Preventing ankle sprain recurrences in sports

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General discussion

Ankle sprains are by far the most common sports injury in a multitude of sports.[1-10] Although incidence numbers on specifically ankle sprain recurrences are not widely available, it has been shown that after an index ankle sprain an increased risk for re-injury remains the first year post-injury.[5,6,11,12] The recurrence rate for lateral ankle sprain in sports has been reported to be as high as 80%.[13] The use of proprioceptive training as a preventive measure against ankle sprain recurrences is warranted, since this is thought to lead to changes in ankle neurophysiology and morphology.

This thesis describes the first large randomized controlled trial (RCT) specifically on prevention of ankle sprain recurrences in athletes who recently sustained an ankle sprain. The first four chapters of this thesis have given insight into the rationale, development, and results of a RCT on the effectiveness and cost-effectiveness of an unsupervised home-based proprioceptive training programme aimed at preventing ankle sprain recurrences. Further, chapter 5 presented the impact compliance has on effect estimates in sports injury prevention studies. Chapter 6 attempted to uncover the black box, in which proprioceptive training is nested.

The first part of this discussion describes important considerations in the development of the intervention, recapitulates the main findings from the previous chapters, and puts them in a broader perspective. Methodological issues are dealt with in the second part of this discussion, ending with implications and recommendations for ankle sprain recurrences prevention and future research.

DEVELOPMENT OF THE INTERVENTION

The development of a proprioceptive training intervention is described in detail in chapter 2. Several considerations from different perspectives were taken into account when designing the intervention.

From an athletes' perspective, intervention feasibility aspects were the primary concern. An extensive pilot study, conducted a year prior to the actual intervention, showed that a full year of low-intensity proprioceptive training was too demanding and would probably lead to significant loss to follow-up. On the other hand research had shown that at least six weeks of training seemed necessary to envoke effects on reducing re-injury risk.[14] As the programme was designed as a continuation of medical treatment, which, judging from Dutch clinical guidelines, on average takes about 6 weeks, an intervention duration of 8 weeks with three training sessions per week was believed optimal. Participants of the pilot study agreed on the feasibility of an eight-week training programme.

Another important issue was the type and difficulty level of exercises chosen in the programme. Pilot testing showed that a modification of a previously proven effective programme in volleyball[15] was feasible for athletes of all types and levels of sports and of all ages. Exercises depicted in Figure 2 of chapter 2 were chosen as the framework of the eight-week training programme. Furthermore, the aim of the intervention was to keep medical costs associated with a prolonged rehabilitation period to a minimum and to put no additional demand on medical practitioners. Therefore, all athletes trained individually, without supervision of a coach or medical practitioner. This made it even more important that exercises of the proprioceptive training programme were fool proof and easy to carry out.

MAIN FINDINGS

Effects of the intervention

Chapter 3 showed that an eight-week proprioceptive training programme after usual care is an effective preventive measure for ankle sprain recurrences and is a useful addition to usual care of an ankle sprain.

It is known that over 50% of all Dutch annual ankle sprains do not seek medical attention for their ankle sprain[16], which equals a total of 124,000 Dutch athletes.

By including both non-medically and medically treated ankle sprains, the present study represented a broad spectrum of injured athletes. As these two types of ankle sprains were used to differentiate in inclusion ankle sprain severity for the stratification procedure, caution needs to be taken to compare between these groups. Nevertheless, valuable information can be gathered from both groups.

As an example, by comparing medically treated with non-medically treated ankle sprains within the control group, information on the effect of medical treatment alone can be established. Table 1 shows that medical treatment significantly lowered incidences of the least severe ankle sprain recurrences (i.e. self-reported ankle sprains). In essence, medical treatment lowers the recurrence risk associated with a non-severe ankle sprain. However, this effect of medical treatment was shown for self-reported ankle sprain recurrences only. These self-reported ankle sprain recurrences are often described as mild and leading to short-term discomfort, by which they are considered less severe than an ankle sprain that causes loss of sports time. Medical treatment alone was not capable of lowering ankle sprain recurrence incidences for these more severe ankle sprains, i.e. those leading to loss of sports time. Hence, it may carefully be concluded that medical treatment of ankle sprains is effective in preventing minor ankle sprain recurrences.

A second example comes from the comparison of non-medically treated and medically treated athletes within the intervention group. The effect on lowering ankle sprain recurrence risk was higher in non-medically treated intervention athletes compared to medically treated intervention athletes. Although non-medically treated ankle sprains were considered the least severe, athletes in this group showed to be more compliant to the programme and showed higher motivational levels compared to medically treated interventions. Compliance and motivation were measured through statements on the self-rated compliance or motivation with the proprioceptive training programme. Statements were answered on

Table 1 Injury incidence (95% confidence interval) in the control group given by injury severity perspective and type of treatment. This table is adapted from Table 3 in chapter 3.

	Treatment	
Ankle sprain	**Medical**	**Non-medical**
Self-reported	**2.12**	**3.79**
	(1.42 to 2.83)	(2.78 to 4.80)
Time loss	**1.13**	**1.22**
	(0.66 to 1.60)	(0.70 to 1.75)
Leading to costs	**1.18**	**0.97**
	(0.69 to 1.67)	(0.51 to 1.43)

a five-point Likert Scale, ranging from complete disagreement (score=1) to complete agreement (score=5) with the statement. Analysis by means of a chi-square of compliance to the programme showed that non-medically treated athletes showed significantly higher levels of full compliance to the intervention than medically treated athletes (p=0.01). Furthermore, motivation to comply with the intervention in medically treated athletes showed significantly lower levels compared to non-medically treated athletes (p=0.01). Perhaps non-medically treated athletes had a higher intrinsic motivation to carry out the exercises, as (on average) six weeks of medical treatment already diminishes most of the intrinsic motivation. Extrinsic motivation provided by participation in a large study as the present might not have triggered medically treated athletes to actually comply to the programme. Perhaps when a medical caregiver had offered the programme, athletes would have displayed higher compliance levels.

Cost-benefits of the intervention

The cost-effectiveness analysis of the intervention, presented in chapter 4, concluded that an unsupervised home-based proprioceptive training programme is cost-beneficial on ankle sprain recurrences. A significant total costs difference per athlete of −€103 in favour of the intervention group was found. Based on the estimated 234,000 annual ankle sprains in the Netherlands[16], this indicates that on a yearly basis a total of €24.1M in Dutch medical costs can be saved. Thereby, from a public health perspective, financial impact of this simple and easy to perform proprioceptive training programme is enormous. After our research group already showed possible cost-benefits on the long term of proprioceptive balance board training programme incorporated in warm-up for volleyball players[17], chapter 4 showed the absolute necessity of incorporating proprioceptive training after an ankle sprain from a cost-perspective.

The effect of compliance on effect estimates

Chapter 5 showed that with a per-protocol (PP) analysis on fully compliant athletes versus control group athletes, the preventive effect of proprioceptive training was over threefold higher when compared to intention-to-treat (ITT) analysis.

Recent studies on the prevention of injuries in sports showed the negative effect poor compliance has on study outcomes.[18,19] Chapter 5 recommended that sports injury prevention studies present a PP analysis alongside analysis according to ITT. Chapter 5 also highlighted the need for proper compliance measurement, since without knowledge of compliance a PP analysis is impossible. Preferably, compliance to prevention programmes should be assessed by an independent person. For all RCTs on sports injury interventions, it is strongly recommended that compliance is assessed at least through multiple compliance questions and at different times points throughout the study. This would help to ascertain the accuracy of the information. However, the best way to assess compliance in this context remains largely unknown and requires future effort.

Furthermore, a PP analysis is justified only if sufficient diversity in compliance to the intervention exists within the intervention group.

Studies with overall high levels of compliance or low levels of compliance to the intervention will not create a better insight in the efficacy of a programme when a PP analysis is compared to the ITT principle. Outcome differences between both analyses types will most likely not be present. Analyses according to a PP principle can lead to distorted conclusions if, by dividing the intervention group into sub-groups of compliance, comparability to the control group is lost. This could be the case if baseline characteristics are significantly different between intervention sub-group and control group. However, this was not the case in the present study.

As a consequence of the above, the CONSORT statement should provide a guideline for proper compliance measurement and reporting, so that all studies are equal in their compliance measurement and reporting. Furthermore, specifically for sports injury prevention studies, the CONSORT guideline should recommend a PP analysis as an analysis option next to analysis from an ITT perspective.

What is the underlying mechanism of proprioceptive training?

The Meeuwisse model[20], described in chapter 1, is widely used to understand the aetiology of sports injuries. It can also be applied to ankle sprain recurrences. In short, an index ankle sprain alters an athlete's intrinsic risk factors[14,21-27], which results in an increased predisposition to re-injury.[20] An ankle sprain is thought to lead to strength deficits, impaired neuromuscular control, and an impaired proprioception. Chapter 6 reviewed the available literature on the effect of sensorimotor training on these risk factors. This chapter used the term sensorimotor training, instead of the more popular term proprioceptive training, to differentiate between the resulting sensory and motor adaptations.

Chapter 6 also introduced a clear distinction between biomechanical and neurophysiological changes on the one hand and functional changes, brought about by changes in biomechanics and neurophysiology, on the other hand. Functional changes can be seen as the resultant of adaptations at a neurophysiological level (i.e. the sensory threshold of specific peripheral mechanoreceptors, nerve conduction velocity, sensorimotor integration at the spinal and/or suprispinal level, alpha motoneuron pool excitability, and/or gamma-motor neuron/muscle spindle function) and changes in morphology (i.e. muscle cross-sectional area, myofibril size, and/or ligament structure).

Biomechanical and neurophysiological entities are closely linked to proprioception and should therefore be measured in future research that proclaims to measure proprioception. Those entities provide more information on proprioception than a functional outcome as for example postural sway.

Even though a combination of biomechanical and epidemiological research is time-consuming and difficult to perform, a multidisciplinary approach is recommended to identify potential solutions to the ankle sprain recurrence problem and thus develop appropriate preventive measures. The challenge is to combine fundamental research with epidemiologic research, despite both research types contain almost complete opposite characteristics (e.g. regarding sample size, type of measurements, and follow-up time). A population with similar characteristics as in the present study, a large group of athletes from different sports and level of sports, who recently sustained an ankle sprain, should become available for kinetic, kinematic, and EMG analysis of both static and dynamic tasks prior to and after the eight-week training programme. A one-year follow-up of these athletes should provide the necessary epidemiologic data on ankle sprain recurrences.

METHODOLOGICAL ISSUES

The conducted study on the prevention of ankle sprain in sports had several shortcomings. Some have already been discussed in the previous chapters.

Randomization & inclusion

Athletes were randomized through stratification for gender, way of enrolment, and severity of their ankle sprain. At first, the Ottawa ankle rules were planned to serve as a differentiation measure of severity. But since hospital emergency rooms (ER) indicated not to use these rules for the treatment of ankle sprains consistently, it was decided to link severity to health care resource utilisation.

Recruitment through medical channels was extremely difficult, time consuming, and not leading to the number of required athletes. A change in method of recruitment was employed in the present study, and resulted in a sample of over 200 injured athletes in about two months, who enrolled through non-medical channels. This is illustrated in figure 1.

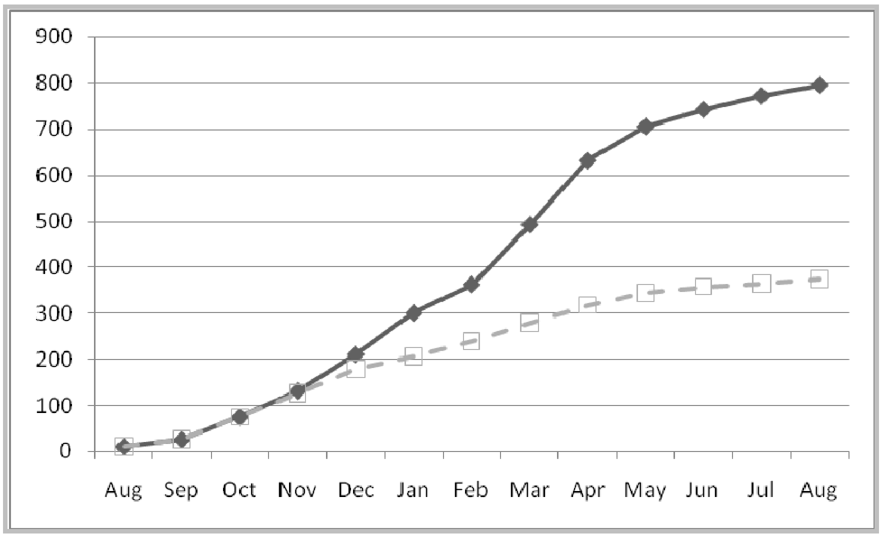

Figure 1 Total monthly athlete recruitment through medical and non-medical channels (solid line) and recruitment through medical channels only (dotted line). From November 2006, non-medical channels were open for recruitment of athletes. Actual number of athletes available for inclusion was different from the numbers presented here.

A slight alteration of the inclusion criteria was necessary to be able to utilize this adapted strategy. The scientific gain through this change in inclusion is that knowledge is also built upon recently sprained athletes who entered the study through non-medical channels. All injured athletes who enrolled through medical as well as non-medical channels were contacted by phone by a physical therapist and were questioned in a standardized manner to assure that the injury was a lateral ankle sprain.

Bias

The athletes' inclusion procedure for this trial was described in detail in chapter 2. Unfortunately, no details and numbers are available on athletes not willing to participate after visiting an ER, PT, or GP or web-based enrolment. Although it was planned to register all approached athletes, this was impossible. Thereby, actual reasons for athletes not to participate are unknown. First, participating medical caregivers were not compliant to handing out information brochures to all athletes, who visited the caregiver with an ankle sprain. We had permission twice to go through all medical files of one participating ER and collected all registered ankle sprains in the previous month. These athletes were contacted by phone and were asked if they had received an information brochure about the present study. Less than 5% of these athletes indicated to have received the brochure. Second, if a brochure was handed to the athlete, it was not returned within the same visit. From an athlete's perspective, possible reasons could have been motivational or time-related. It could be argued that only highly motivated athletes were willing to participate in the present study. However, judging from the motivational statistics presented in this chapter this was probably not the case. Any selection bias is believed to be minimal, since our study group is comparable to the general Dutch sporting population. Data on the general Dutch sporting population were extracted from OBiN[28], which is a yearly phone survey on injuries and physical activities in the Netherlands. First, the distribution of sexes within the general Dutch sporting population is almost equal to the distribution of sexes in the present study (49% female and 51% male vs. 48% female and 52% male). Second, half of all injured athletes in the Dutch sporting population seek medical care for their injury, which is similar to the 50% non-medically treated athletes in the present study depicted in Figure 1 of this chapter. Furthermore, most injuries (55% of all) occurred in the Dutch sporting population aged between 18 and 34; the average age in the present study was 28 years. Finally, the average sports participation in hours per week was similar for the general population and the present study population (3.8 vs. 3.6 hours/week).

In the types of study as the present, a social desirability effect[29] might occur, leading to bias in the observed results. Intervention athletes might report higher levels of sports exposure than actual levels, because they feel this was expected from them. However, if this effect occurred in the present study, this should have happened in control group athletes as well, since similar information on reporting levels of sports activity was provided to them. Furthermore, throughout the one-year follow-up, monthly newsletters were sent to intervention group athletes and control group athletes.

By giving a placebo treatment to control group athletes, blinding of the athletes could have been assured and bias due to a lack of sufficient blinding could have been prevented. To prevent control group athletes from participating in a self-created proprioceptive training programme, a placebo treatment could have been the solution. However, a sham-treatment was considered impossible. Nevertheless, bias due to a lack of sufficient blinding is unlikely to have occurred, since only a small part of the control group athletes (2% of 266 athletes) had participated in proprioceptive training within the one-year follow-up.

Compliance & loss to follow-up

As discussed in chapter 5, full level of compliance with the intervention programme was only achieved by 23% of all intervention group athletes. This poor level of full compliance was mostly ascribable to motivational aspects of the athlete as mentioned in this chapter. Other factors such as that the programme was too time consuming, too boring, too hard, or useless were not shown to be of influence to poor compliance. Nevertheless, maximum efforts had been made to minimize loss of motivation by making the intervention programme as appealing as possible, by using an interactive website including all exercises, and by sending monthly newsletters to all participating athletes.

Loss to follow-up is a stressing problem requiring an a priori relatively high expected drop-out. Previous studies of comparable topic, design, and subjects have learned that an a priori 20% expected drop-out is rarely reached when proper incentives are given, and when time and personal effort are being put in the follow-up of participants. Loss to follow-up in the present study was an acceptable 14% over the whole study period. Unfortunately, reasons for loss to follow-up were predominantly unknown in both groups (59% in the intervention group and 58% in the control group). Other frequently mentioned reasons were lack of time (16% and 19%, respectively), personal reasons (9% and 13%, respectively), or lack of motivation (9% and 0%, respectively).

Validity

Without a proper non-response analysis, evaluation of external validity of a study is hampered. As it was shown that the present study groups is representative for the general Dutch sporting population and since the present study consisted of athletes from all types and levels of sports, implementation of the study results should apply to every athlete. In chapter 3 no confounders or effect-modifiers were found that influenced results. Therefore, this proprioceptive training programme is considered to be generalizable to all athletes.

As there were no differences between groups at baseline, in dropout rates, and in exposure during the study, the internal validity should be high. Although ankle sprain recurrence and exposure registration were based on self-report, good reliability and validity of ankle sprain recurrence and exposure registration were ensured. By using injury registration forms and by having these forms judged by two researchers independently, we feel that the risk of misclassification errors was minimized. This ensured good reliability for comparing the data between the intervention and the control groups.

SIDE EFFECTS

A previous study on a comparable prevention programme in volleyball athletes revealed an increased incidence of self-reported overuse knee injuries resulting from the intervention.[15] The present study found no incidence difference of self-reported knee injuries between intervention and control group. The incidence of self-reported knee injuries was 1.58 (95% confidence interval 1.14 to 2.01) per 1,000 hours of sports in the intervention group, and 1.45 (1.05 to 1.85) in the control group (Table 2). Cox regression analysis adjusted for age, type of sport, and level of sport showed no difference in incidence of self-reported knee injuries between intervention and control group athletes (relative risk 1.08; 95% confidence interval 0.73 to 1.59). Furthermore, intervention group athletes with a history of knee injury did not show significantly higher risk for knee injuries compared to intervention group athletes without a history of knee injury (0.90; 0.55 to 1.46).

In the present study, prevalence for knee injuries in volleyball players was 9%. All knee injuries in volleyball players were reported in the control group. In contrast, prevalence for jumper's knee, which is the main overuse knee injury in volleyball, has been shown to range from 30% to

51%.[30-35] A possible risk factor for the development of jumper's knee is exposure, under the condition that it is excessive in number of hours per week.[30,36] In studies with high jumper's knee prevalence, average training hours ranged from 6 to 12 hours per week.[33,35,37] In high-level volleyball, players' exposure could be seen as a potential risk factor for overuse knee injuries and therefore, volleyball players could be judged as predisposed athletes. Volleyball players in the present study had an average training and match exposure of 2.5 hours per week, which made them less susceptible to knee injuries compared to high-level volleyball players.

A high vertical ground reaction force, deep knee flexion angles, and high tibial moments have been associated with the onset or worsening of jumper's knee.[31] Deep knee flexion angles are part of proprioceptive balance board exercises.

Based on findings in volleyball and the present study no clear statement can be made on a contra-indication for proprioceptive balance board training for high level volleyball players. Despite numerous studies have been undertaken on preventing ankle sprain recurrences[38-41] or knee injuries[42-44] through proprioceptive training, only the abovementioned study in volleyball players[15] and the present study have combined both lower extremity injuries (i.e. ankle and knee) in their analysis. Future studies should also combine these two entities to gain more insight in possible side-effects of proprioceptive training in a population possibly at higher risk.

Implementation of the intervention

The recently presented TRIPP research framework[45] is an addition to the generally applied sequence of prevention model[46] as it translates research into injury prevention practice through two additional steps (Figure 2). As good efficacy or effectiveness research does not ensure the uptake of the interventions and therefore prevention of injuries[45], efforts should be made to create advances in injury prevention through implementation of the study results.

Model stage	TRIPP
1	Injury surveillance
2	Establish aetiology and mechanisms of injury
3	Develop preventive measures
4	"Ideal conditions"/scientific evaluation
5	Describe intervention context to inform implementation strategies
6	Evaluate effectiveness of preventive measures in implementation context

Figure 2 The Translating Research into Injury Prevention Practice (TRIPP) framework. Adapted from Finch (2006).[45]

The effect such evaluation can have on study outcome is presented in chapter 5. To create a situation as close to the ideal situation as possible, understanding of what behavioural changes are needed is necessary. The most important question that needs to be addressed in Tripp Stage 5 is: "What changes are needed in current safety behaviours and how likely are developed interventions adopted?" From the present study it can be concluded that the present training programme should become part of the usual care of every injured athlete, regardless of ankle sprain usual care. In anticipation to Tripp Stage 6, in which focus is on actual implementation of an intervention and evaluating its effectiveness, an actor network analysis could be a useful tool to create insight in how to implement the programme. Such an analysis uses a top-down approach, starting with identifying relevant assets at a government level and ending with the examination of needs at an individual level of the athlete. Although this chapter is not suited for such an analysis, some examples can give ideas on where to start and how to work. Starting at the Dutch government level, monetary injections for research should become available in the yearly budget to be able to perform adequate research on how to best implement a programme. One level down, Dutch health insurance companies should be more than willing to implement the present programme into their standard health insurance policy. It is not unthinkable that health insurance companies send the materials used in the present study (i.e. a balance board, an instructional DVD, and two exercise sheets) to a client who has sprained her or his ankle. As shown in the cost-effectiveness chapter, the total material cost of €27.50 is well worth such a small investment. Furthermore, workers who actively participate in sports and who sprain their ankle in the weekends are often not capable to go to work on Monday. Since in the control group 86% of total ankle sprain recurrence costs were costs due to absenteeism from work, Dutch employers are advised to follow the same example as the health insurance companies.

Another important step is to update the ruling Dutch guidelines on ankle sprain treatment. Current guidelines for acute ankle injury still lack proper description of proprioceptive training as part of rehabilitation. Therefore, this programme should be incorporated into guidelines and this training protocol should become part of usual care treatment. Of the current ruling Dutch guidelines, only the most recent Royal Dutch Society for Physical Therapy (KNGF) guideline on acute ankle injuries (2006) advocates preventive measures after treatment.[47] Herein, a combination of external prophylactic measures during sports and proprioceptive training as home-based exercises is recommended after completion of treatment. The presented proprioceptive training programme fits perfectly in this recently updated guideline. Even so, other ruling guidelines, such as those of the Dutch Orthopaedic Association (NOV), the Dutch College of General practitioners (NHG), the Dutch Association of Sports Medicine (VSG), and the Dutch Institute for Healthcare Improvement (CBO), should follow this example and should recommend the eight-week training programme presented in this thesis as a necessary addition to usual care. These guidelines need to be updated, given that they date back to 2000[48] or even 1998.[49]

The VSG and the Dutch ministry of Health, Welfare, and Sport have taken two important steps by setting up a pilot study aimed at transferring knowledge on ankle sprain treatment to medical caregivers, individual athletes, coaches, insurance companies and other involved parties through the update of guidelines and by introducing a Dutch expert group on ankle sprains. These two steps combined with the collaboration with the Dutch Consumer Safety Institute (SCV) and the Netherlands Olympic Committee (NOC*NSF) strengthens the idea that individual athletes will be reached and will benefit from the presented preventive measure.

Implications of these results should cross the borders of the Netherlands. The Institute for Clinical Symptoms Improvements (ICSI) provides a Health Care Guideline on the treatment of ankle sprains.[50] This guideline was released in 2006 and predominantly uses the same information resources as the Dutch ruling clinical guidelines. The ICSI Health Care Guideline on ankle sprains does not provide a clear and concise proprioceptive training programme for the prevention of ankle sprain recurrences. Therefore, it is recommended that, next to Dutch clinical guidelines, foreign clinical guidelines undergo an update as well, incorporating the present proprioceptive training programme.

Non-medical channels, preferably the internet and athletes' coaches should be utilized to create wide access to the training programme for the large group of athletes that does not seek medical attention. A website has already been created to fit this purpose (see: www.2bfitstudy.nl). Furthermore, NOC*NSF, SCV, and respective sport associations play a vital role, since they have the ability to reach competitive and recreational athletes and coaches in a wide variety of sports, nationwide. Nevertheless, a thorough analysis of how this programme is best implemented is necessary to reach all parties involved in the treatment of ankle sprains.

RECOMMENDATIONS AND IMPLICATIONS FOR HEALTH CARE IN SPORTS

The present study showed that a rehabilitative, unsupervised, home-based proprioceptive training programme is effective in preventing ankle sprain recurrences. Furthermore, it was shown that the use of such a programme was highly cost-effective. An eight-week proprioceptive training programme is therefore recommended for all athletes who have sustained an ankle sprain, regardless of treatment choice of their initial ankle sprain. The abovementioned authorities play a vital role in the success of the implementation of the programme.

As full compliance to the eight-week proprioceptive training programme was poor, mainly due to poor motivational levels, the search for the optimum length and intensity of the training programme continues. From chapter 5 it can be concluded that athletes classified as partially compliant (i.e. four weeks of proprioceptive training, three times a week) had a significantly higher ankle sprain recurrence risk compared to fully compliant athletes. To date, the only proprioceptive training programme effective for ankle sprain recurrences and shorter than eight weeks lasted six weeks and consisted of three training sessions per week.[14] However, this study was not so much an effectiveness study, but rather aimed at establishing biomechanical and neurophysiological adaptations after proprioceptive training. This finds expression in the lower study sample size as compared to the present study (N=92 vs. N=522) and the considerably higher number of athletes who were lost to follow-up compared to the present study (27% vs. 14%). Furthermore, recall bias could have occurred, since information on re-injuries was collected retrospectively one year after the initial ankle sprain instead of every month for 12 months. For now, optimal intensity and duration for proprioceptive training to be effective is considered to be three training sessions per week for eight weeks as in the present study.

PREVENTING ANKLE SPRAIN RECURRENCES: HOW TO MOVE FORWARD?

Evidence presented in chapter 3 is derived from the first large RCT on preventing ankle sprain recurrences in recently sprained athletes. Only one other study[14] has dealt with this issue, but, as mentioned, showed several shortcomings compared to the present study. Nevertheless, both studies add important knowledge to the treatment procedure of acute ankle sprains. These studies showed that proprioceptive training after an acute ankle sprain is effective in preventing ankle sprain recurrences and, therefore, should be part of all treatment procedures, regardless whether an athletes' choice is to non-medically treat the ankle sprain or to have it medically treated.

Although research on the prevention of ankle sprains is abundant[14,15,39,51], little is known about the pathway through which a reduction of ankle sprain recurrence risk is established. A combination of an epidemiological approach and biomechanical and neurophysiological analyses, as described earlier in this chapter, should lead to a better understanding of what causes ankle sprain recurrence risk to go down.

Another interesting challenge is to establish the added value of proprioceptive training in combination with the usage of external support. Bracing and proprioceptive training are equally effective in reducing ankle sprain recurrence rates and have a seemingly equal working mechanism. The question rises whether both preventive measures should be advocated together or whether one of these measures is individually more cost-effective.

CHALLENGES FOR FUTURE RESEARCH

The results of this thesis have created more insight in the effectiveness and cost-effectiveness of proprioceptive training for the prevention of ankle sprain recurrences. However, this thesis also raises new questions that require further research. The following recommendations for future research are made:

- To perform additional randomised controlled trials in a population of athletes who recently sustained an ankle sprain evaluating the effect a proprioceptive programme to support our findings and to investigate the added value of external measures.
- To substantiate current evidence on the monetary benefits of proprioceptive training, more cost-effectiveness evaluations on ankle sprain recurrences are needed in a more international setting.
- To create better understanding of results of injury prevention studies through a priori proper analysis strategies. An important condition to make a PP analysis possible is that compliance measurement is part of the methods of a study.
- To combine in a large cohort epidemiological and biomechanical study approaches of proprioceptive training into one study, to establish the pathway through which proprioceptive training reduces ankle sprain recurrence risk. A comparable population as the present should become available for kinetic, kinematic, and EMG analysis of both static and dynamic tasks prior to and after the eight-week training programme.
- To identify the best channel(s) through which a proprioceptive training programme can be presented to injured athletes. Preferably by performing an actor network analysis.

CONCLUSIONS

This thesis has shown that proprioceptive training should become an integral part of the usual care of an ankle sprain in order to prevent ankle sprains from recurring. The conclusions derived from this thesis are:

- An unsupervised home-based proprioceptive training programme given in addition to usual care is highly effective on ankle sprain recurrences and reduces health care costs significantly within the first year after administration.

- The proprioceptive training programme was effective in preventing ankle sprain recurrences (relative risk 0.63; 95% confidence interval 0.45 to 0.88). Therefore, the use of a proprioceptive training programme is recommended as part of usual care of an ankle sprain. Such a programme should be advocated specifically in non-medically treated athletes.
- This proprioceptive training programme is capable of reducing health care costs with €103 per athlete. Annual costs savings are potentially over €24.1M in the Netherlands.
- Analysis of results from an intention-to-treat perspective and a per-protocol analysis created insight in a better understanding of results of injury prevention studies.
- Based on the literature, the pathway through which training reduces injury risk remains unclear. Evidence was not convincing, if present at all. The main reason for this lack of evidence was that studies on this topic had poor design.

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