Chapter 7

General discussion
INTRODUCTION
The popularity of running has increased in the past years and is still increasing. This is a positive trend, because physical activity is accompanied by many health benefits [1-4]. Therefore, becoming and staying physically active is a cornerstone in today’s public health [5]. Remaining physically active on a regular basis, however, is endangered by a high injury incidence [6]. The high number of running-related injuries (RRI) recorded in runners, particularly in novices, is therefore cause to concern.

The lack of consistent risk factors and preventive measures combined with the high incidence of RRI in novice runners, stresses the need for a large scale prospective cohort study in this population of runners. Therefore, we designed the NLstart2run study, a multi-center prospective cohort study among runners participating in a nationwide “Start to Run” course. The NLstart2run study aimed to increase our knowledge on incidence and determinants for RRI in novice runners. More insight into risk factors for RRI can guide preventive measures.

In this chapter, the research described in the thesis will be placed in a broader context. The incidence of RRI and the impact of injury definition and population of runners followed will be discussed in the first part of the chapter. Secondly, the etiology of RRI will be discussed. In order to solve the puzzle of minimizing RRI risk in runners, some important caveats that were demonstrated in the NLstart2run study should be addressed. These caveats and recommendations for future research will be discussed in the final part of this chapter.

INCIDENCE OF RUNNING-RELATED INJURIES
Many studies have examined the incidence of RRI among runners. These studies reported injury proportions that varied greatly between 1.4% and 94.4% [7, 8]. Several factors, such as injury definition, method of injury assessment, population of runners followed or duration of follow-up, may cause this large range in incidence reports. Increased insight into the burden of injuries might identify populations at increased risk of sustaining an RRI. This information can give direction to future research on the understanding of RRI etiology in these specific populations. Therefore, we conducted an extensive systematic review that was presented in chapter 2. The findings of this review revealed big differences in RRI incidence proportions between different populations of runners. Overall a trend was observed in athletes participating in short track races and ultra marathon runners reporting the highest proportions of time-loss injuries.

Injury incidence versus injury risk
It has often been assumed that novice runners have an increased RRI risk [9-11]. The results presented in chapter 2, however, did not show higher injury proportions in this population
of runners. Novice runners, for instance, had a pooled time-loss injury proportion of 26.4% while this proportion was 64.7% in marathon runners in studies with a follow-up period up to 15 weeks. Incidence proportion is however no synonym for injury risk. To determine the injury risk, the time spent running before the occurrence of an injury should be taken into account as well [12]. Therefore we stratified the analyses in chapter 2 based on duration of follow-up. Because of differences in weekly running duration between different populations of runners, it would have been better to relate the number of injuries to the real time spent running. As a consequence, duration of all running sessions should be registered during follow-up, which increases the impact on participants and researchers. This probably is the reason that only a small number of studies did report incidence densities or cumulative incidence rates that take the time spent running into account [13]. When comparing incidence densities of time-loss injuries between novice runners and middle distance track runners, 33.0 and 5.6 injuries per 1,000 hours of running respectively [14, 15], injury risk seems to be higher in novice runners. A recent systematic review confirmed this higher injury risk in the population of novice runners [16].

As stated in chapter 2, it is highly recommended to include running exposure in future studies, because this enables the calculation of the risk on RRI. Another advantage of expressing RRI incidence in terms of running exposure is the possibility to compare RRI incidences between different studies with varying periods of follow-up. For example, in the NLstart2run study, the injury proportion was 10.9%, which seems low compared to other studies among novice runners in which proportions above 20% were reported [10, 14]. The incidence density, however, was 27.5 RRI per 1,000 hours of running which is comparable to these other studies. Besides differences in injury reporting, comparison of RRI incidences between different studies is also hampered by differences in injury definitions.

**Injury definitions**

Overall, injury definitions can be divided into definitions that register: ‘all complaints’, ‘medical attention complaints’ or ‘time-loss complaints’ [17]. An ‘all complaints’ injury definition registers all physical complaints that occur during sports participation, regardless of its consequences. The use of this definition will result in the highest number of injuries compared to the other definitions [18]. A ‘medical attention’ definition, on the other hand, only registers physical complaints that were reported to a medical professional. Using this definition will therefore result in a lower number of injuries compared to the ‘all complaints’ definition. Whether or not a complaint is reported to a medical professional is highly dependent on accessibility of a medical professional. Given this accessibility, it is likely that complaints to the medical staff are more often reported by elite athletes compared to recreational runners. In addition, a medical attention definition does not tell us anything about the impact
of the complaint on sports participation. A time-loss definition, on the other hand, captures complaints that result in a reduction or complete absence from sports. This third category of injury definitions is often used in cohort studies, including the NLstart2run study [19]. The association between type of injury definition and number of injury complaints is schematically depicted in Figure 1.

![Image of Figure 1](image_url)

**Figure 1**: Interactions between various definitions of injury. Circle-size represents the relative number of incidents likely to be registered (not to scale) (adapted from Clarsen et al., 2014 [17]).

In research among runners, time-loss definitions are most often used to record RRI s. Time-loss definitions, however, allow for a large variety of applications. Time loss can refer to a reduction in sports participation (lower intensity, shorter distance or duration) [9, 20] or complete absence from sports as a result of running-related pain [21, 22]. Also the duration of time loss to be recorded as an RRI differs between studies. In some studies one-day of time loss is considered an RRI [10, 23], while other studies recorded an RRI when time loss persisted for one-week [24, 25] or three-training consecutive sessions [14, 26]. These differences in application of time-loss definitions possibly have a large impact on the reported RRI incidences.

In chapter 6 we examined the impact of six different injury definitions on injury incidence and injury characteristics. The injury definitions used were classified into: all running-related complaints, running-related complaints leading to training reduction and running-related complaints resulting in training absence. These three types of definitions were applied for a minimum duration of complaints of one-day or one-week. The categorization of injury definitions resulted in a total of six different definitions that were applied in the same dataset. We showed that injury definitions indeed had a large impact on the reported injury incidence.
Anatomical locations

The results displayed in chapter 2 showed that the highest proportion of time-loss injuries were sustained around the knee and lower leg in most populations of runners. This is in line with the NLstart2run study, in which 38.4% of the injuries were sustained around the knee, followed by 20.0% in the calf and 13.0% in both the shin and Achilles tendon. In other populations of runners, no large differences in distribution of injury locations existed as shown in chapter 2, except for sprinting athletes. In sprinters (track athletes competing in distances up to 400 meters) most injuries were located in the upper leg (32.9%). This probably is the result of the explosive character of this running discipline in which propulsion is mainly achieved by the hamstrings [27].

As described above, injury definitions have a large impact on the injury incidence. In addition, we showed that the relative distribution of affected body locations was also affected by application of different injury definitions. The proportion of knee complaints was higher when using a time-loss definition, while application of a running-related pain definition resulted in relatively more injuries located at the pelvis/sacrum/buttock region. This stresses the need for standardized injury registration methods, making comparisons between different studies more feasible.

Recurrent injuries

An incidence rate can refer to the number of new injuries, the number of recurrent injuries or the number of new and recurrent injuries [28]. In the NLstart2run study, the RRI incidences are based on the number of new RRIs. This method is similar to most previous studies on injuries in runners. During the course of follow-up it is possible to have multiple RRIs. Including these subsequent injuries in incidence reports gives a better overview of the exact burden of injuries. When taking subsequent injuries into account, it is important to distinguish new injuries from exacerbations and recurrences. Therefore, Fuller et al. proposed a framework to guide research on recurrent injuries [29]. This framework for classifying new injuries (index injuries) and subsequent injuries was extended by Hamilton et al. (Figure 2) [30]. It should be noted that in this framework, the injury definition (e.g. medical attention or time-loss) still determines the start and recovery of injuries. When a time-loss definition is used, return to play would mean recovery from injury and a recurrent injury after return to play would be classified as re-injury [30]. We did not include subsequent injuries in the reports of the NLstart2run study, since our reports describe injury incidence during a short term running program. Studies with a longer period of follow-up are advised to include subsequent injuries in incidence reports and risk factor analyses as well.
Figure 2: Framework for classifying new injuries, re-injuries and exacerbations. (Based on Fuller et al. [29] and Hamilton et al. [30])
Overuse injuries

A recent consensus statement on injury definitions for recreational runners proposed the following RRI definition: “Running-related (training or competition) musculoskeletal pain in the lower limbs that causes a restriction on or stoppage of running (distance, speed, duration or training) for at least seven days or three consecutive scheduled training sessions, or that requires the runner to consult a physician or other health professional” [31]. Application of a time-loss definition like this, however, presents some difficulties in sporting activities like running with a predominance of overuse injuries [18]. Overuse injuries are often the result of repetitive micro-traumas which lead to an injury without an identifiable event responsible for the injury [32]. Overuse injuries often have a slow appearance of pain with a repetitive character. These complaints do not necessarily result in functional limitations (i.e. time loss) and as a result, many of these complaints will be missed under a time-loss definition [33].

The Oslo Trauma Research Center (OSTRC) questionnaire on health problems was developed to monitor overuse problems and illness over time [33]. This questionnaire consists of four questions regarding physical complaints and training participation in which severity of complaints is expressed in a score (Figure 3). This methodology can be used to capture the complete burden of complaints among runners. There are however also some limitations to this questionnaire. The severity score appointed to each answer option is arbitrary as shown in Figure 3. The total severity score ranges from 0 (no complaints) to 100 (severe complaints), but not all scores between 0 and 100 are possible. Therefore the outcome seems to be continuous, but actually is not. Moreover, because this questionnaire is administered weekly, the method that is used to score the severity of complaints is prone to recall bias. This can lead to findings similar to “respondent fatigue” as shown in a recent study on overuse injuries in athletes [34, 35]. What might underlie this phenomenon in the OSTRC questionnaire is that participants relate their answers to previous weeks. Severity assessment with four/five answer options allows recall from previous weeks, which might lead to a “floor effect” during the first few weeks of follow-up. Nevertheless the use of a short, weekly questionnaire to monitor overuse, injury and illness complaints over time is promising and might be the solution for standardizing injury registration in future studies. The above mentioned shortcomings can be solved by the use of a Visual Analogue Scale (VAS) to score the different questions of the questionnaire. For instance, question 1 could be scored with a VAS scale ranging from 0 (full participation without health problems) to 100 (cannot participate due to injury/illness). Conditional questions can be added to record time-loss and medical attention injuries taking the distinction between new injuries, exacerbations and re-injuries into account.
The Oslo Sports Trauma Research Center (OSTRC) Questionnaire on Health Problems

Please answer all questions regardless of whether or not you have experienced health problems in the past week. Select the alternative that is most appropriate for you, and in the case that you are unsure, try to give an answer as best you can anyway.

**Question 1**
Have you had any difficulties participating in normal training and competition due to injury, illness or other health problems during the past week?

- 0 Full participation without health problems
- 8 Full participation, but with injury/illness
- 17 Reduced participation due to injury/illness
- 25 Cannot participate due to injury/illness

**Question 2**
To what extent have you reduced your training volume due to injury, illness or other health problems during the past week?

- 0 No reduction
- 6 To a minor extent
- 13 To a moderate extent
- 19 To a major extent
- 25 Cannot participate at all

**Question 3**
To what extent has injury, illness or other health problems affected your performance during the past week?

- 0 No effect
- 6 To a minor extent
- 13 To a moderate extent
- 19 To a major extent
- 25 Cannot participate at all

**Question 4**
To what extent have you experienced symptoms/health complaints during the past week?

- 0 No symptoms/health complaints
- 8 To a mild extent
- 17 To a moderate extent
- 25 To a severe extent

Figure 3: The four key questions of the Oslo Sports Trauma Research Center Questionnaire on Health Problems with corresponding scores for each answer option. (Based on Clarsen et al. [33, 36])
RISK FACTORS FOR RUNNING-RELATED INJURIES

An important step towards the introduction of preventive measures is the identification of factors and mechanisms that play a role in the occurrence of an injury [37]. Several studies examined factors potentially associated with RRI [38-41]. The number of risk factors consistently associated with RRI is however small. A recent systematic review on the main risk factors for RRIs concluded that the only risk factor consistently reported to increase RRI risk was a previous injury in the past year [41]. The inconsistencies in literature are probably caused by differences in multiple factors (e.g. study design, method of analysis, population of interest). It is likely that inconsistent results in previous prospective cohort studies are caused by small sample sizes. Small sample sizes do not allow for an extensive multifactorial analysis, which is preferred for identification of risk factors [42]. We tried to overcome this limitation by including a large number of runners in the NLstart2run study. In total 1,696 participants were included from who 185 sustained an RRI. This allowed us to include a maximum number of 18 variables into the multifactorial analysis.

Personal characteristics

In chapter 4 we showed that higher age, higher BMI, no previous running experience and previous musculo-skeletal complaints during sports and exercise were associated with RRI occurrence in novice runners. Having no previous running experience turned out to be the strongest risk factor for RRI. Possibly, previous running experience might have led to neuro-muscular or musculoskeletal adaptations that decrease RRI risk in novice runners.

It is generally believed that less running experience is related to an increased RRI risk in runners. However, these conclusions are drawn from studies that were conducted in more experienced runners. This lower risk in more experienced runners might be a reflection of “the healthy runner effect”, whereby runners not suffering from injuries will maintain running activity and therefore have more running experience [10, 43]. This effect is expected to be low in novice runners, because this population of runners generally has little to no running experience, thus no history of severe RRIs. In studies among more experienced runners, the number of years that running was practiced was often used to express running experience [23, 38, 44]. This measure of running experience was not suitable in the current study, because of the population of novice runners who did just pick up running. Running experience was therefore assessed with a question whether participants had been running on a regular basis in the past or not. This is comparable to the methods used in previous studies among novice runners [10, 25]. We categorized running experience into three categories: no experience, experience in the past year and experience more than a year ago, which is in line with the method used in the study of Buist et al. [10]. They also found that having no running experience was associated with an increased RRI risk. In contrast to our
results from the NLstart2run study, RRI risk was not different between participants with running experience longer than a year ago compared to participants without previous running experience. Other studies in novice runners dichotomized running experience and did not find a significantly higher RRI risk in runners without previous running experience [14, 25]. Although the exact reason for this discrepancy is unknown, it might be related to different criteria of inclusion or different purposes for participating in the study or running program.

To comply with the statistical power requirements, previous studies on risk factors for RRI in novice runners had to select the variables that were entered into a multifactorial analysis based on their independent link with RRI or by using stepwise modeling [10, 20, 45]. These techniques do have several limitations that can lead to conflicting results [46]. The selection of possible predictors based on their independent link neglects the complex relations between these variables. Stepwise modeling takes these relations into account, however, due to multiple testing, standard errors become too small, which leads to biased estimates and narrowed confidence intervals [46]. The results from these studies should therefore be interpreted with caution. The large sample size in the current study made it possible to perform a multifactorial analysis in which all variables of interest could be entered into one model [47]. Considering this strength, the results of the NLstart2run study demonstrated that age, BMI, previous injuries and previous running experience were the most important (intrinsic) risk factors for RRI in novice runners. Runners who comply with these characteristics should therefore be extra cautious when starting a running program. The runners could be informed about early signs of injury prior to the running program and preferably an optimized running schedule should be made for these “high risk” novice runners. Future studies should examine the effect of different training factors on RRI risk in novice runners while taking the above mentioned risk factors into account.

**Training characteristics**

In chapter 5, the association of training factors with RRI was examined. Running with a higher intensity was associated with RRI. Weekly training frequency showed a trend towards running three times per week being more hazardous than two times per week. Surprisingly, higher weekly running volume was associated with a lower risk on RRI. This study was the first to include running volume, frequency and intensity while taking into account the time-varying nature of these characteristics.

Based on the results of a systematic review on the association of training factors with RRI, a “U-shaped” pattern between running frequency and RRI risk was suggested [40]. Our study could not confirm this pattern, possibly as a result of the population of runners followed or the statistical methods used. We determined the running frequency based on the number of training sessions in the previous 7 days, while other studies asked for the average weekly
running frequency. The association between perceived running intensity and injury susceptibility has not been studied yet. A few studies did examine the effect or running speed on injury risk [40], however, these studies showed conflicting results, presumably due to the fact that speed is not an equivalent to perceived intensity. Running at a similar speed does not imply a similar perceived intensity, because intensity is highly dependent on the runner’s level which might explain the inconsistencies in previous research.

Higher running volume has often been identified as a risk factor for RRIs [6, 23, 43, 44, 48-55]. Interestingly, our results from the NLstart2run study showed an opposite trend, where participants running more than 60 minutes per week spread over two training sessions had the lowest risk on injury. In chapter 5 several causes for this finding were raised. It is likely that participants with specific characteristics, like lower age, lower BMI, previous running experience or no previous injuries, were able to complete longer training sessions while having a lower RRI risk. Often differences in training exposure are not taken into account when studying the association of different risk factors for RRI. Therefore, it is not surprising that there are many inconsistencies regarding risk factors for RRI when considering the injury mechanism in running.

**INJURY MECHANISM IN RUNNING**

In running most injuries are the result of overuse, which is the cumulative process of tissue damage [34]. Cumulative tissue damage, in turn, is caused by too much load in relation to the load capacity [56]. To better understand the association between risk factors and injury, it is important to realize that load is caused by sports participation. Load capacity, on the other hand, is affected by personal factors (e.g. age, previous injury, previous training). In the end, the load capacity determines whether a (cumulative) training load results in injury or not.

The importance of sports participation in injury occurrence is highlighted by Malisoux et al. who stated that: “Runners do not sustain an injury only because they are overweight, older, or have had a previous injury, injury can only occur when people practice running” [57]. From a causative perspective, this means that running exposure (i.e. the training load) is a necessary cause for sustaining an RRI [12]. For this reason, training characteristics (an indirect measure of training load) should have a direct relation to injury. The amount of training load that can be tolerated is different between individuals and for specific structures, because of differences in structure specific load capacities. The load capacity, however, does not have a direct relation to injury, but it modifies the effect that load has on injury development [57]. This insight is important, because it has several consequences for the method of analysis. The relation between training load, load capacity and injury is schematically depicted in Figure 4.
Training load and load capacity are variables that cannot be measured directly (latent variables). The different risk factors that were studied in chapters 4 and 5 of this thesis, however, are observable variables that partly estimate and influence these latent variables. The personal characteristics age, previous running experience and previous musculoskeletal complaints that had an association with injury (chapter 4) are possibly indicators for the load capacity, while the training factors that were studied in chapter 5 relate to training load.

It should be noted that not all personal characteristics affect the load capacity. BMI for instance, impacts the training load and biomechanics influences the load distribution over different anatomical structures. Personal characteristics (internal risk factors) can therefore both affect the training load and the load capacity as shown in Figure 5. The model that is shown in Figure 5 describes a single training session and the training load and load capacity are structure specific.

Figure 4: Relation between training load, load capacity and injury. Training load has a direct link to injury. This relation is modified by the load capacity (i.e. resulting in an RRI yes/no).

Figure 5: A structure specific model describing the interplay of internal and external risk factors on the training load and load capacity for a single training session.
Consequences for analysis

In Figure 6 the differences between confounding, interaction and effect-measure modification are schematically displayed for both running volume and BMI on RRI [58, 59]. In previous studies on personal and training risk factors for RRI these variables were entered into a multivariable regression model to examine the associations with RRI. This method of analysis treats all variables as confounders. This type of analysis assumes a direct link between all risk factors with RRI, as schematically depicted in Figure 6. As explained in the above described injury mechanism (Figure 5), this is not correct because personal characteristics do not directly influence RRI risk (without running, high BMI will never lead to RRI). Personal characteristics modify the relation between training load and RRI. This would mean that the risk of RRI for different amounts of running volume varies between different strata of BMI. This effect could be observed with an interaction term. In case of interaction, the combined association of running volume and BMI is higher (or lower) than expected based on the separate associations of running volume and BMI with RRI. As can be seen in Figure 6 this is incorrect, because interaction also assumes a direct relation of running volume and BMI with RRI. Personal characteristics should be seen as effect-measure modifiers. As shown in Figure 6, effect-measure modifiers change the association between running volume and RRI for different strata of BMI. BMI does not have a direct relation to RRI which is correct as shown in Figure 5. For this reason, we chose not to include personal characteristics in the analyses of the NLstart2run study as described in chapter 5. To correctly account for the risk factors that were identified in chapter 4 (i.e. age, BMI, previous running experience and previous injuries), the analyses should have been stratified on these variables. Unfortunately it was not justified to do this in the analyses described in chapter 5, because the number of RRIs in each stratum was too low (below 5 RRIs). To correctly account for multiple personal characteristics, participants should be stratified over these characteristics in the analysis. Take age (3 strata), BMI (3 strata), previous injury (2 strata) and previous running experience (2 strata) for example. An analysis in which these factors are taken into account will result in 36 different strata. For meaningful interpretation of the results, each stratum should include around 5 injured participants. To populate each stratum with a sufficient number of injuries, a large cohort of runners is needed.
Figure 6: Schematic representation of confounding, interaction and effect-measure modification of running volume, BMI and injury.

**Statistical challenges**

Hreljac pragmatically stated that: “all overuse running injuries are the result of training errors” [56]. The term training errors is broad, but it is likely related to a time dependent process, like a sudden change in training regimen. The influence of training characteristics on RRI has been subject of several studies [40]. These studies, however, examined the association of training frequency or volume of a “normal training week”. This method treats training behaviors as constants over time. In reality, however, this is not true, as training is characterized by constant changes in volume and frequency. For identification of training errors it therefore is essential to allow training factors to vary over time.

In chapter 5, we allowed training factors to vary over time. In essence, training characteristics were calculated for the seven days prior to each training session. In this manner, these calculated training variables could vary over time (i.e. for each training session). Doing so, the assumption was made that an RRI occurred due to training behavior in the previous week. We chose to calculate the absolute running volume (total duration) for each week and found a higher running volume to be protective for RRI. It can be argued that it would
have been more appropriate to calculate the differences in running volume between weeks. These differences indicate progression or regression which assumable better reflect the differences in training behavior that might be associated with RRI. This would mean that the training data in the first two weeks could not be included into the analysis, because this information is necessary to calculate the difference between two training weeks. Due to the relatively short duration of the NLstart2run study, the amount of missing data, including injuries, would be too high for appropriate interpretation.

The unexpected result that lower weekly running volume was associated with higher RRI risk could be explained by a problem inherent to the inclusion of time-varying training factors into an analysis. It is possible that a participant reduced running volume in the week before an RRI was registered. In the statistical analysis, this would mean that reduced running volume will be associated with RRI. The problem of an observational study design like ours is that we do not know whether the reduced running volume caused the RRI or is the result from complaints preceding an RRI. It might be possible that the participant already suffered from some physical complaints which resulted in a reduced running volume. This would mean that the physical complaints increased RRI risk instead of the reduced running volume. To avoid this uncertainty, future studies are advised to provide a strict running schedule to the participants. Running participation should be monitored closely and in case of deviations from the schedule, questions regarding reasons for deviation should be asked. This information should be taken into account in the analysis.

An important assumption of the Cox regression analysis is the proportionality of hazards [60]. This assumption states that survival curves for different strata must have hazard functions that are proportional over time. It is important to check the proportional hazards assumption for each variable included in a Cox regression model, because when the proportional hazards assumption is not met, results become meaningless [61]. It can be argued whether this assumption holds for analysis with time-varying training variables, because injury risk changes as a result of training and this change is not similar in all participants. Recently a new statistical method, the pseudo values approach [62], was proposed that does not rely on the proportional hazards assumption. A limitation of this method, however, is that injury risks can only be compared at fixed points in time while the Cox regression analysis gives an instantaneous risk based on the complete period of follow-up. Besides, it is not possible to analyze time-varying covariates with the pseudo-values approach yet. For these reasons we chose not to use the pseudo-values approach in the NLstart2run study, but since this method is developing, future studies might consider using this method instead of a Cox regression analysis.
STRENGTHS AND LIMITATIONS

The major strengths of the NLstart2run study include the prospective study design, the large sample size of novice runners and the statistical techniques used. This made it possible to include multiple risk factors into a multifactorial analysis. For this reason, it can be concluded that the risk factors identified in chapter 4 are most important for novice runners. There were several limitations that should be mentioned when interpreting our results. First of all, all data was based on self-report. Personal characteristics were collected with a baseline questionnaire and training characteristics were monitored with weekly running diaries. RRI's were registered based on pain information that was entered into these diaries. Unfortunately no diagnoses of the injured runners were available. Future studies are advised to monitor training behavior more objectively, for instance with GPS devices. Also injury diagnoses are preferred. Next, all registrants of the “Start to Run” course were eligible for inclusion. The program was aimed at novice runners, however, we did not handle an inclusion criteria that only allowed novices in the NLstart2run study. Therefore more experienced runners could have been included in the study population. In addition, a large proportion of the participants were female (78.5%), which may limit the generalizability of our results. On the other hand, our study describes the typical “Start to Run” participant making the results applicable to this large population of runners. Furthermore, in the NLstart2run study participants were given a predefined running program and we did not monitor deviations from this running program closely. For this reason, variation in training exposures was necessary to conduct the analyses described in chapter 5. The predefined running program might have limited variation between runners, however, only one training session was supervised during the running program and the participants were free to plan the other sessions. This freedom resulted in many training variations between participants, allowing the analyses. In addition, due to the short duration of the running program (6 weeks) it was not appropriate to study week-to-week differences in training behavior. It can be argued that especially these changes affect RRI risk [63]. Unfortunately it was not possible to correctly take personal characteristics into account while examining the effect of training characteristics on RRI. In such a case personal characteristics should be handled as effect-measure modifiers for which a large number of RRI's is necessary. Despite of the large sample size only a small proportion of participants sustained an RRI, which limited the possibility of such analyses. Finally, the NLstart2run study did find associations between non-modifiable risk factors and RRI (i.e. higher age, no running experience and previous injuries). This opens the door for a priori screening, but limits the usage for preventive measures. We were not able to identify high-risk training behavior within specific subgroups. Therefore future research should focus on training programs for novice runners having a high risk profile.
FUTURE PERSPECTIVES

More work is needed to properly advice novice runners with a specific risk set about training schedules. The NLstart2run study demonstrated some important caveats that should be considered when studying the effect of training on injury occurrence. As discussed in this chapter, we should realize that running eventually is the main exposure leading to RRI. Intrinsic and extrinsic risk factors impact both the training load and the load capacity as depicted in Figure 5. This distinction has some serious implications that should be addressed in future studies, but before conducting these studies it is important to ensure a solid base.

Solid base for future research

For years, researchers have stressed the need for a standardized RRI definition. With nowadays digital questionnaires that include advanced routing opportunities, it is possible to collect detailed information on physical complaints that occur during training. The main focus for future research should therefore not be to use one uniform injury definition, but to develop a standardized injury registration method that collects all information on physical complaints and illness. The weekly OSTRC overuse injury questionnaire is a good starting point, however as mentioned before, there are some problems with this questionnaire and the interpretation of the severity score that should be addressed. Also additional questions concerning medical attention and time loss, exacerbation or re-injury can be added, making it a tool that can be used to monitor different types of injury complaints over time.

In the NLstart2run study the amount of training was monitored in minutes spent running. This measure of duration is convenient, because time is easy to measure for everybody. It could be argued, however, that duration does not reflect the training load properly. Duration merely reflects the physiological load while an RRI occurs from biomechanical load. From a biomechanical point of view, running distance better reflects the biomechanical load of training. It might therefore be better to monitor running distance instead of duration. Since a large proportion of today’s population has a smartphone, it should be possible to objectively monitor the running distance of each training session and at the same time measure running speed. Making use of these devices, allows us to obtain more objective data on training behavior and collect data on running exposure that better reflects the biomechanical load. Theoretically, it should be possible to record the number of steps for each training session, using the accelerometers that are situated in almost all smartphones. This measure possibly reflects the biomechanical load even better. Future studies are advised to think about more appropriate measures of training load and examine the possibilities to objectively collect these training exposures in a large cohort of runners. Today’s popularity of smartphones and possibly smartwatches in the near future give access to many new possibilities.
Advice on proper training programs

Until now, not much is known about proper running programs for novice runners. The NL-start2run study showed surprising results concerning training behavior and RRI, which highlights the need for different approaches in future research. Taking into account the model described in Figure 5, personal characteristics should be seen as effect-measure modifiers instead of risk factors that directly affect RRI risk. Therefore, future research should focus on identifying the best running program for novice runners with a specific set of personal risk factors (i.e. age, BMI, experience and previous injuries).

Several important questions should be addressed in future studies. 1) Should a training program be based on distance, duration or possibly number of steps? With smartphone applications it is possible to register both distance and duration of a training session. By assigning runners to a duration- or distance-based running program it is possible to analyze which scale best predicts RRI occurrence. 2) At what starting level should a specific participant pick up running? The appropriate starting level is highly dependent on personal characteristics [64]. 3) How much progression should be advised to novice runners and is this amount of progression dependent on personal characteristics? Possibly progression can be linear over time, however, it might be better to introduce some form of periodization.

As discussed before, observational study designs have several limitations when studying the impact of training routine on RRI risk. The best method to answer the above mentioned questions therefore is to randomly assign runners with specific characteristics to different training programs and compare injury risk between these groups. In such studies it is of high importance to monitor training exposures closely and record deviations from the pre-defined training schedule extensively. In the statistical analysis, multi-state transitions can be used to take possible deviations into account.

Return to sports

Until now, most research focused on the prevention of RRLs. This is understandable, because we know that a previous injury is associated with an increased RRI risk. However, little research has been conducted on interventions that lead to the most successful return to sports. That is unfortunate, because injuries are common among runners and are an important reason to quit running [6]. Since an RRI occurs as a result of too much load in a specific structure, reducing load in that specific structure could be beneficial for treatment and secondary prevention, thus full return to sports. The best method to reduce overall load is to lower running distance or speed for a period of time. For overuse complaints in specific structures, however, it should be possible to reduce load in these specific structures by redistributing the load. This could be accomplished by footwear modifications or changes in running technique (gait retraining). Future studies are necessary to examine the exact effect
of these interventions on running continuation. It should be highlighted that these modifications impact the load in a specific structure. Therefore, it is likely that these interventions have the best result for treatment or secondary prevention, because in these cases the weakest link (the injured structure) is known at which the intervention should be targeted. These interventions reduce load in a specific structure, however, this is only effective when the training load is kept constant. Therefore it is important to precisely monitor training behavior and take this into account in the analysis when assessing the effectiveness of these types of interventions, because in the end, an RRI is caused by running too much too soon.

**Digital running coach**

A large part of the running population (67%) is running on a recreational level in an unorganized manner [65]. In this community of unorganized recreational runners there is a high need for training programs [65]. So far, knowledge on correct training programs for specific runners is lacking. More research is needed to properly advice specific runners on their training program. Getting more insight into subject specific responses to specific training programs will be of great value for ensuring a life-long running career.

It will be interesting to study the possibility to identify markers that are associated with a reduced load capacity. Physical complaints after the previous training session or the participant’s feeling just before the next training session might give an indication of a reduced load capacity. Until now, all studies on risk factors for RRI focused on personal characteristics and running characteristics. All activities apart from running participation (e.g. work, spare time activities or sleeping) are neglected while these internal factors might have a large impact on injury risk. Markers for reduced loading capacity can be used to adjust a training session on forehand based on the “form of the day” to decrease injury risk.

With nowadays technology it should be possible to create a smartphone application that can be used to target the large unorganized population of runners. When more is known about subject specific training programs, a smartphone application can be used to select appropriate running programs based on personal information that is entered. Such an application can be used to coach the runner real time and at the same time monitor training behavior and physical complaints. In this manner person specific responses to training over a longer period of time can be collected. Possibly, markers reflecting the loading capacity could be integrated too. This can, in turn, be used to predict injury risk over time more precisely and thereby inform runners about possible subject specific adaptations to reduce injury risk.
CONCLUSIONS

This thesis showed that RRIIs are common in different populations of runners. The results of the NLstart2run study revealed the most important personal characteristics that were associated with RRI in novice runners. In this thesis we also tried to identify training characteristics that had an association with RRI. The counterintuitive results exposed the limitations of observational study designs when studying the relation between training behavior and RRI. Therefore more research in this field is needed. To ensure consistent results in future research, it is advised to develop a standardized injury registration method, because this thesis showed that different injury definitions have a large impact on injury incidence reports. With today’s technological development it becomes possible to monitor running exposures objectively with smartphone or smartwatch applications. These technological advances combined with the new insights in injury causation and methodological consequences, which were presented in this thesis, enable future studies to unravel the person-specific associations between training behavior and RRI. The results from this thesis constitute a first step towards this quest. Eventually, this might allow the development of a digital coaching application that can be used to give evidence-based advice to the large unorganized running community.

REFERENCES


