Targeted Interventions for Patellofemoral Pain (TIPPs): classification of clinical sub-groups

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Study Protocol: Targeted Interventions for Patellofemoral Pain (TIPPs): classification of clinical sub-groups

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Abstract

Introduction

Patellofemoral Pain (PFP) can cause significant pain leading to limitations in societal participation and physical activity. An international expert group has highlighted the need for a classification system to allow targeted intervention for patients with PFP; we have developed a work programme systematically investigating this. We have proposed six potential sub-groups: hip abductor weakness, quadriceps weakness, patellar hypermobility, patellar hypomobility, pronated foot posture and lower limb biarticular muscle tightness. We could not uncover any evidence of the relative frequency with which PFP patients fell into these sub-groups or whether these sub-groups were mutually exclusive. The aim of this study is to provide information on the clinical utility of our classification system.

Methods and Analysis

150 participants will be recruited over 18 months in four NHS physiotherapy departments in England. Inclusion criteria: adults 18-40 years with PFP for longer than three months; PF pain in at least two pre-designated functional activities; PF pain elicited by clinical examination. Exclusion criteria: prior or forthcoming lower limb surgery; co-morbid illness or health condition; lower limb training; or pregnancy. We will record medical history, demographic details, pain, quality of life, psychomotor movement awareness and knee temperature. We will assess hip abductor and quadriceps weakness, patellar hypermobility and hypomobility, foot posture and lower limb biarticular muscle tightness.

The primary analytic approach will be descriptive.
We shall present numbers and percentages of participants who meet the criteria for membership of:
(i) each of the sub-groups;
(ii) none of the sub-groups;
(iii) multiple sub-groups;
Exact (binomial) 95% confidence intervals for these percentages will also be presented.

Ethics and dissemination

This study has been approved by NRES Committee North West – Greater Manchester North (11/NW/0814) and UCLan BuSH Ethics Committee (BuSH 025). An abstract has been accepted for the 3rd International Patellofemoral Pain Research Retreat, Vancouver, September 2013.

Article Summary

Article Focus

- Testing the feasibility of using a clinical practice framework to assign PFP patients into sub-groups
- Assessing the frequency with which PFP patients fall into sub-groups
- Assessing whether sub-groups are mutually exclusive.

Key Messages

- 101/150 patients recruited to date
- Comprehensive psychosocial assessment of demographic details, pain, quality of life, psychomotor movement awareness and knee temperature. (approximately 20 minutes to complete)
- Clinical assessment of hip abductor and quadriceps weakness, patellar hypermobility, patellar hypomobility, foot posture and lower limb biarticular muscle tightness. (approximately 25 minutes to complete)

Strengths and Limitations of this study

- Currently the largest RCT sample size is 176 patients our target sample size of 150 patients for this feasibility study indicates the scale and ambition of our programme of work.
- We have also included a comprehensive set of psychosocial and physiological measures as these may also help us to understand differences between potential sub-groups. Traditionally patellofemoral research has focussed on biomechanical, and to some extent pain measures, and has paid little attention to the wider holistic picture of a patient's complaint.
- We have not included an assessment of cost or resource use in this study. Therefore any differential in the resource use of different sub-groups will remain unknown.
- Qualitative methods would enhance the investigation of psychosocial aspects.
- The study is not longitudinal, but importantly will provide key data to inform such studies.

BACKGROUND

Patellofemoral Pain (PFP) can cause significant pain and dysfunction leading to limitations in societal participation and physical activity. Higher body mass indices and higher than expected levels of disability and psychological morbidity have been observed in patients with PFP [1,2]. A number of studies provide evidence which challenges the common view that PFP is a relatively trivial and self- limiting condition: 91% of patients had pain and dysfunction at a follow up of a minimum of 4 years following diagnosis [3]; 96% reported having problems a mean of 4 years following diagnosis [4]; 73% still had pain at an average of 5.7 years follow up [5]; 94% had on-going problems for on average 16 years following diagnosis [6].

It has also been reported that there is a possibility that PFP predisposes people to osteoarthritis in later life; Stathopulu & Baildam [3] found that 45% of their PFP patients, for whom PFP was the first recorded musculoskeletal problem, were later diagnosed with other arthritic conditions. In a study of people with knee pain aged over 50 years, it was found that 507 (64%) had definite radiographic evidence of patellofemoral osteoarthritis, which suggests that there are specific degenerative processes occurring within the patellofemoral joint, which may not be related to the other articular components of the knee. It is unknown how many of these patients had patellofemoral problems when they were younger [7]. Utting et al, reported that 22% of patients (mean age 67) undergoing uni-compartmental patellofemoral arthroplasty recalled having patellofemoral pain as an adolescent [8]. However, a recent systematic review reported that the link between PFP and patellofemoral osteoarthritis should be interpreted with caution due to the paucity of high quality evidence [9].

PFP is a condition commonly referred for physiotherapy [10] and PFP recently emerged as the 3rd highest ranked topic out of 185 in the Chartered Society of Physiotherapy Musculoskeletal Research Priority Project [11]. In this national survey, there was 94.9% agreement on the importance of PFP with respect to physiotherapy practice, quality of care, cost effectiveness, and public health. The mean number of NHS physiotherapy treatment sessions for patients referred with PFP is reported as eight with the maximum number of sessions reported as 17 [12]. The Cochrane Library lists 4 current reviews [13,14,15,16]; 2 withdrawn reviews [17,18] and 1 protocol [19] which are specific to the conservative management of PFP. Collectively these reviews suggest that there is a weak evidence base for conservative management of PFP, including physiotherapy, mainly due to the poor methodological quality of existing studies. In 2012 we found 52 RCTs recruiting 2667 participants that investigated interventions for PFP, 60% reported results that were not statistically significant. The average sample size was 51 participants and the largest study [20] included 176 participants. As reflected in the number of Cochrane reviews conservative care for PFP is diverse and usually consists of a multimodal package of interventions. The current multimodal approach can include a variety of muscle strengthening and stretching techniques, patellar taping or bracing and foot orthotics. More recent high quality studies [21,22] have proposed that a targeted intervention approach for specific sub-groups of PFP patients may produce improved patient outcomes. Crossley et al [21] also discuss the need for developing PFP patient classification systems so that "*more specific treatment can be designed and evaluated*". The idea of clinically sub-grouping PFP patients and then delivering targeted treatment emerged from the First International PFP

Research Retreat [23]. One of the questions posed, as part of the consensus-building process, was "*Where do we need to go*?" The response was "*Identification of sub-groups of people with PFP is needed. This may be achieved through the use of high quality Randomised Controlled Trials (RCTs), which should only investigate a few potential subgroups for which there is a credible rationale...High quality RCTs for different conservative treatments (e.g. hip muscle retraining, gait re-education) are strongly encouraged. However, these treatments should be targeted to those sub-groups of people who are most likely to benefit*" [23]. The conference proposed three anatomically based sub-groups, proximal (hip and pelvis), local (patella and knee factors) and distal (foot and ankle). The same proximal, local and distal sub-grouping approach was adopted by the Second International PFP Research Retreat [24]. This sub-grouping provides a rationale for researchers to develop targeted treatment interventions. However to date there have been no studies which have further investigated this premise. Interestingly a separate process of international consensus building about the future direction of research in the field of primary care musculoskeletal studies has been conducted [25]. This group has also highlighted the need for future studies to adopt a sub-grouping targeted approach in order to improve our understanding of the mechanisms underlying musculoskeletal problems to optimise patient management. They highlight that in previous studies the heterogeneity of patient samples produces a small treatment effect, which masks a wide range of individual responses leading to the conclusion that non-pharmacological interventions in musculoskeletal conditions lead to little patient benefit.

WORK PLAN

We have developed a work programme consisting of a number of phases to investigate sub-grouping and the targeted intervention approach in PFP. Phase 1: was the theoretical classification of patients with PFP into distinct clinical groups based on clinical assessment tests, which could be used to target intervention in clinical practice, through the development of a clinical practice framework. Phase 2 (the current phase): is developing and testing the feasibility of using a clinical practice framework to assign PFP patients into sub-groups. Phase 3: Randomised controlled trial evaluating the cost-effectiveness of using the clinical practice framework compared to usual care to improve quality of life of patients with PFP. This will incorporate an internal pilot study, to check assumptions about outcome variability which will inform sample size estimates.

Results of Phase 1: **Identification and development of clinical assessment tests**

We have completed Phase 1 of this work. This was a literature review, evidence synthesis and clinical mapping undertaken by the TIPPs research team to establish supporting evidence for the existence of sub-groups. Sub-groups were derived from the literature which conformed to the following criteria: (1) They could potentially be identified by simple evidence based clinical assessment tests; (2) The tests could be used routinely by physiotherapists in a variety of clinical practice settings ranging from Primary Care facilities to Tertiary Teaching Hospitals; (3) Minimal expertise and training was required for competent performance of the tests; (4) Any equipment required for the tests needed to be low cost; (5) Published thresholds for potentially assigning patients to sub-groups had to be available; (6) Any potential sub-group then had to be matched to a specific and credible treatment intervention. Using the

First International PFP Research Retreat sub-groups as a starting point we found that there was often more than one clinical problem at the proximal, local and distal sites, that there were multiple and sometimes complex clinical assessment tests and multiple interventions. For example proximally at the hip a number of different strength factors have been proposed [26, 27]. Locally at the patella and knee patients with proprioceptive deficits have been identified [28, 29], however the problem with this sub-group is that as yet there are no simple and cheap methods to accurately identify proprioceptive deficit in clinical centres that do not have access to dynamometry. Distally at the foot and ankle two clinical prediction rules for the likely success of orthotic intervention have been proposed, however there is no agreement between the two studies as to the individual clinical items. The first [30] lists 3 items: forefoot valgus alignment; great toe extension; navicular drop test and the second [31] lists 4 different items: age; height; worst pain measured using a visual analogue scale; mid-foot width difference from weight bearing to non-weight bearing. Therefore at the end of this work we have proposed 6 rather than 3 sub-groups each of which has a specific clinical test which yields a score from which a threshold has previously been published. The threshold scores will be used to assign patients to sub-group membership (Figure 1). However, the literature was unable to provide any evidence of the relative frequency with which PFP patients fell into each of these sub-groups and whether these sub-groups were mutually exclusive. Therefore the next stage of our developmental work is an investigation of the distribution of patients into the sub-groups when the clinical assessment tests and subsequent threshold scores are applied in routine physiotherapy practice (Phase 2). This is the feasibility study which forms the basis of this paper. The main aims of this feasibility study are to assess the relative frequency with which patients fall into each of the sub-groups, and whether or not the sub-groups are mutually exclusive. By the end of this study we would expect to have greater clarity as to whether all, some or none of our proposed sub-groups could potentially be useful in clinical practice to form the basis of targeted treatment.

Phase 2: Methods

Research Question

Do clinically important sub-groups of PFP patients exist?

Aim of Study

To provide information on the clinical utility of sub-grouping PFP patients.

Study Objectives

This study is designed to provide clinical evidence for theoretically derived sub-groups of PFP patients which may be appropriate for targeted treatment. In this study we will apply evidence based routine clinical assessment tests to a representative sample of patients with PFP referred for physiotherapy in order to examine: i) the relative frequency with which they fall into each of the sub-groups. ii) whether the sub-groups are mutually exclusive or whether, and how frequently, patients fall into two or more sub-groups. iii) whether there are any sub-groups which may not be clinically important in the context of targeted treatment because insufficient patients fall into these sub-groups. iv) whether patient and clinical characteristics vary between the sub-groups. The collection of study data will also allow us to explore the potential for better methods of classifying sub-groups by including patient and/or clinical characteristics or by the use of different test thresholds.

Study design
Observational study, at one time point (commencement of physiotherapy), of adults age 18-40 years with a clinical diagnosis of unilateral or bilateral patellofemoral pain present for longer than three months (For full eligibility criteria see Table 1).

Setting
Four NHS physiotherapy departments in England; Central Manchester University Hospitals NHS Foundation Trust; Harrogate and District NHS Foundation Trust; Lancashire Care NHS Foundation Trust; NHS Solent.

Patient recruitment
One hundred and fifty potential participants in total will be recruited over an eighteen month period across the four collaborating centres. A research physiotherapist based within each of the four physiotherapy departments will check eligibility and obtain informed consent. Each patient that agrees to take part will be assessed once only by a research physiotherapist (one at each participating centre). The research assessment for this feasibility study will consist of two parts. Part 1; assessment of demographic, clinical and psychosocial patient characteristics which will take approximately 20 minutes to complete (Table 2). Data will be collected on characteristics known to have an impact on outcome. This data may help us to further understand differences between potential sub-groups or suggest new sub-groups. Previous studies have used some of these tools, however no other study has attempted to systematically investigate psychosocial issues in PFP patients in the comprehensive manner proposed here. Part 2; clinical assessment tests which take approximately 25 minutes to complete (Table 3). Thresholds, for assigning participants to sub-groups, for each test are based on normative data from healthy populations plus or minus 1 standard deviation (Figure 1).

Clinical assessment tests
Dynamometer measurement of quadriceps muscle strength using a Lafayette Manual Muscle Test System (Range: 0-136kg): The participant will be in a seated position and the hips and knees flexed to 90 degrees. Muscle strength of the knee extensors will be assessed with a portable dynamometer mounted against a stabilisation strap positioned perpendicular to the tibia just above the malleoli. The force exerted against the dynamometer in this position will be recorded and the moment arm of this force around the extension/flexion axis of the knee joint will be measured using a tape measure as the distance from the level of the dynamometer on the tibia to the centre of the knee joint (assumed to coincide with the most prominent point on the femoral epicondyle identified via palpation). These two measurements will be used to calculate the maximum knee extensor moment (Nm) during an isometric maximal voluntary contraction (MVC) test as the product of the force in Newtons (N) and moment arm in metres (m) [32]. *Dynamometer measurement of hip abductors muscle strength:* The participant will be in side lying with the tested leg uppermost in the neutral anatomical position. The participant will be asked to abduct their leg sideways (i.e. towards the ceiling) from this position; the portable dynamometer mounted against a stabilisation strap will be held perpendicular to the side of the leg at a level just above the knee joint. To ensure that abductor muscle strength is tested and that the lower limb does not rotate externally, the participants will be instructed to ensure their toes are pointed horizontally during the contraction. The force exerted against the dynamometer in

this position will be recorded and the moment arm of this force around the adduction/abduction axis of the hip joint will be measured using a tape measure as the distance from the level of the dynamometer on the thigh to the centre of the hip joint. These two measurements will be used to calculate the maximum hip abductor moment (Nm) during an MVC test as the product of the force (N) and moment arm (m) [32]. Strength testing will be performed to assess functional capacity, in particular we are interested in the relative balance between the Quadriceps and Hip Abductors. This simple clinical test procedure will not enable the peripheral and central components of muscle dysfunction to be identified but will provide a useful indication of contractile performance. *Patellar glide:* With the participants in supine, the quadriceps muscles relaxed and the knees in extension, the clinician will apply a medially and then a laterally directed force to the patella. The total displacement of the pole of the patella will be recorded in millimetres in the coronal plane [33]. *Passive knee extension (Hamstrings length):* The participant will be positioned supine on a plinth. The lower limb not being tested will be positioned in hip and knee extension. The research physiotherapist will position the hip and knee of the tested side in 90° of flexion, thus marking the starting position for the test. With one hand supporting the participant's distal thigh and the other hand cupping the heel, the research physiotherapist will passively extend the knee until firm resistance is elicited. At this point the angle of the tibia is recorded with a digital inclinometer [34]. *Passive prone knee bend (Quadriceps length):* The participant will be positioned in prone lying on the edge of a plinth so that the foot on the non-involved side will be placed on the floor at 90° hip flexion. The knee of the tested leg will be passively maximally flexed until resistance or discomfort is elicited. In this position the angle of the tibia will be recorded with a digital inclinometer [33]. *Standing method for assessing calf flexibility:* The length of the gastrocnemius muscle will be obtained by having the participant lean on a solid support 0.6m away with the tested leg behind the contralateral leg and keeping the knee of the tested leg extended. The participants will be instructed to maximally flex their tested ankle while keeping their heel on the floor. The angle of the tibia is recorded relative to vertical with a digital inclinometer [33]. *Foot posture index (FPI):* There are six component assessments: 1. Talar head position, 2. Supra and infra-lateral malleolar curvature, 3. Calcaneal frontal plane position, 4. Prominence in the region of the talonavicular joint, 5. Congruence of the medial longitudinal arch, 6. Abduction/adduction of the forefoot on the rearfoot. Each of the component assessments or observations are graded 0 for neutral, with scores of -2 for clear signs of supination and +2 for clear signs of pronation. Unless the criteria outlined for each of the features are clearly met then the more conservative score will be awarded. When the scores are combined, the aggregate value gives an estimate of the overall foot posture. Large positive aggregate values indicate a pronated posture [35].

Training of research therapists

All research physiotherapists will undertake a full day training session during the first month of the study, when they will be provided with training on the research processes and on how to undertake the standardised clinical assessment tests. During the training sessions, all the therapists will be observed by the PI and Dr Callaghan performing each of the clinical test procedures and provided with peer feedback. Inter-therapist variability will be examined during these sessions and although it will not be possible to conduct a formal inter-rater reliability assessment during the training it will provide an opportunity to observe any variability in

performance and address it. All the physiotherapists will be provided with a comprehensive manual including the standard operating procedures, along with a data recording proforma.

Sample size

Given the nature of the study, power calculations are not applicable. One hundred and fifty participants will enable us to estimate, with 95% confidence, the numbers and percentages of participants who meet the criteria for membership of: (i) each of the 6 sub-groups individually; (ii) none of the sub-groups; (iii) multiple sub-groups (for each represented sub-group combination) to within ±7.5% for well-represented (30% prevalence) sub-groups and to within ±3.5% for sparse (5%prevalence) sub-groups (or multiple sub-groups).

Analysis Plan

As the main purpose of the study is to describe the distribution of PFP patients into the different sub-groups following application of the clinical assessment test criteria, including whether patients meet the criteria for multiple sub-groups or fail to meet the criteria for any of the sub-groups, the primary analytic approach will be descriptive. We shall present numbers and percentages of participants who meet the criteria for membership of:
(i) each of the 6 sub-groups individually;
(ii) none of the sub-groups;
(iii) multiple sub-groups (for each represented sub-group combination).
Exact (binomial) 95% confidence intervals for these percentages will also be presented. We shall also present descriptive statistics (mean [SD], median [IQR], count [%], as appropriate) of the patient characteristics for each sub-group (including the no clinical sub-group) to indicate how these characteristics vary across sub-groups. The data will also enable some further exploratory analyses to be performed. The nature of these analyses will depend on the patterns of the distribution of participants into sub-groups. However, we expect that they will include an exploration of the sensitivity of the distribution of sub-group membership to the choices of thresholds, particularly if substantial numbers of patients fall into either multiple sub-groups or no sub-group; they are also likely to include explorations of the joint effects of patient characteristics on the distribution of patients into sub-groups, using techniques including multiple logistic regression. Demographic, clinical and psychosocial characteristics as previously described may also be included as covariates in later exploratory model-based analyses.

DISCUSSION

Recent literature has strongly promoted the idea of sub-grouping PFP patients and delivering targeted treatment, as it is believed that this may be more beneficial than the current multimodal therapeutic approaches [20,21,22]. Despite these recommendations, this premise has not yet been investigated. The main aims of this feasibility study are therefore to assess the relative frequency with which patients fall into each of the sub-groups, and whether or not the sub-groups are mutually exclusive.

As outlined above, the study has a number of strengths and addresses key gaps in current knowledge. It is ambitious in terms of both scale and scope. There is often controversy and lack of consensus within the field of patellofemoral research, due to

two related factors associated with the nature of the current evidence base. Firstly there are a relatively large number of normative data studies conducted on very small samples of healthy subjects that do little to enhance our understanding of this complex chronic condition [36]. Secondly, as already discussed, there is a limited number of high quality, large scale clinical trials. Set against this context, where currently the largest RCT sample size is 176 patients [20], our target sample size of 150 patients for this feasibility study indicates the scale and ambition of our programme of work. In terms of the scope of this study, we have also included a comprehensive set of psychosocial and physiological measures as these may also help us to understand differences between potential sub-groups. Traditionally patellofemoral research has focussed on biomechanical, and to some extent pain measures, and has paid little attention to the wider holistic picture of a patient's complaint. One study has indicated that psychological morbidity may be important in PFP [2]. The more comprehensive data being obtained in the present study will provide us with a unique insight into the patient's experience of the condition which may also help further our understanding of future treatment options. There are also potential limitations in the scope of this study. We have not included an assessment of cost or resource use in this study. Therefore any differential in the resource use of different sub-groups will remain unknown; we plan to address this in Phase 3 of our programme of work. In the current feasibility study, there is however, a health economics component as we are collecting EQ-5D-5L data so we will gain some insight into the potential health consequences of different sub-groups. Qualitative methods would enhance the investigation of psychosocial aspects. We envisage using mixed methods, as well as more patient and public involvement in subsequent studies. The study is not longitudinal, but importantly will provide key data to inform such studies. The results of the present study are expected in 2014. They will provide answers to a number of questions about the validity and relevance of sub-grouping in PFP in clinical practice, and will inform future trials.

STATUS

The study has currently recruited 101/150 patients and is scheduled to be completed by 29/11/13.

ETHICS

This study has been approved by NRES Committee North West – Greater Manchester North, REC reference: 11/NW/0814 and UCLan BuSH Ethics Committee Reference Number: BuSH 025. All relevant Research and Governance approvals have been secured at the 4 NHS Trusts where data collection is taking place and all licenses obtained for the questionnaire instruments where required.

AUTHORS CONTRIBUTIONS

JS, JR, EW, MC, ER contributed to study conception, design and attained project funding. PD,CS, JD, DM, MS, DT contributed to study design and attained project funding. JJ contributed to project management and study design. All authors contributed to manuscript preparation and have read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Data sharing

No unpublished data have been produced

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Table 1:Eligibility criteria [22,37]

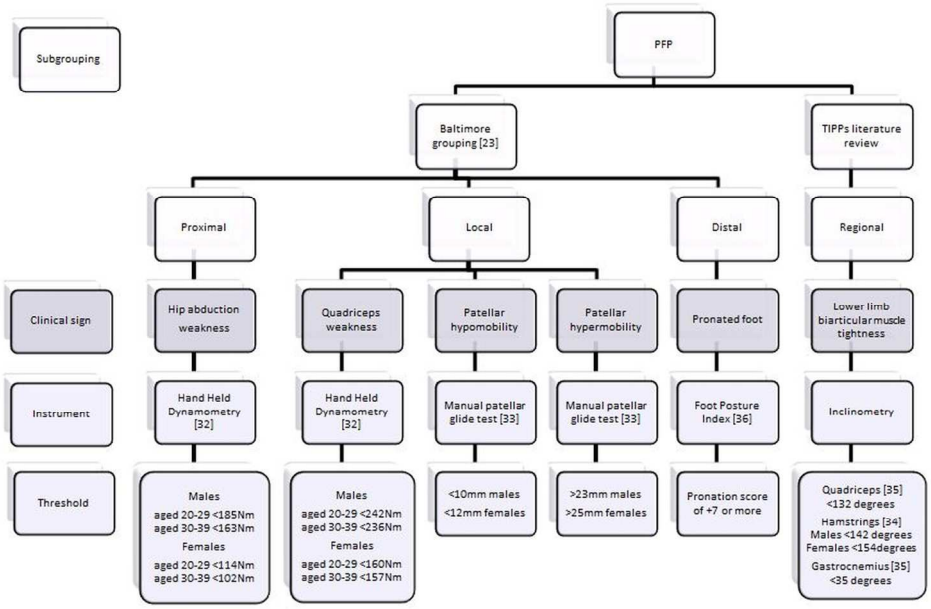
Inclusion criteria
Males and females age 18-40 years able to give informed written consent
Clinical diagnosis of unilateral or bilateral patellofemoral pain longer than three months
Anterior or retropatellar pain reported on at least two of the following activities: prolonged sitting, ascending or descending stairs, squatting, running, kneeling, and hopping/jumping
In addition to the above, at least two of the three following clinical examination findings: • pain during resisted isometric quadriceps contraction • pain with palpation of the posterior borders of the patella • pain during squatting
Exclusion criteria
Previous knee surgery & subjects awaiting surgery for another lower limb joint problem(s).
Ligamentous instability and/or internal derangement
History of patella subluxation or dislocation
Joint effusion when the mid-patellar girth is 5% or more than the non-involved knee
True knee joint locking and/or giving way
Coexistent acute illness or chronic disease
Bursitis, patella or iliotibial tract tendinopathy, Osgood Schlatter's disease, Sinding-Larsen Johansson Syndrome, muscle tears or symptomatic knee plicae
Subjects already involved in active lower limb training programs.
Pregnancy or breast feeding.

Table 2 Patient Characteristics Assessment

Domain	Questionnaire / items
Clinical characteristics	time since onset previous treatment history of trauma physical activity (International Physical Activity Questionnaire IPAQ) [38] physical functioning (Modified Functional Index Questionnaire (MFIQ) [39]
Socio-demographic characteristics	Age gender
Anthropometry	height weight body mass leg length skin fold over the patellae
Psychosocial	
Pain measures	Nociceptive Pain Short Form McGill Pain Questionnaire (SF-MPQ-2) [40] Numeric Pain Rating Scale (NPRS) for average pain during the past week Neuropathic Pain Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire [41]
Quality of life	WHO Disability Assessment Scale 2 (WHODAS 2.0) [42] EQ-5D-5L [43] Hopkins Symptom Checklist 25 (HSCL-25) [44]
Psycho-motor movement awareness	Movement Specific Reinvestment Questionnaire [45]
Physiological parameters	Self-reported indicators of cold knees [46] skin temperature measurement (over centre of patella & muscle belly of tibialis anterior)

Table 3: Clinical Assessment Tests

Proposed Clinical Group	Test
Hip Abductor weakness	Hand Held Dynamometry [32]
Quadriceps weakness	Hand Held Dynamometry [32]
Patellar Hypomobility	Patellar Glide Test [33]
Patellar Hypermobility	Patellar Glide Test [33]
Pronated Foot Posture	Foot Posture Index [35]
Lower Limb Biarticular muscle tightness	Rectus femoris Length test [33] Hamstrings length test [34] Gastrocnemius length test [33]



TIPPs Groups
140x90mm (300 x 300 DPI)