On the Run for Running-Related Injuries

Consequences, role of training load and prevention

Kyra Cloosterman

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CONSEQUENCES, ROLE OF TRAINING LOAD AND PREVENTION

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CONSEQUENCES, ROLE OF TRAINING LOAD AND PREVENTION

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Consequenties, rol van trainingsbelasting en preventie

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Chapter 1

General introduction

INTRODUCTION

Running is one of the most popular sports worldwide. It is estimated that around 50 million people in Europe run on a regular basis, with 1.7 million runners in the Netherlands[1,2]. Running has a range of health-related benefits on both physical and mental well-being (e.g. running improves aerobic fitness and cardiovascular function), is easy to perform, and is an easily accessible sports activity[3-6]. Running can also fulfill a social function, as running groups facilitate interactions between runners which can produce motivational effects[7]. It can even become a place where runners attend for emotional support[7]. Running grew in popularity in the Netherlands, from 4% of the Dutch population in 2001 to 10% in 2018 (+147%)[2]. Unfortunately, many runners are affected by running-related injuries (RRIs) with injury proportions ranging from 3% in cross-country runners up to 85% in novice runners[8]. In the Netherlands, the absolute number of RRIs increased from 750,000 RRIs in 2018 to 1,100,000 RRIs in 2020[7,8]. This makes running the sport with the most reported injuries in the Netherlands[8]. The increase in the number of RRIs was not only due to the increased number of hours of running, but the risk of sustaining an injury also increased from 6.1 RRIs per 1,000 running hours in 2014 to 7.5 injuries per 1,000 hours in 2020[9]. RRIs can result in health and economic burdens, including physical discomfort, decreased workability, increased healthcare utilization, and societal costs[10,11]. This emphasizes the need for prevention of RRIs, especially because RRIs account for 48% of all reasons for running discontinuation[12].

Consequences of running-related injuries

Most RRIs have a serious nature, since 53% of the injured runners in the Netherlands are medically treated by a physiotherapist, general practitioner and/or medical specialist[13]. However, little is known about the severity (e.g. pain severity), consequences (e.g. training adjustments and workability), and prognostic factors of RRIs. So far, only two studies have evaluated prognostic factors of RRIs using different study populations and follow-up times[14,15]. These studies concluded that a previous RRI was related to a poor prognosis of a new RRI in novice runners and that male marathon runners with non-musculoskeletal comorbidities were more likely to have prolonged complaints of their RRI. The large diversity in runner characteristics (e.g. men versus women or novice versus experienced runners) and injury characteristics (e.g. injury location or type of injury) likely results in differences in the impact and prognosis of RRIs. This might be especially important for runners with a running-related knee injury, since the knee is the most frequent injury location in runners[16-18]. It is important to give a more accurate picture of the severity, impact, and prognostic factors of an RRI to inform runners on the course of complaints of their RRI and facilitate them with the most realistic expectations. It will also provide insights into the societal impact of RRIs.

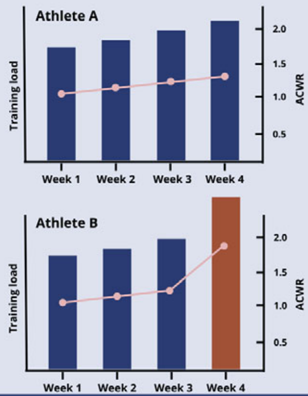
Training load and its association with running-related injuries

Most RRIs are overuse injuries. In 2017, 54% of the RRIs in the Netherlands were reported as a consequence of overuse[13]. In literature, overuse is estimated to account for 64-75% of all RRIs[10,19,20]. Based on research in team sport populations, a sudden increase in training load, also known as the phenomenon "training too much, too soon", has been associated with an increased risk of injury development (See Box 1 for further explanation[21,23]). Change in training load may cause an imbalance between load and recovery in which the training load exceeds the athletes' load capacity for adaptive tissue repair[19,24,25].

Box 1. Interpretation of training load data

First studies investigating the relationship between training load and injury risk were performed in team sport populations. Change in training load was calculated with the use of acute:chronic workload ratios (ACWRs). ACWRs ≥ 1.5 (i.e. the workload in the current week was 1.5 times greater than what the athlete was prepared for) were regarded as high risk. ACWRs within the range of 0.8-1.3 were considered as low risk[34].

This figure shows on the left vertical axis the training load (e.g. km/week), on the right vertical axis the ACWR, and on the horizontal axis the consecutive training weeks. Athlete A increased the weekly training load with ACWRs below 1.5, so the injury risks were low. Athlete B reported a sudden increase in training load in week four with an ACWR above 1.5. Therefore, the injury risk in week four was high.



Only a few studies investigated the association between training load and RRI risk and found conflicting results[26-30]. Possible reasons for these conflicting results are the differences in study populations and the use of different methods to calculate change in training load: the weekly training load method and methods to calculate acute:chronic workload ratios (ACWRs)(Table 1)[26-30]. ACWRs can be calculated by the coupled rolling average (RA) method in which the acute workload (last seven days) is divided by the chronic workload (last 28 days); the uncoupled RA method in which the acute workload is not included in the chronic workload, and the exponentially weighted moving averages (EWMA) in which a decreasing weighting is assigned for load values that have been applied longer ago (Table 1). Another reason for the conflicting results might be the difference in data collection. Most previous RRI studies determined training characteristics by using questionnaires that asked runners for average training distance, frequency, and speed over a certain period of time[19,20,31]. However, this data was collected retrospectively, which may lead to recall bias resulting in inaccurate data[31]. The use of global training data might be an alternative collecting training data, especially because it contains data of each training session performed by a runner. Nowadays, more than 75% of recreational runners use wearable technology such as global positioning system (GPS)-enabled sport watches to track their training activities[32]. Recent research concluded that GPS training data can accurately measure several aspects of training load, such as covered distance, speed and cadence[32]. Therefore, the use of GPS data seems an accurate method to calculate training load in runners[32,33]. However, it is not yet known if it is feasible to collect GPS training data of a large cohort of recreational runners and how this data can be used to calculate change in training load in runners. This emphasizes the need for more insights into the feasibility and usability of GPS data in exploring associations between training load and running injuries.

Table 1. Formulas to calculate training load.

	Weekly training load	Coupled ACWR[a]	Uncoupled ACWR	EWMA[b]
Formula	$\frac{A}{W2} * 100$	$\frac{A}{0.25 * (A+W2+W3+W4)}$	$\frac{A}{0.33 * (W2+W3+W4)}$	$load_{today} * \lambda a + ((1 - \lambda a) * EWMA_{yesterday})$
Definition	A = training load of current training session + 6 days prior to this training session W_t= training load of the previous weeks are represented by W2, W3 and W4, respectively			$\lambda a = 2 / (N + 1)$ N=7 days for the acute workload and 28 days for the chronic workload

[a]Acute:Chronic Workload Ratio; [b]Exponentially Weighted Moving Averages.

Prevention of running-related injuries

To be able to prevent RRIs, it is important to identify risk factors[34]. When risk factors and causes of injuries are known, prevention programs can be developed to inform runners about these risk factors and to give advice to adjust modifiable risk factors (Figure 1)[34,35]. Risk factors for RRIs have been investigated widely throughout the past decades. A large variety of risk factors (e.g. higher body mass index, higher age, and no previous running experience) were identified, but the reported risk factors were often not consistent between studies[17,36,37]. The only consistently reported risk factor for RRIs is a previous injury[17,38].

So far, few randomized-controlled trials (RCTs) investigated the effectiveness of a program to prevent RRIs. Most of these prevention programs targeted one single risk factor (e.g. the effects of training schedules[39], minimalistic shoes[40], or a strength training program[41]) and found no effect on the incidence of RRIs. A reduction of RRI incidence was found in two RCTs, in which the effectiveness of a gait retraining program[42] and a foot core strengthening program were examined[43]. However, both programs will be very hard to implement nationwide because these programs were conducted in a biomechanics laboratory or participants received weekly training by a physical therapist.

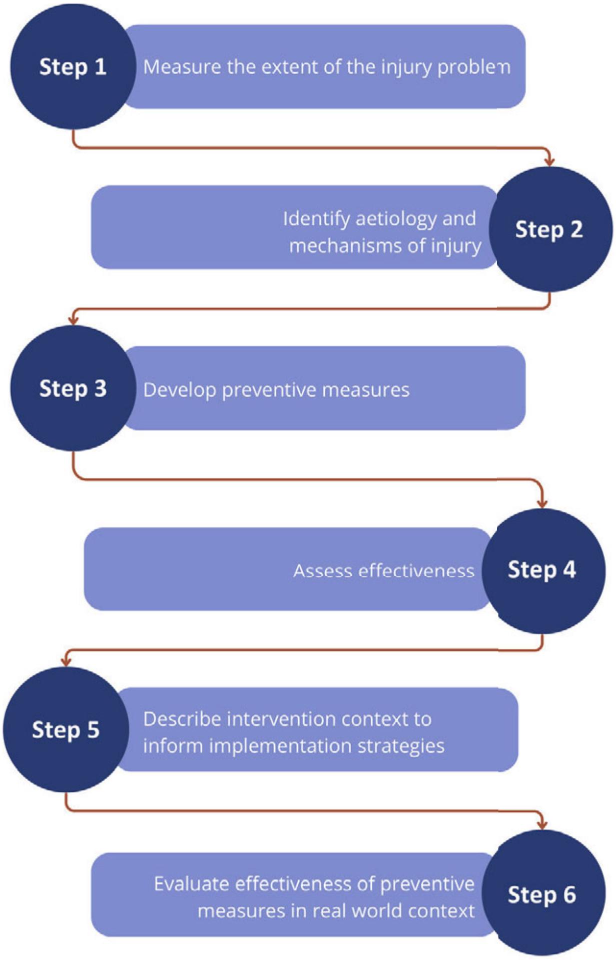


Figure 1. The six steps of the TRIPP model – Translating Research into Injury Prevention Practice that describes sports medical research in injury prevention (modified from Finch et al.[35]).

A reason that most previous RCTs did not find an effect on the number of RRIs might be that all RCTs targeted only one single risk factor, while the cause of injury seems to be multifactorial[25]. Therefore, the INSPIRE trial was designed in 2017[44]. This RCT examined the effect of an online injury prevention program on the number of RRIs in recreational runners using a multifactorial approach. In this prevention program, all participants in the intervention group received information on evidence-based risk factors and advices to reduce their injury risk. However, this RCT did also not decrease the overall number of RRIs in recreational runners[45]. A reason that this program was not effective might be due to the way the information on injury prevention was presented to the included runners. As mentioned by Nielsen et al., to prevent RRIs it is important to distinguish between the prevention of injuries in specific athletes or the wider population of athletes[46]. Generalized population-based prevention of RRIs aims to provide every runner with the same advice. However, the effect of advice on preventing an RRI may vary among runners with different characteristics. Perhaps athlete-specific advices in subgroups of runners are needed to reduce the number of RRIs. An important subgroup to target might be the high-risk group of runners who had a previous injury, especially because the intervention investigated in the INSPIRE trial seemed to have a negative impact on the number of RRIs in the subgroup of runners with no previous RRI[45]. Therefore, this thesis investigated the effect of a new online injury prevention program (the SPRINT study) on the number of RRIs. In this new prevention program, we especially focused on runners with a previous injury and included more online tailored advice and more directed practical information on injury prevention[47,48].

Outline of this thesis

This thesis aims to provide insight into the consequences of RRIs, the role of training load in RRI prevention and to identify new preventive measures for recreational runners. Particularly the use of GPS training data was examined for this purpose. I divided the thesis into three parts. **Part 1** provides insight into the consequences of RRIs and running behavior during the COVID-19 pandemic. **Chapter 2** describes the consequences and prognostic factors of running-related knee injuries. In **Chapter 3**, we examine sex differences in characteristics and factors associated with new RRIs. Because the COVID-19 pandemic was present during our ongoing RCT on running injury prevention (SPRINT study), **Chapter 4** describes changes in running behavior due to the COVID-19 pandemic and identifies whether there was an association between running behavior and the onset of symptoms suggestive for COVID-19. **Part 2** addresses how to define and apply training load in runners and describes the association between change in training load and RRIs. **Chapter 5** focuses on the feasibility and usability of GPS data to explore associations between training load and running-related knee injuries. In **Chapter 6**, we compare different methods to calculate change in training load in running with the use of GPS data. **Chapter 7** investigates the association between change in training load and RRI risk using GPS-based ACWRs. **Part 3** focuses on the SPRINT study, an RCT on the effectiveness of an online prevention program on the number of RRIs in recreational runners. In **Chapter 8**, the results of the SPRINT study are presented. Finally, **Chapter 9** discusses the main findings of this thesis in a broader perspective. This chapter concludes with implications for practice and suggestions for future research.

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Part 1

Consequences of running-related injuries and running behavior during the COVID-19 pandemic

Chapter 2

Consequences and prognosis of running-related knee injuries among recreational runners

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ABSTRACT

Objective: To investigate the consequences and prognostic factors of running-related knee injuries (RRKIs) among recreational runners.

Methods: This study is part of a randomized-controlled trial (RCT) on running injury prevention among recreational runners. At baseline during registration for a running event (5-42 km), demographic and training variables were collected. Participants who reported a new RRKI during follow-up were sent a knee-specific questionnaire at 16 months (range 11.7-18.6) after baseline. To determine the association between potential prognostic factors and time to recovery of an RRKI, a Cox regression analysis was performed.

Results: At 16 months after registration, 71.0% of the participants reported full recovery, with a median time to recovery of 8.0 weeks. Most participants reported iliotibial band syndrome (23.2%) or osteoarthritis (OA)/degenerative meniscopathy (23.2%) as cause of their injury. Male sex was associated with a shorter time to recovery (HR 1.84; 95% CI 1.14-2.97), while suffering knee OA was associated with a longer time to recovery (HR 0.17; 95% CI 0.06-0.46).

Conclusion: Nonrecovered participants adjusted running speed more often and had knee imaging more often than recovered participants. At follow-up, one-third of the participants were not recovered. This emphasizes the need for injury prevention programs for runners. More knowledge on the role of running in knee OA seems important, given the high number of participants with knee OA symptoms.

INTRODUCTION

Recreational running, with its accessibility and low monetary costs, has become increasingly popular among the general population as a primary form of exercise. In the Netherlands, around 12.5% of the total population participated in running activities in 2014[1]. Although several health benefits are attributed to running activities, the increased popularity of running has also led to an increase in running-related injuries (RRIs)[2].

The most common site of running injuries is the knee[3-5]. Running-related knee injury (RRKI) proportions in runners vary from 22.5% in cross-country runners to 30.6% in novice runners[6]. A 1-year prospective follow-up study in novice runners demonstrated that median time to recover from RRKIs in novice runners was 75 up to 88 days for the most common RRKIs (i.e. patellofemoral pain (PFP), meniscopathy, iliotibial band syndrome (ITBS), and patellar tendinopathy)[7]. Furthermore, PFP and meniscopathy were the second and third most common RRIs. Respectively, 15.0% and 26.0% of runners with these injuries reported persistent complaints of their injury after 1-year follow-up[7].

Only a few studies evaluated prognostic factors of RRIs in runners, using different study populations and follow-up times[8,9]. The results of these studies were inconclusive. Van Middelkoop et al.[8] performed a study on the course and 3-month prognosis of RRIs in male marathon runners and found that runners who reported non-musculoskeletal comorbidities were more likely to have prolonged complaints of their injury. This while Fokkema et al.[9] reported that a previous RRI was related to a poor prognosis of a new injury in novice runners. Furthermore, for runners, it is important to be aware on the consequences of RRIs in terms of training adjustments and medical consumption. To the best of our knowledge, no studies have been designed to evaluate the consequences and prognostic factors of RRKIs among recreational runners. When focused on only RRKIs, analysis will be made in a less heterogeneous study population. This will cause a higher chance to find specific factors predicting the course of RRKIs. Identification of these factors would provide practitioners with information about characteristics that may predict the prognosis of their patient's RRKI. Hereby, practitioners can inform their patients about the most likely clinical course of the RRKI and facilitate them with more realistic expectations of treatment outcomes[10]. Therefore, the aim of this study was to investigate the consequences and prognostic factors of RRKIs among recreational runners during a 16-month follow-up period.

METHODS

Study Design and Setting

The current study was part of the INSPIRE trial (Intervention Study on Prevention of Injuries in Runners). The INSPIRE trial was a randomized-controlled trial among recreational runners with a minimum follow-up of three months, in which we investigated the effect of an evidence-based online injury prevention program on the number of RRIs[11]. The INSPIRE trial was funded by the Netherlands Organization for Health Research and Development (ZonMW, 536001001). Medical ethics approvals were obtained by the Medical Ethical Committee of the Erasmus MC University Medical Center Rotterdam, the Netherlands (MEC-2016-292). Participants who reported a new RRKI during the study period were included in the current study and sent a follow-up questionnaire at a mean of 16-month (range 11.7-18.6). A flowchart of the design and follow-up is presented in Figure 1.

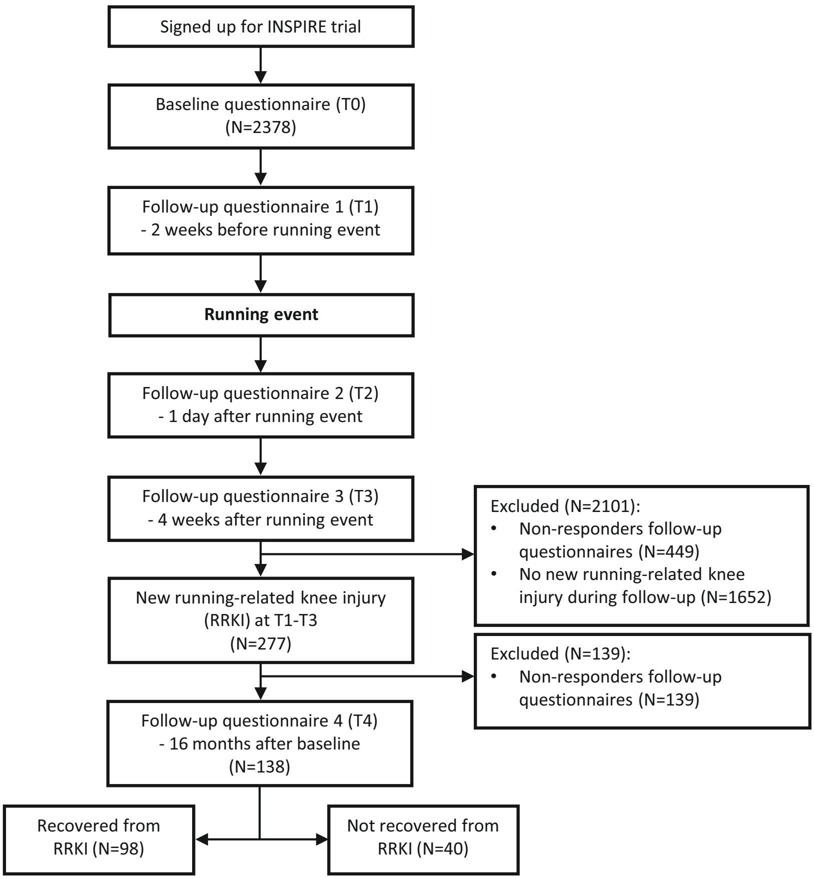

Figure 1. Flowchart of the participants.

Subjects

Runners who registered for the running events NN City Pier City run The Hague (5, 10, and 21.1 km), NN Marathon Rotterdam (10.55 and 42.195 km), and the Ladies Run Rotterdam (5, 7.5, and 10 km) in 2017 were asked if they were interested in participating in the INSPIRE trial. Interested runners were sent additional online information. If they fulfilled the inclusion criteria, runners were asked to provide electronic informed consent and to complete the baseline questionnaire (T0). Both novice and more experienced runners, aged 18 years and older, who returned the baseline questionnaire, were included in the INSPIRE trial. Exclusion criteria were no knowledge of the Dutch language and no access to internet and email. Participants received a follow-up questionnaire two weeks before the running event (T1), one day after the running event (T2), and one month after the running event (T3). Nonresponders were sent a reminder by email within one week. Runners who reported a new knee injury at one of the questionnaires (T1, T2, or T3) were sent an additional knee-specific follow-up questionnaire (T4).

Questionnaires

The baseline questionnaire (T0) consisted of questions on demographic characteristics (sex, age, weight, and height). Weight and height were used to calculate the body mass index (BMI). Participants were asked if they experienced non-musculoskeletal comorbidities (yes/no), if they had an RRI in the preceding 12 months (yes/no), and if this RRI was a knee injury (yes/no). Training-related information was administered with questions on running frequency, hours, distance, and running speed (average per week over the last three months). Furthermore, participants were asked about their running experience (in years), membership of an athletics association (yes/no), and use of a training schedule (yes/no). Information about type of training surface (paved/unpaved), type of training (endurance/interval/specific exercises), and use of orthotics (yes/no) was also obtained. For the current study, running experience was categorized in 0 to 4 years, 4 to 10 years, and ≥ 10 years and training distance in 0 to 15 km, 15 to 30 km, and ≥ 30 km per week. Interval training was dichotomized in more or less than 50% of the training and training on paved surface in more or less than 75% of the training.

For the current study purpose, the follow-up questionnaires (T1-T3) were used to extract information about new RRKIs. Furthermore, severity of knee pain at onset was derived from the questionnaire in which the knee injury was first reported by the participant. Participants scored the severity of knee pain, at rest and while running, on an 11-point Numeric Rating Scale ranging from 0 (no pain) to 10 (worst pain imaginable).

The additional knee-specific follow-up questionnaire (T4) obtained information on long-term consequences of RRKIs. Participants were asked if they were recovered from their RRKI (yes/no). Furthermore, time to recovery (weeks) was questioned. If participants were not recovered, they were asked to score the severity of present knee pain due to the RRKI. Information about the course of the knee pain (constant pain with slight fluctuations/ constant pain with pain attacks/pain attacks, between attacks pain-free/pain attacks, between attacks constant pain) was obtained. The self-reported diagnoses were classified into PFP, ITBS, tendinopathy, knee osteoarthritis (OA)/degenerative meniscopathy, bursitis, traumatic injury, and other/unknown. The self-reported diagnoses were leading, but when a diagnosis remained unclear or unknown, a sports physician gave the participant the most likely diagnosis using reported sublocations of the knee pain and age of the participant. The National Institute for Health and Care Excellence (NICE) guideline was followed to diagnose knee OA. Following this guideline, a participant was diagnosed with knee OA when at least 45 years old, activity-related joint pain, and either no morning joint-related stiffness or morning stiffness that lasted no longer than 30 minutes[12]. Information on medical consumption was obtained by the use of painkillers and/or NSAIDs, treatment by a health professional (general practitioner, medical specialist, and/or physiotherapist), type of treatment received (stretching or exercises, adjustment of running shoes, use of orthotics, and/or other), and imaging (radiography, MRI, and/or ultrasound). In addition, participants were asked whether the RRKI restricted their running in terms of running speed, duration, and/or frequency. The subscales symptoms and sports of the Knee Injury and Osteoarthritis Outcome Score (KOOS) were used to administer OA-specific outcomes at follow-up[13]. The Anterior Knee Pain Scale score (AKPS) was used to evaluate PFP complaints[14]. The scores of the KOOS and AKPS both ranged from 0 (worst pain and/ or disability) to 100 (no pain and/or disability).

Outcome Measures

The primary outcome measure was time to recovery of a knee injury in weeks. An RRKI was defined as any self-reported musculoskeletal complaint of the knee due to running activities, which restricted the amount of running (distance, duration, speed, or frequency) for at least one week or needed medical consultation[3,4,15].

Analysis

Descriptive statistics were used to describe baseline characteristics, expressed in frequency or mean and standard deviations (SDs). Baseline characteristics of responders and nonresponders of the kneespecific 16-month follow-up questionnaire (T4) were compared using independent-sample t-tests or chi-square tests. Recovered and nonrecovered participants were compared on the consequences of RRKIs using independent-sample t-tests and chi-square tests. To test associations between potential prognostic factors and time to recovery from RRKIs, a Cox regression analysis (enter method) was performed with recovery of the RRKI as the event. Potential prognostic factors included sex, age, BMI, non-musculoskeletal comorbidities, RRI in the 12 months before baseline, diagnosis (suspected knee OA based on the NICE guideline, PFP, and ITBS), and severity of knee pain at onset. Hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) were calculated. For participants who did not recover from their RRKI during follow-up, recovery time was set to the time in weeks of the knee complaint up to T4.

Before Cox regression analysis, multiple imputation techniques were performed due to missing data of knee pain at onset. Ten imputations were used in the model. The variables severity of knee pain at onset, at rest and while running, were imputed. Factors used as predictors included sex, age, BMI, non-musculoskeletal comorbidities, recovered (yes/no), recovery time, and diagnosis (suspected knee OA based on the NICE guideline, PFP, and ITBS). P-values <0.05 were regarded as statistically significant. All analyzes were performed using SPSS version 24.0 (SPSS Inc, Chicago, IL).

RESULTS

In total, 2378 runners participated in the INSPIRE trial (Figure 1). Of these, 277 (14.4%) runners reported a new RRKI during follow-up and were sent a knee-specific follow-up questionnaire (T4) after a mean of 16 months (range 11.7-18.6). A total of 138 (49.8%) participants responded to the final follow-up questionnaire and were consequently included in the current study. Compared with the group participants with a new RRKI that did not respond to the knee-specific follow-up questionnaire (T4), responders were on average significantly older (42.3 vs. 39.3 years, p=0.04). No other significant differences between responders and nonresponders were found.

At baseline, study participants with an RRKI (N=277) were on average 42.3 (SD 12.2) years old, had an average BMI of 23.3 (SD 3.0) kg/m^2, and the majority was male (59.4%) (Table 1). Participants trained on average 2.2 (SD 0.9) times a week and spent 2.6 (SD 1.5) hours a week on training with an average running speed of 6.0 (SD 0.9) min/km. A total of 50 (36.2%) of the participants reported an RRKI in the previous 12 months. None of the participants sustained an RRKI at baseline.

After a mean of 16-month follow-up, 71.0% (N=98) of the runners were recovered from their knee injury (Table 2), with a median recovery time of 8.0 weeks. Nonrecovered participants had complaints for 54.5 weeks up to T4. Following the self-reported diagnoses, most participants suffered from ITBS (23.2%) and knee OA/degenerative meniscopathy (23.2%). Following the NICE guideline, 13.8% of the participants were diagnosed with knee OA. A significant difference between recovered and nonrecovered participants was found within the group of participants who had suspected knee OA based on the NICE guideline (5.1% vs. 35.0%, p<0.001).

Table 1. Baseline characteristics of responders and non-responders.

	Responded to follow-up questionnaire		
	Yes (N=138)	**No (N=139)**	**Total (N=277)**
Sex (male)	82 (59.4)	72 (51.8)	154 (55.6)
Age (years)[a]	42.3 (12.2)	39.3 (11.8)	40.8 (12.1)*
BMI (kg/m^2)[a,b]	23.3 (3.0)	23.4 (2.7)	23.3 (2.8)
Non-musculoskeletal comorbidities	30 (21.7)	30 (21.6)	60 (21.7)
Running experience			
0-4 years	67 (48.6)	76 (54.7)	143 (51.6)
4-10 years	37 (26.8)	37 (26.6)	74 (26.7)
≥ 10 years	34 (24.6)	26 (18.7)	60 (21.7)
Weekly training frequency[a]	2.2 (0.9)	2.2 (1.0)	2.2 (1.0)
Weekly training hours[a]	2.6 (1.5)	2.6 (2.1)	2.6 (1.8)
Weekly training distance			
0-15 km	49 (35.8)	60 (43.2)	109 (39.5)
15-30 km	59 (43.1)	54 (38.8)	113 (40.9)
≥ 30 km	29 (21.2)	25 (18.0)	54 (19.6)
Running speed (min/km)[a]	6.0 (0.9)	6.0 (0.9)	6.0 (0.9)
Hard training surface (> 75%)	115 (83.3)	116 (83.5)	231 (83.4)
Interval training (> 50%)	16 (11.6)	11 (7.9)	27 (9.7)
Member of an athletics association	37 (26.8)	42 (30.2)	79 (28.5)
Use of a training schedule	92 (66.7)	82 (59.0)	174 (62.8)
Use of orthotics	61 (44.2)	48 (34.5)	109 (39.4)
RRI[c] 12 months before baseline			
Yes, RRKI[d]	50 (36.2)	48 (34.5)	98 (35.4)
Yes, other RRI	39 (28.3)	32 (23.0)	71 (25.6)
No	49 (35.5)	59 (42.4)	108 (39.0)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between responders and non-responders ($p<0.05$); [b] Body Mass Index; [c] Running-related injury; [d] Running-related knee injury.

Table 2. Severity and type of running-related knee injuries of recovered and non-recovered runners.

		Recovered from knee injury	
	Total (N=138)	**Yes (N=98)**	**No (N=40)**
Severity of knee pain at onset[a,b]			
Rest (NRS[c], 0-10)	3.2 (2.1)	3.0 (2.0)	3.8 (2.1)
Running (NRS, 0-10)	5.7 (2.7)	5.6 (2.7)	6.1 (2.7)
Knee pain at follow-up[a]			
Rest (NRS, 0-10)	-	-	3.1 (2.0)
Running (NRS, 0-10)	-	-	5.1 (2.4)
Diagnosis			
Patellofemoral pain	7 (5.1)	4 (4.1)	3 (7.5)
Iliotibial band syndrome	32 (23.2)	27 (27.6)	5 (12.5)
Tendinopathy	12 (8.7)	10 (10.2)	2 (5.0)
Knee OA / degenerative meniscopathy	32 (23.2)	21 (21.4)	11 (27.5)
Knee OA (NICE guideline[d])	19 (13.8)	5 (5.1)	14 (35.0)*
Bursitis	3 (2.2)	3 (3.1)	0 (0.0)
Traumatic injury	5 (3.6)	1 (1.0)	4 (10.0)
Other / unknown	47 (34.1)	32 (32.7)	15 (37.5)
Course of knee pain			
Constant pain with slight fluctuations	60 (43.5)	45 (45.9)	15 (37.5)
Constant pain with pain attacks	2 (1.4)	2 (2.0)	0 (0.0)
Pain attacks, between attacks pain-free	72 (52.2)	48 (49.0)	24 (60.0)
Pain attacks, between attacks constant pain	4 (2.9)	3 (3.1)	1 (2.5)
Same knee injury in the past	48 (34.8)	32 (32.7)	16 (40.0)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between recovered and non-recovered runners ($p<0.05$). [b] Severity of knee pain at onset derived from the questionnaire in which the knee injury was first reported; [c] Numeric Rating Scale; [d] National Institute for Health and Care Excellence.

More than half (56.5%) of the participants made training adjustments because of the RRKI, of which two-thirds (66.7%) on running speed and 61.5% on frequency (Table 3). Of the 71 participants who received treatment for their RRKI, 87.3% was treated by a physiotherapist. Significant differences between recovered and nonrecovered participants were found in adjustment of running speed during training (75.0% vs. 50.0%, p=0.03), receiving knee radiography, MRI and/or ultrasound (11.2% vs. 30.0%, p=0.01), KOOS Symptoms (89.2 vs. 64.6, p=0.01), KOOS Sports (86.1 vs. 77.8, p<0.001), and AKPS (95.8 vs. 81.4, p<0.001).

Table 3. Consequences of running-related knee injuries of recovered and non-recovered runners after 16 months follow-up.

		Recovered from knee injury	
	Total (N=138)	**Yes (N=98)**	**No (N=40)**
Use of painkillers and/or NSAIDs	15 (10.9)	10 (10.2)	5 (12.5)
Adjustment of training	78 (56.5)	52 (53.1)	26 (65.0)
Running speed	52 (66.7)	39 (75.0)	13 (50.0)*
Hours	25 (32.1)	15 (28.8)	10 (38.5)
Frequency	48 (61.5)	29 (55.8)	19 (73.1)
Treatment of health professional	71 (51.4)	48 (49.0)	23 (57.5)
General practitioner	4 (5.6)	2 (4.2)	2 (8.7)
Medical specialist	7 (9.9)	4 (8.3)	3 (13.0)
Physiotherapist	62 (87.3)	43 (89.6)	19 (82.6)
Kind of treatment			
Stretching or exercises	42 (59.2)	28 (58.3)	14 (60.9)
Adjustment of running shoes	4 (5.6)	3 (6.3)	1 (4.3)
Use of orthotics	5 (7.0)	4 (8.3)	1 (4.3)
Other	23 (32.4)	7 (30.4)	16 (33.3)
Knee radiography, MRI and/or ultrasound	23 (16.7)	11 (11.2)	12 (30.0)*
KOOS (0-100)[a,b]			
Symptoms	82.1 (21.1)	89.2 (15.8)	64.6 (22.4)*
Sports	83.7 (18.0)	86.1 (17.8)	77.8 (17.3)*
AKPS (0-100)[a,c]	91.6 (10.6)	95.8 (6.7)	81.4 (11.6)*

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between recovered and non-recovered runners ($p<0.05$); [b] Knee Injury and Osteoarthritis Outcome; [c] Anterior Knee Pain Scale.

The results of the Cox regression for time to recovery are presented in Table 4. Male sex (HR 1.84; 95% CI 1.14-2.97) was associated with a shorter recovery time, while participants diagnosed with suspected knee OA based on the NICE guideline (HR 0.17; 95% CI 0.06-0.46) had a longer time to recovery. None of the other included variables were significantly associated with time to recovery.

Table 4. Cox Regression Model of prognostic factors associated with a faster recovery from running-related knee injuries.

	HR (95% CI)	p-value
Sex (male)	1.84 (1.14-2.97)*	0.01
Age (years)	1.00 (0.98-1.02)	0.78
BMI (kg/m^2)[a]	0.95 (0.89-1.03)	0.22
Non-musculoskeletal comorbidities	1.31 (0.74-2.32)	0.35
RRI[b] previous 12 months		
No	Reference	
Yes, RRKI[c]	0.86 (0.52-1.42)	0.56
Yes, other RRI	1.45 (0.85-2.47)	0.17
Diagnosis		
Knee osteoarthritis (NICE guideline[d])	0.17 (0.06-0.46)*	<0.001
Patellofemoral pain	0.72 (0.20-2.60)	0.62
Iliotibial band syndrome	1.02 (0.60-1.72)	0.95
Knee pain at onset		
Rest (NRS[e], 0-10)	0.93 (0.83-1.05)	0.25
Running (NRS, 0-10)	0.96 (0.85-1.07)	0.44

* = statistically significant association with time-to-recovery ($p<0.05$); [a] Body Mass Index; [b] Running-related injury; [c] Running-related knee injury; [d] National Institute for Health and Care Excellence; [e] Numeric Rating Scale.

DISCUSSION

The aim of this study was to investigate the consequences and possible prognostic factors for time to recovery from RRKIs in recreational runners. Nonrecovered participants adjusted running speed more often and had knee imaging more often than recovered participants. At follow-up, almost one-third of the participants were not recovered from their RRKI. Male runners were more likely to have a faster recovery from RRKIs compared with females. Runners diagnosed with suspected knee OA based on the NICE guideline were more likely to have a longer time to recovery.

In the current study, 71.0% of the runners with an RRKI were recovered after 16 months, with a median time of 8.0 weeks. The median time to recovery of 8.0 weeks is comparable with a recent study of Mulvad et al.[16], who described a median time to recovery of 7.0 and 8.0 weeks for, respectively, PFP and ITBS. This while Nielsen et al. reported a median recovery time of 10.7 to 12.6 weeks for the most frequent RRKIs (PFP, meniscopathy, ITBS, and patellar tendinopathy)[3]. A possible explanation for this small difference is the use of different study populations because Nielsen et al. performed the study in novice runners. In conclusion, runners suffering an RRKI should expect a recovery time of 7 till 13 weeks if they respond to the initial treatment.

The percentage of participants with knee OA was relatively high because 19 (13.8%) participants were diagnosed with knee OA following the NICE guideline, and even 32 (23.3%) participants reported the diagnosis knee OA. When including all participants with knee OA (suspected knee OA based on the NICE guideline and self-reported knee OA), diagnosis knee OA was still significantly associated with a longer time to recovery from RRKIs (HR 0.43; 95% CI 0.24-0.77, p<0.001). This association is in line with the fact that knee OA is a chronic progressive condition and a major cause of musculoskeletal disability in older populations. Treatments are restricted to pain alleviation by a combination of pharmacological and exercise interventions[17]. In this study, 31.6% of the runners diagnosed with knee OA did not make any training adjustments because of their RRKI. Current clinical guidelines for the management of knee OA recommend exercise among the primary treatments but do not clearly describe recommendations on running[18-21]. A recent study of Lo et al. reported that self-selected running is associated with improved knee pain and not with worsening knee pain or radiographically defined structural progression[21]. More clinical guidance therefore seems required for the middle-aged to older runner with knee complaints, with regard to advice on running intensity, surface, and terrain. Therefore, more evidence from well-designed, prospective studies is needed to determine the role of running in knee OA[22].

Using a Cox regression model, male runners were found to have a faster recovery from RRKIs compared with females. Male runners recovered from their knee injury with a median recovery time of 6.0 weeks, while females recovered with a median recovery time of 10.0 weeks. In none of the other studies about prognostic factors of RRIs, sex was significantly associated with time to recovery[8,9]. Furthermore, no literature has been found to explain the faster recovery in male runners compared with females. Therefore, the difference in recovery time between male and female runners remains unexplained until now.

Strengths and Limitations

This study has a number of strengths. This is the first study providing data on prognostic factors of time to recover from RRKIs, the most common injury in runners. Furthermore, a prospective study design was applied. However, some limitations have to be taken into account when interpreting the results of this study. Information was collected through self-reported questionnaires with a follow-up time of 16 months (range 11.7-18.6), which may have caused recall bias with regard to the injury characteristics. Furthermore, about 43.5% of the participants reported two or more RRIs during the follow-up period. Given answers were likely based on all running injuries and not only on the knee injury. For example, an individual could have been recovered from a knee injury but not yet participating in running activities due to another injury. This may have led to an overestimation of the RRKI duration. Of the participants, 40 (29.0%) did not recover from their RRKI before the end of follow-up. It is not known if participants will recover after follow-up, and if so, when they will recover. To investigate possible prognostic factors, recovery time was defined as the duration of symptoms in weeks up to the knee-specific follow-up questionnaire (T4) for nonrecovered participants. However, this has likely led to an underestimation of time to recovery. Finally, the percentage loss to follow-up (50.2%) was relatively high. Reason for this high percentage might be the long follow-up from questionnaires T3 and T4, without any contact in between with the participants. Because of this long follow-up, participants might have become less interested to participate in the follow-up questionnaire. To remind participants to complete questionnaire T4, a reminder was sent. However, more effort could have been made to keep participants engaged in the study between questionnaires T3 and T4, which would likely have resulted in a higher follow-up at T4. Compared to the group participants with a new RRKI that did not respond to the knee-specific follow-up questionnaire (T4), responders were on average significantly older (42.3 vs. 39.3, p=0.04). Age might be associated with a longer recovery time because older participants are likely to get more often the diagnosis OA. However, a mean difference of three years between responders and nonresponders is not expected to be clinically relevant. In this study, diagnoses were self-reported. Of the 32 participants with the diagnosis knee OA/degenerative meniscopathy, only one participant reported the diagnosis degenerative meniscopathy. Because diagnoses were self-reported and degenerative meniscopathy is a strong risk factor for OA, these two diagnoses were combined.

CONCLUSION

Nonrecovered participants adjusted running speed more often and had knee imaging more often than recovered participants. At follow-up, one-third of the participants were not recovered at 16 months after baseline. Male participants with an RRKI seem to be more likely to have a faster recovery compared with females. Participants diagnosed with knee OA were more likely to have a longer time to recovery. The relatively long duration of knee symptoms after an injury emphasizes the need for optimal treatment, education, and injury prevention programs for recreational runners. Given the high number of participants with knee OA symptoms, more knowledge on the role of running in knee OA seems especially important to provide more clinical guidance toward patients and clinicians.

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Chapter 3

Sex differences in characteristics and factors associated with new running-related injuries among recreational runners

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Submitted

ABSTRACT

Objective: Running is an injury-prone sport. Sex differences in type, location, consequences and risk factors of running-related injuries (RRIs) are understudied. We aim to clarify these sex differences.

Methods: Databases of two randomized-controlled trials were combined. Both trials analyzed injuries among recreational adult runners participating in running events (5-42 km). Participants received a baseline questionnaire and three follow-up questionnaires detailing runners characteristics, injury characteristics (e.g. location and type of injury) and consequences (e.g. painkiller use and pain scores). A predetermined injury definition was used to register RRIs. Data analysis was performed using descriptive statistics and multivariable logistic regression analysis of risk factors.

Results: A total of 6428 participants were analyzed with an average follow-up time of 5.0 months. 82% of the participants finished at least one follow-up questionnaire and 64% completed the follow-up. During follow-up, 2133 (33%) participants (33% men, 34% women) suffered one or more RRIs. We found no sex differences in injury location and type of injury. Men used less medication (13% vs. 15%, p=0.01) and had a lower pain score while running (4.2 (SD 2.9) vs. 4.5 (SD 2.8), p=0.04) compared to women. A history of RRIs was associated with a new RRI in both men (OR 1.9; 95% CI 1.6-2.2) and women (OR 1.7; 95% CI 1.4-2.0).

Conclusion: No relevant differences were found between men and women in location, type, consequences, and factors associated with an increased risk of a new RRI among recreational runners. Our findings do not support accounting for sex-specific factors in the development of personalized prevention for RRIs.

INTRODUCTION

Running is a popular recreational sport, but unfortunately also an injury-prone sport[1]. There is a wide spread in reported injury rates with some studies suggesting an injury rate up to 79.3%[2-4], although the most recent meta-analysis reported an injury rate of 20.8%[5]. A reduction in injury rate could help runners reach their health goals and potentially reduce healthcare costs[6]. The cause of running-related injuries (RRIs) is considered to be multifactorial[3,7].

One factor frequently discussed in association to running injuries is sex[8]. This is because men and women differ in their physiology and anatomy: women tend to have shorter and smaller limbs compared to body size, different hormone levels, increased Q-angle (predisposing for patellofemoral pain syndrome), more laxity of their joints (i.e. the knees), and lower lean body mass for the same BMI when compared to men[9]. Therefore, the relationship between RRIs and sex has been analyzed in multiple studies. There is no evidence that there is a difference in overall injury rate between men and women[5]. Although epidemiological studies have observed mixed evidence on sex differences in type of injury. Women tend to have more knee injuries[2], more bone stress injuries[5,10] and patellofemoral pain[11] compared to men. While men suffer more frequently from Achilles tendinopathy compared to women[5,11]. Although there is also some evidence suggesting that, when comparing exactly the same type of running sports, sex differences might vanish[12].

The evidence on the sex-specific risk factors for new RRIs is conflicting. For example, both long weekly running distances (> 64 km per week)[13], long training distances[3], but also short running distances (< 15 km)[14] are considered to increase RRI risk in men, while for women the association is stronger for shorter running distances (< 10 km)[5].

The association between sex and the prognosis and impact of an RRI is also uncertain. Some potential sex differences have been found in medication use (higher for women)[15-17] and in medical costs of an RRI (higher for men)[18]. But thus far the evidence is limited.

Sex differences in runners have been extensively analyzed, but the studies offer conflicting results. Potential reasons for these conflicting results are the fact that previous studies lack sufficient power, because they differ in type and location of injuries reported, self-reported vs. physician-diagnosed injury, follow-up time, participation rate of the identified target group[13], definition of an injury, and/or classification of the participating runners[2]. In order to tackle previous study limitations we initiated analyzes in a large cohort to identify sex differences in incidence, location, type, consequences, and factors associated with an increased risk of RRIs amongst recreational runners.

METHODS

Study design

This cohort study combined the data of two randomized-controlled trials: the INSPIRE trial (INtervention Study on Prevention of Injuries in Runners at Erasmus MC)[19] and the SPRINT study (Shaping up Prevention of Running Injuries in the Netherlands using Ten steps)[4]. Both studies investigated the effect of an online injury prevention program on the number of RRIs for recreational runners. The INSPIRE trial and SPRINT study were both funded by the Netherlands Organization for Health Research and Development (INSPIRE trial: ZonMW, 536001001, SPRINT study: ZonMW, 50-53600-98-104) and performed in collaboration with Golazo Sports, which organizes various large running events in the Netherlands. Both studies were approved by the Medical Ethical Committee of the Erasmus Medical Center Rotterdam, the Netherlands (INSPIRE trial: MEC-2016-292, SPRINT study: MEC-2019-0136).

Participants

All participants of the included running events were invited to join the study. The INSPIRE trial included: the NN City Pier City The Hague 2017 (5, 10, and 21.1 km), NN Marathon Rotterdam 2017 (10.55 and 42.195 km) and the LadiesRun Rotterdam 2017 (5, 7.5, and 10 km). The SPRINT study included: the DSW Bruggenloop Rotterdam 2019 (15 km), Nacht van Groningen 2020 (10, 16.1, and 21.1km), NN CPC Loop The Hague 2020 (10 and 21.1 km) and NN Marathon Rotterdam 2020 (10.55 and 42.195 km). Both studies applied the same inclusion criteria: 18 years or older, registration at least two months prior to the running event, sufficient mastery of the Dutch language, and access to the internet and email. Additionally, the SPRINT study excluded runners that previously participated in the INSPIRE trial. When participants met these criteria they received more information about the study, were asked to provide their digital informed consent, and were motivated to complete the baseline questionnaire. Only the first event registration was taken into account for runners that registered for multiple of the selected events.

Questionnaires and procedures

Each participant received four questionnaires: a baseline questionnaire and three follow-up questionnaires (Figure 1). In the INSPIRE trial, follow-up questionnaires were sent at: two weeks prior, one day after, and one month after the running event. In the SPRINT study, follow-up questionnaires were sent at: one month prior, one week prior, and one month after the running event. Participants reported whether they suffered a new RRI in the time between two questionnaires. The location of injury was inquired through a multiple choice question. Similarly, the type of injury and diagnosis were inquired, but included the option to provide an open-ended answer. The consequences of the RRI (e.g. painkiller use (yes/no, which?) and numerical rating scale (NRS) pain score (0-10) during rest and running) were asked at every follow-up moment. Supplementary table 1 contains the complete information and the included questions gathered through the baseline and follow-up questionnaires.

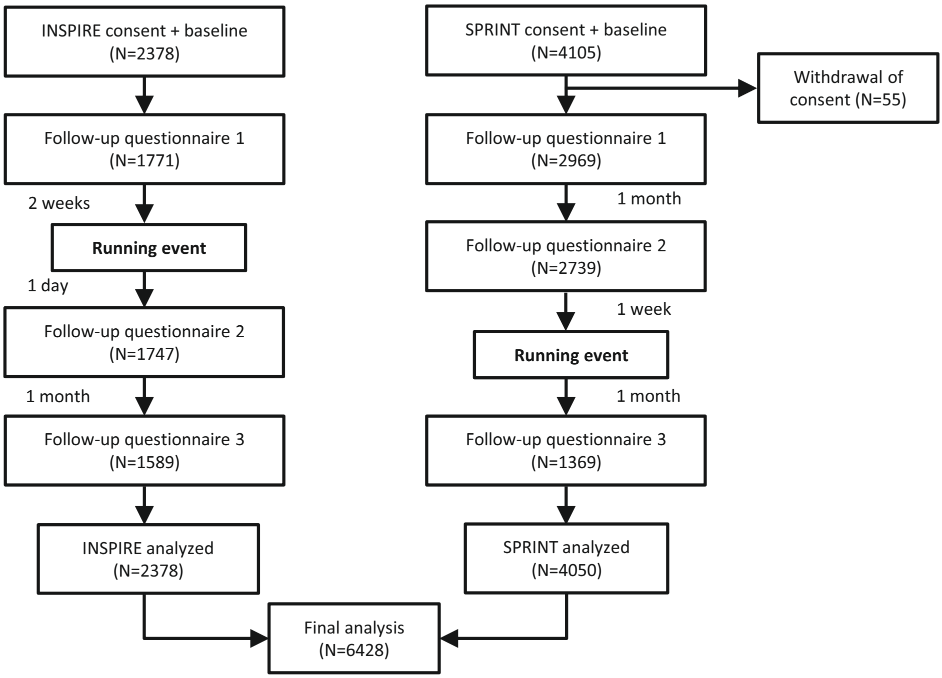

Figure 1. The combined flowchart of the INSPIRE trial and SPRINT study.

The answers to the open-ended questions on type of injury and diagnosis were categorized through a consensus meeting between the first author and a licensed Sports Physician at Erasmus MC. Multiple (new) injuries were allowed per follow-up questionnaire (e.g. a simultaneous injury to the hip and ventral thigh). Injuries were reported if they met a predefined definition. Both the INSPIRE trial and SPRINT study defined an RRI as a self-reported injury of the muscles, joints, tendons, and/or bones in the lower back or lower extremities (hip, groin, thigh, knee, leg, ankle, foot, and toes) that is caused by running (training or competition). The injury had to be severe enough to cause: 1) a reduction in running distance, speed, duration, or frequency for at least seven days or three consecutive scheduled training sessions or 2) the consultation of a physician or other health professional had to be necessary. The INSPIRE trial contained a third inclusion criteria for an RRI: medication was necessary to reduce symptoms as a result of the injury. We verified if participants who reported an RRI also had an RRI at the same location in the previous follow-up questionnaire. If not, the RRI was interpreted as a new RRI.

Statistical Analysis
Baseline characteristics were described using descriptive statistics stratified by sex with presentation of standard deviations (SDs). Normality was assumed because of the relatively large sample size and its effect on the Central Limit Theorem. This was verified using histograms. Significant differences between men and women in baseline characteristics were determined using independent-sample t-tests and chi-square tests for continuous and categorical variables, respectively. Injury proportions were defined as the total number of injuries per anatomical region or type of injury reported in the follow-up questionnaires, divided by the total number of injuries reported from all sites or types of injury. Location and type of injury of a new RRI during follow-up were organized in bar charts stratified by sex including 95% confidence intervals (CIs). Differences in consequences of a new injury between men and women were determined using independent-sample t-tests and chi-square tests for continuous and categorical variables, respectively.

Logistic regression analyzes were used to analyze the association between various factors and their effect on suffering a new RRI, using separate models per sex. First, univariate regression was used to assess the strength of the associations of each variable with a new RRI. Variables with $p \leq 0.2$ were selected to construct the final multivariable regression model. P-values <0.05 were regarded as statistically significant. Only the first reported new injury during follow-up was included when analyzing the consequences and potential factors associated with an increased risk of a new RRI. Analyzes were based on complete data. All analyzes were performed using SPSS version 28.0 (SPSS Inc, Chicago, IL).

RESULTS

The total study population includes 6428 participants (N=3696 men, N=2732 women). Average follow-up time was 5.0 months (range 2.1-10.0 months). At least one follow-up questionnaire was completed by 81.5% of participants with 64.4% completing all questionnaires. During follow-up, 2133 participants (33.2%) suffered one or more new injuries with a total of 3350 reported RRIs. This resulted in an injury rate of 32.7% (N=1698) for men and 33.9% (N=1199) for women, p=0.16. Baseline characteristics are presented in Table 1. Men, on average, ran 1.9 km more than women per week (25.7 km (SD 22.7) vs. 23.8 km (SD 19.7), $p<0.001$). In our dataset, more men ran the marathon (44.4% vs. 37.6%, $p<0.001$), while more women ran the half marathon (18.0% vs. 22.9%, $p<0.001$).

Table 1. Baseline characteristics of study population.

		Men (N=3696)	Women (N=2732)	Total (N=6428)
Demographics				
Age[a]		42.2 (12.2)	41.4 (11.8)	41.9 (12)*
Body mass index (BMI)[a]		23.6 (2.7)	23.2 (2.8)	23.4 (2.7)*
Smoking (yes)		137 (3.7)	100 (3.7)	237 (3.7)
Alcohol consumption (drinks/week)[a]		4.4 (5.0)	4.0 (4.7)	4.2 (4.9)*
Non-musculoskeletal comorbidities		495 (13.4)	373 (13.7)	868 (13.5)
Days per week active for > 30min (days/week)[a]		5.1 (1.8)	5.1 (1.9)	5.1 (1.9)
Training characteristics				
Running experience (years)[a]		9.5 (10.2)	8.0 (8.3)	8.9 (9.5)
Weekly training frequency (times/week)		2.6 (1.3)	2.5 (1.3)	2.5 (1.3)
Hours trained per week[a]		3.2 (3.1)	3.0 (2.7)	3.1 (3.0)*
Distance ran per week (km)[a]		25.7 (22.7)	23.8 (19.7)	24.9 (21.5)*
Running speed last month (min/km)[a]		5.6 (1.4)	5.8 (1.4)	5.7 (1.4)*
Type of training(%)				
Endurance running		70 (22.2)	69.6 (22.8)	69.9 (22.4)
Interval training		23.1 (18.7)	23.0 (19.3)	23.0 (19.0)
Specific exercises[b]		6.9 (10.1)	7.4 (10.1)	7.1 (10.1)
Member of running association/club (yes)		1061 (28.7)	864 (31.6)	1925 (29.9)
Use of training schedule (yes)		2357 (63.8)	1745 (63.9)	4102 (63.8)
Participation in other sports (yes)[c]		2297 (62.1)	1773 (64.9)	4070 (63.3)*
% of time running on	Paved	85.0 (18.3)	84.4 (19.0)	84.8 (18.6)
	Unpaved	15.0 (18.3)	15.6 (19.0)	15.2 (18.6)
% of time running on	Flat ground	83.0 (20.9)	83.2 (20.5)	83.1 (20.7)
	Incline	17.0 (20.9)	16.8 (20.5)	16.9 (20.7)
Running Event				
Distance registered for:				
5/7.5 km		118 (3.2)	19 (0.7)	137 (2.1)*
10/10.55 km		944 (25.5)	853 (31.2)	1797 (28.0)*
15/16.1 km		327 (8.8)	207 (7.6)	534 (8.3)
Half marathon		664 (18.0)	626 (22.9)	1290 (20.1)*
Marathon		1641 (44.4)	1027 (37.6)	2668 (41.5)*
Average running event participations per year[a]		4.5 (4.5)	4.6 (5.1)	4.5 (4.7)
Running-related injury (RRI)				
RRI in last 12 months		1863 (50.4)	1375 (50.3)	3238 (50.4)
RRI at baseline		745 (20.2)	558 (20.4)	1303 (20.3)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = Statistically significant difference between men and women ($p<0.05$); [b] Strengthening, stability, stretching, or running-specific exercises; [c] For at least 30 minutes per week.

Location and type of RRI

The proportions of RRI locations for all sustained injuries for both sexes during follow-up are presented in Figure 2. The most common injury location in both men (21.1%) and women (21.4%) was the knee. Similar injury proportions for all injury locations were found between men and women. Figure 3 shows the proportions for each type of injury for all sustained RRIs for both sexes during follow-up. By far the most common type of injury was muscle or tendon in both men (61.8%) and women (62.1%). We found similar proportion for men and women across all injury types with no significant sex differences.

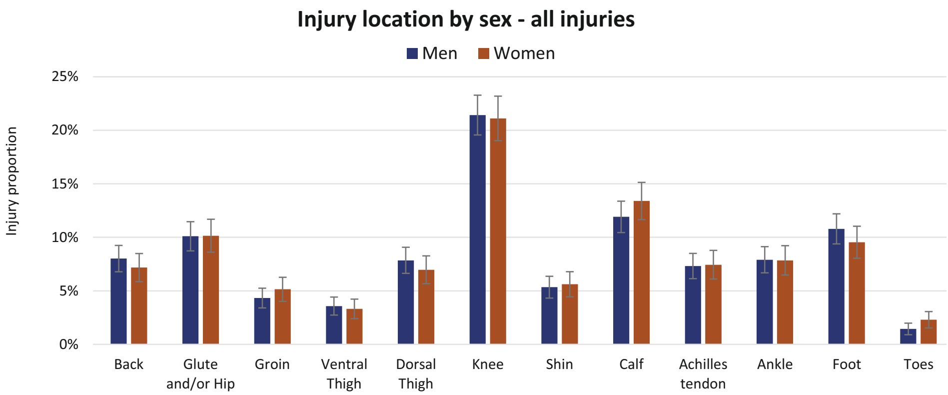

Figure 2. Proportion of injured runners per self-reported location of injury (men N=1872, women N=1478).

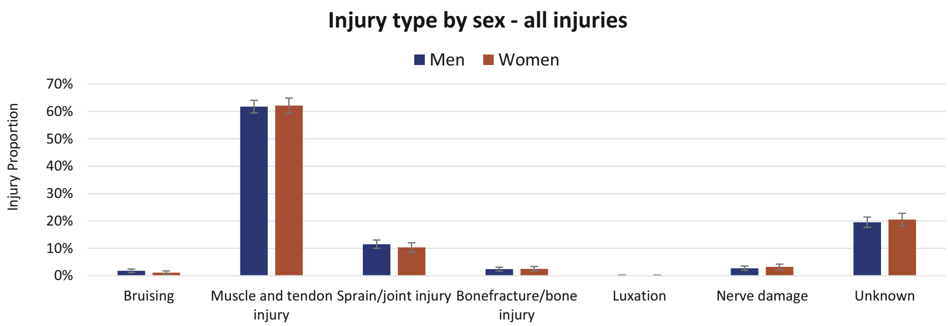

Figure 3. Proportion of injured runners per self-reported injury category (men N=1698, women N=1199).

Table 2. Consequences of first new RRI.

		Men (N=1207)	Women (N=926)	Total (N=2133)
Running-Related Injury				
Pain at rest (0-10)[a]		2.4 (2.3)	2.5 (2.4)	2.4 (2.4)
Pain while running (0-10)[a]		4.2 (2.9)	4.4 (2.8)	4.3 (2.9)*
Injury onset	Acute	571 (53.4)	438 (55.7)	1009 (54.3)
	Gradual	499 (46.6)	349 (44.3)	848 (45.7)
Reduction in day-to-day[b]				
Activities of daily living	Completely	7 (0.7)	8 (1.0)	15 (0.8)
	Partially	46 (4.3)	42 (5.3)	88 (4.7)
Household activities	Completely	21 (2.0)	17 (2.2)	38 (2.0)
	Partially	61 (5.7)	49 (6.2)	110 (5.9)
Work/study	Completely	22 (2.1)	15 (1.9)	37 (2.0)
	Partially	47 (4.4)	35 (4.4)	82 (4.4)
Transportation	Completely	23 (2.1)	19 (2.4)	42 (2.3)
	Partially	129 (12.1)	105 (13.3)	234 (12.6)
Leisure activities	Completely	138 (12.9)	113 (14.4)	251 (13.5)
	Partially	373 (34.9)	284 (36.1)	657 (35.4)
Absenteeism of work (days)		0.2 (1.4)	0.1 (1.0)	0.2 (1.2)
Treatment				
Self-Treated		100 (9.3)	72 (9.1)	172 (9.3)
Untreated		487 (45.5)	359 (45.6)	846 (45.6)
Treated by healthcare provider[c]		481 (45.1)	356 (45.2)	837 (45.2)
General practitioner		41 (8.5)	30 (8.4)	71 (8.5)
Sports physician/Orthopaedic surgeon		35 (7.3)	25 (7.0)	60 (7.2)
Physiotherapist		418 (86.5)	309 (86.8)	727 (86.7)
Other healthcare providers		93 (19.3)	78 (21.9)	171 (20.4)
Pain medication[d]		156 (12.9)	135 (14.6)	291 (13.6)*

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). Because these questions were not mandatory in the INSPIRE trial there was missing data for N=276 runners. * = statistically significant difference between intervention group and control group ($p \leq 0.05$); [b] Reduction in activities for the first week after the new injury; [c] Percentages represent the proportion of participants visiting that specialist compared to the total treated by a healthcare provider. A participant could visit multiple healthcare providers; [d] Contains NSAIDs, paracetamol and opioids.

Table 3. Univariate and multivariable logistic regression for first new injury.

Demographics	
Age	
Body mass index (BMI)	
Smoking (yes)	
Alcohol consumption (drinks/week)	
Non muscular comorbidities	
Days per week active for >30min (days/week)	
Training characteristics	
Running experience (years)	
Weekly training frequency (times/week)	
Hours trained per week	
Distance ran per week (km)	
Running speed last month (min/km)	
Type of training(%)	
Endurance running	
Interval training	
Specific exercises[a]	
Member of running association/club (yes)	
Use of training schedule (yes)	
Participation in other sports (yes)[b]	
% of time running on	Paved
	Unpaved
% of time running on	Flat ground
	Incline
Running Event	
Distance registered for:	
5/7.5 km	
10/10.55 km	
15/16.1 km	
Half marathon	
Marathon	
Average running event participations per year	
Running-related injuries (RRI)	
RRI in last 12 months	
RRI reported at baseline	

Variables in the univariate logistic regression with $p \leq 0.2$ were used to construct the multivariate regression model. * = Statistically significant difference ($p<0.05$);

	Men		Women	
	Univariate OR (95% CI)	**Multivariable OR (95% CI)**	**Univariate OR (95% CI)**	**Multivariable OR (95% CI)**
	1.00 (1.00-1.01)		1.01 (1.00-1.01)	1.01 (1.00-1.01)
	0.97 (0.95-1.00)*	0.99 (0.96-1.01)	1.02 (0.99-1.05)	
	0.94 (0.65-1.36)		0.61 (0.38-0.97)*	0.61 (0.38-0.99)*
	1.00 (0.99-1.02)		0.99 (0.98-1.01)	
	0.97 (0.79-1.19)		1.11 (0.88-1.39)	
	1.02 (0.98-1.05)		0.98 (0.94-1.02)	
	1.00 (1.00-1.00)		1.00 (1.00-1.00)	
	1.05 (1.00-1.11)*	1.02 (0.96-1.09)	1.06 (1.00-1.12)	1.00 (0.94-1.07)
	1.01 (0.99-1.04)	1.00 (0.97-1.03)	1.01 (0.99-1.04)	
	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	
	1.00 (1.00-1.00)		1.00 (1.00-1.00)	
	0.99 (0.99-1.00)*	1.00 (0.99-1.01)	1.00 (0.99-1.00)	
	1.01 (1.00-1.01)*	1.00 (1.00-1.01)	1.00 (1.00-1.00)	
	1.00 (1.00-1.01)		1.01 (1.00-1.02)*	1.01 (1.00-1.02)*
	1.16 (1.00-1.35)*	1.01 (0.85-1.20)	1.07 (0.90-1.27)	
	1.11 (0.97-1.29)	0.96 (0.82-1.13)	1.33 (1.12-1.57)*	1.17 (0.98-1.40)
	1.12 (0.97-1.29)	1.13 (0.98-1.31)	1.02 (0.87-1.21)	
	1.00 (0.99-1.00)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)*
	1.00 (1.00-1.01)	1.00 (0.99-1.00)	1.00 (0.99-1.00)	
	1.00 (0.99-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	
	1.00 (1.00-1.01)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	
	0.79 (0.53-1.20)		0.90 (0.34-2.37)	
	0.86 (0.74-1.01)	0.93 (0.77-1.12)	0.76 (0.64-0.91)*	0.94 (0.35-2.55)
	0.80 (0.63-1.03)	0.85 (0.65-1.11)	0.76 (0.56-1.04)	0.87 (0.31-2.44)
	1.25 (1.05-1.49)*	1.18 (0.97-1.43)	1.18 (0.98-1.42)	1.27 (0.47-3.46)
	1.07 (0.93-1.23)		1.22 (1.04-1.44)*	1.22 (0.45-3.29)
	1.00 (0.99-1.02)		1.00 (0.99-1.02)	
	2.00 (1.74-2.30)*	1.88 (1.60-2.21)*	1.91 (1.63-2.25)*	1.67 (1.38-2.02)*
	1.61 (1.36-1.90)*	1.10 (0.91-1.33)	1.72 (1.42-2.08)*	1.26 (1.01-1.57)*

[a] Strength, stability, stretch, or running-specific training; [b] For at least 30 minutes per week.

Consequences

Table 2 presents the consequences of an RRI for both sexes. Women used more painkillers (14.6% vs. 12.9%, p=0.01) and reported a higher pain score while running (4.4 (SD 2.8) vs. 4.2 (SD 2.9), p=0.04) compared to men. Other analyzed consequences did not differ between men and women. The most common injury consequence was a reduction in leisure activities in both men (34.9%) and women (36.1%).

Associations between baseline characteristics and injury risk

Table 3 presents the results of both the univariate and multivariate logistic regression analysis. An RRI at baseline was associated with an increased risk of suffering a new RRI in women (OR 1.26; 95% CI 1.01-1.57). The strongest association with a new RRI for both men (OR 1.88; 95% CI 1.60-2.21) and women (OR 1.67; 95% CI 1.38-2.02) was an RRI in the previous 12 months. Lastly, smoking was associated with a reduced risk of suffering a new RRI in women (OR 0.61; 95% CI 0.38-0.99).

DISCUSSION

The aim of this study was to identify sex differences in location, type, consequences, and factors associated with an increased risk of a new RRI amongst recreational runners. No relevant differences between men and women were observed. The location and type of injury were similar for men and women. Both men and women had knee injuries as most common injury location and the muscles and tendons were most commonly involved. Women experienced more pain while running when injured and used more painkillers compared to men, although differences were small. There was no sex difference in the consequences of an RRI on various aspects of daily life. We found some statistically significant sex differences in risk factors, but with clinically negligible effect sizes.

In contrast with available literature, no sex difference in injury location and type of injury were observed. Although several comparable studies exist[11,20-23], they differ in either size[20-23], age of study population[21,22], running experience[21,23], injury definition[20,22], event distance[11,20,21,23] or follow-up time[20,22]. In addition, some systematic reviews investigated whether there are sex differences in RRIs[2,5,10]. Pooling of original studies proved difficult, because the underlying studies differed in study population, follow-up duration and definition of outcomes. This limits making firm conclusions. These systematic reviews concluded that women suffer relatively more knee injuries[2] and more bone stress injuries[5,10] when compared to men. One explanation for this contradiction may relate to a difference in age in study populations as conclusions were based on a relatively younger population existing of mostly high school/university athletes, while the average age of our running population is 41.9 years. Since our study is not affected by the heterogeneity among different study populations included in the systematic reviews described above, we conclude that sex differences in injury location, especially for the older runner, are likely smaller than previously assumed.

Analgesic usage in sports is widespread[17,24] with usage reported up to 64% of runners[24], though numbers strongly vary by study[15,17]. In the general population, women tend to use more analgesics compared to men[25]. Previous studies in athletes found that women are more likely to self-medicate than their male counterparts[15,16]. Our study shows similar painkiller usage for RRIs for women (14.6%) as Locquet et al. (14.0%)[15] and lower usage for men (12.9%) compared to women. Part of this difference in painkiller usage could potentially be explained by the higher pain scores while running observed in women (4.4 vs. 4.2 on NRS), although this difference is very small. The observed sex difference in painkiller usage supports previous research that women are more likely to self-medicate after an injury, but the effect size observed is clinically negligible[15,16].

The only factor associated with an increased risk of a new RRI in both men and women in this study was a history of an RRI. This finding is in line with existing literature in runners showing that a previous RRI is the strongest risk factor for a new injury in recreational runners[14, 26-28]. Various other potential factors associated with an increased risk of a new RRI have been identified including age, concrete surface running, marathon participation, event distance, and weekly running distance[3,5,13,14]. However, in this large prospective cohort population we found no clinically relevant associations between the studied factors and injury risk. Earlier research has been performed in smaller study populations, making an incidental finding more likely. Regardless of sex, the only factor strongly associated with an increased risk of a new RRI is a previous RRI.

Strengths and limitations

The main strength of our study is its sample size. To our knowledge, this is the largest prospective cohort study on sex differences in RRIs. Furthermore, the loss to follow-up rate is within acceptable limits and a wide variety of outcomes have been studied. The largest limitation of this study is that parts of the questionnaires are not validated. The data are self-reported, which may have increased the number of reported RRIs and reduced its accuracy compared to relying on an diagnosis by a specialist. Moreover, the participants may have modified their behavior in response to knowing they are being observed (Hawthorne effect). This increased awareness may have caused an overestimation of the injury incidence when compared to an unstudied setting[29].

CONCLUSION

We observed no relevant sex differences between men and women in location, type, consequences, and factors associated with an increased risk of a new RRI among recreational runners. Our findings suggest that there are fewer sex differences than previously assumed in the literature. As a result, the findings of this study do not support accounting for sex-specific factors in the development of future personalized RRI prevention programs.

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SUPPLEMENTARY FILES

Supplementary table 1. Items of the questionnaires.

Questionnaire	Sections	Items
Baseline questionnaire	Demographics	Sex
		Date of birth
		Height (cm)
		Weight (kg)
		Alcohol consumption (yes/no, consumptions per week?)
		Non-running related health problems (yes/no, which?)
		Smoking (yes/no)
		Days per week active for > 30 minutes[a]
	Training	Running experience (years)
		Weekly training frequency (times a week)[b]
		Weekly training hours (hours per week)[b]
		Weekly training distance (km per week)[b]
		Running speed (minutes per km)[b]
		Type of training (endurance, interval, specific exercises (%))
		Membership of a running club (yes/no)
		Use of training schedules (yes/no)
		Participation in another sport than running (yes/no, time per week?)
		Running surface (paved vs. unpaved (%) and flat vs. incline (%))
	Running events	Distance of the registered running event (10-10.55 km/ 15-16.1 km/half marathon/marathon)
		Participation in a previous running event (yes/no)
		Average participations per year
	RRI[c]	Previous RRI in the 12 months before baseline (yes/no)
		Reported RRI at baseline (yes/no)
Follow-up questionnaires	New RRI	New RRI since filling in previous questionnaire (yes/no)
		Location (lower back/buttock/hip/groin/ventral thigh/ dorsal thigh/knee/shin/calf/Achilles tendon/ankle/foot/toe)
		Type (bruising/muscle or tendon injury/sprain or joint injury/bone stress injury or bone fracture/luxation/nerve damage/unknown/open answer)
		Diagnosis (if known, open question)
		Acute vs. gradual injury (%)

Supplementary table 1. Continued

Questionnaire	Sections	Items
		Reduction in activities of daily life (yes/partially/no, categories: activities of daily life, household activities, work/study, transportation, leisure activities)
		Absenteeism from work (%)
		Pain severity (0-10 NRS scale[d]), at rest and while running
		Use of painkillers (paracetamol and NSAIDs) (yes/no, which?)
		Treatment (yes/no/self-treated, and if yes, general practitioner/medical specialist/physiotherapist/others)

[a] Using the SQUASH questionnaire; [b] Asked for the averages over the last month; [c] Running-related injury (definition in methods section); [d] 11-point Numeric Ration Scale (NRS) ranging from 0 (no pain) to 10 (worst pain imaginable).

Chapter 4

Running behavior and symptoms of respiratory tract infection during the COVID-19 pandemic

A large prospective Dutch cohort study

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ABSTRACT

Objective: To explore changes in running behavior due to the Coronavirus Disease 2019 (COVID-19) pandemic, assess presence of symptoms suggestive for COVID-19, and identify whether there is an association between running behavior and COVID-19.

Methods: For this study we used a cohort of runners participating in an ongoing randomized-controlled trial on running injury prevention among recreational runners. At baseline, demographic and training variables were collected. Seven weeks after starting the lockdown, information on running behavior (interval training, training with partner, and physical distancing during training) and running habits (training frequency, duration, distance, and speed) were obtained. Furthermore, healthcare utilization and symptoms suggestive for COVID-19 were assessed. To determine the association between running and symptoms suggestive for COVID-19, univariate and multivariate logistic regression analyzes were performed.

Results: Of the 2586 included participants, 2427 (93.9%) participants continued running during lockdown with no significant changes in mean weekly training variables. A total of 253 participants (9.8%) experienced symptoms suggestive for COVID-19 and 10 participants tested positive for COVID-19. Two participants were admitted to hospital due to COVID-19 with both one day of admission. Running behavior and running habits were not associated with the onset of symptoms suggestive for COVID-19.

Conclusion: The large majority of runners in the Netherlands did not change their running habits during lockdown. No association between running behavior or running habits and onset of symptoms suggestive for COVID-19 was identified. This implicates that running outdoor during lockdown does not negatively affect health of runners.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) has been reported world-wide in more than a million cases and resulted in more than 300,000 deaths since May 2020[1]. This new pandemic led to governments implementing lockdown with the aim to prevent healthcare services beyond its limits. In several countries athletes were strictly forbidden to perform outdoor physical activities. Overall this might have resulted in people undertaking less physical activities than normal for prolonged periods[2]. The Dutch government decided to implement a 'targeted lockdown' (March 9, 2020) with advices on meticulous hygiene measures and physical distancing and restrictions in traveling and group meetings. The Dutch authorities advised to stay home as much as possible, but performing outdoor physical activities was not restricted.

Running is a popular sport all over the world. In the Netherlands, approximately 12.5% of the Dutch population perform regular running activities[3]. These regular physical activities offer numerous health benefits, of which an improved immune function is of potential importance during this COVID-19 pandemic[4]. The immune system provides a potent and multi-layered defense against virus attacks. Depression of this immune system can occur during recovery from intense exercise[5], so high-intensity interval training might result in invading viruses.

In the current phase of the COVID-19 pandemic, many countries are liberalizing their lockdown measures[6], so individuals will have the ability to perform their outdoor sports again. A recent aerodynamics simulation experiment–however–demonstrated that there is substantial droplet exposure during running which would need a physical distance of 10 meter[7]. These results questioned whether physically active people can safely participate in outdoor sports[8]. Another recent study highlighted that physically active individuals are more susceptible to wellbeing issues during a strict lockdown in China[9]. This strict lockdown has been used in multiple countries all over the world and might have had similar impact on the physically active population. It implicates that runners will probably have a strong desire to perform outdoor running activities again.

It is unknown whether Dutch runners changed their running behavior due to the pandemic and there are no data on the relationship between outdoor physical activities and symptoms of community-acquired respiratory tract infections (CARTI) or COVID-19 specifically. We therefore send out an additional questionnaire in our currently running large prospective study in runners with the aim to (1) explore changes in running habits due to the COVID-19 period, (2) assess presence of symptoms suggestive for COVID-19, and (3) identify whether there is an association between outdoor running activities and symptoms suggestive for COVID-19.

METHODS

This study is part of the Shaping up Prevention for Running Injuries in the Netherlands using Ten steps (SPRINT) study. The SPRINT study is an ongoing randomized-controlled trial (RCT) among recreational runners with a minimum follow-up of three months, to investigate the effect of an online injury prevention program on the number of running-related injuries (Dutch Trial Registry; NL7694). Follow-up questionnaires were sent one month before, one week before and one month after the registered running event (not used for current study purpose). During follow-up, the Dutch government implemented a targeted lockdown due to COVID-19. Seven weeks after the start of the targeted lockdown, all participants received an additional COVID-19 questionnaire. A flowchart of the design is presented in Figure 1. The SPRINT study was funded by the Netherlands Organization for Health Research and Development (ZonMW, grant number 50-53600-98-104). Medical ethics approvals for the SPRINT study and the additional COVID-19 questionnaire (using an amendment) were obtained by the Medical Ethical Committee of the Erasmus MC University Medical Center Rotterdam, the Netherlands (MEC-2019-0136).

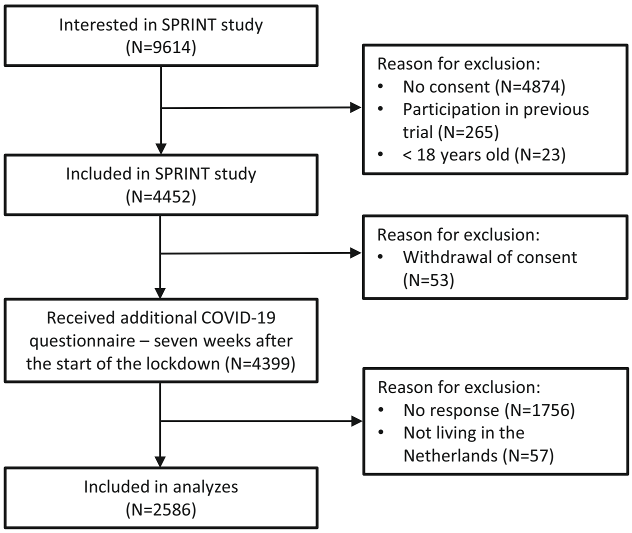

Figure 1. Flowchart of the participants included in the SPRINT study.

Runners who registered for the running events DSW Bruggenloop Rotterdam 2019, Nacht van Groningen 2020, NN CPC Loop The Hague 2020, and NN Marathon Rotterdam 2020 (distances ranging from 10.0 to 42.2 km) were invited to participate in the SPRINT study. Interested runners, aged 18 years or older, were asked to provide electronic informed consent and complete the baseline questionnaire. Exclusion criteria were participation in our previous trial on RRI prevention[10], no knowledge of the Dutch language and no access to internet and email.

In the baseline questionnaire information on demographics (sex, age, weight, and height) were assessed. Weight and height were used to calculate the body mass index (BMI). Furthermore, participants were asked if they suffered from non-musculoskeletal comorbidities, and if yes which comorbidity. Only the comorbidities hypertension, cardiovascular disease and diabetes were included in this study, since these were reported as the most common underlying conditions in hospitalized patients with COVID-19[11,12]. Training-related information were administered with questions on running frequency, duration, distance, and speed (average per week over the last three months). The additional COVID-19 questionnaire obtained information on five items:

- *Running habits:* running habits during lockdown were assessed by asking whether participants continued running outdoor (yes/no), and if yes their mean weekly training frequency, hours, distance, and running speed were obtained (average per week over the last seven weeks).
- *Symptoms and healthcare utilization:* participants were asked whether they experienced symptoms of CARTI (yes/no) in the preceding seven weeks, including running nose, sore throat, fever, dry or productive cough, dyspnea during rest or exertion, myalgia, headache, chest pain, diarrhea, nausea or vomiting, eye infection, dyssomnia, and fatigue. If yes, participants were questioned whether they consulted a general practitioner (GP) due to symptoms (yes/no), if they were tested for COVID-19 (yes/no), the result of this test (positive/negative), and if they were hospitalized due to COVID-19 (yes/no). If a participant was hospitalized, information on the amount of days and admission to intensive care (yes/no) was obtained.
- *Running behavior in relation to prevention of CARTI and COVID-19:* running behavior during lockdown was assessed by asking about type of training (endurance/interval/specific exercises), training with a partner who was not family related (yes/no), and maintaining a physical distance of 1.5 meter during running (yes/no). Interval training was dichotomized in more or less than 50% of the training.
- *Preventive measures for CARTI and COVID-19:* participants were asked if they followed measures to prevent transmission of COVID-19. Measures questioned were meticulous hand hygiene, avoiding touching face, eyes and mouth, using face masks, physical distancing, no unnecessary travel, and avoiding group meetings.
- *General risk factors for CARTI and COVID-19:* to obtain information about the risk of getting symptoms of CARTI or COVID-19 specifically, participants were asked if they had contact with possible infected individuals (yes/no), provided care to COVID19 patients (yes/no) and if they experienced psychosocial stress and sleep disruption (five points scale form 5 (strongly agree) to 1 (strongly disagree)). For the current study purpose, experience of psychosocial stress and sleep disruption were categorized in yes ((strongly) agree) and no (sometimes and (strongly) disagree). Last, participants

were asked in which province of the Netherlands they lived. Based on national data, living in the provinces Noord-Brabant and Limburg were risk factors for COVID-19 (Supplementary figure 1). Therefore, living in the province Noord-Brabant or Limburg was included and categorized in yes and no.

The primary outcome measures of this study were the percentage of runners continuing running training outdoor and the mean weekly training frequency, hours, distance and running speed during lockdown. Secondary outcome was the experience of symptoms suggestive for a COVID-19 infection. The most commonly reported COVID-19 symptoms are fever and cough, followed by dyspnea, sputum production and fatigue[13-15]. Experience of symptoms suggestive for COVID-19 was defined as reported fever or cough with at least one other commonly reported symptom (fever, cough, sputum production, dyspnea or fatigue). To be more inclusive, we selected an additional outcome measure defined as runners who experienced at least two symptoms of CARTI.

Descriptive statistics were used to describe characteristics obtained at baseline and follow-up, expressed in frequency or mean and standard deviations (SDs). Participants who completed the additional COVID-19 questionnaire and participants who did not complete this questionnaire were compared using independent sample t-tests (continuous data), Mann–Whitney U tests (continuous data) and chi–square tests (dichotomous data). To determine changes in running habits, differences in mean weekly training frequency, duration, hours and running speed between baseline and lockdown were evaluated with Wilcoxon signed rank tests. Participants who experienced symptoms suggestive for COVID-19 and with ≥ 2 CARTI symptoms were compared with participants without these symptoms using independent sample t-tests (continuous data) and chi–square tests (dichotomous data). Logistic regression analysis was used to examine the association between running behavior and running habits and symptoms suggestive for COVID-19. Four separate univariate and multivariate models (enter-method) were performed for each category: (1) demographic characteristics; (2) measures to prevent COVID-19; (3) general risk factors for COVID-19; (4) running habits and running behavior. Variables with a p-value <0.20 in the multivariate logistic regression analyzes in these separate models were entered together in the final multivariate model. Results of the logistic regression analyzes are presented as odds ratios (ORs) with 95% confidence intervals (CIs). P-values <0.05 were regarded as statistically significant. All analyzes were performed using SPSS version 25.0 (SPSS Inc, Chicago, Illinois).

RESULTS

In total, 4452 participants were included in SPRINT study (Figure 1). During follow-up, 53 participants withdrew their consent. A total of 4399 participants were sent the additional COVID-19 questionnaire after a mean of 5.5 months (range 2.5–8.5). 2643 (60.1%) participants responded to the additional COVID-19 questionnaire. Of the responders, 57 (2.2%) participants reported not living in the Netherlands. As the lockdown measures varied between countries, these participants were excluded. A total of 2586 participants were included for further analyzes. Compared to the participants who did not respond, responders were on average significantly older (44.4 vs. 39.1, $p<0.001$) and trained more frequently (2.6 vs. 2.5 times a week, $p=0.01$) (Supplementary table 1).

A total of 2427 (93.9%) participants continued running training outdoor during the lockdown (Table 1). The mean (SD) weekly running frequency (2.6 (1.2) to 2.6 (1.3) times), duration (3.1 (2.8) to 3.0 (2.7) hours), distance (26.8 (21.6) to 25.8 (18.0) km) and speed (5.8 (0.9) min/km at both time points) did not change significantly between baseline and lockdown period (p-values 0.10, 0.12, 0.42, and 0.13, respectively).

Of the included participants, 253 (9.8%) participants experienced symptoms suggestive for COVID-19 during lockdown (Table 1). Participants who experienced these symptoms, were significantly younger (41.2 vs. 44.7, $p<0.001$) and less often male (51.8% vs. 63.1%, $p<0.001$) with an underlying condition (7.4% vs. 3.7%, $p<0.01$). A total of 894 participants (34.6%) reported the experience of ≥ 2 CARTI symptoms during lockdown (Supplementary table 2). Of the participants who experienced ≥ 2 CARTI symptoms, 83 participants (9.3%) contacted their GP due to their symptoms, of which 37 (4.1%) participants were tested for COVID-19 with a total of 10 positive tests (1.1%). Two participants (0.2%) were admitted to hospital due to COVID-19 with both one day of admission. No participants reported having been treated on the intensive care unit.

Frequently adapted measures to prevent symptoms of COVID-19 were meticulous hand hygiene (N=2446, 94.6%), physical distancing (N=2495, 96.5%), avoiding unnecessary travel (N=2221, 85.9%) and avoidance of group meetings (N=2307, 89.2%) (Table 1). Of the participants who continued running during lockdown, 2361 (97.3%) participants followed physical distancing during training and 581 (23.9%) participants trained with a non-family partner. Furthermore, 100 (4.1%) participants performed interval training of more than 50% of their trainings.

Table 1. Characteristics of participants who experienced symptoms suggestive for COVID-19[a].

	COVID-19 symptoms		
	Total (N=2586)	**Yes (N=253)**	**No (N=2333)**
Baseline			
Demographic characteristics			
Sex (male)	1604 (62.0)	131 (51.8)	1473 (63.1)*
Age (years)[b]	44.4 (12.2)	41.2 (12.6)	44.7 (12.1)*
BMI (kg/m^2)[b,c]	23.2 (2.6)	23.3 (2.7)	23.2 (2.6)
Underlying condition[d]	94 (4.0)	16 (7.4)	78 (3.7)*
Living in province of South Holland	1469 (56.8)	145 (57.3)	1324 (56.8)
During lockdown period			
Running behavior			
Continuing running training outdoor	2427 (93.9)	229 (90.5)	2198 (94.2)*
Physical distancing during training[e]	2361 (97.3)	223 (97.4)	2138 (97.3)
Interval training (> 50%)[e]	100 (4.1)	5 (2.2)	95 (4.3)
Training with partner[e]	581 (23.9)	45 (19.7)	536 (24.4)
Measures to prevent COVID-19			
Meticulous hand hygiene	2446 (94.6)	241 (95.3)	2205 (94.5)
Avoiding touching face, eyes and mouth	1095 (42.3)	112 (44.3)	983 (42.1)
Using face masks	101 (3.9)	10 (4.0)	91 (3.9)
Physical distancing	2495 (96.5)	245 (96.8)	2250 (96.4)
No unnecessary travel	2221 (85.9)	230 (90.9)	1991 (85.3)*
Avoiding group meetings	2307 (89.2)	235 (92.9)	2072 (88.8)*
General risk factors for COVID-19			
Contact with possible infected individuals	466 (18.0)	99 (39.1)	367 (15.7)*
Providing care to COVID-19 patients	137 (5.3)	22 (8.7)	115 (4.9)*
Psychosocial stress	319 (12.3)	44 (17.4)	275 (11.8)*
Sleep disturbance	201 (7.8)	31 (12.3)	170 (7.3)*
Living in a province with high COVID-19 infection rate	291 (11.3)	32 (12.6)	259 (11.1)

Categorical data are presented as N (%) and continuous data ([b]) as means (SD). * = statistically significant difference between participants ($p<0.05$); [a] Fever or cough with at least one other commonly reported symptom (fever, cough, sputum production, dyspnea, or fatigue); [c] Body Mass Index; [d] Hypertension, cardiovascular disease, and/or diabetes; [e] Based on participants who continued running training during lockdown (total of 2427 participants).

Table 2 presents the four separate defined regression models for symptoms suggestive for COVID-19 and Table 3 presents the final multivariate model. In the final model, male sex (OR 0.71; 95% CI 0.53-0.97) and lower age (OR 0.98; 95% CI 0.97-0.99) were negatively associated with symptoms suggestive for COVID-19 (Table 3). No unnecessary travel (OR 1.6; 95% CI 1.04-2.69) and contact with possible infected individuals (OR 3.29; 95% CI 2.45-4.42) were positively associated with symptoms suggestive for COVID-19. There was no association with running habits or running behavior. Association between included characteristics and CARTI symptoms are presented in Supplementary tables 3–5. With this more inclusive approach, lower age (OR 0.99; 95% CI 0.98-0.99) was negatively associated with at least two symptoms of CARTI. Contact with possible infected individuals (OR 2.19; 95% CI 1.78-2.70), psychosocial stress (OR 2.36; 95% CI 1.83-3.04) and sleep disturbance (OR 1.65; 95% CI 1.21-2.26) were positively associated with at least two symptoms of CARTI. There was also no association with running behavior or running habits.

Table 2. Univariate and multivariate logistic regression analyzes of characteristics associated with symptoms suggestive for COVID-19[a].

Model 1 - Demographic characteristics
Sex (male)
Age (years)
BMI (kg/m^2)[c]
Model 2 - Measures to prevent COVID-19
Meticulous hand hygiene
Avoiding touching face, eyes and mouth
Using face masks
Physical distancing
No unnecessary travel
Avoiding group meetings
Model 3 - General risk factors for COVID-19
Contact with possible infected individuals
Providing care to COVID-19 patients
Psychosocial stress
Sleep disturbance
Living in a province with high COVID-19 infection rate
Model 4 – Running habits and running behavior
Weekly training hours
Interval training (>50%)
Training with partner
Physical distancing during training

* = statistically significant association ($p<0.05$); [a] Fever or cough with one other commonly reported symptom (fever, cough, sputum production, dyspnea, or fatigue); [b] $p<0.2$ presented in bold; [c] Body Mass Index.

Univariate analysis		Multivariate analysis	
OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value[b]**
0.63 (0.48-0.81)*	<0.001	0.67 (0.51-0.89)*	**0.01**
0.98 (0.97-0.99)*	<0.001	0.98 (0.97-0.99)*	**<0.001**
1.01 (0.96-1.06)	0.66	1.05 (1.00-1.10)	**0.07**
1.17 (0.64-2.14)	0.62	1.00 (0.53-1.86)	0.99
1.09 (0.84-1.42)	0.51	1.04 (0.79-1.36)	0.79
1.01 (0.52-1.97)	0.97	1.01 (0.51-1.97)	0.99
1.13 (0.54-2.36)	0.75	0.93 (0.44-1.98)	0.85
1.72 (1.10-2.68)*	0.02	1.56 (0.97-2.49)	**0.06**
1.65 (1.00-2.70)*	0.05	1.40 (0.82-2.37)	0.22
3.44 (2.61-4.54)*	<0.001	3.34 (2.53-4.42)*	**<0.001**
1.84 (1.14-2.96)*	0.01	1.39 (0.85-2.28)	**0.19**
1.58 (1.11-2.23)*	0.01	1.38 (0.95-2.01)	**0.10**
1.78 (1.18-2.67)*	0.01	1.56 (1.01-2.43)*	**0.05**
1.16 (0.78-1.72)	0.46	1.06 (0.70-1.58)	0.80
0.92 (0.86-0.99)*	0.02	0.95 (0.88-1.02)	**0.13**
0.49 (0.20-1.23)	0.13	0.50 (0.20-1.25)	**0.14**
0.76 (0.54-1.07)	0.11	0.78 (0.56-1.11)	**0.17**
1.04 (0.45-2.44)	0.92	0.98 (0.42-2.32)	0.97

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Table 3. Final multivariate logistic regression model for characteristics associated with symptoms suggestive for COVID-19[a].

	Multivariate analysis	
	OR (95% CI)	**p-value**
Sex (male)	0.71 (0.53-0.97)*	0.03
Age (years)	0.98 (0.97-0.99)*	<0.01
BMI (kg/m^2)[b]	1.03 (0.98-1.09)	0.25
No unnecessary travel	1.67 (1.04-2.69)*	0.03
Contact with possible infected individuals	3.29 (2.45-4.42)*	<0.001
Providing care to COVID-19 patients	1.25 (0.73-2.12)	0.41
Psychosocial stress	1.09 (0.72-1.64)	0.69
Sleep disturbance	1.51 (0.93-2.44)	0.09
Weekly training hours	0.98 (0.92-1.05)	0.58
Interval training (>50%)	0.51 (0.20-1.29)	0.15
Training with partner	0.74 (0.52-1.05)	0.10

* = statistically significant association (p<0.05); [a] Fever or cough with one other commonly reported symptom (fever, cough, sputum production, dyspnea, or fatigue); [b] Body Mass Index.

DISCUSSION

In this large prospective cohort study, we found that the large majority of runners maintained their normal running habits during the lockdown period due to COVID-19. Mean weekly running frequency, duration, distance and speed were all similar to values before the lockdown. Only a small number of runners were tested positive for COVID-19 (N=10) or were shortly admitted to hospital due to COVID-19 (N=2). A higher proportion of the included runners (N=253, 9.8%) experienced symptoms suggestive for COVID-19. We did not identify an association between running behavior or running habits and onset of symptoms suggestive for COVID-19. This implicates that only a small minority of the runners experienced COVID-19 related problems and that running behavior does not seem to be an important factor associated with COVID-19.

These findings are very relevant because many countries are currently liberalizing their lockdown measures. In the Netherlands, people were able to perform outdoor sports activities during the lockdown. Our findings show that the large majority of runners did not change their running habits. It is hard for governments to establish which sport activities are safe to restart. A recent aerodynamics simulation study implicated that running outdoor is potentially unsafe due to substantial droplet exposure during running[8]. In our large cohort study, we did not identify an increased risk for COVID-19 infection using multiple outcome parameters[7]. A small portion of this relatively healthy population did have a positive COVID-19 test (0.4%) or a short (one day) hospital admission (0.08%). This is comparable to the Dutch national COVID-19 infection (0.3%) and hospital admission (0.08%) data (Supplementary figure 2). Another frequently mentioned drawback of continuing intensive running with interval training, is the temporary decreased immune function and thereby increased susceptibility for infection[4]. We did–however–not find an association between runners continuing interval training and onset of symptoms suggestive for COVID-19. This finding is in line with recent scientific views; the risk for infectious disease in athletes seems to be multifactorial and not only associated with training intensity[16].

Restraining individuals from participation in outdoor running activities does not only further decrease their fitness level and health status, but also their mental status which is very important during a lockdown period[9]. The clinical and societal relevance of our findings will even further increase if we will encounter a second wave of the COVID-19 pandemic. During the liberalization of the preventive measures, countries must thoroughly revisit the scientific evidence of their measures before the second wave may come[17].

Strengths and Limitations

The major strength is that this is the first prospective study to evaluate associations between running activity and COVID-19 related symptoms. The study topic is actual and it will probably remain important in the near future. It is one of the largest cohort studies performed in an athletic population, thereby making the findings more robust. The fact that we have prospectively collected data ensures that we can adequately answer our primary research question regarding change in running habits during the lockdown period.

This study has a number of limitations. The response rate (60.1%) was not optimal. However, there were no relevant differences in characteristics between responders and non-responders. It may be that non-responders did not respond to the questionnaire because they were admitted to hospital, died due to COVID-19 within this period or experienced no problems related to COVID-19 at all. However, it is more likely that a larger number of responders experienced COVID-19 related problems. A potential limitation of the study was that the study parameters were collected using a questionnaire. Due to this study design, it is impossible to test whether the answers provided are the true answers (e.g. did the participants actually implement the precautions for COVID-19 or were they prone to provide a socially desirable answer?). Another limitation is the choice of outcome measures for COVID-19. Due to the limited test capacity for COVID-19 in the Netherlands, this outcome measure has limitations. For that reason, we used symptoms suggestive for COVID-19 and CARTI as outcome measures. As we did not detect an association between running behavior and COVID symptoms using both these strict and inclusive symptom based outcome measures, we are more confident that this finding is correct. The absence of associations between running parameters and COVID-19 are potentially due to the strict adherence to the other preventive measures by the Dutch population. Results may differ when more people are outside. Furthermore, this study only assessed health parameters of the runners but not of potential subjects they might encounter during running (e.g. walkers). The runners might be protected by a well-functioning immune system and potentially infect walkers during their run.

Future research could be focused on the safety of running in small groups. If these runners respect the preventive measures for transmission of CARTI, it is potentially safe to start up running habits at the club.

CONCLUSION

The COVID-19 pandemic leads to a lot of changes worldwide, but the large majority of Dutch runners were able to maintain their normal running habits during the targeted lockdown period. Mean weekly running frequency, duration, distance, and speed were all similar to values before the lockdown. Only a small number of runners were tested positive for COVID-19 or were shortly admitted to hospital due to COVID-19. 9.8% of the included runners experienced symptoms suggestive for COVID-19. We did not identify an association between running habits or running behavior and onset of symptoms suggestive for COVID-19. This implicates that running outdoor during lockdown due to the COVID-19 pandemic may not negatively affect the health of Dutch runners.

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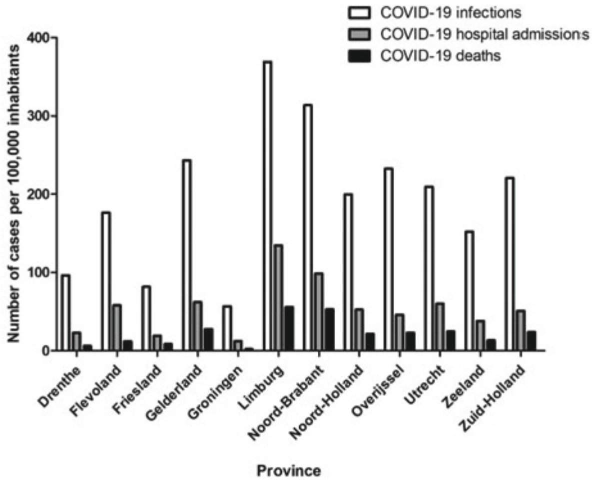
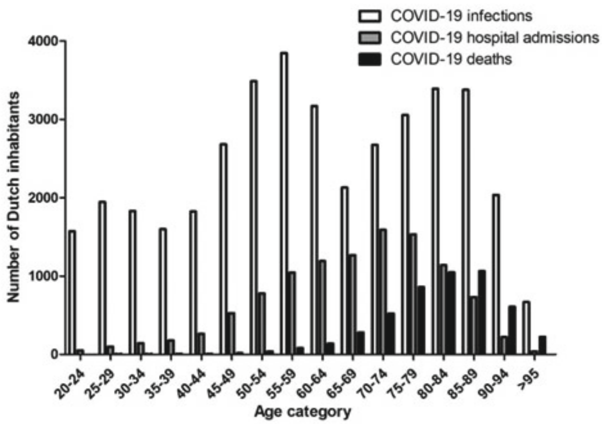
SUPPLEMENTARY FILES



Supplementary figure 1. Number of cases of COVID-19 infections, COVID-19 hospital admissions, and COVID-19 deaths in the Dutch population on 1st May 2020 per province (Source: BD Dataplan).



Supplementary figure 2. Distribution of COVID-19 related outcomes in the Dutch adult population on 1st May 2020 per age category (Source: BD Dataplan). A total of 39,277 adults were infected with COVID-19, 10,776 were admitted to hospital, and 4,891 were registered as death due to COVID-19. The total Dutch adult population is 13,490,325 inhabitants (Source: Statistics Netherlands). The proportion of Dutch adults with registered COVID-19 infections is 0.3%, with registered COVID-19 hospital admissions 0.08%, and registered COVID-deaths is 0.04%.

Supplementary table 1. Baseline characteristics of responders and non-responders.

	Responded to COVID-19 questionnaire		
	Total (N=4399)	**Yes (N=2586)**	**No (N=1813)**
Demographic characteristics			
Sex (male)	2765 (62.9)	1604 (62.0)	1161 (64.0)
Age (years)[a]	42.2 (12.1)	44.4 (12.2)	39.1 (11.3)*
BMI (kg/m^2)[a,b]	23.3 (2.6)	23.2 (2.6)	23.4 (2.7)
Underlying condition[c]	146 (3.6)	94 (4.0)	52 (3.1)
Training characteristics			
Weekly training frequency[a]	2.6 (1.3)	2.6 (1.2)	2.5 (1.3)*
Weekly training hours[a]	3.0 (2.7)	3.1 (2.8)	3.0 (2.6)*
Weekly training distance (km)[a]	26.2 (22.3)	26.8 (21.6)	25.4 (23.1)*
Running speed (min/km)[a]	5.8 (0.9)	5.8 (0.9)	5.7 (0.9)*
Interval training (>50%)	226 (5.1)	154 (6.0)	72 (4.0)*

Categorical data are presented as N (%) and continuous data ([a]) as means (SD).
* = statistically significant difference between responders and non-responders (p<0.05); [b] Body Mass Index; [c] Hypertension, cardiovascular disease, and/or diabetes.

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Supplementary table 2. Reported symptoms of CARTI[a] and COVID-19[b] during the lockdown period.

	Symptoms of CARTI (N=894)
Fever	109 (12.2)
Cough	281 (31.4)
Sputum production	172 (19.2)
Dyspnea	217 (24.3)
Fatigue	480 (53.7)
Running nose	549 (61.4)
Sore throat	394 (44.1)
Myalgia	312 (34.9)
Headache	452 (50.6)
Chest pain	93 (10.4)
Diarrhea	144 (16.1)
Nausea and/or vomiting	72 (8.1)
Eye infection	27 (3.0)
Dyssomnia	51 (5.7)
	Symptoms suggestive for COVID-19 (N=253)
Fever	93 (36.8)
Cough	209 (82.6)
Sputum production	77 (30.4)
Dyspnea	112 (44.3)
Fatigue	188 (74.3)

Data are presented as N (%). [a] Community-acquired respiratory tract infections; [b] Fever or cough with one other commonly reported symptom (fever, cough, sputum production, dyspnea, or fatigue).

Supplementary table 3. Characteristics of participants who experienced at least two symptoms of CARTI[a].

	≥ 2 symptoms of CARTI		
	Total (N=2586)	**Yes (N=894)**	**No (N=1692)**
Baseline			
Demographic characteristics			
Sex (male)	1604 (62.0)	512 (57.3)	1092 (64.5)*
Age (years)[b]	44.4 (12.2)	42.4 (12.0)	45.4 (12.2)*
BMI (kg/m^2)[b,c]	23.2 (2.6)	23.3 (2.7)	23.2 (2.5)
Underlying condition[d]	94 (4.0)	43 (5.5)	51 (3.3)*
Living in province of South Holland	1469 (56.8)	513 (57.4)	956 (56.5)
During lockdown period			
Running behavior			
Continuing running training outdoor	2427 (93.9)	832 (93.1)	1595 (94.3)
Physical distancing during training[e]	2361 (97.3)	809 (97.2)	1552 (97.3)
Interval training (>50%)[e]	100 (4.1)	39 (4.7)	61 (3.8)
Training with partner[e]	581 (23.9)	184 (22.1)	397 (24.9)
Measures to prevent COVID-19			
Meticulous hand hygiene	2446 (94.6)	848 (94.9)	1598 (94.4)
Avoiding touching face, eyes and mouth	1095 (42.3)	382 (42.7)	713 (42.1)
Using face masks	101 (3.9)	31 (3.5)	70 (4.1)
Physical distancing	2495 (96.5)	865 (96.8)	1630 (96.3)
No unnecessary travel	2221 (85.9)	763 (85.3)	1458 (86.2)
Avoiding group meetings	2307 (89.2)	807 (90.3)	1500 (88.7)
General risk factors for COVID-19			
Contact with possible infected individuals	466 (18.0)	234 (26.2)	232 (13.7)*
Providing care to COVID-19 patients	137 (5.3)	47 (5.3)	90 (5.3)
Psychosocial stress	319 (12.3)	181 (20.2)	138 (8.2)*
Sleep disturbance	201 (7.8)	108 (12.1)	93 (5.5)*
Living in a province with high COVID-19 infection rate	291 (11.3)	103 (11.5)	188 (11.1)

Categorical data are presented as N (%) and continuous data ([b]) as means (SD). * = statistically significant difference between participants ($p<0.05$); [a] Community-acquired respiratory tract infections; [c] Body Mass Index; [d] Hypertension, cardiovascular disease, and/or diabetes; [e] Based on participants who continued running training during lockdown (total of 2427 participants).

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Supplementary table 4. Univariate and multivariate logistic regression analyzes of characteristics associated with at least two symptoms of CARTI[a].

Model 1 - Demographic characteristics
Sex (male)
Age (years)
BMI (kg/m^2)[c]
Model 2 - Measures to prevent COVID-19
Meticulous hand hygiene
Avoiding touching face, eyes and mouth
Using face masks
Physical distancing
No unnecessary travel
Avoiding group meetings
Model 3 - General risk factors for COVID-19
Contact with possible infected individuals
Providing care to COVID-19 patients
Psychosocial stress
Sleep disturbance
Living in a province with high COVID-19 infection rate
Model 4 - Running habits and running behavior
Weekly training hours
Interval training (>50%)
Training with partner
Physical distancing during training

* = statistically significant association ($p<0.05$); [a] Community-acquired respiratory tract infections; [b] $p<0.2$ presented in bold; [c] Body Mass Index.

Univariate analysis		Multivariate analysis	
OR (95% CI)	p-value	OR (95% CI)	p-value[b]
0.74 (0.62;0.87)*	<0.001	0.79 (0.66;0.94)*	**0.01**
0.98 (0.97;0.99)*	<0.001	0.98 (0.97;0.99)*	**<0.001**
1.01 (0.98;1.04)	0.67	1.04 (1.00;1.07)*	**0.04**
1.08 (0.76;1.56)	0.66	1.06 (0.73;1.54)	0.77
1.02 (0.87;1.21)	0.77	1.02 (0.86;1.21)	0.81
0.83 (0.54;1.28)	0.40	0.82 (0.53;1.27)	0.38
1.14 (0.72;1.78)	0.58	1.09 (0.69;1.73)	0.72
0.94 (0.74;1.18)	0.57	0.86 (0.67;1.11)	0.24
1.19 (0.91;1.55)	0.21	1.24 (0.93;1.66)	**0.15**
2.23 (1.82;2.74)*	<0.001	2.29 (1.85;2.82)*	**<0.001**
0.99 (0.69;1.42)	0.95	0.81 (0.56;1.19)	0.28
2.86 (2.25;3.63)*	<0.001	2.57 (2.00;3.30)*	**<0.001**
2.36 (1.77;3.16)*	<0.001	1.74 (1.28;2.38)*	**<0.001**
1.04 (0.81;1.35)	0.75	1.01 (0.78;1.31)	0.95
0.96 (0.93;1.00)*	0.03	0.97 (0.94;1.01)	**0.10**
1.24 (0.82;1.87)	0.31	1.27 (0.84;1.92)	0.26
0.86 (0.70;1.05)	0.13	0.88 (0.72;1.07)	0.20
0.98 (0.58;1.63)	0.92	0.93 (0.56;1.57)	0.80

Supplementary table 5. Final multivariate logistic regression model for characteristics associated with at least two symptoms of CARTI[a].

	Multivariate analysis	
	OR (95% CI)	**p-value**
Sex (male)	0.86 (0.72;1.04)	0.12
Age (years)	0.99 (0.98;0.99)*	<0.001
BMI (kg/m^2)[b]	1.03 (0.99;1.06)	0.11
Avoiding group meetings	1.20 (0.91;1.59)	0.20
Contact with possible infected individuals	2.19 (1.78;2.70)*	<0.001
Psychosocial stress	2.36 (1.83;3.04)*	<0.001
Sleep disturbance	1.65 (1.21;2.26)*	<0.01
Weekly training hours	0.98 (0.95;1.02)	0.33

* = statistically significant association (p<0.05); [a] Community-acquired respiratory tract infections; [b] Body Mass Index.

Part 2

GPS-based training load and its association with running-related injuries

Chapter 5

Feasibility and usability of GPS data in exploring associations between training load and running-related knee injuries in recreational runners

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ABSTRACT

Objective: To explore the feasibility of collecting GPS data and the usability of GPS data to evaluate associations between the training load and onset of running-related knee injuries (RRKIs).

Methods: Participants of the INSPIRE-trial, a randomized-controlled trial on running injury prevention, were asked to participate in this study. At baseline, demographic variables were collected. Follow-up questionnaires assessed information on RRKIs. Participants with a new reported RRKI and uninjured participants were sent a GPS export request. Weekly GPS-based training distances were used to calculate acute:chronic workload ratios (ACWRs).

Results: A total of 240 participants (62.7%) tracked their running training sessions with the use of a GPS-enabled device or platform and were willing to share their GPS data. From the participants (N=144) who received a GPS export request, 50.0% successfully shared their data. The majority (69.4%) of the shared GPS data were usable for analyzes (N=50). GPS data were used to present weekly ACWRs of participants with and without an RRKI eight weeks prior to RRKI onset or running event.

Conclusion: It seems feasible to collect GPS data from GPS-enabled devices and platforms used by recreational runners. The results indicate that GPS data is usable to calculate weekly ACWRs to evaluate associations between training load and onset of RRKIs in recreational runners. Therefore, GPS-based ACWR measures can be used for future studies to evaluate associations between training load and onset of RRIs.

INTRODUCTION

Running is one of the most popular forms of physical exercise and is associated with positive effects on a range of health benefits[1]. However, a high number of runners experience a running-related injury (RRI)[2-4]. A recent systematic review of Kakouris et al. showed an overall injury incidence of 40.2%[5]. Up to 80% of all RRIs are thought to develop as a consequence of overuse[6]. Overuse injuries can occur when the training load exceeds the runners' load capacity for adaptive tissue repair[7,8]. Therefore, it is believed that the onset and development of RRIs is strongly related to an imbalance between training and recovery[8-10]. However, the estimation of load capacity is difficult since the training load varies due to variation within and between individuals[10,11].

The acute:chronic workload ratio (ACWR) can be used to calculate changes in training load and is calculated by dividing the acute training load (e.g. covered distance in the past week) by the chronic workload (e.g. covered distance in the past four weeks)[12,13]. Research within team sport populations, like football, soccer and rugby, reported that a ratio of 1.5 or higher is associated with increased injury risk compared to a ratio of 0.8 to 1.3[12,14]. One study investigated the relationship between ACWR and injury risk in a mixed endurance sports population[15]. The authors concluded that endurance athletes could minimize their injury risk by maintaining moderate to high chronic training loads while avoiding high spikes in acute training load. Furthermore, a recent study in competitive runners showed that a fortnightly low increase of the ACWR (0.10–0.78) is related to an increased risk of sustaining an injury[16]. Last, a recent study in competitive trail runners reported a significant weekly increase in ACWR for session-rate of perceived exertion, total distance, and training time in the weeks prior to an injury's occurrence[17].

Questionnaires used to determine training characteristics retrospectively are reported to include inaccuracy due to recall bias[18]. Therefore, the use of global positioning systems (GPS) data to collect training information may be a more accurate method. Nowadays, more than 75% of runners use GPS-enabled devices, like sports watches, smartphone applications, and activity trackers, to track their training activities[19,20]. These devices can accurately measure several aspects of training load, such as distance and speed[20-22]. However, little is known about the feasibility of collecting GPS data and the usability of GPS data to study the ACWR to assess injury risk in runners. Examining injury risk is especially important in runners with a running-related knee injury (RRKI), since this is the most commonly reported injury in runners with an incidence of 26.2% in non-ultramarathoners and up to one-third of the runners with an RRKI still experience complaints after one year[2,5,23]. Therefore, the aims of this study were to 1) explore the feasibility of collecting GPS data from recreational runners and 2) examine the usability of GPS data to evaluate associations between training load and onset of RRKIs with the use of ACWR.

METHODS

Study design

This study is part of the INtervention Study on Prevention of Injuries in Runners (INSPIRE) trial, a randomized-controlled trial to investigate the effect of an online injury prevention program on the number of RRIs[24]. After completing the baseline questionnaire, follow-up questionnaires were sent (i) two weeks before the running event; (ii) one day after the running event; (iii) four weeks after the running event. Participants with a new RRKI during follow-up were sent an additional knee-specific follow-up questionnaire at an average of 16 months (range 11.7–18.6) after baseline. GPS usage questions were sent at an average of 20 months (range 15.8–23.0) after baseline. The INSPIRE trial (trial registration number NTR5998) was funded by the Netherlands Organization for Health Research and Development (ZonMW, grant number 536001001). Medical ethics approval was obtained by the Medical Ethical Committee of the Erasmus Medical Center Rotterdam, The Netherlands (MEC-2016-292).

Participants

Runners who registered for one of three selected running events (distances 5.0–42.2 kilometer (km)) in 2017 were invited to participate in this study. Interested runners, aged 18 years or older, were asked to provide informed consent and to fill in the baseline questionnaire. For the current study purpose, participants with a new RRKI during follow-up and participants without an RRI in the past and during follow-up were included. Exclusion criteria were no knowledge of the Dutch language and no access to internet and email. For the current study purpose, participants were excluded if they did not train with the use of a GPS-enabled device or platform or if they were not willing to share their GPS data. Furthermore, exclusion criteria were the use of a GPS-enabled device or platform without option to export GPS data and the estimated use of a device or platform in less than 80% of training sessions. Participants without an RRI were excluded if they reported a new RRI between baseline and the GPS usage questions.

Questionnaires and procedures

The flowchart of the procedures is presented in Figure 1. In the baseline questionnaire, information on demographics (sex, age weight and height) and training characteristics (average weekly training frequency, hours, distance (km), and running speed (minutes per km) over the previous three months) were collected. Furthermore, information on running experience (years), RRI in the 12 months before baseline (yes/no), and distance of registered running event were obtained. In the follow-up questionnaires, participants were asked if they sustained a new RRI since completing the previous questionnaire (yes/no). If yes, location of RRI and number of weeks the participant suffered from the RRI were collected.

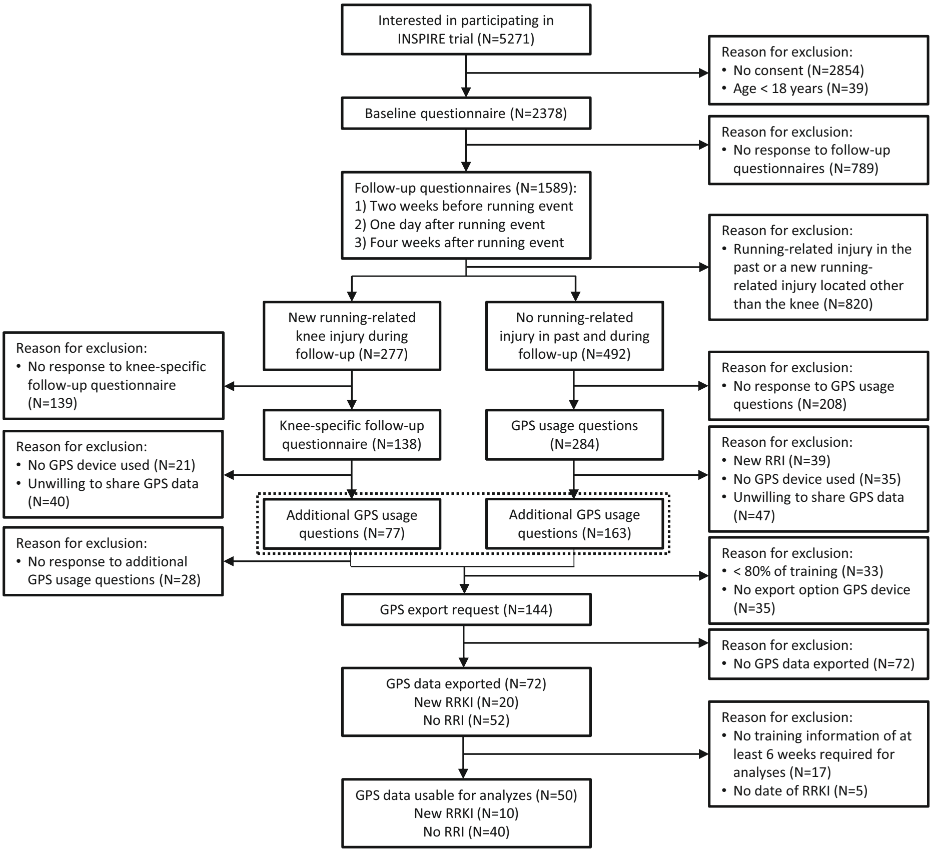

Figure 1. Flowchart of the participants.

In the knee-specific follow-up questionnaire, participants were asked if they tracked their training sessions with a GPS-enabled device or platform (yes/no) and if yes, if they were willing to share these data. The same questions were asked to the participants without an RRI. Furthermore, these participants were asked if they suffered a new RRI since completing the last follow-up questionnaire (yes/no). Next, additional GPS usage questions were sent to participants who were willing to share GPS data. The additional GPS usage questions collected information on the brand of GPS-enabled device or platform, the number of recorded training sessions (< 80% or 80–100% of all sessions), and training type (all training sessions, endurance training, tempo training, and interval training). A GPS export request was sent to the participants who met the inclusion criteria for the current study purpose. Manuals on how to share GPS data with the researchers were provided for the most popular platforms (i.e. Garmin, Strava, TomTom, Runkeeper, and Runtastic). In order of the researchers, Move-Metrics, a company specialized in data analysis for sport and health, standardized the different activity file formats (.tcx, .fit, .json, .gpx) and derived descriptives from the activity files required for this study[25]. Details on characteristics measured with GPS are outlined in Supplementary table 1.

Measurements

Body Mass Index (BMI) was calculated using weight and height. Based on the registered distances of the running event, participants were categorized into a short-distance group (i.e. 5–10.55 km) and long-distance group (i.e. 21.1–42.2 km) for comparison. If participants reported that they suffered an RRKI, the date of RRKI onset was calculated using the date of completion of the questionnaire minus the number of weeks a participant already suffered from the RRKI. If the date of RRKI onset could not be calculated within two weeks of certainty due to missing values, participants were excluded.

GPS data of the 11 weeks before the onset of the RRKI were selected to evaluate the associations between training load and the onset of RRKIs. We chose the 11 weeks of training load based on a combination of clinical experience and availability of data. For participants without an RRI, GPS data of the 11 weeks before the running event were selected. GPS data were divided into weekly blocks from Monday to Sunday and usable for analyzes if it contained training information of at least six out of 11 weeks required for analyzes. With the use of the GPS data, the average training minutes, distance (km) and running speed (minutes per km) were calculated for every training session. For each week, training loads were calculated as the total sum of the training distance. If a participant did not perform a training session for a week, a value of zero was included. Weekly ACWRs were calculated with the use of the coupled rolling average model in which acute training load (average training load of the present week) is divided by the chronic load (average training load of the present week and previous three weeks)[13].

Outcomes

The primary outcome measure of this study was the feasibility of collecting GPS data in terms of the percentage of participants who were willing to share GPS data and the percentage of collected GPS data useable for analyzes. The secondary outcome measure was the usability of GPS data to determine the weekly ACWR of participants with and without an RRKI. An RRKI was defined as any self-reported musculoskeletal complaint of the knee due to running activities, which restricted the amount of running (distance, duration, speed, or frequency) for at least one week or needed medical consultation[2,3,26].

Statistical analyzes

Normality of the data was checked statistically using the Shapiro–Wilk test. Descriptive statistics were used to describe baseline characteristics, expressed in frequency or average and standard deviations (SDs). Baseline characteristics between participants who did and did not share GPS data were compared using independent sample t-tests (normally distributed continuous data), Mann–Whitney U tests (not normally distributed continuous data) and chi-square tests (dichotomous data). The same tests were used to explore differences in baseline characteristics between participants with an RRKI and without an RRI who shared GPS data usable for analyzes. With the use of GPS data, training characteristics and corresponding SDs were calculated and compared between participants with an RRKI and without an RRI using independent sample t-tests. The same tests were used to examine differences between the long-distance and short-distance group. P-values <0.05 were regarded as statistically significant. All analyzes were performed using SPSS version 25.0 (SPSS Inc, Chicago, Illinois).

RESULTS

In total, 2378 runners participated in the INSPIRE trial (Figure 1). On one hand, 277 (14.4%) participants reported an RRKI during follow-up and received an additional knee-specific follow-up questionnaire. A total of 138 (49.8%) participants responded to this additional questionnaire. Of those, 117 participants (84.8%) reported the use of a GPS-enabled device or platform to track their training sessions, of which 77 participants (65.8%) were willing to share their GPS data and received additional GPS usage questions. A total of 49 (63.6%) participants responded to these additional questions. On the other hand, 492 participants without an RRI in the past and during follow-up received GPS usage questions. Of the 284 (57.7%) responders, 39 (13.7%) participants reported a new RRI and were therefore excluded. Of the remaining participants, 210 (85.7%) participants used a GPS-enabled device or platform, of which 163 (77.6%) participants were willing to share their GPS data and received additional GPS usage questions.

Feasibility of GPS data collection

From both RRKI and RRI branches, a total of 212 participants responded to the additional GPS usage questions. Most reported GPS-enabled devices or platforms were Strava (30.2%) and Garmin (28.3%) (Table 1). Participants were excluded from receiving the GPS export request if they tracked less than 80% of their training sessions (N=33) or if their GPS-enabled device or platform had no option to export GPS data (N=35). Of the participants who received a GPS export request, 72 (50.0%) participants shared their GPS data. After receiving GPS data, 17 participants were excluded because their GPS data did not contain training information of at least six out of 11 weeks required for analyzes and five participants were excluded because the date of RRKI onset could not be given within a certainty of two weeks. GPS data of a total of 50 (69.4%) participants were usable for analyzes.

Table 1. GPS usage responses.

	Responders to the additional GPS usage questions (N=212)
GPS-enabled device	
Strava	64 (30.2)
Garmin	60 (28.3)
TomTom	43 (20.3)
Runkeeper	33 (15.6)
Polar	30 (14.2)
Runtastic	8 (3.8)
Nike+ running	10 (4.7)
Other	14 (6.6)
Use of ≥ 2 GPS-enabled devices	53 (25.0)
GPS used ≥ 80% of training sessions	179 (84.4)
All training sessions recorded[a]	167 (93.3)

Data are presented as N (%).[a] Based on runners who tracked at least 80% of their training sessions.

Usability of GPS data to determine the training load

Compared to the participants (N=72) who received the GPS export request but did not share GPS data, participants (N=72) who shared GPS data had significantly more running experience (9.1 years vs. 8.3 years, p=0.02) and trained more times a week (2.7 vs. 2.6, p=0.01) (Supplementary table 2). Participants (N=50) who shared GPS data usable for analyzes were on average 44.9 (SD 11.6) years old and the majority registered for a long-distance running event (72.0%) (Table 2). No significant baseline differences between participants with an RRKI and without an RRI who shared GPS data usable for analyzes were found (Table 2).

Table 3. Training characteristics measured by GPS eight weeks before onset of RRKI or running event.

	Total	
	RRKI[a] (N=10)	No RRI[b] (N=40)
Weekly training frequency	3.2 (1.4)	2.9 (1.2)
Each training session		
Average training duration (min)	51.1 (26.2)	56.0 (32.8)
Average training distance (km)	8.2 (4.2)	9.6 (5.3)
Average running speed (min/km)	6.0 (1.0)	5.6 (1.1)

Data are presented as means (SD). * = statistically significant difference between participants with an RRKI and participants with no RRI (p<0.05). [a] Running-related knee injury; [b] Running-related injury.

Participants with an RRKI trained on average 51.1 (SD 26.2) minutes with a distance of 8.2 (SD 4.2) km per training in the eight weeks prior to the RRKI onset (Table 3). Participants with an RRKI in the long distance group trained significantly more often compared to participants without an RRI (3.5 vs. 2.9 times a week, p≤0.01). Of the participants who registered for a short-distance running event, participants without an RRI trained at a significantly higher speed (5.3 vs. 5.6 min/km, p≤0.01) compared to participants with an RRKI.

Table 2. Baseline characteristics of runners who shared GPS data usable for analyzes.

	Total (N=50)	RRKI[a] (N=10)	No RRI[b] (N=40)
Demographic characteristics			
Sex (male)	36 (72.0)	8 (80.0)	28 (70.0)
Age (years)[c]	44.9 (11.6)	49.7 (12.6)	43.7 (11.2)
BMI (kg/m^2)[c,d]	23.2 (2.1)	23.3 (1.1)	23.2 (2.3)
Training characteristics			
Running experience (years)[c]	9.2 (10.5)	14.3 (16.8)	7.9 (8.0)
Weekly training frequency[c]	2.5 (0.9)	2.3 (0.8)	2.6 (1.0)
Weekly training hours[c]	2.8 (1.5)	2.6 (1.3)	2.9 (1.5)
Weekly training distance (km)[c]	25.0 (15.0)	21.6 (10.3)	25.9 (15.9)
Running speed (min/km)[c]	5.9 (0.9)	5.8 (0.7)	5.9 (1.0)
Running event			
Distance registered for:			
Short-distance (5-10.55km)	14 (28.0)	4 (40.0)	10 (25.0)
Long-distance (21.1-42.2km)	36 (72.0)	6 (60.0)	30 (75.0)

Categorical data are presented as N (%) and continuous data ([c]) as means (SD). No statistically significant difference between participants who did and did not share GPS data usable for analyzes.
[a] Running-related knee injury; [b] Running-related injury; [d] Body Mass Index.

	Short-distance event		**Long-distance event**	
	RRKI (N=4)	**No RRI (N=10)**	**RRKI (N=6)**	**No RRI (N=30)**
	2.8 (1.2)	2.7 (1.2)	3.5 (1.5)	2.9 (1.1)*
	36.7 (13.0)	33.1 (13.9)	60.4 (28.4)	63.3 (33.7)
	1.7 (10.8)	6.0 (2.4)	9.9 (4.5)	10.8 (5.4)
	5.6 (1.0)	5.3 (1.0)*	5.9 (1.0)	5.6 (1.1)

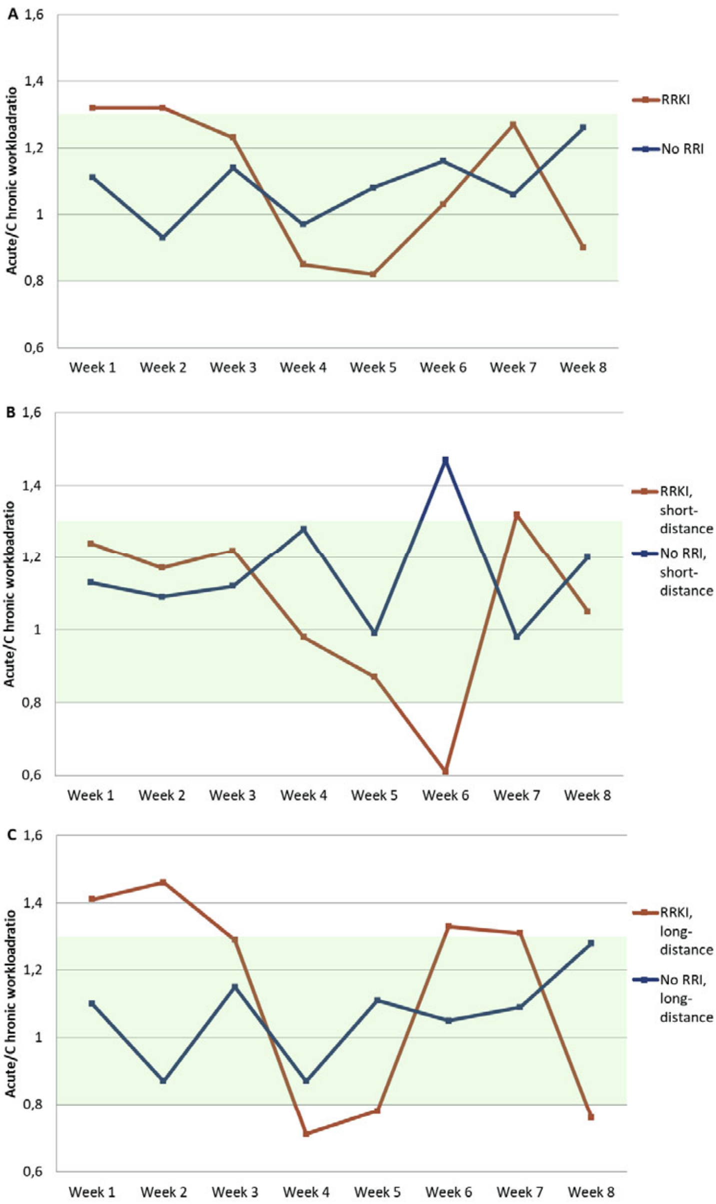

Figure 2. Weekly acute:chronic workload ratios (ACWRs) of participants with a running-related knee injury (RRKI) and without a running-related injury (RRI). ACWRs were calculated by weekly training distance. **A** For participants with an RRKI, weekly ACWR was calculated for the eight weeks before onset of the RRKI. For participants without an RRI, weekly ACWR was calculated for the eight weeks before start of the running event. For both groups the ACWRs were also calculated based on registered distance of running event: **B** short-distance (5–10.55 km) and **C** long-distance (21.1–42.2 km). ACWRs within the range of 0.8 to 1.3 ("green zone") were regarded as normal[12].

Figure 2 and Supplementary table 3 present weekly ACWRs of participants with and without an RRKI eight weeks prior to RRKI onset or registered running event. Weekly ACWRs of participants for a long-distance and short-distance running event are also presented. As observed in Figure 2A, participants without RRI showed relative stable average values of ACWR over the eight week period, while participants with an RRKI showed more fluctuated average values of ACWR. Participants with an RRKI who registered for a long-distance running event showed more fluctuated average values of ACWR compared to participants without an RRI (Figure 2C).

DISCUSSION

Almost two-thirds of the participants used a GPS-enabled device or platform to track their running training sessions and were willing to share GPS data. It therefore seems feasible to collect data from GPS-enabled devices and platforms that are used by recreational runners. However, caution is advised since only half of the participants who received a GPS export request did actually share their GPS data and of this data two-thirds was usable for analyzes. Our study showed that GPS data derived from GPS-enabled devices and platforms from recreational runners contained variables like training frequency, duration, distance, and speed and these can be used for calculation of ACWR values.

More than 85% of the participants used a GPS-enabled device or platform to track their running training sessions. This is comparable with previous studies in which more than 75% of runners used GPS-enabled devices[19,20]. Since GPS data were collected from devices owned by the participant, no effort and costs were made for these measurements. Of the participants (N=144) who received a GPS export request, 50% did not share GPS data. Possible reasons to not share GPS data are the need to perform multiple steps to share GPS data and concerns about privacy handling of data. Therefore, we expect that user-friendly sharing, with more information on privacy handling of data may improve data collection for research purposes. Nevertheless, this study shows that it seems feasible to collect GPS data from several brands of GPS-enabled devices and platforms used and owned by recreational runners.

Next, it is important that GPS data contain useful data to calculate training load. Our study showed that GPS data derived from GPS-enabled devices and platforms from recreational runners contained variables like training frequency, duration, distance, and speed. With the use of the variable training distance we calculated ACWRs. Furthermore, previous research reported that GPS-enabled devices can accurately measure this variable, perhaps even more accurate than questionnaires[20-22]. So GPS data derived from GPS-enabled devices offer a better alternative to calculate training load compared to questionnaires. However, there is much debate about the best model to calculate training load in runners. For many years, runners were advised to limit the increase in their weekly training load to < 10% in order to minimize the risk of injury[27]. Recently, studies concluded that the ACWR can be used to examine the relationship between training load and injury risk[12,14]. The best model to calculate ACWR is unclear and some studies reported that the exponentially weighted moving average (EWMA) is a more sensitive model to detect associations between training load and injury[28]. So far, only a few studies examined associations between training load and injury risk in runners[15-17]. Future prospective studies with large sample sizes are necessary to determine the best method to calculate training load in recreational runners and to explore associations between training load and onset of RRIs.

Strengths and limitations

A strength of the current study is that it is the first study that provides information on the feasibility of GPS data collection in recreational runners. Furthermore, this is the first study that explored the usability of GPS data to evaluate associations between training load and onset of RRKIs with the use of ACWRs. However, this study has a number of limitations. The loss to follow-up (51.2%) was relatively high. Reason for this high percentage might be the long follow-up of 20 months (range 15.8–23.0). Besides the knee-specific follow-up questionnaire, there was no contact with the participants between the follow-up questionnaires and the GPS usage questions. Due to this long follow-up, participants might have become less interested to answer this questionnaire, which was also not announced when this study started. The questionnaires were not validated. However, the definition of RRIs and data collection using this approach has been frequently applied and published in the past[29,30]. Another limitation is the date of RRKI onset. Participants were asked to estimate the duration of their RRKI. Because only three follow-up questionnaires were sent to the participants, this may have caused recall bias. Furthermore, ACWRs of participants without an RRI were calculated based on the 11 weeks before the running event. For participants with a new reported RRKI, ACWRs were calculated based on the 11 weeks before RRKI onset. However, these weeks included at least five out of the 11 weeks before the running event and were therefore comparable to the weeks selected for participants without an RRI. A loss of training data in a specific period might have large impact on the ACWR in that period. This might have influenced the results, although we cannot estimate the impact of the missing data. The threshold to determine whether GPS data collection is feasible was not defined as it depends on multiple factors such as population heterogeneity and population size. Furthermore, due to the small sample sizes per subgroup, no statistical test was performed to compare ACWR values between participants with and without an RRKI. We described the use of GPS-enabled devices or platforms used by the participants. However, for some devices or platforms it was not clear if a sports watch or smartphone was used to track the running training. When using GPS data derived from different GPS-enabled devices or platforms, differences in training recording and device differences can be expected. Therefore, researchers should keep in mind potential bias to usage, device specifications and sensor-position.

CONCLUSION

This study shows that it seems feasible to collect training characteristics from GPS-enabled devices and platforms used by recreational runners. The results indicate that GPS data is usable to calculate weekly ACWRs to evaluate associations between training load and onset of RRKIs in recreational runners. Therefore, GPS-based ACWR measures can be used for future studies to evaluate associations between training load and onset of RRIs.

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SUPPLEMENTARY FILES

Supplementary table 1. Characteristics measured by GPS-enabled device or platform.

	GPS-enabled device			
	Strava	**Garmin**	**Runkeeper**	**TomTom**
Duration (sec)	Yes	Yes	Yes	Yes
Distance (meters)	Yes	Yes	Yes	Yes
Average speed (km/h)	Yes	Yes	Yes	Yes
Heart rate (bpm)	Product[a]	Product	No	Product
Cadence (spm)	Product	Product	No	No
Altitude (meters)	Yes	Yes	Yes	Yes
Stance time (ms)	Product	Product	No	No
Vertical oscillation (cm)	Product	Product	No	No
Total steps	Product	No	No	No

[a] Characteristic measured depending on type of GPS-enabled device.

Supplementary table 2. Baseline characteristics of participants who did and did not share GPS data after receiving the GPS export request.

		GPS data shared	
	Total (N=144)	**Yes (N=72)**	**No (N=72)**
Demographic characteristics			
Sex (male)	91 (63.2)	51 (70.8)	40 (55.6)
Age (years)[a]	44.9 (12.6)	44.5 (12.0)	45.2 (13.2)
BMI (kg/m^2)[a,b]	23.5 (2.9)	23.1 (2.4)	23.9 (3.3)
Training characteristics			
Running experience[a]	8.7 (10.1)	9.1 (10.6)	8.3 (9.6)*
Weekly training frequency[a]	2.6 (1.3)	2.7 (1.0)	2.6 (1.4)*
Weekly training hours[a]	2.8 (1.4)	2.9 (1.5)	2.7 (1.3)
Weekly training distance (km)[a]	26.2 (19.3)	25.3 (14.8)	27.1 (22.9)*
Running speed (min/km)[a]	6.1 (1.1)	5.9 (0.9)	6.2 (1.3)
Injuries			
RRI[c] 12 months before baseline	11 (7.6)	8 (11.1)	3 (4.2)
New RRKI[d] during follow-up	35 (24.3)	20 (27.8)	15 (20.8)
Running event			
Distance registered for:			
Short-distance (5-10.55km)	55 (38.2)	22 (30.6)	33 (45.8)
Long-distance (21.1-42.2km)	89 (61.8)	50 (69.4)	39 (54.2)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between responders and non-responders ($p<0.05$); [b] Body Mass Index; [c] Running-related injury; [d] Running-related knee injury.

Supplementary table 3. Weekly acute:chronic workload ratios (ACWRs) calculated by weekly training distance in participants with an RRKI and without an RRI.

ACWR	**Total**		**Short-distance event**[a]		**Long-distance event**[a]	
	RRKI[b] (N=10)	No RRI[c] (N=40)	RRKI (N=4)	No RRI (N=10)	RRKI (N=6)	No RRI (N=30)
Week 1	1.34 (1.1)	1.11 (0.5)	1.24 (0.8)	1.13 (0.5)	1.41 (1.4)	1.10 (0.5)
Week 2	1.35 (0.4)	0.93 (0.7)	1.17 (0.3)	1.09 (1.1)	1.46 (0.5)	0.87 (0.5)
Week 3	1.26 (0.4)	1.14 (0.8)	1.22 (0.3)	1.12 (1.1)	1.29 (0.5)	1.15 (0.7)
Week 4	0.82 (0.5)	0.97 (0.6)	0.98 (0.8)	1.28 (0.8)	0.71 (0.4)	0.87 (0.5)
Week 5	0.81 (0.5)	1.08 (0.5)	0.87 (0.6)	0.99 (0.7)	0.78 (0.5)	1.11 (0.5)
Week 6	1.04 (0.5)	1.16 (0.8)	0.61 (0.6)	1.47 (1.1)	1.33 (0.2)	1.05 (0.7)
Week 7	1.32 (0.4)	1.06 (0.7)	1.32 (0.4)	0.98 (0.5)	1.31 (0.5)	1.09 (0.8)
Week 8	0.87 (0.5)	1.26 (0.6)	1.05 (0.4)	1.20 (0.4)	0.76 (0.6)	1.28 (0.7)

Data are presented as means (SD). [a] ACWRs are calculated based on registered distance of running event, short-distance (5-10.55km) and long-distance (21.1-42.2km); [b] Running-related knee injury; [c] Running-related injury.

Chapter 6

Comparison of weekly training load and acute:chronic workload ratio methods to estimate change in training load in running

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ABSTRACT

Objective: To investigate differences between four methods to calculate change in training load: (1) weekly training load; (2) acute:chronic workload ratio (ACWR), coupled rolling average (RA); (3) ACWR, uncoupled RA; (4) ACWR, exponentially weighted moving averages (EWMA).

Methods: This study is part of a randomized-controlled trial on running injury prevention among recreational runners. Runners who registered for running events (distances 10-42.195 kilometers) in the Netherlands received a baseline questionnaire and a request to share global positioning system (GPS) training data. Primary outcome measure was the predefined significant increase in training load (weekly training loads ≥ 30% progression and ACWRs ≥ 1.5), based on training distance. Proportional Venn diagrams visualized the differences between the methods.

Results: 430 participants (73.3% men; age 44.3 years) shared their GPS training data with in total 22,839 training sessions. For the weekly training load, coupled RA, uncoupled RA, and EWMA method, respectively 33.4% (95% CI 32.8-34.0), 16.2% (95% CI 15.7-16.6), 25.8% (95% CI 25.3-26.4), and 18.9% (95% CI 18.4-19.4) of the training sessions were classified as significant increase in training load. Of the training sessions with significant increase in training load, 43.0% expressed in the weekly training load method showed a difference with the coupled RA and EWMA method. Training sessions with significant increase in training load based on the coupled RA method showed 100% overlap with the uncoupled RA and EWMA method.

Conclusion: The difference in change in training load measured by weekly training load and ACWR methods was high. To validate an appropriate measure of change in training load in runners, future research on the association between training loads and RRI risk is needed.

INTRODUCTION

Running is a time-efficient, easily accessible and relatively inexpensive activity[1]. Despite health benefits[2], running has a substantial risk of injury. A recent systematic review (literature search up to June 2020) among middle- and long-distance runners reported an overall running-related injury (RRI) incidence and prevalence of 40% and 45% respectively[3]. An RRI accounts for 48% of all reasons for running discontinuation[4]. To help people staying active and to work towards a healthy society, development of preventive interventions for RRIs is highly important.

Overuse injuries are estimated to account for 64-75% of all RRIs[5,6]. These injuries are characterized by a multifactorial aetiology[6,7]. It is assumed that the training load (the amount of training in a defined time period) imposed by running plays an important role in the development of overuse injuries as a consequence of "running too much, too soon"[8]. This significant change in training load may cause an imbalance between training and recovery in which the training load exceeds the runners' load capacity for adaptive tissue repair, especially if there is inadequate recovery time[7-9]. In order to define change in training load, accurate methods to collect training data need to be used. Training characteristics retrospectively collected from questionnaires might be inaccurate due to recall bias[10]. The use of global positioning systems (GPS) might be a more accurate method to collect training data[11,12]. Collecting GPS data was recently also found to be feasible to estimate training load in runners[13].

Traditionally, change in training load in running was expressed as the week-to-week training progression in running distance[11,14,15]. Runners who progressed their training distance by more than 30% seemed to be more vulnerable to sustain an RRI[15]. In 2014, the acute:chronic workload ratio (ACWR) was launched to estimate change in training load and this measure has been frequently used, especially in team sports populations[16,17]. An association between an increase in ACWR and the risk of injury was identified in several competitive team sports, such as Australian football, rugby, cricket, and soccer and ACWRs greater than 1.5 were considered as high risk for sustaining an injury[16,18,19]. Though, the use of the ACWR for training-load management and recommendations is subject of discussion in literature[20]. So far, only few studies examined the ACWR in running populations, with conflicting results[21-24].

A possible reason for the conflicting results is that these studies used different methods to calculate ACWRs. Possible methods for calculating the ACWR are: (1) coupled rolling average (RA) method in which the acute workload (last seven days) is divided by the chronic workload (last 28 days); (2) uncoupled RA method in which the acute workload is not included in the chronic workload; (3) exponentially weighted moving averages (EWMA) in which a decreasing weighting is assigned for load values that have been applied longer ago (Supplementary table 1)[25,26]. Regardless of sport type, most studies used the coupled RA method to calculate ACWR[18,27]. However, the uncoupled RA method might be a better method since mathematical coupling of ACWR is controversial as it influences the chronic workloads and therefore the ACWR itself[28]. Compared to the RA methods, studies suggested that the EWMA method is a more sensitive indicator to assess injury risk[27,29,30], whilst others suggested that there are no differences between the RA and EWMA methods[31]. To examine the impact of change in training load on the risk for sustaining an RRI, it is first important to gain insight in the differences between the applied methods that are used to express change in training load in runners. Therefore, the aim of this study was to investigate differences between four methods to calculate significant increase in training load in recreational runners: (1) weekly training load; (2) acute:chronic workload ratio (ACWR), coupled rolling average (RA); (3) ACWR, uncoupled RA; (4) ACWR, exponentially weighted moving averages (EWMA).

METHODS

Study design

The current study was part of the Shaping up Prevention for Running Injuries in the Netherlands using Ten steps (SPRINT) study. The SPRINT study was a randomized-controlled trial (RCT) among recreational runners with a minimum follow-up of three months, to investigate the effect of an online injury prevention program on the number of RRIs[32]. After participants completed the baseline questionnaire, follow-up questionnaires were sent one month before, one week before, and one month after the registered running event. Additionally, by the end of the follow-up period all participants were asked to share their GPS training data. Because it was not possible for each platform to share GPS data of a specific timeframe, participants were asked to share all their GPS data up to date of upload. GPS training data within six months prior to the running event registered for were included in this study. A flowchart of the design is presented in Figure 1. The SPRINT study was funded by the Netherlands Organization for Health Research and Development (ZonMW, grant number 50-53600-98-104). Medical ethics approval was obtained by the Medical Ethical Committee of the Erasmus Medical Center Rotterdam, the Netherlands (MEC-2019-0136).

Participants

Runners who registered for the DSW Bruggenloop Rotterdam 2019 (15 kilometer (km)), Nacht van Groningen 2020 (10, 16.1, and 21.1 km), NN CPC Loop The Hague 2020 (10 and 21.1 km) or NN Marathon Rotterdam 2020 (10.55 and 42.195 km) were invited to participate in the SPRINT study. Interested runners, aged 18 years or older, were asked to provide digital informed consent. Exclusion criteria were registration < 60 days before the running event, no sufficient knowledge of the Dutch language, no access to internet and email, and participation in our previous trial on RRI prevention[33]. For the current study purpose, participants were excluded if they: (1) did not share GPS training data, or (2) shared GPS training data, but did not include training data six months before the running event registered for.

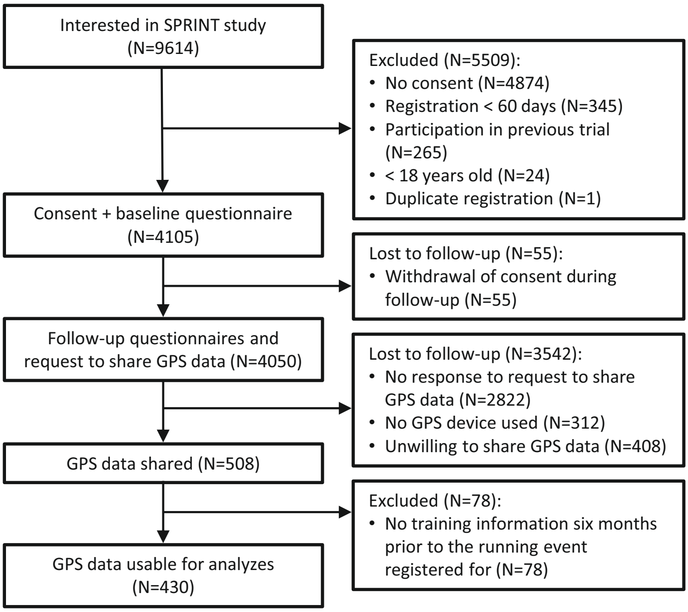

Figure 1. Flowchart of the participants.

Data collection

In the baseline questionnaire, information on demographics (sex, age, weight, and height) was collected. Weight and height were used to calculate the body mass index (BMI). Information on training characteristics (average weekly training frequency, hours, distance (km), and running speed (minutes per km) over the last three months), running experience (years), RRI in the 12 months before baseline (yes/no), RRI at baseline (yes/no), use of a GPS-enabled device or platform (yes/no), and distance of the registered running event was obtained. Based on the registered distance of the running event, participants were categorized into 10/10.55 km, 15/16.1 km, half marathon, and marathon. In the follow-up questionnaires, participants were asked if they sustained a new RRI since completing the previous questionnaire (yes/no). An RRI was defined as a self-reported injury of the muscles, joints, tendons and/or bones in the lower back or lower extremities (hip, groin, thigh, knee, leg, ankle, foot, and toes) that is caused by running (training or competition). The injury had to be severe enough to cause a reduction in running distance, speed, duration, or frequency for at least seven days or three consecutive scheduled training sessions or the consultation of a physician or other health professional had to be necessary[34,35]. At the end of follow-up, an email with a request to share GPS training data was sent to all participants. In this request, participants were asked to upload their GPS data through a personalized link to a cloud-based digital environment. This digital environment was especially developed for this study by MoveMetrics, a company specialized in data analysis for sport and health[36]. After uploading, the GPS data was automatically standardized and pseudonymized. Sensitive metadata (like user credentials) were automatically removed, and the GPS-position data was converted into relative distances. Accordingly, researchers downloaded the data through a password protected link.

Training load analysis

Training load was calculated based on the distance of each running activity derived from GPS data within six months prior to the running event registered for. Of each running session, change in training load was calculated by the weekly training load, coupled RA, uncoupled RA, and EWMA method (Supplementary table 1). To begin the EWMA calculation, the distance of the first recorded running activity of the participants was used as the first training load value. To define the weekly training load, the week-to-week change in training load was divided into one of the following categories: (1) regression between 0% and 10%; (2) regression between 10% and 30%; (3) regression between 30% and 50%; (4) regression ≥ 50%; (5) progression between 0% and 10%; (6) progression between 10% and 30%; (7) progression between 30% and 50%; (8) progression ≥ 50%[15]. ACWRs (coupled RA method, uncoupled RA method, and EWMA) were categorized into: (1) < 0.8; (2) between 0.8 and 1.3; (3) between 1.3 and 1.5; (4) between 1.5 and 2.0; (5) ≥ 2.0[16,27]. If a participant did not train in the days used to calculate the denominator (the denominator was zero), it was not possible to calculate the workload of that training session. These training sessions were categorized into a ‘not available’ group.

Outcome measures

The primary outcome is the number of training sessions with a predefined significant increase in training load. Runners who train with a significant increase in training load are suspected to be at higher risk for sustaining an RRI[15,16,18]. A significant increase in training load was defined as ≥ 30% progression[11,15]. For the ACWR methods, a significant increase in training load was defined as ACWRs ≥ 1.5[16,19].

Statistical analyzes

Descriptive statistics were used to describe all variables, expressed in frequency or mean and standard deviations (SDs). Participants who shared GPS data eligible for analyzes and participants who did not share GPS data were compared with independent sample t-tests (continuous data), Mann-Whitney U tests (continuous data) and chi-square tests (dichotomous data). Frequencies of the training sessions with 95% confidence intervals (CIs) were calculated for the predefined change in training load categories of the weekly training load, coupled RA, uncoupled RA, and EWMA method. Differences between training sessions with significant increase in training load expressed in the weekly training load, coupled RA, and EWMA method were calculated. A proportional Venn diagram was used to visualize these differences with the use of the online software EulerAPE[37]. Additionally, differences between training sessions with significant increase in training load expressed in coupled RA, uncoupled RA, and EWMA method were calculated and a second proportional Venn diagram was used to visualize these differences. All analyzes were performed in SPPS Statistics 25 and p-values <0.05 were regarded as statistically significant.

RESULTS

Participants

Of the 9,614 runners interested in participation in the SPRINT study, 4,050 participants were included and consequently asked to share their GPS data (Figure 1). A total of 312 (7.7%) participants reported no use of GPS device or platform. Of the remaining 3,738 participants, 408 (10.9%) participants were unwilling to share GPS data and 2,822 participants did not respond to the request to share GPS data. A total of 508 (13.6%) participants shared GPS data. Of those, 78 (15.4%) participants were excluded because they did not share GPS data six months prior to the running event registered for. Therefore, GPS data of 430 participants was useable for analyzes with a total of 22,839 training sessions. Compared to the participants who did not share (usable) GPS data, participants who shared GPS data were more often males (73.3% vs. 62.3%, p<0.001), on average (SD) older (44.3 (12.2) vs. 42.0 (12.1), p<0.001), with more running experience (10.9 (10.3) vs. 10.2 (10.1), p=0.04), trained at a higher weekly training distance (30.4 (22.5) vs. 26.0 (22.6), p<0.001), and were more often member of an athletic association (39.8% vs. 28.7%, p<0.001) (Table 1). Furthermore, participants who shared GPS data more often reported an RRI during follow-up compared to the participants who did not share GPS data useable for analyzes. (46.3% vs. 34.2%, p<0.001).

Outcome measures

Tables 2 and 3 show the number of training sessions within the predefined change in training load categories of the weekly training load method and ACWR methods (coupled RA, uncoupled RA, and EWMA). For the outcome weekly training load, a total of 33.4% (95% CI 32.8-34.0) of the training sessions were classified as significant increase in training load. For the coupled RA method, uncoupled RA method, and EWMA method, a total of respectively 16.2% (95% CI 15.7-16.6), 25.8% (95% CI 25.3-26.4), and 18.9% (95% CI 18.4-19.4) of the training sessions were classified as significant increase in training load.

Table 1. Baseline characteristics of participants who shared GPS data usable for analyzes.

		GPS data shared	
	Total (N=4050)	**Yes (N=430)**	**No (N=3620)**
Demographic characteristics			
Sex (male)	2570 (63.5)	315 (73.3)	2255 (62.3)*
Age (years)[a]	42.3 (12.1)	44.3 (12.2)	42.0 (12.1)*
BMI (kg/m^2)[a,b]	23.3 (2.6)	23.0 (2.5)	23.3 (2.6)*
Training characteristics			
Running experience[a]	10.3 (10.1)	10.9 (10.3)	10.2 (10.1)*
Weekly training frequency[a]	2.6 (1.3)	2.8 (1.1)	2.5 (1.3)*
Weekly training hours[a]	3.1 (2.8)	3.2 (1.7)	3.1 (2.9)*
Weekly training distance (km)[a]	26.5 (22.7)	30.4 (22.5)	26.0 (22.6)*
Running speed (min/km)[a]	5.8 (0.9)	5.6 (0.7)	5.8 (0.9)*
Member of athletic association (yes)	1210 (29.9)	171 (39.8)	1039 (28.7)*
Use of training schedule (yes)	2636 (65.1)	300 (69.8)	2336 (64.5)*
Running events			
Distance registered for:			
10/10.55 km	894 (22.1)	56 (13.0)	838 (23.1)*
15/16.1 km	534 (13.2)	62 (14.4)	472 (13.0)
Half marathon	579 (14.3)	93 (21.6)	486 (13.4)*
Marathon	2043 (50.4)	219 (50.9)	1824 (50.4)
Running-related injury			
RRI[c] 12 months before baseline (yes)	2000 (49.4)	225 (52.3)	1775 (49.0)
Reported RRI at baseline (yes)	763 (18.8)	75 (17.4)	688 (19.0)
RRI during follow-up (yes)	1436 (35.5)	199 (46.3)	1237 (34.2)*

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between responders and non-responders ($p<0.05$); [b] Body Mass Index; [c] Running-related injury.

Figure 2A and Supplementary table 2 present that 15.6% of the training sessions with significant increase in training load showed an overlap between the coupled RA, weekly training load, and EWMA method. A total of 43.0% of the training sessions with significant increase in training load based on the weekly training load method showed a difference with the coupled RA and EWMA method. Between the three ACWR methods (coupled RA, uncoupled RA, and EWMA), an overlap of 29.6% of training sessions with significant increase in training load was reported (Figure 2B and Supplementary table 3). Training sessions with significant increase in training load based on the uncoupled RA method showed a difference of 23.6% with the coupled RA and EWMA method and 17.3% of the training sessions with significant increase in training load calculated by the EWMA method showed a difference with the coupled and uncoupled RA method. Training sessions with significant increase in training load based on the coupled RA method showed 100% overlap with the uncoupled and EWMA method.

Table 2. Number of training sessions per category of the weekly training load.

	N	% (95% CI)
Weekly training load		
Weekly regression		
0-10%	2196	9.6 (9.2-10.0)
10-30%	3328	14.6 (14.1-15.0)
30-50%	1837	8.0 (7.7-8.4)
≥ 50%	1210	5.3 (5.0-5.6)
Weekly progression		
0 -10%	2242	9.8 (9.4-10.2)
10-30%	3368	14.7 (14.3-15.2)
30-50%	2033	8.9 (8.5-9.3)
≥ 50%	5589	24.5 (23.9-25.0)
Not available	1036	4.5 (4.3-4.8)

All training loads are based on the distance of each training activity extracted from GPS data.

Table 3. Number of training sessions for each ACWR[a] method (coupled, uncoupled, and EWMA[b]).

	Coupled ACWR		Uncoupled ACWR		EWMA	
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
< 0.8	3167	13.9 (13.4-14.3)	3730	16.3 (15.9-16.8)	781	3.4 (3.2-3.7)
0.8-1.3	13111	57.4 (56.8-58.0)	10192	44.6 (44.0-45.3)	13050	57.1 (56.5-57.8)
1.3-1.5	2872	12.6 (12.1-13.0)	2819	12.3 (11.9-12.8)	4692	20.5 (20.0-21.1)
1.5-2.0	2511	11.0 (10.6-11.4)	3231	14.1 (13.7-14.6)	3508	15.4 (14.9-15.8)
≥ 2.0	1178	5.2 (4.9-5.5)	2678	11.7 (11.3-12.1)	808	3.5 (3.3-3.8)
Not available	0	0.0 (0.0-0.0)	189	0.8 (0.7-1.0)	0	0.0 (0.0-0.0)

All training loads are based on the distance of each training activity extracted from GPS data. [a] Acute:Chronic Workload Ratio; [b] Exponentially Weighted Moving Averages.

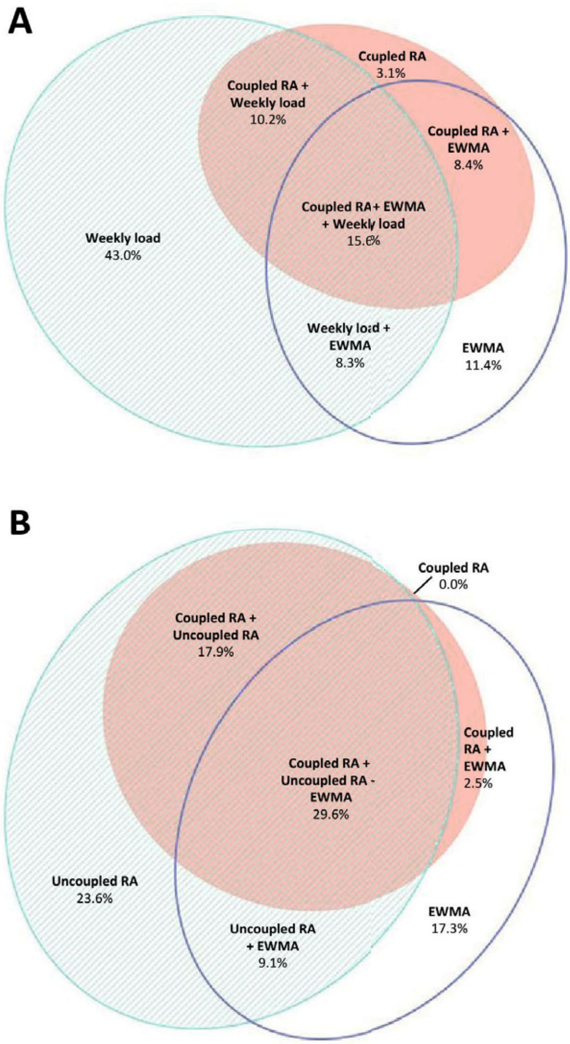

Figure 2. Proportional Venn diagram of high load training sessions. **A** Training loads calculated by the weekly training load[1], coupled RA method, and EWMA method[2] (N=9886). **B** Training loads calculated by the coupled RA method, the uncoupled RA method, and EWMA method (N=7916).

[1] For the weekly training load, values ≥ 30% were regarded as high risk for sustaining a running-related injury.

[2] For the rolling-average (RA) methods and exponentially weighted moving averages (EWMA) method, values ≥ 1.5 were regarded as high risk.

DISCUSSION

This is the first study that investigated differences in calculations of estimated training sessions with significant increase in training load between the weekly training load method and ACWR methods in recreational runners. With the use of the weekly training load method, the percentage of training sessions with significant increase in training load was almost two times higher compared to the coupled RA and EWMA method (33% vs. 16% and 19%) and 1.5 times higher compared to the uncoupled RA method (33% vs. 26%). Almost half of the training sessions with significant increase in training load calculated by the weekly training load method showed a difference with the coupled RA and EWMA method. Only one-third of the training sessions with significant increase in training load showed an overlap between the coupled RA, uncoupled RA, and EWMA method.

We categorized the change in training load of each training session and reported that 16-33% of the training sessions were classified as significant increase in training load. These percentages were higher compared to the percentages calculated in a recent study that described the association between ACWR and RRIs[23]. This study included 435 runners with a median follow-up time of 26 weeks and reported a total of 5-15% of the ACWRs higher than 1.5[23]. A reason for this difference might be that Nakaoka et al. used questionnaires to calculate training load with retrospectively collected data, which might have caused recall bias. This study also calculated ACWRs with the use of biweekly cumulative distance of running sessions, which may have smoothed training load variations over time[23].

In recent years, the assessment of change in training load in athletes has been studied widely. A possible reason for the growing interest was the creation and further detailing of the ACWR[17,19,38]. Despite the great interest, no consensus has been reached on the preferred method to calculate change in training load. Furthermore, the utility of the ACWR has prompted significant discourse in scientific literature mainly related to potential biased estimates of the ACWR[20,39,40]. We found that almost half of the training sessions with significant increase in training load calculated by the weekly training load showed no overlap with the ACWR methods (coupled RA and EWMA method). A reason for this high difference is likely that the weekly training load method calculates change in training load based on the training sessions performed in two weeks rather than the four weeks used in the ACWR methods. By using training sessions over a longer period of time, small differences in training load will have less impact on the ACWR. Moreover, there was an actual difference in cut-offs, as the week-to-week progression of 30% is lower than the 1.5 used for the ACWR, resulting in more training sessions when weekly progression exceeds the cut-off for significant increase in training load. Therefore, the ACWR methods might be more sensitive in identifying change in training load spikes using repeated measurements. Furthermore, smaller differences were seen between the three ACWR methods compared to the difference between the weekly training load method and ACWR methods. However, still 24% and 17% of the training sessions with significant increase in training load expressed in the uncoupled RA and EWMA method respectively showed a difference compared to the other methods. While these ACWR methods are frequently reported in literature as one method, there are considerable differences between the different methods to calculate these ratios.

In our study, we used the distance of each running activity to calculate training loads. We used distance because it is an accurate and objective variable to collect from GPS training data in runners[11,12]. There is a high variability in the variables used to calculate training load since the rate of change in load may be more problematic than the absolute load experienced by an athlete[16]. Therefore, external loads (i.e. the amount of external work performed by the athlete measured by kilometers ran or duration of training session) and internal loads (i.e. internal response factors within the biological system, measured by subjective rate of perceived exertion (sRPE) for example) can be combined to calculate training load[8]. In our study, no information on internal loads was collected. However, there is no consensus which variables need to be taken into account[16]. Future research is needed to validate an appropriate method to calculate training load in runners and to examine which internal and external variables have to be used.

Only few studies examined the association between change in training load and RRI risk. Traditionally, runners have been advised to not increase their total training distance by more than 10% relative to the previous week[41]. However, a preventive randomized trial among novice runners found no effect of a graded '10% rule' training program on the number of RRIs[14]. Nielsen et al. reported that runners who progressed their training distance by more than 30% seemed more vulnerable to sustain an RRI compared to runners who increased their running distance by less than 10%[15]. Studies that examined the association between ACWR and running injury risk showed conflicting results[21-24]. Reasons for these conflicting results might be the differences in sample size, data collection (questionnaire or GPS data) and the methods used to calculate ACWRs. Dijkhuis et al. calculated change in training load with the coupled RA method in a small study of 23 competitive runners with the use of questionnaires and expressed ACWRs as the combination of training duration and sRPE[21]. This study demonstrated that a fortnightly low increase of ACWR (0.10-0.78) led to a 4.5-fold increase in injury risk and a low increase (0.05-0.62) of the week-to-week ACWR difference between week three and two before an injury led to a 2.7-fold increase in injury risk[21]. Nakaoka et al. calculated ACWRs with the use of a database composed of data from three studies in which questionnaires were used to collect running distance and duration of 435 recreational runners and concluded that the higher the ACWR (uncoupled and coupled RA method), the lower the risk of an RRI[23]. Also, no association was found between EWMA values and risk for sustaining an RRI[23]. In another small study, Matos et al. calculated training loads in 25 competitive male trail runners with the use of GPS data and calculated ACWRs for running duration, distance, and sRPE values separately[22]. This study reported significant weekly increases in all ACWR measures in the weeks prior to the onset of an RRI[22]. A recent study by Toresdahl et al. calculated the number of days when the ACWR was ≥ 1.3 or ≥ 1.5 and showed that increases in training volume ≥ 1.5 were associated with more injuries among runners training for a marathon[24]. The high variability of the previous studies makes it difficult to conclude if and how change in training load is associated with injury risk in runners. Therefore, future research on the complex relation between training loads, the most sensitive method to calculate change in training load, and risk for sustaining an RRI is needed.

Strengths and limitations

A strength of this study was the large sample size of 430 participants who shared usable GPS training data with a total of 22,839 training sessions. To our knowledge, only one other study collected this large amount of GPS training data to calculate change in training load in runners[24]. A limitation of this study was that participants who shared GPS data were more often males who had on average more running experience, were more often member of an athletic association and more often used a training schedule compared to participants who did not share GPS data (Table 1). This could jeopardize the generalizability of this study. However, because our study purpose was to investigate differences in training load methods, this selective population was not expected to impact the study outcomes. Another limitation was that the ACWR is measured based on the training load of the previous seven days and the previous 28 days per training session. Therefore, the first 27 days of data could not be used to calculate ACWRs. To calculate change in training load of the same number of training sessions for the ACWR methods and weekly training load method, the first 27 days of data was removed for all methods. However, this decreased the number of total data that we could use for calculating our outcome measure.

CONCLUSION

The difference in calculated change in training load expressed in weekly training load method and ACWR methods (coupled ACWR and EWMA) was high. We found smaller differences between the three ACWR methods (coupled ACWR, uncoupled ACWR, and EWMA method). To validate an appropriate measure of change in training load in runners, future research on the complex relation between training loads, the most sensitive method to calculate change in training load, and risk for sustaining an RRI is needed.

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SUPPLEMENTARY FILES

Supplementary table 1. Formulas to calculate training load.

	Weekly training load	Coupled ACWR[a]	Uncoupled ACWR	EWMA[b]
Formula	$\frac{A}{W2} * 100$	$\frac{A}{0.25 * (A+W2+W3+W4)}$	$\frac{A}{0.33 * (W2+W3+W4)}$	$load_{today} * \lambda a + ((1 - \lambda a) * EWMA_{yesterday})$
Definition	A = training load of current training session + 6 days prior to this training session W_t= training load of the previous weeks are represented by W2, W3 and W4, respectively			$\lambda a = 2 / (N + 1)$ N=7 days for the acute workload and 28 days for the chronic workload

[a]Acute:Chronic Workload Ratio; [b]Exponentially Weighted Moving Averages.

Supplementary table 2. Number of training sessions with significant increase in training load calculated by the weekly training load, coupled RA, and EWMA.

	N (%)
Coupled RA (yes)	310 (3.1)
Weekly training load (yes)	4252 (43.0)
EWMA (yes)	1128 (11.4)
Coupled RA and weekly training load (yes)	1008 (10.2)
Coupled RA and EWMA (yes)	826 (8.4)
Weekly training load and EWMA (yes)	817 (8.3)
Coupled RA, EWMA, and weekly training load (yes)	1545 (15.6)

For the weekly training load method, a significant increase in training load was defined as ≥ 30% progression. For the rolling-average (RA) method and exponentially weighted moving averages (EWMA) method, a significant increase in training load was defined as ACWRs ≥ 1.5.

Supplementary table 3. Number of training sessions with significant increase in training load calculated by the coupled RA, uncoupled RA, and EWMA.

	N (%)
Coupled RA (yes)	1 (0.0)
Uncoupled RA (yes)	1741 (23.6)
EWMA (yes)	1277 (17.3)
Coupled RA and uncoupled RA (yes)	1317 (17.9)
Coupled RA and EWMA (yes)	188 (2.5)
Uncoupled RA and EWMA (yes)	668 (9.1)
Coupled RA, uncoupled RA, and EWMA (yes)	2183 (29.6)

For the rolling-average (RA) methods and exponentially weighted moving averages (EWMA) method, a significant increase in training load was defined as ACWRs ≥ 1.5.

Chapter 7

Association between GPS-based training load and injury risk in recreational runners
a large prospective study

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Submitted

ABSTRACT

Objective: To investigate the association between training load and injury risk in recreational runners with the use of global positioning system (GPS) data.

Methods: We conducted a study in runners who registered for running events (distances 10-42.195 kilometers). Adult runners who provided informed consent received three follow-up questionnaires and were requested to share GPS data. GPS-based training load was calculated as acute:chronic workload ratio (ACWR) based on distance, duration, or speed of each training session. Cox regression models were performed to evaluate the association (hazard ratio; HR) between ACWR and RRI onset.

Results: GPS data of 461 participants (72.9% men; mean (SD) age 43.8 (12.4) years; 42.3% reported a new RRI during follow-up) were used for analyzes with a total of 20,425 training sessions. A positive association between ACWR and RRI onset was found for distance (HR 1.32; 95% CI 1.00-1.74) and duration (HR 1.39; 95% CI 1.07-1.79). Though in the analyzes adjusted for known risk factors only ACWR based on duration (HR 1.33; 95% CI 1.02-1.74) remained positively associated with RRI onset. No significant association was found between ACWR and RRI onset when excluding runners with an RRI at baseline (15.8%).

Conclusion: We identified an association between ACWR and RRI onset in runners based on distance and duration respectively. The clinical relevance of the identified associations are questionable given the small HRs and inconsistency in outcomes which makes the role of general training load advice in the prevention of RRIs uncertain.

INTRODUCTION

Running is a highly popular form of exercise for adults worldwide[1]. In 2020, running was the sport with most reported injuries in the Netherlands, with an incidence of 7.5 RRIs per 1,000 running hours[2]. RRIs can lead to both health and economic burden, including physical discomfort, decreased workability, increased healthcare utilization, and societal costs[3,4]. Regarding the injury mechanism, overuse is considered the most important cause of RRIs as it accounts for 64-75% of all RRIs[3,5]. Compared to acute RRIs, overuse injuries tend to be more severe and costly over time, resulting in a greater health and economic burden[3]. This emphasizes the need for interventions to prevent overuse injuries in runners.

Training load is believed to play an important role in the development of overuse RRIs, because high training loads might create an imbalance between the cumulative loads and load-bearing capacity of the musculoskeletal tissues[6-8]. Prevention of RRIs with training load advice has been widely implemented by coaches, physiotherapists, and sport associations, despite absence of clear evidence. In runners, only a few studies examined the relationship between training load and RRIs and found conflicting results[9-13]. The main reason for these findings is the heterogeneity in study methodology. Studies differed in study populations, applied methods, definition of training load, and data collection (questionnaires versus global positioning system (GPS) data). Training characteristics determined by means of questionnaires are collected retrospectively, which may lead to recall bias resulting in inaccurate data[14]. GPS data can accurately measure several aspects of training load and is feasible to collect GPS data in a large cohort of runners[15-17]. Currently, there is a lack of appropriately sized cohorts using adequate data collection methods, valid outcome measures, and appropriate statistical methods to identify the potential association between training load and running injuries. Understanding the relationship between training load and injury in runners may provide information on how to reduce the risk of RRIs and might eventually result in a prediction of the appropriate load advice for runners. Therefore, the aim of this study was to investigate the association between training load and injury risk in recreational runners with the use of GPS training data.

METHODS

Study design

This study is part of the Shaping up Prevention for Running Injuries in the Netherlands using Ten steps (SPRINT) study, a randomized-controlled trial (RCT) on the effectiveness of an online RRI prevention program[18]. One month before, one week before, and one month after the registered running event follow-up questionnaires were sent to the participants by email. In addition, all participants received biweekly newsletters with a hyperlink to an online injury questionnaire including the question to actively register any new RRI. By the end of follow-up all participants were asked to share their GPS data. The online prevention program did not decrease the number of RRIs, which is why we consider this study as a prospective cohort. The SPRINT study was funded by the Netherlands Organization for Health Research and Development (ZonMW), grant number 50-53600-98-104. Medical ethics approval was obtained by the Medical Ethical Committee of the Erasmus University Medical Center Rotterdam, Netherlands (MEC-2019-0136).

Participants

Recreational runners who registered in 2019-2020 for one of four selected running events in the Netherlands (distances ranging from 10 to 42.2 kilometer (km)) were invited to participate in the SPRINT study. Interested runners who met the inclusion criteria (18 years or older, registration at least 60 days before the running event, sufficient knowledge of the Dutch language, access to internet and email, and no participation in our previous trial on RRI prevention[19]) were asked to provide digital informed consent and subsequently complete the online baseline questionnaire. For the current study purpose, participants were excluded if they did not share GPS training data at the end of follow-up, if their estimated use of a GPS-enabled device or platform was less than 80% of their total running sessions, or if they shared GPS data that did not contain information on running sessions (e.g. GPS data of other sports activities, like cycling or hiking). Participants with a new RRI during follow-up were excluded if the date of the new RRI was unknown.

Data collection

In the baseline questionnaire, information on participants' demographics (sex, age, weight, and height) as well as their training characteristics (average weekly training frequency, hours, distance (km), and running speed (minutes per km) over the last three months) was obtained. Body mass index (BMI) was calculated based on the weight and height. Participants were also asked about their running experience (years), whether they were member of a running club (yes/no), use of training schedule (yes/no), experience of an RRI in the 12 months before baseline (yes/no) and at baseline (yes/no), use of a GPS-enabled device or platform (yes/no), and number of recorded training sessions (< 80% or 80-100% of all sessions). Based on the registered distance of the running event, participants were categorized into 10/10.55 km, 15/16.1 km, half marathon, and marathon. In the follow-up and biweekly questionnaires, participants were asked if they sustained a new RRI since completing the previous questionnaire (yes/no). An RRI was defined as a self-reported injury of the muscles, joints, tendons and/or bones in the lower back or lower extremities (hip, groin, thigh, knee, leg, ankle, foot, and toes) that is caused by running (training or competition). The definition of an RRI was that the injury had to be severe enough to cause a reduction in running distance, speed, duration, or frequency for at least seven days or three consecutive scheduled training sessions or the consultation of a physician or other health professional had to be necessary[20]. Participants who reported a new RRI during follow-up were asked to fill in the date of new RRI (biweekly questionnaires) or the number of weeks they already suffered from the RRI (follow-up questionnaires). At the end of follow-up, participants were asked to upload their GPS data to a personalized cloud-based digital environment developed by MoveMetrics[21]. GPS data was automatically standardized, pseudonymized, sensitive metadata (like user credentials) were removed, and GPS-position data was converted into relative distances. Accordingly, researchers downloaded the data through a password protected link.

Acute:chronic workload ratio

Training load was determined by the acute:chronic workload ratio (ACWR). The variables distance, duration, and speed were obtained from collected GPS data. For every running session, ACWR was calculated for each variable, using the coupled RA method, in which the acute workload (the sum of the distance or duration or speed of the running sessions performed in the last seven days) was divided by the chronic workload (the sum of the distance or duration or speed of the running sessions performed in the last 28 days)[22,23]. On the days a participant did not perform a running session, no ACWR was calculated because the runner was not considered to be exposed to an RRI on those days.

Statistical analyzes

Descriptive statistics were used to describe baseline characteristics, expressed in frequency or mean and standard deviations (SDs). Participants who reported a new RRI during follow-up and participants who did not report a new RRI were compared using independent sample t-tests (continuous data), Mann-Whitney U tests (continuous data), and chi-square tests (dichotomous data). We used the same tests to compare participants who did and did not share GPS training data. Cox regression analyzes were performed to examine the association between ACWR and RRI onset. The ACWR was included as a time-varying variable, recalculated for each training. Cox regression models were conducted for ACWRs based on running distance, duration, and speed. ACWRs calculated in the seven days before the running event or RRI onset were not included in the models due to the injury definition in which participants were asked to report an RRI if they have reduced their running distance, speed, duration, or frequency in the last seven days. The time axis of the Cox model was defined to count towards the running event that a participant trained for (and which is considered to be time zero). First, Cox regression analyzes were performed for each variable separately. Second, all analyzes were adjusted for possible pre-defined confounding factors including sex, age, BMI, running experience, registered distance of the running event, previous RRI in the last 12 months, and RRI at baseline. Last, (un)adjusted Cox regression analyzes were performed without participants with an RRI at baseline. Hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) were calculated. P-values <0.05 were regarded as statistically significant. Analyzes were performed using SPSS version 28.0 (SPSS Inc, Chicago, Illinois) and R version 4.3.0 (R Core team (2023)).

RESULTS

Of the 4,050 participants included in the SPRINT study, 508 participants shared their GPS data (Figure 1). Of these, 19 (3.8%) were excluded because they recorded less than 80% of their training sessions (N=15) or did not share GPS data containing information on their running sessions (N=4). Of the remaining 489 participants, 28 (5.7%) participants reported a new RRI during follow-up with an unknown date of injury onset and were excluded for analyzes. Therefore, GPS data of 461 participants (72.9% men; age 43.8 (12.4) years, 10.7 (10.4) years running experience) were used for analyzes with a total of 20,425 training sessions (Table 1). Of the included participants, 51.6% reported an RRI in the 12 months before baseline and 15.8% an RRI at baseline. The mean follow-up duration was 5.0 (range 3.0 – 7.7) months. Compared with participants who did not share GPS data, participants who shared GPS data were more often men (72.9%, vs. 62.2%, p<0.01), had a higher age (43.8 (12.4) vs. 42.1 (12.1), p<0.01), ran more km per week (29.7 (22.2) vs. 26.1 (22.7), p<0.001), and more often reported a new RRI during follow-up (42.3% vs. 34.6%, p<0.01) (Supplementary table 1). Of the participants who shared GPS data, 195 (42.3%) participants reported a new RRI during follow-up. Participants with a new RRI registered less often for the distance 10/10.55 km (8.7% vs. 18.0%, p<0.01) and more often reported a previous RRI in the last 12 months (63.6% vs. 42.9%, p<0.001) compared to participants without a new RRI (Table 1).

The unadjusted Cox regression analyzes showed a positive association between ACWR and RRI onset for running distance (HR 1.32; 95% CI 1.00-1.74, p=0.05) and duration (HR 1.39; 95% CI 1.07-1.79, p=0.01) (Table 2). When Cox regression analyzes were adjusted for known risk factors, a positive association was seen between ACWR based on running duration (HR 1.33; 95% CI 1.02-1.74, p=0.04) and RRI onset. No association between ACWR (based on running distance, duration, or speed) and RRI onset was found when runners with an RRI at baseline (15.8%) were excluded (Table 3). All adjusted Cox regression analyzes showed a positive significant association between the confounding factor previous RRI in the last 12 months and RRI onset (distance: HR 1.63; 95% CI 1.15-2.30, p=0.01, duration: HR 1.63; 95% CI 1.15-2.31, p=0.01, speed: HR 1.62; 95% CI 1.15-2.30; p=0.01). No other confounding factors were significantly associated with RRI onset in the multivariable models.

Table 1. Baseline characteristics of the study population.

	Total (N=461)	RRI (N=195)	No RRI (N=266)
Demographic characteristics			
Sex (male)	336 (72.9)	146 (74.9)	190 (71.4)
Age (years)[a]	43.8 (12.4)	43.3 (12.3)	44.1 (12.4)
BMI (kg/m^2)[a,b]	23.1 (2.5)	23.0 (2.4)	23.1 (2.6)
Training characteristics			
Running experience[a]	10.7 (10.4)	10.3 (9.9)	10.9 (10.8)
Weekly training frequency[a]	2.8 (1.1)	2.9 (1.1)	2.7 (1.2)
Weekly training hours[a]	3.1 (1.7)	3.3 (1.6)	3.0 (1.7)
Weekly training distance (km)[a]	29.7 (22.2)	30.7 (22.6)	29.0 (22.0)
Running speed (min/km)[a]	5.6 (0.7)	5.6 (0.8)	5.7 (0.8)
Membership of a running club (yes)	174 (37.7)	78 (40.0)	96 (36.1)
Use of training schedule (yes)	326 (70.7)	140 (71.8)	186 (69.9)
Running events			
Distance registered for:			
10/10.55 km	65 (14.1)	17 (8.7)	48 (18.0)*
15/16.1 km	67 (14.5)	25 (12.8)	42 (15.8)
Half marathon	98 (21.3)	48 (24.6)	50 (18.8)
Marathon	231 (50.1)	105 (53.8)	126 (47.4)
Running-related injury			
Previous RRI[c] in the last 12 months (yes)	238 (51.6)	124 (63.6)	114 (42.9)*
Reported RRI at baseline (yes)	73 (15.8)	38 (19.5)	35 (13.2)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between participants with and without an RRI during follow-up ($p<0.05$); [b] Body Mass Index; [c] Running-related injury.

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Table 2. Cox Regression Models of variables associated with a running-related injury (N=461).

	Distance	
	HR[a] (95% CI)	**p-value**
Unadjusted		
ACWR[b]	1.32 (1.00-1.74)*	0.05
Adjusted		
ACWR	1.26 (0.95-1.68)	0.15
Sex (male)	0.93 (0.66-1.32)	0.68
Age (years)	0.99 (0.97-1.00)	0.09
BMI (kg/m²)[c]	1.03 (0.97-1.09)	0.40
Running experience (years)	1.00 (0.98-1.01)	0.65
Registered distance running event		
10/10.55 km	Reference	
15/16.1 km	0.94 (0.50-1.79)	0.86
Half marathon	1.29 (0.79-2.10)	0.30
Marathon	0.78 (0.49-1.23)	0.28
Previous RRI[d] in the last 12 months	1.63 (1.15-2.30)*	0.01
Reported RRI at baseline	1.17 (0.80-1.71)	0.41

* = statistically significant association with a running-related injury ($p<0.05$); [a] Hazard ratio; [b] Acute:Chronic Workload Ratio; [c] Body Mass Index; [d] Running-related injury.

Table 3. Cox Regression Model of variables associated with a running-related injury excluding participants with a running-related injury at baseline (N=388).

	Distance	
	HR[a] (95% CI)	**p-value**
Unadjusted		
ACWR[b]	1.18 (0.84-1.66)	0.35
Adjusted		
ACWR	1.16 (0.82-1.64)	0.41
Sex (male)	0.90 (0.60-1.36)	0.62
Age (years)	0.99 (0.97-1.00)	0.10
BMI (kg/m²)[c]	1.02 (0.95-1.09)	0.61
Running experience (years)	1.00 (0.98-1.02)	0.79
Registered distance running event		
10/10.55 km	Reference	
15/16.1 km	1.16 (0.55-2.46)	0.70
Half marathon	1.41 (0.74-2.68)	0.29
Marathon	0.70 (0.53-1.77)	0.92
Previous RRI[d] in the last 12 months	1.57 (1.11-2.23)*	0.01

* = statistically significant association with a running-related injury ($p<0.05$); [a] Hazard ratio; [b] Acute:Chronic Workload Ratio; [c] Body Mass Index; [d] Running-related injury.

	Duration		Speed	
	HR (95% CI)	p-value	HR (95% CI)	p-value
	1.39 (1.07-1.79)*	0.01	1.31 (0.96-1.78)	0.09
	1.33 (1.02-1.74)*	0.04	1.25 (0.91-1.72)	0.17
	0.93 (0.66-1.32)	0.68	0.93 (0.66-1.32)	0.69
	0.99 (0.97-1.00)	0.09	0.99 (0.97-1.00)	0.09
	1.03 (0.97-1.09)	0.41	1.03 (0.97-1.09)	0.40
	1.00 (0.98-1.01)	0.66	1.00 (0.98-1.01)	0.65
	Reference		Reference	
	0.95 (0.50-1.80)	0.87	0.94 (0.50-1.78)	0.85
	1.30 (0.80-2.11)	0.29	1.29 (0.79-2.10)	0.31
	0.78 (0.49-1.24)	0.29	0.77 (0.49-1.23)	0.27
	1.63 (1.15-2.31)*	0.01	1.62 (1.15-2.30)*	0.01
	1.17 (0.80-1.70)	0.42	1.18 (0.81-1.72)	0.39

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	Duration		Speed	
	HR (95% CI)	p-value	HR (95% CI)	p-value
	1.22 (0.88-1.69)	0.24	1.15 (0.79-1.68)	0.48
	1.20 (0.86-1.68)	0.29	1.12 (0.76-1.65)	0.57
	0.90 (0.60-1.36)	0.62	0.90 (0.60-1.36)	0.63
	0.99 (0.97-1.00)	0.11	0.99 (0.97-1.00)	0.10
	1.02 (0.95-1.09)	0.62	1.02 (0.95-1.09)	0.61
	1.00 (0.98-1.02)	0.79	1.00 (0.98-1.02)	0.79
	Reference		Reference	
	1.17 (0.55-2.47)	0.69	1.16 (0.55-2.45)	0.70
	1.42 (0.75-2.69)	0.29	1.40 (0.74-2.67)	0.30
	0.97 (0.53-1.79)	0.93	0.96 (0.53-1.77)	0.91
	1.58 (1.11-2.23)*	0.01	1.57 (1.11-2.22)*	0.01

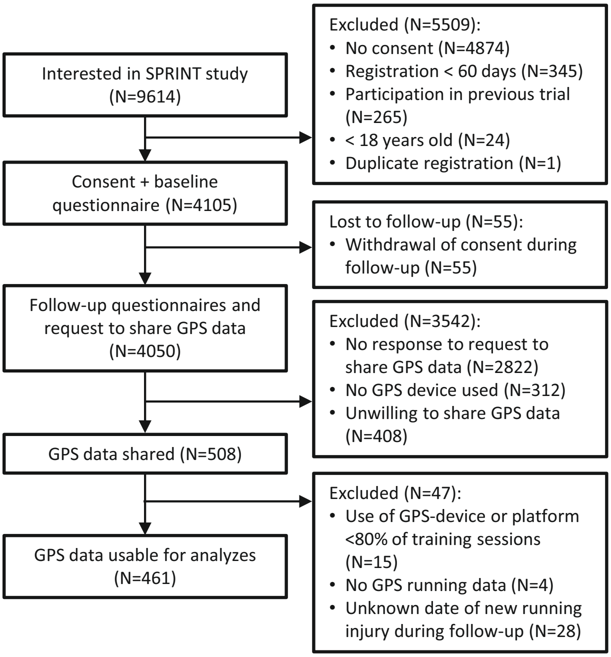

Figure 1. Flowchart of the participants.

DISCUSSION

The purpose of this study was to explore the association between ACWR and injury onset in recreational runners. We identified a positive association between ACWR (based on running distance and duration) and RRI onset, with relatively small hazard ratios. When adjusting for possible predefined confounding factors, only the positive association between ACWR based on running duration and RRI onset remained. No association was found between ACWR (based on running distance, duration, or speed) and RRI onset when runners with an RRI at baseline were excluded.

The association between ACWR and injury risk has been examined across a wide range of team sports populations[24]. These studies concluded that the risk of injury was relatively low if the ACWR ranges from 0.8 to 1.3[22,24,25]. More recently, few studies among runners examined the association between ACWR and injury risk[9,11,12]. Dijkhuis et al. reported that a fortnightly low increase of the ACWR and a low increase between the second and third week before an RRI lead to an increased injury risk[9]. Nakaoka et al. found an association between ACWR and RRIs, suggesting that the higher the ACWR, the lower the RRI risk, while Toresdahl et al. concluded that increases in training volume ≥ 1.5 ACWR were associated with more

RRIs[11,12]. Matos et al. reported significant weekly increases in ACWR in the three weeks prior to an injury's occurrence in trail runners[10].These studies found conflicting results, likely due to the heterogeneity in ACWR definition and applied study methodology. There is a large heterogeneity in variables used to calculate ACWR, including covered distance[10-12], duration of activity [10,11], rate of perceived exertion[10], or a combination of duration and rate of perceived exertion[9]. We calculated ACWRs based on distance, duration, or speed and considered these variables most valuable as running progression is usually monitored and assessed by these variables and are relatively easy to collect with high reliability[15-17]. It remains however unknown which variable can best be used to calculate training load in running.

Study methodology is heterogeneous in studies that investigated the association between ACWR and RRI risk. Recent studies used different statistical models to analyze the association between ACWR and injury risk[9,11-13]. It is likely that the relationship between training load and injury risk is non-linear and that the training load of a runner vary over time due to multiple training load exposures in the past[26,27]. Therefore, a Cox regression model seems the most appropriate model to calculate the association between ACWR and RRI onset, taking both non-linearity and time varying concept into account. A recent study by Toresdahl et al. calculated the number of days when the ACWR was ≥ 1.3 or ≥ 1.5 before analyzing the results[12]. These thresholds were selected because they have been associated with injury risk in other sport populations. However, it is unknown if these thresholds can be applied in running. Last, ACWR can be calculated weekly, for each training session, or per day. In the present study, the ACWR was calculated for each day a running session was performed and not for the days participants were not exposed to running. However, little is known if runners are at injury risk on days that the runner is not exposed to a running training. Future studies should try to further deepen our understanding of training load and injuries. Since there are different types of overuse injuries, it may be especially important to investigate certain types of overuse injuries instead of all injuries together. We currently used GPS data with general load parameters as outcome. This might be imprecise for specific injuries. Development of Smart garments can accurately assess local tissue loads. This might increase the likelihood of finding associations between local tissue load and specific injuries in future studies.

Clinical Implications

The ACWR based on running duration showed a significant association with RRI onset in the unadjusted and adjusted analyzes. In the adjusted analysis, a hazard ratio of 1.33 was reported, meaning that a runner is 33% more likely to suffer an RRI if the ACWR increases by one point on a given training day. Of the 20,425 training sessions, only 0.7% showed an increase of more than one point ACWR compared to the previous training session. Given this low percentage, the clinical relevance of the significant associations found is questionable.

Without participants with an RRI at baseline, no association between ACWR and RRI onset was identified for all variables examined (distance, duration, and speed). A reason that no association was found when excluding this subgroup of runners might be associated with their potential increase in training volume while recovering from their RRI during study follow-up resulting in an increase of the ACWR compared to participants with no injury. Another reason that no association was found might be the reduced power of the analyzes since 15.8% of the participants were excluded. Due to the reasons stated above we feel that the significant associations found in this study should be interpreted with caution. It is important for healthcare providers working with RRIs and sport associations to realize that we found no compelling evidence that 'overuse' leads to more injuries in recreational runners.

Strengths and limitations

To our knowledge, this is one of the largest prospective cohort study using GPS data to examine associations between training load and injury onset in runners so far. A limitation of this study was the selection of participants. Participants who did not share GPS data were on average younger runners who trained less often and less often used a training schedule compared to participants who shared GPS data (Supplementary table 1). Due to the small differences between participants who did and did not share GPS data, we do not expect that this selective population impact the study outcomes. Another limitation was the lack of information about the onset of first symptoms of a new RRI. An RRI was defined as an injury that was caused by running which was severe enough to cause reduction in running for at least seven days or three consecutive scheduled training sessions or if it was necessary to consult a health professional. Participants might experience first symptoms of an RRI before meeting the definition of an RRI. Due to these symptoms, they might have already changed their running behavior which influenced the ACWR. Therefore we chose to calculate the ACWR until seven days before the date of RRI onset. However, it is not known if participants already altered their running behavior before those seven days.

CONCLUSION

We identified a small association between training load, expressed in ACWR based on running distance and duration, and RRI onset in runners. When adjusting for known risk factors, only ACWR based on running duration remained positively associated with injury onset. No association between ACWR and RRI onset was found when excluding participants with an RRI at baseline. The clinical relevance of the identified associations are questionable given the small HRs and inconsistency in outcomes.

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SUPPLEMENTARY FILES

Supplementary table 1. Baseline characteristics of participants who did and did not share GPS data.

		GPS data shared	
	Total (N=4050)	**Yes (N=461)**	**No (N=3589)**
Demographic characteristics			
Sex (male)	2570 (63.5)	336 (72.9)	2234 (62.2)*
Age (years)[a]	42.3 (12.1)	43.8 (12.4)	42.1 (12.1)*
BMI (kg/m²)[a,b]	23.3 (2.6)	23.1 (2.5)	23.3 (2.6)*
Training characteristics			
Running experience (years)[a]	10.3 (10.1)	10.7 (10.4)	10.2 (10.1)
Weekly training frequency[a]	2.6 (1.3)	2.8 (1.1)	2.5 (1.3)*
Weekly training hours[a]	3.1 (2.8)	3.1 (1.7)	3.1 (2.9)*
Weekly training distance (km)[a]	26.5 (22.7)	29.7 (22.2)	26.1 (22.7)*
Running speed (min/km)[a]	5.8 (0.9)	5.6 (0.7)	5.8 (0.9)*
Member of athletic association (yes)	1210 (29.9)	174 (37.7)	1036 (28.9)*
Use of training schedule (yes)	2636 (65.1)	326 (70.7)	2310 (64.4)*
Running events			
Distance registered for:			
10/10.55 km	894 (22.1)	65 (14.1)	829 (23.1)*
15/16.1 km	534 (13.2)	67 (14.5)	467 (13.0)
Half marathon	579 (14.3)	98 (21.3)	481 (13.4)*
Marathon	2043 (50.4)	231 (50.1)	1812 (50.5)
Running-related injury			
RRI[c] 12 months before baseline (yes)	2000 (49.4)	238 (51.6)	1762 (49.1)
Reported RRI at baseline (yes)	763 (18.8)	73 (15.8)	690 (19.2)
New RRI during follow-up (yes)	1436 (35.5)	195 (42.3)	1241 (34.6)*

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between participants who did and did not share GPS data ($p<0.05$); [b] Body Mass Index; [c] Running-related injury.

Part 3

Prevention of running-related injuries

Chapter 8

Educational online prevention program (the SPRINT study) has no effect on the number of running-related injuries in recreational runners

a randomized-controlled trial

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ABSTRACT

Objective: The aim of this study was to examine the effectiveness of an enhanced online injury prevention program on the number of running-related injuries (RRIs) in recreational runners.

Methods: We conducted a randomized-controlled trial in runners who registered for running events (distances 10–42.195 km) in the Netherlands. Adult runners who provided informed consent were randomized into the intervention or control group. Participants in the intervention group received access to the online prevention program, which included items to prevent RRIs. Participants in the control group followed their regular preparation for the running event. The primary outcome measure was the number of new RRIs from baseline to one month after the running event. To determine differences between injury proportions, univariate and multivariate logistic regression analyzes were performed.

Results: This study included 4050 recreational runners (63.5% males; mean (SD) age 42.3 (12.1) years) for analyzes. During follow-up, 35.5% (95% CI 33.5-37.6) of the participants in the intervention group sustained a new RRI compared with 35.4% (95% CI 33.3-37.5) of the participants in the control group, with no between-group difference (OR 1.03; 95% CI 0.90-1.17). There was a positive association between the number of items followed in the injury prevention program and the number of RRIs (OR 1.05; 95% CI 1.00-1.11).

Conclusion: The enhanced online injury prevention program had no effect on the number of RRIs in recreational runners, and being compliant with the program paradoxically was associated with a slightly higher injury rate. Future studies should focus on individual targeted prevention with emphasis on the timing and application of preventive measures.

Trial registration number: NL7694.

INTRODUCTION

Running is a popular form of physical activity: it is easy to perform, easily accessible and has a range of health-related benefits[1-3]. Unfortunately, running can also be associated with a high number of running-related injuries (RRIs) with a prevalence between 10% and 92%[4-6]. This large range is likely due to a lack of consistency in defining an injury heterogeneity of studied running populations and variable exposure times[4].

As first steps towards prevention of RRIs, risk factors have been assessed in multiple studies. These studies identified several risk factors, including a previous RRI, no previous running experience, higher body mass index, higher age, and a high weekly running distance[7-9]. The large variety of risk factors indicates that the cause of RRIs is multifactorial[10]. However, most prevention studies focused on modifying one single risk factor for RRIs, for example no previous running experience and increasing training load too fast[11,12]. These studies found no effect on the number of RRIs, which may be due to the fact that they targeted only one single risk factor. In addition, literature shows that runners' assumptions on RRI prevention is not supported by scientific evidence which demonstrates the need to inform runners on known risk factors[13,14]. In 2017, we designed the Intervention Study on Prevention of Injuries in Runners at Erasmus MC (INSPIRE) trial, a randomized-controlled trial (RCT) in which the effect of a multifactorial online injury prevention program on the number of RRIs was investigated[15]. This program did not decrease the number of RRIs in recreational runners. However, new insights were gained to enhance injury prevention in runners, including runners' opinions, barriers, and facilitators of injury prevention[16,17]. We found indications that the prevention program even increased the number of new RRIs in runners with no previous RRI[17]. Therefore, we concluded that research on RRI prevention should target runners who previously reported injuries, because these runners seem to be more motivated to perform preventive measures than runners with no history of RRIs[16]. Furthermore, runners reported that a website and application were the most preferred routes of information delivery. Last, participants indicated that 'not knowing what to do' was an important barrier for injury prevention[16]. As shown by Hesphanol et al. in trail runners, online tailored advice may have the potential to prevent RRIs[18]. Specific potential educational content was earlier suggested by Murray et al. and Blagrove et al. in terms of registration and monitoring of weekly training load and the integration of running-specific strengthening exercises in training schedules[19,20]. Runners clearly prefer practical and straight instructions with the use of animations and interactive tools, which can be integrated into their training sessions with great ease.

Therefore, we designed an enhanced online injury prevention program entitled '10 steps 2 outrun injuries'. The aim of this study was to examine the effectiveness of this prevention program on the number of RRIs in recreational runners.

METHODS

Study design

The Shaping up Prevention of Running Injuries in the Netherlands using Ten steps (SPRINT) study is an RCT in recreational runners with a minimum follow-up of three months. A detailed study protocol of the SPRINT study has been published elsewhere[21]. This study was funded by the Netherlands Organization for Health Research and Development (ZonMW, grant number 50-53600-98-104) and was performed in collaboration with the Rotterdam Marathon Study Group of Golazo Sports, the organizer of large running events in the Netherlands.

Participants

Runners who registered for the DSW Bruggenloop Rotterdam 2019 (15 km), Nacht van Groningen 2020 (10, 16.1 and 21.1 km), NN CPC Loop The Hague 2020 (10 and 21.1 km), or NN Marathon Rotterdam 2020 (10.55 and 42.195 km) were asked to participate in this study through a question on the online registration form. Interested runners who met the inclusion criteria (18 years or older, registration at least two months before the running event, sufficient knowledge of the Dutch language, access to internet and email, and no participation in the previous INSPIRE trial) received more information about the SPRINT study by email. If they were still interested, participants were asked to provide digital informed consent and complete the baseline questionnaire. For runners who registered for multiple selected running events only the first registration was taken into account.

Randomization and follow-up

After completing the baseline questionnaire, participants were randomized into either the intervention or control group, using a computer-generated randomization list (Microsoft Access) with block sizes of 40. The allocation was concealed, as the randomization table was generated by an individual from outside the research group and was not accessible for the research team during the inclusion and data collection. The participants were informed on the outcome of the randomization by a member of the research team. Participants in the intervention group received a personal login code to the website that included the prevention program, to which they had unlimited access. Moreover, a Web App version was made available. Participants in the control group followed their regular preparation for the running event. During follow-up, all participants received three follow-up questionnaires to inform on new RRIs in the time frame between the last questionnaire and current questionnaire: one month and one week before the running event, and one month after the running event. In addition, all participants received every two weeks a newsletter with updates on the SPRINT study and a hyperlink to an online injury questionnaire with the question to actively register any new RRI. The newsletters for the intervention group additionally highlighted one of the items of the prevention program.

The ‘10 steps 2 outrun injuries’ prevention program

The prevention program was based on literature, the expertise of clinicians and researchers and the results and knowledge gained through the INSPIRE trial[15-17]. This program included 10 items with specific advice and tools to prevent RRIs (Supplementary figure 1). More detailed information about the items can be found elsewhere[21].

Measurements

Items of the four sections (demographics, training, running events, and previous RRI) collected through the baseline questionnaire are presented in Supplementary table 1. Information on new RRIs was obtained with the follow-up questionnaires and the biweekly injury questionnaires (Supplementary table 1).

Outcome measures

The primary outcome measure of this study is the difference in injury proportion between the intervention and control group from baseline to one month after the running event, based on participants with at least one new injury reported in the follow-up questionnaires and the injury questionnaires filled-in through the biweekly newsletters. An RRI was defined as a self-reported injury of the muscles, joints, tendons, and/or bones in the lower back or lower extremities (hip, groin, thigh, knee, leg, ankle, foot, and toes) that is caused by running (training or competition). The injury had to be severe enough to cause a reduction in running distance, speed, duration, or frequency for at least seven days or three consecutive scheduled training sessions or the consultation of a physician or other health professional had to be necessary[22]. Secondary outcome measures included the clustered injury location, severity of RRIs based on the OSTRC Overuse Injury Questionnaire, and medical consumption.

Sample size

Based on the INSPIRE trial, an injury incidence of 38% was expected in recreational runners who register for a running event (distance 10–42.195 km) at least two months before the running event until one month after the running event[17]. Since the prevention program was focused on runners with a previous RRI, the sample size calculation was based on the subgroup analysis of runners with a previous RRI. With a risk difference of 5%, 0.05 significance level (two-sided testing and a power of 80%), a minimum of 1414 runners with a previous RRI had to be included in the analyzes to detect a relevant difference in RRIs. Since the INSPIRE trial reported that 52.1% of the participants sustained a previous RRI, the sample size was doubled in order to obtain enough power for the primary analyzes in the entire study population[15]. Taking a loss to follow-up of 20% into account, at least 3394 runners had to be included in this study.

Statistical analyzes

Descriptive statistics were used to describe all variables, expressed in frequency or mean and standard deviations (SDs). Participants in the intervention and control group were compared with independent sample t tests (continuous data), Mann-Whitney U tests (continuous data) and chi-square tests (dichotomous data). Consistent with the Consolidated Standards of Reporting Trials (CONSORT) statement, an intention-to-treat analysis was performed[23]. Injury proportions with 95% confidence intervals (CIs) were calculated for all participants and for the intervention and control group separately, for which a difference in injury proportion was calculated. To correct for errors, we checked whether participants who reported an RRI filled in an RRI on the same location in the previous questionnaire. If not, the RRI was interpreted as a new RRI. If they did, this RRI was not regarded as a new RRI. Additionally, odds ratios (ORs) with 95% CI were calculated using univariate logistic regression analysis. Potential confounders (age, body mass index (BMI), and a previous RRI) and baseline characteristics with a significant difference between the intervention and control group were added one by one to the univariate regression model. If a potential confounder altered the unadjusted estimate effect by 10% or more, this confounder was added to the multivariate logistic regression model to calculate adjusted ORs and to the generalized linear models to calculate adjusted risk ratios. Predefined subgroup analyzes were performed for distance of running event, sex, running experience (≤ 1 year/> 1 year), a previous RRI, and reported RRI at baseline. Moreover, between-group differences in the clustered injury locations (lower back, hip/groin, upper leg/knee, lower leg (shin/calf/Achilles tendon/ankle), and foot/toe) were analyzed. Based on the request of peer reviewers, we made a minor protocol deviation in the predefined subgroup analysis; we calculated the injury proportion and adjusted ORs for participants without an RRI at baseline. With the OSTRC Overuse Injury Questionnaire, the OSTRC severity score (0–100) of new RRIs was calculated and every new RRI was categorized into a substantial overuse injury (yes/no)[24]. Next, between-group differences in OSTRC severity score, substantial overuse injury, pain score (Numeric Rating Scale (0-10)), use of painkillers and/or non-steroidal anti-inflammatory drugs (NSAIDs), and medical attention were calculated. A sensitivity analysis was performed to compare the injury proportion of participants in the intervention group who were compliant with the prevention program with the injury proportion of the control group. Participants were regarded compliant if they reported that they applied at least one item from the prevention program to their training sessions. Last, an explorative additional analysis on the number of used items in relation to the injury risk was performed using univariate logistic regression analyzes. All analyzes were performed in SPPS Statistics V.25 and p-values <0.05 were regarded as statistically significant. Missing data were not imputed and analyzes were based on complete data.

RESULTS

Participants

After registration for one of the selected running events, 9614 runners were interested in participation in the SPRINT study (Figure 1). Of these, 4105 participants were included and randomized into either the intervention group (N=2054) or control group (N=2051). During follow-up, 55 participants were lost due to withdrawal of consent. A total of 2023 participants in the intervention group and 2027 participants in the control group were included for analyzes. Compared with participants in the control group, participants in the intervention group were at baseline on average (SD) older (42.8 (12.4) vs. 41.7 (11.9), p=0.01) and had a higher BMI (23.4 (2.6) vs. 23.2 (2.6), p=0.01) (Table 1). A total of 2000 (49.4%) participants reported a previous RRI in the last 12 months. Compared with participants in the control group, participants in the intervention group reported less RRIs at baseline (17.4% vs. 20.3%, p=0.02).

Follow-up questionnaires

The mean follow-up duration was 5.0 (range 3.0–7.8) months, with no between-group difference. A total of 3312 (81.8%) participants completed at least one of the follow-up questionnaires, while 2329 (57.5%) participants completed all follow-up questionnaires. Participants who did not complete any of the follow-up questionnaires were on average (SD) younger (37.8 (10.7) vs. 43.3 (12.2), p<0.001), had less running experience (8.0 (8.6) vs. 10.8 (10.3) years, p<0.001) and participated less often in a previous running event (89.8% vs. 94.4%, p<0.001) compared with participants who completed at least one follow-up questionnaire (Supplementary table 2).

Primary outcome measure

During follow-up, 1436 participants (35.5%, 95% CI 34.0-36.9) sustained a new RRI, with a total of 2245 new injuries (1131 RRIs in the control group and 1114 RRIs in the intervention group) (Table 2). The injury proportion for the intervention group was 35.5% (95% CI 33.5-37.6) and for the control group 35.4% (95% CI 33.3-37.5), with no differences between groups (adjusted OR 1.03; 95% CI 0.90-1.17).

Subgroup analyzes and secondary outcome measures

In all participants, the most reported injured location was the knee (11.0% in the control group and 10.4% in the intervention group) (Figure 2). There were no significant differences in the clustered injury locations between the intervention and control group (Table 2). Subgroup analyzes performed for the distance of running event registered for, sex, running experience, previous RRI, and reported RRI at baseline showed no significant differences in injury proportions between the intervention and control group either (Table 3). In participants without an RRI at baseline, the injury proportion was 33.1% (95% CI 30.8-35.3) in the intervention group and 32.6% (95% CI 30.3-34.9) in the control group, with no differences between groups (adjusted OR 1.03; 95% CI 0.89-1.20) (Supplementary table 3).

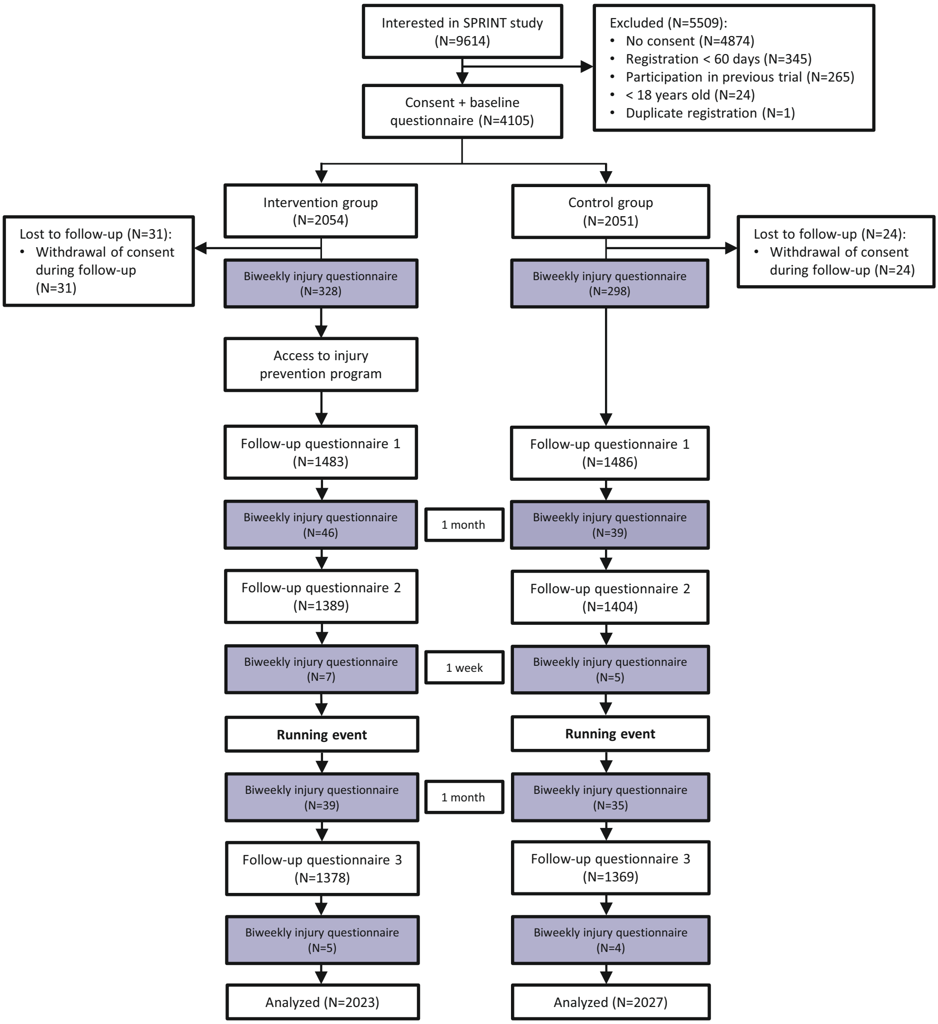

Figure 1. Flowchart of the SPRINT study. SPRINT, Shaping up Prevention of Running Injuries in the Netherlands using Ten steps.

Table 1. Baseline characteristics of the study population.

	Total (N=4050)	Intervention group (N=2023)	Control group (N=2027)
Demographics			
Sex (male)	2570 (63.5)	1299 (64.2)	1271 (62.7)
Age (years)[a]	42.3 (12.1)	42.8 (12.4)	41.7 (11.9)*
BMI (kg/m²)[a, b]	23.3 (2.6)	23.4 (2.6)	23.2 (2.6)*
Training characteristics			
Running experience (years)[a]	10.3 (10.1)	10.4 (10.2)	10.1 (10.0)
Weekly training frequency[a]	2.6 (1.3)	2.6 (1.3)	2.6 (1.3)
Weekly training hours[a]	3.1 (2.8)	3.1 (2.6)	3.1 (3.0)
Weekly training distance (km)[a]	26.5 (22.7)	26.8 (21.4)	26.2 (23.8)
Running speed (min/km)[a]	5.8 (0.9)	5.8 (0.8)	5.8 (0.9)
Type of training (%)			
Endurance training	70.6 (21.4)	70.5 (21.4)	70.7 (21.4)
Interval training	22.5 (17.7)	22.6 (17.9)	22.4 (17.6)
Specific exercises	6.9 (9.9)	6.9 (9.8)	7.0 (10.1)
Membership of a running club (yes)	1210 (29.9)	612 (30.3)	598 (29.5)
Use of training schedule (yes)	2636 (65.1)	1307 (64.6)	1329 (65.6)
Participation in another sport than running (yes)	3276 (80.9)	1634 (80.8)	1642 (81.0)
Running events			
Distance registered for:			
10/10.55 km	894 (22.1)	455 (22.5)	439 (21.7)
15/16.1 km	534 (13.2)	268 (13.2)	266 (13.1)
Half marathon	579 (14.3)	291 (14.4)	288 (14.2)
Marathon	2043 (50.4)	1009 (49.9)	1034 (51.0)
Participation in a previous running event (yes)	3791 (93.6)	1901 (94.0)	1890 (93.2)
Average participations per year[a]	8.1 (8.7)	8.3 (8.8)	8.0 (8.6)
RRI[c]			
Previous RRI in the last 12 months (yes)	2000 (49.4)	979 (48.4)	1021 (50.4)
Reported RRI at baseline (yes)	763 (18.8)	351 (17.4)	412 (20.3)*

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between intervention and control group ($p<0.05$); [b] Body Mass Index; [c] Running-related injury.

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Table 2. Total number of injuries and per clustered injury location with differences between the intervention group and control group (N=4050).

	Total N (%)	Intervention group N (%)
Primary outcome		
Newly reported RRI[c] during follow-up (yes)	1436 (35.5)	719 (35.5)
Secondary outcome: injury location		
Lower back	170 (4.2)	86 (4.3)
Hip/groin	247 (6.1)	128 (6.3)
Upper leg/knee	637 (15.7)	314 (15.5)
Lower leg	597 (14.7)	304 (15.0)
Foot/toe	243 (6.0)	120 (5.9)

[a] Adjusted for the variables age, BMI, RRI in previous 12 months, and reported RRI at baseline; [b] Control group is reference; [c] Running-related injury.

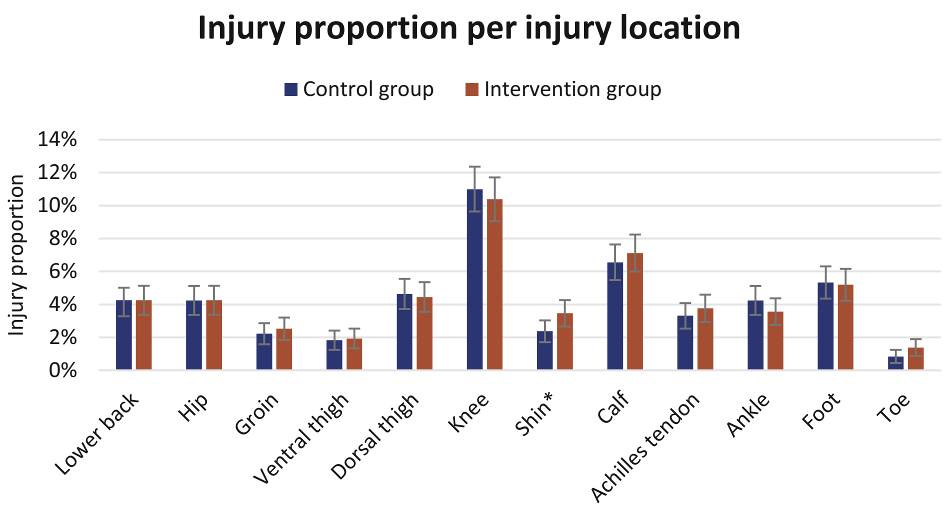

Figure 2. Number of injured runners per anatomical side. * statistically significant difference between intervention and control group ($p<0.05$).

Control group N (%)	Crude Difference % (95% CI)	Adjusted odds ratio[a] (95% CI)	Adjusted risk ratio[a,b] (95% CI)
717 (35.4)	0.2 (-2.8-3.2)	1.03 (0.90-1.17)	1.02 (0.94-1.11)
84 (4.1)	0.1 (-1.2-1.4)	1.02 (0.75-1.39)	1.02 (0.76-1.37)
119 (5.9)	0.5 (-1.1-2.0)	1.10 (0.85-1.43)	1.09 (0.86-1.39)
323 (15.9)	-0.4 (-1.9-2.7)	0.99 (0.84-1.18)	1.00 (0.87-1.15)
293 (14.5)	0.6 (-1.7-2.8)	1.06 (0.89-1.26)	1.05 (0.91-1.22)
123 (6.1)	-0.1 (-1.4-1.6)	0.98 (0.75-1.27)	0.98 (0.77-1.25)

Data on RRI severity on 13 of the 2245 reported new RRIs were missing due to a questionnaire error. The OSTRC severity score was on average 53.2 (SD 26.1) for all participants, with no difference between the intervention and control group (53.2 (SD 25.9) vs. 53.2 (SD 26.4)). A total of 1441 (64.6%) RRIs were classified as a substantial overuse injury, with a significant difference between the intervention and control group (747 (66.6%) vs. 694 (62.5%), $p<0.05$). Of the participants (N=1250) who reported a new RRI in the follow-up questionnaires, 198 (15.8%) participants used painkillers and/or NSAIDs and 548 (43.8%) participants received medical attention (Table 4).

Sensitivity analysis

Of the participants in the intervention group who completed the last follow-up questionnaire (N=1378), 922 (66.9%) participants reported that they read at least one item of the injury prevention program, of whom 491 (53.3%) participants read at least five items, and 256 (27.8%) participants read all 10 items. A total of 680 (49.3%) participants reported that they applied at least one item to their training sessions and were therefore compliant with the prevention program. The most applied items were 'take enough time for rest and recovery' (N=351, 51.6%), 'make sure there is variety in movement using specific exercises' (N=343, 50.4%) and 'do not train too much' (N=333, 49.0%). The injury proportion of the participants in the intervention group who were compliant was 44.0% (95% CI 40.2-47.7) compared with 35.4% (95% CI 33.3-37.5) of the participants in the control group. Furthermore, there was a positive association between the number of items applied and the number of RRIs (OR 1.05; 95% CI 1.00-1.11).

Table 3. Subgroup analyzes of injury proportions for the intervention and control group.

	Intervention group N (%)
Distance running event	
10/10.55 km	137 (30.1)
15/16.1 km	88 (32.8)
Half marathon	102 (35.1)
Marathon	392 (38.9)
Sex	
Male	477 (36.7)
Female	242 (33.4)
Running experience[d]	
≤ 1 year	82 (39.0)
> 1 year	637 (35.2)
Previous RRI[e]	
Yes	439 (44.8)
No	280 (26.8)
Reported RRI at baseline	
Yes	166 (47.3)
No	553 (33.1)

[a] Control group is reference; [b] Adjusted for the variables age, BMI, RRI 12 months before baseline, weekly training frequency, and weekly training distance; [c] Adjusted for the variables age, BMI, RRI 12 months before baseline, and reported RRI at baseline;

Table 4. Severity and medical consumption of new RRIs reported in the follow-up questionnaires.

	Total (N=1250)	Intervention group (N=618)	Control group (N=632)
Pain score of RRI[b]			
Rest (NRS[c], 0-10)[a]	2.4 (2.3)	2.3 (2.3)	2.5 (2.3)
Running (NRS, 0-10)[a]	4.1 (2.8)	4.0 (2.8)	4.2 (2.8)
Use of painkillers and/or NSAIDs	198 (15.8)	88 (14.2)	110 (17.4)
Treatment of health professional	548 (43.8)	265 (42.9)	283 (44.8)
Physiotherapist	517 (41.4)	248 (40.1)	269 (42.6)
General practitioner	52 (4.2)	27 (4.4)	25 (4.0)
Medical specialist	48 (3.8)	19 (3.1)	29 (4.6)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). No statistically significant differences between intervention and control group. [b] Running-related injury; [c] Numeric Rating Scale.

Control group N (%)	Crude difference % (95% CI)	Adjusted odds ratio[a] (95% CI)	Adjusted risk ratio (95% CI)
130 (29.6)	0.5 (-5.7-6.6)	1.08 (0.80-1.45)[b]	1.06 (0.87-1.29)[b]
87 (32.7)	0.1 (-8.1-8.3)	1.08 (0.75-1.58)[b]	1.06 (0.83-1.34)[b]
107 (37.2)	-2.1 (-5.9-10.1)	0.94 (0.66-1.33)[b]	0.98 (0.79-1.20)[b]
393 (38.0)	0.8 (-3.4-5.1)	1.03 (0.86-1.24)[b]	1.03 (0.92-1.14)[b]
466 (36.7)	0.1 (-3.7-3.8)	1.03 (0.87-1.21)[c]	1.02 (0.92-1.26)[c]
251 (33.2)	0.2 (-4.6-5.1)	1.03 (0.83-1.28)[c]	1.02 (0.89-1.18)[c]
90 (36.1)	2.9 (-6.2-12.1)	1.15 (0.78-1.69)[c]	1.10 (0.87-1.39)[c]
627 (35.3)	-0.1 (-3.1-3.3)	1.02 (0.89-1.17)[c]	1.02 (0.93-1.11)[c]
438 (42.9)	1.9 (-2.5-6.4)	1.09 (0.91-1.30)[f]	1.05 (0.95-1.16)[f]
279 (27.7)	-0.9(-3.0-4.8)	0.96 (0.79-1.17)[f]	0.97 (0.84-1.12)[f]
191 (46.4)	0.9 (-6.3-8.2)	1.05 (0.79-1.39)[g]	1.02 (0.88-1.18)[g]
526 (32.6)	0.5 (-2.8-3.8)	1.03 (0.89-1.19)[g]	1.02 (0.92-1.13)[g]

[d] Running experience is missing for 3 participants; [e] Running-related injury; [f] Adjusted for the variables age and reported RRI at baseline; [g] Adjusted for the variables age and BMI.

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DISCUSSION

The aim of this study was to investigate the effect of a specifically designed injury prevention program on the number of RRIs in recreational runners. This enhanced online injury prevention program did not decrease the number of RRIs. Neither were there any differences in the number of RRIs in any of the investigated subgroups of runners. Compliance with the injury prevention program had a negative effect on injury proportion. Of the new RRIs, almost two-thirds were classified as a substantial overuse injury and almost half of the participants with a new RRI needed medical attention.

The injury prevention program did not decrease the overall number of RRIs in runners. Notably, we found that being compliant (applied at least one item) with the injury prevention program negatively affected the injury proportion. Similar results were found in participants who applied at least five items of the intervention program (injury proportion 47.9%, 95% CI

40.8-55.1). Moreover, there was a positive association between the number of items applied and the number of RRIs. The negative effect of compliance might be due to the timing of applying the prevention program: the prevention program may have been initiated as a result of an RRI (tertiary prevention) and not proactively to prevent an RRI. Due to the design of this study, we were not able to determine the time frame between the occurrence of the RRI and the use of the program. Furthermore, only 49.3% of the participants in the intervention group were complaint to the prevention program which was only slightly higher compared with the INSPIRE trial (44.1%). Perhaps, more targeted educational interventions, as argued by Nielsen et al. and Hespahanol et al. may increase compliance[18,25]. So future studies should focus on how to improve compliance and the timing and application of prevention programs.

In step six of the prevention program, runners were advised to stop running or adapt their training when they experienced discomfort or mild pain during running as this can be the first sign of an RRI. As a consequence, this may have interfered with the primary study outcome, since a reduction in running for more than seven days or three consecutive training sessions was considered as an injury according to our definition of an RRI. Of the 680 participants who were compliant to the prevention program, 231 (34.0%) participants applied the information from step six in their training sessions. In these participants, the injury proportion was 56.3% (95% CI 49.8-62.7). Given this high proportion, we analyzed the injury proportion for participants in the intervention group who did not apply step six to their training sessions (N=1792), resulting in an overall injury proportion of 32.9% (95% CI 30.7-35.1). As this injury proportion was 2.6% lower compared with the injury proportion of all participants in the intervention group, the impact of the advice of step six on the number of reported RRIs seemed relatively high. Furthermore, we expected that participants who applied step six to their training sessions reported less substantial overuse injuries. However, significantly more RRIs of the participants in the intervention group were classified as a substantial overuse injury compared with the RRIs of the participants in the control group (747 (66.6%) vs. 694 (62.5%), p=0.05).

Because the INSPIRE trial indicated that running prevention advices should be directive and personalized, we aimed to make items more actionable (e.g. if your step frequency is low, gradually build up your step frequency) and included animations, videos, and interactive tools in the new prevention program (Supplementary figure 1). Moreover, we removed the information on forefoot strike as this seemed to have a negative impact on the occurrence of lower limb injuries[17]. The prevention program used in the INSPIRE trial pointed to a negative effect on the occurrence of new RRIs in the subgroup of runners with no previous RRI[17]. Therefore, runners without previous RRIs were advised not to change anything in their running behavior in step one of the enhanced injury prevention program (Supplementary figure 1). This prevention program was especially focused on runners who had an RRI in the past. However, we did not detect any between-group differences in the subgroup of participants with a previous RRI. Therefore, the enhanced injury prevention program did not decrease the number of RRIs in this subgroup.

Strengths and limitations

A strength of this study was the large sample size of 4105 participants. To our knowledge, this is the largest RCT on RRI prevention so far. We adhered to the criteria of the CONSORT statement. Furthermore, the loss to follow-up was relatively low since more than 80% of the participants completed at least one of the follow-up questionnaires. A limitation of this study was that participants who did not complete any of the follow-up questionnaires were on average younger and less experienced runners (Supplementary table 2). However, these small differences between responders and non-responders are not expected to impact the primary study outcomes. A reported RRI during follow-up was not regarded as new injury if participants reported an RRI on the same location in the previous questionnaire, and if they had reported in that same previous questionnaire not yet to be recovered. Therefore, we may have missed new RRIs on the same location while the previous injury was still present. Hypothetically, this new RRI could have had a different origin than the previous reported RRI (e.g. the first RRI may have been patellofemoral pain and the second additional RRI a meniscal tear). We expect that this may have occurred in the vast minority. Another potential limitation is the inclusion of participants with an RRI at baseline, since an existing injury may impact the risk of new injuries at other locations due to dysfunction of the kinetic chain. However, sensitivity analyzes excluding those participants with an RRI at baseline showed similar results compared with analyzes including all participants. Information on the injury severity and medical consumption was based on the follow-up questionnaires only since this information was not collected through the biweekly injury questionnaires. Therefore, information on the consequences of newly reported RRIs was missing for a total of 186 participants who reported a new RRI in the biweekly injury questionnaire only.

CONCLUSION

An educational online prevention program had no effect on the number of RRIs in recreational runners. The prevention program also had no impact on the occurrence of new RRIs in the subgroup of runners with a previous RRI even though it was specifically aimed at this subgroup of runners. Runners compliant to the program reported more injuries compared with those in the control group. Therefore, future studies should consider focusing on individual targeted prevention with attention to the timing and application of the preventive measures.

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SUPPLEMENTARY FILES

	Advice	Tools
Step 1	Do not change anything if you have no experience with running injuries	None
Step 2	Do not train too much	Training load scheme Video interview with a medical specialist Training load management tool
Step 3	Make sure there is variety in movement using specific exercices	Video illustration of running exercices
Step 4	Take enough time for rest and recovery	Animation Pain ladder scheme Training load management tool
Step 5	Participate in other sports	Animation
Step 6	Do not ignore pain during and after running	Pain ladder scheme
Step 7	Wear shoes that feel comfortable	Video interview with a medical specialist
Step 8	Run with a high step rate	Animation Link to app to detect step frequency
Step 9	Plan a gradual increase in race distance within the first year of running experience	Link to training schedules
Step 10	Run with joy	None

Supplementary figure 1. Ten items with advice and tools designed with the aim to prevent running-related injuries included in the '10 steps 2 outrun injuries' prevention program. More detailed information about these items can be found elsewhere[21].

Supplementary table 1. Items of the questionnaires in the SPRINT study.

Questionnaire	Section	Items
Baseline questionnaire	Demographics	Sex
		Date of birth
		Height (cm)
		Weight (kg)
	Training	Running experience (years)
		Weekly training frequency (times a week)[a]
		Weekly training hours (hours per week)[a]
		Weekly training distance (km per week)[a]
		Running speed (minutes per km)[a]
		Type of training
		Endurance training (%)
		Interval training (%)
		Specific exercises (%)
		Membership of a running club (yes/no)
		Use of training schedules (yes/no)
		Participation in another sport than running (yes/no)
	Running events	Distance of the registered running event (10-10.55 km/ 15-16.1 km/half marathon/marathon)
		Participation in a previous running event (yes/no)
		Average participations per year
	RRI[b]	Previous RRI in the 12 months before baseline (yes/no)
		Reported RRI at baseline (yes/no)
Follow-up questionnaire	New RRI*	New RRI since filling in previous questionnaire (yes/no)
		Location (lower back/buttock/hip/groin/ventral thigh/ dorsal thigh/knee/shin/calf/Achilles tendon/ankle/foot/ toe) OSTRC Overuse injury questionnaire[c] Pain severity (0-10 NRS scale[d]), at rest and while running Use of painkillers and/or NSAIDs (yes/no)
		Treatment (yes/no, and if yes, general practitioner/ medical specialist/physiotherapist) Complete recovery (yes/no)
	Injury prevention programe[e]	Read program (yes/no, and if yes, which advices)
		Applied program to training (yes/no, and if yes, which advices)

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Supplementary table 1. Continued

Questionnaire	Section	Items
Injury questionnaire	New RRI	New RRI (yes/no)
		Location (lower back/buttock/hip/groin/ventral thigh/ dorsal thigh/knee/shin/calf/Achilles tendon/ankle/foot/toe)
		OSTRC Overuse injury questionnaire
		Complete recovery (yes/no)

* Specific question: " Did you suffer a running injury between the previous questionnaire and now? This can also be an injury that was already present when you completed the previous questionnaire and that still bothered you in the past period."

[a] Asked for the averages over the last month; [b] Running-related injury; [c] Oslo Trauma Research Center Overuse Injury Questionnaire; [d] 11-point Numeric Ration Scale (NRS) ranging from 0 (no pain) to 10 (worst pain imaginable); [e] Only included in the last follow-up questionnaire of the intervention group (one month after the running event).

Supplementary table 2. Baseline characteristics of participants who responded to at least one follow-up questionnaire.

	Total (N=4050)	Yes (N=3312)	No (N=738)
Demographics			
Sex (male)	2570 (63.5)	2081 (62.8)	489 (66.3)
Age (years)[a]	42.3 (12.1)	43.3 (12.2)	37.8 (10.7)*
BMI (kg/m^2)[a,b]	23.3 (2.6)	23.2 (2.6)	23.6 (2.7)*
Training characteristics			
Running experience (years)[a]	10.3 (10.1)	10.8 (10.3)	8.0 (8.6)*
Weekly training frequency[a]	2.6 (1.3)	2.6 (1.3)	2.5 (1.3)
Weekly training hours[a]	3.1 (2.8)	3.1 (2.8)	2.9 (2.7)*
Weekly training distance (km)[a]	26.5 (22.7)	27.0 (23.3)	24.2 (19.5)*
Running speed (min/km)[a]	5.8 (0.9)	5.8 (0.9)	5.7 (0.9)
Type of training (%)			
Endurance training	70.6 (21.4)	70.4 (21.4)	71.5 (21.2)
Interval training	22.5 (17.7)	22.7 (17.7)	21.7 (17.7)
Specific exercises	6.9 (9.9)	7.0 (9.9)	6.9 (9.9)
Membership of a running club (yes)	1210 (29.9)	1030 (31.1)	180 (24.4)*
Use of training schedule (yes)	2636 (65.1)	2164 (65.3)	472 (64.0)
Participation in another sport than running (yes)	3276 (80.9)	2660 (80.3)	616 (83.5)*
Running events			
Distance registered for:			
10/10.55 km	894 (22.1)	740 (22.3)	154 (20.9)
15/16.1 km	534 (13.2)	456 (13.8)	78 (10.6)
Half marathon	579 (14.3)	490 (14.8)	89 (12.1)
Marathon	2043 (50.4)	1626 (49.1)	417 (56.5)
Participation in a previous running event (yes)	3791 (93.6)	3128 (94.4)	663 (89.8)*
Average participations per year[a]	8.1 (8.7)	8.6 (9.0)	6.0 (7.0)*
Running-related injury			
Previous RRI[c] in the last 12 months (yes)	2000 (49.4)	1635 (49.4)	365 (49.5)
Reported RRI at baseline (yes)	763 (18.8)	614 (18.5)	149 (20.2)

Categorical data are presented as N (%) and continuous data ([a]) as means (SD). * = statistically significant difference between intervention and control group ($p<0.05$); [b] Body Mass Index; [c] Running-related injury.

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Supplementary table 3. Total number of injuries of participants with no running-related injury at baseline with differences between the intervention group and control group (N=3287).

	Total N (%)	Intervention group N (%, 95% CI)
Primary outcome		
Newly reported RRI[c] during follow-up (yes)	1079 (32.8)	553 (33.1, 95% CI 30.8-35.3)

[a] Adjusted for the variables age and BMI; [b] Control group is reference; [c] Running-related injury.

Control group N (%, 95% CI)	Crude Difference % (95% CI)	Adjusted odds ratio[a, b] (95% CI)	Adjusted risk ratio[a] (95% CI)
526 (32.6, 95% CI 30.3-34.9)	0.5 (-2.7-3.7)	1.03 (0.89-1.20)	1.02 (0.92-1.13)

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Chapter 9

General discussion

GENERAL DISCUSSION

Running is a popular sport worldwide and has many health-related benefits for both physical and mental well-being[1-3]. Unfortunately, many runners experience a running-related injury (RRI), with overuse being the most common cause of an RRI[4-6]. Little is known about the consequences of RRIs, which is important for informing runners about the course of their RRIs and providing them with the most realistic expectations. Furthermore, no effective prevention program has yet been identified to reduce the risk of injuries in recreational runners[7-10]. It might be especially important to include training load and RRIs.

The aims of this thesis were to 1) provide insight into the consequences of RRIs and running behavior during the Coronavirus Disease 2019 (COVID-19) pandemic, 2) investigate how to define and apply a measure of training load in runners and examine its association with RRIs, and 3) evaluate if a multifactorial prevention program reduces the number of RRIs. The previous chapters described the presented studies' findings, strengths and limitations. In this final chapter, the main findings will be discussed in a broader perspective. This chapter concludes with implications for practice and suggestions for future research.

Consequences of running-related injuries

In the first part of this thesis, we focused on the consequences and prognosis of running-related knee injuries (RRKIs) in recreational runners. We directed our attention toward knee injuries since the knee is identified as the most frequent location for an RRI, as confirmed in the SPRINT study (**Chapter 5**)[11-13]. Various conditions can cause knee pain in runners. Knee structures that can get involved in these conditions and are particularly prone to non-traumatic running injuries include articular cartilage, ligaments, and tendons[11]. Of our participants with an RRKI, 23.2% reported iliotibial band syndrome, 8.7% tendinopathy, and 5.1% patellofemoral pain as the cause of their injury (**Chapter 2**). All diagnoses were self-reported by the participants. The reliability of self-reported knee injury diagnoses for diagnosing knee pain is uncertain, as knee pain in a specific area around the knee can be associated with various diagnoses, and not all of these diagnoses have established gold standards[14]. For a reliable diagnosis of knee pain, the expertise of a healthcare professional who performs an anamnesis and a physical examination may be necessary. An accurate diagnosis might be important, because it can help in setting realistic expectations regarding the prognosis of knee pain. In our study, the median duration of the knee injury was eight weeks and 71% of the runners had recovered within 16 months (**Chapter 2**). The median duration was based on all participants with an RRKI. We did not differentiate between the most common diagnoses of an RRKI. Other studies have reported a similar median time to recovery of 7-13 weeks for the most common knee injuries in runners, such as patellofemoral pain, iliotibial band syndrome, and meniscopathy[15,16]. Based on the knowledge so far, an accurate diagnosis cannot yet predict the prognosis of knee pain in runners. But will an accurate diagnosis of knee pain affect treatment in runners? Runners with patellofemoral pain and tendon-related knee injuries are advised to reduce running and gradually increase running again when the symptoms have subsided[17]. Neuromuscular strengthening exercises of the muscles around the hip and knee joints may reduce pain and/or improve knee function[14,18]. Based on systematic review and randomized-controlled trial (RCT) evidence, for patients with patellofemoral pain a combined intervention approach (hip and knee exercises with at least one of the following: foot orthoses, patellar taping or manual therapy) is recommended[18]. Compared to patellofemoral pain, less interventional research examined treatment options in patients with iliotibial band syndrome and robust evidence for effective treatments is lacking[19-21]. Based on current literature, we can conclude that it remains unclear whether treatment approaches for runners with knee pain should be differentiated, especially due to a lack of appropriate interventional research for some specific diagnoses.

In this thesis, 14% of the participants with a new RRKI were diagnosed with knee osteoarthritis (OA) following the case definition of the NICE guideline[22], and even 23% of the participants reported the diagnosis OA/degenerative meniscopathy as cause of their knee pain (**Chapter 2**). This implies that knee OA might be an important factor in running. OA is estimated to become the most prevalent disease in the Dutch population, as the prevalence of OA is rising due to the aging population, the increase in obesity rates, and the increase of anterior cruciate ligament injuries[23-25]. Of all joints where OA can occur, the knee is the most commonly affected joint and the most disabling[23,26]. A number of risk factors for knee OA have been identified, including age, obesity, female sex, and previous knee injury[23,27]. Given the high number of runners who experience knee OA symptoms, it is important to know the impact of running on these symptoms. Recent systematic reviews reported that running is not correlated with detrimental structural or molecular cartilage adaptation, and that changes to lower limb cartilage following running are transient[28,30]. A recent systematic review by Dhillon et al. reported that running is not associated with worsening disease-specific patient-reported outcomes (i.e. presence of knee pain or functioning) or radiological features of knee OA in the short term (mean follow-up time of 55.8 months in the running group and 99.7 months in the non-running group)[31]. So, although OA is a chronic condition, continuation of running may not necessarily worsen the symptoms. However, the included studies in this systematic review demonstrated heterogeneity in the amount of running, number of participants, age of the participants, outcome variables, follow-up duration, and study designs. Therefore, the impact of running on OA symptoms remains unclear and this relationship is further complicated by several confounding factors. More research is needed to provide runners with OA with appropriate advice, such as whether it is advisable to continue running or if they should consider alternative sports like cycling or swimming.

An example of this is a prospective cohort study in runners with knee OA. An ongoing study, the LoaD project, will examine the interactions between running and OA progression and will provide insights into how running may impact the progression of knee OA in the individual patient[32]. These insights can be used to develop personalized advice and guidelines for runners with knee OA. This will also be helpful for clinicians, so they can provide their patients with recommendations based on scientific evidence.

Training load and its association with running-related injuries

In the past decades, research into the role of training load on injury risk has received increasing attention. A search in the MEDLINE database shows that in the past 20 years, there has been rapid growth in the number of publications per year using the search syntax ("training load" AND "injury"), increasing from 15 papers in 2002 to 306 in 2022. An important belief in sports injury research is that a sudden increase in training load plays a key role in injury development, also called "training too much, too soon, too often"[33]. From a theoretical viewpoint, injury might occur when the cumulative training load over several training sessions exceeds the body's load capacity for adaptive tissue repair[33-35]. The identification of an association between change in training load and sports injuries is seen as a very important step in injury prevention, since training load might be a readily modifiable factor when developing injury prevention strategies.

In running, a substantial amount of research has examined the association between change in training load and RRIs in the past years[36-38]. In these studies, several measurement methods were used to measure change in training load. In previous years the '10% rule' was a popular method to regulate increases in training load in runners. However, there is no evidence that this 10% rule reduces the RRI risk in novice runners[39]. A possible explanation for not finding an effect could be that the 10% rule only includes weekly changes in training load and does not account for the load-bearing capacity of an individual athlete over a longer timespan (chronic load). A newer method to calculate change in training load is the acute:chronic workload ratio (ACWR)[40-42]. In the ACWR method, the acute workload represents the fatigue component and the chronic workload reports the fitness component[43]. An advantage of the use of the ACWR method is the possibility of calculating ACWR for each training session. This is important, because training load has to be considered as a time-dependent variable since training load continuously changes over time. An association between high ACWRs and increased injury risk was found in team sport population studies (such as cricket, rugby league and basketball)[43]. These studies concluded that the risk of injury was relatively low if the acute training load remains below, similar to, or slightly above the chronic training load (ACWR within the range of 0.8-1.3) and that the risk of injury was high with an ACWR ≥ 1.5[40,41]. In running, only a few studies examined the relationship between ACWRs and injury risk and found inconclusive and conflicting results[37,38,44]. Dijkhuis et al. reported that a fortnightly low increase of the ACWR and a low increase between the second and third week before an RRI lead to an increased injury risk[44]. Nakaoka et al. found an association between ACWR and RRIs, suggesting that the higher the ACWR, the lower the RRI risk, while Toresdahl et al. concluded exactly the opposite: increased training volume ≥ 1.5 ACWR was associated with more RRIs[37,38]. Matos et al. reported significant weekly increases in ACWR in the three weeks prior to an injury in trail runners[45]. The main reason for these inconclusive results is a lack of appropriately sized cohorts using adequate data collection methods, valid outcome measures, and appropriate statistical methods to identify associations between change in training load and RRIs.

In part two of this thesis, we addressed the use of global positioning system (GPS) data for training load calculation. In our study population, almost two-thirds of the recreational runners tracked their running training sessions with the use of a GPS-enabled device or platform and were willing to share their GPS training data (**Chapter 5**). We concluded that it seemed feasible to collect GPS data from a large cohort of recreational runners and that GPS data was usable to calculate training load (**Chapter 5**). In **Chapter 6** of this thesis, we examined the differences between the applied methods that were previously used to express change in training load in runners (the weekly training load method and three methods to calculate ACWR). We concluded that the difference between the weekly training load method and ACWR methods was high. We found smaller differences between the three ACWR methods (i.e. coupled ACWR, uncoupled ACWR, and EWMA method as introduced in the first chapter of this thesis). With this information, we conducted a study on the association between change in training load and injury risk in a large cohort of runners (**Chapter 7**). In this study, we identified associations between ACWR and RRI, but the clinical relevance of these associations was questionable given the small hazard ratios and inconsistency in outcomes. For runners, it is important to know how to train best to minimize their injury risk. However, based on the results of our research and previous studies it is not possible to provide runners with specific advice on their training load to prevent RRIs.

Prevention of running-related injuries

The third part of this thesis focused on the prevention of RRIs in recreational runners (SPRINT study) (**Chapter 8**). In this RCT, the intervention group received access to an online prevention program that consisted of 10 items, each addressing a specific advice or tool related to RRI prevention. The control group followed their regular training program. The online prevention program did not reduce the number of RRIs in recreational runners.

Based on the results of a previously conducted RCT on running injury prevention (INSPIRE trial), the injury prevention program developed for the SPRINT study was especially aimed at runners who had an RRI in the past[7,46]. In this prevention program, runners without a previous RRI were advised not to change anything in their running behavior. Runners with a previous RRI were advised to follow the 10 items of the prevention program. However, the prevention program also did not decrease the number of RRIs in the subgroup of runners with a previous RRI. We hypothesized that no effect was found because of the low compliance and the fact that we found a positive association between the number of items of the prevention program applied and the number of RRIs. The negative effect of compliance might be due to the way the program was applied by the runners: the prevention program may have been initiated as a result of an RRI (tertiary prevention) and not proactively to prevent an RRI (primary prevention). Due to the design of this study, we were unfortunately not able to determine the time frame between the occurrence of the RRI and the use of the prevention program. Therefore, it is important to focus on the timing of the programs used by the participants to prevent injuries in future prevention studies.

Policymakers emphasize that people should engage in sports to prevent health conditions as physical activity has proven to be a cost-effective method to improve overall well-being and decrease morbidity and mortality[1-3]. Despite the numerous health benefits, athletes are prone sustaining sports-related injuries. In 2022, an estimated 3.9 million athletes in the Netherlands experienced at least one injury, with 2.4 injuries per 1,000 hours of sports activities[47]. Funding was made available for research into sports injury prevention to reduce the incidence of sports injuries and the number of athletes who stop exercising due to their injuries. Sports injuries cost society money, not only for the required care but also through absenteeism from work and education[48]. Therefore, it is also important to reduce sports injuries to increase the positive balance between the benefits and costs of sport and exercise. Findings from the SPRINT study (**chapter 8**), as well as other RCTs[7,10], suggest that reducing the number of RRIs through a prevention program is challenging. Only a few RCTs were effective in reducing injury risk among small groups of runners by targeting a single risk factor. For example, a foot core strengthening protocol was effective in reducing the incidence of RRIs in recreational long-distance runners[49] and a treadmill-based gait retraining program reduced the injury risk in novice runners[50]. However, both programs will be very hard to implement nationwide because these programs were conducted in a biomechanics laboratory or participants received training by a physical therapist. Perhaps the ability to design targeted prevention programs for runners is limited by an incomplete understanding of the causes of injuries. It might be necessary to take a step back in the TRIPP model of prevention to better understand RRIs (**Figure 1, Introduction**)[51]. Running injuries may result from a complex interaction between internal (e.g. body weight and heart rate) and external risk factors (e.g. training distance and number of steps). Furthermore, risk factors may change over time and might not remain consistent between baseline and point of injury[52]. Therefore, it is especially important to address the multifactorial nature of RRIs to obtain a complete understanding of the cause of injuries. Although it is not within my expertise, an interesting research area involves the use of computational models to model the impact of internal and external risk factors on the lower-limb structures in an individual. These new techniques may provide new insights on injury development that may be translated to clinical practice. Another reason for the lack of effective prevention programs in running is that the optimal intervention approach will differ between each individual. Targeted group prevention strategies to reduce the number of RRIs may require individual risk factor modification based on existing risk factors and the variability of risk factors over time. These interventions can be conducted online, are easy to implement and reachable for a large number of runners. Therefore, future studies should focus on how to improve multifactorial injury prevention programs, especially by more targeted and individual interventions. Last, injury prevention programs may not be effective as they often address all lower-limb RRIs instead of focusing on specific injury locations, structures, or diagnosis. Injury prevention programs in athletes that focused on a specific injury, such as anterior cruciate ligament injuries[53] or hamstring injuries[54,55], have shown to be effective. This indicates that it might be important to focus preventive research on specific injury locations in (at risk) runners.

Challenges in injury prevention research for runners

A previous running-related injury as a risk factor

Based on existing literature, a previous RRI is the strongest risk factor for a new RRI[56-58]. This thesis also demonstrated the significant impact of previous RRIs. We concluded in **Chapter 3** that a previous RRI is a strong risk factor in both men and women for the development of a new RRI. The results of the SPRINT study indicated its high prevalence as a risk factor, since almost half of the participants reported a previous RRI in the last 12 months (**Chapter 8**). Reasons why a previous running injury increases the risk of a new RRI are still unclear. Some runners seem prone to develop multiple RRIs compared to other runners, and are perhaps not 'made for running'. A previous RRI is a risk factor for a new RRI, possibly due to incomplete healing of the initial injury, a combination of structural and functional factors, or changed biomechanics due to a previous injury resulting in an overload of other structures or joints[57]. If we want to prevent the first RRI of a runner, we have to know more about previous injuries and their relation with new RRIs. Furthermore, previous studies on risk factors for RRIs showed heterogeneity in how they collected information on previous injuries: the definition of a previous injury varied, which ranged from unspecified absence from sports practice to injuries caused by running in the 12 months prior to an event[56]. There is insufficient knowledge about the nature of previous injuries (e.g. type of injury) and whether the recurring injury was related to the previous one. Also, little is known about the characteristics of the runners with a previous RRI. Only one study investigated the characteristics of runners with a previous RRI who suffered a new RRI and concluded that registration for a marathon event and a previous injury in the upper or lower leg were associated with a higher risk of new running injuries[59]. More research is needed on the association between previous and new injuries to find out why some runners do not get injured while others suffer from repeated injuries.

The complexity of training load measurement

Studies in team sports populations reported an ACWR window of 0.8-1.3 in which athletes have a lower risk of sustaining an injury[40,41]. In runners, this optimal training window has not been identified. Each runner likely has a personal training load window in which the risk of an overuse injury is low. Some runners will sustain injuries at ACWRs much lower than 1.5, while other runners will tolerate ACWRs far above 1.5. It is even possible that this individualized training load window will change over time. But which factors contribute to the variation in the tolerance of training load among runners? It is possible that due to the multifactorial nature of running injuries, high training load alone does not increase injury risk and that it might be an interplay of multiple risk factors of running injuries. In our study (**Chapter 7**), we included running distance, duration, and speed of each training session to examine the association between training load and running. Training load in runners might be influenced by both external (the mechanical physical stress applied to an athlete) and internal training load factors (the physiological and psychological stress in response to external loads)[60,61]. Therefore, it might be better to interpret training load in conjunction with other variables, for example, historical factors (e.g. age, previous injury, and training experience), external factors (e.g. ground reaction forces, contact time, and number of steps), and physiological internal factors (e.g. body weight, heart rate, and session-rate of perceived exertion). The genetic profile of a runner may also play a role, with some runners being more susceptible to an RRI than others. Furthermore, applied loads may be distributed differently at a structural level, depending on distribution-related factors (e.g. equipment, technique, and surface). Last, runners enter each training session with a certain tolerance to withstand load. We are unable to measure this tolerance exactly. However, variables like current injury, state of recovery (e.g. time between training sessions, stiffness, and strength), and daily stress (e.g. sleep, work, and diet) could affect the tolerance to withstand a given session load. It is challenging to calculate training loads and the interaction with other variables due to the session-to-session variability since most factors vary between training sessions, and sometimes even within one training session. Understanding how other variables interact with training load might result in a more precise measurement of training load and prediction of the load tolerance of a runner.

The impact of daily physical activity and sedentary behavior

An underexposed variable in the research on training load and injury risk is the influence of other physical and sport activities in daily life. Training load research focuses on the effect of sudden changes in load during running training sessions. However, little is known about the physical activity patterns of runners outside training. Perhaps runners perform other sports activities, cycle to work every day, or are exposed to work-related physical activity. The accumulated loading from other sports activities, physical activities of daily living, and occupational activities can cause substantial load on the musculoskeletal system, especially lower-limb load[62]. Therefore, daily physical activity might play a role in the development of musculoskeletal injuries due to load exposure and possible repetitive forces. In contrast, sedentary behavior might also be of interest when calculating training load. Runners who work in the office might sit all day before going home and perform a running training. However, it is not known what the impact of a running training is on the lower-limb load if a runner has been sitting all day. Perhaps these runners are at higher risk of sustaining an injury due to the sudden increase of lower-limb load during their training. Future research is needed to evaluate the effect of daily physical activity and sedentary behavior on lower-limb load in runners.

Practical implications

RRIs are a major reason to discontinue running, but also result in a health and economic burden. Recreational runners most frequently experience knee injuries (**Chapter 5**). Based on current literature, the courses for the most common RRKIs are comparable. Due to a lack of appropriate interventional research for some specific diagnoses of RRKIs, it is unclear whether treatment options for runners with knee pain should differentiate. However, healthcare professionals (such as physiotherapists or sports physicians) play an important role in educating patients about the course and prognosis of their RRKI and to guide them during their recovery with personalized strength exercises and training schedules.

The relationship between training and injury has been of interest to researchers and clinicians for considerable time. The use of technology, like a sports watch or platform to collect training data, has become common in recreational running. Some platforms, like Strava, even offer running plans to runners, which can be used to train for a race. Training data collection can provide runners, as well as clinicians, with data that offers accurate insights into training load. Based on the conclusions in this thesis, it is important for clinicians to realize that there seems to be an association between change in training load (calculated as ACWRs) and injury risk in runners, but that the clinical relevance of this association is questionable. Healthcare professionals, as well as sports trainers, should be aware that the role of general training load advice in the prevention of RRIs is uncertain.

So far, no effective multifactorial RRI prevention program has been identified. The online prevention program examined in this thesis was also not effective in reducing the number of RRIs in recreational runners (**Chapter 8**). It is therefore very hard to come up with new practical evidence-based advice for runners and clinicians to reduce injury risk.

Suggestions for future research

This thesis indicates that, with the current knowledge, it is challenging to provide runners with advice on preventing running injuries. Before developing a new prevention program, it is important to take a step back in the TRIPP model of prevention to gain more insight into the risk factors of RRIs. Policymakers can influence existing knowledge by providing funding to facilitate research that is relevant to injury prevention. For future trials, it is advisable to focus on two important topics: 1) training load calculation in runners, and 2) a previous RRI as a risk factor for a new RRI.

Long-term studies with large sample sizes are required to better understand how to calculate (change in) training load in runners with the selection of the most reliable factors for training load assessment. In this type of research, change in training load (like ACWR) should be included as a primary exposure, whereas historical factors, external factors, internal psychosocial factors, distribution-related factors, and tolerance-related variables may be included as effect measure modifiers. Special focus on the difference between time-fixed variables (e.g. previous injury) and variables that change over time (e.g. session rate of perceived exertion, state of recovery, or daily stress) or even within a training session (e.g. heart rate or surface) is needed. Because of the large variability in personal factors and training characteristics within a group of runners, it might be a key implication to examine the impact of training load in a subgroup of runners, or even within individual runners. These subgroups of runners can be classified based on age, but also the years of running experience, a previous running injury (and type of this injury), or biomechanical characteristics. Using subgroups can help to identify the association between training load and injury risk. This might eventually give specific training load advice and perhaps optimal training load windows to reduce injury risk in runners.

The effect of daily physical activity and sedentary behavior on the lower-limb load of runners is unknown. Therefore, these variables might be important in training load calculations. An interesting future research question would be to examine whether specific physical activity patterns have an impact on the lower-limb load in runners. In this study, important variables are the type and amount of physical activity, but also the timing of the activity (e.g. moment during the day). Physical activity and sedentary behavior can be monitored with the use of an accelerometer. Data collection through a wearable device is a noninvasive way to monitor mobility and physical activity and will collect data more objectively compared to self-reported questionnaires[63,64]. Accelerometers are widely used to measure physical activity and sedentary time[65]. Some studies indicate that the use of an GPS sensor in combination with an accelerometer generates better results for the detection of physical activity compared to the use of an accelerometer alone[66-68]. In the past years, there has been an increased interest in the use of wearable inertial measurement units (IMUs) to assess lower-limb load. IMUs are small sensors that consist of accelerometers, gyroscopes and/or magnetometers[69]. They are able to acquire data on the inertial motion and 3D orientation of individual limb segments in unconstrained environments[70,71]. In future RRI prevention research, it would be interesting to provide a subgroup of participants with an IMU to collect variables like the duration of daily physical activity, amount of steps, and the intensity of the activities on specific limb segments.

Experienced runners who have never been injured are a group of interest for future research. We can probably learn from these runners, because they excel in a particular aspect or possess a highly protective genetic makeup, preventing them from getting injured. Perhaps they have other training habits compared to runners who are getting injured or have non-modifiable characteristics that are ideal for running. With this information, we might be able to give runners who are repeatedly injured specific advice to prevent RRIs. Another important topic in future research is runners who fully recovered from their previous running injury, but have not yet suffered a new RRI. These runners seem to have developed a form of injury resistance, which may be due to an effective treatment, discontinuing factors that contributed to their previous injury or adopting a running technique that is more resistant to injuries. Only one study so far has compared runners with a previous RRI to runners who have never been injured and those who were recently injured[72]. The main focus of this study was the difference in clinical measures of strength, joint motion, and functional foot alignment during a treadmill run. This study concluded that those clinical measures were not superior in injury-resistant runners compared with recently injured runners. Differences in biomechanics and training characteristics were not examined in this study. It would be interesting to follow a cohort of runners to explore how a new RRI affects training habits (such as training frequency and strength exercises), biomechanics and medical consumption. These runners should be followed for a longer period (e.g. > one or two years) to examine whether they become re-injured. After the follow-up period, differences in the recovery process between injured runners who did and did not become re-injured can be examined. This might give some new insights on the recovery process of an RRI and how to reduce the risk of re-injury.

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Part 4

Appendices

Chapter 10

Summary

Samenvatting

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SUMMARY

Running is one of the most popular sports worldwide. Unfortunately, many runners experience a running-related injury (RRI) and an RRI is often a reason to stop running. Little is known about the consequences of running injuries, which is important for informing runners about the course of their RRIs and providing them with the most realistic expectations. The identification of an association between change in training load and RRI risk might be an important step in RRI prevention. However, there is a lack of appropriately sized cohorts using adequate data collection methods and valid outcome measures to identify associations between training load and RRIs. Last, no effective multifactorial prevention program has been identified to reduce the risk of RRIs. Therefore, the aims of this thesis were to 1) provide insight into the consequences of RRIs and running behavior during the Coronavirus Disease 2019 (COVID-19) pandemic (**Part 1: Chapters 2-4**), 2) examine how to define and apply a measure of training load in runners and investigate its association with RRIs (**Part 2: Chapters 5-7**), and 3) evaluate if a multifactorial prevention program reduces the number of RRIs (**Part 3: Chapter 8**).

All studies presented in this thesis were based on data collected in two large randomized-controlled trials (RCTs) on injury prevention: the INSPIRE trial (INtervention Study on Prevention of Injuries in Runners at Erasmus MC) and the SPRINT study (Shaping up Prevention of Running Injuries in the Netherlands using Ten steps) (**Chapter 8**). In both RCTs, demographic and training variables were collected through a baseline questionnaire. All participants received three follow-up questionnaires to gather information about new RRIs and their consequences. Data collected in the INSIPIRE trial was utilized in **Chapters 2 and 5**. In **Chapter 3**, the combined dataset from the INSPIRE trial and SPRINT study was used. Data from the SPRINT study was utilized in **Chapters 4, 6, and 7**.

Part 1: Consequences of running-related injuries and running behavior during the COVID-19 pandemic

In **Chapter 2** we investigated the consequences and prognostic factors of running-related knee injuries (RRKIs). Participants of the INSPIRE trial who reported a new RRKI during follow-up were sent a knee-specific questionnaire. To determine the association between potential prognostic factors and time to recovery of an RRKI, a Cox regression analysis was performed. A total of 138 participants responded to the knee-specific questionnaire. At 16 months after registration, 71.0% of the participants reported full recovery, with a median time to recovery of 8.0 weeks. Most participants reported iliotibial band syndrome (23.2%) or osteoarthritis (OA)/degenerative meniscopathy (23.2%) as cause of their injury. Suffering knee OA was associated with a longer time

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to recovery (HR 0.17; 95% CI 0.06-0.46). The relatively long duration of knee symptoms after an injury emphasizes the need for optimal treatment, education, and injury prevention programs for recreational runners. Given the high number of participants with knee OA symptoms, more knowledge on the role of running in knee OA seems especially important to provide more clinical guidance toward patients and clinicians.

Sex differences in runners have been extensively analyzed, but these studies provide conflicting results. Moreover, the evidence regarding sex-specific risk factors for new RRIs is also contradictory. The objective of **Chapter 3** was to identify sex differences in the location, type, consequences, and risk factors of RRIs in a large cohort of recreational runners. In this study, data from the INSPIRE trial and SPRINT study were combined. Data analysis was performed using descriptive statistics and multivariable logistic regression analyzes. A total of 6428 participants were included with an average follow-up time of 5.0 months. During follow-up, 2133 participants (33% men, 34% women) suffered one or more RRIs. We found no relevant sex differences between men and women among recreational runners. Our findings suggest that there are fewer sex differences than previously assumed in the literature. Based on these findings, it may not be necessary for future personalized RRI prevention programs to account for sex-specific factors.

During the ongoing SPRINT study, the global outbreak of COVID-19 occurred. The Dutch government decided to implement a 'targeted lockdown' with advice on meticulous hygiene measures and physical distancing, and restrictions in traveling and group meetings. The Dutch authorities advised to stay home as much as possible, but performing outdoor physical activities was not restricted. In **Chapter 4** we explored the changes in running behavior due to the COVID-19 pandemic and assessed the presence of symptoms suggestive for COVID-19 in recreational runners. Furthermore, this study identified whether there was an association between outdoor running activities and symptoms suggestive for COVID-19. Seven weeks after the start of the lockdown, information on running behavior, running habits, healthcare utilization, and symptoms suggestive for COVID-19 was obtained through an additional questionnaire. To determine the association between running and symptoms suggestive for COVID-19, univariate and multivariate logistic regression analyzes were performed. Of the included participants (N=2586), the large majority (93.9%) was able to maintain their normal running habits during the targeted lockdown period. A total of 253 participants (9.8%) experienced symptoms suggestive for COVID-19 and 10 participants tested positive for COVID-19. Running behavior and running habits were not associated with the onset of symptoms suggestive for COVID-19. This implies that outdoor running during lockdown due to the COVID-19 pandemic has no negative consequences for the health of Dutch runners.

Part 2: GPS-based training load and its association with running-related injuries
Most previous RRI studies determined training characteristics by means of questionnaires. The use of global positioning system (GPS) data may serve as an alternative for accurately collecting training data. The purpose of **Chapter 5** was to explore the feasibility of collecting GPS data in recreational runners and to examine the usability of GPS data to evaluate associations between training load and RRKIs. Participants of the INSPIRE trial with a new reported RRKI and uninjured participants were sent an additional questionnaire and a GPS export request. Weekly GPS-based training distances were used to calculate acute:chronic workload ratios (ACWRs). Almost two-thirds of the participants (N=240) tracked their running training sessions using a GPS-enabled device or platform and were willing to share their GPS data. From the participants (N=144) who received a GPS export request, 50.0% successfully shared their data. Therefore, we concluded that it seems feasible to collect training characteristics from GPS-enabled devices and platforms used by recreational runners. The majority (69.4%) of the shared GPS data was usable to present weekly ACWRs, indicating that GPS data is usable to calculate ACWRs. Therefore, GPS-based ACWR measures can be used for future studies to evaluate associations between training load and onset of RRIs.

After concluding that GPS training data can be used to measure change in training load, we explored the best method to calculate change in training load in runners. In previous studies, several methods were utilized to calculate change in training load. In **Chapter 6**, we examined the difference between four methods: 1) weekly training load; 2) ACWR, coupled rolling average (RA); 3) ACWR, uncoupled RA; 4) ACWR, exponentially weighted moving averages (EWMA). At the end of the follow-up period of the SPRINT study, all participants were asked to share their GPS training data. Primary outcome measure was the predefined significant increase in training load (weekly training loads ≥ 30% progression and ACWRs ≥ 1.5), based on training distance. GPS data of 430 participants were used for analyzes with a total 22,839 training sessions. We concluded that the difference in calculated change in training load expressed in the weekly training load method and ACWR methods was high, since 43.0% of the training sessions with significant increase in training load expressed in the weekly training load method showed a difference with the coupled RA and EWMA method. We found smaller differences between the three ACWR methods. To validate an appropriate measure of change in training load in runners, future research on the complex relation between training loads, the most sensitive method to calculate change in training load, and risk for sustaining an RRI is needed.

The association between training load and injury risk was examined in **Chapter 7**. In this study, we utilized data obtained through questionnaires and GPS requests in the SPRINT study. Change in training load was calculated as ACWRs (coupled RA method) based on distance, duration, or speed of each training session. Cox regression models were performed to evaluate the association between ACWR and RRI onset. GPS data of 461 participants were used for analyzes with a total of 20,425 training sessions. We identified an association between ACWR and RRI onset in runners based on the variables running distance (HR 1.32; 95% CI 1.00-1.74) and duration (HR 1.39; 95% CI 1.07-1.79), respectively. Though in the analyzes adjusted for known risk factors, only ACWR based on duration (HR 1.33; 95% CI 1.02-1.74) remained positively associated with RRI onset. No significant association was found between ACWR and RRI onset when excluding runners with an RRI at baseline (15.8%). We concluded that the clinical relevance of the identified associations are questionable given the small HRs and inconsistency in outcomes. This makes the role of general training load advice in the prevention of RRIs uncertain.

Part 3: Prevention of running-related injuries

In 2017, the INSPIRE trial was designed in which the effect of a multifactorial online injury prevention program on the number of RRIs was investigated. This program did not decrease the number of RRIs in recreational runners. However, new insights were gained to enhance RRI prevention, such as the indication that an RRI prevention program should focus on runners with a previous RRI. With the use of these new insights, we developed an enhanced online injury prevention program, especially aimed at runners with a previous RRI (the SPRINT study). In **Chapter 8** we presented the results of the SPRINT study (N=4050). To determine differences between injury proportions, univariate and multivariate logistic regression analyzes were performed. During follow-up, 35.5% of the participants sustained a new RRI, with no difference between the intervention and control group. The prevention program also had no impact on the occurrence of new RRIs in the subgroup of runners with a previous RRI. Runners compliant to the program reported more injuries compared with runners in the control group. Therefore, future studies should consider focusing on individual targeted prevention with attention to the timing and application of the preventive measures.

Finally, the main findings of this thesis were summarized in **Chapter 9** and discussed in a broader context. This chapter concluded with clinical implications and suggestions for future research.

SAMENVATTING

Hardlopen is een van de meest populaire sporten ter wereld. Helaas ervaren veel hardlopers een blessure en is een hardloopblessure vaak een reden om te stoppen met hardlopen. Er is weinig bekend over de gevolgen van hardloopblessures. Het is van belang om meer te weten over de gevolgen van hardloopblessures om hardlopers adequaat te kunnen informeren over het verloop van hun blessure en realistische verwachtingen te kunnen bieden. Het aantonen van een associatie tussen de verandering in trainingsbelasting en het risico op het krijgen van een blessure kan een belangrijke stap zijn in de preventie van hardloopblessures. Er is echter een gebrek aan adequaat opgezette cohorten die gebruikmaken van geschikte methoden voor gegevensverzameling en geldige uitkomstmaten om associaties tussen trainingsbelasting en hardloopblessures aan te tonen. Tot slot bestaat er geen effectief multifactorieel preventieprogramma om het risico op hardloopblessures te verminderen. Daarom waren de doelstellingen van dit proefschrift om: 1) inzicht te krijgen in de gevolgen van hardloopblessures en het hardloopgedrag tijdens de COVID-19 pandemie (**Deel 1: Hoofdstukken 2-4**), 2) te onderzoeken hoe trainingsbelasting bij hardlopers berekend kan worden en te onderzoeken of er een associatie is tussen trainingsbelasting en hardloopblessures (**Deel 2: Hoofdstukken 5-7**) en 3) te evalueren of een multifactorieel preventieprogramma effectief is in het verminderen van het aantal hardloopblessures (**Deel 3: Hoofdstuk 8**).

Alle studies in dit proefschrift zijn gebaseerd op gegevens die verzameld zijn in twee grote gerandomiseerde gecontroleerde onderzoeken (RCT's): de INSPIRE-studie (INtervention Study on Prevention of Injuries in Runners at Erasmus MC) en de SPRINT-studie (Shaping up Prevention of Running Injuries in the Netherlands using Ten steps) (**Hoofdstuk 8**). In beide RCT's werden demografische gegevens en trainingsvariabelen verzameld via een baseline vragenlijst. Alle deelnemers ontvingen drie follow-up vragenlijsten om informatie te verzamelen over nieuwe hardloopblessures en de gevolgen van deze blessures. Gegevens die verzameld zijn in de INSPIRE-studie werden gebruikt in de **Hoofdstukken 2 en 5**. In **Hoofdstuk 3** werd de gecombineerde dataset van de INSPIRE-studie en de SPRINT-studie gebruikt. Gegevens uit de SPRINT-studie zijn gebruikt in de **Hoofdstukken 4, 6 en 7.**

Deel 1: Gevolgen van hardloopblessures en het hardloopgedrag tijdens de COVID-19 pandemie

In **Hoofdstuk 2** onderzochten we de gevolgen en prognostische factoren van knieblessures bij recreatieve hardlopers. Deelnemers van de INSPIRE-studie die tijdens de follow-up een nieuwe knieblessure rapporteerden, ontvingen een knie-specifieke vragenlijst. Om de associatie tussen mogelijke prognostische factoren en de tijd tot herstel van een knieblessure te bepalen, werd een Cox-regressieanalyse uitgevoerd. In totaal reageerden

138 deelnemers op de knie-specifieke vragenlijst. 16 maanden na registratie was 71,0% van de deelnemers met een knieblessure volledig hersteld, met een mediane tijd tot herstel van 8 weken. De meeste deelnemers rapporteerden als oorzaak van hun blessure het iliotibiale bandsyndroom (23,2%) of artrose/degeneratieve meniscopathie (23,2%). Het hebben van knieartrose was geassocieerd met een langere tijd tot herstel (HR 0,17; 95% CI 0,06-0,46). De relatief lange duur van knieblessures benadrukt de noodzaak van optimale behandeling, educatie en blessurepreventieprogramma's voor recreatieve hardlopers. Gezien het hoge aantal deelnemers met symptomen die passen bij knieartrose is het belangrijk om meer kennis te krijgen over de rol van hardlopen bij knieartrose, zodat patiënten op de juiste manier begeleid kunnen worden.

Geslachtsverschillen bij hardlopers en geslachtsspecifieke risicofactoren voor nieuwe hardloopblessures zijn uitgebreid onderzocht in de literatuur, met tegenstrijdige resultaten. Het doel van **Hoofdstuk 3** was om geslachtsverschillen aan te tonen in de locatie, het type, de gevolgen en de risicofactoren van blessures in een groot cohort van recreatieve hardlopers. In deze studie combineerden we de datasets van de INSPIRE-studie en de SPRINT-studie. Beschrijvende statistieken en multivariate logistische regressieanalyses werden gebruikt om de data te analyseren. In totaal werden 6428 deelnemers geïncludeerd met een gemiddelde follow-up van 5 maanden. Tijdens de follow-up kregen 2133 deelnemers (33% mannen, 34% vrouwen) één of meerdere hardloopblessures. We vonden geen relevante verschillen tussen mannen en vrouwen onder recreatieve hardlopers. Onze bevindingen suggereren dat er minder geslachtsverschillen zijn dan voorheen werd aangenomen in de literatuur. Het is daarom in toekomstige preventieprogramma's voor hardloopblessures mogelijk niet nodig om rekening te houden met geslachtsspecifieke factoren.

Tijdens de SPRINT-studie vond de wereldwijde uitbraak van COVID-19 plaats. De Nederlandse regering besloot een 'gerichte lockdown' in te voeren met adviezen over hygiënemaatregelen en fysieke afstand, en beperkingen op reizen en groepsbijeenkomsten. De Nederlandse autoriteiten adviseerden om zoveel mogelijk thuis te blijven, maar het was wel toegestaan om buiten te sporten. In **Hoofdstuk 4** onderzochten we de veranderingen in hardloopgedrag als gevolg van de COVID-19 pandemie en rapporteerden we de aanwezigheid van symptomen suggestief voor COVID-19 bij recreatieve hardlopers. Bovendien werd in deze studie onderzocht of er een verband was tussen buiten hardlopen en symptomen suggestief voor COVID-19. Zeven weken na het begin van de lockdown werd informatie over hardloopgedrag, hardloopgewoonten, gezondheidszorggebruik en symptomen suggestief voor COVID-19 verzameld via een extra vragenlijst. Om de associatie tussen hardlopen en symptomen suggestief voor COVID-19 te onderzoeken werden univariate en multivariate logistische regressieanalyses uitgevoerd. Van de geïncludeerde deelnemers (N=2586) slaagden de overgrote meerderheid (93,9%) erin hun normale hardloopgewoonten tijdens de lockdown te handhaven. In totaal ervaarden 253 deelnemers (9,8%) symptomen suggestief voor COVID-19 en 10 deelnemers testten positief op COVID-19. Het hardloopgedrag en de hardloopgewoonten waren niet geassocieerd met symptomen suggestief voor COVID-19. Dit impliceert dat buiten hardlopen tijdens de lockdown geen negatieve gevolgen heeft voor de gezondheid van Nederlandse hardlopers.

Deel 2: Op GPS gebaseerde trainingsbelasting en de associatie met hardloopblessures

Eerdere studies die onderzoek deden naar hardloopblessures gebruikten meestal vragenlijsten om trainingsgegevens te verzamelen. Het gebruik van sporthorloges of mobiele telefoons die gegevens verzamelen middels global positioning system (GPS) kan dienen als een alternatief voor het nauwkeurig verzamelen van trainingsgegevens. Het doel van **Hoofdstuk 5** was om te onderzoeken of het haalbaar is om GPS-gegevens te verzamelen van recreatieve hardlopers. Daarnaast was het doel van deze studie om te evalueren of GPS-gegevens gebruikt kunnen worden om de associatie tussen trainingsbelasting en knieblessures bij hardlopers te onderzoeken. Deelnemers aan de INSPIRE-studie met een nieuwe knieblessure en deelnemers zonder een nieuwe blessure ontvingen een extra vragenlijst en een verzoek om hun GPS-gegevens met ons te delen. Acute:chronic workload ratios (ACWRs) werden berekend met behulp van de wekelijkse trainingsafstand (gebaseerd op GPS-gegevens). Bijna twee derde van de deelnemers (N=240) gebruikte een GPS-apparaat of platform om zijn hardlooptrainingen vast te leggen en was bereid zijn GPS-gegevens te delen. Van de deelnemers (N=144) die een verzoek kregen om GPS-gegevens met ons te delen, deelden 50,0% succesvol hun gegevens. We concludeerden dat het haalbaar lijkt om trainingsgegevens te verzamelen van GPS-apparaten en platforms die worden gebruikt door recreatieve hardlopers. Het merendeel (69,4%) van de gedeelde GPS-gegevens was bruikbaar om wekelijkse ACWRs te berekenen. Daarom kunnen in toekomstige studies op GPS gebaseerde ACWRs worden gebruikt om associaties tussen trainingsbelasting en hardloopblessures te onderzoeken.

Nadat we hadden geconcludeerd dat GPS-gegevens kunnen worden gebruikt om trainingsbelasting te berekenen bij hardlopers, hebben we onderzocht wat de beste methode is om verandering in trainingsbelasting te berekenen. In eerdere onderzoeken werden verschillende methoden gebruikt om de verandering in trainingsbelasting te berekenen. In **Hoofdstuk 6** onderzochten we het verschil tussen vier methoden: 1) wekelijkse trainingsbelasting; 2) ACWR, gekoppeld voortschrijdend gemiddelde; 3) ACWR, ontkoppeld voortschrijdend gemiddelde; 4) ACWR, exponentieel gewogen voortschrijdend gemiddelde (EWMA). Aan het einde van de follow-up van de SPRINT-studie werd aan alle deelnemers gevraagd om hun GPS-gegevens met ons te delen. De primaire uitkomstmaat was de vooraf gedefinieerde significante toename in trainingsbelasting (wekelijkse trainingsbelasting ≥ 30% progressie en ACWRs ≥ 1,5), gebaseerd op trainingsafstand. GPS-gegevens van 430 deelnemers werden gebruikt voor de analyses met in totaal 22.839 hardlooptrainingen. We concludeerden dat het verschil tussen de wekelijkse trainingsbelasting methode en de ACWR-methoden groot was, aangezien 43,0% van de hardlooptrainingen met een significante toename in trainingsbelasting berekend door de wekelijkse trainingsbelasting methode een verschil toonde met de gekoppeld voortschrijdend gemiddelde- en EWMA-methode. We vonden kleinere verschillen tussen de drie ACWR-methoden. Om een geschikte methode te valideren voor het meten van de verandering in trainingsbelasting bij hardlopers, is het nodig om onderzoek te doen naar de complexe relatie tussen trainingsbelasting, de meest gevoelige methode om verandering in trainingsbelasting te berekenen en het risico op het krijgen van een hardloopblessure.

De associatie tussen trainingsbelasting en het krijgen van een hardloopblessure werd onderzocht in **Hoofdstuk 7**. In dit onderzoek maakten we gebruik van de vragenlijsten en de GPS-gegevens die verzameld waren in de SPRINT-studie. Verandering in trainingsbelasting werd berekend via ACWRs (gekoppeld voortschrijdend gemiddelde methode) gebaseerd op afstand, duur of snelheid van elke hardlooptraining. Cox-regressieanalyses werden uitgevoerd om de associatie tussen ACWR en hardloopblessures te evalueren. GPS-gegevens van 461 deelnemers werden gebruikt voor de analyses met in totaal 20.425 hardlooptrainingen. We identificeerden een associatie tussen ACWR en hardloopblessures op basis van de variabelen trainingsafstand (HR 1,32; 95% CI 1,00-1,74) en trainingsduur (HR 1,39; 95% CI 1,07-1,79) respectievelijk. In de analyses gecorrigeerd voor bekende risicofactoren bleef alleen de ACWR op basis van trainingsduur (HR 1,33; 95 % CI 1,02-1,74) positief geassocieerd met het ontstaan van hardloopblessures. Er werd geen significante associatie gevonden tussen ACWR en hardloopblessures wanneer hardlopers die een blessure hadden bij de start van de SPRINT-studie geëxcludeerd werden (15,8%). We concludeerden dat de klinische relevantie van de geïdentificeerde associaties twijfelachtig is gezien de kleine hazard ratio's en inconsistentie in uitkomsten. Dit maakt de rol van trainingsbelasting voor de preventie van hardloopblessures onzeker.

Deel 3: Preventie van hardloopblessures

In 2017 werd de INSPIRE-studie uitgevoerd waarin het effect van een multifactorieel online blessurepreventieprogramma op het aantal hardloopblessures werd onderzocht. Dit programma verminderde echter niet het aantal hardloopblessures bij recreatieve hardlopers. Desalniettemin werden nieuwe inzichten verworven om het blessurepreventieprogramma te verbeteren, zoals het inzicht dat het preventieprogramma zich moet richten op hardlopers met een eerdere hardloopblessure. Met behulp van deze nieuwe inzichten ontwikkelden we een verbeterd online blessurepreventieprogramma, speciaal gericht op hardlopers met een eerdere hardloopblessure (de SPRINT-studie). In **Hoofdstuk 8** presenteerden we de resultaten van de SPRINT-studie (N=4050). Om verschillen tussen blessurepercentages vast te stellen, werden univariate en multivariate logistische regressieanalyses uitgevoerd. Tijdens de follow-up kreeg 35,5% van de deelnemers een nieuwe hardloopblessure, met geen verschil tussen de interventie- en controlegroep. Het preventieprogramma had ook geen invloed op het voorkomen van nieuwe blessures in de subgroep van hardlopers met een eerdere blessure. Hardlopers die het programma volgden meldden meer blessures in vergelijking met degenen in de controlegroep. Daarom zouden toekomstige studies zich moeten richten op individueel gerichte preventie met aandacht voor de timing en toepassing van de preventieve maatregelen.

Tot slot werden de belangrijkste bevindingen van dit proefschrift samengevat in **Hoofdstuk 9** en besproken in een bredere context. Dit hoofdstuk werd afgesloten met klinische implicaties en suggesties voor toekomstig onderzoek.

DANKWOORD

Nu komt het meest gelezen hoofdstuk van het hele proefschrift. Een plek om alle mensen te bedanken die een bijdrage hebben geleverd tijdens mijn promotietraject. Ik weet dat het onmogelijk is om iedereen bij naam te noemen, maar ik wil graag iedereen die voor mij belangrijk is of geweest is bedanken!

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Al tijdens mijn masterstage kwam ik in contact met mijn tweede copromotor; Robert-Jan de Vos. Beste **Robert-Jan**, ondanks jouw drukke agenda reageerde je altijd heel snel en prettig op mijn e-mails. Ook al gaf je aan dat de feedback wel even ging duren, vaak ontving ik dan nog binnen een week uitgebreide feedback van jou. Bedankt dat je altijd open stond om mee te denken over lastige kwesties of je met jouw klinische blik te mengen in belangrijke discussies. Jouw achtergrond als sportarts zorgde ervoor dat ook de klinische waarde van mijn onderzoek niet vergeten werd.

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Joy, samen zijn we volwassen geworden en zijn we elkaar altijd blijven zien. Bedankt voor de goede gesprekken en de interesse die jij in mijn onderzoek hebt getoond. Jij bood altijd een luisterend oor wanneer dit nodig was. Ik vind het heel leuk dat jij nu ook begonnen bent aan een promotietraject, iets wat zeker bij jou past en wat jij gaat rocken!

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CURRICULUM VITAE

Kyra Cloosterman is geboren op 16 september 1992 in Nijmegen. Na het behalen van haar gymnasiumdiploma aan het Dominicus College, begon zij in 2010 met de studie Biomedische Wetenschappen aan de Radboud Universiteit in Nijmegen. Tijdens de bachelorfase en het verrichtten van vrijwilligerswerk in Nepal kwam ze erachter ook interesse te hebben in de studie Geneeskunde. In 2013 begon zij met de master Biomedical Sciences, met als specialisatie bewegingswetenschappen. Daarnaast begon zij in 2015 met de premaster Geneeskunde, waarna ze in 2016 doorstroomde naar de master Geneeskunde. Tijdens het volgen van coschappen werd haar duidelijk dat zij het meest geïnteresseerd was in het vak als huisarts. Dit was voor haar de reden om ervoor te kiezen haar masterstage te volgen aan het Erasmus Medisch Centrum in Rotterdam, waar zij onderzoek kon doen naar de preventie van hardloopblessures op de afdeling Huisartsgeneeskunde. In 2019 rondde zij beide studies succesvol af. Na het behalen van haar artsenexamen heeft zij gewerkt als arts-assistent (ANIOS) psychiatrie bij het Vincent van Gogh Instituut. Per 1 maart 2020 is zij gestart als arts in opleiding tot huisarts en onderzoeker (AIOTHO) aan het Erasmus Medisch Centrum in Rotterdam. Tijdens het AIOTHO-traject heeft zij de opleiding tot huisarts gecombineerd met een promotieonderzoek naar de consequenties en preventie van hardloopblessures. Zij verwacht in februari 2025 haar huisartsopleiding af te ronden.

PHD PORTFOLIO

Erasmus MC Department: General Practice
PhD Period: 2020-2024
Promotor: Prof.dr. S.M.A. Bierma-Zeinstra
Copromotors: Dr. M. van Middelkoop and Dr. R.J. de Vos

	Year	Workload (ECTS)
Professional education		
Vocational training in general practitioner, Erasmus MC, Rotterdam	2020-2025	
Courses and training		
BROK (Basic course Rules and Organization for Clinical researchers) course	2020	1.5
Workshop Microsoft Excel 2016: Basic	2020	0.3
Workshop Microsoft Excel 2016: Advanced	2020	0.4
Photoshop and Illustrator CC 2020	2020	0.3
Scientific Integrity Course	2022	0.3
Basic course on R	2022	1.5
Presentations		
Oral presentation Sportmedisch Wetenschappelijk Jaarcongres, Ermelo	2018	1.0
Oral presentations Department of General Practice, Rotterdam (1/yr)	2020-2023	2.0
Poster presentation American College of Sports Medicine, online	2021	1.0
Poster presentation Scandinavian Sports Medicine Congress, Copenhagen	2023	1.0
Participation (inter)national conferences		
Annual meeting North American Primary Care Research Group, online	2020	1.5
NHG-Wetenschapsdag	2021-2022	0.6
Teaching activities		
Clinical reasoning for master students	2020	2.0
Supervision student session ‘How to judge a paper’	2020	0.3
Supervision of master research project medical student (2x)	2021-2023	8.0

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	Year	Workload (ECTS)
Supervision of master research project student Business Analytics	2021	2.0
Supervision of master research project student Physiotherapy (2x)	2020-2023	8.0
Other activities		
Peer review British Journal of Sports Medicine (2x)	2021-2022	2.0
Hiring committee general practitioners	2023-2024	1.5

LIST OF PUBLICATIONS
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Cloosterman KLA, van Middelkoop M, Krastman P, de Vos RJ. Running behavior and symptoms of respiratory tract infection during the COVID-19 pandemic: A large prospective Dutch cohort study. J Sci Med Sport. 2021 Apr;24(4):332-337.

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Cloosterman KLA, de Vos RJ, Willemsen S, van Oeveren B, Visser E, Bierma-Zeinstra SMA, van Middelkoop M. Association between GPS-based training load and injury risk in recreational runners: a large prospective study. Submitted.

Van Hoek JPKD, **Cloosterman KLA**, de Vos RJ, van Middelkoop M. Sex differences in characteristics and factors associated with new running-related injuries among runners. Submitted.

OTHER PUBLICATIONS

Mans MFT, van der Most F, **Cloosterman KLA**. Letter to the Editor on: "Effectiveness of Multi-activity, High-intensity Interval Training in School-aged Children". Int J Sports Med. 2021 Jan;42(1):96-97.

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