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RISK FACTORS AND THEIR ASSOCIATION(S) IN RELATION TO OVERUSE INJURIES IN RECREATIONAL MALE RUNNERS

BY
RENÉ B.K. BRUND

DISSERTATION SUBMITTED 2018

AALBORG UNIVERSITY
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DISSERTATION SUBMITTED TO DEPARTMENT OF HEALTH SCIENCE

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CURRICULUM VITAE

René Boerge Korsgaard Brund (RKB) received his Master degree in Sports Science from Aalborg University in 2012. RKB enrolled in the doctoral school at Faculty of Medicine at AAU under supervision of Professor Michael Voigt and Professor Uwe Kersting in 2012. RKB have published 3 peer-reviewed papers, 2 non-peer reviewed papers, held 4 oral presentations at conferences, of these 3 were invited. Additionally, RKB has reviewed 5 scientific papers. RKB has been teaching academically since 2010, which is summing up to more than 3000hours of teaching at bachelor level within outdoor life, biomechanics and statistics. His academic research interest are sports biomechanics, etiology and prevention of running-related overuse injury, statistics, running shoes, tendon development and musculo-skeletal loading and simulation.

PREFACE

The present study was carried out in the Physical Activity and Human Performance group, SMI®, Department of Health Science and Technology, Aalborg University, Denmark, between 2012 and 2017. The PhD stipend was funded by Aalborg University.

The thesis is based on three original articles. In the thesis, these are referred to as paper I, paper II, and paper III (the full-length articles are included in the Appendix).

Paper I: Brund, R.B.K., Rasmussen, S., Nielsen R.O., Kersting, U.G., Laessoe, U. and Voigt, M. The association between eccentric hip abduction strength and hip and knee angular movement in recreational male runners: an explorative study. *Scandinavian Journal of Medicine and Science in Sports, 2018;28(2):473-478*

Paper II: Brund, R.B.K., Rasmussen, S., Nielsen R.O., Kersting, U.G., Laessoe, U. and Voigt, M. Medial shoe-ground pressure and specific running injuries: A 1-year prospective cohort study. *Journal of Science and Medicine in Sport, 2017;20(9): 830-834*

Paper III: Brund, R.B.K., Rasmussen, S., Nielsen R.O., Parner, E.T. and Voigt, M. Changes in the running-related injury rate ratio in a 1000km explorative prospective cohort study involving two unspecific shoe changes. *in revision*

The reporting of the observational studies complies with the recommendation of strengthening the reporting of observational studies in epidemiology (STROBE statement).

This thesis has been submitted for assessment in partial fulfilment of the PhD degree. The thesis is based on the submitted or published scientific articles which are listed above. Parts of the articles are used directly or indirectly in the extended summary of the thesis. As part of the assessment, co-author statements have been made available to the assessment committee and are also available at the Faculty.

ENGLISH SUMMARY

Running is associated with injuries, mainly overuse injuries, and a great proportion of active runners sustain one or more overuse injury yearly. A multitude of biomechanical factors have been proposed to elicit running-related overuse injuries. However, these factors or combinations of factors that are leading to the most frequent running-related overuse injuries, are inconclusive. Therefore further evidence is needed to clarify the etiology of running-related overuse injuries. The purpose of this PhD thesis is to provide further insight into the etiology leading to the most frequent running-related overuse injuries and to investigate potential relationships between risk factors associated with running-related overuse injuries. Three specific research questions were asked to pursue the purpose:

Research question 1: *Is eccentric hip abduction strength associated with specific hip and knee joint kinematic patterns, which again may be related to knee injury?*

Research question 2: *Is medial shoe-ground pressure associated with the development of Achilles tendinopathy, plantar fasciitis and/or medial tibial stress syndrome (APM injuries) among recreational male runners?*

Research question 3: *How does the injury incidence rate ratio (IIRR) change over a one year prospective study involving two changes of running shoes?*

A group of 99 recreational male runners were monitored with respect to running activity and running injury for one year. At baseline, runners were provided with a pair of neutral running shoes, in which they should run the first 500km. Eccentric hip abduction strength, shoe-ground pressure profiles and kinematics during running were measured before (baseline) and approximately after the first 500km of running in the provided pair of neutral running shoes. In case of a running-related overuse injury, the injury was clinically examined, diagnosed and recommendations concerning recovery strategies were given.

The answer to research question 1 provided further insights into identifying a subgroup of runners displaying an association between eccentric hip abduction strength and hip and knee kinematics. Overall, no associations between eccentric hip abduction strength and hip and knee kinematics were found in the main group. In a subgroup demonstrating simultaneous hip adduction and knee abduction (valgus) during the first half of the stance phase, an association between eccentric hip abduction strength and the magnitude of the knee abduction angular excursion was demonstrated.

The answer to research question 2 provided evidence to the effect shoe-ground pressure distributions has on the risk of APM-injuries. The group of runners with higher medial shoe-ground pressure during running sustained a greater proportion of APM-injuries. It is not certain if all three types of injuries (Achilles tendinopathy, plantar fasciitis and medial tibial stress syndrome) are associated with higher medial shoe-ground pressure. Since only rather few APM-injuries in total occurred during the period of observation this uncertainty could not be addressed with the present data set. The exact associations between higher medial shoe-ground pressure and each of the specific injuries need further clarification.

The answer to research question 3 can be viewed as a first step to shed light on the association between changing running shoes and running injury incidence rate. Running-related overuse injury incidence rate ratio (IIRR) was increased above one around the changes of running shoes and below one in the intermediate periods. However, it was not possible to confirm that the increased IIRRs were caused by the running shoe changes per se. Additionally, it could not be excluded that differences in weekly running distance had an influence on the results, together with other unidentified risk factors. Large scale studies involving alternative experimental protocols are needed to provide further insight into the association between running-related overuse injury incidence rate and running shoe changes.

In summary, the results of this thesis have provided further insights into the etiologies leading to some of the most frequent running-related overuse injuries. Although the applied experimental design applied and the data collection methods used in the present study possess limitations, the valuable knowledge generated in this thesis may act as a foundation for future studies investigating the etiology of running-related overuse injuries. It is suggested that future studies of running-related overuse injury etiology should amongst other things consist of large scale studies including enough injuries of interest to account for important covariates. In addition, instrumentation with which it is possible to assess loads on specific structures in the musculo-skeletal system in the field may be used as the exposure scale.

DANSK RESUMÉ

Fysisk aktivitet er vigtig for sundhed. Næsten 30% af den danske befolkning løber regelmæssigt, hvilket er gavnligt for bl.a. fysisk velvære og reduktion af kropsfedt. Dog er løb forbundet med skader og en stor andel af de aktive løbere bliver skadet årligt. Derfor er det vigtigt at identificere faktorer forbundet med løberelaterede skader. Det er ikke muligt at fremskaffe evidens for mekanismerne bag de hyppigst forekommende løbeskader. Derfor er formålet med dette projekt at udvide den viden der findes omkring etiologien, som leder til de hyppigste skader. Dette har ført til følgende tre specifikke forskningsspørgsmål:

Forskningsspørgsmål 1: Er ekcentrisk hofte abduktionsstyrke relateret til hofte og knæ beveægelse, som igen er relateret til knæskader?

Forskningsspørgsmål 2: Øger medial fod tryk, risikoen for Akillesene tendinopathy, plantar fasciitis og medial tibial stress syndrome (APM-skader)?

Forskningsspørgsmål 3: Stiger incidence raten efter et skoskift?

Dette blev undersøgt i et studie som fulgte 99 mandlige motionsløbere over et år. Løberne fik udleveret et par neutrale test sko, som de skulle gennemføre de første 500km i. Løbernes excentrisk hofte abduktionsstyrke, fodtryk, løbestil og løbesko blev testet ved start og efter omkring 500 kilometers løb, i de udleverede sko. I perioden, hvor de blev fulgt, blev skadede løbere klinisk diagnosticeret og fik anbefalinger til gode rehabiliteringsstrategier.

Forskningsspørgsmål 1 undersøgte ekcentrisk hoftestyrkes påvirkning af hofte og knæ bevægelse. Resultaterne viste ingen sammenhæng mellem ekcentriske hofte abduktions styrke og hofte og knæ vinklerne i hele kohorten. Dog blev der fundet en sammenhæng mellem ekcentriske hofte abduktions styrke og knæ abduktions vinklen i løbere med hofte adduktion og knæ abduktion under løb.

Forskningsspørgsmål 2 undersøgte skader forbundet med medialt tryk på foden. Løbere med et højere medialt tryk på foden pådrager sig flere plantar fasciitis, Akilles tendinopati og skinnebensbetændelse end løbere med et højere lateral tryk på foden. Der var for få løbeskader til at kunne tage højde for tidligere skader, hvilket kan være årsagen til fundet, da tidligere skade øger risikoen for en ny skade.

Forskningsspørgsmål 3 undersøgte risikoen ved at skifte løbesko. Resultaterne viste at skadesraten steg lige efter inklusionen og det første skoskifte, samt omkring det frivillige skoskifte omkring 500km. Grundet studiedesignet, så kan det hverken bekræftes eller afkræftes at der er en sammenhæng mellem skoskifte og øget risiko for løbeskader.

Denne adhandling præsenterer nye resultater vedrørende etiologien som fører til løberelatederede skader. Resultaterne har begrænsninger, som skal fortolkes varsomt. Resultaterne bygger videre på tidligere fund og skaber fundament for yderligere undersøgelser på området. Fremtidige undersøgelser kan fokusere på store kohorte undersøgelser med mere end 100 løbeskader og med en duration skala som måler/estimere kræfterne i de væv som undersøges.

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Completion of the thesis would not have been possible without the economic support from Aalborg University Hospital and the participating runners. I send my best running wishes to all the runners that were interested in participating and a special thanks to those participating.

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Last but very important, I would like to acknowledge the love and support from my family and friends. Especially the joy and endless support from my fiancée and our two daugthers have been the most important. This PhD project would not have been possible without my family support and therefore its dedicated to them.

LIST OF ABBREVIATIONS

RunTech	Running technique study
km	Kilometers
GPS	Global Postion System
APM-injuries	Achilles tendinopathy, plantar fasciitis and medial tibial stress syndrome injuries
CI	Confidence interval
STD	standard deviation
OR	Odds ratio
RR	Relative risk
HR	Hazard ratio
RD	Risk difference
IIRR	Injury incidenc rate ratio
IRR	Incidence rate ratio
BMI	Body mass index
RQ	Research question
BM	Body mass
Min	Minutes

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CHAPTER 1. INTRODUCTION

The introduction will describe the increasing popularity of running which unfortunately also leads to a greater running-related overuse injury burden. Risk factors for running-related overuse injuries will be reviewed together with the etiology of the six most common running-related overuse injuries. Finally, a number relevant problems are identified and the research questions which are addressed in this thesis are formulated.

Popularity of running

Since the middle of the 20th century participation in recreational sport activities has continously increased year by year in the Danish population, reaching 64% of the Danish population in 2011 (Laub and Pilgaard, 2013). Running alone has also grown in popularity and is the preferred recreational physical activity among Danish adults. Especially adults between 25 years to 45 years prefer to run probably owing to the flexibility and highly self-organizing quality of the activity (Forsberg, 2012). Additionally, between 1975 and 2016, the proportion of the Danish population involved in running on a regular basis has increased from 2% to 29% of all citizens (Laub and Pilgaard, 2013) (Figure 1). In comparison to our Swedish neighbours, 40% of the Swedish population is running (Hillevi, 2016), with men between 30 and 49 years running the most (Åkerström, 2017).

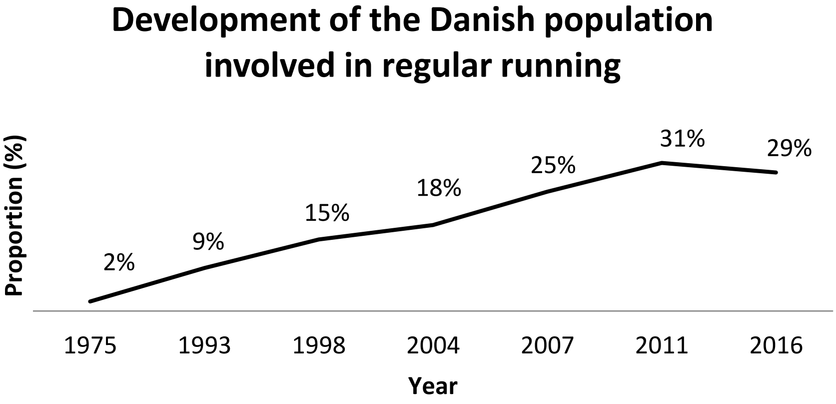


Figure 1: The development in running on a regular basis in the Danish population from 1975 to 2016, indicated as proportions (modified from Laub and Pilgaard, 2013).

Unfortunately, running-related overuse injuries have become a major problem. In Denmark, running is the sport activity contributing with the most injuries. More than twice as many injuries are sustained from running compared to soccer and strength training, which are the second and third sport activities contributing with the most injuries in absolute numbers (Nielsen et al., 2017). As a consequence, injury problems have been in the focus of research for more than 40 years. Many factors have been examined and identified as being associated with running-related overuse injuries. These factors include training errors, equipment, clinical/pathological issues (e.g. previous injury history), anthropometrical factors (e.g. height, weight and leg length), anatomical factors (e.g. bone alignment and joint surface geometry) and biomechanical factors (e.g. load magnitude, distribution and direction). Despite the intense focus on running-related overuse injury research, the literature is sparse concerning the etiology of running-related overuse injuries. Studies of running-related overuse injury including the reviews show divergent results, most likely owing to limitations in the methodologies of the particular studies.

RUNNING-RELATED OVERUSE INJURIES

A running-related overuse injury may develop with repeated stresses on the musculoskeletal tissues, causing microtrauma, which cumulatively together with insufficient rest between the applied stresses may decrease the capacity to tolerate the exposure (Hreljac, 2005). Although, no consensus exists regarding definition of running-related overuse injury, which makes it difficult to compare incidence rates between studies and different populations. Kluitenberg et al. (2016) concluded that the definition of injury has a great impact on injury incidence and location. Presently, at least three injury definitions have been used: 1) medical attention, 2) physical complaint and 3) time loss (Yamato et al., 2015). A consensus-based definition from 2015 defined a running-related overuse injury as: 'Running-related (training or competition) musculoskeletal pain in the lower limbs that causes a restriction or stoppage of running (distance, speed, duration, or training) for at least 7 days or 3 consecutive scheduled training sessions, or that requires the runner to consult a physician or other health professional' (Yamato et al., 2015). However this definition was not published at the collection of data for this PhD-study. Therefore an injury was defined as *"absence of running for a minimum of one week due to complaints concerning musculoskeletal problems in the lower extremity or back caused by running*'. This definition is though not much different from the consensus-based definition. In the following when injury incidences, prevalences and distributions are reported, the numbers should be interpreted with caution, due to the lack of a proper injury definition in the past as explained above

Injury incidence, prevalence and distribution

The injury incidence rate has been reported to range from 0.18 to 2.85 injuries per 1000km of running, depending on the population investigated (Videbaek et al., 2015). Novice runners sustains 0.86 injuries per 1000km of running (Bovens et al., 1989), while recreational and ultra marathon runners sustains 0.76 and 2.28 injuries per 1000km of running (Krabak et al., 2011;Wen et al., 1998). Since three different injury definitions were used, the comparison of incidence rate may not be appropriate. Although, Bovens et al. (1989) and Wen et al. (1998) used at similar time loss definition. Using a uniform injury definition, Kluitenberg et al. (2015) have reported that the running-related overuse injury prevalence was less than 30% for novice runners while exceeding 50% for recreational runners and ultra-marathoners during a one-year follow-up period (Figure 2).

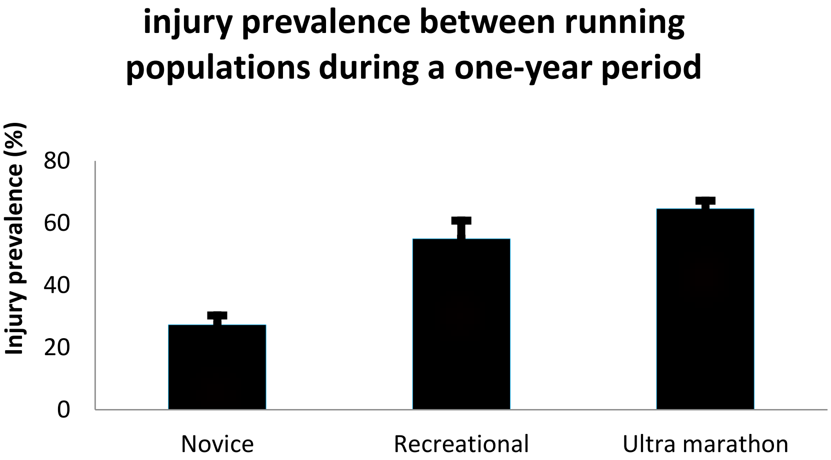


Figure 2: A graphical presentation of the injury prevalence for a one-year period in three different running populations (modified from Kluitenberg et al. 2015).

Injury location and diagnoses

Running-related overuse injuries are mainly related to excessive exposure and the knee and lower leg are the most frequent locations of overuse injury (Figure 3) (Kluitenberg et al., 2015).

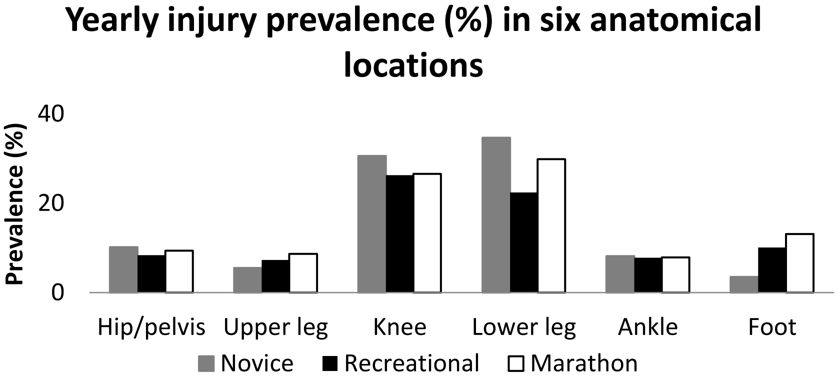


Figure 3: A graphical presentation of a one-year period prevalence of overuse injuries in each injury location in in three populations of runners (modified from Kluitenberg et al. 2015)

Within the knee and lower leg, some of the most frequent running-related overuse injuries were plantar fasciitis, patellar tendinopathy, iliotibial band syndrome and patellofemoral pain, medial tibial stress syndrome and Achilles tendinopathy, as illustrated in Table 1 (Lopes et al., 2012). Based on the fact that in the general population one out of four of the 5.8 mio. citizens is a recreational runner more than 1.4 mio. Danish citizens are recreational runners (Danmarks Statistik, 2018). Since the injury prevalence is 50% for recreational runners, it is reasonable to assume that more than 700.000 recreational runners are injured at any given day of the year. These runners may benefit from in depth knowledge concerning the etiology of these injuries

Table 1: Most frequent running-related overuse injuries (based on/derived from Lopes et al. 2012)

Diagnoses	Prevalence (%)
Plantar fasciitis	17.5
Patellar tendinopathy	12.5
Iliotibial band syndrome	10.5
Medial tibial stress syndrome	9.5
Achilles tendinopathy	9.5
Patellofemoral syndrome	5.5

RISK FACTORS

In the following section risk factors of running-related overuse injuries will be reviewed. A risk factor is defined by Ryan et al. (2006) as: “as a variable that, while not necessarily proven to be causative, is considered to be associated with the onset of injury”. Identification of risk factors should be based on biologically plausible mechanisms. This section will focus on risk factors that are modifiable. Modifiable risk factors are factors that are possible to modify by the runner without surgical treatment or factors that otherwise are impossible to change (e.g., age, gender or phenotype). This section and future research should focus on this, since these risk factors are amendable to change, which is necessary to develop injury prevention guideline (Cameron, 2010). However age, gender and previous injury will also be described since the literature indicates their importance and their importance for the results (of studies on injuries) (Cameron, 2010). Therefore, the following section will review the literature regarding training habits, equipment and environment, anthropometry and the musculoskeletal system’s association with running-related overuse injuries.

TRAINING HABITS

Several authors have proposed training errors (excessive distance, sudden change of training routines, sudden increases in running speed) as the cause of around 70% of all running-related overuse injuries (Johnson, 1983;Lysholm and Wiklander, 1987;Renstrom, 1993). Changes in the normal training routine, such as greater running distance, speed have been discussed as possible risk factors. In the following section the injury patterns related to running distance, time, frequency, speed and sudden changes in training will be reviewed.

Running distance

Running distance is defined as one of the greatest indicators for developing running-related overuse injury. Hootman et al. (2002) demonstrated an increased risk of running-related overuse injuries in adults running more than 20 miles per week in both males (HR=1.66; 95%CI:1.43-1.94) and females (HR=2.08; 95% CI:1.45-2.98) compared to running less than 20 miles per week. Moreover, running more than 40 miles per week more than doubled the risk of running-related overuse injury compared to those running less than 10 miles per week. Macera et al. (1989) demonstrated that an increased risk was found for recreational male runners performing more than 40 miles per week over a period of three months (OR:2.9; 95%CI: 1.1-7.5). In the same study, the risk of running-related overuse injury in recreational female runners did not differ between different mileage (Macera et al., 1989). Moreover Walter et al. (1989) reported no significant difference in relative risk between running less than 10 miles per week and running between 10 and 39 miles per week in runners. Three prospective studies on recreational runners did not find a significant relationship between weekly mileage and running-related overuse injury (Fields et al., 1990;Hespanhol Junior et al., 2013;Van Middelkoop et al., 2008). In contradiction, two prospective studies investigating recreational runners reported the opposite relationship, that increasing the mean session distance (HR: 0.8; 95% CI: 0.73-0.87) or km per week (HR:0.97) reduces the risk of running-related overuse injury (Malisoux et al., 2015;Theisen et al., 2014).

The relationship between mileage and specific running injuries has been investigated by several authors. Satterthwaite et al. (1999) demonstrated that marathon runners increasing mileage by 6 miles per week were reducing the risk of knee injuries (OR: 1.13; 95%CI: 1.04-1.23) but increasing the risk of hamstring injuries (OR:1.07; 95%CI: 1.02-1.13). Moreover, Wen et al. (1997) found marathon runners with greater weekly mileage were significantly associated with a greater risk of developing hamstring injuries (p-value = 0.012) and they also found that increasing weekly mileage and hours of running per week reduced knee and foot injuries. Messier et al. (1991;1995) reported that those runners having patellofemoral pain (21 miles per week) ran significantly less compared to healthy controls (30 miles per week), while those sustaining iliotibial band syndrome (31 miles per week) ran significantly more compared to another group of healthy controls (26 miles per week).

A study conducted by Nielsen et al. (2014) revealed that novice runners progressing more than 30% in distance per week increased their risk of developing patellofemoral pain, iliotibial band syndrome and patellar tendinopathy compared to novice runners progressing less than 10% in distance per week. In the same study, Running-related overuse injuries and non-running-related overuse injuries were not significantly related to progression of running distance on a weekly basis

Running time

Pollock et al. (1977) demonstrated that novice runners displayed an increase in injury proportion of 22%, 24% and 54% of the 15, 30 and 45-min duration groups, respectively. Moreover, Jakobsen et al. (1994) reported that marathon runners running on average 2.7 or 3.4 hours per week over a year had 6.9 and 7.4 injuries per 1000 hours of running. Buist et al. (2008) compared dfferences in running-related overuse injuries between novice runners progressing on average 10% or 24% in distance per week. These runners developed 30 (95%CI: 22-38) and 38 (95%CI: 27-49) running-related overuse injuries per 1000 hours of running, respectively. Although, this difference was not statistically significant. Hespanhol Junior et al. (2013) reported a significant Odds ratio of 1.01 (95%CI:1-1.02) with longer duration (min) per session in recreational runners. However Theisen et al. (2014) found no relationship between weekly running hours and running-related overuse injuries in recreational runners. In contradiction reported Malisoux et al. (2015;2016b) that for recreational runners increasing their mean session duration was reducing the risk of running-related overuse injuries (HR:0.96 and 0.98). This was confirmed by Bovens et al. (1989) that reported marathon runners running 162, 192 and 240 minutes per week sustained 12.1, 10 and 7 injuries per 1000 hours of running over a period of 18 months. Lastly Chang et al. (2012) found that runners spending more than 60 min per session compared to running less than 30 min per session had a lower risk of hip pain (OR:0.34; 95%CI: 0.11-0.86) but a higher risk of foot pain (OR:3.04; 95%CI: 1.47-6.28) during a 10-km, half marathon or marathon race. In the same study, time spent running was not significantly related with knee and ankle pain.

Training frequency

The frequency of running has been demonstrated to increase the risk of running-related overuse injury (Hespanhol Junior et al., 2013;Jacobsen et al., 2013;Kluitenberg et al., 2016;Macera et al., 1989;Malisoux et al., 2015;McKean et al., 2006;Pollock et al., 1977;Theisen et al., 2014;Walter et al., 1989;Wen et al., 1997) and some have reported that a greater running frequency could more than double the risk of running-related overuse injury in recreational runners (Knobloch et al., 2008). However, Kluitenberg et al. (2016) and Hespanhol Junior et al. (2013) did not find this to be significantly associated. Malisoux et al. (2016b) demonstrated that every one day increase in running frequency per week would increase the risk of running-related overuse injury (HR: 1.28; 95%CI:1.17-1.41). Moreover, Satterthwaite et al. (1999) found that every one increase in sessions per week in marathon runners would increase the risk of an injury in the anterior thigh (OR: 1.19; 95%CI: 1.05-1.34). Additionally, Knobloch et al. (2008) reported that recreational runners doing more than four times per week increased the risk of medial tibial stress syndrome (RR: 2.3; 95%CI. 1.09-4.96).

Running speed

A seperate risk factor of running-related overuse injuries may also be the running speed as greater speed increases the magnitude of the ground reaction force. However, only few studies have demonstrated a relationship between average running speed and running-related overuse injuries. Jacobs et al. (1986) reported that injured runners ran faster than the non-injured runners (p-value<0.05). Hootman et al. (2002) reported recreational male runners running below 15 min per mile to face a lower risk for running-related overuse injuries compared to runners doing running above 15 min per mile (HR:0.51; 95% CI: 0.35-0.74). A similar hazard ratio was found for women but this was only a trend. Kluitenberg et al. (2016) demonstrated that higher intensity was associated with increased injury occurrence (HR: 1.28; 95% CI 1.18–1.40). Moreover, runners doing tempo runs increased the risk of running-related overuse injuries (OR: 3.96; 95% CI 1.35–11.61) compared to those not performing tempo runs (Hamstra-Wright et al., 2013). In addition, the risk of running-related overuse injuries was increased in runners doing very high speed interval bouts (OR: 1.46; 95% CI: 1.02-2.1), while the risk was reduced in runners doing interval training (OR: 0.61; 95% CI: 0.43-0.88) compared to performing less intervals per week (Hespanhol Junior et al., 2013). However, the majority of the studies indicate no such relationship (Jakobsen et al., 1994;Malisoux et al., 2015;Malisoux et al., 2016b;Messier et al., 1991;Rauh et al., 2006;Theisen et al., 2014;Van Mechelen et al., 1993;Walter et al., 1989;Wen et al., 1998). Additionally, Ramskov et al. (2018) investigated differences in risk between groups of recreational runners progressing in running distance or running speed, repsectively. The study comprised a 16 week intervention divided in blocks of 4 weeks, which had a 23% progression in the first week and a 10% regression in the fourth week. The authors found that those runners increasing their running speed displayed an insignificant risk reduction of 14%-point (95%CI: -36.9%-8.9%) compared with the group increasing running distance.

Sudden changes in Training

Jacobs and Berson (1986) reported that one of three injured competitive and recreational runners had changed training schedule or running shoe. This was supported by a review comparing training schedules and concluded that sudden changes of weekly running distance or other kinds of training (surface change, hill workout or interval training) may be the key to the understanding of development of running-related overuse injuries (Ryan et al., 2006). A recently published study found that novice runners changing running distance increase the risk of running-related overuse injuries (OR: 1.28; 95%CI: 0.99-1.64), although it was only trending towards significance (Linton and Valentin, 2018). Moreover, Rauh (2014) reported injury rates to gradually increase the first three to four weeks after the transition from the cross-country preseason to the cross country season. The increased injury risk of sudden changes in training have also been reported in other sports (Gabbett et al., 2014;Hulin et al., 2014;Hulin et al., 2016;McNamara et al., 2017;Soligard et al., 2016).

In summary, evidence in general point both ways. Moreover, evidence on running distance indicates slightly greater proportion of the studies found a relationship *between high mileage and greater risk of injury. However, a number of high-quality studies revealed no association or demonstrated that high mileage was protective against injuries. Some studies investigated the effect of high mileage and specific injuries and found high mileage associated with increased risk of hamstring injuries and iliotibial band syndrome while it reduced the risk of patellofemoral pain, knee and foot injuries. The factor running duration indicates that increased weekly running hours increased the risk of running-related overuse injuries, although some evidence points towards no or a reverse relationship regarding running duration. Finally, the evidence of the impact of training frequency is rather clear, increasing the running frequency lead to increased risk of running-related overuse injuries. Moreover, the influence running speed have on running-related overuse injury is inconclusive. However, there seems to be agreement that sudden changes in training routine increases the risk of running-related overuse injuries, although evidence was sparse.*

EQUIPMENT AND ENVIRONMENT

The equipment and environment may influence the risk of running-related overuse injuries and are easily modified by changing running shoes, orthotics or the surface of running. In the following section running shoes, orthotics and running surface will be reviewed.

Running shoes

The possible influence of running shoe type and wear on the occurrence of running-related overuse injuries is highly debated (Malisoux et al., 2016a;Nielsen et al., 2013;Ryan et al., 2011), in spite of active runners have reported that they experience that running shoes have an influence on the development of running-related overuse injuries (Saragiotto et al., 2014).

Excessive pronation of the foot has been proposed to be related with an increased risk of developing running-related overuse injuries (Richards et al., 2009). Although foot pronation have been linked to running-related overuse injuries, the etiology of these type of injuries is still debated and results point against an effect of pronation or overpronation on the risk of running-related overuse injuries (Chang et al., 2014;Chuter and Janse de Jonge, 2012;Clements et al., 1984;Neal et al., 2014;Sharma et al., 2011). Nielsen et al. (2013) reported, based on a prospective study, that no difference in injury incidence proportion in novice runners was demonstrated across different foot posture indexes, while wearing neutral running shoes. Moreover, Ryan at al. (2011) found that runner wearing motion controls shoes reported greater levels of pain independent of the foot type. These results are contradicted by Malisoux et al. (2016a) based on a randomized controlled trial, who reported reduced risk of sustaining running-related overuse injuries in recreational runners with overpronated feet wearing motion control shoes in comparison to a group of runners with neutral feet wearing neutral running shoes (HR: 0.34; 95%CI: 1.01-3.22).

Running shoes are typically built with a heel-to-toe drop and varying midsole hardness, which is expected to influence the risk of running-related overuse injury.

Theisen et al. (2014) and Malisoux et al. (2016b) demonstrated that the risk of running-related overuse injuries was not significantly different in runners wearing different midsole hardness (asker-C: 54 vs 62au) or different heel-to-toe drop. Although, Malisoux et al. (2015) reported a reduced risk for runners who alternate their footwear regularly (HR:0.614; 95%CI:0.389-0.969).

Changing to new running shoes may increase the risk of running-related overuse injuries. One-third of the injured competitive and recreational runners had changed training technique, schedule or running shoe prior to the injury (Jacobs and Berson, 1986). This observation is supported by the fact that marathon runners developing injuries were changing running shoes every 7th month while non-injured runners were changing every 10th month (p-value < 0.05). Moreover, Duffey et al. (2000) found that injured distance runners were only running 536 miles (862km) before changing to a new shoe, while non-injured runners were using their running shoe for 693 miles (1135km) before changing to new running shoes (p-value < 0.05). Finally, Fuller et al. (2017) demonstrated that runners changing to minimalist shoes had more pain compared to runners changing to conventional running shoes. In a different study, Salzler et al. (2012) reported that seven out of ten runners were injured in the first two months after changing to minimalist shoes and the rest were injured after three, four and 10 months. All injuries occurred in the foot or ankle and nine out of ten were stress fractures.

Orthotics

Foot orthotics may be used as a replacement for the common insole in running shoes. Foot orthotics may reduce the risk of injury by changing unwanted movement patterns or reduce stress concentrations in vulnerable structures. Foot orthotics can be custom made in opposition to running shoes, which enables the possibility to target and potentially remove a specific unwanted movement.

Several cross-sectional studies have investigated the effect of foot orthotics on running-related overuse injuries. Marti et al. (1988) found that foot orthotics were associated with an increased risk of getting running-related overuse injuries while

McKean et al. (2006) confirmed that using orthotics increased the Odds of sustaining running-related overuse injuries by 1.91 and 1.83 in runners below and above the age of 40 compared to those not using orthotics. Wen et al. (1997) demonstrated that 22.78% of the marathon runners using shoe inserts, while only 3.88% of runners not using shoe insert were developing foot injuries (p-value<0.001). However, Reinking et al. (2013) revealed no effect of orthotic use. In contradiction, Chang et al. (2012) found that soft insoles (OR:0.31, 95%CI:0.11-0.86) and insoles with medial arch support (OR:0.66, 95%CI:0.47-0.92) reduced the risk of getting running-related overuse injuries significantly during a 10-km, half marathon and marathon competition compared to non-users.

Running surface

Most runners have preferences regarding their running surface. Some prefer the hardness of asphalt and concrete and others prefer the softness and variety of grass and trails.

The vast majority of the studies found no associations between running surface and the risk of running-related overuse injuries (Hespanhol Junior et al., 2013;Jacobs and Berson, 1986;Malisoux et al., 2015;Marti et al., 1988;Rauh et al., 2006;Taunton et al., 2003;Theisen et al., 2014;van Gent et al., 2007;Walter et al., 1989;Wen et al., 1997). However, there seems to be a relationship between running surface and specific injuries. Wen et al. (1997) demonstrated a significantly greater prevalence of back injuries (49.2% vs 71.6%; p-value = 0.005) and thigh injuries (42.2% vs 71.1%; p-value = 0.011) in runners spending less time running on concrete or asphalt. Knobloch et al. (2008) reported that running on asphalt decreased the risk of Achilles tendinopathy (RR: 0.47; 95%CI: 0.25-0.89), while sand increased the relative risk for Achilles tendinopathy (RR:10; 95%CI:1.12-92.8).

In summary, the choice of running footwear is not conclusively related with risk of getting running-related overuse injuries. However, there seems to be sparse but consistent results showing that a change of running shoes increases the risk of getting running-related overuse injuries. In addition, orthotics and running surface are not conclusively related with the risk of getting running-related overuse injuries. Although harder training surface seems to increase the prevalence of back and thigh injuries, while reducing the risk of Achilles tendinopathy. However, it remains unknown whether subgroups of runners may favour the use of running shoes, orthotics and/or specific running surfaces.

NON-MODIFIABLE RISK FACTORS

Non-modifiable risk factors are usually not of interest but some of these have been demonstrated to be important and have an effect on running-related overuse injury (Cameron, 2010). In the following the influence of age, gender and previous injury will be discussed.

Age

Several studies have investigated the relationship between age and running-related overuse injury. Nielsen et al. (2013a) found that novice runners between 45 and 65 were trending towards a greater risk of running-related overuse injury compared to runners between 30-45 years of age (RD:14.7%; 95%CI:-2.1 31.5%), while runners between 18-30 years of age did not show any statistical differences in injury risk when compared to the runners between 30-45 year/s of age. Kluitenberg et al. (2015) demonstrated an increased injury risk in novice runners by one unit increase in age (HR:1.02; 95%CI: 1-1.04). On the contrary, Malisoux et al. (2015) and Buist et al. (2010a) did not find any statistically significant relationship between age and running-related overuse injuries in both novice and recreational runners. Moreover, the opposite relationship has been reported. Buist et al. (2010b) found that increasing age by ten years would significantly decrease the risk of running-related overuse injuries in recreational male runners (HR: 0.63; 95%CI: 0.48-0.82) and a trend towards a significant reduced effect was demonstrated for recreational female runners (HR:0.82; 95%CI: 0.66-0.1.02). Satterthwaite et al. (1999) reported a higher age in marathon runners to reduce the risk of injury, with those above 35years to face the lowest risk (OR: 0.43; 95%CI:0.21-0.87). However, in the same study a complex relationship for specific injuries was revealed. The risk of injury in the anterior thigh had a reversed-U relationship with age, with those between 30-34 years to face the greatest risk (OR:1.83; 95%CI: 1.04-3.22) and those below 25 and above 40 years facing the lowest risk (OR: 0.96; 95%CI: 0.56-1.63). Moreover, increased age reduced the risk of injury in the calves, with those above 40 years facing the lowest risk (OR:0.4; 95%CI: 0.23-0.73). Hootman et al. (2002) found that a 10 year increase in age would reduce the risk of injury in both recreational men (HR:0.88;95%CI:0.86-0.91) and recreational women (HR: 0.74; 95%CI:0.69-0.80).

Some studies have addressed age and specific injuries. Wen et al. (1997) reported higher age to be a risk factor for hamstring injuries. Hirschmüller et al. (2012) demonstrated that runners with Achilles tendinopathy were older compared to asymptomatic runners (48 vs 43 year; p-value<0.05). Taunton et al. (2002) reported that increasing age was increasing the risk for patellofemoral pain, iliotibial band syndrome, patellar tendinopthy, medial tibial stress syndrome and reduced the risk of plantar fasciitis, meniscal injuries and Achilles tendinopathy. The data of Wen et al (1998) may suggest that at higher age the risk for knee injuries was increased (RR:2.09; 95%CI:0.95-4.48) and at a low(er) age the risk of injuries was decreased (RR:0.38; 95%CI:0.15-0.97). Marti et al. (1988) found that runners with Achilles tendinopathy and pulled calf muscle were significantly older, while those having knee pain were significantly younger. Although, Kelsey et al. (2007) did not find any association between age and risk of stress fractures either. Van Ginckel et al. (2009) did not find any association between age and risk of Achilles tendinopathy. Thijs et al. (2011) did not find any association between age and risk of patellofemoral pain syndrome.

Gender

Few of the studies have demonstrated that gender might have an influence on the risk of running-related overuse injuries. Buist et al. (2010a) found that novice male runners had a greater risk of running-related overuse injuries compared to women (HR: 1.5; p-value = 0.04). In the same study, a one unit increase in body mass index increased the hazard ratio by 1.12 for running-related overuse injury in novice male runners (p-value = 0.01) but not in novice female runners (HR:0.99; p-value = 0.84). Satterthwaite et al. (1999) revealed that male marathon runners were in increased risk of getting hamstring and calves injuries, while the risk of the male runners getting hip injuries compared to women was lower. However, the majority of the evidence point towards no differences in the risk of running-related overuse injuries between males and females (Hirschmüller et al., 2012;Kluitenberg, van Middelkoop, Smits et al., 2015;Malisoux et al., 2015; Nielsen, Buist, Parner, Nohr, Sørensen, Lind, and Rasmussen, 2013a;Reinking et al., 2007;Reinking et al., 2013;Theisen et al., 2014).

Previous injury

The vast majority of the literature, including one randomised controlled trial and 11 prospective studies demonstrated previous injury to increase the risk of running-related overuse injury with odds ratio, hazard ratio or relative risk being above 1.2 and the most extreme cases were greater than seven (Buist et al., 2010a;Hespanhol Junior et al., 2013;Hirschmüller et al., 2012;Hootman et al., 2002;Kelsey et al., 2007;Kluitenberg et al., 2016;Macera et al., 1989;Malisoux et al., 2015;Marti et al., 1988;Parker et al., 2011;Rasmussen et al., 2013;Reinking et al., 2007;Theisen et al., 2014;Walter et al., 1989). Moreover, it seems like the severity of the injury and the closer the previous injury was in time, the higher is the running-related overuse injury risk (Buist et al., 2010a;Buist et al., 2010b;Parker et al., 2011). However, five studies reported no association between previous injury and risk of running-related overuse injury (Buist et al., 2010b;Kluitenberg, van Middelkoop, Smits et al., 2015; Nielsen, Buist, Parner, Nohr, Sørensen, Lind, and Rasmussen, 2013a;Taunton et al., 2002;van Middelkoop et al., 2007), although Nielsen et al. (2013a) revealed previous non-running-related overuse injury to be a risk factor of running-related overuse injury.

In summary, evidence on the association of age with the development of running-related overuse injuries point in both directions, indicating that both being young and being old is a risk factor. Moreover, a few studies found that males were at increased risk of developing running-related overuse injuries, while the majority of the evidence did not find a significant difference between genders/sexes or the difference was not clinically relevant. Lastly, the vast majority of the evidence indicates that previous injury has an effect on running-related overuse injury risk, however, some studies failed to confirm this relationship. It seems like the more severe the injury was and the shorter the time after an injury, the greater the risk of developing a new running-related overuse injury.

ANTHROPOMETRY

Anthropometry is the science, which measure human body size and proportions. Anthropometric factors may affect the risk of getting running-related overuse injuries and are considered important by many in the analysis of risk factors. The following anthropometrical factors will be discussed: body weight and body mass index.

Body weight

Wen et al. (1997) reported that female marathon runners with back injuries had a greater body weight (76.6kg vs 63.3kg; p-value = 0.002) compared to controls. Wen et al. (1998) demonstrated that increased body weight may reduce the risk of foot injuries (RR: 0.94; 95%CI:0.89-0.99) slightly. Taunton et al. (2002) found that lower weight reduced the risk of plantar fasciitis in recreational runners (OR: 0.38; 95%CI: 0.203-0.706). Duffey et al. (2000) reported that lower weight increased the risk of anterior knee pain in distance runners. Two prospective studies found no statistically significant association between body weight and running-related overuse injuries in competitive and novice runners (Ghani Zadah Hesar et al., 2009;Valliant, 1981). Prospective studies investigating body weights relationship with specific injuries did neither demonstrate a relationship. Kelsey et al. (2007) revealed no association between body weight and risk of stress fractures in female cross country runners. Hirschmüller et al. (2012) and Van Ginckel et al. (2009) found no association between body weight and risk of Achilles tendinopathy in both novice and recreational runners. Thijs et al. (2011) reported no association between body weight and risk of patellofemoral pain syndrome in novice runners.

Studies have reported body mass index to increase and decrease the risk of running-related injuries. Hootman et al. (2002) reported that increased body mass index in recreational adult women increased the risk of running-related overuse injuries. This was confirmed by Buist et al. (2010a) that found one unit increase in body mass index increased the risk of running-related overuse injury in novice male runners (HR: 1.12; p-value = 0.01) but not in novice female runners (HR:0.99; p-value = 0.84). In line with this Buist et al. (2010b) confirmed that higher body mass index increased the risk of running-related overuse injuries in recreational female runners but not significantly in recreational male runners. Moreover, Kluitenberg et al. (2015) verified an increased risk with increases in body mass index for both novice male runners (HR:1.04; 95%CI:1.01-1.08) and novice female runners (HR: 1.04; 95%CI:1-1.07). In addition were back injuries associated with greater body mass index (27.2 kg/m^2 vs 23.4 kg/m^2; p-value = 0.009) in female marathon runners (Wen et al., 1997). On the contrary, several studies revealed no effect. Theisen et al. (2014) and Malisoux et al. (2015) demonstrated no significant relationship between body mass index and running-related overuse injuries in recreational runners. In addition, Nielsen et al. (2013) found no increased risk of running-related overuse injury in novice runners between four different body mass index groups. However the risk of running-related injury was insignificantly increased with an increase in body mass index. Moreover no associations between body mass index and risk of stress fractures (Kelsey et al., 2007), Achilles tendinopathy (Hirschmüller et al., 2012;Van Ginckel et al., 2009), patellofemoral pain syndrome (Thijs et al., 2011), medial tibial stress syndrome (Yagi et al., 2013) and anterior knee pain (Duffey et al., 2000) have been demonstrated. Finally, Taunton et al. (2003) found that recreational runners with higher body mass index strongly decreased the risk of running-related overuse injuries in a prospective study.

In summary, no clear relationships between any of the anthropometric factors have been demonstrated but it cannot be excluded that the risk of running injury is within specific groups of runners associated with both body weight and body mass index.

MUSCULOSKELETAL SYSTEM

Factors related to the musculoskeletal system are often suggested or identified as risk factors for running-related overuse injuries. The influence of muscle strength/weakness, flexibility, lower limb alignment and foot posture, kinetic and kinematics will be reviewed below.

Muscle strength/weakness

Lack of muscle strength has been suggested as a potential risk factor for running-related overuse injuries. The influence of hip, kne and ankle muscle strength will be discussed below.

Hip muscle strength

The vast majority of studies on hip strength and specific running-related overuse injuries are performed as cross-sectional studies. No significant difference in hip abduction strength between recreational runners developing iliotibial band syndrome and controls was found, unaffected by the measure of contraction type (isometric and isokinetic) (Brown et al., 2016;Foch et al., 2015;Grau et al., 2008;Noehren et al., 2014). However Fredericson et al. (2000) demonstrated that male and female distance runners with iliotibial band syndrome had less than 8% of bodyweight x height in isometric hip abduction strength, while non-injured distance runners had more than 9% of bodyweight x height in isometric hip abduction strength (p-value<0.05). Cross-sectional studies investigated the relationship between hip strength and patellofemoral pain with inconclusive result. Plastaras et al. (2016) reported recreational female runners with patellofemoral pain having greater absolute hip abduction strength compared to the weaker limb of controls (9.9N vs 8.9N; p-value = 0.03). Moreover, Esculier et al. (2015) confirmed this relationship in recreational runners (34.2% strength of bodyweight vs 33.9% strength of body weight). On the contrary, recreational runners with patellofemoral pain have been demonstrated to have weaker hip strength normalized to bodyweight (0.29N/BW vs 0.37N/BW; p-value = 0.03 and 0.13N/BW vs 0.18N/BW; p-value < 0.05) (Cichanowski et al., 2007;Ferber et al., 2011). This was verified by a study normalizing to bodyweight and height (15.3 kg x cm / BW vs 17.3 kg x cm / BW; p-value=0.045) (Dierks et al., 2008). However, Esculier et al. (2015) found no significant differences between external hip rotation and hip extension strength and the risk of patellofemoral pain in recreational runners. Lastly only one of the identified studes has investigated isometric hip abductor strength and the risk of getting an Achilles tendinopathy. They reported that recreational runners with Achilles tendinopathy have reduced hip abduction strength compared to controls (Niemuth et al., 2005).

Prospective studies focusing on the link between hip strength and patellofemoral pain indicate weak hip abductors is a risk factor. Ramskov et al. (2015) reported that a weak eccentric hip abduction strength increased the risk of patellofemoral pain syndrome over the first 50 kilometers in novice runners. To support this, Luedke et al. (2015) found that high school cross country runners developing anterior knee pain were all in the lowest tertile of isometric hip abductor strength, although only three of 68 runners developed anterior knee pain. However, two studies reported no difference (Finnof et al., 2011;Thijs et al., 2011). Moreover, Finnof et al. (2011) reported weaker hip external rotators as risk factors in high school running athletes. Last, Thijs et al. (2011) reported hip muscle strength not to be a risk factor for the development of patellofemoral pain syndrome in novice runners. Moreover, studies investigating the relationship between isometric hip abduction strength and the risk of developing either medial tibial stress syndrome or Achilles tendinopathy demonstrated no significant difference in hip abduction strength between injured and controls (Hein et al., 2013;Luedke et al., 2015;Yagi et al., 2013).

Knee muscle strength

Knee muscle strength has been proposed as a potential risk factor for the development of running-related overuse injuries such as anterior knee pain, shin injury and Achilles tendinopathy. Luedke et al. (2015) found that high school cross country runners developing anterior knee pain were all in the lowest tertile of isometric knee extensor and flexor strength, although only three of 68 runners developed anterior knee pain. In support, knee extensor and flexor strength was significantly reduced in distance runners with anterior knee pain (Duffey et al., 2000). However, isometric knee extensor and flexor strength was not a predictor of shin injury in high school cross country runners (Luedke et al., 2015).

Ankle muscle strength

Haglun-Åkerlind et al. (1993) found that middle distance runners with Achilles tendon injury had significantly lower eccentric torques of the plantar-flexors at 30, 60, 120 and 180 degrees per second ranging between 15-25Nm lower muscle torque compared to controls. McCrory et al. (1999) confirmed that peak isokinetic ankle plantar flexion strength at 180 degrees per second was reduced in Achilles tendon injured runners (33.84Nm vs 29.47Nm; p-value=0.008). This relationship was also demonstrated for competivtive and recreational runners suffering from plantar fasciitis. These runners had lower isokinetic ankle plantar flexor strength at 60 and 180 degrees per second compared to controls and their non-injured ankle (p-value<0.001) (Kibler et al., 1991). Moreover, Saeki et al. (2017) found an insignificant lower isokinetic ankle plantar flexor strength for the runners suffering from medial tibial stress syndrome compared to controls.

In summary, the literature is inconsistent with regard to the association between hip strength and running-related overuse injuries, although some prospective studies demonstrated statistical significant weaker hip abductors to be related with patellofemoral pain. Weak knee muscles seem to be associated with anterior knee pain, and Achilles tendinopathy but not shin injury, although evidence is sparse. Weak ankle plantar flexor muscles seem to be a predictor of Achilles tendinopathy, plantar fasciitis and maybe also medial tibial stress syndrome, although evidence is sparse.

Flexibility

Stretching is considered by many as a part of the training routine for runners, as a tool for preparation, performance enhacement and injury prevention. Although, the basis of recommending stretching for injury prevention is not based on scientific evidence associating reduced flexibility to an increased risk of running-related overuse injury. In the following the influence of flexibility on the risk of developing running-related overuse injuries will be reviewed.

To date, very little evidence exists with respect to the relationship between flexibility and running-related overuse injuries. Hreljac et al. (2000) found that ankle range of motion was not significantly different between injured and non-injured runners. Additionally, Duffey et al. (2000) reported that distance runners with anterior knee pain had significantly reduced knee flexion range of motion compared to controls (137.3 degrees vs 139.5 degrees, p-value<0.05). Noehren et al. (2014) demonstrated that hip abduction flexibility was statistically significantly reduced in recreational male runners suffering from ilitiotibial band syndrome when compared to controls

(18.8degrees vs 17.6 degrees; p-value = 0.03). In contrast Miller et al. (2007) revealed no significant differences in flexibility of the iliotibial band between recreational runners with iliotibial band syndrome and controls, although flexibility was reduced in both legs and at 0 and 90 degrees of hip flexion in the injured runners compared to the controls. Lastly, Kibler (1991) reported that ankle range of motion was reduced in competivtive and recreational runners with plantar fasciitis compared to controls (p-value < 0.001).

In summary, evidence is sparse, but reduced hip abduction range of motion may be a risk factor for ilitiotibial band syndrome and reduced ankle range of motion may be a risk factor for Achilles tendon injuries and plantar fasciitis.

Lower limb alignment and foot posture

Lower limb alignment or an abnormal/mal alignment have been suspected to be a crucial part of running-related overuse injuries. Malalignment of the lower limb which have been discussed as potential risk factors for running-related overuse injuries circulates around alignment of the knee and foot

Foot posture

The relationship between the risk of running-related overuse injury and foot posture, such as arch index, navicular drop and foot posture index respectively, have been investigated.

Arch index seems not to be associated with running-related overuse injuries (Hespanhol Junior et al., 2015;Hreljac et al., 2000;Taunton et al., 2003;Wen et al., 1997). However, evidence is sparse on arch index and specific injuries. Arch index was not found to be associated with patellofemoral pain (Messier et al., 1991). However recreational runners with plantar fasciitis displayed reduced arch index (Arch index 0.32 vs 0.34; p-value = 0.01 and 0.17 vs 0.22; p-value = 0.009) (Pohl et al., 2009;Ribeiro et al., 2011).

Navicular drop seems not to be associated with running-related overuse injuries (Bennett et al., 2012;Buist et al., 2010a), although Bennet et al. (2012) found that cross country runners with a navicular drop greater than 10mm displayed a higher odds of developing running-related overuse injuries on the medial side (OR:<3; p-value<0.001). Moreover, Bennett et al. (2001) demonstrated that cross country runners developing medial tibial stress syndrome displayed significantly greater navicular drop compared to non-injured runners (6.8mm vs 3.6mm; p-value < 0.01). Last, Plisky et al. (2007) revealed no association between navicular drop and the risk of medial tibial stress syndrome.

It has been demonstrated that foot posture index is not significantly associated with injuries in novice runners (Nielsen et al., 2013). however two studies indicated that feet with a neutral foot posture index displayed the lowest percentage of running-related overuse injuries compared to pronated foot postures in experienced runners (combined prevalence: neutral feet=27.1% vs pronated feed= 36.8%) (Malisoux et al., 2016a;Ryan et al., 2011), although no statistical analyses were performed.

Knee alignment

Factors for quantification of knee alignment are: Q-angle and Frontal knee alignment. The relationship between these factors and running-related overuse injuries have been investigated.

Evidence on the association between Q-angle and running-related overuse injuries is rather clear. No association between Q-angle and running-related overuse injuries have so far been demonstrated in runners (Hespanhol Junior et al., 2015;Rasmskov et al., 2013;Zifchock et al., 2008). This is also the case for: patellofemoral pain (Duffey et al., 2000;Messier et al., 1991;Thijs et al., 2011), medial tibial stress syndrome (Yagi et al., 2013), plantar fasciitis (Messier and Pittala, 1988), Achilles tendinopathy (McCrory et al., 1999). However, Rauh et al. (2007) reported that highschool cross-country runners with a Q-angle above 20 degrees had a higher risk of getting knee injuries compared to those with a Q-angle between 10 and 15 degrees (RR:1.7; 95%CI: 2.3-14.1).

Regarding frontal knee alignment, evidence is sparse but knee varus seems not to be a risk factor for developing running-related overuse injuries in marathon runners (Wen et al., 1997). However, Becker et al. (2017) found that greater knee varus may be a predictor for medial tibial stress syndrome in recreational runners (8.63 deg vs 6.63deg; p-value <0.05), which was in agreement with Wen et al. (1998) that confirmed the same relationship for marathon runners (IRR:1.09; 95%CI: 1.032-1.146).

In summary, evidence on relationships between factors describing foot posture or lower limb alignment and running-related overuse injuries is inconclusive. The association between lower limb alignment and specific running-related overuse injuries is sparse and it is questionable if the inconclusive results are owing to the measurements of malalignment are obtained in static and not dynamic situations, since static measurements may not represent the dynamic situation of the musculoskeletal system.

Kinematics and kinetics

The lower extremity is composed of a chain of interconnected segments that influence each other (Loudon and Reiman, 2012). Each segment transfers forces and motions to the adjacents segments through the joints in a specific and highly specialized pattern under natural circumstances (Bunton et al., 1993;Heller et al., 2003;Lima et al., 2018;Sakaguchi et al., 2015). Therefore, theoretically, deviations in the kinematics and kinetics of the basic pattern may be an indication of unwanted stress concentrations on specific structures, which again may increase the risk of specific injuries. For example limited ankle range of motion may be related with increased knee abduction angle and knee abduction impulse, which again may increase the risk of some knee injuries (Lima et al., 2018;Sakaguchi et al., 2015).

Hip kinematics and kinetics

The relationship between the magnitude of hip adduction during running and running-related overuse injuries has been studied intensively leading to no consensus. It has been demonstrated that peak hip adduction was reduced in recreational female runners (15.4deg vs 16.8deg; p-value = 0.27)(Brown et al., 2016), recreational runners (9deg vs13deg; p-value<0.05)(Grau et al., 2011) and recreational runners with a history of iliotibial band syndrome (13.4 vs 16.6; p-value = 0.02)(Foch et al.,

2015) compared to controls. However, Foch et al. (2015) did not find this difference between runners with current iliotibial band syndrome and controls. This was contradicted by Ferber et al. (2010) and Noehren et al. (2007) who found peak hip adduction angle to be significantly increased in recreational female runners with a history of iliotibial band syndrome (14.1 vs 10.6; p-value = 0.01) and competitive female runners developing iliotibial band syndrome (10.39 vs 7.92; p-value <0.05). Moreover, recreational runners with iliotibial band syndrome displayed less hip adduction velocity (119deg/sec vs 30 deg/sec; p-value:<0.05) (Grau et al., 2011), higher peak iliotibial band strain (8.5% vs. 7.5%; p-value<0.05) (Miller et al., 2007) compared to controls. However, three studies did not demonstrate any association between hip abduction moment and iliotibial band syndrome in recreational and competitive runners (Ferber et al., 2010;Foch et al., 2015;Noehren et al., 2007). Moreover, two studies consisting mostly of recreational female runners demonstrated that patellofemoral pain development was associated with more than three degree increased hip adduction angle compared to controls (Dierks et al., 2011;Noehren et al., 2013). This was verified by several other studies (Luz et al., 2018;Watari et al., 2018;Willson and Davis, 2008). Moreover, hip internal rotation does not seem to be associated with either iliotibial band syndrome, patellofemoral pain or Achilles tendinopathy in novice runners (Buist et al., 2010a).

Knee kinematics and kinetics

Few studies have investigated the relationship between knee kinematic factors and running-related overuse injuries. Female runners with iliotibial band syndrome display more than two degrees greater knee internal rotation angle compared to controls (Ferber et al., 2010;Noehren et al., 2007), although knee external rotational moment was not significantly different from controls (Ferber et al., 2010;Noehren et al., 2007). Recreational male runners with iliotibial band syndrome displayed greater peak knee adduction angle (3.6deg; p-value:0.001) compared to controls (Noehren et al., 2014). Recreational runners with Patellofemoral pain displayed more than 3 degrees reduced knee flexion angle (Dierks et al., 2011). Moreover, Dierks et al. (2011) revealed a subgroup of recreational runners with patellofemoral pain displayed more that 15% greater knee abduction angle (4.7deg vs -1.3deg), while the rest of the runners with patellofemoral pain displayed less hip adduction (3.8deg vs 11.8deg) compared to controls. Lastly, Azevedo et al. (2009) found that knee flexion range of motion during eccentric phase of running stance was significant reduced in runners with Achilles tendinopathy compared to controls (26.3deg vs 22deg; p-value = 0.011).

Foot and ankle kinematics and kinetics

Studies have demonstrated varying effect of foot and ankle kinematics and kinetics on the risk of specific injuries. Female runners with iliotibial band syndrome have been associated with reduced peak rearfoot eversion angle (9.7deg vs 11.6deg; p-value = 0.07) (Noehren et al., 2007). Peak rearfoot inversion moment was not associated with iliotibial band syndrome in both recreational and competitive female runners (Ferber et al., 2010;Noehren et al., 2007). Noehren et al. (2013) revealed no significant association between rearfoot eversion angle during running and development of patellofemoral pain, although rearfoot eversion angle was reduced in female runners with patellofemoral pain. Moreover, Thijs et al. (2008) reported that novice and recreational runners with patellofemoral pain reached peak force on the medial (0.061s vs 0.081s; p-value = 0.016) and lateral heel (0.04s vs 0.054s; p-value = 0.037) earlier than controls. Runners developing Achilles tendinopathy displayed greater peak pronation (11.98 vs. 11.42; p-value<0.05), peak pronation velocity (376.5 deg per second vs 374.3 deg per second; p-value < 0.05), while time to maximum pronation was shorter (37.3 % of stance vs 40.32 % of stance; p-value <0.05) (McCrory et al., 1999). Moreover, novice runners with Achilles tendinopathy reached peak force on the medial heel earlier (0.016s vs 0.02s; p-value = 0.032) compared to controls (Van Ginckel et al., 2009).

In summary, hip adduction angle during running appears to be associated with both increased and decreased risk for iliotibial band syndrome. Hip adduction angle seems strongly related with increased risk for patellofemoral pain. Reduced hip internal rotation angle during running was associated with patellofemoral pain, while an increased hip internal rotation angle may be a risk factor for medial tibial *stress syndrome. Evidence of associations between knee kinematic and kinetic factors and running-related overuse injuries is sparse, although it seems that greater knee internal rotation and greater peak knee adduction angle may be associated with iliotibial band syndrome. Increased peak knee abduction angle is associated with Patellofemoral pain. Lastly Achilles tendinopathy seems to be related to the magnitude of foot pronation and time to peak force.*

Summary of risk factors review

Training habits indicated varying association with running-related overuse injuries. Greater and reduced running distance was both increasing and decreasing the risk of running-related overuse injuries. Moreover, evidence on running duration indicates that increased weekly running hours increased the risk of running-related overuse injuries. Although, some evidence points against no or the reverse relationship regarding running duration. Finally, the evidence of the impact of training frequency and running speed on running-related overuse injury is inconclusive. However, there seems to be agreement that sudden changes in training routine increases the risk of running-related overuse injuries.

Age and gender was not coclusively related with developing running-related overuse injuries. The vast majority of the literature found previous injury to be associated with the risk of developing a new injury. It seems that the more severe the injury was and the shorter the time after an injury; the greater the risk of developing a new running-related overuse injury. This may explain why a few studies did not find this result, since the previous injury may not have been severe enough or potentially too much time have elapsed from the injury and the runner have fully recovered from the injury

None of the risk factors related with, equipment, environment and anthropometry was conclusively related with developing running-related overuse injuries. However, there seems to be agreement that sudden changes in training routine increases the risk of running-related overuse injuries, although evidence was sparse

Moreover, the literature is inconsistent with regard to the association between hip strength and running-related overuse injuries, although some prospective studies demonstrated weaker hip abduction strength to be related with increased risk of developing patellofemoral pain. Weak knee muscles seems to be associated with anterior knee pain, and Achilles tendinopathy but not shin injury, although evidence was sparse. Weak ankle plantar flexor muscles seem to be associated with Achilles tendinopathy, plantar fasciitis and maybe also medial tibial stress syndrome, although evidence is sparse.

Evidence of the effect of flexibility on the risk of running-related overuse injury is sparse, but reduced hip abduction range of motion may be a risk factor for iliotibial band syndrome and reduced ankle range of motion may be a risk factor for Achilles tendon injuries and plantar fasciitis. Moreover, evidence on the relationships between factors describing the foot posture and lower limb alignment and running-related overuse injuries is inconclusive. The association between lower limb alignment and specific running-related overuse injuries is sparse and it is questionable if the results are owing to static malalignment measurement. Static measurements may not represent the dynamic situation of the musculoskeletal system.

Finally, evidence is sparse regarding kinematics and kinetics association with running-related overuse injuries, although increased hip adduction angle was associated with patellofemoral pain. Reduced hip internal rotation angle during running was associated with patellofemoral pain, while an increased hip internal rotation angle may be a risk factor of medial tibial stress syndrome. Evidence on the association between knee kinematic and kinetic factors and running-related overuse injuries is sparse, although it seems that greater knee internal rotation and greater peak knee adduction angle may be associated with iliotibial band syndrome. Increased peak knee abduction angle is associated with Patellofemoral pain. Lastly Achilles tendinopathy seems to be related to the magnitude of foot pronation and time to peak force.

ETIOLOGY OF THE MOST COMMON RUNNING-RELATED OVERUSE INJURIES

As explained previously the most frequent running-related overuse injuries are plantar fasciitis, patellar tendinopathy, iliotibial band syndrome, medial tibial stress syndrome, Achilles tendinopathy and patellofemoral pain. The following paragraph will describe current state of understanding of the etiologies associated with these injuries.

Plantar fasciitis

Plantar fasciitis is characterized by pain in the plantar region of the heel after prolonged period of rest (Beeson, 2014;Ferreira, 2014). Pain is typically worse in the morning and improves after the first few steps of the day (Prichasuk, 1994). It is more prevalent in male runners (54% vs 46%) (Taunton et al., 2002). Several etiologies have been proposed, such as inflammation (irritated fascia) of the plantar fascia or a degenerated (worn fascia, which is not inflamed so pain stems from something else) plantar fascia (Johnson et al., 2014;Neufeld and Cerrato, 2008), although they are not fully supported by the literature (Prichasuk, 1994). Plantar fasciitis is more likely a combination of inflammation and degeneration of the plantar fascia, although it seems plausible that the injury is initiated by a inflammation developing into a degenerated fascia. The plantar fascia or aponeurosis is a band of connective tissue that supports the arch of the foot (Cutts et al., 2012;Orchard, 2012). During the weight bearing phase, the sole of the foot is compressed and a traction force of the plantar fascia is generated (Ferreira, 2014). This traction force increases with increased dorsiflexion of the great toe (Caravaggi et al., 2009). The traction force is repeated for each step, which over time may result in degeneration and micro tears at the origin of the plantar fascia, at the medial site of the calcaneal tuberosity (Cutts et al., 2012;Ferreira, 2014;Neufeld and Cerrato, 2008;Prichasuk, 1994). These micro tears may lead to an inflammatory process together with a degradation of the plantar fascia over time if recovery between running sessions is insufficient.

Risk factors for plantar fasciitis include excessive pronation (Buchbinder, 2004;Chang et al., 2014;Chuter and Janse de Jonge, 2012), reduced arch index (Pohl et al., 2009;Ribeiro et al., 2011), reduced ankle plantar flexor strength (Kibler et al., 1991), limited ankle dorsiflexion (Kibler et al., 1991;Buchbinder, 2004;Pohl et al., 2009;Riddle et al., 2003), greater instantaneous vertical loading rate (Pohl et al., 2009), being younger (1994;Taunton et al., 2002), being employed at occupations with prolonged standing (Buchbinder, 2004;Riddle et al., 2003), being obese (Buchbinder, 2004;Prichasuk, 1994;Riddle et al., 2003;Taunton et al., 2002;van Leeuwen et al., 2016). From these risk factors it seems like all are either increasing the magnitude of force or the rate the force is applied to the plantar fascia

Patellar tendinopathy

Patellar tendinopathy is one source of anterior knee pain with a prevalence above 20% in runners (Lopes et al., 2012;Malliaras et al., 2015). Patellar tendinopathy is characterized with local pain at apex of the patella and increasing pain related with increased demand on the knee extensors (Ferretti et al., 1983;Lian et al., 2005;Malliaras et al., 2015;Rudavsky and Cook, 2014). Patellar tendinopathy is prevalent in younger male athletes between 15-30 years old, who participate in activities with repetitive landings, which gives high loads on the patellar tendon during the eccentric phase (Lian et al., 2005;Visnes and Bahr, 2013). Patellar tendinopathy is an overuse injury with a gradual onset of pain, which often is neglected in the initial phase of the gradual onset of pain and training is continued (Rudavsky and Cook, 2014). The gradual onset of pain may likely be introduced by sudden increases in running distance which may be linked with patellar tendinopathy (Grau et al., 2008; Nielsen et al., 2014). Greater running distance increases the number of stride cycles. Each stride cycle puts stress on the patellar tendon and insufficient rest between each running session (Shepherd and Screen, 2013), can reduce the capacity of the tendons to withstand load, which may increase the risk of patellar tendinopathy (Cook et al., 2001;Malliaras, Cook et al., 2006a).

Runners sustaining patellar tendinopathy demonstrated increased knee flexion velocity, foot pronation velocity and greater hip adduction angle, although the latter was only a trend (Grau et al., 2008). It is plausible that these movements put greater stress on the patellar tendon during the stance phase. These movements or the unwanted stress on the patellar tendon could be owing to a lack of inter-joint coordination (Grau et al., 2008), motor cortex inhibition of the quadriceps or a later onset of rectus femoris, vastus lateralis or biceps femoris (Janssen et al., 2015). Moreover, the risk for patellar tendinopathy may increase with limited quadriceps and hamstring flexibility (Cook et al., 2004;Crossley et al., 2007;Witvrouw et al., 2001), reduced ankle dorsiflexion range of motion (Backman and Danielson, 2011;Malliaras, Cook et al., 2006b), lower foot arch height (Crossley et al., 2007). Lastly, greater strength of the quadriceps have been associated with reduced patellar tendon pain (Crossley et al., 2007), although two studies found the opposite (Lian et al., 1996;Visnes and Bahr, 2013).

Illiotibial band syndrome

Illiotibial band syndrome is characterized by pain on the lateral aspect of the knee (Lavine, 2010;Louw and Deary, 2014). Pain occurs typically only after running. The etiology of illiotibial band syndrome is debated. Several authors have proposed a friction theory where the iliotibial band grinds anterior-posteriorly over the lateral femoral epicondyle during repetitive knee motion, sometimes accompanied with tightening of the iliotibial band (Lavine, 2010;Strauss et al., 2011). Fairclough et al. (2006;2007) demonstrated that iliotibial band syndrome may evolve from repetitive cycles of tightening of the lateral fascia. This is in line with the observations by Miller et al. (2007) who reported reduced iliotibial band flexibility to be a risk factor of iliotibial band syndrome.

Risk factors for iliotibial band syndrome includes sudden increases in running distance (Messier et al., 1995; Nielsen et al., 2014), weak hip abduction strength (Brown et al., 2016;Foch et al., 2015;Grau et al., 2008;Noehren et al., 2014), greater peak hip adduction impulse (MacMahon et al., 2000) and increased iliotibial band strain (Hamill et al., 2008). Moreover, kinematic risk factors associated with iliotibial band syndrome include a reduced peak hip adduction angle (Brown et al., 2016;Foch et al., 2015;Grau et al., 2011) or in contradiction increased peak hip adduction angle

(Ferber et al., 2010;Noehren et al., 2007). Moreover, a greater knee internal rotation angle (Ferber et al., 2010;Noehren et al., 2007) and an increased knee flexion angle (Miller et al., 2007;Noble, 1980;Orchard et al., 1996). Running downhill has also been proposed as a risk factor, probably owing to the increased knee flexion during heel strike (Noble, 1980;Orchard et al., 1996).

Medial tibial stress syndrome

Medial tibial stress syndrome is characterized by pain on the medial aspect of the tibia. Pain is typically elevated by running or other impact activities loading the lower limb. The pain lasts for hours after running and is often limiting normal running activity (Hubbard et al., 2009;Newman et al., 2013). At least two etiologies have been proposed to be the mechanism of medial tibial stress syndrome: 1) repetitive stress on the distal tibial cortex (Gaeta et al., 2006) or 2) tibial fascial traction (Noh, 2018).

Medial foot pressure or foot pronation is an often proposed risk factor of medial tibial stress syndrome (Messier and Pittala, 1988;Neal et al., 2014;Newman et al., 2013;Sharma et al., 2011;Viitasalo and Kvist, 1983). Moreover, navicular drop appears to be a risk factor (Bennett et al., 2001;Yagi et al., 2013), although Plisky et al. (2007) found no association between the magnitude of navicular drop and the risk for medial tibial stress syndrome. In addition to foot pronation, an increased peak internal hip rotation angle (Loudon and Reiman, 2012;Yagi et al., 2013), sudden increases in running distance (Knobloch et al., 2008), knee varus alignment (Becker et al., 2017;Wen et al., 1998) and obesity (Newman et al., 2013;Plisky et al., 2007) are risk factors of/for medial tibial stress syndrome.

Achilles tendinopathy

Achilles tendinopathy has been characterized by pain in the Achilles tendon during running, morning stiffness in the ankle joint the first steps in the morning (Wyndow et al., 2013). Achilles tendinopathy is commonly experienced in sporting activities involving running (Wyndow et al., 2010). The Achilles tendon is the largest and strongest tendinous structure in the body, which is defined anatomically as the tendinous structure connecting the soleus and the gastrocnemii muscles to the heel bone while the tendon of plantaris longus is often included (Freedman et al., 2014). Clement et al. (1984) have indicated a “whipping or bowstring action” of the Achilles tendon in the frontal plane during stance when going from supination into a pronated foot. This whipping action may produce tensile forces along the medial side of the tendon, causing microtears in the tendon (Kannus, 1997;Maffulli et al., 2003;Schepsis et al., 2002). This together with the internal rotation of the tibia possibly caused by foot pronation, may induce wringing of the tendons resulting in degenerative changes (Clements et al., 1984;Kannus, 1997;Lersch et al., 2012;Nigg et al., 1993;Schepsis et al., 202). A common hypothesis causing the pain associated with Achilles tendinopathy is excessive loading, which could cause a loss of tissue homeostasis (Arnoczky et al., 2007) or inflammation of the tendon (Abate et al., 2009;Fu et al., 2010) or maybe it is a combination of both factors which is causing the pain (O'Neill et al., 2016). Essentially, Achilles tendinopathy seems to be linked with the rate of stress being greater than the rate of tissue repair (Magnusson et al., 2010;O'Neill et al., 2016;Scott et al., 2013). This is supported by the fact that sudden increases in running pace have been linked with Achilles tendinopathy (Clements et al., 1984;Hein et al., 2013; Nielsen et al., 2014).

Risk factors for developing Achilles tendinopathy are being male (Taunton et al., 2002;Wyndow et al., 2010), increasing age (Hirschmüller et al., 2012), limited ankle dorsiflexion range of motion (Haglund-Akerlind and Eriksson, 1993), running on sand (Knobloch et al., 2008), reduced hip abduction strength (Niemuth et al., 2005), reduced knee flexor strength (Hein et al., 2013), greater hip adduction impulse (Creaby et al., 2017) and excessive foot pronation (Clements et al., 1984;Creaby et al., 2017;Donaghue et al., 2008;McCrory et al., 1999;M. Ryan et al., 2009;Van Ginckel et al., 2009).

Patellofemoral pain

Patellofemoral pain is defined (or diagnosed) in several ways including retropatellar or peripatellar pain (Earl and Vetter, 2007;Waryasz and McDermott, 2008). Pain is possibly induced by physical and biochemical changes in the patellofemoral joint. Patellofemoral pain is believed to be owing to an altered tracking of the patella within the trochlear grove (Earl and Vetter, 2007;Liao et al., 2015). Pain is described as a gradual or acute ache behind the patella, which worsens with activities such as running and sitting. The location of pain is diffuse and often described as situated under or around the patella (Cavazzuti et al., 2010;Willson et al., 2011). Females are more likely to sustain patellofemoral pain (Barton et al., 2009;Myer et al., 2010; Petersen et al., 2014). Oblique lateral patella tracking may result from an increased knee abduction angular movement (Powers, 2010), which potentially results from increased hip internal rotation (Souza and Powers, 2009;Souza et al., 2010), increased knee internal rotation (Bolgla et al., 2008) and increased hip adduction (Noehren et al., 2013;Souza and Powers, 2009). Many risk factors are involved with both distal and proximal factors affecting patella tracking (Powers, 2010).

Risk factors identified for Patellofemoral pain are sudden increases in running distance (Messier et al., 1991; Nielsen et al., 2014;Thijs et al., 2008). Moreover, increased hip adduction angle (Dierks et al., 2011;Luz et al., 2018;Noehren et al., 2013;Watari et al., 2018;Willson and Davis, 2008), increased hip internal rotation (Dierks et al., 2011;Noehren et al., 2013), increased peak knee abduction angle (Dierks et al., 2011;Ferber et al., 2011;Watari et al., 2018), reduced pronation the first 10% of stance (Duffey et al., 2000) and increased pronation during stance (Duffey et al., 2000;Noehren et al., 2013) have been associated with increased risk of patellofemoral pain. Moreover, eccentric hip abduction strength has been investigated both in case-control and prospective studies with inconclusive results. Based on case-control studies, Plastaras et al. (2016) and Esculier et al. (2015) reported recreational runners to have greater hip abduction strength compared to controls, although most of these runners were females. On the contrary, runners with patellofemoral pain have demonstrated weaker hip abduction strength (Cichanowski et al., 2007;Dierks et al., 2008;Ferber et al., 2011). However, Duffey et al. (2000) found that hip endurance was significantly lower in patellofemoral pain runners. Additionally, two prospective studies demonstrated that runners developing patellofemoral pain had weaker hip abduction strength (Luedke et al., 2015;Ramskov et al., 2015), although two studies revealed no difference (Finnof et al., 2011;Thijs et al., 2011). Moreover, Dierks et al. (2011) discovered a subgroup of runners with patellofemoral pain to display increased knee abduction angle, while the other part of the patellofemoral pain runners displayed increased hip abduction. This could indicate that knee abduction angle and hip abduction is only a part of the etiological chain but not the direct cause of patellofemoral pain.

OVERALL SUMMARY OF THE RISK FACTORS

From the review the underlying etiology of specific running-related overuse injuries is poorly understood and often conflicting result. The problem is that the studies despite being selected after consistent criteria for inclusion use quite different methodologies and, more importantly, different samples and groups of runners which make a quantitative comparison/analysis problematic. To identify/suggest the most important risk factors a criterion was introduced that when being statistically significant in at least three studies it was considered an important risk factor. This approach leads to one or more important risk factors for the six most common running-related overuse injuries.

Plantar fasciitis *is commonly associated with greater foot pronation, limited ankle dorsiflexion and obesity.*

Patellar tendinopathy *is commonly associated with limited quadriceps flexibility, limited hamstring flexibility and restricted ankle dorsiflexion range of motion*.

Iliotibial band syndrome *is commonly associated with weak hip abduction strength, increased knee flexion angle.*

Medial tibial stress syndrome *is commonly associated with greater foot pronation.*

Achilles tendinopathy *is commonly associated with greater foot pronation.*

Patellofemoral pain *is commonly associated with weak hip abduction strength, increased hip adduction angle, increased peak knee abduction angle and sudden increases in running distance.*

Overall, these injuries are commonly associated with different risk factors. However, there seems to be a common denominator between Plantar fasciitis, medial tibial stress syndrome and Achilles tendinopathy, which is greater foot pronation. Moreover, iliotibial band syndrome was related with weak hip abductors and increased knee flexion angle, while patellofemoral pain seem related with weak *hip abductors, greater hip adduction angle and knee abduction angle during running.*

DISCUSSION OF RISK FACTORS

The majority of the relationships between risk factors and the actual risk of getting a running-related overuse injury demonstrated contradictory results and very little consensus has been found. This may be owing to the typically applied retrospective designs and lack of accounting for co-variables with a mediating effect on running-related overuse injuries. The retrospective design has a disadvantage since the cause and effect relationship cannot be investigated. Instead a prospective design investigating the exposure to injury is warranted to elaborate on the difference in how much a runner can tolerate when presenting a given risk factor compared to not having that risk factor. However, applying a prospective design with an exposure to event analysis may not be enough since these studies still have shortcomings, such as lack of accounting for co-variables and addressing risk of specific injuries. When lacking to account for co-variables incorrect relationships may be identified since it any relationship would be influenced by such co-variables. For example, age was both increasing the risk of injury and reducing the risk of injury in different studies, let's say study A and study B. This seems rather contradictory but may be explained from a biological and statistical point of view. If study A demonstrates that increasing age is increasing the risk of injuries, which is biologically plausible since aging among other things reduces the ability to recover from the training load and is connected with reduction of the strength/capacity of musculo-skeletal structures. However, study B find the reverse association that increasing age is reducing the risk of injury, which may be contradictory to a biological plausible mechanism. This finding may however be explained by the unmeasured variable running experience, since increasing age most likely will increase the likelihood of having more experience. Having more running experience may increase the capacity to tolerate the load applied during running, which may actual cause this relationship. Therefore it becomes plausible that study A found the actual association between age and injury risk and study B found a mediated association between running experience and risk of injury. Since running-related overuse injuries are multifactorial of nature it is important to be able to account for the risk factors which may mediate the association *of interest. The existing prospective studies often associate risk factors with all running-related overuse injuries. This may not be appropriate since not all running-related overuse injuries may be caused by the same mechanism. If a risk factor such as foot pronation is only associated with injuries around the foot, then only studies with an overweight of foot injuries will identify foot pronation as a risk factor. Therefore, the analysis should be based on biological and biomechanical plausible mechanisms leading to the specific injury if possible. Lastly, cross-sectional studies are still warranted to elaborate on potential mechanisms leading to the different risk factors. This information may increase the understanding of the causative/underlying mechanisms and be beneficial for the development of injury prevention programs.*

Future research should be conducted prospectively or in cross-sectional studies, and should elaborate more on the establishement of cause and effect relationships. A step closer to a cause and effect relationship may be to focus on specific injuries and/or aacounting for co-variates.

IDENTIFICATION OF THE RELEVANT PROBLEMS

It seems clear that weak hip abduction strength was related with both iliotibial band syndrome and patellofemoral pain. Increased knee flexion angle was related with iliotibial band syndrome and greater hip adduction angle knee abduction angle was related with patellofemoral pain. Moreover, foot pronation was associated with three of the most common running-related overuse injuries, Achilles tendinopathy, medial tibial stress syndrome and plantar fasciitis. Also, sudden changes to the training schedule have been proposed by several authors while evidence is sparse but seems to be consistent regarding that sudden changes may increase the risk of running-related overuse injuries. Based on this it is proposed to conduct three studies investigating 1) the influence of hip abduction strength on hip and knee angular movement to elaborate on the potential injury mechanisms; 2) the medial shoe-ground pressure's influence on specific injuries (APM-injuries; Achilles tendinopathy, medial tibial stress syndrome and plantar fasciitis); 3) the potential risk of sudden training changes using a change of footwear as one of the previously suggested alterations. In the following paragraph the motivation for the mentioned studies will be further elaborated.

The influence of hip abduction strength on hip and knee angular movement

Weak hip abduction strength has been associated with two of the most common running-related overuse injuries (iliotibial band syndrome and patellofemoral pain). Hip abduction strength is modifiable (Ferber et al., 2011;Snyder et al., 2009;Willy and Davis, 2011). Patellofemoral pain subjects was after 8 weeks of hip abductor strength training able to reduce the knee abduction joint moment more than 15Nm (p-value=0.05) and patellar pain was reduced from 40 to 5mm on a VAS scale (p-value <0.0005) (Earl and Hoch, 2011). This was in agreement with Wouters et al. (2012) which found the knee abduction moment to reduce more than 20Nm (p-value = 0.033) by increasing hip abduction strength. Moreover Dolak et al. (2011) demonstrated hip strengthening exercises to increase the hip abduction strength, which reduced the subjective pain related with patellofemoral pain after 4 weeks (p-value <0.05).

As described above in the risk factor section, cross-sectional studies did not find consistent results regarding difference in hip abduction strength between runners with either iliotibial band syndrome or patellofemoral pain. However, one prospective study demonstrated that after 50km of running was novice runners with a high eccentric hip abduction strength displaying 0.9%-point fewer patellofemoral pain injuries compared to the normal strength runners (p-value = 0.03) (Ramskov et al., 2015). This is interesting, although the effect was small and it does not identify the potential mechanism that weak eccentric hip abduction strength may have on patellofemoral pain. It is plausible that the potential mechanisms could be that weak eccentric hip abduction strength may not have the ability to control the pelvis and thigh motion during the stance phase, which may result in increased hip adduction and knee abduction angles. Moreover, greater knee valgus alignment increases the abduction moment while greater knee varus increases the adduction moment (Heller et al., 2003). Additionally, static knee valgus alignment in novice runners displayed knee abduction angle of 1.55deg, while the control group displayed a knee adduction angle of 2.03deg (p-value = 0.015) (Barrios et al., 2016). This may suggest that eccentric hip abduction strength is important to control knee abduction angle and moment in runners with a knee valgus morphology.

Still, evidence on the relationship between weak eccentric hip abduction strength and hip and knee kinematics in runners remains unclear. Cashman (2012) reported a lack of agreement between studies investigating the influence of eccentric hip abduction strength on knee abduction angle and moment. Moreover, Cashman was not able to make definitive conclusions. Currently, the relationship between weak hip abduction strength and knee joint kinematics and kinetics has been investigated in several tasks such as a single leg squat (Baldon et al., 2011;Claiborne et al., 2006) and in a double legged jump landing (Homan et al., 2013). However, this relationship remains to be investigated in a large sample during running using 3D motion analysis and isokinetic strength measurement (Cashman, 2012).

Medial shoe-ground pressures influence on APM-injuries

Shoe-ground pressure may be affected by running shoes. It has been demonstrated that runners wearing motion control shoes reduced the navicular drop rate by 35mm/s (Hoffman et al., 2015). In line with this displayed runners wearing motion controls shoes increased subtalar joint inversion the first 40% of stance compared to when they ran barefoot or in minimalist running shoes (p-value < 0.05) (Peltz et al., 2014).

The influence of excessive foot pronation on running-related overuse injuries is still debated. Greater foot pronation seems to be a common feature of APM-injuries, as described in the risk factor section. Eversion (i.e., pronation) of the foot demonstrates a dynamic coupling mechanism with internal rotation of tibia (Nigg et al., 1993). This leads to a so-called 'whipping bowstring action' which implicates potential tears of the Achilles tendon (Clements et al., 1984). This has been supported by a cadaver study demonstrating the greater the eversion or inversion angle of calcaneus induces over 2%-point more strain on the distal aspect of the tibia compared to neutral calcaneus alignment (Lersch et al., 2012). It has been demonstrated that runners with plantar fasciitis display greater maximal pronation compared to their controls (7.4 deg vs 6.2 deg; p-value < 0.05) (Chang et al., 2014), which may be owing to increased strain that foot pronation creates on the plantar fascia. In addition, recruits displaying higher medial foot pressure have 1.15 times greater odds of sustaining medial tibial stress syndrome compared to those displaying a more lateral pressure (p-value < 0.001) (Sharma et al., 2011). A graphical comparison indicated this difference was in the first 20% and last 30% of stance, although it was only the first 20%, which was significantly different between injured and non-injured recruits (p-value < 0.03). Finally, Neal et al. (2014) found that foot posture indicating overpronation to be a risk factor for developing medial tibial stress syndrome, in a systematic review and meta-analysis, although the overall effect was small. Medial shoe-ground pressure was demonstrated to predict medial tibial stresss syndrome in recruits, which makes it reasonable to assume that similar effects exist in runners. Similar findings remain to be demonstrated in runners with Achilles tendinopathy and plantar fasciitis. Therefore a prospective study investigating medial shoe-ground pressures effect on the development of APM-injuries would be relevant to clarify this effect.

The risk of changing running shoes

In several biomechanical studies, vertical impact peak, loading rate, knee and ankle flexion moment have been demonstrated to change with differences in shoe properties. For example vertical impact peak increases with lower midsole hardness (soft:1.7BW medium:1.64 hard:1.54 p-value<0.001) (Baltich et al., 2015) and pressure time integral increases approximately 10% when changing to new shoes (p-value < 0.05) (Rethnam and Makwana, 2011). In addition, the loading rate is increased by reducing heel-to-toe drop in shoes during overground running with more than $20BWs^{-1}$ (Chambon et al., 2015). Finally, knee flexion moment during push–off phase is reduced in zero drop shoes (p-value < 0.001) while ankle flexion moment is increased in zero drop shoes compared to shoes with 6 and 10mm heel-to-toe drop (p-value < 0.001) (Besson et al., 2017). This indicates that changes in the mechanical characteristics of running shoes may change the way the mechanical stress is distributed in the anatomical structures of the lower extremities during running. This implies that any change in running shoes without changing running habits may change the distribution of lower extremity tissue loads, and acutely reorganized tissue loads may reveal injurious because the acute redistribution may load non-adapted tissues and/or structures above their capacity (Bertelsen et al., 2017;Hreljac, 2005).

Any change of type and/or property of running shoes may theoretically change the distribution of loads on the anatomical structures in the lower extremities during running, which again potentially increases the risk of obtaining a running-related overuse injury. This may be a plausible mechanism behind the increased risk of sudden changes described in the risk factor section. For example, Clement and Taunton (1980) proposed that changing running surface could be injurious if performed too sudden at the same training volume. This observation has later been supported by a study of Dixon et al. (2000), which indicated changes of running surface may change the peak impact force and loading rate unsystematically.

Moreover, one study demonstrated that runners preferring to run on asphalt had less risk of sustaining Achilles tendinopathy (RR: 0.47; 95%CI: 0.25-0.89), while those preferring to run on sand had a higher risk of developing Achilles tendinopathy (RR:10; 95%CI:1.12-92.8) (Knobloch et al., 2008), which indicates different loading of the musculoskeletal system between running surfaces. Moreover, Rauh (2014) found that injury rate increased gradually in the first 3-4 weeks after engaging into the summer season, which may indicate to be the latency of the expression of the injuries after too sudden changes. Changing into new running shoes is associated with increases in the risk of running-related overuse injury. Jacobs and Berson (1986) reported that one out of three injured runners changed training technique, schedule or running shoe prior to their running-related overuse injuriy. This is supported by the fact that injured runners used their running shoes 7 months before changing them, while non-injured runners waited 10 months (p-value < 0.05) (Wen et al., 1997). In line with this, another study demonstrated that injured runners were also covering fewer miles (536 miles (862km)) before changing to a new pair, while non-injured were covering 693 miles (1135km) before changing to new running shoes (p-value < 0.05). This could imply an injurious effect of changing running shoes too often. Moreover, Logan et al. (2010) proposed that this risk could be reduced by gradually changing running shoes over time, to avoid too sudden changes in kinematics and kinetics.

PURPOSE, RESEARCH QUESTIONS AND HYPOTHESES

On the basis of the information presented above the purpose of the PhD-thesis was to provide further insight into the etiology of some of the most frequent running-related overuse injuries and to investigate potential relationship between selected risk factors potentially associated with the development of running-related overuse injuries. The available evidence for possible mechanisms leading to the most frequent running-related overuse injuries in many cases is inconclusive. Therefore, there is a need for further clarification of the etiologies of most running-related overuse injuries. Therefore the related research question proposed to fullfil this purpose and provide further evidence was:

How can we establish further evidence on the etiology leading to some of the most frequent running-related overuse injuries?

This was accomplished by a 1-year prospective study on 100 recreational male runners, with a baseline measure before engaging into the follow-up study and after 500km of training distance/amount.

The specific research questions posed in this PhD-thesis were:

1. *Is eccentric hip abduction strength associated with specific hip and knee joint kinematic patterns, which again may be related to knee injury?*
2. *Is medial shoe-ground pressure associated with the development of Achilles tendinopathy, plantar fasciitis and/or medial tibial stress syndrome (APM injuries) among recreational male runners?*
3. *How does the injury incidence rate ratio (IIRR) change over a one year prospective study involving two changes of running shoes?*

The research questions were answered in three papers in the order given above.

The hypothesis for research question 1 was*: the magnitude of eccentric hip abduction strength is not associated with either the magnitude of hip adduction or knee abduction angular movement in the total sample but only in runners where hip adduction and knee abduction angular movement occur simultaneously, immediately following foot strike.*

The hypothesis for research question 2 was: *runners displaying primarily medial shoe-ground pressure will sustain the most APM-injuries compared with runners displaying lateral pressure dominance.*

The hypothesis for research question 3 *was:* Any change in running shoes will increase the injury incidence rate above the average injury incidence rate over a given period of running

CHAPTER 2. METHODS

This PhD-thesis is based on data collected in one large study. The RUNning TECHnique study (RunTech). The study was designed as an epidemiological observational prospective cohort study with 1-year follow-up. A study overview of RunTech is presented in Figure 4, visualizing how the collected data were used to answer the different research questions. Data were collected after inclusion of runners at a baseline examination, at the 500km examination, during the follow-up of the runners and in case of injuries, these were diagnosed and collected as well (see Figure 4).

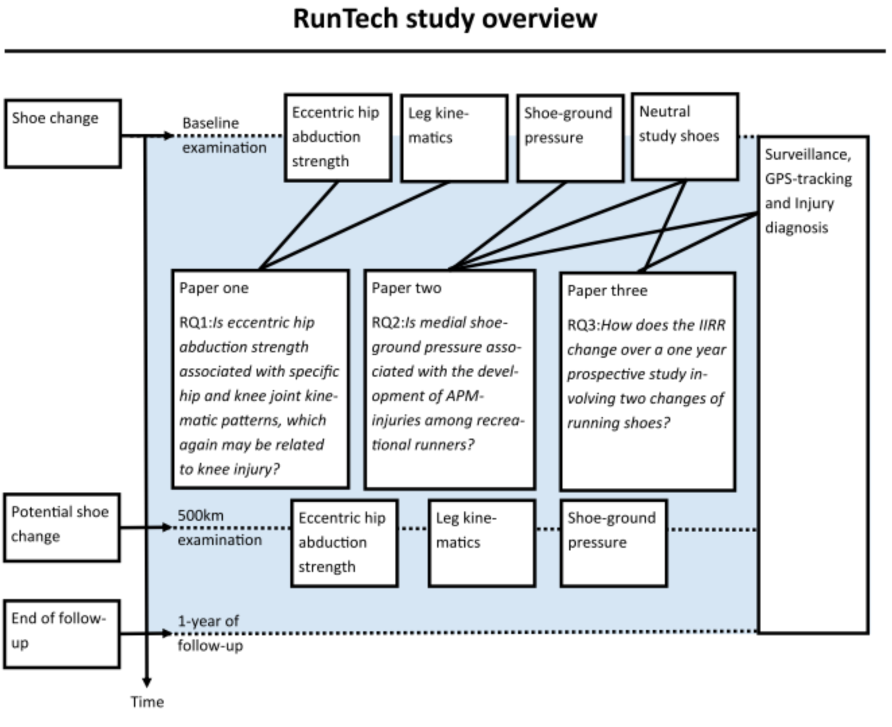


Figure 4: The RunTech study overview and how the collected data are used to answer each research question and in which papers there are answered

STUDY DESIGN

At baseline, runners were provided with a pair of experimental running shoes, which was a neutral running shoe and eccentric hip abduction strength, shoe-ground pressure and leg kinematics during running were collected in the laboratory. The baseline examination provided the basis for all three studies. The eccentric hip abduction strength and hip and knee angular kinematics collected at the baseline examination, was used in paper one (RQ1). The shoe-ground pressure collected at baseline, running kilometers and clinical diagnosed injuries were used in paper two (RQ2). The baseline and 500km examinations were used to define a change and potential change of running shoes in paper three (RQ3).Trainingsessions from each runner were obtained based on GPS data and a weekly questionnaire were collected during the follow-up. After 500km of running using the experimental running shoe a 500km examination were performed, which collected the eccentric hip abduction strength and shoe-ground pressure. Runners reported injuries during the weekly questionnaire, which was diagnosed by a sports physiotherapist or sports physician.

Ethics approval

The study design was presented to the local ethical committee of Region Nordjylland, who approved the study, N-20130074. The Danish Data protection agency accepted the study, approval number 2008-58-0028. All runners signed an informed written consent prior to the test according to the declaration of Helsinki.

Recruitment

Runners were recruited in northern part of Jutland, Denmark, between February and June 2014. Runners were recruited through advertising at local races and by e-mail distribution to local companies, hospitals and at the local University. All persons who received the advertising material about the study were allowed to forward it to others, who might be interested in participating in the study. During the 5-month of recruitment, in total 207 persons signed up for the study by completing an online questionnaire.

Inclusion and exclusion criteria

Inclusion criteria were: (1) male between 18-60 years, (2) running at least 2 times per week, (3) minimum 2 years of running experience, (4) no injuries within the past 3 months prior completing the baseline questionnaire, (5) experienced in treadmill running. Runners were excluded due to: (1) no e-mail address or access to the internet, (2) participation in other sports for more than 4 hours a week, (3) necessity for the use of insoles while running, (4) previous stroke, heart diseases, or pain in the chest during training, (5) unwillingness to run in a neutral pair of running shoes or to use a global position system (GPS) watch or smartphone to quantify the running characteristics.

Procedure for inclusion of runners

The 207 persons were screened and all persons eligible for inclusion were interviewed by phone. Runners that still were eligible for inclusion, were invited to a baseline investigation. The baseline procedure is described later in this section and the consort flow diagram of the inclusion process is described in the initial part of the results (see Figure 10).

Procedure after inclusion

A pair of standard “neutral” running shoes (Asics Gel-pulse5; designed with a medial arch support, heel rise and a 12mm heel to toe drop) (See Figure 5) and an armband suitable for their smartphone were handed out to the included runners. The runners had to run in the provided neutral running shoes from the time of inclusion and at least to the 500km examination in the laboratory (described later). This involved potentially two changes of running shoes: 1) at 0km and 2) a possible change of running shoes around approximately 500km. Runners had to run more than 10km in total within at least two running sessions per week during the 1-year follow-up. Besides the minimum of running two times a week byond 10km in total, no restrictions were provided concerning where to run, when to run and at which pace to run. Thus, the runners completing a minimum of 500km within the follow-up year, were rewarded with the armband and shoes for free. The standardization of running shoes should ensure that the collected baseline measures were comparable between runners and the shoe conditions comparable between runners during the first approximately 500km. A standardized “neutral” running shoe was chosen since RQ2 was addressing the effect of medial foot pressure and a motion control shoe may affect this relationship.

Figure 5: The type of running shoes (Asics Gel-pulse5) given to the participants . The participating runners used these shoes during datacollection at baseline and during the first approximately 500km of running.

A personal profile of all included runners was created on the personal running diary at www.mit-løbeprogram.dk, that automatically uploaded data from each running session collected by smartphones or GPS watches. The personal running diary allowed self-reporting of time spent running and distance in case of missing GPS data, which the runners had to recall, which was the optimal solution when GPS data were missing (Dideriksen et al., 2015).

BASELINE AND 500-KM EXAMINATION AND DATA ANALYSIS

Runners were informed and again screened at baseline, for eligibility and their GPS watches or smartphone were checked for uploading data to our database (http://www.mit-løbeprogram.dk), which were used to collect injury status and training distance of the runners during follow-up. At baseline eccentric hip abduction strength, shoe-ground pressure and leg kinematics during running were collected in the laboratory after this screening. Additionally, following the first approximalely 500km of running the participants visited the laboratory again and the eccentric hip abduction strength and shoe-ground pressure were collected (See Figure 5).

Eccentric hip abduction strength (research question 1)

A isokinetic dynamometer (Biodex Multi-Joint System 2; Biodex Medical Systems, Inc, Shirley, NY) was used to obtain eccentric hip abduction strength at two angular velocities, 30 and 60 degrees per second (Nakagawa et al., 2012b) for both hip joints over a range of motion of 20 degrees from 20 degrees abducted hip to neutral hip alignment in frontal plane (See Figure 6). The proximal aspect of the iliac crest and contralateral tibia were fixed with straps to avoid compensatory movements. Due to small range of motion of hip abduction, 30 deg s^{-1} was used as the outcome measure for eccentric hip abduction strength, to allow the participants to build up maximal force.

[redacted]

Figure 6: The body position in the Biodex dynamometer just before the start of a measurement of eccentric hip abduction strength.

The length of the lever arm on the dynamometer was kept constant during all tests. Biodex standard test procedures were applied and data being sampled at 100Hz. Isokinetic data were collected in a .txt format and imported to Matlab (Matworks, Natick MA) for further processing. Isokinetic data from seven subjects were lost due to problems with the Biodex database. To calculate the outcome the highest and lowest peak value of five repetitions were deleted and the average of the remaining three was divided by the runners body mass.

Assesment of running kinematics and kinetics (paper 1 and 2)

Running kinematics and eccentric hip abduction strength was used in paper one, while the shoe-ground pressure was used in paper two. Ground reaction force and shoe-ground pressure during running was captured on a force and pressure sensitive treadmill (Zebris FDM-T, 1.8kW; Medical GmbH, Germany), which was synchronized with a Codamotion active marker system (Charnwood Dynamics Ltd., Leicestershire, UK). The data from the treadmill and the Codamotion system were sampled at 100Hz. Running movements were captured at 1) a running speed of 10km per hour and 2) at a running speed corresponding to the average speed during a self estimated best 5000-meter run. Recordings were obtained after six minutes of adaptation to the given running speed. The six minutes of familiarization were performed to reduce variation (Lavcanska et al., 2005). The 10km per hour was chosen for the analysis of research question 1, while the self-estimated speed was chosen for the analysis of research question 2.

Shoe-ground pressure during running (paper 2)

Left and right shoe-ground pressure was measured during running on the pressure sensitive treadmill. The data from the treadmill-system were exported in asci-format (‘text-files’) and imported into Matlab (Matworks, Natick MA) for further processing. From the pressure data, time of initial ground contact and toe off were determined. Initial contact and toe off were defined as the points in time where the vertical ground reaction force calculated from the pressure data either exceeded 10N or fell below 10N respectively, during each stride cycle. Shoe-ground pressure ratio was estimated in the following way: 1) the mean pressure profile shoe prints for each stance phase was calculated and 2) the longitudinal axis of each shoe print separating this in a medial and lateral side was determined. This longitudinal axis was defined as the line connecting the most anterior and the most posterior active pressure cells in each mean pressure profile shoe print (See Figure 7) (De Cock et al., 2008).

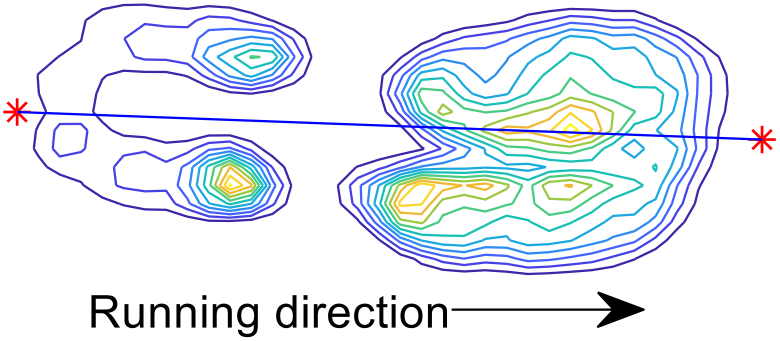


Figure 7: Contour plots of mean pressure shoe-prints from a right foot during the stance phases obtained from a running trial. The red asterisks indicate the positions of the most anterior and the most posterior pressure cells, respectively. The blue line between these is defined as the longitudinal axes of the shoe-print. Medio-lateral shoe-ground pressure ratio was calculated as*: ∑average medial shoe-ground pressure / ∑average lateral shoe-ground pressure*.

The average of shoe-ground pressures on the medial side of this axis was divided with the average of the shoe-ground pressures on the lateral side of this axis, and a ratio between average medial and lateral shoe-ground pressures during each stance phase was obtained (Sharma et al., 2011). For each participant the shoe-ground pressure ratio was calculated for the first 15 stride cycles from each recording and the two extreme values in both the high and low end of the ratios were deleted and an average of the 11 remaining stride cycles was calculated and used as a measure of the individual shoe-ground pressure ratio. If the medio-lateral shoe-ground pressure ratio was smaller than 1 the lateral shoe-ground pressure was considered to dominate (LP). If the ratio was above 1, the medial shoe-ground pressure was considered to dominate (MP). Based on this shoe pressure ratio, each left and right foot were categorized as LP or MP.

Leg kinematics during running (paper 1)

Kinematics of both legs were collected with the Codamotion active marker system. Three Codamotion racks containing three sensors each, were positioned in a triangle with each camera placed approximately 2 m away from the center of the treadmill. One sensor was placed in front, another on rear left and the last on the rear right side of the treadmill. Active tracking markers were placed on 1) the shoe over the following landmarks: posterior surface of calcaneus, head of fifth metartarsal, navicularis, cuboideum and 2) directly on the skin over the following anatomical landmarks: anterior superior iliac spine, posterior iliac spine. Two tracking marker clusters, each including four markers, were attached on the outside of femur and tibia on the least bulky location, respectively. Both anatomical and cluster markers were secured with tape to assure minimal movement in relation to the skin. The relative positions of tracking markers and calibration markers were determined with a virtual point marker. The following calibration marker positions were recorded: the medial and lateral femoral epicondyles and the malleolis and the head of first metatarsal. Hip joint centers were estimated according to Leardini et al. (1999) and pelvic width were measured with a slide caliper.

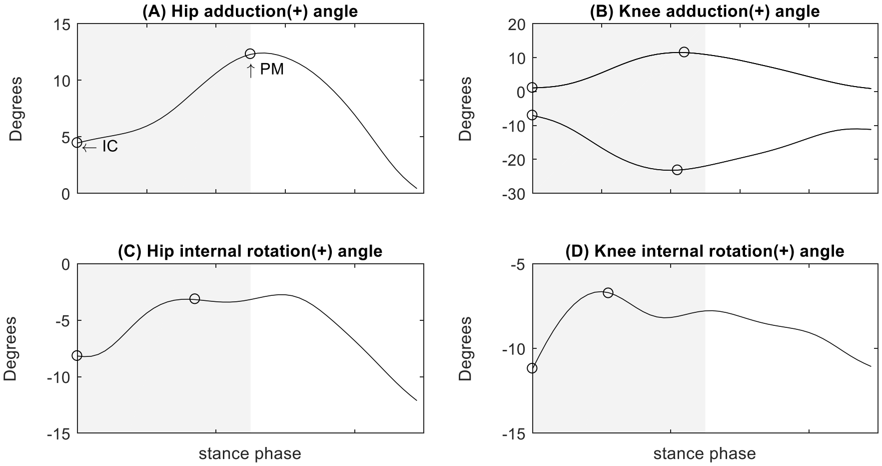


Figure 8: Illusstration of the location of initial shoe contact (IC) and position of the initial movement peak (IMP) for the four kinematical variables of interest. The shaded area represents the first 50% of the stance phase. Figure 8B has two curves since the knee either display a abduction or adduction angle during stance. Based on Figure 8B, the subgroup is identified by the curve moving in a negative direction, indicating those runners displaying knee abduction angle during stance.

Kinematic data were exported to Matlab (Matworks, Natick MA) for further processing. The pressure data from the treadmill were used to identify the individual stride cycles and foot contact times as explained above. The first recorded 30 stride cycles of each data sequence for each leg were used to calculate the hip and knee joint angular movement parameters. The five most extreme parameter values in both ends of each parameter range were discarded, and each parameter was determined as the average of the remaining 20 values. The joint angles were calculated as Euler angles using joint coordinate systems (Grood and Suntay, 1983). The angular movements of interest were calculated as the difference between joint angle at the time of initial shoe contact (IC) and peak angular movement (PM) in the initial movement direction during the first 50% of the stance phase (i.e. initial varus or valgus angular movements in the knee and initial adduction or abduction angular movement in the hip) (See Figure 8).

Selection of runners displaying both hip adduction and knee abduction angular movement (knee valgus subgroup)

Several movement patterns may be associated with a weak eccentric hip abduction strength. One of these is the combination of simultaneous hip adduction and knee abduction. A priori, this subgroup of runners was defined as follows: Those increasing both their hip adduction and knee abduction angles in the range between initial shoe contact and 50% of the stance phase.

Injury surveillance and diagnosis (Paper 2 and 3)

During the follow-up, our database http://www.mit-løbeprogram.dk was used to monitor injuries. Runners received one e-mail per week with a link to a web-based questionnaire about injury status, which was examined weekly. In case of reported injuries, missing training data or lack of response to the weekly questionnaire, the runners were contacted and an appointment was made for attending a clinical examination performed by a sports physiotherapist or sports physician. Only diagnosed injuries sustained from running or in combination with running were included in the analysis.

STATISTICAL ANALYSES

The statistical analyses performed in the thesis were:

1) a multiple regression analysis in research question one, 2) time to first APM-injury with other injuries handled as competing risk in research question two, 3) incidence rates across the follow-up period in research question three. All statistical analyses were performed using Stata Version 12 or later (StataCorp LP, College Station, TX).

Research question 1: A multiple linear regression of hip- and knee angular movement with eccentric hip abduction strength as the explanatory variable was performed. In addition, a subgroup analysis of the knee valgus subgroup was performed to elaborate on the relationship between eccentric hip abduction strength and hip and knee angular movements. The ability of eccentric hip abduction strength to explain the variability of hip- and knee angular movements respectively was assessed with an R-squared value derived from the regression model. The variables were inspected visually for a linear relationship and outliers using a scatterplot of explanatory variables versus the dependent variable. The homoscedasticity and normal distribution was evaluated using p-p plots. Due to concerns about right-skewness of data, a sensitivity analysis was performed using robust variance estimation and a bootstrap with 1000 replications to confirm the confidence interval ranges. Variables were obtained on data from both legs and each individual was considered as one cluster with two legs.

Research question 2: The runners were right censored in case of disease, lack of motivation, non-running-related overuse injury causing a permanent stop of running or end of follow-up after 1 year, whichever occurred first. Generalized linear regressions using the pseudo observation method were used to assess cumulative risk difference (absolute difference) in injury survival between exposure groups of different mediolataral shoe-ground pressure distribution ratio (Klein et al., 2007). In the analyses, a model on cause-specific hazards of two endpoints (APM-injuries and other injuries) was calculated as competing injuries (Putter et al., 2007). The pseudo observation method considers the possible dependency between the two legs by clustering the individual runners as one cluster with 2 legs (Klein et al., 2007). When one leg sustained an injury, the contralateral leg was still followed until the end of the follow-up, censoring or injury. Confounders potentially affecting the result would be age, BMI, previous type of running shoe being used while entering the study, the previous amount of different running shoes used per week and previous injuries. Since only rather few injuries occurred during the follow up, a sensitivity analysis was performed using a bootstrap with 50 replications to confirm the confidence interval range.

Research question 3: The cumulated running distance was used as the duration scale. In the analyse/is, cause-specific hazards of the instantaneous risk of injury from a specific injury category (Running-related overuse injuries, non-running-related overuse injuries) were calculated using competing risks. Only first time injuries were used in the present analysis, however runners recovering from their injury were still followed for 1-year in total and had to run in the prescribed pair of running shoes. The injury incidence rate as a function of cumulated running distance was estimated using a Poisson regression with restricted cubic spline knots at 50, 100, 500, 600 and 1000km, which was based on the empirical-based rationale that the influence of changing running shoes was greatest during the first100km. Based on the knots, five risk periods was defined, P1(0-50km), P2(50-100km), P3(100-500km), P4(500-600km), P5(600km-end). The injury incidence rate is plotted after the 5th incidence to increase robustness of the estimated incidence rates. The IIRR was calculated as the instantaneous injury incidence rate divided by the average injury incidence rate over the entire follow-up period. A Wald-test was used to investigate the relative levels of the injury incidence rate curve between risk periods. An exploratory analysis describing the potential differences in training distance between injured and non-injured runners were performed to elaborate on training distances the potential influence of the training distances on injury risk. The influence of distance per training session as a function of cumulated kilometres in the study assessed using a regression with restricted cubic splines with similar knots as in the primary analysis.

The difference in training distance between injured and non-injured runners was evaluated with an unpaired t-test. All statistical analyses were performed using Stata Version 15 (StataCorp LP, College Station, TX).

CHAPTER 3. RESULTS

The main results are summarized in the following section. Further details are presented in the orginal papers/manuscripts.

DESCRIPTION OF THE POPULATION INCLUDED

In the following, the inclusion proces and a description of running exposure and observed injuries during the follow-up is described. Ninety-nine recreational male runners were included in the study following the inclusion process, and a flow chart of the entire process is presented in Figure 9.

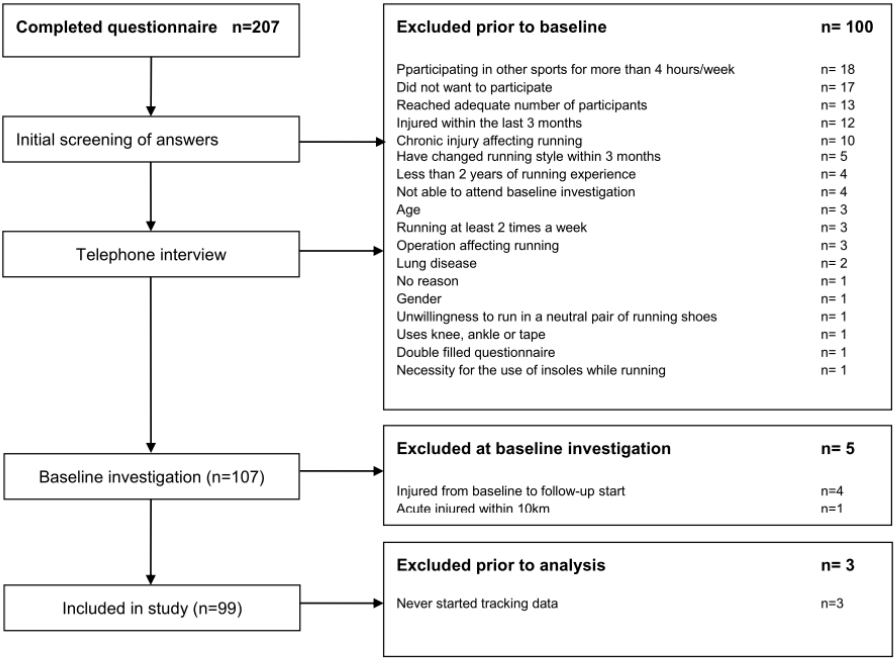


Figure 9: Flow chart of the inclusion procedure.

At baseline, the average self-estimated pace by the runners, was 13km/hour and 25% estimated to run on average 12km/hour or slower, while 25% estimated an ability to run 14km/hour or faster on a 5-kilometer distance.

Description of the running exposure during follow-up

During the 1-year follow-up, the runners ran 99.800 kilometres in total in 9663 running sessions with a mean covered distance of 975 (±790km) per year. No clear difference in the total number of runningsessions per week day and total running mileage per session was found, but sundays seems to be the preference running day and on average was the longest distances covered on fridays and saturdays (Figure 10).

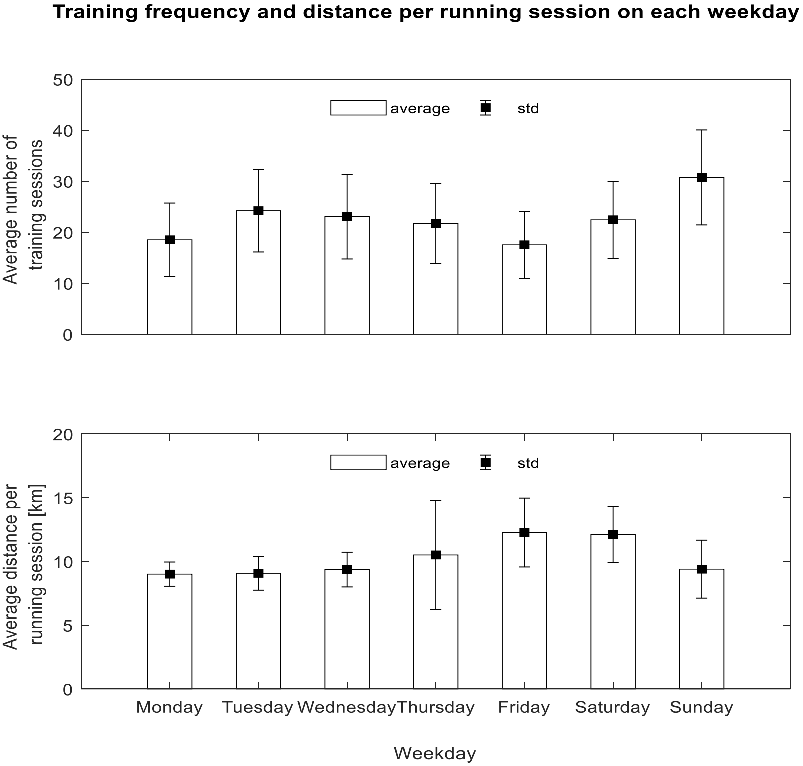


Figure 10: Average number of training sessions and kilometers being run on each weekday during the 1-year of follow-up. Std: standard deviation. n=99

In Figure 11 the average running mileage per session and the number of running sessions per month is presented. During the first three months the runners steadily increased the mileage pr. session. All runners was included in the end of July 2014 and at this time point the most monthly running sessions was covered. From July 2014 until the first runners had been included for a year in the end of March 2015 a gradual decreased in total number of running sessions was seen each month. The average kilometer per running session over the year, was approximately 10km.

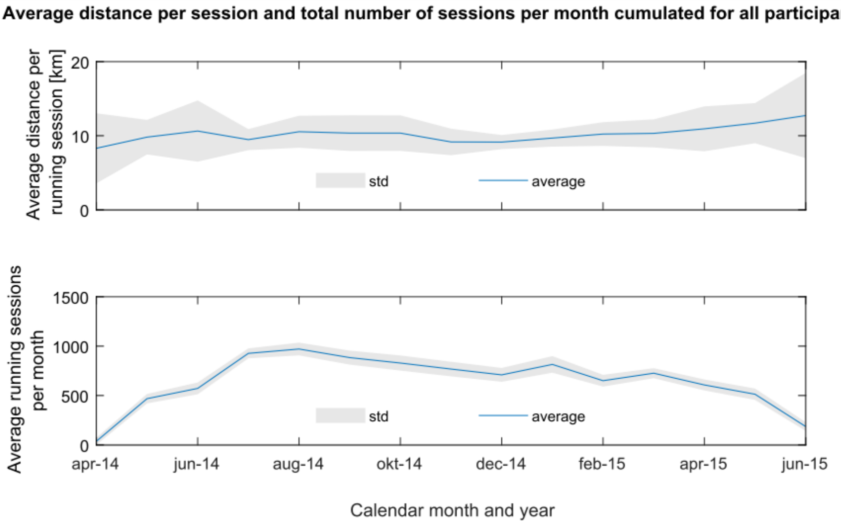


Figure 11: Average of kilometers per session and sessions being run each month during the 1-year follow-up period of 99 recreational male runners. Std: standard deviation. Average standard deviation of running sessions per month: 6 sessions per month. From April to July there was 21, 51, 78 and 99 runners in the end of each month.

Description of the observed injuries

In Figure 12 a graphical representations of the Kaplan-Meier failure is presented. The injury incidence rate was 0.41 injuries per 1000km of running. 40 running-related overuse injuries were reported in total, while 30 of these were first time injuries, six of the runners had a second injury, while two had a third injury during the follow-up period. The first 500km account for the most of the injuries and after 1500km of running, nearly half of the cohort has been injured or censored.

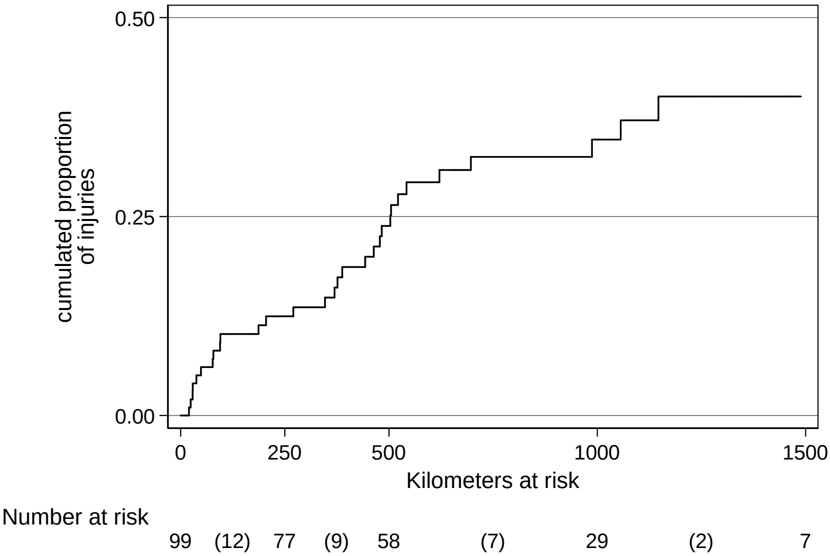


Figure 12: Kaplan-Meier failure function. Estimated number of runners at risk is presented for different time periods and events between time periods are presented in parentheses. Numbers at risk, indicates how many subjects that is able to sustain an injury, while the number in parantheses is the amount of running-related overuse injuries between the two periods.

The most often sustained injury was Achilles tendinopathy followed by injuries in the lower back. The lower leg was the most injured location sustaining more than 50% of the injuries (Table 2). Median recovery time for all injuries was 16 days with a interquartile range of 14 days. Recovery time was dependent on injury type e.g iliotibial band syndrome and plantar fasciitis injuries corresponded to 13% of the total amount of injuries which had a median recovery time of 30 days. However, Achilles tendinopathy and low back pain had a greater prevalence (34% and 18%) but shorter median recovery times (12 and 17 days respectively) (Table 2).

Table 2: Descriptive data on types of running-related overuse injuries and recovery time in descending order based on injury frequency.

Injury type	Number of first time injuries	Number of second time injuries	Number of third time injuries	Percent of injuries	Median recovery time (days)	Diff. in recovery time (days)
	N	N	N	%	median	IQR
Achilles tendinopathy	10	2	1	34%	12	5
Low back injuries	6	1	0	18%	17	8
Plantar fasciitis	3	0	0	8%	30.5	61.5
Medial tibialis stress syndrome	1	2	0	8%	13	8
Gastrocnemius injuries	2	0	1	8%	14	13
Iliotibial band syndrome	1	1	0	5%	42	86
Adductor injuries	2	0	0	5%	26	45
Bursitis hip	2	0	0	5%	29	44
Patellofemoral pain	1	0	0	3%	26	0
Hamstring injuries	1	0	0	3%	22	0
Other	1	0	0	3%	39	0
Tot injuries	**33**	**7**	**3**			

IQR: interquartile range; Diff: difference; Tot injuries: Total number of running-related overuse injuries

ECCENTRIC HIP ABDUCTION STRENGTH AND HIP AND KNEE ANGULAR MOVEMENT (RESEARCH QUESTION 1)

In paper 1, the answer to **research question 1** was approached using a multiple regression analysis between eccentric hip abduction strength and hip and knee angular movement. In this analysis, a total sample of 186 knees were included, after losing seven runners (14 knees) from the Biodex database. The hip- and knee angular movement was used as the dependent variables being explained by eccentric hip abduction strength in a multiple linear regression analysis.

Table 3: The regression coefficient between eccentric hip abduction strength and kinematic variables.

All subjects; N=186 knees	**Independent variable:**				
Dependent variables:	Eccentric hip abduction strength Nm/kg BM				
	Coef	L CI	U CI	R-squared	**p-value**
Knee abduction	1.86	-0.39	4.11	0.18	0.1
Knee internal rotation	0.89	-1.25	3.04	0.29	0.41
Hip internal rotation	0.69	-1.41	2.79	0.24	0.52
Hip adduction	-1.01	-3.22	1.19	0.19	0.36
Knee valgus subgroup; N=46 knees					
Knee abduction	-2.84	-4.56	-1.12	0.35	**0.002***
Knee internal rotation	-3.03	-7.88	1.82	0.41	0.21
Hip internal rotation	-3.02	-8.14	2.09	0.29	0.24
Hip adduction	2.14	-0.05	4.33	0.41	**0.06**

In Table 3, the relationships between eccentric hip abduction strength and hip and knee kinematic variables are presented. In the total sample, eccentric hip abduction strength was not significantly related with hip adduction (p-value = 0.36), hip internal rotation (p-value = 0.52), knee abduction (p-value = 0.1) and knee internal rotation (p-value = 0.41). Additionally, a subgroup analysis (n = 46) comprising runners with both knee valgus and hip adduction was performed. This subgroup analysis, revealed that 1Nm/kg BM increase in eccentric hip abduction strength reduces knee abduction angular movement 2.8 degrees (p-value = 0.002; 95% CI -4.56: -1.12). However, insignificant relationships between eccentric hip abduction strength and hip adduction angular movement (p-value = 0.06), hip internal angular rotation (p-value = 0.24) and knee internal angular rotation (p-value = 0.21) were found.

THE INFLUENCE OF INCREASED MEDIAL SHOE-GROUND PRESSURE ON APM-INJURY RISK (RESEARCH QUESTION 2)

In paper 2**, research question 2** was approached using a pseudo regression analysis. From the 99 runners recruited, only 79 runners were included in the analysis, owing to incomplete pressure data recordings from 20 runners. Shoe-ground pressures from both feet were analysed giving 158 mean pressure shoe-prints for the analysis. Fifty nine of these were classified as LP and 99 were classified as MP (See Figure 13).

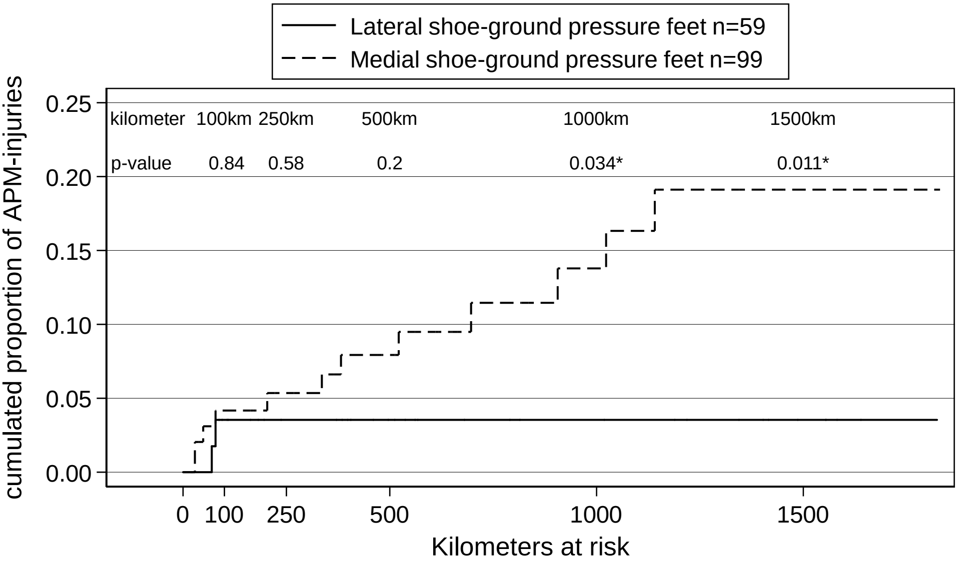


Figure 13: Injury survival among lateral shoe-ground pressure, medial shoe-ground pressure, categorized by the mediolateral shoe-ground pressure ratio. APM-injuries: Achilles tendinopathy, plantar fasciitis and medial tibial stress syndrome. An asteristisk indicates significant more injuries in the medial shoe-ground pressure group compared to the lateral shoe-ground pressure feet.

Nineteen APM-injuries were sustained during follow-up of which 14 were first time injuries. Medial shoe-ground pressure runners (MP) had 16% -point more APM-injuries after 1500km of running (p-value = 0.011 ; 95% CI 0.03 to 0.28) compared to runners displaying lateral shoe-ground pressure (LP) (See Table 4).

Table 4: Crude cumulative risk differences (RD) for APM (Achilles tendinopathy, plantar fasciitis and medial tibial stress syndrome) according to shoe-ground pressure distribution

Analysis time	MLPDR	Number of feet remaining	Number of injuries	Risk difference (Percent point)	Standard error	95% Confidence interval	P>|z|
100km	LP (ref)	53	2				
	MP	90	4	0.006	0.03	-0.05 to 0.06	0.836
250km	LP (ref)	45	2				
	MP	80	5	0.018	0.03	-0.04 to 0.08	0.578
500km	LP (ref)	37	2				
	MP	64	7	0.04	0.05	0.0003 to 0.11	0.2
1000km	LP (ref)	28	2				
	MP	37	10	0.10	0.048	0.007 to 0.19	0.034*
1500km	LP (ref)	18	2				
	MP	24	12	0.16	0.06	0.03 to 0.28	0.011*

Analyses are presented at 100, 250, 500, 1000 and 1500 km. MLPDR was defined as average medio-lateral shoe-ground pressure distribution ratio. LP was defined as lateral pressure ratio. MP was defined as medial shoe-ground pressure ratio.

INJURY INCIDENCE RATE FOLLOWING SHOE CHANGES (RESEARCH QUESTION 3)

In paper 3, **research question 3** was approached using a Poisson regression with restricted cubic splines. The mileage for the individual runners at the time of the ‘500km’ examination varied between 385 and 714km (mean 530km; Standard deviation of 51km).

Injury incidence rate was overall significantly different between the five risk periods based on the Wald-test (p-value = 0.03). Based on the estimated instantaneous injury incidence rate ratios from the Poisson regression presented in Table 5, the average injury incidence rate the first 50km (risk period 1, P1) of running after the first compulsory running shoe transition was not clinically relevant different from one (IIRR = 0.98 [95%CI: 0.97; 0.99]). Contrastingly, the average IIRR was above one between 50 and 100km (1.61 [95%CI: 1.15; 2.24]) (risk period 2) and reduced between 100 and 500km (0.56 [95%CI: 0.37; 0.84]) (risk period 3). Finally, the average IIRR was insignificantly above one between 500 and 600km of running (1.47 [95%CI: 0.77; 2.79]) (risk period 4, P4) and insignificantly below one after 600km of running (0.71 [95%CI: 0.25; 2.02]) (risk period 5).

Table 5: Injury incidence rate ratio during the follow-up period

Risk period	Kilometer period	Running-related overuse injuries	Injury incidence rate ratio	95% Confidence interval	P> |z|
	3 month before inclusion to inclusion				
	0 km	**Transition into the neutral pair of running shoes**			
Risk period 1	0-50km	6	0.98	0.97 - 0.99	0.003
Risk period 2	50-100km	4	1.64	1.13 - 2.24	0.009
Risk period 3	100-500km	11	0.55	0.34 - 0.87	0.011
	387-714km	**Possible shoe change period**			
Risk period 4	500-600km	4	1.47	0.77 - 2.79	0.24
Risk period 5	600km-end	5	0.71	0.25 - 2.02	0.52

‘500km’ examination varied between 385 and 714km (mean 530km; Standard deviation of 51km). Incidence rate ratio = rate in a certain risk period / the average incidence rate during the entire follow-up period (reference rate = 0.41 injuries per 1000km of running).

Graphical presentations of the development of the injury incidence rate and IIRR as a function of kilometers of running are shown in Figure 14A and15B. Figure 15A illustrates the instantaneous injury incidence rate and after how many kilometers of running each of the 30 injured runners were covering before they were injured in the follow-up period, while Figure 14B visualize the modulation of the IIRR. The IIRR-curve indicates that the included runners are at increased risk from the beginning of the curve (starting after 5 incidences) to around 75km and between approx. 375 and 575km of running (Figure 14B).

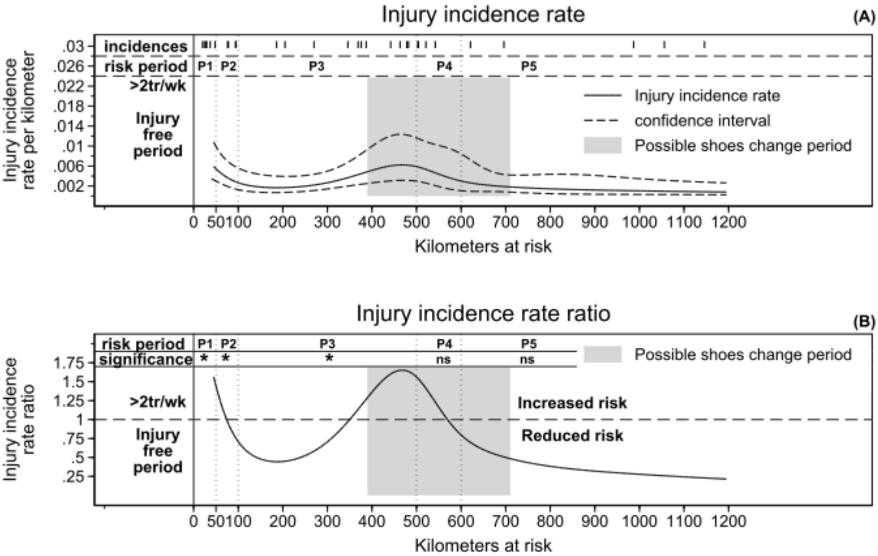


Figure 14: **A)** Injury incidence rate across running distance (curves) and after how many kilometers of running each of the 30 injured runners were covering before they were injured in the follow-up period (markings in the top of the figure). The figure contains data from 99 runners changing to the same type of ‘neutral’ and compulsory running shoe at 0km and with the possibility to change to optional shoes after a biomechanical assessment at about 500km of running. Risk periods: P1: first 100km after changing to the “neutral” running shoes; P2: 100km to the 500km investigation; P3: period after the 500km investigation with the possibility to change to any given running shoes; P4: 500-600km; P5: 600 – end of study. Due to practical issues the 500-km examination in reality occurred over an interval ranging 385-714km of running, which is marked with grey on both A and B. The curves illustrating the incidence rate and confidence intervals start after the fifth incidence, since these five injuries were used to establish a starting point and thereby to increase robustness of the predicted incidence rate. **B)** Predicted injury incidence rate ratio, based on the data illustrated in the panel above. The curve for predicted injury incidence ratio was divided with the average injury incidence rate over the observation period. The horizontal dashed line indicates the average injury

incidence level level (reference rate = 0.41 injuries per 1000km of running). Risk periods significantly different from one (p-value <0.01) is marked with an asterisk.

The average self-reported running distance per week before the inclusion in the study for all the included runners was 29.6km/wk (SD: 20.0). For the group of later non-injured runners (n= 69) it was 26.7km/wk (SD: 17.0) and for the later injured runners (n= 30) it was 31.7km/wk (SD: 28.2) which was significantly higher than the former (p < 0.00001) (see also Fig 15). Additionally, the group of injured runners trained significantly more in risk periods one to three (P1: 5.0km, P2: 12.0km and P3: 6.5km greater weekly running distance), but no statistical differences were found in period four and five (Figure 15). The fitted curves of the development of the weekly running distance during the follow up period are shown in Figure 15. For the non-injured runners there was a tendency to that the weekly running distance increases slightly during the first about 600km, where after the distance began steadily to increase further (Figure 15). The injured runners increased their weekly running distance during the first 100km of running and from 500-700km which suggests that these runners may have decreased the training distance immediately after inclusion and increased it again over the first 100km of running. Overall the injured runners were running more kilometers per week before the inclusion in the study and during the first 1000km of running when compared to the non-injured runners. The injured runners were not followed in the analysis in the present study after their injury and consequently the increase after 600km on the fitted line for the injured runners (Figure 15) is only based on five runners or below. This may explain why the increase is not significant. However, it can still not be excluded that the development in weekly running distance could have had an influence on the IIRR around the optional shoe change.

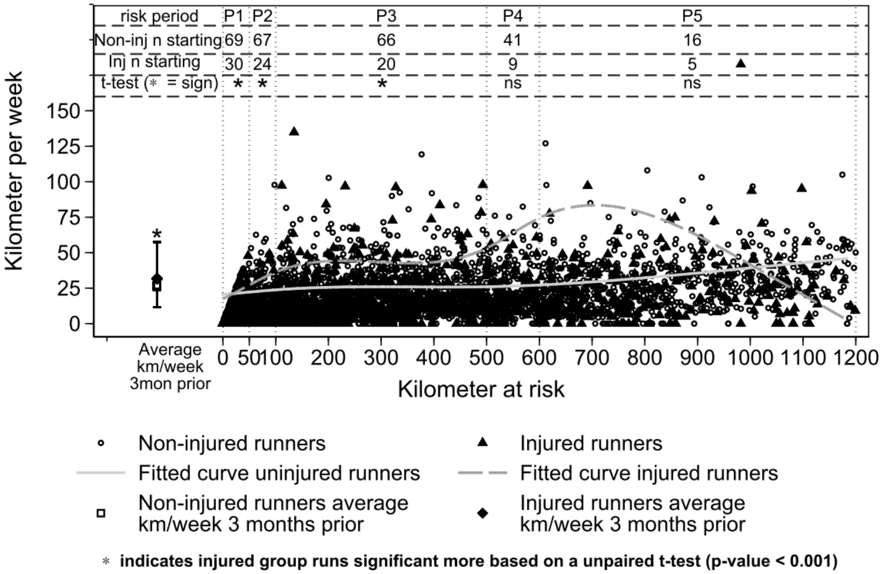


Figure 15: Weekly training distance between runners sustaining an injury and non-injured runners during the follow-up. P1-5: risk periods one to five (see Figure 14); Non-inj n starting: Number of non-injured runners starting in each risk period; Inj n Starting: number of injured runners starting in each risk period; Unpaired t-test (∗ = p-value <0.001)

CHAPTER 4. DISCUSSION

The overall purpose of this PhD-thesis was to provide further insight into the etiology of certain/selected the most frequent running-related overuse injuries and to investigate potential relationships between risk factors associated with running-related overuse injuries. Three main findings were obtained: **1)** in a subgroup of recreational male runners (N = 46 out of 186 knees) increased eccentric hip abduction strength was related with decreased knee abduction angular movement immediately after shoe strike in runners displaying hip adduction and knee abduction immediately after shoe strike. **2)** In a group of 79 recreational male runners 59 feet were classified as LP and 99 were classified as MP. MP feet cumulated a 16%-point greater proportion of plantar fasciitis, Achilles tendinopathy and medial tibia stress syndrome (APM-injuries) compared to lateral pressure feet runners after 1500km of running. **3)** The magnitude of the running-related overuse injury incidence rate ratio (IIRR) modulated over a one year follow-up period including two running shoe changes, one at the time of inclusion, and one after about 500km of running. The IIRR was increased above one around the time-points where the runners changed running shoes and decreased below one in the intermediate period. Hovewever, based on the present results it could not be documented that the running shoe changes were the main determinants of the elevated IIRR levels.

RESEARCH QUESTION 1

Is eccentric hip abduction strength associated with specific hip and knee joint kinematic patterns, which again may be related to knee injury?

Based on the data collected in this study the answer is yes for a subgroup showing simultaneous knee abduction and hip adduction angular movement immediately after initial contact. This observation indicates that hip strength alone is only a risk factor when this pattern is observed which on the one hand means that both factors would be needed to be screened for identifying runners at risk. On the other hand, it underlines the multifactorial nature of running injuries requiring to screen many to better understand these interrelationships. It should be recognized that this observation does not establish direct evidence concerning the etiology of running-related overuse injuries because no direct relationship to injuries was investigated. However, it provided insight on the association between two risk factors associated with knee injuries, which could influence the risk of a knee injury in this sub-group.

HIP STRENGTH MEASURES

A computer-assisted isokinetic dynamometer was used to measure the maximal eccentric hip abduction strength in this study. The strength was measured starting from 20 degrees hip abduction continuously throughout five repetitions of eccentric/concentric sinusoidal movement with an amplitude of 20 degrees at 30 deg s^{-1}. The measured eccentric hip abduction strength was 0.79 Nm/kg (±0.35), which was low compared to the 1.6-1.85 Nm/kg BM range reported in other studies (Baldon et al., 2011;Claiborne et al., 2006). However, the angular velocity and range of motion, in this thesis were similar to Baldon et al. (2011), while the authors initiated the measure at 10 degrees hip adduction, compared to the neutral hip alignment in the present thesis. Claiborne et al. (2006), estimated the eccentric hip abduction strength at 60 deg s^{-1}, with a range of motion of 40 degress starting at 10 degrees hip adduction. Moreover, Claiborne et al. (2006) had 4-5 submaximal and maximal familiarization repetitions before the 3 maximal contractions, which likely increases the maximal strength owing to an effect from familiarization. These differences most likely influence the individual results. The rather low values for maximal eccentric hip abduction strength obtained in this study most likely is the result of the specific manner the maximal strength test was performed.

FACTORS INFLUENCING KNEE ABDUCTION ANGLE

A recently published systematic review and meta-analysis reported several modifiable risk factors that either increase or decrease the knee abduction angle, although with high variations in r-values (Cronström et al., 2016a). Reduced trunk strength, reduced gluteus maximus activity, decreased ankle range of motion, and increased external hip rotation range of motion was moderately associated with increased knee abduction angle. In addition, decreased strength of the hip abductors, external rotators, and extensors and knee flexors were at most weakly associated with increased knee abduction angle. Moreover, other modifiable risk factors, such as increasing peak hip adduction angle (Coef: 0.62deg per one deg increase in peak hip adduction angle; p-value < 0.05) and reducing peak foot eversion (-0.84deg per one deg increase in peak foot eversion; p-value < 0.001) increases the peak knee abduction angle (Sakaguchi et al., 2014). Lastly, Lima et al. (2018) found in a systematic review evidence for a reduced ankle dorsiflexion increasing dynamic knee valgus. It has to be asked why the relationship is not for all. The subgroup analysis indicate it is a matter of the initial movement direction of the knee and only runners with an initial knee abduction angle may display this relationship. From a biomechanical view this subgroup seems to benefit from a greater hip strength. This is probably owing to stronger hip abductors is able to control/resist the amount of hip adduction angle during stance (Baggaley et al., 2015), which leads to a smaller knee abduction angle (Sakaguchi et al., 2014).

CAPTURING DYNAMIC HIP AND KNEE ANGULAR MOTIONS DURING RUNNING

In the present study motion capture was performed with skin mounted active markers. However motions can be captured in various ways. The collection methods range from retro-reflective or active marker systems using either skin mounted or bone pin mounted markers (Benoit et al., 2006), electrogoniometers (Higginson, 2009), electrogyroscopes (Higginson, 2009), inertial magnetic measurement units (Reenalda et al., 2016). The use of skin mounted markers seems to be a generally accepted data collection method during motion capture of running, but due to skin (and marker) movement in relation to the underlying bones the use of skin mounted markers has a drawback compared to bone pin mounted markers which are fixed to the bones (Benoit et al., 2006;Reinschmidt et al., 1997b;Reinschmidt et al., 1997c). However, the use of bone pin markers has a rather invasive nature, and is therefore for ethical reasons not suitable for regular motion capture (Reinschmidt et al., 1997a). It has been demonstrated that knee flexion/extension angular movement agrees rather well when results based on kinematic recordings using both skin mounted and bone pin mounted markers simultaneously (Reinschmidt et al., 1997b), while the knee int/ext and ab/adduction angular movements ranged from poor to good agreememt, with maximal angular differences of 3.9-11.3 degrees and 4.3-13.3 degrees, respectively. An error range of 4.3-13.3 degrees of abduction/adduction between measurements based on bone pin mounted marker and skin mounted markers, corresponding to a measure of validity of the use of skin mounted markers. This is an unavoidable limitation of skin mounted markers in 3-dimensional motion analysis; however considering the subject pool consisted of physically active runners the magnitude of this error would be smaller than if our subjects were obese.

Even though the use of skin markers is generally accepted, differences may also exist in the accuracy of different motion capture systems. The Codamotion system has been demonstrated to have a root mean square error (RMSerror) of 0.225 cm between a rotating plate with 9 cm between markers (Richards, 1999). In comparison to other motion capture systems, this was similar to the Qualisys (0.221 RMSerror) but a doubling of the Vicon system (0.129 RMSerror)(Richards, 1999). Although, the distance between markers is relevant, the measures of angles may be a better estimate of the precision of the motion capture system in relation to the measure of hip and knee angle. In this regard, the Codamotion system displayed a root mean square error of 3.4 deegress on the same plate, with a maxial error of 9 degrees. In comparison the Qualisys and Vicon system displayed a root mean square error of 4.5 and 1.4 degrees and a maximal error of 19.3 and 4.6 degrees (Richards, 1999). It should be recognized that the study is nearly 20 years old and the presented errors is definetly assumed to be smaller today due to improved camera resolution. Overall, it seems like the Codamotion systems is sufficiently accurate in comparison to the commonly used systems. However, a downside of the Codamotion system compared to passive marker systems, was the rather low sampling frequency. Increasing the number of markers, requires the Codamotion system to capture at lower sample frequencys, to accurately capture all markers. This is a limitation of using active marker systems for high frequency movements, such as running. The Nyquist sample theorem states that the sampling frequency must at least be twice as high as the highest frequency in the signal. During running, the step rate is between 2-5Hz, depending on the running speed, giving a sample rate of at least 10Hz. Since the movement of interest, was the path length of the hip and knee during the eccentric phase, which would have four times as high signal frequency. Therefore, at least 40Hz is needed to capture the motions, indicating 100Hz was sufficient.

TREADMILL RUNNINGS EFFECT ON RUNNING MOTION

Treadmill running elicits minor but systematic differences in foot pressure, but no difference in hip and knee angular motion compared to overground running(García-Pérez et al., 2013;Riley et al., 2008). Foot pressure is in general underestimated in treadmill running but demonstrates similar pressure patterns with overground running (García-Pérez et al., 2013;Hong et al., 2012). The pressure is in general lower in the heel and forefoot during treadmill running, which could be owing to the longer contact time displayed in treadmill running (García-Pérez et al., 2013). No general pattern seems to exist regarding the effect treadmill running might have on hip adduction, hip internal rotation knee abduction and knee internal rotation angles (Riley et al., 2008;Schache et al., 2001;Sinclair et al., 2013). Moreover, the treadmill belt was lubricated with silicone oil weekly or after 25-30 operating hours during data collection, dependent on the intensity of use. Based on these results and precautions we assume that foot pressure and hip and knee angular kinematics measured during running on this treadmill can be generalized to overground running.

POST HOC POWER ANALYSES (RQ1)

Sample size calculation is an important tool to ensure sufficient sample size to detect or reject the differences of interest. However in the present study, no sample size calculation was performed beforehand. A post hoc power estimation analysis was performed for the main analysis and sub analysis using an alpha level of 0.05, four covariates, and the total sample size of 186 and 46 and the corresponding estimated r-square values. For the main analysis, the power ranged from 0.99 to 1 and for the sub analysis it ranged from 0.92 to 0.99. This indicates that the analysis for RQ1 was sufficiently powered to reject the main hypothesis and accept the hypothesis for the sub analysis.

Summary of research question 1

Further insight was provided by the identification of a subgroup of runners displaying an association between eccentric hip abduction strength and hip and knee kinematics. Overall, no association existed between eccentric hip abduction strength and hip and knee kinematics in the main group. The subgroup analysis indicate that runners displaying hip adduction and initial movement direction of the knee, only display an association between reduced eccentric hip abduction strength and increased knee abduction angle. From a biomechanical view this group of runners benefit from stronger hip abductor. This is because stronger hip abductors is able to control/resist the amount of hip adduction angle during stance (Baggaley et al., 2015), which leads to a smaller knee abduction angle (Sakaguchi et al., 2014).

RESEARCH QUESTION 2

Is medial shoe-ground pressure associated with the development of APM-injuries among recreational male runners?

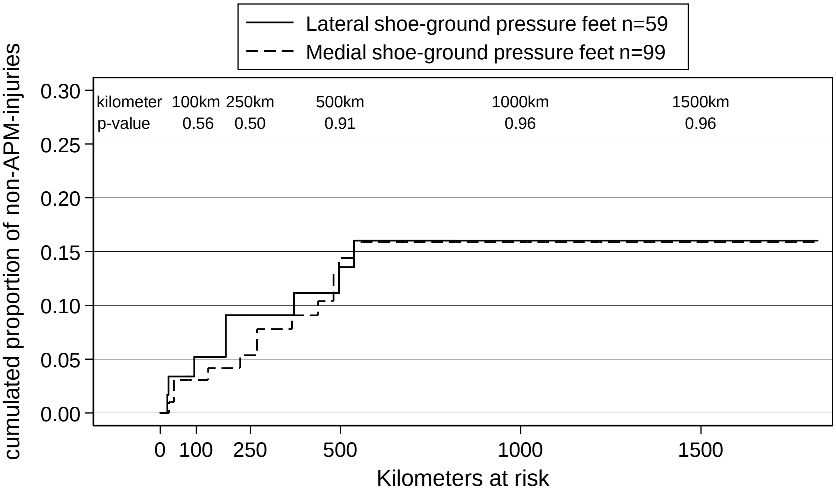
Based on the data from the present study the answer to this question must be yes. It was found that medial shoe-ground pressure runners sustain a significantly greater proportion of APM-injuries compared to lateral pressure feet runners.

ETIOLOGY OF APM-INJURIES

It has been shown previously that the medial shoe-ground pressure exposes greater strain on the medial aspect of the plantar fascia (Chang et al., 2014;Irving et al., 2007), the Achilles tendon (Lersch et al., 2012;Wyndow et al., 2010) and the medial wall of the tibia (Franklyn and Oakes, 2015). Although the medial shoe-ground pressure explains the risk of APM-injuries it is not known in detail exactly how an overweight in medial shoe-ground pressure is translated in to stress concentrations in the plantar fascia, the Achilles and at the medial tibial surface. The mechanisms possibly differ in nature. For example, medial tibial stress syndrome has been identified to be connected with a greater medial longitudinal arch angle at toe-off compared to controls (Bandholm et al., 2008) and greater medial shoe-ground pressure during first 20% and last 30% of the stance phase compared to control recruits (Sharma et al., 2011). This differs from the suggested mechanism of plantar fasciitis that displays a greater inversion-eversion range of motion angle during running, which may increase the rearfoot eversion velocity compared to the controls (Chang et al., 2014), while Achilles tendinopathy may be related to a prolonged rearfoot eversion angle (Donoghue et al., 2008). However, it is important to highlight that the cited studies were case-control studies and the kinematic patterns may have been changed by the injuries and not vice versa, and primary causes of these injuries has not been fully clarified.

MEDIAL SHOE-GROUND PRESSURE AND NON-APM INJURIES

RQ2 proposed only APM-injuries to be associated with medial shoe-ground pressure. Figure 16, indicates no difference in injury survival between MP and LP when investigating running-related overuse injuries excluding APM-injuries). A sufficient number of injuries (10) to develop a robust statistical model, was developed after 250km of running. Eigth of the 59 developed a non-APM-injury (13.5%) in the lateral shoe-ground pressure group, while 13 out of 99 legs developed a non-APM-injury (13.1%) in the medial shoe-ground pressure group after 1500km of running.



Figur 16: Injury survival among lateral shoe-ground pressure, medial shoe-ground pressure, categorized by the mediolateral shoe-ground pressure ratio. Non-APM-injuries: Running-related overuse injuries excluding Achilles tendinopathy, plantar fasciitis and medial tibial stress syndrome.

PROSPECTIVE DESIGN

A prospective design was used to follow each runner with regard to running exposure and injury to answer research questions 2 and 3. The prospective design has several major strengths and assures that the exposure always is measured before the outcome (Meeuwisse, 1994a;Meeuwisse et al., 2007). The running exposure in paper 2 and 3 was measured as the cumulated running distance in kilomters. Running exposure is identified on a duration scale, which is the overall term of the scale used to measure the duration at risk while following runners. Duration scale in running can also be time spent running (minutes), steps or training frequency etc. However, different scales may give different results and therefore it is important to consider the duration scale/s carefully. Time spent running may represent an exposure to running but are limited in cases where runners participate with different pace and/or training distance, since training distance and pace may influence running-related overuse injury location (Nielsen et al., 2013b;Petersen et al., 2015). However, using steps as the duration scale may be closer related with injuries, if steps together with other running metrics can be correlated with distribution of load applied to the musculoskeletal structures in each step (Bertelsen et al., 2017).

INJURY DEFINITION, MEASUREMENT AND DIFFERENT ETIOLOGY OF INJURIES

In the present investigation, the definition of running-related overuse injuries was: absence of running for minimum one week due to lower extremity or lower back musculoskeletal complaints caused by running (Nielsen et al., 2013). Based on the clinical examinations, all musculoskeletal complaints were classified as either running-related overuse injury, injury from other sport or acute injury. The specific classification of each individual injury was a major strength of the present investigation, as the etiology leading to specific injuries is likely different in nature. In study 2, the association between an overweight in medial shoe-ground pressure with APM-injuries was assessed, however it is plausible that not all three APM-injuries are associated with medial shoe-ground pressure alone. In future studies assessing the association between an overweight in medial shoe-ground pressurs and APM-injury, the analysis of the association with each of these injuries separately is needed to finally confirm these findings.

CAPTURING THE SHOE-GROUND PRESSURE

The shoe-ground pressures were captured at each subjects self-estimated 5000m running speed with a sampling frequency of 100Hz. The fastest pace were intended to mimick the pace each runner were exposed to during the follow-up period. In future studies, it may be warranted to use an instrument with the ability to measure shoe-ground pressure continuously during follow-up. This could be used to change the shoe-ground pressure ratio from sessions to session, dependent on the subjects shoe-ground pressure in the specific session (Nielsen et al., 2016). It is likely, that this approach will display an even closer relationship between medial shoe-ground pressure and APM-injuries. Moreover, the shoe-ground pressure was captured at 100Hz, which is enough to average the pressure on the foot. However, it should be recognized that the sampling frequency is too low to capture the impact peak accurately. The missing impact peak, may slightly favor the probability of indentifying medial pressure runners, since the foot pressure is on the lateral aspect of foot during the impact. This is a small proportion of the stance phase and may therefore have very little influence on the shoe-ground pressure ratio.

LIMITATIONS OF THE INTERPRETATION OF STUDY 2

The fact that two out of three feet in the MP group have previously been injured compared to one out of two in the LP group may have affected the results, since previous injuries are known to be a risk factor of subsequent running-related overuse injury (Wen, 2007). Although research question 2 was answered positively, the few injuries limit the possibility to account for previous injuries (Keyes and Galea, 2017). This would have revealed the effect of previous injuries and medial shoe-ground pressure on APM-injury. An additional analysis investigating the risk of previous running-related overuse injury on APM-injury using a Pseudo regression analysis was performed. This analysis demonstrated an insignifincat reduced risk of sustaining a APM-injury after 1500km of running in runners with a previous running-related overuse injury compared to runners which have never experienced a running-related overuse injury before inclusion (p-value = 0.239 ; 95% CI -0.23 to 0.06). Based on this, it is likely that previous injury was not a risk factor of subsequent injuries, which could be speculated based on the literature. In the statistical approach the individuals were kept in the analysis if they were injured in one leg but not the other, which reduces the risk of sustaining another injury on the non-injured leg in the rehabilitation period of the injured leg. This may therefore not reflect the true kilometers at risk after an unilateral injury. Runners preferring other brands or supporting shoes may have been reluctant to participate in this study resulting in the study population being a convenience sample which therefore may not have represented the whole population of recreational male runners.

POST HOC VALIDATION (RQ2)

No sample size calculation was performed A priori. However, we ensured in the analysis to have a minimum of 10 injuries per explanatory variable (Hansen et al., 2014;Nielsen et al., 2016). Based on this, the analysis for RQ2 is not sufficiently robust before the 1000km comparative analysis. Therefore, interpretation of the risk difference before 1000km of running should be done with caution.

Summary of research question 2

Runners with an overweight in medial shoe-ground pressure sustained a greater proportion of APM-injuries compared to runners with an overweight in lateral shoe-ground pressure. This indicates that certain running mechanics may lead to an increased risk of specific running-related overuse injuries. It is not certain if all three APM-injuries are associated with increased medial foot pressure. To understand the exact association between increased medial shoe-ground pressure and the development of each of the specific APM-injuries, further elaboration is needed in future studies.

RESEARCH QUESTION 3

How does the IIRR change over a one year prospective study involving two changes of running shoes?

The primary observation in the results for RQ3 was that the magnitude of the running-related overuse injury incidence rate ratio (IIRR) changed over the follow-up period. A significantly elevated IIRR between 50-100km of running, a significantly decreased IIRR between 100 and 500km of running and an insignificant elevated IIRR between 500 and 600km of running were demonstrated. The elevated IIRR occurred close to the changes of running shoes. It was not possible to confirm that the increased IIRRs were caused by the running shoe changes per se, since it could not be excluded that another risk factor, namely the weekly running distance and other unidentified risk factors were involved too.

A plausible mechanism was that injured runners were, on average, running more kilometers per week during the first 700km of the follow-up period and potentially also progressing more in kilometers (Figure 15). This indicated a greater training load during the observation period, which leaves them at increased risk of injury compared to the non-injured runners. All runners should preferably be under constant injury risk during the observation period apart from the possible added risk imposed by the change of running shoes, if it should have been possible to elaborate on the effect on IIRR of the shoe changes alone.

PROSPECTIVE DESIGN

A prospective design was used to follow each runner regarding running exposure and injury to answer research question 3. All the running-related overuse injuries observed were used to asses the potential risk of changing into new pair of running shoes. It is likely that not all types of running-related overuse injuries are associated with the transition of running shoes. For example, when changing from a conventional running shoe to a minimalist running shoe has been revealed to increase pain in the ankle, calf, shin and knee (Fuller et al., 2017). Therefore, it is possible, that a change of running shoes, primarily increases the risk of lower leg injuries as proposed by Rethnam and Makwana (2011). In the present study, nearly half of the injuries occurred in the lower leg.

LIMITATIONS OF THE INTERPRETATION OF STUDY 3

The increased injury incidence rate above the average incidence rate of the follow-up period may be explained by (a): change in training patterns immediately after being enrolled in the study, (b): the change of running shoes (c): the examination at inclusion into the study, or (d): various other factors. Moreover, the magnitude of changes in biomechanics is unknown, since it is loading of the musculoskeletal system form both the previous running shoe and the experimental running shoe is unknown. A future study should include a preconditioning period of sufficient length, which ensures similar training load before changing to a new running shoe. This would allow for a comparison between the injury incidence rate before and after the shoe change, which would have strengthened the study.

POST HOC VALIDATION (RQ3)

No sample size calculation was performed A priori. However, we ensured in the analysis to have a minimum of five injuries before interpreting the incidence rate and IIRR. It should be recognized that after 600km of running, very few injuries occurred, which reduces robustness of estimating IIRR.

Summary of research question 3

A running-related overuse injury incidence rate ratio above one was found around the time-points at which runners changed running shoes. It remains to be investigated if the increased rates were caused by the changes in shoes or by other factors e.g. running exposure. Additionally, it could not be excluded that differences in weekly running distance have had an influence on the results, together with other unidentified risk factors.

RUNNING-RELATED OVERUSE INJURY ETIOLOGY

An understanding of the causes of running-related overuse injuries is the key to advance knowledge, particularly to predict an injury and develop and implement prevention strategies (Finch, 2006; Meeuwisse, 1994). Despite decades of research, the main problem associated with existing research is that little progress has been made regarding identifying biologically and/or mechanically plausible risk factors with a causal chain to injury (Nielsen et al., 2012;Saragiotto, Yamato, Hespanhol et al., 2014;van Gent et al., 2007). The RunTech study was developed to increase our knowledge on risk factors' influence on developing running-related overuse injuries. This knowledge will be useful when introducing preventive measures by establishing guideline for runners. This chapter will discuss running-related injury etiology and propose how to move beyond prediction and towards causation and intervention.

A MULTIFACTORIAL RUNNING-RELATED OVERUSE INJURY MODEL

Bertelsen et al. (2017) have developed a causal framework for the etiology of running-related overuse injuries. In their paper, the authors argue that future research should address running participation (running distance, time spent running, session frequency or stride number) alone or together with other risk factors (muscle strength, running shoes, running kinematics) to move towards causation (Bertelsen et al., 2017). Therefore, to provide a better understanding of the causes of injury, study designs should be developed according to causal frameworks (Bertelsen et al., 2017;Nielsen et al., 2017). By developing a study design according to running-related overuse injury within its causal framework, research will move beyond prediction and towards causation and intervention by asking questions such as "How much running participation can runners with a specific variable tolerate, compared to runners not having that variable?" (Bertelsen et al., 2017; p. 5, l.47-49). This type of question was investigated in RQ2, which found that at a similar running distance, the runners with an overweight in medial shoe-ground pressure were developing a greater amount of APM-injuries. Asking this type of questions moves towards causation, since runners displaying medial shoe-ground pressure are not at risk of running-induced APM-injuries, if they are not exposed to running. Therefore it is utmost important that the research questions are asked in a similar way as research question 2.

In Figure 17, a modified version of the causal framework by Bertelsen et al. (2017) is presented. The Figure describes the balance between the structure-specific load capacity and structure-specific cumulative load in one training. A runner engages into a running session with an initial structure-specific load capacity (SSLC), which is the amount of load each structure is able to withstand before developing a running-related overuse injury. The SSLC is reduced every running stride during a running session and the amount of reduction is dependent on the magnitude of the load applied per stride and how this magnitude is distributed over tissue structures (Bertelsen et al., 2017). The magnitude of load applied per stride (MLPS) is amongst other things influenced by the running speed, bodyweight and terrain. The distribution of load over tissue structure applied per stride (DLPS) is amongst other things influenced by the muscle strength, running kinematics, running shoes. MLPS and DLPS results in a structure-specific load per stride (SSLPS) for any given structure in the musculoskeletal system. By applying a greater SSLPS than the SSLC is able to withstand results in a running-related overuse injury.

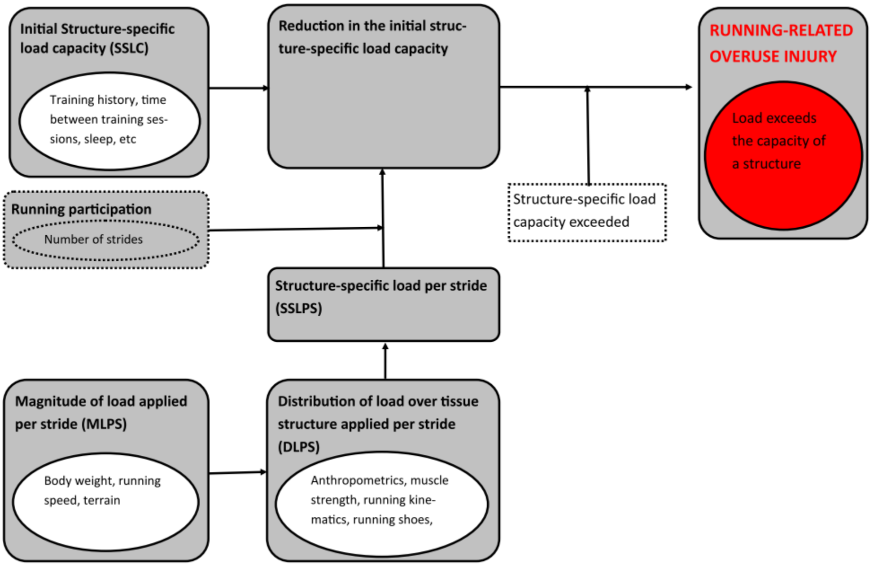


Figure 17: A conceptual framework describing the mechanisms behind a running-related overuse injury within one single running session. The relationship between initial Structure-specific load capacity, Structure-specific cumulative load per running session, and running-related overus injury. (modified from Bertelsen et al. (2017) with permission).

Based on the framework, a necessary cause for developing a running-related overuse injury is the exposure of running participation, which preferably should be expressed as ‘number of strides’. Running distance, time spent running or days of running will not equate to the load a given runner’s musculoskeletal system is exposed to (Bertelsen et al., 2017). However, using running distance or time spent running as running participation may still be in favour of not using running participation at all to address risk factors influence on the risk of running-related overuse injury. This is because the participation in running is crucial to identify how much running participation runners with a specific variable/risk factor can tolerate compared to runners without this variable/risk factor. Therefore future research should, as mentioned above, form hypothesis asking how much runners are able to participate with a certain risk factor compared to not having that risk factor and carefully consider how running participation is expressed and used in the statistical model.

Development of RQ1, 2 and 3 in relation with the causal framework

Paper 1 was not intended to move towards a causative relationship of running-related overuse injuries, but was intended to elaborate on potential mechanism leading to the selected risk factors. Therefore, Paper 1 provided further insights into a possible etiology of running-related overuse injuries, which may be beneficial for alignment of future study designs with this causal framework

Paper 2 was alignet with the causal framework by addressing how much runners are able to participate when showing a certain risk factor (medial shoe-ground pressure) compared to not generating this loading pattern. It has to be noted that several authors have proposed that running-related overuse injuries develop as a consequence of running “too much, too soon” (Nielsen et al., 2012;Renstrom, 1993;Wen, 2007) which is a very different argument. To proof if such a relationhip is correct, study 2 should have included the differences in progression of running distance to elaborate on how much progression is feasible with and without medial shoe-ground pressure. This would potentially indicate a lower threshold of progression, which would increase the risk of APM-injuries in the medial shoe-ground pressure group compared to the lateral shoe-ground pressure group. By establishing a lower threshold, preventive studies can be designed to compare differences in injury risk between runners displaying medial shoe-ground pressue and runners progressing less than the threshold with those progressing more than the threshold.

Paper 3 was not alignet with this causal framework, although the novelty of this study may prove important. When investigating the effect of footwear changes, future studies should align with the causal framework by using a randomized controlled trial starting with a preconditioning period where the included runners should run with a standardized running shoe. Thereafter, two lines of intervention arms could be introduced with one arm changing to another standardized running shoe and the other arm should continue with the same running shoe for an appropriate time period. The difference in injury risk between the two groups after the intervention period, would then give the effect of changing running shoes. If feasible, running exposure should be controlled to ensure an even exposure between groups. This design will ensure that all runners are preconditioned to the same running shoe and the preconditioning period will ensure the most fragile runners is injured before the intervention starts and thereby not influence the results. If future studies confirm the increased risk after changing running shoes and/or the distribution of load to the musculoskeletal system, the importance of preparing for footwear changes and slowly implementing the new shoes after a change should be highlighted both to the running community and to running injury researchers.

CHAPTER 5. IMPLICATIONS OF THE THESIS

The results from Paper 1 are beneficial when selecting runners that could benefit from strengthening the eccentric hip abduction strength to reduce the knee abduction angle. Strengthening the hip abductors may not reduce the general risk of injury but may increase the total amount of running exposure a specific athlete can withstand before exceeding the load capacity of the specific structures (Keyes and Galea, 2017). A reduced knee abduction angle may lead to an altered tracking of the patella and with that reduce the cause of pain. Stefanyshyn *et al.* (2006) have previously demonstrated, in a prospective matched case-control study, that runners developing patellofemoral pain had a greater knee abduction moment but similar running participation, running experience and bodymass compared to their controls. This risk factor together with the fact that resistance training and functional movement training reduces the knee abduction moment makes it plausible that greater eccentric hip abduction strength is beneficial in a selected group of runners (Snyder et al., 2009;Wouters et al., 2012). It is important to highlight that a reduced knee abduction angle may reduce the knee joint abduction moment but may increase the load in other structures that may face an increased risk for injuries in structures which have not adapted to the redistributed load.

Paper 2 investigated the medial shoe-ground pressure relationship with specific injuries (medial tibial stress syndrome, Achilles tendinopathy and plantar fasciitis). To date, only few prospective studies have investigated the relationship between foot function and running-related overuse injuries (Malisoux et al., 2016a;Nielsen et al., 2013;Ryan et al., 2011) and none of these investigated foot function in relation to specific injuries. In the current study, medial shoe-ground pressure feet runners sustained a greater proportion of plantar fasciitis, Achilles tendinopathy and medial tibial stress syndrome compared to lateral pressure feet. The fact that this has been related to specific injuries may prove beneficial in runners with initial pain in the plantar fascia; Achilles tendon or medial wall of the tibia. Such runners could possibly change to motion control shoes with the ability to move the medial pressure to the lateral side. This may potentially reduce the applied load to the medial aspect of the tibia, Achilles tendon and plantar fascia and therefore increase the recovery in those areas (Magnusson et al., 2010). The change in shoe-ground pressure may have a downside of increasing risk of injuries in other structures (Thijs et al., 2007). However, this is rather speculative since it was the natural shoe-ground pressure that was investigated in this thesis. It remains uncertain if a change from higher medial to higher lateral shoe-ground pressure elicits similar foot function as the natural lateral shoe-ground pressure.

Paper 3, was designed based on the observation that the body slowly adapts to certain musculoskeletal loads and a major change in this load may increase the risk of sustaining an running-related overuse injury. The present results indicate that it cannot be verified that changing running shoes increases the risk of sustaining injuries briefly after the shoe change. Several uncertainties were present in this study, which leaves the question on the injurious effects of changing shoes open. Therefore, more studies on changing footwear are warranted and these should elaborate on the magnitude of change and duration of increased injury risk following shoe change. Moreover, if feasible, the potential preventive effect of using multiple shoes at specific frequency/ies should be investigated. Using multiple shoes theoretically reduces the magnitude of sudden changes, since the body has adapted to a range of different loading patterns. Multiple shoe users have been proven to sustain fewer injuries compared to single shoe users (Malisoux et al., 2015), but the optimal interval(s) between shoe changes are still unknown.

CHAPTER 6. CONCLUSION

The purpose of this thesis was to provide further insight into the etiology leading to some of the most frequent running-related overuse injuries and to investigate potential relationships between risk factors and running-related overuse injuries. Running-related overuse injuries were assessed by a combination of biomechanical and epidemiological methods that allowed for an identification of associations, evaluating and identifying risk factors based on biomechanical variables. The overall purpose was approached by posing three research questions.

The answer to **research question 1** provided further insight into identifying a subgroup of runners demonstrating simultaneous hip adduction and knee abduction (valgus) during the first half of the stance phase. In this subgroup, an association between reduced eccentric hip abduction strength and increased magnitude of the knee abduction angular excursion was discovered. This new insight may prove beneficial to reduce the knee abduction angle in this subgroup, while runners displaying knee adduction may not benefit from increasing the eccentric hip abduction strength. Reducing the knee abduction angle may increase the amount of exposure a specific athlete can withstand before exceeding the load capacity of the specific structures.

The answer to **research question 2** provided evidence to the effect shoe-ground pressure distribution has on the risk of APM-injuries. To date, only few prospective studies have investigated the relationship between foot function and running-related overuse injuries and none of them investigated the relationships of foot function with specific injuries. The group of runners with higher medial shoe-ground pressure during running sustained a greater proportion of APM-injuries. The fact that this has been related to specific injuries may prove beneficial in runners with initial symptoms of pain in the plantar fascia; Achilles tendon or medial wall of the tibia. Such runners could possibly change to motion control shoes which may have the ability to move the medial pressure on the foot to the lateral side. This may potentially reduce the applied load to these three structures and therefore potentially prevent overloading or increase recovery.

The answer to **research question 3**, has shedded light on the association between changing running shoes and running injury incidence rate. Running-related overuse injury incidence rate ratio (IIRR) was increased above one around the changes of running shoes and below one in the intermediate periods. Large scale studies involving alternative experimental protocols are needed to provide further insight into the association between running-related overuse injury incidence rate and running shoe changes.

In summary, the results of this thesis have provided further insights into the etiologies leading to some of the most frequent running-related overuse injuries. Although the applied experimental design applied and the data collection methods used in the present study possess limitations, the valuable knowledge generated in this thesis may act as a foundation for future studies.

CHAPTER 7. PERSPECTIVES

Certainly more research is needed to improve our understanding of etiologies leading to running-related overuse injuries. Prospective studies and trials have previously included between 100 and 2000 runners (Bredeweg et al., 2010;Kluitenberg et al., 2013;Nielsen et al., 2011). However, together with the present study, these studies were limited in numbers of injuries, which restricted the studies to include between 2-7 exposure variables (Nielsen et al., 2016). Larger studies with more injuries, increases the possibility of including more variables, since a minimum of 10 injuries per variable is needed (Peduzzi et al., 1995).

Moreover, larger studies with more injuries should also include both training variables, such as progression in running distance and exposure variables such as shoe-ground pressure and changing running shoes. This would enable the possibility to compare the effect and interplay between training variables and exposure variables, which most likely will increase our understanding of which variables influence the running-related overuse injury risk the most. Although, larger studies definitely may advance the understanding of the etiologies leading to specific running-related overuse injuries, the current measures of training load/exposure, such as changes in kilometers, speed etc., are indirect in that these measures are not directly reflected as structure-specific loads. Since injuries occur in specific structures (i.e. plantar fasciaa, Achilles tendon), tools for quantifying the resulting load in specific structures need to be developed and implemented. Recent developments in computational musculo-skeletal modelling methods (The AnyBody Modelling System (AMS), AnyBody Technology, Aalborg, Denmark) and/or shear wave propagation (Martin et al., 2018) have made it possible to estimate structure-specific loads. Combining these biomechanically estimated structure-specific loads with training load variables measured in a epidemiological study will further increase our understanding of how running-related overuse injuries develop. Training load variables could be number of strides, cadence, ground contact time, stride length, and vertical oscillation. This will increase our understanding of training loads effect on specific structures loading and hopefully be able to predict the structure-specific load in epidemiological studies. Furthermore, determining ways of reducing load on the specific musculoskeletal structure, may also be useful in epidemiological studies. Based on this, researchers could modify the running exposure variables associated with cumulated loading on specific structures. Therefore future studies, should focus on: 1) large scale studies with more than 100 injuries of interest, to investigate both changes in training load and exposure of interest and 2) the development of instruments to estimate cumulated loading on specific structures and use in-field measurable training load variables to predict this estimated structure-specific load.

CHAPTER 8. THESIS AT A GLANCE

Title of paper	Research question	Method	Main finding
Paper I			
The association between eccentric hip abduction strength and hip and knee angular movement in recreational male runners: an explorative study.	Is eccentric hip abduction strength associated with specific hip and knee joint kinematic patterns, which again may be related to knee injury?	A multiple linear regression analysis on 186 knee investigating the relationship between eccentric hip abduction strength and hip and knee angular movement.	No relationship were found in the main group. However, weak hip abductors was related with increased knee abduction angular movement in runners displaying increased hip adduction and increased knee abduction immediately after foot strike.
Paper II			
Medial shoe-ground pressure and specific running injuries: A 1-year prospective cohort study.	Is medial shoe-ground pressure associated with the development of APM-injuries among recreational runners?	A time-to-event model was used to compare differences in incidence between shoe-ground pressure groups.	Runners displaying medial shoe-ground pressure during stance phase sustained a greater amount of plantar fasciitis, Achilles tendinopathy and medial tibia stress syndrome (so called APM-injuries) compared to those displaying a lateral shoe-ground pressure during stance phase.
Paper III			
Increased rate of running-related overuse injury immediately after transitioning to a conventional running shoe: A 1-year prospective cohort study	Is the incidence rate of obtaining a running-related overuse injury increased after changing running shoes?	99 recreational male runners volunteered to engage in a self-structured running program, provided with a pair of neutral running shoes.	A running-related overuse injury incidence rate ratios above one was found around the time-points at which runners changed running shoes. However, it remains to be investigated if the increased rates were caused by the changes in shoes or by other factors e.g. running exposure.

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