General introduction
Although the positive societal, psychological, and physiological effects of sports are well known, physical inactivity is a major problem in today’s society. To overcome this problem, people are encouraged to have a physically active lifestyle and to actively participate in sports. Despite the abovementioned positive effects, physical activity and sports is accompanied by a public health hazard, namely injuries.\textsuperscript{1-3} In the Dutch sporting population a total of 1,500,000 sports injuries is sustained annually by a population of 7,700,000 athletes.\textsuperscript{4} More than half of these injuries (780,000) require any form of medical treatment, costing about €540 million in direct medical and indirect costs.\textsuperscript{4} In addition to high associated costs, athletes suffer from the severity and the subsequent negative long-term, potentially disabling, consequences of an injury. The associated high medical costs, long-term health effects, and negative personal consequences make sports injuries a public health problem, warranting preventive measures.

Injuries in sports are diverse in nature and in cause, ranging from a bruise due to physical contact in soccer to anterior cruciate ligament injury in skiing. Other common sports injuries include stress fractures of the foot, shin splints, tendinitis, runner’s knee, hamstring injuries, tennis elbow, foot injuries, and myriad other sprains and pulled muscles.\textsuperscript{3} This thesis focuses on the overall most common injury in sports: i.e. the ankle sprain.

**WHAT IS THE PROBLEM?**

*Incidence rates of ankle sprains*

The best way to grasp the magnitude of the injury problem is by expressing injury rates by incidence numbers. Despite the fact that direct comparison of injury risk in sports is often hampered by different definitions of injury and different ways of reporting injury incidence, the magnitude of the problem can still be illustrated by calculating the incidence of sports injuries as the number of injuries per, for example, 1,000 hours of sports exposure or per 1,000 athlete exposures. From available descriptive injury
incidence figures it can be concluded that ankle sprain is the most common sports injury across a wide variety of sports (Table 1).

**Table 1** The most common injured body sites in different sports illustrated as weighted percentages of all injuries. Adapted from: Fong et al.

<table>
<thead>
<tr>
<th>Sport</th>
<th>Most common injured body sites (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Badminton</td>
<td>Ankle (23.5) Knee (14.0) Foot (12.5) Arm (8.0) Leg (5.4)</td>
</tr>
<tr>
<td>Basketball</td>
<td>Ankle (15.9) Knee (10.7) Trunk (6.5) Thigh (5.4) Leg (5.0)</td>
</tr>
<tr>
<td>Field Hockey</td>
<td>Head (34.4) Ankle (34.0) Arm (13.6) Knee (4.1) Trunk (1.1)</td>
</tr>
<tr>
<td>Gymnastics</td>
<td>Ankle (32.3) Arm (25.9) Knee (9.4) Trunk (6.8) Hand (4.4)</td>
</tr>
<tr>
<td>Soccer</td>
<td>Ankle (21.2) Knee (16.3) Thigh (12.2) Leg (9.0) Hip (4.3)</td>
</tr>
<tr>
<td>Softball</td>
<td>Ankle (18.3) Knee (11.1) Hand (6.6) Leg (4.4) Head (2.2)</td>
</tr>
<tr>
<td>Volleyball</td>
<td>Ankle (45.6) Arm (15.4) Knee (11.4) Shoulder (4.8) Hand (4.3)</td>
</tr>
</tbody>
</table>

**Aetiology of ankle sprains**

An ankle sprain is a forced plantar-flexed inversion of the foot, exceeding the anatomical range of motion. During participation in sports, an athlete is exposed to risk factors and is at risk of sustaining an ankle sprain. To explore the interrelationships between risk factors and their contribution to the occurrence of an ankle sprain, the dynamic, recursive model as postulated by Meeuwisse et al. can be used (Figure 1). This model is a modification of the previous multifactorial model of athletic injury aetiology. This model is different from the previous model in that it incorporates the consequences of repeated participation in sports, both with and without injury. In line with this approach, preventive measures
should be aimed at improving effects of modifiable risk factors through the introduction of appropriate and timely ankle sprain prevention strategies.\textsuperscript{10} When looking at ankle sprains it can be stated that intrinsic risk factors act from within the athlete, predisposing the athlete to an ankle sprain. Intrinsic factors are related to individual psychosocial or biological characteristics, for example age, muscle strength, neuromuscular control, psychosocial stress, proprioception, history of injury, and adequacy of rehabilitation. Extrinsic risk factors relate to environmental variables that act on the predisposed athlete from outside. These factors are classified as enabling factors in that they facilitate the manifestation of injury. Level of play, exercise load, position played, protective equipment such as mouth guards, bracing, and shoes, weather conditions, playing field conditions, rules, and fair play are examples of extrinsic risk factors.

The combination of intrinsic and extrinsic risk factors and the interaction between them make the athlete susceptible to an ankle sprain. The
inciting event is described as the final link in the chain that causes an injury. For instance, landing on a teammate’s foot after a block in volleyball or enduring a tackle on the ankle during soccer. Physiological alterations after an ankle sprain form a major intrinsic risk factor, predisposing the athlete to sustain a re-injury of the same ankle. There is strong evidence that a history of injury, especially when followed by inadequate rehabilitation, places an athlete at an increased risk for suffering a re-injury. An ankle sprain might cause changes in morphology (changes in ankle structure) or neurophysiology (changes in nervous system function) of the ankle, or a combination of both. This might become apparent through alterations in intrinsic risk factors. Strength deficits, impaired neuromuscular control, and an impaired proprioception are thought to occur. These alterations could lead to a change in the predisposition to re-injury, making the athlete more susceptible to an ankle sprain recurrence. Research in volleyball has shown that an increased ankle sprain recurrence risk is apparent in the first year after the initial ankle sprain. A similar result was found in other sports and in military recruits.

**PREVENTION OF ANKLE SPRAINS**

*Preventive measures*

Over the years, measures to prevent ankle sprains have been evaluated. A reduction in ankle sprains was found for taping and bracing, with an up to a twofold reduction in ankle sprains for bracing. Research on the effectiveness of proprioceptive balance board training as a preventive measure showed a similar 50% ankle sprain risk reduction. For several reasons proprioceptive training can be considered the most promising of these three measures: (1) whereas taping and bracing are external functionally supportive devices of the ankle, proprioceptive training is aimed at changing ankle morphology and neurophysiology by re-strengthening muscles and ligaments and by restoring proprioception of
the damaged structures around the ankle\textsuperscript{37-39}; (2) tape can be irritating to the skin and tape loosening has been shown to occur after as little as ten minutes of exercise\textsuperscript{40}, resulting in a loss of support; (3) it is generally assumed that the use of tape or brace is accompanied by relatively high costs, as compared to proprioceptive balance board training.\textsuperscript{41}

In addition, a sensitivity analysis on costs associated with proprioceptive training showed that in the long term proprioceptive balance board training is cost-beneficial.\textsuperscript{42}

**Only effective in preventing ankle sprain recurrences**

The finding that preventive measures reduce ankle sprain risk needs to be put in the right perspective. Randomized controlled trials (RCT) that showed an effect of proprioceptive training on ankle sprain risk\textsuperscript{14,34,36}, found that these effects were greater for subjects with a history of ankle sprain compared to subjects without such a history. It thus seems as if there is not so much a primary preventive effect of proprioceptive training on ankle sprains, but rather a preventive effect on ankle sprain recurrences. A similar secondary preventive effect was ascribed to taping\textsuperscript{43} and to bracing.\textsuperscript{32} Incorporating these findings into the Meeuwisse model\textsuperscript{10}, it is reasonable to assume that a first ankle sprain is the most important risk factor for an ankle sprain recurrence.

Since in most of these studies\textsuperscript{34,36} the observed secondary preventive effect was based on sub-group analyses of large study samples, this assumption regarding this secondary preventive effect should be interpreted with caution. To assure sufficient statistical power, studies on sports injury prevention rely on large sample sizes. A priori sample size calculations in the current literature are based on athletes with and without a history of injury. Thereby, significant loss of power is bound to occur if sub-group analyses are employed. A recent study by McGuine and Keene on high school athletes suffered from this limitation and most likely therefore failed to show an effect of proprioceptive training on athletes with a
Chapter 1 General introduction

history of ankle sprain.\textsuperscript{35} Furthermore, recall bias could have occurred when subjects were asked retrospectively about their history of ankle sprains\textsuperscript{34,35,44}, or were asked retrospectively about ankle sprain recurrences one year after their first ankle sprain.\textsuperscript{14} Research has shown that the time interval since exposure and the degree of detail required influenced the recall of a variety of exposures, such as medication usage\textsuperscript{45-47} or work history.\textsuperscript{48,49}

\textbf{Treatment of ankle sprains}

Next to a history of ankle sprain, inadequate rehabilitation or premature return to play has shown to be an important risk factor for ankle sprain recurrences.\textsuperscript{12} It was shown that soccer players, who were improperly rehabilitated, or who were not ready to return to a pre-injury level of competition, were at increased risk of suffering re-injury.\textsuperscript{50,51} From reports on top-level volleyball players it can be concluded that treatment of the initial ankle sprain was not sufficient to prevent an ankle sprain to recur.\textsuperscript{52} These soccer and volleyball specific examples on improper rehabilitation after injuries indicate the premature termination of treatment by health care professionals.

\textbf{Establishing true effects}

History of ankle sprain as the most important risk factor of a recurrent ankle sprain warrants a comprehensive RCT, accounting for statistical power and preventing the occurrence of recall bias. Furthermore, to adequately tackle the problem of inadequate rehabilitation and the supposedly premature termination of treatment by health care professionals, athletes should be studied after treatment of the ‘first’ ankle sprain. To do so, athletes with an acute ankle sprain should be subjected to a proprioceptive training programme immediately following the termination of treatment by the initial health care professional. This programme should be easy to perform and should be executable as
adjuvant home exercises after termination of treatment. Through this design it can be determined whether proprioceptive training as a preventive measure is truly capable of reducing ankle sprain recurrence risk. To establish the added value of this training programme compared to usual care of an ankle sprain, the proprioceptive training programme should be performed after treatment by usual care.

THESIS OUTLINE
The main objective of this thesis is to describe an RCT on the effectiveness on ankle sprain recurrences of an unsupervised home-based proprioceptive training programme that was applied after termination of usual care of an acute ankle sprain.

Chapter 2 describes the study design of this randomized controlled trial. This chapter gives an in-depth look into the intervention study. The effectiveness of this trial is described in Chapter 3, while its cost-effectiveness is described in Chapter 4. Chapter 5 contains a methodological article on analysis considerations in injury prevention studies. This chapter attempts to create a better understanding of results of injury prevention studies by comparing results of this trial from two analyses perspectives. Analysis from an intention-to-treat approach, which is gold standard in RCT’s, are compared with a per-protocol analysis. Chapter 6 provides a critical review of biomechanical studies on ankle sprain recurrences in order to give insight in the working mechanism of the proprioceptive training programme. Finally, Chapter 7 contains a general discussion of the methods and results presented in Chapters 3 to 6, after which our conclusions are summarised, implications of the findings for the prevention of ankle sprain recurrences are discussed, and recommendations for future research are made.
REFERENCES


21. Hale SA, Hertel J, Olmsted-Kramer LC. The effect of a 4-week comprehensive rehabilitation program on postural control and lower


