Thesis Submission for Doctor of Philosophy

# The influence of lower limb biomechanics on the development, persistence and management of patellofemoral pain in recreational runners

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'Submitted in part fulfilment of the requirements

of the degree of Doctor of Philosophy'

# i. Statement of originality

I, Bradley Stephen Neal, 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.

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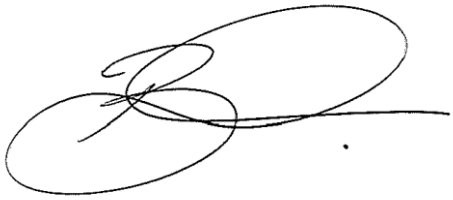

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## ii. Abstract

**Background** Patellofemoral pain (PFP) is a common complaint characterised by diffuse retropatellar or peripatellar pain during activities such as running, stair descent or squatting. We aimed to determine the influence of lower limb biomechanics on the development, persistence and management of PFP in recreational runners.

**Methods** Two systematic reviews with meta-analysis explored risk factors for, and the associations between, PFP and lower limb biomechanics respectively. A case-control study investigated lower limb kinematics during treadmill running and a feasibility study explored recruitment, retention and delivery of a step rate intervention in mixed-sex runners. Finally, a validity study investigated the potential for two-dimensional (2D) video to predict three-dimensional (3D) running kinematics.

**Results** Understanding of which variables contribute to PFP development is inadequate, requiring further exploration. Multiple retrospective associations between and potential treatment mechanisms for lower limb biomechanics and PFP were identified, but prospective data is lacking. A mixed-sex cohort of runners demonstrated higher peak hip adduction compared to controls. Higher peak hip adduction was also observed when comparing females with PFP to controls, but data for males were non-significant. Recruitment and retention of a mixed-sex cohort of runners with PFP to a step rate intervention was feasible. Clinically relevant changes in pain and potential kinematic treatment mechanisms were identified post-retraining, though these mechanisms were not detectable with 2D video.

**Conclusion** Potential influences of lower limb biomechanics once a recreational runner has PFP are well established. Further work is required to determine what biomechanical variables may contribute to PFP development, with novel approaches required. Sex influences lower limb kinematics and as such, males and females may have different symptom drivers requiring individual treatment strategies. Step rate retraining demonstrated potential efficacy and treatment mechanisms that warrant further appraisal in an adequately powered randomised controlled trial to long-term follow up.

## iii. Publications and presentations related to thesis work

### Resultant publications

**Neal, BS**, Barton, CJ, Gallie, R, O'Halloran, P, Morrissey, D. Runners with patellofemoral pain have altered biomechanics which targeted interventions can modify: A systematic review and meta-analysis. Gait & Posture. 2016;45:69-82.

**Neal, BS**, Barton, CJ, Birn-Jeffrey, A, Daley, M, Morrissey, D. The effects and mechanisms of increasing running step rate: a feasibility study in a mixed-sex group of runners with patellofemoral pain. Physical Therapy in Sport. 2018;32:244-251.

**Neal, BS,** Lack, SD, Lankhorst, NE, Raye, AD, Morrissey, D and Van Middelkoop, M. Risk factors for patellofemoral pain: a systematic review and meta-analysis. British Journal of Sports Medicine. *(Article currently in production)*

**Neal, BS**, Barton, CJ, Birn-Jeffrey, A, Morrissey, D. Increased hip adduction during running is associated with patellofemoral pain and differs between males and females: a case-control study. *(Article currently in review).*

### Related publications

**Neal, BS**, Griffiths, IB, Dowling, GJ, Murley, GS, Munteanu, SE, Franettovich-Smith, MM, et al. Foot posture as a risk factor for lower limb overuse injury: a systematic review and meta-analysis. Journal of Foot and Ankle Research. 2014;7(1):55.

Dowling, GJ, Murley, GS, Munteanu, SE, Franettovich-Smith, MM, **Neal, BS**, Griffiths, IB, et al. Dynamic foot function as a risk factor for lower limb overuse injury: a systematic review. Journal of Foot and Ankle Research. 2014;7(1):53.

Barton, CJ, Bonanno, DR, Carr, J, **Neal, BS**, Malliaras, P, Franklyn-Miller, A, et al. Running retraining to treat lower limb injuries: a mixed-methods study of current evidence synthesised with expert opinion. British Journal of Sports Medicine. 2016;50(9):513-26.

Lack, SD, **Neal, BS**, Silva, DD, Barton, CJ. How to manage patellofemoral pain - Understanding the multifactorial nature and treatment options. Physical Therapy in Sport. 2018;32:155-166.

### Resultant conference presentations

Neal, BS, 2015. Runners with patellofemoral pain have altered biomechanics which targeted interventions can modify: A systematic review and meta-analysis. Danish Sports Medicine Congress, Copenhagen and the International Patellofemoral Pain Research Retreat, Manchester. Podium Presentations.

Neal, BS, 2015. The effects and mechanisms of increasing running step rate: a feasibility study in a mixed-sex group of runners with patellofemoral pain. International Patellofemoral Pain Research Retreat, Manchester. Podium Presentation.

Neal, BS, 2016. The effects and mechanisms of increasing running step rate: a feasibility study in a mixed-sex group of runners with patellofemoral pain. Danish Sports Medicine Congress, Kolding. Podium Presentation.

Neal, BS, 2017. The effects and mechanisms of increasing running step rate: a feasibility study in a mixed-sex group of runners with patellofemoral pain. International Patellofemoral Pain Research Retreat, Gold Coast, Australia. Podium Presentation.

Neal, BS, 2017. Risk factors for patellofemoral pain: a systematic review and meta-analysis. International Patellofemoral Pain Research Retreat, Gold Coast, Australia. Podium Presentation.

Neal, BS, 2018. Risk factors for patellofemoral pain: a systematic review and meta-analysis. Danish Sports Medicine Congress, Copenhagen. Podium Presentation (presented by Dr Marienke Van Middelkoop).

### Related conference presentations

Neal, BS, et al, 2014. Foot posture as a risk factor for lower limb overuse injury: a systematic review and meta-analysis. Sports Medicine Australia Conference, Canberra, Australia. Podium Presentation (Presented by Dr Christian Barton).

Neal, BS, et al, 2014. Foot posture as a risk factor for lower limb overuse injury: a systematic review and meta-analysis. British Association of Sports and Exercise Medicine (BASEM) Annual Conference. Poster Presentation.

Neal, BS, 2016. Gait retraining for running related injury: what, why and how? 14th Groningen Sports Medicine Symposium, Groningen, Holland. Invited Plenary Presentation and Paralell Workshop.

Rathleff, M, Lack, SD and Neal, BS, 2016. Moving beyond exercise for patellofemoral pain. International Federation of Orthopaedic and Manual Therapists (IFOMPT) Conference, Glasgow. Invitied Podium Presentation

Rathleff, M, Lack, SD and Neal, BS, 2017. Moving beyond exercise for managing the common knee complaints. Danish Sports Medicine Congress, Copenhagen. Invitied Podium Presentation.

Neal, BS, 2018. An exploration into the incidence, prevalence and treatment outcomes of patellofemoral pain in uk sports medicine: a mixed methods study. Danish Sports Medicine Congress, Copenhagen. Poster Presentation.

Neal, BS, 2018. An exploration into the incidence, prevalence and treatment outcomes of patellofemoral pain in UK sports medicine: a mixed methods study. Physiotherapy Research Society Annual Conference, Newcastle Upon-Tyne. Podium Presentation.

## iv. List of Figures

## v. Tables

## vi. List of abbreviations

PFP – patellofemoral pain

UK – United Kingdom

BMI – body mass index

SMD – standardised mean difference

sEMG – surface electromyography

HADD – hip adduction

HIR – hip internal rotation

VAS – visual analogue scale

LEFS – lower extremity functional scale

RCT – randomised controlled trial

KOOS – knee osteoarthritis outcome score

AVLR – average vertical loading rate

2D – two-dimensional

3D – three-dimensional

ICC – intraclass correlation coefficient

*r* – Pearson's correlation coefficient

*d* – Cohen's *d*

FADD – femoral adduction

CLPD – contralateral pelvic drop

PRISMA – preferred reporting items for systematic reviews and meta-analyses

NOS – Newcastle Ottawa Scale

HQ – high quality

MQ – moderate quality

LQ – low quality

RR – risk ratio

VMO – vastus medialis obliqus

NRS – numerical rating scale

KFLEX – knee flexion

HFLEX – hip flexion

GMAX – gluteus maximus

GMED – gluteus medius

ST - semitendinosus

## vii. Acknowledgements

Completing my PhD has been a deeply rewarding experience that would not have been possible without the support of multiple people, whom it would be remiss not to acknowledge in detail.

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# 1. Introduction

Patellofemoral pain (PFP) is a common musculoskeletal complaint, affecting 22.7% of the United Kingdom (UK) general population (1). Long-term treatment outcomes are suboptimal, with more than one in two patients reporting an unfavourable outcome more than five years after diagnosis (2). PFP is thought to be the start of a continuum which may culminate in Patellofemoral Osteoarthritis (3). This means improving management in young adults may have positive implications for both individuals and the health care system in both the short and long term. Aggravating factors associated with PFP include squatting, stair ascent/descent, running or hopping/jumping (4). There is no singular diagnostic test for PFP (5), with a clinical diagnosis instead reached in the presence of pain located at, around or behind the patella (4) after the exclusion of alternative or concomitant pathologies such as patella tendinopathy, iliotibial band syndrome or tibiofemoral pathology as the primary symptom driver. Imaging is not recommended as part of the primary diagnostic process owing to the questionable relevance of articular structure changes, which are prevalent in symptomatic and asymptomatic individuals (6).

## 1.1. Running participation and health benefits

Participation in recreational running has nearly doubled in the past 6 years. Specifically, the number of people running once per week in the UK throughout 2016 approached 30,000 people, compared to just 15,000 in 2010 (7). The popularity of running is likely due to the ease of accessibility and relative low cost associated with recreational running participation (8). Running is also associated with multiple positive health benefits. A recent systematic review and meta-analysis reports moderate evidence that running improves cardiovascular function and aerobic fitness, and reduces adiposity (9). There is further level one evidence that regular running reduces body fat percentage, blood triglycerides and resting heart rate in inactive individuals (10). Finally, regular running has been reported to reduce all-cause mortality by 30-45% after adjustment for age and sex (11).

## 1.2. Running injury prevalence

Despite multiple health benefits, recreational running also increases risk of musculoskeletal injury (12). Dependent on the chosen source and injury definition (8,

13), 18-79% of recreational runners are reported to sustain a musculoskeletal injury in a calendar year. PFP is reported as the most prevalent injury, accounting for 17% of all running-related injuries presenting to Sports Medicine facilities (14), twice as common as the next most prevalent injury (iliotibial band syndrome, 8%). Additionally, a recent injury surveillance study completed in the UK reported that 49.8% of recreational runners described themselves as having a musculoskeletal injury related to running, with injury to the knee region the most prevalent (15).

### 1.3. PFP incidence

New incident cases of PFP appear to vary dependent on the population studied. A recent meta-analysis from Smith et al (16) reported that the incidence of PFP within military recruits ranges from 9.7 to 574.1 cases per 1,000 person-years and from 5.1-14.9% amongst adolescent athletes. Among recreational runners, new incident cases of PFP have been reported to range from 17% to 26% during a ten-week 'start to run programme' (17, 18) and from 3% to 4% over a one to two year period (19, 20).

### 1.4. Influence of sex on PFP incidence

Amongst military recruits, females have been reported to be twice as likely to develop PFP compared to males (21). Both high (43%) (22) and low (3%) (23) incidence rates have been reported amongst military recruits, with the higher figure coming from an all female cohort. Amongst adolescent athletes, there is further support for the notion of a female sex bias in PFP, with studies by Foss et al (24) and Herbst et al (25) reporting the highest incidence of 15% from all female cohorts, compared to the lower incidence of 5% reported by Finnoff et al (26), who investigated a mixed-sex cohort. However, it should be stressed that higher incidence rates have been reported by studies involving mixed-sex or male dominant cohorts in the military (27) and low rates of PFP incidence reported by studies involving adolescent females (28, 29).

Amongst recreational runners there is further confliction regarding the role of sex and PFP development, with Noehren et al (20) and Ramskov et al (19) having reported identical incidence figures of 4% despite a clear sex discrepancy in populations studied. Overall, the role of sex as a confounding factor in PFP development is conflicting and requires further exploration.

## 1.5. Factors associated with PFP development and persistence

Two recent systematic reviews have synthesised research evaluating factors associated with PFP (30, 31). A prospective review, summarising work to November 2010, highlighted a dearth of evidence, with just seven studies eligible for inclusion at the time of searching (30). Multiple risk factors were investigated in single studies, which require further exploration in future studies to allow for data pooling. A review of cross-sectional literature highlighted a greater breadth of evidence, with 47 eligible studies and data pooling possible for eight factors (31). Additionally, a number of other systematic reviews evaluating the cross-sectional relationship of various factors with PFP have been published (32-37).

### 1.5.1. Quadriceps function

The strongest risk factor for future PFP development reported by Lankhorst et al (30) was reduced knee extension strength, with standardised mean differences (SMD) ranging from small (0.11) to moderate (0.84). These pooled data included only two studies investigating military recruits (22, 38). Therefore, it is unknown if knee extension weakness is a risk factor for PFP development in other cohorts such as recreational runners.

Two cross-sectional studies have reported an association between lower peak knee extensor torque and PFP in recreational runners, compared to asymptomatic runners (31, 39, 40). Global atrophy of the quadriceps (41) and delayed vastus medialis obliqus (VMO) onset during functional tasks (42) has also been reported in people with PFP. Not all cohorts with PFP have demonstrated such muscle weakness, with Selfe et al (43) reporting a cross-sectional subgroup with significantly greater isokinetic quadriceps strength. This subgroup were predominantly male and demonstrated higher levels of both function and quality of life, suggesting that muscle deficits in those with PFP may be subgroup specific.

### 1.5.2. Hip muscle function

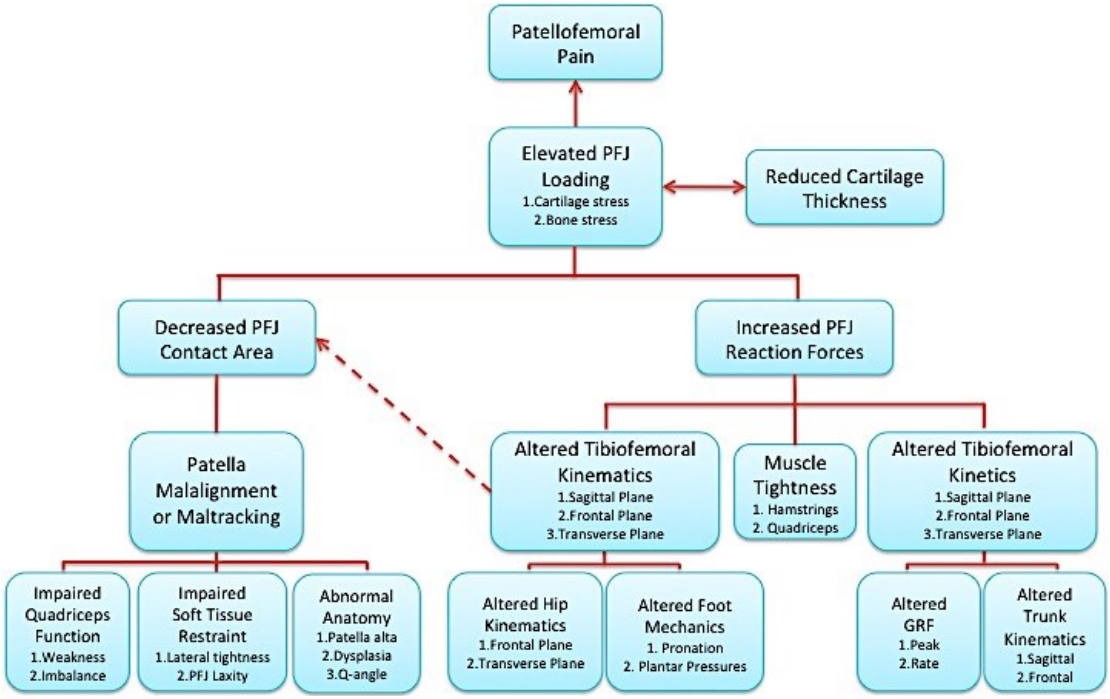
The association between hip muscle strength and PFP is conflicting. A recent systematic review by Rathleff et al (44) reported moderate evidence of no association between isometric hip strength and future PFP development. There is moderate evidence of an association between reduced isometric hip abduction and extension

strength and persistent PFP in both sexes (31, 32), but also evidence of a subgroup that demonstrate significantly greater isokinetic hip abductor strength (43). Delayed gluteus medius (GMED) onset and reduced activation duration, measured with surface electromyography (sEMG), have also been reported during both stair negotiation and running (34).

Since the review of Rathleff et al (32), studies have emerged reporting that *increased* isometric hip abduction strength is predictive of future PFP development in adolescents (25, 26). However, Ramskov et al (19) reported that higher eccentric hip abduction strength was associated with a lower risk of future PFP development in an adult novice running cohort. These conflicting data suggest that the relationship between hip strength and PFP may be individual within specific homogenous populations, and that variable methods of testing (e.g. hand held versus isokinetic dynamometers) may result in differing outcomes.

### 1.5.3. Lower limb biomechanics

There is an extensive body of literature investigating lower limb biomechanics in individuals with PFP, owing to the theory that PFP is intrinsically related to abnormal tracking of the patella relative to the underlying trochlear groove (45). This prevalent theory is summarised by the recently published pathoanatomical model of PFP (see figure 1) (46). Theoretically, altered patella tracking is thought to result in increased patellofemoral joint stress, by reducing patellofemoral contact area over which subsequent patellofemoral joint reaction force is applied (47). This is suggested to contribute to articular cartilage pathology and result in increased nociceptive output from the highly innervated subchondral bone (48). However, to date there is a lack of confirmatory evidence that increased patellofemoral joint stress, reported in some cohorts during some tasks, relates strongly to pain. Nonetheless, a large body of research has explored biomechanics related to this theoretical paradigm.




*1. The pathoanatomical model of PFP reproduced from Powers et al (46)*

### 1.5.4. Hip kinematics

As the quadriceps tendon anchors the patella to the femur during closed chain tasks, recent literature has focused on the influence of frontal and transverse plane hip kinematics underneath this stable extensor mechanism (45). Both increased hip adduction (HADD) and internal rotation (HIR) have been reported to increase lateral patella displacement during weight bearing in observational studies (49, 50), which will theoretically increase patellofemoral joint stress. Prospectively, Noehren et al (20) reported that increased peak HADD during running is a risk factor for future PFP development in female runners. In addition, Boling et al (23) reported that an increase in peak HIR during a jump-landing task is a risk factor for future PFP development in in a mixed-sex military cohort.

Multiple studies report significant cross-sectional associations between altered hip kinematics and PFP during running (39, 51-54), with data predominantly coming from mixed sex cohorts. Only Willy et al (51) has presented data for both sexes separately, reporting significantly greater HADD in females with PFP compared to males with PFP. Overall, the influence of sex on lower limb biomechanics in relation to PFP development and persistence is under-evaluated and warrants further investigation (55), since this may lead to differences in treatment targets. Currently, a number of

proximally targeted interventions have been explored for both female and mixed sex cohorts in the literature (56).

### 1.5.5. Foot biomechanics

Despite the historic suggestion that foot kinematics, specifically increased rearfoot eversion, are associated with patellofemoral loading (57), evidence for this relationship is conflicting (55). Individuals with PFP have been reported to have a more pronated foot posture than controls (31), which has also been observed prospectively in a military cohort using navicular drop (36). However, these static tests are not strongly related to dynamic foot function (58-60), and no dynamic differences in foot function are reported to exist in those with PFP compared to controls during running (52). Furthermore, variation in foot kinematics during gait in asymptomatic individuals is reported to be both varied and normal (61). Consistent evidence suggests that individuals with PFP exert higher forces through specific regions of the foot (lateral forefoot and medial metatarsal heads) during running (18), although ability to measure these forces in clinical practice is limited.

### 1.5.6. Non-mechanical contributors to PFP

There is growing evidence to support the role of non-physical factors in persistent musculoskeletal pain (35). Consistent with this suggestion, local and widespread hyperalgesia have been reported in both adolescents (62) and adults (63) with PFP, thought to reflect peripheral and central sensitization. Higher levels of depression, anxiety and catastrophising behavior have also been reported in individuals with PFP (35), alongside a lower quality of life (33), all of which are reported to alter an individual's pain processing (55). The suggestion of a singular nociceptive tissue source in PFP is also questioned by the work of Boudreau et al (64), who report considerably heterogeneous visual pain maps amongst a cohort of adolescents and young adults with PFP (see figure 2).

*2. Heterogeneous visual pain maps in PFP from Boudreau et al (64)*

## 1.6. Passive PFP interventions

Some treatment adjuncts are advocated in the management of pain that is severe or irritable as part of a combined treatment battery (65). A recent systematic review reports statistically, but not clinically significant reductions in pain after local manual therapy in participants with PFP (66), though the methodology of this review has recently been challenged (67). Patellar mobilisation, except in the presence of objective patellar hypomobility (65), therapeutic ultrasound (68) and stretching (69) are not supported by the current patellofemoral consensus statement (65). Furthermore, dry needling has been reported to add no additional benefit to multimodal Physiotherapy consisting of manual therapy and strengthening exercise (70).

### 1.6.1. Taping

Patellar taping was developed to target theoretical abnormal patella tracking (45, 71, 72). A Cochrane review including only data from randomized controlled trials (RCT) to 2011 reports insufficient evidence to support the effectiveness of patellar taping (71). However, a more recent systematic review including data from multiple study designs to 2013 supports the use of tailored patellar taping to immediately reduce pain during stair ambulation and squatting (73). The mechanisms of effect for patellar taping are poorly understood, with Ho et al (74) reporting no significant alterations in patellar

arthrokinematics during a step down task after the application of either McConnell or Kinesio taping designed to improve frontal plane alignment. Pelletier et al (75) report significant favourable alterations in both hip and knee flexion angles at initial contact during treadmill running in individuals with PFP, but no inference on symptoms was made by this observational study. Effects of patellar taping are therefore yet to be evaluated in a recreational running cohort.

#### 1.6.2. Foot orthoses

Whilst the evidence surrounding both static and dynamic foot function and PFP development and persistence is conflicting, there is supporting evidence for the use of prefabricated foot orthoses to effectively reduce pain at six week follow up compared to both sham devices and a 'wait and see' approach (76, 77). In a recreational running cohort, orthoses intervention is reported to reduce both peak rearfoot eversion and eversion velocity (78), but again no inference on symptoms was made by this observational study. Positive effects of foot orthoses were recently reported in a recreational running cohort by Bonacci et al (79), but were inferior to step rate retraining and minimalist shoe use in this pilot randomised controlled trial (RCT).

### 1.7. Active PFP interventions

#### 1.7.1. Exercise therapy

Exercise therapy is the gold standard conservative intervention for PFP (65, 69, 80), with level one evidence to support the use of both hip (proximal) and knee (local) exercise (56, 81). This aligns well with the proximal and local muscle weaknesses reported in those with PFP in comparison to asymptomatic controls (31, 32). In a running specific population, exercise therapy is reported to result in significant improvements in both pain and function (82-84) at short-term follow up. However, only one of these case series identified a potential mechanism of effect, being a reduced knee abduction moment during the stance phase of running (84), with no significant running kinematic changes reported. Moreover, the recent three-arm RCT of Esculier et al (85) reported that exercise therapy was no more effective than load management education, or load management education combined with step rate retraining. Thus, the mechanism(s) for improved outcomes following exercise therapy in runners with PFP remains unclear. This lack of clarity limits the ability of clinicians

and researchers to act on the suggestion that interventions should be tailored to specific individual deficits (43), and questions the role for exercise therapy as an intervention for runners with PFP that may primarily be associated with altered lower limb kinematics.

### 1.7.2. Running retraining in PFP: emerging effects and mechanisms

Multiple observational studies involving asymptomatic participants report no significant differences to either hip or knee kinematics during running after hip strengthening programmes, irrespective of significant increases in hip abductor or external rotator strength (86-88). A novel finding reported by Willy et al (88) was a significant reduction in both HADD and HIR during a single leg squat task post-exercise therapy. The authors hypothesised that these changes may reflect the acquisition of a new movement skill as opposed to being the result of increased isometric strength (88). In keeping with this suggestion, an intervention termed '*running retraining'* has an emerging evidence base and is best described as 'the implementation of any cue or strategy designed to alter an individual's running biomechanics, or technique' (89).

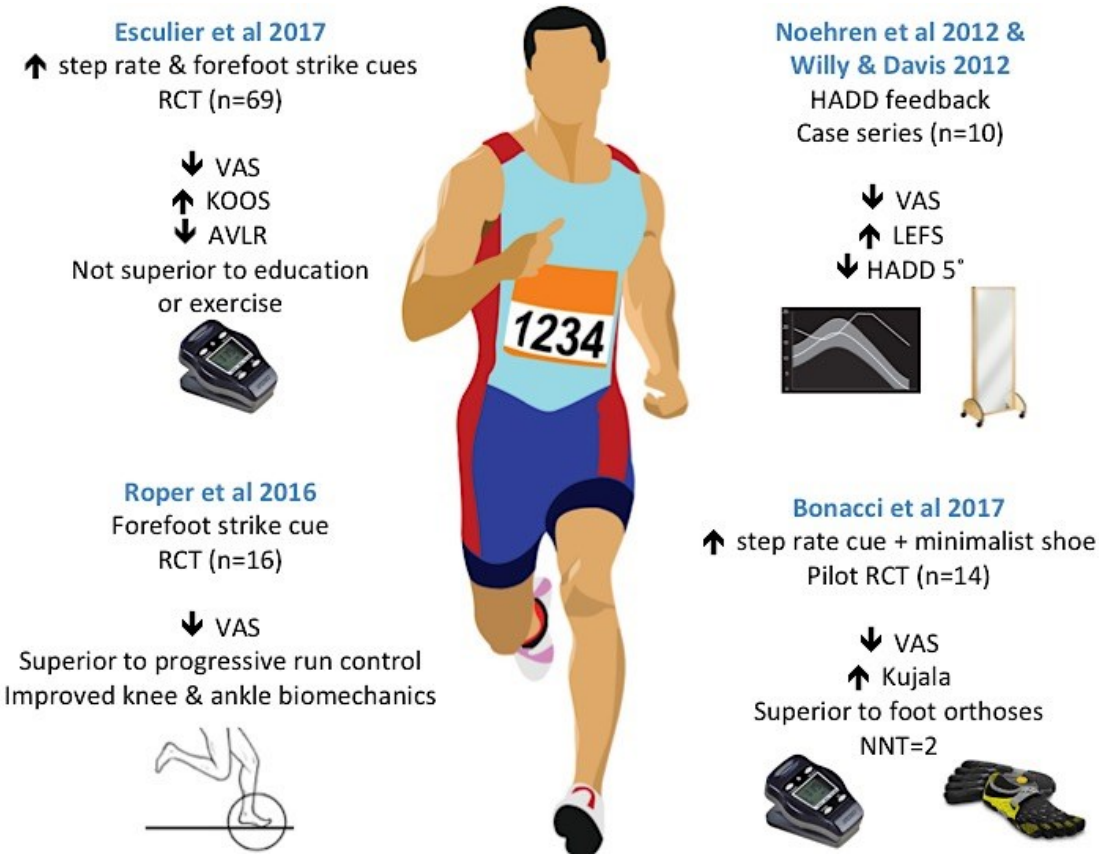
A large number of observational studies indicate running cues can alter an individual's running biomechanics (90). Multiple studies report that increasing running step rate (the number of steps a runner takes in a given period of time) by 5-10% results in reduced peak HADD (91-93). Studies also report that increasing running step rate results in reduced patellofemoral joint stress (94, 95) and increased gluteal muscle activation duration (96). However, as all of these studies have been observational, mostly in asymptomatic runners, inferences in relation to runners with PFP should be made with caution.

Barefoot running as a potential tool to facilitate changes to running technique has been reported to reduce patellofemoral joint stress (97), although not greater than the aforementioned work on step rate increase (94, 95). A trial investigating the effects or mechanisms of barefoot running in a PFP population is yet to be completed. Cueing transition from a rearfoot to a forefoot strike pattern has also been reported to reduce patellofemoral joint stress (98, 99), although again not greater than step rate cues (99).

Two initial case series in female runners with PFP (100, 101) have reported significant improvements in both pain (measured with a visual analogue scale {VAS}) and function (measured with the lower extremity functional scale {LEFS}). Despite employing differing forms of feedback, a live display of real-time HADD during stance and mirror feedback respectively, both reported similar reductions in peak HADD (5˚) that may provide a potential kinematic mechanism for pain reduction. Both authors suggest that this reduction in peak HADD was likely to alter nociceptive output from the subchondral bone by way of reducing patellofemoral joint stress. In addition, a smaller case study (n=2) by Willy et al (102) reported similar kinematic outcomes but also earlier GMED onset relative to foot contact and a longer GMED activation duration post-mirror gait retraining, measured with sEMG.

The primary limitation of these case series was the investigation of an all female cohort, making these data inapplicable to male runners with PFP. Further limitations include the absence of a control group and the lack of clinical applicability of the feedback provided. Specifically, Noehren et al (100) delivered live visual feedback via laboratory-based technology (three dimensional {3D} motion analysis), which is not commercially available. The work of Willy et al (101, 102) is more clinically applicable, involving mirror feedback, but involved eight intervention sessions in a two-week period, which is likely to be an unrealistic expectation of the average clinical facility.

More recently, two small RCT's have been published in the literature. The first was conducted by Roper et al (103), who reported a significant reduction in pain when transitioning a PFP cohort to a forefoot strike pattern over and above a control group consisting of a graduated increase in running. However, the potential negative of transitioning to a forefoot strike pattern is the load that may be shifted consequentially to the ankle joint (104), reflected by a 25% rate of secondary ankle pain in the treatment group at one month follow up. A second pilot RCT conducted by Bonacci et al (79), reported a significant reduction in pain in a cohort of runners with PFP after a combined step rate and minimalist shoe intervention, compared to prescription of prefabricated foot orthoses. Whilst positive effects were observed in this pilot RCT, the combined approach of increasing step rate and graduated use of a minimalist shoe make it impossible to determine what aspect of the retraining protocol resulted in the positive outcome.




*3. Summary of run retraining interventions and outcomes in PFP*

Key: RCT; randomised controlled trial; VAS=visual analogue scale; KOOS; knee osteoarthritis outcome score; AVLR; average vertical loading rate; HADD=hip adduction; LEFS=lower extremity functional scale; NNT=number needed to treat.

One proposed explanation for the positive clinical benefits from running retraining interventions, is that they are derived as a result of *load management* (105). The monitoring and subsequent manipulation of workload has been reported to be an effective method of reducing injury risk in elite sport (106). As running retraining protocols contain a progressive increase in running duration (100, 101), it is certainly plausible that a load management mechanism is at least partially involved in the positive effects derived.

This hypothesis is supported by the recent high quality RCT conducted by Esculier et al (85), who reported that increasing step rate and/or transitioning to a forefoot strike pattern was no more effective than load management education alone, or load management education combined with exercise therapy. All groups within this RCT improved significantly for the outcomes of usual, worst and running-related pain, as well as improvements in the activities of daily living subscale of the Knee Osteoarthritis Outcome Score (KOOS). The running retraining group was reported to have a

significant reduction in average vertical loading rate (AVLR) compared to both education and exercise, but this identified mechanism did not affect the primary outcome.

Whilst this RCT identifies the novel benefit of an education intervention in runners with PFP, there are some limitations to the design of their step rate retraining intervention. Step rate retraining was completed without adhering to a faded feedback protocol, used successfully by previous studies and reported to be necessary to facilitate skill acquisition (107). This is supported by the recent RCT of Roper at al (103), which reported significant improvements in both pain and function in runners with PFP compared to a load management control. Whilst both groups in this trial completed a graduated return to running, only the intervention group was given a cue designed to induce a forefoot strike pattern. There was also no monitoring of adherence in the field, with adherence closely controlled in previous studies.

## 1.8. Literature gaps of relevance to this thesis

### 1.8.1. PFP epidemiology

When last reviewed, the dearth of prospective literature limited ability to define causal relationships between given variables and the risk of future PFP, particularly in recreational runners. An updated systematic review of the prospective literature was hypothesised to result in a greater understanding of causal relationships for PFP. There are reported associations between several kinematic variables and PFP, with the most consistent evidence indicating the presence of greater peak HADD. However, the majority of data is presented pooled for both sexes. There is currently minimal evidence comparing males and females with PFP, with a significant increase in peak HADD reported in female runners (46) when data are presented for individual sexes. This requires further exploration as if consistent, will indicate that males and females with PFP may present with potentially differing kinematic treatment targets.

### 1.8.2. Running retraining

Short-term effects of running retraining and associated biomechanical mechanisms indicate further research is warranted in relation to this treatment approach for recreational runners. Feedback approaches previously explored in PFP cohorts have inherent limitations. The work of Noehren et al (100) and Willy et al (101) lack clinical

applicability due to the technology involved and the frequency of sessions delivered. Transitioning from a rearfoot to a forefoot strike which was investigated by Roper et al (103) may result in the adverse outcome of secondary ankle pain. Increasing step rate has only been explored in combination with a minimalist shoe (79), or without the use a faded feedback protocol (85). Additionally, all previous running retraining studies have a significant female sex bias in sampling. Given the plausibility of increasing step rate reported in observational cohort studies (91, 94), an investigation into increasing step rate in a mixed-sex PFP cohort with increased clinical applicability is warranted. Additional exploration of both kinematic and muscle function post-intervention is also justified, to aid in understanding the mechanisms of any observed positive effects.

### 1.8.3. Clinical applicability of biomechanics

A further limitation to current running retraining research is the divide between research and clinical practice, with respect to the measurement of human biomechanics. This fault lies not with our understanding of how biomechanics can contribute to PFP, but with the paucity of validated tools suitable for use in a clinical setting that can measure the relevant variables described in the literature. A pragmatic and clinically applicable solution to this problem is the use of two-dimensional (2D) video. Maykut et al (108) reported a moderate correlation with 3D peak HADD during over ground running ($r$=0.62). Furthermore, Dingenen et al (109) recently reported a significant, positive correlation between 3D and 2D measurement for femoral adduction (FADD), contralateral pelvic drop (CLPD) and HADD during running stance phase in asymptomatic runners.

A limitation of all work completed to date is the normative cohorts chosen for validation, as one cannot presume that participants with pain will move in the same way as those who are asymptomatic. Furthermore, all previous studies have used Dartfish software, which is not fully clinically applicable due to prohibitive costs. Analysis of software that is free at the point of access may reduce barriers between laboratory biomechanical analysis and clinical practice. In addition, the correlation between 3D biomechanics and 2D video for the knee in the sagittal plane is yet to be explored. Whilst knee position in the sagittal plane has been reported to be unaffected by patellofemoral taping or bracing during step descent (110), it has been reported to

correlate positively with patellofemoral joint stress during running (94) and can be successfully manipulated using step rate retraining.

This opening thesis chapter has broadly explored the literature surrounding the development, persistence and management of PFP, with a specific focus on PFP in the recreational runner.

This remainder of this thesis will:

1. Further explore the magnitude of the patellofemoral problem by exploring the epidemiology and incidence of PFP.
2. Synthesise the literature relating to biomechanical factors of interest for PFP development, persistence and treatment in a running specific cohort.
3. Explore the reliability of kinematic marker placement, before determining the kinematic differences between males and females during treadmill running.
4. Present data on the feasibility, effects, biomechanical mechanisms and clinical applicability of a step rate intervention in a mixed sex recreational running population with PFP.
5. Investigate the validity of high frame rate 2D video in relation to 3D kinematic motion capture.

The subsequent aims and objectives of this PhD thesis in chapter two arise from the research space described within this introduction.

# 2. Aims, objectives, impact and hypotheses

The overarching aim of this thesis was to synthesise and extend the existing knowledge base, in order for clinicians to have the information and procedures required to understand lower limb biomechanics in relation to PFP in recreational runners. More specifically, I aimed to better understand and generate answers to unaddressed questions in the literature relating to the influence(s) of running biomechanics on the development, persistence and management of PFP.

The impact should be improved clinical outcomes and better engagement with running as an exercise for health initiative in a large group of people with recurrent problems. More specifically, this information should allow clinicians to better implement biomechanical strategies for managing PFP in the recreational runner, resulting in longer-term treatment effects and potentially the development of preventative strategies.

## 2.1. Specific aims and objectives

The aims of the introduction were to provide a broad overview of the existing literature, to identify the resultant research space, to consider strengths and weaknesses of potential methodologies and to orientate the reader to the subsequent experimental chapters.

The studies completed as part of this thesis had the following aims, objectives and alternate hypotheses:

1. Quantify the etiology of PFP in multiple cohorts and determine the strength of identified evidence. The objectives for this aim were:
    a. Review and critically appraise the current prospective literature for risk factors for future PFP development (performing meta-analyses for variables where homogeneity allows), to determine factors of highest relevance (chapter three).
    b. Calculate the specific incidence of PFP from studies included within this systematic review (chapter three).

        $H_1$ – that there would be an extended range, and increased strength of evidence, for potentially modifiable risk factors for PFP development,

both associative and causative, since the previous review. In addition, these risk factors would be of relevance to clinicians treating people with PFP.

The impact of successfully achieving aim one should be to inform clinicians about the current evidence base relating to PFP incidence and risk factors for development, and the extent to which they can apply this knowledge to specific patient groups.

2. Determine the role of lower limb biomechanics on the development, persistence and management running-related PFP, determining the strength of identified evidence. The objectives for this aim were:

    a. Review and critically appraise the current literature for risk factors, associated factors and treatment effects/mechanisms specific to lower limb biomechanics in running specific PFP cohorts (performing meta-analyses for variables where homogeneity allows) and determine the factors of greatest relevance (chapter four).

    $H_1$ – that a coherent narrative would emerge of modifiable biomechanical factors specific to a running population, that are also amenable to treatment. Further, that there would be multiple treatments of proven efficacy, but that the populations to which this was of proven relevance would be limited.

    b. Perform preliminary reliability testing on marker placement for kinematic motion analysis (chapter five).

    c. Conduct a case-control study to further determine the kinematic differences between runners with and without PFP during a treadmill run, to understand how prolonged running might influence mechanics and intervention design and simultaneously investigate the difference between the sexes (chapter five).

    $H_1$ – that kinematic data collected during a prolonged run would identify significant differences when comparing PFP runners to matched controls, but also when comparing males and females.

The impact of successfully achieving aim two should be to inform clinicians about the current evidence base relating to lower limb biomechanics and their contribution to

PFP development and persistence, and how these factors can extend to treatment mechanisms in recreational runners.

3. To guide clinicians with respect to whether running retraining, formed of a 7.5% step rate increase, in a mixed sex PFP cohort, has similar efficacy and biomechanical mechanisms to those established in previous studies. The objectives for this aim were:

    a. Obtain feasibility study funding (chapter six).

    b. Conduct a feasibility study to determine if a running retraining intervention (increasing step rate by 7.5% cued with an audio metronome) is feasible in a mixed-sex, UK cohort, at short-term (six week) follow up (chapter six).

    c. Collect symptom, function and mechanisms data throughout the course of a feasibility study to begin to inform upon biomechanical mechanisms, comparing to current existing literature (chapter six).

    $H_1$ - that recruitment of a mixed sex cohort of runners with PFP would be successful and that a six-week step rate intervention would achieve significant changes in both pain and function. Furthermore, the likely kinematic mechanism through which these positive effects are derived would be predominantly hip driven.

The impact of successfully achieving aim three should be to affirm the potential for running retraining (delivered using step rate feedback) in a mixed-sex UK cohort, giving clinicians a tailored treatment to apply where indicated.

4. Increase the subsequent clinical applicability of biomechanical interventions to maximise impact and ensure that the procedures can be readily applied in usual clinical practice. The objectives for this aim were:

    a. Determine the validity and intra-rater reliability of high frame rate 2D video with respect to 3D kinematic motion capture (chapter seven).

    $H_1$ - that high frame rate 2D video would give useful data that has acceptable accuracy with respect to 3D kinematic analyses.

The impact of successfully achieving aim four should be to inform clinicians whether they can use a pragmatic, clinically applicable tool to measure relevant running biomechanics in patients with PFP, particularly pre/post intervention.

# 3. Risk factors for patellofemoral pain: a systematic review & meta-analysis

In the introduction chapter, only a limited number of risk factors associated with the development of PFP were identified based on pooled data from previous meta-analysis. Additionally, the most recent systematic review synthesising research related to risk factors completed their search in 2010, eight years ago. Consequently, a review of the epidemiology of PFP (risk factors and incidence) are presented in this chapter.

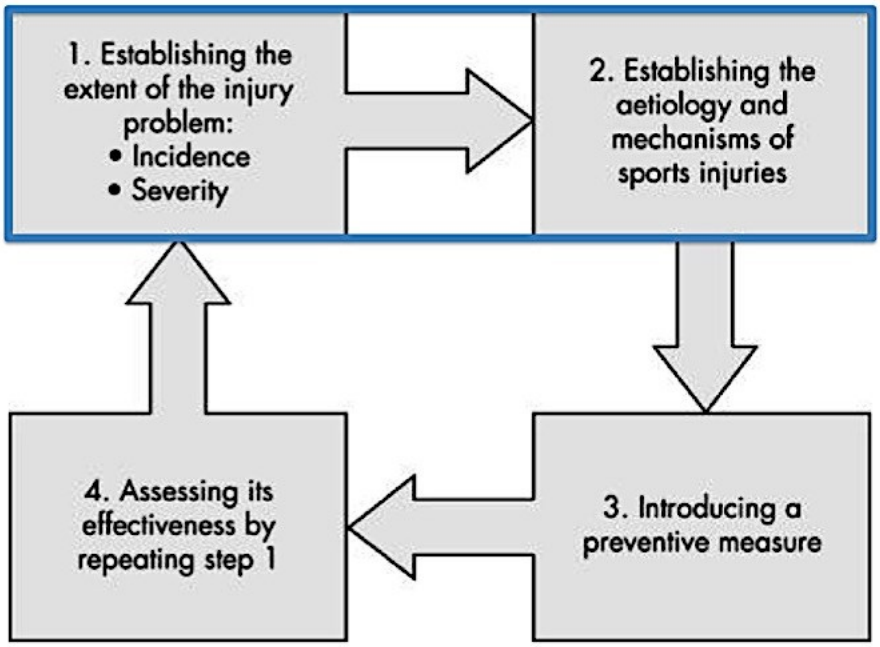
Preliminary results of this review were presented at the 2017 International Patellofemoral Pain Research Retreat in Australia and the 2018 Danish Sports Medicine Congress in Copenhagen. This review was accepted for publication in the British Journal of Sports Medicine (Impact Factor 6.557) after two comprehensive rounds of peer review (appendix A), with proofs yet to be provided.

The results presented within this chapter informed the subsequent systematic review investigating the association between lower limb biomechanics and recreational runners with PFP (chapter four), given the absence of data pertaining to risk factors for PFP development in this patient group group.

## 3.1. Introduction

PFP is characterised by diffuse retropatellar or peripatellar symptoms throughout activities that load the knee during flexion, such as running, stair descent or squatting (4). It is described as a common pathology in both adolescents (111) and adults (21), with prevalence in the general population reported as 22.7% (16). However, the factors associated with PFP development and the incidence of the condition across a variety of populations remains under-evaluated due to limited prospective data and the homogeneity of studied populations (16, 112). As PFP is reported to be common across the lifespan and may be the precursor to patellofemoral osteoarthritis (3, 113), an improved understanding of the factors associated with the development of PFP and its incidence in differing populations is essential to prevent symptom development.

With the incidence of PFP reported to be high (16) and symptoms persisting despite evidence based interventions (2), further investigation is warranted to understand variables that are associated with PFP development and subsequently deliver evidence based preventative strategies. In 1992, Van Mechelen et al. presented a theoretical model described as the 'sequence of prevention' for sports injury (see figure 4) to guide injury prevention development (114). With the incidence of PFP defined across populations (16) (stage one), an understanding of the aetiology (stage two) is required to identify the variables associated with the pathology development. A variable that has been found to be associated with future pathology development should be manipulated as a preventative strategy within a randomised controlled trial (RCT) (stage 3). The effectiveness of the implemented strategy should then be appraised by re-examining the incidence within a specific population (stage 4).




*4. The Van Mechelen model of injury prediction*

In 2012, Lankhorst et al. completed a systematic review of risk factors for PFP development (30), which identified a clear association between low knee extension strength and subsequent risk of PFP irrespective of measurement method, but no associations with other investigated variables. This is likely due to the low number of included studies (n=7), high data heterogeneity and data pooling being possible for just 13 out of 137 identified variables, but was unexpected given the known crossectional association between PFP and multiple pathomechanical variables such as muscle function and lower limb biomechanics (46).

Additional risk factors for future PFP development have been identified within other systematic reviews using data from single studies. Increased navicular drop in military recruits (36), greater peak hip adduction during running (82) and increased forces at foot level during both walking and running (37) have all been shown to increase the risk of future PFP development. Whilst these findings are statistically significant, the absence of data pooling and the small to moderate effect sizes limit the impact and clinical applicability. Given the number of subsequently published prospective studies, an updated systematic review on this topic is now appropriate.

The aim of this systematic review was to provide researchers and clinicians with evidence synthesis concerning predictive variables for PFP to aid the development of

preventative interventions. The review was designed to synthesise the available evidence at stage two (aetiology) of the Van Mechelen model (see figure 1), and enable addressing stage three (preventative strategies). A secondary aim was to determine the incidence of PFP within the included studies, both as a heterogeneous condition and within specific homogenous cohorts. Specific objectives were to (i) establish prospective links between all investigated variables and future PFP development (ii) identify risk factors and PFP incidence specific to individual homogenous cohorts and (iii) inform future studies on PFP prevention.

## 3.2. Methods

This systematic review was completed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (115) and was registered with PROSPERO prior to completion of the initial search (registration number: CRD42016049327).

### 3.2.1. Search strategy

The search terms used by Lankhorst et al (30) were duplicated for the purpose of this review. The following terms were used for PFP: arthralgia AND knee joint OR anterior knee pain OR (patell* OR femoropatell* OR femoro-patell* OR retropatell*) AND (pain OR syndrome OR dysfunction). Key words used for risk factors were: risk factor OR association OR relative risk OR odds ratio. We searched MEDLINE, Web of Science and SCOPUS from inception until February 2017, limited to papers published in the English language involving human subjects.

MEDLINE was searched as it is listed as an essential database by the Cochrane group, with approximately 50% of RCTs indexed for MEDLINE (116). Web of Science was searched as it is reported as a minimum requirement of a systematic search by a recent exploratory study (117). SCOPUS was searched as an additional third database given its wide, interdisciplinary coverage and reported complimentary design to Web of Science (118) In order to be compliant with a PRISMA systematic search strategy, (116), an additional citing reference search was undertaken using Google Scholar up to March 2018, as well as hand searching of the reference lists of identified papers.

### 3.2.2. Inclusion criteria

A single investigator (AR) exported all studies identified by the search strategy to Endnote X7 (Thomson Reuters, Philadelphia). Eligibility criteria were adapted from the original review of Lankhorst et al (30), described as follows: (i) studies involving male or female subjects who developed subsequent PFP (synonyms including retropatella pain, chondromalacia or anterior knee pain); (ii) at least one variable investigated as a risk factor for PFP; and (iii) prospective study designs. Studies with less than 20 PFP subjects were excluded by the review of Lankhorst et al (30), but were included in this review. Two independent authors (BN and NL) reviewed all abstracts to determine

eligibility. Full texts were screened where eligibility could not be determined by the abstract alone and any discrepancies were resolved at a consensus meeting.

### 3.2.3. Quality assessment

Methodological quality and risk of bias of included studies was determined by combining the Newcastle-Ottawa scale (119) (NOS) and appraising the number of events per variable described by Peduzzi et al (120). The NOS is advocated by the Cochrane group for determining epidemiological cohort study quality (121) and was used successfully by the previous review of Lankhorst et al (30). The number of events per variable described by Peduzzi et al (120) was employed so that studies previously excluded by Lankhorst et al (30) could be included, but the eventual level of evidence appropriately adjusted should studies be found to have a high risk of bias.

Eligible studies were independently rated by two authors blind to study authors and institutions (SL and NL), with discrepancies resolved at a consensus meeting. The NOS contains 8 categories relating to methodological quality and each study was given an eventual score out of a maximum of 8 points. A score of 0-3 points equated to a low quality (LQ) study, a score of 4-6 points equated to a moderate quality (MQ) study, with a score of 7-8 points required for a study to be given a score of high quality (HQ). In addition, HQ or MQ studies were reduced to either MQ or LQ respectively if they were determined to have a high risk of bias as a result of having less than 10 PFP participants for each investigated variable within their total sample (120). Inter-rater reliability of the NOS was calculated using the percentage agreement method.

### 3.2.4. Data extraction

Data related to study characteristics were initially extracted from all included studies by one author (AR) and subsequently reviewed by a second author (BN). This included participant numbers (separating those who developed PFP and those who did not), characteristics of these groups (such as population), study duration and publication details (author and year). A second author (BN) extracted all data pertaining to potential risk variables to be included in the meta-analysis. Means and standard deviations (SD) were extracted for variables of interest, which included (but were not limited to: anthropometrics and demographics (such as sex, body mass index (BMI)),

biomechanical variables (such as kinematics and kinetics) and muscle function (such as strength or onset timing).

### 3.2.5. Statistical methods

Statistical analyses were undertaken using Review Manager 5.0 (The Cochrane Collaboration, Copenhagen, Denmark). Analyses were completed initially by one author (BN) and subsequently reviewed by a second author (SL). Means and SD's were extracted for continuous scaled variables and used to calculate a standardised mean difference (SMD) with 95% confidence intervals (CI's). Calculated individual or pooled SMDs were categorised as small (0.59), medium (0.60–1.19) or large (1.20) as described by Hume et al (122). For nominal scaled variables, raw counts of injured and uninjured participants (e.g. PFP incidence in males and females) were extracted and used to calculate risk ratios (RR) with 95% CI's, with a small effect indicated by a RR ≥ 2.0 and a large effect by a RR ≥ 4.0 (122).

Data were pooled and has been presented as both a heterogeneous PFP cohort and further pooled by specific homogeneous subgroup where possible. Where methodological approaches between studies were deemed to be adequately comparable a meta-analysis was performed and the level of statistical heterogeneity for pooled data were determined using $I^2$ statistics (heterogeneity defined as $I^2 > 50\%$, $p < 0.05$). A random effects model (rather than a fixed effects model) was used due to the variation in study methods and populations, and the typically low number of studies, therefore reducing the possibility of a type 1 error (123). This decision was made apriori, as the Cochrane group state that the choice between a fixed-effects and random-effects meta-analysis should never be made on the basis of a statistical test for heterogeneity.

Only outcomes incorporating data from a minimum of two studies are presented in the main body of the review, due to the risk of reporting inappropriate levels of evidence where data pooling were not possible.

### 3.2.6. Evidence based recommendations

Levels of evidence were assigned to each calculated variable (pooled or otherwise) as described by Van Tulder et al (116), which incorporate both assigned methodological quality of included studies and statistical outcomes:

Strong evidence: Pooled results derived from three or more studies, including a minimum of two high quality studies that are statistically homogenous.

Moderate evidence: Pooled results derived from multiple studies, including at least one high quality study, that are statistically heterogeneous; or from multiple moderate or low quality studies which are statistically homogenous.

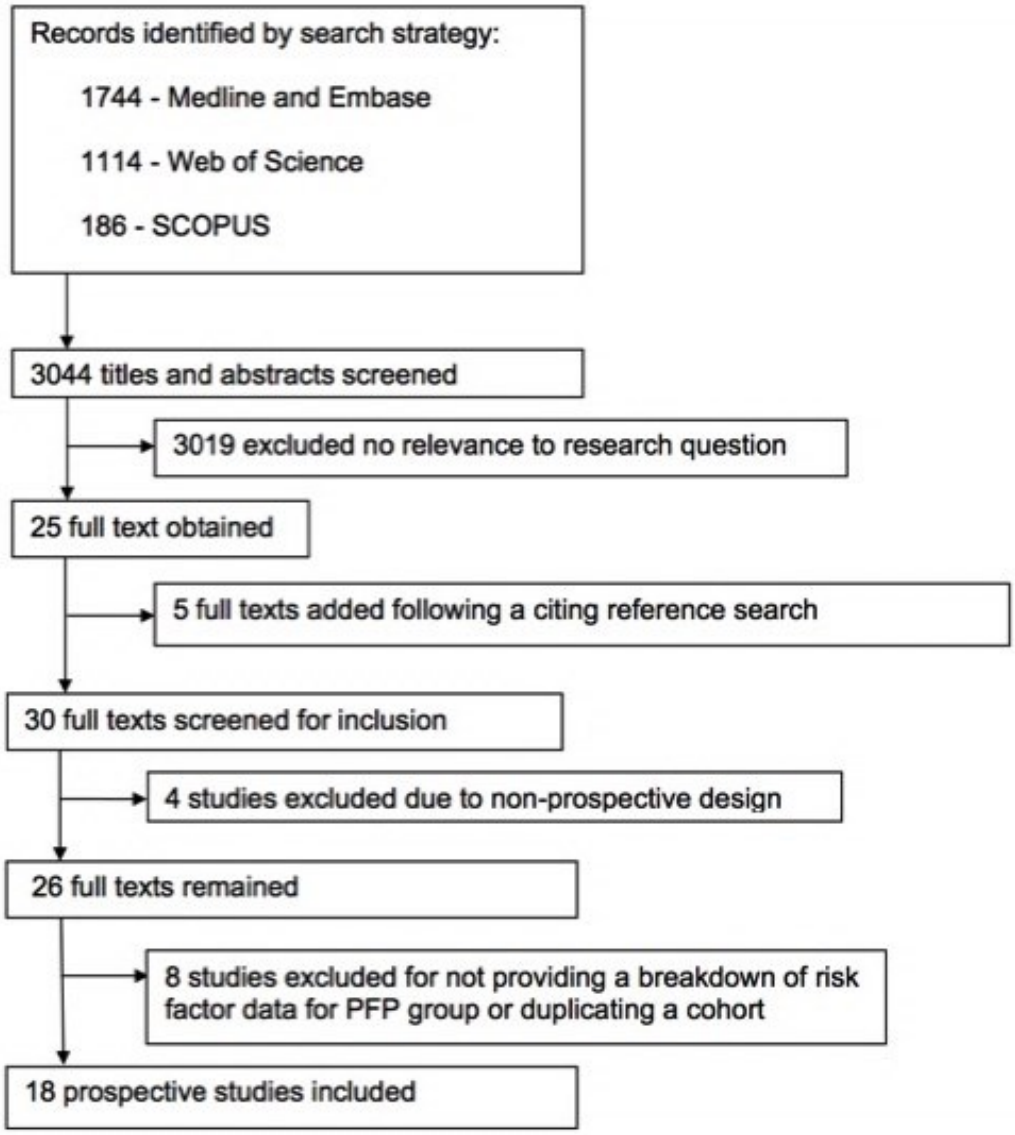
Limited evidence: Results from one high quality study or multiple moderate or low quality studies that are statistically heterogeneous.

Very limited evidence: Results from one moderate or low quality study.

## 3.3. Results

### 3.3.1. Search results

The search resulted in 3044 titles and abstracts identified for screening. Following the removal of duplicates and studies that did not meet the inclusion criteria of the review, 18 studies involving a total of 4818 participants were included (see figure 5) (17-20, 22, 23, 25-29, 38, 42, 124-128), 483 of whom went on to develop symptoms consistent with PFP. This is indicative of a heterogeneous PFP incidence of 10%. Extracted data relating to study characteristics are presented in table 1.




*5. Search flow chart for risk factors systematic review & meta-analysis adhering to PRISMA guidelines*

1. Study characteristics for risk factors systematic review & meta-analysis

| Study | NOS Score | Risk of Bias | Cohort | PFP | Sample Size | Incidence | Study Duration (Months) |
|---|---|---|---|---|---|---|---|
| **Boling '09 (23)** | H | L | Military (USA) | 40 (M=16, F=24) | 1319 | 3% | 30 |
| **Duvigneaud '08 (22)** | H | L | Military (Belgium) | 26 (F=26) | 62 | 42% | 1.5 |
| **Finnoff '11 (26)** | MD | H | Adolescents (USA) | 5 (M=2, F=3) | 98 | 5% | 9 |
| **Foss '12 (124)** | H | L | Adolescents (USA) | 39 (F=39) | 262 | 15% | 24 |
| **Herbst '15 (25)** | H | L | Adolescents (USA) | 38 (F=38) | 255 | 15% | 12 |
| **Hetsroni '06 (126)** | H | L | Military (Israel) | 61 (M/F=?) | 405 | 15% | 4 |
| **Holden '15 (29)** | MD | H | Adolescents (Ireland) | 8 (F=8) | 76 | 11% | 24 |
| **Luedke '16 (127)** | MD | H | Recreational Runners (USA) | 3 (M=1, F=2) | 57 | 5% | 12 |
| **Milgrom '91 (125)** | MD | L | Military (Israel) | 60 (M=60) | 390 | 15% | 3.5 |
| **Myer '10 (28)** | MD | H | Adolescents (USA) | 14 | 145 | 10% | 9 |
| **Noehren '13 (20)** | MD | H | Recreational Runners (USA) | 15 (F=15) | 400 | 3% | 24 |
| **Ramskov '15 (19)** | H | L | Recreational Runners (Denmark) | 24 (M=10, F=14) | 629 | 4% | 12 |
| **Thijs '07 (27)** | H | L | Military (Belgium) | 36 (M=25, F=11) | 84 | 43% | 1.5 |
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Thijs '08 (18)** | MD | H | Recreational Runners (Belgium) | 17 (M=1, F=16) | 102 | 17% | 2.5 |
| **Thijs '11 (17)** | MD | H | Recreational Runners (Belgium) | 16 (F=16) | 77 | 21% | 2.5 |
| **Van Tiggelen '04 (38)** | H | L | Military (Belgium) | 31 (M=31) | 96 | 32% | 1.5 |
| **Van Tiggelen '09 (42)** | H | L | Military (Belgium) | 26 (M=26) | 79 | 33% | 1.5 |
| **Witvrouw '00 (128)** | MD | H | Adolescents (Belgium) | 24 (M=11, F=13) | 282 | 9% | 24 |

Key: H=high; MD=moderate; L=low; M=male; F=female, USA=United States of America

### 3.3.2. Subgroups and PFP incidence

Three distinct subgroups were identified during the data extraction process. There were a total of seven studies involving military recruits (22, 23, 27, 38, 42, 125, 126), six studies involving adolescents (25, 26, 28, 29, 124, 128) and five studies involving recreational runners (17-20, 127). Studies involving military recruits involved a total of 2435 participants, 280 of whom went on to develop PFP, reflective of an incidence of 11% (range 3%-43%). Studies involving adolescents involved a total of 1118 participants, 128 of whom went on to develop PFP, reflective of an incidence of 11% (range 5%-15%). Studies involving recreational runners involved a total of 1265 participants, 75 of whom went on to develop PFP, reflective of an incidence of 6% (range 4%-21%).

### 3.3.3. Quality assessment

After evaluation of study quality and risk of bias (119, 120), a total of 9 HQ studies (19, 22, 23, 25, 27, 38, 42, 124, 126) and a further 9 MQ studies were identified (17, 18, 20, 26, 28, 29, 125, 127, 128). Mean percentage agreement for the NOS was 95% (range 89%-100%), indicating high inter-rater reliability (see table 2). The questions with the lowest percentage agreement were question five (does the study control for any confounding variables) and question seven (was follow up time clearly defined).

2. Individual study NOS scores and percentage agreement for risk factor systematic review & meta-analysis

| Question | The cohort was truly or somewhat representative of a typical PFP cohort | | Selection of the non-PFP cohort was from the same community as the PFP cohort | | Ascertainment of PFP was made via secure record OR structured interview | | Demonstration that outcome of interest was not present at start of study | | Cohorts were comparable on the basis of the design OR confounders controlled for | | Assessment of outcome was independent OR linked to medical records | | Follow up time was clearly defined | | Follow up was adequate (all subjects accounted for or ≤20% attrition) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 |
| **Boling ('09) (23)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | N | Y | Y |
| **Duvigneaud ('08) (22)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | ? | Y | Y | Y | N | Y | Y |
| **Finnoff ('11) (26)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| **Foss ('12) (124)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| **Herbst ('15) (25)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| **Hetsroni ('06) (126)** | Y | Y | Y | Y | Y | Y | N | N | N | Y | Y | Y | Y | Y | Y | Y |
| **Holden ('15) (29)** | Y | Y | Y | Y | Y | Y | Y | Y | N | N | Y | Y | Y | Y | Y | Y |
| **Luedke ('16) (127)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Y |
| **Milgrom ('91) (125)** | N | Y | N | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | Y |
| **Myer ('10) (28)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| **Noehren ('13) (20)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | ? |
| **Ramskov ('15) (19)** | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Thijs (‘07) (27)** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** |
| **Thijs (‘08) (18)** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **N** | **N** |
| **Thijs (‘11) (17)** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** |
| **Van Tiggelen (‘04) (38)** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **?** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** |
| **Van Tiggelen (‘09) (42)** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** |
| **Witvrouw (‘00) (128)** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **Y** | **N** | **N** |
| **Percentage Agreement** | **94%** | | **94%** | | **100%** | | **100%** | | **89%** | | **100%** | | **89%** | | **94%** | |

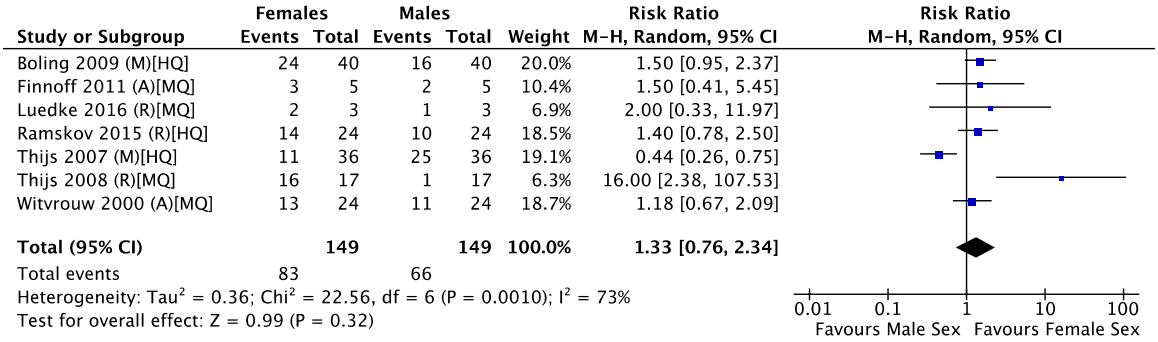
Key: R=rater; Y=yes; N=no; ?=unable to determine

### 3.3.4. Anthropometrics and demographics

Data pooling were possible for seven individual variables (sex, height, weight, BMI, body fat percentage, age and limb length).

*Sex*

There is moderate evidence from three HQ (19, 23, 27) and four MQ (18, 26, 127, 128) studies that sex is not a risk factor for future PFP development ($I^2$=73%, RR 1.33, CI 0.76,2.34) (see figure 6). This outcome does not change when pooling data only for military subjects (moderate evidence, $I^2$=91%, RR 0.82, CI 0.25,2.74), adolescents (moderate evidence, $I^2$=0%, RR 1.23, CI 0.38,2.07) or recreational runners (moderate evidence, $I^2$=76%, RR 3.08, CI 0.59,15.99). Whilst subgroup data pooling were non-significant, six of the seven included studies that reported data on sex had a greater proportion of females in their PFP cohort (19, 23, 26, 27, 127, 128), the highest of which was observed in the recreational runner subgroup.



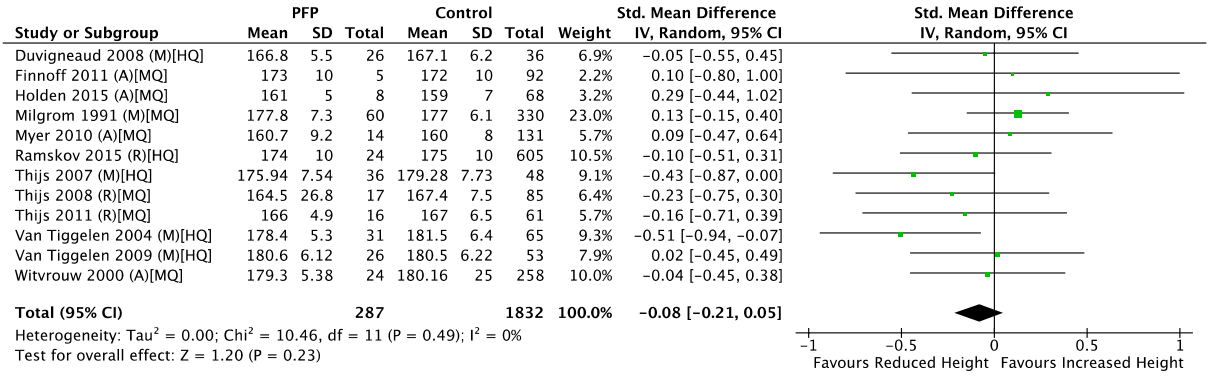

*6. Forrest plot detailing risk ratios for sex when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain

*Height*

There is strong evidence from five HQ (19, 22, 27, 38, 42) and seven MQ (17, 18, 26, 28, 29, 125, 128) studies that height is not a risk factor for future PFP development ($I^2$=0%, SMD -0.08, CI -0.21,0.05) (see figure 7). This outcome does not change when pooling data for only military recruits (strong evidence, $I^2$=41%, SMD -0.15, CI -

0.42,0.12), adolescents (moderate evidence, $I^2$=0%, SMD 0.06, CI -0.23,0.35) or recreational runners (moderate evidence, $I^2$=0%, SMD -0.15, CI -0.43,0.13).

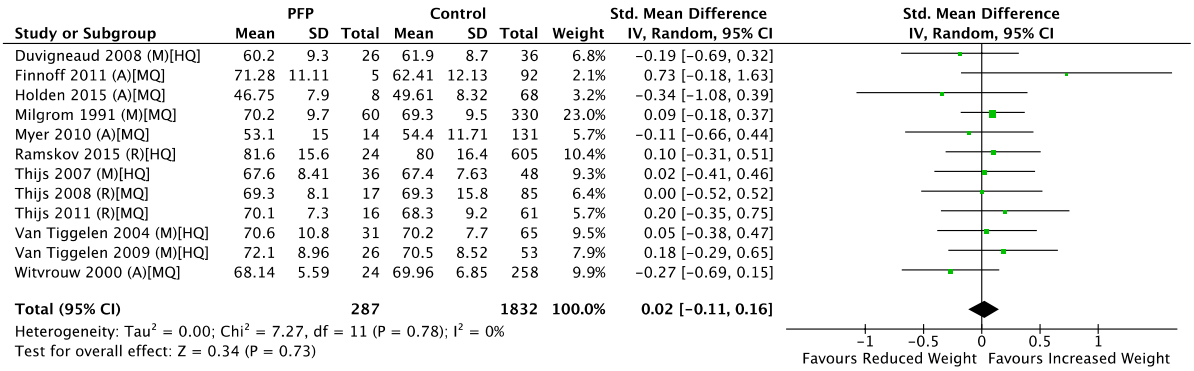



*7. Forrest plot detailing standardised mean differences for height when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain

*Weight*

There is strong evidence from five HQ (19, 22, 27, 38, 42) and seven MQ (17, 18, 26, 28, 29, 125, 128) studies that weight is not a risk factor for future PFP development ($I^2$=0%, SMD 0.02, CI -0.11,0.16) (see figure 8). This outcome does not change when pooling data for only military recruits (strong evidence, $I^2$=0%, SMD 0.05, CI -0.12,0.23), adolescents (moderate evidence, $I^2$=28%, SMD -0.10, CI -0.46,0.25) or recreational runners (moderate evidence, $I^2$=0%, SMD 0.10, CI -0.18,0.37).

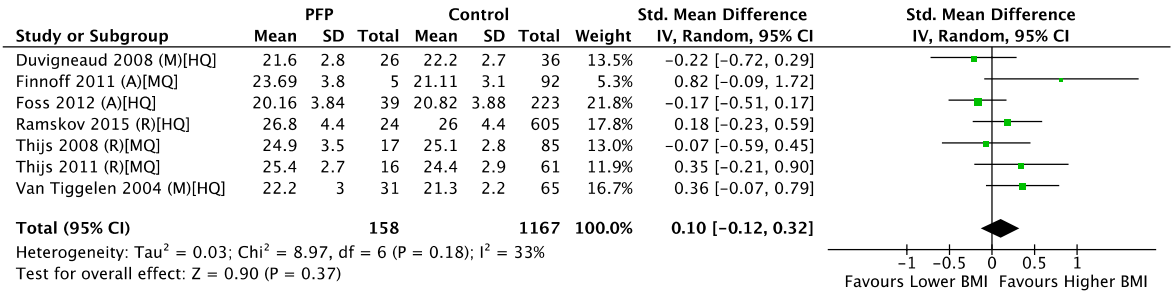



*8. Forrest plot detailing standardised mean differences for weight when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain

*BMI*

There is strong evidence from four HQ (19, 22, 38, 124) and three MQ (17, 18, 26) studies that BMI is not a risk factor for future PFP development ($I^2$=33%, SMD 0.10, CI -0.12,0.32) (see figure 9). This outcome does not change when pooling data for only military recruits (moderate evidence, $I^2$=65%, SMD 0.09, CI -0.48,0.65), adolescents (moderate evidence, $I^2$=75%, SMD 0.23, CI -0.72,1.18) or recreational runners (moderate evidence, $I^2$=0%, SMD 0.15, CI -0.13,0.43).

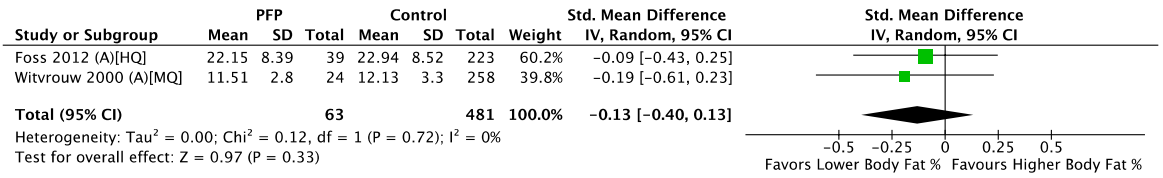



*9. Forrest plot detailing standardised mean differences for BMI when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain; BMI – body mass index

*Body fat percentage*

There is moderate evidence from one HQ study (124) and 1 MQ study (128) that body fat percentage is not a risk factor for future PFP development in adolescents ($I^2$=0%, SMD -0.13, CI -0.40,0.13) (see figure 10). This variable was not investigated in either military recruits or recreational runners.

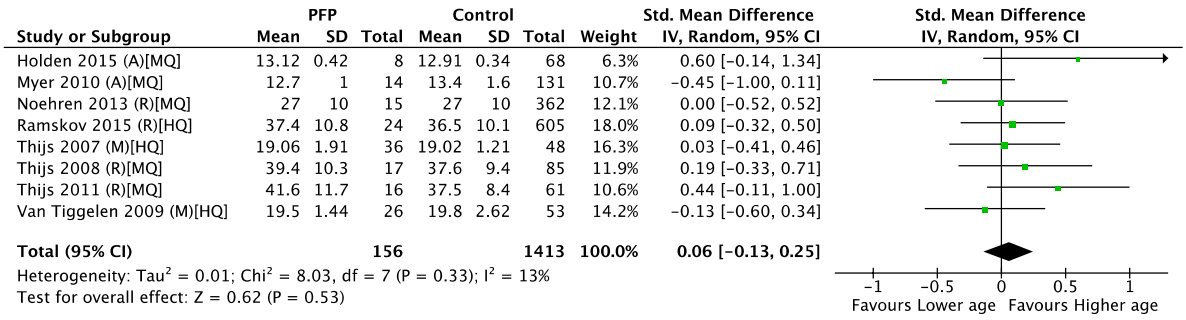



*10. Forrest plot detailing standardised mean differences for body fat percentage when comparing adolescents who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; A – adolescents; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain; % - percentage

*Age*

There is strong evidence from three HQ (19, 27, 42) and five MQ studies (17, 18, 20, 28, 29) that age is not a risk factor for future PFP development ($I^2$=13%, SMD 0.06, CI -0.13,0.25) (see figure 11). This outcome does not change when pooling data for only military recruits (moderate evidence, $I^2$=0%, SMD -0.05, CI -0.36,0.27), adolescents (limited evidence, $I^2$=80%, SMD 0.04, CI -0.98,1.07) or recreational runners (moderate evidence, $I^2$=0%, SMD 0.16, CI -0.09,0.40).




*11. Forrest plot detailing standardised mean differences for age when comparing participants who developed PFP with controls.*

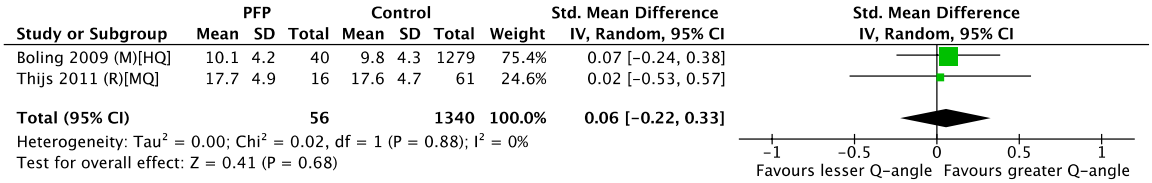
Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

*Limb length*

There is limited evidence from two MQ studies (26, 125) that limb length is not a risk factor for future PFP development ($I^2$=0%, SMD -0.01, CI -0.28,0.25). This variable was not investigated in recreational runners and no data pooling were possible within any individual subgroups.

### 3.3.5. Lower limb alignment

Data pooling were only possible for static Q-angle. Limited evidence from one HQ (23) and one MQ study (17) indicates that Q-angle is not a risk factor for future PFP development ($I^2$=0%, SMD 0.06, CI -0.22,0.33) (see figure 12). No data pooling were possible for any identified subgroup.




*12. Forrest plot detailing standardised mean differences for Q-angle when comparing participants who developed PFP with controls.*

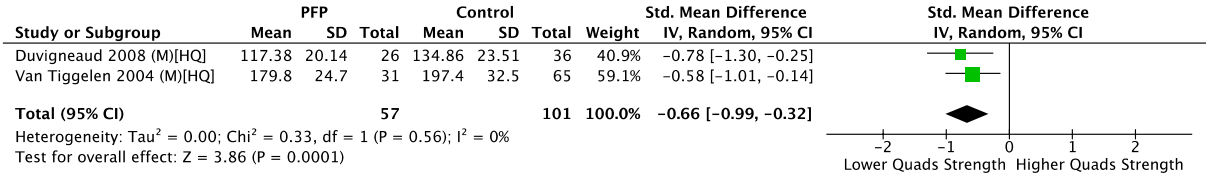
Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

### 3.3.6. Strength measures

*Quadriceps strength*

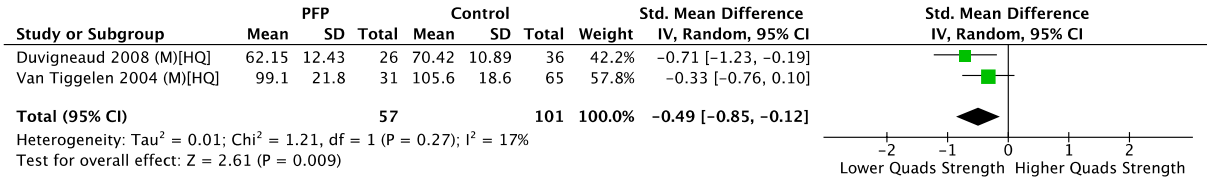
When pooling all available data for quadriceps strength, regardless of cohort or measurement method, there is strong evidence that low quadriceps strength is a risk factor for future PFP development (moderate evidence, $I^2$=65%, small SMD -0.32, CI -0.42, -0.22).

Data pooling were only possible for the military subgroup for all quadriceps strength measures. There is moderate evidence from two HQ studies (22, 38) that lower quadriceps strength is a risk factor for future PFP development when measured with an isokinetic dynamometer concentrically at 60˚/second ($I^2$=0%, moderate SMD -0.66, CI -0.99,-0.32) (see figure 13) or concentrically at 240˚/second ($I^2$=17%, small SMD -0.49, CI -0.85,-0.12) (see figure 14).




*13. Forrest plot detailing standardised mean differences for Quadriceps strength measured concentrically at 60˚/s when comparing military recruits who developed PFP with controls.*

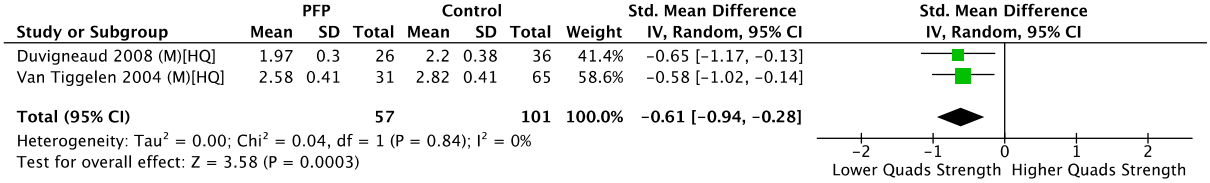
Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;




*14. Forrest plot detailing standardised mean differences for Quadriceps strength measured concentrically at 240˚/s when comparing military recruits who developed PFP with controls.*

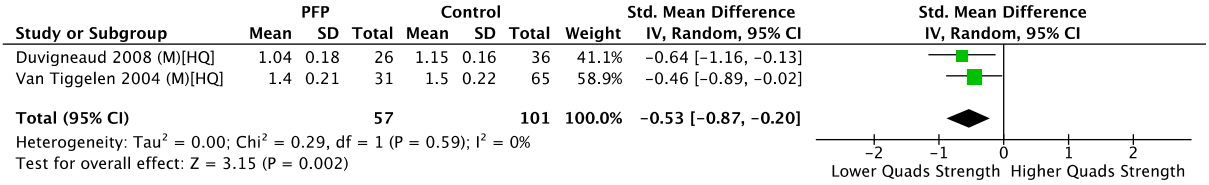
Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

For normalised quadriceps strength measured with an isokinetic dynamometer, there is moderate evidence from two HQ studies (22, 38) that lower quadriceps strength is a risk factor for future PFP development when normalised by body mass at 60˚/second ($I^2$=0%, moderate SMD -0.61, CI -0.94,-0.28) (see figure 15) or at 240˚/second ($I^2$=0%, small SMD -0.53, CI -0.87,-0.20) (see figure 16). When normalised by BMI, moderate evidence remains that lower quadriceps strength is a risk factor for future PFP development when measured at both 60˚/second ($I^2$=0%, moderate SMD -0.69, CI -1.02,-0.35) (See figure 17) and 240˚/second ($I^2$=0%, small SMD -0.51, CI -0.84,-0.18) (see figure 18).



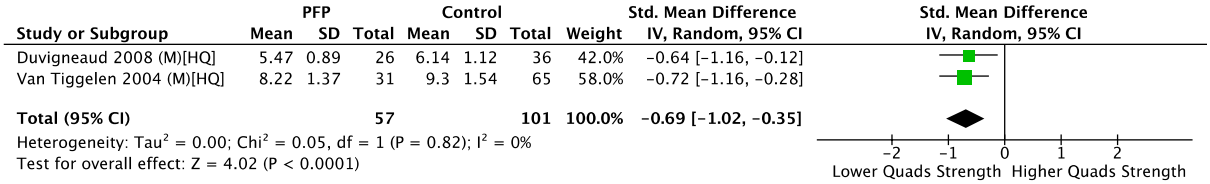

*15. Forrest plot detailing standardised mean differences for Quadriceps strength normalized by body mass and measured concentrically at 60˚/s when comparing military recruits who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;



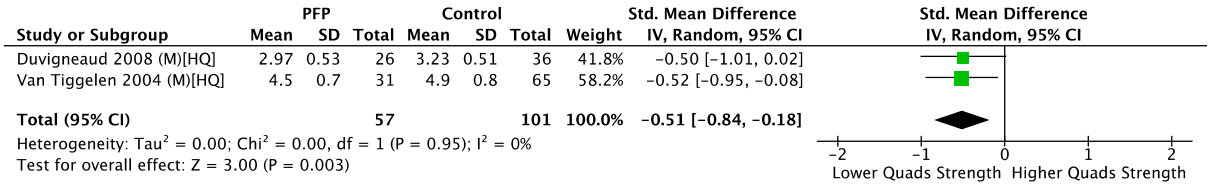

*16. Forrest plot detailing standardised mean differences for Quadriceps strength normalized by body mass and measured concentrically at 2400˚/s when comparing military recruits who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;




*17. Forrest plot detailing standardised mean differences for Quadriceps strength normalized by BMI and measured concentrically at 60˚/s when comparing military recruits who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;




*18. Forrest plot detailing standardised mean differences for Quadriceps strength normalized by BMI and measured concentrically at 240˚/s when comparing military recruits who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

For quadriceps strength measured isometrically with a hand-held dynamometer (HHD), there is moderate evidence from one HQ (23) and one MQ study (125) that lower quadriceps strength is not a risk factor for future PFP development ($I^2$=82%, small SMD -0.25, CI -0.74,0.25).

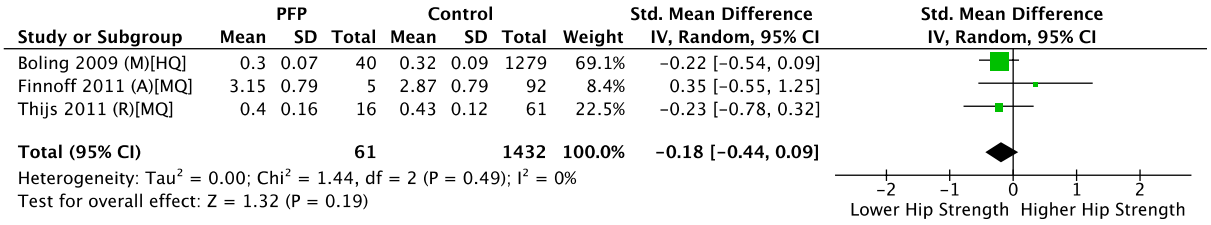
*Hamstrings strength*

There is moderate evidence from two HQ studies (22, 38) that hamstring strength is not a risk factor for future PFP development in the military when measured with an isokinetic dynamometer concentrically at 60˚/second ($I^2$=0%, SMD -0.09, CI -0.42,0.24)

or 240˚/second ($I^2$=0%, SMD -0.10, CI -0.43,0.22). This variable was not investigated in either adolescents or recreational runners.

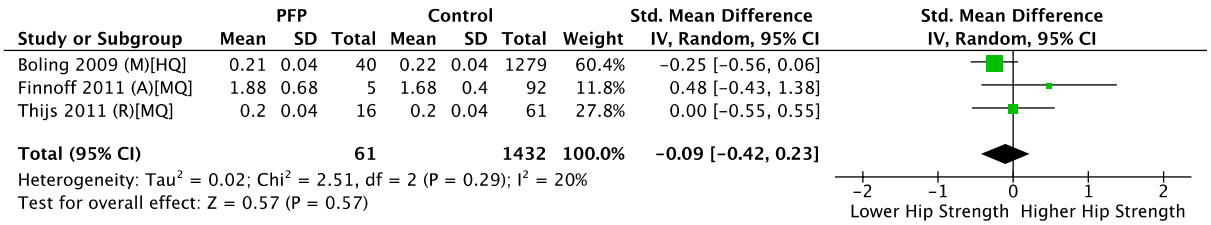
*Hip strength*

There is moderate evidence from one HQ (23) and two MQ studies (17, 26) that hip extension ($I^2$=0%, SMD -0.18, CI -0.44,0.09) (see figure 19), hip internal rotation ($I^2$=20%, SMD -0.09, CI -0.42,0.23) (see figure 20) and hip external rotation (I2=0%, SMD -0.17, CI -0.43,0.10) (see figure 21) strength, measured isometrically with a HHD, are not risk factors for future PFP development. There is also limited evidence from two MQ studies (17, 26) that both hip adduction strength ($I^2$=0%, SMD -0.20, CI -0.67,0.28) (see figure 22) and hip flexion strength ($I^2$=52%, SMD -0.08, CI -0.82,0.67) (see figure 23) are not risk factors for future PFP development when measured with a HHD. No data pooling were possible for any identified subgroup for these strength measures.



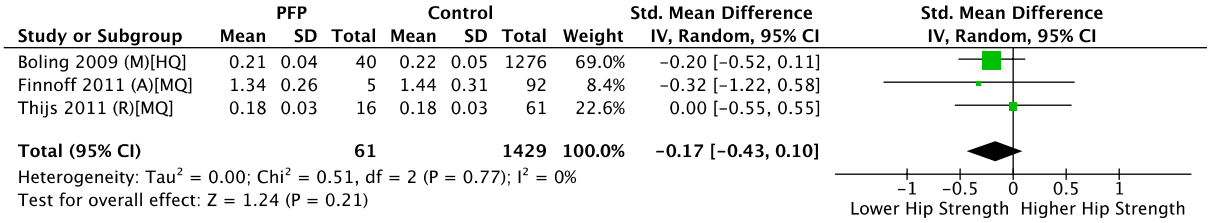

*19. Forrest plot detailing standardised mean differences for hip extension strength when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;



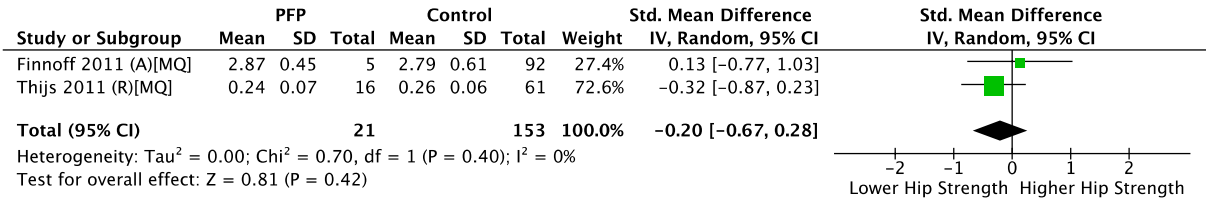

*20. Forrest plot detailing standardised mean differences for hip internal rotation strength when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;



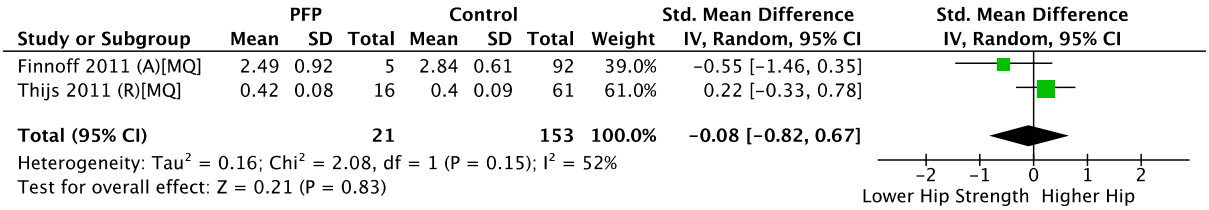

*21. Forrest plot detailing standardised mean differences for hip external rotation strength when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;




*22. Forrest plot detailing standardised mean differences for hip adduction strength when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

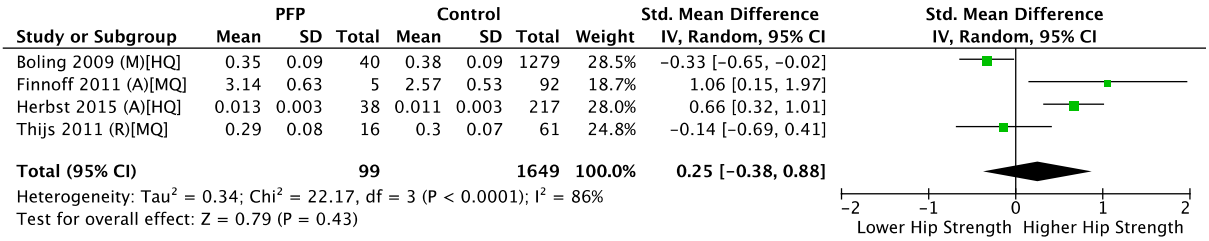



*23. Forrest plot detailing standardised mean differences for hip flexion strength when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

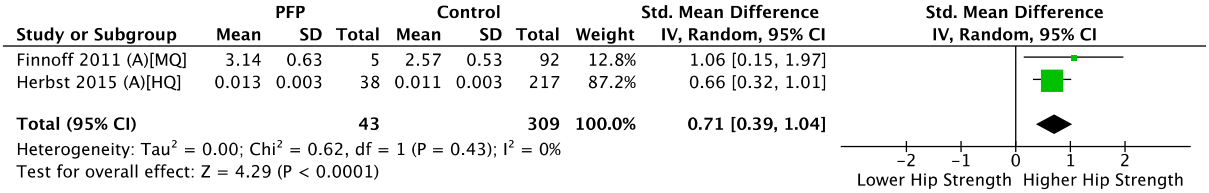
There is moderate evidence from two HQ (23, 25) and two MQ (17, 26) that hip abduction strength is not a risk factor for future PFP development ($I^2$=86%, SMD 0.25, CI -0.38,0.88) (see figure 24) when measured isometrically with a HHD. When data were pooled for the adolescent cohort, there is moderate evidence from one HQ (25) and one MQ study (26) that higher hip abduction strength is a risk factor for future PFP development ($I^2$=0%, SMD 0.71, CI 0.39,1.04) (see figure 25) when measured with

isometrically a HHD. Data pooling were not possible for the military or recreational runner subgroups.




*24. Forrest plot detailing standardised mean differences for hip abduction strength when comparing participants who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;




*25. Forrest plot detailing standardised mean differences for hip abduction strength when comparing adolescents who developed PFP with controls.*

Key: HQ – high quality; MQ – medium quality; LQ – low quality; M – military recruits; A – adolescents; R – recreational runners; SD – standard deviation; IV – inverse variance; CI – confidence intervals PFP – patellofemoral pain;

### 3.3.7. Biomechanics

*Dynamic knee valgus angle*

Moderate evidence from one HQ study (23) and one MQ study (29) indicates that knee valgus angle during a jump land task is not a risk factor for future PFP development ($I^2$=99%, SMD 4.17, CI -4.19,12.53). No data pooling were possible for any identified subgroup.

*Foot kinetics*

One HQ study (27) and one MQ study (18) investigated foot kinetics during walking and running respectively. When these data were pooled, moderate evidence indicates no significant associations between time to peak force at any investigated region of the foot, which included the hallux, the metatarsal heads and the medial/lateral heel.

## 3.4. Discussion

This systematic review aimed to provide a synthesis of the evidence concerning predictive variables for PFP development. Despite the inclusion of 11 additional prospective studies and 55 additional variables when compared to the previous review of Lankhorst et al (30), high data heterogeneity and a limited ability to pool da/ta remained. Just two predictive variables, lower isokinetic quadriceps strength in the military and higher isometric hip abduction strength in adolescents, were identified. Heterogeneous incidence of PFP was found to be 10%, with incidence also identified within the specific homogenous cohorts of military recruits (11%), adolescents (11%) and recreational runners (6%).

The finding that lower isokinetic quadriceps strength is predictive of future PFP development in a military cohort (22, 38) is in agreement with the previous review of Lankhorst et al (30). Unfortunately, the strength of this evidence has not changed, as no new prospective studies using an isokinetic dynamometer to measure quadriceps strength have been published since 2011. Data from two studies investigating isometric quadriceps strength in military cohorts (23, 125), not included by Lankhorst et al, have been included in this review and demonstrated no significant association with future PFP development. Whilst this could be interpreted as conflicting evidence, it could be that isometric muscle testing may not be sensitive enough to identify military recruits at risk of PFP. This limits the clinical applicability of these results, as isometric testing with a HHD is a more accessible tool for clinicians to use when measuring muscle strength.

Data from a single study (25) reports that low baseline isokinetic quadriceps strength was not identified as a risk factor for future PFP development in an adolescent group. Whilst this further validates the importance of investigating risk factors within homogenous groups, it is also important to consider the implications of these findings in relation to risk modification interventions within differing populations. A similar disparity between adult and adolescent populations has been observed crossectionally, with no differences in hip or knee strength having been reported when comparing adolescents with PFP to a group of asymptomatic controls matched for

both age and sex (129), but significant strength deficits identified in adults with PFP compared to control groups (31, 44). These findings offer indications as to why rehabilitation programmes have been shown to be of significant benefit in adults with PFP (130, 131), but are of only limited additional benefit to education alone in adolescents (132).

In contrast to the quadriceps data, low baseline hip strength, regardless of test direction, was not found to be a risk factor for future PFP development in military recruits or recreational runners. However, pooled data from two studies (25, 26) indicate that higher baseline isometric hip abduction strength predicts future PFP development in adolescents. Herbst et al (25) make the suggestion that greater hip abduction strength could be the result of increased eccentric hip abductor demands due to increased peak hip adduction during dynamic tasks. When pooling data from both military and adolescent cohorts, dynamic knee valgus angle was also not found to be a risk factor for future PFP development. However, Holden et al (29) reported higher knee valgus displacement in adolescent females who develop PFP (mean difference 7.8˚). Despite these reported kinematic deficits, hip strength and altered kinematics during dynamic tasks are consistently negatively correlated (133), contradicting this hypothesis.

A more plausible explanation for the association between higher isometric hip abduction strength and future PFP in young adolescents is a high level of physical activity, common within this age group (134). The mean age of the Herbst et al (25) cohort is 12.7 years and may therefore have higher lower limb muscle strength as a consequence of high physical activity levels. It may be that lower limb muscle strength correlates with duration of symptoms in adolescents, with strength deficits presenting later in life when symptoms persist and if activity levels subsequently reduce (129). As a result, it is sensible to question the role of increasing muscle strength in adolescent cohorts as a preventative measure. It is advised that future prospective studies both report and stratify for activity levels when investigating the association between strength variables and future PFP development.

In 2011 Coppack et al (135) reported a significant reduction in PFP risk after completion of a quadriceps and gluteal strengthening programme when compared to a

non-specific control group. It is surprising that an exercise intervention designed to increase quadriceps strength has not been investigated further, given both level one (30) and two (135) evidence identifying quadriceps weakness as a preventative treatment target. Future studies aiming to reduce the incidence of PFP in the military should give priority to exercise protocols designed to increase quadriceps strength. Whilst higher baseline hip abduction strength was found to increase the risk for future PFP development in adolescents, this is potentially a surrogate indicator of activity level. Given the promise that education and load management interventions are demonstrating within this population (132), we suggest that these strategies are prioritised in future studies designed to reduce the incidence of PFP in adolescents.

Multiple variables often described as risk factors for future PFP development, perhaps due to strong associations in cross-sectional studies, were not found to be so in this meta-analysis. Participant height, weight, BMI, body fat percentage, age and Q-angle were not to predict future PFP development in any cohort. The recent systematic review of Hart et al (136) reports a crosssectional association between high BMI and both PFP and patellofemoral osteoarthritis (PFOA) in adults, again perhaps due to a reduction in activity levels after symptom development (137). Higher BMI was not reported to be a risk factor for future PFP development in either adults or adolescents, nor was a high BMI linked to intervention outcomes in participants with PFP (136). Whilst these data question the biologically plausible suggestion that a high BMI contributes to PFP development, it remains plausible that high BMI may influence treatment outcomes and this suggestion requires further investigation (136).

Using data from the work of Boling et al (23), the previous 2012 review of Lankhorst et al (30) reported that females are at a higher risk of developing PFP within the military (odds ratio: 2.23, 95% CI 1.16,4.10). Our results are in conflict with this, with pooled data from 7 studies (18, 19, 23, 26, 27, 127, 128) identifying no significant links between the female sex and future PFP development. Pooling data for the identified individual subgroups is also non-significant, but six of the seven studies including data on sex report a greater proportion of females developing subsequent PFP. The largest proportion of females occurs amongst the recreational runner subgroup and this is in fact statistically significant when a fixed-effects model is used for the meta-analysis,

meaning observed results are most likely a result of selection bias in source studies. However, given the low number of studies (n=3) and high heterogeneity, a fixed-effects model is inappropriate and increases the chance of sustaining a type I error (123). Given the absence of a causal association between the female sex and future PFP development, the frequent bias towards the female sex in trial sampling and the need to control for sex as a confounder may not be necessary.

Using data only from studies included in this review, heterogeneous incidence of PFP was found to be 10%, demonstrating that PFP affects up to one in ten persons across multiple populations. The recent systematic review of PFP incidence and prevalence by Smith et al (16) identified a wide range of PFP incidence amongst military recruits (9.7-571.4 cases per 1000 person-years), which is similar to the incidence range identified by this review (3-43%). The variance is likely explained by the four studies (22, 38, 42, 126) included in this review not included by Smith et al (16), and the three studies included by Smith et al (16) not eligible for inclusion within this review (135, 138, 139). The incidence range for PFP within adolescent cohorts are identical (5-15%), despite two studies from this review (29, 124) not being included by Smith et al (16).

### 3.4.1. Limitations and future research directions

This review is not without limitations, which must be considered when interpreting the results. There is currently no accepted method for determining study methodological quality or ascertaining risk of bias. Whilst the NOS is advocated by the Cochrane Group, it is possible that using a different quality appraisal tool may have yielded different levels of eventual evidence. It should also be considered that the NOS does not have a component pertaining to the reliability of exposure data collection, focussing more on the validity of outcome data. As per the PRISMA guidelines (115) three databases were searched, but is it also possible that increasing the number of databases searched may have yielded additional studies for inclusion. An attempt was made to mitigate this risk by completing a citing reference search in Google Scholar in addition to hand searching the reference lists of included studies. It must be stressed that incidence data has been calculated only from included studies, and the addition of other epidemiology studies that do not fit the inclusion criteria of this review would have affected the figures reported. It was also not possible to express incidence data

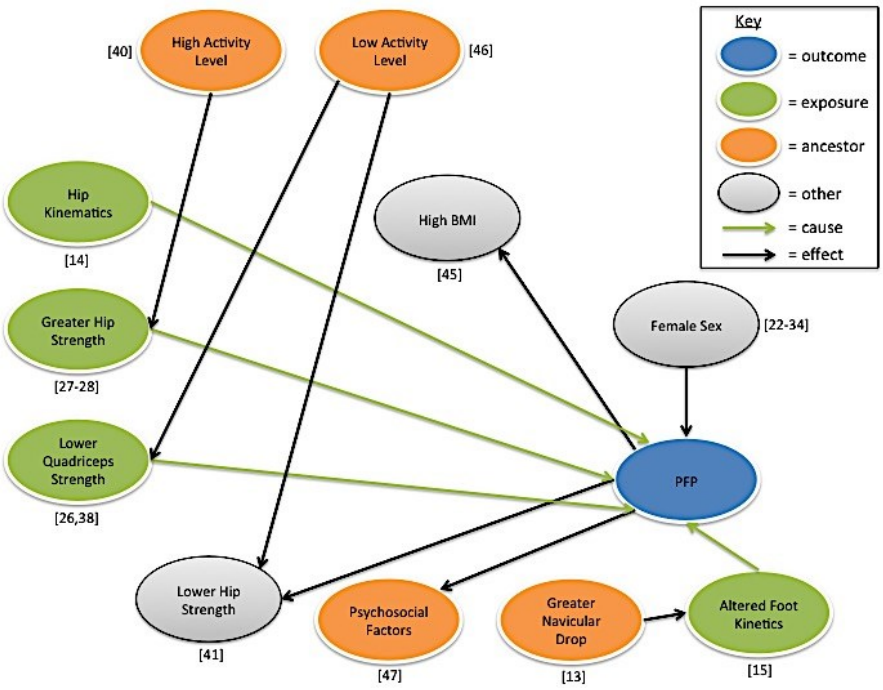
relative to a timeframe given the high heterogeneity observed between included studies.

Some included studies provided data that were not suitable for inclusion in a meta-analysis (i.e. no mean/SD or raw counts) and efforts to obtain raw data directly from study authors were unsuccessful. Despite the addition of 11 new studies, ability to pool data were limited, which is partly attributable to the 116 individual variables investigated across the 18 included studies that could not be pooled. A total of 8 studies (17, 18, 20, 26, 28, 29, 127, 128) failed to adhere to the rule of 10 (120), that is ensuring a minimum of 10 PFP events for each variable of interest, resulting in a high risk of bias and reduced methodological quality. Future studies are encouraged to investigate an appropriate number of variables within an adequate sample, that have the potential for future pooling with existing data to affect the strength of level 1 evidence, unless there is clear plausibility to investigate a novel variable.

Given the lack of associations identified by this review (pooled data or otherwise), it is sensible to suggest that perhaps the current body of research is not placing appropriate focus on variables of interest. Altered hip and knee kinematics during running are known to have moderate to strong cross-sectional association with PFP (82), yet there remains just one prospective investigation of these variables in female runners only (20). There is also an emerging evidence base surrounding the association between psychological variables and PFP, with levels of anxiety, depression, catastrophising and fear of movement reported to be elevated in persons with PFP by a recent systematic review (35). Future studies should focus on attempting to establish an association between these variables and PFP development.

The prospective studies included within this review have sought to detect an association between single variables and risk of PFP development. The inherent limitation of this approach is the inability to consider interactions between multiple variables. Consequently, research needs to move towards a complex systems approach to better understand injury aetiology (140). Rather than endeavouring to identify a singular causal factor, studies should be designed to investigate the interactions between a ‘web of determinants’ that are likely to be non-linear in nature (141). This approach has significant methodological challenges and requires the use of a statistical

learning approach such as a Bayesian network (142). Examples of variables that could fit into a web of determinants for PFP from the published literature include muscle strength (quadriceps and gluteal), hip/knee kinematics, activity levels/sporting workload and psychosocial measures (see figure 26).




*26. Potential causal inference diagram for PFP*

No variable included within this systematic review identified a link with future PFP development in recreational runners. High peak hip adduction is known to be associated with future PFP development in female runners (20), and future studies should further explore the causal associations between lower limb kinematics and PFP. Whist not presented in a fashion that allowed for data pooling, Ramskov et al (19) report that higher eccentric hip abduction strength reduces the risk of future PFP development in recreational runners, using a time to event analysis. The distinct limitation of this study design is that no guidance was given to the included runners regarding training frequency or intensity which is likely to be a significant confounder, as more aggressive run volume progressions have been shown to increase the risk of injury development (143). Future studies should focus on further exploring the causal associations between both muscle strength and activity level with respect to future PFP development in recreational runners.

## 3.5. Conclusion

Low quadriceps strength, measured using an isokinetic dynamometer and whether or not normalised to either bodyweight or BMI, is a risk factor for future PFP development in military recruits and should be investigated as a preventative strategy in a future RCT. Whilst higher hip abduction strength is a risk factor for future PFP development in adolescents, this may simply be a composite of activity level. PFP is a common pathology in multiple populations, with incidence found to be 10%, with a higher incidence seen amongst military recruits and adolescents compared to recreational runners. Overall, our understanding of what contributes to the development of PFP is inadequate and requires further scientific exploration, though the relationship between given variables and PFP risk is likely to be both complex and individual. This work represents a strong case for future trials requiring stronger preliminary risk factor identification to improve outcomes.

# 4. Runners with patellofemoral pain have altered biomechanics which targeted interventions can modify: a systematic review and meta-analysis

Limited risk factors for the development of future PFP were identified in the systematic review that forms chapter three. Furthermore, no risk factors associated with the development of running-related PFP from pooled data were identified. As a result, a systematic review of the specific biomechanical factors that are associated with the development, persistance and management of running-related PFP are presented in this chapter.

Preliminary results of this review were presented at the 2015 Danish Sports Medicine Congress in Copenhagen and the 2015 International Patellofemoral Pain Research Retreat in Manchester. This review was accepted for publication in Gait & Posture (Impact Factor 2.347) after two rounds of comprehensive peer review (appendix B). A translational publication for the Physio First 'In Touch' journal was also produced as part of a special issue on PFP, based on data from this systematic review (appendix C).

The results presented within this chapter informed the subsequent case-control study (chapter five), by identifying a dearth of literature investigating running kinematics when comparing between the sexes. Additionally, the results informed the subsequent step rate feasibility study (chapter six), by identiying potential efficacy and kinematic treatment targets following *running retraining* interventions.

## 4.1. Introduction

Participation in running has increased in recent years, as a result of the increased awareness of exercise for good health (8). Although running has been linked to improvements in cardiovascular disease (144), improved mental health (145) and a reduced risk of diabetes (146), it is also associated with a greater incidence of musculoskeletal injury (12). Dependent on the source (8, 13), the overall lower extremity injury incidence is suggested to range from 18% to 92%, with the most significant risk factor for injury being a previous running injury (12). The most common running overuse injury is patellofemoral pain (PFP), with an incidence of 3% to 15% in active populations stated amongst the literature (23, 112, 126).

The source of symptoms in PFP remains highly debated (147). A well-established explanatory reason is increased patellofemoral joint stress. Elevated patellofemoral joint stress has been reported in individuals with PFP during fast walking (148) and squatting tasks (149) and is thought to result in afferent nociceptive drive from subchondral bone (48), although it must be stated that the most recent PFP consensus statement highlighted that the source of pain in PFP remains unclear (80). Small changes in patellofemoral joint kinematics, of the order of five degrees of femoral internal rotation, have been shown to increase osteochondral shear stress (50), and therefore increased patellofemoral lateral patella facet contact pressures. Increases in vertical loading rates (and subsequent patellofemoral reaction forces) have also been reported in runners with PFP (150). Therefore, a link between possible biomechanical mechanisms and pain development can be suggested, making such variables of great interest from a treatment mechanism perspective.

The cause of altered kinematics and PFJ stress in PFP is considered multifactorial, with various intrinsic and extrinsic factors thought to contribute. Several kinematic factors, including excessive frontal/transverse plane motion of the lower limb (dynamic knee valgus), have been theorised to increase loading forces acting on the lateral facet of the patella (45). One previous systematic review summarising literature to 2008 (151) reported that rearfoot eversion, knee external rotation and hip adduction were increased in runners with PFP (151). However, findings related to hip internal rotation

and adduction were reported to be inconsistent, with a paucity of data preventing meta-analysis. Further, a dearth of prospective research at that time prevented conclusions about causal relationships between kinematics and PFP presentation and intervention outcomes (151).

Alongside kinematics, muscle function of the quadriceps and gluteals is thought to play a role in both the development and management of PFP. Reduced knee extension strength has been identified as a risk factor (30). Additionally, weakness or delayed activation of vastus medialis obliquus (VMO) is also historically described as a risk factor and rehabilitation target for PFP, although recent research has questioned its importance (152). There is known to be an association between reduced gluteal strength and PFP (34), but the causative relationship of this factor has recently been questioned, highlighting a discrepancy between prospective and cross-sectional findings (17, 32, 34).

PFP is often recalcitrant, with as many as 91% of suffers continuing to report symptoms beyond four years following diagnosis (153). This is particularly problematic given the recent suggestion that PFP may be an early stage of a continuum ultimately leading to patellofemoral joint osteoarthritis (3). Typical exercise interventions (encompassing both the hip and the knee) appear to have a positive effect on pain and function (56, 154, 155), but have been reported not to alter running kinematics such as knee valgus linked to PFP (88). Given that a kinematic mechanism may be required to achieve a long-term resolution in PFP, research surrounding movement feedback interventions and running retraining are starting to be explored (156, 157). Foot orthoses are another intervention which aims to alter lower limb kinematics and have been shown to improve outcomes in PFP patients at six weeks follow up, but their long-tem outcomes and place within a multi-modal rehabilitation, particularly in a running population, remains unclear (69).

The aim of this systematic review was to guide the treatment and prevention of PFP by synthesising prospective, observational and intervention studies that measure clinical and biomechanical outcomes in symptomatic running populations. Specific objectives included (i) to establish the biomechanical differences (including kinematics, kinetics and neuromuscular) between individuals with and without PFP in a running

population, identifying causal relationships where possible; and (ii) define the biomechanical outcomes of interventions used in the conservative management of PFP. It is anticipated that the impact of this review will be to improve upon the prevention and treatment outcomes of PFP during running by identifying when biomechanical variables should be targeted as part of a management plan, and by what mechanisms these variables may be best approached.

## 4.2. Methods

The protocol for this systematic review was designed in accordance with the PRISMA statement (115).

### 4.2.1. Search strategy

MEDLINE, Web of Science and CINAHL were searched from inception until April 2015. MEDLINE and Web of Science were searched using the rationale described in chapter three. CINAHL was searched as an allied health professional specific database that offers an alternative source of primary studies, and has been reported to result in unique search results (158). The search strategy was limited to publications in the English language and those involving human subjects. In order to be compliant with a PRISMA systematic search strategy (116), additional hand searching of the reference lists of identified papers and discussions with field experts (e.g. physiotherapists and podiatrists) regarding relevant publications were conducted, alongside a citing reference search using Google Scholar.

### 4.2.2. Eligibility criteria

All studies identified by the search strategy were exported to Endnote version X7 (Thomson Reuters, Philadelphia) by one investigator. Adapted from the original review of Barton et al (151), eligibility criteria applied to manuscript titles were: (i) studies involving male or female subjects with PFP (multiple terms including retropatellar pain, chondromalacia or anterior knee pain) ; (ii) a 3D kinematic, kinetic or EMG outcome measure captured during treadmill or over-ground running; and (iii) prospective, case-control or intervention study design. Exclusion criteria included studies that used 2D methods of kinematic measurement (due to insufficient validity and reliability), studies where data was collected during a task other than running and studies using a case series methodology design. Two authors (BN and PH) reviewed all abstracts to determine eligibility and full texts were screened to confirm eligibility where there was uncertainty from the abstract alone. A third reviewer (CB) was available for any discrepancies but was not required.

### 4.2.3. Quality assessment

The Downs and Black Quality Index (159) was used to determine quality for case-control and prospective studies. Use of Downs and Black is advocated by the Cochrane Group (121) and is a validiated tool for both randomised and non-randomised control trials, with intra-class correlation coefficients (ICC) of 0.75 to 0.89 previously reported (159). A modified version for case-control studies (scored out of 16) as used by Barton et al (151), which has been reported to have good inter-rater reliability when grading similar studies, was applied. Studies with scores of eleven or greater were considered to be 'high quality' (HQ), studies with scores from six to ten were considered to be 'moderate quality (MQ) and studies with scores five or lower were considered to be 'low quality' (LQ).

The PEDro scale was used to determine the quality of the intervention studies, as it was specifically designed to evaluate the quality of physical therapy interventions (160). The PEDro scale has previously been reported to be a valid and reliable tool, with ICC's of 0.68 for consensus ratings (160). A score of 6-8 on the PEDro scale was considered to be HQ, scores of 4-5 were considered to be MQ and studies that scored below 4 were considered to be LQ, based on the work of Moseley (161).

Two independent raters (BN and RG), blinded to author and publication details appraised each study, with any discrepancies resolved at a consensus meeting. Inter-rater reliability was calculated using percentage agreement.

### 4.2.4. Data management

Data pertaining to study characteristics were extracted from all included studies by one author (162). This included participant numbers and characteristics of the PFP and control groups, publication details (author, year, and country), biomechanical variables analysed, examiner details, PFP outcome, duration of study and covariates investigated, for analysis of possible mechanisms (see tables 3 and 4). Corresponding authors were contacted where appropriate data was not included in the publication and recorded as 'not reported' (NR) if this was unsuccessful. Variables of interest in this review included (but were not limited to) peak hip adduction, internal rotation and

flexion, contralateral pelvic drop, rearfoot eversion, peak metatarsal force, patellofemoral joint stress and peak/average gluteal electromyography.

3. Summary of study characteristics for included prospective and case-control studies for biomechanics systematic review & meta-analysis

| Study | Study Population | Study Design | Injury Outcome | Injured | | Control | | Outcome Variables |
|---|---|---|---|---|---|---|---|---|
| | | | | Total | Age (Mean ±) | Total | Age (Mean ±) | |
| **Rodrigues 2013 (78)** | Heel Strike Runners | Case-Control | Anterior Knee Pain | 17 | 29.8 ±7.0 | 19 | 34.0 ±10.0 | Kinematics |
| **Rodrigues 2013 (163)** | Heel Strike Runners | Case-Control | Anterior Knee Pain | 17 | 29.8 ±7.0 | 19 | 34.0 ±10.0 | Kinematics |
| **Souza 2009 (39)** | Local Orthopaedic Clinics | Case-Control | Patellofemoral Pain | 21 | Not Reported | 20 | Not Reported | Kinematics, EMG |
| **Willson 2011 (164)** | University Fitness Centre | Case-Control | Patellofemoral Pain | 20 | 21.3 +2.6 | 20 | 21.6 ±4.5 | Kinematics, EMG |
| **Besier 2009 (165)** | Not Stated | Case-Control | Patellofemoral Pain | 27 | 30.5 +4.5 (m)<br>28.7 ±4.6 (f) | 16 | 27.2 +3.0 (m)<br>28.8 ±4.7 (f) | EMG |
| **Bazett-Jones 2013 (166)** | University Community | Case-Control | Patellofemoral Pain | 19 | 26.0 ±5.5 | 19 | 24.3 ±4.3 | Kinematics |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Cunningham 2014 (167)** | Recreational Runners | Case-Control | Patellofemoral Pain | 19 | 25.8 ±6.1 | 11 | 26.5 ±13.4 | Kinematic Coupling |
| **Dierks 2011 (168)** | Recreational Runners | Case-Control | Patellofemoral Pain | 20 | 24.1 ±7.4 | 20 | 22.7 ±5.6 | Kinematics |
| **Noehren 2012 (52)** | Competitive Runners | Case-Control | Patellofemoral Pain | 16 | 27.0 ±6.0 | 16 | 25.0 ±4.0 | Kinematics |
| **Noehren 2012 (53)** | Recreational Runners | Case-Control | Patellofemoral Pain | 15 | 27.0 ±6.0 | 15 | 25.0 ±4.0 | Kinematics |
| **Souza 2009 (54)** | Local Physiotherapy Clinics | Case-Control | Patellofemoral Pain | 19 | 27.0 ±6.0 | 19 | 26.0 ±4.0 | Kinematics |
| **Stefanyshyn 2006 (162)** | Sports Medicine Clinic | Case-Control | Patellofemoral Pain | 20 | 34.6 ±9.8 | 20 | 34.3 ±10.3 | Kinematics |
| **Willy 2012 (51)** | University Running Club | Case-Control | Patellofemoral Pain | 18 | 24.7 +4.9 (m)<br>22.2 ±3.8 (f) | 18 | 23.4 ±3.6 | Kinematics |
| **Willson 2008 (169)** | Active Females | Case-Control | Patellofemoral Pain | 20 | 23.3 ±3.1 | 20 | 23.7 ±3.6 | Kinematics |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Wirtz 2012 (170)** | Recreational Runners | Case-Control | Patellofemoral Pain | 20 | 21.3 ±2.6 | 20 | 21.6 ±4.4 | Joint Stress |
| **Pal 2011 (171)** | University Sports Clinic | Case-Control | Patellofemoral Pain | 40 | 28.9 ±4.6 | 15 | 28.2 ±3.9 | EMG |
| **Esculier 2015 (172)** | Recreational Runners | Case-Control | Patellofemoral Pain | 21 | 34.1 ±6.0 | 20 | 33.2 ±6.0 | Kinematics, Kinetics, EMG |
| **Chen 2014 (173)** | Orthopaedic Clinic | Case-Control | Patellofemoral Pain | 20 | 27.9 ±6.7 | 20 | 26.1 ±7.2 | Patellofemoral Reaction Force |
| **Thijs 2008 (18)** | Novice Recreational Runners | Prospective | Patellofemoral Pain | 17 | 39.4 ±10.3 | 85 | 37.6 ±9.4 | Plantar Pressures |
| **Noehren 2013 (20)** | Heel Strike Runners | Prospective | Patellofemoral Pain | 15 | 27.0 ±10.0 | 15 | 27.0 ±10.0 | Kinematics |
| **Macintyre 1992 (174)** | Recreational Runners | Case-Control | Patellofemoral Pain | 5 | Not Reported | 12 | Not Reported | EMG |

Key: ± = standard deviation; EMG = electromyography; m=male; f=female

4. Summary of study characteristics for included intervention studies for biomechanics systematic review & meta-analysis

| Study | Study Population | Intervention Period | Injury Outcome | Injured | | Control | | Outcome Variables |
|---|---|---|---|---|---|---|---|---|
| **Exercise Therapy** | | | | Total | Age (Mean ±) | Total | Age (Mean ±) | |
| Earl 2011 **(84)** | Female College Students | 8 Weeks | Patellofemoral Pain | 19 | 22.7 ±7.2 | N/A | N/A | Kinematics, Kinetics |
| Ferber 2011 **(83)** | Recreational Runners | 3 Weeks | Patellofemoral Pain | 15 | 35.2 ±12.2 | 10 | 29.9 ±8.3 | Kinematics |
| **Orthoses** | | | | | | | | |
| Boldt 2013 **(175)** | Recreational Runners | Immediate | Patellofemoral Pain | 20 | 21.3 ±2.6 | 20 | 21.6 ±4.5 | Kinematics |
| Rodrigues 2014 **(176)** | Heel Strike Runners | Immediate | Patellofemoral Pain | 17 | 29.8 ±7.2 | 16 | 34.2 ±10.9 | Kinematics |

| **Running Retraining** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Noehren 2012 (100) | Recreational Runners | 2 Weeks | Patellofemoral Pain | 10 | 23.3 ±5.8 | N/A | N/A | Kinematics, Kinetics |
| Willy 2012 (101) | Recreational Runners | 2 Weeks | Patellofemoral Pain | 10 | 22.4 ±5.0 | N/A | N/A | Kinematics |
| Willson 2014 (95) | Heel Strike Runners | Immediate | Patellofemoral Pain | 10 | 20.8 ±3.7 | 10 | 21.0 ±2.3 | Joint Stress |

### 4.2.5. Statistical methods

All statistical analyses were completed in Review Manager 5.0 (The Cochrane Collaboration, Copenhagen, Denmark) initially by one author (BN) and subsequently checked by a second author during a consensus meeting (CB). Means and SD's for continuous scaled variables were extracted and used to calculate standardised mean differences (SMD) with 95% confidence intervals (CI's). No dichotomous data were identified in the results of any included study. Data for men and women were analysed independently and directly compared where this breakdown was published, also contributing to the pooled SMD produced where relevant. Meta-analysis was performed where homogeneity between studies was deemed to be adequate and the level of statistical heterogeneity for pooled data were established using $I^2$ statistics (heterogeneity defined as $I^2 > 50\%$, $p < 0.05$) (177). Calculated individual or pooled SMDs were categorised as small (≤ 0.59), medium (0.60 to 1.19) or large (≥ 1.20) (122).

### 4.2.6. Evidence based recommendations

Based on the previous work of van Tulder *et al* (116), levels of evidence were assigned for each evaluated variable or intervention, incorporating statistical outcomes and the methodological quality of included studies.

*Strong evidence*: pooled results derived from three or more studies, including a minimum of two high quality studies that are statistically homogenous; may be associated with a statistically significant or non-significant pooled result.

*Moderate evidence:* statistically significant pooled results derived from multiple studies that are statistically heterogeneous, including at least one high quality study; or from multiple moderate quality or low quality studies which are statistically homogenous.

*Limited evidence*: results from one high quality study or multiple moderate or low quality studies that are statistically heterogeneous.

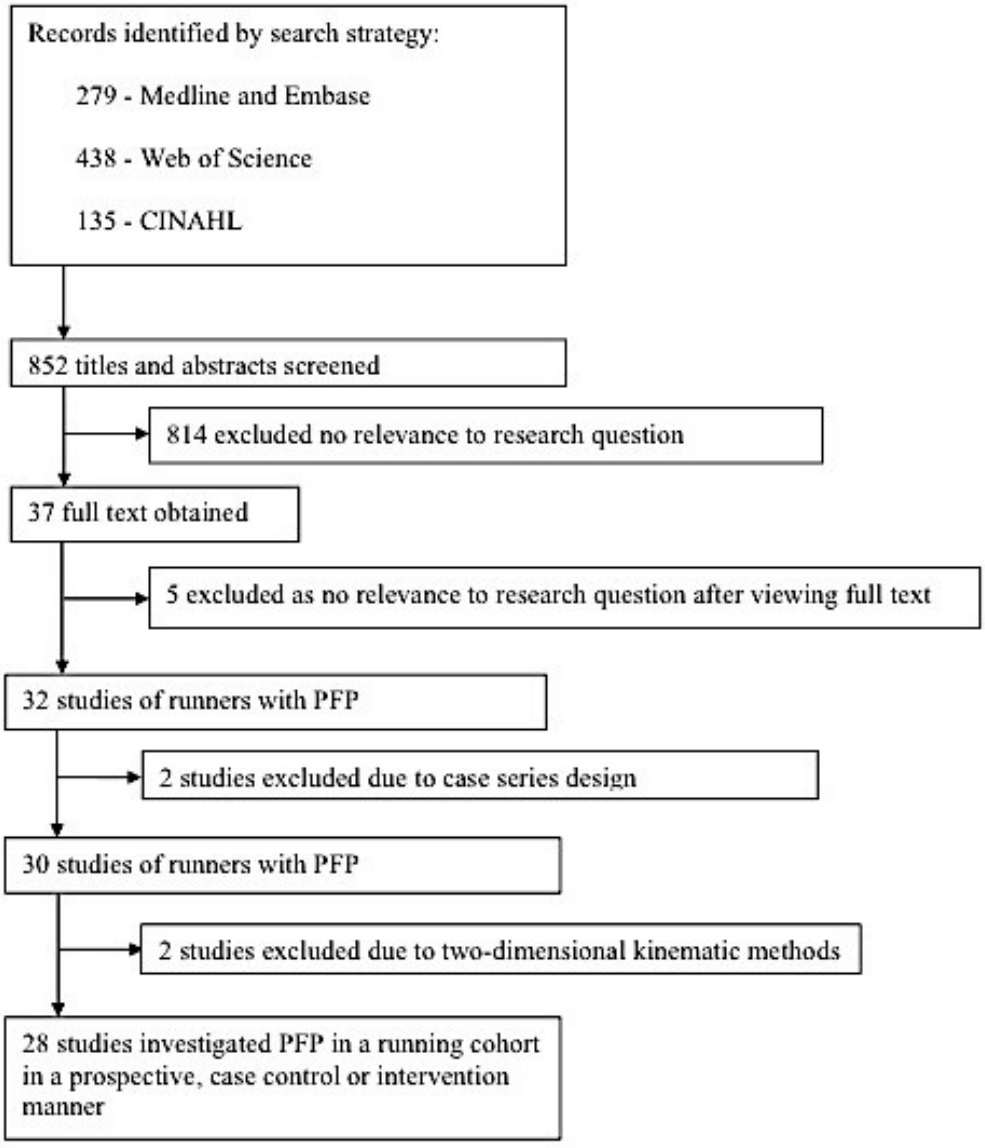
*Very limited evidence*: results from one moderate quality study or one low quality study.

*No evidence:* pooled results insignificant and derived from multiple studies regardless of quality that are statistically heterogeneous.

## 4.3. Results

### 4.3.1. Search results

The electronic database search yielded 852 citations. After a sequential review of titles, abstracts and full texts, and removal of studies that were not completed using a running population or studies involving two dimensional kinematic analysis, 28 studies were included – three prospective studies (18, 20, 162) 18 case-control studies (39, 51-54, 163-174, 176) and seven intervention studies (78, 83, 84, 95, 100, 101, 175) (Figure 27).




*27. Search flow chart for biomechanics systematic review & meta-analysis adhering to PRISMA guidelines*

### 4.3.2. Quality assessment of included studies

*Prospective/Case-Control studies*

Based on evaluation with the Down's and Black, quality scores ranged from 6 to 14 (out of a maximum score of 16). Of the 21 prospective and case-control studies included in this review, 13 studies were scored as HQ (18, 39, 51-54, 162, 165, 166, 168, 170, 172, 173), 8 studies were scored as MQ (20, 163, 164, 167, 169, 171, 174, 176) and no studies were scored a LQ. Inter-rater reliability was calculated using percentage agreement for all prospective and case-control studies and mean agreement was calculated to be 83%. For the 15 items included in the modified Down's and Black evaluation, percentage agreement ranged from 35% to 100%, with a mean of 80%. Item 20, relating to the reliability and validity of the main outcome measures displayed the lowest percentage agreement, with perfect agreement identified for only 7 of the included studies.

*Intervention studies*

Based on evaluation with the PEDro scale, quality scores ranged from 3 to 6 (out of a maximum possible score of 10). Of the 7 intervention studies included in this review, 2 studies were scored as HQ (95, 175), 4 studies were scored as MQ (78, 83, 100, 101) and 1 study was classified LQ (84). Inter-rater reliability was calculated using percentage agreement for all intervention studies and mean agreement was calculated to be 92%. For the 11 items included in the PEDro evaluation, percentage agreement ranged from 71% to 100%, with a mean of 94%. Item 3 concerning similarity at baseline regarding prognostic indicators displayed the lowest percentage agreement, with perfect agreement identified for only 5 included studies.

### 4.3.3. Study characteristics

Study characteristics are presented in tables 3 and 4, including recruitment population and participant characteristics to inform upon potential subgroups, observation periods and injury outcomes to inform upon potential recovery timeframes and biomechanical variable(s) to inform upon symptom development and intervention mechanisms.

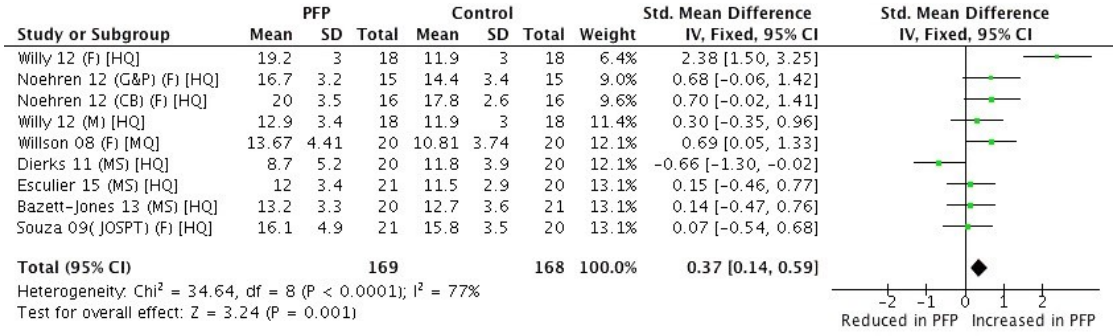
*Case-Control*

Unless a specific sex is mentioned, results described are in relation to a mixed sex cohort.

### 4.3.4. Retrospective kinematics (peak)

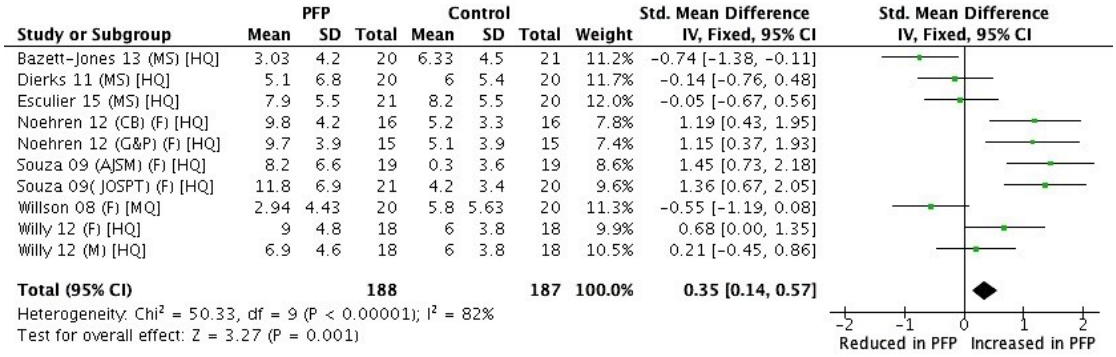
*Proximal*

There is moderate evidence from 7 HQ studies (39, 51-53, 166, 172, 178) and one MQ study (169) of an association between PFP and increased peak hip adduction ($I^2$ *=84%,* small significant SMD 0.37, 0.14 to 0.59) (see figure 28) and peak hip internal rotation ($I^2$*=83%,* small significant SMD 0.35, 0.14 to 0.57) (see figure 29). Additionally, moderate evidence from 4 HQ studies (51, 52, 166, 172) indicates an association between PFP and increased peak contralateral pelvic drop ($I^2$*=63%,* medium significant SMD 0.67, 0.37 to 0.97) (see figure 30). There is also limited evidence from one HQ study (166) of a significant association between PFP and reduced stance phase peak hip flexion (medium SMD -0.69, -1.32 to -0.06) (see figure 31).



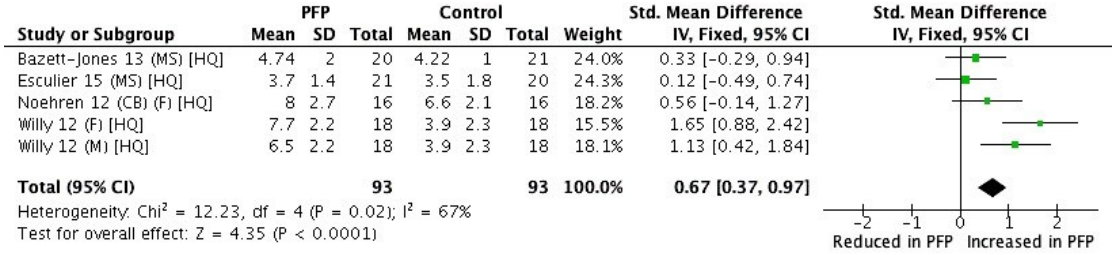

*28. Forest plot detailing standardised mean difference for peak hip adduction when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain



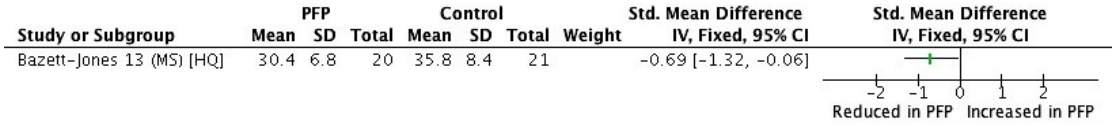

*29. Forest plot detailing standardised mean difference for peak hip internal rotation when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain




*30. Forest plot detailing standardised mean difference for peak contralateral pelvic drop when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain



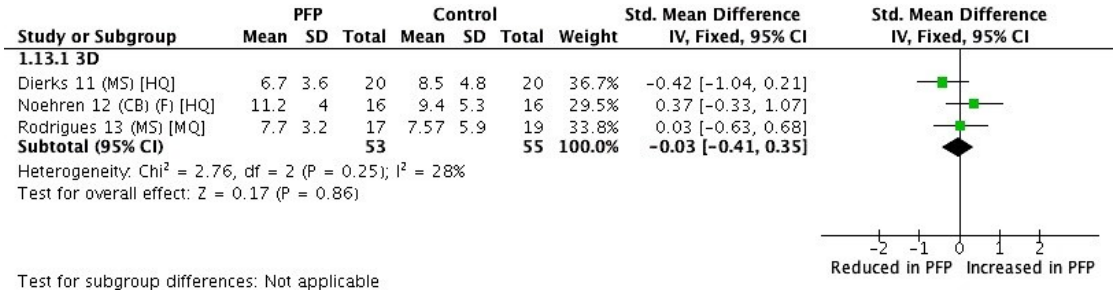

*31. Forest plot detailing standardised mean difference for peak hip flexion when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

*Distal*

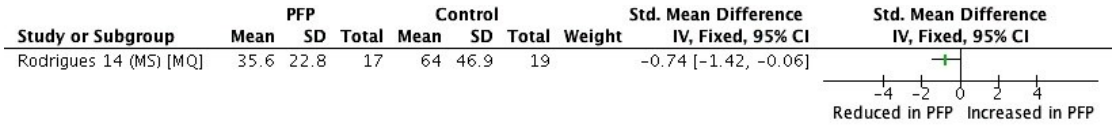
There is strong evidence from 2 HQ studies (52, 168) and 1 MQ (163) study of no association between PFP and increased peak rearfoot eversion ($I^2$*=28%,* small non-significant SMD -0.03, -0.41 to 0.35) (see figure 32). There is very limited evidence from one MQ study (176) of a significant reduction in 'minimum time to contact the

ankle joint complex range of movement boundary' (an expression of pronation velocity) in runners with PFP (medium SMD -0.74, -1.42 to -0.06) (see figure 33).




*32. Forest plots detailing standardised mean differences for peak rearfoot eversion when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

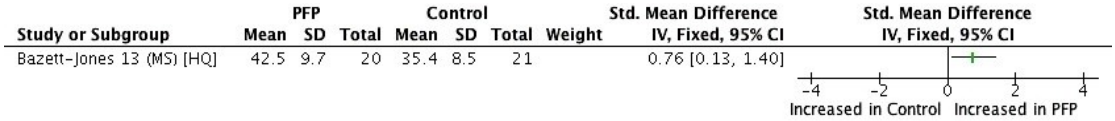



*33. Forest plots detailing standardised mean differences for minimum time to contact ankle range of motion boundary when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

### 4.3.5. Retrospective kinematics (peak): post-fatigue

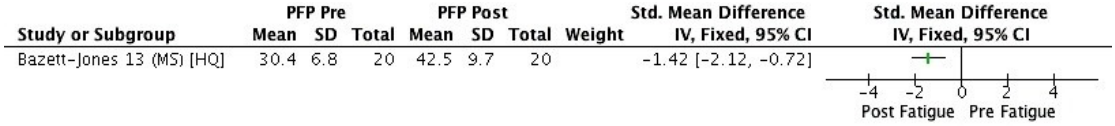
Three HQ studies (53, 166, 168) investigated the effect of fatigue on lower limb kinematics in runners with and without PFP. Limited evidence from one HQ study (166) indicates an association between increased peak hip flexion (medium SMD 0.76, 0.13 to 1.40) and runners with PFP in a fatigued state (see figure 34).




*34. Forest plots detailing standardised mean differences for peak hip flexion when comparing runners with PFP to controls post-fatigue.*

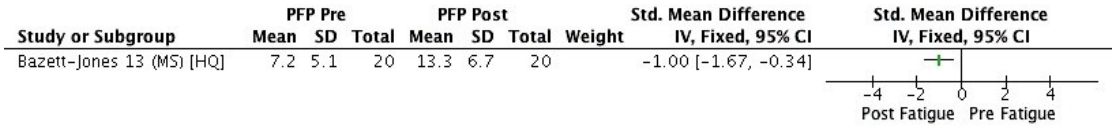
Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

When analysing kinematic changes in runners with PFP as a result of fatigue, this same limited evidence of increased peak hip flexion remains (large SMD 1.42, 0.72 to 2.12) (see figure 35), as well as limited evidence of increased anterior pelvic tilt (medium SMD 1.00, 0.34 to 1.67), from the same HQ study (166) (see figure 36).




*35. Forest plots detailing standardised mean differences for peak hip flexion when comparing runners with PFP pre/post-fatigue.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain



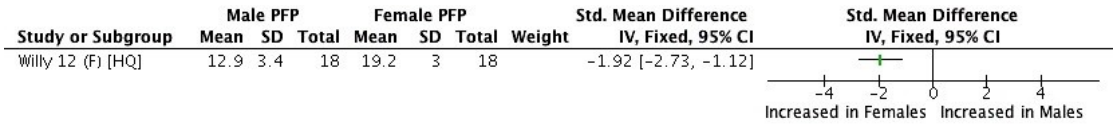

*36. Forest plots detailing standardised mean differences for peak anterior pelvic tilt when comparing runners with PFP pre/post-fatigue.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

No significant differences were identified post-fatigue for any of the kinematic variables analysed by the above stated three HQ studies (53, 166, 168).

### 4.3.6. Retrospective kinematics (peak): male compared to female

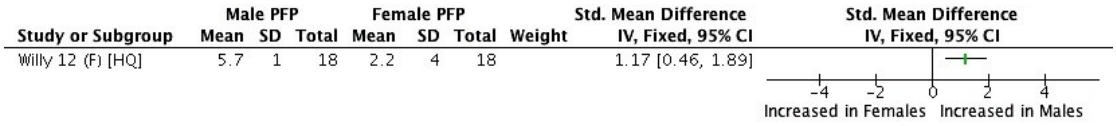
Limited evidence from one HQ study (51) indicates that female runners with PFP have significantly increased peak hip adduction (large SMD -1.92, -2.73 to -1.12) in comparison to male runners with PFP (see figure 37).




*37. Forest plots detailing standardised mean differences for peak hip adduction when comparing male and female runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

Limited evidence from the same HQ study also indicates that male runners with PFP have significantly increased peak knee adduction (medium SMD 1.17, 0.46 to 1.89) compared to female runners with PFP (see figure 38).




*38. Forest plots detailing standardised mean differences for peak knee abduction when comparing male and female runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

No significant differences were identified for any other kinematic variables investigated, including contralateral pelvic drop or hip internal rotation.

### 4.3.7. Retrospective kinematics (coupling angle variability)

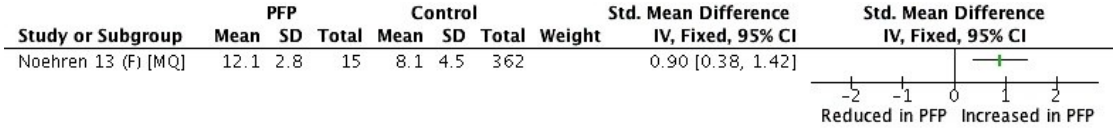
Coupling angle variability is a measure used to describe the degree of variation of coordinated segments, with reduced variability thought to be associated with repetitive use injury development (167). However, very limited evidence from one MQ study (167) identified a significant association between *greater* kinematic coupling angle variability and runners with PFP in comparison to control, for the following variables: Knee Flexion/Extension and Ankle Dorsiflexion/Plantarflexion at heel strike (medium SMD 0.91, 0.12 to 1.69); Knee Internal/External Rotation and Ankle Dorsiflexion/Plantarflexion at mid-stance (medium SMD 0.81, 0.03 to 1.58); Knee Valgus and Ankle Dorsiflexion/Plantarflexion at swing acceleration (medium SMD 1.03, 0.23 to 1.83); Knee Valgus and Ankle Inversion/Eversion at swing deceleration (medium SMD 1.05, 0.25 to 1.84); Knee Valgus and Ankle Dorsiflexion/Plantarflexion during the first 40% stance (medium SMD 1.10, 0.30 to 1.90) and Knee Valgus and Ankle Inversion/Eversion throughout the gait cycle (medium SMD 0.81, 0.04 to 1.59).

### 4.3.8. Prospective kinematics (peak)

*Proximal*

Very limited evidence from one MQ study (20) indicates that increased peak hip adduction was predictive of PFP development in female runners, associated with a significant, medium SMD (0.90, 0.38 to 1.42) (see figure 39). No significant links were

identified for peak hip internal rotation (SMD 0.25, -0.27 to 0.76) or knee angular impulse (SMD 0.31, -0.52 to 1.15).

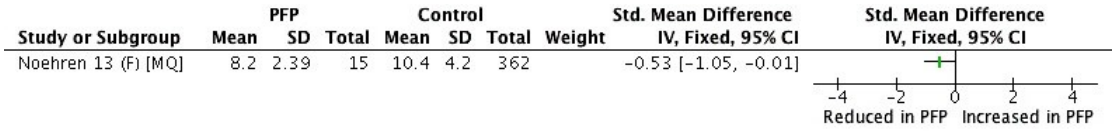



*39. Forest plots detailing standardised mean differences for prospective peak hip adduction when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

*Distal*

Very limited evidence from one MQ study (20) indicates that reduced peak rearfoot eversion is predictive of PFP development in female runners, associated with a small but significant SMD (-0.53, -1.05 to -0.01) (see figure 40).

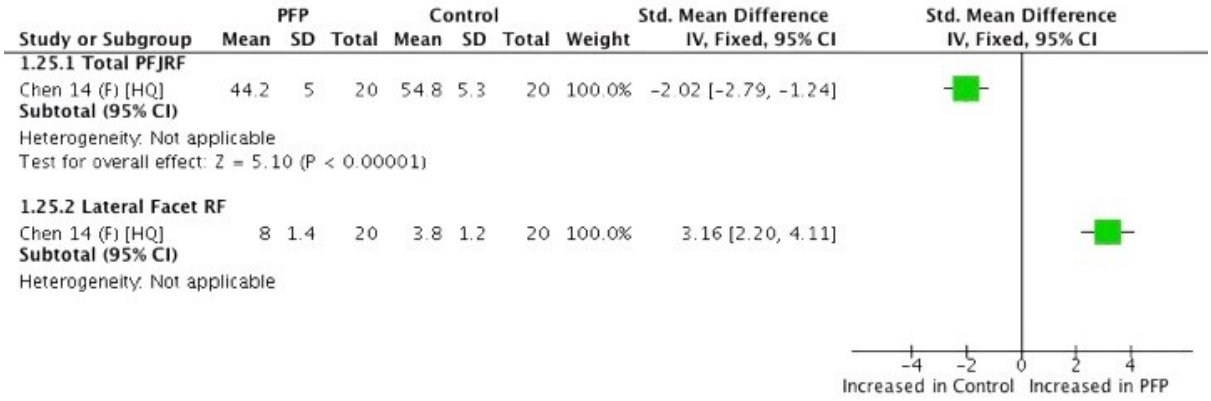



*40. Forest plots detailing standardised mean differences for prospective rearfoot eversion when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

### 4.3.9. Retrospective kinetics

Two HQ studies (170, 173) investigated the correlation between joint stress or patellofemoral reaction forces and female runners with PFP. Limited evidence of no significant difference was identified for peak patellofemoral joint stress during running from one HQ study (170) (SMD 0.46, -0.17 to 1.09). Limited evidence of significantly lower patellofemoral reaction force during running in participants with PFP was also identified from one HQ study (173) (large SMD -2.02, -2.79 to -1.24), but a significant increase in patellofemoral reaction force specific to the lateral facet of the patella was also identified in runners with PFP by the same HQ study (large SMD 3.16, 2.20 to 4.11) (see figure 41).

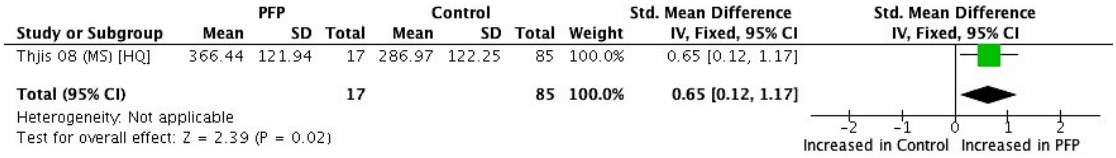



*41. Forest plot detailing standardised mean differences for patellofemoral reaction force when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

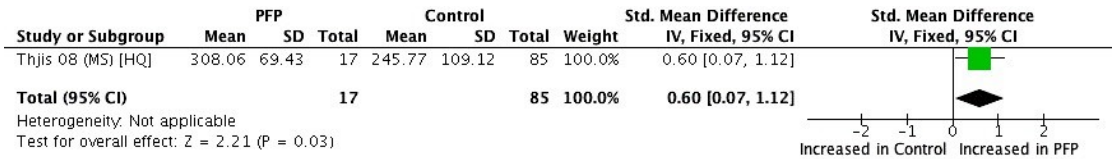
### 4.3.10. Prospective kinetics

Limited evidence from one HQ study (18) indicates that runners who go on to develop PFP have a significantly higher peak vertical force under the second (medium SMD 0.65, 0.12 to 1.17) (see figure 42) and third (medium SMD 0.60, 0.07 to 1.12) (see figure 43) metatarsals and a significantly lower time to peak force underneath the lateral heel (small SMD -0.56, -1.08 to -0.03) (see figure 44).



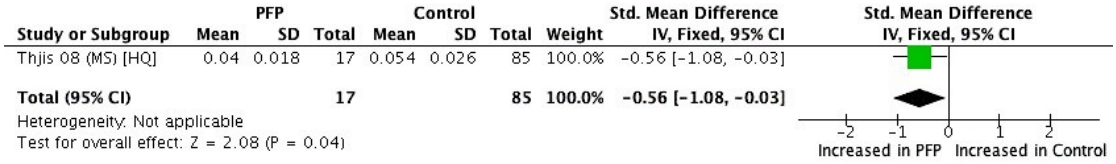

*42. Forest plots detailing standardised mean differences for peak vertical force under the 2nd metatarsal head when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain




*43. Forest plots detailing standardised mean differences for peak vertical force under the 3rd metatarsal head when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

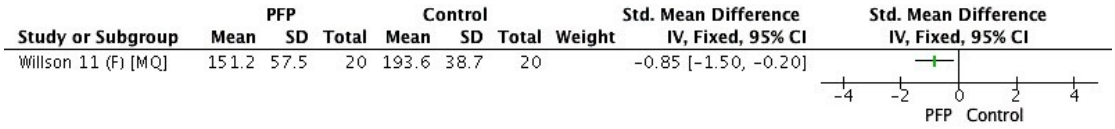



*44. Forest plots detailing standardised mean differences for time to peak vertical force at the lateral heel when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

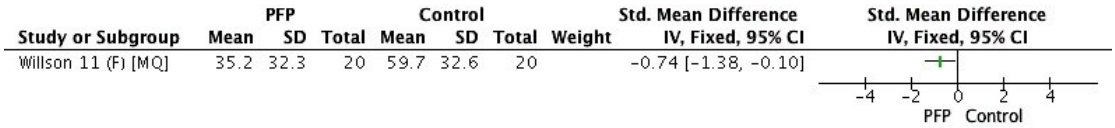
### 4.3.11. Lower limb EMG

One HQ study (172) and one MQ study (164) investigated the differences in gluteal muscle EMG in runners with PFP. Very limited evidence from one MQ study (164) was identified that female runners with PFP have significantly lower Gluteus Medius activation duration (medium SMD -0.85, -1.50 to -0.20) (see figure 45) and delayed onset prior to foot contact (medium SMD -0.74, -1.38 to -0.10) (see figure 46). No significant differences were identified for Gluteus Medius peak activation or average activation, or for any of the aforementioned variables for Gluteus Maxiumus from either study (164, 172).




*45. Forest plots detailing standardised mean differences for gluteus medius muscle activation duration when comparing runners with PFP to controls.*

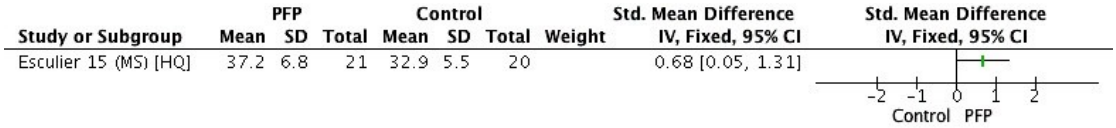
Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain




*46. Forest plots detailing standardised mean differences for gluteus medius muscle onset prior to foot contact when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

Additionally, very limited evidence of no significant differences in timing of VMO activation during running were identified by one MQ study (171), nor VMO peak activation from one HQ study (limited evidence) (172). Limited evidence from one HQ study (172) was identified that runners with PFP have a greater soleus activation duration (expressed as a percentage of the running cycle) compared to controls (medium SMD 0.68, 0.05 to 1.31) (see figure 47), but no significant differences were identified for any other muscle group investigated by this study, including the gluteals and quadriceps.



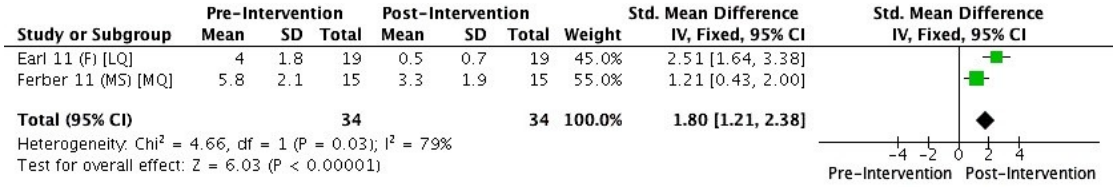

*47. Forest plots detailing standardised mean differences for soleus muscle activation duration when comparing runners with PFP to controls.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

### 4.3.12. Interventions and their effects

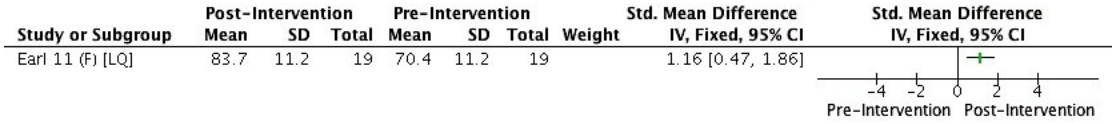
*Exercise*

Two studies investigated the effects of proximal (hip) strengthening exercise in the management of running-related PFP (83, 84), both of which provided data suitable for SMD calculation. There is limited pooled evidence that proximal strengthening exercise can reduce pain (large SMD 1.80, 1.21 to 2.38) (see figure 48) and very limited evidence that proximal strengthening exercise can improve function (medium SMD 1.16, 0.47 to 1.86) (see figure 49) in runners with PFP. However, no significant differences were observed for any of the kinematic variables, including hip adduction and internal rotation, rearfoot eversion, knee abduction or genu valgum, with no data pooling being possible.




*48. Forest plots detailing standardised mean differences for pain post-strengthening exercise in runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

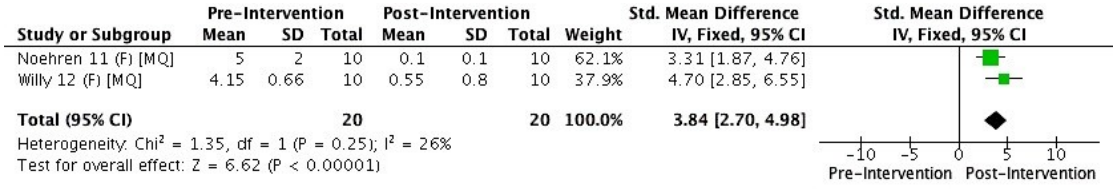



*49. Forest plots detailing standardised mean differences for function post-strengthening exercise in runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

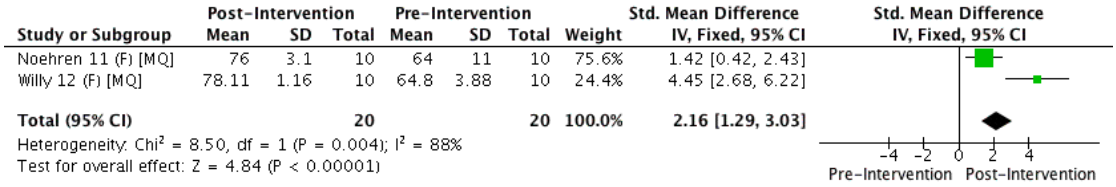
*Running retraining*

Three studies investigated the effects of running retraining in the management of females with running-related PFP (95, 100, 101). Limited evidence from two MQ studies (100, 101) indicates that running retraining using either visual display of real-time hip adduction (100), or mirror feedback to reduce hip adduction (101) significantly reduces pain (large SMD 3.84, 2.70 to 4.98) (see figure 50) and improves function (large SMD 2.16, 1.29 to 3.03) (see figure 51) at short-term follow up. Limited evidence from the same MQ studies indicates that peak hip adduction during running is reduced post-intervention, associated with a large and significant pooled SMD ($I^2$=0%, p=0.72, large SMD 2.10, 1.30 to 2.91) (see figure 52). No significant differences were identified for either hip internal rotation or contralateral pelvic drop at short-term follow up. No significant differences in patellofemoral joint kinetics were identified from one HQ study using metronome cadence re-training (+/- 10% from baseline) (95), but a trend towards significance for vertical impact peak was identified from one MQ study using real-time visual feedback to reduce peak hip adduction (100) (medium SMD 0.91, -0.02 to 1.84).



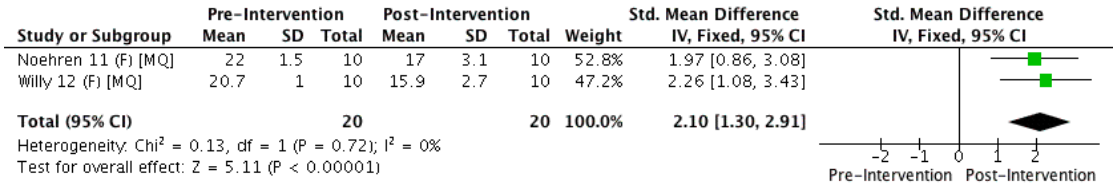

*50. Forest plots detailing standardised mean differences for pain post-running retraining in runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain




*51. Forest plots detailing standardised mean differences for function post-running retraining in runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain




*52. Forest plots detailing standardised mean differences for peak hip adduction post-running retraining in runners with PFP.*

Key: HQ – high quality; MQ – moderate quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – Gait & Posture; CB – Clinical Biomechanics; SD – standard deviation; IV – inverse variance; CI – confidence interval; PFP – patellofemoral pain

### *Orthoses*

Two studies (78, 175) investigated the kinematic effects of orthoses in runners with PFP, one of which (78) provided data suitable for SMD calculation. Neither study concurrently reported the effects of orthoses on either pain or function. Limited evidence from one MQ study (78) indicates that peak rearfoot eversion is reduced in runners with PFP following orthoses intervention, associated with a significant medium SMD (0.79, 0.29 to 1.29). There is also limited evidence from the same MQ study that orthoses intervention reduces peak ankle joint complex velocity (medium SMD -0.70, -

1.20 to -0.20) and increases the ankle joint angle at foot strike (medium SMD 0.64, 0.14 to 1.14), with both variables expressions of pronation velocity.

## 4.4. Discussion

This systematic review identified very limited evidence that increased peak hip adduction is a risk factor for PFP development in female runners, which can be modified with symptomatic benefit using running retraining. Increased peak hip adduction in runners with PFP is further supported by moderate cross-sectional evidence. Additionally, significant associations of PFP with increased peak hip internal rotation and contralateral pelvic drop, and a reduction in peak hip flexion were identified in both female and mixed-sex PFP populations. An association was also identified between PFP and both delayed and shorter Gluteus Medius activation duration in female runners. There are, therefore, clear outcomes from this systematic review relevant to clinicians treating runners with PFP.

Current findings related to the biomechanical effects of conservative interventions for management of runners with PFP indicate running retraining and proximal strengthening exercise both reduce pain. Running retraining was also found to reduce peak hip adduction; an established risk factor for PFP development (20), and this biomechanical change may provide a mechanistic explanation for running retraining effectiveness. Conversely, this review indicates that biomechanical mechanisms explaining the therapeutic effects of proximal strengthening exercise remain unclear. Foot orthoses were found to reduce peak rearfoot eversion, however without concurrent reporting of their effects on symptoms, it remains unclear if this kinematic mechanism can explain previously reported positive clinical outcomes (76, 77, 179).

### 4.4.1. Biomechanics associated with PFP during running

Very limited evidence that increased peak hip adduction was a risk factor for PFP development in female runners was identified (20), a finding supported by moderate cross-sectional evidence indicating greater hip adduction in individuals with existing PFP (39, 51-53, 166, 169, 172, 178). Additionally, meta-analysis revealed moderate evidence of greater peak hip internal rotation (39, 51-53, 166, 172, 178) and contralateral pelvic drop (51, 52, 166, 172) in individuals with PFP. Whilst hip adduction in both female and male symptomatic subjects was found to be greater than controls, limited evidence was identified that females with PFP may possess greater peak hip adduction in comparison to males with PFP, with males found to have

significantly greater knee adduction in one study (51). Considering that previous prospective research linking greater hip adduction to risk of PFP development was limited to a female population, future prospective research should include both sexes and sub-group them to establish if different biomechanical risk profiles exist in relation to the hip.

Distally, very limited evidence was identified that reduced peak rearfoot eversion was a risk factor for PFP (20), which was inconsistent with strong evidence from pooled cross-sectional findings that identified no association between peak rearfoot eversion and PFP during running (52, 163, 168). It should be highlighted that two studies (40, 180) which were excluded for 2D methods of quantifying rearfoot eversion do suggest that increased rearfoot eversion is associated with PFP. However, quantification of 2D rearfoot motion is known to have a measurement error up to four degrees (181), while the between group differences from these studies were below this figure (0.5 degrees (40) and 3.1 degrees (180)). Inclusion of these studies could have biased the findings of this review towards a false positive for this variable, hence their exclusion.

Limited evidence of both greater peak force under the 2$^{nd}$ and 3$^{rd}$ metatarsals, as well as a shorter time to peak force under the lateral heel were identified as risk factors for PFP in runners (18). Thijs et al (18) suggested that the increased forces described above could indicate a reduction in pronation, consistent with findings from Noehren et al (20), and thus reduction in shock attenuation at the foot during the loading phase of gait, with potential transfer of ground reaction forces to proximal structures such as the patellofemoral joint (37). When considering these limited findings in light of greater navicular drop being reported as a risk factor for PFP (23, 36) and evidence supporting the prescription of foot orthoses designed to control foot pronation (76, 77, 179), it is clear the relationship between foot biomechanics and PFP is poorly understood at this time.

The influence of fatigue on kinematics was highlighted as an under-researched area by the 2014 PFP consensus statement (80). Limited evidence identified that when fatigued, runners with PFP demonstrate greater peak stance phase hip flexion in comparison to controls and greater peak hip flexion and anterior pelvic tilt in comparison to their pre-fatigue state (166). This may indicate runners with PFP increase both trunk flexion and limb compliance throughout a period of running,

possibly as a result of fatigue (182, 183), or in an attempt to reduce PFJ stress (184). Interestingly, moderate evidence indicates that the differences in hip adduction, internal rotation and contralateral pelvic drop between runners with PFP when compared to asymptomatic runners is no longer present once in a fatigued state (53, 166, 168). It is important to note that the kinematics of runners with PFP do not change (e.g. reduced hip adduction) when fatigued, but rather the kinematics of asymptomatic runners become more akin to those with PFP (i.e. increased hip adduction). This suggests that runners with PFP demonstrate biomechanical features causally related to PFP from early in a run whereas those without pain only demonstrate these features when fatigued and likely close to finishing their run. This manifestation of injurious biomechanics from the initiation of high load exercise may be an important factor leading to symptom development.

Electromyographic investigations have yielded limited evidence of shorter, and delayed, activation prior to foot contact of Gluteus Medius is present in runners with PFP, while no significant differences were identified for Gluteus Maximus (164). Impaired gluteal function may partially explain altered kinematics in runners with PFP. Supporting this notion is work by Willson et al (164), which identified a correlation between gluteus medius activation delay at foot contact and increased hip adduction excursion. Limited evidence of no differences in VMO activity were identified by this review (171, 172), which is in support of previous analyses that VMO impairment is highly variable, present in some individuals with PFP but also highly prevalent amongst asymptomatic individuals (185).

Limited evidence identified a significant increase in patellofemoral reaction forces specific to the lateral facet of the patella during running (173), but no difference in peak total patellofemoral joint stress (170). These findings related to stress are inconsistent with other tasks evaluated in the literature, which indicates greater PFJ stress in individuals with PFP during walking (148) and squatting (149). It is plausible that it is not the total joint stress or reaction force, but spatially concentrated reaction forces leading to shear stress in specific patellofemoral joint facets, that may be responsible for symptom development (173). Another explanation may be variations in modelling approaches used. Wirtz et al (170), who provided running data for this review, suggest a possible underestimation of PFJ stress in their analyses, with an

absence of transverse plane kinematics in their modelling, which may explain the inconsistent findings. Importantly, hip internal rotation has been reported to contribute significantly to patellofemoral joint stress (50). Given the significant association between increased peak hip internal rotation and PFP identified by this review, further investigation to allow for greater understanding of joint stress and its mechanism on PFP development is warranted.

### 4.4.2. Biomechanical effects of interventions

Limited evidence indicates running retraining and proximal strengthening exercise both achieve improvements in pain and function in runners with PFP at short-term follow up. When evaluating the biomechanical effects and mechanisms for symptomatic improvement from running retraining, a significant reduction in peak hip adduction up to three months following a two-week running retraining intervention was identified (100, 101). However, findings from this review indicate no kinematic changes following exercise intervention (83, 84), indicating benefits may be derived by other mechanisms such as limb stiffness changes or nociceptive input processing alterations. Findings from Earl *et al* (84) provide some possible biomechanical explanation for the benefits of exercise rehabilitation in runners with PFP, reporting a significant reduction in peak internal knee abduction moments following an 8 week proximal strengthening program, although the data extracted did not produce a significant finding for this variable in the current review. Regardless, these changes to knee joint moments may be of potential clinical relevance and should be considered in future investigations.

Whilst no definite mechanism have yet been identified to explain the efficacy of proximal strengthening exercise in reducing running-specific PFP, it is possible that changes to both instantaneous and average loading rates can be achieved alongside positive clinical outcomes, identified in a recent study by Escullier et al (186). It is essential however, to realise that this study was multi-modal in nature, encompassing exercise, advice on load management and training error, as well as instruction to alter running cadence and foot strike patterns. Therefore, these positive effects cannot be solely attributed to any one of these interventions in isolation, but the developing hypotheses about loading rates certainly warrant further investigation.

Foot orthoses are known to have positive effects on pain and function in individuals with PFP (76, 77, 179), but do not improve outcomes when combined with multi-modal physiotherapy (179). The exact mechanism by which foot orthoses exert therapeutic effects is unclear, with several different paradigms outlined in the literature to explain the observed effects. This review identified limited evidence for a small reduction in both peak rearfoot eversion and peak ankle joint complex velocity with the prescription of medially posted foot orthoses designed to reduce rearfoot eversion (78, 175). Interestingly, this approach to prescription, which is similar to approaches with therapeutic supporting evidence (76, 77, 179), conflicts with findings suggesting that reduced rearfoot eversion may be a risk factor for PFP development (20). However, as concurrent measures of pain or function were not taken in these biomechanical orthoses studies (78, 175), the clinical relevance of these findings as potential mechanisms is unclear. Interestingly, research has suggested that rearfoot kinematic changes do not correlate well with pain reduction (187) or reduced tissue loads/demands (188), which potentially suggests that the modification of kinetic parameters may be of greater relevance to symptom change. However, the kinetic effects of foot orthoses in runners with PFP are currently unclear due to a paucity of research, indicating this is an area of research requiring attention.

### 4.4.3. Clinical implications

The findings of this review indicate that peak hip adduction may be a modifiable risk factor for PFP in female runners. Based on the data included in this meta-analysis, results also suggest that a change in hip adduction of 5 degrees post-intervention could be considered clinically meaningful, with these changes associated with marked reductions in running-related pain (100, 101). Recent evidence has emerged that 2D video movement analysis demonstrates good intra-rater reliability and acceptable concurrent validity with respect to detailed three-dimensional movement analysis, but currently only for hip adduction measurement (108). As such there is a useful, readily accessible assessment tool when managing runners with PFP. It may be that future work on new methods for 2D measurement will improve reliability of measurement for variables such as rear-foot motion, which would yield a very useful clinical tool. Additionally, previous research also indicates functional tasks such as single leg small knee bend or single leg step down may provide an indication of hip adduction during

running (189), indicating possible valuable clinical correlates in clinical settings where running cannot be easily assessed.

Both running retraining and proximal strengthening exercise have been reported to improve pain and function (83, 84, 100), but may have different effect mechanisms based on the findings of this review. Considering this, it is possible that a combination of the two interventions could lead to superior results. Considering the positive clinical outcomes identified for running retraining to reduce hip adduction, other running retraining strategies aimed at altering mechanics related to PFP may also be effective. For example, cadence manipulation has recently shown positive clinical outcomes in the management of tibial stress fractures (93) and has also shown favourable changes to patellofemoral joint forces (94) and lower limb joint mechanics (91) in normative cohorts. These additional running modification strategies may be positively augmented by proximal muscle training undertaken in a parallel fashion.

### 4.4.4. Limitations and future research

Some limitations must be considered when interpreting findings of this review. Not all studies provided data that allowed effect size calculation and subsequent potential for inclusion in meta-analysis. To address this, attempts to obtain data from corresponding authors were made, however, this did not prove successful in all instances, meaning some findings could not be considered when making conclusions and recommendations.

Common themes of methodological limitation were identified during the quality assessment process. For the prospective and case-control studies, only one study (18) ensured that their sample was representative of the entire recruitment population (failing to adequately state population source and subsequent participation percentages), only 6 studies reported reliability of their outcome measures (18, 20, 39, 51, 53, 54) and no studies attempted to blind those measuring the main outcome measures in the case-control studies. Similar themes were identified for the intervention studies, where all studies failed to blind either subjects or raters to groupings and no randomisation was performed, although it should be recognised that this was due to the absence of a control group in the design.

The presence of just one HQ (18) and two MQ (20, 162) prospective studies highlights a dearth of research to differentiate between cause and effect, and addressing this should be a priority for future work. Subsequent prospective or cross-sectional studies of the biomechanics of runners with PFP should focus on variables that have been found to be associated with the condition. Future prospective or cross-sectional investigation is warranted for peak hip internal rotation, hip flexion, contralateral pelvic drop, anterior pelvic tilt, gluteal EMG, joint stress and plantar pressures.

Only one cross-sectional study (51) provided a breakdown of kinematics for the individual sexes and only 5 studies (163, 165, 166, 168, 172) utilised a genuine mixed-sex cohort. This means that applying kinematic findings of this review to male runners with PFP requires particular caution. Future studies investigating cohorts involving both sexes with enough participants to complete between sex comparisons are needed to better understand biomechanics associated with PFP in males.

The clinical outcomes for running retraining can currently only be discussed relative to a short-term follow up (maximum 3 months) and future studies should seek to establish if these outcomes extend to a long-term follow up, with a minimum of 12 months suggested to meet the Cochrane Group guidelines (190). Running retraining has not been evaluated in relation to a control group and this is essential to determine the efficacy of the intervention. Positive clinical outcomes are known to extend to long term follow up for proximal strengthening exercise (56), but this needs to be confirmed in a running specific population, alongside an analysis of potential mechanisms. This should also be a priority for future research, alongside establishing if a combined running retraining and exercise intervention yields superior results to either intervention in isolation. The recent best practice guide for PFP (69) has outlined strong efficacy for both tailored patella taping and bracing in relation to short-term pain relief in conjunction with multi-modal physiotherapy. The biomechanical effects of these interventions have not been investigated in a running population and this would be a positive direction for future studies to take. Intervention using orthoses during running needs to be examined in conjunction with assessment of both symptoms and function, to determine the clinical efficacy of this intervention in a running cohort.

## 4.5. Conclusion

The quantity and quality of published literature concerning lower limb running biomechanics and the relationship to PFP has progressed markedly since the last systematic review on the topic, enabling more varied and stronger conclusions to be drawn. These conclusions relate to both symptom development and maintenance, as well as potential explanatory mechanisms for treatment effects. Very limited prospective evidence indicates that increased peak hip adduction is a risk factor for PFP development in female runners; in addition to limited evidence that running retraining changes both symptoms and function via a likely kinematic mechanism of reduced peak hip adduction. This is supported by moderate evidence from cross-sectional research in mixed sex cohorts, with a correlation also identified between PFP during running and increased peak hip adduction, internal rotation and contralateral pelvic drop. Further prospective research is needed to clarify if these relationships are of a causal or associative nature, and therefore better target interventions aimed at treatment and prevention. Limited evidence also indicates that proximal strengthening exercise changes both symptoms and function at short-term follow up, but currently potential biomechanical mechanisms are unclear. Further research to establish long-term efficacy for running retraining and an improved understanding of potential mechanisms for proximal strengthening exercise is needed

# 5. Increased peak hip adduction during running is associated with patellofemoral pain but differs between males and females: a case-control study

The systematic review presented in chapter 4 included eight case-control studies that reported peak kinematic variables during running, identifying clear associations between persistent PFP and altered running kinematics. Just one of these case-control studies reported their data for male and female participants separately, identifying a significant difference between the sexes for peak hip adduction. Given the strength of evidence for kinematic associations identified when data is pooled for both sexes, this case-control study was designed to further determine if sex influences previously reported differences in kinematics between runners with and without PFP.

As this chapter presents the first original data contribution within this thesis, the methodology for kinematic data collection during running is described in detail. The intra-rater reliability of marker placement for kinematic analysis is also presented.

This study has been submitted for peer review in Clinical Biomechanics (impact factor 1.874) and is currently awaiting an initial round of peer review.

## 5.1. Introduction

Patellofemoral pain (PFP) is described as either retropatellar or peripatellar pain of atraumatic onset, associated with knee joint loading into flexion (4). Running is a common aggravating factor, with incidence rate reported to range from as low as 4% throughout a two year period (20), to as high as 21% during a ten week 'start to run' programme (17). A recent systematic review and meta-analysis identified no risk factors from pooled data for the development of PFP in a running population (191).

Whilst there is a paucity of prospective research investigating risk factors for PFP in running populations, female runners with PFP have been reported to be at an increased risk of developing PFP in the presence of high peak hip adduction during running (20). Additionally, runners with persistent PFP have been reported to run with increased peak hip adduction and internal rotation, and reduced peak hip flexion compared to asymptomatic controls (82, 192). It is thought that these kinematic variations may contribute to the development and persistence of PFP by way of increasing patellofemoral joint stress, and thus provide treatment targets when using interventions such as gait retraining (100, 101).

A higher prevalence of PFP is reported amongst females (21). However, despite the breadth of literature evaluating the kinematics of runners with PFP, current understanding of the influence of sex on kinematic differences is unclear. Multiple studies have evaluated females only (52, 53), while others have evaluated mixed-sex cohorts with no sub-analysis of the individual sexes (166, 172, 178).

One previous study evaluated kinematic differences between males and females with PFP during running (51), reporting that females with PFP demonstrate greater peak hip adduction compared to both males with PFP and male controls. In contrast, males with PFP were reported to run with greater peak knee adduction when compared to both females with PFP and male controls. Limitations of this study include use of a fixed speed (3.35m/sec), which may result in different findings to when running at a self-selected speed; and the lack of a female control group. Improving understanding of how kinematic associations with PFP may differ between sexes is important to guide the development of more tailored interventions for this often persistent condition (2).

3D motion analysis is a widely used tool for the assessment of human locomotion, to understand both the epidemiology of a condition and to assess the effects of a given intervention. Accurate placement of the chosen marker set is fundamental to the collection of reliable data, with 75-90% of day to day variability reported to be explained by inconsistent marker placement by Gorton et al (193). Whilst there will always be a degree of inherent variability between trials when assessing human locomotion, accurate marker placement was found to significantly reduce both the standard error of measure (SEM) and minimum detectable change (MDC) for multiple peak kinematic variables by Noehren et al (194).

This case-control study aimed to evaluate running kinematics at self-selected speeds during a treadmill run between a mixed sex cohort with and without PFP, with further analysis of kinematics when these cohorts are divided into males and females. A further specific objective was to determine the intra-rater reliability of marker placement for kinematic data collection during a static standing calibration trial.

## 5.2. Methods

The Queen Mary Ethics of Research Committee granted ethical approval for this study (QMREC2014/63) and all participants provided written informed consent prior to participation.

### 5.2.1. Kinematic reliability participants

Prior to recruitment of the case-control participants, a convenience sample of asymptomatic individuals was sought from a local university student population. Ten participants (four males, six females) aged 27.7 (+3.1) years, height 171.4 (±8.7) centimeters and weight 65.9 (±14.5) kilograms volunteered to participate.

### 5.2.2. Case-Control participants

A convenience sample of participants with and without PFP was sought from local sports medicine clinics and running clubs respectively. Using peak hip adduction data from previous work (51) (males with PFP 12.9˚ [±3.4], females with PFP 19.2˚ [3.0]), an a priori analysis revealed that 5 participants were required to determine the difference between males and females with PFP ($\alpha$=5%, $\beta$=0.80). We therefore recruited 20 participants per group defined either by sex or presence of PFP.

20 runners with PFP (11 females, 9 males) and 20 asymptomatic runners (11 females, 9 males) were recruited (see table 5). To be included in the PFP group, participants were required to have retropatellar or peripatellar pain rated at a minimum of three (out of a maximum of 10) using a numerical rating scale (NRS) during running and one other activity described by the most recent PFP consensus document (4). This definition of PFP was used as inclusion criteria to ensure that the outcomes of this study would be comparable to other studies completed in this field.

Participants with patellofemoral instability, tibiofemoral pathology or previous lower limb surgery were excluded. To be included in the control group, participants were required to be free of running-related injury (RRI) for a minimum of three months and have no previous history of PFP. All participants were of either sex, currently or recently running a minimum of three times or $\geq$10 km/week and aged between 18 and 45 years, to ensure a cohort of participants that met the criteria for a recreational runner described by Niemuth et al (102). Two-tailed, independent samples t-tests were used to determine statistical differences between pairs of groups (PFP versus

control) for participant characteristics, with the corresponding *P* value detailed in the final column of table 5.

5. Participant characteristics for case-control kinematic study

| Variable | PFP Mean (SD) | Controls Mean (SD) | *P* |
|---|---|---|---|
| Age (Years) | 31.9 (5.8) | 30.7 (4.8) | 0.47 |
| Height (cm) | 173.3 (8.4) | 171.8 (7.7) | 0.57 |
| Mass (kg) | 67.5 (9.2) | 65.7 (1.4) | 0.59 |
| Average run volume (km) | 17.9 (8.9) | 19.7 (11.9) | 0.58 |
| Step rate (SPM) | 164.6 (5.6) | 167.1 (7.4) | 0.23 |
| Symptom duration (Months) | 55.8 (51.6) | N/A | N/A |
| Kujala scale | 87.6 (6.8) | N/A | N/A |
| Average NRS | 3.3 (1.5) | N/A | N/A |
| Worst NRS | 6.8 (1.5) | N/A | N/A |

Key: SD=standard deviation; cm=centimeters; kg=kilograms; km=kilometers; SPM=steps per minute; NRS=numerical rating scale; N/A=not applicable.

### 5.2.3. Experimental protocol

Participants were required to present to the Human Performance Laboratory at Queen Mary University of London. Data pertaining to one limb, rather than two, was entered into the analysis to reduce type I error potential (195). For participants with bilateral symptoms, the limb that rated the highest on the numerical rating scale was included. For participants with equivalent symptoms, or for the control participants, the dominant limb (defined as the limb that would be used to kick a ball) was included (101). Prior to data collection, participants in the PFP group were required to rate their average and worst pain in the past week from 0 to 10 using an NRS. Participants in the PFP group also completed the Kujala Scale (196), a 13-question appraisal of subjective function in those with PFP, with a score of 100 representing no symptoms and a score of zero indicating complete disability. The Kujala Scale was chosen as it was originally

validated using participants that were recruited from a 10km running event (196), with 10km the minimum weekly run distance required for participant eligibility.

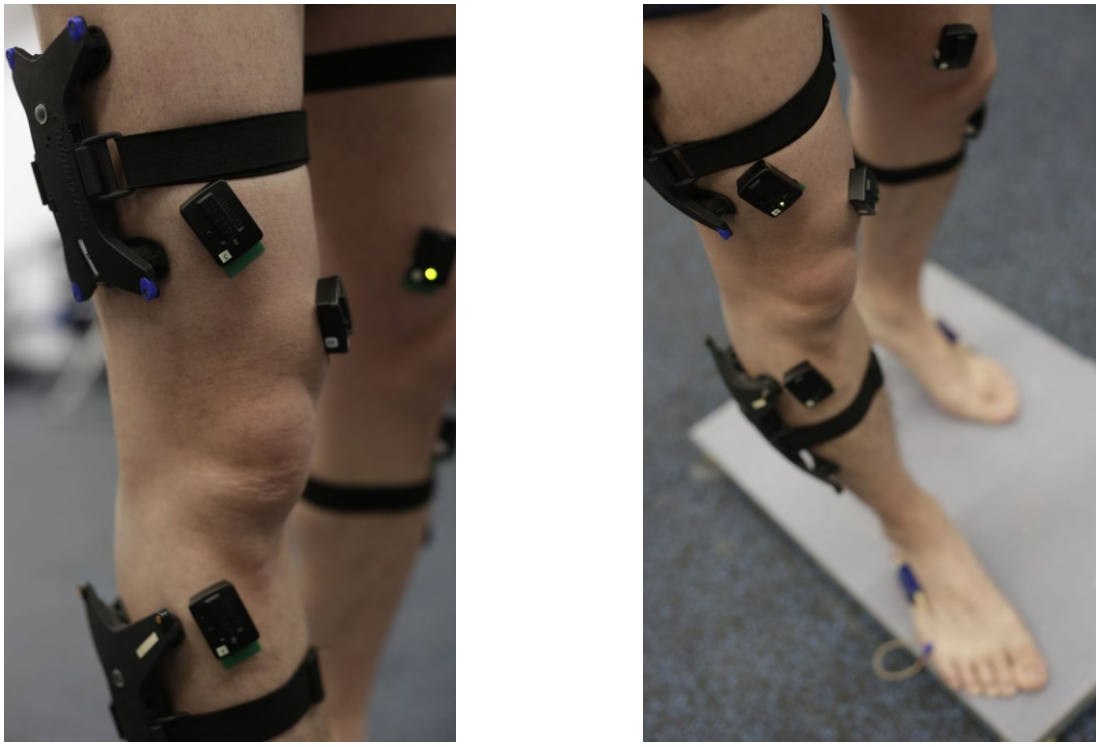
### 5.2.4. Kinematic measures

Kinematic data were collected during running using a four-camera, infrared motion analysis system (CX-1, Codamotion, Charnwood Dynamics Limited, Leicestershire, UK) (197) (see figure 53).


*53. Component parts of the Codamotion analysis system*

24 infrared markers were placed on standard pelvic and lower limb anatomical landmarks adhering to the CAST protocol (198). Eight individual markers (powered by a drive box) were placed on bilateral pelvic (ASIS and PSIS) (see figure 57) and foot landmarks (lateral calcaneal tuberosity and head of fifth metatarsal). Specifically, bilateral foot markers were placed on a participant's shoe as an estimation of the anatomical location (see figure 54), given the potential for barefoot running to effect running kinematics (199). Additionally, four rigid clusters of four markers were placed on the thigh and shank segments bilaterally (see figure 55).


*54. Neutral Asics Nimbus shoe with bilateral infrared foot markers applied*



*55. Location of thigh (left) and shank (right) rigid clusters prior to securement*

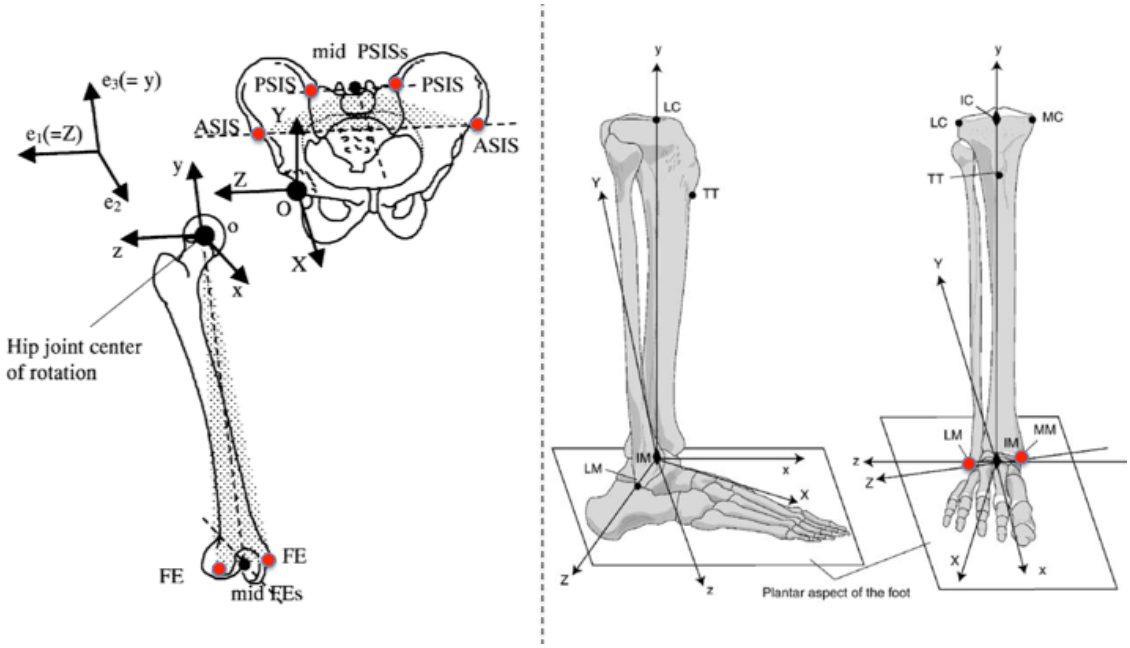
Rigid clusters were applied using adjustable elastic straps and were secured with cohesive self-adherent bandage, to minimize the potential for cluster displacement during high force activity (see figure 56). Individual markers were applied using double-sided adhesive tape and secured with transparent surgical tape.

*56. Use of cohesive self-adherent bandage to secure rigid cluster position*

Virtual markers were also identified on the femoral epicondyles and the ankle malleoli, to allow for the calculation of relevant joint centers during an upright standing trial (see figure 57), which did not differ between male and female participants. The knee joint centre was estimated as the mid-point between the femoral epicondyle markers and the hip joint centre was estimated as a projection within the pelvis frame using the equation previously described by Bell et al (200):

$$RHJC = [0.36 \times \text{ASIS\_Distance} \quad -0.19 \times \text{ASIS\_Distance} \quad -0.3 \times \text{ASIS\_Distance}]^T$$

$$LHJC = [-0.36 \times \text{ASIS\_Distance} \quad -0.19 \times \text{ASIS\_Distance} \quad -0.3 \times \text{ASIS\_Distance}]^T$$




*57. Positioning of individual pelvic markers and identified virtual markers at knee and ankle, identified by the red dots*

Kinematic data were sampled at 200Hz. Whilst lower collection frequencies are acceptable for low velocity movements such as walking, high velocity movements such as running require a higher sampling frequency to ensure that movement peaks are not excluded. 200Hz is the sampling frequency used most commonly by studies collecting running kinematic data in PFP participants (20, 51, 52, 101) and is also the maximum collection frequency for the Codamotion system when using between 13-28 infrared markers.

For the assessment of reliability of kinematic marker placement, participants stood on a marked line on the laboratory floor, with their feet positioned underneath their hips and their arms crossed over their chest. 10 seconds (s) of data were collected one week apart whilst the participant was instructed to stand as still as possible.

For the case-control study, participants were required to run in their usual running shoes and at a self-selected 'steady state' running speed on the laboratory treadmill (Kistler Gaitway, Kistler Group, Winterthur, Switzerland). Participants in the PFP group were given the option to cease data collection if their symptoms increased to four or greater on the NRS. Participants ran for a total of three kilometers (km), with 10s of data collected at 0.8/1.8/2.8km. A three km run with initial data collection at 0.8km was selected to ensure that a minimum of six minutes of running had been completed prior to data collection, reported to allow for normalisation to running surface and

thus ensure validity of kinematic data (201). Distance, as opposed to time, was chosen to act as a constant measure across a cohort of participants running at differing speeds.

A minimum of 10 gait events has previously been reported to increase the intra-rater reliability of kinematic gait analysis completed using Codamotion hardware (202). As such, three separate acquisitions of kinematic data (10s), containing approximately 12-15 foot strikes, were collected during a prolonged run, in attempt to ensure the most reliable pooled mean for each kinematic parameter. Variables of interest included peak hip adduction (HADD), internal rotation (HIR) and flexion (HFLEX) and peak knee flexion (KFLEX), based on between condition-determined group differences identified in our recent meta-analysis (82).

### 5.2.5. Data analysis

Data were analysed offline using a customised Matlab program (version 2015, Mathworks, Natick, Massachusetts, USA).

For the reliability data, kinematic marker position was determined using Euclidean distance, the absolute distance between two markers in three-dimensional space, using the following equation (where *d*=distance, p=marker 1, q=marker2, $_1$= *x* plane, $_2$= *y* plane and $_3$= *z* plane):

$$d(\mathbf{p}, \mathbf{q}) = \sqrt{(p_1 - q_1)^2 + (p_2 - q_2)^2 + (p_3 - q_3)^2}.$$

Euclidean distance for the following segments were determined: 'ASIS' [left ASIS to right ASIS]; 'PSIS' [left PSIS to right PSIS]; 'left pelvis' [left ASIS to left PSIS]; 'right pelvis' [right ASIS to right PSIS]; 'left knee' [left MFC to left LFC]; 'right knee' [right MFC to right LFC]; 'left lateral shank' [left LM to left LFC]; 'left medial shank' [left MM to left MFC]; 'right lateral shank' [right LM to right LFC]; 'right medial shank' [right MM to right MFC].

For the case-control data, initial foot contact and toe off were identified using the calcaneal tuberosity marker and the metatarsal head marker in the vertical (Z) plane. Consistent with previously described methods, initial foot contact was defined as the point at which the calcaneal tuberosity marker ceased its descent in the vertical plane

(203). Toe off was identified by determining peak acceleration of the fifth metatarsal marker within a specific time point, defined as ≥70% of the absolute maximum velocity region of the calcaneal tuberosity marker (203). All kinematic data were aligned to initial foot contact, interpolated and normalised to percentage of stride cycle (0% = initial contact, 100% = terminal stance).

### 5.2.6. Statistical analysis

All statistical testing were performed offline using Microsoft Excel (Microsoft Corporation, Albuquerque, New Mexico, USA). Data normality were determined using Kolmogorov-Smirnov (K-S) test, with all data identified to be normally distributed (*P*= 0.29 – 0.97) and parametric statistical tests therefore employed.

For the reliability data, single measure ICC with 95% confidence intervals were calculated using a two-way fixed effects model. ICC were interpreted as excellent (≥ 0.90), good (0.75-0.90), moderate (0.50-0.75) and poor (≤ 0.50) respectively (204). Standard errors of measure [SD x $\sqrt{}$1-ICC] and minimum detectable change [SEM x 1.96 x $\sqrt{}$ (2)] were also calculated.

For case-control data, a one-way analysis of variance (ANOVA) with four sub-groups defined by sex and symptoms were conducted, with a Tukey's post-hoc test, which does not require statistical correction for multiple comparisons. Two-tailed, independent samples t-tests were used to determine statistical differences between pairs of groups (PFP versus control). Statistical significance of data was set at $\alpha \leq 0.05$, with a trend defined as $\alpha \leq 0.10$. Cohen's *d* was also calculated to determine the effect size of all identified inter-group differences, alongside the reporting of mean differences and 95% confidence intervals (CI). Cohen's *d* was interpreted as small (≤ 0.2), medium (>0.5) and large (>0.8) respectively (205). Minimum detectable change (MDC) data from previous work (194) were used to determine the clinical relevance of identified kinematic differences.

## 5.3. Results

### 5.3.1. Participant characteristics

Analyses of all characteristics between groups were non-significant and are detailed in table 5. Participants in the PFP group demonstrated a prolonged duration of pain (55.8 [±51.6] months), but only a mild impairment in function, reflected by a mean Kujala scale score of 87.6 (±6.8).

### 5.3.2. Kinematic reliability

Reliability of kinematic marker placement was found to be moderate to excellent (ICC 0.62-0.93) (table 6). The most reliable segment was found to be the 'left pelvis' (ICC 0.93) and the least reliable segment the 'left knee' (ICC 0.62).

6. Kinematic marker placement reliability data

| Variable | Mean Difference | ICC | 95% CI | | SEM | MDC |
|---|---|---|---|---|---|---|
| | (mm) | | Lower | Upper | (mm) | (mm) |
| ASIS (IR) | 4.2 | 0.78 | 0.37 | 0.94 | 4.9 | 13.7 |
| PSIS (IR) | 5.0 | 0.66 | 0.15 | 0.90 | 7.8 | 21.6 |
| Left Pelvis (IR) | 3.9 | 0.93 | 0.73 | 0.98 | 1.5 | 4.12 |
| Right Pelvis (IR) | 0.6 | 0.89 | 0.62 | 0.97 | 2.9 | 8.1 |
| Left Knee (V) | 5.5 | 0.62 | 0.07 | 0.89 | 4.2 | 11.6 |
| Right Knee (V) | 1.0 | 0.75 | 0.28 | 0.93 | 2.6 | 7.1 |
| Left Lateral Shank (V) | 7.4 | 0.65 | 0.12 | 0.89 | 11.7 | 32.5 |
| Left Medial Shank (V) | 1.7 | 0.79 | 0.35 | 0.94 | 8.9 | 24.9 |
| Right Lateral Shank (V) | 3.1 | 0.66 | 0.08 | 0.90 | 14.7 | 40.7 |
| Right Medial Shank (V) | 5.9 | 0.84 | 0.52 | 0.95 | 6.2 | 17.1 |

Key: IR=infrared; V=virtual; ASIS=anterior superior iliac spine; PSIS=posterior superior iliac spine; mm=millimeters; ICC=intra class correlation coefficient; CI=confidence interval; SEM=standard error of measure; MDC=minimum detectable change.

### 5.3.3. PFP versus control (mixed-sex)

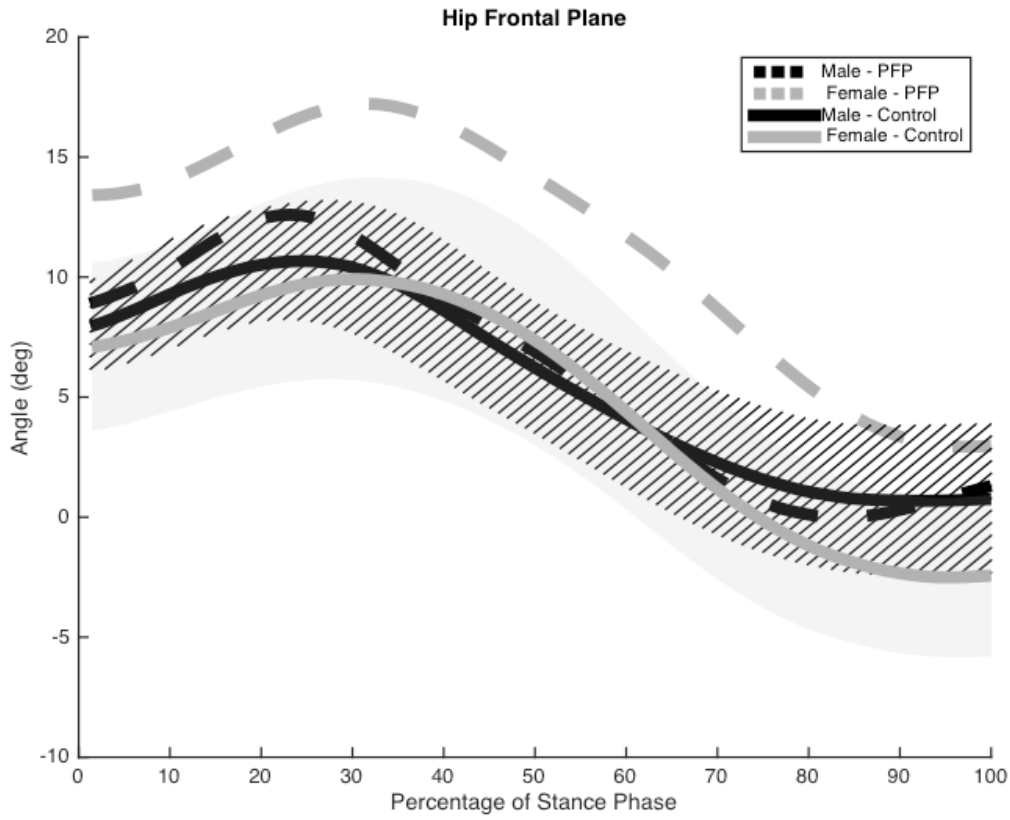
The mixed-sex PFP cohort ran with significantly greater peak hip adduction (mean difference=4.9˚, *P*=0.01, *d*=0.91, 95% CI 1.4-8.2) when compared to the control group

(see figure 58). No significant differences were identified for any other variable (table 7).

7. Comparison between participants with PFP and matched controls for kinematic data

| Variable | PFP Mean (SD) | Controls Mean (SD) | Mean Difference | *P* | *d* | 95% CI |
|---|---|---|---|---|---|---|
| **KFLEX** | 37.7˚ (5.5) | 36.6˚ (5.7) | 1.1˚ | 0.54 | 0.19 | -2.5 to 4.7 |
| **HFLEX** | 26.0˚ (7.4) | 23.8˚ (8.2) | 2.2˚ | 0.38 | 0.28 | -2.8 to 7.2 |
| **HADD** | 16.5˚ (4.5) | 11.6˚ (6.2) | 4.9˚ (+) | 0.01* | 0.92 | 1.4 to 8.2 |
| **HIR** | 9.4˚ (7.6) | 7.3˚ (7.0) | 2.1˚ | 0.37 | 0.28 | -2.6 to 6.8 |

Key: SD=standard deviation; KFLEX=peak knee flexion; HFLEX=peak hip flexion; HADD=peak hip adduction; HIR=peak hip internal rotation; CI=confidence interval; *=indicates significance; (+) mean difference exceeds MDC.




*58. Graph depicting pooled mean hip adduction for all four groups during running stance phase.*

Key: Solid and dashed error bars reflect 95% confidence intervals for female and male control subjects respectively.

### 5.3.4. Sub-group analysis

Females with PFP ran with significantly greater peak hip adduction compared to female controls (mean difference=6.6˚, *P*=0.02, F=3.41, 95% CI 0.4 to 12.8), with a trend towards female runners having significantly greater peak hip adduction when compared to male controls (mean difference=6.3˚, *P*=0.06, F=3.41, 95% CI -0.3 to 12.8) (see figure 27). No significant differences were identified for any other variable. Full details can be found in table 8.

8. Kinematic sub-analyses for the individual sexes when comparing between participants with and without PFP

| | **Female Controls (n=11) Mean (SD)** | **→*P*←** | **Female PFP (n=11) Mean (SD)** | **→*P*←** | **Male PFP (n=9) Mean (SD)** | **→*P*←** | **Male Controls (n=9) Mean (SD)** |
|---|---|---|---|---|---|---|---|
| **KFLEX** | 35.3˚ (4.8) | 0.74 | 37.7˚ (6.3) | 1.00 | 37.7˚ (5.0) | 0.99 | 38.2˚ (6.6) |
| **HFLEX** | 23.4˚ (9.7) | 1.00 | 23.1˚ (7.7) | 0.26 | 29.5˚ (5.6) | 0.46 | 24.2˚ (6.5) |
| **HADD** | 11.5˚ (7.5) | 0.03* | 18.1˚ (3.8) | 0.47 | 14.6˚ (4.7) | 0.70 | 11.8˚ (4.5) |
| **HIR** | 9.6˚ (5.3) | 0.99 | 10.2˚ (7.3) | 0.94 | 8.4˚ (8.3) | 0.67 | 4.5˚ (8.2) |

Key: SD= standard deviation; KFLEX=peak knee flexion; HFLEX=peak hip flexion; HADD=peak hip adduction; HIR=peak hip internal rotation; *=indicates significance.

## 5.4. Discussion

Our findings indicate greater peak hip adduction during running in the PFP group, compared to matched controls when mixed sex comparisons are made. However, this difference appears to be influenced by participant sex, with greater peak hip adduction in female runners compared to female controls, but no differences in males with and without PFP.

### 5.4.1. Frontal plane hip kinematics

Findings of greater peak hip adduction in our mixed-sex cohort of runners with PFP compared to matched controls are consistent with Fox et al, who recently reported greater frontal plane hip motion during running in their chronic PFP cohort (defined by symptom duration >three months) (192). However, they conflict with other mixed-sex studies (166, 168, 172), which have reported no differences in peak hip adduction when comparing runners with PFP to asymptomatic runners.

One potential explanation for this conflict is the inclusion of participants with more acute PFP by both Dierks et al (168) and Bazett-Jones et al (166) (minimum symptom duration one to two months), in contrast to our data from participants with more persistent symptoms (mean symptom duration 55.8 [±51.6] months). This hypothesis is supported by the recent case-control study by Fox et al (192), who did not report a difference in peak hip adduction for their acute PFP cohort compared to asymptomatic runners. Interestingly, the cohort from Esculier et al (172) included participants with more prolonged PFP symptoms (mean duration 38.1 [45.5] months), with no differences between groups reported for their mixed-sex comparison. However, they did report a significant difference in peak hip adduction between participants with and without PFP when performing a sub-analysis for female participants only, which is consistent with our findings.

### 5.4.2. Frontal plane hip kinematics: the influence of sex

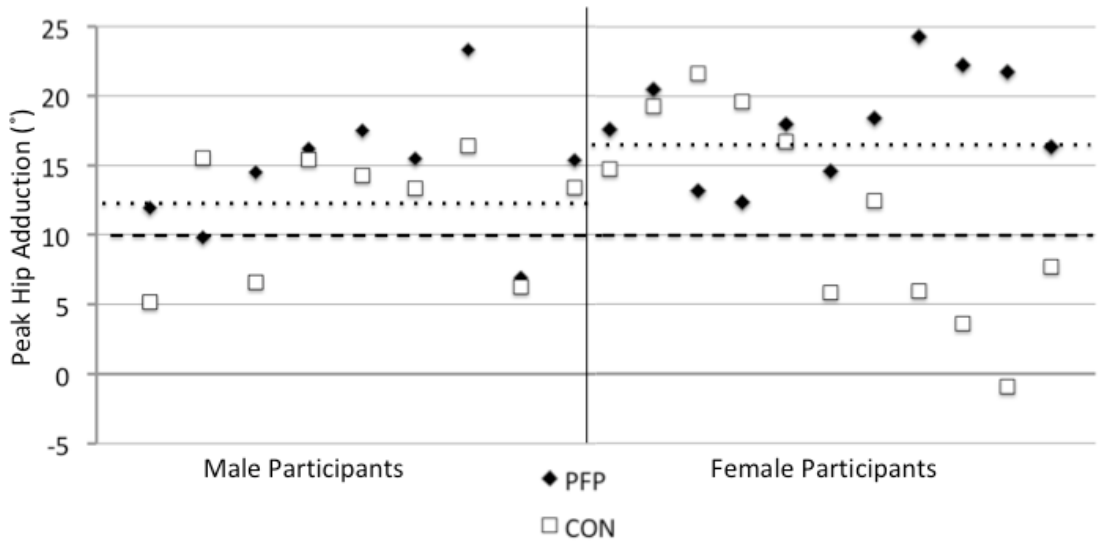
Our findings indicate greater peak hip adduction in females with PFP compared to female controls. These data are in agreement with the three previous case-control studies comparing females with PFP to female controls (52, 53, 169), all of which reported higher peak hip adduction during running in the PFP cohorts. Our findings

indicate a trend toward greater peak hip adduction in females with PFP compared to male controls, but not males with PFP.

These findings are interesting when considered alongside those reported by Willy et al. Consistent with our findings, they reported that females with PFP ran with greater peak hip adduction compared to male controls (51). However, contrary to our findings, they also reported that their female PFP cohort ran with significantly greater hip adduction compared with their male PFP cohort. As the mean difference from our data is above the MDC for hip adduction reported by Noehren et al (194) when comparing these groups (3.5˚ greater in the female PFP group), it is likely that our smaller sample size (n=11 versus n=18) accounts for the lack of statistical significance in our findings. Considering sex specific differences identified in our current, and previous studies, future studies evaluating running kinematics are advised to report data for males and females separately, irrespective of study design.

### 5.4.3. Individual kinematic responses

Some participants from both sexes do demonstrate individual kinematic patterns that are in contrast to the mean pooled data (see figure 59). In the male subgroup, there were two PFP participants with a peak hip adduction value below the pooled mean of the control group (9.8˚ and 6.9˚ respectively), and three control participants with a peak hip adduction value above the pooled mean of the PFP group (15.4˚, 15.5˚ and 16.4˚ respectively). However, in the female subgroup, there were no PFP participants with a with a peak hip adduction value below the pooled mean of the control group and three control participants with a peak hip adduction value above the pooled mean of the PFP group (19.2˚, 19.6˚ and 21.6˚ respectively). Therefore, whilst there is an association between increased peak hip adduction during running and PFP, especially in females, it may not be a contributor to symptom development or persistence in all cases, and not all runners with increased peak hip adduction will develop PFP.




*59. Individual peak hip adduction data points for participants with and without PFP, with each sex presented individually.*

Key: Dotted line - pooled mean of the PFP group; dashed line - pooled mean of the control group (CON).

### 5.4.4. Kinematic treatment targets

Running retraining, defined as any intervention that aims to modify an individual's running technique (89), has an emerging evidence base. In previous observational case series, verbal and visual cues to reduce peak hip adduction during running have been reported to reduce pain and improve function in females with excessive frontal plane hip motion (defined as peak hip adduction $\geq$ 20˚). The mean reduction in peak hip adduction from both studies was approximately 5˚, which is similar to the magnitude of difference between our female PFP cohort and female controls (6.6˚). Considering this, and the fact that hip adduction does not seem to be associated with PFP in male runners in our, and other groups data (51), it could be suggested that retraining runners to reduce peak hip adduction may only be applicable to female runners with PFP. However, an absence of benefit from running retraining targeting the hip in males with PFP would need to be identified through further research to confirm this. If choosing to implement running retraining in males with PFP, alternative strategies such as transitioning to non-rearfoot strike or increasing step-rate may be more applicable (103, 206, 207).

### 5.4.5. Limitations and future directions

Findings from this study should be interpreted within the context of its limitations. The retrospective, case-control design does not allow for the interpretation of causality

and it may be that the observed kinematics are simply adaptations to persistent pain rather than the primary driver of symptoms (55). Whilst there is some data to support the notion that altered hip kinematics may increase the risk of future PFP development in female runners (20), there remains a dearth of prospective literature. Further research is needed to determine if males and females might have different running kinematic risk profiles for the development of PFP. Important participant characteristics data such as years of running experience, the presence of bilateral symptoms, training volume details and participant footwear choice were not collected. As a result, caution needs to be applied with respect to generalising these results to all runners in clinical practice and instead considered with respect to the characteristics data presented (table 5).

Treadmill running gait, which was evaluated in this study, may not fully reflect kinematics of over ground running. However, it has been reported that hip and knee kinematics (208), as well as peak and rate of patellofemoral joint stress (209) are not significantly different when comparing treadmill with over ground running in asymptomatic populations. As participants were also given approximately six minutes to normalise their running gait to the treadmill condition (201), appropriate steps have been taken to ensure that the reported results are representative of a participant's typical running gait.

## 5.5. Conclusion

Our findings indicate runners with PFP have significantly greater peak hip adduction when compared to matched controls. This finding appears to be influenced by sex, as females, but not males, were found to have significantly greater peak hip adduction when compared to sex matched controls. These differences between sexes in kinematic profiles may highlight the need for different treatment targets in males and females. Future research is encouraged to report lower limb kinematic variables in runners with PFP separately for males and females.

# 6. The effects & mechanisms of increasing running step rate: a feasibility study in a mixed-sex group of runners with patellofemoral pain

The systematic review presented in chapter four identified limited evidence of short-term efficacy for *running retraining* in runners with PFP. Furthermore, it also identified limited evidence of a kinematic mechanism of effect, being a reduction in peak HADD. At the time of the design of this study, no investigations into the feasibility or efficacy of step rate retraining had been completed in a patellofemoral pain cohort. This chapter therefore presents a study designed to investigate the feasibility of a step rate intervention in a mixed sex cohort of runners with PFP, in addition to data collected to determine the effects and potential biomechanical mechanisms of the intervention.

Preliminary results from this study were presented at both the 2015 (Manchester, UK) and 2017 (Gold Coast, Australia) International Patellofemoral Pain Research Retreats and the 2016 Danish Sports Medicine Congress in Copenhagen. This study was accepted for publication in Physical Therapy in Sport (impact factor 1.919) after two rounds of robust peer review (appendix D). A translational publication was also produced for the College of Podiatry 'Podiatry Now' journal, detailing the clinical application of step rate retraining using a case study (appendix E).

## 6.1. Introduction

Recreational running positively influences cardiac (144), metabolic (146) and mental (145) health. Despite the reported benefits, recreational running is reported to bring about an increased risk of musculoskeletal pain (8, 12). Overall incidence of musculoskeletal pain amongst recreational runners ranges from 19% to 94% (8), with patellofemoral pain (PFP) thought to be the most common (14). Specific annual incidence of PFP amongst recreational runners ranges from 4% to 21% (19, 20, 27), with overall prevalence in sports medicine facilities suggested to be 17% (14).

Running biomechanics have been reported to be a risk factor for, and associated with, running related PFP. Specifically, peak hip adduction during running has been reported to be significantly higher in female runners who develop subsequent PFP when compared to those who remain asymptomatic (20, 82). In addition, based on our recent meta-analysis (82), peak hip adduction, peak hip internal rotation and contralateral pelvic drop are also significantly higher in runners with PFP when compared to asymptomatic controls. For neuromuscular function, females with PFP have been reported to have a delayed gluteal onset prior to foot contact and shorter gluteal activation duration compared to asymptomatic controls (164).

At present, evidence suggests that exercise interventions, whilst effective at reducing symptoms in runners with PFP in the short-term, do not result in full symptom resolution (83, 84). Moreover, exercise may not derive its effects by way of a kinematic mechanism, as multiple studies have demonstrated that exercise programs designed to increase hip strength do not alter running kinematics reported to be associated with PFP (84, 86-88). This brings into question the ability of exercise interventions to provide a long-term resolution to running related PFP, as it fails to target factors reported to be associated with the development and persistence of the condition. It is this premise that originally led to the development of what has been termed running retraining (210), or more specifically 'the implementation of any cue or strategy designed to alter an individual's running technique' (89).

Reports from observational studies, involving visual and verbal cues to reduce peak hip adduction, indicates running retraining may reduce pain and improve function in female runners with PFP who demonstrate more than 20˚ peak hip adduction during

running (82, 100, 101). The key limitation of this work is that the results can only be extrapolated to a minority of runners with PFP (i.e. females with high peak hip adduction). The majority of PFP research is done with female subjects, previously thought to reflect relative incidence, and there are retrospective indications that sub-groups exist based on a range of presenting factors including sex (43). For these reasons, it was necessary to make sure recruitment was feasible for both sexes.

In addition, a recently completed RCT has established efficacy for cues to transition from rearfoot to forefoot strike in combination with a load management running program in a mixed-sex, but again a predominantly female, cohort (103). The limitation of this study is that cues to transition to a forefoot strike are only applicable to those who rearfoot strike at baseline. Additionally, it is thought that such a change to running mechanics may also be injurious by virtue of the increase in Achilles tendon load that is observed with forefoot strike running compared to rearfoot strike running (104). This is reinforced by the fact that 25% (2/8) of the runners in this RCT who transitioned to a forefoot strike pattern reported ankle soreness at follow up (103).

It has been reported that cues to increase running step rate do not increase Achilles tendon load (211) and thus may be a more widely applicable running retraining option to those previously studied. A recent feasibility study has reported that a step rate increase of 10% combined with running in a minimalist shoe was superior to foot orthoses at reducing pain and improving function at 12 week follow up in runners with PFP (79). An increase in step rate of 10% has also been reported to favourably alter patellofemoral joint stress in both runners with PFP and asymptomatic runners (95), though the actual reduction in step length reported was much greater (14%). In addition, no evaluation of symptoms could be reported in this study due to the limitation of the cross-sectional, observational design. Observational work in asymptomatic runners also indicates that more modest increases in running step rate of 5% or 7.5% may still reduce peak hip adduction (91, 93), albeit of a smaller magnitudes. The collection of biomechanical measures, and an indication of their magnitude, was therefore an important feasibility target.

A recent three-arm RCT (85) found that a running retraining intervention to increase step rate was no more effective than education focused on load management, or compared to the same education combined with exercise therapy in runners with PFP.

Whilst no treatment group had superior outcomes, the step rate intervention did result in significant reductions in both worst and running specific pain. All three groups remained symptomatic at the primary end point (20 weeks), and running-related pain was higher (2.5/10) in the step rate group compared to previous studies where hip adduction (0.5/10) (100, 101) and strike pattern (1.0/10) (103) has been targeted. This could be explained by the absence of a faded-feedback protocol to facilitate the retraining intervention (107), which has been found to be effective by previous studies (100, 101, 103).

A feasibility study design was chosen to prepare for a future efficacy study. Typical feasibility outcomes can include intervention development, randomisation mechanisms, and delivery experience and randomisationd acceptability, with a full range of possible outcomes considered for this study. PFP is a heavily researched topic, with a range of trials reported in a variety of groups (including running retraining interventions) in similar groups and care delivery settings to those in this study design, giving confidence that the feasibility focus could be narrowed. No issues have previously been identified suggesting recruitment would be problematic, nor were there any no-treatment or sham-treatment groups in the planned future efficacy study. It was therefore judged not to be a priority to assess the feasibility of randomization. In contrast, the nuances of cueing and the potential difficulties in collection of kinematic data were deemed as priorities for feasibility, as these included novel aspects hypothesised to be particularly challenging.

The primary aim of this study was to investigate the feasibility of a pragmatic running retraining intervention, by cueing a 7.5% increase in running step rate using a faded feedback protocol. Specific objectives included (i) the recruitment of an appropriate number of both males and females from a clinical population and (ii) the collection of both symptom and function data to determine an estimate of the effects derived from the intervention. The secondary aim was to investigate the potential kinematic and muscle function mechanisms explaining any effects induced by the intervention.

## 6.2. Methods

### 6.2.1. Participants

Ethical approval for this study was granted by the Queen Mary Ethics of Research Committee (QMREC2014/63). All participants provided written informed consent prior to study commencement. Using the justification outlined in chapter five, PFP participants were recruited from a local sports medicine clinic. Sample size was based on the apriori power analysis conducted by the authors of the previous work on running retraining (100, 101), leading to a total of 10 participants being sought. Participants were of either sex, currently or previously running a minimum of three times or $\geq$ 10 km/week and aged between 18 and 45 years. To be included, participants were required to have atraumatic retropatellar or peripatellar pain during running and one other activity described by the most recent PFP consensus document, which includes squatting, stair ambulation and jumping (4). Patellofemoral symptoms needed to be rated at a minimum of three (out of a maximum of 10) using a numerical rating scale (NRS). Potential participants with patellofemoral instability, previous surgery, tibiofemoral pathology or any pathology (musculoskeletal or otherwise) that precluded running participation were excluded.

### 6.2.2. Experimental protocol

Included participants were required to present to the Human Performance Laboratory at Queen Mary University of London. In the presence of bilateral symptoms, the knee that scored highest on the numerical rating scale was analysed. In the presence of equivalent symptoms, the dominant limb that would be used to kick a ball was analysed (101). Both limbs were not entered into the analysis in the presence of bilateral symptoms given the potential for type I error (195).

### 6.2.3. Feasibility outcomes (in order)

The primary aim of this study was to determine the feasibility of a step rate intervention. The following feasibility outcomes were therefore explored, which link closely to those explored in other feasibility studies such as Drew et al (212), with the planned exceptions as outlined in the introduction. These outcomes are presented in the same order throughout the relevant sections below.

*Recruitment and eligibility*

Recruitment was assessed using the rate of eligibility (%) and conversion to consent (%), as well as the ability to recruit a mixed sex cohort.

*Adherence and acceptability*

Adherence was assessed by attendance to the weekly-supervised step rate retraining with the primary investigator (%) and a subjective report of adherence to the additional twice-weekly independent retraining sessions (%). Acceptability was assessed using the rate of attrition (%) and the number of adverse events reported by participants (n).

*Outcome measures*

The percentage of missing outcome data (symptoms, function, mechanistic) was to be recorded.

### 6.2.4. Treatment efficacy outcomes

Prior to data collection, participants were also required to rate their average and worst pain in the past week from 0 to 10 using an NRS. Participants also completed the Kujala Scale as a subjective measure of function (196). The Kujala Scale is a 13-question appraisal of subjective function in those with PFP, with a score of 100 representing no symptoms and a score of 0 indicating complete disability. Whilst there is no definitive outcome measure for use with a PFP cohort, the NRS and Kujala Scale are reported to be the most valid and responsive measures for detecting change at time of study commencement (213). Symptom and function outcomes were repeated at six weeks follow up.

### 6.2.5. Mechanistic outcomes

*Running kinematics*

Previously described in detail in chapter five, participant movement data were collected during running using a four-camera, infrared motion analysis system (CX-1, Codamotion, Charnwood Dynamics Limited, Leicestershire, UK) (214). 24 infrared markers, consisting of eight individual markers and four rigid clusters of four markers, were placed on standard pelvic and lower limb anatomical landmarks using the CAST protocol (198). Markers from the pelvis frame to the knee joint centre tracked the

thigh segment and markers from the knee joint centre to the ankle joint centre tracked the shank segment. Individual markers were applied using double-sided adhesive tape and secured with transparent surgical tape, with the rigid clusters applied using adjustable elastic straps and secured with cohesive self-adherent bandage. Virtual markers were also identified on the femoral epicondyles and the ankle malleoli, to allow for the calculation of relevant joint centers during an upright standing trial.

Participants were asked to run in their usual running shoes and self-select their typical 'steady state' running speed on the laboratory treadmill (Kistler Gaitway, Kistler Group, Winterthur, Switzerland). Participants were instructed to run for a total of three kilometers (km), with the option to cease if symptoms increased to four or greater on the NRS. 10 seconds of data sampled at 200Hz were collected at 0.8/1.8/2.8km, with distance as opposed to time chosen to act as a constant measure across a cohort of participants running at differing speeds. Multiple data collections were completed to increase reliability of gait analysis (202). In order to address between group differences identified in our recent meta-analysis (82) (chapter four) and the empirical data collected in chapter five, variables of interest included peak hip adduction, internal rotation and flexion, peak knee flexion and contralateral pelvic drop, given their cross-sectional association with PFP.

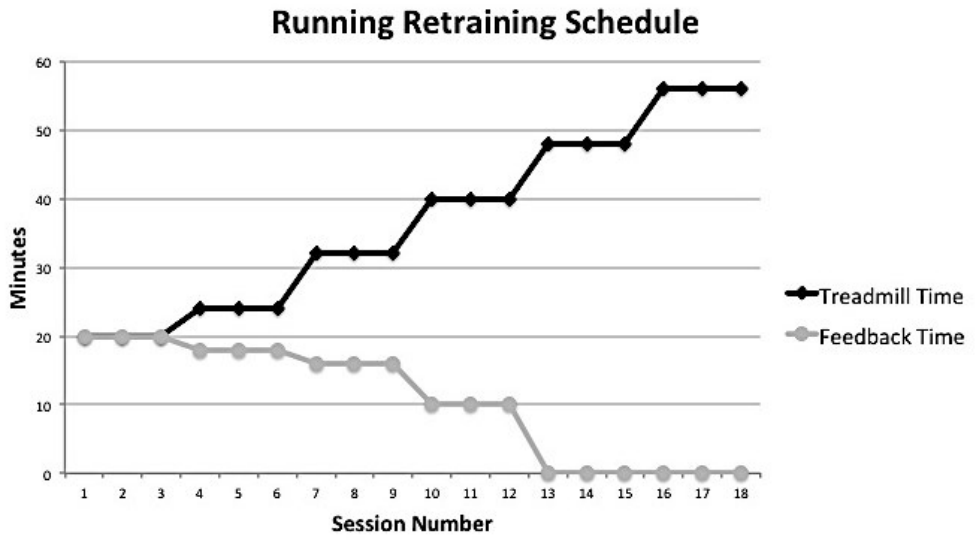
*Electromyography measures*

sEMG were collected simultaneously with the kinematic data using a wireless Delsys TRIGNO system (DELSYS Inc., Natick, Massachusetts, USA). Prior to application, participant's skin was marked, shaved and cleaned with an alcohol swab. Self-contained bipolar electrodes were placed at the motor points of the Gluteus Maximus (GMAX), Gluteus Medius (GMED), Semitendinosus (ST) and Vastus Medialis Obliqus (VMO) adhering to SENIAM guidelines (215). 10 seconds of sEMG data were sampled at 1926Hz, an intrinsic setting within the Delsys Trigno sensors designed to optimize the communication bandwidth and signal conditioning, and cannot be altered. sEMG data were collected at three specific distance points as described above, but were not synchronised to the kinematic data as digital synchronicity between Codamotion Odin and Delsys Trigno systems was not available at the time of data collection.

### 6.2.6. Running retraining intervention

Participants completed 18 retraining sessions over the course of six weeks. Each week involved a total of three individual runs, equating to 18 runs in total. For the first four weeks, the initial run was completed in a supervised fashion with the primary investigator (BN). The additional two runs each week were completed independently. During the retraining sessions, participants were cued via an audio metronome set at 7.5% above their baseline step rate (calculated during data acquisition by counting the number of foot contacts a participant made in 30 seconds and multiplying by two). The decision to increase step rate by 7.5% (rather than 5% or 10%) was made using the previous work of Willy et al (93), who reported significant reductions in peak HADD with this more modest increase. Whilst not measured by this study, a more modest step rate increase was chosen with the premise that it may be more sustainable for participants, as biomechanical changes to running gait can have a negative effect on running economy (216).

A faded feedback protocol successfully used previously was adopted (100, 101). Feedback exposure was gradually reduced and treadmill run time was gradually increased from 10 minutes to 30 minutes (see figure 60), to facilitate skill acquisition. A slower progression from 10-30 minutes was used (18 sessions over six weeks) compared to previous work (8-10 sessions over two to four weeks), to better adhere to contemporary training progression approaches (105). Further, this pace of progression is used clinically in the chosen recruitment centre, minimising ethical issues from varying usual care. For the final two weeks, all completed sessions were performed independently, without any metronome feedback. All data were collected prior to, and after completion of, the running retraining intervention.




*60. Running retraining schedule depicting the faded feedback protocol employed*

### 6.2.7. Kinematic data analysis

Data were analysed offline using a custom written Matlab program (version 2015, Mathworks, Natick, Massachussets, USA). Initial foot contact and toe off were identified using the heel marker on the calcaneal tuberosity and the metatarsal marker on the fifth metatarsal head in the vertical (Z) plane. Consistent with previously described methods, initial foot contact was defined as the point at which the heel marker ceased its descent in the vertical plane (203). Toe off was identified using a combination of the heel and metatarsal markers. Specifically, peak acceleration of the metatarsal marker was identified within a specific time point, defined by 70% or greater of the absolute maximum velocity region of the heel marker (203). All kinematic data were aligned to initial foot contact, interpolated and normalised to percentage of stride cycle (0% = initial contact, 100% = terminal stance) to facilitate data analysis. Clinical relevance of kinematic data was interpreted with reference to the minimum detectable change data reported by Noehren et al (194).

### 6.2.8. sEMG data analysis

sEMG data were processed using an in-built band-pass filter from 25-500 Hz. Raw sEMG data were decomposed using wavelets (217). Post-wavelet decomposition, data were cut into strides using the mean total wavelet power of the VMO muscle, as the typical activation pattern of this muscle (onset/offset) during running is reported to

align closely to the initial contact (onset) and toe off (offset) phases of running gait (218). These stride cycle timings were then applied to all sEMG data. Pre and post retraining data were cut into strides independently, but were not used to describe sEMG data as though it were synchronised to the true kinematic gait cycle of the participant. As participants are unlikely to reach signal intensity akin to maximal voluntary isometric contraction (MVIC) during steady state running, data were normalised to the mean of the peak dynamic signal intensity across a single set of strides (0.8km trial, pre-retraining), which has been reported to be more valid than normalizing to maximal dynamic signal peak (219).

### 6.2.9. Statistical analysis

All statistical testing were performed offline using Microsoft Excel (Microsoft Corporation, Albuquerque, New Mexico, USA). Data normality were determined using Kolmogorov-Smirnov (K-S) test, with all data identified to be normally distributed ($P$= 0.39 – 0.91) and parametric statistical tests therefore employed.

Cohen's *d* was calculated to determine the size of all identified interactions, alongside the reporting of mean differences and 95% confidence intervals (CI). Cohen's *d* was interpreted as small ($\leq$ 0.2), medium (>0.5) and large (>0.8) respectively (205). As a feasibility study, not powered apriori to detect statistical significance, dependent sample *t-tests* were not performed and p-values for differences not reported because of the potential for type II error and to avoid giving the impression of there being robust findings from a feasibility study design. The main outcomes were those of recruitment, retention and measurement feasibility.

## 6.3. Results

### 6.3.1. Feasibility outcomes

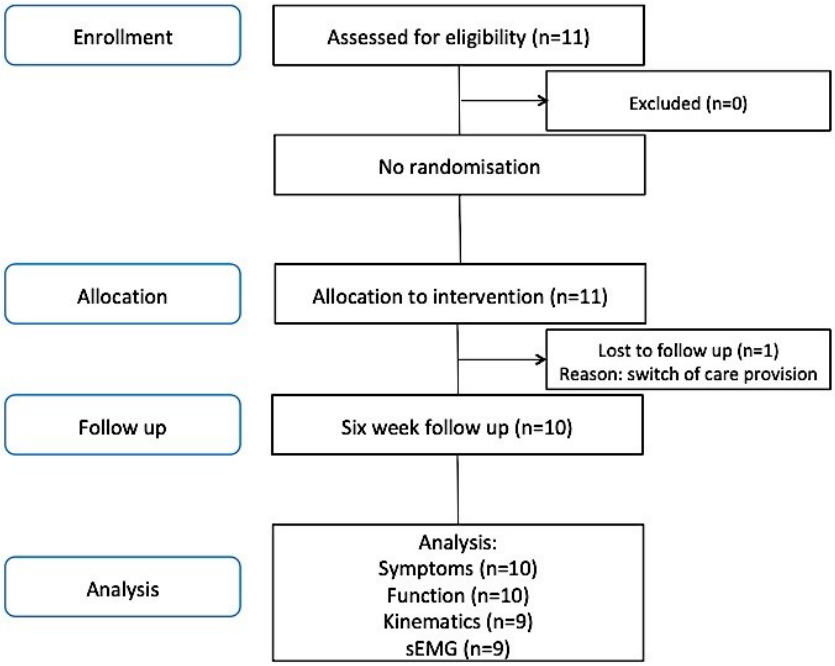
*Recruitment and eligibility*

Potential participants presenting to the recruitment site were sequentially approached. All 11 participants approached were eligible to participate and consented to commence the study. A total of 10 (out of 11) participants (four male, six female) completed the study, reflecting successful recruitment of a mixed-sex cohort. One female participant was lost to follow up due to a switch of care provision to the National Health Service prior to commencing the intervention. Demographics and baseline characteristics of the participants who completed the study are described in table 9, which includes details of recruitment according to sex.

9. Feasibility study participant characteristics

| Variable | Mean (SD) |
|---|---|
| Sex (male/female) | 4/6 |
| Age (years) | 31.6 (5.5) |
| Height (cm) | 170.6 (7.8) |
| Mass (kg) | 67.7 (9.8) |
| Symptom duration (months) | 45.1 (32.1) |
| Average run volume (km) | 17.0 (9.8) |
| Step rate (SPM) | 163.6 (4.7) |
| Kujala scale | 86.4/100 (6.9) |
| Average NRS | 3.0/10 (1.6) |
| Worst NRS | 6.8/10 (1.5) |

Key: cm=centimeters; kg=kilograms; km=kilometers; SPM=steps per minute; NRS=numerical rating scale.




*61. Participant flow through the study (CONSORT diagram)*

*Adherence and acceptability*

All 10 participants attended all four of their supervised retraining sessions with the primary investigator (100% adherence) and reported completing all of their additional independent retraining sessions (100% adherence), although this was not objectively measured. There was no additional attrition outside of the participant who was lost to follow up prior to study commencement and no participants reported an adverse event as a result of completing the study.

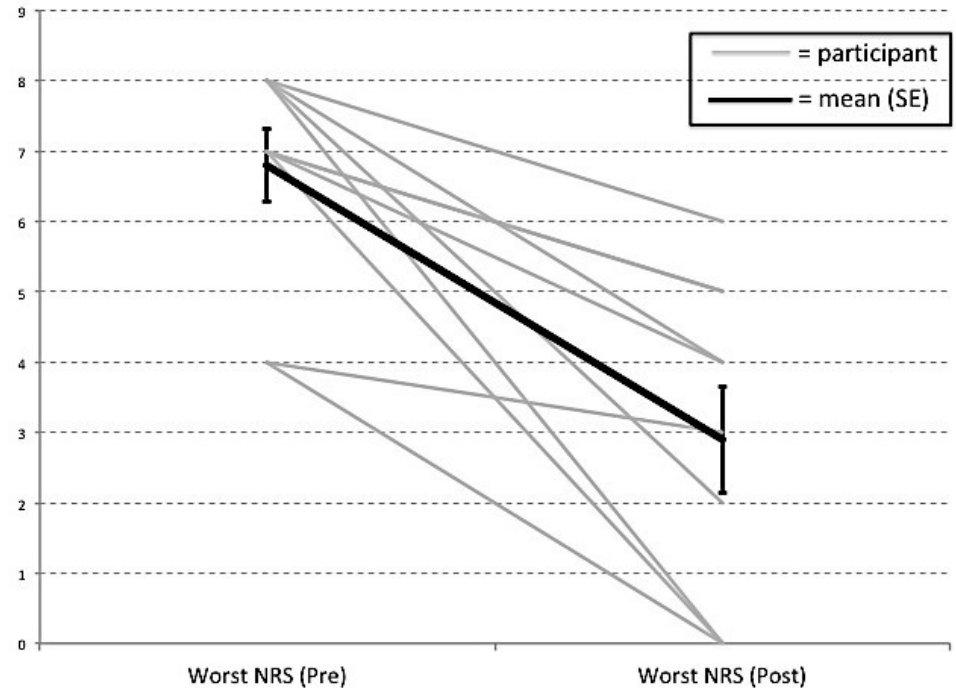
*Outcome measures*

All symptoms and function data were completed successfully without data loss. One participant's kinematic data were corrupted and were excluded from the analysis and a different participant's sEMG data were corrupted and also excluded from the analysis, reflecting 90% data retention.

### 6.3.2. Treatment efficacy outcomes

Large reductions in both average (*d*=1.7) and worst (*d*=2.0) pain were identified post-retraining. The mean difference (MD) of these reductions was 2.1 and 3.9 NRS points respectively and individual participant worst pain responses to the retraining intervention ranged from 1 to 8 NRS points (see figure 61). A modest improvement in

function measured with the Kujala Scale was also identified (*d*=0.12), with a mean difference of 4.4 points.




*62. Mean pooled and individual worst pain responses at baseline (pre) and six weeks follow up (post)*

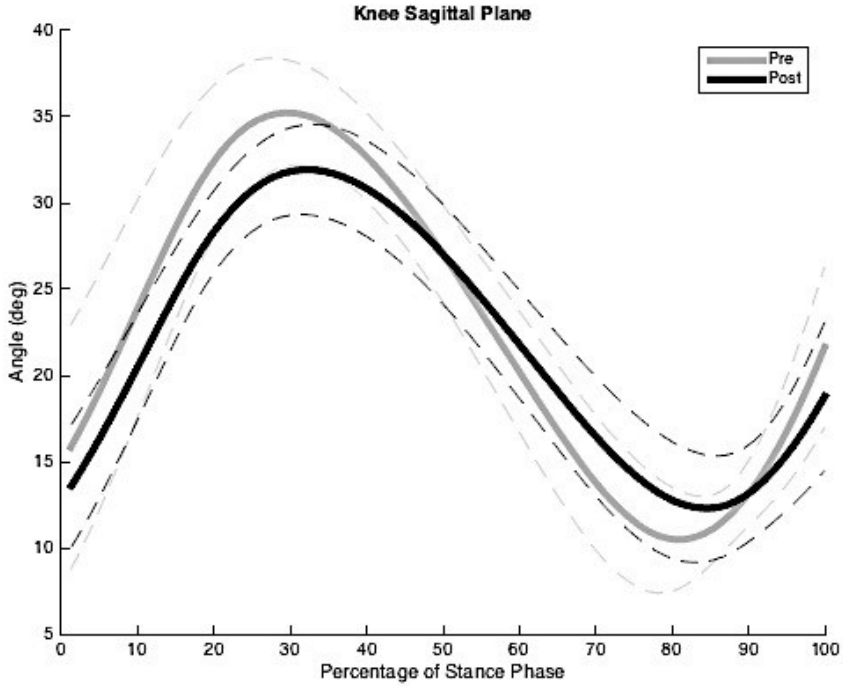
### 6.3.3. Mechanistic outcomes

*Spatiotemporal*

An increase in running step rate at six weeks follow up was observed, with a mean increase of 7.8% (range 2.3% - 11.1%). 3 participants did not achieve a step rate of ≥ 7.5% post retraining.

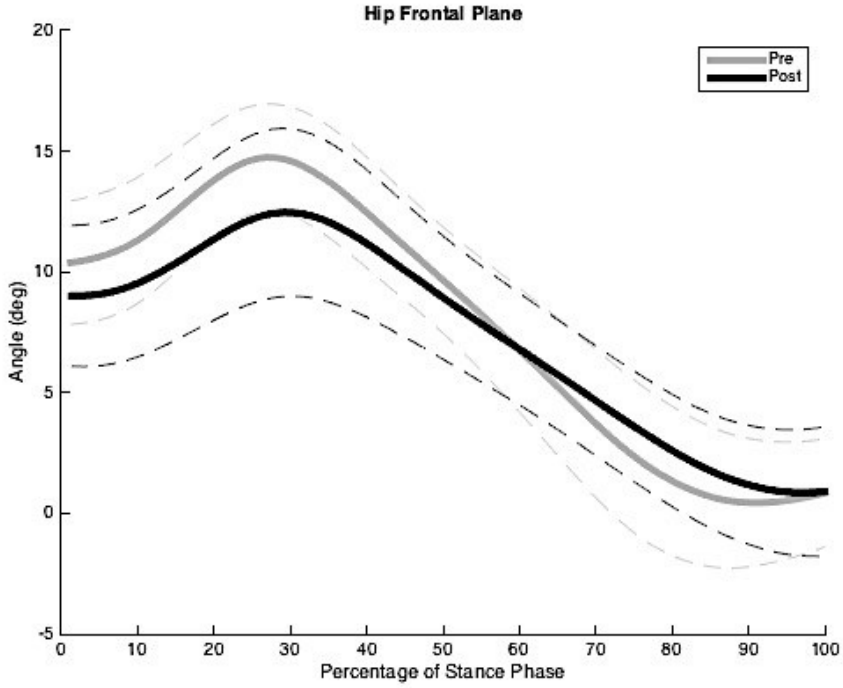
*Kinematics*

One participant was found to have consistently corrupted marker data throughout their trials and was therefore removed from the kinematic analysis. This resulted in a kinematic sample of nine participants (five females, four males). Moderate reductions in both peak knee flexion (MD=3.7˚, *d*=0.78) (see figure 62) and peak hip adduction (MD=2.4˚, *d*=0.54) (see figure 63) were identified post-retraining. A large reduction in peak hip internal rotation was also identified post retraining (MD=5.1˚, *d*=0.96) (see figure 64). A full breakdown of the kinematic analysis can be seen in table 10 and individual participant spatiotemporal and kinematic responses in relation to average/worst pain at six-week follow up are presented in table 11.



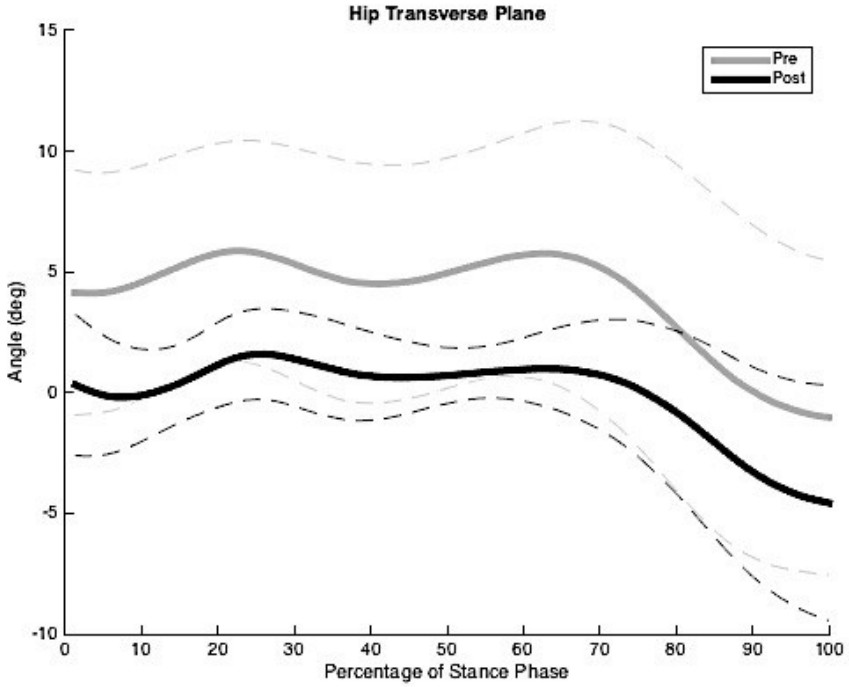

*63. Mean pattern of hip knee flexion throughout stance at baseline (pre) and six week follow up (post).*

Key: Knee flexion is positive. Solid line = mean. Dashed line = 95% confidence intervals




*64. Mean pattern of hip adduction throughout stance at baseline (pre) and six week follow up (post).*

Key: Hip adduction is positive. Solid line = mean. Dashed line = 95% confidence intervals




*65. Mean pattern of hip internal rotation throughout stance at baseline (pre) and six week follow up (post).*

Key: Hip internal rotation is positive. Solid line = mean. Dashed line = 95% confidence intervals

10. Pre and post step-rate retraining means, standard deviations, mean differences, 95% confidence intervals and effect sizes

| Variable | Pre | Post | Mean Difference | 95% CI | Cohen's *d* |
|---|---|---|---|---|---|
| | Mean (SD) | Mean (SD) | | | |
| **Average Pain** | 3.0/10 (1.6) | 0.90/10 (0.9) | 2.1 (*) | 0.88, 3.32 | 1.7 |
| **Worst Pain** | 6.8/10 (1.5) | 2.9/10 (2.3) | 3.9 (*) | 2.08, 5.72 | 2.0 |
| **Kujala Scale** | 86.4/100 (6.9) | 90.8/100 (5.4) | 4.4 | -10.22, 1.42 | 0.1 |
| **Peak KFLEX** | 36.2˚ (5.3) | 32.5˚ (4.2) | 3.7˚ | -1.08, 8.48 | 0.78 |
| **Peak HFLEX** | 26.7˚ (9.3) | 23.1˚ (4.9) | 3.6˚ | -3.83, 11.03 | 0.51 |
| **Peak HADD** | 15.6˚ (3.5) | 13.2˚ (5.4) | 2.4˚ | -2.15, 6.95 | 0.54 |
| **Peak CLPD** | 4.3˚ (2.7) | 2.8˚ (2.4) | 1.5˚ | -1.05, 4.05 | 0.59 |
| **Peak HIR** | 9.1˚ (7.7) | 4.0˚ (2.9) | 5.1˚ (*) | -0.71, 10.91 | 0.96 |

Key: (*)=mean difference exceeds MDC; SD=standard deviation; CI=confidence interval; HADD=hip adduction; HIR=hip internal rotation; CLPD=contralateral pelvic drop; KFLEX= knee flexion; HFLEX= hip flexion

11. Individual participant kinematic, spatiotemporal and symptom responses to step-rate retraining

| Participant | Peak KFLEX at Follow Up | Peak HADD at Follow Up | Peak HIR at Follow Up | Peak KFLEX at Follow Up | Baseline Step Rate | Step Rate % Increase | Average Pain at Follow Up (x/10) | Worst Pain at Follow Up (x/10) |
|---|---|---|---|---|---|---|---|---|
| 1 | ↓ | ↓ | ↓ | ↓ | 160 | 11.1% | 1 | 6 |
| 2 | ↓ | ↓ | ↓ | ↓ | 172 | 2.3% | 2 | 5 |
| 3 | ↓ | ↓ | ↓ | ↓ | 168 | 7.7% | 0 | 0 |
| 4 | ↓ | ↓ | ↓ | ↓ | 164 | 8.9% | 0 | 3 |
| 5 | ↓ | ↑ | ↓ | ↓ | 168 | 7.7% | 0 | 0 |
| 6 | ↓ | ↓ | ↑ | ↓ | 164 | 8.9% | 2 | 2 |
| 7 | ↑ | ↑ | ↓ | ↑ | 164 | 5.7% | 0 | 0 |
| 8 | ↓ | ↓ | ↑ | ↓ | 158 | 10.2% | 1 | 4 |
| 9 | ↑ | ↓ | ↑ | ↑ | 158 | 6.0% | 2 | 4 |

Key: HADD=hip adduction; HIR=hip internal rotation; KFLEX=knee flexion; A-NRS= average pain; W-NRS=worst pain.

*sEMG*

One participant was found to have consistently corrupted sensor data throughout their trials and was therefore removed from the sEMG analysis. This resulted in a sEMG sample of 9 participants (6 females, 3 males). A mean of peak muscle amplitudes, in addition to an integral (amplitude x duration) of each decomposed signal were calculated for each muscle pre and post retraining. For mean amplitude, minimal changes post-retraining were identified for GMAX (*d*=0.02), GMED (*d*=0.07) and ST (*d*=0.05). However, for VMO, an increase in mean amplitude was observed post-retraining, associated with a medium effect size (*d*=0.53, 95% CI -0.09, 0.03). For muscle integral, a similar interaction was identified, with minimal changes seen post-retraining for GMAX (*d*=0.04), GMED (*d*=0.04) and ST (*d*=0.09). For VMO, an increase was observed, associated with a medium effect size (*d*=0.58, 95% CI -0.06, 0.02).

## 6.4. Discussion

The results of this study suggest that a faded feedback protocol to increase running step rate by 7.5%, is feasible in a clinical setting. A mixed sex cohort was successfully recruited and a low dropout rate (n=1) was achieved. Furthermore, potential clinically relevant changes in both average and worst pain were identified post-retraining, suggesting that the intervention has potential efficacy and warrants further appraisal in an adequately powered RCT.

The mean reductions in both average and worst pain seen within this study are smaller than those identified by previous running retraining studies (100, 101, 103), although no inference on average or worst pain as individual outcomes were made by these studies and the feedback employed was different. Further, both this feasibility study and the referenced works were essentially underpowered for all but the most preliminary of conclusions. When analysing the reductions in worst pain from this study, only 3/10 participants were asymptomatic at six-week follow up and just one participant had pain $\leq$ 3/10. This means that the 6 remaining participants would continue to be eligible for inclusion into a clinical trial using currently accepted criteria (4), meaning that the intervention could be defined as unsuccessful in 60% of our cohort if using worst pain as the primary outcome.

A recent high quality RCT identified that a 7.5% step rate increase, with the option of transitioning to a forefoot strike pattern if deemed necessary, was no more effective than comparative education or exercise interventions (85). When comparing the symptom reductions achieved in this study (6 week follow up) to the most relevant time point in the Esculier et al RCT (8 week follow up) (85), both average and worst VAS are comparable for our step rate intervention compared to all 3 intervention groups (education, exercise plus education, running retraining plus education). It could be suggested that running retraining is in fact a form of load management or graded exposure, which may explain why it was found to be no more effective than education on training loads by Esculier et al (85). However, Roper et al (103) reported efficacy of retraining from rearfoot to forefoot strike running. Importantly, this retraining strategy produced larger pain reductions when delivered using a faded feedback protocol, over

and above an equivalent progressive duration running protocol. This suggests that a form of feedback is required over and above a load management intervention where there is a clinical need. A further potential explanation for the more modest symptom responses to step rate retraining reported by Esculier et al (85), is that feedback is likely to have needed to be subject or subgroup specific and not all participants will have a baseline step rate amenable to an increase.

Previous studies on running retraining have established a potential kinematic mechanism at the hip to explain their positive effects, specifically a 5˚ reduction in peak hip adduction (100, 101). The results of this study are in line with this, identifying a smaller but still clinically meaningful mean difference of 2.4˚ that was associated with a moderate effect size (table 10). Our mixed-sex sample could explain this smaller mean difference, as the previous work of both Noehren et al (100) and Willy et al (101) purposefully recruited female participants with higher than average peak hip adduction, which may be more amenable to change. However, as our results have identified a reduction in peak hip adduction equivalent to a previous 7.5% step rate increase study in asymptomatic runners (93), it is suggested that a larger increase in step rate (10%) will result in greater reductions in peak hip adduction equivalent to those seen in asymptomatic runners (91). A 10% step rate increase is reported to reduce both patellofemoral joint stress (95) and pain (79) in runners with PFP, whereas a 7.5% step rate increase (85) resulted in non-significant changes in both peak patellofemoral reaction force and average patellofemoral loading rate in a recent RCT. Clinically, it may be sensible to start retraining with a more modest 7.5% step rate increase, increasing to 10% or greater if tolerated, especially in those with low baseline step rate.

In addition to reducing peak hip adduction, the results of this study have identified two novel potential kinematic mechanisms, being a reduction in both peak hip internal rotation and knee flexion. The identified mean difference in peak hip internal rotation of 5.1˚ is above the MDC of 3.7˚ reported by Noehren et al (194) and was associated with a large effect size (*d*=0.96). Peak hip internal rotation is associated with running related PFP (82) and can result in increased patellofemoral joint stress by increasing contact pressures at the lateral patellar facet (220). Thus, given the plausibility for

reducing hip internal rotation during running gait to favourably alter PFP symptoms and the size of the identified effect, one could argue that a clinically meaningful change has been identified.

A reduction in peak knee flexion of 3.7˚ is in line with the work of Lenhart et al (94), who reported a reduction in peak knee flexion of 3.3˚ with a 10% step rate increase in a normative cohort. Within this musculoskeletal model, (94) peak knee flexion correlates positively with patellofemoral joint force, indicating this finding may be clinically relevant. This effect is likely due to changes in patella contact pressures, as a subsequent modeling study reports that lateral patellar arthrokinematics were not significantly altered by a 10% step rate increase (221). At an individual level, kinematic changes seem to correlate poorly with symptom improvements post-step rate retraining (see table 11). For example, two participants (one male, one female) had an increased peak hip adduction post-retraining (see table 11), with both participants asymptomatic for both average and worst pain variables. For the female participant, the increase in peak hip adduction (6.6˚) exceeds the MDIC (2.6˚) and is thus less likely to be related to measurement error. Future studies should look to investigate alternative potential mechanisms of running retraining, such as kinetic changes, load management or graded exposure.

Previous observational research investigating increasing step rate by 10% has identified increased quadriceps activation (96) comparable to the increase seen within this study. VMO activity is known to be altered in some individuals with PFP (185) and VMO weakness is reported to correlate with lateral patella shift (222). Whilst this study design prohibits inference of causality, this sEMG finding may be associated with the reduction in pain seen post-retraining.

The lack of change in mean gluteal EMG identified by this study is perhaps not surprising given the work of Willson et al (164), who reported no differences in mean gluteal sEMG when comparing female runners with PFP to matched controls. Willson et al (164) do however report that female runners with PFP demonstrate a shorter GMED activation window and delayed onset prior to foot contact in females with PFP. Additionally, Willy & Davis (102) reported earlier GMED activation and an increased GMED activation duration in a small case series of two female runners with PFP post-

mirror running retraining. Combined with findings from our study, this indicates that changes to gluteal muscle activation patterns rather than magnitude may provide mechanistic explanation for the reduction in pain. Further research is needed to explore this and a limitation of the current study is the fact that the sEMG were not synchronised to the kinematic system, meaning not all variables of interest from the previous literature could be investigated.

### 6.4.1. Limitations and future directions

Based on the results of this feasibility study, a future RCT should look to compare a step rate intervention against an exercise therapy control, with investigation of effects to long-term follow up at 12 months advocated. However, as no control arm was included in this feasibility study, the results cannot be used to directly inform a sample size calculation for a definitive trial. Post-intervention data from the exercise group of a comparable high quality study in a similar population (85) were therefore used to estimate required sample size. When using post-retraining 'worst pain' data from this study (mean NRS 2.9 ±2.3) and post-exercise 'worst pain' data taken from Esculier et al (85) at a comparative time point (four weeks post-intervention, mean NRS 4.4 ±2.5), a sample size of 42 participants per group with a two-tailed hypothesis is required to achieve $\alpha$=0.05, 1-$\beta$=0.20, with a Cohen's *d* of 0.6 (calculated using G*Power 3.1.9.2, Heinrich-Heine University, Germany).

A further limitation of the absence of a control arm in this study is that it is difficult to be certain about the feasibility of recruitment and subsequent randomisation to a choice of interventions – in this case, usual care consisting of exercise therapy which is of proven efficacy. It could be suggested that the potential randomisation to an exercise therapy arm would not affect recruitment negatively, given the frequently reported effectiveness of exercise therapy for PFP and the genuine equipoise that could be communicated to, and engendered in, potential participants. Furthermore, an unusually high rate of eligibility was observed in this study (100%). This is likely to be reflective of either significant fortune or the nature of the recruitment centre (a private sports medicine facility), which is unlikely to be replicable in other settings.

Perhaps reflecting the relative ease of performing RCTs for PFP, feasibility studies are not commonly published in this field. Further, qualitative evaluation of the trial process and intervention delivery has not been found in any recently published PFP RCT, nor any recently published feasibility studies (79, 212), but could have been useful to inform subsequent trial design. For example, it may have informed the package of PPI activities essential to future efficacy trial design and delivery (www.invo.org.uk). Further, it would have added an additional element of process evaluation, such as helping develop a logic model and complementing the existing elements such as adherence. These improvements will be considered for future studies.

If I, or other colleagues, were considering using our results to inform a large-scale intervention study, then a nested pilot study would be an appropriate part of the design. This would be particularly useful if an effectiveness rather than efficacy study were planned, given the difficulties in extrapolating efficacy findings to real-world usual-care settings, allowing for the investigation of both recruitment and randomization. A 'stop/go' approach should be applied, with the trial ceasing if issues with participant safety or difficulties in recruiting resultant from the comparative treatment arm were encountered. If one intervention arm was identified to demonstrate significant superiority over the other prior to the planned trial end point, the trial should also be ceased.

Future work on running retraining should consider use of a faded feedback protocol, as it appears to result in superior outcomes. Recruitment of participants with a step rate of <160 (>1 SD below the mean of this cohort), who are more likely to be amenable to step rate retraining, or stratifying outcome analysis by baseline cadence, is worth considering – a strategy that would require greater samples but produce more generalisable findings. Sub-group analysis by baseline kinematic variables associated with PFP such as hip adduction may also be indicated, though kinematic variables do not appear to be sensitive to predicting those who may respond to a step rate intervention.

Future studies should also ensure that a full compliment of participant characteristics is collected, to allow for results to be fully generalisable. Potentially important data

such as the presence of bilateral symptoms, the percentage of participants who had received previous intervention and years of running experience were not collected in this study, meaning that the results may not be applicable to all recreational runners with PFP.

Whilst this feasibility trial was not powered apriori to investigate treatment effects, a post-hoc calculation using the mean difference of both average and worst pain revealed that a sample of 10 participants is adequate to investigate symptom changes post-step rate retraining with adequate statistical power ($\alpha$=0.05, $\beta$=0.20). It is therefore advisable that future trials adhere to the so-called rule of 10, ensuring recruitment of 10 participants per individual variable investigated to minimize risk of bias (120). 10% of the biomechanical data in this study was lost due to data corruption and it is advisable that this be factored in to any sample size calculation for mechanistic outcomes in future studies.

Comparing the results of this study to the previous work on running retraining proved challenging given the heterogeneity of pain outcomes collected. It is advisable that future work collects data on both average/usual and worst/running related symptoms to allow for more clinically meaningful comparisons. The mean difference in the Kujala scale identified falls well below the accepted MCID of 10 points (213) and given the high baseline scores seen in the population studied, a ceiling effect can be suggested. Future studies are advised to consider an alternative measure of subjective function, with the LEFS, used by previous studies (100, 101), and the recently developed patellofemoral subscale of the Knee Osteoarthritis Outcome Score (KOOS) (223), particularly worthy of consideration.

## 6.5. Conclusion

The results of this study confirm that increasing running step rate using a faded-feedback protocol is a feasible intervention, within the constraints of the feasibility outcomes assessed by this study, that has potential efficacy in a mixed sex UK cohort. Future studies should focus on investigating the long-term efficacy of running retraining in a cohort that have a clear treatment target (e.g. low step rate), compared to an appropriate control. A nested pilot study may be useful if effectiveness studies are planned. Based on this feasibility study, a sample size of ten participants per group/variable is adequate to detect minimum clinically important differences with adequate statistical power, although a more sophisticated calculation may be required if stratification is planned. In addition to future work establishing efficacy, exploration of different forms of feedback and treatment mechanisms is encouraged.

# 7. Is two-dimensional video a valid and reliable measure of three-dimensional kinematics in runners with PFP?

The previous chapters presented in this thesis have identified data which suggest that lower limb biomechanics are associated with the development (chapter four), persistence (chapters four and five) and management (chapter six) of PFP in recreational runners. Specifically, peak HADD was identified to be associated with the development of PFP in female recreational runners, as well as being associated with the persistence of PFP in mixed-sex cohorts of runners. Furthermore, both reduced peak HADD and KFLEX were identified to be potential mechanisms of effect following step rate retraining.

A limitation of these above data is the current divide between research and clinical practice, with respect to the measurement of human biomechanics. This fault lies not with our understanding of how biomechanical variables are associated with PFP, but with the paucity of validated clinical tools suitable for use in the clinical setting. Given the new knowledge identified by the previous chapters of this thesis, it was deemed an important translational piece of work to consider a solution to enable clinicians to measure the relevant variables described in the wider literature and in this thesis. This penultimate thesis chapter therefore aimed to determine the accuracy of video gait analysis, which presents a pragmatic and clinically applicable solution to this problem.

Data are presented for the concurrent validity and intra-rater reliability of high frame rate 2D video, with respect to 3D kinematic analysis.

## 7.1. Introduction

Recreational running is a common form of exercise (15) associated with both positive health benefits (11) and high rates of musculoskeletal injury (12). The knee is reported to be the most prevalent joint involved in running-related musculoskeletal injury (14, 15), with patellofemoral pain (PFP) reported as the most prevalent diagnosis (14). Whilst all musculoskeletal injuries are likely to be multi-factorial (140), peak hip adduction (HADD) has been reported as a risk factor for future PFP development in female runners (20) and is associated with the persistence of PFP in mixed-sex cohorts (82). Peak HADD of >20˚ and a reduction in peak HADD of 5˚ are also reported to be the treatment target and mechanism of effect underpinning running retraining in PFP, respectively (82, 90).

Despite understanding of the associations between lower limb biomechanics and PFP improving positively in recent years, there remains a paucity of validated, clinical tools with which to measure these variables (82). Accurate 2D measurement of running kinematics has the potential to positively influence clinical practice, with guidelines for 2D running gait analysis available (224). Multiple studies have reported intra- and inter-rater reliability of 2D video analysis during running in asymptomatic cohorts, covering gait phases (225), foot strike (226) and uniplanar hip and knee kinematics (227). However, 2D video has limited value unless construct validity in injured runners can be established, confirming that 2D observations are truly representative of three-dimensional (3D) kinematic motion capture (228).

Two previous studies provide support for the concurrent validity and reliability of high frame rate 2D video for measuring peak HADD in asymptomatic runners, in comparison to 3D kinematic motion capture (108, 109). Maykut et al (108) reported a significant moderate correlation between 2D and 3D measurement for peak HADD during treadmill running ($r$=0.53-0.62). In addition, Dinengen et al (109) reported a significant, positive correlation for peak HADD during over ground running, using a discrete 2D variable to predict the entire 3D kinematic curve from initial ground contact through to toe off. Both of these studies reported their 2D video methodology to be reliable (ICC 0.90-0.99). These findings are based on asymptomatic runners,

limiting the external applicability to clinical populations. Kinematics of runners with PFP may affect the relationship between 3D and 2D measurement, as runners in pain are theorized to have greater movement variability (167), and have been reported to move differently in multiple planes in comparison to asymptomatic runners. Investigating the validity and reliability of 2D and 3D measures of lower limb kinematics within a symptomatic population is therefore justified.

Previous studies investigating construct validity for 2D video to measure peak HADD have failed to report perfect agreement between 3D and 2D measurement. Runners with PFP have also been reported to demonstrate increased peak hip internal rotation (HIR) in comparison to controls (39, 51-54, 82). Transverse plane motion at the hip is theorized to be coupled with HADD and tibial abduction, referred to in combination as dynamic knee valgus (45). Determining the impact of this movement direction on the variability observed between 3D and 2D measurement may therefore yield the answer as to the source of the expected imperfect agreement (229).

A further limitation of previous studies has been their focus primarily on establishing validity for frontal plane variables, given their reported associations with common running-related pathology (82, 230, 231). In runners with PFP, peak knee flexion is also a variable of interest, as it is reported to affect patellofemoral joint stress (94) and may be associated with symptomatic improvements after a step rate retraining intervention (206). An investigation into the validity of clinical measurement of variables in the sagittal plane was therefore warranted.

This study aimed to determine the accuracy of 2D video gait analysis for runners with PFP. The primary objective was to investigate the concurrent validity and intra-rater reliability of high frame rate 2D video in relation to 3D kinematic motion capture. Given the expected imperfect agreement between 3D and 2D kinematics, a secondary objective was to investigate the source of any identified disagreement using logistic regression, with peak HIR used as a covariate. The null hypothesis was that 2D video would not give useful measurements of acceptable accuracy with respect to 3D kinematic analyses.

## 7.2. Methods

The Queen Mary Ethics of Research Committee (QMREC2014/24/103) gave approval for this study.

### 7.2.1. Participants

To be eligible, participants were required to report retropatellar or peripatellar pain for a minimum of one month, during at least one activity of running, squatting, stair ambulation and jumping (4). As described in chapter five, this definition of PFP was used to ensure that the outcomes from this study would be comparable to other studies in the field. A specific recreational running cohort was not sought for this chapter, as recruitment was nested within recruitment for a larger study requiring greater heterogeneity of sports and hobbies during which symptoms were present. Participants with patellofemoral instability, tibiofemoral pathology or other concomitant pathology were excluded.

The Tegner Activity Scale was collected to act as a constant measure across a heterogeneous cohort of participants with PFP who participated in a variety of sports and hobbies (232). Height and mass were collected to allow for the calculation of BMI, reported to be higher in those with persistent PFP (136). Symptom duration, Kujala scale and average pain using an NRS were collected as a reflection of symptom severity and persistence, reported to alter running kinematics (192).

### 7.2.2. Sample size calculation

Using peak HADD 3D and 2D means and a pooled SD for the right limb from Maykut et al (108) (2D HADD 11.2˚ [±2.7], 3D HADD 14.0˚ [3.7]), a sample size of 21 participants was required to achieve α 5% and β 80%. 21 participants with PFP (10 male, 11 female) were conveniently sampled from local sports medicine clinics (see table 12). All participants provided written informed consent prior to participating.

12. Participant characteristics for 3D/2D study

| Variable | Mean (SD) |
|---|---|
| Age (years) | 32.1 (12.9) |
| Height (cm) | 169.1 (45.2) |
| Mass (kg) | 69.8 (19.6) |
| BMI | 23.2 (2.6) |
| Tegner score | 5.5 (1.3) |
| Symptom duration (months) | 53.1 (84.5) |
| Kujala scale | 76.2 (12.9) |
| Average NRS | 4.7 (2.0) |

Key: SD=standard deviation; cm=centimeters; kg=kilograms; BMI=body mass index; NRS=numerical rating scale.

### 7.2.3. 3D kinematics

3D kinematic data were collected during running using a four-camera, infrared motion analysis system runnung Odin software (CX-1, Codamotion, Charnwood Dynamics Limited, Leicestershire, UK) (214).

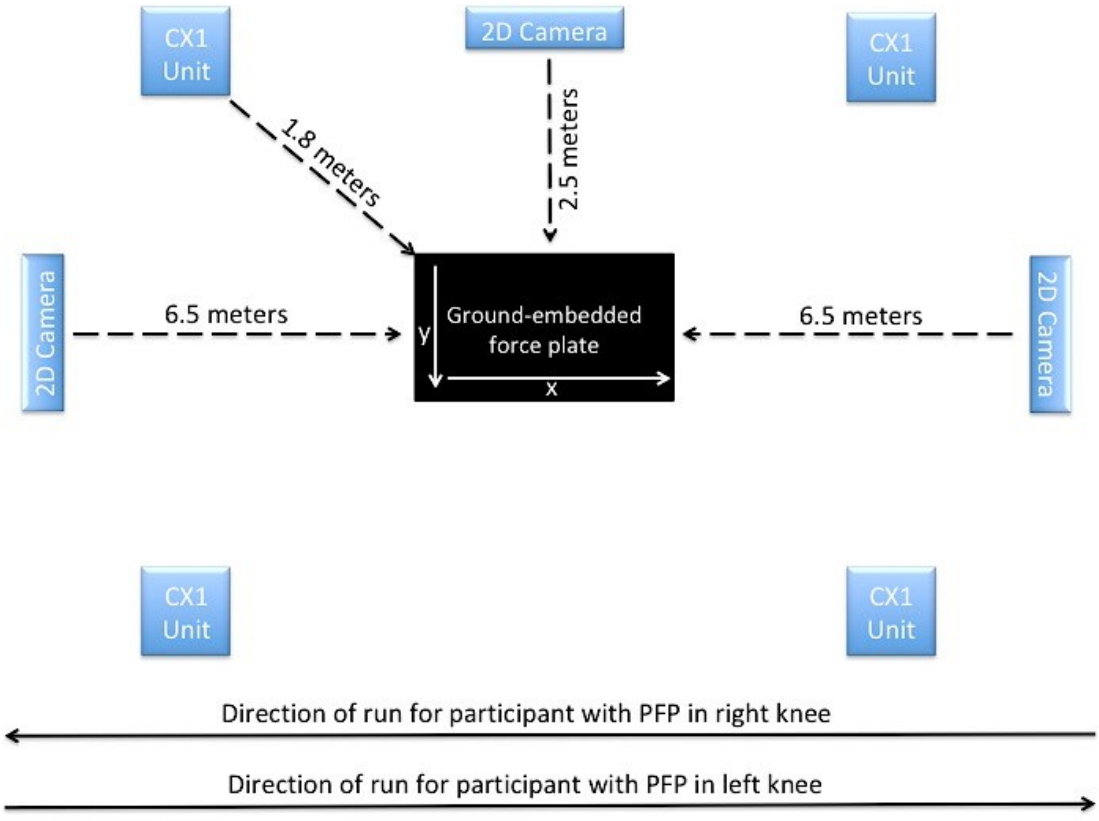
As described in detail in chapter five, a total of 24 infrared markers were placed on standard pelvic and lower limb anatomical landmarks using the CAST protocol (198). Intra-rater reliability of kinematic marker placement for the primary investigator (BN) had previously been identified to be moderate to excellent (ICC 0.62 – 0.93). Eight individual markers (powered by a drive box) were placed on bilateral pelvic landmarks (ASIS and PSIS) and foot landmarks (lateral calcaneal tuberosity and head of fifth metatarsal). Specifically, bilateral foot markers were placed on the participant's shoe as an estimate of the anatomical location, given the potential for running barefoot to effect running kinematics (199). Additionally, four rigid clusters of four markers were placed on the bilateral thigh and shank segments.

Individual markers were applied using double-sided adhesive tape and secured with transparent surgical tape. Rigid clusters were secured using a combination of adjustable elastic straps and cohesive self-adherent bandage, to minimise the potential for cluster displacement during a high force activity. Virtual markers were also identified on the femoral epicondyles and the ankle malleoli bilaterally, using a

pointer tool during a static calibration trial. These virtual markers allowed for the calculation of relevant joint centres, which did not differ between male and female participants.

### 7.2.4. 2D kinematics

2D kinematic data were captured using two high frame-rate smartphone cameras (iPhone 6, Apple Corporation, California, USA) recording at 240/frames per second. Cameras were mounted on stable tripods 1.0 metre from the laboratory floor. The camera recording in the sagittal plane was placed at a distance of 2.5 metres from the centre of a ground-embedded force plate, which participants subsequently ran past. The camera recording in the frontal plane was placed 6.5 metres from the centre of a ground-embedded force plate, which participants ran directly towards (see figure 66).

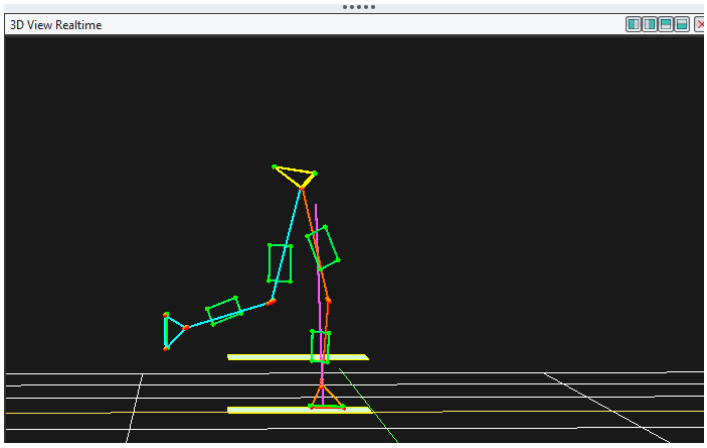



*66. Laboratory set up for 3D/2D motion analysis project*

### 7.2.5. Experimental protocol

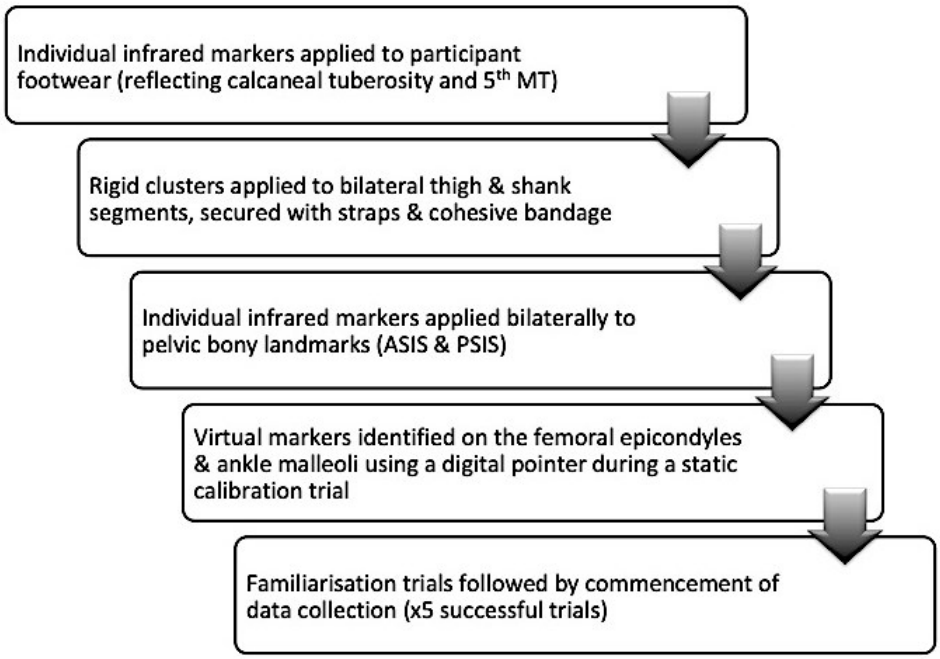
Participants presented to the Human Performance Laboratory at Queen Mary University of London. Both 3D and 2D data were captured during trials of over-ground

running. Participants were provided with neutral running shoes in their required size (Asics Nimbus, Asics, Cheshire, UK), to minimise potential effects of footwear variation on running kinematics (233). Participants were instructed to run in a straight line for a distance of 10.0 meters at a self-selected speed, landing the foot of their symptomatic limb on a ground-embedded force plate (Type 9281CA, Kistler Corporation, Switzerland).




*67. 3D real time view within Odin software detailing force plate contact and vertical ground reaction force output (pink)*

The ground-embedded force plate was 5.0 metres from the trial start-point, with participants typically making contact with their fifth step. Several practice runs were permitted to allow for familiarisation and to ensure adequate force plate contact during a participant's natural running gait (see figure 67). This process was repeated until five successful trials were obtained, with a successful trial defined as an appropriate landing of the correct foot directly onto the force plate without visual adjustment of running gait. Each trial was initiated by a member of the research team, with the 3D system and both 2D cameras manually synchronised using a numerical countdown.



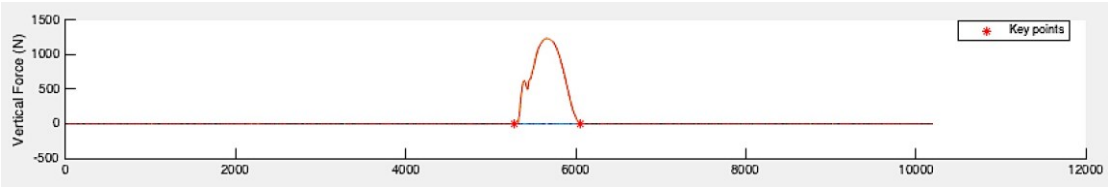

*68. Flowchart depicting application of infrared markers, virtual markers and subsequent data collection*

### 7.2.6. Data analysis

To reduce the potential for type I error, data pertaining to one limb only were entered into the analysis (195). For participants with bilateral symptoms, the limb that rated the highest on the numerical rating scale was evaluated. In the presence of equivalent symptoms the dominant limb was evaluated, defined by the limb that the participant would use to kick a ball.

*3D kinematic analysis*

Data were analysed offline using a customised Matlab program (version 2015, Mathworks, Natick, Massachussets, USA), using a graphical user interphase (GUI). Initially, a 20*N* threshold from the ground-embedded force plate was used to determine initial contact and toe-off respectively (see figure 69).




*69. Vertical ground reaction force within data analysis GUI*

Kinematic data were processed within this event window, defined as running stance phase. An International Society of Biomechanics advocated XYZ (sagittal, frontal,

transverse) cardan rotation sequence was used. Peak joint angles for both peak hip adduction (HADD) and knee flexion (KFLEX) were visualised and subsequently exported to a Microsoft Excel 'comma separated value' (.csv) file for statistical analysis.

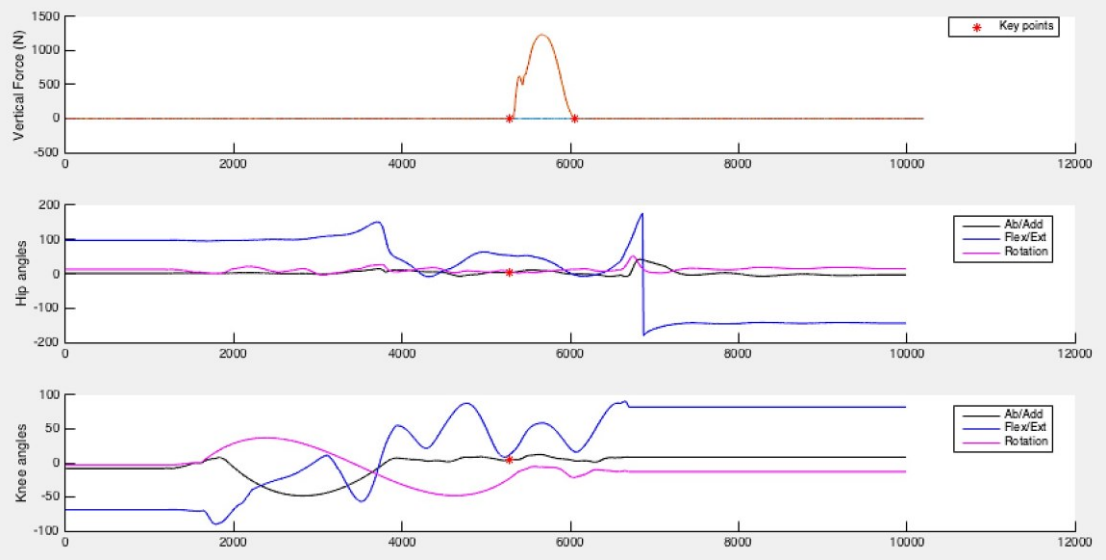
```
%%%%%%%%%%%%%%%%% KINEMATIC OUTCOME CALCULATIONS %%%%%%%%%%%%%%%%%
%Find the correct leg dependent on dominance
if strcmp(handles.legSelect,'R')
    curHipAbAdd = handles.curFileDetails.newAngleData.JointAngle.RHip.Data(curEventRange(1):curEventRange(2),1);
    curKneeRot = handles.curFileDetails.newAngleData.JointAngle.RKnee.Data(curEventRange(1):curEventRange(2),3);
    curKneeFlexExt = handles.curFileDetails.newAngleData.JointAngle.RKnee.Data(curEventRange(1):curEventRange(2),2);

    %Looking for adduction
    [peakHip,tempHipIdx] = max(curHipAbAdd);
    %Looking for internal rotation
    [peakKnee, tempKneeIdx] = max(curKneeRot);
    %Looking for max knee flexion
    [peakKneeFlex, tempKneeFlexIdx] = max(curKneeFlexExt);

    %Find the absolute timing of these features
    peakHipTime = ((curEventRange(1)+tempHipIdx)-1)/max(handles.curFileDetails.allFreq);
    %Looking for internal rotation
    peakKneeTime = ((curEventRange(1)+tempKneeIdx)-1)/max(handles.curFileDetails.allFreq);
    %Looking for max knee flexion
    peakKneeFlexTime = ((curEventRange(1)+tempKneeFlexIdx)-1)/max(handles.curFileDetails.allFreq);

else %must be a left leg
```

*70. Section of Matlab code within GUI detailing identification of relevant peak joint angles*



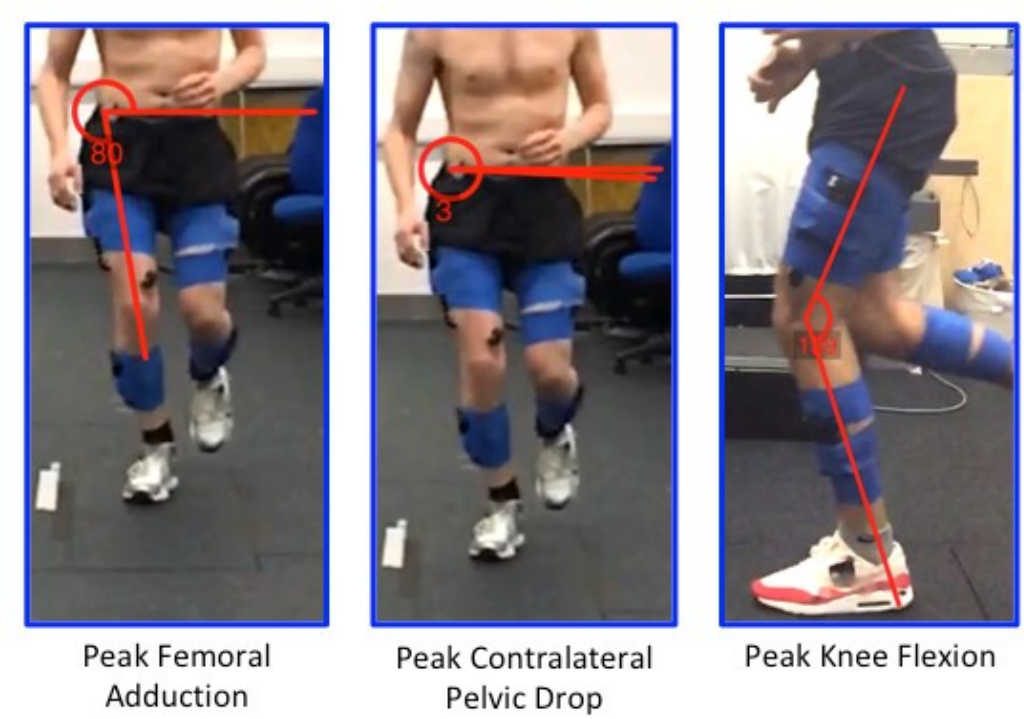

*71. Raw kinematic data trace for both hip and knee within running stance phase event window*

### *2D kinematic analysis*

Videos from successful trials were subsequently imported into the Hudl Technique application (Hudl, Agile Sports Technologies Inc., Nebraska, USA) for analysis. Two independent 2D angles, hip adduction (HADD) and knee flexion (KFLEX) were identified. HADD was determined using methods described by Dingenen et al (109), where the contralateral pelvic drop (CLPD) angle is added to the femoral adduction (FADD) angle. CLPD was defined as the angle formed by a horizontal line from the

stance limb anterior superior iliac spine (ASIS) (referenced from the laboratory floor) and the swing limb ASIS (see figure 72). FADD was defined as the angle formed by a horizontal line from the stance limb ASIS (referenced from the laboratory floor) and the centre of the stance limb tibiofemoral joint (an estimation of the knee joint centre) (see figure 72). Infrared ASIS and PSIS markers used for 3D kinematic data collection were used to determine the location of these landmarks on 2D video.

KFLEX was defined as the angle formed by a line drawn from the stance limb greater trochanter to the lateral femoral condyle and a second line drawn from the stance limb lateral femoral condyle to the stance limb lateral malleolus (see figure 72). For both variables, a peak angle was estimated, determined to be when the participant reached the peak of mid-stance, manually defined as the point where maximal foot contact had occurred and no upward/downward motion was occurring (108).




*72. Figure demonstrating the calculation of 2D joint angles*

### 7.2.7. Statistical analysis

All analyses were performed using SPSS (version 22 for MacOS, IBM, New York, USA). Data normality were determined using Kolmogorov-Smirnov (K-S) test, with all data identified to be normally distributed ($P$= 0.31 – 0.74) and parametric statistical tests therefore employed.

*Concurrent validity*

Means of the five 3D and 2D trials were calculated, leaving one pooled mean 3D and 2D value for each participant for both variables of interest (HADD and KFLEX). The difference between the 3D and 2D means was determined using two-tailed, paired t-tests. Scatter plots were used to visualise the directionality of the relationship between 3D and 2D measurement. To determine concurrent validity between 3D and 2D measurement, single measure ICCs with 95% confidence intervals were calculated using a two-way mixed effects model with absolute agreement. ICCs were defined as excellent (> 0.90), good (0.75-0.90), moderate (0.50-0.75) and poor (< 0.50) respectively (204). Bland and Altman plots with 95% limits of agreement (LOA) were used to visually represent the agreement between the 3D and 2D values (234). In addition, a backward linear regression was performed to assess the effect of including 3D hip internal rotation (HIR) in a predictive model, with the F change statistic used to determine the significance of 3D HIR as a covariate.

*Intra-rater reliability*

Peak HADD and KFLEX values from the first run trial of all participants was analysed twice, with 24 hours between analyses. Reliability was determined using single measure ICCs with 95% confidence intervals using a two-way mixed effects model with absolute agreement.

## 7.3. Results

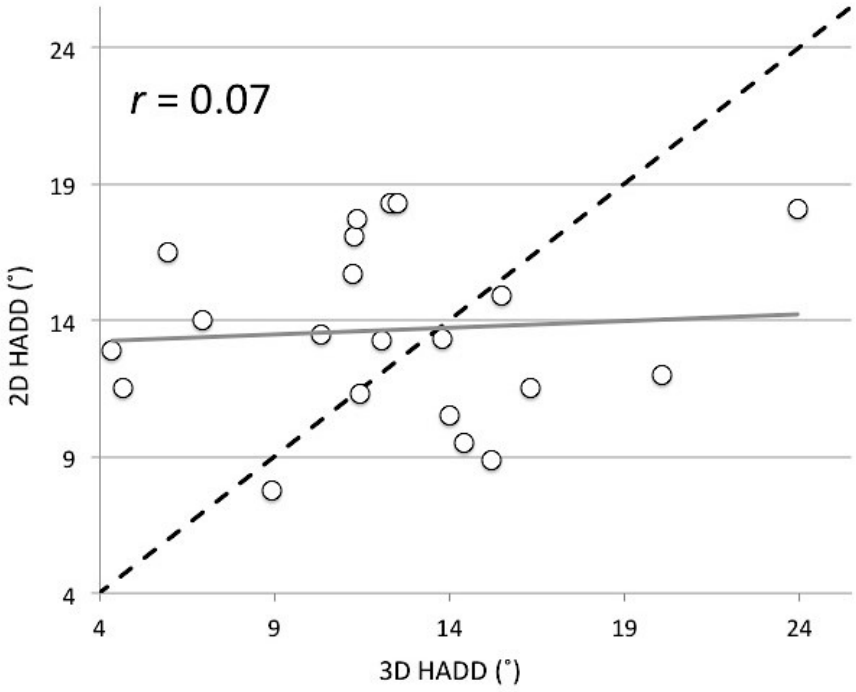
### 7.3.1. Concurrent validity

There was a significant difference between 3D and 2D measured peak KFLEX, but peak HADD was not significantly different between 3D and 2D measures (table 13). ICC's identified poor agreement for both peak HADD and peak KFLEX between 3D and 2D measurement (table 14).

13. 3D and 2D data for both peak HADD and KFLEX

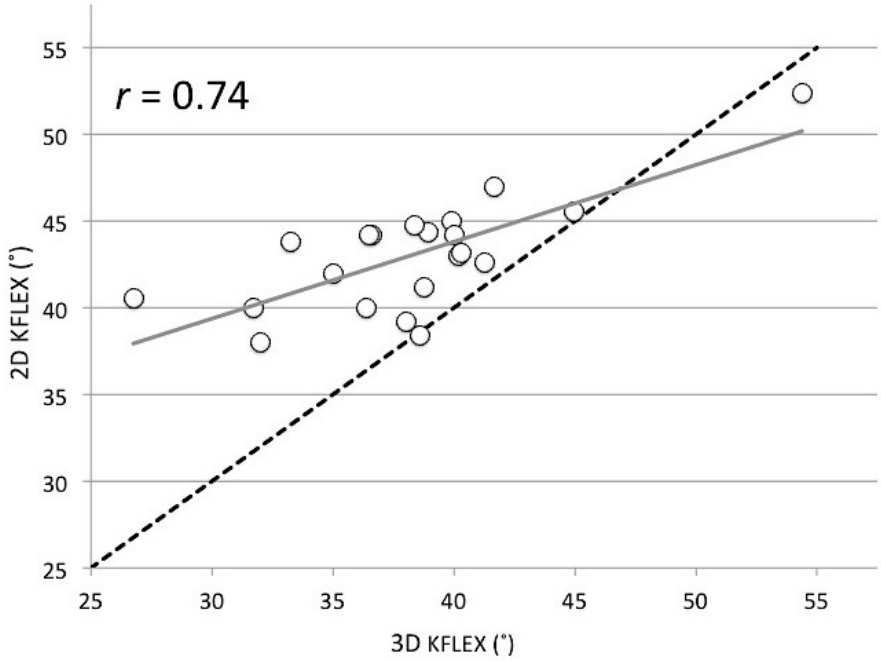
| Variable | 3D Measurement Mean (SD) | 2D Measurement (Mean (SD) | Difference Mean | *P* | *d* |
|---|---|---|---|---|---|
| **HADD** | 12˚ (4.7) | 13˚ (3.2) | -1˚ | 0.25 | -0.27 |
| **KFLEX** | 38˚ (5.5) | 43˚ (3.3) | -5˚ | <0.01* | -1.13 |

Key: 3D= three-dimensional; 2D=two-dimensional; SD=standard deviation; *HADD=hip adduction; KFLEX=knee flexion.*




*73. Scatter plot for peak 2D and 3D peak HADD*

Key: dashed lines represent a line of identity, solid line represents the line of best fit.




*74. Scatter plot for peak 2D and 3D peak KFLEX*

Key: dashed lines represent a line identity, solid line represents the line of best fit.

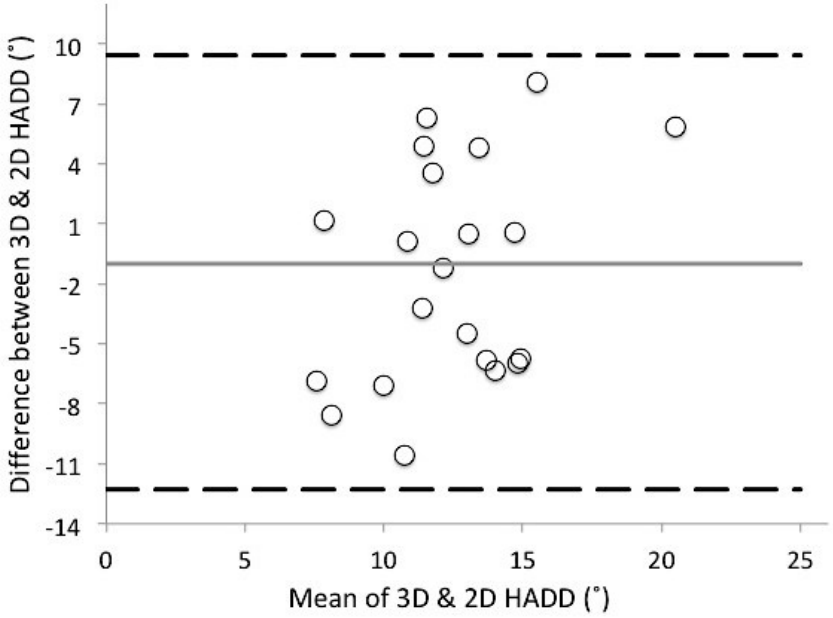
14. Construct validity data for peak HADD and KFLEX comparing 3D and 2D measurement

| Outcome | HADD | KFLEX |
|---|---|---|
| **ICC (95% CI)** | 0.06 (-0.35, 0.47) | 0.42 (-0.10, 0.75) |
| **Upper LOA** | 9.4 | 2.6 |
| **Lower LOA** | -12.3 | -12.1 |

Key: HADD=hip adduction; KFLEX=knee flexion; ICC=intraclass correlation coefficient; CI=confidence interval; LOA=limits of agreement.

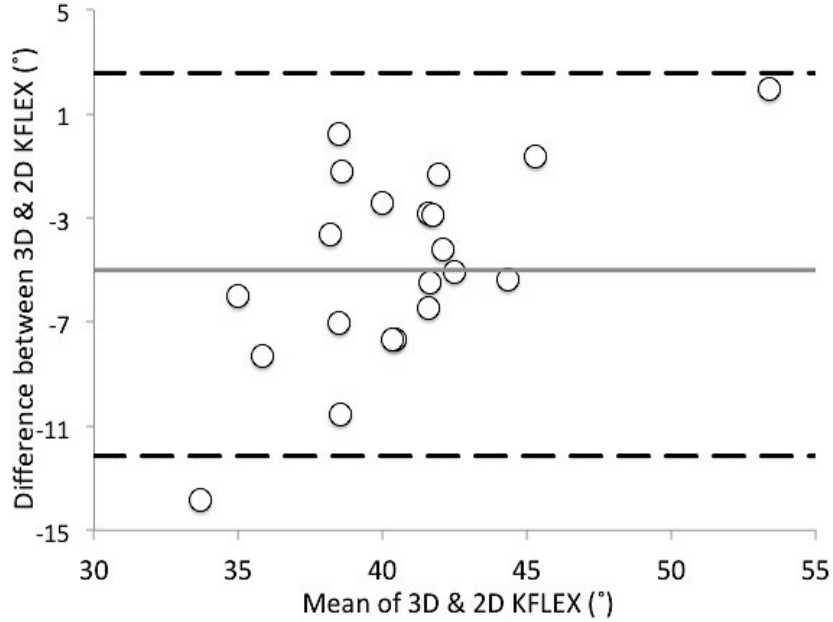
For peak HADD, Bland and Altman analysis identified wide limits of agreement and a broad spread of data with no bi-modal distribution (see figure 75). This indicates poor agreement (ICC 0.06) between 3D and 2D measurement that is not resultant of a systematic bias. For peak KFLEX, Bland and Altman analysis again reveals wide limits of agreement indicating poor agreement between 3D and 2D measurement (see figure

76). There is however a linear directionality to these data, suggesting the identified poor agreement (ICC 0.42) is result of a systematic bias, further indicated by the line of equivalence observed on the scatter plot for these data (see figure 73).




*75. Bland and Altman plot for peak HADD*

Key: dashed lines represent upper and lower limits of agreement, solid line represents the pooled mean difference between 3D and 2D measurement.




*76. Bland and Altman plot for peak KFLEX*

Key: dashed lines represent upper and lower limits of agreement, solid line represents the pooled mean difference between 3D and 2D measurement.

### 7.3.2. Intra-rater reliability

Moderate intra-rater reliability was identified for peak HADD (ICC 0.65 95% CI 0.34, 0.83) and peak KFLEX (ICC 0.61 95% CI -0.09, 0.87).

### 7.3.3. Logistic regression

A multiple variable, backward linear regression was calculated to predict 3D peak HADD (dependent variable) using 2D HADD (independent variable$_1$) and 3D HIR (independent variable$_2$). $R^2$ of the model was 0.06, with a non-significant F change (0.07, $p$ = 0.93) identified after the removal of 3D HIR ($R^2$ change = -0.01).

A second multivariable backward linear regression was calculated to predict 3D KFLEX (dependent variable) using both 2D KFLEX (independent variable$_1$) and 3D HIR (independent variable$_2$). $R^2$ of the model was 0.60, with a non-significant F change (3.76, $p$ = 0.06) identified after the removal of 3D HIR ($R^2$ change = -0.08).

## 7.4. Discussion

This study aimed to determine the appropriateness of clinical gait analyses for runners with PFP, by investigating the concurrent validity and intra-rater reliability of high frame rate 2D video. Accepting our null hypothesis, a poor correlation between 3D and 2D measurement was found for both peak HADD and peak KFLEX, reflected by poor ICCs and wide limits of agreement. In the presence of acceptable intra-rater reliability, these data suggest that pragmatic 2D video does not have acceptable accuracy with respect to 3D kinematic outcomes for runners with PFP when measuring both peak HADD and peak KFLEX.

Our findings for peak HADD conflict with the work of both Maykut et al (108) and Dingenen et al (109), who reported significant correlations between 3D and 2D measured peak HADD. The primary explanation for this disagreement is the investigation of a cohort of participants with PFP in comparison to participants who are asymptomatic. Reflective of a typical cohort with persistent PFP (mean symptom duration 53.1 months), our participants had a higher BMI (mean 23.2) than the previously studied asymptomatic cohorts. This may have negatively affected the accuracy of 2D video digitisation by increasing the visual distortion of necessary bony landmarks. Furthermore, our PFP cohort had a lower physical activity level (mean Tegner Scale 5.5) in comparison to the elite asymptomatic cohorts investigated by both Maykut et a(108) and Dingenen et al (109) (estimated Tegner Scale 8-10). Elite runners are reported to have more consistent kinematics than recreational runners (235), which is likely to have resulted in a more stable mean and thus, increased agreement between 3D and 2D measurement (236).

A further explanation for this conflict is the statistical methodologies employed. Maykut et al (108) calculated a Pearson's Correlation Coefficient (*r*) which may over-estimate the agreement between two variables when data demonstrates a linear trend (237). Peak HADD data from our study does not appear to have a systematic bias (i.e. consistently over or under predict) and the data does not follow a linear trend, with a Pearson's *r* comparable to the calculated ICC (*r*=0.07). Dingenen et al (109) employed statistical parametric mapping, which does not confirm that the 2D method

used can accurately predict a discrete 3D value at a specific point within the gait cycle. Clinicians often seek a discrete kinematic variable within the gait cycle to employ clinical prediction rules, such as a 5˚ reduction in peak HADD as a predictor for running retraining success (100, 101), and the clinical applicability of this study is therefore limited.

An additional discrepancy between our study and the work of both Maykut et al (108) and Dingenen et al (109) is the software used to assess the 2D videos. We evaluated the construct validity of the Hudl Technique application (Hudl, Agile Sports Technologies Inc., Nebraska, USA), given its ease of clinical application. Hudl Technique is free of cost at the point of access and can be installed on a variety of devices (mobile phones and tablets) and operating systems. The Dartfish software (Dartfish, Fribourg, Switzerland) used in previous studies may offer greater precision, where digitizing 2D video is completed using a mouse rather than the assessor's finger on a touch screen. The limitation of Dartfish as a method of 2D video digitization is the associated cost (£204-£880 per calendar year). Table 15 summaries the similarities and differences between this study and the previous work of both Maykut et al (108) and Dingenen et al (109).

15. Similarities/differences between this study and previous 3D/2D running kinematic measurement

| | This study | Maykut et al (108) | Dingenen et al (109) |
|---|---|---|---|
| **Population studied** | Physically active persons with PFP (m=10, f=11) | Asymptomatic elite runners (m=14, f=10) | Asymptomatic elite athletes (m=6, f=9) |
| **Participant BMI Mean (SD)** | 23.2 (2.6) | 20.0 (1.4) | 21.1 (2.1) |
| **Participant age (years) Mean (SD)** | 32.1 (12.9) | 19.9 (1.3) | 18.7 (1.6) |
| **Running method** | Over ground | Treadmill | Over ground |
| **2D analysis software** | HUDL | Dartfish | Dartfish |
| **Statistical method** | ICC | Pearson's *r* | SPM |
| **Frontal plane camera distance from axis** | 6.5 meters | ? | 4.5 meters |

Key: SD=standard deviation; 2D=two dimensional; m=male; f=female; ICC=intraclass correlation coefficient; SPM=statistical parametric mapping; ?=unable to determine.

Our novel investigation of peak KFLEX also resulted in a poor correlation between 2D video and 3D kinematic motion capture. There is a linear pattern to these data, which results in a Pearson's *r* that over-estimates construct validity (*r*=0.74). There also appears to be a systematic bias within these data, with 2D video consistently over-predicting peak KFLEX by a mean of 5˚. Ortiz et al (229) hypothesised that transverse plane hip motion may affect the accuracy of 2D measured frontal plane hip and knee kinematics. Consistent with this hypothesis, there is a statistical trend towards 3D peak HIR being a covariate for this outcome (F change 3.76, *p*=0.06, $R^2$ change -0.08). Whilst this may explain the systematic bias within these data, this potential model has limited clinical applicability, as transverse plane hip data is not readily collectable by a 2D camera.

## 7.5. Limitations and future directions

This study is not without limitations, which must be considered when interpreting the results. In an attempt to best replicate clinical practice, participants completed only a short over ground run, with data collected on the fifth step on average. Dingenen et al (236) recently reported that a minimum of seven steps are required to allow for a stable mean of a 2D measured kinematic variable. These data refer to analysis completed with Kinovea (http://www.kinovea.org), software that is free of cost at the point of access to Microsoft Windows users. Kinovea offers similar precision to digitization with Dartfish and has been reported to be reliable for measuring a variety of 2D running kinematic variables (236) when data were collected using retroflective markers. Given the apparent potential for increased precision to result in greater construct validity, a future study using either Dartfish or Kinovea involving runners with PFP is warranted.

It could also be that repeating this study using a treadmill running protocol similar to that used by Maykut et al (108) may return a different outcome. Although kinematic comparisons between treadmill and over ground running have been reported to be equivalent (238), a treadmill protocol would allow for the frontal plane camera to be placed closer to the runner, increasing the video quality and reducing the potential for parallax error. Retroflective markers should also be encouraged to increase the precision of 2D video digitisation in future studies, regardless of the chosen analysis method.

Whilst not statistically significant, there is a trend for peak HIR data to explain the observed poor agreement between 3D and 2D measurement, particularly for peak KFLEX. As a result, future studies are encouraged to investigate methods for clinical gait analysis that may allow for measurement of all movement planes, such as an inertial measurement unit (239). Inertial measurement unit data has been collected in a small sample during a marathon run (240), but is yet to be completed in the clinical setting or be compared to 3D motion capture to the best of our knowledge.

## 7.6. Conclusion

A poor correlation between 3D kinematic motion capture and high frame rate 2D video was identified for both peak HADD and KFLEX in runners with PFP. This may be attributed to the increased variability in running kinematics in runners with PFP, but could also be explained by employed 2D video or statistical methodologies. Further investigation of software with increased precision, such as Dartfish or Kinovea, is warranted, aiming to improve the ability of high frame rate 2D video to accurately predict 3D kinematics in the clinical setting. At present, clinical gait analysis conducted using the Hudl Technique application should be interpreted with caution, as the accuracy of 2D measurement cannot be guaranteed, even in the presence of moderate intra-rater reliability.

# 8. Discussion and conclusions

This thesis had the overarching aim of determining the influence(s) of lower limb biomechanics on the development, persistence and management of PFP in recreational runners. Given the reported high prevalence of musculoskeletal injury amongst runners (18-92%) (12), the first thesis aim centred on defining the magnitude of PFP by exploring its epidemiology (risk factors and incidence).

## 8.1. Risk factors for PFP development

The primary finding from the systematic review completed to fulfil aim one was that limited risk factors from pooled data existed to explain the development of PFP. Furthermore, no risk factors from pooled data existed to explain the development of PFP in recreational runners. This highlights a clear dearth of prospective literature that can guide the design of interventions aiming to prevent future PFP and is suggested as the primary research priority for the field.

Multiple variables often reported as being cross-sectionally associated with PFP such as height, body mass, BMI, body fat percentage, age and Q-angle, were not found to be causally associated with PFP in any cohort. As such, preventative programmes for PFP that seek to modify these variables are unlikely to yield success. For body mass and body fat percentage, reported to be associated with PFP once symptoms have developed (136), these data suggest that persistence of PFP (2) results in wider health problems. As recreational running has been reported to reduce both adiposity (9) and body fat percentage (10), there is a clear need to improve understanding of the epidemiology of PFP amongst recreational runners.

We identified moderate evidence that quadriceps weakness is a risk factor for future PFP in military recruits. This aligns well with the study by Coppack et al (135), where a predominantly quadriceps-based exercise programme reduced the incidence of PFP in the military. However, the most recent consensus statement from the international patellofemoral research network (241), and the most recent systematic reviews relating to exercise therapy in PFP (56, 81) both report superior outcomes when gluteal and quadriceps exercises are combined. It may therefore be that exercise programmes designed to either prevent or manage PFP in the military have different

treatment targets to other populations. No study to date has investigated the role of quadriceps strength in the development of PFP amongst recreational runners. As quadriceps weakness has been reported in this group once PFP has developed (31), prospective investigation is encouraged to aid in determining if this variable is associated more with the development or persistence of PFP in a recreational running cohort.

Moderate evidence also existed that identified increased hip abduction strength as a risk factor for future PFP development in adolescents, questioning the preventative role that exercise interventions may have in this population. Given the identified high incidence figure (11%) and wider health implications of a musculoskeletal disorder with a poor prognosis in young people (134), the development of preventative strategies should be of an urgent priority. As muscle strength deficits have also not been reported in adolescents once PFP is persistent (129) and the reported effectiveness of education as an intervention (132), it is here that preventative strategies may be best placed.

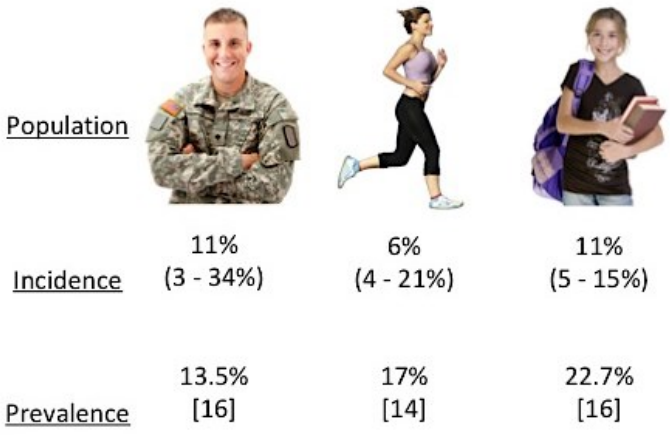
Prospective hip abduction strength data in adolescents is in conflict with the limited data that exists investigating the role of gluteal muscle strength in relation to PFP development in recreational runners. Ramskov et al (19) reported that higher eccentric hip abduction strength reduced the incidence of PFP amongst novice recreational runners, though these data were not presented in a manner allowing for meta-analysis. This suggests that an exercise programme targeting eccentric gluteal strength may reduce the risk of PFP development in novice runners (19), though this hypothesis is yet to be investigated.

Previous systematic reviews looking to identify risk factors for running-related injury as a heterogeneous entity have reported associations between running frequency/volume and risk of future injury (8, 12). More specifically, runners who increased their weekly volume by more then 30% were reported to be at a greater risk by Nielsen et al (143), compared to runners who progressed by a more conservative 10%. Furthermore, measurement of activity using the acute:chronic workload method has been reported to both predict and prevent subsequent injury in multiple sports (242-245).

It is plausible to suggest that both quadriceps weakness (in the military) and increased hip abduction strength (in adolescents), which we identified to be risk factors for future PFP, could be confounded by participant activity level. In support of this hypothesis, Smith et al (16) highlight that the highest incidence rate for PFP amongst military recruits come from populations where military conscription remains a law. It is therefore advised that future prospective studies both record and investigate activity level as an exposure, especially in recreational runners where future PFP is the outcome.

## 8.2. Incidence and prevalence of PFP

When heterogeneous data were pooled from all included prospective studies, PFP incidence was identified to be 10%. Within the identified homogenous populations, incidence figures for military recruits, adolescents and recreational runners were in agreement with the recent systematic review and meta-analysis of Smith et al (16). These identified incidence data, and prevalence data reported by both Smith et al (16) and Taunton et al (14) are summarised in figure 77, with prevalence exceeding incidence for all populations. The discrepancy between incidence and prevalence questions the notion that PFP is a self-limiting condition (16, 246) and affirms the suggestion that long-term outcomes for PFP are currently sub-optimal in all populations (2).

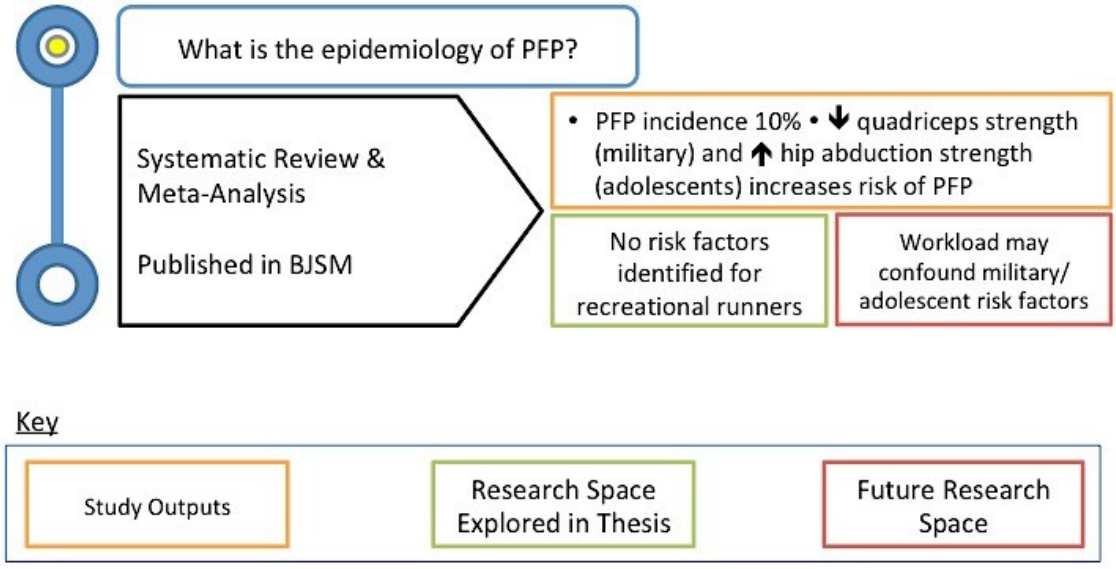



*77. A summary of PFP incidence and prevalence data in multiple cohorts*

There is a frequent suggestion throughout the wider literature, often without substantiation, that females are more at risk of developing PFP than males (112). This

is perhaps due to the increased risk of females developing other knee injuries that have an equivalent theoretical biomechanical mechanism, such as ACL rupture (247). That said, females have previously been reported to be twice as likely to develop PFP than males during basic military training (21). Data from studies included in the systematic review completed to fulfil aim one did not identify sex as a risk factor for future PFP development, but the largest proportion of females developing PFP was identified amongst recreational runners. This may explain why such a significant proportion of both case-control and intervention studies relating to running investigate all female populations. This identified parity between the sexes in terms of PFP development resulted in the decision to investigate mixed-sex samples in the studies that formed chapters five through seven.

Figure 78 incorporates the study designed to complete and achieve the aim of exploring the epidemiology of PFP. Having identified limited risk factors for PFP development and defined the incidence of the condition, the second aim of this thesis centered on determining the biomechanical factors associated with the development, persistence and management of PFP in recreational runners.




*78. Study, outputs and research space(s) identified by work completed in relation to aim one*

## 8.3. Biomechanics and running-related PFP

### 8.3.1. Biomechanics and PFP development

Only data from a single study indicated that a kinematic variable, peak HADD, was a risk factor for future PFP development in recreational runners (20). Despite the statistical significance, caution is advised in interpreting this very limited evidence. Noehren et al (20) investigated a female only cohort and had a high risk of bias resulting from the low patellofemoral sample size. This is consistent with another prevalent running injury, iliotibial band syndrome (ITBS), with peak HADD reported as the only kinematic risk factor in female runners (231). As a result, evidence for isolated kinematic variables as risk factors for PFP development amongst recreational runners is therefore extremely limited and ripe for further scientific exploration.

A similar kinematic risk profile has also been reported for both ACL injury and PFP in adolescent females, with an eight degree increase in peak HADD increasing the risk of subsequent ACL rupture (248). In a subsequent study a kinetic variable, a higher knee abduction moment (>25Nm), determined those who developed subsequent ACL rupture rather than PFP (249). It is reasonable to suggest that those with an appropriate biomechanical profile may be at risk of either PFP or ACL rupture, dependent on their choice to perform a predominantly sagittal plane, lower force sport (recreational running) or a multiplanar, higher force sport.

Limited evidence was also identified to indicate that increased peak force under the $2^{nd}/3^{rd}$ metatarsal heads and time to peak force at the lateral heel during running increased the risk of future PFP development. Such plantar loading variables have also been reported as risk factors for the development of Achilles tendinopathy (37). As increased vertical load rate has also been reported as prospectively associated with future injury in female runners (250), it could be that total limb loading, rather than increased load at a specific anatomical region, is the variable that increases injury risk.

Very limited evidence for an association between reduced rearfoot eversion (20) and future PFP development was also identified. This is in conflict with the wider literature where increased navicular drop has also been reported to be a risk factor for future PFP development (36). This conflict is perhaps unsurprising, given that global foot

kinematics in asymptomatic participants have been reported to be highly variable (61). Consequently, understanding of the role of foot biomechanics in relation to PFP risk amongst recreational runners is limited, requiring further investigation.

### 8.3.2. Biomechanics and PFP persistence

Despite limited prospective links, multiple associations were observed between altered running kinematics and PFP, including increased peak HADD, HIR and CLPD when compared to controls. As these associations come from the case-control literature, it is not possible to determine if these kinematic differences existed prior to symptom development, or are simply adaptations to pain. This is again consistent with the literature surrounding ITBS, with both male and female runners with ITBS reported to run with greater peak HADD when compared to controls (230, 251, 252).

There is a plausible mechanistic explanation as to why an equivalent kinematic variable (peak HADD) is associated with two differing types of knee pain. It could be that trochlear dysplasia, reported to result in reduced patellofemoral contact area during both open and closed chain tasks (253), magnifies the effect of increased peak HADD during running. Including an imaging component to future prospective and case-control studies would add a significant amount to the understanding relating to kinematics and their association with knee pain. An example of where imaging has improved treatment outcomes is patellofemoral arthroplasty, with implants customised to the recipients geometry reported to be superior in those with trochlear dysplasia (254).

It may also be that running kinematics are effected by symptom persistence, with a recent case-control study (192) reporting that increased peak HIR and increased peak HADD were associated with acute (< one month duration) and persistent (> three months duration) PFP respectively. This suggests that increased peak HADD could therefore be an adaptation to persistent pain, but conflicts with the data of Noehren et al (20), who reported increased peak HADD as a risk factor for future PFP in female runners.

Overall, the strength of evidence for the association between running biomechanics and PFP is typically associative rather than causal. A longitudinal cohort study would

be required to investigate the biomechanical variables that contribute to the development and subsequent persistence of PFP, which may differ, and may also not provide plausible treatment targets. However, the identified associations between hip kinematics and persistent PFP justified the inclusion of these variables in the experimental studies that form chapters five through seven.

Whilst the first systematic review of this thesis did not identify the female sex as a risk factor for future PFP development, larger proportions of females were observed in the included recreational running studies. Asymptomatic females have previously been reported to demonstrate both increased peak HADD and HIR during running in comparison to asymptomatic males (255). Despite the strength of evidence identified for cross-sectional associations between altered running kinematics and PFP, the majority of included studies (seven out of eight) reported data on either female only or mixed-sex cohorts. It was therefore plausible to suggest that the females amongst the cohorts may have significantly affected any differences identified between mixed-sex PFP and control cohorts.

Just one previous case-control study reported kinematic data for both sexes separately (51), with females demonstrating increased peak HADD during running when compared to both males with PFP and asymptomatic males. The mean difference between males and females with PFP (6.3˚) is greater than the mean difference reported by Chumanov et al (255) in asymptomatic runners (2.9˚). This suggested that kinematic data from females with PFP might significantly alter the pooled mean for peak HADD when data for both sexes are combined. Given the emergence of interventions that are reported to have a potential kinematic treatment target and mechanism such as *running retraining* (>20˚ peak HADD reduced by ~5˚) (100, 101), it was deemed necessary to determine if these altered hip kinematics exist in both sexes.

Having confirmed the reliability of kinematic marker placement, our mixed-sex data further confirmed that runners with PFP demonstrated increased peak HADD when compared to controls. When sub-grouped by sex, females with PFP demonstrated significantly greater peak HADD during running when compared to asymptomatic females, but not asymptomatic males or males with PFP. The absence of statistically significant differences between males and females with PFP in our analysis was

attributed to the sample imbalance towards females (n=11 versus n=9), but was considered clinically relevant as the mean difference between the groups exceeded the accepted MDC (3.5˚) (194). Thus, when considered in combination with the data of Willy et al (51), it is suggested that future studies investigating lower limb kinematics in a PFP cohort during running report data for males and females separately. This will mitigate the potential for a spurious outcome that may arise when pooling data for both sexes.

### 8.3.3. Biomechanics and observed mechanisms of treatment effects

Three interventions; exercise therapy, orthoses and *running retraining*, were investigated by studies included in the systematic review completed to partially fulfil aim two. Whilst exercise therapy and orthoses have been included in multiple previous PFP consensus documents (65, 80, 241), *running retraining* is a novel intervention for which the evidence base is in its infancy. Data from these studies were pooled in relation to both treatment effects and biomechanical mechanisms.

*Foot orthoses*

Increased peak rearfoot eversion has been reported in individuals with PFP during running (256) and very limited evidence of reduced peak rearfoot eversion with foot orthoses in-situ was identified. However, no inferences on treatment effects were made by the observational study from which these data come, heavily limiting their clinical applicability. In keeping with the previously reported efficacy of foot orthoses in other cohorts (76, 77, 179), the recent study of Sinclair et al (257) also reported positive short-term effects of foot orthoses in runners with PFP. In conflict with Rodrigues et al (78), no significant kinematic changes at the rearfoot were reported by Sinclair et al (257).

On the whole, the evidence for foot orthoses in managing runners with PFP is conflicting, both with respect to treatment effects and biomechanical mechanisms. This is a consistent theme throughout the literature, with two recent systematic reviews reaching conflicting conclusions regarding the use of orthoses in plantar heel pain (258, 259). This may be explained by the methodological challenges presented by attempting to investigate the effects and mechanisms of orthoses; namely a likely

inability to control biomechanical effects across a population, rendering mean pooled data insignificant secondary to high variability (260). Despite this, there is an emerging positive narrative in the field of PFP, meaning that future investigation of both the effects and mechanisms of foot orthoses in recreational runners is worthwhile.

*Exercise therapy*

Exercise therapy is described as the gold standard intervention for PFP by the most recent consensus statement from the international patellofemoral research network (241). Consistent with this statement, moderate evidence was identified that exercise therapy reduces pain and improves function in recreational runners to short-term follow up. In keeping with previous work in asymptomatic runners (88), no kinematic changes were identified after exercise therapy. This means that the mechanism underpinning these positive effects is unknown, leaving clinicians unable to tailor exercise therapy to a biomechanical treatment target in recreational runners.

It could be that the mechanisms of exercise therapy in recreational runners with PFP are not biomechanical in nature. For example, improvements in both strength and proprioception have been reported as potential mediators of the effects of exercise therapy in osteoarthritis management (261). Alternatively, it may be that exercise therapy can improve the kinetic factors associated with knee injury, as observed in females who are 'at risk' of subsequent ACL injury after a neuromuscular protocol (262). There is limited evidence of this skill transfer in recreational runners, with single leg squat kinematics, but not running kinematics, improving after an exercise protocol in asymptomatic runners (88).

Moreover, it has recently been reported that clinicians are currently unable to replicate published exercise therapy protocols for PFP secondary to inadequate reporting standards (263). This may go some way to explaining why exercise therapy was not found to be superior to an education intervention in runners with PFP at six month follow up (85). As a result, future work would be necessary to determine if and how exercise therapy should be best implemented to manage PFP in recreational runners.

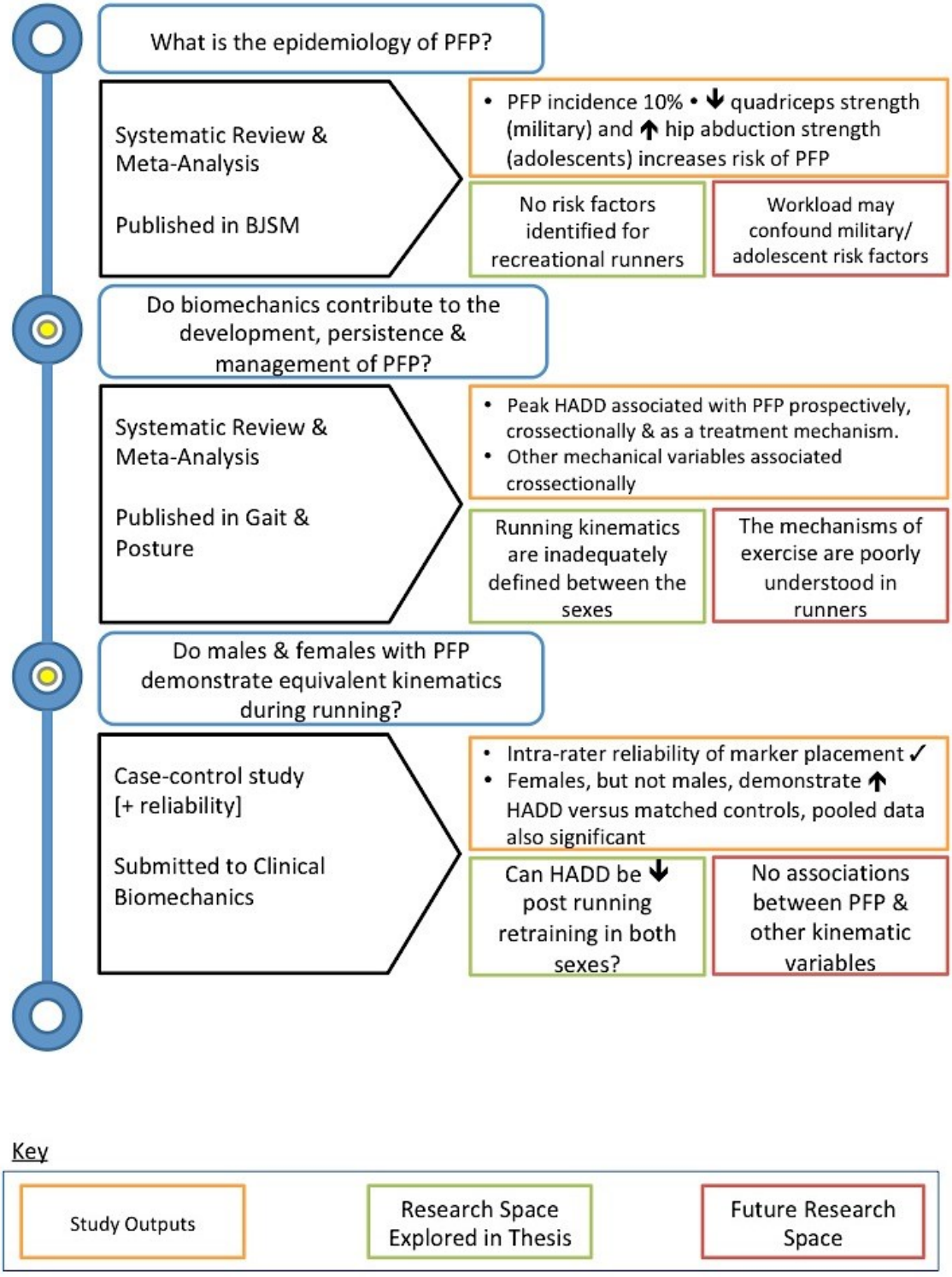
*Running retraining*

Best defined as 'the implementation of any cue or strategy designed to alter an individual's running biomechanics or technique' (89), *running retraining* was also identified to reduce pain and improve function in recreational runners at short-term follow up. Pooled data for the effect of *running retraining* on symptoms resulted in a larger SMD when compared to pooled data for exercise therapy (3.8 [2.7,5.0] versus 1.8 [1.2,2.4]), though the identified level of evidence (limited) was equivalent. As an advantage over exercise therapy, *running retraining* had an apparent kinematic mechanism of effect, being a reduction in peak HADD during running of 5˚. This limited evidence is now supported by two further studies (79, 103), both of which reported short-term reductions in pain, despite again using different forms of feedback (forefoot strike and step rate plus minimalist shoe respectively). The identified larger effect size and potential mechanism of effect lead to the decision to investigate a *running retraining* intervention within the projects forming this thesis.

Figure 79 incorporates the studies designed to completed and achieve the second aim of this thesis into the overall thesis narrative. Having identified associations between running kinematics and PFP persistence, and the effects and biomechanical mechanisms of *running retraining* from pooled data, the third aim of this thesis centered on determining the feasibility, effects and potential biomechanical mechanisms of a step rate intervention in runners with PFP. As there was a clear female bias in the sampling of the previous studies on the topic, and having affirmed the potential for the female sex to influence kinematic outcomes, a mixed-sex cohort was actively sought.

Increasing step rate was chosen as the form of feedback for multiple reasons. It has greater clinical applicability than the direct HADD feedback by Noehren & Willy (100, 101) and a lower potential to result in secondary ankle pain compared to the forefoot strike feedback used by of Roper et al (103). When combined with the use of a minimalist shoe, data from a pilot RCT suggested efficacy of increasing step rate in runners with PFP (79), with further favourable biomechanical changes post-step rate increase reported amongst the observational literature (90). It was yet to be investigated in a manner necessary to meet the requirements of a *running retraining*

intervention described by Davis (107) in a PFP cohort; requiring extrinsic feedback delivery within a faded feedback protocol.




*79. Study, outputs and research space(s) identified by work completed in relation to aim two*

## 8.4. Step-rate retraining and running-related PFP

Determined by investigating recruitment and eligibility and adherence and acceptability, we determined that increasing running step rate appears to be a feasible intervention in a mixed-sex group of runners with persistent PFP. Whilst not anticipated to present a problem for a future efficacy trial, the absence of a control arm in this study prohibited the investigation of randomisation. As a result, we advise that a future efficacy trial commence with a nested pilot study design, allowing for trial cessation should randomisation to a comparative arm prove to be difficult.

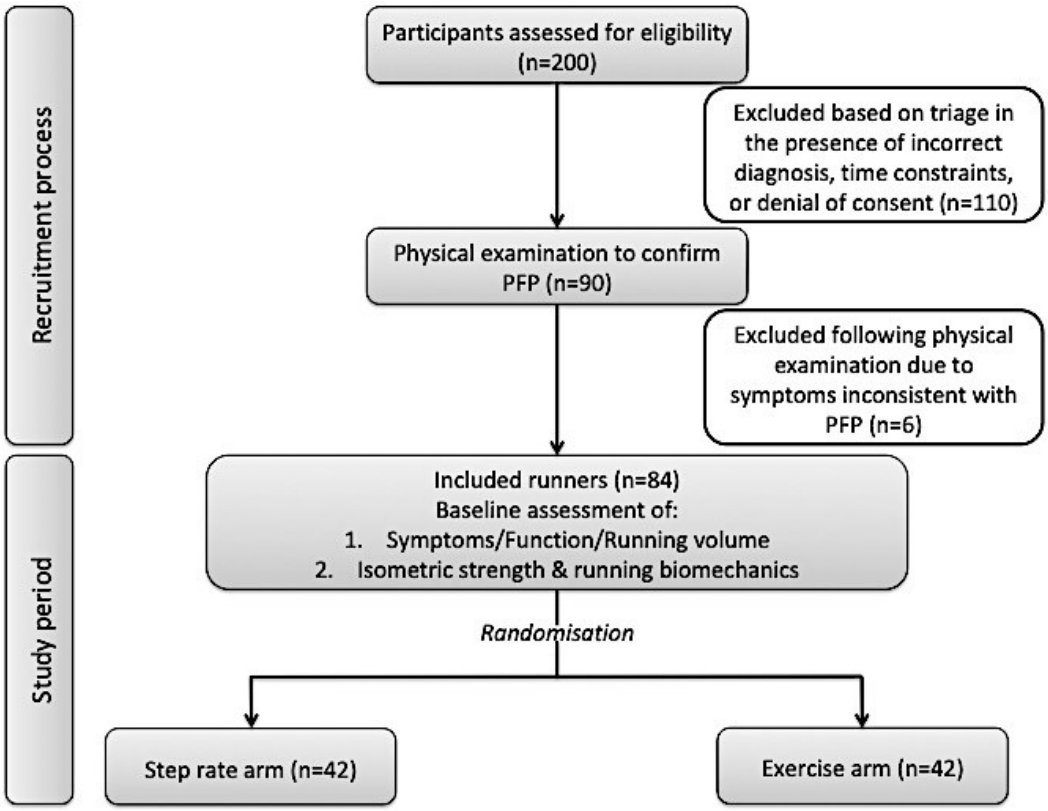
Consistent with the previous *running retraining* literature, we identified that a step rate intervention resulted in a significant reduction in pain at short-term (six-week) follow up. In agreement with the work of Noehren and Willy (100, 101), we also identified a reduction in peak HADD post-retraining, though the difference was small (2.4˚). This was most likely explained by our mixed-sex sample, as the mean difference in peak HADD was consistent with other observational studies completed using asymptomatic, mixed-sex samples (91, 93). Significant reductions in both peak HIR and KFLEX following step rate retraining were also identified. This suggests that the kinematic mechanisms of step rate retraining may exist outside of the frontal plane and should be included in future mechanistic investigations post-*running retraining*.

Female runners with PFP have previously been reported to have delayed gluteal onset relative to foot contact and reduced gluteal activation duration when compared to controls (264). Increasing step rate in an asymptomatic group of runners has previously been reported to result in an earlier onset of lower limb musculature, but have no effect on muscle activity during running stance phase (96). Consistent with the work of Chumanov et al (96), we did not identify any changes to muscle amplitudes during running stance phase post-step rate retraining. Future mechanistic sEMG investigations post-*running retraining* should allow for the analysis of muscle activity relative to kinematic data rather than in isolation, which is a limitation of our work.

Whilst data following step rate retraining add weight to the suggestion of a kinematic mechanism, there are clearly some participants in our small cohort for whom this is not the case. Increasing step rate has been reported to reduce average vertical loading

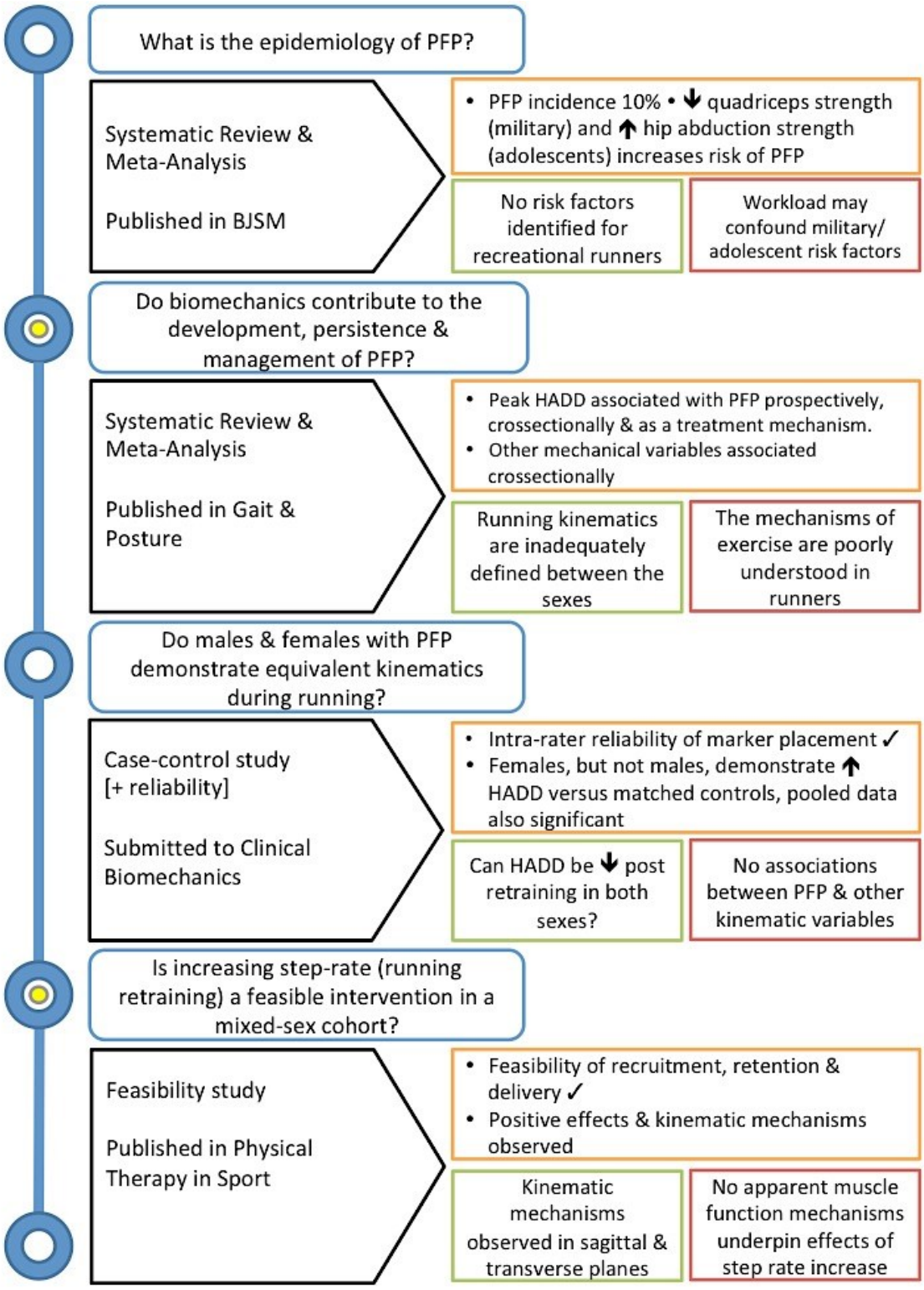
rate (265), a variable which is associated with both injury risk (250) and injury prevention in recreational runners (207). Increasing step rate has also been reported to result in a consequential shift towards a forefoot strike pattern (99), which in turn has been reported to be effective in managing both PFP (103) and exercise induced leg pain (90). There are therefore a plethora of potential mechanisms that may underpin the positive effects observed following step rate retraining, all of which warrant further investigation. Furthermore, expert opinion taken from a mixed methods study with which I was involved, advocates *running retraining* as an intervention for multiple conditions, which future work should seek to explore (90).

Based on the systematic review findings from chapter four and the intervention data reported in chapter six, both exercise therapy and *running retraining* (irrespective of feedback) appear effective in reducing symptoms of PFP at short-term follow up. A future RCT comparing a high quality and clinically replicable exercise therapy intervention with a *running retraining* intervention delivered using a faded feedback protocol is advocated, with a comparative load management education arm similar to that included by Esculier et al (85). Adhering to the suggestion from the international patellofemoral research network (241) that treatment be tailored, it would be desirable to stratify by a specific deficit, such as a low baseline step rate. Secondary analyses could also seek to explore if a strength programme is more effective in participants with true muscle weakness or an education intervention in participants who breach recommended acute:chronic workload ratios. To truly examine this hypothesis of tailored treatment, one could also include treatment arms where the intervention is delivered to participants without said specific deficit, though this would present challenges with stratification and require a significant sample size. Figure 80 depicts a CONSORT diagram for this potential RCT design, using the sample size calculation performed in chapter six using empirical data from this chapter and comparative data from Esculier et al (85).




*80. Potential design for three-arm RCT to investigate optimal management of PFP in recreational runners*

Figure 81 incorporates the study designed and completed to achieve the third aim of this thesis into the overall thesis narrative. Having adequately established feasibility for the future investigation of the efficacy of step rate retraining in a mixed-sex cohort of runners with PFP, there was motivation to further increase the clinical applicability of this potentially impactful intervention. There was preliminary evidence to suggest that a kinematic mechanism may underpin the positive effects of step-rate retraining, and chapters four through six of this thesis identified associations between altered lower limb kinematics and PFP, both with respect to symptom development and persistence. In attempt to increase the clinical applicability of measuring these kinematic variables, the final aim of this thesis was to investigate the accuracy of 2D video gait analysis.




*81. Study, outputs and research space(s) identified by work completed in relation to aim three*

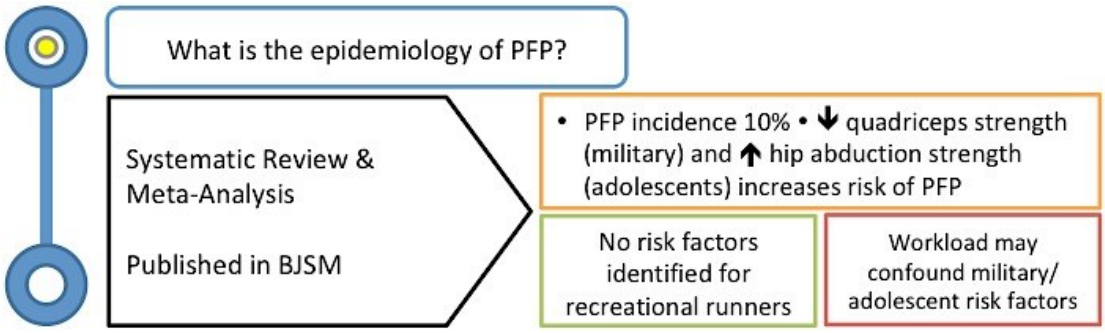
## 8.5. Bridging the gap between laboratory and clinical practice

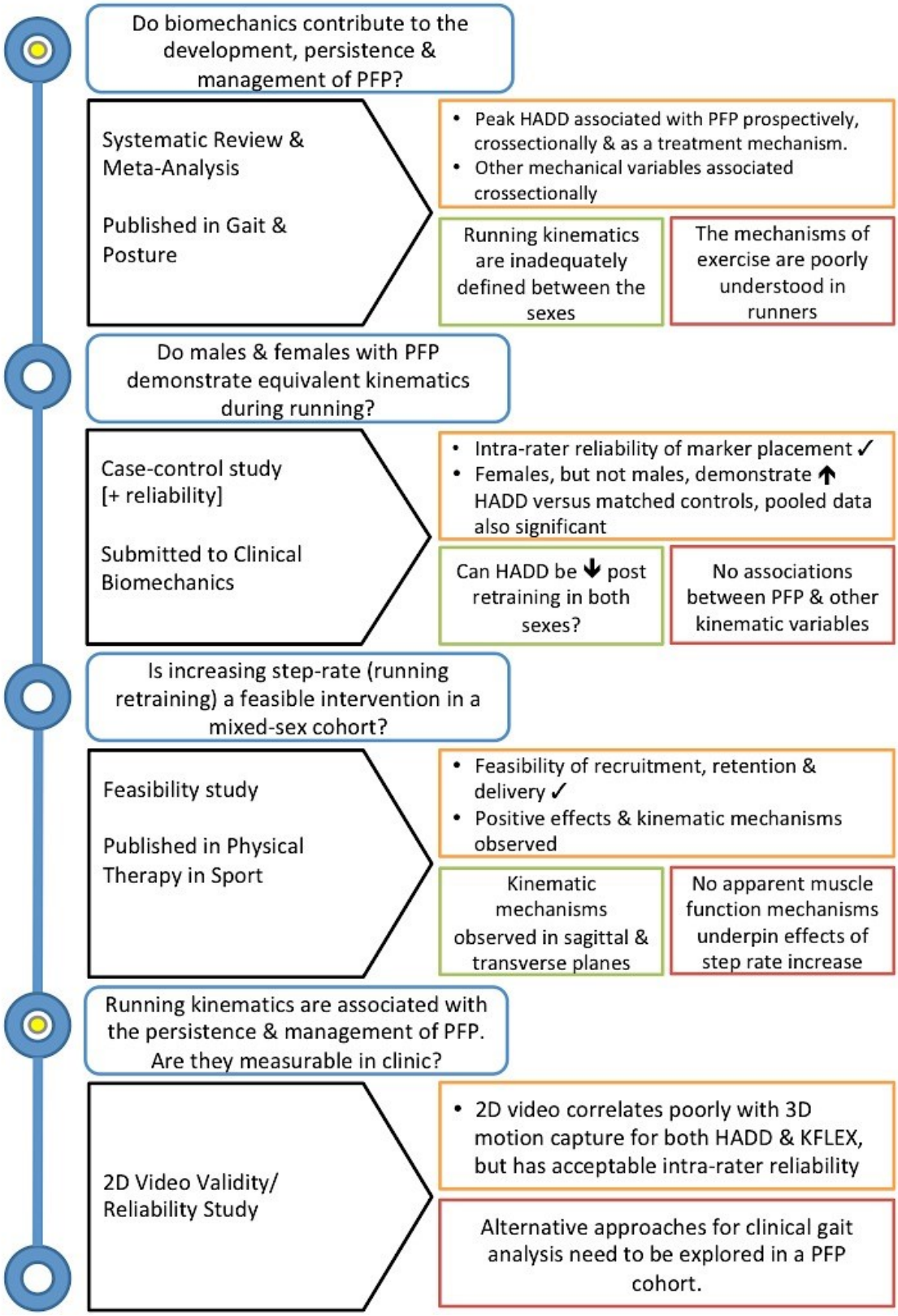
In conflict with the previous 2D video studies that used asymptomatic runners, our investigation identified poor agreement between 3D and 2D kinematic motion analysis

for both peak HADD and KFLEX, despite acceptable intra-rater reliability. This disagreement could simply be explained by our investigation of a cohort of runners with PFP, who we identified to demonstrate more variable running kinematics compared to runners without symptoms (82). However, in an attempt to make this investigation as clinically applicable as possible, there were also differences in 2D video data collection and digitisation that could also account for the identified discrepancies.

Improving upon the clinical applicability of kinematic gait analysis in runners with PFP therefore remains a priority area for further research. A repeat investigation of the treadmill analysis protocol used by Maykut et al (108) in runners with PFP is advocated. This would allow for the frontal plane camera to be much closer to the participant, and should therefore increase the precision of data analysis via increased video footage quality. It is also plausible to investigate the concurrent validity of Kinovea software, as this was recently reported to be both inter- and intra-rater reliable for a variety of running kinematics (236). Until such time, clinicians are advised to exercise caution with their use of 2D video to analyse kinematics in runners with PFP, as collected data may not reflect the gold standard measurement.

Figure 82 incorporates the study designed and completed to fulfill this final aim into the overall thesis narrative.






*82. Study, outputs and research space(s) identified by work completed in relation to aim four*

## 8.6. Conclusions

This thesis had the overarching aim of determining the influence of lower limb biomechanics on the development, persistence and management of PFP in recreational runners. Limited data existed to support the premise that biomechanics influence the development of PFP. Innovative approaches are required to further develop understanding regarding the development of PFP. Multiple associations between PFP and running biomechanics were identified from the cross-sectional literature, with an inability to distinguish cause from effect. Further studies are encouraged to investigate which variables are genuine mediators of either persistent symptoms or treatment effects. For peak HADD, the variable with the strongest association with PFP, it is important that future data be both presented and analysed for the individual sexes, given the potential for data from females to influence outcomes.

Increasing step rate was associated with multiple potential mechanisms. These should be further investigated to determine if the intervention could be tailored to individually determined treatment targets, such as sub-groups defined by baseline activity level or step rate. There remains a clear barrier between laboratory and clinical practice, as the kinematic variables determined to be of interest by this thesis were not accurately measurable using pragmatic 2D video. This needs to be addressed to allow for understanding of the influence of lower limb biomechanics on PFP to fully impact upon the management of PFP in recreational runners.

Overall, optimal management for PFP in recreational runners is yet to be determined. However, increasing step rate appears to be a feasible intervention with indications of efficacy in runners with PFP from both sexes, warranting further appraisal in an efficacy trial. Future studies should also seek to determine if exercise therapy and *running retraining* could be used as a combined intervention, as advocated by the international patellofemoral research network.

This thesis has added to the understanding of PFP epidemiology. It has explored how lower limb biomechanics are associated with both the development (limited evidence) and the persistence (moderate to strong evidence) of PFP in recreational runners. The

impact of the female sex on running kinematics is now better understood and should allow for increased validity in future analyses. This thesis has identified adequate feasibility for a running retraining (step rate) intervention and has prepared the ground for future clinical trials in the field. Finally, the translation of kinematic data into clinical practice has been shown to be warranted.

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# 10. Appendix A: Peer reviewed publication – Risk factors for Patellofemoral Pain: a systematic review and meta-analysis (British Journal of Sports Medicine)

06-Aug-2018

Dear Mr. Bradley Neal,

bjsports-2017-098890.R3 - Risk Factors for Patellofemoral Pain: a Systematic Review and Meta-Analysis

We are pleased to accept your article for publication in the British Journal of Sports Medicine.

Your paper will be now sent for editing and typesetting and you will receive a proof to check in around 10-15 working days; please check your junk mail if you have not received your proof within this time, in case the automatic email goes there.

# 11. Appendix B: Peer reviewed publication – Runners with Patellofemoral pain have altered biomechanics which targeted interventions can modify: a systematic review and meta-analysis (Gait & Posture)

Gait & Posture 45 (2016) 69–82

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## Runners with patellofemoral pain have altered biomechanics which targeted interventions can modify: A systematic review and meta-analysis

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ABSTRACT

Patellofemoral pain (PFP) is the most prevalent running pathology and associated with multi-level biomechanical factors. This systematic review aims to guide treatment and prevention of PFP by synthesising prospective, observational and intervention studies that measure clinical and biomechanical outcomes in symptomatic running populations. Medline, Web of Science and CINAHL were searched from inception to April 2015 for prospective, case-control or intervention studies in running-related PFP cohorts. Study methodological quality was scored by two independent raters using the modified Downs and Black or PEDro scales, with meta-analysis performed where appropriate. 28 studies were included. Very limited evidence indicates that increased peak hip adduction is a risk factor for PFP in female runners, supported by moderate evidence of a relationship between PFP and increased peak hip adduction, internal rotation and contralateral pelvic drop, as well as reduced peak hip flexion. Limited evidence was also identified that altered peak force and time to peak at foot level is a risk factor for PFP development. Limited evidence from intervention studies indicates that both running retraining and proximal strengthening exercise lead to favourable outcomes in both pain and function, but only running retraining significantly reduces peak hip adduction, suggesting a possible kinematic mechanism. Put together, these findings highlight limited but coherent evidence of altered biomechanics which interventions can alter with resultant symptom change in females with PFP. There is a clear need for high quality prospective studies of intervention efficacy with measurement of explanatory mechanisms.


### 1. Introduction

Participation in running has increased in recent years, as a result of the increased awareness of exercise for good health [1]. Although running has been linked to improvements in cardiovascular disease [2], improved mental health [3] and a reduced risk of diabetes [4], it is also associated with a greater incidence of musculoskeletal injury [5]. Dependent on the source [1,6], the overall lower extremity injury incidence is suggested to range from 18% to 92%, with the most significant risk factor for injury being a previous running injury [5]. The most common running overuse injury is patellofemoral pain (PFP), with an incidence of 3–15% in active populations stated amongst the literature [7–9].

The source of symptoms in PFP remains highly debated [10]. A well-established explanatory reason is increased patellofemoral joint stress. Elevated patellofemoral joint stress has been reported in individuals with PFP during fast walking [11] and squatting tasks [12] and is thought to result in afferent nociceptive drive from subchondral bone [13], although it must be stated that the most recent PFP consensus statement highlighted that the source

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of pain in PFP remains unclear [14]. Small changes in patellofemoral joint kinematics, of the order of 5° of femoral internal rotation, have been shown to increase osteochondral shear stress [15], and therefore increased patellofemoral lateral patella facet contact pressures. Increases in vertical loading rates (and subsequent patellofemoral reaction forces) have also been reported in runners with PFP [16]. Therefore, a link between possible biomechanical mechanisms and pain development can be suggested, making such variables of great interest from a treatment mechanism perspective.

The cause of altered kinematics and PFJ stress in PFP is considered multifactorial, with various intrinsic and extrinsic factors thought to contribute. Several kinematic factors, including excessive frontal/transverse plane motion of the lower limb (dynamic knee valgus), have been theorised to increase loading forces acting on the lateral facet of the patella [17]. One previous systematic review summarising literature to 2008 [18] reported that rearfoot eversion, knee external rotation and hip adduction were increased in runners with PFP [18]. However, findings related to hip internal rotation and adduction were reported to be inconsistent, with a paucity of data preventing meta-analysis. Further, a dearth of prospective research at that time prevented conclusions about causal relationships between kinematics and PFP presentation and intervention outcomes [18].

Alongside kinematics, muscle function of the quadriceps and gluteals is thought to play a role in both the development and management of PFP. Reduced knee extension strength has been identified as a risk factor [19]. Additionally, weakness or delayed activation of vastus medialis obliquus (VMO) is also historically described as a risk factor and rehabilitation target for PFP, although recent research has questioned its importance [20]. There is known to be an association between reduced gluteal strength and PFP [21], but the causative relationship of this factor has recently been questioned due to a discrepancy between prospective and cross-sectional findings [21–23].

PFP is often recalcitrant, with as many as 91% of suffers continuing to report symptoms beyond 4 years following diagnosis [24]. This is particularly problematic given the recent suggestion that PFP may be an early stage of a continuum ultimately leading to patellofemoral joint osteoarthritis [25]. Typical exercise interventions (encompassing both the hip and the knee) appear to have a positive effect on pain and function [26–28], but have been reported not to alter running kinematics such as knee valgus linked to PFP [29]. Given that a kinematic mechanism may be required to achieve a long-term resolution in PFP, research surrounding movement feedback interventions and running retraining are starting to be explored [30,31]. Foot orthoses are another intervention which aims to alter lower limb kinematics and have been shown to improve outcomes in PFP patients at 6 weeks follow up, but their long-tem outcomes and place within a multi-modal rehabilitation, particularly in a running population, remains unclear [32].

The aim of this systematic review was to guide the treatment and prevention of PFP by synthesising prospective, observational and intervention studies that measure clinical and biomechanical outcomes in symptomatic running populations. Specific objectives included (i) to establish the biomechanical differences (including kinematics, kinetics and neuromuscular) between individuals with and without PFP in a running population, identifying causal relationships where possible; and (ii) define the biomechanical outcomes of interventions used in the conservative management of PFP. It is anticipated that the impact of this review will be to improve upon the prevention and treatment outcomes of PFP during running by identifying when biomechanical variables should be targeted as part of a management plan, and by what mechanisms these variables may be best approached.

## 2. Methods

The protocol for this systematic review was designed in accordance with the Preferred Reporting of Systematic Reviews and Meta Analysis (PRISMA) statement [33].

### 2.1. Search strategy

MEDLINE, Web of Science and CINAHL were searched from inception until April 2015. The search strategy was limited to publications in the English language and those involving human subjects. Additional hand searching of the reference lists of identified papers and discussions with field experts (e.g. physiotherapists and podiatrists) regarding relevant publications were conducted. A citing reference search was undertaken using Google Scholar.

### 2.2. Eligibility criteria

All studies identified by the search strategy were exported to Endnote version X7 (Thomson Reuters, Philadelphia) by one investigator (PO'H). Adapted from the original review of Barton et al. [18], eligibility criteria applied to manuscript titles were: (i) studies involving male or female subjects with PFP (multiple terms including retropatella pain, chondromalacia or anterior knee pain); (ii) a 3D kinematic, kinetic or EMG outcome measure captured during treadmill or over-ground running; and (iii) prospective, case-control or intervention study design. Exclusion criteria included studies that used 2D methods of kinematic measurement (due to insufficient validity and reliability), studies where data was collected during a task other than running and studies using a case series methodology design. Two authors (BSN and PO'H) reviewed all abstracts to determine eligibility and full texts were screened to confirm eligibility where there was uncertainty from the abstract alone. A third reviewer (CJB) was available for any discrepancies but was not required.

### 2.3. Quality assessment

The Downs and Black Quality Index [34] was used to determine quality for case-control and prospective studies. This is a validiated tool for both randomised and non-randomised control trials, with intra-class correlation coefficients (ICC) of 0.75–0.89 reported [34]. A modified version (scored out of 16), as used by Barton et al. [18] which has been shown to have good inter-rater reliability when grading similar studies was applied. Studies with scores of 11 or greater were considered to be 'high quality' (HQ), studies with scores from 6 to 10 were considered to be 'moderate quality' (MQ) and studies with scores 5 or lower were considered to be 'low quality' (LQ).

The PEDro scale [35] was used to determine the quality of the intervention studies and has been shown to be a valid and reliable tool, with ICC's of 0.68 for consensus ratings [35]. A score of 6–8 on the PEDro scale was considered to be HQ, scores of 4–5 were considered to be MQ and studies that scored below 4 were considered to be LQ, based on the work of Moseley [36].

Two independent raters (BSN and RG), blinded to author details and publication details appraised each study, with any discrepancies resolved at a consensus meeting. Inter-rater reliability was calculated using percentage agreement.

### 2.4. Data management

Data pertaining to study characteristics was extracted from all included studies by one author. This included participant numbers and characteristics of the PFP and control groups, publication details (author, year, and country), biomechanical variables

analysed, examiner details, PFP outcome, duration of study and covariates investigated, for analysis of possible mechanisms (See Tables 1 and 2). Corresponding authors were contacted where appropriate data was not included in the publication and recorded as 'not reported' (NR) if this was unsuccessful. Variables of interest in this review included (but were not limited to) peak hip adduction, internal rotation and flexion, contralateral pelvic drop, rearfoot eversion, peak metatarsal force, patellofemoral joint stress and peak/average gluteal electromyography.

### 2.5. Statistical methods

All statistical analyses were completed in Review Manager 5.0 (The Cochrane Collaboration, Copenhagen, Denmark) initially by one author (BSN) and subsequently checked by a second author during a consensus meeting (CJB). Means and SD's for continuous scaled variables were extracted and used to calculate standardised mean differences (SMD) with 95% confidence intervals (CI's). No dichotomous data was identified in the results of any included study. Data for men and women was analysed independently and directly compared where this breakdown was published, also contributing to the pooled SMD produced where relevant. Meta-analysis was performed where homogeneity between studies was deemed to be adequate and the level of statistical heterogeneity for pooled data was established using $I^2$ statistics (heterogeneity defined as $I^2 > 50\%$, $p < 0.05$) [37]. Calculated individual or pooled SMDs were categorised as small ($\leq$0.59), medium (0.60–1.19) or large ($\geq$1.20) [38].

### 2.6. Evidence based recommendations

Based on the previous work of van Tulder et al. [39], levels of evidence were assigned for each evaluated variable or intervention, incorporating statistical outcomes and the methodological quality of included studies.

#### 2.6.1. Strong evidence:
Pooled results derived from three or more studies, including a minimum of two high quality studies that are statistically homogenous; may be associated with a statistically significant or non-significant pooled result.

#### 2.6.2. Moderate evidence:
Statistically significant pooled results derived from multiple studies that are statistically heterogeneous, including at least one high quality study; or from multiple moderate quality or low quality studies which are statistically homogenous.

#### 2.6.3. Limited evidence:
Results from one high quality study or multiple moderate or low quality studies that are statistically heterogeneous.

#### 2.6.4. Very limited evidence:
Results from one moderate quality study or one low quality study.

#### 2.6.5. No evidence:
Pooled results insignificant and derived from multiple studies regardless of quality that are statistically heterogeneous.

## 3. Results

### 3.1. Search results

The electronic database search yielded 852 citations. After a sequential review of titles, abstracts and full texts, and removal of studies that were not completed using a running population or studies involving two dimensional kinematic analysis, 28 studies were included – 3 prospective studies [40,41,42] 18 case-control studies [43–60] and 7 intervention studies [61–67] (Fig. 1).

### 3.2. Quality assessment of included studies

#### 3.2.1. Prospective/case-control studies
Based on evaluation with the Down's and Black, quality scores ranged from 6 to 14 (out of a maximum score of 16). Of the 21 prospective and case-control studies included in this review, 13 studies were scored as HQ [40,42,43,45,46,48,50–52,56,57,59,60], 8 studies were scored as MQ [41,44,47,49,53–55,58] and no studies were scored a LQ. Inter-rater reliability was calculated using percentage agreement for all prospective and case-control studies and mean agreement was calculated to be 83%. For the 15 items included in the modified Down's and Black evaluation, percentage agreement ranged from 35% to 100%, with a mean of 80%. Item 20, relating to the reliability and validity of the main outcome measures displayed the lowest percentage agreement, with perfect agreement identified for only seven of the included studies.

#### 3.2.2. Intervention studies
Based on evaluation with the PEDro scale, quality scores ranged from 3 to 6 (out of a maximum possible score of 10). Of the seven intervention studies included in this review, two studies were scored as HQ [61,66], four studies were scored as MQ [63–65,67] and one study was classified LQ [62]. Inter-rater reliability was calculated using percentage agreement for all intervention studies and mean agreement was calculated to be 92%. For the 11 items included in the PEDro evaluation, percentage agreement ranged from 71% to 100%, with a mean of 94%. Item 3 concerning similarity at baseline regarding prognostic indicators displayed the lowest

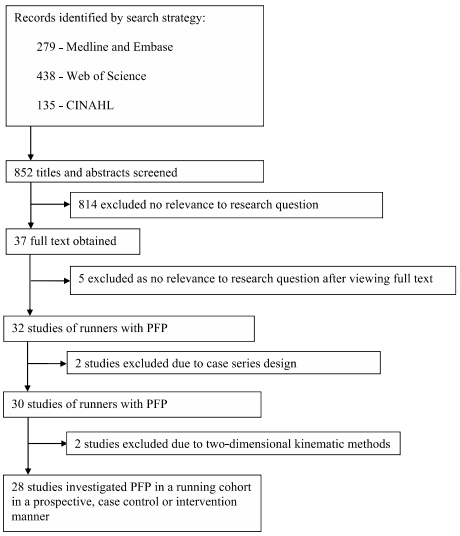


**Fig. 1.** Flow chart detailing the systematic search process as per the PRISMA guidelines.

**Table 1**
Summary of study characteristics for included prospective and cross-sectional studies.

| Study | Study population | Observation period | Injury outcome | Injured | | Control | | Outcome variable(s) |
|---|---|---|---|---|---|---|---|---|
| | | | | Total | Age | Total | Age | |
| Rodrigues et al. [65] (GP) | Heel strike runners | Case-control | Anterior knee pain | 17 | 29.8 ± 7 | 19 | 34 ± 10 | Kinematics |
| Rodrigues et al. [54] (JAB) | Heel strike runners | Case-control | Anterior knee pain | 17 | 29.8 ± 7 | 19 | 34 ± 10 | Kinematics |
| Souza and Powers [57] (JOSPT) | Local orthopaedic clinics | Case-control | Patellofemoral pain | 21 | Not reported | 20 | Not reported | Kinematics, EMG |
| Willson et al. [58] | University and fitness centres | Case-control | Patellofemoral pain | 20 | 21.3 ± 2.6 | 20 | 21.6 ± 4.5 | Kinematics, EMG |
| Besier et al. [48] | Not stated | Case-control | Patellofemoral pain | 27 | 30.5 ± 4.5 (male)<br>28.7 ± 4.6 (female) | 16 | 27.2 ± 3.0 (male)<br>28.8 ± 4.7 (female) | EMG |
| Bazett-Jones et al. [43] | University community | Case-control | Patellofemoral pain | 19 | 26 ± 5.5 | 19 | 24.3 ± 4.3 | Kinematics |
| Cunningham et al. [49] | Recreational runners | Case-control | Patellofemoral pain | 19 | 25.8 ± 6.1 | 11 | 26.5 ± 13.4 | Kinematic coupling |
| Dierks et al. [50] | Recreational runners | Case-control | Patellofemoral pain | 20 | 24.1 ± 7.4 | 20 | 22.7 ± 5.6 | Kinematics |
| Noehren et al. [51] (CB) | Competitive runners | Case-control | Patellofemoral pain | 16 | 27 ± 6 | 16 | 25 ± 4 | Kinematics |
| Noehren et al. [52] (GP) | Recreational runners | Case-control | Patellofemoral pain | 15 | 27 ± 6 | 15 | 25 ± 4 | Kinematics |
| Souza and Powers [56] (AJSM) | Local clinics and university | Case-control | Patellofemoral pain | 19 | 27 ± 6 | 19 | 26 ± 4 | Kinematics |
| Stefanyshyn et al. [40] | Sports medicine clinic | Case-control | Patellofemoral pain | 20 | 34.6 ± 9.8 | 20 | 34.4 ± 10.3 | Kinematics |
| Willy et al. [59,67] | Students and running clubs | Case-control | Patellofemoral pain | 18 | 24.7 ± 4.9 (male)<br>22.2 ± 3.8 (female) | 18 | 23.4 ± 3.6 | Kinematics |
| Willson and Davis [47] | Active females | Case-control | Patellofemoral pain | 20 | 23.3 ± 3.1 | 20 | 23.7 ± 3.6 | Kinematics |
| Wirtz et al. [60] | Recreational runners | Case-control | Patellofemoral pain | 20 | 21.3 ± 2.6 | 20 | 21.6 ± 4.4 | Joint stress |
| Pal et al., [53] | University and sports clinics | Case-control | Patellofemoral pain | 40 | 28.9 ± 4.6 | 15 | 28.2 ± 3.9 | EMG |
| Esculier et al. [46] | Recreational runners | Case-control | Patellofemoral pain | 21 | 34.1 ± 6 | 20 | 33.2 ± 6 | Kinematics, kinetics, EMG |
| Chen and Powers [45] | University and orthopaedic clinics | Case-control | Patellofemoral pain | 20 | 27.9 ± 6.7 | 20 | 26.1 ± 7.2 | Patellofemoral joint reaction forces |
| Thijs et al. [42] | Novice recreational runners | 10 weeks | Patellofemoral pain | 17 | 39.4 ± 10.3 | 85 | 37.6 ± 9.4 | Kinetics – plantar pressures |
| Noehren et al. [41] | Heel strike runners | 2 years | Patellofemoral pain | 15 | 27 ± 10 | 15 | 27 ± 10 | Kinematics |
| Macintyre and Robertson [44] | Recreational runners | Case-control | Patellofemoral pain | 8 | Not reported | 12 | Not reported | EMG |

**Table 2**
Summary of study characteristics for included interventional studies.

| Study | Study population | Intervention period | Injury outcome | Injured | | Control | | Outcome variable(s) |
|---|---|---|---|---|---|---|---|---|
| | | | | Total | Age | Total | Age | |
| Strengthening exercise | | | | | | | | |
| Earl and Hoch [62] | Not reported | 8 Weeks | Patellofemoral pain | 19 | 22.68 ± 17.9 | N/A | N/A | Kinematics |
| Ferber et al. [63] | Recreational runners | 3 weeks | Patellofemoral pain | 15 | 35.2 ± 12.2 | 10 | 29.9 ± 8.3 | Kinematics |
| Orthoses | | | | | | | | |
| Boldt et al. [61] | Recreational runners | Immediate | Patellofemoral pain | 20 | 21.3 ± 2.6 | 20 | 21.6 ± 4.5 | Kinematics |
| Rodrigues et al. [55] | Heel strike runners | Immediate | Anterior knee pain | 17 | 29.8 ± 7.2 | 16 | 34.2 ± 10.9 | Kinematics |
| Running retraining | | | | | | | | |
| Noehren et al. [51,52] | Recreational runners | 2 weeks | Patellofemoral pain | 10 | 23.3 ± 5.8 | N/A | N/A | Kinematics, kinetics |
| Willson et al. [66] | Heel strike runners | Immediate | Patellofemoral pain | 10 | 20.8 ± 3.7 | 13 | 21 ± 2.3 | Joint stress |
| Willy and Davis [29] | Recreational runners | 2 weeks | Patellofemoral pain | 10 | 22.4 ± 5 | N/A | N/A | Kinematics |

percentage agreement, with perfect agreement identified for only five included studies.

### 3.2.3. Study characteristics

Study characteristics are presented in Tables 1 and 2, including recruitment population and participant characteristics to inform upon potential subgroups, observation periods and injury outcomes to inform upon potential recovery timeframes and biomechanical variable(s) to inform upon symptom development and intervention mechanisms.

## 3.3. Case-control

Unless a specific sex is mentioned, results described are in relation to a mixed sex cohort.

## 3.4. Retrospective kinematics (peak)

### 3.4.1. Proximal

There is moderate evidence from seven HQ studies [43,46,50,51,52,57,59] and one MQ study [47] of an association between PFP and increased peak hip adduction ($I^2$ = 84%, small significant SMD 0.37, 0.14–0.59) (see Fig. 2a) and peak hip internal rotation ($I^2$ = 83%, small significant SMD 0.35, 0.14–0.57) (See Fig. 2b). Additionally, moderate evidence from four HQ studies [43,46,51,59] indicates an association between PFP and increased peak contralateral pelvic drop ($I^2$ = 63%, medium significant SMD 0.67, 0.37–0.97) (see Fig. 2c). There is also limited evidence from one HQ study [43] of a significant association between PFP and reduced stance phase peak hip flexion (medium SMD −0.69, −1.32 to −0.06) (See Fig. 2d).

### 3.4.2. Distal

There is strong evidence from two HQ studies [50,51] and one MQ [54] study of no association between PFP and increased peak rearfoot eversion ($I^2$ = 28%, small non-significant SMD −0.03, −0.41–0.35) (See Fig. 3a). There is very limited evidence from one MQ study [55] of a significant reduction in 'minimum time to contact the ankle joint complex range of movement boundary' (an expression of pronation velocity) (medium SMD −0.74, −1.42 to −0.06) in runners with PFP (see Fig. 3b).

## 3.5. Retrospective kinematics (peak): post fatigue

Three HQ studies [43,50,52] investigated the effect of fatigue on lower limb kinematics in runners with and without PFP. Limited evidence from one HQ study [43] indicates an association between increased peak hip flexion (medium SMD 0.76, 0.13–1.40) and runners with PFP in a fatigued state (see Fig. 4a).

When analysing kinematic changes in runners with PFP as a result of fatigue, this same limited evidence of increased peak hip flexion remains (large SMD 1.42, 0.72–2.12) (see Fig. 4b), as well as limited evidence of increased anterior pelvic tilt (medium SMD 1.00, 0.34–1.67) (see Fig. 4c), from the same HQ study [43].

No significant differences were identified post-fatigue for any of the kinematic variables analysed by the above stated three HQ studies [43,50,52].

## 3.6. Retrospective kinematics (peak): male compared to female

Limited evidence from one HQ study [59] indicates that female runners with PFP have significantly increased peak hip adduction (large SMD −1.92, −2.73 to −1.12) in comparison to male runners with PFP (see Fig. 5a). Limited evidence from the same HQ study also indicates that male runners with PFP have significantly increased peak knee adduction (medium SMD 1.17, 0.46–1.89) compared to female runners with PFP (see Fig. 5b). No significant differences were identified for any other kinematic variables investigated, including contralateral pelvic drop or hip internal rotation.

## 3.7. Retrospective kinematics (coupling angle variability)

Coupling angle variability is a measure used to describe the degree of variation of co-ordinated segments, with reduced variability thought to be associated with repetitive use injury development [49]. However, very limited evidence from one MQ study [49] identified a significant association between *greater* kinematic coupling angle variability and runners with PFP in comparison to control, for the following variables: Knee Flexion/Extension and Ankle Dorsiflexion/Plantarflexion at heel strike (medium SMD 0.91, 0.12–1.69); Knee Internal/External Rotation and Ankle Dorsiflexion/Plantarflexion at mid-stance (medium SMD 0.81, 0.03–1.58); Knee Valgus and Ankle Dorsiflexion/Plantarflexion at swing acceleration (medium SMD 1.03, 0.23–1.83); Knee Valgus and Ankle Inversion/Eversion at swing deceleration (medium SMD 1.05, 0.25–1.84); Knee Valgus and Ankle Dorsiflexion/Plantarflexion during the first 40% stance (medium SMD 1.10, 0.30–1.90) and Knee Valgus and Ankle Inversion/Eversion throughout the gait cycle (medium SMD 0.81, 0.04–1.59).

## 3.8. Prospective kinematics (peak)

### 3.8.1. Proximal

Very limited evidence from one MQ study [41] indicates that increased peak hip adduction was predictive of PFP development in female runners (see Fig. 6a), associated with a significant, medium

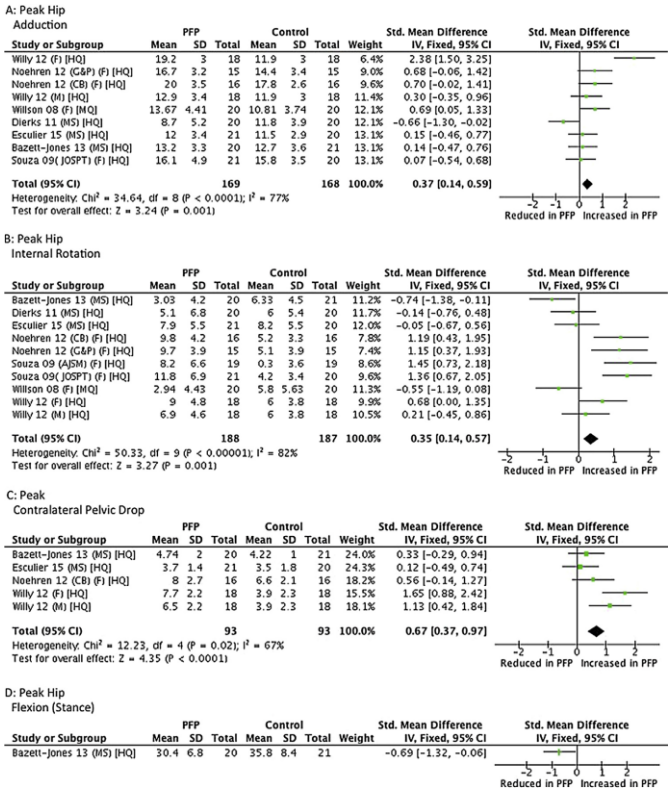


**Fig. 2.** a Forrest plot detailing standardised mean differences for peak hip adduction when comparing runners with PFP to controls. HQ – high quality; MQ – medium quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – gait and posture; CB – clinical biomechanics; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for peak hip internal rotation when comparing runners with PFP to controls. HQ – high quality; MQ – medium quality; LQ – low quality; F – female; M – male; MS – mixed sex; G&P – gait and posture; CB – clinical biomechanics; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. c Forrest plot detailing standardised mean differences for peak contralateral pelvic drop when comparing runners with PFP to controls. HQ – high quality; MQ – medium quality; LQ – low quality; F – female; M – male; MS – mixed sex; CB – clinical biomechanics; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. d Forrest plot detailing standardised mean differences for peak hip flexion when comparing runners with PFP to controls. HQ – high quality; MQ – medium quality; LQ – low quality; F – female; M – male; MS – mixed sex; CB – clinical biomechanics; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

SMD (0.90, 0.38–1.42). No significant links were identified for peak hip internal rotation (SMD 0.25, −0.27 to 0.76) or knee angular impulse (SMD 0.31, −0.52 to 1.15).

### 3.8.2. Distal

Very limited evidence from one MQ study [41] indicates that reduced peak rearfoot eversion is predictive of PFP development in female runners, associated with a small but significant SMD (−0.53, −1.05 to −0.01) (see Fig. 6b).

## 3.9. Retrospective kinetics

Two HQ studies [45,60] investigated the correlation between joint stress or patellofemoral reaction forces and female runners with PFP. Limited evidence of no significant difference was identified for peak patellofemoral joint stress during running from one HQ study [60] (SMD 0.46, −0.17–1.09). Limited evidence of significantly lower patellofemoral reaction force during running in participants with PFP was also identified from one HQ study [45] (large SMD −2.02, −2.79 to −1.24), but a significant increase in patellofemoral reaction force specific to the lateral facet of the patella was also identified in runners with PFP by the same HQ study (large SMD 3.16, 2.20–4.11) (see Fig. 7).

## 3.10. Prospective kinetics

Limited evidence from one HQ study [42] indicates that runners who go on to develop PFP have a significantly higher peak vertical force under the second (medium SMD 0.65, 0.12–1.17) (see Fig. 8a) and third (medium SMD 0.60, 0.07–1.12) (see Fig. 8b) metatarsals and a significantly lower time to peak force underneath the lateral heel (small SMD −0.56, −1.08 to −0.03) (see Fig. 8c).

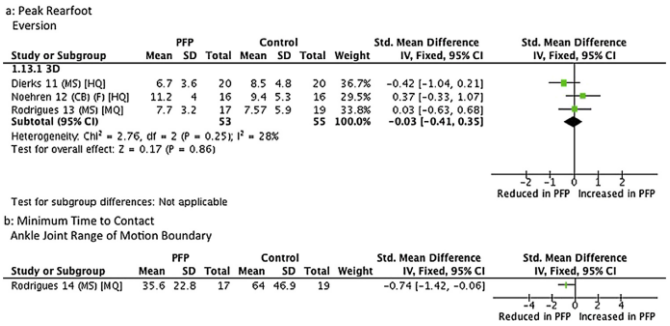


**Fig. 3.** a Forrest plot detailing standardised mean differences for peak rearfoot eversion when comparing runners with PFP to controls. HQ – high quality; MQ – medium quality; LQ – low quality; F – female; MS – mixed sex; CB – clinical biomechanics; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for minimum time to contact ankle range of movement boundary when comparing runners with PFP to controls. HQ – high quality; MQ – medium quality; LQ – low quality; F – female; MS – mixed sex; CB – clinical biomechanics; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

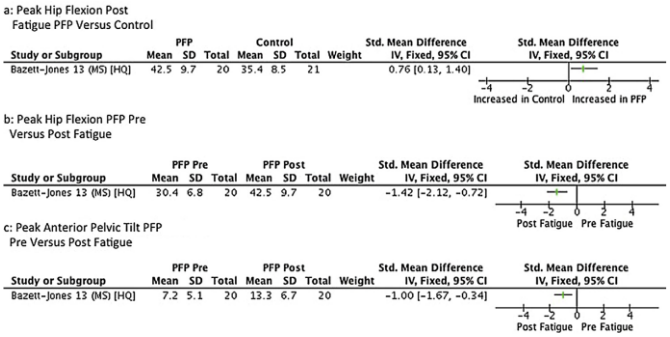


**Fig. 4.** a Forrest plot detailing standardised mean differences for peak hip flexion when comparing runners with PFP to controls when fatigued. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for peak hip flexion when comparing runners with PFP pre and post fatigue. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. c Forrest plot detailing standardised mean differences for peak anterior pelvic tilt when comparing runners with PFP pre and post fatigue. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

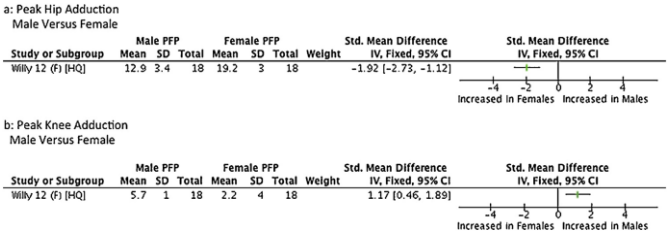


**Fig. 5.** a Forrest plot detailing standardised mean differences for peak hip adduction when comparing males and females with PFP. HQ – high quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for peak knee abduction when comparing males and females with PFP. HQ – high quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

### *3.11. Lower limb EMG*

One HQ study [46] and one MQ study [58] investigated the differences in gluteal muscle EMG in runners with PFP. Very limited evidence from one MQ study [58] was identified that female runners with PFP have significantly lower Gluteus Medius activation duration (medium SMD −0.85, −1.50 to −0.20) (see Fig. 9a) and delayed onset prior to foot contact (medium SMD

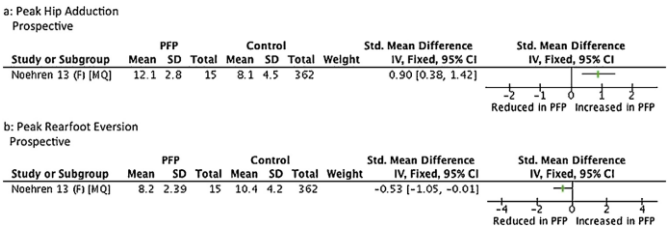


**Fig. 6.** a Forrest plot detailing standardised mean differences for peak hip adduction when comparing runners with PFP to controls prospectively. LQ – low quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for peak rearfoot eversion when comparing runners with PFP to controls prospectively. LQ – low quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

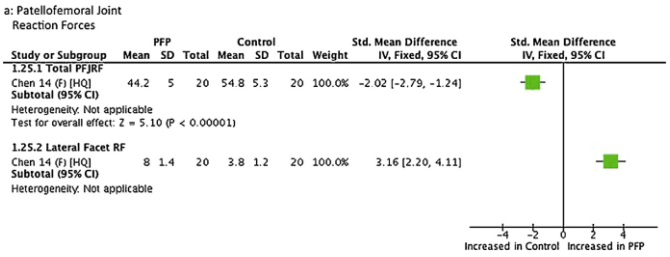


**Fig. 7.** Forrest plot detailing standardised mean differences for patellofemoral joint reaction forces when comparing runners with PFP to controls. HQ – high quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

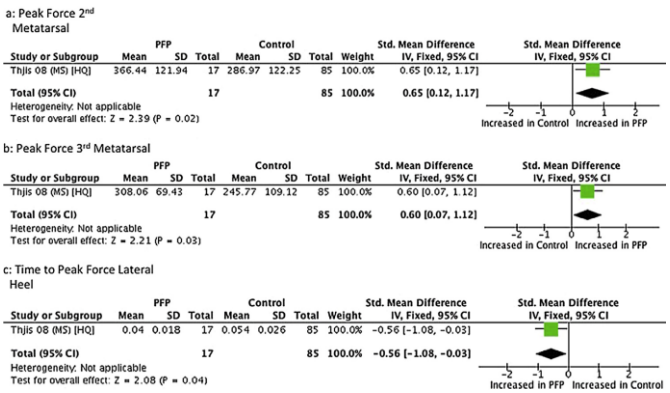


**Fig. 8.** a Forrest plot detailing standardised mean differences for peak force under the 2nd metatarsal when comparing runners with PFP to controls prospectively. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for peak force under the 3rd metatarsal when comparing runners with PFP to controls prospectively. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. c Forrest plot detailing standardised mean differences for time to peak force under the lateral heel when comparing runners with PFP to controls prospectively. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

−0.74, −1.38 to −0.10) (see Fig. 9b). No significant differences were identified for Gluteus Medius peak activation or average activation, or for any of the aforementioned variables for Gluteus Maxiumus from either study [46,58]. Additionally, very limited evidence of no significant differences in timing of VMO activation during running were identified by one MQ study [53], nor VMO peak activation from one HQ study (limited evidence) [46]. Limited evidence from one HQ study [46] was identified that runners with PFP have a greater soleus activation duration (expressed as a percentage of the running cycle) compared to controls (medium SMD 0.68,

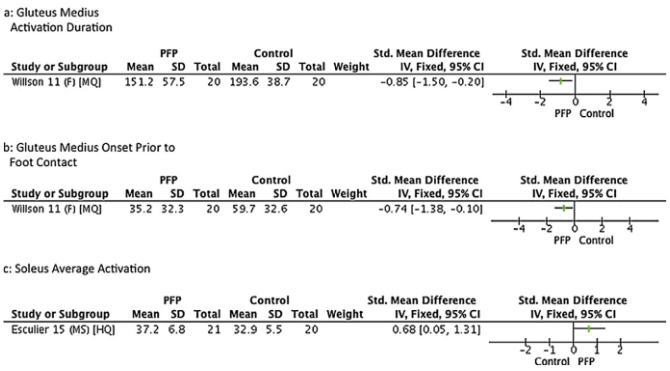


**Fig. 9.** a Forrest plot detailing standardised mean differences for gluteus medius activation duration when comparing runners with PFP to controls. HQ – high quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for gluteus medius onset prior to foot contact when comparing runners with PFP to controls. HQ – high quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. c Forrest plot detailing standardised mean differences for soleus average activation duration when comparing runners with PFP to controls. HQ – high quality; MS – mixed sex; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

0.05–1.31) (see Fig. 9c) but no significant differences were identified for any other muscle group investigated by this study, including the gluteals and quadriceps.

### 3.12. Interventions and their effects

#### 3.12.1. Exercise

Two studies investigated the effects of proximal (hip) strengthening exercise in the management of running-related PFP [62,63], both of which provided data suitable for SMD calculation. There is limited pooled evidence that proximal strengthening exercise can reduce pain (large SMD 1.80, 1.21–2.38) (see Fig. 10a) and very limited evidence that proximal strengthening exercise can improve function (medium SMD 1.16, 0.47–1.86) (see Fig. 10b) in runners with PFP. However, no significant differences were observed for any of the kinematic variables, including hip adduction and internal rotation, rearfoot eversion, knee abduction or genu valgum, with no data pooling being possible.

#### 3.12.2. Running retraining

Three studies investigated the effects of running gait retraining in the management of females with running-related PFP [64,66,67]. Limited evidence from two MQ studies [64,67] indicates that running retraining using either visual display of real-time hip adduction [64], or mirror feedback to reduce hip adduction [67] significantly reduces pain (large SMD 3.84, 2.70–4.98) (see Fig. 11a) and improves function (large SMD 2.16, 1.29–3.03) (see Fig. 11b) at short-term follow up. Limited evidence from the same MQ studies indicates that peak hip adduction during running is reduced post-intervention, associated with a large and significant pooled SMD ($I^2 = 0\%$, $p = 0.72$, large SMD 2.10, 1.30–2.91) (see Fig. 11c). No significant differences were identified for either hip internal rotation or contralateral pelvic drop at short-term follow up. No significant differences in patellofemoral joint kinetics were identified from one HQ study using metronome cadence retraining (±10% from baseline) [66], but a trend towards significance for vertical impact peak was identified from one MQ

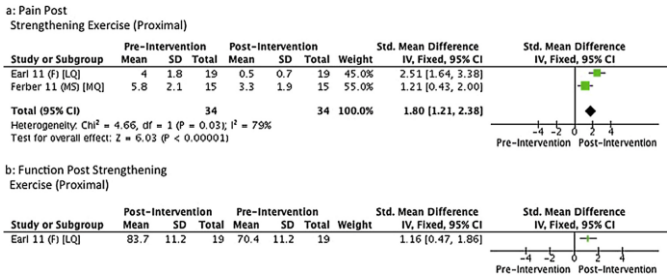


**Fig. 10.** a Forrest plot detailing standardised mean differences for pain when comparing runners with PFP pre and post strengthening exercise. MQ – medium quality; LQ – low quality; MS – mixed sex; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for function when comparing runners with PFP pre and post strengthening exercise. MQ – medium quality; LQ – low quality; MS – mixed sex; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

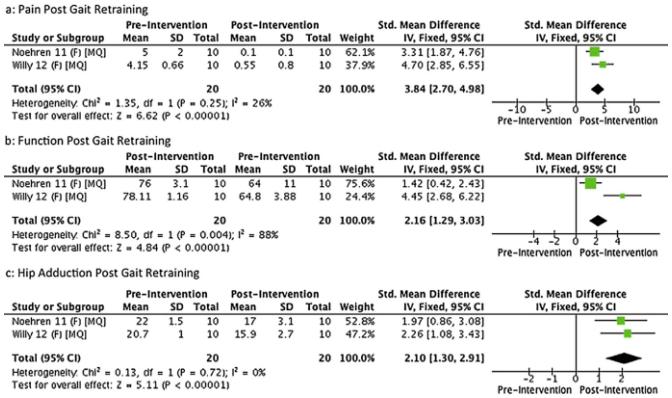


**Fig. 11.** a Forrest plot detailing standardised mean differences for pain when comparing runners with PFP pre and running retraining. MQ – medium quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for function when comparing runners with PFP pre and running retraining. MQ – medium quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain. b Forrest plot detailing standardised mean differences for peak hip adduction when comparing runners with PFP pre and running retraining. MQ – medium quality; F – female; SD – standard deviation; IV – inverse variance; PFP – patellofemoral pain.

study using real-time visual feedback to reduce peak hip adduction [64] (medium SMD 0.91, −0.02 to 1.84).

### 3.13. Orthoses

Two studies [61,65] investigated the kinematic effects of orthoses in runners with PFP, one of which [65] provided data suitable for SMD calculation. Neither study concurrently reported the effects of orthoses on either pain or function. Limited evidence from one MQ study [65] indicates that peak rearfoot eversion is reduced in runners with PFP following orthoses intervention, associated with a significant medium SMD (0.79, 0.29–1.29). There is also limited evidence from the same MQ study that orthoses intervention reduces peak ankle joint complex velocity (medium SMD −0.70, −1.20 to −0.20) and increases the ankle joint angle at foot strike (medium SMD 0.64, 0.14–1.14), with both variables expressions of pronation velocity.

## 4. Discussion

This systematic review identified very limited evidence that increased peak hip adduction is a risk factor for PFP development in female runners, which can be modified with symptomatic benefit using running retraining. Increased peak hip adduction in runners with PFP is further supported by moderate cross-sectional evidence. Additionally, significant associations of PFP with increased peak hip internal rotation and contralateral pelvic drop, and a reduction in peak hip flexion were identified in both female and mixed-sex PFP populations. An association was also identified between PFP and both delayed and shorter Gluteus Medius activation duration in female runners. There are, therefore, clear outcomes from this systematic review relevant to clinicians treating runners with PFP.

Current findings related to the biomechanical effects of conservative interventions for management of runners with PFP indicate running retraining and proximal strengthening exercise both reduce pain. Running retraining was also found to reduce peak hip adduction; an established risk factor for PFP development [41], and this biomechanical change may provide a mechanistic explanation for running retraining effectiveness. Conversely, this review indicates that biomechanical mechanisms explaining the therapeutic effects of proximal strengthening exercise remain unclear. Foot orthoses were found to reduce peak rearfoot eversion, however without concurrent reporting of their effects on symptoms, it remains unclear if this kinematic mechanism can explain previously reported positive clinical outcomes [69–71].

## 5. Biomechanics associated with PFP during running

Very limited evidence that increased peak hip adduction was a risk factor for PFP development in female runners was identified [41], a finding supported by moderate cross-sectional evidence indicating greater hip adduction in individuals with existing PFP [43,46,47,50,51,52,57,59,68]. Additionally, meta-analysis revealed moderate evidence of greater peak hip internal rotation [43,46,51,50,52,57,59,68] and contralateral pelvic drop [43,46,50,51,59] in individuals with PFP. Whilst hip adduction in both female and male symptomatic subjects was found to be greater than controls, limited evidence was identified that females with PFP may possess greater peak hip adduction in comparison to males with PFP, with males found to have significantly greater knee adduction in one study [59]. Considering that previous prospective research linking greater hip adduction to risk of PFP development was limited to a female population, future prospective research should include both sexes and sub-group them to establish if different biomechanical risk profiles exist in relation to the hip.

Distally, very limited evidence was identified that reduced peak rearfoot eversion was a risk factor for PFP [41], which was inconsistent with strong evidence from pooled cross-sectional findings that identified no association between peak rearfoot eversion and PFP during running [50,51,54]. It should be highlighted that two studies [72,73] which were excluded for 2D methods of quantifying rearfoot eversion do suggest that increased rearfoot eversion is associated with PFP. However, quantification of 2D rearfoot motion is known to have a measurement error up to 4° [74], whilst the between group

differences from these studies were below this figure (0.5° [72] and 3.1° [73]). Inclusion of these studies could have biased the findings of this review towards a false positive for this variable, hence their exclusion.

Limited evidence of both greater peak force under the 2nd and 3rd metatarsals, as well as a shorter time to peak force under the lateral heel were identified as risk factors for PFP in runners [42]. Thijs et al. [42] suggested that the increased forces described above could indicate a reduction in pronation, consistent with findings from Noehren et al. [41], and thus reduction in shock attenuation at the foot during the loading phase of gait, with potential transfer of ground reaction forces to proximal structures such as the patellofemoral joint [75]. When considering these limited findings in light of greater navicular drop being reported as a risk factor for PFP [7,76] and evidence supporting the prescription of foot orthoses designed to control foot pronation [69–71], it is clear the relationship between foot biomechanics and PFP is poorly understood at this time.

The influence of fatigue on kinematics was highlighted as an under-researched area by the 2014 PFP consensus statement [14]. Limited evidence identified that when fatigued, runners with PFP demonstrate greater peak stance phase hip flexion in comparison to controls and greater peak hip flexion and anterior pelvic tilt in comparison to their pre-fatigue state [43]. This may indicate runners with PFP increase both trunk flexion and limb compliance throughout a period of running, possibly as a result of fatigue [77,78], or in an attempt to reduce PFJ stress [79]. Interestingly, moderate evidence indicates that the differences in hip adduction, internal rotation and contralateral pelvic drop between runners with PFP when compared to asymptomatic runners is no longer present once in a fatigued state [43,50,52]. It is important to note that the kinematics of runners with PFP do not change (e.g. reduced hip adduction) when fatigued, but rather the kinematics of asymptomatic runners become more akin to those with PFP (i.e. increased hip adduction). This suggests that runners with PFP demonstrate biomechanical features causally related to PFP from early in a run whereas those without pain only demonstrate these features when fatigued and likely close to finishing their run. This manifestation of injurious biomechanics from the initiation of high load exercise may be an important factor leading to symptom development.

Electromyographic investigations have yielded limited evidence of shorter, and delayed, activation prior to foot contact of Gluteus Medius is present in runners with PFP, whilst no significant differences were identified for Gluteus Maximus [58]. Impaired gluteal function may partially explain altered kinematics in runners with PFP. Supporting this notion is work by Willson et al. [58], which identified a correlation between gluteus medius activation delay at foot contact and increased hip adduction excursion. Limited evidence of no differences in VMO activity were identified by this review [46,53], which is in support of previous analyses that VMO impairment is highly variable, present in some individuals with PFP but also highly prevalent amongst asymptomatic individuals [80].

Limited evidence identified a significant increase in patellofemoral reaction forces specific to the lateral facet of the patella during running [45], but no difference in peak total patellofemoral joint stress [60]. These findings related to stress are inconsistent with other tasks evaluated in the literature, which indicates greater PFJ stress in individuals with PFP during walking [11] and squatting [12]. It is plausible that it is not the total joint stress or reaction force, but spatially concentrated reaction forces leading to shear stress in specific patellofemoral joint facets, that may be responsible for symptom development [45]. Another explanation may be variations in modelling approaches used. Wirtz et al. [60], who provided running data for this review, suggest a possible underestimation of PFJ stress in their analyses, with an absence of transverse plane kinematics in their modelling, which may explain the inconsistent findings. Importantly, hip internal rotation has been reported to contribute significantly to patellofemoral joint stress [15]. Given the significant association between increased peak hip internal rotation and PFP identified by this review, further investigation to allow for greater understanding of joint stress and its mechanism on PFP development is warranted.

## 6. Biomechanical effects of interventions

Limited evidence indicates running retraining and proximal strengthening exercise both achieve improvements in pain and function in runners with PFP at short-term follow up. When evaluating the biomechanical effects and mechanisms for symptomatic improvement from running retraining, a significant reduction in peak hip adduction up to 3 months following a 2-week running retraining intervention was identified [64,67]. However, findings from this review indicate no kinematic changes following exercise intervention [62,63], indicating benefits may be derived by other mechanisms such as limb stiffness changes or nociceptive input processing alterations. Findings from Earl and Hoch [62] provide some possible biomechanical explanation for the benefits of exercise rehabilitation in runners with PFP, reporting a significant reduction in peak internal knee abduction moments following an 8 weeks proximal strengthening program, although the data extracted did not produce a significant SMD for this variable in the current review. Regardless, these changes to knee joint moments may be of potential clinical relevance and should be considered in future investigations.

Whilst no definite mechanism have yet been identified to explain the efficacy of proximal strengthening exercise in reducing running-specific PFP, it is possible that changes to both instantaneous and average loading rates can be achieved alongside positive clinical outcomes, identified in a recent study by Esculier et al. [81]. It is essential however, to realise that this study was multimodal in nature, encompassing exercise, advice on load management and training error, as well as instruction to alter running cadence and foot strike patterns. Therefore, these positive effects cannot be solely attributed to any one of these interventions in isolation, but the developing hypotheses about loading rates certainly warrant further investigation.

Foot orthoses are known to have positive effects on pain and function in individuals with PFP [69–71], but do not improve outcomes when combined with multi-modal physiotherapy [70]. The exact mechanism by which foot orthoses exert therapeutic effects is unclear, with several different paradigms outlined in the literature to explain the observed effects. This review identified limited evidence for a small reduction in both peak rearfoot eversion and peak ankle joint complex velocity with the prescription of medially posted foot orthoses designed to reduce rearfoot eversion [61,65]. Interestingly, this approach to prescription, which is similar to approaches with therapeutic supporting evidence [69–71], conflicts with findings suggesting that reduced rearfoot eversion may be a risk factor for PFP development [41]. However, as concurrent measures of pain or function were not taken in these biomechanical orthoses studies [61,65], the clinical relevance of these findings as potential mechanisms is unclear. Interestingly, research has suggested that rearfoot kinematic changes do not correlate well with pain reduction [82] or reduced tissue loads/demands [83], which potentially suggests that the modification of kinetic parameters may be of greater relevance to symptom change. However, the kinetic effects of foot orthoses in runners with PFP are currently unclear due to a paucity of research, indicating this is an area of research requiring attention.

## 7. Clinical implications

The findings of this review indicate that peak hip adduction may be a modifiable risk factor for PFP in female runners. Based on the data included in this meta-analysis, results also suggest that a change in hip adduction of 5° post-intervention could be considered clinically meaningful, with these changes associated with marked reductions in running-related pain [64,67]. Recent evidence has emerged that 2D video movement analysis demonstrates good intra-rater reliability and acceptable concurrent validity with respect to detailed three-dimensional movement analysis, but currently only for hip adduction measurement [84]. As such there is a useful, readily accessible assessment tool when managing runners with PFP. It may be that future work on new methods for 2D measurement will improve reliability of measurement for variables such as rear-foot motion, which would yield a very useful clinical tool. Additionally, previous research also indicates functional tasks such as single leg small knee bend or single leg step down may provide an indication of hip adduction during running [85], indicating possible valuable clinical correlates in clinical settings where running cannot be easily assessed.

Both running retraining and proximal strengthening exercise have been reported to improve pain and function [62–64], but may have different effect mechanisms based on the findings of this review. Considering this, it is possible that a combination of the two interventions could lead to superior results. Considering the positive clinical outcomes identified for running retraining to reduce hip adduction, other running retraining strategies aimed at altering mechanics related to PFP may also be effective. For example, cadence manipulation has recently shown positive clinical outcomes in the management of tibial stress fractures [86] and has also shown favourable changes to patellofemoral joint forces [87] and lower limb joint mechanics [88] in normative cohorts. These additional running modification strategies may be positively augmented by proximal muscle training undertaken in a parallel fashion.

## 8. Limitations and future research

Some limitations must be considered when interpreting findings of this review. Not all studies provided data that allowed effect size calculation and subsequent potential for inclusion in meta-analysis. To address this, attempts to obtain data from corresponding authors were made, however, this did not prove successful in all instances, meaning some findings could not be considered when making conclusions and recommendations.

Common themes of methodological limitation were identified during the quality assessment process. For the prospective and case-control studies, only one study [42] ensured that their sample was representative of the entire recruitment population (failing to adequately state population source and subsequent participation percentages), only six studies reported reliability of their outcome measures [41,42,52,56,57,59] and no studies attempted to blind those measuring the main outcome measures in the case-control studies. Similar themes were identified for the intervention studies, where all studies failed to blind either subjects or raters to groupings and no randomisation was performed, although it should be recognised that this was due to the absence of a control group in the design.

The presence of just one HQ [42] and two MQ [40,41] prospective studies highlights a dearth of research to differentiate between cause and effect, and addressing this should be a priority for future work. Subsequent prospective or cross-sectional studies of the biomechanics of runners with PFP should focus on variables that have been found to be associated with the condition. Future prospective or cross-sectional investigation is warranted for peak hip internal rotation, hip flexion, contralateral pelvic drop, anterior pelvic tilt, gluteal EMG, joint stress and plantar pressures.

Only one cross-sectional study [59] provided a breakdown of kinematics for the individual sexes and only five studies [43,46,48,50,54] utilised a genuine mixed-sex cohort. This means that applying kinematic findings of this review to male runners with PFP requires particular caution. Future studies investigating cohorts involving both sexes with enough participants to complete between sex comparisons are needed to better understand biomechanics associated with PFP in males.

The clinical outcomes for running retraining can currently only be discussed relative to a short-term follow up (maximum 3 months) and future studies should seek to establish if these outcomes extend to a long-term follow up, with a minimum of 12 months suggested to meet the Cochrane Group guidelines [89]. Running retraining has not been evaluated in relation to a control group and this is essential to determine the efficacy of the intervention. Positive clinical outcomes are known to extend to long term follow up for proximal strengthening exercise [27], but this needs to be confirmed in a running specific population, alongside an analysis of potential mechanisms. This should also be a priority for future research, alongside establishing if a combined running retraining and exercise intervention yields superior results to either intervention in isolation. The recent best practice guide for PFP [32] has outlined strong efficacy for both tailored patella taping and bracing in relation to short-term pain relief in conjunction with multi-modal physiotherapy. The biomechanical effects of these interventions have not been investigated in a running population and this would be a positive direction for future studies to take. Intervention using orthoses during running needs to be examined in conjunction with assessment of both symptoms and function, to determine the clinical efficacy of this intervention in a running cohort.

## 9. Conclusion

The quantity and quality of published literature concerning lower limb running biomechanics and the relationship to PFP has progressed markedly since the last systematic review on the topic, enabling more varied and stronger conclusions to be drawn. These conclusions relate to both symptom development and maintenance, as well as potential explanatory mechanisms for treatment effects. Very limited prospective evidence indicates that increased peak hip adduction is a risk factor for PFP development in female runners; in addition to limited evidence that running retraining changes both symptoms and function via a likely kinematic mechanism of reduced peak hip adduction. This is supported by moderate evidence from cross-sectional research in mixed sex cohorts, with a correlation also identified between PFP during running and increased peak hip adduction, internal rotation and contralateral pelvic drop. Further prospective research is needed to clarify if these relationships are of a causal or associative nature, and therefore better target interventions aimed at treatment and prevention. Limited evidence also indicates that proximal strengthening exercise changes both symptoms and function at short-term follow up, but currently potential biomechanical mechanisms are unclear. Further research to establish long-term efficacy for running retraining and an improved understanding of potential mechanisms for proximal strengthening exercise is needed.

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## Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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# 12. Appendix C: Translational publication – Running retraining in the management of patellofemoral pain (Physio First In Touch Journal)

# Running retraining in the management of patellofemoral pain

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**Running is becoming increasingly popular as a form of general exercise and so, for clinicians, the prevention and management of running injuries, and patellofemoral pain (PFP) in particular, is an ongoing challenge. This article explores the options for intervention and retraining runners in order to reduce the instances of injury and PFP.**

**Learning outcomes**

1. Understand the established evidence base behind running retraining as an intervention for PFP.
2. Identify the differing mechanisms behind the varied forms of feedback used in running retraining interventions.
3. Understand the potential dual role for both running retraining and rehabilitative exercise.

## Introduction

Despite the growing popularity of running as a form of exercise, it remains associated with a high incidence of musculoskeletal injury (Saragiotto *et al* 2014). Patellofemoral pain is, depending on the literature cited, the most common running-related musculoskeletal condition, affecting up to 15% of runners (Hetsroni *et al* 2006; Callaghan & Selfe 2007; Boling *et al* 2009). While the source of pain in PFP can be heavily debated, a well-established explanation is increased joint stress, as a result of altered patellofemoral kinematics (Davis *et al* 2010; Liao *et al* 2015). Given that exercise interventions designed to improve altered running kinematics have proven ineffective (Willy & Davis 2011), strategies by way of internal or external feedback, known as "gait retraining", are starting to be explored (Agresta & Brown 2015; Napier *et al* 2015).

## Running retraining

At present, just two observational trials (Noehren *et al* 2011, Willy *et al* 2012) have investigated the effects and mechanisms of running retraining in PFP specific cohorts. Both studies identified significant improvements in pain, measured with a visual analogue scale, and function, measured with the lower extremity functional index in female runners at short-term follow-up. The mechanism attributed to these positive effects was a reduction in peak hip adduction, which was significantly reduced in both studies.

The limitation of these quality observational trials is the mechanism of feedback used. Noehren *et al* (2011) employed a method of feedback based around a live display of peak hip adduction, whereas Willy *et al* (2012) used multiple mirror feedback and cueing to reduce peak hip adduction. While the external feedback methods used in both of these studies is known to be more effective than internal feedback for facilitating skill acquisition (Wulf *et al* 2010), both methods used here have a significant lack of clinical carry-over.

A more clinically viable form of external feedback is increasing step rate or cadence via audio metronome, which has been evaluated to a degree in relation to PFP. One high quality observational trial (Willson *et al* 2014) investigated the immediate effects of cadence increase using external metronome feedback in both asymptomatic and PFP runners. A significant reduction in patellofemoral joint stress was identified in both groups, both in relation to stress per step and stress per mile. Unfortunately, no concurrent measures of pain or function were taken in this study, most likely due to the immediate nature of the data collection and, at present, it is not known if this reduction in patellofemoral joint stress will result in associated reductions in pain or improvements in function. This positive finding is supported by a more recent piece of observational research (Willy *et al* 2015) which identified that 7.5% cadence increase, cued via audio metronome, significantly reduced both peak hip adduction and vertical loading

rates, factors known to be associated with PFP development and maintenance (Davis *et al* 2010; Noehren *et al* 2013).

## Is there a role for barefoot running?

Switching to barefoot running is often suggested by clinicians and academics alike as a potential means to reduce running injury rates (Hall *et al* 2013). A recent, high quality observational laboratory study (Bonacci *et al* 2014) investigated patellofemoral specific kinetic and kinematic outcomes achieved when switching to barefoot running, using a cohort of asymptomatic runners. A 12% reduction in patellofemoral joint stress was achieved in the barefoot condition, attributed to a reduction in stride length, an increase in baseline cadence and a reduced peak knee flexion angle at mid-stance of running (Bonacci *et al* 2014). Another observational laboratory study (McCarthy *et al* 2015) has also identified positive changes to hip kinematics when comparing barefoot to shod running.

Despite this positive finding, it must be highlighted that equivocal reductions in patellofemoral joint stress and favourable changes to hip kinematics have been shown to be achievable with a 10% increase in cadence alone (Heiderscheit *et al* 2011; Lenhart *et al* 2014).

The limitation of all of these findings is that they come from asymptomatic populations but, given that a secondary increase in injury may occur with a switch to barefoot running (Murphy *et al* 2013), and that clear clinical guidance for the use of barefoot running as a feedback tool remains absent (Hall *et al* 2013), other forms of external feedback should be advocated for the majority of runners before suggesting a switch to barefoot running.

## Where does this place rehabilitative exercise?

It must be highlighted that the two intervention studies investigating the effects and mechanisms of rehabilitative exercise in runners with PFP also yielded significant improvements in pain and function at short-term follow up (Earl & Hoch 2011; Ferber *et al* 2011). Although a reduction in peak knee abduction moment was identified by one of these studies (Earl & Hoch 2011), no other significant biomechanical mechanisms were identified. It is becoming clear that, while rehabilitative exercise is an effective management strategy for PFP especially when targeting muscles proximal to the hip (Lack *et al* 2015), no apparent mechanisms of effectiveness can be suggested.

It is possible that in a running population, a programme of rehabilitative exercise leads to a reduction in vertical loading rates (Esculier *et al* 2015), although this has only been shown when rehabilitative exercise was combined with advice and education on training error, and instruction to change cadence and foot strike pattern (Esculier *et al* 2015). However, it is certainly plausible that a combination of gait retraining and proximal exercise may lead to superior clinical outcomes, and the authors would suggest that this should become a future research priority.

## Conclusion

Patellofemoral pain is a challenging condition to treat, particularly in the running population. Selecting an intervention that targets appropriate mechanisms is, therefore, of paramount importance. The early positive outcomes of gait retraining appear to be the result of a kinematic mechanism, targeting the primary risk factor for PFP development, established among the literature. As such a mechanism has not been determined for rehabilitative exercise, it can be suggested that gait retraining should be the primary intervention when managing running-specific PFP. However, this must not detract from the positive effects of rehabilitative exercise when managing PFP on the whole, and a combination of interventions may well bring about superior clinical outcomes.

## About the author

Bradley is a physiotherapist and clinical academic. He is a lower quadrant specialist, taking an interest in knee pathology, tendinopathy and overload conditions. Bradley began his PhD studies at Queen Mary University, London, in April 2014, investigating the effects and mechanisms of running retraining in the management of PFP. He combines his research and clinical roles with regular teaching.

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# 13. Appendix D: Peer reviewed publication – The effects & mechanisms of increasing running step rate: a feasibility study in a mixed-sex group of runners with patellofemoral pain (Physical Therapy in Sport)

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Original Research

## The effects & mechanisms of increasing running step rate: A feasibility study in a mixed-sex group of runners with patellofemoral pain

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ABSTRACT

*Objectives:* To explore feasibility of recruitment and retention of runners with patellofemoral pain (PFP), before delivering a step rate intervention.
*Design:* Feasibility study.
*Setting:* Human performance laboratory.
*Participants:* A mixed-sex sample of runners with PFP (n = 11).
*Main outcome measures:* Average/worst pain and the Kujala Scale were recorded pre/post intervention, alongside lower limb kinematics and surface electromyography (sEMG), sampled during a 3 KM treadmill run.
*Results:* Recruitment and retention of a mixed-sex cohort was successful, losing one participant to public healthcare and with kinematic and sEMG data lost from single participants only. Clinically meaningful reductions in average (MD = 2.1, $d = 1.7$) and worst pain (MD = 3.9, $d = 2.0$) were observed. Reductions in both peak knee flexion (MD = 3.7°, $d = 0.78$) and peak hip internal rotation (MD = 5.1°, $d = 0.96$) were observed, which may provide some mechanistic explanation for the identified effects. An increase in both mean amplitude ($d = 0.53$) and integral ($d = 0.58$) were observed for the Vastus Medialis Obliqus (VMO) muscle only, of questionable clinical relevance.
*Conclusions:* Recruitment and retention of a mixed sex PFP cohort to a step rate intervention involving detailed biomechanical measures is feasible. There are indications of both likely efficacy and associated mechanisms. Future studies comparing the efficacy of different running retraining approaches are warranted.



### 1. Introduction

Recreational running positively influences cardiac (Petrovic-Oggiano, Damjanov, Gurinovic, & Glibetic, 2010), metabolic (Williams, 2014) and mental (Ghorbani et al., 2014) health. Despite the reported benefits, recreational running is reported to bring about an increased risk of musculoskeletal pain (Saragiotto et al., 2014; van Gent et al., 2007). Overall incidence of musculoskeletal pain amongst recreational runners ranges from 19% to 94% (van Gent et al., 2007), with patellofemoral pain (PFP) thought to be the most common (Taunton et al., 2002). Specific annual incidence of PFP amongst recreational runners ranges from 4% to 21%, (Noehren, Hamill, & Davis, 2013; Ramskov, Barton, Nielsen, & Rasmussen, 2015; Thijs, Van Tiggelen, Roosen, De Clercq, & Witvrouw, 2007), with overall prevalence in sports medicine facilities suggested to be 17% (Taunton et al., 2002).

Running biomechanics has been reported to be a risk factor for,

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and associated with, running related PFP. Specifically, peak hip adduction during running has been reported to be significantly higher in female runners who develop subsequent PFP when compared to those who remain asymptomatic (Neal, Barton, Gallie, O'Halloran, & Morrissey, 2016; Noehren et al., 2013). In addition, based on our recent meta-analysis (Neal et al., 2016), peak hip adduction, peak hip internal rotation and contralateral pelvic drop are also significantly higher in runners with PFP when compared to asymptomatic controls. For neuromuscular function, females with PFP have been reported to have delayed gluteal muscle onset prior to foot contact and shorter gluteal muscle activation duration compared to asymptomatic controls (Willson, Kernozek, Arndt, Reznichek, & Scott Straker, 2011).

At present, evidence suggests that exercise interventions, whilst effective at reducing symptoms in runners with PFP in the short-term, do not result in full symptom resolution (Earl & Hoch, 2011; Ferber, Kendall, & Farr, 2011). Moreover, exercise may not derive its effects by way of a kinematic mechanism, as multiple studies have demonstrated that exercise programs designed to increase hip strength do not alter running kinematics reported to be associated with PFP (Earl & Hoch, 2011; Sheerin, Hume, & Whatman, 2012; Willy & Davis, 2011; Wouters et al., 2012). This brings into question the ability of an exercise intervention to provide long-term resolution to running related PFP, as it fails to target factors known to be associated with the development and persistence of the condition. It is this premise that originally led to the development of what has been termed running retraining (Heiderscheit, 2011), or more specifically 'the implementation of any cue or strategy designed to alter an individual's running technique' (I. Davis, 2005).

Reports from observational studies, involving visual and verbal cues to reduce peak hip adduction, indicates running retraining may reduce pain and improve function in female runners with PFP who demonstrate more than 20° peak hip adduction during running (Neal et al., 2016; Noehren, Scholz, & Davis, 2011; Willy, Scholz, & Davis, 2012). The key limitation of this work is that the results can only be extrapolated to a minority of runners with PFP (i.e. females with high peak hip adduction). In addition, a recently completed randomised controlled trial (RCT) has established efficacy for cues to transition from rearfoot to forefoot strike in combination with a load management running program in a mixed-sex, but again a predominantly female, cohort (Roper et al., 2016). The limitation of this study is that cues to transition to a forefoot strike are only applicable to those who rearfoot strike at baseline. Additionally, it is thought that such a change to running mechanics may also be injurious by virtue of the increase in Achilles tendon load that is observed with forefoot strike running compared to rearfoot strike running (Rice & Patel, 2017). This is reinforced by the fact that 25% (2/8) of the runners in this RCT who transitioned to a forefoot strike pattern reported ankle soreness at follow up (Roper et al., 2016).

It has been reported that cues to increase running step rate do not increase Achilles tendon load (Lyght, Nockerts, Kernozek, & Ragan, 2016) and thus may be a more widely applicable running retraining option to those previously studied. A recent feasibility study has reported that a step rate increase of 10% combined with running in a minimalist shoe was superior to foot orthoses at reducing pain and improving function at 12 week follow up in runners with PFP (Bonacci, Hall, Saunders, & Vicenzino, 2017). An increase in step rate of 10% has also been reported to favourably alter patellofemoral joint stress in both runners with PFP and asymptomatic runners, (Willson, Sharpee, Meardon, & Kernozek, 2014), though the actual reduction in step length reported was much greater (14%). In addition, no evaluation of symptoms could be reported in this study due to the limitation of the cross-sectional, observational design. Observational work in asymptomatic runners also indicates that more modest increases in running step rate of 5% or 7.5% may still reduce peak hip adduction (Heiderscheit, Chumanov, Michalski, Wille, & Ryan, 2011; Willy et al., 2015), albeit of a smaller magnitude.

A recent three-arm RCT (Esculier et al., 2017) found that a running retraining intervention to increase step rate was no more effective than education focused on load management, or compared to the same education combined with exercise therapy in runners with PFP. Whilst no treatment group had superior outcomes, the step rate intervention did result in significant reductions in both worst and running specific pain. All three groups remained symptomatic at the primary end point (20 weeks), and running-related pain was higher (2.5/10) in the step rate group compared to previous studies where hip adduction (0.5/10) (Noehren et al., 2011; Willy et al., 2012) and strike pattern (1.0/10) (Roper et al., 2016) has been targeted. This could be explained by the absence of a faded-feedback protocol to facilitate the retraining intervention (Irene Davis, 2017), which has been found to be effective by previous studies (Noehren et al., 2011; Roper et al., 2016; Willy et al., 2012).

The primary aim of this study was to investigate the feasibility of a pragmatic running retraining intervention, by cueing a 7.5% increase in running step rate using a faded feedback protocol. Specific objectives included (i) the recruitment of an appropriate number of both males and females from a clinical population and (ii) the collection of both symptom and function data to determine an estimate of the effects derived from the intervention. The secondary aim was to investigate the potential kinematic and muscle function mechanisms explaining any effects induced by the intervention.

## 2. Methods

### 2.1. Participants

Ethical approval for this study was granted by the Queen Mary Ethics of Research Committee (QMREC2014/63). All participants provided written informed consent prior to study commencement. Participants were recruited from local sports medicine clinics. Sample size was based on the apriori power analysis conducted by the authors of the previous work on running retraining (Noehren et al., 2011; Willy et al., 2012), leading to a total of 10 participants being sought. Participants were of either sex, currently or previously running a minimum of 10 km/week and aged between 18 and 45 years. To be included, participants were required to have atraumatic retropatellar or peripatellar pain during running and one other activity described by the most recent PFP consensus document, which includes squatting, stair ambulation and jumping (Crossley et al., 2016). Patellofemoral symptoms needed to be rated at a minimum of three (out of a maximum of 10) using a numerical rating scale (NRS). Potential participants with patellofemoral instability, previous surgery, tibiofemoral pathology or any pathology (musculoskeletal or otherwise) that precluded running participation were excluded.

### 2.2. Experimental protocol

Included participants were required to present to the Human Performance Laboratory at Queen Mary University of London. In the presence of bilateral symptoms, the knee that scored highest on the numerical rating scale was analysed. In the presence of equivocal symptoms, the dominant limb that would be used to kick a ball was analysed (Willy et al., 2012). Both limbs were not entered into the analysis in the presence of bilateral symptoms given the potential

for type I error (Menz, 2005). Prior to data collection, participants completed the Kujala Scale as a subjective measure of function (Kujala et al., 1993). The Kujala Scale is a 13-question appraisal of subjective function in those with PFP, with a score of 100 representing no symptoms and a score of 0 indicating complete disability. Participants were also required to rate their average and worst pain in the past week from 0 to 10 using an NRS. Whilst there is no definitive outcome measure for use with a PFP cohort, the NRS and Kujala Scale are reported to be the most valid and responsive measures for detecting change at time of study commencement (Crossley, Bennell, Cowan, & Green, 2004).

### 2.3. Kinematic measures

Participant movement data were collected during running using a four-camera, infrared motion analysis system (CX-1, Codamotion, Charnwood Dynamics Limited, Leicestershire, UK) (Lack et al., 2014). 24 infrared markers, consisting of eight individual markers and four rigid clusters of four markers, were placed on standard pelvic and lower limb anatomical landmarks using the CAST protocol (Cappello, Cappozzo, La Palombara, Lucchetti, & Leardini, 1997). Markers from the pelvis frame to the knee joint centre tracked the thigh segment and markers from the knee joint centre to the ankle joint centre tracked the shank segment. Individual markers were applied using double-sided adhesive tape and secured with transparent surgical tape, with the rigid clusters applied using adjustable elastic straps and secured with cohesive self-adherent bandage. Virtual markers were also identified on the femoral epicondyles and the ankle malleoli, to allow for the calculation of relevant joint centers during an upright standing trial. The hip joint centre was estimated as a projection within the pelvis frame using the methods described by Bell et al. (Bell, Pedersen, & Brand, 1990) and did not vary between male and female subjects. The knee joint centre was estimated as the midpoint between the femoral epicondyle markers.

Participants were asked to run in their usual running shoes and self-select their typical 'steady state' running speed on the laboratory treadmill (Kistler Gaitway, Kistler Group, Winterthur, Switzerland). Participants were instructed to run for a total of 3 km, with the option to cease if symptoms increased to four or greater on the NRS. 10 s of data sampled at 200 Hz were collected at 0.8/1.8/2.8 km, with distance as opposed to time chosen to act as a constant measure across a cohort of participants running at differing speeds. Multiple data collections were completed to increase reliability of gait analysis (Monaghan, Delahunt, & Caulfield, 2007). Based on between group differences identified in our recent meta-analysis (Neal et al., 2016), variables of interest included peak hip adduction, internal rotation and flexion, peak knee flexion and contralateral pelvic drop, given their retrospective association with PFP.

### 2.4. Electromyography measures

Surface muscle electromyography (sEMG) were collected simultaneously with the kinematic data using a wireless Delsys TRIGNO system (DELSYS Inc., Natick, Massachusetts, USA). Prior to application, participant's skin was marked, shaved and cleaned with an alcohol swab. Self-contained bipolar electrodes were placed at the motor points of the Gluteus Maximus (GMAX), Gluteus Medius (GMED), Semitendinosus (ST) and Vastus Medialis Obliqus (VMO) adhering to SENIAM guidelines (Hermens, Freriks, Disselhorst-Klug, & Rau, 2000). 10 s of sEMG data sampled at 1926 Hz were collected at three specific distance points as described above, but were not synchronised to the kinematic data.

### 2.5. Running retraining intervention

Participants completed 18 retraining sessions over the course of six weeks. Each week involved a total of three individual runs, equating to 18 runs in total. For the first four weeks, the initial run was completed in a supervised fashion with the primary investigator (BSN). During the retraining sessions, participants were cued via an audio metronome set at 7.5% above their baseline step rate (calculated during data acquisition), based on the previous work of Willy et al. (Willy et al., 2015). The additional two runs each week were completed independently. A faded feedback protocol successfully used previously was adopted (Noehren et al., 2011; Willy et al., 2012). Feedback exposure was gradually reduced and treadmill run time was gradually increased from 10 min to 30 min (see Fig. 1), to facilitate skill acquisition. A slower progression from 10 to 30 min was used (18 sessions over six weeks) compared to previous work (8–10 sessions over two to four weeks), to better adhere to contemporary training progression approaches (Gabbett, 2016). Further, this pace of progression is used clinically in the chosen recruitment centre, minimising ethical issues from varying usual care. For the final two weeks, all completed sessions were performed independently, without any metronome feedback. All data were collected prior to, and after completion of, the running retraining intervention.

### 2.6. Kinematic data analysis

Data were analysed offline using a custom written Matlab program (version 2015, Mathworks, Natick, Massachussets, USA). Initial foot contact and toe off were identified using the heel marker on the calcaneal tuberosity and the metatarsal marker on the fifth metatarsal head in the vertical (Z) plane. Consistent with previously described methods, initial foot contact was defined as the point at which the heel marker ceased its descent in the vertical plane (Zeni, Richards, & Higginson, 2008). Toe off was identified using a combination of the heel and metatarsal markers. Specifically, peak acceleration of the metatarsal marker was identified within a specific time point defined by the 70% or greater of the absolute maximum velocity region of the heel marker (Zeni et al., 2008). All kinematic data were aligned to initial foot contact, interpolated and normalised to percentage of stride cycle (0% = initial contact, 100% = terminal stance) to facilitate data analysis. Clinical relevance of kinematic data was interpreted with reference to the minimum detectable change data reported by Noehren et al. (Noehren, Manal, & Davis, 2010)

### 2.7. sEMG data analysis

sEMG data were processed using an in-built band-pass filter from 25 to 500 Hz. Raw sEMG data were decomposed using wavelets (Reaz, Hussain, & Mohd-Yasin, 2006). Post-wavelet decomposition, data were cut into strides using the mean total wavelet power of the VMO muscle, as the typical activation pattern of this muscle (onset/offset) during running is known to align closely to the initial contact (onset) and toe off (offset) phases of running gait (Flynn & Soutas-Little, 1993). These stride cycle timings were then applied to all sEMG data. Pre and post retraining data were cut into strides independently, but were not used to describe sEMG data as though it were synchronised to the true kinematic gait cycle of the participant. As participants are unlikely to reach signal intensity akin to maximal voluntary isometric contraction (MVIC) during steady state running, data were normalised to the mean of the peak dynamic signal intensity across a single set of strides (0.8 km trial, pre-retraining), which has been reported to be more valid than normalizing to maximal dynamic signal peak (Bolgla & Uhl, 2007).

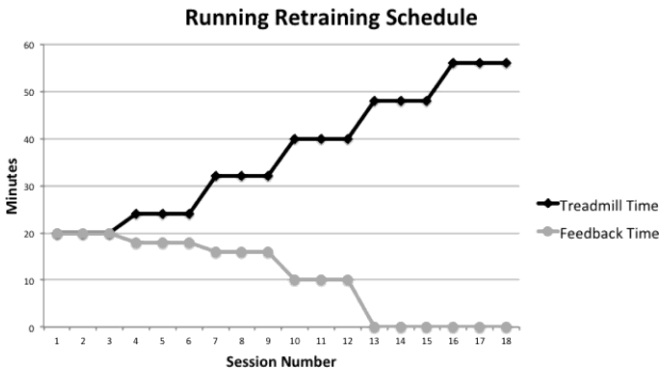


**Fig. 1.** Running retraining schedule depicting the faded feedback protocol employed.

### 2.8. Statistical analysis

All statistical testing were performed offline using Microsoft Excel (Microsoft Corporation, Albuquerque, New Mexico, USA). A Cohen's *d* was calculated to determine the size of all identified interactions, alongside the reporting of mean differences and 95% confidence intervals (CI). Cohen's *d* was interpreted as small (≤0.2), medium (>0.5) and large (>0.8) respectively (Sullivan & Feinn, 2012). As a feasibility study, not powered apriori to detect statistical significance, dependent sample *t-tests* were not performed and p-values for differences not reported because of the potential for type II error and to avoid giving the impression of there being robust findings from a feasibility study design. The main outcomes were those of recruitment, retention and measurement feasibility.

## 3. Results

A total of 10 (out of 11) participants (four male, six female) completed the study. One female participant was lost to follow up due to a switch of care provision to the National Health Service. Demographics and baseline characteristics of the participants who completed the study are described in Table 1.

### 3.1. Effects

Large reductions in both average ($d = 1.7$) and worst ($d = 2.0$) pain were identified post-retraining. The mean difference (MD) of these reductions was 2.1 and 3.9 NRS points respectively and individual participant worst pain responses to the retraining intervention ranged from 1 to 8 NRS points (see Fig. 2). A modest improvement in function, measured with the Kujala Scale, was also identified ($d = 0.12$), with a mean difference of 4.4 points.

**Table 1**
Participant characteristics.

| Variable | Mean (SD) |
|---|---|
| Sex (Male/Female) | 4/6 |
| Age (Years) | 31.6 (5.5) |
| Height (cm) | 170.6 (7.8) |
| Mass (kg) | 67.7 (9.8) |
| Symptom duration (Months) | 45.1 (32.1) |
| Average run volume (km) | 17.0 (9.8) |
| Step rate (SPM) | 163.6 (4.7) |
| Kujala scale | 86.4/100 (6.9) |
| Average NRS | 3.0/10 (1.6) |
| Worst NRS | 6.8/10 (1.5) |

Key: cm = centimeters; kg = kilograms; km = kilometers; SPM = steps per minute; NRS = numerical rating scale.

### 3.2. Mechanisms

#### 3.2.1. Spatiotemporal

An increase in running step rate at six weeks follow up was observed, with a mean increase of 7.8% (range 2.3%–11.1%). 3 participants did not achieve a step rate of ≥7.5% post retraining.

#### 3.2.2. Kinematics

One participant was found to have consistently corrupted marker data throughout their trials and was therefore removed from the kinematic analysis. This resulted in a kinematic sample of nine participants (five females, four males). Moderate reductions in both peak knee flexion (MD = 3.7°, $d = 0.78$) (see Fig. 3a) and peak hip adduction (MD = 2.4°, $d = 0.54$) (see Fig. 3b) were identified post-retraining. A large reduction in peak hip internal rotation was also identified post retraining (MD = 5.1°, $d = 0.96$) (see Fig. 3c). A full breakdown of the kinematic analysis can be seen in Table 2 and individual participant spatiotemporal and kinematic responses in relation to average/worst pain at six-week follow up are presented in Table 3.

#### 3.2.3. sEMG

One participant was found to have consistently corrupted sensor data throughout their trials and was therefore removed from the sEMG analysis. This resulted in a sEMG sample of 9 participants (6 females, 3 males). A mean of peak muscle amplitudes, in addition to an integral (amplitude x duration) of each decomposed signal were calculated for each muscle pre and post retraining. For mean amplitude, minimal changes post-retraining were identified for GMAX ($d = 0.02$), GMED ($d = 0.07$) and ST ($d = 0.05$). However, for VMO, an increase in mean amplitude was observed post-retraining, associated with a medium effect size ($d = 0.53$, 95% CI -0.09, 0.03). For muscle integral, a similar interaction was identified, with minimal changes seen post-retraining for GMAX ($d = 0.04$), GMED ($d = 0.04$) and ST ($d = 0.09$). For VMO, an increase was observed, associated with a medium effect size ($d = 0.58$, 95% CI -0.06, 0.02).

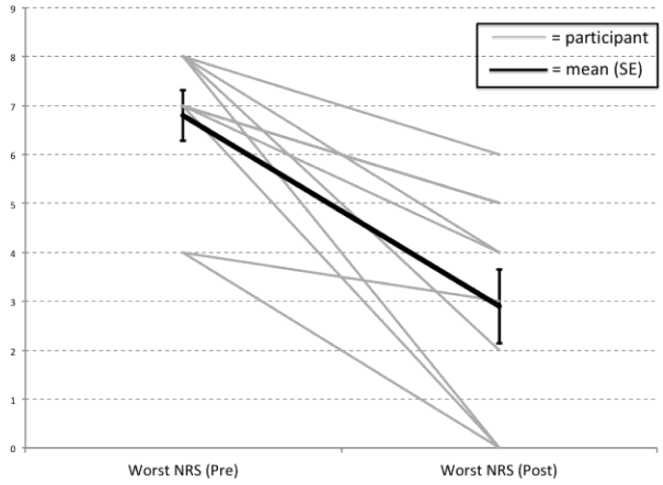


**Fig. 2.** Mean pooled and individual worst pain responses at baseline (pre) and six weeks follow up (post).

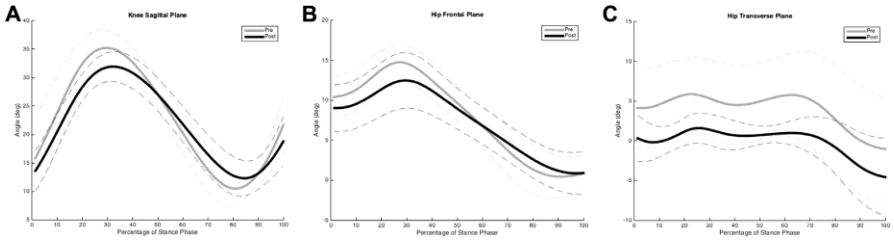


**Fig. 3.** a: Mean pattern of hip knee flexion throughout stance at baseline (pre) and six week follow up (post). Knee flexion is positive. Solid line = mean. Dashed line = 95% confidence intervals. b: Mean pattern of hip adduction throughout stance at baseline (pre) and six week follow up (post). Hip adduction is positive. Solid line = mean. Dashed line = 95% confidence intervals. c: Mean pattern of hip internal rotation throughout stance at baseline (pre) and six week follow up (post). Hip internal rotation is positive. Solid line = mean. Dashed line = 95% confidence intervals.

**Table 2**
Pre and post retraining means, standard deviations, mean differences, 95% confidence intervals and effect sizes.

| Variable | Pre Mean (SD) | Post Mean (SD) | Mean Difference | 95% CI | Cohen's *d* |
|---|---|---|---|---|---|
| Average Pain | 3.0/10 (1.6) | 0.90/10 (0.9) | 2.1 (*) | 0.88, 3.32 | 1.7 |
| Worst Pain | 6.8/10 (1.5) | 2.9/10 (2.3) | 3.9 (*) | 2.08, 5.72 | 2.0 |
| Kujala Scale | 86.4/100 (6.9) | 90.8/100 (5.4) | 4.4 | −10.22, 1.42 | 0.1 |
| Peak KFLEX | 36.2° (5.3) | 32.5° (4.2) | 3.7° | −1.08, 8.48 | 0.78 |
| Peak HFLEX | 26.7° (9.3) | 23.1° (4.9) | 3.6° | −3.83, 11.03 | 0.51 |
| Peak HADD | 15.6° (3.5) | 13.2° (5.4) | 2.4° | −2.15, 6.95 | 0.54 |
| Peak CLPD | 4.3° (2.7) | 2.8° (2.4) | 1.5° | −1.05, 4.05 | 0.59 |
| Peak HIR | 9.1° (7.7) | 4.0° (2.9) | 5.1° (*) | −0.71, 10.91 | 0.96 |

Key: (*) = mean difference exceeds MDC; SD = standard deviation; CI = confidence interval; HADD = hip adduction; HIR = hip internal rotation; CLPD = contralateral pelvic drop; KFLEX = knee flexion; HFLEX = hip flexion.

## 4. Discussion

The results of this study suggest that a faded feedback protocol to increase running step rate by 7.5% is feasible in a clinical setting. A mixed sex cohort was successfully recruited and a low dropout rate (n = 1) was achieved. Furthermore, potential clinically relevant changes in both average and worst pain were identified post-retraining, suggesting that the intervention has potential efficacy

**Table 3**
Individual participant kinematic, spatiotemporal and symptom responses to retraining.

| Participant | Peak KFLEX at Follow Up | Peak HADD at Follow Up | Peak HIR at Follow Up | Peak KFLEX at Follow Up | Baseline Step Rate | Step Rate % Increase | Average Pain at Follow Up (x/10) | Worst Pain at Follow Up (x/10) |
|---|---|---|---|---|---|---|---|---|
| 1 | ↓ | ↓ | ↓(*) | ↓ | 160 | 11.1% | 1 | 6 |
| 2 | ↓(*) | ↓(*) | ↓(*) | ↓(*) | 172 | 2.3% | 2 | 5 |
| 3 | ↓ | ↓(*) | ↓(*) | ↓ | 168 | 7.7% | 0 | 0 |
| 4 | ↓(*) | ↓(*) | ↓(*) | ↓(*) | 164 | 8.9% | 0 | 3 |
| 5 | ↓ | ↑(*) | ↓(*) | ↓ | 168 | 7.7% | 0 | 0 |
| 6 | ↓ | ↓(*) | ↑ | ↓ | 164 | 8.9% | 2 | 2 |
| 7 | ↑ | ↑ | ↓(*) | ↑ | 164 | 5.7% | 0 | 0 |
| 8 | ↓(*) | ↓(*) | ↑ | ↓(*) | 158 | 10.2% | 1 | 4 |
| 9 | ↑ | ↓ | ↑(*) | ↑ | 158 | 6.0% | 2 | 4 |

Key: (*) = difference exceeds MDC; HADD = hip adduction; HIR = hip internal rotation; KFLEX = knee flexion; A-NRS = average pain; W-NRS = worst pain.

and warrants further appraisal in an adequately powered RCT.

The mean reductions in both average and worst pain seen within this study are smaller than those identified by previous running retraining studies (Noehren et al., 2011; Roper et al., 2016; Willy et al., 2012), although no inference on average or worst pain as individual outcomes were made by these studies and the feedback employed was different. Further, both this feasibility study and the referenced works were essentially underpowered for all but the most preliminary of conclusions. When analysing the reductions in worst pain from this study, only 3/10 participants were asymptomatic at six-week follow up and just one participant had pain ≤3/10. This means that the 6 remaining participants would continue to be eligible for inclusion into a clinical trial using currently accepted criteria (Crossley et al., 2016), meaning that the intervention could be defined as unsuccessful in 60% of our cohort if using worst pain as the primary outcome.

A recent high quality RCT identified that a 7.5% step rate increase, with the option of transitioning to a forefoot strike pattern if deemed necessary, was no more effective than comparative education or exercise interventions (Esculier et al., 2017). When comparing the symptom reductions achieved in this study (6 week follow up) to the relevant time point in the Esculier et al. RCT (8 week follow up) (Esculier et al., 2017), both average and worst VAS are comparable for our step rate intervention compared to all 3 intervention groups (education, exercise plus education, running retraining plus education). It could be suggested that running retraining is in fact a form of load management or graded exposure, which may explain why it was found to be no more effective than education on training loads by Esculier et al. (Esculier et al., 2017) However, Roper et al. (Roper et al., 2016) reported efficacy of retraining from rearfoot to forefoot strike running. Importantly, this retraining strategy produced larger pain reductions when delivered using a faded feedback protocol, over and above an equivocal progressive duration running protocol. This suggests that a form of feedback is required over and above a load management intervention where there is a clinical need. A further potential explanation for the more modest symptom responses to step rate retraining reported by Esculier et al. (Esculier et al., 2017), is that feedback is likely to have needed to be subject or subgroup specific and not all participants will have a baseline step rate amenable to an increase.

Previous studies on running retraining have established a potential kinematic mechanism at the hip to explain their positive effects, specifically a 5° reduction in peak hip adduction (Noehren et al., 2011; Willy et al., 2012). The results of this study are in line with this, identifying a smaller but still clinically meaningful mean difference of 2.4° that was associated with a moderate effect size (Table 2). Our mixed-sex sample could explain this smaller mean difference, as the previous work of both Noehren et al. (Noehren et al., 2011) and Willy et al. (Willy et al., 2012) purposefully recruited female participants with higher than average peak hip adduction, which may be more amenable to change. However, as our results have identified a reduction in peak hip adduction equivalent to a previous 7.5% step rate increase study in asymptomatic runners (Willy et al., 2015), it is suggested that a larger increase in step rate (10%) will result in greater reductions in peak hip adduction equivalent to those seen in asymptomatic runners (Heiderscheit et al., 2011). A 10% step rate increase is known to reduce both patellofemoral joint stress (Willson et al., 2014) and pain (Bonacci et al., 2017) in runners with PFP, whereas a 7.5% step rate increase (Esculier et al., 2017) resulted in non-significant changes in both peak patellofemoral reaction force and average patellofemoral loading rate in a recent RCT. Clinically, it may be sensible to start retraining with a more modest 7.5% step rate increase, increasing to 10% or greater if tolerated, especially in those with low baseline step rate.

In addition to reducing peak hip adduction, the results of this study have identified two novel potential kinematic mechanisms, being a reduction in both peak hip internal rotation and knee flexion. The identified mean difference in peak hip internal rotation of 5.1° is above the MDC of 3.7° reported by Noehren et al. (Noehren et al., 2010) and was associated with a large effect size ($d = 0.96$). Peak hip internal rotation is associated with running related PFP (Neal et al., 2016) and can result in increased patellofemoral joint stress by increasing contact pressures at the lateral patellar facet (Salsich & Perman, 2007). Thus, given the plausibility for reducing hip internal rotation during running gait to favourably alter PFP symptoms and the size of the identified effect, one could argue that a clinically meaningful change has been identified.

A reduction in peak knee flexion of 3.7° is in line with the work of Lenhart et al. (Lenhart, Thelen, Wille, Chumanov, & Heiderscheit, 2014), who reported a reduction in peak knee flexion of 3.3° with a 10% step rate increase in a normative cohort. Within this musculoskeletal model (Lenhart et al., 2014), peak knee flexion correlates positively with patellofemoral joint force, indicating this finding may be clinically relevant. This effect is likely due to changes in patella contact pressures, as a subsequent modeling study reports that lateral patellar arthrokinematics were not significantly altered by a 10% step rate increase (Lenhart et al., 2015). At an individual level, kinematic changes seem to correlate poorly with symptom improvements post-step rate retraining (see table 3). For example, two participants (one male, one female) had an increased peak hip adduction post-retraining (see table 3), with both participants asymptomatic for both average and worst pain variables. For the female participant, the increase in peak hip adduction (6.6°) exceeds the MDIC (2.6°) and is thus less likely to be related to measurement error. Future studies should look to investigate alternative potential mechanisms of running retraining, such as kinetic changes, load management or graded exposure.

Previous observational research investigating increasing step

rate by 10% has identified increased quadriceps activation (Chumanov, Wille, Michalski, & Heiderscheit, 2012) comparable to the increase seen within this study. VMO activity is known to be altered in some individuals with PFP (Chester et al., 2008) and VMO weakness is reported to correlate with lateral patella shift (Sakai, Luo, Rand, & An, 2000). Whilst this study design prohibits inference of causality, this sEMG finding may be associated with the reduction in pain seen post-retraining.

The lack of change in mean gluteal EMG identified by this study is perhaps not surprising given the work of Willson et al. (Willson et al., 2011), who report no differences in mean gluteal sEMG when comparing female runners with PFP to matched controls. Willson et al. (Willson et al., 2011) do however report that female runners with PFP demonstrate a shorter GMED activation window and delayed onset prior to foot contact in females with PFP. Additionally, Willy & Davis (Willy & Davis, 2013) reported earlier GMED activation and an increased GMED activation duration in a small case series of 2 female runners with PFP post-mirror running retraining. Combined with findings from our study, this indicates that changes to gluteal muscle activation patterns rather than magnitude may provide mechanistic explanation for the reduction in pain. Further research is needed to explore this and a limitation of the current study is the fact that the sEMG were not synchronised to the kinematic system, meaning not all variables of interest from the previous literature could be investigated.

### 4.1. Future directions

Based on the results of this feasibility study, a future RCT should look to compare a step rate intervention against an exercise therapy control and investigation of effects to long-term follow up (~12 months) is advocated. Future work on running retraining should seek to use a faded feedback protocol, as it appears to result in superior outcomes. Recruitment of participants with a step rate of <160 (>1 SD below the mean of this cohort) who are more likely to be amenable to step rate retraining or stratifying outcome analysis by baseline cadence is worth considering – a strategy that would require greater samples but produce more generalisable findings. Sub-group analysis by baseline kinematic variables associated with PFP such as hip adduction may also be indicated, though kinematic variables do not appear to be sensitive to predicting those who may respond to a step rate intervention.

Whilst this feasibility trial was not powered apriori to investigate these effects, a post-hoc calculation using the mean difference of both average and worst pain revealed that a sample of 10 participants is adequate to investigate symptom changes post-step rate retraining with adequate statistical power ($\alpha = 0.05$, $\beta = 0.80$). It is therefore advisable that future trials adhere to the so-called rule of 10, recruiting 10 participants per individual variable investigated to minimize risk of bias (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996) 10% of the biomechanical data in this study was lost due to data corruption and it is advisable that this be factored in to any sample size calculation for mechanistic outcomes in future studies.

Comparing the results of this study to the previous work on running retraining proved challenging given the heterogeneity of pain outcomes collected. It is advisable that future work collects data on both average/usual and worst/running related symptoms to allow for more clinically meaningful comparisons. The mean difference in the Kujala scale identified falls well below the accepted MCID of 10 points (Crossley et al., 2004) and given the high baseline scores seen in the population studied, a ceiling effect can be suggested. Future studies are advised to consider an alternative measure of subjective function, with the lower extremity functional scale (LEFS), used by previous studies (Noehren et al., 2011; Willy et al., 2012), and the recently developed patellofemoral subscale of the Knee Osteoarthritis Outcome Score (KOOS) (Crossley, Macri, Cowan, Collins, & Roos, 2017), particularly worthy of consideration.

## 5. Conclusion

The results of this study confirm that increasing running step rate using a faded-feedback protocol is a feasible and effective intervention for use in a mixed sex UK cohort. Future studies should focus on investigating the long-term efficacy of running retraining in a cohort that have a clear treatment target (i.e. low step rate), compared to an appropriate control. A sample size of ten participants per group/variable is adequate to detect minimum clinically important differences with adequate statistical power. In addition to future work establishing efficacy, exploration of both forms of feedback and treatment mechanisms is encouraged.

## Conflicts of interest

The authors declare that they have no conflicts of interest in relation to this study.

## Ethical approval

Ethical approval was sought and subsequently granted by the Queen Mary Ethics of Research Committee (QMREC2014/63).

## Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ptsp.2018.05.018.

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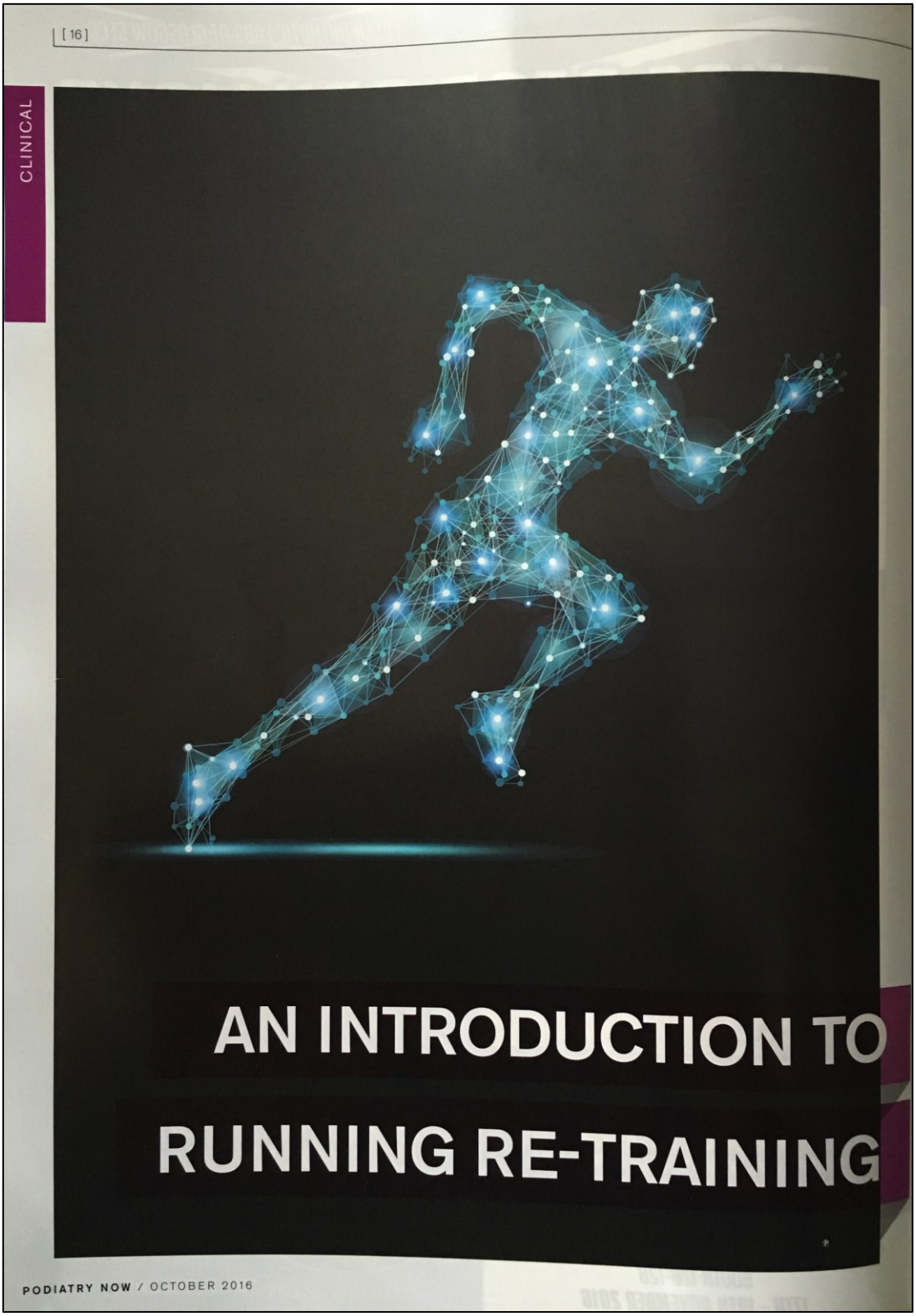
## 14. Appendix E: Translational publication surrounding *running retraining* in Podiatry Now



Griffiths, Neal and Dunne investigate the benefits of running re-training on certain running-related pathologies, and the role that podiatrists could play in this

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## INTRODUCTION

**The role of the podiatrist within a multidisciplinary musculoskeletal team is often erroneously assumed to be solely limited to the provision of foot orthoses. Whilst for the appropriate patient/pathology, orthoses can be an incredibly useful tool, the literature suggests that they are more likely to exert their primary effects via their modulation of kinetic variables (i.e. forces), rather than by re-aligning the skeleton or placing an individual back into a fictitious 'normal' position.[1,2]**

It is therefore more sensible to consider foot orthoses as 'load modifiers' rather than 'arch supports', and managing load is currently considered one of the key tenets of rehabilitating any mechanically based lower-extremity pathology.[3]

Podiatrists need to be aware of other ways to influence load management if foot orthoses are not a viable option, and something that has been shown to warrant consideration in clinical practice is running re-training.[4] Although delivery of this intervention is unlikely to be podiatrist-led, they may be the first practitioner that an injured athlete consults with and as such the first practitioner to analyse running gait. It is therefore crucial they have an appropriate understanding of the current evidence base in this area.

Running re-training was developed as a result of the apparent link between kinematics and certain running-related pathology.[5] Contrary to the proposed hypotheses of many, rehabilitative exercise has not been shown to alter running kinematics.[6] As such, running re-training began to be investigated. As with any intervention, running re-training will not be appropriate for every athlete. It should also be noted that whilst there is developing evidence for its application in the presence of certain pathologies such as patellofemoral pain,[7,8] tibial stress[9] and biomechanical overload syndrome,[10] the intervention is very much in its infancy. Currently, there are no strong data that support modifying characteristics of a runner's gait for any other pathology, nor support the recommendation to change the way an uninjured athlete runs. Some experts believe that altering the running pattern of an uninjured runner may be more likely to give them an injury than prevent them from getting one they have not yet sustained.[11]

## CASE STUDY 1: STRIDE LENGTH AND PATELLOFEMORAL PAIN

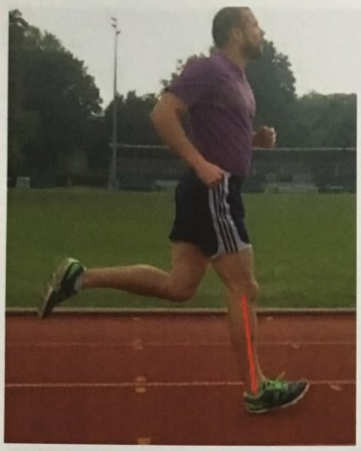
A 25-year-old athlete presented to clinic, having suffered with bilateral anterior knee pain associated with his running for over six months. Onset was insidious with no antecedent trauma and not related to any sudden changes in training load. Pain was reported as a sharpness behind the kneecap(s) at any distance beyond 5km, or if he ran for two consecutive days. Pain completely resolved with running cessation for more than a week but then returned upon resuming running. No red flags were identified.

He was referred by a Consultant Sports Physician and a recent MRI scan had showed no structural defects and suggested symptoms were patellofemoral in origin. He ran in a pair of Asics DS racers and had done for the previous four years; he reported they were the most comfortable pair of shoes he had ever used. He did not currently wear foot orthoses and had no history of doing so. On questioning he was particularly reticent to consider these unless absolutely necessary.

Video gait analysis in the frontal plane highlighted good control at pelvic level, but an apparent increase in peak hip adduction. In the sagittal plane there was a tendency for foot contact to occur anterior to both the hip and the knee joint axes (Figure 1a), with this stride length increasing the net extension moment at the knee and contributing to increased contact times in stance. Cadence was calculated at 160 steps per minute at a self-selected running speed of 11.0km/h. Treatment direction tests suggested that he might not be a suitable candidate for orthosis use (low dye taping did not alter his pain[12] and his foot mobility score was <10mm).[13]

Following a discussion of the level 1 evidence regarding patellofemoral pain in runners[14] between the athlete, the podiatrist and the physiotherapist, it was agreed that running re-training was to be trialled and was to focus primarily on stride-length reduction, achieved by concentrating on increasing cadence (as these variables are inversely proportionate) whilst controlling for speed. An increase of 7.5% of the athlete's baseline cadence was chosen, which has been shown to reduce patellofemoral joint forces by up to 14% and reduce peak hip adduction.[15] This was achieved by fixing the speed (11.0km/h) on the treadmill and providing an audible metronome set at a cadence of 172 via a faded feedback design[16] over a period of 12 weeks.

At review the athlete reported complete resolution of his symptoms and a weekly running volume of 30km over three to four runs, with plans to increase this further over future months. Video gait analysis review highlighted that his stride length and cadence appeared to have altered from his initial presentation to clinic (~166), despite the metronome not being in use for the previous four weeks (Figure 1b). He was referred to a running coach for ongoing guidance



**Left: Figure 1a.** Showing the ankle joint anterior to the knee joint at contact; often referred to as an 'overstride'.
**Right: Figure 1b.** A reduction in stride length following cadence modification; note verticality in tibia.

regarding his load management and running drills.

## CASE STUDY 2: STRIDE WIDTH AND MEDIAL TIBIAL STRESS SYNDROME

A 19-year-old athlete presented with a clinical presentation giving a high index of suspicion for bilateral medial tibial stress syndrome. Many of the numerous other causes of exercise-induced leg pain were excluded following a detailed history taking, and bone stress was ruled out via MRI scan. Symptoms were running related and appeared to have been triggered following an increase in running volume whilst training for an event. Symptoms had been present over two years and despite dramatically modifying activity still persisted when attempting to run for longer than 10 minutes. In this two-year period the athlete had seen many different consultants, physiotherapists and podiatrists. He was wearing a pair of Asics 1000 trainers (with a dual density midsole) and was using a pair of custom made devices that had been prescribed approximately one year before.

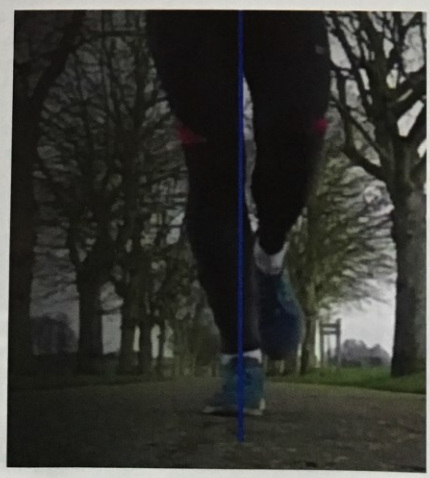
On examination it was clear that control at pelvic level was suboptimal, and literature has previously identified this as a risk factor for tibial stress.[17] A tibial varum was evident, which will usually increase tibial bending moments; a key causative factor in medial tibial stress syndrome.[18, 19] However, this was also exacerbated by a very narrow stride length being adopted when viewing the gait analysis footage in the frontal plane with some 'crossing over' relative to the midline (Figure 2a). Whilst a functional limb varus is a common feature when running,[20] significant crossing over or scissoring may be an observation worth noting in the context of the work showing that increasing step width will reduce tibial stress.[9] The foot orthoses being used were reviewed by the podiatrist and considered to be well made and have the design features present that have been suggested to effectively modify tibial bending moments,[21] but despite this the athlete was still symptomatic when using them.

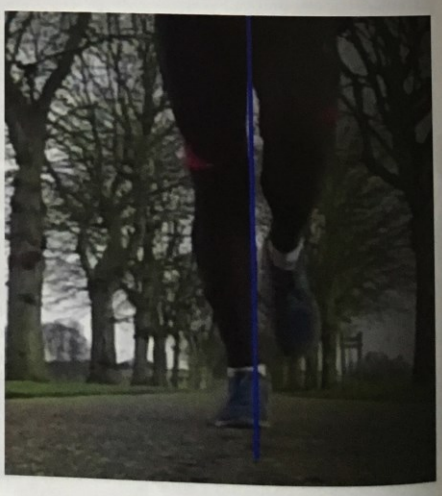
The team discussed running re-training with the athlete and agreed it was worthy of trial. This consisted of physiotherapy input for the proximal structures (a strength-endurance programme for the hip abductors, extensors and external rotators) and the running coach providing internal and external cues to help with increasing step width. The most effective approach for this athlete was using an actual visible line (the painted lane line on the running track) and being asked to 'miss it left' with his left foot and 'miss it right' with his right foot. This is in keeping with the data which has concluded that external cues seem to be more effective at facilitating change than internal cues.[22, 23]

Following eight weeks of rehabilitation in this way the athlete was able to run for 45-60 minutes twice a week with no shin pain being experienced. There was a visible increase in his step width, which appeared to persist even when he was

**Left: Figure 2a.** Illustrating narrow step width with tendency to scissor or cross over midline.

**Right: Figure 2b.** Increase in step width observed following gait re-training with external cues.





analysed in a distractive environment without a line present (Figure 2b).

## CONCLUSION

Case studies of two very commonly seen pathologies have been presented, and a description of how running re-training was the key component of their rehabilitation strategies. In both cases the equipment used was inexpensive and readily available to anyone with a tablet or smartphone, and as such exhibits the ease with which this intervention can be applied to clinical practice.

Whilst it is not the suggestion that running re-training should completely replace any current approaches for lower extremity pathology, it is hoped that these case studies highlight that it can be an incredibly useful approach to consider in cases of patellofemoral pain and tibial stress.

It may be particularly useful for athletes who are not keen to consider foot orthoses (due to the cost being prohibitive or to a personal stance against them) or when many of the more traditional approaches have already been put in situ (including foot orthoses) and the desired outcome has still not been achieved.

A multidisciplinary approach is encouraged for both optimum patient outcomes and also improved inter-practitioner development. It is crucial that podiatrists have these professional relationships in situ for such cases. ■

**EQUIPMENT USED IN ABOVE CASE STUDIES:**

- Video Capture; iPad with Hudl Technique (free app)
- Metronome; MetroTimer (free app)
- Theraband; cost approx. £2

**NOTE**

*Images used are to illustrate concepts and are not of actual athletes/patients referred to.*

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# 15. Appendix F: Kujala Knee Pain Questionnaire

ANTERIOR KNEE PAIN (Sheet code: _____)

Name: _____ Date: _____

Age: _____

Knee: L/R

Duration of symptoms: _____ years _____ months

For each question, circle the latest choice (letter), which corresponds to your knee symptoms.

**1. Limp**
(a) None (5)
(b) Slight or periodical (3)
(c) Constant (0)

**2. Support**
(a) Full support without pain (5)
(b) Painful (3)
(c) Weight bearing impossible (0)

**3. Walking**
(a) Unlimited (5)
(b) More than 2 km (3)
(c) 1-2 km (2)
(d) Unable (0)

**4. Stairs**
(a) No difficulty (10)
(b) Slight pain when descending (8)
(c) Pain both when descending and ascending (5)
(d) Unable (0)

**5. Squatting**
(a) No difficulty (5)
(b) Repeated squatting painful (4)
(c) Painful each time (3)
(d) Possible with partial weight bearing (2)
(e) Unable (0)

**6. Running**
(a) No difficulty (10)
(b) Pain after more than 2 km (8)
(c) Slight pain from start (6)
(d) Severe pain (3)
(e) Unable (0)

**7. Jumping**
(a) No difficulty (10)
(b) Slight difficulty (7)
(c) Constant pain (2)
(d) Unable (0)

**8. Prolonged sitting with the knees flexed**
(a) No difficulty (10)
(b) Pain after exercise (8)
(c) Constant pain (6)
(d) Pain forces to extend knees temporarily (4)
(e) Unable (0)

**9. Pain**
(a) None (10)
(b) Slight and occasional (8)
(c) Interferes with sleep (6)
(d) Occasionally severe (3)
(e) Constant and severe (0)

**10. Swelling**
(a) None (10)
(b) After severe exertion (8)
(c) After daily activities (6)
(d) Every evening (4)
(e) Constant (0)

**11. Abnormal painful kneecap (patellar) movements (subluxations)**
(a) None (10)
(b) Occasionally in sports activities (6)
(c) Occasionally in daily activities (4)
(d) At least one documented dislocation (2)
(e) More than two dislocations (0)

**12. Atrophy of thigh**
(a) None (5)
(b) Slight (3)
(c) Severe (0)

**13. Flexion deficiency**
(a) None (5)
(b) Slight (3)
(c) Severe (0)

# 16. Appendix G: Step rate retraining protocol from feasibility study


## Running Retraining Instructions

Participant:_____ Metronome setting:_____ Treadmill speed:_____

**INITIAL TEST**

**Week 1:** 3 sessions of: ***(Run 1min : Walk 1min)*** *x 10 (metronome feedback for all)*

**Week 2:** 3 sessions of: ***(Run 2min : Walk 1min)*** *x 8 (metronome feedback on numbers 1-3 and 5-7)*

**Week 3:** 3 sessions of: **(Run 3min : Walk 1min)** x 8 (metronome feedback on numbers 1, 3, 5, 7)

**Week 4:** 3 sessions of: **(Run 4min : Walk 1min)** x 8 (metronome feedback on numbers 1 and 5)

**Week 5:** 3 sessions of: **(Run 5min : Walk 1min)** x 6 (no metronome feedback)

**Week 6:** 3 sessions of: **(Run 10min : Walk 1min)** x 3 (no metronome feedback)

**RE – TEST**

**Week 7:** 3 sessions of: **(Run 15min : Walk 1min) x 2**

**Week 8:** 3 sessions of: **Run 20min continuous**

**Week 9:** 3 sessions of: **Run 25min continuous**

**Week 10:** 3 sessions of: **Run 30min continuous**

**Week 11:** 3 sessions of: **Run 35min continuous**

**Week 12:** 3 sessions of: **Run 40min continuous**

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University of London

# 17. Appendix H: Tegner activity scale

Name: _____ Side: Right / Left
Date: _____

**QUESTIONS**

1. **Activity Levels, please look at the scale below and answer the score for your activity level before and after the problem began or the surgery took place.**

## TEGNER ACTIVITY LEVEL SCALE

**Please indicate in the spaces below the HIGHEST level of activity that you participated in BEFORE YOUR INJURY and the highest level you are able to participate in CURRENTLY.**

**BEFORE INJURY: Level_____ CURRENT: Level_____** See scale below

| | |
|---|---|
| **Level 10** | **Competitive sports- soccer, football, rugby (national elite)** |
| **Level 9** | **Competitive sports- soccer, football, rugby (lower divisions), ice hockey, wrestling, gymnastics, basketball etc** |
| **Level 8** | **Competitive sports- racquetball, squash or badminton, track and field athletics (jumping, etc.), down-hill skiing etc** |
| **Level 7** | **Competitive sports- tennis, running, motorcars speedway, handball**<br>**Recreational sports- soccer, football, rugby, bandy, ice hockey, basketball, squash, racquetball, running,MTB,dancing etc** |
| **Level 6** | **Recreational sports- tennis and badminton, handball, racquetball, down-hill skiing, jogging at least 5 times per week** |
| **Level 5** | **Work- heavy labor (construction, etc.)**<br>**Competitive sports- cycling, cross-country skiing,**<br>**Recreational sports- jogging on uneven ground at least twice weekly** |
| **Level 4** | **Work- moderately heavy labor (e.g. truck driving, etc.)** |
| **Level 3** | **Work- light labor (nursing, etc.)** |
| **Level 2** | **Work- light labor**<br>**Walking on uneven ground possible, but impossible to back pack or hike** |
| **Level 1** | **Work- sedentary (secretarial, etc.)** |
| **Level 0** | **Sick leave or disability pension because of hip problems** |

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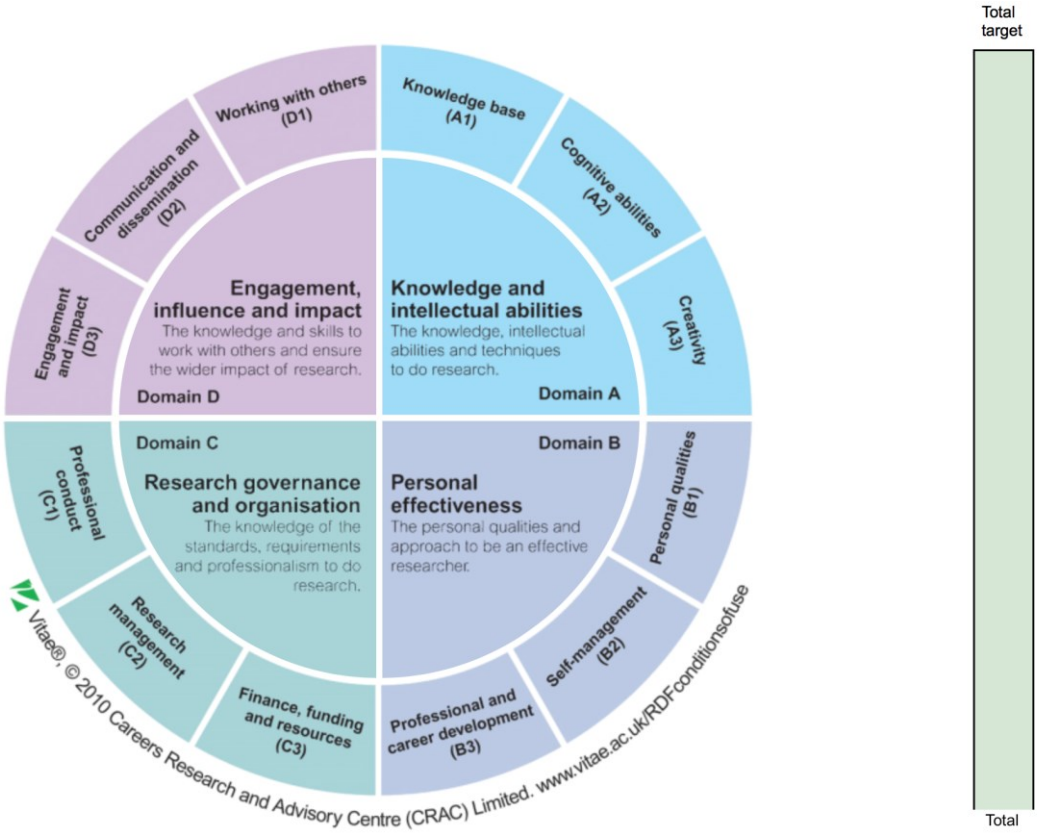
# 18. Appendix J: Skills points record

The knowledge and skills that I have developed during the course of my PhD extend beyond the chapters presented in this thesis. Over the past four and a half years I have immersed myself amongst the literature, not just in relation to my topic of patellofemoral pain, but also in relation to the wider scientific method. These skills have been tested and strengthened further by the submission and subsequent presentation of abstract findings at a variety of national and international conferences.

I have developed my teaching skills by successfully completing the first module of my certificate in learning and teaching (CILT), which I shall formally complete in the next academic year. I have successfully supervised three MSc students to the successful completion of their dissertation and subsequent degrees. I am particularly proud of the patellofemoral pain research group that I co-supervised throughout 2016/17 with my colleague Dr Simon Lack, which contained five iBSc students, all of whom successfully passed their dissertation component.

I have no doubt that the knowledge and skills that I have gained throughout the course of my PhD will serve me well throughout my future career, both as an academic and as a clinician.




| | | | |
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## Supervisors

| Title | Given Names | Last Name | Telephone | Email | Active |
|---|---|---|---|---|---|
| Dr | Aleksandra Victoria | Birn-Jeffery | | a.birn-jeffery@qmul.ac.uk | true |
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| Year | Type | Pts: | A | B | C | D | Total | Cap: | A | B | C | D | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1st | **Conference attendance sub-total** | | **9.0** | **6.0** | **0.0** | **0.0** | **15.0** | | | | | | |
| | *Other Teaching/demonstrating training* | | 0.0 | 3.0 | 0.0 | 3.0 | 6.0 | | | | | | |
| | **Course/event attendance sub-total** | | **0.0** | **3.0** | **0.0** | **3.0** | **6.0** | | | | | | |
| | *Standard Ethical Approval* | | 3.0 | 0.0 | 9.0 | 3.0 | 15.0 | | | | | | |
| | **Ethical approval sub-total** | | **3.0** | **0.0** | **9.0** | **3.0** | **15.0** | | | | | | |
| | *External funding application >£10,000* | | 4.0 | 0.0 | 6.0 | 4.0 | 14.0 | | | | | | |
| | **Funding application sub-total** | | **4.0** | **0.0** | **6.0** | **4.0** | **14.0** | | | | | | |
| | *Conference Presentation (Oral)* | | 3.0 | 3.0 | 0.0 | 4.0 | 10.0 | | | | | | |
| | *Conference Presentation (Poster)* | | 3.0 | 3.0 | 0.0 | 4.0 | 10.0 | | | | | | |
| | **Giving presentations sub-total** | | **6.0** | **6.0** | **0.0** | **8.0** | **20.0** | | | | | | |
| | *Organising Conference (with external speaker(s)) claim per day* | | 2.0 | 0.0 | 2.0 | 2.0 | 6.0 | | | | | | |
| | **Organising events/seminars sub-total** | | **2.0** | **0.0** | **2.0** | **2.0** | **6.0** | | | | | | |
| | *Refereed Publication (Journal Paper, Book chapter, not abstract) acceptance* | | 2.0 | 0.0 | 0.0 | 8.0 | 10.0 | | | | | | |
| | **Written publications sub-total** | | **2.0** | **0.0** | **0.0** | **8.0** | **10.0** | | | | | | |
| | **Year 1 Total (with caps applied)** | | **26.0** | **15.0** | **17.0** | **28.0** | **86.0** | | | | | | |
| 2nd | *Conference Attendance (Three days)* | | 18.0 | 12.0 | 0.0 | 0.0 | 30.0 | | | | | | |
| | **Conference attendance sub-total** | | **18.0** | **12.0** | **0.0** | **0.0** | **30.0** | | | | | | |
| | *Other course/event attendance* | | 0.0 | 0.5 | 0.5 | 0.5 | 1.5 | | | | | | |
| | **Course/event attendance sub-total** | | **0.0** | **0.5** | **0.5** | **0.5** | **1.5** | | | | | | |
| | *Conference Presentation (Oral)* | | 9.0 | 9.0 | 0.0 | 12.0 | 30.0 | | | | | | |
| | **Giving presentations sub-total** | | **9.0** | **9.0** | **0.0** | **12.0** | **30.0** | | | | | | |
| | *Seminar attendance (single)* | | 0.0 | 0.0 | 1.0 | 0.0 | 1.0 | | | | | | |
| | **Seminar attendance sub-total** | | **0.0** | **0.0** | **1.0** | **0.0** | **1.0** | | | | | | |
| | *Mentoring/supervising of Project Student* | | 4.0 | 2.0 | 0.0 | 4.0 | 10.0 | | | | | | |
| | **Teaching sub-total** | | **4.0** | **2.0** | **0.0** | **4.0** | **10.0** | | | | | | |
| | *Refereed Publication (Journal Paper, Book chapter, not abstract) acceptance* | | 4.0 | 0.0 | 0.0 | 16.0 | 20.0 | | | | | | |
| | *Refereed Publication (Journal Paper, Book chapter, not abstract) submission* | | 2.0 | 0.0 | 0.0 | 8.0 | 10.0 | | | | | | |
| | **Written publications sub-total** | | **6.0** | **0.0** | **0.0** | **24.0** | **30.0** | | | | | | |
| | **Year 2 Total (with caps applied)** | | **37.0** | **23.5** | **1.5** | **40.5** | **102.5** | | | | | | |
| 3rd | *Conference Attendance (Three days)* | | 9.0 | 6.0 | 0.0 | 0.0 | 15.0 | | | | | | |
| | **Conference attendance sub-total** | | **9.0** | **6.0** | **0.0** | **0.0** | **15.0** | | | | | | |
| | *CILT Module 1* | | 0.0 | 5.0 | 0.0 | 5.0 | 10.0 | | | | | | |
| | *Other Teaching/demonstrating training* | | 0.0 | 3.0 | 0.0 | 3.0 | 6.0 | | | | | | |
| | *Researcher Development Course* | | 0.0 | 1.0 | 0.0 | 3.0 | 4.0 | | | | | | |
| | *Statistics* | | 18.0 | 0.0 | 0.0 | 0.0 | 18.0 | | | | | | |
| | **Course/event attendance sub-total** | | **18.0** | **9.0** | **0.0** | **11.0** | **38.0** | | | | | | |
| | *External funding application >£10,000* | | 4.0 | 0.0 | 6.0 | 4.0 | 14.0 | | | | | | |
| | **Funding application sub-total** | | **4.0** | **0.0** | **6.0** | **4.0** | **14.0** | | | | | | |
| | *Conference Presentation (Oral)* | | 3.0 | 3.0 | 0.0 | 4.0 | 10.0 | | | | | | |
| | **Giving presentations sub-total** | | **3.0** | **3.0** | **0.0** | **4.0** | **10.0** | | | | | | |
| | *Teaching/demonstrating/marking/preparation* | | 0.0 | 2.5 | 0.0 | 2.5 | 5.0 | | | | | | |
| | **Teaching sub-total** | | **0.0** | **2.5** | **0.0** | **2.5** | **5.0** | | | | | | |
| | **Year 3 Total (with caps applied)** | | **34.0** | **20.5** | **6.0** | **21.5** | **82.0** | | | | | | |
| 4th | *Educational Development Course* | | 0.0 | 1.5 | 0.0 | 1.5 | 3.0 | | | | | | |
| | *Researcher Development Course* | | 0.0 | 1.0 | 0.0 | 2.0 | 3.0 | | | | | | |
| | **Course/event attendance sub-total** | | **0.0** | **2.5** | **0.0** | **3.5** | **6.0** | | | | | | |
| | **Year 4 Total (with caps applied)** | | **0.0** | **2.5** | **0.0** | **3.5** | **6.0** | | | | | | |

## Points Summary

⊞ Show Yearly Totals

| Year | Type | Pts: | A | B | C | D | Total | Cap: | A | B | C | D | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total | *Conference Attendance (Three days)* | | 36.0 | 24.0 | 0.0 | 0.0 | 60.0 | | | | | | |
| | **Conference attendance sub-total** | | **18.0** | **12.0** | **0.0** | **0.0** | **30.0** | | **18.0** | **12.0** | | | **30.0** |
| | *CILT Module 1* | | 0.0 | 5.0 | 0.0 | 5.0 | 10.0 | | | | | | |
| | *Educational Development Course* | | 0.0 | 1.5 | 0.0 | 1.5 | 3.0 | | | | | | |
| | *Other Teaching/demonstrating training* | | 0.0 | 6.0 | 0.0 | 6.0 | 12.0 | | | 10.0 | | 10.0 | 20.0 |
| | *Other course/event attendance* | | 0.0 | 0.5 | 0.5 | 0.5 | 1.5 | | | | | | |
| | *Researcher Development Course* | | 0.0 | 2.0 | 0.0 | 5.0 | 7.0 | | | | | | |
| | *Statistics* | | 18.0 | 0.0 | 0.0 | 0.0 | 18.0 | | 20.0 | | | | 20.0 |
| | **Course/event attendance sub-total** | | **18.0** | **15.0** | **0.5** | **18.0** | **51.5** | | | | | | |
| | *Standard Ethical Approval* | | 3.0 | 0.0 | 9.0 | 3.0 | 15.0 | | 3.0 | | 9.0 | 3.0 | 15.0 |
| | **Ethical approval sub-total** | | **3.0** | **0.0** | **9.0** | **3.0** | **15.0** | | | | | | |
| | *External funding application >£10,000* | | 8.0 | 0.0 | 12.0 | 8.0 | 28.0 | | | | | | |
| | **Funding application sub-total** | | **8.0** | **0.0** | **12.0** | **8.0** | **28.0** | | | | | | |
| | *Conference Presentation (Oral)* | | 9.0 | 9.0 | 0.0 | 12.0 | 30.0 | | 9.0 | 9.0 | | 12.0 | 30.0 |
| | *Conference Presentation (Poster)* | | 3.0 | 3.0 | 0.0 | 4.0 | 10.0 | | 9.0 | 9.0 | | 12.0 | 30.0 |
| | **Giving presentations sub-total** | | **12.0** | **12.0** | **0.0** | **16.0** | **40.0** | | | | | | |
| | *Organising Conference (with external speaker(s)) claim per day* | | 2.0 | 0.0 | 2.0 | 2.0 | 6.0 | | 8.0 | | 8.0 | 8.0 | 24.0 |
| | **Organising events/seminars sub-total** | | **2.0** | **0.0** | **2.0** | **2.0** | **6.0** | | | | | | |
| | *Seminar attendance (single)* | | 0.0 | 0.0 | 1.0 | 0.0 | 1.0 | | | | | | |
| | **Seminar attendance sub-total** | | **0.0** | **0.0** | **1.0** | **0.0** | **1.0** | | **30.0** | | | | **30.0** |
| | *Mentoring/supervising of Project Student* | | 4.0 | 2.0 | 0.0 | 4.0 | 10.0 | | 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** | | **4.0** | **4.5** | **0.0** | **6.5** | **15.0** | | | | | | |
| | *Refereed Publication (Journal Paper, Book chapter, not abstract) acceptance* | | 4.0 | 0.0 | 0.0 | 16.0 | 20.0 | | 4.0 | | | 16.0 | 20.0 |
| | *Refereed Publication (Journal Paper, Book chapter, not abstract) submission* | | 2.0 | 0.0 | 0.0 | 8.0 | 10.0 | | 4.0 | | | 16.0 | 20.0 |
| | **Written publications sub-total** | | **6.0** | **0.0** | **0.0** | **24.0** | **30.0** | | | | | | |
| | **Total (with caps applied)** | | **71.0** | **43.5** | **24.5** | **77.5** | **216.5** | | | | | | |
| | Target | | 60.0 | 20.0 | 15.0 | 30.0 | 210.0 | | | | | | |