey (191). Number 12 and 29 refer to the inferior pole of the patella.
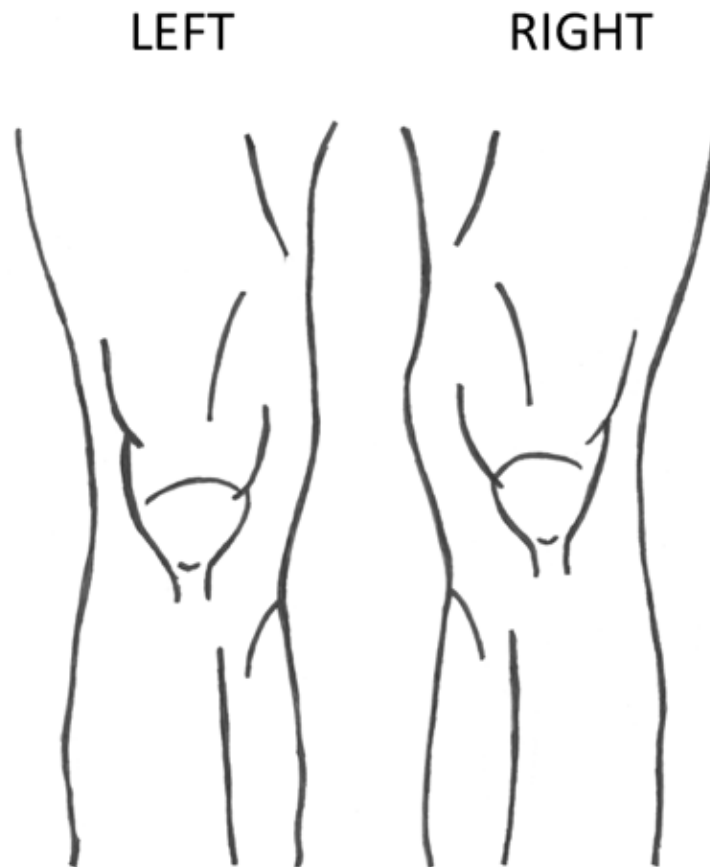
Figure 18: Improved picture of anterior aspect of the knee for a drawable pain map

ST has a drawable pain map feature in their system. They provide different pictures, sex option, type of pain, severity, and so on. However, there were some missing key features such as zoom option and adjustable pen size which would make hard to draw pain for a specific area. Furthermore, there were also some errors listed below;

- Not working very well with a smartphone,
- Length of pain severity line were changing based on screen size,
- Being able to draw out of the picture (Figure 19).

Therefore, ST pain map was not good enough and was decided not to be used. Pain map data was decided to be collected in Navigate Pain (NP) software (Figure 20) as NP covers all the missing points and errors of ST, plus it provides data analysis. NP has the same or similar abovementioned features (e.g. ISO quality standards, secure data storage etc.) just like ST. Moreover, both ST and NP are approved platforms and follow Queen Mary's privacy notice for research participants.
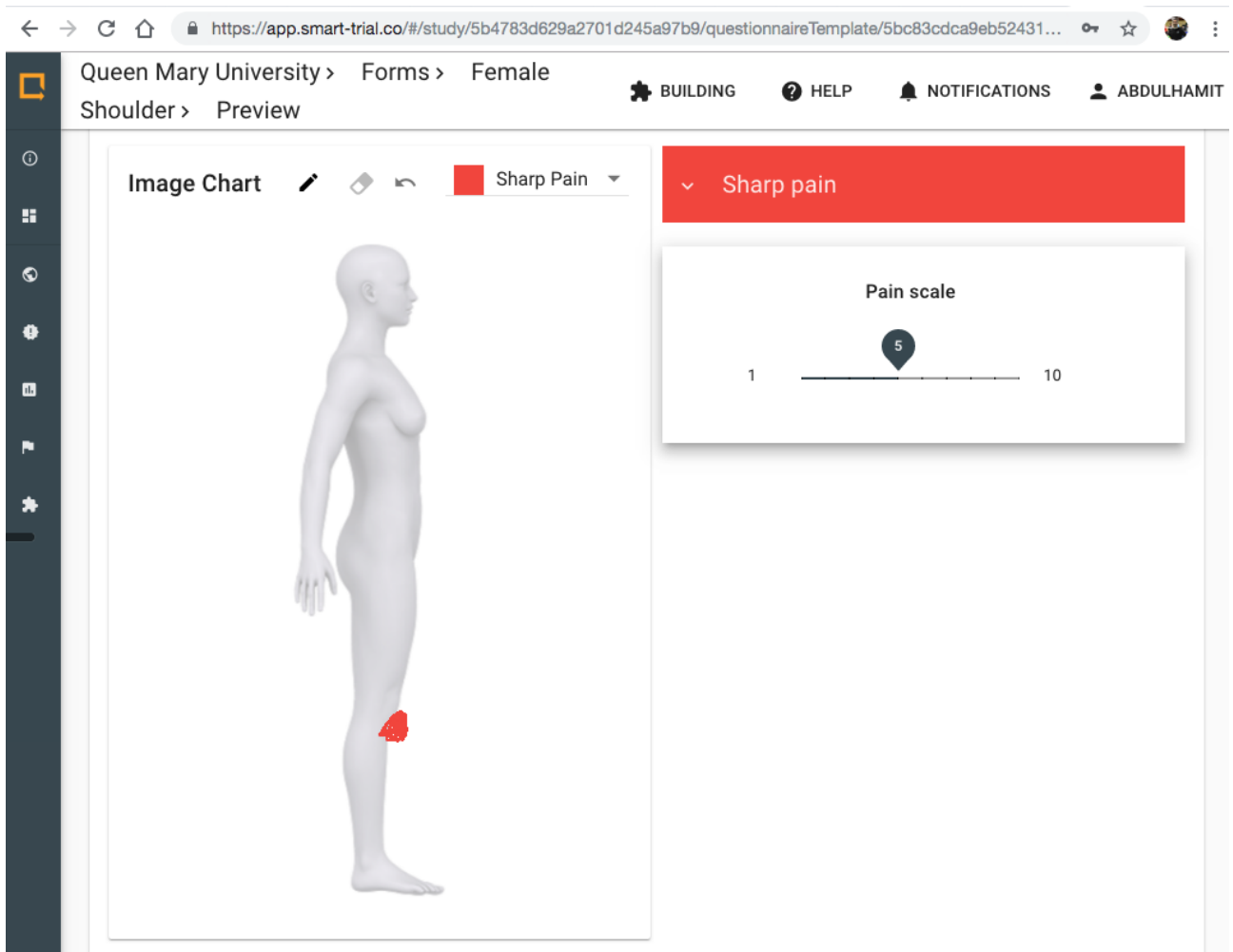
Figure 19: Drawable whole body chart in Smart Trial. Red drawing refers to the error of being able to draw out of the picture.
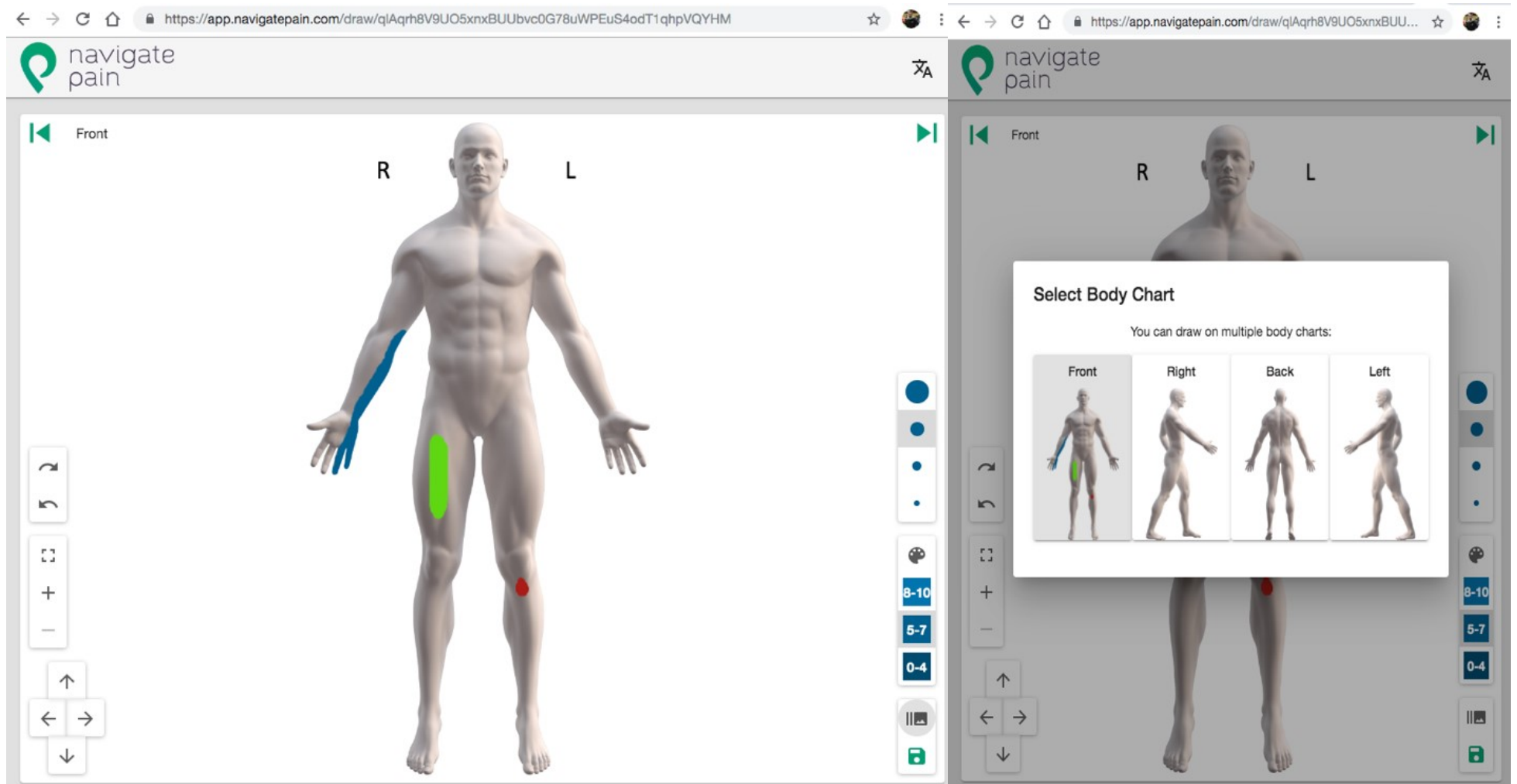
Figure 20: Drawable whole body chart in Navigate Pain. Different colours refers to different types of pain (e.g. pain, stabbing, electric). It provides 4 different aspects of body (front, back, left and right side views), sex, zoom and pen size options.

As using two different software, ST and NP, it was needed to link both system to each other. It was a totally technical issue between ST and NP, and I had to wait until, 45 days, they sort this connection between two software. After this connection, the process of enrolment was tested. The communication of two systems was good as when a participant was enrolled in ST, they were also enrolled by NP automatically in a few seconds. As a result, clinical and survey data were being captured electronic forms and saved directly ST and NP systems. While participants can fill out the online survey and pain map by themselves with remote accessibility, I entered the clinical data.

4.1.3 Re-piloting

Re-piloting of the online survey has been conducted because of the new setup in ST and NP. Additionally, I was unable to check follow up surveys in the feasibility study (Chapter 5). Therefore, baseline survey and only first four follow up surveys were piloted with a 1-hour time interval for follow up surveys instead of 3 weeks to save time. The aims of this re-piloting were;

1. To test ST and NP with real people to find out if there is any problem,
2. To test whether both ST and NP work together very well for the eligibility survey,
3. To test whether e-mails and SMS texts were sent on time,
4. To test whether follow up surveys were sent on time,
5. To test whether reminders were sent on time.

There were two other PhD students who were using ST and NP systems in people with shoulder and foot problems. Re-piloting was conducted for all PhDs at the same time because of the second aim mainly. Therefore, 21 people in total (8 females, 13 males) were recruited, 8 people in knee part and the rest in shoulder or foot part. We asked questions below to get participants feedback;

1. Which device/browser did you use?
2. Have you had any trouble with the system?
3. Have you had any trouble with pain map drawing?
4. Is there any question(s) that you had difficulty to understand?
5. Do you think that survey is relevant with your condition?
6. What do you feel could be improved in this survey?

Feedback analysis was done for per knee survey pathway specifically and for all the system generally. Please see the Table 5 for the feedback.

In conclusion, 5 participants gave at least 1 feedback for overall survey and system, 3 participants with no problem. Overall, participants were happy with the system and survey (answers of question 2 and 6) as the problems they mentioned were minor.

Table 5: Specific feedback from re-piloting for only knee part (n=8). Keys: EQ5D5L, Health related quality of life scale; ✓, solution applied; NA, not applicable; NP, Navigate Pain.

Feedback	Number of People	Solution	Status
Grammar and spelling corrections	1	Editing and corrections	✔
Missing instruction for EQ5D5L	1	Add instruction	✔
The Patient-Specific Functional Scale (PSFS) did not work in follow ups	2	Exclude PSFS form the survey	✔
Table question type did not work properly with smaller screen sizes like smartphone	2	Add instruction to remind participants	✔
Confusion for follow up surveys	1	It was because of 1-hour follow up duration. Thus, there will be no problem in the main study.	✔
Completion time of survey was long but acceptable	1	Did not change	✔
Saving pain map drawing in NP	1	Add instruction into NP email	✔
People with no feedback	3	NA	NA
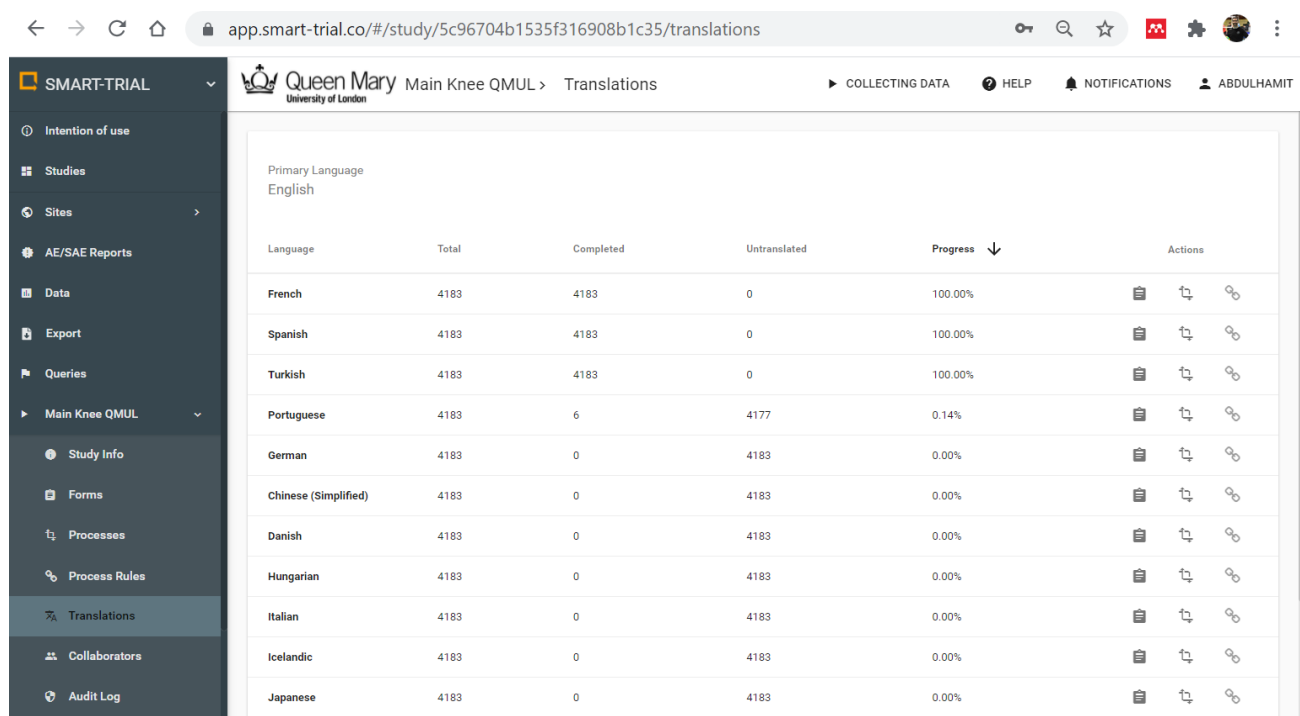
4.1.4   Patient and Public Involvement

Patient and Public Involvement event was organised on 7th January 2019 at a private restaurant by Team Cohort (AT, HG, MD, and supervisor DM). Two sessions were completed, and four attendees were recruited for each session. First session lasted one hour, while second session was 45 minutes. We had two main sections which were 'Baseline' and 'Retention' in order to get feedback on the planned prospective cohort study. Sections were mainly included questions about survey duration, how to motivate people to join in the study, retain in the study and fill out the long surveys, type of reminder, reminder time and frequency and solutions for email junk/spam box.

There were number of risks and benefits identified by the attendees. These included the data sharing with third parties or private companies, the need for repeated consent if using the data for multiple purposes, suggestions or potential solutions on recruitment and retention strategies, timing of the surveys, frequency and number of the reminders, communication methods, and motivation methods for joining in the study. These inputs helped us to improve the recruitment and retention strategies of the cohort study. For instance, attendees suggested that using e-mail and SMS instead of phone calls would be a better way to reach the participants. We set reminders, two times with three days intervals, based on attendees' suggestion as they stated that every 3-day for the frequency of reminders is good enough, but still need to put some limits (e.g. maximum 3 reminders). Please see Appendix 6 for the details of the questions and responses.

4.1.5 Translations into other languages

Online questionnaire battery was carefully translated to Turkish, Spanish and French to optimise recruitment. If PROMs have already been translated into targeted languages, their existing versions were used (Turkish: VISA-P (192), TSK-11 (193), PCS (194), eHEALS (195); Spanish: VISA-P (196), TSK-11 (197), PCS (198), eHEALS (199); French: VISA-P (200), TSK-11 (201), PCS (202)) or accessed from official websites for KOOS and KOOS-PF (http://koos.nu), EQ5D5L (https://euroqol.org/), and GSE (http://userpage.fu-berlin.de/health/selfscal.htm). We used Google Translation for missing PROMs (Turkish: PASS, SANE; Spanish: KOOS-PF, PASS, SANE; French: KOOS-PF, PASS, SANE, eHEALS), miscellaneous questions, e-mail/SMS content, PIS and ICF forms. After using Google translation for forward and backward translation, collaborators were asked (Turkish: HG and MD, Spanish: IS, French: GLS and KJF) to check all translations for their own language. Also, we used existing translations of KOOS and TSK for the same items in KOOS-PF and TSK-11, respectively. Once translations were received, I applied them into ST system (Figure 21). However, ST system allows the users to enter translated content one by one, there being 4183 strings for each language. Therefore, applying translations took a lot of time about 7-10 days for one language.

Figure 21: Applying translation in ST

4.2 Changes for clinical and US examinations

The feasibility study outputs for the clinical and US imaging examination were to reduce time burden and repetitions. Furthermore, categorical data was decided to be used as potential variables which

could go into the causal model were planned to be categorised. For instance, hamstring muscle flexibility will be categorised as normal or tight. Categorization were also useful to reduce time burden of the examinations. Completion time was around 45 minutes for clinical and US examinations compared to feasibility study which was about 75 minutes. On the other hand, when using categorical data, it is very important how to do categorization for each variable. Therefore, each categorization was decided based on literature (Table 6). Reasoning for each clinical measurement was presented in Table 6. I applied clinical measurements and a GE Logiq S8 device used for US imaging (Figure 22). Please see Appendix 7 for the final version of data collection form for clinical and US examination.
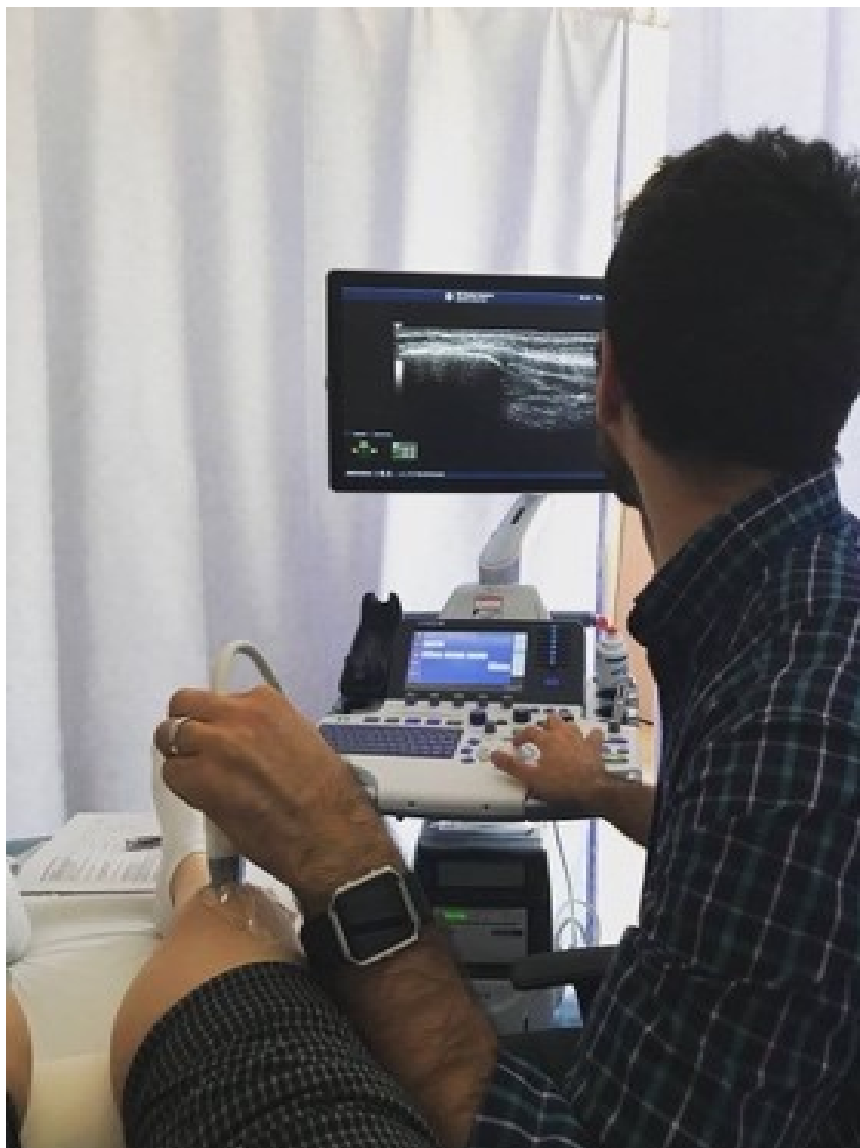
*Figure 22: US imaging with **GE Logiq S8***

Table 6: Justifications for each clinical measurement. Keys: VAS, Visual Analogue Scale; PT, patellar tendinopathy.

Tools	To measure	Justification of measuring variables	Justifications of measurement tools
Navigate Pain (Digital Pain Map Drawing) including VAS.	Pain localisation, distribution, type, severity and frequency.	Important as diagnostic criteria, especially localisation based on inferior patella pole (25,26).	Shown to reflect chronicity irrespective of problem (203). Good studies (204–206) showing utility for digital pain map. VAS is widely used for pain severity (207).
Weber-Barstow measurement.	Leg length discrepancy.	Clear place on literature (83,91), plus part of standard lower limb assessment.	This method is quick and easy to apply in the clinic (208). Differences mean >5mm.
Observation of lower limb posture. Magee's Method for knee. Visual assessment of foot type.	Knee alignment (genu varus, valgus and recurvatum) Foot posture (supinated and pronated).	Lower limb alignment (64) and lower foot arch height (78,83) have a clear place on literature. They are mentioned in the literature as potential variables. Plus, part of standard lower limb assessment.	The method described by Magee categorizes varus, valgus, or neutral alignment based on visual observation and is quick and easy to apply in the clinic (208,209). Procedure to categorise foot type (supinated, neutral, pronated) by observation (210).
Pain on Palpation (before and after graded loaded challenge (GLC).	Inferior patella pole, patellar mid-tendon and insertion, tibial tuberosity, thigh muscles, retropatellar, quadriceps tendon.	Confirmational and differential diagnostic criteria, especially for pain distribution (211–214). Plus part of standard lower limb assessment.	Flexion of the knee tightens the extensor tendons (213). Therefore, supine position with knee flexed 20-30° allows as suitable examination for all palpations except retropatellar. Extended knee position is needed for retropatellar as it allows patella to move to the sides (211).
Hoffa's Test (before and after GLC).	Hoffa fat pad involvement.	Differential diagnostic criteria (24).	Difficult to diagnose clinically, but Hoffa's test might be quite helpful and quick (215).
Hand-held dynamometer and Oxford Scale.	Muscle strength (Knee extension-flexion and hip extension-flexion-abduction).	Quadriceps and hamstring strength have a place on literature as they were investigated as potential factors (74). Plus, part of standard lower limb assessment.	Hand-held dynamometer (break test) (216) will be used for the key muscles (quadriceps and hamstring). Oxford scale (217) for hip as it is quick and easy to apply in the clinic. Procedure for all strength tests (217).
Active- and Passive range of motion (AROM/ PROM) by categorising.	AROM and PROM for knee extension and hip abduction. Only PROM for knee flexion and hip extension.	Biomechanical studies demonstrate association between range of motion and PT (103,174,177,184,218,219). Plus, part of standard lower limb assessment. These range on motion assessments will be measured during jump-landing with biomechanics as well.	Categorizations were used to reduce the time burden for participants as I am interested in the outcomes that could go into the model, instead of actual degrees of range of motion. Knee extension (limited, normal, lax), normal means fully extended. Hip abduction (limited, normal, lax) normal means 45°. Knee is bilaterally fully flexed (means heel to bottom), then check the asymmetry. Hip extension (limited, normal, lax) normal means 20° by stabilising from tuber ischia.
Observational flexibility measurement by categorising.	Hamstring and quadriceps flexibility.	It is reported that decreased quadriceps and hamstring flexibility are associated with PT (74,78,84).	For hamstring flexibility, from hip and knee 90° flexion positon to reach full knee extension means normal, <90° means tight hamstring (83). Deep quadriceps is same as PROM for knee flexion, so no need to do it again. Fully flexed knee (heel to bottom) with a slight hip extension for rectus femoris flexibility. Fully flexed means normal, otherwise tight.
Ober Test.	Iliotibial Band flexibility.	Part of standard lower limb assessment.	Procedure for side lying position and categorising (220). Normal means horizontal to the bed, above horizontal is tight, below horizontal is flexible.
Modified Thomas Test.	Hip flexors flexibility.	Part of standard lower limb assessment.	Procedure for supine position and categorising (220). Normal means horizontal to the bed, above horizontal is tight, below horizontal is flexible. Plus, if tight check the main muscle (Iliopsoas, rectus femoris of tensor fascia lata).
Knee to Wall test by using inclinometer.	Total ankle dorsiflexion range of motion, plus gastrocnemius flexibility.	Reduced ankle dorsiflexion range is identified as a risk factor for PT (93,94).	Reliable bilateral measurement, front and back limb (221–223).
Graded Loaded Challenge (GLC) including Modified Borg Scale (MBS, 0-10).	Loading on tendon with graded tasks, end of protocol based on pain severity by numerical rating scale (NRS) (>5/10) plus following fatigue during tasks.	Load dependent pain is important as diagnostic criteria (1,23,24). Jump landing activities are associated with PT (99), and have a clear place on literature with fatigue (174,219,224).	Pain based on NRS >5/10 to stop the protocol (225). Standardized version of the MBS (226). Order of tasks validity and reliability was checked with the feasibility study. Two tasks were removed to reduce the burden and order was reorganised.

4.3 Changes for biomechanics

I performed biomechanical tests in the Human Performance Laboratory by using an active infra-red motion capture system (CX-1, Codamotion, Charnwood Dynamics Limited, Leicestershire, UK), two embedded force plates (Kistler Type 9281CA, Kistler Corporation, Switzerland) (Figure 23), and wireless electromyography (DELSYS Inc., Natick, Massachusetts, USA). ISB guidelines (227) and the CAST protocol (228) determined marker placement, while Seniam Guideline (229) determined EMG channels placement (Figure 24). The feasibility study outputs for the biomechanical tests were to reduce time burden and system problems, and to increase the quality of data. There were lots of troubleshooting or corruption in the system due to time for recording. To solve this problem number of jump-landing tasks and repetition were decreased based on feasibility study data. Number of EMG channels were reduced from 22 to 14 to avoid second PC preparation and to ease data analyses. However, number of markers and reference points were increased to improve visibility, hence the quality of data. Completion time was around 75 minutes for biomechanics compared to feasibility study which was about 90 minutes. Please see Appendix 8 for the final version of biomechanical data collection form.
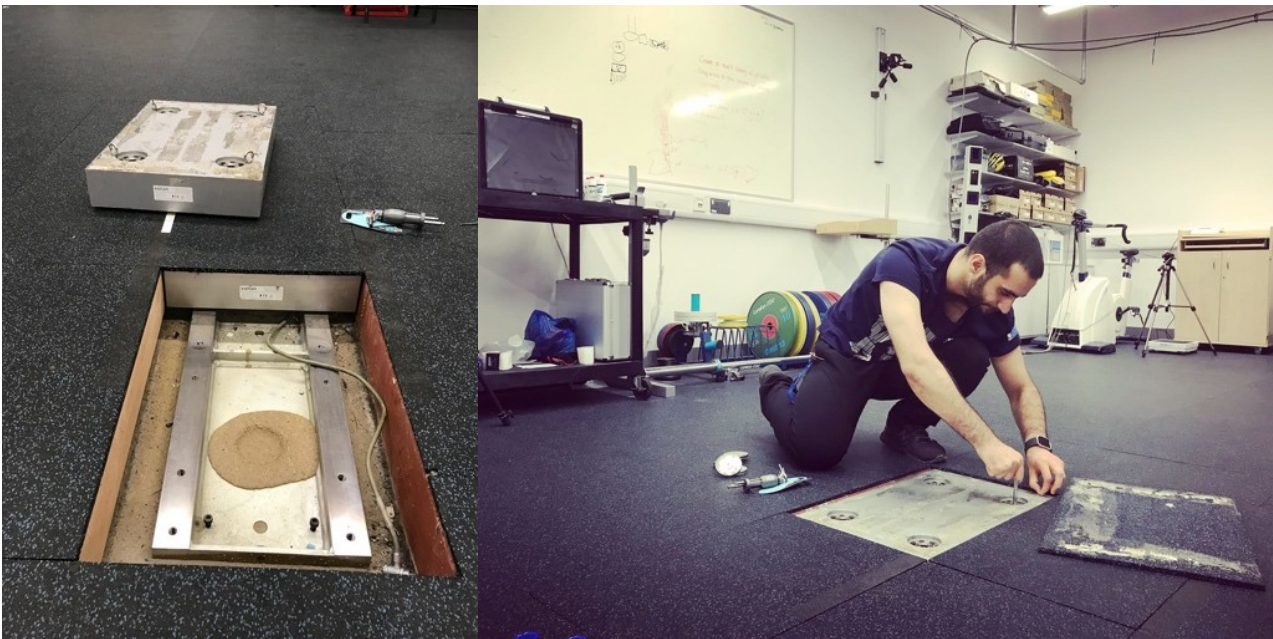
Figure 23: Preparation of the force plates (e.g. positioning specific to my tasks)

Markers:
1. R.1MT (M1)
2. R.5MT (M3)
3. R.Heel (M4)
4. L.1MT (M5)
5. L.5MT (M7)
6. L.Heel (M8)
7. R.ASIS (M9)
8. R.PSIS (M10)
9. L.PSIS (M11)
10. L.ASIS (M12)
11. R.IC (M13)
12. L.IC (M14)
13. R.AC (M15)
14. R.HLE (M16)
15. L.AC (M17)
16. L.HLE (M18)
17. X (M19)
18. T8 (M20)
19. C7 (M21)
20. SJN (M22)
21. R.Shank (25-28)
22. L.Shank (29-32)
23. R.Thigh (33-36)
24. L.Thigh (37-40)

- Double Marker Drive Box x2 (1-3)
- Double Marker Drive Box x2 (4-6)
- Double Marker Drive Box x3 (7-12)
- Double Marker Drive Box x2 (13-16)
- Double Marker Drive Box x2 (19-20)
- Clusters for each one (21-24)

Landmarks for Pointer:
1. R Med Malleolus
2. R Lat Malleolus
3. L Med Malleolus
4. L Lat Malleolus
5. R Med Femoral Epicondyle
6. R Lat Femoral Epicondyle
7. L Med Femoral Epicondyle
8. L Lat Femoral Epicondyle
9. R ASIS
10. L ASIS
11. Static Acquisition

Stick Figures:
1. Legs R & L
2. Trunk
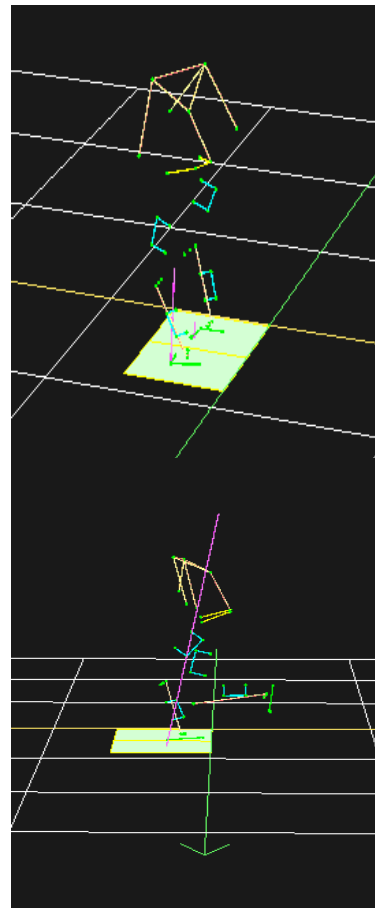
Calculations and Centroid Joints:
1. R.Ankle: MM & LM
2. L.Ankle: MM & LM
3. R.Knee: MFE & LFE
4. L.Knee: MFE & LFE
5. Hip R: ASIS + PSIS
6. Hip L: ASIS + PSIS
7. Force
8. CB
9. EA angles
10. Other calculations

Graphs and Live Graphs:
1. EMG channels
2. Forces
3. EA Angles

EMG Channels:
1. Vastus Medialis
2. Vastus Lateralis
3. Rectus Femoris
4. Semitendinosus
5. Biceps Femoris
6. Med Gastrocnemius
7. Lat Gastrocnemius

In total 14 channels for double legs

Figure 24: Lab protocol. Kinetics, kinematics, and stick figure configuration of the body. Basic foot (heel, first and fifth metatarsal), shank, thigh, pelvis (anterior and posterior superior iliac spine), trunk (xiphoid and T8 vertebrae), and arm (acromion and lateral epicondyle) markers were used. EMG sensors placements for both legs (yellow points). Keys: M, markers; R, right; L, left; MT, metatarsal; ASIS, anterior superior iliac spine; PSIS, posterior superior iliac spine; IC, iliac crista; AC, acromion; HLE, humerus lateral epicondyle; X, xiphoid; T8, T8 vertebrae; C7, C7 vertebrae; SJN, sternum jugular notch; MM, medial malleolus; LM, lateral malleolus; MFE, medial femoral epicondyle; LFE, lateral femoral epicondyle

4.4 Study scheme diagram

Please see Figure 25 for the participant journey and life cycle of the study in a schematic form.
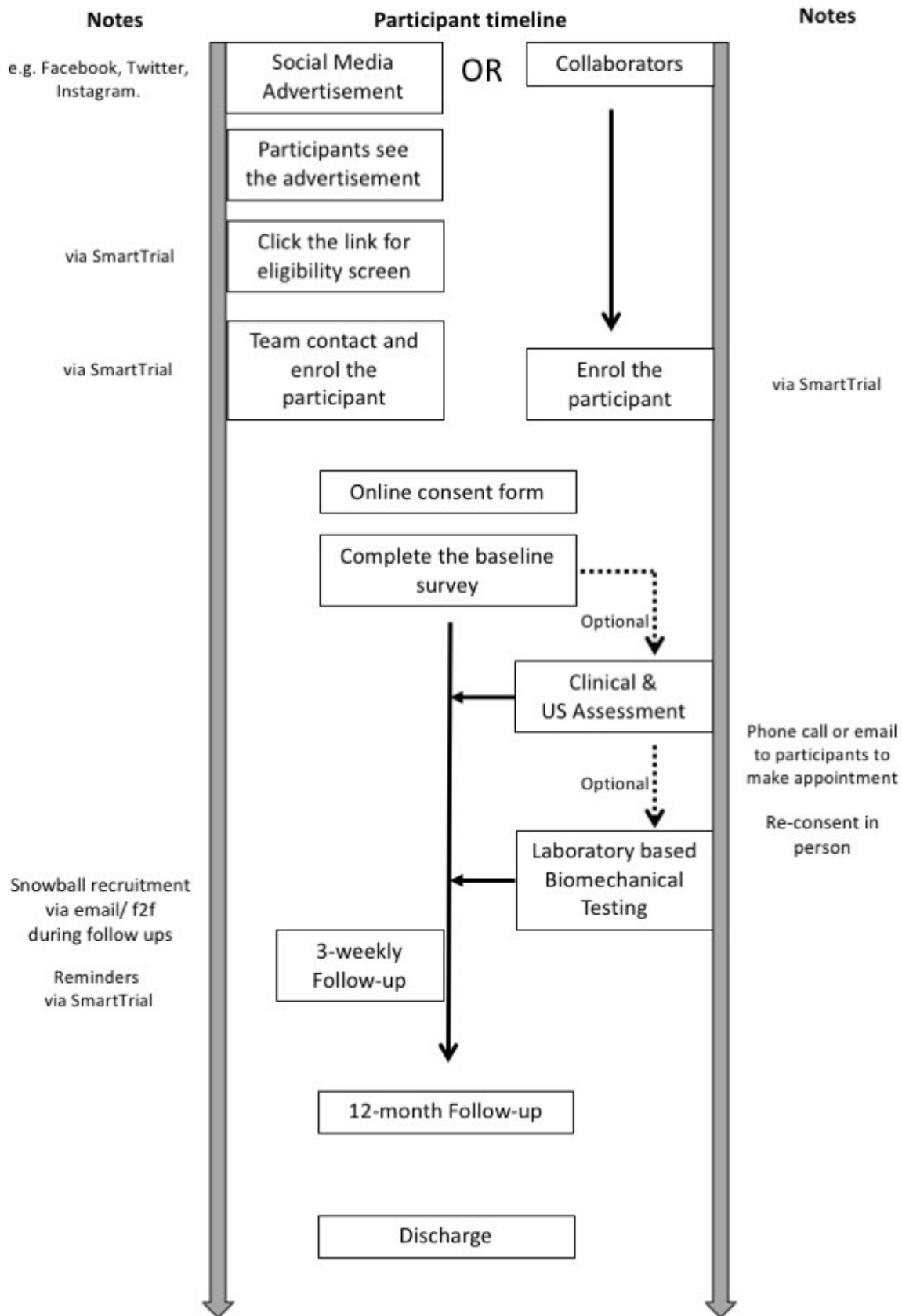
Figure 25: A typical participant journey. Keys: US, ultrasound; f2f, face-to-face.

4.4.1 Collaborators

There were over 40 collaborators from 10 different countries who joined this international cohort study. However, all of the collaborators did not recruit actively. The process of working with a large number of collaborators started with a site feasibility survey hosted on Survey Monkey (https://www.surveymonkey.co.uk/r/3T_10000) to learn the potential collaborators' target population and the number or people they had access. We visited them in person or arranged video calls, if they were available. We also prepared a recruitment package in case of being unable to reach collaborators in person or via video calls. Recruitment package included;

- Guideline for the recruitment package: Brief explanation of documents and how to use the package.

- Video showing how to enrol a participant into the survey:
  https://www.dropbox.com/sh/t68ifetyl5y8z6a/AACH6SztZ9_3FPo7XEG87BPSa?dl=0&preview=6-)+how+to+enrol+participants+by+eligibility+survey.mp4

- The main eligibility survey short cut link.

- Ten Thousand Tendons study protocol.

- Ten Thousand Tendons study Queen Mary ethics application and approval letter.

- Ten Thousand Tendons study presentation from Prof Dylan Morrissey:
  https://www.dropbox.com/sh/t68ifetyl5y8z6a/AACH6SztZ9_3FPo7XEG87BPSa?dl=0&preview=2-)3T+presentation+from+Dylan+Morrissey.url

- Ten Thousand Tendons study recruitment presentation_08.05.19: Brief presentation about the study and recruitment process chart.

- Eligibility criteria of the study and key points.

- Study flyers (Appendix 9).

- The package link is here:
  https://www.dropbox.com/sh/t68ifetyl5y8z6a/AACH6SztZ9_3FPo7XEG87BPSa?dl=0

5 Patellar tendinopathy outcome predictors in jumping athletes: Feasibility of measures for a cohort study

In the study development chapter, I presented the progress of the online questionnaire, clinical and ultrasound assessments and biomechanical tests of the planned cohort study. To assess these data collection procedures I conducted a feasibility study. Therefore, feasibility, validity and reliability of the planned cohort study measurements are presented in this chapter.

Preliminary results of this feasibility study were presented at the 2018 5th International Scientific Tendinopathy Symposium in Netherlands and the 2019 21st Annual Conference in Sport & Exercise Medicine in QMUL, UK. This study has been accepted for publication by Physical Therapy in Sport (Impact Factor=2.365, https://doi.org/10.1016/j.ptsp.2020.05.004) after two rounds of comprehensive peer review and has been adapted for the thesis.

5.1 Introduction

The planned cohort study used an online self-administered questionnaire battery to obtain data from a large number of participants. Clinical assessment should yield more detailed information compared to questionnaire via physical examination and Ultrasound (US) imaging data from a subset of participants. The most detailed information was planned to be obtained via biomechanical data from a further subset. The aim was to build a statistical causal model to describe why PT does not recover fully, and what the predictors of recovery are. It has been shown that a multivariable model predicts non-recovery better than a single variable in the case of shoulder pain (158). Therefore, a casual model could enable clinicians to improve their decisions about prognosis for athletes with PT and manage patients' expectations accordingly.

To achieve the main study aims, epidemiological data needs to be collected from a large number of participants who are then followed up to determine causal relationships between how jumping athletes present and how they recover. There are some shared potential factors between PT and other knee problems (OP) such as quadriceps strength (74,230), playing surface (66,231) and body mass index (83,85,232) for patellofemoral pain, anterior cruciate ligament injury or osteoarthritis. Therefore, we do not know which factors are specifically associated with PT presence due to the commonality of the variables with other knee problems.

It is essential to determine methodological feasibility in such a complex study (233). The Consolidated Standards of Reporting Trials extension to pilot and feasibility trials (Consort-PF, (234))

gives useful guidance on the constituent elements of a high-quality feasibility study as does the Prediction model Risk Of Bias ASsessment Tool (PROBAST) for epidemiological studies (235). Based on these checklists, the focus of this feasibility study was to evaluate suitability of outcome measures for online use, data collection procedures and processes, and to determine potential problems for the planned cohort study design.

The main aim was to assess feasibility, by testing data collection procedures in order to optimise the success of a planned large international cohort study. Feasibility measures included completion time, recruitment and the time burden for participants. Secondary objectives were to test measurement validity and reliability. The impact of success would include useful information about data collection procedures such as remote questionnaire use and the validity of a graded loaded challenge suitable for use in clinical practice as an objective measure of severity, and guide the necessary amendments to optimise the planned cohort study. The alternative hypothesis was that data collection procedures of the planned cohort study were feasible, valid and reliable.

5.2   Materials and methods

The Consort-PF statement (234) guided the design and reporting of this feasibility study (Appendix 10).

5.2.1   Participants

This study was approved by Queen Mary Ethics of Research Committee with reference number QMREC2014/24/153 (Appendix 11). 36 jumping athletes equally distributed between those with PT, OP and healthy controls were recruited from private clinics and sports clubs. Eligibility was checked after consent (Appendix 12) had been granted: with the inclusion criteria being aged between 18 and 64; performing a minimum of one-hour training once per week; previously or recently having a clinical diagnosis of PT (PT group) or another musculoskeletal condition affecting the anterior knee (OP group) from a clinician or having had no knee related diagnosis (healthy control group). The exclusion criteria were having cardiovascular or neurological disorders for all groups.

5.2.2   Procedures

Recruitment was done with two equally populated pathways (Figure 26). The first pathway completed one online survey, assisted or non-assisted, then attended clinic and ultrasound

examination. 9 participants completed two biomechanical examinations. The second pathway completed the survey twice, both assisted and non-assisted, 2-7 days apart in a randomised order.

5.2.3   Measures

5.2.3.1   Online questionnaire battery

The composite battery included six patient reported outcome measures (PROMs) plus miscellaneous questions (MQs) concerning demographics, condition related details, treatments, training load in the previous 6 weeks and a pain map (https://www.surveymonkey.co.uk/r/t-team3a-pt). There were some minor formatting adaptations for online PROM administration as previously reported 'faithful migrations' from paper to electronic platforms (236). The adaptations included one extra logic question in the VISA-P to link to the last item, 'placing a tick' and 'drawing a line from the box' were changed with 'clicking' and 'by adjusting the slider', respectively, in the instruction of EQ5D5L, and 'ticking' was changed with 'clicking' for the instruction of KOOS.
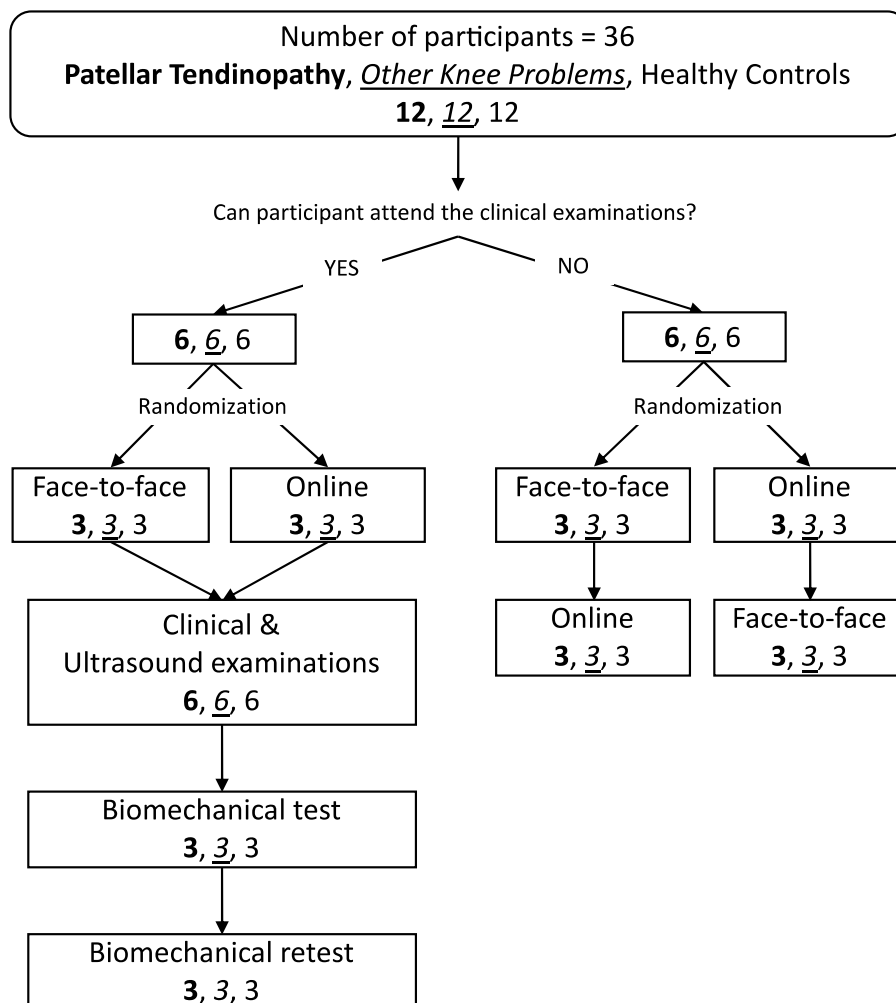
Figure 26: Feasibility study design showing participant test order

The Knee injury and Osteoarthritis Outcome Score (KOOS) (237) with Patellofemoral subscale (KOOS-PF) (238) and Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon (VISA-P) (239) measure knee-specific condition severity. Health-related Quality of Life (EQ5D5L) (240) was included due to likely chronicity (4,7). Psychosocial factors are associated rehabilitation outcomes (241) while catastrophisation (Pain Catastrophizing Scale (PCS) (242)) and kinesiophobia (Tampa Scale for Kinesiophobia (TSK) (243)) have not been investigated in PT but have in other tendinopathies (244).

5.2.3.2 Clinical and ultrasound assessment

Clinical measurements were applied in clinic by an experienced clinician (AT) and a GE Logiq S8 device used for US imaging. Clinical and US assessments are variably reliable in the literature so we chose commonly used measurements already reported to be reliable with a minimum moderate reliability, i.e. ICCs=0.5-0.75 (245), set as a criterion. Patellar tendon palpation (pearson r=0.82; (27)), hamstring range of motion (ICC=0.84; (83)), ankle dorsiflexion range of motion (ICCs=0.97-0.99; (83,246)) and single leg hop test (ICCs=0.76-0.92; (247)) were shown to be reliable measurements and therefore selected.

Ultrasonography was also included as it supports the diagnosis of PT (28) and helps with detection of structural patellar tendon changes (115). A recent systematic review demonstrated that inter- and intra-rater US reliability was good to excellent when measuring tendon thickness and cross-sectional area, despite variation in examiner experience (248). Reliability of US measurements (such as thickness, structural changes, neovascularization) were investigated in various tendinopathies showing moderate to excellent intra-rater and inter-rater reliability in supraspinatus tendinopathy (k=0.60-0.96; ICCs>0.85; (249,250), good inter-observer reliability (ICC=0.85; (251)) in mid-portion Achilles tendinopathy, poor to excellent inter-observer reliability (thickness: ICCs=0.96-0.99; neovascularisation: r=0.77-0.99; structural changes: r=0.38-0.84; (252)) and intra-observer reliability (structural changes: k=0.54-0.87; neovascularisation (k=0.64-0.86; (252)) in Achilles and patellar tendinopathies and good inter-tester reliability (Pearson r>0.87; (253)) in patellar tendinopathy. Ultrasound reliability was therefore not specifically assessed in this feasibility study.

Clinical assessment included pain map annotation (191) (Figure 17), palpation (214), observational lower limb posture analysis (208), anthropometrics (83), range of motion (94), muscle strength and flexibility tests (74), functional tests (29) and a graded loaded challenge (GLC).

The GLC is a functional test specifically designed for clinic use. The GLC aim was pain-provocation with condition-specific movements to indicate severity, using progressively higher load and speed

demands from double leg to single leg squat and jump landing activities. Progression was stopped when participants experienced pain of 5/10 on a numeric rating scale (225) or movement failure such as contralateral limb compensation.

US measurement of patellar and quadriceps tendon thickness (Figure 27), neovascularisation (254), presence of teno-osseal changes, cortical irregularity, bone spurs in distal portion of patellar tendon, presence of pre- and infra-patellar bursitis, Osgood Schlatter, swelling, tear and calcification was performed.
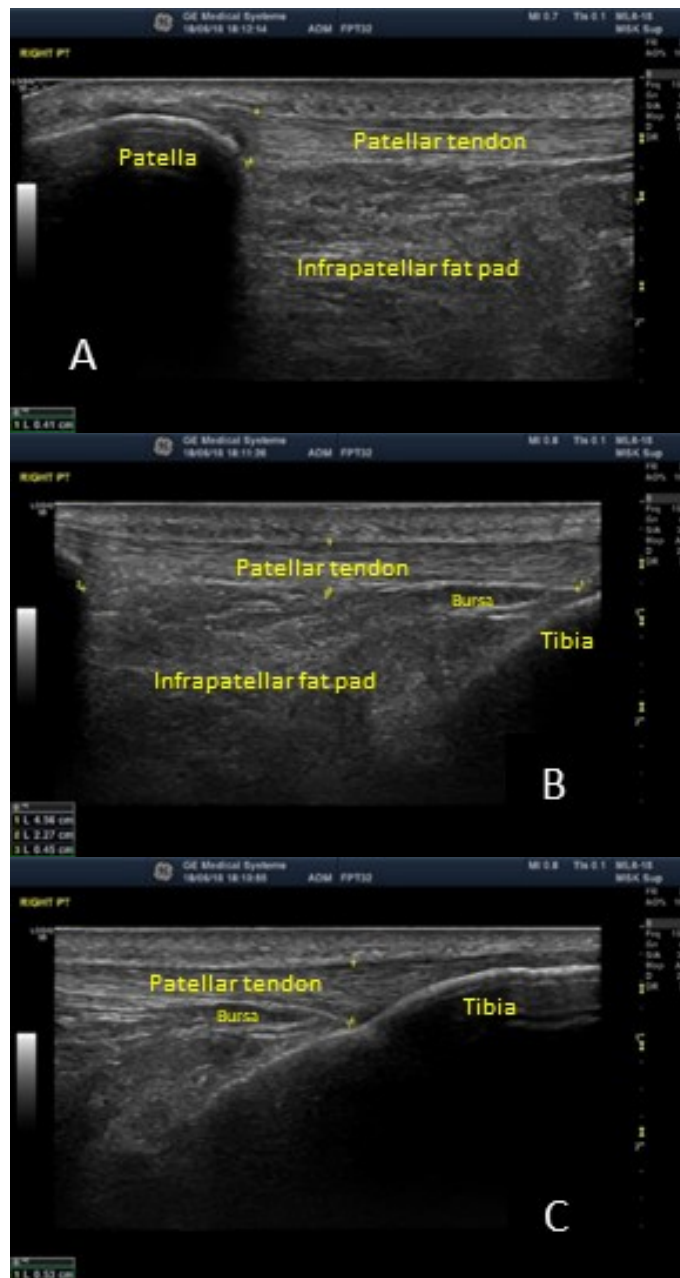
Figure 27: Anterior-posterior thickness for A) proximal B) middle C) distal parts of the patellar tendon in longitudinal section

95
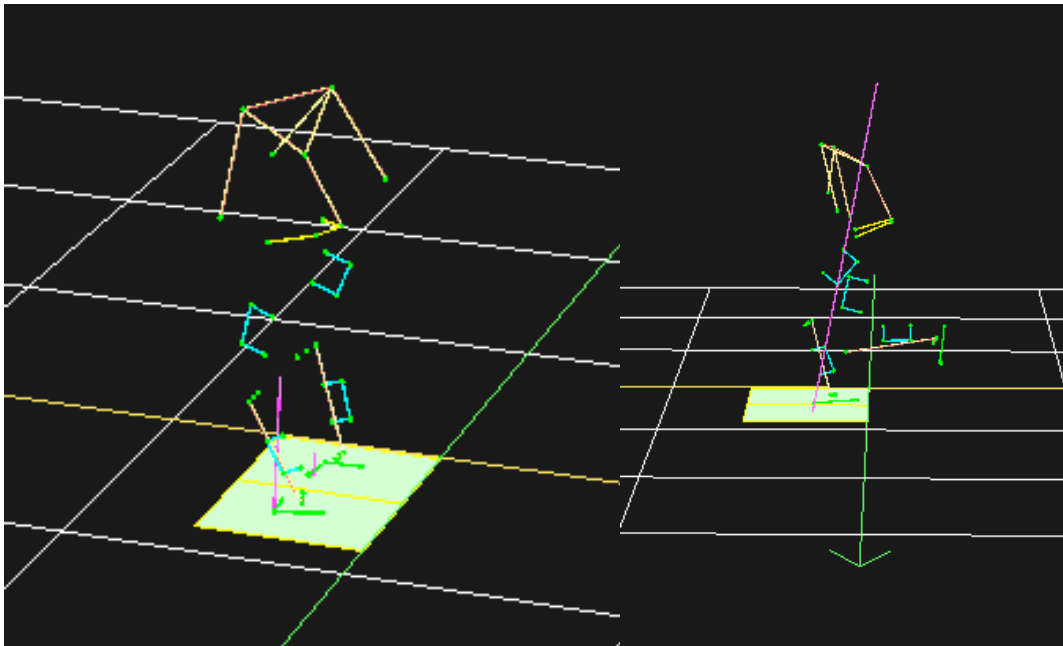
Figure 28: Kinetics, kinematics, and stick figure configuration of the body. Basic foot (heel, first and fifth metatarsal), shank, thigh, pelvis (anterior and posterior superior iliac spine), trunk (xiphoid and T8 vertebrae), and arm (acromion and lateral epicondyle) markers were used.

5.2.3.3 Biomechanical measures

Biomechanical testing was performed using an active infra-red motion capture system (CX-1, Codamotion, Charnwood Dynamics Limited, Leicestershire, UK) and two embedded force plates (Kistler Type 9281CA, Kistler Corporation, Switzerland). ISB guidelines (227) and the CAST protocol (228) determined marker placement (Figure 28). Only kinetic analyses focusing on peak vertical ground reaction force (vGRF), time to peak vGRF and rate of force development (RFD) were extracted (Figure 29).

5.2.4 Validity and reliability

Questionnaire validity was assessed by comparing non-assisted versus assisted survey administration, while clinical and US examination measures were compared to published values. Kinetic analysis informed GLC movement progression validity evaluation. Reliability was assessed by repeated measures (Figure 26) for questionnaire and biomechanical tests.

5.2.5 Feasibility

Survey, clinical, US and biomechanical assessment feasibility was evaluated with participant feedback on content, percentage completion, time burden and recruitment analysis.

Specifically, we tested whether we can measure acute: chronic workload ratio (ACWR), as it may be a recovery predictor, being associated with onset (79,127,137), but has never been investigated for

PT outcome prediction. Therefore, training load duration, intensity (rating of perceived exertion (150)), and jump number were retrospectively collected for a 6-week period. Participant recall duration was the key outcome to see how long athletes could recall their training related information for.
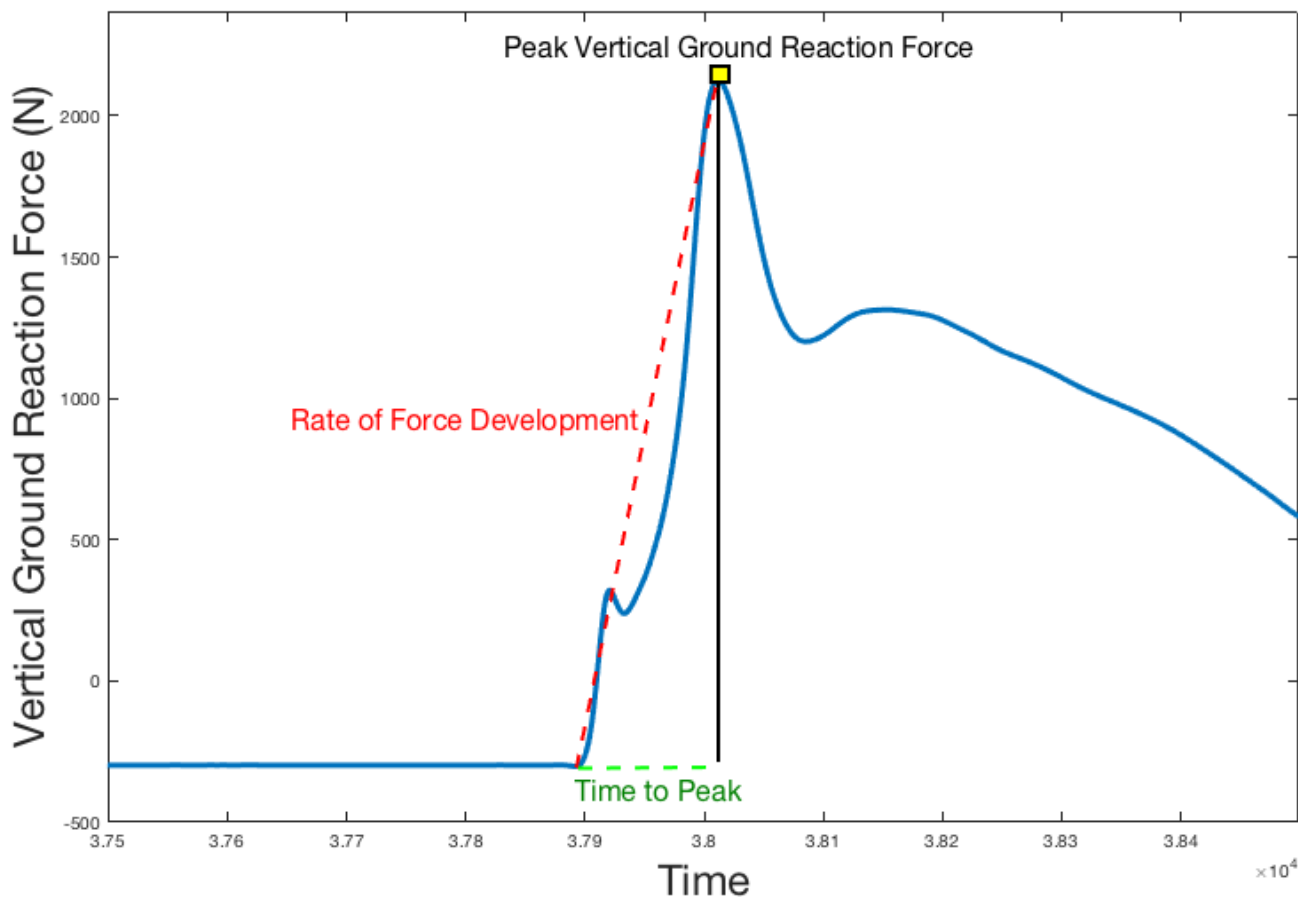
Figure 29: Parameters of the kinetic analysis

5.2.6 Sample size

Sample size was calculated using G*Power (version 3.1) with an expected mean score of 64 points from VISA-P for tendinopathy, 70 for OP, 95 for athletes without PT, and a standard deviation of 19 (1,196,255). A score of 70 was expected for OP as it has been shown VISA-P is often similar in people with PT and OP, and people with OP was slightly higher (196,255). F test (ANOVA: Repeated measures, between factors) were used with a power of 80% and an alpha of 5%, suggesting 21 participants, were needed. Reliability sample size was based on expected ICC values (256) of 0.9 for excellent reliability (245). 14 participants were needed, within the validity calculation parameters.

5.2.7 Data analysis

The data were used from the injured side, or dominant side on controls. If a participant had a bilateral condition, we used the most severe side.

5.2.7.1 Online questionnaire battery

PROMs data were calculated using their usual formulae in original papers or official calculators ((239,242,243,257); http://koos.nu). We devised a risk factor scoring system to analyse MQs which Morton et al. (191) developed (Table 7). Four questions (foot arch height, flexibility of quadriceps, hamstring and ankle) were removed from total score calculation as they were measured by clinical assessment.

5.2.7.2 Clinical and ultrasound assessment

Clinical and US data were electronically transcribed, and methods of collection compared. Single leg hop (SLH) test length was normalized to leg length ((SLH distance/leg length)*100) to obtain a percentage value (247).

Table 7: PT Risk Factor Scoring System to analyse miscellaneous questions together (191). Scores for each miscellaneous question were summed to obtain a total score which is 13.

Miscellaneous Questions	Score
Weight	1 if calculated Body Mass Index > 25
Sex	1 if male
Main sport	1 if basketball or volleyball was defined as main sport
Hours of training	1 if 5-10 hours a week training or 2 if > 10 hours a week training
High cholesterol/familial hypercholesterolemia	1 if raised cholesterol selected as a health condition
Family history of rheumatoid arthritis/ psoriasis/ ankylosing spondylitis	Maximum of 1 if rheumatoid arthritis, ankylosing spondylitis or psoriasis selected or yes selected to a family history of any of these conditions
Diabetes diagnosis	1 if diabetes selected as a health condition
Use of statins	1 if yes – currently taken selected
Menopausal status of women	1 if peri-menopausal or post-menopausal selected
Smoking	1 if yes – active smoker selected
Family history of tendon disorders	1 if yes selected to family history of tendon problems and 2 if participant currently has other tendon problems in addition to PT or 1 if participant previously has had other tendon problems

5.2.7.3 Biomechanical measures

Data were analysed using MATLAB (version R_2018a 9.4.0, MathWorks). The raw vGRF data were filtered by using a fourth-order zerophase-shift Butterworth digital low-pass filter (fc=50Hz) and normalised to body weight.

5.2.8 Statistical analysis

Validity of the survey administration methods were analysed with Cohen's d effect sizes with 0.2, 0.5, and 0.8 considered small, medium, and large, respectively (258). Additionally, limits of agreement with Bland and Altman plots (259) and modality (questionnaire administration) order effect were analysed with t-tests. One-way ANOVA with post hoc Tukey tests were used to assess differences between groups for demographics, clinical and US examinations. Reliability was analysed using the Intraclass Correlation Coefficient (ICC, two-way random, absolute agreement), classified as <0.5, 0.5 to 0.75, 0.75 to 0.9, and >0.90 being poor, moderate, good, and excellent, respectively (245). Statistical analysis was conducted by using SPSS (version 24.0, IBM, NY, USA) and Excel (version 16.22, Microsoft).

5.3 Results

5.3.1 Demographics

67 responses were collected between 20th March and 10th July 2018. 13 responses were excluded due to missing data giving a completion rate of 81%. 19 male and 17 female jumping athletes were recruited, half completed the questionnaire battery twice which makes 54 completed responses in total. Demographics and VISA-P scores were shown in Table 8. Volleyball was the main sport for athletes with PT and OP (Table 8). Post hoc Tukey tests showed VISA-P scores and height differed between condition groups and healthy controls.

Table 8: Mean ± SD values for the participants' descriptive features. P-values for differences in means between groups calculated using One-Way ANOVA or Kruskal Wallis tests based on normal distributions. Chi-square was used for categorical variables. * p < 0.05 compared to healthy controls, † p < 0.05 compared to OP. Keys: n, number of participants; VISA-P, Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon.

Demographics	Patellar Tendinopathy (n=12)	Other knee problems (n=12)	Healthy controls (n=12)
Male: Female	9: 3	5: 7	5: 7
Recreational: Professional	4: 8	6: 6	8: 4
Age (years)	28.7±7.9	29.7±7.1	25.6±4.0
Sporting Age (years)	14.3±6.6	15.4±6.9	8.8±8.4
Body Mass (kg)	82.0±18.0	76.2±22.9	64.9±8.7
Height (cm)	*186.7±15.7	*180.4±17.1	171.6±7.8
Body Mass Index (kg/m^2)	23.3±2.4	23.0±4.8	22.0±2.1
Weekly hours trained	11.7±9.7	11.8±7.8	8.2±7.1
VISA-P score	*65.8±21.3	*71.9±26.4	96.5±4.5
Sports disciplines			
Volleyball	7	5	1
Basketball	3	2	1
Fitness	1	2	3
Running	-	-	3
Others (single n)	Hockey	Rugby Dancing Tennis	Football Wing Tsun Kayaking Cricket

5.3.2 Validity

5.3.2.1 Online questionnaire battery

Limits of agreements were shown for PROMs and MQs in Table 9 and Figure 30. There was no systematic difference between assisted and non-assisted methods for PROMs and MQs (range of d=-0.32 to 0.26), without any order effect (all p>0.05) except KOOS-PF (p=0.02) (Figure 31). 9 athletes with PT clearly identified the inferior patellar pole in the pain map, and pain was spreading around the patella in 69%.

5.3.2.2 Clinical and ultrasound assessment

Clinical and US assessments were shown in Table 9. According to post hoc Tukey test, single leg hop test percentage values were significantly greater in PT group compare with other groups. Thickness for proximal, middle and distal patellar tendon was greater than other groups, but there was a significant difference compare to healthy controls for middle part only. There were significant differences in pain during single leg (SL) squat, double leg (DL) jump SL land and SL jump SL land tasks of the GLC between PT group and healthy controls.

5.3.2.3 Biomechanical measures

Peak vGRF and landing impact rate of force development was presented in Table 9 for the GLC tasks. There were 2 patterns in peak vGRF progression of GLC, an increase in the first 4 tasks and steadiness for the rest of the tasks (Figure 32).

5.3.3 Reliability

5.3.3.1 Online questionnaire battery

Inter-session ICC values were moderate to excellent (range of ICC=0.68-0.93) for the PROMs and MQs shown in Table 9. Pain maps were 94% matched between assisted and non-assisted methods without any order effect.

5.3.3.2 Clinical and ultrasound assessment

Reliability has not been tested for clinical and US imaging examinations.

5.3.3.3 Biomechanical measures

Inter-session reliability was moderate to excellent for peak vGRF, time to peak vGRF and RFD during the GLC jump tasks (Table 9). ICC statistics was not applicable for time to peak vGRF and RFD variables as we did not standardize the time for squat tasks.
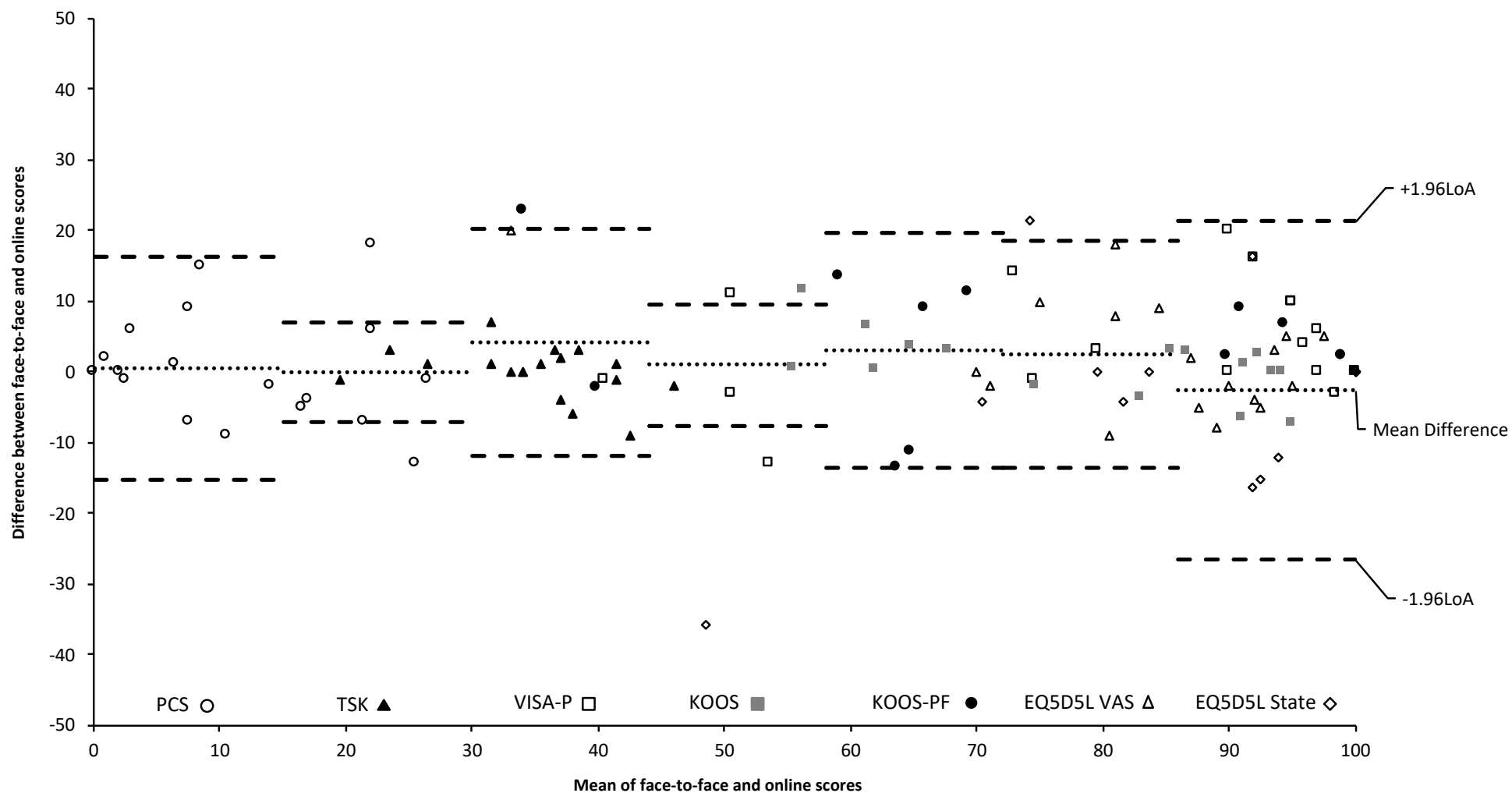
Figure 30: Bland and Altman Plots: No systematic difference between face-to-face (assisted) and online (non-assisted) methods. EQ5D5L State subscale scores were normalized to 100 and also KOOS subscales (pain, symptom, activity daily life, sports & recreational, quality of life) scores were summed and then divided by 5 to obtain a total score to use in this graph. Each PROM was aligned with their mean difference and ±1.96LoA lines. Keys: LoA, Limits of Agreement; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale for Kinesiophobia; VISA-P, Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon; KOOS, Knee injury and Osteoarthritis Outcome Score; KOOS-PF, KOOS Patellofemoral subscale; EQ5D5L, Health-related Quality of Life.
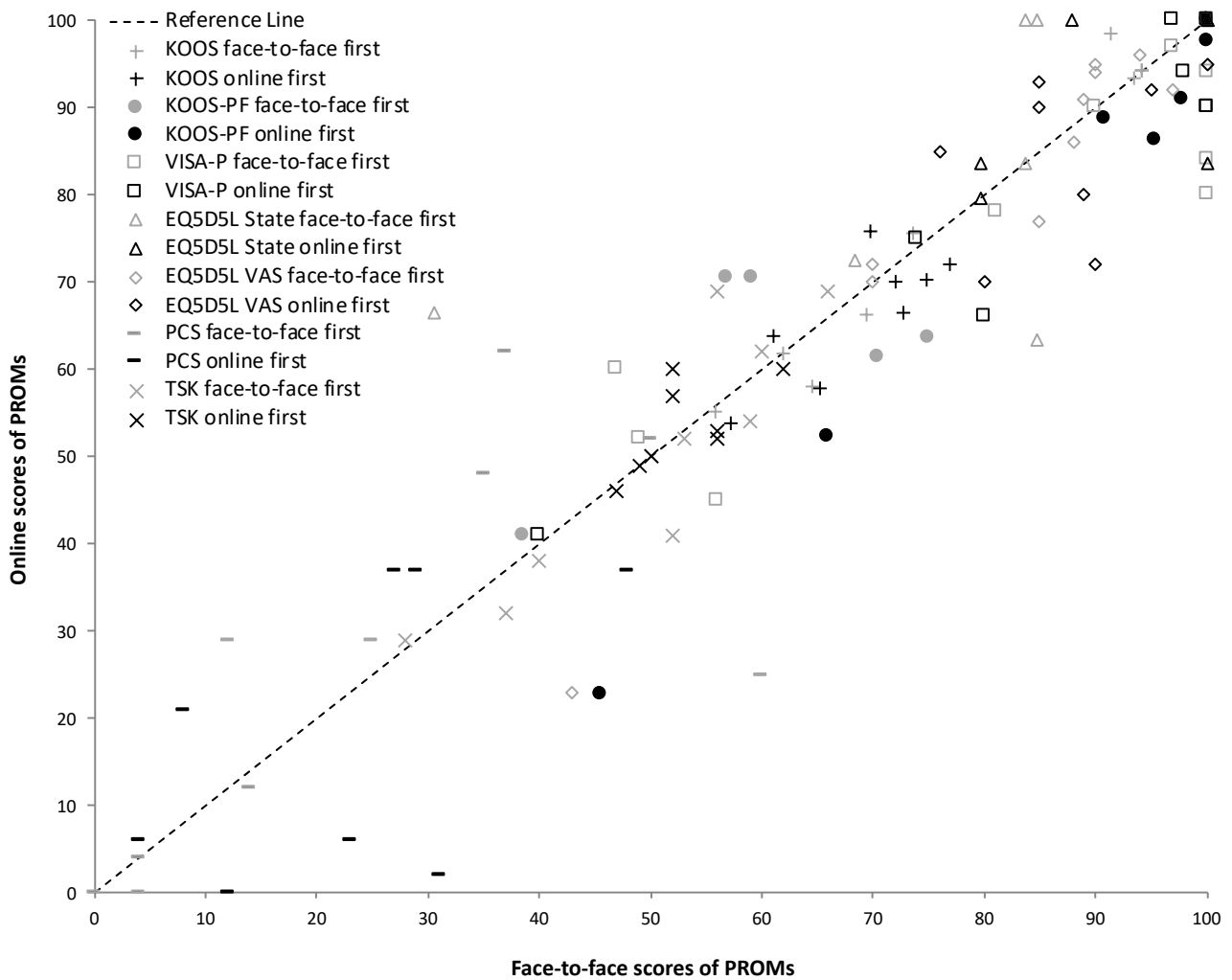
Figure 31: No order effect between assisted and non-assisted methods for PROMs (all p > 0.05) except KOOS-PF subscale (p = 0.02). EQ5D5L State subscale, TSK and PCS scores were normalized to 100 and also KOOS subscales (pain, symptom, activity daily life, sports & recreational, quality of life) scores were summed and then divided by 5 to obtain a total score to use in this graph. Keys: PROMs, patient reported outcome measures; KOOS, Knee injury and Osteoarthritis Outcome Score; KOOS-PF, KOOS Patellofemoral subscale; VISA-P, Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon; EQ5D5L, Health-related Quality of Life; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale for Kinesiophobia.
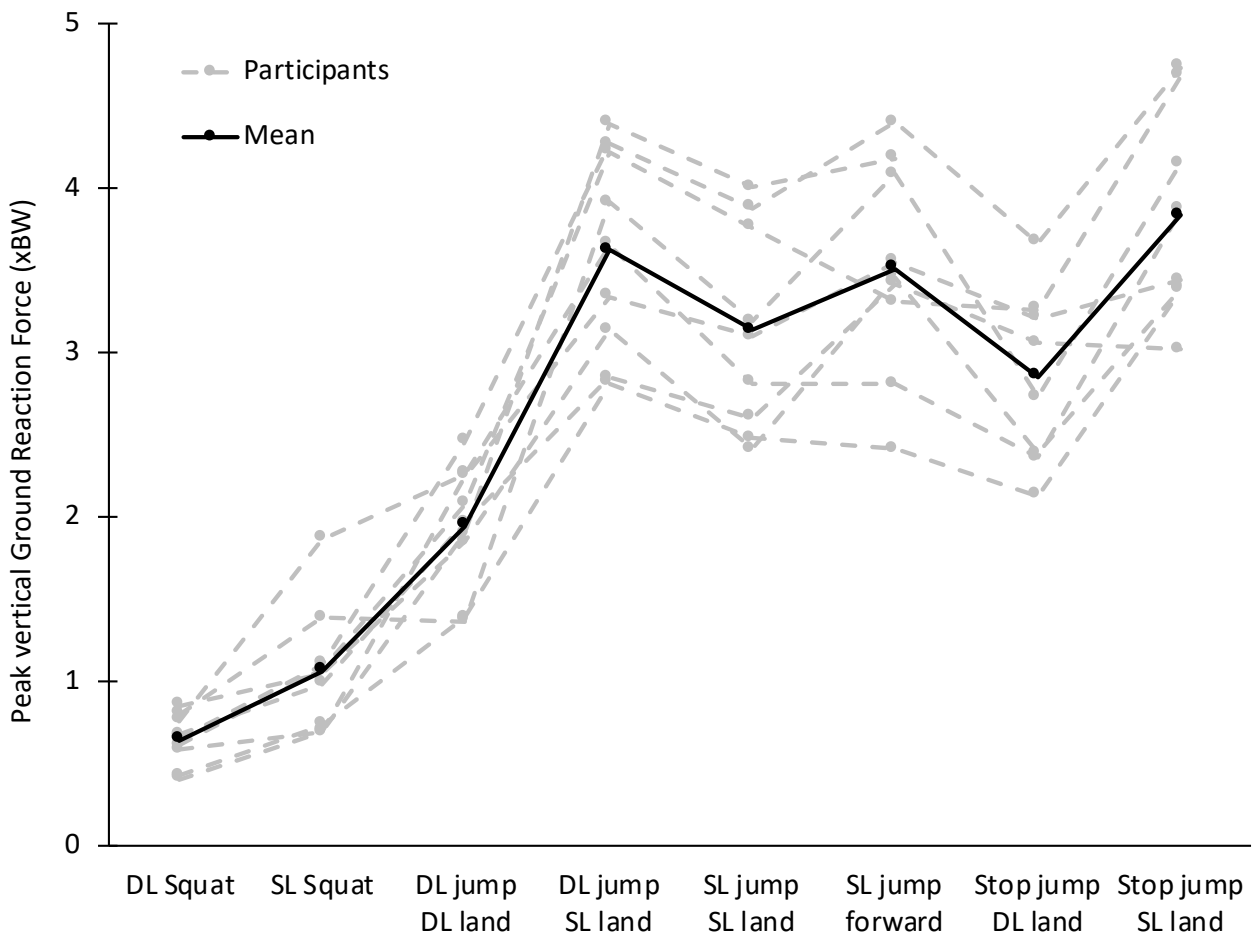
Figure 32: Peak vertical ground reaction force values, normalised to body weight, for each participant and mean values for each task showing the graded loaded challenge movement load progression between tasks. Keys: BW, body weight; DL, double leg; SL, single leg.

*Table 9: All the measures with their contents, purpose, relative results and outcomes were presented at columns in order. For questionnaire analysis, limit of agreement (mean bias ± 1.96*SD) and Cohen's d for effect of modality, p value for modality order effect, and ICC values for reliability were reported. Mean ± SD values for clinical, ultrasound and biomechanical findings were given. P-values for differences in means between groups calculated using One-Way ANOVA or Kruskal Wallis tests based on normal distributions. Keys: n, number of participants; LoA, Limit of agreement; ICC, Intra-class Correlation Coefficients; d, Cohen's d; SD, Standard deviation of mean values; VAS, Visual Analogue Scale; JPTs, jumping athletes with patellar tendinopathy; RoM, range of motion; DF, dorsiflexion; K90, knee 90 degrees flexion; NRS, numerical rating scale; DL, double leg; SL, single leg; max, maximum; AP, anterior-posterior; vGRF, peak vertical ground reaction force; RFD, rate of force development; BW, body weight.*

Measurements	Domain	N	Validity / Reliability / Feasibility	Results	Outcomes
PATIENT REPORTED OUTCOME MEASURES					
Knee injury and Osteoarthritis Outcome Score (KOOS)	Physical factors	18	V	LoA= 0.9±8.6; d=-0.32 to 0.26; p>0.05	Online use valid
			R	*Subscales Moderate to Good (ICC = 0.68 - 0.88)*	*Reliable measure*
			F	**Too long for one page**	**Separate subscale pages**
KOOS Patellofemoral subscale (KOOS-PF)	Physical factors	18	V	LoA= 2.9±16.7; d=0.13; p=0.02	Online use valid
			R	*Excellent (ICC = 0.93)*	*Reliable measure*
			F	**Applicable with KOOS**	**Use with KOOS**
Victorian Institute of Sport Assessment Questionnaire - Patellar Tendon (VISA-P)	Physical factors	18	V	LoA= 4.1±15.9; d=0.2; p=0.98	Online use valid
			R	*Excellent (ICC = 0.91)*	*Reliable measure*
			F	**Presentation improvement needed**	**Alter page view**
Pain Catastrophizing Scale (PCS)	Psychosocial factors	18	V	LoA= 0.4±15.8; d=0.05; p=0.33	Online use valid
			R	*Moderate (ICC = 0.68)*	*Reliable measure*
			F	**Different response types needed**	**Alter response mode**
Tampa Scale for Kinesiophobia (TSK)	Psychosocial factors	18	V	LoA= -0.1±7.1; d=0.01; p=0.85	Online use valid
			R	*Good (ICC = 0.87)*	*Reliable measure*
			F	**Different response types needed**	**Alter response mode**
Health-related Quality of Life (EQ5D5L)	Quality of Life	18	V	State: LoA = -2.8±23.9; d=-0.18; p=0.6	Online use valid overall
			V	VAS: LoA = 2.4±16.1; d=0.16; p=0.6	
			R	*State: Moderate (ICC = 0.69)*	*Reliable measure overall*
			R	*VAS: Good (ICC = 0.86)*	
			F	**VAS: Different response types needed**	**Alter response mode**
Miscellaneous Questions	Related factors (PT risk factor scoring)	18	V	LoA= 0.17±1.39; d=0.11; p=0.75	Online use valid
			R	*Good (ICC = 0.90)*	*Reliable measure*
			F	**Too time consuming**	**Reduce time**
	Pain grid	36	V	9 JPTs identified the inferior patellar pole.	Online use valid
			V	Pain-spreading around the patella in 69%.	
			R	*94% matching between administration method*	*Reliable measure*
			F	**Difficult to use**	**Use professional software designed specifically to map painful body regions**
	Training diary	36	**F**	**Almost 50% recall by week 3**	**Online use feasible**
			F	**Taking time was the feedback on daily version**	**Use weekly version**
			F	**Too time consuming**	**Reduce time**

CLINICAL EXAMINATION

Measurements	Domain	N	Validity/Reliability/Feasibility	Patellar Tendinopathy	Other knee problems	Healthy controls	Outcomes
Anthropometric measurements	Hamstring RoM (°)	18	V	63.7±20.0	63.3±10.9	74.8±14.8	Overall: Valid measures, need categorization and reduction (e.g. functional tests were excluded to avoid repetition with GLC)
	Navicular drop (cm)		V	1.07±0.46	0.83±0.26	0.78±0.37	
	Ankle DF RoM (°)		V	35±8	37.0±9.5	34.8±9.1	
Strength (Oxford Scale /5)	Hip flexors		V	4.6±0.7	3.8±0.3	4.3±0.6	
	Hip extensors in K90		V	4.5±0.6	4.3±0.5	4.5±0.6	
Functional tests	Single leg squat (°)		V	60.3±27.8	60.5±17.9	80±16.7	
	Single leg hop (%)		V	†*158±20	96±24	114±27	
Graded Loaded Challenge (GLC)	Pain (NRS /10)		V				Need further analysis
	DL squat	18		0.7±0.8	1.3±3.3	0±0	
	SL squat	18		*2±2.1	2±3.6	0±0	
	DL jump DL land	16		ª0.4±0.6	ª0±0	0±0	
	DL jump SL land	16		*1.2±1.3	0±0	0±0	
	SL jump SL land	16		*1.2±0.8	0.4±0.9	0±0	
	SL jump forward	16		0.6±0.9	0±0	0±0	
	Stop jump (DL land)	16		0±0	0±0	0±0	
	Stop jump (SL land)	16		1.6±2.3	0.6±1.3	0±0	
		18	**F**	**50 minutes**			**Reduce time**

(* p < 0.05 compared to healthy controls, † p < 0.05 compared to other knee problems, a = GLC was stopped for participants with pain >5)

ULTRASOUND ASSESSMENT

Measurements	Domain	N	Validity	Patellar Tendinopathy	Other knee problems	Healthy controls	Outcomes
Thickness in Longitudinal Section	Patellar tendon	18	V				Overall: Valid measures, need reduction (e.g. one
	Proximal (mm)			4.37±1.7	3.62±0.8	3.32±1.0	

			vGRF (x BW) / vGRF	Time to vGRF	RFD (BW.s⁻¹) / RFD	
Middle (mm)			*3.95±0.6	3.43±0.4	2.98±0.5	thickness measurement
Distal (mm)			4.98±1.1	4.17±0.8	3.83±0.6	instead prox, mid and dist
Quadriceps Tendon		V				
Max AP (mm)			6.03±1.8	4.27±1.1	4.17±0.7	
	18	F	25 minutes			Reduce time

(* $p < 0.05$ compared to healthy controls, † $p < 0.05$ compared to other knee problems)

BIOMECHANICAL ASSESSMENT

Graded loaded challenge	Functional test		vGRF (x BW)	Time to vGRF	RFD (BW.s⁻¹)	
	DL squat	9	V	0.65 ± 0.16		NA	Valid measure overall
	SL squat	9		1.07 ± 0.38		NA	
	DL jump DL land	9		1.95 ± 0.38		24.20 ± 7.53	
	DL jump SL land	9		3.63 ± 0.62		47.86 ± 13.72	
	SL jump SL land	9		3.14 ± 0.62		38.44 ± 15.42	
	SL jump forward	9		3.52 ± 0.64		107.00 ± 31.64	
	Stop jump (DL land)	8		2.86 ± 0.53		74.81 ± 29.62	
	Stop jump (SL land)	8		3.84 ± 0.64		71.33 ± 26.37	
				vGRF	Time to vGRF	RFD	
	DL squat	9	R	ICC= 0.63	NA	NA	*Reliable measure overall*
	SL squat	9		ICC= 0.87	NA	NA	*(Moderate to Excellent)*
	DL jump DL land	8		ICC= 0.84	ICC= 0.80	ICC= 0.79	
	DL jump SL land	8		ICC= 0.97	ICC= 0.82	ICC= 0.94	
	SL jump SL land	8		ICC= 0.97	ICC= 0.90	ICC= 0.94	
	SL jump forward	8		ICC= 0.97	ICC= 0.93	ICC= 0.97	
	Stop jump (DL land)	7		ICC= 0.95	ICC= 0.78	ICC= 0.79	
	Stop jump (SL land)	7		ICC= 0.98	ICC= 0.77	ICC= 0.89	
		9	F	90 minutes			**Need helper, and need reduction in number of tasks and repetitions to reduce time**

5.3.4   Feasibility

5.3.4.1   Online questionnaire battery

Total survey completion rate was 81%, the most common reason for cessation being survey length, median 45 minutes. There were two patterns for retrospective training load monitoring (Figure 33). Training load recall percentage decreased until week-3 with only the 20% maintaining a training diary completing the full 6 weeks. Both assisted and non-assisted methods presented similar patterns.

5.3.4.2   Clinical and ultrasound assessment

Measurement time of clinical and ultrasound scanning was 50 and 25 minutes, respectively.

5.3.4.3   Biomechanical measures

Measurement time of biomechanics was 90 minutes in total for participants' preparation and GLC procedure applying. Recording tasks took around 45 minutes as GLC consisted of 10 repetitions for each task.
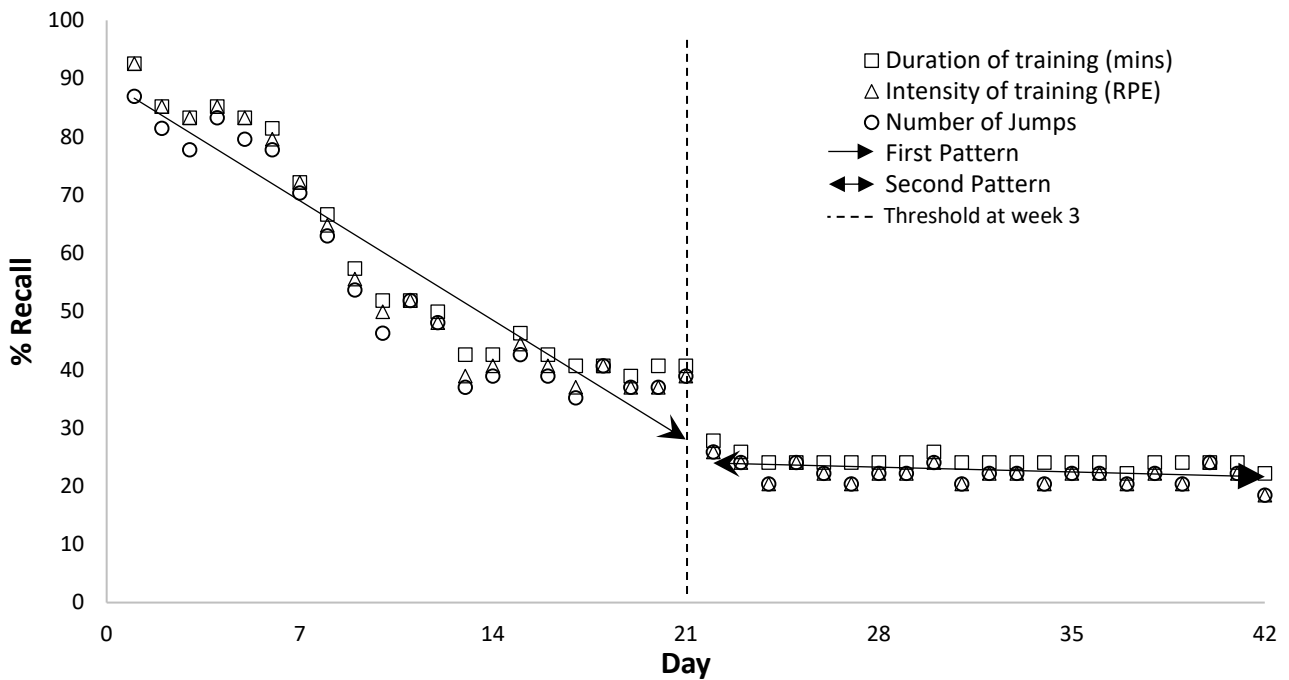
Figure 33: Recall rate for online daily retrospective training load monitoring. Keys: mins, minutes; RPE, rating of perceived exertion.

5.4 Discussion

This study was designed to test validity, reliability and feasibility of the methodology for a large international prospective cohort study, represents the first to test the online use of most of these questionnaires and showed them to be valid, reliable, and feasible for remote use. Recruitment lessons, participants' feedback and time burden analysis provided important information on how to improve feasibility. It is important to collect valid and reliable data remotely in large population based epidemiological studies to decrease the burden and cost of data collection.

5.4.1 Validity

Online use of PROMs provides advantages such as easier participant access, lower cost, faster completion and efficient data management (260). Gwaltney et al. (236) reported good or excellent equivalence between electronic and paper administrations for over 200 PROMs. Similarly, we found online use of PROMs to yield equivalent results to traditional administration. Gudbergsen et al. (261) reported that paper-based and computerized versions of KOOS were comparable with regard to psychometrics thus supporting our findings, although we found an order effect for KOOS-PF. There was no identified pattern when checking the responses for each item. Of note is that the KOOS-PF was the final questionnaire in the test battery, so participants may have rushed in order to finish. VISA-P scores between study groups correlated with the literature (196,255) as there were significant difference between condition groups and healthy athletes and no differences between

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PT and OP groups. Parker et al. (262) reported the minimum clinically important difference threshold ranged from 0.14 to 0.24 for the EQ5D which matched our results. We also tested the miscellaneous question validity and found no systematic differences or order effects. Overall, the questionnaire battery and pain map should provide useful data.

The clinical and ultrasound examination showed some expected trends and between group differences. Hamstring flexibility was lower in PT and OP compared to healthy athletes, which is a known risk factor for patellar tendinopathy (74,78,79). We tested single leg hop test as jump performance is related to PT (75), and found that PT group had higher performance. Hip strength was measured as there is no data on the relation to PT recovery, but it is often clinically addressed with no between group differences but flexor weakness being observed in OP group. Thickness of both patellar and quadriceps tendons was greater in PT group, with patellar mid-tendon thickness significantly so. We found trends towards lower foot arch (79,83), reduced ankle dorsiflexion range (83,93,94) and decrease in single leg squat range (29) similar to previous work. The feasibility study was not powered to reveal definitive differences, but the findings suggest the clinical and ultrasound examinations should yield useful predictive findings.

We expected an increase in total lower limb load progression based on peak vGRF through the GLC tasks. However, there were two patterns in our task order, an increase in the first 4 tasks and steadiness for the rest. Unexpectedly, RFD progression was higher during DL jump-SL land when compared to SL jump-SL land, likely due to higher jumping height. We found similar peak vGRF or RFD results with literature for the selected tasks (188,263). Therefore, GLC may well represent a valid clinical measurement but less manoeuvres are needed and further testing in the main study will confirm its utility or otherwise.

5.4.2   Reliability

The questionnaires were reliable measurements for an online based survey. Alviar et al. (264) reported ICC range in patients with knee injuries for each KOOS subscale. Our ICC values were in the reported range except Symptoms and Activity Daily Life subscales which were lower than the reported range. KOOS-PF reliability was excellent and higher compare to its development study (238). ICC for VISA-P was excellent and in the reported range (0.74-0.99) (196,239,255,265,266). We found moderate or good reliability for EQ5D5L (267), PCS (268–270), TSK (269,271) and MQs (191) similar to the previous literature. Additionally, our biomechanical results showed that GLC is a

reliable measurement for clinical use as inter-session reliability ranged from moderate to excellent and was in the reported ranges (272).

5.4.3   Feasibility

Survey completion rate was acceptable with 80% as 20% is an expected dropout rate for observational studies (273). Time was one of the biggest problems for each step. Reduction in time was found to be required to improve feasibility and reduce the participants' burden. The training load diary was too time consuming as participants had to enter retrospective daily data for 6 weeks. Therefore, using a shorter recall duration and asking participants to keep diary to improve data quality and to reduce time burden were identified solutions. Additionally, improving inter-question logic and reducing repetitive miscellaneous questions were implemented to decrease the time burden.

The main methodological amendments were to the protocol and hosting technology, in addition to the changes already described. The study protocol was trimmed in line with the feasibility findings to reduce the time burden and to improve data quality. Two high quality data collection tools were employed to collect the data (Smart Trial) and pain maps (Navigate Pain). Navigate Pain provides a digital pain map including all aspects of the knee with whole body chart and bone landmarks, plus sex, severity and pain type options. Features of the new pain map will help to reduce the time burden as pain related miscellaneous questions (such as location, type of pain, severity) will be removed from the questionnaire. We decided to use categorical outcomes for clinical and US assessments because potential variables which could go into the causal model will be categorised. For instance, hamstring muscle flexibility will be categorised as normal or tight instead of measuring range of motion. Categorization will also be useful to make the recording faster. Functional tests, SL squat and hop test, were removed to avoid repetition with GLC. GLC will also be shortened according to biomechanical results and recruitment lessons to increase the clinical applicability and to ease biomechanical measurements burden. GLC for the future cohort consisted of 6 tasks instead of 8. Repetition for each task was decreased from 10 to 5. However, number of markers were increased to improve visibility, hence the quality of data.

5.4.4   Limitations

One of the difficulties with remote data collection is that training load validity and reliability could not be fully established, there being no direct measurement to compare with. Another difficulty was

that diagnosis was established by self-report of prior consultation with a medical professional, in response to questions in our online survey so could not be verified by physical examination. Reliability was not performed for clinical and US imaging examinations however established procedures were applied by an experienced clinician (AT). The main limitation was that the follow-up process for the online surveys could not be tested and the issue of retention could not be addressed, requiring within-study development due to timelines.

5.5 Conclusion

The cohort study plan is feasible with the online questionnaire battery performing equivalently to traditional administration. The tested questionnaires were valid and reliable for online use, which is therefore suitable for clinical and research purposes. To improve feasibility, we need a shorter survey to reduce questionnaire burden, and collecting training load measures more regularly to facilitate recall. The biomechanical measures were valid and reliable, and a graded loaded challenge, suitable for further testing, has been defined.

6 Self-reported bio-psycho-social factors partially distinguish patellar tendinopathy from other knee problems and explain patellar tendinopathy severity in jumping athletes: A case-control study

In the feasibility study chapter, I concluded that the cohort study plan is feasible. In this chapter, I specifically focused on how jumping athletes with PT (JPTs) present and differ from athletes with other knee problems. We also lack a clear understanding of why some athletes present with worse severity than others. I aimed to improve our understanding of JPTs by determining what combinations of self-reported factors distinguish PT from other knee problems, and explain the variance of PT severity. Therefore, the findings from the baseline surveys of the cohort study are presented in this chapter as a case-control study.

Preliminary results of this case-control study were presented online at the 2020 LASEM Sports Medicine Student Showcase, La Trobe University, Australia and the 2021 Virtual Physiotherapy Conference, Chartered Society of Physiotherapy, UK. This study was submitted to the American Journal of Sports Medicine (Impact Factor=6.202) for publication and currently is under review.

6.1   Introduction

PT presence has been shown to be associated with self-reported variables such as sex, hours of training, hamstring flexibility, previous knee injury, current or previous back pain, family history, and age (79). There are also factors associated with both PT and other knee problems (e.g. patellofemoral pain, anterior cruciate ligament injury or osteoarthritis) such as quadriceps strength (74,230), playing surface (66,231), age (78,79,274), sex (78,79,274,275) or body mass index (83,85,232,275). The commonality of these associations means that we do not know which factors are specifically associated with PT presence. Recent research has focussed on physical examination and imaging, with the absence of statistical models (78) considering combinations of various risk factors potentially obscuring understanding of how jumping athletes with PT (JPTs) present, progress and differ from athletes with other knee problems. This lack of tendinopathy specific information limits the understanding of PT presence and therefore management.

In addition to the specificity of PT from other knee problems, we also lack a clear understanding of why some athletes present with worse severity than others. Morton et al (79) reported some associated variables (i.e. sex, previous knee injury, family history) with PT presence, but found no association between these variables and PT severity. PT symptoms such as pain or functional

limitation generally occur insidiously, and athletes often continue to play through symptoms (58). Additionally, there is a mismatch between tendon abnormalities seen on imaging and symptoms, although the presence of abnormalities is a risk for symptom development (276). This limited understanding is likely to partly explain poor treatment outcomes. Therefore, investigating the factors that explain the variance of PT severity would be helpful to understand the condition better, and inform efforts to improve treatment.

The primary aim of this study was to improve our understanding of JPTs by determining what combination of self-reported factors distinguishes JPTs from athletes with other knee problems. In other words, we were primarily looking for factors that are specific to PT presence, rather than differentiating PT diagnosis from other knee problems. We aimed to build exploratory models from the baseline data of a large international cohort of jumping athletes, considering training load descriptors and a range of biopsychosocial factors. The secondary aim was to investigate the variance of PT severity. Successfully accomplishing the study aims should lead to a better understanding and management of JPTs. The alternative hypothesis was that multivariable statistical regression models distinguish PT from other knee problems and explain both the variance of condition severity and compromised participation in jumping athletes.

6.2   Materials and methods

The STROBE statement (277), Strengthening the Reporting of Observational Studies in Epidemiology, guided the design and reporting of this case-control study (Appendix 13).

6.2.1   Participants

This study was approved by Queen Mary Ethics of Research Committee (QMERC2018/92), the UK National Health Service (NHS) (264615) and University of Liège Hospital-Faculty Ethics Committee (2019/182). Please see the Appendix 11 for all approval letters. A previously validated, reliable online questionnaire battery (278) yielded data from an international sample of jumping athletes recruited via social media, private practice, sporting teams and the NHS through a large network of collaborators. Eligibility was checked after consent (Appendix 12) had been granted, with the inclusion criteria being: aged 18 and over; performing any jump-related sport with a minimum of an hour of training once per week; having a clinical diagnosis of PT or another musculoskeletal condition affecting the knee from a clinician in the last 6 months. The exclusion criterion was having any neurological disorders.

There were two main recruitment strategies (Figure 34). Firstly, we advertised the study via flyers (Appendix 9) in social media. When we received the eligibility survey answers we enrolled participants into the relevant study groups according to inclusion/exclusion criteria. After this point, everything was automated via SmartTrial such as receiving survey link via email and text message. Secondly, collaborators directly recruited participants from their practice, sporting teams or NHS and enrolled them. Additionally, we targeted snowball recruitment with automated emails via SmartTrial. If participants consented to take part in the study, we recorded them as recruited, and calculated retention rates after consent had been granted.
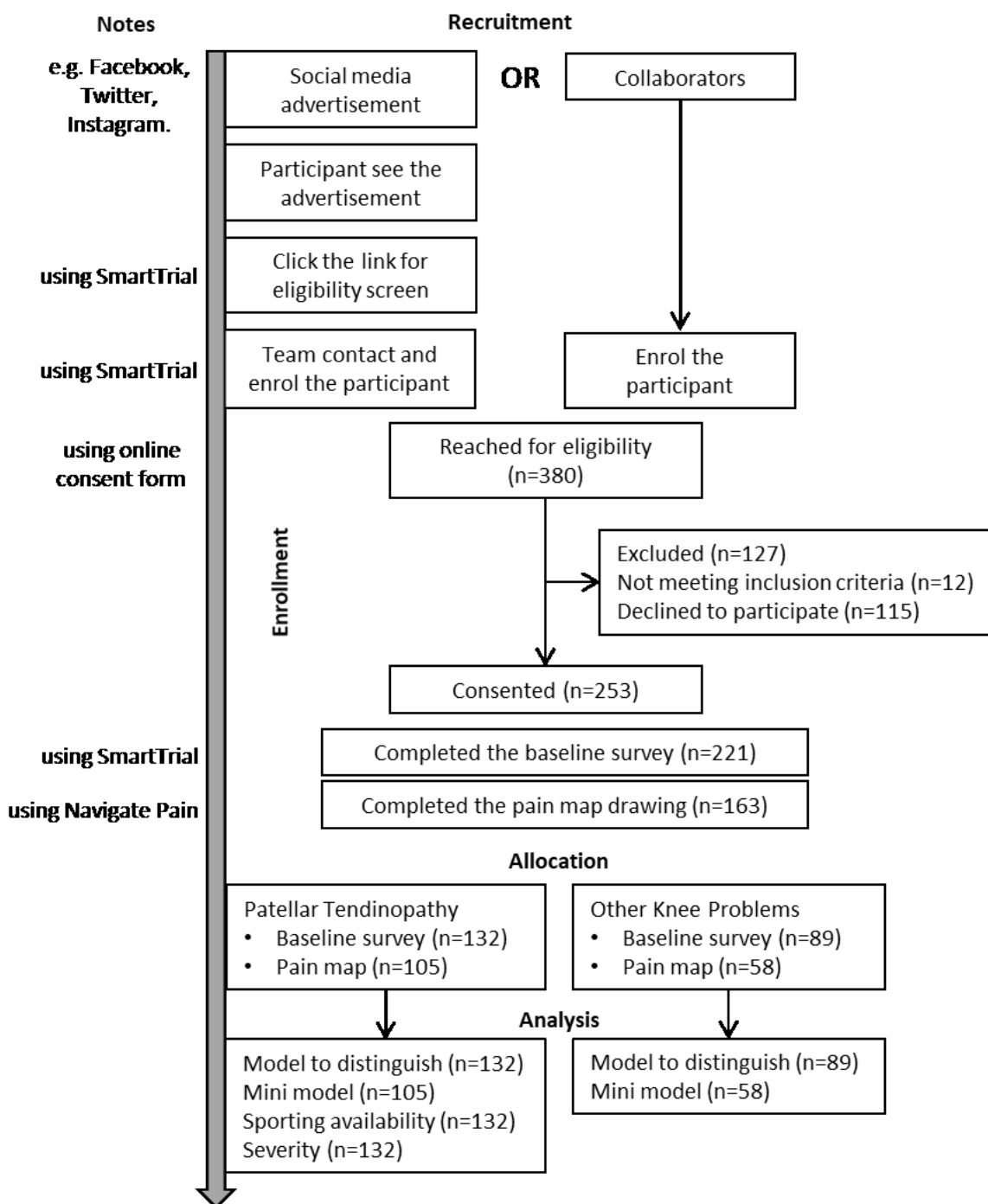
Figure 34: A typical participant journey showing the screening and enrolment process.

6.2.2 Online questionnaire battery

The composite battery included 10 patient-reported outcome measures (PROMs) and miscellaneous questions concerning demographics, condition related details, treatments and training load in the previous 3 weeks (278). Participant completed the online questionnaire battery by using SmartTrial (version 4.0, MEDEI ApS, Aalborg, Denmark). Additionally, we collected pain related details such as location, pain type and severity with digital online self-reported pain map drawings by using Navigate Pain (Aalborg University, Version 1). Questionnaires were carefully translated to Turkish, Spanish and French to optimise recruitment. If PROMs have already been translated into targeted languages, their existing versions were used as described in the section 4.1.5. For the survey, please see the documents here:

https://www.dropbox.com/sh/hd7152qgun781gi/AADNF5zgMVzzrsqZ-wvZ8sEPa?dl=0

The Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon (VISA-P) (239) and the Knee injury and Osteoarthritis Outcome Score (KOOS) (237) with Patellofemoral subscale (KOOS-PF) (238) were used to measure knee-specific condition severity. For the global knee assessment, Patient Acceptable Symptom State (PASS) (279), a single-item binary (yes/no) question, was used to define the global satisfaction over time, while the Single Assessment Numeric Evaluation (SANE) (280) rating scale was used for the degree of normal. Psychosocial factors are associated with rehabilitation outcomes (241) while kinesiophobia (Tampa Scale for Kinesiophobia-11 (TSK-11)) (281) and catastrophisation (Pain Catastrophizing Scale (PCS)) (242) have not been investigated in PT but have in other tendinopathies (244). Health-related Quality of Life (EQ5D5L) (240) was included due to likely chronicity (4). General Self Efficacy Scale (GSE) (282) was used as a cognitive factor that facilitates the recovery as it has been found useful in other knee conditions such as anterior cruciate ligament injuries (283) or osteoarthritis (284). The eHealth Literacy Scale (eHEALS) (285) was used as a check of online health self-efficacy.

6.2.3 Main outcome measurements

For the primary aim, we considered clinical diagnosis (having PT vs having other knee problems) as the dependent variable for the regression model to be able to determine what combination of self-reported factors distinguishes JPTs from athletes with other knee problems. Therefore, cases were defined as athletes with a clinical diagnosis of PT by a clinician in the last 6 months, while controls were defined as athletes with a clinical diagnosis of another musculoskeletal knee condition but not PT by a clinician in the last 6 months.

For the secondary aim, we used the VISA-P (239) score as the main dependent variable for tendon specific severity. As many athletes continue to train and compete despite injury (58), consensus has identified *'Full availability for training and competition'* as the preferred marker of recovery in athletic populations (45), and so we included this as a second dependent variable to understand the factors associated with the sporting impact of PT.

6.2.4 Variables of interest

We considered over 45 potentially plausible self-reported factors as independent variables in the regression models (Table 1). These were derived from published literature suggesting an association with PT (2,64,67,74,78,79,83,85) or other musculoskeletal problems (65,66,137,230–232,241,244), and categorized under five different subheadings: demographics, sports specific, biomedical, psychological and social.

Number of body regions	Number of sites around the knee (anterior/ posterior/ medial/ lateral) (x/4)	Focal pain on inferior patella pole (no=0 yes=1)	Focal pain on superior patella pole (no=0 yes=1)	Diffuse pain around the patella (no=0 yes=1)	Current pain level (x/10)	Usual pain level (x/10)	Type of pain* (0=pain, 1=dull aching, 2=stabbing, 3=tingling, 4=electric, 5=throbbing, 6=numbness, 7=burning, 8=Other/multiple)
2	1	0	0	1	2.1	2.0	2

Figure 35: An example of processing pain map drawing. *Every colour refers one type of pain (e.g. Green = stabbing) in the software.

6.2.5 Data analysis

We have previously published total score calculations for PROMs (278). We manually converted pain map drawings into binary categorical (i.e. focal pain on inferior patella pole) and continuous (i.e. number of body regions) variables for location (286), and directly exported the data for pain severity and pain type from the software (204) (Figure 35). For training load details, we collected range of duration and number of jumps with categorical miscellaneous questions (feasible (278), validity and reliability have not been tested). Then, we took the mid-point of ranges and treated the training load data as continuous. We also calculated acute:chronic workload ratio (ACWR) with the rolling average method in both minutes and jumps (137). ACWR was categorised as low 0-0.8, optimal 0.8-1.3 and high >1.3 severity as per recommendations (137). Other categories in certain categorical factors were shown in Table 1. Sparsely populated sub-categories that were sufficiently similar were combined prior to analysis (287). For instance, injured side was categorised as unilateral (right or left sides) and bilateral (both sides), while sport type was categorised as court base jumping sports (volleyball, basketball and handball) and other jump related sports (athletics, football, running, dance, fitness etc.).

6.2.6 Statistical analysis

Statistical analysis was conducted using STATA (version 16.0, StataCorp LP, College Station, TX, USA). We commenced with calculation of descriptive statistics to profile each study group, visualised the data and compared groups with independent t-tests or chi square procedures according to data type. Univariate regression was used to analyse associations between each plausible independent variable and having PT (logistic), sporting impact (logistic) or severity (linear).

Independent variables with $p<0.10$ (288) in the univariate regression analysis were retained for multivariable regression using a manual forward approach. The order of forward inclusion of independent variables into multivariable model was from demographic to social factors. Independent variables which improved the model were retained, as determined with the likelihood-ratio test (289) at the 5% significance level (i.e. $p<0.05$). To avoid multicollinearity, correlations between independent variables were tested with Pearson or Cramer's V based on data type and variance inflation factor (VIF) (288,290). If correlation (288) or individual VIF (291) was greater than 0.75 or 10, respectively, for any two independent variables, they were not used together in the model, and the variable with better explanatory power retained.

For the final multivariable logistic model performance, we tested goodness of fit with the Hosmer-Lemeshow test (>0.05), model accuracy with the area under the receiver operating characteristic curve (AUC; >0.7 acceptable, >0.8 excellent) and model sensitivity and specificity (288). For the final multivariable linear model performance, we reported R^2 as a measure of the proportion of explained variance, and checked normality of residuals. We used the odds ratio (logistic) and beta coefficient values (linear) of individual items to interpret the models.

6.3 Results

6.3.1 Participants

We reached 380 international jumping athletes between 5th April 2019 and 16th November 2020. 253 athletes consented to the study and 221 completed the survey giving a completion rate of 87% (Figure 34). 32 responses were excluded from analysis due to missing data. 132 athletes with PT (31.2±8.9 years; 80 males; VISA-P=61.6±16.0) and 89 athletes with other knee problems (32.1±9.9 years; 47 males; VISA-P=62.9±21.2) were included. 74% participants (n=163) completed the separate pain map drawing (Figure 34).

Reported ability to use electronic health resources was similar between PT and other knee problem groups according to the eHEALS responses (Table 11). Height, sport type, player level, full availability to training and competitions, some training details and symptoms differed (p<0.05) between groups. There was no difference between groups in any PROMs measuring knee condition severity (VISA-P, KOOS, KOOS-PF), global knee assessment (SANE) and psychosocial factors (TSK-11, PCS, EQ5D5L, GSE), except PASS (p=0.03, V=-0.14).

Localised inferior patella pole pain was more commonly reported by PT group (OR=10.2, 95%CI 4.4-23.6, p<0.001), while pain around the patella was more commonly reported by the other knee problems group (OR=0.28, 95%CI 0.13-0.58, p<0.001). Patellofemoral pain, osteochondral lesions, cruciate ligament, collateral ligament and meniscus injuries were the common diagnoses in the other knee problems group (Table 10). In PT group, 32 athletes had other knee conditions in addition to PT.

Table 10: Diagnosis for other knee problems group (multiple response)

Diagnosis for other knee problems group (n=89)	Right	Left	Total
Patellar tendon partial or full tears	3	0	3
Cruciate ligament injuries (anterior/ posterior)	14	13	27
Collateral ligament injuries (medial/ lateral)	6	9	15
Meniscus injuries (medial/ lateral)	18	21	39
Patellofemoral pain syndrome	14	15	29
Growth plate injuries (Osgood-Schlatter/ Sinding-Larsen-Johansson)	3	1	4
Osteochondral lesions	19	6	25
Osteoarthritis	6	3	9
Other	14	11	25
Iliotibial band syndrome	2	2	4
Quadriceps tendinopathy	1	1	2
Rheumatoid arthritis	1	1	2
Infrapatellar bursitis	1	1	2
Pes Anserinus tendinopathy	1	0	1
Bone oedema	1	0	1
Medial plica syndrome	1	0	1
Fracture around knee	1	0	1
Baker's cyst	0	1	1

6.3.2 Model development

6.3.2.1 Model to distinguish JPTs from those with other knee problems

Univariate logistic regression analysis was performed for each plausible independent variable (Table 12), with twenty-two being retained for model construction. The final model consisted of seven variables (Table 14A); hours trained in the last week (OR=1.10, 95%CI=1.03-1.17, p=0.01), sport type (OR for court base jumping sports=2.31, 95%CI=1.24-4.32, p=0.01), injured side (OR for bilateral=2.28, 95%CI=1.09-4.77, p=0.03), pain onset (OR for gradual=1.97, 95%CI=1.07-3.60, p=0.03), morning pain (OR for yes=1.89, 95%CI=1.01-3.53, p=0.047), PASS (OR for yes=0.39, 95%CI=0.21-0.73, p=0.003) and swelling (OR for yes=0.37, 95%CI=0.18-0.74, p=0.01). Therefore, JPTs tend to train/play more, to play court base jumping sports (volleyball, basketball and handball), to have bilateral injury, to have gradual pain onset, to have morning pain, not to be satisfactory and not to have swelling in comparison to other knee problems. Model fit was good (Hosmer-Lemeshow test=0.33, p<0.001) with acceptable accuracy (AUC=0.76), specificity (70.8%) and sensitivity (70.5%). We also constructed a mini model with pain map drawing data (n=163) to explore whether pain location has any role to distinguish injured groups. The final multivariable model consisted of six variables (Table 14B). Model fit was good (Hosmer-Lemeshow test=0.47, p<0.001) with excellent accuracy (AUC=0.85) and acceptable specificity (77.8%) and sensitivity (76.2%).

6.3.2.2 Model to explain sporting availability in JPTs

Individual relationships between each plausible independent variable and full availability were calculated (Table 13), with twenty-six being retained for multivariable model construction. The final

multivariable model consisted of two variables (Table 14C); KOOS - sports (OR=1.02, 95%CI=1.01-1.04, p=0.01) and player level (OR for professional=4.11, 95%CI=1.90-8.87, p<0.001); meaning better sporting availability in JPTs was associated with a better sports specific function and being professional athlete. Model fit was good (Hosmer-Lemeshow test=0.73, p<0.001) with acceptable accuracy (AUC=0.72), specificity (65.5%) and sensitivity (66.2%).

6.3.2.3   Model to explain severity in JPTs

Individual relationships between each plausible independent variable and VISA-P score were calculated (Table 13), with twenty-eight being retained for multivariable model construction. The final multivariable model consisted of three variables (Table 14D); EQ5D5L index (β coef=0.32, p<0.001), KOOS-sports (β coef=0.38, p<0.001) and age (β coef=-0.17, p=0.02); meaning higher PT severity was associated with a lower quality of life, a worse sports specific function and being older. Overall, multivariable linear regression model was explaining 44% of the variance in PT severity (p<0.001, R^2=0.44, Figure 36).

6.3.2.4   Example of how to use the models

Equations for each model were provided in Table 15. For instance, the severity model equation was used for a 34 years old participant with 0.498 EQ5D5L index score and 30 KOOS-sports score. The severity was high with 46.7 and similar with the actual VISA-P score (34). On the other hand, the severity was low with 71.0 for another 28 years old participant with 0.837 EQ5D5L index score and 80 KOOS-sports score and similar with the actual VISA-P score (79). However, there is an over-estimation at the lower values and an under-estimation at the higher values in the results (Figure 36). This suggests there is potential a/some hidden variable(s) (e.g. clinical and/or biomechanical assessments) that we are not capturing yet.

Table 11: Self-reported baseline participant characteristics. Mean ± SD values for the continuous variables. P-values for differences in means between groups calculated using Independent t-test or Mann-Whitney U test based on normal distributions with Cohen's d effect size. Chi-square was used for categorical variables with Cramer's V effect size. Higher score means worse outcome for PCS and TSK-11, but better outcome for the rest of the PROMs. Keys: n, number of participants; N, no; Y, yes; EN, English; TR, Turkish; SP, Spanish; FR, French; RPE, rating of perceived exertion; ACWR, acute: chronic workload ratio; VISA-P, Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon; KOOS, Knee injury and Osteoarthritis outcome score; EQ5D5L, Health-related Quality of Life; VAS, visual analogue scale; NA, not applicable; DNK, do not know.

VARIABLES	Patellar Tendinopathy (n=132)	Other knee problems (n=89)	Effect sizes
A) DEMOGRAPHICS	* p < 0.05 vs other knee problems		
Age (years)	31.2 ± 8.9	32.1 ± 9.9	d= 0.10
Body Mass (kg)	79.1 ± 14.8	76.3 ± 16.8	d= -0.18
Height (cm)	*182.7 ± 12.9	178.3 ± 11.6	d= -0.35
Sex (Female: Male)	52: 80	42: 47	V= 0.08
Dominance (Right: Left: Not sure)	110: 21: 1	75: 11: 3	V= 0.11
Language (EN: TR: SP: FR)	28: 90: 6: 8	18: 62: 2: 7	V= 0.07
Ethnicity (White: Arab: Asian: Black: Mixed: Others: Prefer not to say)	71: 2: 6: 6: 5: 22: 20	58: 0: 4: 0: 1: 12: 14	V= 0.19
B) SPORTS SPECIFIC			
Sporting Age (years)	13.1 ± 7.3	13.3 ± 8.9	d= 0.02
KOOS - sports subscale score (0-100)	56.2 ± 21.6	58.8 ± 27.1	d= 0.11
Sport Type (Other: Court base Jumping Sports)	*61: 71	57: 32	V= 0.18
Player Level (Amateur: Professional)	*49: 83	52: 37	V= 0.21
Training details (including competition)			
Weekly hours trained	*5.3 ± 6.5	3.3 ± 4.5	d= -0.35
Average hours trained in the last 3 weeks	*5.6 ± 5.8	3.9 ± 4.7	d= -0.31
Weekly number of jumps	327.3 ± 678.1	168.8 ± 471.7	d= -0.26
Average number of jumps in the last 3 weeks	374.7 ± 627.3	229.0 ± 542.5	d= -0.25
Intensity in the last week (RPE)	4.3 ± 3.4	3.6 ± 3.2	d= -0.21
Average intensity in the last 3 weeks (RPE)	4.3 ± 2.8	3.7 ± 2.8	d= -0.22
ACWR minutes (n=185)	0.99 ± 0.64	0.87 ± 0.75	d= -0.17
ACWR jumps (n=187)	0.83 ± 0.79	0.67 ± 0.82	d= -0.19
ACWR minutes (Low: Optimal: High) (n=185)	32: 54: 25	27: 36: 11	V= 0.11
ACWR jumps (Low: Optimal: High) (n=187)	51: 36: 24	42: 23: 11	V= 0.11
Playing surface (multiple response)			
Artificial grass (N: Y)	*115: 17	66: 23	V= -0.17
Natural grass: Tartan: Polished hardwood or marple: Multi-purpose plastic: Taraflex: Sand: Concrete: Asphalt: Others (Yes)	25: 9: 53: 16: 40: 5: 19: 13: 12	19: 10: 28: 8: 19: 4: 13: 14: 13	V$_{range}$= -0.09 to 0.10
Shoes (multiple response)			
Basketball sneakers (N: Y)	*83: 49	70: 19	V= 0.17
Cross-trainer shoes (N: Y)	*125: 7	77: 12	V= -0.14
Volleyball shoes: Soccer cleats: Running shoes: Walking shoes: Tennis shoes: Hiking boots: Cycling shoes: Minimalist/Lacrosse shoes: Others (Yes)	37: 22: 48: 9: 4: 2: 3: 0: 9	15: 18: 34: 9: 3: 0: 3: 0: 8	V$_{range}$= -0.06 to 0.13
C) BIOMEDICAL			
Body Mass Index (kg/m^2)	23.6 ± 3.2	23.8 ± 3.5	d= 0.05
Injured side (Right: Left: Both)	*57: 31: 44	43: 32: 14	V= 0.21
VISA-P score (0-100)	61.6 ± 16.0	62.9 ± 21.2	d= 0.07
KOOS - symptom subscale score (0-100)	54.3 ± 12.5	55.1 ± 11.7	d= 0.06
KOOS - pain subscale score (0-100)	73.3 ± 15.9	75.8 ± 18.7	d= 0.15
KOOS - activity daily life subscale score (0-100)	82.6 ± 14.0	82.7 ± 18.0	d= 0.004
KOOS - Patellofemoral score (0-100)	58.8 ± 20.8	62.8 ± 25.1	d= 0.18
Patient Acceptable Symptom State (N: Y)	*77: 55	39: 50	V= -0.14
Single Assessment Numeric Evaluation (0-100)	60.1 ± 24.0	61.0 ± 24.5	d= 0.04
Current condition duration (months)	19.3 ±13.3	17.6 ± 13.7	d= -0.12
Time-off from sport (weeks)	*5.1 ± 5.0	7.4 ± 5.0	d= 0.46
Previous injury presence (N: Y)	91: 41	65: 24	V= 0.04
Current other injury presence (N: Y)	*100: 32	55: 34	V= -0.15
Adequate recovery time from previous injury (N: Y: No previous injury)	26: 25: 81	22: 11: 56	V= 0.10
Direct hit to the knee (N: Y)	116: 16	71: 18	V= -0.11
Family tendon disorder history (N: Y)	118: 14	82: 7	V= 0.05
Family systemic disease history (N: Y)	114: 18	71: 18	V= -0.09
Having any systemic disease (N: Y)	95: 37	61: 28	V= -0.04

Tendon problem other than PT (Currently: Previously: Never)	15: 33: 84	10: 15: 64	V= 0.10
Symptoms (N: Y)			
Pain	12: 120	13: 76	V= 0.09
Stiffness	114: 18	69: 20	V= -0.12
Swelling	*105: 27	60: 29	V= -0.14
Others	*129:3	81: 8	V= -0.15
Pain Onset (Sudden: Gradual)	*51: 81	50: 39	V= 0.17
Morning pain (N: Y)	*38: 94	39: 50	V= 0.16
Morning stiffness (N: Y)	67: 65	42: 47	V= -0.04
Pain at night (N: Y)	*85: 47	71: 18	V= 0.17
Movement effect on symptoms (Get better: Get worse: No effect)	46: 58: 28	29: 30: 30	V= 0.15
Medicine (Currently: Previously: Never)			
Statin use	0: 1: 131	0: 2: 87	V= 0.06
Glucocorticoid use	0: 1: 131	0: 4: 85	V= 0.12
Fluoroquinolone use	*0: 2: 130	1: 7: 81	V= 0.18
Others			
Hormonal contraception use (NA: Y: N)	44: 7: 81	32: 9: 48	V= 0.10
Menopausal status (NA: Pre: Current: Post)	95: 34: 2: 1	60: 28: 0: 1	V= 0.10
Hormone replacement therapy (NA: Y: N)	54: 1: 77	43: 0: 46	V= 0.09
Low back pain presence (Current: Previous: N)	16: 77: 39	14: 53: 22	V= 0.07
Low back pain association with leg pain (N: Y)	*64: 29	60: 7	V= 0.22
Smoking (Active: Passive: Ex-smoker: Never)	39: 16: 13: 64	19: 5: 13: 52	V= 0.16
Daily sleep time (hours)	7.7 ± 1.1	7.6 ± 1.2	d= -0.10
Sleep difficulty (N: Y)	100: 32	66: 23	V= -0.02
Feeling rested after sleep (Y: Partially: N)	51: 67: 14	35: 45: 9	V= 0.01
D) PSYCHOLOGICAL			
Full availability (N: Y)	*58: 74	54: 35	V= 0.16
KOOS - quality of life subscale score (0-100)	53.7 ± 20.6	54.8 ± 24.1	d= 0.05
EQ5D5L index score (-1 to 1)	0.76 ± 0.20	0.74 ± 0.23	d= -0.12
EQ5D5L VAS score (0-100)	77.7 ± 20.9	78.0 ± 17.3	d= 0.01
Pain Catastrophizing score (0-52)	13.9 ± 11.7	12.4 ± 11.2	d= -0.13
Tampa-11 Kinesiophobia score (11-44)	23.6 ± 6.8	23.2 ± 6.2	d= -0.05
General Self-Efficacy score (10-40)	31.8 ± 5.1	31.6 ± 5.0	d= -0.03
Patient recovery predictions			
Get better: Stay the same: Get worse: DNK	82: 19: 9: 22	53: 15: 7: 15	V= 0.04
If better,			
Confidence on recovery prediction (%) (n=134)	82.6 ± 20.1	86.6 ± 13.6	d= 0.22
Time prediction (months) (n=93)	*4.6 ± 4.8	6.8 ± 5.5	d= 0.44
Confidence on time prediction (%) (n=91)	75.4 ± 24.3	83.0 ± 16.9	d= 0.35
E) SOCIAL			
E-Health Literacy score (8-40)	28.9 ± 6.2	27.6 ± 6.8	d= -0.21
Education level (Did not attend or Elementary school: High school: Undergraduate: Postgraduate)	3: 45: 63: 21	0: 20: 48: 21	V= 0.17
Work Status (Full time: Part time: N)	67: 19: 46	49: 13: 27	V= 0.05
Change in work participation (N: Y)	115: 17	70: 19	V= -0.11

F) PAIN MAP DRAWING	**Patellar Tendinopathy (n=105)**	**Other knee problems (n=58)**	**Effect sizes**
Number of body regions	2.0 ± 1.4	1.9 ± 1.5	d= -0.04
Number of sites around the knee (anterior/posterior/medial/lateral)	1.8 ± 1.1	1.7 ± 1.1	d= -0.14
Focal pain on inferior patella pole (N: Y)	*40: 65	50: 8	V= 0.46
Focal pain on superior patella pole (N: Y)	*80: 25	52: 6	V= 0.16
Diffuse pain around the patella (N: Y)	*51: 54	12: 46	V= -0.27
Current pain level (VAS)	3.8 ± 2.2	3.4 ± 2.4	d= -0.16
Usual pain level (VAS)	3.7 ± 2.3	3.5 ± 2.5	d= -0.09
Pain Type (Pain: Dull aching: Stabbing: Tingling: Electric: Throbbing: Numbness: Burning: Other/Multiple)	69: 17: 7: 0: 1: 4: 2: 2: 3	33: 12: 6: 2: 2: 0: 0: 0: 3	V= 0.26

Table 12: Univariate logistic regression analysis. Dependent variable is having PT vs having other knee problems. Odds ratios were the membership of having PT, meaning >1.00 increases the possibility of having PT, while <1.00 decreases the possibility of having PT. Variables with *p < 0.05, $^\$$p < 0.10 were retained for multivariable regression. Key: PT, patellar tendinopathy; OP, other knee problems; CI, confidence interval; ref, reference.

VARIABLES (n=221; PT=132, OP=89)	Odds Ratio	95% CI	Prob>chi2
A) DEMOGRAPHICS			
Age	0.99	0.96 - 1.02	0.43
Body Mass	1.01	0.99 - 1.03	0.19
Height	1.03	1.01 - 1.05	*0.01
Sex	Male: 1.38	0.80 - 2.37	0.25
Dominance (ref: right)	Left: 1.30	0.59 - 2.86	0.29
B) SPORTS SPECIFIC			
Sporting Age	1.00	0.96 - 1.03	0.86
KOOS - sports	1.00	0.98 - 1.01	0.43
Player Level (ref: amateur)	Professional: 2.38	1.37 - 4.13	*0.002
Sport Type (ref: other jumping sports)	Court base jumping sports: 2.07	1.19 - 3.60	*0.01
Weekly hours trained	1.07	1.01 - 1.14	*0.01
Average hours trained in the last 3 weeks	1.07	1.01 - 1.13	*0.02
Weekly number of jumps	1.00	0.99 - 1.00	*0.046
Average number of jumps in the last 3 weeks	1.00	0.99 - 1.00	$^\$$0.07
Intensity in the last week	1.07	0.98 - 1.16	0.13
Average intensity in the last 3 weeks	1.08	0.98 - 1.19	0.12
ACWR			
Minutes continuous (n=185)	1.30	0.83 - 2.02	0.24
Jumps continuous (n=187)	1.28	0.88 - 1.87	0.20
Minutes categorical (ref: optimal) (n=185)	Low: 0.79, High: 1.52	Range: 0.41 - 3.46	0.34
Jumps categorical (ref: optimal) (n=187)	Low: 0.78, High: 1.39	Range: 0.40 - 3.38	0.35
C) BIOMEDICAL			
Body Mass Index	0.99	0.91 - 1.07	0.72
Injured side (ref: unilateral)	Bilateral: 2.68	1.36 - 5.27	*0.003
VISA-P	1.00	0.98 - 1.01	0.62
KOOS - symptom	0.99	0.97 - 1.02	0.65
KOOS - pain	0.99	0.98 - 1.01	0.28
KOOS - activity daily life	1.00	0.98 - 1.02	0.98
KOOS - Patellofemoral	0.99	0.98 - 1.00	0.20
Patient Acceptable Symptom State	Yes: 0.56	0.32 - 0.96	*0.03
Single Assessment Numeric Evaluation	1.00	0.99 - 1.01	0.79
Current condition duration	1.01	0.99 - 1.03	0.36
Time-off from sport	0.91	0.87 - 0.97	*0.001
Previous injury presence	Yes: 1.22	0.67 - 2.21	0.51
Current other injury presence	Yes: 0.52	0.29 - 0.93	*0.03
Adequate recovery time from previous injury	Yes: 1.92	0.78 - 4.77	0.36
Direct hit to the knee	Yes: 0.54	0.26 - 1.14	0.11
Family tendon disorder history	Yes: 1.39	0.54 - 3.59	0.49
Family systemic disease history	Yes: 0.62	0.30 - 1.28	0.20
Having any systemic disease	Yes: 0.85	0.47 - 1.53	0.58
Tendon problem other than PT (ref: never)	Currently: 1.14	0.48 - 2.71	0.33
	Previously: 1.68	0.84 - 3.35	
Symptom (Swelling)	Yes: 0.53	0.29 - 0.98	*0.04
Pain Onset (ref: sudden)	Gradual: 2.04	1.18 - 3.52	*0.01
Morning pain	Yes: 1.93	1.10 - 3.39	*0.02
Morning stiffness	Yes: 0.87	0.51 - 1.49	0.60
Pain at night	Yes: 2.18	1.16 - 4.09	*0.01
Movement effect on symptoms (ref: no effect)	Get better: 1.70	0.85 - 3.40	$^\$$0.10
	Get worse: 2.07	1.05 - 4.08	
Hormonal contraception use	Yes: 0.46	0.16 - 1.32	0.32
Low back pain presence (ref: never)	Current: 0.65	0.27 - 1.57	0.62
	Previous: 0.82	0.44 - 1.54	
Low back pain association with leg pain	Yes: 3.88	1.58 - 9.53	*0.004
Smoking (ref: never)	Range: 0.81 - 2.60	Range: 0.35 - 7.57	0.12

Sleep time	1.09	0.86 - 1.40	0.47
Sleep difficulty	Yes: 0.92	0.49 - 1.71	0.79
Feeling rested after sleep (ref: no)	Fully: 0.94	0.37 - 2.40	0.99
	Partially: 0.96	0.38 - 2.40	

D) PSYCHOLOGICAL

Full availability	Yes: 1.97	1.14 - 3.40	*0.01
KOOS - quality of life	1.00	0.99 - 1.01	0.73
EQ5D5L index	1.77	0.50 - 6.27	0.38
EQ5D5L VAS	1.00	0.99 - 1.01	0.92
Pain Catastrophizing	1.01	0.99 - 1.04	0.33
Tampa-11 Kinesiophobia	1.01	0.97 - 1.05	0.70
General Self-Efficacy	1.01	0.95 - 1.06	0.81

E) SOCIAL

E-Health Literacy	1.03	0.99 - 1.08	0.14
Education Level (ref: DNA or Elementary)	Range: 1.00 - 2.25	Range: 0.64 - 5.01	0.104
Work Status (ref: no)	Full time: 0.80	0.44 - 1.46	0.77
	Part time: 0.86	0.37 - 2.01	
Change in work participation	Yes: 0.55	0.27 - 1.12	$0.097

F) PAIN MAP DRAWING (n=163; PT=105, OP=58)

Number of body regions	1.03	0.82 - 1.29	0.81
Number of sites around the knee	1.14	0.84 - 1.54	0.40
Focal pain on inferior patella pole	Yes: 10.2	4.4 - 23.6	*<0.001
Focal pain on superior patella pole	Yes: 2.71	1.04 - 7.05	*0.03
Diffuse pain around the patella	Yes: 0.28	0.13 - 0.58	*<0.001
Current pain level	1.07	0.93 - 1.24	0.33
Usual pain level	1.04	0.91 - 1.20	0.56

Table 13: Univariate logistic (dependent variable: Full availability) and linear (dependent variable: VISA-P) regression analysis for PT severity. Odds ratios were the likelihood of being fully available, meaning >1.00 increases the possibility of being fully available, while <1.00 decreases the possibility of being fully available. Variables with *p < 0.05, $ p < 0.10 were retained for multivariable regression. Key: PT, patellar tendinopathy; CI, confidence interval; coef, coefficient values; ref, reference.

VARIABLES (n=132)	Logistic Regression Model (Full Availability)			Linear Regression Model (VISA-P)		
	Odds Ratio	95% CI	Prob>chi2	Coef	R²	Prob>F
A) DEMOGRAPHICS						
Age	0.96	0.93 - 1.00	$0.07	-0.44	0.06	*0.01
Body Mass	1.02	1.00 - 1.05	$0.054	0.02	<0.001	0.86
Height	1.05	1.02 - 1.09	*<0.001	0.21	0.03	$0.06
Sex	Male: 1.71	0.84 - 3.46	0.14	3.28	0.01	0.25
B) SPORTS SPECIFIC						
Sporting Age	1.03	0.98 - 1.08	0.22	-0.24	0.01	0.21
KOOS - sports	1.02	1.01 - 1.04	*0.01	0.44	0.35	*<0.001
Player Level (ref: amateur)	Professional: 4.13	1.95 - 8.73	*<0.001	6.06	0.03	*0.04
Sport Type (ref: other jumping sports)	Court base: 3.21	1.57 - 6.57	*0.001	4.73	0.02	$0.09
Weekly hours trained	1.10	1.03 - 1.19	*0.003	0.30	0.01	0.17
Average hours trained in the last 3 weeks	1.12	1.03 - 1.22	*0.002	0.46	0.03	$0.06
Weekly number of jumps	1.00	1.000 - 1.002	*0.003	0.002	0.01	0.36
Average number of jumps in the last 3 weeks	1.00	1.000 - 1.001	*0.004	0.002	0.01	0.29
Intensity in the last week	1.08	0.97 - 1.20	0.14	0.86	0.03	*0.04
Average intensity in the last 3 weeks	1.07	0.95 - 1.21	0.27	1.26	0.05	*0.01
ACWR (n=111)						
Minutes continuous	1.44	0.78 - 2.65	0.24	2.73	0.01	0.26
Jumps continuous	1.65	0.98 - 2.77	*0.048	5.14	0.06	*0.01
Minutes categorical (ref: optimal)	L: 0.78, H: 0.88	Range: 0.32 - 2.28	0.85	L: -6.5, H: -8.1	0.05	$0.06
Jumps categorical (ref: optimal)	L: 0.41, H: 0.70	Range: 0.17 - 2.04	0.13	L: -4.5, H: 1.22	0.02	0.29
C) BIOMEDICAL						
Body Mass Index	0.94	0.84 - 1.05	0.25	-0.84	0.03	$0.051
VISA-P	1.05	1.02 - 1.07	*<0.001	NA	NA	NA
KOOS - symptom	1.02	1.00 - 1.05	$0.09	0.36	0.08	*0.001
KOOS - pain	1.03	1.00 - 1.05	*0.03	0.51	0.26	*<0.001
KOOS - activity daily life	1.03	1.00 - 1.06	*0.02	0.60	0.27	*<0.001
KOOS - Patellofemoral	1.03	1.01 - 1.05	*0.001	0.49	0.41	*<0.001
Patient Acceptable Symptom State	Yes: 4.54	2.10 - 9.81	*<0.001	13.73	0.18	*<0.001
Single Assessment Numeric Evaluation	1.03	1.01 - 1.04	*0.001	0.31	0.22	*<0.001
Current condition duration	1.01	0.98 - 1.03	0.56	-0.01	<0.001	0.89
Time-off from sport	0.90	0.84 - 0.97	*0.003	-0.85	0.07	*0.002
Previous injury presence	Yes: 1.16	0.55 - 2.44	0.70	-4.54	0.02	0.13
Current other injury presence	Yes: 0.86	0.39 - 1.90	0.70	-1.92	0.003	0.56
Adequate recovery time from previous injury	Yes: 0.93	0.31 - 2.83	0.98	-3.14	0.02	0.25
Direct hit to the knee	Yes: 1.01	0.35 - 2.89	0.99	4.82	0.01	0.26
Family tendon disorder history	Yes: 0.76	0.25 - 2.31	0.63	2.96	0.003	0.52
Family systemic disease history	Yes: 0.98	0.36 - 2.66	0.96	-1.52	0.001	0.71
Having any systemic disease	Yes: 0.57	0.26 - 1.22	0.15	-2.25	0.004	0.47
Tendon problem other than PT (ref: never)	Currently: 0.99	0.33 - 2.98	0.60	-3.42	0.01	0.69
	Previously: 1.52	0.66 - 3.47		0.85		
Symptom (pain/stiffness/swelling)	Range: 0.61 - 0.98	Range: 0.18 - 6.64	All>0.10	-4.28 to -1.95	All<0.01	All>0.10
Pain Onset (ref: sudden)	Gradual: 1.23	0.61 - 2.49	0.57	-0.77	0.001	0.79
Morning pain	Yes: 0.77	0.36 - 1.67	0.51	-10.2	0.08	*0.001
Morning stiffness	Yes: 0.58	0.29 - 1.16	0.12	-8.91	0.08	*0.001
Pain at night	Yes: 0.64	0.31 - 1.31	0.22	-2.88	0.01	0.32
Movement effect on symptoms (ref: no effect)	Get better: 1.17	0.45 - 3.03	0.64	4.30	0.06	*0.03
	Get worse: 0.80	0.32 - 1.99		-4.22		
Hormonal contraception use	Yes: 0.12	0.01 - 1.04	$0.06	5.11	0.02	0.37
Low back pain presence (ref: never)	Current: 1.58	0.48 - 5.21	0.72	-0.79	<0.001	0.98

	Previous: 1.27	0.59 - 2.75		-0.62		
Low back pain association with leg pain	Yes: 1.03	0.43 - 2.52	0.77	-3.16	0.01	0.67
Smoking (ref: never)	Range: 0.74 - 1.71	Range: 0.33 - 5.50	0.55	-7.2 to 2.3	0.03	0.28
Sleep time	1.23	0.88 - 1.72	0.22	0.63	0.002	0.64
Sleep difficulty	Yes: 1.20	0.53 - 2.68	0.66	-0.52	<0.001	0.87
Feeling rested after sleep (ref: no)	Fully: 2.79	0.82 - 9.54	0.24	12.9	0.06	*0.03
	Partially: 2.36	0.71 - 7.79		9.3		

D) PSYCHOLOGICAL

Full availability	NA	NA	NA	Yes: 10.2	0.10	*<0.001
KOOS - quality of life	1.04	1.02 - 1.06	*<0.001	0.46	0.35	*<0.001
EQ5D5L index	8.95	1.33 - 60.5	*0.02	43.4	0.30	*<0.001
EQ5D5L VAS	1.02	1.01 - 1.04	*0.01	0.26	0.11	*<0.001
Pain Catastrophizing	0.96	0.93 - 0.99	*0.01	-0.46	0.12	*<0.001
Tampa-11 Kinesiophobia	0.94	0.89 - 0.98	*0.01	-0.68	0.08	*0.001
General Self-Efficacy	1.08	1.00 - 1.15	*0.04	0.44	0.02	0.11

E) SOCIAL

E-Health Literacy	0.97	0.92 - 1.03	0.32	0.05	<0.001	0.81
Education Level (ref: DNA or Elementary)	Range: 0.31 - 0.91	Range: 0.02 - 10.8	0.24	-6.8 to 1.71	0.04	0.18
Work Status (ref: no)	Full time: 0.90	0.42 - 1.93	0.18	1.88	0.02	0.38
	Part time: 0.38	0.12 - 1.13		6.14		
Change in work participation	Yes: 0.66	0.24 - 1.83	0.43	0.95	<0.001	0.82

Table 14: Final models' properties. A&B) Multivariable logistic regression analysis: dependent variable is having PT vs having other knee problems. Odds ratios were the likelihood of having PT, meaning >1.00 increases the possibility of having PT, while <1.00 decreases the possibility of having PT. C) Multivariable logistic regression analysis: dependent variable is Full availability. Odds ratios were the likelihood of being fully available, meaning >1.00 increases the possibility of being fully available, while <1.00 decreases the possibility of being fully available. D) Multivariable linear regression analysis: dependent variable is VISA-P. Key: PT, patellar tendinopathy; JPTs, jumping athletes with PT; OP, other knee problems; OR, odds ratio; CI, confidence interval; coef, coefficient values.

FINAL MULTIVARIABLE REGRESSION MODELS

A) Model to distinguish JPTs from those with other knee problems (n=221; PT=132, OP=89)

Independent Variables	OR (95% CI)	Beta coef.	P > |z|	Interpretation: JPTs … in comparison to other knee problems
Hours trained in the last week	1.10 (1.03-1.17)	0.09	0.01	Tend to train/play more
Sport Type (Court base jumping sport)	2.31 (1.24-4.32)	0.84	0.01	Play court base jumping sports
Injured side (Bilateral)	2.28 (1.09-4.77)	0.83	0.03	Tend to have bilateral injury
Pain onset (Gradual)	1.97 (1.07-3.60)	0.68	0.03	Tend to have gradual pain onset
Morning Pain (Yes)	1.89 (1.01-3.53)	0.63	0.047	Tend to have morning pain
Patient Acceptable Symptom State (Yes)	0.39 (0.21-0.73)	-0.94	0.003	Tend not to be satisfactory
Swelling (Yes)	0.37 (0.18-0.74)	-1.01	0.01	Tend not to have swelling

B) Mini model with pain map drawing data to distinguish JPTs from those with other knee problems (n=163; PT=105, OP=58)

Independent Variables	OR (95% CI)	Beta coef.	P > |z|	Interpretation: JPTs … in comparison to other knee problems
Full availability (Yes)	2.80 (1.22-6.46)	1.03	0.02	Tend to be more available to train/compete
Focal pain on inferior patella pole (Yes)	9.08 (3.66-22.5)	2.21	<0.001	Tend to have focal pain on inferior pole
Pain onset (Gradual)	2.95 (1.25-6.94)	1.08	0.01	Tend to have gradual pain onset
Morning Pain (Yes)	2.95 (1.16-7.46)	1.08	0.02	Tend to have morning pain
Swelling (Yes)	0.29 (0.11-0.75)	-1.25	0.01	Tend not to have swelling
Daily sleep time (hours)	1.74 (1.16-2.61)	0.55	0.01	Tend to sleep more

C) Model to explain sporting availability in JPTs (n=132; PT=132)

Independent Variables	OR (95% CI)	Beta coef.	P > |z|	Interpretation: Better sporting availability was associated with …
KOOS - sports	1.02 (1.01-1.04)	0.02	0.01	A better sports specific function
Player Level (Professional)	4.11 (1.90-8.87)	1.41	<0.001	Being professional athlete

D) Model to explain severity in JPTs (n=132; PT=132)

Independent Variables	Coef. (95% CI)	Beta coef.	P > |z|	Interpretation: Higher PT severity was associated with …
EQ5D5L index	25.1 (12.1-38.1)	0.32	<0.001	A lower quality of life
KOOS - sports	0.28 (0.16-0.40)	0.38	<0.001	A worse sports specific function
Age	-0.30 (-0.54 to -0.06)	-0.17	0.02	Being older

Table 15: Equations for each model. *Court base jumping sports include volleyball, basketball and handball. Key: JPTs, jumping athletes with patellar tendinopathy; LP, linear predictor.

FINAL MULTIVARIABLE REGRESSION MODELS

A) Model to distinguish JPTs from those with other knee problems

Independent Variables	Coding	Model formula: $LP=beta_1x_1+beta_2x_2+...+constant\ value$
Hours trained in the last week	Hours	
Sport Type	Other jump related=0	
	*Court base jumping=1	LP= 0.09(Hours trained in the last week) + 0.84(Sport Type) +
Injured side	Unilateral=0, Bilateral=1	0.83(Injured side) + 0.68(Pain onset) + 0.63(Morning pain) +
Pain onset	Sudden=0, Gradual=1	(-0.94(Patient Acceptable Symptom State)) + (-1.01(Swelling)) + (-0.59)
Morning Pain	No=0, Yes=1	
Patient Acceptable Symptom State	No=0, Yes=1	
Swelling	No=0, Yes=1	

B) Mini model with pain map drawing data to distinguish JPTs from those with other knee problems

Independent Variables	Coding	Model formula: $LP=beta_1x_1+beta_2x_2+...+constant\ value$
Full availability	No=0, Yes=1	
Focal pain on inferior patella pole	No=0, Yes=1	LP= 1.03(Full availability) + 2.21(Focal pain on inferior patella pole) +
Pain onset	Sudden=0, Gradual=1	1.08(Pain onset) + 1.08(Morning Pain) +
Morning Pain	No=0, Yes=1	(-1.25(Swelling)) + 0.55(Daily sleep time) + (-5.82)
Swelling	No=0, Yes=1	
Daily sleep time	Hours	

C) Model to explain sporting availability in JPTs

Independent Variables	Coding	Model formula: $LP=beta_1x_1+beta_2x_2+...+constant\ value$
KOOS - sports	Value	LP= 0.02(KOOS - sports) + 1.41(Player Level) + (-1.90)
Player Level	Amateur=0, Professional=1	

D) Model to explain severity in JPTs

Independent Variables	Coding	Model Formula: $y=a_1x_1+a_2x_2+...+constant\ value$
EQ5D5L index	Value	$VISA\text{-}P_{model\_score}$= 25.06(EQ5D5L index) + 0.28(KOOS - sports) +
KOOS - sports	Value	(-0.30(Age)) + 36.05
Age	Years	
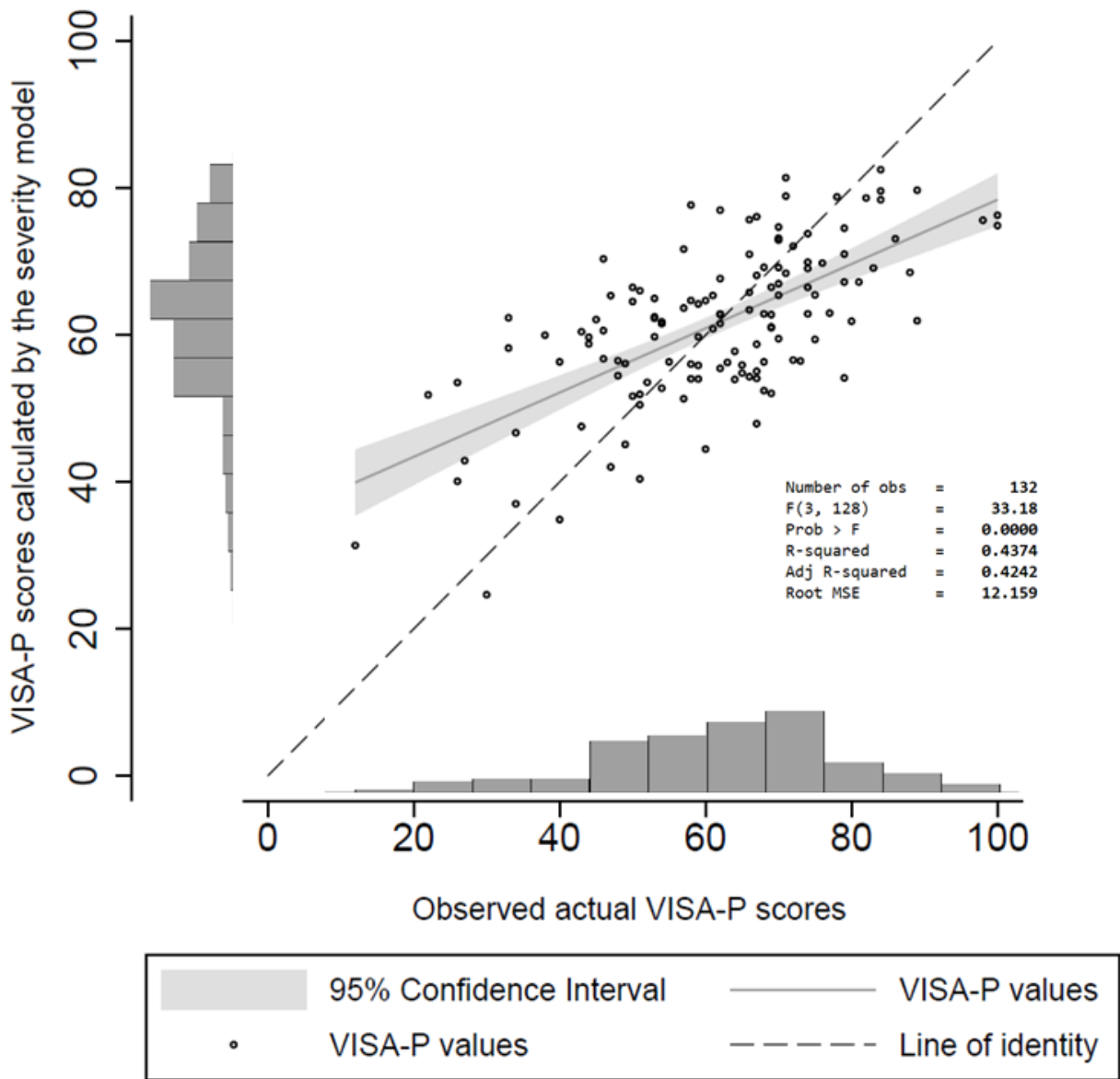
Figure 36: The final multivariable linear regression model visualization for PT severity. The model consisted of three variables: EQ5D5L index, KOOS-sports and age. There is an over-estimation at the lower values and an under-estimation at the higher values in the results. This suggests there is potential a/some hidden variable(s) (e.g. clinical and/or biomechanical assessments) that we are not capturing yet.

6.4 Discussion

We aimed to explore what distinguishes jumping athletes with patellar tendinopathy (JPTs) from those with other knee problems by determining the best combination of self-reported demographics, sports specific and bio-psycho-social factors to inform clinical profiling. Secondary aim was to explain the variance of PT severity as defined either by condition severity or sporting availability. Patient-reported measurements are easy, cheap and quick to collect (292), and we found that various sports specific, biomedical and psychological factors partially distinguish PT from other knee problems. In other words, the combination of these factors were specific to jumping

athletes with PT presence and differentiated their profile from those with other knee problems, rather than having a diagnostic role between conditions. An international effort with many collaborators enabled sufficient data collection to build multivariable models. These models are associative, so the reported findings should not be taken as being causal, but adding sports specific and bio-psycho-social assessments into athlete monitoring in at-risk cohorts, individual assessment and future research will likely improve our understanding of the presentation in JPTs.

Analysis of the data revealed an interesting and complex relationship between athlete groups, pain, function and availability. Within our study, JPTs play more despite having equal severity to those with other knee problems yet are less satisfied with their condition. It has been previously reported in anterior cruciate ligament injuries (293) that satisfaction is associated with return to pre-injury physical activity level, which we do not observe in JPTs. This could be one of the reasons for the reported low satisfaction level in JPTs as they do not present with marked functional limitations and sudden changes in symptoms compared to acute onset knee problems. Another reason could be that the typically used PROMs may not be sensitive enough to the correct condition-specific factors as neither the VISA-P nor the KOOS and KOOS-PF differentiated between the conditions. For instance, many symptoms associated with PT presence in our model are not represented in the VISA-P. Therefore, investigating sports specific and bio-psychological factors in addition to knee pain and function PROMs might improve the identification and grading of PT.

The mini model analysis showed that the combination of pain location with sport specific/psychological and biomedical factors also distinguishes JPTs from those with other knee problems. Despite lower numbers due to incomplete data, the mini model had better accuracy, specificity and sensitivity compared to the larger model therefore illustrating the importance of pain location. The biomedical symptoms (pain onset, morning pain and swelling) were similar between the models, with the exception of 'injured side'. The addition of pain location and reduced numbers meant full availability, daily sleep time and pain location were included instead of training duration, sport type and symptom satisfaction. Full availability could be equivalent to training duration as they both show JPTs to be more active. Daily sleep time seemed to explain the variance otherwise attributed to playing level and a sensitivity analysis found that professional athletes in PT group have higher daily sleep time. It is plausible that professional JPTs with more availability and busy training schedule require, and can take, more rest. Localised inferior patella pole pain was expected since it is an important diagnostic criterion (25) for PT. However, self-reported pain map data is also another factor missing from typically used musculoskeletal PROMs. Collecting the data found to be

useful in the modelling could complement the more commonly collected physical examination in usual clinical care as well as future research.

Sporting availability within the JPTs was partially explained by associations with a combination of sports specific function and player level. Better sports specific function and being a professional athlete were associated with better sporting availability. It is plausible that better sports specific function could result in better availability. However, player level may represent reverse causality. It is unknown whether amateur athletes are more likely to stop playing or professional athletes have better access to medical professionals, which result in better tendinopathy management, hence better availability. Therefore, investigating sports specific factors could be useful to help explain the availability, and yield a better understanding of the interaction of sporting level and PT severity.

The variance in PT severity was partially explained by associations with a combination of age, sports specific function and quality of life. Being cautious for the interpretation of multivariable linear regression models was suggested (294) as there are potential changes between univariate and multivariable regression analysis in terms of the amplitude and direction of coefficient values for each independent variable. In our analysis, amplitudes of the variables have decreased by %32-42 without any directional change, although there was no multicollinearity. Being older was expected to be associated with higher severity due to accumulated pathology and longer recovery times (295). Possibility of recurrence might also increase with age, in association with reduced tendon health (295), hence increasing severity. Better sports specific function and quality of life may cause, but also result from, lower severity. Associations between quality of life and the severity of other tendinopathies have been widely investigated and aligned with our findings. For example, it has been reported that musculoskeletal conditions impact on health related quality of life, especially physical function compromise, pain level, and role limitations caused by physical problems (296). Poorer quality of life was present in people with Achilles tendinopathy (297) and associated with higher severity in gluteal tendinopathy (298). A recent systematic review also showed that various psychological factors were associated with quality of life in people with rotator cuff tendinopathy (299). Quality of life, perhaps measured with EQ5D5L or KOOS-QoL, could be another useful assessment to help explain the psychosocial aspects of patients' presentation – irrespective of whether the relationship is causal or not.

The majority of human health conditions are complex. The multifactorial nature of sports injuries has been proposed (300) as it arises from the interaction of a web of determinants on timescales that differ from one athlete to another, but not from linear interactions between exploratory

factors. There were some variables, which despite having univariate associations with PT and a plausible rationale, did not either distinguish PT from other knee problems or help explain the variance in severity. For instance, it has been reported that PT was more prevalent in elite (1) and non-elite (2) male jumping athletes, and being male (79) was a risk factor for PT. Similarly, a positive family history of tendon disorders (79,123) or previous knee injury (79) has been suggested as risk factors. However, these variables did not contribute to our exploratory models, which is a study strength that arises due to the variety of measures made in a large sample. Additionally, we used multivariable regression analysis which has been recommended (78) to identify outcome predictors while accounting for other pertinent variables with previous literature (78) mainly employing univariate statistical approaches and often yielding conflicting findings. Effectively, confounded or indirectly related measures were identified and removed prior to settling on the final associative model rather than being retained and misleading the interpretation of results.

One of the study limitations was that diagnosis was established by self-report of prior consultation with a medical professional, instead of verifying in person. In terms of analysis, diagnostic groups may not be homogenous, but having a large sample size and robust analysis are a trade-off for heterogeneity. Additionally, we performed a sensitivity analysis by removing the athletes who had other knee conditions in addition to PT (n=32) in the PT group from model building for contamination concerns. Although original model (PT=132, OP=89; AUC=0.76, specificity=70.8%, sensitivity=70.5%) and contamination free model (PT=100, OP=89; AUC=0.78, specificity=73.0%, sensitivity=72.0%) were similar in model performance, there were small differences in the variables included in the models. Playing level and time-off from sport included in the contamination free model instead of training duration and sport type from the original model. Less time-off from the sport could be similar to higher training duration as both meaning more active players. On the other hand, there could be an interaction between sport type and playing level as professional athletes were mainly playing court base jumping sports. Regardless of contamination, small changes were also expected in the analysis due to different number of events, and there were only two variables different between models and the rest of the five variables stayed the same which shows how robust the analysis and the model are. Therefore, contamination in the PT group was very minimum. Another limitation was that we could not fully include the variables from the pain maps in our main models due to unequal participant numbers. The main reason for this was that we collected pain map drawings with a second software package that could not be fully integrated from the online survey and increased participant effort. However, we constructed a mini model with pain map data by removing missing data from all dataset. The main limitation was the lack of variables from

physical examination, imaging and biomechanical assessments. These assessments were initiated, and would be expected to give stronger models, but data collection had to be curtailed due to the COVID-19 pandemic.

6.5   Conclusion

This study showed that self-reported sports specific and bio-psycho-social factors partially distinguish PT from other knee problems and partially explain both the variance of condition severity and compromised participation in jumping athletes. These findings could complement the more commonly collected physical examination and imaging findings in clinical care and research. The findings are generalizable because of the uniquely large sample size, diverse range of analysed variables enabling multivariable analysis and relevant international sample of elite and non-elite athletes (78). Adding sports specific and bio-psycho-social factors into assessments might help better identification and management of jumping athletes with patellar tendinopathy. We will carry out a prospective international cohort study of jumping athletes to investigate the outcome predictors for recovery of PT in order to support clinical decision making by addressing who gets better, why and when.

7 Outcome predictors for recovery of patellar tendinopathy in jumping athletes: An international prospective cohort study

In the case-control study chapter, I presented how jumping athletes with PT (JPTs) present and differ from athletes with other knee problems. Specifically, PT severity and compromised participation were partially explained by the exploratory multivariable models. In this chapter, I focus on outcome predictors for recovery of PT. I aimed to improve our understanding of PT prognosis by determining what combination of self-reported factors predicts PT recovery in jumping athletes. Therefore, the findings from the follow-up surveys of the cohort study are presented in this chapter.

Preliminary results of this cohort study will be presented at the 2022 Scandinavian Sports Medicine Congress in Denmark.

7.1 Introduction

To our knowledge there is no study that investigates prognostic factors for PT. Thus, we do not know who gets better, when they get better or why they get better. Associations between condition outcome and various factors have been widely investigated in other musculoskeletal conditions. For example, Collins et al. (55) reported that poor recovery of patellofemoral pain either at 3-month (55%) or 12-month (40%) was associated with longer baseline pain duration and greater baseline pain severity. Another cohort of knee complaints (54) reported that worse outcome at 3-month (75%) and 12-month (56%) was associated with previous knee complaints, a longer duration of the current episode, other coexisting musculoskeletal complaints, and a higher level of distress. It has been reported (301,302) that baseline psychosocial (e.g. patient expectations and self-efficacy) and baseline biomedical (e.g. disability and severity) factors were associated with clinical outcome at 6 months in people with shoulder pain. A recent scoping review (303) also concluded that better understanding of the factors during rehabilitation might assist with optimising management, encouraging return to sport, and long term quality of life, as various psychosocial and contextual factors were present and had an impact on recovery of sport-related traumatic knee injuries. Similarly, a systematic review (241) reported an association between psychosocial factors and a range of sports injury rehabilitation outcomes in competitive athletes. PT symptoms such as pain or functional limitation generally occur insidiously, and athletes often continue to play through symptoms despite PT presence (58), hence non-recovery. There is also a mismatch between tendon abnormalities seen on imaging and symptoms, although the presence of abnormalities is a risk for

symptom development (276). This limited understanding is likely to partly explain poor treatment outcomes. Therefore, investigating the factors that predict PT recovery would be helpful to understand the prognosis better, therefore improving management.

There is a strong link between the use of prognostic models and personalized or stratified healthcare, as risk communication and clinical decisions are informed by an individual's profile of predictor values (304–306). Prognostic models assist clinicians with their prediction of a patient's future outcome and to enhance clearer communication with their patient and informed decision making together (304,307). Additionally, knowing the likely course of the condition might help athletes with PT to come to terms with, and plan for, the future (308). Knowledge of the risk of worse outcomes or the likelihood of self-resolution of symptoms is critical in predicting and planning the likely effect of management (309). Recent research has focussed on interventions, with the absence of statistical models (78) considering combinations of various risk factors potentially obscuring understanding of how jumping athletes with PT (JPTs) progress and recover.

The aim of this study was to improve management by determining what combination of self-reported factors predicts PT recovery. We planned to build exploratory recovery model from the one-year follow-up data of a large international cohort of jumping athletes, considering training load descriptors and a range of biopsychosocial factors. Successfully accomplishing the study aim should lead to a better understanding of PT prognosis and management of JPTs by identifying modifiable variables in the recovery model. The alternative hypothesis was that multivariable statistical survival model predicts outcome for PT in jumping athletes.

7.2 Materials and methods

The STROBE statement (277), Strengthening the Reporting of Observational Studies in Epidemiology, guided the design and reporting of this cohort study, while PROBAST, the Prediction model Risk Of Bias ASsessment Tool (235,310), was used to assess the risk of bias and applicability (Appendix 14).

7.2.1   Participants

This study was approved by Queen Mary Ethics of Research Committee (QMERC2018/92), the UK National Health Service (NHS) (264615) and University of Liège Hospital-Faculty Ethics Committee (2019/182). Please see Appendix 11 for all approval letters. A previously validated, reliable online questionnaire battery (278) yielded data from an international sample of jumping athletes recruited

via social media, private practice, sporting teams and the NHS through a large network of collaborators (Figure 37). Eligibility was checked after consent (Appendix 12) had been granted, with the inclusion criteria being: aged 18 and over; performing any jump-related sport with a minimum of an hour of training once per week; and having a clinical diagnosis of PT or another musculoskeletal condition affecting the knee from a clinician in the last 6 months. The exclusion criterion was having any neurological disorders.

7.2.2   Recruitment and retention strategies

There were two main recruitment strategies (Figure 37). First, we advertised the study via flyers (Appendix 9) in social media. When we received the eligibility survey answers we enrolled participants based on the inclusion/exclusion criteria. After this point, everything was automated via SmartTrial. This automation included survey link distribution via email and text message for 3-weekly follow-up surveys for a year. Secondly, collaborators directly reached the participants in their private practice, sporting teams or NHS and enrolled them. Additionally, we targeted snowball recruitment with automated emails via SmartTrial. If participants consented to take part in the study, we recorded them as recruited, and calculated the retention rates if they dropped out after giving consent. We used automated emails and text messages via SmartTrial to send reminders two times with three days intervals if a participant did not complete the current follow-up survey.

7.2.3   Online questionnaire battery

7.2.3.1   Baseline survey

The composite battery included 10 patient reported outcome measures (PROMs) plus miscellaneous questions concerning demographics, condition related details, treatments, full availability to training and competition and training load in the previous 3 weeks (278). Participants completed the questionnaire battery online remotely using SmartTrial. Additionally, we collected pain related details such as location, pain type and severity with digital online self-reported pain map drawings using Navigate Pain. Questionnaires were carefully translated to Turkish, Spanish and French to optimise recruitment. If PROMs have already been translated into targeted languages, their existing versions were used as described in the section 4.1.5. For the survey, please see the documents here:

https://www.dropbox.com/sh/hd7152qgun781gi/AADNF5zgMVzzrsqZ-wvZ8sEPa?dl=0
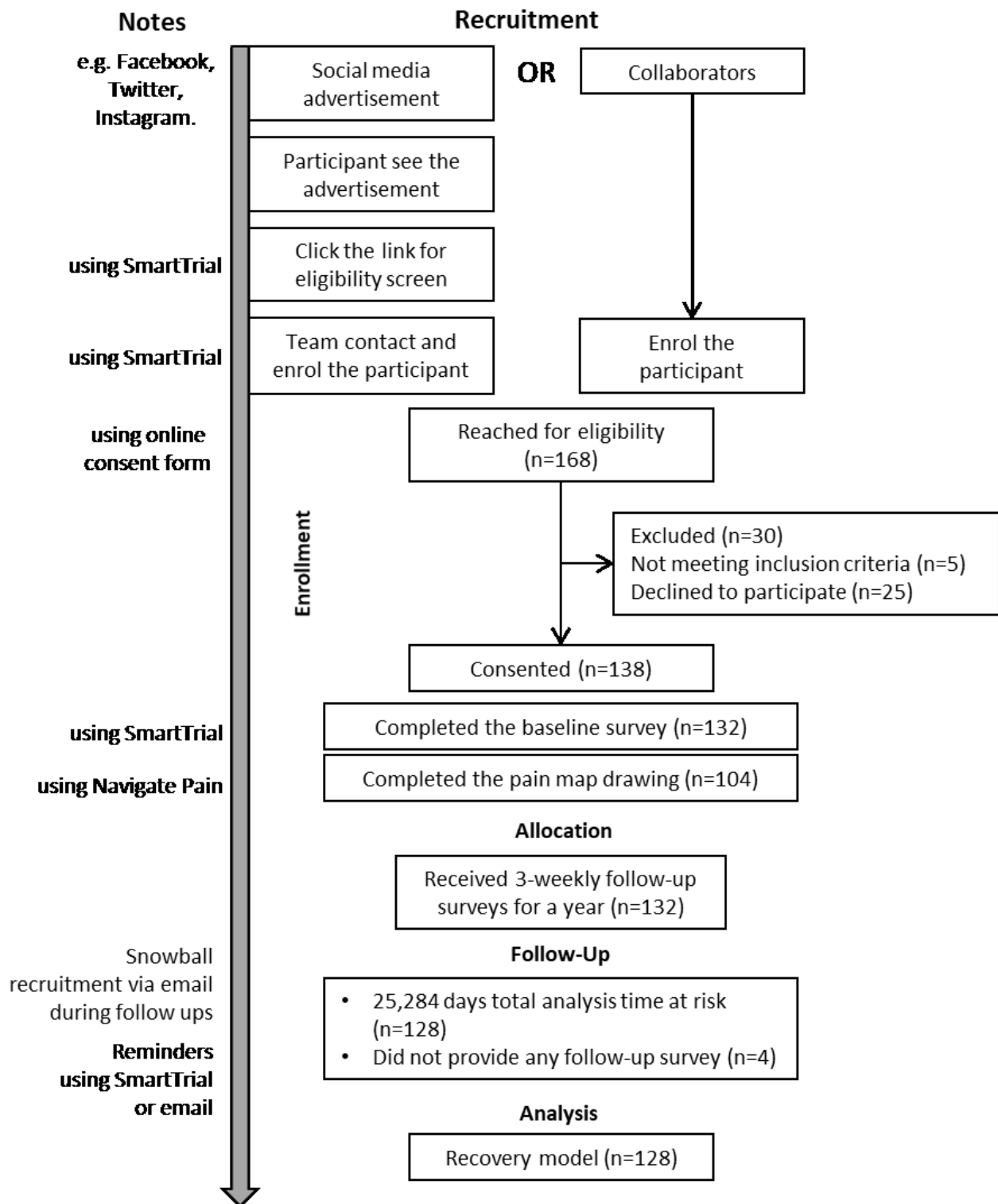
Figure 37: A typical participant journey showing the screening and enrolment process.

The Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon (VISA-P) (239) and the Knee injury and Osteoarthritis Outcome Score (KOOS) (237) with Patellofemoral subscale (KOOS-PF) (238) were used to measure knee-specific condition severity. For the global knee assessment, Patient Acceptable Symptom State (PASS) (279), a single-item binary (yes/no) question, was used to define the global satisfaction over time, while the Single Assessment Numeric Evaluation (SANE)

(280) rating scale was used for the degree of normal. Psychosocial factors are associated with rehabilitation outcomes (241) while kinesiophobia (Tampa Scale for Kinesiophobia-11 (TSK-11)) (281) and catastrophisation (Pain Catastrophizing Scale (PCS)) (242) have not been investigated in PT but have in other tendinopathies (244). Health-related Quality of Life (EQ5D5L) (240) was included due to likely chronicity (4,7). General Self Efficacy Scale (GSE) (282) was measured as a cognitive factor that facilitates the recovery and has been useful in other knee conditions such as anterior cruciate ligament injuries (283) or osteoarthritis (284). The eHealth Literacy Scale (eHEALS) (285) was used as a check of online health self-efficacy.

7.2.3.2   3-weekly follow-up surveys

Change in progress was measured with the combination of the Global Rating of Change (GRoC) scale (46) and full availability for training and competition during follow-ups.

7.2.4   Main outcome measurements

Recovery was collected as a main outcome with the combination of GRoC scale (46) and full availability for training and competition (Figure 38). GRoC is an 11-point scale in which the participant is asked to rate their perceived overall change in the condition, as 'Worse', 'No Change', or 'Better' (311). If they indicate worse or better, the participant will then be asked how much worse or better on a five-point scale (46). Using scales like GRoC to measure patient perceived change has previously (312) been demonstrated to be clinically relevant and a stable concept for interpreting meaningful improvements from an individual perspective. On the other hand, as many athletes continue to train and compete despite PT presence (58), consensus has identified 'Full availability for training and competition at any time point' as the preferred marker of recovery in athletic populations (45). If an athlete is not fully available for training and competitions, it is considered as non-recovered. To our knowledge, there is no valid and reliable question for full availability. To capture this information, if an athlete is able to train and compete without restriction it is considered as full availability. Overall, if an athlete states top two categories of GRoC and is being fully available for both training and competitions, it is considered as recovered (Figure 38).

With respect to your knee pain, how satisfied are you with your condition?

◉ Better
○ No change
○ Worse

How much better?

○ Slightly better
○ Somewhat better
○ Moderately better
◉ Much better
○ Very much better

Are you currently fully available* for training?

◉ Yes
○ No

*Full availability means that you are able to train/compete without restriction.

Are you currently fully available* for competition?

○ Yes
◉ No

Figure 38: Global Rating of Change (GRoC) scale and binary questions for full availability. Circle refers the top two categories of GRoC. In this figure, the participant is not fully recovered due to being unavailable for the competition.

7.2.5 Variables of interest

We considered over 45 potentially plausible self-reported factors as independent variables in the regression models (Table 18). These were derived from published literature suggesting an association with PT (2,64,67,74,78,79,83,85) or other musculoskeletal problems (65,66,137,230–232,241,244), and categorized under five different subheadings: demographics, sports specific, biomedical, psychological and social.

7.2.6 Bradford Hill criteria of causality

We followed the Bradford Hill criteria (313) which consists of nine principles as a guide for assessing causality. The principles and their status in this study were presented in Table 16.

Table 16: Bradford Hill criteria (313) and their availability in this cohort study. Keys: NA, not applicable; ✓, meets criterion.

Bradford Hill criteria	Definitions	Status
Strength	Effect size, the strong association supports causality, while weak association does not mean that there is no causal effect.	✓
Consistency	Reproducibility across studies, different situations, researchers, places and/or populations.	NA - As this is the first study in this field. Need external validity by other researchers.
Specificity	The more specific association, the higher the probability of causality.	✓
Temporality	The outcome has to occur after the cause (event).	✓
Biological gradient	Dose-response relation, amount of exposure should impact on incidence of the outcome.	✓
Plausibility	A plausible mechanism between variables and outcome.	✓
Coherence	Coherence between laboratory and epidemiological findings. However, lack of laboratory findings cannot nullify the epidemiological observations.	NA - As we do not have laboratory findings, all self-reported.
Experiment	Experimental evidence.	NA - Due to observational study design.
Analogy	The use of analogies between the associations.	✓

7.2.7 Sample size

To obtain a robust sample size calculation, the primary outcome measure was calculated using the AUC, checked with events per variable (EPV). The AUC gives information about the overall predictive accuracy of outcome (314). It is a metric recommended to perform sample size estimation (315). The AUC is also equivalent of other discriminative model performance statistics such as R-squared or C-statistics (316). Thus, sample size was calculated based on AUC. This PhD project was planned to produce a tool for clinicians examining patients, so they can more reliably predict patient outcome. Therefore, an excellent score >0.8 (288) was defined as an indicator of a useful model with a power of 80% and an alpha of 5% in order to yield robust data for clinical approaches. To our knowledge no data are available that describe the single variable prediction of outcome for recovery of PT. Thus, single variable prediction of outcome was estimated at 0.7 based on work in other fields. Ratio of sample sizes in negative/positive groups was considered 0.54 (35%:65%) based on recovery rates from the previous patellar tendinopathy studies (4,5). Negative and positive groups were defined as non-recovery and recovery, respectively. Computer based MedCalc software (version

18.6) was used to calculate the required sample size. The sample size was 193 participants (125 participants is for positive group, 68 is for negative group, Table 17, Figure 39). Lastly, an estimated drop out of 20% (273,317) was added, to give a required number of 242 participants (157 participants is for positive group, 85 is for negative group) for the total sample size.

*Table 17: Sample size calculation according to different recovery rate based on AUC. *chosen sample size.*

Non-recovery: Recovery		30:70		35:65		40:60	
	Alpha	0.05	0.01	0.05	0.01	0.05	0.01
Beta	**0.20**	140+61	213+92	**125+68***	189+103	114+76	172+114
1-Power	**0.10**	181+78	262+113	161+87	233+126	147+98	213+141
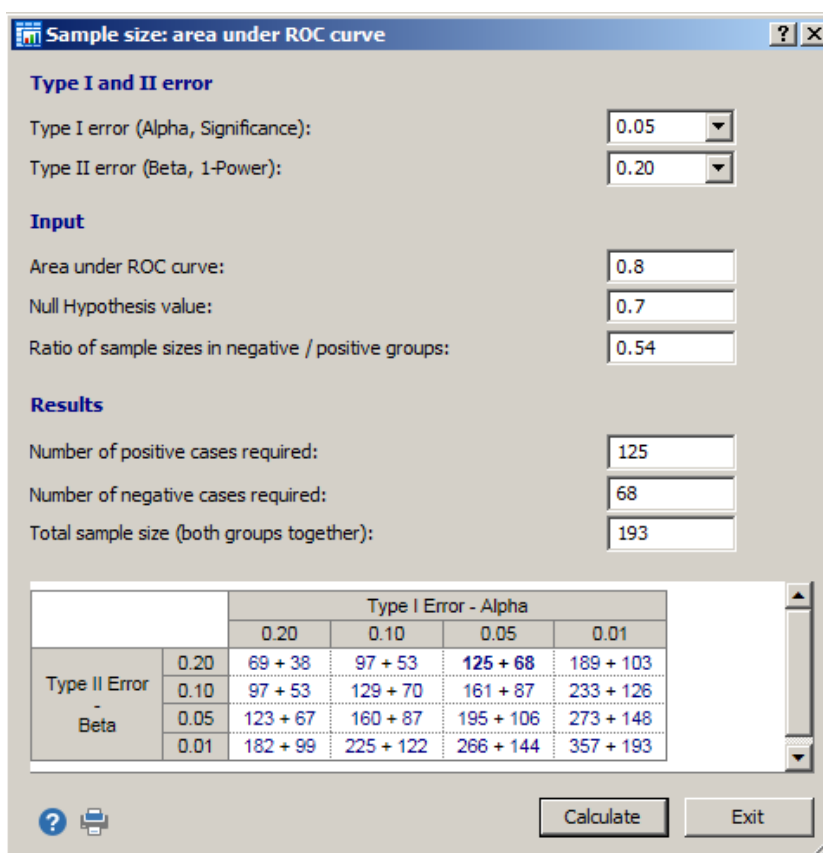
Figure 39: MedCalc software for the sample size calculation based on AUC

7.2.8 Data analysis

We have previously published total score calculations for PROMs (278). The details of the data analysis and processing was explained in section 6.2.5.

7.2.9 Statistical analysis

Statistical analysis was conducted using STATA. We calculated descriptive statistics to profile the study sample and visualised the data. We used univariate cox proportional-hazards regression to

calculate time to event, analysing individual predictive associations between recovery (outcome) and each plausible independent variable at baseline.

Independent variables associated with in the univariate regression analysis (p<0.10 (288)) were retained for multivariable cox proportional-hazards regression using a manual forward approach. The order of forward inclusion of independent variables into multivariable model was from demographic to social factors. Independent variables which improved the model were retained, as determined with the likelihood-ratio test (289) at the 5% significance level (i.e. p<0.05). To avoid collinearity, correlations between independent variables were tested with Pearson or Cramer's V based on data type (288). If correlation (288) was greater than 0.75 for any two independent variables, they were not used together in the model, and the variable with better explanatory power retained.

We constructed cox proportional-hazards regression model with the number of days at risk as the time variable to evaluate the time to recovery (304). For the final multivariable cox proportional-hazards model fit, we tested the proportional-hazards assumption by estimating the Schoenfeld residuals (estat phtest >0.05) (318). We also checked the assumption by visualising the survival time proportional-hazards plots (stphplot; plot curve for each category should be parallel) and Kaplan-Meier survival plots (stcoxkm; predicted and observed curves should be close together). We used the hazard ratio values of individual items to interpret the model. Additionally, Akaike's information criterion (AIC) (319) and Bayesian information criterion (BIC) (320) were used for model comparisons.

We evaluated the predictive performance of the final model by conducting discrimination and calibration analysis. We first calculated Harrell's C-statistics for the discrimination (316) to display how well the model differentiate between the athletes who recovered and those who had not recovered. Values of C-statistics near 1 indicate that the discrimination is good at determining which of two athletes will have the outcome. For the calibration, we calculated the calibration slope and visualised the calibration plot to demonstrate how well the model predictions match the observed data. Calibration slope reflects the average strength of the predictor effects and is the regression coefficients between predicted and observed outcomes (321). A value of calibration slope less than or greater than 1 indicates that the model systematically overestimates or underestimates predicted outcomes, respectively. Calibration plots reflect the agreement between observed and predicted outcomes and were assessed graphically (321). If well calibrated, predictions should lie around the 45° reference line of the calibration plot.

For the model internal validation, the bootstrap resampling technique (322) was conducted in order to adjust the apparent (original) C-statistics and calibration slope for optimisation. In the bootstrap procedure, we repeated the modelling process in 1000 bootstrap samples drawn with replacement from the original sample and tested on the original sample to estimate optimism in model performance (323). For potential overfitting or underfitting, we used the optimism-corrected calibration slope as a uniform shrinkage factor to adjust the regression coefficients (effects) of the variables in order to improve the model's calibration (316).

7.3 Results

7.3.1 Participants

We reached 168 international jumping athletes with PT between 5th April 2019 and 14th January 2021. 138 athletes consented to the study and 132 completed the baseline survey giving a completion rate of 95%. 4 participants did not provide any follow-up surveys and were excluded prior to the analysis. The major milestones of 3-month, 6-month, 9-month and 12-month, follow-up surveys' retention rates were 88%, 78%, 68% and 71%, respectively. Retention rates for 3-weekly follow-up surveys ranged from 45-92%. Participants journey were shown in Figure 40. 128 participants (30.9±8.9 years; 77 males; VISA-P=61.5±16.2) provided 25,284 days total analysis time at risk (198±141 days, minimum=21, median=177, maximum=397) in the survival analysis. Recovery rate was 45% occurring around 6-month (198 days). Baseline characteristics of the participants for each statistical model are shown in Table 18.
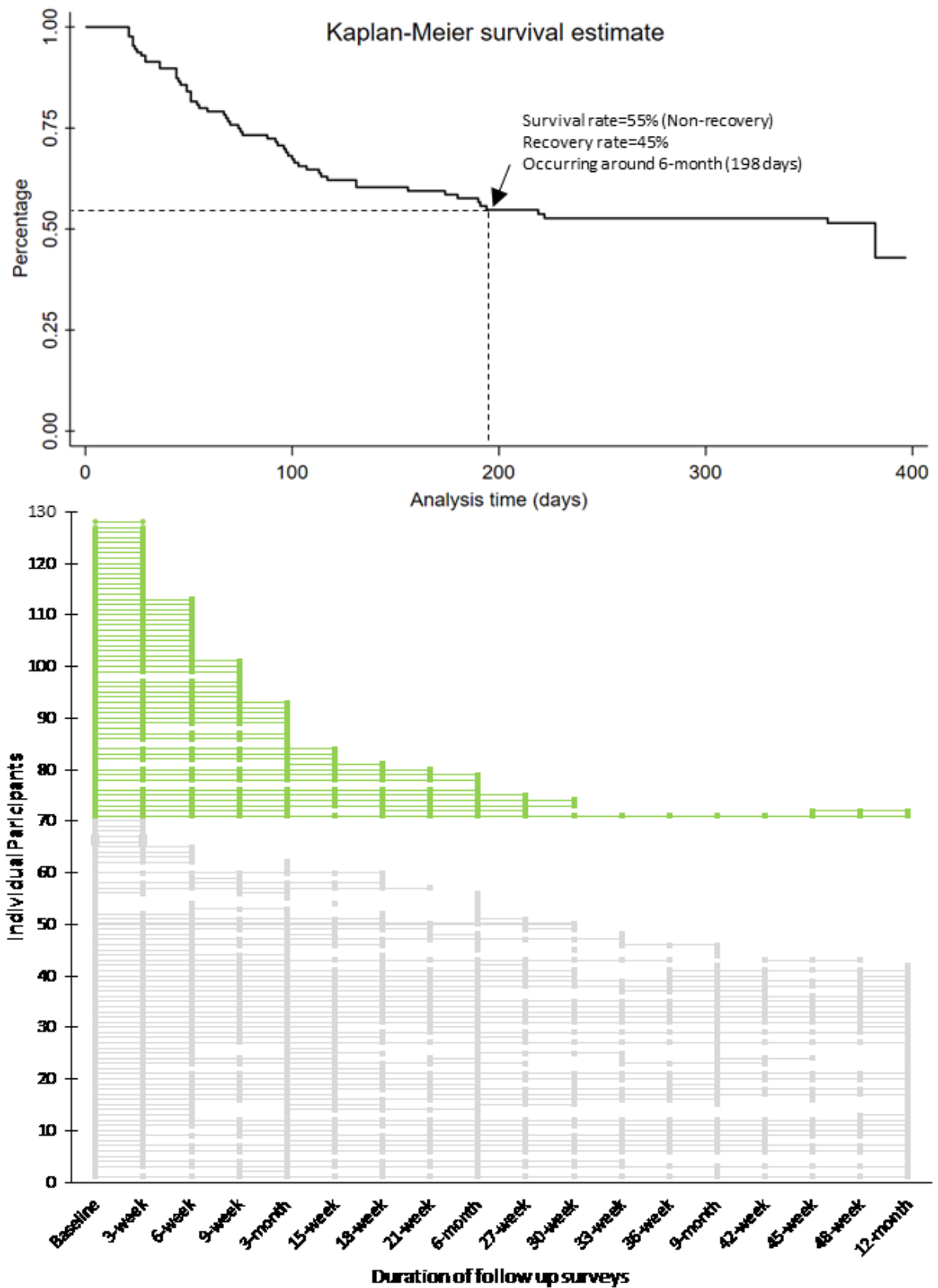
Figure 40: Kaplan-Meier survival estimate graph and individual participants' journey. Keys for colours: green; individual participants who recovered, grey; those who did not recover.

7.3.2 Multivariable cox proportional-hazards regression model (n=128)

Univariate cox proportional-hazards regression analysis showed forty-one variables individually predicted PT recovery and being retained for multivariable model construction (Table 18). The final multivariable model comprising six factors predicted PT recovery (Table 19); KOOS-PF (HR=1.03, 95%CI=1.02-1.05, p<0.001), time-off from sport (HR=0.93, 95%CI=0.87-0.99, p=0.03), feeling rested after sleep (HR for yes=1.93, 95%CI=1.13-3.28, p=0.02), current other tendon problem (HR for yes=0.23, 95%CI=0.07-0.69, p=0.01), average 3-weekly hours trained (HR=1.05, 95%CI=1.01-1.10, p=0.01) and movement effect on symptoms (HR for effect=2.71, 95%CI=1.21-6.09, p=0.02); meaning recovery in JPTs was associated with the combination of a higher KOOS-PF score (lower severity), a shorter time-off from sport, feeling rested after sleep, not having current other tendon problem, higher training duration and change in symptoms with movement.

Model fit was good as the proportional-hazards assumption has not been violated (estat phtest=0.69, p value for the model<0.001). Additionally, KOOS-PF (AIC=470.6, BIC=487.7) was interchangeable with VISA-P (HR=1.03, 95%CI=1.01-1.05, p=0.002, AIC=480.6, BIC=497.7, estat phtest=0.43) in the model, but current other tendon problem was insignificant (p=0.07) when VISA-P in instead of KOOS-PF.

For the model performance (Table 20), apparent Harrell's C-statistics was 0.79 showing that the model differentiate the outcome in almost 8 out of 10 athletes. Apparent calibration slope was 1.000 and calibration plot showed that the most of the predictions lied around the 45° reference line (Figure 41). We adjusted the model with internal validation outputs for optimisation. The optimism-corrected C-statistics and calibration slope were 0.77 and 0.86 (Table 20), respectively. The optimism-corrected calibration slope showed that the model systematically overestimates predicted outcomes. Therefore, we adjusted the regression coefficients of the variables to improve the calibration (Table 19) with the optimism-corrected calibration slope as a uniform shrinkage factor.

Table 18: Self-reported baseline participant characteristics and univariate cox regression analysis for jumping athletes with PT. Mean±SD values for the continuous variables, and proportions for the categorical variables in characteristics. Dependent variable is recovery vs non-recovery. Hazards ratios were the likelihood of recovery, meaning >1.00 increases the possibility of recovery, while <1.00 decreases the possibility of recovery. Variables with *p<0.05, $^{\$}$p<0.10 were retained for multivariable regression. Higher score means worse outcome for PCS and TSK-11, but better outcome for the rest of the PROMs. Keys: PT, patellar tendinopathy; n, number of participants; N, no; Y, yes; EN, English; TR, Turkish; SP, Spanish; FR, French; RPE, rating of perceived exertion; VISA-P, Victorian Institute of Sport Assessment Questionnaire-Patellar Tendon; KOOS, Knee injury and Osteoarthritis outcome score; EQ5D5L, Health-related Quality of Life; VAS, visual analogue scale; NA, not applicable; DNK, do not know; HR, hazards ratio; CI, confidence interval.

VARIABLES (n=128)	Baseline Characteristics	Univariate Cox Proportional-Hazards	
Recovery (Non-recovered: Recovered)	NA	70: 58 (Recovery rate: 45%)	
A) DEMOGRAPHICS		HR (95% CI)	Prob>chi2
Age (years)	30.9 ± 8.9	0.98 (0.95-1.01)	0.19
Body Mass (kg)	79.5 ± 14.7	1.01 (1.00-1.03)	0.15
Height (cm)	182.8 ± 12.9	1.03 (1.01-1.05)	*0.01
Sex (Female: Male)	51: 77	Male:1.61 (0.92-2.81)	$^{\$}$0.09
Dominance (Right: Left: Not sure)	108: 19: 1	Left:0.82 (0.39-1.74)	0.45
Language (EN: TR: SP: FR)	26: 89: 6: 7	NA	NA
Countries (UK: Turkey: Spain: France: USA/Canada: Belgium: Australia: Netherlands)	18: 90: 6: 4: 4: 3: 2: 1	NA	NA
Ethnicity (White: Arab: Asian: Black: Mixed: Others: Prefer not to say)	68: 2: 6: 6: 5: 22: 19	NA	NA
B) SPORTS SPECIFIC			
Sporting Age (years)	13.2 ± 7.3	1.02 (0.99-1.06)	0.27
KOOS - sports subscale score (0-100)	55.8 ± 21.6	1.02 (1.01-1.04)	*<0.001
Player Level (Amateur: Professional)	46: 82	Professional:3.07 (1.55-6.06)	*<0.001
Sport Type (Other: Court base Jumping Sports)	58: 70	Court base:1.53 (0.90-2.63)	0.11
Training details (including competition)			
Weekly hours trained	5.5 ± 6.5	1.04 (1.01-1.08)	*0.02
Average 3-weekly hours trained	5.8 ± 5.8	1.07 (1.03-1.10)	*0.001
Weekly number of jumps	338 ± 686	1.00 (0.999-1.001)	$^{\$}$0.08
Average 3-weekly number of jumps	386 ± 634	1.00 (1.00-1.001)	*0.01
Weekly intensity (RPE)	4.4 ± 3.3	1.06 (0.98-1.15)	0.14
Average3-weekly intensity (RPE)	4.4 ± 2.8	1.12 (1.01-1.23)	*0.02
Acute: Chronic Workload Ratio			
Minutes continuous (n=108)	1.00 ± 0.63	1.67 (1.02-2.74)	*0.04
Jumps continuous (n=107)	0.86 ± 0.78	1.96 (1.34-2.87)	*0.001
Minutes categorical (Low: Optimal: High) (n=108)	30: 53: 25	Low:0.42 (0.19-0.93) High:0.69 (0.34-1.43)	$^{\$}$0.07
Jumps categorical (Low: Optimal: High) (n=107)	47: 36: 24	Low:0.37 (0.18-0.74) High:0.82 (0.40-1.69)	*0.01
C) BIOMEDICAL			
Body Mass Index (kg/m^2)	23.7 ± 3.2	0.97 (0.90-1.05)	0.49
Injured side (Right: Left: Both)	54: 30: 44	Bilateral:1.13 (0.66-1.93)	0.66
VISA-P score (0-100)	61.5 ± 16.2	1.04 (1.02-1.06)	*<0.001
KOOS - symptom subscale score (0-100)	54.0 ± 12.5	1.03 (1.00-1.05)	*0.02
KOOS - pain subscale score (0-100)	73.2 ± 15.9	1.02 (1.00-1.04)	*0.02
KOOS - activity daily life subscale score (0-100)	82.3 ± 14.0	1.03 (1.01-1.05)	*0.003
KOOS - Patellofemoral score (0-100)	58.4 ± 20.8	1.03 (1.02-1.05)	*<0.001
Patient Acceptable Symptom State (N: Y)	74: 54	Yes:2.17 (1.29-3.65)	*0.003
Single Assessment Numeric Evaluation (0-100)	59.7 ± 24.0	1.02 (1.01-1.04)	*<0.001
Current condition duration (<6M: >6M)	35: 93	>6M:0.77 (0.44-1.35)	0.37
Current condition duration (months)	19.2 ± 13.3	0.98 (0.96-1.00)	$^{\$}$0.08
Time-off from sport (weeks)	5.0 ± 5.0	0.89 (0.84-0.95)	*<0.001
Previous injury presence (N: Y)	88: 40	Yes:0.73 (0.42-1.29)	0.27
Current other injury presence (N: Y)	97: 31	Yes:0.52 (0.26-1.03)	*0.045
Adequate recovery time from previous injury (N: Y: No previous injury)	25: 25: 78	Yes:1.02 (0.43-2.41)	0.42
Direct hit to the knee (N: Y)	114: 14	Yes:0.89 (0.38-2.06)	0.77
Family tendon disorder history (N: Y)	110: 18	Yes:1.27 (0.58-2.81)	0.56
Family systemic disease history (N: Y)	92: 36	Yes:0.69 (0.30-1.61)	0.37
Having any systemic disease (N: Y)	66: 20	Yes:0.50 (0.25-0.99)	*0.03
Other tendon problem (Current: Previous: Never)	15: 32: 81	Current:0.40 (0.15-1.12)	*0.048
Symptoms (N: Y)			
Pain	10: 118	0.85 (0.34-2.12)	0.73

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Stiffness	111: 17	0.95 (0.43-2.08)	0.89
Swelling	101: 27	0.87 (0.45-1.67)	0.66
Pain Onset (Sudden: Gradual)	50: 78	Gradual:0.84 (0.50-1.41)	0.51
Morning pain (N: Y)	35: 93	Yes:0.78 (0.45-1.37)	0.39
Morning stiffness (N: Y)	63: 65	Yes:0.54 (0.32-0.92)	*0.02
Pain at night (N: Y)	81: 47	Yes:0.84 (0.49-1.45)	0.53
Movement effect on symptoms (Get better: Get worse: No effect)	45: 57: 26	Get better:2.82 (1.23-6.48) Get worse:1.54 (0.66-3.58)	*0.02
Movement effect on symptoms (No effect: Effect)	26:102	Effect:2.04 (0.93-4.51)	$0.053
Investigations (N: Y)			
X-ray	102: 26	NA	NA
MRI	37: 91	NA	NA
US	98: 30	NA	NA
Blood Test	125: 3	NA	NA
Physical Examination	56: 72	NA	NA
Medicine (Current: Previous: Never)			
Statin use	0: 1: 127	NA	NA
Glucocorticoid use	0: 1: 127	NA	NA
Fluoroquinolone use	0: 2: 126	NA	NA
Treatment (N: Y)	27: 101	Yes:1.61 (0.76-3.40)	0.19
Footwear changes	100: 28	Yes:1.49 (0.84-2.66)	0.19
Education	115: 13	NA	NA
Provision of information	117: 11	NA	NA
Physiotherapy	41: 87	Yes:1.37 (0.76-2.47)	0.28
Orthoses	120: 8	NA	NA
Injection	86: 42	Yes:1.06 (0.62-1.80)	0.83
Electrotherapy	103: 25	Yes:0.86 (0.45-1.66)	0.65
Medication	89: 39	Yes:1.23 (0.71-2.11)	0.47
Surgery	121: 7	NA	NA
Number of Visits			
General Practitioner	0.75 ± 1.53	NA	NA
Physiotherapist	5.70 ± 4.54	NA	NA
Rheumatologist	0.50 ± 1.67	NA	NA
Occupational Therapist	0.43 ± 1.76	NA	NA
Sport Physician	3.08 ± 3.76	NA	NA
Orthopaedic Surgeon	0.83 ± 2.03	NA	NA
Other	0.36 ± 1.51	NA	NA
Total	11.7 ± 10.0	1.01 (0.99-1.04)	0.34
Others			
Hormonal contraception use (NA: Y: N)	44: 6: 78	Yes:0.30 (0.04-2.20)	0.19
Menopausal status (NA: Pre: Current: Post)	91: 34: 2: 1	NA	NA
Hormone replacement therapy (NA: Y: N)	52: 1: 75	NA	NA
Low back pain presence (Current: Previous: Never)	16: 75: 37	Current:1.38 (0.56-3.39) Previous:1.21 (0.66-2.21)	0.74
Low back pain association with leg pain (N: Y)	99: 29	Yes:0.81 (0.43-1.53)	0.50
Smoking (Active: Passive: Ex-smoker: Never)	38: 16: 13: 61	Active:1.14 (0.63-2.07) Passive:1.53 (0.76-3.09) Ex:0.32 (0.08-1.36)	0.12
Daily sleep time (hours)	7.6 ± 1.0	1.10 (0.86-1.42)	0.46
Sleep difficulty (N: Y)	97: 31	Yes:1.00 (0.55-1.83)	0.99
Feeling rested after sleep (Y: Partially: N)	49: 65: 14	Yes:2.22 (1.33-3.73)	*0.003
D) PSYCHOLOGICAL			
Full availability (N: Y)	56: 72	NA	NA
KOOS - quality of life subscale score (0-100)	53.9 ± 20.5	1.03 (1.02-1.05)	*<0.001
EQ5D5L index score (-1 to 1)	0.76 ± 0.20	28.6 (4.32-189.1)	*<0.001
EQ5D5L VAS score (0-100)	77.3 ± 21.0	1.03 (1.01-1.05)	*<0.001
Pain Catastrophizing score (0-52)	13.8 ± 11.5	0.98 (0.95-1.00)	*0.049
Tampa-11 Kinesiophobia score (11-44)	23.6 ± 6.7	0.94 (0.90-0.97)	*0.001
General Self-Efficacy score (10-40)	31.8 ± 5.1	1.06 (1.01-1.12)	*0.03
Patient recovery predictions			
Get better: Stay the same: Get worse: DNK	80: 19: 9: 20	Get better:1.83 (0.82-4.08) Get worse:1.25 (0.36-4.28) DNK:0.49 (0.14-1.67)	*0.02
If better,			
Confidence on recovery prediction (%) (n=80)	82.3 ± 20.2	1.03 (1.00-1.05)	*0.01
Time prediction (months) (n=55)	4.5 ± 4.8	0.90 (0.81-1.01)	*0.04

Confidence on time prediction (%) (n=54)	75.1 ± 24.4	1.02 (1.00-1.05)	*0.01	

E) SOCIAL

E-Health Literacy score (8-40)	28.9 ± 6.2	1.00 (0.96-1.04)	0.99	
Education level (Did not attend or Elementary school: High school: Undergraduate: Postgraduate)	3: 44: 61: 20	HighSchool:0.58 (0.14-2.46) Undergrad:0.52 (0.12-2.18) Postgrad:0.13 (0.02-0.75)	*0.01	
Work Status (Full time: Part time: N)	65: 17: 46	Full time:1.26 (0.71-2.26) Part time:1.59 (0.71-3.56)	0.50	
Change in work participation (N: Y)	112: 16	Yes:0.66 (0.28-1.54)	0.31	

F) PAIN MAP DRAWING (n=104)

Number of body regions	2.0 ± 1.4	0.86 (0.68-1.09)	0.17	
Number of sites around the knee (anterior/posterior/medial/lateral)	1.8 ± 1.1	0.91 (0.69-1.19)	0.46	
Focal pain on inferior patella pole (N: Y)	40: 64	Yes:1.06 (0.58-1.94)	0.85	
Focal pain on superior patella pole (N: Y)	79: 25	Yes:2.56 (1.42-4.65)	*0.003	
Diffuse pain around the patella (N: Y)	50: 54	Yes:0.61 (0.34-1.10)	$0.10	
Current pain level (VAS)	3.8 ± 2.2	0.94 (0.83-1.07)	0.36	
Usual pain level (VAS)	3.8 ± 2.3	0.96 (0.85-1.10)	0.58	
Pain Type (Pain: Dull aching: Stabbing: Tingling: Electric: Throbbing: Numbness: Burning: Other/Multiple)	69: 16: 7: 0: 1: 4: 1: 3: 3	NA	NA	

Table 19: Final recovery model properties. Dependent variable is recovery vs non-recovery. Hazards ratios were the likelihood of recovery, meaning >1.00 increases the possibility of recovery, while <1.00 decreases the possibility of recovery. Key: HR, hazards ratio; CI, confidence interval; coef, coefficient values.

Independent Variables (n=128)	HR (95% CI)	Beta coef.	Optimism-corrected coef.	P > |z|	Interpretation:
KOOS-Patellofemoral (higher is better)	1.03 (1.02-1.05)	0.033	0.028	<0.001	Lower severity is associated with getting better
Time-off from sport (weeks)	0.93 (0.87-0.99)	-0.072	-0.062	0.03	Longer time-off from sport is associated with less likely to recover
Feeling rested after sleep (Yes)	1.93 (1.13-3.28)	0.655	0.565	0.02	Feeling rested after sleep is associated with getting better
Current other tendon problem (Yes)	0.23 (0.07-0.69)	-1.494	-1.288	0.01	Having current tendon problem other than PT is associated with less likely to recover
Average 3-weekly hours trained	1.05 (1.01-1.10)	0.052	0.045	0.01	Higher training duration is associated with getting better
Movement effect on symptoms (Yes)	2.71 (1.21-6.09)	0.998	0.860	0.02	Change in symptoms with movement is associated with getting better

Model formula: LP=$beta_1 x_1 + beta_2 x_2 + ...$

LP= 0.028(KOOS-Patellofemoral) + (-0.062(Time-off from sport)) + 0.565 (Feeling rested after sleep) + (-1.288(Current other tendon problem)) + 0.045(Average 3-weekly hours trained) + 0.860(Movement effect on symptoms)

Coding: Values for KOOS-Patellofemoral, Time-off from sport and Average 3-weekly hours trained.
No=0, Yes=1 for Feeling rested after sleep, Current other tendon problem and Movement effect on symptoms.

Table 20: Internal validation outputs for the final recovery model.

Final Model Properties	C-statistics	Calibration Slope
Apparent (Original)	0.79	1.000
1000 Bootstrap samples	0.80	1.000
Average Optimism	0.02	0.14
Optimism-corrected	0.77	0.86
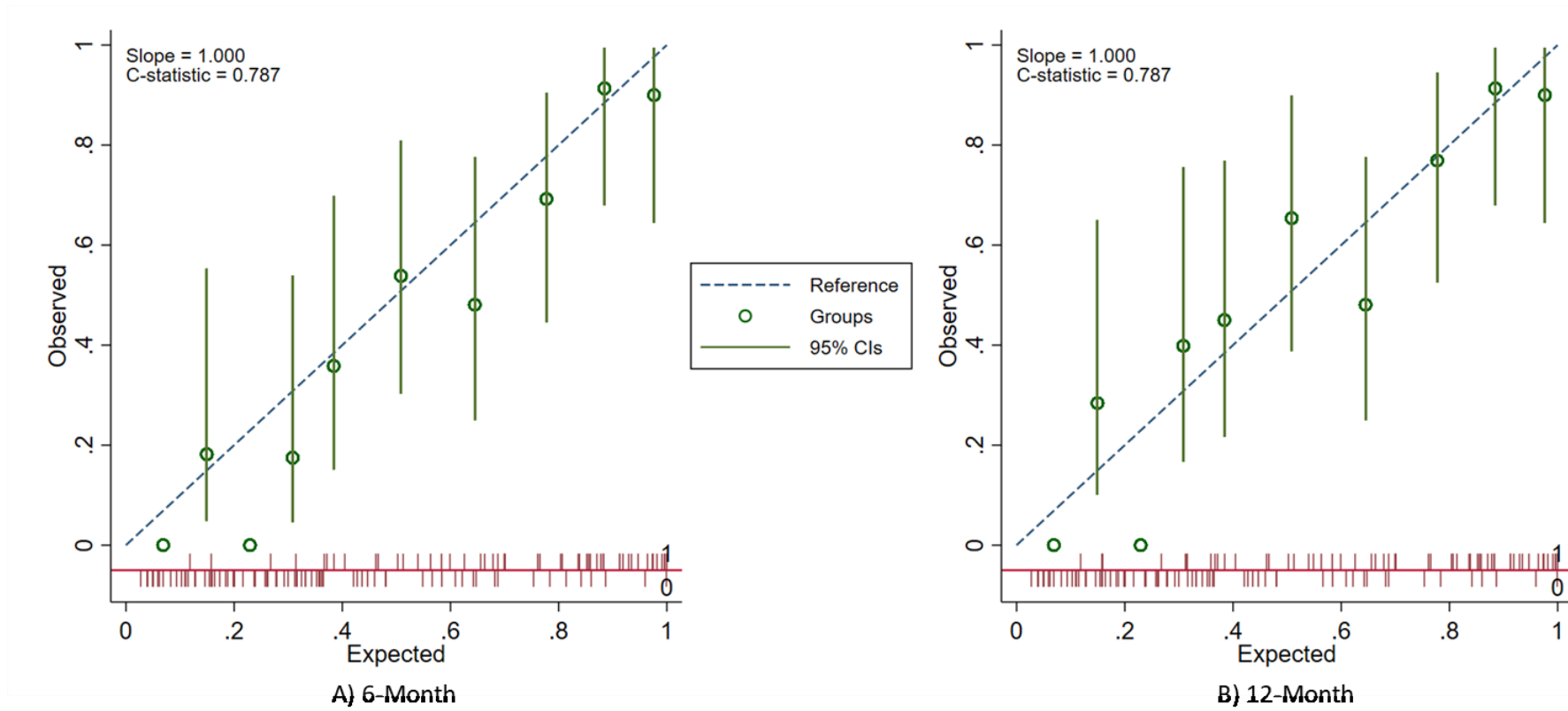
Figure 41: Calibration plot at specific time points; A) 6-month, B) 12-month. 10 groups were established by STATA as a default feature based on range of probabilities. Calibration plot showed that the most of the predictions lied around the 45° reference line.

7.4   Discussion

This is the first study investigating outcome predictors for recovery of patellar tendinopathy (PT) in an international sample of elite and non-elite jumping athletes. Patient reported measurements are easy, cheap and quick to collect (292). An international effort with many collaborators enabled sufficient data collection to build a multivariable model. The statistical causal model showed that the combination of self-reported sports specific and biomedical variables potentially predicted PT recovery. Demographic or psychosocial variables did not contribute to our exploratory recovery model. Having treatment also did not predict recovery. Recovery rate was 45% occurring around 6-month. These findings could support clinical decision making by helping to clarify who gets better, why they get better and when they get better. Our exploratory recovery model is easily applicable in clinical practice as it consists only of self-reported measurements and could help researchers and clinicians to better understand the prognosis of PT in jumping athletes. All predictive factors in the model, except current other tendon problem, are modifiable which could help improve the recovery outcome.

Recovery rates are around 50% for knee conditions (54,55). Only 25% recover after 3 months, increasing to 44% after 12 months has been reported in patients with a new episode of knee complaints (54). PT also has similar unsatisfactory recovery rates, with the highest reported being 65% at 6 months in observational studies irrespective of intervention (4,5). Higher (75%) recovery rates of PT have been reported in soccer players (6,56) resolving in less than a week. In contrast, survival analysis revealed a lower recovery rate being 45% around 6-month in our cohort. Definition of recovery could be the reason of different recovery rates. We defined the recovery with the Global Rating of Change (GRoC) scale and full availability for training and competition, while definition was based on time loss from training or match play in soccer players (6,56). When standard methods of injury registration, typically relying on a "time-loss", are used in epidemiological studies, overuse injuries such as PT are difficult to record (57). Symptoms of PT such as pain or functional limitation generally occur insidiously, and athletes often continue to play through symptoms despite the PT presence (58), hence non-recovery. While improvements have been reported for different treatments in randomised controlled trials, full-recovery was not achieved in terms of VISA-P or VAS scores in either the short- or long-term (59–61). The number of fully recovered people is generally missing in trial reporting which makes it difficult to understand effectiveness or efficacy of an intervention, hence limiting prognostic clarity. Therefore, future research investigating prognosis of PT should take into account relevant definitions and detailed reporting.

Recovery of PT was partially explained in my data, with the combination of a lower severity, a shorter time-off from sport, feeling rested after sleep, not having current other tendon problem, higher training duration and change in symptoms with movement. It is plausible that athletes with less severity are more likely to recover or vice versa. Thus, severity was an expected finding and is an important indicator of the prognosis and clinical decision making, as it is the most commonly used measurement to track prognosis in RCTs and usual care. Time-off from sport and training duration are both very similar predictors as they refer to athlete availability, but there was no multicollinearity between these variables. If athletes are more available to play, they are more likely to recover. This could seem like reverse causality, but we used the information at baseline to predict future outcome. It is possible that athletes may be close to recovery at baseline, hence more available. However, we should consider that recovery is a process rather than a sudden event. Thus, time-off from sport and training duration predicting recovery is plausible.

Good quality sleep has been reported as one of the best promotors of recovery, especially for elite athletes considering their chronic sleep deprivation (324). Growth hormone which plays a substantial role in tissue regeneration and repair is secreted during the non-rapid eye movement (NREM) sleep (325). There is also a reported association between NREM sleep and accelerated healing by decreased oxygen consumption, building proteins, and transporting free fatty acids (325). We assumed that feeling rested after sleep indicates good quality sleep, hence being a plausible predictor of recovery. It is logical that currently having another tendon problem decreases the probability of recovery, as the body dealing with multiple injuries at the same time. This was also consistent for having any systemic disease in the univariate analysis. Longer recovery duration (326) and poor outcome (327) were reported in multiple injuries compared to monotrauma in other fields. The mechanism of change in symptoms with movement is unclear as we did not specifically investigate the type of movement. We assumed that if symptoms could be modified by movement, especially with exercise strategies, athletes are more likely to get better due to responsiveness. Therefore, investigating these sports specific and biomedical factors in usual care might improve the prediction of recovery in JPTs.

We should be cautious about implying prediction. The Bradford Hill criteria (313) were followed as a guide for assessing causality. The most important principle for causality is 'Temporality' which has been achieved through the prospective study design and survival analysis. The model is predictive with ~80% accuracy and has been rigorously internally validated, with biologically plausible relationships having been identified. The criteria currently missing are the external validation and

experimental checking of the model. However, these are further steps in epidemiological studies and their absence does not necessarily mean that our developmental model is not predictive – at least potentially.

As this is the first study investigating outcome predictors for recovery of PT, it is not possible to directly compare our model properties. However, van der Waal et al. (54) investigated the prognosis of new knee complaints (baseline n=251) with self-administered questionnaires at 3 months (89% retention) and at 12 months (81% retention) in general population. They found that four variables; being male, shorter duration of the knee symptoms, less stiffness at baseline and being in menopause predicted better outcome at 3 months with acceptable accuracy (AUC=0.77), while two variables; not having previous knee complaints and less pain at baseline predicted better outcome at 12 months with acceptable accuracy (AUC=0.72) (54). Sex related factors and previous injury presence were the main differences from our model, as these factors did not predict PT recovery, either individually or in combination, in our cohort. The current presence of other tendon problems also differed between models as it was not a predictor in the prognosis model for knee complaints, although they indirectly measured the coexisting musculoskeletal complaints (54). We do not know whether sleep, movement effect on symptoms and training duration actually differed between models, as these factors were not investigated for knee complaints, potentially due to the study sample being from the general population (54), especially for sports specific factors. Regarding similarities, less pain and stiffness could be equivalent to lower severity, while shorter duration of symptoms could be equivalent to time-off from sport in our model. Another similarity was that psychosocial factors also did not contribute to either prognostic model (54). Overall, severity and duration related factors were the most consistent biomedical predictors for both prognosis of knee problems and PT, while coexisting injuries, sleep and sports specific predictors could be more specific to PT prognosis.

The multifactorial nature of sports injuries has been proposed due to complexity of health conditions (300). It arises from the complex interaction between a web of determinants and timescale that differ from one athlete to another instead of the linear interaction between isolated and predictive factors. There were some variables, which despite being individually associated with recovery and/or having a plausible rationale, did not contribute to the final model. For instance, we expected that treatment at baseline could be one of the main predictors of recovery as a recent systematic review (328) reported that various interventions improved VISA-P scores. However, as we discussed earlier, improvement and full recovery are not same which could explain why

treatment was not prognostic. In other words, athletes often continue to play despite PT presence and non-recovery, meaning interventions could help management of the condition with some improvement or maintain tolerable symptoms without resolution. Similarly, it was reported that increased symptoms duration resulted in poorer outcomes in improvement (1% decrease per additional month, p=0.004) regardless of treatment (328). Current condition duration did not predict recovery (binary, p=0.37; continuous, p=0.08) in our cohort, but time-off from sport improved the recovery model as a duration related variable. This suggests that a specific time-off period from the activity seems a better predictor than an overall condition duration for PT. On the other hand, health-related quality of life and self-efficacy individually predicted recovery as expected due to likely chronicity (4,7) and as a cognitive factor that facilitates recovery (283,284), respectively. However, these variables did not contribute to our exploratory recovery model, represents a study strength that arises due to the variety of measures. For instance, we assumed that severity in our recovery model covers or confounds quality of life measures, as our case-control study (Section 6.3.2.3) showed that the quality of life was one of the variables that explains PT severity. Additionally, we used multivariable regression analysis which was suggested (78) to identify outcome predictors while accounting for other pertinent variables, as previous literature (78) mainly consisted of univariate statistical approaches and often yielding conflicting findings. Effectively, confounded or indirectly related measures were identified and removed prior to settling on the final model rather than being retained and misleading the interpretation of results.

The variables in our exploratory recovery model, except current other tendon problem, are modifiable. Several studies (3,328–330) showed that better clinical outcome in PT resulted from exercise strategies, mainly improved pain and function. This matched with severity and change in symptoms with movement in the model, showing clinicians could modify these variables – for example with exercise strategies. Monitoring time-off from sport and training duration could help professionals individualise management strategies. Modification of these time-related variables could be indirect. For instance, modification of both variables could be integrated with severity and load management suggesting a holistic approach. Load management is very important, especially in clinical progression for PT, and it was suggested that correlating severity during training with change on the load is essential (331). Thus, time could be used and modified as an indicator of dose and frequency in the severity and load management either during training or time-off period. Better load and severity management could result in shorter time-off from sport and higher training duration, hence better outcome. Lastly, we could modify feeling rested after sleep by improving sleep quality. Professionals could consider using sleep hygiene education that has been proven to

improve sleep quality in various athletic populations by facilitating sleep, avoiding behaviours that interfere with sleep and managing environmental factors (e.g. light, noise, and temperature) that affect sleep (332–334). Therefore, alongside understanding the prognosis, professionals could also modify the predictors in our model in order to influence and improve PT outcome.

There were limitations that need to be acknowledged for this cohort study. We used self-reported diagnosis of prior consultation with a medical professional, instead of verifying in person to boost recruitment. Although this study has the largest cohort in this field, sample size was still underpowered mainly missing positive events (recovered athletes). Thus, there was not enough data (events) for clustering or building a multivariable model specific to ethnicity or country. Although this is an international cohort study, I did not aim to investigate differences in ethnicity or perform an ecological study with country as a key independent variable. The main reason of international design was to boost data collection to reach large number of athletes and to be able to generalize the findings, with the premise being that the similarities amongst athletes meeting our inclusion criteria would exceed any differences due to country of origin. Underpowered sample size was also the main reason for overfitting. However, robust statistical analysis and clear findings compensate for the heterogeneity and overestimation and enabled model calibration. Another limitation was that we could not include ACWR, patient recovery predictions and pain map variables into multivariable model building due to missing data. The main reasons were the nature of calculation, non-mandatory questions and a second software package that could not be fully integrated from the online survey increasing participant effort. Lack of external validity was another limitation due to not having an external dataset as the whole dataset was used for internal validation. Although bootstrapping method is the best option for internal validation, it requires using the whole dataset for the model building to avoid dividing dataset and losing events, and tests model's internal validity within the dataset. However, it is not feasible to collect an external data within the PhD timeline, and external validity should be done by other researchers to avoid the bias of developers. Therefore, we encourage researchers to assess external validity in future research. The main limitation was the lack of variables from physical examination, imaging and biomechanical assessments which could add more to understanding. These assessments were initiated, and would be expected to give a stronger model, but data collection had to be curtailed due to the COVID-19 pandemic.

7.5   Conclusion

This is the first study investigating outcome predictors for recovery of PT in a large international sample of elite and non-elite jumping athletes. The statistical causal model showed that the combination of sports specific and biomedical variables were potentially predictive of recovery. Demographic or psychosocial variables did not contribute to the model. The findings are generalizable because of the uniquely large sample size, diverse range of analysed variables enabling multivariable survival analysis and relevant international sample of elite and non-elite athletes (78). Our exploratory recovery model is easily applicable in clinical practice and could help researchers and clinicians to better understand PT prognosis, and we encourage researchers to assess model reproducibility in future research. All predictive factors in the model, except current other tendon problem, are modifiable which could help better management of jumping athletes with patellar tendinopathy, hence improve the recovery outcome. These findings could support clinical decision making by helping to clarify who gets better, why they get better and when they get better.

8   Discussion and conclusion

The presentation and progression of patellar tendinopathy (PT) in jumping athletes is poorly understood. One of the reasons for this lack of clarity is the absence of statistical models including a wide range of factors plausibly associated with PT. This PhD thesis explored PT presentation in jumping athletes and outcome prediction for PT recovery (Figure 42). The systematic review identified that landing biomechanics might be associated with PT presence, but the level of evidence was limited with a high risk of bias. I therefore focused on conducting a prospective cohort study to establish multi-factorial causality which included biomechanical factors such as workload and a wide range of other bio-psycho-social factors. Validity, reliability and feasibility of the online questionnaire battery, physical examination, US imaging and biomechanical measures for the cohort study were established with the feasibility study. However, physical examination, imaging and biomechanical assessments had to be curtailed due to the COVID-19 pandemic.

The analysis of the online questionnaire battery revealed a complex relationship between athlete groups, pain, function and availability (Figure 43). Within our case-control study, the jumping athletes with PT (JPTs) reported playing more despite having equal severity to those with other knee problems yet are less satisfied with their symptoms. Within JPTs, sports specific function and player level partially explained sporting availability, while quality of life, sports specific function and age partially explained PT severity. The prospective cohort study showed that PT recovery was partially predicted with the combination of severity, time-off from sport, sleep quality, other tendon problem presence, training duration, and movement effect on symptoms (Figure 43). In contrast to PT presence, demographic or psychosocial variables did not contribute to the recovery model. Our exploratory models are readily applicable in clinical practice, and could support clinical decision making by helping researchers and clinicians to better understand how JPTs present and progress. The model merits prospective validation. The overarching aim of this thesis was achieved by building these statistical models that explained how PT presents in jumping athletes, predicted PT outcome and are potentially Figure 43 for clinic (Figure 43).
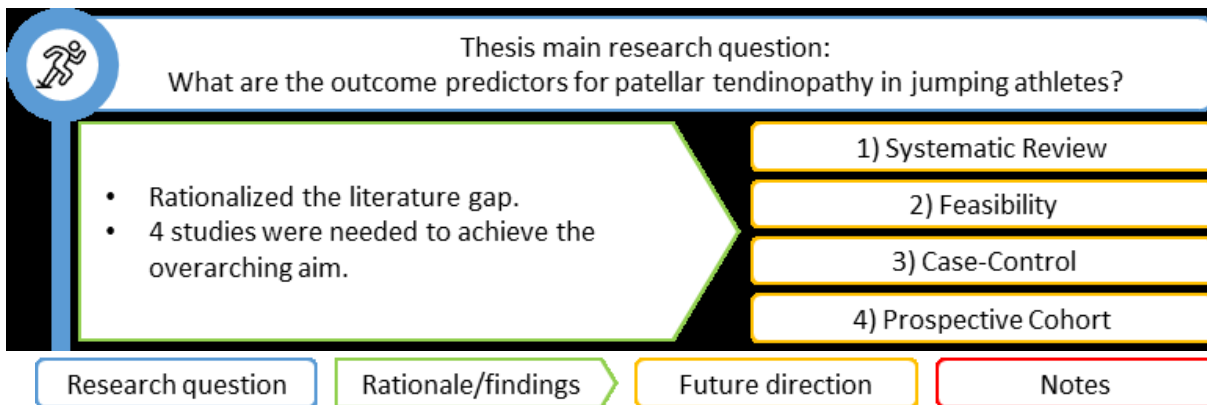
Figure 42: Thesis overall story diagram established by the work completed in relation to overarching aim.

Due to the complexity of the health conditions such as PT, building multivariable models would be superior to using a single variable in order to understand and explain the nature of the condition, and to predict outcome. This better mimics clinical reasoning, and was evident in the case of shoulder pain as multivariable model predicted non-recovery better than a single variable (158). Bittencourt et al. (300) also proposed multivariable approaches to sports injuries because of the complex interaction between the constituent elements of the web of determinants and timescales that differ from one athlete to another rather than simplistic interactions between isolated factors. However, in the field of PT as a common sports injury, the multivariable approach was lacking as van der Worp et al. (78) reported that the literature mainly consisted of univariate statistical approaches in their systematic review on PT onset. After recommendation of multivariable approach (78), trend of univariate approach shifted in the field as multivariable approach is growing (68,69,71,72,128,135) in the recent literature with few univariate exceptions (79,113), mainly for the development of PT. Effectively, the multivariable approach allows researchers to identify confounders or covariates and remove them prior to settling on the final model rather than retaining them and reaching a misleading interpretation. Therefore, using a model could enable clinicians to understand the condition better and improve decisions, and this PhD represents the first investigating both presence and prognosis of PT with multivariable analyses.

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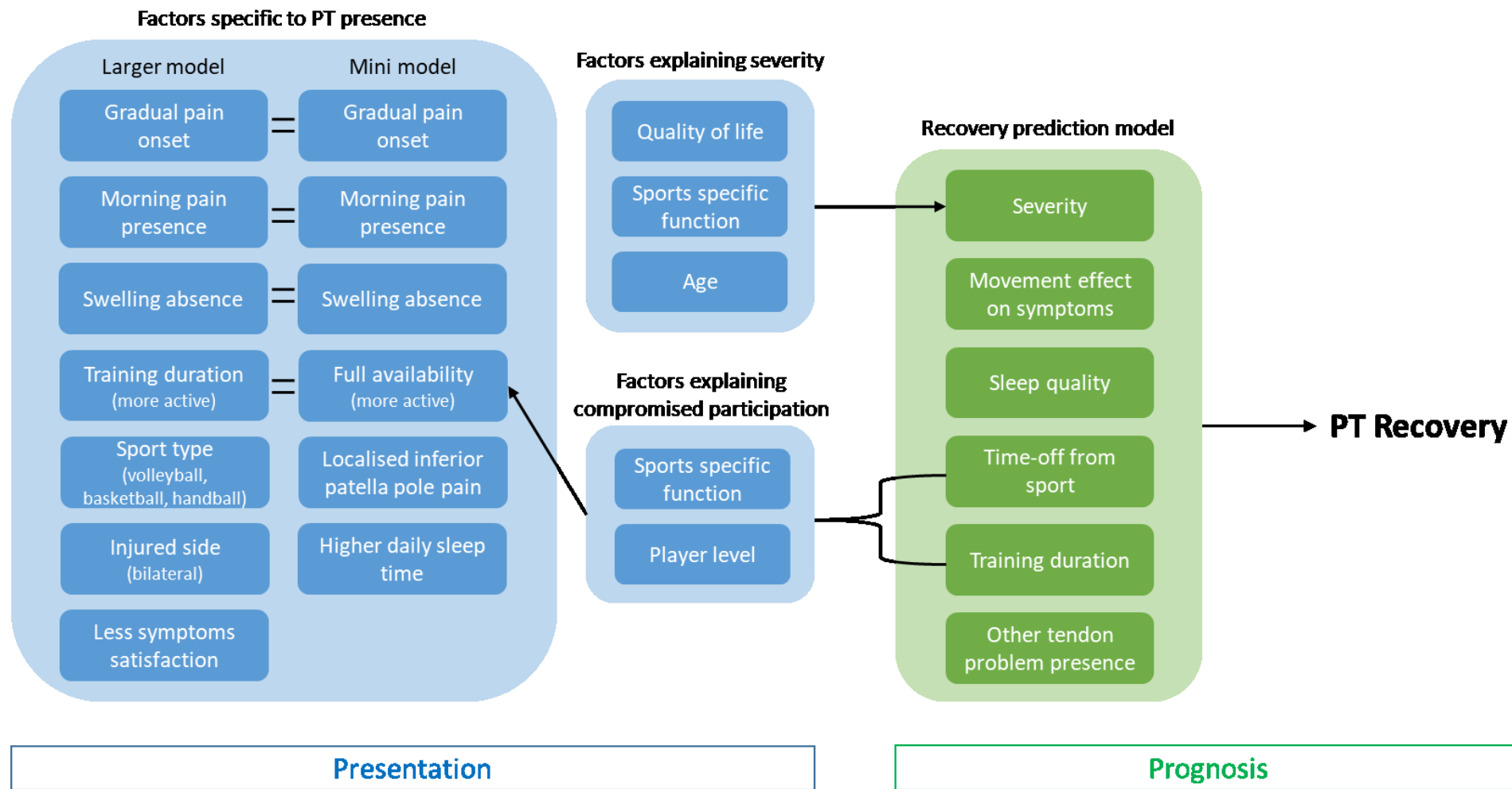
Figure 43: Outcome predictors for PT in jumping athletes. Keys: PT; patellar tendinopathy.

Specifically, the systematic review had the aim of determining whether jump-landing biomechanics are altered among JPTs and can predict onset. Previous literature (78,96,99,160) suggested mechanical explanations and potential associations between landing patterns and PT onset and presence. Thus, I hypothesized that there is a strong level of evidence with low risk of bias showing an association between jump-landing biomechanics and PT in jumping athletes. However, the alternative hypothesis was rejected as the evidence of identified associations were mainly limited with high risk of bias (335). The systematic review also showed that the existing literature is currently insufficient for robust recommendations in usual care, and causal relationships are scarce due to the absence of prospective studies, there being only one cohort with a problematically small sample size of JPTs (64). The main limitation of our systematic review was high variability of the existing literature in terms of differences in the tasks implemented, population or variable of interest measured.

Van der Worp et al. (2014) (99) conducted the first systematic review on this topic with six studies reporting horizontal landing kinematics potentially linked to PT onset. While I was finalising the review, two more systematic reviews (161,162) were published. Harris et al. (2020) (161) reported 37 biomechanical variables to be associated with PT with 15 studies. De Bleecker et al. (2020) (162) investigated only jump-landing kinematics for a range of lower extremity overuse injuries with meta-analysis, including nine reports specific to PT, which concluded that the kinematic associations with PT are poorly understood. However, no recent comprehensive review has scoped the literature to demonstrate evidence gaps, graded the evidence, assessed the risk of bias and pooled data. Our systematic review with 16 studies equating to a ~20% source material difference (three different included papers to review by Harris et al.) addressed these deficits. I have produced an evidence gap map that shows the pattern of work that has, and has not, been done in this field (335). This map is a key translational output and shows both the findings and where suitable work has not been performed.

The systematic review had the impact of guiding the future research by providing evidence gaps in the available literature and suggesting potential roles of non-biomechanical factors. Therefore, I concluded that high quality prospective cohort studies are essential to establish multi-factorial causality including both biomechanical and non-biomechanical factors (Figure 44). It is important to determine methodological design in such a complex epidemiological study. STROBE (277) and PROBAST (235) give useful guidance on the constituent elements of a high-quality epidemiological studies. These elements mainly consist of recruitment, selection of variables, outcome definition,

data collection, data processing and statistical analysis. Additionally, good examples in the literature for high quality prospective studies (69,128,135,336) were checked to observe applications with real data in terms of recruitment and retention strategies, variables of interest, data collection and analysis. Therefore, in addition to the existing literature, key guidelines were followed to improve the quality and reduce the risk of bias in order to facilitate the success for designing, conducting and reporting of our prospective cohort study.

Figure 44: Thesis overall story diagram established by the work completed in relation to aim of systematic review. Keys: PT; patellar tendinopathy.

Feasibility study had the primary aim of testing data collection procedures to optimise the success of the planned international prospective cohort study. The secondary aim was to test measurements validity and reliability. I hypothesized that data collection procedures of the planned cohort study are feasible, valid and reliable. This study represents the first to test the online use of most of the questionnaires (e.g. KOOS, EQ5D5L, PCS, TSK, GSE) and showed them to be valid, reliable, and feasible for remote use (278). It was reported (236,337) that paper-based PROMs adapted to online use are equivalent or even superior to original paper version. Online use of questionnaires offers many advantages over paper version such as easier participant access, lower cost, faster completion and efficient data management (260,337). Thus, it is important to collect valid and reliable data remotely in large population based epidemiological studies to decrease the burden and cost of data collection. The importance of remote data collection also became obvious during the COVID-19 pandemic. For instance, guidelines recommended limiting direct contact

between therapists and patients with COVID-19 and proposed using telerehabilitation options (338,339) which include assessment, monitoring, prevention, intervention, supervision, education, consultation, and coaching (340). Therefore, increased need for telerehabilitation during COVID-19 pandemic warranted readily applicable remote online tools.

On the other hand, findings from the feasibility study suggested that the clinical, ultrasound and biomechanical assessments should yield useful predictive findings. I also introduced a novel graded loaded challenge (GLC) which may represent a valid and reliable clinical measurement (278), but further testing is needed to confirm its utility. Although load dependent pain is an important diagnostic criteria of PT (23), there is no progressive condition-specific movement set as a validated clinical test to indicate PT severity in the literature. However, we are seeing papers like Gulle et al. (341), Gheidi et al. (342) and Baxter et al. (343) that are developing GLC in other musculoskeletal conditions. The single leg decline squat test (29) is the most common approach to test load dependent PT pain. However, this approach does not grade PT severity and does not address all movement patterns related to PT as it is a single movement pattern. In our novel GLC, we incorporated vertical and horizontal jump-landing activities in addition to squat to grade the severity by establishing progressively higher load and speed demands from double leg to single leg activities. The impact of the GLC would be assessing change in PT severity over time, before and after treatment which could improve management strategies for PT.

Overall, the cohort study plan was feasible with amendments and the alternative hypothesis of the feasibility study was accepted. To improve overall feasibility, the protocol was trimmed to reduce the time burden and improve data quality. The main limitation of the feasibility study was that the follow-up process for the online questionnaire battery could not be tested, hence the issue of retention could not be addressed, required within-study development due to timelines. Feasibility study had the impact of providing useful information about data collection procedures with detailed measurement properties for researchers, especially online use compared to traditional. For this thesis, impact of the feasibility study was guiding the necessary amendments to optimise the planned cohort study success (Figure 45).
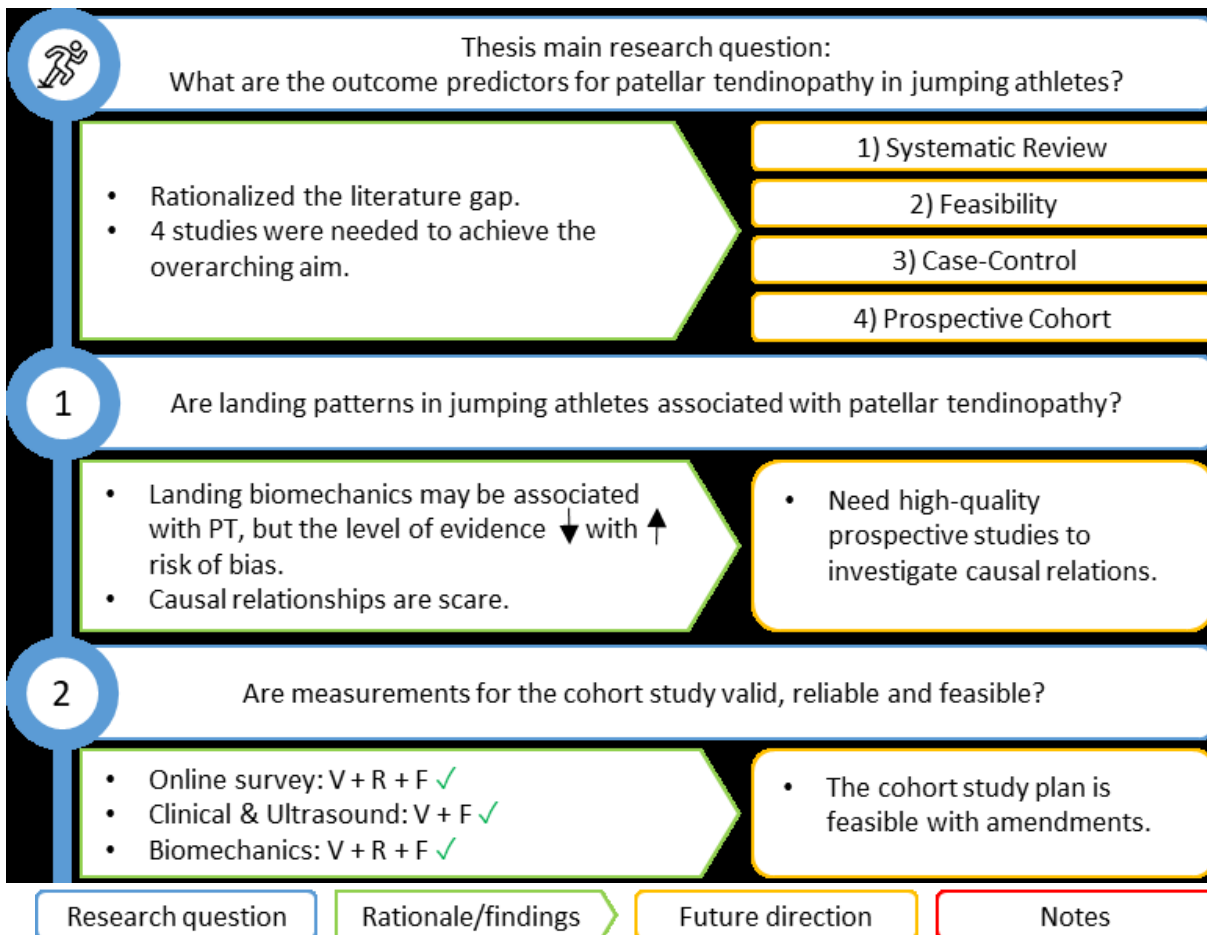
Figure 45: Thesis overall story diagram established by the work completed in relation to aim of feasibility study. Keys: PT; patellar tendinopathy; V; validity, R; reliability; F, feasibility; ✓, meets criterion.

Case-control study had the primary aim of determining what combination of self-reported factors distinguishes JPTs from those with other knee problems. The secondary aim was to investigate PT severity as defined either by condition severity or sporting availability. Due to the proposed multifactorial nature of sports injuries (300), I hypothesized that multivariable statistical regression models distinguish PT from other knee problems and explain both the variance of condition severity and compromised participation. There is an important distinction between diagnosis and assessment that has led to the careful choice of words. In our case control study, I used the word 'distinguish' to perceive a difference between characteristics of jumping athletes with PT presence and those with other knee problems. As we discussed earlier, the commonality of associated factors between PT and other knee conditions existed in the literature. Therefore, I primarily looked for factors that are specific to PT presence, rather than investigating their diagnostics roles between PT and other knee problems.
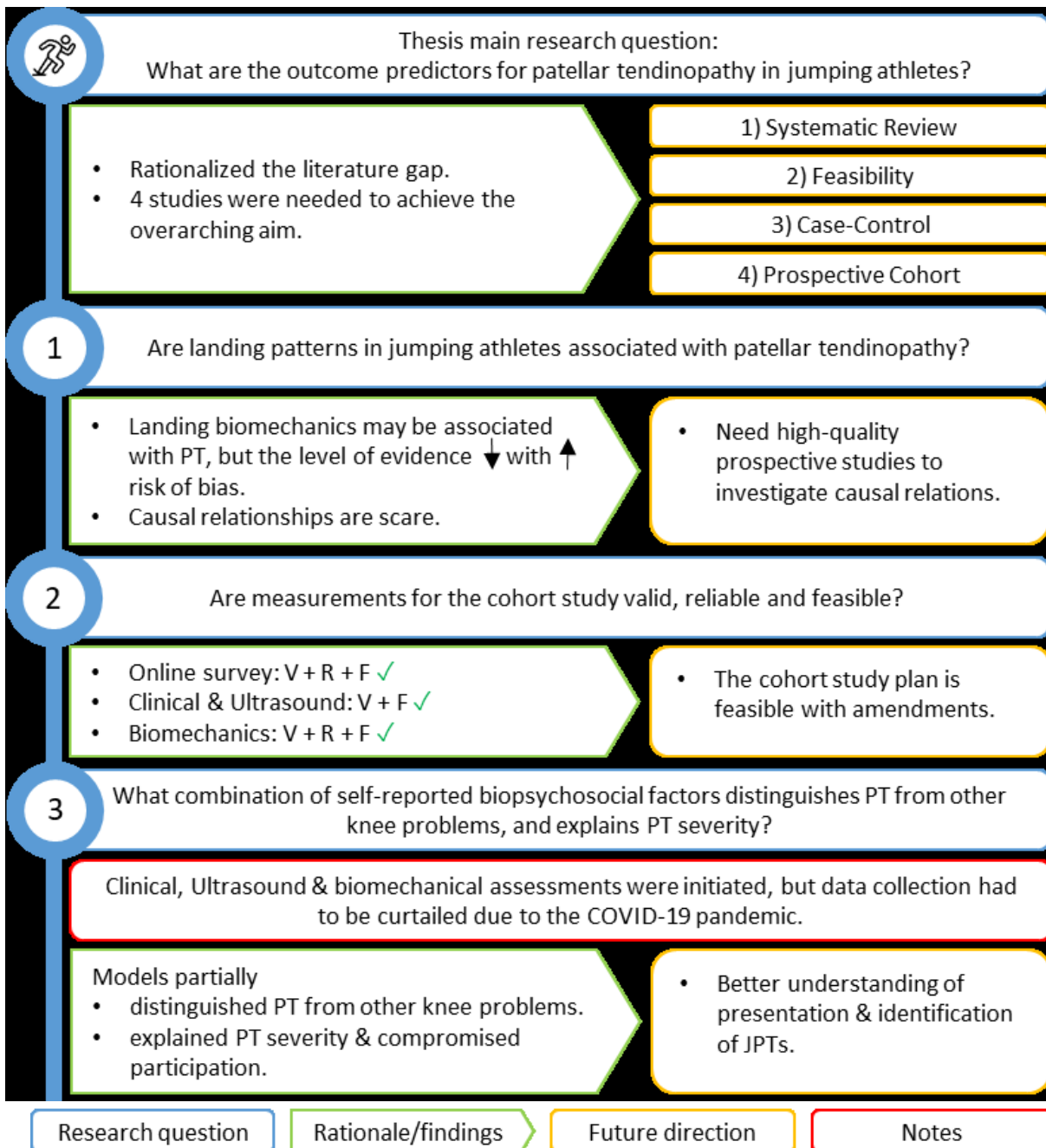
Figure 46: Thesis overall story diagram established by the work completed in relation to aim of case-control study. Keys: PT; patellar tendinopathy; V; validity, R; reliability; F, feasibility; ✓, meets criterion; JPTs, jumping athletes with PT.

This case-control represents the first to investigate factors specific to PT presence and to explain the variance of PT severity by using multivariable modelling approach. An international effort with many collaborators enabled sufficient data collection to build multivariable models. I found that various self-reported sports specific, biomedical and psychological factors partially distinguish PT from other knee problems (Figure 43), in other words these factors were specifically associated with PT presence. This study also showed that availability is mainly explained by sports specific factors, while psychosocial factors impact on severity (Figure 43). Thus, the alternative hypothesis was accepted and these findings suggest that adding sports specific and bio-psycho-social assessments

into athlete monitoring in at-risk cohorts, individual assessment and future research will likely improve our understanding of the presentation in JPTs. Therefore, case-control study will have the primary impact of informing clinical profiling that leads to a better understanding of presentation and identification of JPTs (Figure 46). The secondary impact will be providing deeper explanation of the variance in PT severity, hence better management of the condition.

Prospective cohort study had the aim of determining what combination of self-reported factors predicts PT recovery in order to improve the understanding of PT prognosis. I hypothesized that multivariable statistical survival model predicts PT outcome. This is the first cohort investigating outcome predictors for recovery of PT in an international sample of elite and non-elite jumping athletes. With survival analysis, this cohort revealed that poor recovery outcome (45% ~6-month) for PT was evident with carefully established recovery definition taking into account sporting availability. The novel exploratory causal model showed that the combination of self-reported sports specific and biomedical variables partially predicted PT recovery, while demographic or psychosocial variables did not contribute to the model (Figure 43). Therefore, the alternative hypothesis was accepted and our exploratory recovery model could help researchers and clinicians to better understand PT prognosis in jumping athletes.

Another contribution to existing literature is that I provided the outcome predictors to professionals, so they can focus on these factors and modification could potentially influence prognosis. With clinical decisions informed by an individual's profile of predictor values, a strong link between the use of prognostic models and personalized or stratified healthcare has been reported (304–306). Precision medicine is a major research goal of major funders (e.g. NIHR Biomedical Research Centres call currently underway) and has realised major advances in outcomes for many conditions such as cancer and rheumatoid arthritis - the latter led from our centre at QMUL (344). It is important to assist clinicians with their prediction of a patient's future outcome by using prognostic models in order to enhance clearer communication with the patient and informed decision making together (304,307). On the other hand, knowing the likely course of the condition might also help JPTs to come to terms with, and plan for, the future (308). It is critical to have knowledge of the risk of worse outcomes or the likelihood of self-resolution of symptoms in predicting and planning the likely effect of management (309). Thus, cohort study will have the impact of providing an explanation of PT recovery, hence better understanding of PT prognosis and management of JPTs (Figure 47). Therefore, outputs from this cohort could support clinical decision making by helping to clarify who gets better, why they get better and when they get better.
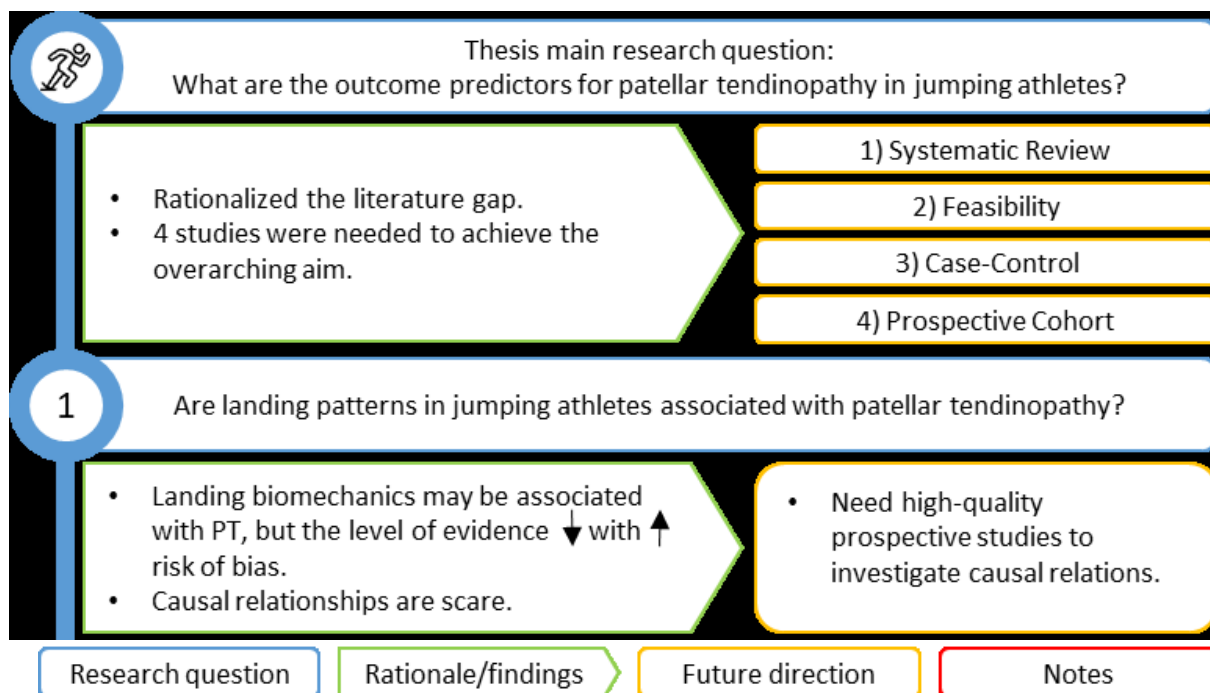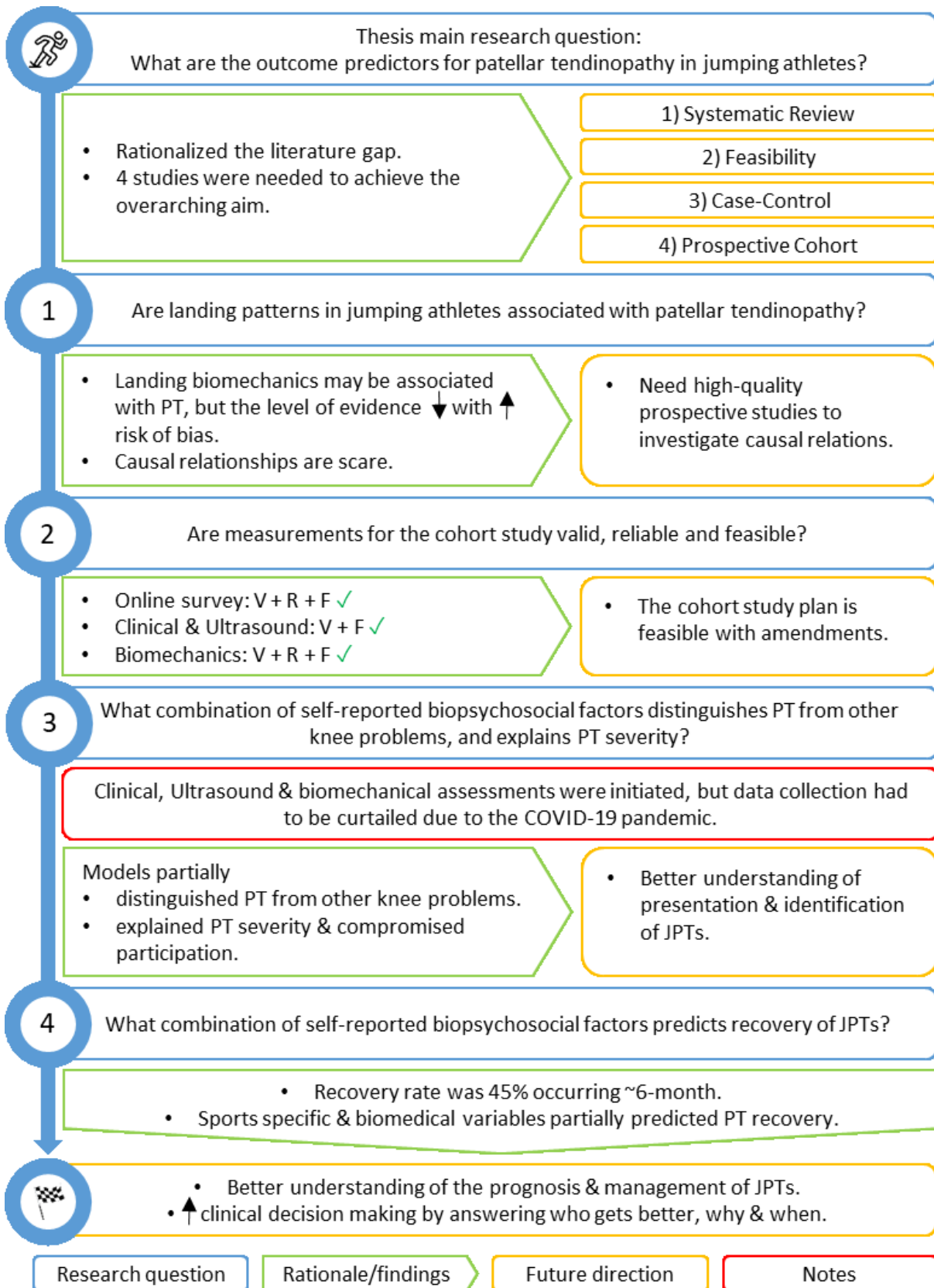
Figure 47: Thesis overall story diagram established by the work completed in relation to aim of prospective cohort study. Keys: PT; patellar tendinopathy; V; validity, R; reliability; F, feasibility; ✓, meets criterion; JPTs, jumping athletes with PT.

This PhD had limitations that need to be acknowledged. A limitation for the feasibility, case-control and cohort studies was that diagnosis was established by self-report of prior consultation with a

medical professional, instead of verifying in person. This was a deliberate decision in order to facilitate recruitment of a large number of international athletes. Although this PhD has the largest cohort of international JPTs, it was underpowered due to the low number of recovery events. This was also the main reason for overfitting, as our recovery model barely provided the minimum requirement of 10 'events per variable' of interest (190) with 58 recovered athletes and six variables in the model giving 9.7 events per variable. However, robust statistical analysis allowed addressing overestimation by adjusting model calibration. The main limitation for the overall PhD was the COVID-19 pandemic, especially influenced case-control and cohort studies. My thesis was relying on data collected from three sources – online survey, clinical measures (stopped) and laboratory measures (also stopped). During this pandemic, the Tendon clinic (NHS Trust) and QMUL Human Performance Laboratory have been closed. Also, my PhD project included recruiting people from the NHS. I had an NHS amendment for recruiting in five different NHS sites, which was also halted. These mainly affected my biomechanical and clinical data collection, and existing data was not enough (clinical: n=35, 10 with PT and biomechanics: n=11, 3 with PT) to be used in the analyses. Therefore, variables from physical examination, imaging and biomechanical assessments were lacking from the analyses.

8.1   Future directions

This PhD clearly showed that how definitive, adequately powered, well-designed prospective cohort studies with self-reported measurements and adequate follow up could improve our understanding of multifactorial relationships when determining outcome predictors for PT presence and prognosis. We encourage researchers to test external validity, hence reproducibility, in order to confirm established exploratory recovery model(s). Future work should also consider focusing on whether clinical, imaging and biomechanical factors play a part in explaining PT presence and/or predicting recovery. For instance, adding physical examinations such as strength, flexibility, range of motion and functional tests could improve the clinical symptom presentation, while imaging could help to explain associations between tendon structural changes and prognosis. Adding biomechanical factors such as patellar tendon force, knee moment, landing stiffness and lower limb joint kinematics could add more to understanding of loading on the tendon and altered movement patterns. It is highly likely that some of these additional factors may confound some of the variables in the current model, but evaluating these by self-report would still be desirable, perhaps prior to initial or remote consultation. Future prospective cohort studies could also investigate PT recurrence, as explanation of PT re-injury remains scarce despite the high prevalence of recurrence.

Future randomised controlled trials (RCT) could integrate our established models to improve the interpretation of their findings. For instance, checking study groups, different interventions, with the outcome predictors from established models could help to explain better or worse outcome. With this approach, future research could explain whether the different outcomes are actually due to interventions or population characteristics. Thus, researchers could also use outcome predictors as matching criteria to test actual efficacy and effectiveness of the interventions. Lastly, with the recent development of machine learning and artificial intelligence in medical research, future research could focus on dissemination of model usability by establishing websites (e.g. http://calculator.oarisk.org/) or mobile applications in order to ease screening and monitoring in tendinopathy usual care.

Personally, conducting this PhD taught me so much about epidemiology. As a physiotherapist, this was the first time I systematically and academically focussed on a bigger picture such as associations and causality, instead of applying examinations and treatments based on clinical reasoning driven by personal work experience. Especially, establishing international collaborations, collecting a large international data, and managing a huge dataset with robust statistical approaches were my biggest achievements. This PhD also gave me a chance to prove myself as an academic with two publications in good journals and several international conference presentations. My next personal step is to become a clinical-academic in order to produce publishable work, improve skills and knowledge as a researcher, and incorporate this into my clinical approach.

8.2 Conclusion

The overarching aim of this PhD thesis was achieved by building statistical models that explained how PT presents in jumping athletes, predicted PT outcome and are potentially useful for clinic. This PhD represents the first to investigate factors specific to PT presence, to explain the variance of PT severity and to determine the predictors for PT prognosis by using multivariable modelling approach in a large international cohort of elite and non-elite jumping athletes. Jumping athletes with PT play more despite having equal severity to those with other knee problems yet are less satisfied with their symptoms. Sporting availability is mainly explained by sports specific factors, while psychosocial factors impact on severity. The developmental statistical causal model showed that the combination of sports specific and biomedical variables were potentially predictive of PT recovery. In contrast to PT presence, demographic or psychosocial variables did not contribute to the recovery model. Our exploratory models are readily applicable in clinical practice, and could

support clinical decision making by helping researchers and clinicians to better understand how jumping athletes with PT present and progress, likely leading to better management of the condition. Therefore, this thesis will have the impact of improving clinical decision making and practice by clarifying who gets better, why and when.

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10 Appendices

Appendix 1: Full version of the completed Skill Point Database.

Activity Record

Type	Code	Title	Provider	From	To	Hours	A	B	C	D	Total
School/Institute Induction		Sports & Exercise Medicine Induction Day	WHRI	25-Eyl-2017 00:00	25-Eyl-2017 00:00	0,0	1,0	1,0	1,0	1,0	4,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	27-Eyl-2017 00:00	27-Eyl-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)	WHR6026	Literature Reviewing Lecture	WHRI	27-Eyl-2017 00:00	13-Ara-2017 00:00	24,0	24,0	0,0	0,0	0,0	24,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)	WHR7026	Research Methods Lecture	WHRI	28-Eyl-2017 00:00	14-Ara-2017 00:00	24,0	24,0	0,0	0,0	0,0	24,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Introduction to MSK Ultrasound Imaging Course	SMUG	29-Eyl-2017 00:00	30-Eyl-2017 00:00	14,0	14,0	0,0	0,0	0,0	14,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	04-Eki-2017 00:00	04-Eki-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Other course/event attendance	EAL4710	Reading and Writing Critically	Language Centre	05-Eki-2017 00:00	14-Ara-2017 00:00	0,0	20,0	0,0	0,0	0,0	20,0
Conference Attendance (Two days)		The Second World Congress of Sports Physical Therapy	IFSPT	06-Eki-2017 00:00	07-Eki-2017 00:00	0,0	6,0	4,0	0,0	0,0	10,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	11-Eki-2017 00:00	11-Eki-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Other course/event attendance		PG Tips	Doctoral College	18-Eki-2017 00:00	18-Eki-2017 00:00	0,0	0,0	1,0	0,0	0,0	1,0
Mentoring/supervising of Project Student		Mentoring of iBSc Student Research Project	PhD Supervisor	18-Eki-2017 00:00	14-Ara-2017 00:00	0,0	2,0	1,0	0,0	2,0	5,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	18-Eki-2017 00:00	18-Eki-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Doctoral College event/course	DC100	PhD Induction	Doctoral College	24-Eki-2017 09:30	24-Eki-2017 17:00	0,0	0,0	2,0	3,0	2,0	7,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Push to Web Survey	City University of London	25-Eki-2017 00:00	25-Eki-2017 00:00	1,0	1,0	0,0	0,0	0,0	1,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Introduction to Good Clinical Practice eLearning (Primary Care)	NIHR	27-Eki-2017 00:00	28-Eki-2017 00:00	4,0	4,0	0,0	0,0	0,0	4,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	07-Kas-2017 00:00	07-Kas-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Conference Attendance (Three days)		9th Turkish Sports Physiotherapists Congress	Turkish Sports Physiotherapists Association	09-Kas-2017 00:00	11-Kas-2017 00:00	0,0	9,0	6,0	0,0	0,0	15,0
Conference Presentation (Oral)		Sports Specific Performance Tests for Volleyball	Turkish Sports Physiotherapists Association	11-Kas-2017 00:00	11-Kas-2017 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	15-Kas-2017 00:00	15-Kas-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	22-Kas-2017 00:00	22-Kas-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	29-Kas-2017 00:00	29-Kas-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Researcher Development Course	RD104	Critical Thinking	QMUL	05-Ara-2017 10:00	05-Ara-2017 13:00	0,0	3,0	0,0	0,0	0,0	3,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	06-Ara-2017 00:00	06-Ara-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Tendinopathy Lecture	KCL & PhD Supervisor	06-Ara-2017 00:00	06-Ara-2017 00:00	2,0	2,0	0,0	0,0	0,0	2,0

Activity Record

Type	Code	Title	Provider	From	To	Hours	A	B	C	D	Total
Other course/event attendance		Teaching Exercises & ACL Event	PhD Supervisor & International Speakers	12-Ara-2017 00:00	13-Ara-2017 00:00	0,0	4,0	2,0	0,0	2,0	8,0
Researcher Development Course	RD004	Endnote for Medicine and Dentistry	QMUL	12-Ara-2017 10:00	12-Ara-2017 12:00	0,0	2,0	0,0	0,0	0,0	2,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisior	13-Ara-2017 00:00	13-Ara-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	20-Ara-2017 00:00	20-Ara-2017 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Other course/event attendance		Patient and Public Involvement: Inspiring New Researchers - PILOT (eLearning)	NIHR	23-Ara-2017 00:00	23-Ara-2017 00:00	0,0	2,0	0,0	0,0	0,0	2,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		The Basics of The Coda Technology and How to Use It	Codamotion & PhD Supervisor	03-Oca-2018 00:00	03-Oca-2018 00:00	6,0	6,0	0,0	0,0	0,0	6,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	10-Oca-2018 00:00	10-Oca-2018 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Odin/Gait and force plate/EMG integration	Codamotion & PhD Supervisor	10-Oca-2018 00:00	10-Oca-2018 00:00	5,0	5,0	0,0	0,0	0,0	5,0
Mentoring/supervising of Project Student		Mentoring of iBSc Student Research Project	PhD Supervisor	15-Oca-2018 00:00	11-Haz-2018 00:00	0,0	2,0	1,0	0,0	2,0	5,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	17-Oca-2018 00:00	17-Oca-2018 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Other CPD course	GCP009	Good Practice for Interventional studies	Joint Research Management Office	17-Oca-2018 12:30	17-Oca-2018 17:00	0,0	0,0	0,0	4,5	0,0	4,5
Internal Presentation (< or =30 mins)		PhD Project Presentation	PhD Supervisor	19-Oca-2018 00:00	19-Oca-2018 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Researcher Development Course	RD019	Writing a Scientific Abstract	Researcher Development	19-Oca-2018 10:00	19-Oca-2018 11:00	0,0	0,0	0,0	0,0	1,0	1,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	24-Oca-2018 00:00	24-Oca-2018 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Researcher Development Course	RD204	Managing your time and workload effectively in a research environment	QMUL	30-Oca-2018 10:00	30-Oca-2018 13:00	0,0	0,0	2,0	1,0	0,0	3,0
Journal Club/Reading Group/lab meeting/mentoring group - attendance		PhD Weekly Meeting	PhD Supervisor	31-Oca-2018 00:00	31-Oca-2018 00:00	2,0	1,0	0,0	0,0	0,0	1,0
Researcher Development Course	RD302	Preparing for Your Viva	QMUL	01-?ub-2018 13:30	01-?ub-2018 16:30	0,0	0,0	0,0	1,0	2,0	3,0
Internal Presentation (< or =30 mins)		PhD Project Presentation	PhD Supervisor	07-?ub-2018 00:00	07-?ub-2018 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Researcher Development Course	RD203	Reading Strategically and Analytically	QMUL	12-?ub-2018 14:00	12-?ub-2018 17:00	0,0	3,0	0,0	0,0	0,0	3,0
Standard Ethical Approval		QMREC2014/24/136	QM ERC	19-?ub-2018 00:00	01-May-2019 00:00	0,0	3,0	0,0	9,0	3,0	15,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Epidemiology: The Basic Science of Public Health	Coursera	19-?ub-2018 00:00	19-Mar-2018 00:00	6,0	6,0	0,0	0,0	0,0	6,0
Standard Ethical Approval		QMREC2014/24/153	QM ERC	01-Mar-2018 00:00	01-May-2019 00:00	0,0	3,0	0,0	9,0	3,0	15,0
Researcher Development Course	RD109	Speed-reading for Researchers	QMUL	06-Mar-2018 09:30	06-Mar-2018 12:30	0,0	0,0	3,0	0,0	0,0	3,0
Conference Attendance (One day)		6th Annual Foot & Ankle Conference	AFAP	17-Mar-2018 00:00	17-Mar-2018 00:00	0,0	3,0	2,0	0,0	0,0	5,0
Conference Attendance (Two days)		Sports Traumatology and Rehabilitation Congress	Uskudar University	30-Mar-2018 00:00	31-Mar-2018 00:00	0,0	6,0	4,0	0,0	0,0	10,0
Conference Presentation (Oral)		Rehabilitation of Isolated MCL Injuries	Uskudar University	30-Mar-2018 00:00	30-Mar-2018 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Researcher Development Course	RD014	Project Management for Researchers	QMUL	12-Haz-2018 10:00	12-Haz-2018 17:00	0,0	0,0	3,0	3,0	0,0	6,0

Activity Record

Type	Code	Title	Provider	From	To	Hours	A	B	C	D	Total
Internal Presentation (< or =30 mins)		Ten Thousand Tendons (3T) Project Presentation	PhD Supervisor	04-Tem-2018 00:00	04-Tem-2018 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Conference Attendance (One day)		20th Annual Conference in Sport&Exercise Medicine	Centre for Sports and Exercise Medicine, QMUL	14-Eyl-2018 00:00	14-Eyl-2018 00:00	0,0	3,0	2,0	0,0	0,0	5,0
Mentoring/supervising of Project Student		Mentoring of MSc Student Research Project	PhD Supervisor	24-Eyl-2018 00:00	21-Ara-2018 00:00	0,0	2,0	1,0	0,0	2,0	5,0
Conference Attendance (Three days)		5th International Scientific Tendinopathy Symposium	University Medical Center Groningen	27-Eyl-2018 00:00	29-Eyl-2018 00:00	0,0	9,0	6,0	0,0	0,0	15,0
Conference Presentation (Poster)		Are Jump Landing Patterns Associated with Patellar Tendinopathy in Competitive Athletes? - A Systematic Review	University Medical Center Groningen	28-Eyl-2018 00:00	28-Eyl-2018 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Conference Presentation (Poster)		Patellar Tendinopathy Outcome Predictors in Competitive Athletes: Feasibility for a Cohort Study	University Medical Center Groningen	28-Eyl-2018 00:00	28-Eyl-2018 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Doctoral College event/course	DC102	International PhD Student Welcome	Doctoral College	08-Eki-2018 13:30	08-Eki-2018 17:00	0,0	0,0	1,0	1,0	1,0	3,0
Researcher Development Course	RS125	Introduction to Statistics and R	Researcher Development	31-Eki-2018 09:00	05-Ara-2018 12:00	0,0	15,0	0,0	0,0	0,0	15,0
Ethical Approval (standard, not fast-track)		QMERC2018/92	QM ERC	01-Ara-2018 00:00	31-Ara-2021 00:00	0,0	3,0	0,0	9,0	3,0	15,0
Teaching/demonstrating/marking/preparation		Marking of iBSc&MSc Students' Essays	PhD Supervisor	20-Ara-2018 00:00	20-Ara-2018 00:00	5,0	0,0	2,5	0,0	2,5	5,0
Mentoring/supervising of Project Student		Mentoring of MSc Student Research Project	PhD Supervisor	07-Oca-2019 00:00	13-Eyl-2019 00:00	0,0	2,0	1,0	0,0	2,0	5,0
Other course/event attendance	EAL7620	Research Writing Workshop	Language Centre	15-Oca-2019 00:00	19-Mar-2019 00:00	0,0	14,0	3,0	0,0	3,0	20,0
Conference Attendance (Three days)		Scandinavian Sports Medicine Congress	Danish Society of Sports Medicine and Danish Society of Sports Physical Therapy	31-Oca-2019 00:00	02-?ub-2019 00:00	0,0	9,0	6,0	0,0	0,0	15,0
Conference Presentation (Poster)		Are Jump Landing Patterns Associated with Patellar Tendinopathy in Competitive Athletes? - A Systematic Review	Danish Society of Sports Medicine and Danish Society of Sports Physical Therapy	31-Oca-2019 00:00	31-Oca-2019 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Hackathon - Combining models to optimise gait assessment	Sports and Exercise Medicine Department	02-Mar-2019 00:00	02-Mar-2019 00:00	7,0	7,0	0,0	0,0	0,0	7,0
Internal Presentation (< or =30 mins)		Patellar tendinopathy outcome predictors in jumping athletes:feasibility for a cohort study	Sports and Exercise Medicine Department	28-Mar-2019 00:00	28-Mar-2019 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Internal Presentation (< or =30 mins)		Patellar tendinopathy outcome predictors in jumping athletes:feasibility for a cohort study	Sports and Exercise Medicine Department	03-Nis-2019 00:00	03-Nis-2019 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Ethical Approval (NHS)		Tendinopathy TEAM 3a – predictors of outcome for tendinopathy	NHS	26-Haz-2019 00:00	30-Haz-2021 00:00	0,0	5,0	0,0	15,0	5,0	25,0
Internal Presentation (< or =30 mins)		Outcome predictors for recovery of Patellar Tendinopathy in jumping athletes: Viva presentation	Sports and Exercise Medicine Department	02-Tem-2019 00:00	02-Tem-2019 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Doctoral College event/course	DC300	3rd Year PhD Cohort Day - Employability	Doctoral College	03-Eyl-2019 09:45	03-Eyl-2019 17:00	0,0	0,0	4,0	0,0	2,0	6,0
Conference Attendance (Three days)		21st Annual Conference in Sport & Exercise Medicine	Sports and Exercise Medicine Department at QMUL	12-Eyl-2019 00:00	14-Eyl-2019 00:00	0,0	9,0	6,0	0,0	0,0	15,0

Activity Record

Type	Code	Title	Provider	From	To	Hours	A	B	C	D	Total
Conference Presentation (Oral)		Reliability and Validity of a Graded Loaded Challenge for Patellar Tendinopathy: A Laboratory Study	Sports and Exercise Medicine Department at QMUL	13-Eyl-2019 00:00	13-Eyl-2019 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Sports Medicine Ultrasound Group (SMUG) Pedret & Ballius Advanced Lower Limb Muscle & Tendon Injury Masterclass	Sports Medicine Ultrasound Group	14-Eyl-2019 00:00	15-Eyl-2019 00:00	14,0	14,0	0,0	0,0	0,0	14,0
Other CPD course	GCP003	Good Clinical Practice (GCP) Refresher	Joint Research Management Office	28-Eki-2019 14:00	28-Eki-2019 16:30	0,0	0,0	0,0	2,0	0,0	2,0
Internal Presentation (< or =30 mins)		Patellar Tendinopathy Outcome Predictors in Jumping Athletes: A Case-Control Study	Sports and Exercise Medicine Department	20-Kas-2019 00:00	20-Kas-2019 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Researcher Development Course	RD028	Introduction to meta-analysis	Researcher Development	27-?ub-2020 10:00	27-?ub-2020 17:00	0,0	6,0	0,0	0,0	0,0	6,0
Internal Presentation (< or =30 mins)		Are Jump Landing Patterns Associated with Patellar Tendinopathy in Jumping Athletes? - A Systematic Review	Sports and Exercise Medicine Department	11-Mar-2020 00:00	11-Mar-2020 00:00	0,5	1,0	1,0	0,0	2,0	4,0
Refereed Publication (Journal Paper, Book chapter, not abstract) acceptance		Patellar tendinopathy outcome predictors in jumping athletes: feasibility of measures for a cohort	Physical Therapy in Sport	24-May-2020 00:00	24-May-2020 00:00	0,0	2,0	0,0	0,0	8,0	10,0
Internal Presentation (< or =30 mins)		Biopsychosocial factors explain the variance of Patellar Tendinopathy severity in jumping athletes better than training related factors: Baseline analysis of an international prospective cohort study	Sports and Exercise Medicine Department	01-Tem-2020 00:00	01-Tem-2020 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Internal Presentation (< or =30 mins)		Biomedical and sport specific factors distinguish Patellar Tendinopathy from other knee problems in jumping athletes: Baseline analysis of an international prospective cohort study (update)	Sports and Exercise Medicine Department	23-Eyl-2020 00:00	23-Eyl-2020 00:00	0,0	1,0	1,0	0,0	2,0	4,0
Education & Learning Course (Queen Mary Academy)	QMATYFS03	Teach Your First Session (SE) Split over 2 days	QMUL	12-Eki-2020 10:00	14-Eki-2020 12:00	0,0	0,0	2,0	0,0	2,0	4,0
Researcher Development Course	RD-QMA-010	Let's Write! Online Writing Retreat (full day)	Researcher Development	23-Eki-2020 10:00	23-Eki-2020 16:00	0,0	0,0	2,0	1,0	1,0	4,0
Conference Attendance (Three days)		LASEM Sports Medicine Student Showcase	La Trobe University Sports and Exercise Medicine Research Centre	27-Eki-2020 00:00	29-Eki-2020 00:00	0,0	9,0	6,0	0,0	0,0	15,0
Conference Presentation (Oral)		Outcome predictors for recovery of patellar tendinopathy in jumping athletes: a cohort study	La Trobe University Sports and Exercise Medicine Research Centre	27-Eki-2020 00:00	27-Eki-2020 00:00	0,0	3,0	3,0	0,0	4,0	10,0
Researcher Development Course	RD-QMA-009	Let's Write! Online Writing Retreat (half day)	Researcher Development	05-Kas-2020 13:30	05-Kas-2020 16:30	0,0	0,0	1,0	0,5	0,5	2,0
Researcher Development Course	RD-QMA-010	Let's Write! Online Writing Retreat (full day)	Researcher Development	18-Kas-2020 10:00	18-Kas-2020 16:00	0,0	0,0	2,0	1,0	1,0	4,0
Researcher Development Course	RD-QMA-009	Let's Write! Online Writing Retreat (half day)	Researcher Development	27-Kas-2020 10:00	27-Kas-2020 13:00	0,0	0,0	1,0	0,5	0,5	2,0
Researcher Development Course	RD-QMA-010	Let's Write! Online Writing Retreat (full day)	Researcher Development	10-Ara-2020 10:00	10-Ara-2020 16:00	0,0	0,0	2,0	1,0	1,0	4,0
Researcher Development Course	RD-QMA-010	Let's Write! Online Writing Retreat (full day)	Researcher Development	16-Mar-2021 10:00	16-Mar-2021 16:00	0,0	0,0	2,0	1,0	1,0	4,0

Activity Record

Type	Code	Title	Provider	From	To	Hours	A	B	C	D	Total
Researcher Development Course	RD-QMA-009	Let's Write! Online Writing Retreat (half day)	Researcher Development	25-Mar-2021 13:30	25-Mar-2021 16:30	0,0	0,0	1,0	0,5	0,5	2,0
Researcher Development Course	PHD-QMA-301	Writing Your Thesis (2-part course)	Researcher Development	12-Nis-2021 10:00	13-Nis-2021 12:00	0,0	0,0	0,0	1,0	2,0	3,0
Researcher Development Course	RD-QMA-010	Let's Write! Online Writing Retreat (full day)	Researcher Development	15-Nis-2021 10:00	15-Nis-2021 16:00	0,0	0,0	2,0	1,0	1,0	4,0
Researcher Development Course	RD-QMA-009	Let's Write! Online Writing Retreat (half day)	Researcher Development	27-Nis-2021 10:00	27-Nis-2021 13:00	0,0	0,0	1,0	0,5	0,5	2,0
Researcher Development Course	RD-QMA-009	Let's Write! Online Writing Retreat (half day)	Researcher Development	05-May-2021 13:30	05-May-2021 16:30	0,0	0,0	1,0	0,5	0,5	2,0
Core research knowledge or methods course (e.g. LTCC, IALS courses, masters lectures)		Statistical Methods for Risk Prediction and Prognostic Models	Keele University	19-May-2021 00:00	21-May-2021 00:00	24,0	24,0	0,0	0,0	0,0	24,0
Researcher Development Course	RD-QMA-009	Let's Write! Online Writing Retreat (half day)	Researcher Development	27-May-2021 10:00	27-May-2021 13:00	0,0	0,0	1,0	0,5	0,5	2,0
Researcher Development Course	RD-QMA-024	Fundamentals of Data Visualisation	Researcher Development	17-Haz-2021 13:00	18-Haz-2021 16:00	0,0	3,0	0,0	0,0	3,0	6,0

Appendix 2: The PRISMA checklist for the reporting of the systematic review.

Section/topic	#	Checklist item	Status
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	✓
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	✓
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	✓
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	✓
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	✓
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	✓
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	✓
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	✓
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	✓
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	✓
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	✓
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	✓
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	✓
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	✓
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			

Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.		✓
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.		✓
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).		✓
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.		✓
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.		✓
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).		✓
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).		NA
DISCUSSION				
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).		✓
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).		✓
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.		✓
FUNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.		✓
Keys: NA, not applicable; ✓, meets criterion.				

Appendix 3: Search strategy for all databases.

Latest search performed on 24.05.2020.

Pubmed:
("Tendinopathy" OR "tendinopathies" OR "tendinitis" OR "tendonitis" OR "tendinosis" OR "tenosynovitis" OR "paratendinopathy" OR "Paratenonitis" OR "noninsertional" OR "insertional" OR "Patella-tendon" OR "Patellar-tendon" OR "Patella-tendinopathy" OR "Patellar-tendinopathy" OR "Patella-tendinitis" OR "Patellar-tendinitis" OR "Patella-tendinosis" OR "Patellar-tendinosis" OR "Patella-paratenonitis" OR "Patellar-paratenonitis" OR "patella-apicitis" OR "patellar-apicitis" OR "patella-apex-syndrome" OR "patellar-apex-syndrome" OR "patella-tip-syndrome" "patellar-tip-syndrome" OR "patella-tenosynovitis" OR "patellar-tenosynovitis" OR "jumpers-knee" OR "Jumper's-knee" OR "tendon injury")
AND
("jump" OR "jumping" OR "touchdown" OR "land" OR "landing" OR "kinematics" OR "biomechanics" OR "Mechanical-stress" OR "Mechanical-stresses" OR "take-off" OR "Jump-landing")

Web of Science Search:
ALL FIELDS: ("Tendinopathy" OR "tendinopathies" OR "tendinitis" OR "tendonitis" OR "tendinosis" OR "tenosynovitis" OR "paratendinopathy" OR "Paratenonitis" OR "noninsertional" OR "insertional" OR "Patella-tendon" OR "Patellar-tendon" OR "Patella-tendinopathy" OR "Patellar-tendinopathy" OR "Patella-tendinitis" OR "Patellar-tendinitis" OR "Patella-tendinosis" OR "Patellar-tendinosis" OR "Patella-paratenonitis" OR "Patellar-paratenonitis" OR "patella-apicitis" OR "patellar-apicitis" OR "patella-apex-syndrome" OR "patellar-apex-syndrome" OR "patella-tip-syndrome" OR "patellar-tip-syndrome" OR "patella-tenosynovitis" OR "patellar-tenosynovitis" OR "jumpers-knee" OR "Jumper's-knee" OR "tendon injury")
AND
ALL FIELDS: ("jump" OR "jumping" OR "touchdown" OR "land" OR "landing" OR "kinematics" OR "biomechanics" OR "Mechanical-stress" OR "Mechanical-stresses" OR "take-off" OR "Jump-landing")

Cochrane Library:
"Tendinopathy" OR "tendinopathies" OR "tendinitis" OR "tendonitis" OR "tendinosis" OR "tenosynovitis" OR "paratendinopathy" OR "Paratenonitis" OR "noninsertional" OR "insertional" OR "Patella-tendon" OR "Patellar-tendon" OR "Patella-tendinopathy" OR "Patellar-tendinopathy" OR "Patella-tendinitis" OR "Patellar-tendinitis" OR "Patella-tendinosis" OR "Patellar-tendinosis" OR "Patella-paratenonitis" OR "Patellar-paratenonitis" OR "patella-apicitis" OR "patellar-apicitis" OR "patella-apex-syndrome" OR "patellar-apex-syndrome" OR "patella-tip-syndrome" "patellar-tip-syndrome" OR "patella-tenosynovitis" OR "patellar-tenosynovitis" OR "jumpers-knee" OR "Jumper's-knee" OR "tendon injury" in All Text
AND

"jump" OR "jumping" OR "touchdown" OR "land" OR "landing" OR "kinematics" OR "biomechanics" OR "Mechanical-stress" OR "Mechanical-stresses" OR "take-off" OR "Jump-landing" in All Text - (Word variations have been searched)

No Additional Filters.
No language restrictions.
Sorted by 'Most Recent' in Pubmed.
All fields search in all databases.

RESULTS
PUBMED: 1608
WOS: 2122
COCHRANE: 999
OVERALL: 4729

Appendix 4: Jump-landing kinematic analyses.

Keys: H, high; M, moderate; L, low; PT, patellar tendinopathy; PTA, asymptomatic patellar tendon abnormality; JPTs, jumping athletes with PT; vGRF, vertical ground reaction force; LR, loading rate; DF, dorsiflexion; PF, plantarflexion; IR, internal rotation; ER, external rotation; RoM, range of motion; IC, initial contact; PTF, patellar tendon force.

Kinematic variables	Findings	Quality (n)			Evidence Level
		H	M	L	
Joints angles at IC (ankle, knee, hip)	Lower ankle PF, higher likelihood of previous PT (103).		1		Very Limited
	More limited knee flexion, higher likelihood of previous PT (103).		1		Very Limited
	PTA group landed with greater knee flexion (178,184).		1	1	Limited
	Hip angles may be related to PTA; a trend for greater hip flexion (184) & significantly smaller hip ER in fatigue (174).		2		Very Limited
	No relation between joint angles at IC and PT (175,177,179,185).	1	3		Moderate
Joints velocities at IC (knee, hip)	Slower knee flexion velocity possibly related to PTA (174,184).		2		Limited
	Hip joint velocity may be related to PTA; hip extension displaying significantly faster hip extension velocity (184).		1		Very Limited
Joints RoM (ankle, knee, hip)	An association of smaller ankle dorsiflexion with PT (64,175,180,183).	1	3		Moderate
	No relation between sagittal plane ankle kinematics and PT in young athletes (179).	1			Limited
	No relation between sagittal plane ankle kinematics and PTA (180).	1			Limited
	No relation between sagittal plane ankle kinematics and previous PT (183).		1		Very Limited
	PTA group had greater ankle inversion at PTF (184).		1		Very Limited
	JPTs had lower peak knee flexion angles (64,177).		2		Limited
	A deeper knee flexion predicted 100% cases for PT (100).			1	Very Limited
	PTA group had greater knee IR at vGRF and lower peak knee flexion angles (184).		1		Very Limited
	No relation between sagittal plane knee RoM and PT (175,179–181).	3	1		Strong
	JPTs had more hip flexion (64).		1		Very Limited
	JPTs had lower peak hip flexion (177).		1		Very Limited
	PTA group had lower hip flexion RoM (178).			1	Very Limited
	PTA group had greater hip adduction at vGRF (184).		1		Very Limited
	Athletes with PTA had smaller hip ER at vGRF when fatigued (174).		1		Very Limited
	No relation between PT and hip flexion RoM (175,179,180).	2	1		Strong
	JPTs had less Lower Extremity Contact Angle (175).		1		Very Limited
	JPTs (n=3) displayed no common landing technique or kinematic patterns (64).		1		Very Limited
	Similar joint positions from IC to peak PTF when fatigued in athletes with PTA (174).		1		Very Limited
Trunk Position	Decreased pain with greater trunk flexion during landing in JPTs (180).	1			Limited
	No relation between PT and trunk kinematics (179,180).	2			Moderate
	No relation between PT and forward head projection (180).	1			Limited
Joint angular velocities, acceleration, & angular displacement	Higher LR of ankle angular velocities in previous PT (103).		1		Very Limited
	A relation between higher knee angular velocity and previous PT (103,183).		2		Limited
	PTA group had a slower knee flexion velocity at PTF (184).		1		Very Limited
	JPTs had lower maximum knee angular displacement (177).		1		Very Limited
	Hip angular velocity (184) & angular displacement (177) might be related to PT.		2		Very Limited
	No relation between knee angular velocity and PT (181,183).	1	1		Moderate
	Similar ankle, knee & hip angular velocities from IC to peak PTF in PTA when fatigued (174).		1		Very Limited
	No group difference in landing velocity (185).		1		Very Limited

Keys: H, high; M, moderate; L, low; PT, patellar tendinopathy; PTA, asymptomatic patellar tendon abnormality; JPTs, jumping athletes with PT; vGRF, vertical ground reaction force; LR, loading rate; DF, dorsiflexion; PF, plantarflexion; IR, internal rotation; ER, external rotation; RoM, range of motion; IC, initial contact; PTF, patellar tendon force.

Kinetic variables	Findings	Quality (n) H	M	L	Evidence Level
Peak Patellar Tendon Force and its Loading rate	JPTs had smaller PTF than PTA group (180).	1			Limited
	JPTs had smaller PTF than controls (176).		1		Very Limited
	No relation between PT and PTF (179).	1			Limited
	No relation between PTA and PTF (176,184).		2		Very Limited
	An association of greater truncal-flexion with decreased PTF (180).	1			Limited
	JPTs had lower LR of PTF (179).	1			Limited
	JPTs had less PTF impulse vs PTA and controls (176).		1		Very Limited
	PTA had similar PTF impulse vs controls (176).		1		Very Limited
	Similar LR of PTF and duration from IC to PTF between groups (184).		1		Very Limited
	No relation between fatigue state and landing technique or net PTF (174).		1		Very Limited
Ground Reaction Forces (GRF) and its Loading rate	Greater peak vGRF might be related to PT (100,185).		1	1	Limited
	JPTs showed 22% lower peak vGRF (181).	1			Limited
	Greater peak braking GRF might be related to PT (185).		1		Very Limited
	No group difference in average vGRF (181).	1			Limited
	No relation between peak vGRF and PT (175,179,180,183).	2	2		Strong
	No relation between peak vGRF and PTA (180,184).	1	1		Moderate
	No relation between peak braking GRF and PT (175).		1		Very Limited
	Smaller vGRF in landing with a flexed trunk position (180).	1			Limited
	Athletes with PTA had a greater peak anterior-posterior GRF when fatigued (174).		1		Very Limited
	JPTs had lower LR of vGRF during stop jump horizontal landing (179).	1			Limited
	Higher LR of vGRF in athletes with previous PT (183) and with PTA when fatigued (174).		2		Very Limited
	PTA group had a lower LR of vGRF during vertical landing phase (184).		1		Very Limited
	Longer duration from IC to first and second peak vGRF between groups (179).	1			Limited
	Similar LR of vGRF & duration (IC to peak vGRF) during horizontal landing phase (184).		1		Very Limited
	Greater vertical (15%) & braking impulses (126%) in dancers with PT (185).		1		Very Limited
	No group difference in vGRF impulse (175,179,181).	2	1		Strong
	No group difference in peak propulsive GRF (185), propulsive (185) & braking impulse (175).		2		Very Limited
Joint moments	Foot inversion moment might be related to PT (101).			1	Very Limited
	Higher LR of ankle moment development in previous PT (183).		1		Very Limited
	No relation between PT and ankle joint contribution to the total support moment (182).	1			Limited
	An association of smaller knee moments with PT vs healthy controls (183).		1		Very Limited
	An association of smaller knee moments with PT vs PTA (180).	1			Limited
	ER moment at the left knee might be implicated in PT (100).			1	Very Limited
	Peak tibial ER moment predicted 8/10 cases for PT (100).			1	Very Limited
	JPTs displayed lower knee joint contribution to the total support moment (182).	1			Limited
	A relation between higher LR of knee moment and previous PT (103,183).		2		Limited
	JPTs had less knee extensor moment impulse vs PTA & controls (176).		1		Very Limited
	PTA group had similar knee extensor moment impulse vs controls (176).		1		Very Limited
	JPTs displayed greater hip joint contribution to the total support moment (182).	1			Limited
	No relation between PT and peak knee moments (179–181).	3			Strong
	No relation between PT and peak ankle (179,180) and hip (179,180) moments.	2			Moderate
	No relation between PT and average ankle, knee and hip moments (182).	1			Limited
	No relation between PT and total support moment (182).	1			Limited
	No relation between PT and sagittal plane trunk joint moments (179).	1			Limited
Joint energetics	Lower knee joint power in JPTs (181,183).	1	1		Moderate
	Lower negative knee joint work in JPTs (176,181,183).	1	2		Moderate
	No group difference in positive knee joint work (181).	1			Limited
	JPTs & previous PT had similar and ankle & hip joints power & work (183).		1		Very Limited
	Similar knee joint power (PT & PTA) & work (PTA) (176).		1		Very Limited
Leg stiffness	JPTs (64) and previous PT (183) had higher leg stiffness.		2		Very Limited
Muscle activation	Athletes with PTA might have different muscle recruitment order (184).		1		Very Limited
	No group differences in onset time or peak muscle burst activity relative to peak PTF (184).		1		Very Limited

Appendix 6: Questions of Patient and Public Involvement event and attendees' responses.

Baseline Section

Q1. What is the best way to explain long (around 45 minutes) initial questionnaire aim? Is this kind of explanation acceptable to convince people?

Answers:
- Inform people individually, like "we need your help/this info to help you" to convince them.
- 10 minutes is acceptable for a day to fill out the survey (e.g. 10 mins/day to finish all, 1-hour survey could take 6 days).
- Some of them were not happy about the duration and one of them said that the study is not going to work, and we can have a high rate of drop out. (He also said he would not attend this study).

Judgement: We should focus on the positive features of the study, then use these features to sell the study.

Q2. Please tell us three things how to motivate people to join the study and fill out the long survey including monthly follow-ups?

Answers:
- To be able to go back to survey wherever they left as a feature would be great.
- Examples of happy participants from previous studies.
- Some results from previous research they have attended would be a good motivation for them.
- End goals are important for participants to join a study.
- Getting better is more important than money for them.
- Flexibility for the time to complete the survey could be good.

Judgement: We should focus on our previous study outputs and happy participants in order to recruit new people for the cohort study. Need to prepare a clear explanations for the end goals which are the benefits taking out the study.

Q3. What time of the day you want to fill in the survey?

Answers:
- Lunch time could work.
- The time of the day is not really important as it is an online survey and available all the time.

Judgement: We are going to send the survey link after enrolling the participant.

Q4. How do you want to receive reminder? (calling, mailing, text, etc.)

Answers:
- SMS and email for reminders.
- Good titles for the email subjects.
- Calling participants is not a good option.
- They do not answer phone calls.

- If they did not fill out the survey for a long time (e.g. 2 weeks), we should think that they do not want to do it.

Judgement: We have already planned to use SMS and email at the same time. This event is confirmed we are on the right truck. We should consider an attractive subject title for the emails as well.

Q5. If it is email: How can we ask you to add our email address in your address list in case of receiving study reminders in junk/spam box?

Answers:
- Junk/spam; participants can confirm our emails (e.g. confirmation emails from companies, so smart trial may work on it?).

Judgement: We will investigate whether we can find out to use a confirmation email via Smart Trial.

Q6. What kind of way is more useful to attend to the study? Why? (Social media, by clinician, etc.).

Answers:
- Social media is highly recommended.
- They recommended us to find some people from Facebook groups (sports related, disease related, etc.).

Judgement: We will use social media advertisement to spread our study as planned.

Retention Section

Q1. What would it be helpful to complete monthly follow-up surveys?

Answers:
- It is difficult to remember a month ago for them.
- Short follow-up is good.

Judgement: We should stick with short follow ups and also consider about how they can easily remember their last month. Keeping a diary?

Q2. During follow-up, if we cannot reach a person when exact time they need to fill-out the survey or they left the survey half way through, how frequently should we call or send a reminder without leading any disturbance.

Answers:
- Every 3-day for the frequency of reminders is good enough, but still need to put some limit (e.g. maximum 3 reminders) for this.

Judgement: The ideal number of reminder would be once in three days.

Q3. What kind of things would be helpful to complete study as a reward? (Drawing, voucher, money, gift, food & drinks)

Answers:
- Rewards are also important for them, especially treatment.

- Giving explanation/advice on their condition for self-management.

Judgement: Some people are expecting to receive any benefits. The benefit can be an advice, information about their condition or treatment. To provide that, we are planning to prepare a report as mentioned below.

Q4. How we can keep you in the study when you recovered and do not have problem anymore as the study requires follow up even after getting better?

Answers:
- After getting better: they all said yes to continue study to help other people.
- We can sell this idea to get people as well (or to keep them) → "You recovered but we still following your condition" to provide information for you and other people.

Judgement: 'Feeling good' as a component is discussed in the overall part.

Q5. Apart from the survey, we have some parts like keeping diary. How can we motivate people to perform these extra things?

Answers:
- Diary issue: need to give an example of a good participant.
- Talking about data protection can convince people for other extra things.
- Some of them were not happy for any other study parts as they thought it is already too much.

Judgement: Patient information sheet can be reorganized by highlighting data protection and explaining clearly what we want them to do.

Overall Judgements

A. What you will take forward and why:

1. Participants request to know all steps of study before joining the study. For instance, initial and follow up survey duration, the number of follow up questionnaires, the number of exercise diary.

2. Make participants feeling good that they can get help from the study and to help other people by participating our study = 'feeling good' as a component. So, how can we help them:

   o Preparing a report to inform them about their information context (e.g. consisting of questionnaire score with their meanings) in five working days after a participant fill the initial survey OR automatic replies if it is possible.

   o Format could be like a blood test sheet. So we will give the actual results and their meaningful ranges. That's it. We will not give any comment on it to avoid treatment/advice issue.

- o We may inform clinicians if participants prefer to show our report to their clinicians. This is really matter because this help us to understand relationship between prognosis and treatment.

- o This should be individually and require low effort. (i.e. we can use mail merge).

- o As another report, we can prepare an infographic about outcome predictor related to recovery at the end of the study and show which features of them associated with tendinopathy. At the begging of the study we can sent an example infographic in order to explain what we will try to figure out and what we provide as end points. We can explain the infographic as following sentences; 'These factors are considered as associated at the beginning but we found these that are not related your problem. Apart from these factors, other two or three lead to getting you better or worse.'

3. Ways for selling the study:

- o Using logo of our collaborators as an endorsement (e.g. using FC Barcelona logo to attract athletes).

- o Including previous participant views for emphasizing the study that it really worth to attend.

- o Including clinicians' views as well to show this is a worthful study which helps clinicians to choose better treatment strategies (impact of the study].

B. What you will not / consider later and why:
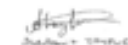
- o The feedbacks should not include a treatment/advice because the study do not focus giving treatment.

- o Feedbacks should not contaminate the study as well.

Appendix 7: Data collection form for clinical and US examinations.

SOP Title	Case report form – Assessment
SOP Reference	Combined CRF and PAB Team_Cohort
Version Number	Cohort T-TEAM 3a_feasibility CRF Assessment v 1.9 29.01.19
Approval Date	29.01.19
Effective Date	29.01.19

Approved by	Dylan Morrissey	
	Chief Investigator	

Author	Abdulhamit Tayfur	
Reviewed by	Dylan Morrissey	

Clinical Examination

Height (cm): _____   Weight (kg): _____

Leg length discrepancy (>5mm)	According to bottom of MM	L=R / L > R / R > L
Observation of LL posture	Knee Normal ☐ Genu Varus ☐ Genu Valgus ☐ Genu Recurvatum ☐ Flexed ☐	Foot L: Supinated / Neutral / Pronated R: Supinated / Neutral / Pronated

Please tick or circle the option (Keys: MM; medial malleolus, LL; lower limb, L; left, R; right)

L	Pain on Palpation	R
	(Knee 20-30°, Before Graded Loaded Challenge, please circle)	
+ve / -ve	Inferior Patella Pole	+ve / -ve
+ve / -ve	Patellar Mid-tendon	+ve / -ve
+ve / -ve	Patellar Tendon Insertion	+ve / -ve
+ve / -ve	Tibial Tuberosity	+ve / -ve
+ve / -ve	Thigh Muscles	+ve / -ve
+ve / -ve	Retropatellar (extended knee)	+ve / -ve
+ve / -ve	Quadriceps Tendon	+ve / -ve
	Main pain is _____	

Hoffa's test

L		R
+ve / -ve	Starting Position: Supine with flexed knee 20-30° Test: Pressing both thumbs deeply along the sides of patellar tendon, then ask active knee extension +ve: If it is painful behind the tendon, in the fat pad region	+ve / -ve

	L	Muscle Strength	R	
		Hand Dynamometer - Break Test		
		Knee Ext (Sitting)		
		Knee Flex 90° (Prone)		
		Oxford Scale x/5		
	<5 / 5	**Hip Ext** (Prone, Knee 90°)	<5 / 5	
	<5 / 5	**Hip Abd** (Side-lying)	<5 / 5	
	<5 / 5	**Hip Flex** (Sitting)	<5 / 5	

Please measure muscle strength three times for knee ext & flex and write the maximum value of the three repetitions.

Lower Limb RoM

Knee Extension (Supine)	Active	L: Limited / Normal / Lax R: Limited / Normal / Lax
	Passive	L: Limited / Normal / Lax R: Limited / Normal / Lax
Hip Abduction (Supine)	Active	L: Limited / Normal / Lax R: Limited / Normal / Lax
	Passive	L: Limited / Normal / Lax R: Limited / Normal / Lax
Knee Flexion (Prone)	Fully flexed (passive, heel to bottom)	Y / N
	Asymmetry (based on passive RoM)	L=R / L > R / R > L
Hip Extension (Prone)	Passive (stabilize from tuber ischia)	L: Limited / Normal / Lax R: Limited / Normal / Lax

Please circle the option (Keys: RoM, range of motion; L; left, R; right, Y; yes, N; no)

L	Flexibility (please circle)	R
Normal / Tight	**Rectus Femoris**	Normal / Tight
Normal / Tight	**Hamstring (Knee & Hip 90°)**	Normal / Tight
Flex / Normal / Tight	**ITB (Ober)**	Flex / Normal / Tight
Flex / Normal / Tight	**Modified Thomas**	Flex / Normal / Tight
Iliopsoas / TFL / RecFem	↓If tight Primary limit for hip ext	Iliopsoas / TFL / RecFem

Knee to Wall	L	R
Total Ankle DF RoM (front limb)	°	°
Gastrocnemius (back limb)	°	°

Graded Loaded Challenge

After 3 mins warm-up – consisting of walk for 1 min, brisk walk on the spot for 1 min, and dynamic stretch for Quadriceps and Hamstring muscles for 30 seconds each (see video 1)

The patient is asked to perform the following set of tests:

1. in order
2. with good form: comment on RoM, stabilization, speed
3. stopping at the point at which pain is reproduced at >5/10
4. record the challenge level and number of reps to get to that point

Task	Reps		Pain (NRS x/10)		MBS (0-10)		Comment on form
Warm-up (Video 1)		mins	R	L			
Double leg (DL) squat (Video 2)		/5	R	L		/10	RoM Stabilization Speed Other
Single leg (SL) squat (Video 3)	R L	/5 /5	R	L	R L	/10 /10	RoM Stabilization Speed Other
DL jump DL landing (Video 4)		/5	R	L		/10	RoM Stabilization Speed Other
DL jump SL landing (Video 6)	R L	/5 /5	R	L	R L	/10 /10	RoM Stabilization Speed Other
Stop Jump (DL land) (Video 8)		/5	R	L		/10	RoM Stabilization Speed Other
Stop Jump (SL land) (Video 9)	R L	/5 /5	R	L	R L	/10 /10	RoM Stabilization Speed Other

Keys: NRS; numerical rating scale, MBS; modified Borg Scale

L	Pain on Re-palpation	R
	(Knee 20-30°, After GLC, please circle)	
less / same / more	Inferior Patella Pole	less / same / more
less / same / more	Patellar mid-tendon	less / same / more
less / same / more	Patellar Insertion	less / same / more
less / same / more	Tibial Tuberosity	less / same / more
less / same / more	Thigh Muscles	less / same / more
less / same / more	Retropatellar (extended knee)	less / same / more
less / same / more	Quadriceps Tendon	less / same / more
	Main pain is _____	
less / same / more	**Hoffa's test**	less / same / more

Ultrasound report form

Position: Knee 20-30°	Left	Right
Maximum A-P Thickness for PT	LS TS mm	LS TS mm
Neovascularisation grade for PT (modified Ohberg's according to Chan)	0 1 2 3 4 5	0 1 2 3 4 5
Maximum A-P Thickness for Lateral Retinaculum (in TS with Knee 10°)	mm	mm
Pre- or Infrapatellar Bursa?	Y / N Comment:	Y / N Comment:
Swelling?	Y / N	Y / N
Tears seen?	No / Partial / Full Prox / Mid / Distal	No / Partial / Full Prox / Mid / Distal
Calcification seen?	Y / N	Y / N
Comments		

Keys: LS, longitudinal section; TS, transvers section

Appendix 8: Data collection form for biomechanical measures.

Lab report form

Height:

Weight:

Pelvic Width:

Leg Length:

EMG norm records:

- Quads:
- Hams:
- Gastrocs:

Static record in standing position:

Task	Reps		NRS (x/10)	MBS (0-10)		Trial Number	Correct Reps
Warm-up	mins		R L		/10	NA	NA
Double leg (DL) squat		/5	R L		/10		
Single leg (SL) squat	R L	/5 /5	R L	R L	/10 /10	R: L:	R: L:
DL jump DL landing		/5	R L		/10		
DL jump SL landing	R L	/5 /5	R L	R L	/10 /10	R: L:	R: L:
Stop Jump (DL land)		/5	R L		/10		
Stop Jump (SL land)	R L	/5 /5	R L	R L	/10 /10	R: L:	

Appendix 10: CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial.

Section/Topic	Item No	Checklist item	Status
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	✔
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	✔
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	✔
	2b	Specific objectives or research questions for pilot trial	✔
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	✔
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	✔
Participants	4a	Eligibility criteria for participants	✔
	4b	Settings and locations where the data were collected	✔
	4c	How participants were identified and consented	✔
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	NA
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	✔
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	✔
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	✔
Sample size	7a	Rationale for numbers in the pilot trial	✔
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	✔
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	✔
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	NA
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	✔
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	NA
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	✔
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	✔
	13b	For each group, losses and exclusions after randomisation, together with reasons	✔
Recruitment	14a	Dates defining the periods of recruitment and follow-up	✔
	14b	Why the pilot trial ended or was stopped	Partly
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	✔
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	✔
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	Partly
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	✔

Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)		NA
	19a	If relevant, other important unintended consequences		✔
Discussion				
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility		✔
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies		✔
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence		✔
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments		✔
Other information				
Registration	23	Registration number for pilot trial and name of trial registry		X
Protocol	24	Where the pilot trial protocol can be accessed, if available		X
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		Partly
	26	Ethical approval or approval by research review committee, confirmed with reference number		✔
Keys: NA, not applicable; √, meets criterion; X, does not meet criterion; Partly, partially meets criterion.				

Appendix 11: Ethics approval letters; A) Feasibility study, B) Case-control and cohort studies.

A) Feasibility study:

Queen Mary
University of London

Queen Mary, University of London
Room E16
Queen's Building
Queen Mary University of London
Mile End Road
London E1 4NS

Queen Mary Research Ethics Committee
Hazel Covill
Research Ethics Administrator
Tel: +44 (0) 20 7882 2207
Email: h.covill@qmul.ac.uk

Dr Dylan Morrissey
Department of Sports Medicine
Mile End Hospital
Bancroft Road
London E1 4NS

16th December 2019

To Whom It May Concern:

Re: QMREC2014/24 – Human performance measurement and surveys – a generic ethics application.

This is to confirm that the following study was agreed under the above ethical approval:

Re: QMERC2014/24/153 - Tendinopathy TEAM 3a – predictors of outcome for tendinopathy: *a feasibility study.*

(Running title: T-TEAM 3(a): predictors of outcome for tendinopathy)

Date of approval
This was noted and fully approved on the 1st March 2018

Yours faithfully

Dr Helen Jenner – QMREC Chair.

Patron: Her Majesty the Queen
Incorporated by Royal Charter as Queen Mary
and Westfield College, University of London

B) Case-control and cohort studies:

Queen Mary
University of London

Queen Mary, University of London
Room W104
Queen's Building
Queen Mary University of London
Mile End Road
London E1 4NS

Queen Mary Ethics of Research Committee
Hazel Covill
Research Ethics Facilitator
Tel: +44 (0) 20 7882 7915
Email: h.covill@qmul.ac.uk

c/o Professor Dylan Morrissey
Department of Sports Medicine
Mile End Hospital
Bancroft Road
London

15th May 2019

To Whom It May Concern:

Re: QMERC2018/92 – Tendinopathy Team 3a – predictors of outcomes for tendinopathy.

The above study was conditionally approved by The Queen Mary Ethics of Research Committee (Review Panel G) on the 19th December 2018; full approval was ratified by Chair's Action on the 21st February 2019.

This approval is valid for three years, (if the study is not started before this date then the applicant will have to reapply to the Committee).

Amendment
1. A minor amendment (small changes to materials) was agreed via Chair's Action on the 14th May 2019.

Yours faithfully

Dr Helen Jenner – QMERC Chair.

NHS
Health Research Authority

London - City & East Research Ethics Committee
Bristol Research Ethics Committee Centre
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 02071048033/53

> **Please note:** This is an acknowledgement letter from the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

10 September 2019

Professor Dylan Morrissey
Bart's Health NHS Trust and the WHRI, QMUL
Sports and Exercise Medicine
Mile End Hospital, Bancroft Road
London E1 4DG

Dear Professor Morrissey

Study title:	3T - the 10000 Tendons study, outcome prediction for tendinopathy: an international cohort study
REC reference:	19/LO/1340
Protocol number:	v1.0 23-52019
IRAS project ID:	264615

Thank you for your letter of 09 September 2019. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 26 August 2019

Documents received

The documents received were as follows:

Document	Version	Date
Confirmation of any other Regulatory Approvals (e.g. CAG) and all correspondence [Email HRA questions]	1	03 September 2019
Covering letter on headed paper [Covering letter]		27 August 2019
IRAS Application Form [IRAS_Form_09092019]		09 September 2019
Response to Additional Conditions Met		09 September 2019
Schedule of Events or SoECAT	1.1	02 September 2019
Schedule of Events or SoECAT [Soecat]	1	02 September 2019

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	Version	Date
Confirmation of any other Regulatory Approvals (e.g. CAG) and all correspondence [Email HRA questions]	1	03 September 2019
Covering letter on headed paper [Covering letter]		19 July 2019
Covering letter on headed paper [Covering letter]		27 August 2019
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		
IRAS Application Form [IRAS_Form_09092019]		09 September 2019
Letter from funder [Fudning letter from EPSRC for portfolio adoption]		
Letter from sponsor		19 July 2019
Other [Instruction of Video Method]	0.5	
Other [Response to Validation]		29 July 2019
Participant consent form [ICF]	1.0	
Participant information sheet (PIS) [PIS]	1.0	23 June 2019
Referee's report or other scientific critique report [Peer review]	1.0	18 July 2019
Research protocol or project proposal [Protocol]	1.0	23 May 2019
Response to Additional Conditions Met		09 September 2019
Schedule of Events or SoECAT	1.0	19 July 2019
Schedule of Events or SoECAT	1.1	02 September 2019
Schedule of Events or SoECAT [Soecat]	1	02 September 2019
Summary CV for Chief Investigator (CI) [CV]		15 March 2019
Validated questionnaire [Survey battery for all 15 routes]	1.0	19 July 2019

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

19/LO/1340	Please quote this number on all correspondence

Yours sincerely

Rajat Khullar
REC Manager

E-mail: nrescommittee.london-cityandeast@nhs.net

Approbation d'une demande d'étude clinique (suite)
Approval form for a clinical trial (following page)

Protocole

| Tendinopathy Team 3a - predictors of outcome for tendinopathy. |

Service de :
Clinical unit <u>**MEDECINE PHYSIQUE**</u>

Chef de Service : <u>**Prof. J.-F. KAUX**</u>
Director of the clinical unit
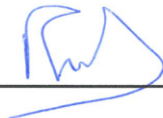
Expérimentateur principal : <u>**Prof. J.-F. KAUX**</u>
Principal investigator

Par décision collégiale, le Comité d'Ethique (voir liste des membres en annexe) :
By collegial decision, the Ethics Committee (see enclosed list of the members) :

Oui/*Yes*   Non/*No*

■ **estime que l'étude peut être réalisée**
has accepted the performance of the study | X | | |

Signature _____   **Nom :** <u>**Prof. V. SEUTIN Président**</u>
Signature   *Printed name :*

Date, *Date* **:**   26/02/2020

The Ethics Committee states that it is organized and operates according to the ICH/GCP guidelines, the applicable laws and regulations, and their own written operating procedures

Cette approbation ne signifie pas que le comité prend la responsabilité de l'étude.
This approval does not mean that the Ethics Committee takes the responsibility of the study

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MEMBRES DU COMITE D'ETHIQUE MEDICALE
HOSPITALO-FACULTAIRE UNIVERSITAIRE DE LIEGE

Monsieur le Professeur **Vincent SEUTIN** Pharmacologue, membre extérieur au CHU	**Président**
Monsieur le Professeur **Jean DEMONTY** Interniste, CHU	**Vice Président**
Monsieur le Docteur **Guy DAENEN** Honoraire, Gastro-entérologue, membre extérieur au CHU	**Secrétaire exécutif**

Monsieur **Resmi AGIRMAN**
Représentant des volontaires sains

Monsieur le Docteur **Etienne BAUDOUX**
Expert en Thérapie Cellulaire, CHU

Madame le Professeur **Adélaïde BLAVIER**
Psychologue, membre extérieur au CHU

Madame le Professeur **Florence CAEYMAEX**
Philosophe, membre extérieur au CHU

Madame **Marie Noëlle ENGLEBERT**
Juriste, membre extérieur au CHU

Monsieur le Professeur **Pierre FIRKET**
Généraliste, membre extérieur au CHU

Madame **Isabelle HERMANS**
Assistante sociale, CHU

Monsieur le Professeur **Maurice LAMY**
Honoraire, Anesthésiste-Réanimateur, membre extérieur au CHU

Madame le Docteur **Marie LEJEUNE** / Madame le Docteur **Sophie SERVAIS** (suppléante)
Hématologues, CHU

Monsieur **Pierre LISENS** / Madame **Viviane DESSOUROUX** (suppléante)
Représentant (e) des patients

Madame **Patricia MODANESE**
Infirmière chef d'unité, CHU

Madame le Professeur **Anne Simone PARENT**
Pédiatre, CHU

Monsieur le Professeur **Marc RADERMECKER**
Chirurgien, CHU

Monsieur le Professeur **Régis RADERMECKER**
Expert en méthodologie de la recherche clinique, CHU

Madame **Isabelle ROLAND**
Pharmacie, CHU
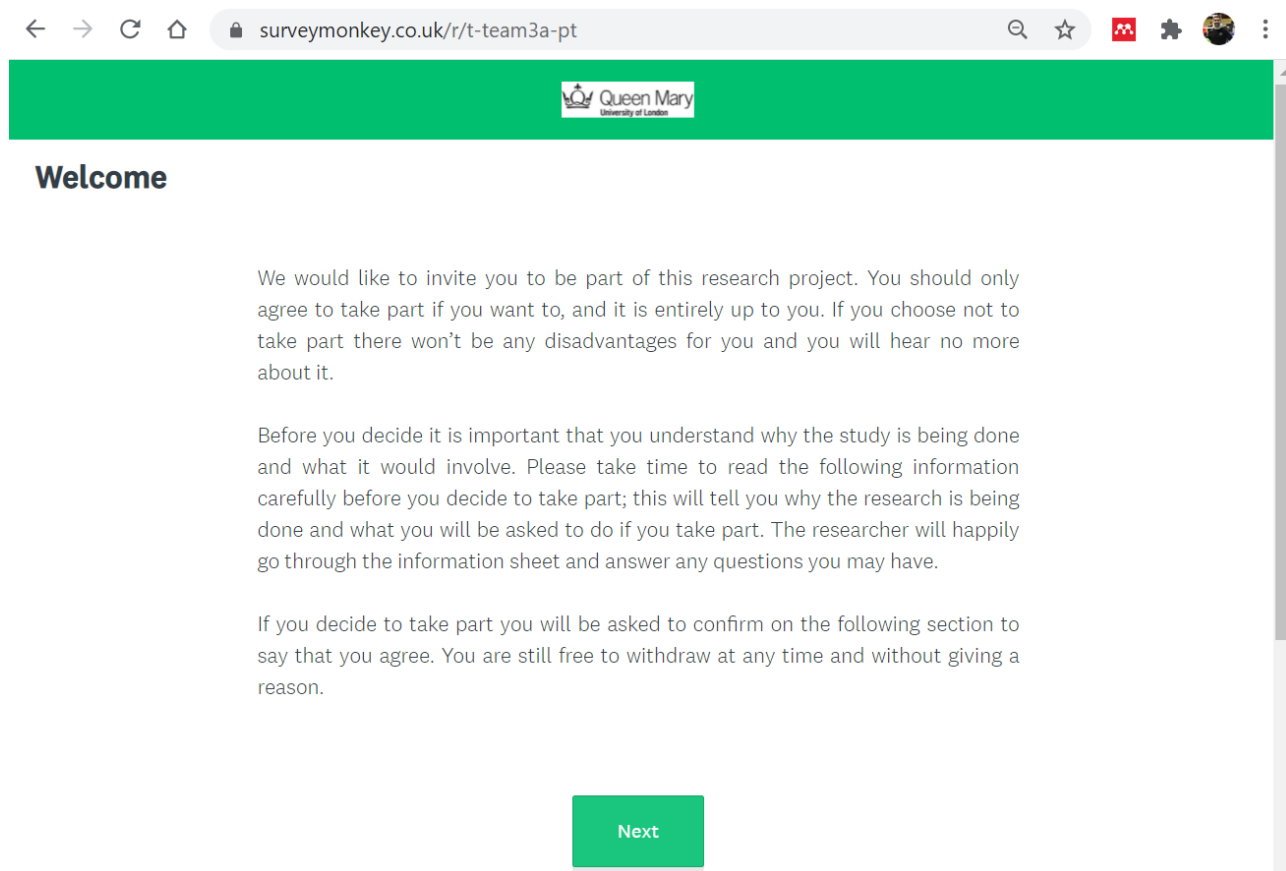
Madame le Docteur **Isabelle RUTTEN**
Radiothérapeute, membre extérieur CHU

Madame **Carine THIRION**
Infirmière chef d'unité, CHU   26/02/2020

Appendix 12: Patient Information Sheets and Informed Consent Forms; A) Feasibility study, B) Case-control and cohort studies.

A) Feasibility study:

Welcome

We would like to invite you to be part of this research project. You should only agree to take part if you want to, and it is entirely up to you. If you choose not to take part there won't be any disadvantages for you and you will hear no more about it.

Before you decide it is important that you understand why the study is being done and what it would involve. Please take time to read the following information carefully before you decide to take part; this will tell you why the research is being done and what you will be asked to do if you take part. The researcher will happily go through the information sheet and answer any questions you may have.

If you decide to take part you will be asked to confirm on the following section to say that you agree. You are still free to withdraw at any time and without giving a reason.

Next

Participant Information Sheet

What is the purpose of the study and why have I been invited to take part?

You have been invited to take part because you have been diagnosed with a tendon problem affecting the hip, knee, shoulder or foot. We will apply different questionnaires and physical examinations depending on your diagnosed condition. Alternatively, you may have another musculoskeletal condition affecting these areas in which case we are also keen to find out more about you to compare to the main group. We are also very keen to recruit people without such problems so we can be sure that the findings of the research are true. For example, for every person with a knee tendon problem, we would like to recruit one person of similar age and background with a different hip problem and one with no such problems.

Tendinopathy is common and problematic if it does not resolve. It also affects daily quality of life. Surprisingly, although tendinopathy is a common problem, the causes of non-recovery or recurrence of tendinopathy remain unclear. There are some potential risk factors associated with the condition.

This is a feasibility study to test the data collection process and tools, and to establish the validity and reliability of the questionnaire, laboratory, clinical, and imaging approaches. In other words, this is essential preparatory work to help us make sure the future study runs really well and gives us trustworthy information.

Do I have to take part?

No. Whether or not you join the study is up to you. We will describe the study and go through this information sheet with you. If you agree to take part, then you will be asked to sign a consent form. You are free to withdraw at any time, without giving a reason. If you do wish to withdraw or you are asked to withdraw from the study, it will not affect you in any way.

What will happen to me if I take part?

Firstly: If you decide to take part in the study we will ask you to fill out a questionnaire. These questionnaires are about your general health, physical and musculoskeletal health conditions. The questionnaires will take about 30-40 minutes. We will ask you to do this twice, once an online version and another time with a paper version in clinic. We will tell you the order. If you find any of this difficult we can help you to fill it out.

Our contact e-mail is teamcohort@qmul.ac.uk

Secondly, we are keen to collect as much data from your clinical or ultrasound examination as possible. This is mainly information that clinicians usually collect from a thorough examination. The link for an online form is here. Again, we are happy to help your clinician fill this out.

Finally, we will invite people who live near London to come for an assessment of how they move in our laboratory. We will ask you to do some tasks depend on your condition such as walking for people with foot pain, jumping for people with knee pain, walking for people with hip pain, and arm movement for people with shoulder pain. We are happy to discuss this further.

Expenses and payments

We are happy to pay reasonable travel expenses to come to the laboratory.

For people who complete all the questionnaires and the clinical examination, we will give you a **£10 Amazon voucher** as a token of our appreciation.

What are the possible risks of taking part?

We do not foresee any risks from taking part in this study.

What are the possible benefits of taking part?

We cannot promise the study will help you personally, however the study findings should help us prevent and understand pain and tendinopathy better in the future. We are happy to send you the results of the study if you would like.

What happens if there is a problem?

If you have any questions or concerns about any aspect of the study or about the way of the study was conducted please, in the first instance, contact the researcher responsible for the study (project e-mail is teamcohort@qmul.ac.uk). They will try their best to answer your questions. If this is unsuccessful, or not appropriate, or you wish to make a formal complaint, please contact Hazel Covill, the Secretary at the Queen Mary Ethics of Research Committee, Room W104, Queen's Building, Mile End Campus, Mile End Road, London or research-ethics@qmul.ac.uk tel: 020 7882 7915/6947

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. Any data, which may identify you, will be held on secure servers. The research team will be the only ones allowed access to this information. By consenting to be involved in this study you give the research team permission to access your information. All information collected about you during the study and after completion will be kept strictly confidential and all researchers of the research team will abide by the Data Protection Act 1998 and the rights you have under this Act.

What happens if I don't want to carry on with the study?

You are free to withdraw at any time, without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect you. If you withdraw from the study, we will stop any future data collection, but we will need to use the anonymised data collected up until your withdrawal.

What will happen to the results of the study?

The results of the study will be analysed and presented as written work, presentation material and possible publication in a peer reviewed journal as a part of a postgraduate study. Provided that your data will be anonymized, the results may be presented at meetings and help to inform future practice. You can request to have a copy of the completed results. If this is your wish please let a member of the research team know.

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Queen Mary

CONSENT

Please complete this form after you have read the Information Sheet about the research.

Title of Study 1: **Tendinopathy TEAM 3a – predictors of outcome for tendinopathy: a feasibility study**

Queen Mary Ethics of Research Committee Ref: **QMREC2014/24/153**

Title of Study 2: **How training loads are associated with patellar tendinopathy.**

Queen Mary Ethics of Research Committee Ref: **QMREC2014/24/136**

* Please complete this form after you have read the Information Sheet.

☐ I confirm I have read and understood the participant information sheet for the above study and have had the opportunity to consider the information, to ask questions and to have these answered.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, this will not affect how I am treated in any way.

☐ I understand that all information about me will be kept in a confidential way and destroyed once the study is completed.

☐ I would like to learn my study results.

☐ I am happy to come and discuss further steps of the study such as clinical examination and movement analyses.

☐ I would consider attending for a second test in 7 days.

* I am between 18 and 64 years old.

○ Yes
○ No

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B) Case-control and cohort studies:

Participant Information Sheet

Tendinopathy TEAM 3*a* – predictors of outcome for tendinopathy:

Invitation paragraph

We would like to invite you to be part of this research project. If you choose not to take part there won't be any disadvantages for you. Before you decide we would like you to understand why the study is being done and what it would involve. Please take time to read the following information carefully before you decide to take part as it will tell you why the research is being done and what you will be asked to do. Please ask the researchers if there is anything that is not clear or if you would like more information.

If you decide to take part you will be asked to electronically sign a consent form on the next page. You are still free to withdraw at any time and without giving a reason.

What is the purpose of the study and why have I been invited to take part?
You have been invited to take part because you have been diagnosed with a tendinopathy affecting the hip, knee, ankle, shoulder or foot (plantar heel pain, or plantar fasciitis). Alternatively, you have another musculoskeletal condition affecting these areas. We are also very keen to recruit people without such problems so we can be sure that the findings of the research are true.

Tendinopathy is common and problematic if it does not resolve. It also affects quality of life. Surprisingly, although tendinopathy is a common problem, the causes of non-recovery or recurrence of tendinopathy remain unclear. The main study aim is to develop ways of predicting the course of tendinopathy and then inform clinicians. This may provide better health care services for patients.

What will happen if I take part?

We will firstly ask you to fill out some questionnaires about your general health and physical conditions which will take about half an hour. If you find any of this difficult we can help you.

We will send you a short (5 minutes maximum to fill out) follow-up questionnaire every four weeks for a year to help record your progress and find out when you recover.

Secondly, we are keen to collect information from your clinical or ultrasound examination that clinicians usually collect from a thorough examination. We are happy to help your clinician fill this out.

Thirdly, if you have shoulder pain, we are interested in shoulder blade movement which is important for shoulder. We want you to record your scapular movement video. When you send the video we will examine your scapular and shoulder movement.

Finally, we will invite people who live in London or cities surrounding London for an assessment of how they move in Human Performance Laboratory at Queen Mary University of London. We are happy to discuss this further.

No expenses or payments will be offered, but we are happy to pay reasonable travel expenses to come to the laboratory.

We do not foresee any risks from taking part in this study. We will keep your data safe, in accordance with QMUL data protection policies which are GDPR compliant. For people with shoulder pain although the back is being filmed you can be identified the due to physical differences. However, the videos will not be used to identify you and the video will be kept in locked cabinet by anonymising. Moreover, please record the video with your primary relatives or friend who you can trust.

We cannot promise the study will help you personally, however the study findings should help us

manage tendinopathy better in the future. You will play an active role in shaping this development by taking part in the study, and would gain a deeper understanding of your condition. We are happy to send you the results of the study if you would like.

What happens if there is a problem?

If you have any questions or concerns about any aspect of the study please, in the first instance, contact the researcher responsible for the study Professor Dylan Morrissey and his team via teamcohort@qmul.ac.uk or 07305249149. They will try their best to answer your questions. If this is unsuccessful, or not appropriate, or you wish to make a formal complaint, please contact Hazel Covill, the Secretary at the Queen Mary Ethics of Research Committee, Room W117, Queen's Building, Mile End Campus, Mile End Road, London or research-ethics@qmul.ac.uk tel: 02078827915

Will my taking part in this study be kept confidential?

Yes. We will use secure online data collection tools called 'SmartTrial' and 'Navigate Pain' . These are approved platforms and follow Queen Mary's privacy notice for research participants.

You can find important information about your personal data and your rights at: http://www.arcs.qmul.ac.uk/media/arcs/policyzone/Privacy-Notice-for-Research-Participants.pdf.

What happens if I don't want to carry on with the study?

You are free to withdraw at any time, without giving a reason. If you withdraw from the study, we will stop any future data collection, but will use the de-identified data collected up until your withdrawal.

What will happen to the results of the study?

The results of the study will be analysed and presented as written work, presentation material and possible publication in peer reviewed journals as a part of postgraduate study. Your data will be anonymized, and the results may be presented at meetings. You can request to have a copy of the completed results.

Consent form
Title of Study: Tendinopathy TEAM 3a – predictors of outcome for tendinopathy
Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

The study has been ethically approved by NHS, Ethics Ref: 264615, Version 1.0, Date: 26/06/2019

I confirm

◉ I have read and understood the participant information sheet dated 23062019 for the above study and have had the opportunity to consider the information, to ask questions and to have these answered.

I understand

☑ that my participation is voluntary and that I am free to withdraw at any time without giving a reason, this will not affect how I am treated in any way.

☑ that all information about me will be kept in a confidential way and destroyed once the study is completed.

☑ I would like to learn the study results.

☑ I would like to be sent a copy of my questionnaire results.

☑ I consent to attend the clinical and ultrasound examination part of the study.

☐ People with shoulder pain only: I consent to the analysis of my shoulder movement video and I understand the risks of video recording.

I agree

☑ to take part in this study

Appendix 13: STROBE Statement checklist of items that should be included in reports of case-control studies.

	Item No	Recommendation	Status
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls.	✓
		(*b*) For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	X
Study size	10	Explain how the study size was arrived at	X
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	✓
		(*d*) If applicable, explain how matching of cases and controls was addressed	NA
		(*e*) Describe any sensitivity analyses	✓
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	✓
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	✓
Outcome data	15	Report numbers in each exposure category, or summary measures of exposure	✓
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓
Keys: NA, not applicable; ✓, meets criterion; X, does not meet criterion.			

Appendix 14: STROBE Statement checklist of items that should be included in reports of cohort studies, and PROBAST assessment results for the prospective cohort study.

	Item No	Recommendation	Status
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	✓
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	X
Study size	10	Explain how the study size was arrived at	✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	✓
		(*d*) If applicable, explain how loss to follow-up was addressed	✓
		(*e*) Describe any sensitivity analyses	✓
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	✓
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	✓
		(c) Summarise follow-up time (eg, average and total amount)	✓
Outcome data	15	Report numbers of outcome events or summary measures over time	✓
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

Keys: NA, not applicable; ✓, meets criterion; X, does not meet criterion.

Risk of bias				Applicability			Overall	
Participants	Predictors	Outcome	Analysis	Participants	Predictors	Outcome	Risk of Bias	Applicability
+	+	+	+	+	+	+	+	+

+ indicates low risk of bias/low concern regarding applicability