# Spraino

*A new concept in lateral ankle sprain injury prevention*

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# SPRAINO: A NEW CONCEPT IN LATERAL ANKLE SPRAIN INJURY PREVENTION

BY
FILIP GERTZ LYSDAL

DISSERTATION SUBMITTED 2020

AALBORG UNIVERSITY
DENMARK

# SPRAINO: A NEW CONCEPT IN LATERAL ANKLE SPRAIN INJURY PREVENTION

## PHD THESIS

by

Filip Gertz Lysdal

AALBORG UNIVERSITY
DENMARK

Dissertation submitted

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# CV

Filip Gertz Lysdal received his bachelor's degree in sports science in 2014, and his master's degree in sports technology in 2016, both at Aalborg University. Before graduating, Filip had an exchange semester at German Sport University Cologne in 2015, where he also wrote his master's thesis in 2016.

Upon receiving a grant from Innovation Fund Denmark (Grant 7038-00087B), Filip was enrolled as an Industrial PhD student in the doctoral school of biomedical science and engineering at the Department of Health Science and Technology where he would complete his PhD degree while upholding his employment as Scientific Project Manager in Spraino ApS.

Filip is an active member in multiple scientific communities, including International Society of Biomechanics, Footwear Biomechanics Group, Danish Society of Biomechanics, American College of Sports Medicine, International Ankle Consortium, International Foot and Ankle Biomechanics Community, Japanese Society of Biomechanics, and International Society of Biomechanics in Sports.

It is obvious that Filip is a social fellow, and he has been very active in attending conferences both nationally and internationally, at which he has given multiple oral- and poster presentations, as well as being an invited symposia speaker and workshop holder. Filip has received multiple nominations and awards for his conference contributions and presentations, as well as being on the receiving end of a handful of travel grants.

During his PhD, Filip has shown proof-of-concept of a new lateral ankle sprain injury preventive device that modifies the friction characteristics of indoor sports footwear. Filip will continue down this path in his upcoming employment as postdoc at Institute of Mechanical Engineering at Technological University of Denmark as part of Uwe G. Kersting's recent grant from the Independent Research Fund Denmark (Grant 0136-00283A).

# ENGLISH SUMMARY


Physical activity is not only fun, but essential for general wellbeing. However, despite the obvious benefits, injuries seem to form an almost inevitable part of practicing an active lifestyle, potentially outweighing the health benefits of regular physical activity. Sports injuries are reportedly accountable for up to 37% of all leisure time accidents in Denmark, with the ankle joint being the most common site of acute injury. In Denmark alone, ~40,000 people attend the emergency rooms every year due to something as “trivial” as a twisted ankle, of which by far most of these ankle injuries are characterized by a sprain to one or more of the lateral ligaments of the ankle joint. Indoor sports are very popular in Denmark, especially handball, badminton, and basketball, activities that in recent times have been singled out as particular high-risk activities for sustaining lateral ankle sprain injuries.

It has previously been hypothesized that the high friction between shoe and surface in indoor sports could be directly linked with the higher rate of lateral ankle sprain injuries, when compared to outdoor sports. Spraino (“**NO**” + “**SPRAIN**”) is an injury preventive measure specifically designed to prevent friction-related lateral ankle sprain injuries in indoor sports. Spraino comprises of low-friction patches that are attached on the lateral outside of indoor sports shoes, to minimize shoe-surface friction whenever the foot is placed in an inappropriate position against the floor.

The overall aim of this PhD project was to deliver a comprehensive scientific evaluation of Spraino as a new concept for lateral ankle sprain injury prevention. The thesis is structured around the ‘sequence of prevention’, and its four steps is covered by three separate studies. Study 1 established the prevalence of previous lateral ankle sprain injuries among active Danish indoor sport athletes, as well as the mechanism by which their most recent injury occurred. Study 2 introduced and preclinically evaluated Spraino as a new preventive measure. Finally, Study 3 established clinical ‘proof-of-principle’ through a pragmatic pilot randomized controlled trial with 510 participants with previous ankle sprain injuries.

In summary, Study 1 showed that three out of four active Danish indoor sport athletes had sustained a lateral ankle sprain injury at some point while playing, and that more than half of their most recent injuries were incurred without contact with an opponent or object. Study 2 found strong preclinical and biomechanical indications of an injury preventive mechanism. Finally, Study 3 established clinical effectiveness and found that allocation to Spraino significantly reduced both rate and severity of lateral ankle sprain injuries, as well as reducing ankle pain and fear-of-ankle sprain injury. Future research should explore the possibility of permanently integrating Spraino into indoor sports shoes, and the promising risk reductions should be confirmed in a future definitive RCT.

# DANSK RESUME

Sport og fysisk aktivitet er både sjovt og sundt, men er desværre også forbundet med en øget risiko for skader i muskler og led. Disse helbredstruende konsekvenser kan være fatale og potentielt set opveje de sundhedsfremmende effekter vi ellers forbinder med regelmæssig motion. Idrætsskader udgør 37% af alle forekomne fritidsulykker i Danmark, hvoraf ankelleddet er den mest udsatte kropsdel. Ifølge tal fra *Landspatientregistret* er der hvert år i Danmark ca. 40.000 skadestuebesøg - alene på grund af en forvreden ankel. Heraf er langt de fleste af disse ankelskader karakteriseret ved en forstuvning af et eller flere ledbånd på ydersiden af anklen. I Danmark er indendørs idræt meget populært, hvor især håndbold og badminton, og i nyere tid basketball, oplever stor tilslutning. Disse sportsgrene er imidlertid forbundet med en særlig stor risiko for ankelforstuvninger.

Mange har tidligere diskuteret (og antaget), at det er den høje gnidningsmodstand imellem sko og gulv der er årsag til, at ankelforstuvninger forekommer hyppigere i indendørs idræt, end i udendørs. Spraino (”**SPRAIN** + **NO** / FORSTUV + EJ”) er et nyt skadesforebyggende tiltag, som netop er designet til at forebygge de ankelforstuvninger, der antageligvis skyldes den høje gnidningsmodstand imellem sko og gulv. Spraino består af en særlig glat ”tape”, som påklistres på ydersiden af sportsskoene, for dermed at nedsætte gnidningsmodstanden mod gulvet, i tilfælde af at man træder forkert.

Formålet med denne ph.d. var at lave en omfattende videnskabelig evaluering af Spraino, da dette var et helt nyt koncept til forebyggelse af ankelforstuvninger. Afhandlingen er struktureret omkring en såkaldt ’forebyggelsessekvens’, hvor dennes fire trin er forsøgt afdækket gennem tre separate studier. Studie 1 fastslog omfanget af udøvere i dansk indendørs idræt, der havde oplevet at forstuve anklen mens de dyrkede deres sport, samt måden hvorpå deres seneste ankelskade var opstået. Studie 2 introducerede Spraino og beskrev de forebyggende mekanismer gennem laboratorieforsøg. Studie 3 fastslog den tidlige kliniske effektivitet af Spraino gennem et pragmatisk lodtrækningsstudie blandt aktive indendørs idrætsudøvere med tidligere ankelskader.

Kort fortalt viste Studie 1, at tre fjerdedele af de aktive danske indendørs idrætsudøvere havde oplevet at forstuve anklen under sport, og at mere end halvdelen af deres seneste ankelskader var hændt uden direkte kontakt. Studie 2 viste særlige prækliniske indikationer mod at Spraino kunne have en skadesforebyggende funktion. I sidste ende fastlagde Studie 3, at den gruppe udøvere, som modtog Spraino, i mindre grad forstuvede deres ankler, og at de skader, de fik, tilmed var mindre alvorlige. Derudover fik denne gruppe mindre ondt i anklerne og var i mindre grad bange for at nye skader skulle opstå. Fremtidig forskning bør undersøge om det er muligt at bygge Spraino ind i sko, samt efterprøve de lovende fund i et endeligt lodtrækningsstudie.

# ACKNOWLEDGEMENTS

This PhD study would never have begun without the generous financial support from Innovation Fund Denmark, who showed great trust in our ambitious project.

I wish to thank all the people whose assistance was essential to the completion of this project. First and foremost, I wish to express my sincere appreciation to my supervisors. Without your help, the goals of this project would never have been realized. My main supervisor, Professor Uwe G Kersting, who convincingly guided and encouraged me to be a creative professional and to look for the odd solution when the road got tough. Thor Buch Grønlykke, for being my daily contact, and for providing a roof over my head in a great time of need. Professor Kristian Thorborg for your immense help throughout, and for being a true beacon and a great source of inspiration. Associate Professor Ion Marius Sivebæk for always encouraging me to "know my literature".

Secondly, I wish to recognize the invaluable assistance that all my co-authors provided during our studies. I especially wish to express my deepest gratitude to Professor Janne Tolstrup. Your great advice and assistance proved monumental towards the success of this study. From Hvidovre Hospital: Thomas Bandholm, Mikkel Bek Clausen, and Stephanie Mann in particular, for your perseverance and countless hours and efforts put into the clinical surveillance. I also wish to extent my thanks to my international collaborators: Professors Eamonn Delahunt and Daniel Fong, true leaders in ankle sprain research.

I want to thank The National Olympic Committee and Sports Confederation of Denmark (DIF), especially Anne Mette Trier, and the governing bodies: DHF, Badminton Denmark and DBBF for your help in recruiting athletes for the clinical trial, and not least all the participants taking part in our studies.

I am thankful for all students I have supervised at Aalborg University, for your help during various projects that all affected the outcome of this thesis. Lasse Jakobsen for helping construct the mechanical test setup.

Finally, I wish to acknowledge the great love and support of my family and friends. I wish to thank my parents and siblings, not to mention Emil and his family, and all my friends, the P4 guys and my two AAU office mates, Kent, and Anders. You all kept me going and are always there for me.

To my Copenhagen roommates, Magnus, and Riccardo, and later *The Bastardi*: Brando and Andre. Thanks for making our home a place of joy, laughter, and amazing cooking - not least during the challenging times of the Coronavirus pandemic.

*/Filip*
*October 2020, Copenhagen*

# PREFACE

This PhD thesis is centered around the scientific value of 'Spraino' - a new technology designed to prevent lateral ankle sprain injuries in indoor sports. The thesis is based on three separate studies, with entirely different methodology, that are tied together through what is known as the 'sequence of prevention' model (1). This model and the three studies below are introduced together in the first chapter, after which the studies are presented separately in the chapters 2-5, before an overall discussion sums up the findings and reflects upon these in a wider context (**Figure 0-1**).

**STUDY 1**
Lysdal FG, Thorborg K, Bandholm T, Petersen K, Clausen MB, Hansen M, Jensen N, Grønlykke TB, Kersting UG. High prevalence of lateral ankle sprain injuries in Danish indoor sports: a cross-sectional survey among 91 sub-elite indoor sports teams. *Manuscript in preparation.*

**STUDY 2**
Lysdal FG, Fong DTP, Grønlykke TB, Thorborg K, Kersting UG. Spraino: a new concept for preventing lateral ankle sprain injuries in indoor sports. *Manuscript in preparation.*

**STUDY 3**
Lysdal FG, Bandholm T, Tolstrup JS, Clausen MB, Mann S, Petersen PB, Grønlykke TB, Kersting UG, Delahunt E, Thorborg K. Does the Spraino low-friction shoe patch prevent lateral ankle sprain injury in indoor sports? a pilot randomized controlled trial with 510 participants with previous ankle injuries. *British Journal of Sports Medicine.* 2020. Doi: 10.1136/bjsports-2019-101767

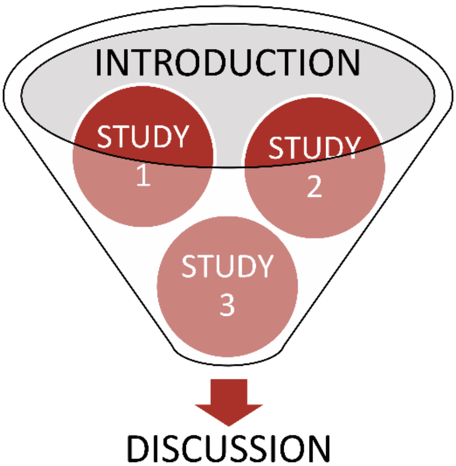

*Figure 0-1. Flow of thesis*

# DISCLOSURES

Filip Gertz Lysdal is a paid employee in Spraino ApS under the Industrial PhD Program, financially supported by Innovation Fund Denmark (grant number 7038-00087A). Thor Grønlykke (Co-author and company supervisor) is the founder and CEO of Spraino ApS. These conflicts were accommodated by restricting Spraino ApS, and authors Filip Gertz Lysdal and Thor Grønlykke from having any final deciding role in the design, execution, analysis and interpretation of data, and decision to submit results of the clinical trial. Kristian Thorborg (PhD Co-supervisor) had full authority of the clinical trial administration. The senior clinical researchers, Kristian Thorborg, Thomas Bandholm, and Eamonn Delahunt, had full authority in terms of submission for publication. The remaining authors have no competing interests to declare.

Copenhagen Center for Health Technology (CACHET) financially supported the clinical trial (grant number RFH-15-00013), for which Spraino ApS provided the low-friction patches (worth approx. €19 000). Innovation Fund Denmark and Copenhagen Center for Health Technology (CACHET) had no scientific role in Study 3 or any other part of this PhD.

*Figure 0-2. Research partners and supporting funding agencies*

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# CHAPTER 1. INTRODUCTION

According to the World Health Organization, physical inactivity is responsible for 3.2 million deaths annually, and is thus considered the fourth-biggest risk factor on global health (2,3). This is backed by research conducted for the Danish Health Authority (*Sundhedsstyrelsen*), in which it is estimated that 7-8% of all deaths in Denmark are due to physical inactivity (4). Practicing sports is in this regard considered health-beneficial and would be the obvious choice for battling the issue, that is inactivity. Sport and physical activity may help reduce the risk of premature mortality in general, as well as obesity, coronary heart disease, and diabetes in particular (5,6). It is thus not without reasoning that regular physical activity is highly recommended by both the World Health Organization and the Danish Health Authority (7). Physical activity is not only fun, but essential for general wellbeing. However, despite the obvious benefits, injuries seem to be an almost inevitable part of practicing an active lifestyle (8), potentially outweighing the health benefits of regular physical activity (9).

## 1.1. SPORTS INJURIES

Injuries are among the most common causes of death, as well as a leading cause of long term disability and lower life expectancy (3), and it is also in this light that physical activity presently finds itself. Sporting activities is considered one of the major causes of injuries, comparable to occupational- and home accidents, thereby eclipsing traffic accidents and violence (10–14). Moreover, illnesses and injuries are among the greatest barriers for performing regular physical activity (9), why prevention of injuries is considered vital for maintaining a good public health (7,15).

Injuries have previously been defined as *"any unintentional or intentional damage to the body … caused by acute exposure to physical agents such as mechanical energy, heat, electricity, chemical, and ionizing radiation interacting with the body in amounts or rates that exceed the threshold of human tolerance"* (8). From a biomechanical perspective this would be the equivalent to the failure of a machine or structure, due to a stress that exceeds the tolerance of a given structure (16). The definition of injury in sports was recently refined by the International Olympic Committee *(Injury and Illness Epidemiology Consensus Group)* as:

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*"Injury is tissue damage or other derangement of normal physical condition due to participation in sports, resulting from rapid or repetitive transfer of kinetic energy"*
Bahr *et al* (17)

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In short (and in layman's terms), a sports injury can simply be defined as *any harm or damage to the human body sustained while (or due to) participating in sports or physical activity*. A common definition that has been largely consistent in sports injury research over the years (1,18,19).

Injuries occurring during sports is not an uncommon phenomenon, and a staggering 37% of all leisure time accidents in Denmark are reportedly sports injuries (15). A recent national survey (20) uncovered that 18.4% of the population in Denmark aged 15 and above had (within a year) sustained a sports-related injury that resulted in at least seven days restriction from physical activity, and/or treatment from a health care professional. The prevalence among kids (age: 7 to 15) was 19.3% (20). These high numbers are also reflected in the number of hospital visits, with 10-19% of all acute injuries that are treated in the emergency rooms in Scandinavia stemming from incidents occurring during sports (16,21).

While the number on the billboard below (**Figure 1-1**) might be a simple extrapolation of the reported prevalence (20) it still reflects a recent increased attention towards sports-related injuries.


*Figure 1-1. Picture of a billboard from a Danish train station with the message; "900.000 sports injuries incurred yearly in Denmark"*

### 1.1.1. WHAT GETS INJURED?

Interestingly, sports-related injuries seem to occur basically everywhere in/on the human body (**Figure 1-2**). This was highlighted in a widely acclaimed systematic review from 2007 (11) that synthesized injury data from 70 different sports. In general, however, the lower extremities appeared more susceptible to injury during sports. Knee injuries accounted for 13.2-27.0% (10,22–42); ankle injuries for 11.2-20.8% (10,22–42); foot injuries for 10.0-15.6% (10,22,33,35,41,42); and leg/thigh injuries for 4.1-10.0% (10,22–42). Additionally, hand injuries accounted for 9.1-21.8% (10,22–28,33,42); arm injuries for up to 11.0% (23); shoulder injuries for 3.3-5.8% (29–32,34,36,38–40); trunk injuries for 4.9-8.5% (24–32,34,37–40); and finally head injures for up to 10.0% (37).

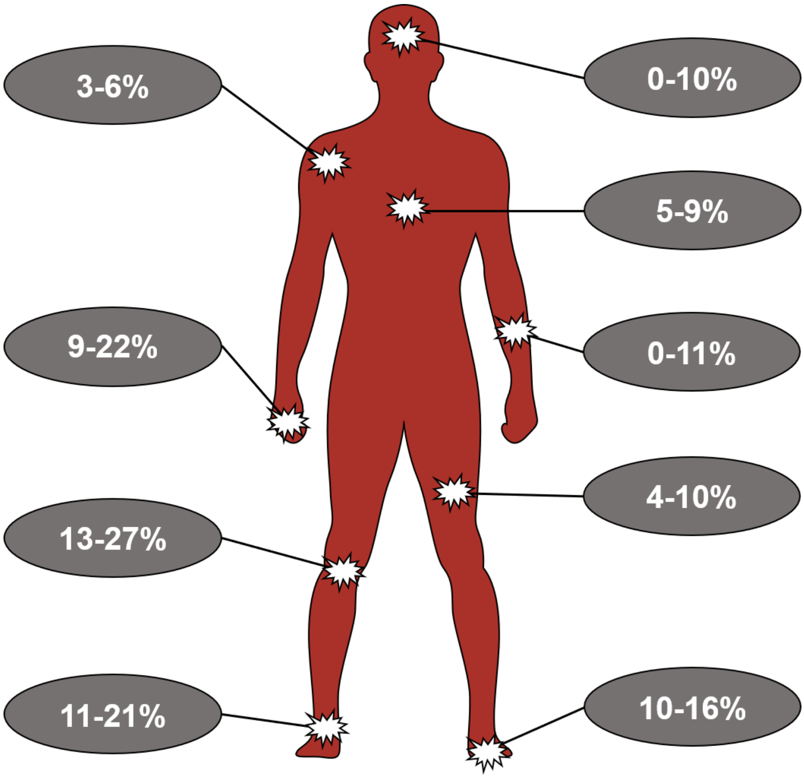


*Figure 1-2. Weighted percentages of the most common injured body sites in sports, numbers from Fong et al* (11)

The same review also found the ankle joint to be the most commonly injured body part in 34% (24 out 70) of all included sports and that the most common type of injury was a sprain injury (11).

## 1.2. ANKLE SPRAINS

A ‘sprain’, also known as a ‘torn ligament’, is a rupture of collagen fibers forming the ligaments (19) that passively connect the bones of our skeletal system (43). The tearing of a ligament (sprain) typically occurs as a result of an acute trauma, in which a joint is suddenly forced into an extreme position (19). This causes a sudden stress that exceeds the ligament’s structural capacity (44). Ligamentous injuries are universally classified within the grades 1-3, ranging from mild to severe, based on the level of structural damage (19): A grade 1 sprain injury is considered mild with only microscopic structural tearing, typically associated with slight local tenderness. A grade 2 sprain is considered moderate with partial macroscopic tearing of the ligament and typically notable pain and swelling. Grade 3 sprains are considered severe and are characterized by a complete rupture of the ligament (19,45,46).

In human anatomy, the ankle is the joint where the foot and lower leg segments connect (**Figure 1-3**). It comprises of three major articulations: the distal tibiofibular syndesmosis, the talocrural joint, and the subtalar joint (47,48). These articulations allow for three-dimensional movements of the foot in relation to the lower leg, namely: plantar flexion and dorsal flexion, inversion and eversion, and internal and external rotation (47). This enables the foot to do very precise movements and to participate in anything from ballet to soccer.
The joints of the ankle are passively supported by multiple ligaments, and as such, an ‘ankle sprain’ is a tearing of one or more of these ligaments of the ankle joint (47,49).

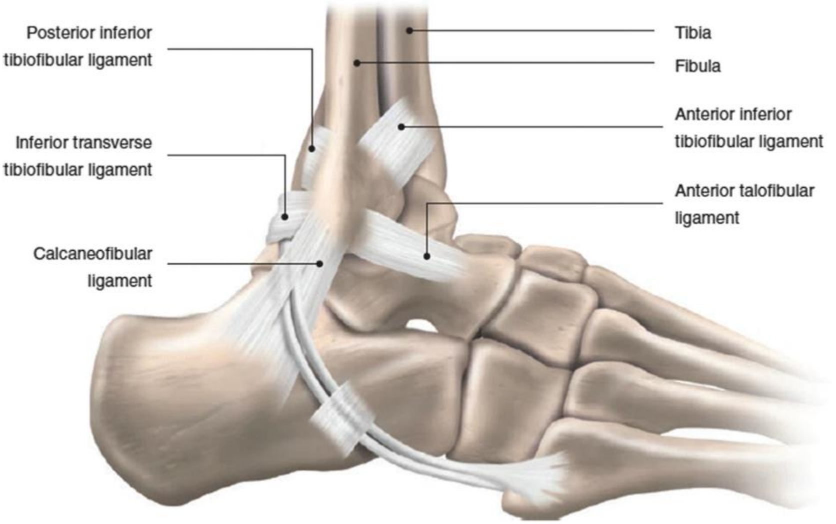


*Figure 1-3. The lateral ligaments of the ankle joint.*
*Reused with permission from D’Hooghe et al* (50)

The particular focus given to 'sprains', as opposed to other ankle injuries, is grounded in the unique characteristic of ankle injuries being almost exclusively characterized by sprains (11,49,51).

We focus our attention on *'lateral ankle sprains'*, since by-far most of these sprain injuries involve the same ligaments on the outside of the ankle joint. This makes the *lateral ligament complex* the most commonly injured single-structure in the human body (11,47,49,51). The lateral ligament complex of the ankle refers to the three separate ligaments on the outside of the ankle joint (**Figure 1-3**): the anterior talofibular ligament, the calcaneofibular ligament, and the posterior talofibular ligament. Lateral ankle sprains are thus not completely structure specific (as e.g. an ACL injury). Instead, lateral ankle sprains were defined by Delahunt et al (52) as

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> *"an acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot."*
> Delahunt *et al* (52)

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This definition has later been endorsed by the International Ankle Consortium (49), and highlights that a lateral ankle sprain is an injury to any of the three ligaments of the lateral ligament complex. This definition is now widely used in ankle sprain research, and unlike many other injury definitions, it includes the mechanism by which lateral ankle sprain injuries occur (47,49,53). A rapid excessive inversion of the rear foot typically results in tissue damage to the calcaneofibular ligament. However, when the foot is in plantar flexion, the anterior talofibular ligament is typically the first to injure (45,54).

The ankle joint is without question the most common site of injury among the general population (49), with up to 27 injuries per 1000 person-years (55). It is further estimated that one lateral ankle sprain injury occur for every 10,000 people each day (56,57). This equals to 25,000 lateral ankle sprains occurring daily in the United States (57–59). In Denmark ~40,000 people attend the emergency rooms every year due to an ankle distortion, according to the national patient register *(Landspatientregisteret).*

### 1.2.1. ANKLE SPRAINS IN SPORTS

Although ankle injuries are very prevalent among the general population (49,55), it is worth noting that about 40% of all traumatic injuries to the ankle joint are estimated to occur during sports (48,60,61). Around 80% these ankle injuries are characterized by sprain injuries, of which ~80% affect the lateral ligament complex, thereby making the lateral ankle sprain the most common type of acute injury in sports. Even in some sports, ankle injuries are solely reported as lateral ankle sprain injuries, thereby representing 100% of the ankle injury cases (11,47,51,62). Lateral ankle sprains have been shown to most frequently occur in indoor and court sports with a cumulative incidence rate of 4.9 sprains per 1000 hours of sports participation.

### 1.2.2. THE IMPACT OF ANKLE SPRAINS IN SPORTS

The high incidence rate of lateral ankle sprains in sports (11,62) represents a considerable risk of injury to anyone who actively participate (49). These injuries are often regarded as benign (57,62), but lateral ankle sprains injuries can have a significant impact on sports performance, especially in team sports, where lateral ankle sprains account for 1/6 of all injury related absence from sports participation (51). Apart from decreased (team) performance and absence from sports, ankle sprains are also debilitating in the form of pain and swelling, reduced mobility, occupational absence, and adverse psychological effects (47,62). Additionally, the risk of long term injury-associated residual symptoms following a lateral ankle sprain is significant (49,57,63,64), with up to 75% reporting recurring or chronic issues following injury (57,63). These issues include functional and mechanical insufficiency, commonly labelled chronic ankle instability, which is defined as persistent pain, swelling, giving way episodes and recurrent sprain injuries for more than 12 months after the first ankle sprain (49,61,65,66). There is also a notable increased risk of post-traumatic osteoarthritis (49,57).

Ankle instability is, as one would think, related with a high risk of re-injury (66), and an athlete escaping an index ankle sprain without any chronic issues, might not be so lucky after the second (or third) ankle sprain. In fact, the rate with which lateral ankle sprains reoccur is the highest among all musculoskeletal injuries, with a reported 9.8 times increased risk of injury in the first six months following a first-time lateral ankle sprain (49,67).

The sheer magnitude of lateral ankle sprains is naturally associated with substantial socioeconomic costs, with annual health-care costs of €187,200,000 in the Netherlands alone (68), and $2,000,000,000 annually in the US (58). The high prevalence and incidence rate of ankle sprains, coupled with the high associated economic costs of treatment, and the substantial risk of chronic issues, demands effective measures to prevent lateral ankle sprain injuries in sports (49,57,63).

## 1.3. SEQUENCE OF PREVENTION

When fighting the global disease burden that is sports injuries, it is important to know where and what to target. The 'sequence of prevention' is a four-step cyclic framework (**Figure 1-4**) originally proposed by van Mechelen et al. in 1987 (1). This framework has since its introduction been widely adopted (and debated) within this field of research (69–71). In essence, the 'sequence of prevention' describes injury prevention research as a step-by-step process in which information is systematically collected with the goal of developing (and implementing) effective injury preventive measures (1,71).

The model can be used to understand and describe sports injury prevention research in its wider context (11,16), and it is implied that one aspect of the prevention cycle should not stand alone (1). This thesis is no exception where this model is used as a framework to tie the studies together.

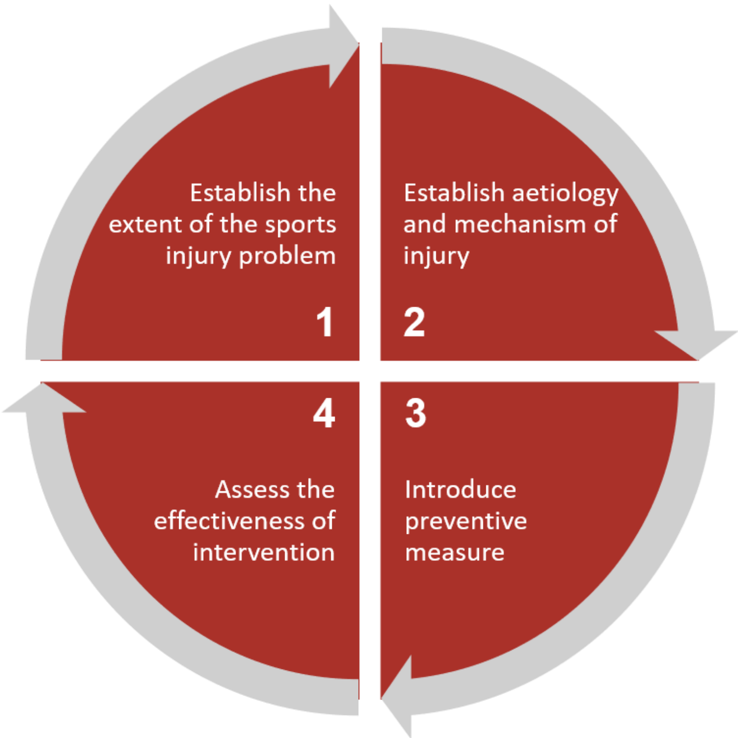



*Figure 1-4. The 'sequence of prevention' of sports injuries. Adapted from van Mechelen et al. 1992* (1)

### 1.3.1. STEP 1: ESTABLISHING THE EXTENT OF THE SPORTS INJURY PROBLEM

The first step in the sequence of prevention is to establish the extent of the sports injury problem. The problem is typically quantified by epidemiological measures such as prevalence, incidence, and severity. Ideally, injury incidence should be expressed in rates, and preferably as the number of injuries per 1000 hours of sports participation. In this way, exposure is taken into account, thereby enabling comparisons between sports and/or preventions strategies (1,72).

Injury severity is another important aspect when investigating the extent of a sports injury problem (1). A simple and widely implemented measure of sports injury severity is 'time lost from sports participation'. This duration of absence (or affected participation) gives a precise estimate of the consequences following injury for the individual. Injury severity is typically classified into 'minor' (< 1 week of affected participation), 'moderate' (1-3 weeks of affected participation) and 'severe' (≥ 3 weeks of affected participation) (1,40).

### 1.3.2. STEP 2: ESTABLISHING THE ETIOLOGY AND MECHANISM OF THE SPORTS INJURY

The second step in the sequence of prevention is to establish the etiology and mechanism of the sports injury (1). Establishing the cause of injury is a crucial step in the prevention cycle that includes information on risk factors and injury mechanism (1,16,71).

Risk factors are typically divided into two categories, *intrinsic* and *extrinsic* risk factors(1,16,73). Intrinsic risk factors cover all factors related to the athlete itself such as sex, age, body composition, anatomy, health, flexibility, skill level, and previous injury etc., that might predispose an individual athlete to injury. Extrinsic risk factors cover possible risks outside of the athlete, relating to factors such as the environment in which the sport is practiced (e.g. weather, floor/turf type and maintenance, visibility), protective equipment (e.g. helmets and shin guards), sports equipment (e.g. shoes, skis, bike), and even the nature and rules of the sport (16,73).

And while risk factors, irrespective of how many they might be, might predispose an athlete to injury, they remain distant from the injury outcome and are not what causes the injury in itself (16,71,73). For a sports injury to occur, we still need an inciting event (proximal to the injury outcome), that coupled with the risk factors result in a sports injury (16,73). This can occur during anything from the mere sports exposure, to a specific playing situation, or the behavior of a player or opponent (e.g. violent conduct). It is argued that a precise description of the inciting event is fundamental to understand the specific cause(s) of a given injury in order to design an effective preventive strategy (1,69,71,73).

### 1.3.3. STEP 3: INTRODUCING A PREVENTIVE MEASURE

The third step in the sequence of prevention is to introduce a measure that targets the established etiology and mechanism of injury from the second step. This measure is thus presumed likely to reduce the risk and/or severity of the sports injury in question (1,16,70). Injury preventive measures have typically been divided into three main categories: training (e.g. proprioceptive training), equipment (e.g. a helmet), and regulatory (e.g. enforced use of helmets) (74). The introduced preventive measure should be specific and well defined on the type of injury, the hypothesized risk factor targeted, and under which setting/sport the proposed measure is intended to prevent the sports injury in question (1,70). However, the same preventive measure can be introduced in multiple sports, provided that the injuries occur in a similar way - under the same conditions and with a similar mechanism (1).

### 1.3.4. STEP 4: ASSESSING THE PREVENTIVE EFFECTIVENESS

The fourth step in the sequence of prevention is to assess the preventive effectiveness of the introduced preventive measure (1). Again, this is ideally done by looking at incidence rates per 1000 hours of sports participation (17), as well as severity per injury incurred (1). Testing whether the introduced injury preventive measure actually does work (as intended), is preferably evaluated in a randomized controlled trial (RCT) (16,75). An RCT is considered the gold standard in medical research (76) since it allows for a direct comparison between groups. It is strongly encouraged to design RCT's as pragmatic effectiveness studies, using an intention-to-treat approach, where the participants are analyzed as randomized (77,78). These trials should mimic real life behavior as closely as possible (75,77,79), and adherence should be reported for evaluation into whether a proposed measure is adopted by the athletes. These steps are considered important to provide information on long term effectiveness in injury prevention (79–81), something which should be acknowledged already in the design phase of such trial (82).

## 1.4. AIMS AND HYPOTHESES

In summary, lateral ankle sprains are the most common injury among the general population (55), yielding incredible sums in health-care costs (68), with high risk of recurring issues and long term sequalae (49). Since this injury type is a particular problem in indoor sports (62), the overall aim of this PhD was to introduce and give scientific evaluation a new concept (Spraino) for preventing lateral ankle sprain injuries in indoor sports. As such, the aims of this PhD are closely related to the 'sequence of prevention' (1), and three separate studies were conducted to cover the four steps.

The first study (Study 1) was a cross-sectional survey in which the aim was to establish the prevalence and etiology of lateral ankle sprain injuries among Danish indoor sports participants. The participants in Study 1 who had sustained a recent lateral ankle sprain injury were invited to participate in the clinical trial (Study 3). The aim of Study 3 was to establish the preventive effectiveness of Spraino, when used as an intervention to prevent lateral ankle sprain injuries in indoor sports. Here, 50% of the included participants received Spraino as an intervention to prevent lateral ankle sprain injuries. Spraino was preclinically evaluated in Study 2 through different mechanical and biomechanical tests, with the aim of introducing and thoroughly describe 'Spraino', a new concept for preventing lateral ankle sprain injuries in indoor sports. The flow of the thesis is illustrated below (**Figure 1-5**).

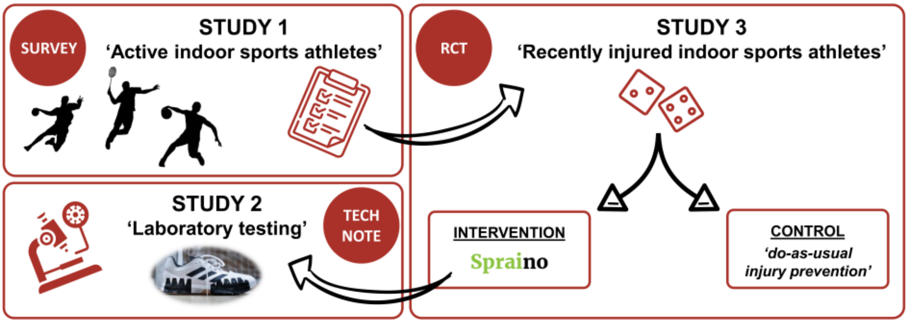
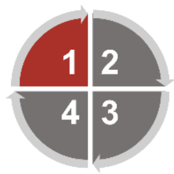



*Figure 1-5. Flow of included studies.*

It was expected that lateral ankle sprain injuries would be very prevalent among indoor sport athletes in Denmark, and that most of these injuries would be non-contact injuries (occurring without stepping/landing onto something other than the floor). The pilot randomized controlled trial of Spraino was considered exploratory, but with a working hypothesis that Spraino would be an effective and safe intervention when used to prevent lateral ankle sprain injuries in indoor sports.

# CHAPTER 2. EXTENT OF SPORTS INJURY PROBLEM




Denmark has strong tradition of practicing organized sports, and indoor sports are particularly popular among the nation's population (83). It has previously been described how ankle sprain injuries are most common in indoor sports (11), with cumulated incidence rates as high as 4.9 injuries per 1,000 hours of exposure (61,62). It was therefore expected that Danish indoor sports participants would be no exception to this "rule" and to a large extent would be familiar with lateral ankle sprain injuries.

## 2.1. PREVALENCE OF LATERAL ANKLE SPRAIN INJURIES IN DANISH INDOOR SPORTS

Handball, badminton and basketball are among the most popular indoor sports with millions of participants worldwide (84–86). In Denmark, only badminton and handball are among the most popular sports. However, basketball is rapidly growing in popularity and is registering an ever-increasing number of participants (83). These sports are associated with an notable high risk of suffering lateral ankle sprains (11,49,62). Lateral ankle sprains account for ~20% of all injuries in badminton, ~15% of basketball injuries, and ~14% of all handball injuries (11). The incidence rate though was found to be highest in handball, followed by basketball and badminton, respectively (62). However, proportion of sports injuries (11) or injury incidence rates (62) might cause a minority of participants to distort the overall picture due to injury recurrences - a particular concern for lateral ankle sprain injuries (49).

To this date it remained unknown how big a proportion of active indoor sport athletes that have experienced a lateral ankle sprain injury while playing, and whether there would be any difference in prevalence between the investigated sports.

### 2.1.1. METHODS

#### 2.1.1.1 Design

We designed and conducted a cross-sectional survey to establish the prevalence of lateral ankle sprain injuries among active danish indoor sports participants. The study was approved by the North Denmark Region Committee on Health Research Ethics on 5 July 2017 and deemed exempt by the Danish Data Protection Agency on 25 August 2017. Respondents were approached between 19 October 2017 and 28 February 2018. We report the study adhering to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative (87) using the IOC extension for Sports Injury and Illness Surveillance (STROBE-SIIS) (17).

#### 2.1.1.2 Participants and Setting

Respondents were recruited by physical approach at the local training facilities of sub-elite indoor sport teams competing in handball, basketball, or badminton at divisional or league level in Denmark. Respondents were eligible for inclusion in the study if they: (i) played handball, basketball or badminton in a Danish indoor sports club at divisional level or higher, and (ii) could read, speak and understand Danish.

#### 2.1.1.3 Data collection

All participants completed a modified Danish version of the previously validated NCAA Injury Surveillance System questionnaire (88), that was piloted beforehand with help from 25 field sport athletes. The questionnaire included information on the occurrence and mechanism of their most recent of lateral ankle sprain injury, as well as information on anthropometry and demography (gender, age, height, body mass, sports, shoe size, exposure, level of competition). The questionnaire was distributed on paper on site of the training residence before, or immediately after, a training session, and collected once filled. A lateral ankle sprain was further explained verbally in layman's terms to the athletes as a lateral distortion of the ankle/foot resulting in pain, stiffness and/or swelling of the ankle, adhering to the International Ankle Consortium endorsed definition by Delahunt *et al* (49,52).

Respondents who had previously sustained a lateral ankle sprain in their primary indoor sport were asked to classify their most recent injury as being either a 'contact' or 'non-contact' injury. A contact sprain was defined as an injury to the lateral ligament complex incurred by stepping/landing directly onto an object (i.e., opponent's foot). A non-contact sprain was defined as an injury incurred without stepping onto something (other than the floor), regardless of any player-to-player interaction prior to the event.

#### 2.1.1.4 Statistical analysis

Respondent characteristics were reported as mean and standard deviation, all rounded to the nearest integer. Prevalence of lateral ankle sprains was calculated with 95% confidence interval for each sport individually, and in total. Univariate logistic regressions were used to determine whether the prevalence of a recent lateral ankle sprain sustained could be predicted by the type of sport practiced (handball, badminton, or basketball). A Chi-squared test was used to test for differences in proportions of lateral ankle sprains suffered by contact and non-contact mechanisms between handball, badminton, and basketball players, respectively (Chapter 3). All statistical analyses were conducted as 'available case analysis' using SPSS software version 25.0 (IBM SPSS Statistics Inc., Chicago, IL, USA) with a critical probability level of 0.05 used throughout all tests.

## 2.1.2. RESULTS

### 2.1.2.1 Recruitment and response rate

A total of 1339 indoor sports participants were approached at the local training facilities of 91 indoor sports teams competing in handball, basketball, or badminton at divisional or league level in Denmark. Twelve hundred seventy-three participants accepted the invitation and complete responses were received from 1238 participants at a rate of 93% (1238 out of 1339 invited) (**Figure 2-1**). A total of 101 responses were not received, of which 66 had declined to participate before receiving the questionnaire. Eight respondents did not provide info on level of competition, and five respondents did not provide info on injury mechanism of most recent ankle sprain.

The sample of the present survey corresponded to 18% of the total population in divisional handball, 27% of the population in badminton and 12% of the population in basketball (Lysdal FG; in an email from R. Larsen (rla@basket.dk) and K. Hansen (kiha@badminton.dk) in May 2018; and personal communication with administration in Danish Handball Federation (May 2018).

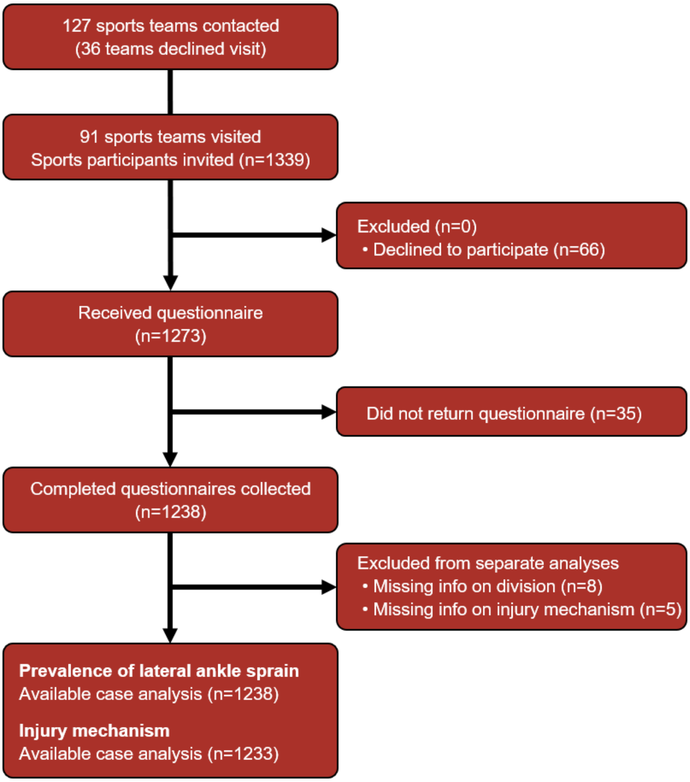



*Figure 2-1. Flow diagram of respondents, as recommended by the STROBE initiative* (17,87)

### 2.1.2.2 Trial population

The mean age of respondents was 23.4 years and 53% were men. Handball players made up 75% of the sample (925 out of 1238), followed by 17% badminton players (207 out of 1238) and 9% basketball players (106 out of 1238). More than half of the sample (53%) competed in the third division (654 of 1238) (**Table 2-1**).

**Table 2-1:** Respondent characteristics

| | Handball | Badminton | Basketball | Total |
|---|---|---|---|---|
| Respondents, n (%) | 925 (75) | 207 (17) | 106 (9) | 1238 (100) |
| Male, n (%) | 458 (50) | 127 (61) | 73 (69) | 658 (53) |
| Age, mean (SD) | 23.5 (4.3) | 22.8 (7.2) | 23.7 (6.8) | 23.4 (5.2) |
| Height (cm), mean (SD) | 180 (10) | 178 (10) | 185 (11) | 180 (10) |
| Body mass (kg), mean (SD) | 79.4 (14) | 72.0 (12) | 80.6 (15) | 78.2 (14) |
| Weekly practice (hours), mean (SD) | 5.3 (2.3) | 6.8 (3.6) | 7.4 (4.6) | 5.8 (2.9) |
| Level of play, n (%) | | | | |
| League | 17 (1) | 4 (0) | 23 (2) | 44 (4) |
| 1st division | 190 (15) | 11 (1) | 32 (3) | 233 (19) |
| 2nd division | 246 (20) | 35 (3) | 18 (1) | 299 (24) |
| 3rd division | 469 (38) | 152 (12) | 33 (3) | 654 (53) |

### 2.1.2.3 Prevalence of lateral ankle sprain injuries

Almost three quarters (74%) of all responding divisional indoor sports participants reported to have sustained a lateral ankle sprain at some point when participating in their sport (912 of 1238) (**Figure 2-2**). Almost two thirds (59%) of these injuries had been sustained within the preceding 24 months (541 of 912), and 37% within the preceding 12 months (335 of 912).

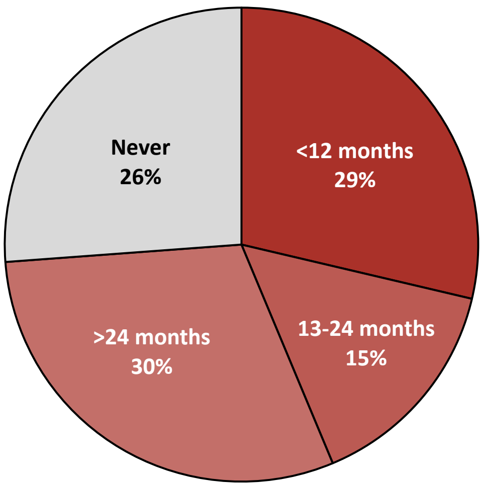



*Figure 2-2. Prevalence of lateral ankle sprains in Danish indoor sports.*
*Have you ever sustained a lateral ankle sprain when playing your primary sport?*

A historic lateral ankle sprain injury was most prevalent among handball players and basketball players. Here 78% (723 of 925 and 83 of 106) had sustained this injury at some point during their sport, while this was "only" the case for just over half of the badminton players (51%; 106 of 207) (**Table 2-2**).

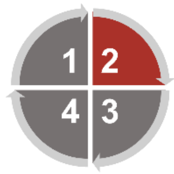
Within the preceding 24 months, 46% (430 of 925) of all handball players had sustained an ankle sprain, and 31% (290 of 925) within the preceding 12 months. In basketball, this was the case among 57% (60 of 106) and 39% (41 of 106), respectively.

One quarter (25%) of the badminton players had sustained a lateral ankle sprain within the preceding 24 months (51 of 207) and 12% (24 of 207) within the preceding 12 months (**Table 2-2**).

**Table 2-2:** Proportion of respondents with a historic lateral ankle sprain (95% CI)

| | Handball | Badminton | Basketball | Total |
|---|---|---|---|---|
| Ankle sprain (all-time) | 78.2% (75.5, 80.8) | 51.2% (44.4, 58.0) | 78.3% (70.5, 86.1) | 73.7% (71.2, 76.1) |
| Ankle sprain (< 24 months) | 46.5% (43.3, 49.7) | 24.6% (18.8, 30.5) | 56.6% (47.2, 66.0) | 43.7% (40.9, 46.5) |
| Ankle sprain (< 12 months) | 31.4% (28.4, 34.3) | 11.6% (7.2, 16.0) | 38.7% (29.4, 48.0) | 28.7% (26.2, 31.2) |

# CHAPTER 3. ETIOLOGY AND MECHANISM OF INJURY




That the lateral ankle sprain is the most common single type of acute sports injury (11,47), could be explained by the ankle being the first group of major articulations to be loaded when taking a step (89). Over the years there have been extensive investigations into the mechanism with which this injury occurs (47–49,90). This has led to a deep understanding of the movements the foot has to make in relation to the lower leg segment, for the lateral ligaments of the ankle to be stretched past their tolerance and ultimately tear (49).

The lateral ankle sprain is a "closed-loop" injury where the injury promoting distortion of the ankle is characterized by a rapid excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot (47,52). This distortion can be initiated in different ways that traditionally have been classified into two major categories, *'non-contact'*, and *'contact'* mechanisms (16). Although lateral ankle sprain injuries are predominantly reported to be non-contact injuries (11,49,61,62), variations in injury patterns are found between sports disciplines (11,71).

Studies on soccer for instance, report that the inciting events for distortions of the ankle, leading to lateral ankle sprain injuries, were predominantly characterized by a direct impact from the opponent on the medial aspect of the lower leg just before (or at) initial weightbearing, causing the player to land with an exposed inverted foot position; and a forced plantar flexion due to a tackle/block when striking the ball (47,71,91). For goalkeepers in soccer, a non-contact inciting event characterized 79% of all lateral ankle sprains (91). In indoor sports, where the risk of ankle sprains is highest (62), ankle sprain injuries are predominantly characterized by occurring without direct contact (11,61,62). And while a direct hit to the leg or ankle is punishable by law in most sports (92), no regulations are designed to help prevent non-contact ankle injuries.

The traditional classification of injuries being instigated by either contact or non-contact events have been rather rigid in its form. Formerly, injuries with even the slightest of touch between opponents has been classified as 'contact injuries', even if this touch ("contact") appeared distant from the injury site. More recent studies have instead added a third dimension, by dividing contact injuries into two subcategories (17,19), *indirect contact* and *contact*. Contact is here defined as a direct blow that is responsible for the injury occurrence, while an *indirect contact* injury could be any other player-player interaction (i.e. ACL injury occurring following a shove from an opponent).

However, when the aim is to prevent lateral ankle sprains, where we have such great existing evidence on the specific injury mechanism (49,51,53,93), it seems redundant to consider indirect contact injuries as a group by itself, unless the aim is to change the rules of a game (92). At the same time, it is not ideal to group these as contact injuries, since the indirect contact would often occur just before the inciting event and/or appear isolated from the injury site (19).

Instead we propose a grouping of 'indirect contact' and 'non-contact' lateral ankle sprains, since these injuries are all characterized by the foot being distorted solely by the floor (94). As such, lateral ankle sprain injuries would be defined by:

- A contact lateral ankle sprain is an injury incurred by stepping/landing directly onto an object (i.e., opponent's foot) (94) or by the result of a direct blow (91).

- A non-contact lateral ankle sprain is an injury incurred without stepping onto something (other than the floor), regardless of any player-to-player interaction prior to the event (94).

## 3.1. INJURY MECHANISM IN DANISH INDOOR SPORTS

The respondents in our cross-sectional survey (**Study 1**), being handball, badminton, and basketball players, were asked to categorize the nature of their most recent lateral ankle sprain injury using only the two definitions above. The results revealed that more than half (56%; 511 of 907) of the participants with a historic sports-related lateral ankle sprain, had experienced their most recent ankle sprain injury to occur without stepping onto something (other than the floor) (**Table 3-1** and **Figure 3-1**).

**Table 3-1:** Injury mechanism of most recent ankle sprain (95% CI)

| | Handball | Badminton | Basketball | Total |
|---|---|---|---|---|
| Contact injury | 46.6% (42.9, 50.2) | 14.2% (7.5, 20.8) | 56.1% (45.4, 66.8) | 43.7% (40.4, 46.9) |
| Non-contact injury | 53.4% (49.8, 57.1) | 85.8% (79.2, 92.5) | 43.9% (33.1, 54.6) | 55.9% (52.7, 59.1) |

Among the handball players, 53% (384 of 719) of the participants' most recent ankle sprains were incurred without contact, while this was the case for 86% (91 of 106) of the badminton players, and 44% (36 of 82) of the basketball players.

A Chi-squared test on injury mechanism revealed that the badminton players' last ankle sprains were significantly more characterized by having resulted from a non-contact injury mechanism. No statistically significant differences were found between the injury mechanisms in handball and basketball (**Figure 3-1**).

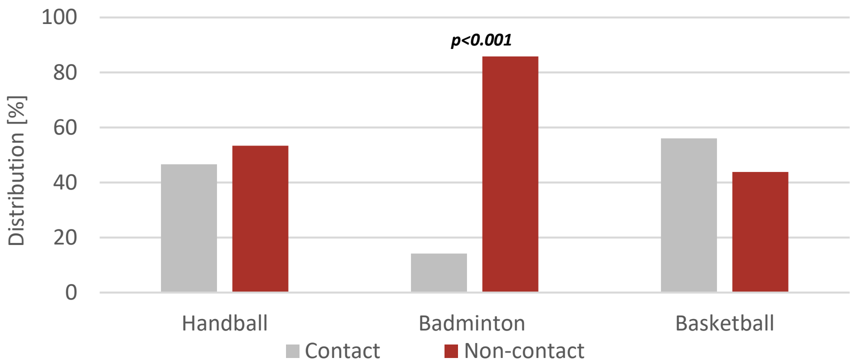



*Figure 3-1. Distribution of lateral ankle sprain injury mechanism in Danish indoor sports.*

That the most recent badminton sprain injuries were significantly more characterized by a non-contact injury mechanism was expected beforehand, and it seems likely that this is due to the obvious trait of badminton being a sport with a net separating the players, as opposed to the more chaotic nature of basketball and handball.

## 3.2. INJURY MECHANISM IN THE NBA 2013-2017

In the National Basketball Association (NBA), 25.8% of the players sustained one or more ankle sprains every season, on average during four seasons (2013-14 through 2016-17). Of these injuries, 71.2% (567 of 796) were reported to involve a contact mechanism of injury (95). However, only 33.3% (189 of 567) of these contact injuries occurred directly from stepping onto an opponent's foot, while 42.3% (240 of 567) occurred due to general contact with another player (i.e. indirect contact) (95). Thus, when employing the same definitions of injury mechanism as proposed previously (94), only 23.7% (189 of 796) of the injuries sustained can with certainty be classified as contact injuries (**Figure 3-2**), while 59.0% (469 of 796) were non-contact injuries. The remaining 17.3% (138 of 796) of unclassified injuries remains unknown (95).

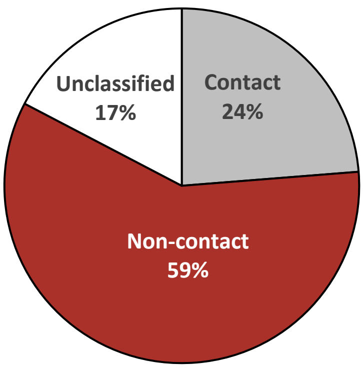



*Figure 3-2. Ankle sprain mechanisms during the NBA seasons 2013-14 to 2016-17. Recalculated from numbers in Herzog et al. 2019* (95)

## 3.3. HOW AETIOLOGY AFFECTS MECHANISM

While the presented injury characteristics from the NBA might seem contrary to those reported by the basketball players in our retrospective cross-sectional survey, the difference most likely lies in the fact that in our survey, they could only report their most recent injury, that in turn could date back their entire playing career.

This serves to highlight that injury recurrences, which are so highly associated with lateral ankle sprain injuries (49,67), to a larger extent, than first-time injuries, might be characterized by a non-contact injury mechanism (67,96). For instance, if an athlete sustains a lateral ankle sprain by stepping onto an opponent's foot, then he/she could be at a heightened risk of sustaining that same injury without 'contact' in the future (96,97).

The same injury mechanism (rapid excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot (47,52)) can be initiated in different ways, that they vary between sports (11) and positions (91). This is important knowledge that tells us that the inciting moment, just before the injury is about to happen, plays an important role in the occurrence of lateral ankle sprains. Here, initial foot positioning at touch down reportedly plays a pivotal role in the occurrence of lateral ankle sprains (47,49,90,93), where initial inversion of the foot in relation to the lower leg segment is a particular concern (93). Inversion of the ankle joint can occur prior to touchdown due to an inadequate contraction of the peroneus muscles (98), that opposes ankle supination (47), or in the early loading phase if landing on an object (e.g. an opponent's foot) or an inclination (e.g. uneven surface) (90). If the foot in addition is plantarflexed during touchdown, the moment arm around the subtalar joint axis is increased, and thereby also the resultant joint torque, causing a rapid inversion and adduction of the foot (47,90).

## 3.4. IS HIGH FRICTION A RISK FACTOR?

It has long been hypothesized that the interaction between shoe and surface plays a pivotal role in the incidence of lateral ankle sprains in sports (99). Specifically, high shoe-surface friction has been suggested as a direct risk factor for non-contact lower extremity injuries (100,101), and for lateral ankle sprains in particular (101–104).

It is widely acknowledged, that lateral ankle sprain injuries are caused by an excessive supination moment around the subtalar joint (47,90,105). In biomechanics, this joint moment is a direct result of the position, magnitude, and orientation of the ground reaction force vector (90,105). Here, the orientation of the ground reaction force vector is directly affected by the friction between the bodies in contact (106).
This means that the *friction coefficient* is not just a unitless descriptor of the exact relationship between the horizontal (breaking) forces and normal force (from the gravity and mass), but is directly related to the moment around the ankle joint (104).

The friction coefficient is derived by dividing the sum of friction (breaking) forces with the normal force (**Equation 3-1**) (106).

$$\mu = \frac{F_f}{F_n} \qquad \textbf{Eq. 3-1}$$

Thus, the ground reaction force vector in **Figure 3-3** is representative of a friction coefficient of 1.0 since the angle of the vector is 45 degrees. This theoretical friction coefficient is a completely normal value for shoes with a rubber outsole against a traditional floor material (107,108). However, this might not be ideal in a situation where the foot is placed in a vulnerable position, such as depicted (**Figure 3-3**).

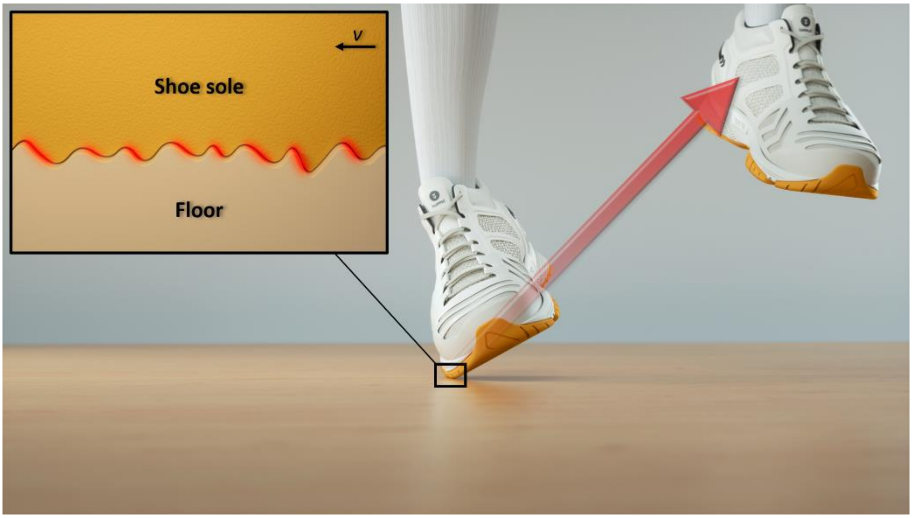



*Figure 3-3. High shoe-surface friction during a bad landing.*
*Adapted with permission from Lysdal et al. (94)*

High friction can in this case create a local anchor. This ultimately leads to a high supination moment that puts the lateral ligaments of the ankle, the anterior talofibular ligament in particular, under high stress (47,105). Shoe-surface friction is traditionally higher in indoor sports, compared to e.g. outdoor and field sports. since the outsole of these shoes typically comprise of a rubber material (109,110). Rubber materials possess friction characteristics that are highly pressure-dependent (111). This essentially means that the friction coefficient can appear higher than usual, during the inciting event of a lateral ankle sprain injury. This is due to the smaller contact area on the edge of the shoe (112), and thereby a greater local compression of the rubber material against the surface roughness (**Figure 3-3**) (111,113).

Thus, it remains plausible that the higher friction between shoe and floor (100,108) in indoor sports explains the higher incidence rate of lateral ankle sprains compared to outdoor/field sports (11,61,62).

**TRY THIS YOURSELF:** IF WEARING SHOES WITH A RUBBER OUTSOLE. FEEL THE DIFFERENCE WHEN SLIDING YOUR SHOE AGAINST THE FLOOR IN A FLAT AND TILTED POSITION, RESPECTIVELY.

# CHAPTER 4. SPRAINO: A PREVENTIVE MEASURE

Provided that high lateral shoe-surface friction, as hypothesized, is indeed a risk factor, then modifying the friction properties at this area of the sports shoes could prove a viable method to prevent lateral ankle sprain injuries (1).

The interaction between shoes (equipment) and surface (sports setting) naturally lies outside of the body, and shoe-surface friction is therefore considered an extrinsic risk factor (1,16,73). It has been proclaimed how targeting external risk factors for ankle sprain injuries has the potential to benefit a wide range sports participants (61), while it has previously been discussed how preventive devices requiring minimal effort for the athlete has a greater chance of being adopted into general use, than complex preventive training regimes (61,64,69,114).

## 4.1. WHAT IS SPRAINO?

Spraino (*"no"* + *"sprain"*) is an injury preventive measure that comprises of low-friction shoe patches (**Figure 4-1**) specifically designed to prevent friction related lateral ankle sprain injuries (94).


*Figure 4-1. A package of Spraino low-friction shoe patches*

The front patch is attached along the edge of the lateral forefoot, with 2-4 mm covering the shoe sole. The rear patch is attached along the edge of the lateral rearfoot but does not cover the sole (**Figure 4-2**). The patches are intended for use during indoor sports and have a durability of 40-60 hours of playing time.

*Figure 4-2. Spraino low-friction shoe patches on an indoor sports shoe.*
*Reused with permission from Lysdal et al.* (94)

### 4.1.1. HOW SPRAINO WORKS

Spraino works by minimizing friction between the lateral edge of the shoe sole and the floor. The minimized friction causes a reorientation of the ground reaction force vector (105). When bringing the resulting GRF vector closer to the joint center, the joint torque around the subtalar joint axis is lowered, which could mitigate the risk and severity of lateral ankle sprain injuries (47). At the same time if the friction between shoe and floor is sufficiently low (106,115), then the shoe can slide “freely” against the floor surface. This removes the anchor between shoe and floor, around which lateral ankle sprain injuries take place (53), thereby allowing for a re-alignment of the foot and the prevention of rapid excessive inversion and internal rotation (116).

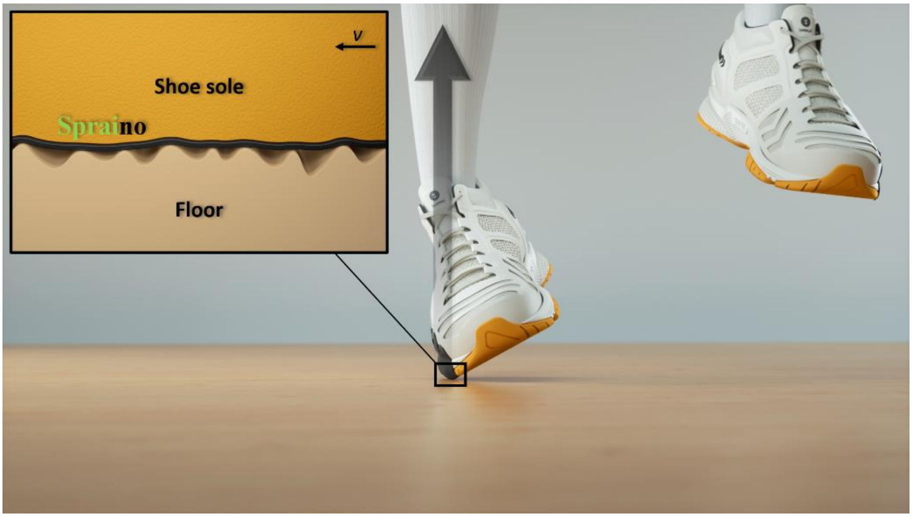



*Figure 4-3. Low shoe-surface friction during a bad landing due to Spraino. Adapted with permission from Lysdal et al.* (94)

## 4.2. MECHANICAL TESTING OF SPRAINO

People have been shown to be able to detect relative changes in coefficient of friction as low as 11% when comparing specimens or materials directly up against one another by hand (117). However, to quantify to which extent Spraino reduces lateral shoe-surface friction in indoor sports, we designed and conducted a modified version of the *Personal protective equipment – Test method for slip resistance* (ISO: 12387:2019) (110).

### 4.2.1. METHODS

The modification of this test lied in the orientation of the test shoe being positioned in a 15º pitch and 30º roll angle in relation to the floor surface, and instead of moving the floor and shoe surfaces against one another along the longitudinal axis of the shoe, the shoe was rotated 90° to conduct a lateral translation.

Lateral shoe-surface friction was then tested on a Yonex badminton shoe (SHB-65 Z2 M, Yonex Co., Ltd., Tokyo, Japan), with and without Spraino attached to the lateral side, in a test setup at Aalborg University. The mechanical test setup comprised of a steel frame that was bolted to the floor above a force plate (AMTI-OPT464508HF-1000, Advanced Mechanical Technology, Watertown MA, USA) equipped mechanical hydraulic platform (Serman & Tipsmark, Brønderslev, Denmark) (118). The steel frame made sure that the shoe would remain in the same (horizontal) position when the force plate was moved against the shoes by the hydraulic platform. The force plate was covered by a standard vinyl sports floor (7.5 mm Taraflex – Evolution, Gerflor, Lyon, France) that is used for badminton and other indoor sports.

The shoe was fitted (and bolted) to a nylon shoe last (Framas Kunststofftechnik GmbH, Pirmasens, Germany) and had the freedom to move vertically inside a vertical steel lead.

The hydraulic arms that powered the platform movements could provide robust and repeatable vertical and horizontal movement (118) making it possible to mimic different shoe-floor interactions. A constant passive load of 50 kg standard weight plates was added atop the test shoe through a vertical load distributor (**Figure 4-4**). The two shoe conditions were each tested against the floor surface five times, respectively, at a sliding speed of 0.3 m/s as per ISO: 13287-2019 (110).

*Figure 4-4. Mechanical setup of the modified ISO: 13287:2019 slip resistance test. Shoe is fixed in 15º pitch and 30º roll angle in relation to the floor surface and loaded with 50 kg.*

Force plate data were recorded with a sample frequency of 1200 Hz and the movement of the force plate was captured via a single retro-reflective marker fixed on the hydraulic platform using eight infrared cameras sampling at 500 Hz (Oqus 300+, Qualisys AB, Gothenburg, Sweden). The hydraulic platform was controlled using Mr. Kick software (Mr. Kick version 3.0, Aalborg, Denmark) and an analog TLL-signal from the platform was used to trigger the data collection from all trials.

The raw force plate data were imported into MATLAB (R2018a, The MathWorks, Massachusetts, USA) where it was low-pass filtered with a cut-off frequency of 30 Hz and 10 Hz, respectively, using a 2$^{nd}$ order Butterworth filter. Zero-phase filtering was performed using MATLAB function FiltFilt, filtering both forwards and backwards. All measurements were synchronized using the kinematics of the single retro-reflective marker by calculating cross-covariance and aligning data by circular shift. Ten empty (no contact) force plate movements were also recorded for later subtraction of the inertial contribution from the hydraulics accelerating the force plate.

The friction coefficient was computed using the force plate-measured reaction forces (**Equation 4-1**) where $F_x$ and $F_y$ are the horizontal reaction forces and $F_z$ the reaction force in the vertical direction (normal force).

$$\mu = \frac{\sqrt{F_x^2} + \sqrt{F_y^2}}{|F_z|} \qquad \textbf{Eq. 4-1}$$

The friction coefficients were computed over 0.50 seconds (600 frames), with the start of the measurement being defined as exceeding a threshold value of 50 N in frictional force. The mean was calculated from 0.17 to 0.42 seconds due to a particular interest in the dynamic friction coefficient (average value after peak in static friction) as per the test standard (110).

### 4.2.2. RESULTS

The friction coefficient increased steadily from the start of the measurement in the control condition, until around 0.21 s after which it became relatively constant. With Spraino attached on the shoe, the friction coefficient peaked after 0.08 s after which it became relatively constant after 0.1 s (**Figure 4-5**).

The mean dynamic coefficient of friction was 0.76 (± 0.02) without Spraino (Control), and 0.41 (± 0.01) with Spraino attached on the shoe.

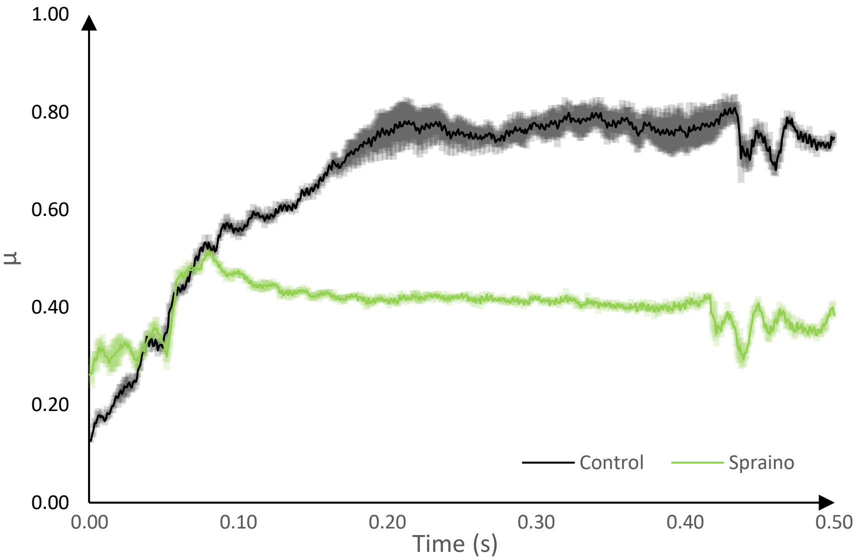



*Figure 4-5. Friction coefficient of a sports shoe with and without Spraino attached in a modified ISO: 13287:2019 standard test.*

## 4.3. BIOMECHANICAL TESTING OF SPRAINO

Preclinical evaluations are essential to inform about initial safety and potential clinical relevance of an intervention (119,120). Biomechanical analyses of interventions are in this regard the typical "next step" in sports injury prevention research (1). The mechanical test established that Spraino minimized lateral shoe-surface friction. However, it remained unknown whether this feature would prevent the foot from twisting, during an inverted and plantarflexed foot position at initial floor contact.

### 4.3.1. REALIGNMENT MECHANISM

The major limitations when evaluating interventions for sports injury prevention in biomechanical laboratories are safety and ethical issues (121). Since it remains highly unethical to sprain the ankles of living subjects intentionally (121,122), we designed a test to simulate a typical initial contact of non-contact lateral ankle sprain injuries (47,90), to test if the added low-friction properties of Spraino would realign the foot.

We had a special focus on the "roll" angle, which is the angle between shoe and floor, around the longitudinal axis of the shoe. We chose this focus due to our interest in evaluating whether Spraino would realign (or not) against the surface, and due to the close resemblance to ankle inversion, which at initial contact is a reported risk for lateral ankle sprain injuries (47,90).

#### 4.3.1.1 Methods

The 'realignment mechanism' was tested on one healthy male subject age, 27 years; height, 1.74 m; body mass, 75.5 kg) with his left leg securely fixed above the same robotic platform (Serman & Tipsmark A/S, Denmark) as used in the mechanical test of Spraino (**Figure 4-6**) fitted with a vinyl indoor sports floor (7.5 mm Taraflex – Evolution, Gerflor, Lyon, France) that is used for badminton and other indoor sports. The subject wore a Li-Ning Ranger indoor sports shoe designed for badminton (Li Ning, Beijing, China) equipped with six retroreflective markers, and with Spraino attached to the lateral outside in the intervention condition (116).

The traveling distance of the robotic platform was set up so that only the early phase of non-contact inversion sprain injuries was simulated. The platform was then moved repeatedly against the foot of the fixed leg in a medially and upwards movement with a resultant speed of 1.12 m/s. Ten trials were recorded for each condition (116).

Shoe kinematics were recorded at 244 Hz (due to active filtering) using eight infrared highspeed cameras (Oqus 300+, Qualisys AB, Gothenburg, Sweden). These signals were digitally low-pass filtered using a 4$^{th}$ order Butterworth filter with a 14 Hz cut-off frequency and roll angle of the shoe was analyzed between start and end position of the moving platform using Visual 3D v6 (C-Motion Inc., Maryland, USA) (116).

#### 4.3.1.2 Results

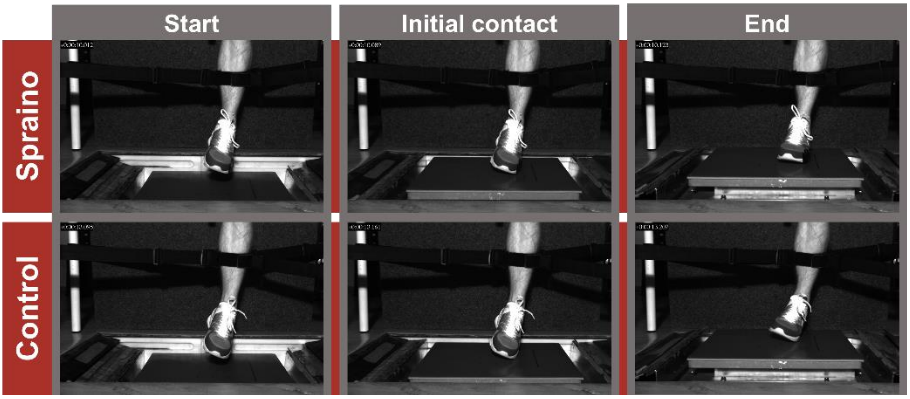



*Figure 4-6. Realignment test with and without Spraino. The left leg of the subject is hanging freely, but fixed in the horizontal plane, above the hydraulic platform.*

Adding Spraino to the lateral outside of this indoor sports shoe facilitated a complete change in frontal plane kinematics (**Figure 4-6**). Instead of twisting any further, or being kept in the relatively high roll angle, Spraino allowed the shoe to realign against the floor surface in 0.1 s (**Figure 4-7**) with a peak angular velocity of -247°/s. In direct contrast, the roll angle increased slightly initially with a peak angular velocity of 165°/s in the control condition (116).

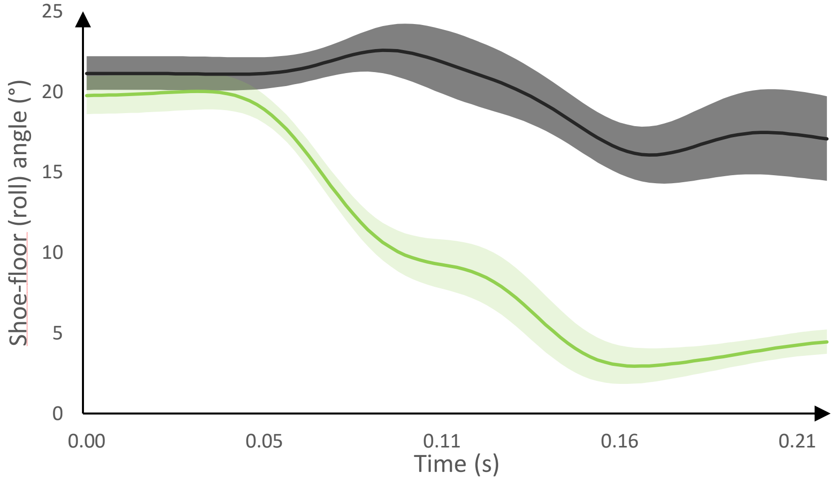



*Figure 4-7. Rotation around the shoe's longitudinal axis (roll angle) between start and end of platform movement against the hanging leg. Adapted from Lysdal et al.* (116)

## 4.3.2. CASE REPORT FROM A LABORATORY INCIDENT

One male PhD student (age, 26 years; height, 1.74 m; body mass, 75.5 kg) tested Spraino in a biomechanics laboratory by performing a series of lateral cutting movements, landing with his right foot onto a force platform equipped with a standard vinyl sports floor (7.5 mm Taraflex – Evolution, Gerflor, Lyon, France). He felt cocky, and started to land with an initially plantarflexed and inverted foot, thus making initial contact with the lateral edge of the shoe; a foot position associated with lateral ankle sprain injuries (47,90). Following a series of successful trials (foot realigning) with Spraino attached, the student removed the Spraino patches from the test shoe and performed one additional trial. This resulted in a grade 1 lateral ankle sprain to his right ankle (19).

The PhD student immediately felt acute pain and tenderness at the location of the anterior talofibular ligament, as well as suffering from local swelling at the injured ankle shortly hereafter. There was minimal or no pain around the other supporting structures. The PhD student's last ankle sprain injury occurred 12 years earlier, and he had no symptoms of pain or functionality limitations in the feet for years prior to this incident. The PhD student returned to full 'Sunday League' football participation after three and a half weeks.

### 4.3.2.1 Methods

Three-dimensional kinematics from 26 retroreflective markers was recorded by eight infrared highspeed cameras sampling at 500 Hz (Oqus 300+, Qualisys AB, Gothenburg, Sweden). Ground reaction force (GRF) data were recorded using a force platform (AMTI OPT464508HF-1000, Advanced Mechanical Technology, Watertown MA, USA) recording with a 1000 Hz sample rate.

Kinematic and force platform data were low-pass filtered using a $4^{th}$-order Butterworth filter with a cut-off frequency of 14 Hz and 100 Hz, respectively. A non-injury (Spraino) trial with pre-contact kinematics that resembled the injury trial the most was chosen for direct comparison between conditions. Ankle joint angles were then analyzed using Visual 3D v6 (C-Motion Inc., Maryland, USA). The trials were synchronized using the vertical ground reaction force, and ankle joint kinematics of the right ankle was analyzed from 0.5 seconds before, until 0.3 seconds after initial contact ($F_z > 20$ N) with the force platform. Inverse dynamics analyses were not conducted due to faulty settings in the amplification of the force platform signals (too-much signal gain), with mid-stance GRF data saturating.

#### 4.3.2.2 Results

Despite being practically identical prior to landing, with similar ankle angles at foot strike, the analysis of ankle joint kinematics revealed completely different progressions in all three planes following initial contact (**Figure 4-8**).

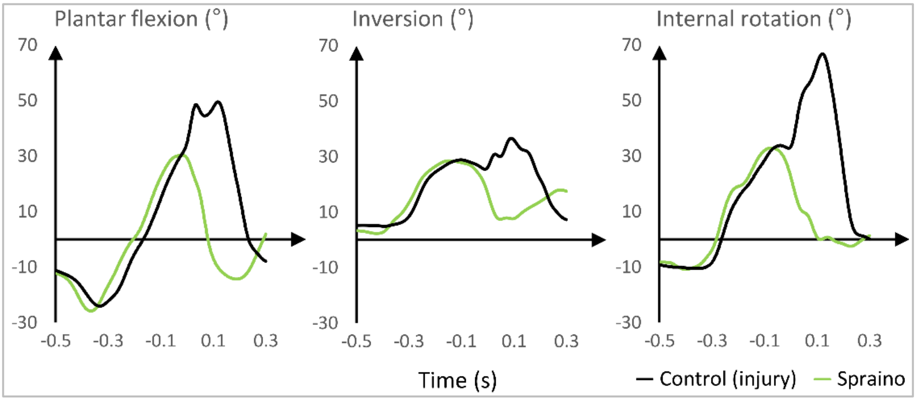



*Figure 4-8. Ankle angles (degrees) around three axes for the Control (injury) trial and the most resembling Spraino trial.*

In the Control (injury) trial, the right foot rapidly stopped its motion in the horizontal plane, causing the injured ankle to be further plantar flexed until 49.6°, further inverted until 36.7°, and further internally rotated until 66.9°, all peaking within 0.12 seconds after initial contact (**Figure 4-8**).

In the closely resembling Spraino trial, the foot did not stop immediately after initial contact, and the foot's motion in relation to the lower leg was directly opposite compared to the injury trial. Instead, the ankle returned to a "safe" position within 0.05 seconds after initial contact, through a combined dorsi flexion, eversion, and external rotation (**Figure 4-8**).

These obvious differences in ankle angles were naturally also reflected in the angular velocities. With the injury trial reaching substantially higher velocities in the lateral ankle sprain injury-promoting directions (**Figure 4-9**).

The Control (injury) trial reached 341°/s in plantar flexion velocity, 468°/s in ankle inversion velocity, and 299°/s in internal rotation velocity, all of which characterizes a typical lateral ankle sprain mechanism (47,93), and with all of them peaking just after initial contact and within 0.03 seconds (**Figure 4-9**).

The Spraino trial was rapidly realigned with a dorsiflexion velocity of 568°/s, eversion velocity of 440°/s, and external rotation velocity of 196°/s immediately after initial contact (**Figure 4-9**).

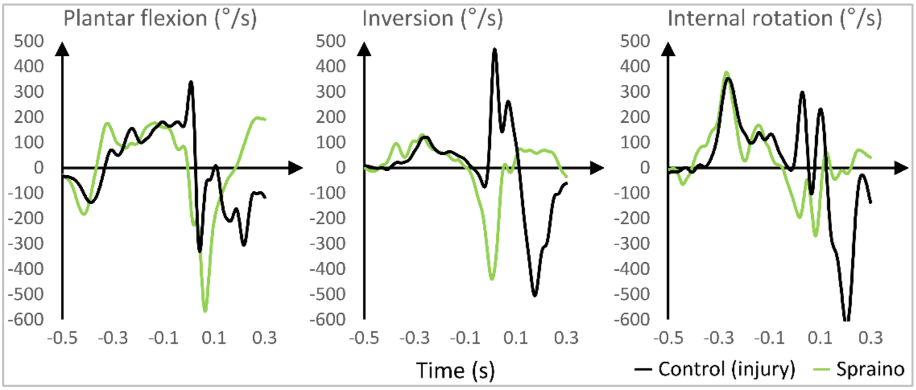



*Figure 4-9. Ankle angular velocities (deg/s) around three axes for the Control (injury) trial and the most resembling Spraino trial.*

During the first five frames (0.01 s) after initial contact the mean coefficient of friction was 1.1 in the Control (injury) trial and 0.37 in the Spraino trial (**Figure 4-10**). Thus, it seems highly likely that the complete change in post foot strike kinematics is directly facilitated by the minimized friction on the lateral edge, as hypothesized.

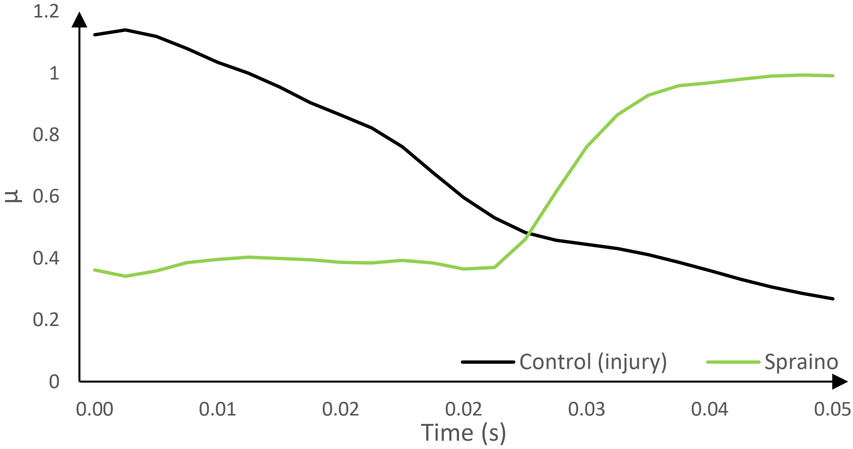



*Figure 4-10. Early contact coefficient of friction for the Control (injury) and Spraino trial.*

Being directly derived from the GRFs, the difference in friction coefficient is naturally reflected in the orientation of the GRF vector (**Figure 4-11**). The high friction at initial contact in the Control (injury) trial produces a medially deviated GRF vector producing combined inversion and internal rotation moments, that coupled with the risky position of the foot is a direct cause of injury (90,105).

The GRF vector in the Spraino trial is naturally more vertical in the early contact (i.e. low friction). This ensures that the GRF vector stays lateral of the ankle joint center (**Figure 4-11**), producing initial eversion and external rotation moments. Friction increases (**Figure 4-10**) as the foot realigns (**Figure 4-8**).

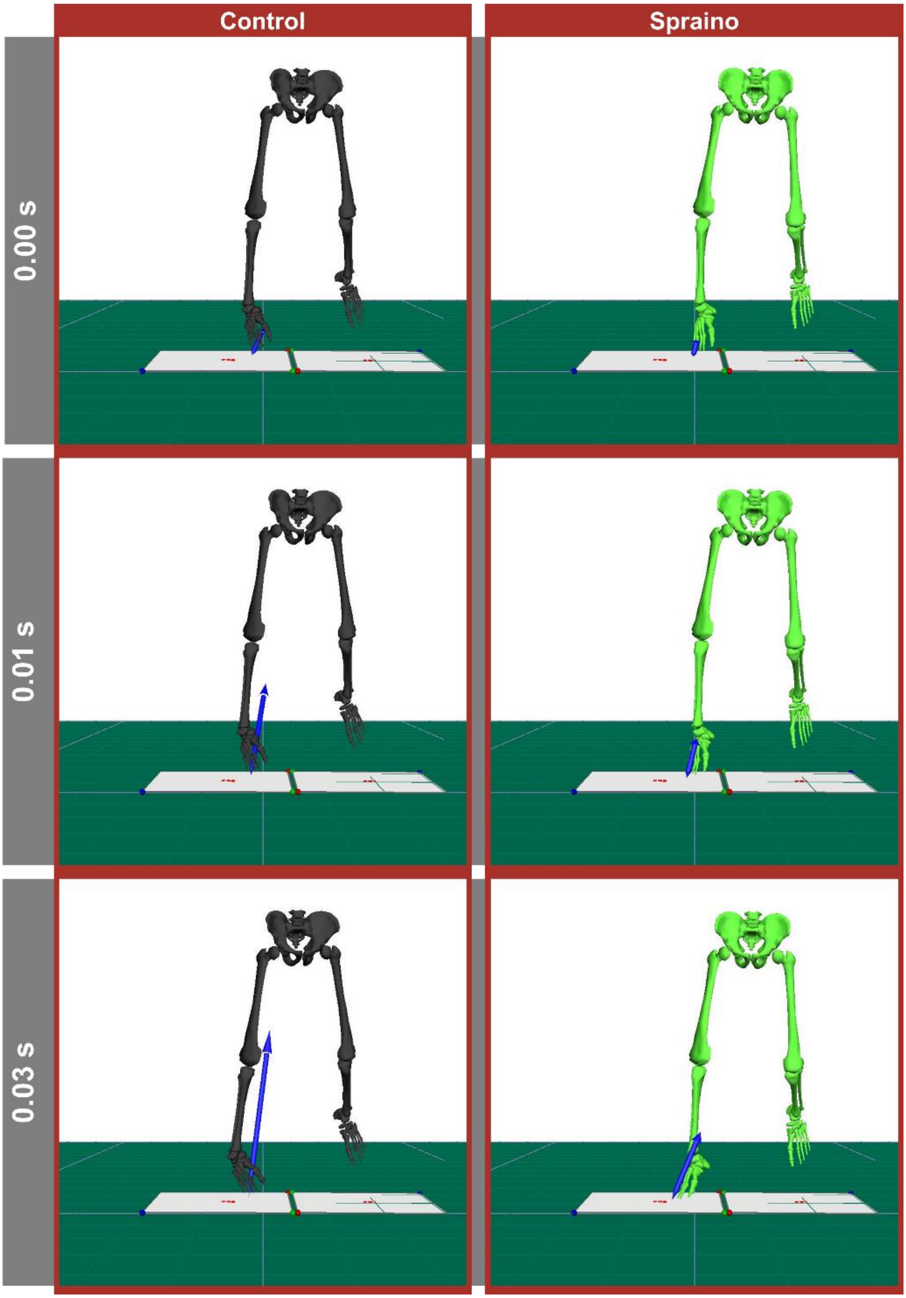



*Figure 4-11. Early contact of the Control (injury) and Spraino trial – visually depicting the early orientation of the ground reaction force vector in relation to the ankle joint center.*

### 4.3.3. ADDITIONAL BIOMECHANICAL TESTS

Our additional biomechanical tests supported the notion that high friction on the lateral edge of the shoe is not a necessity for athletic performance, and that Spraino could be used in indoor sports without affecting performance and safety.

A single-blinded randomized crossover study on 11 healthy team sports practitioners saw no Spraino-related alterations of ground contact mechanics or ankle joint loading during 180° change of direction maneuvers (123). There was no effect on ground contact time, vertical and horizontal GRFs of the turning foot, as well as no differences in ankle kinematics and ankle inversion moments – despite an excessive attachment of Spraino covering 10 mm of the lateral shoe sole in the intervention condition. Plantar flexor muscle activity did change, but only during late stance.

Spraino did also not affect performance and safety among nine elite female handball players testing Spraino while performing submaximal 90° lateral side-cut movements at the same time as receiving a pass. With this single-blinded randomized crossover study finding no differences in ground contact time, ground reaction forces, and ankle joint kinetics (124).

Crucially, no slipping occurred and no subjects reported any adverse experiences during all tests, and Spraino did not compromise performance and safety during 180° change of direction maneuvers or 90° lateral side-cut movements (123,125). An important note is however that in all these laboratory tests, initial contact was made with the medial aspect of the shoe, not covered by Spraino (123–125).

A randomized crossover study of 21 international elite badminton players saw no reduction in performance and safety when performing a novel speed test for evaluation of badminton specific movements (126) despite the highly erratic pattern of movements in this test. On the contrary, a strong tendency was found towards an overall faster completion time when wearing Spraino ($p=0.08$). No differences were found in lower extremity kinematics between conditions in the short backhand corner, despite initial contact on the lateral aspect of the heel (127,128).

# CHAPTER 5. EFFECTIVENESS OF SPRAINO AS PREVENTIVE MEASURE


The first natural step following promising laboratory testing is to establish "proof-of-principle", on clinically relevant endpoints (119). Hence, the aims of this exploratory pilot trial were to determine preliminary effectiveness and safety of using Spraino to prevent lateral ankle sprains among sub-elite indoor sport athletes with a previous lateral ankle sprain, when compared to a "do-as-usual" control group (94).

## 5.1. METHODS

### 5.1.1.1 Design

The trial was designed as a two-arm, parallel-group, exploratory pilot randomized controlled trial (RCT) to assess preliminary effectiveness and safety of Spraino in lateral ankle sprain injury prevention among indoor sport athletes at high risk of new injury. The participants were randomly allocated (1:1) to an intervention (Spraino) group or a control ("do-as-usual") group. Ethical approval was granted by The North Denmark Region Committee on Health Research Ethics on July 5th, 2017; the trial was registered at ClinicalTrials.gov (NCT03311490) on October 17th, 2017 and enrolment was conducted between October 19th, 2017 and February 28th, 2018. The trial protocol was developed using the PREPARE trial guide (120) and SPIRIT checklist (129). (94)

### 5.1.1.2 Participants

The participants for this pilot RCT were recruited among the responding athletes in Study 1, who reported to have incurred a lateral ankle sprain injury within the previous two years. The other eligibility criteria required that the participants: [I] were aged 18 years or older; [II] could read, speak and understand Danish; [III] could receive and reply to text messages using Short Message Services (SMS); [IV] performed indoor sport in a sub-elite level team with at least two weekly practice sessions; and [V] had returned to play at the commencement of our trial (94).

The reason for only including athletes with a previous lateral ankle sprain, was because they are at particularly "high risk" of new injury (64,67). Injury risk mitigation is thus highly relevant for this population. At the time of recruitment, all athletes were participating fully in sport and reported no acute injury symptoms (94).

#### 5.1.1.3 Sample size

The sample size was determined by **Equation 5-1**, where $n$ is the number of participants in each arm, $T$ the observation time, and $\theta_0$ and $\theta_1$ the incidence rates in the control and intervention group (130).

$$n = \frac{4}{T\left(\sqrt{\theta_0} - \sqrt{\theta_1}\right)^2} \qquad \textbf{Eq. 5-1}$$

Based on previous literature, we expected an incidence rate of 4.9 ankle sprains per 1000 hours of exposure (62) without Spraino, and an incidence rate of 2.94 per 1000 hours among participants randomized to Spraino (40% lower). With a power of 80% and an α of 5% an exposure time of ~15350 hours would thus be needed in each arm. Assuming an average exposure of 3 hours of court activities per week per participant, 250 participants would be needed to be observed for 20 weeks. Assuming a dropout rate of 15%, the 250 participants should be observed for at least 23 weeks. (94)

#### 5.1.1.4 Randomization

Randomization was performed after the included participants had provided written consent and the completed baseline questionnaires had been collected. The two comparison groups were generated using balanced block randomization, in which the random component in the sequence generation process was a drawing of lots. Block sizes were determined by the number of enrolled participants within a given team. An equal amount of lots (representing allocation for intervention and control) was used to assure a 1:1 allocation ratio. This meant in praxis that if i.e. a team had 11 enrolled players, then 12 lots, six representing each group, were included. The lots were made of wooden beads and were identical in appearance. They were drawn from an opaque bag, and it was ensured that allocation was concealed for participants and investigators enrolling participants (94).

#### 5.1.1.5 Intervention

The intervention group received Spraino and application instructions on the same day of inclusion, along with a letter containing information on how to report adverse events associated with its use, and how to order new patches when running out. They were encouraged to use Spraino during all indoor sport activities. Participants of both groups were also permitted to use (or keep using) any other injury preventive measure of their choice (94).

#### 5.1.1.6 Injury registration and data collection

All participants completed a baseline questionnaire (88), from which mobile phone numbers were obtained to prospectively collect data in SMS-Track (86,131) through answers to six weekly standardized questions (94).

When replying to these questions via SMS, the participants were required to report: (Q1,Q2) their weekly training and match exposure; (Q3) whether they had sustained a lateral ankle sprain; (Q4) whether their participation was restricted due to a lateral ankle sprain; (Q5) whether they used any ankle injury preventive measure; (Q6) whether they adhered to the intervention. Reminder messages were sent out after 48 hours if an answer to a text message had not been collected. They received a reminding phone call if answers had not been received on time for two consecutive weeks (94).

A lateral ankle sprain injury was defined using the International Ankle Consortium endorsed definition by Delahunt et al. (52)(49), that resulted in:

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*"An immediate sensation of pain, discomfort, or loss of functioning associated, by an athlete, with an isolated exposure to physical injury during sports training or competition having an intensity and quality making the sensation being interpreted by the athlete as discordant with normal body functioning"*
*Timpka et al.* (18)

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Whenever a lateral ankle sprain injury, or restricted sports participation due to an ankle-related problem, was reported via the SMS system, a follow-up telephone interview was conducted by a member of the research team. If a lateral ankle sprain injury had indeed occurred, a detailed injury registration form was completed (94).

#### 5.1.1.7 Outcome measures

Being exploratory, the trial was designed without a predetermined hierarchy among outcome measures. Data on contact and non-contact lateral ankle sprains, as well as in-trial first-time injuries and injury recurrences were documented. A contact sprain was defined as an injury sustained by stepping/landing directly onto an object (e.g. an opponent's foot). A non-contact sprain was defined as an injury sustained without stepping onto something (other than the floor), regardless of any player-to-player interaction prior to the event (94). A recurrent sprain was defined as a subsequent sprain to that same ankle previously injured within the trial period (52,94,132).

Time-loss following a lateral ankle sprain was defined as the number of calendar weeks with time lost from unrestricted participation due to injury-associated symptoms (18,133). This was based on the received responses to Question 4. An ankle sprain resulted in time-loss if: (Q4=1) the participant had reduced participation in their primary sport; or (Q4=2) the participant took part but was affected. A sprain was considered "severe" if the participant experienced time-loss for more than three weeks (1,40,134). Time-loss recordings for each injury was stopped on the first day of a consecutive three-week period during which the participant could participate unrestricted in his/her primary sport, to assure a causal link between injury-related time-loss and the acute lateral ankle sprain (94).

Subjective outcomes included pain in the ankle joint during sport (11-NRS: 0-10) (135) and fear of injury (11-NRS: 0-100) (136). These were assessed at baseline and follow-up using numeric rating scales (NRS). Additionally, the intervention group were instructed to report any adverse events they associated with using Spraino (94).

#### 5.1.1.8 Statistical analysis

Lateral ankle sprain injury incidence rates (per 1000 hours of exposure) and injury incidence rate ratios (Spraino vs. control) were estimated using Poisson regression with the sum of match-play and practice hours as exposure. The effectiveness estimates were adjusted for *sex*, *age*, *type of sport* and *level of play*. Injury recurrences were estimated similarly but theses analyses only contained exposure from in-trial injured participants. Mean injury-related time-loss for participants sustaining an ankle sprain was calculated using negative binomial regression. Robust standard errors were calculated to adjust for the repeated nature of measurements (within-participant correlation) (94).

Change from baseline to follow-up, in fear of sustaining a new lateral ankle sprain, and ankle pain, were calculated using negative binomial regression. These analyses were adjusted for the values reported at baseline (137). Multiple imputations by chained equations were performed to account for missing values (138). The imputation procedure included variables (*age*, *sex*, *group allocation* and *type of sport*) pre-hypothesized to potentially predict missing information. Data were analyzed using the mi estimate command in Stata (20 imputations). This analysis runs the estimation command on each imputation separately first and then combines the results using Rubin's rule (139). These analyses were also conducted for participants with full information only (complete case analysis) (94).

The outcome assessor was blinded to group allocation. All statistical analyses were conducted in Stata/IS 13.1 and performed as intention-to-treat, using inverse probability-of-censoring weighting to account for participant dropout (137,140). Adhering to the intention-to-treat principle, Spraino-adherence and co-interventions were not taken into account in the analyses (94).

## 5.2. RESULTS

### 5.2.1.1 Recruitment and trial completion

We recruited and randomized 510 participants from 1339 approached athletes of which 576 were eligible for inclusion (**Figure 5-1**). A total of 480 participants completed the trial; 246 in the intervention (Spraino) group and 234 in the control ("do-as-usual") group, respectively. Completion was defined as having responded at least once to the weekly text messages. The mean number of participating weeks was a little higher in the intervention (Spraino) group compared to the control ("do-as-usual") group (20.7 vs 18.2 weeks) (94).

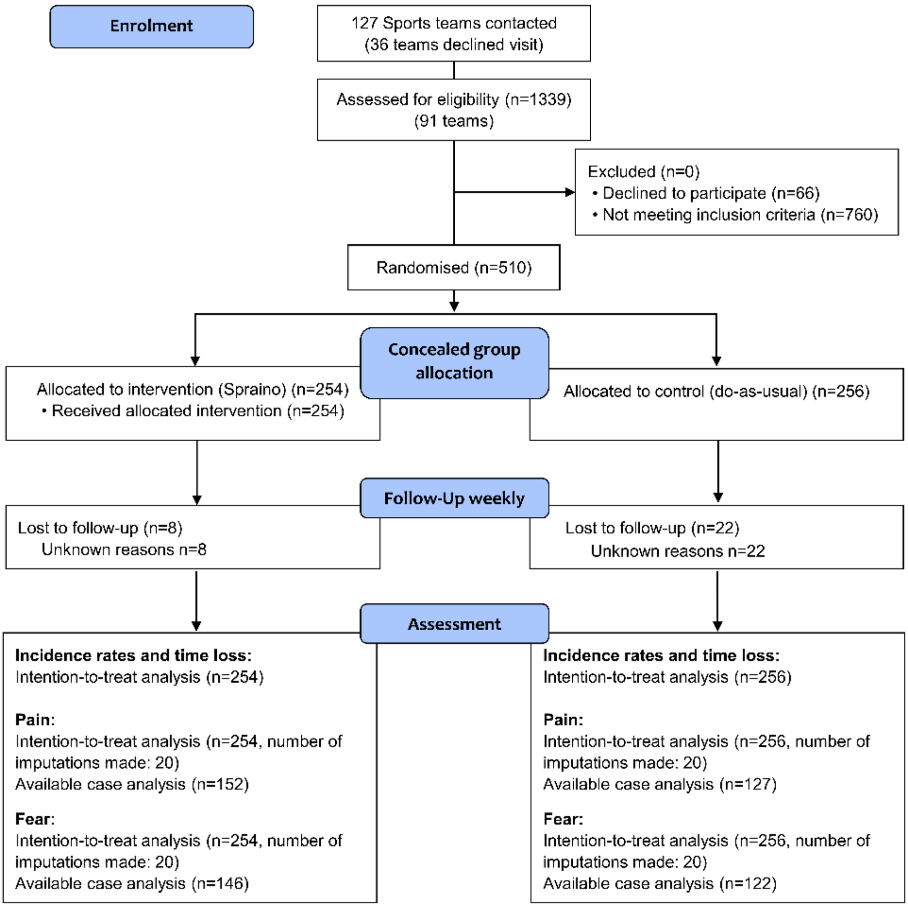



*Figure 5-1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram. Reused with permission from Lysdal et al.* (94)

#### 5.2.1.2 Trial population

The participants were 22.7 years old on average, 57% of them were men, and the majority were handball players. No clinically relevant between-group differences appeared present (**Table 5-1**) and we performed no baseline hypothesis, as suggested by the CONSORT group (77,141).

**Table 5-1:** Baseline characteristics

| | Spraino | Control | Total |
|---|---|---|---|
| Participants, n | 256 | 254 | 510 |
| Male, n (%) | 146 (57) | 146 (57) | 292 (57) |
| Age, mean (SD) | 22.3 (4.0) | 23.0 (4.5) | 22.7 (4.3) |
| Height (cm), mean (SD) | 181 (10) | 182 (11) | 182 (11) |
| Body mass (kg), mean (SD) | 80.8 (14) | 80.3 (14) | 80.5 (14) |
| Fear*, median (IQR) | 70 (40;90) | 70 (50;90) | 70 (40;90) |
| Pain**, median (IQR) | 2 (0;3) | 1 (0;2) | 1 (0;3) |
| Sport, n (%) | | | |
| Handball | 204 (80) | 205 (81) | 409 (80) |
| Basketball | 26 (10) | 31 (12) | 57 (11) |
| Badminton | 26 (10) | 18 (7) | 44 (9) |
| Weekly practice (hours), mean (SD) | 6.1 (3.1) | 6.1 (3.0) | 6.1 (3.0) |
| Level of play, n (%) | | | |
| League | 10 (4) | 12 (5) | 22 (4) |
| 1st division | 80 (31) | 78 (31) | 158 (31) |
| 2nd division | 64 (25) | 70 (28) | 134 (26) |
| 3rd division | 102 (40) | 94 (37) | 196 (38) |

*Fear of ankle sprain during primary sport (100=no fear, 0=highest fear imaginable)
**Pain in ankle joint during primary sport (0=no pain, 10=highest pain imaginable)

*Table 5-1 reused with permission from Lysdal et al.* (94)

#### 5.2.1.3 Intervention effectiveness on incidence rates and severity

A grand total of 151 lateral ankle sprains were sustained over the course of the trial. Ninety-six of these were categorized as non-contact injuries, and 50 were categorized as severe injuries. The injury incidence rate (sprains per 1000 hours of exposure) was lower in the intervention (Spraino) group compared to the control ("do-as-usual") group for all collected outcomes (**Table 5-2**) (94).

The injury incidence rate ratio was 0.87 (95% CI: 0.62 to 1.23) for any type of lateral ankle sprain, with an associated mean time-loss of 1.8 weeks (95% CI: 1.3 to 2.3) in the intervention (Spraino) group and 2.8 weeks (95% CI: 2.2 to 3.4) in the control ("do-as-usual") group. The resultant time-loss difference was 1 week (95% CI: -1.8 to -0.2) (**Table 5-2**).

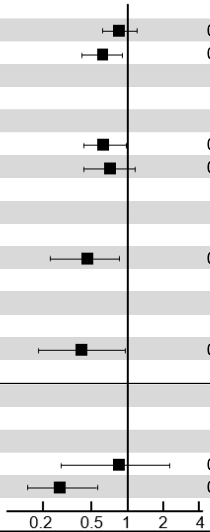
The 96 non-contact ankle sprains occurred at a lower rate in the intervention (Spraino) group compared to the control ("do-as-usual") group. The injury incidence rate ratio was 0.64 (95% CI: 0.42 to 0.98) with a time-loss difference per non-contact sprain of 0.9 weeks (95% CI: -2.0 to 0.2).

For all severe lateral ankle sprains, the incidence rate ratio was 0.47 (95% CI: 0.25 to 0.88). For severe non-contact sprains the incidence rate ratio was 0.43 (95% CI: 0.19 to 0.97), both favoring the intervention (Spraino) group (94).

The 19 in-trial injury recurrences occurred with an incidence rate ratio of 0.85 (95% CI: 0.31 to 2.34), with 2.3 weeks (95% CI: -3.7 to -0.9) less injury-related time-loss in the intervention (Spraino) group (**Table 5-2**) (94).

**Table 5-2:** Incidence rates, event-related time-loss and effectiveness estimates (Spraino vs Control)

| | Spraino (n=256) | Control (n=254) | Spraino vs Control Ratio* |
|---|---|---|---|
| Total exposure (hours) | 18,803 | 14,185 | |
| Events [151] | | | |
| Number | 81 | 70 | |
| Incidence rate† | 4.30 (3.30, 5.30) | 4.93 (3.68, 6.18) | 0.87 (0.62, 1.23) |
| Time-loss (weeks) | 1.8 (1.3, 2.3) | 2.8 (2.2, 3.4) | 0.63 (0.44, 0.92) |
| Non-contact events [96] | | | |
| Number | 44 | 52 | |
| Incidence rate† | 2.33 (1.67, 3.00) | 3.67 (2.54, 4.77) | 0.64 (0.42, 0.98) |
| Time-loss (weeks) | 1.9 (1.1, 2.7) | 2.7 (2.0, 3.4) | 0.67 (0.41, 1.10) |
| Severe events [50] | | | |
| Number | 19 | 31 | |
| Incidence rate† | 1.01 (0.51, 1.50) | 2.20 (1.36, 3.04) | 0.47 (0.25, 0.88) |
| Non-contact severe events [34] | | | |
| Number | 12 | 22 | |
| Incidence rate† | 0.63 (0.25, 1.02) | 1.56 (0.82, 2.30) | 0.43 (0.19, 0.97) |
| In-trial recurrent events [19] | | | |
| Total exposure (hours) | 1889 | 1428 | |
| Number | 10 | 9 | |
| Incidence rate† | 5.27 (1.68, 8.85) | 6.29 (1.81, 10.8) | 0.85 (0.32, 2.24) |
| Time-loss (weeks) | 1.1 (0.5, 1.7) | 3.5 (2.1, 4.86) | 0.33 (0.15, 0.72) |




* Incidence rate ratio or relative time-loss duration
† per 1000 h of participation in primary sport
Numbers in parenthesis represent 95% confidence intervals
Spraino vs Control, Ratio <1 indicates preventive effect

*Table 5-2 adapted with permission from Lysdal et al.* (94)

### 5.2.1.4 Intervention effectiveness on fear-of-injury and ankle pain

Four hundred and fifty-five participants provided full information on fear and pain at baseline, and 281 provided full information at follow-up. The mean fear of sustaining a new ankle sprain during sport decreased in both groups. A between-groups difference of 13.7 points (95% CI: 9.2 to 18.3) was detected (**Table 5-3**). The mean level of ankle pain decreased in the intervention group while it increased in the control group. A between-groups difference of -1.2 points (95% CI: -1.5 to -0.9) was detected (**Table 5-3**) (94).

| **Table 5-3:** Fear of new ankle sprain* and pain in the ankle† | | | |
|---|---|---|---|
| | **Mean (95% CI)** | | |
| | **Spraino** | **Control** | **Between-groups difference for change** |
| Fear*, intention-to-treat [n] | 254 | 256 | |
| Baseline | 62.9 (59.1, 66.6) | 66.6 (63.1, 70.1) | 13.7 (9.2, 18.3) |
| Follow-up | 84.7 (82.2, 87.2) | 70.9 (67.2, 74.7) | |
| Fear*, available case [n] | 146 | 122 | |
| Baseline | 62.9 (59.1, 66.6) | 66.6 (63.1, 70.1) | 15.4 (10.2, 20.7) |
| Follow-up | 85.0 (82.4, 87.5) | 69.5 (65.2, 73.9) | |
| Pain†, intention-to-treat [n] | 254 | 256 | |
| Baseline | 1.9 (1.7, 2.1) | 1.6 (1.4, 1.8) | -1.2 ( -1.5, -0.9) |
| Follow-up | 0.6 (0.5, 0.7) | 1.8 (1.6, 2.0) | |
| Pain†, available case [n] | 152 | 127 | |
| Baseline | 1.9 (1.7, 2.1) | 1.6 (1.4, 1.8) | -1.3 (-1.6, -1.0) |
| Follow-up | 0.6 (0.4, 0.7) | 1.9 (1.6, 2.2) | |

* Fear of sustaining a new ankle sprain during sport was measured on a scale from 100 representing no fear to 0 representing maximum fear. A change of >0 reflects less fear at follow-up as compared to baseline.

† Pain in the ankle during sport was measured on a scale from 0 representing no pain to 10 representing worst pain imaginable. A change of <0 reflects less pain at follow-up as compared to baseline.

Numbers in parenthesis represent 95% confidence intervals.

*Table 5-3 reused with permission from Lysdal et al.* (94)

A clinically relevant reduction can naturally only take place among participants with a relevant level of fear and/or pain at baseline. In continuation, a further analysis among participants with a relevant fear at baseline (≤ 70 NRS) (142) revealed that 87% experienced less fear of at least the size of minimally clinical important difference (MCID) in the intervention (Spraino) group, compared to 60% in the control ("do-as-usual") group (**Table 5-4**).

Among the participants with relevant pain at baseline (≥ 3 NRS) (143), the distribution of participants who experienced an MCID reduction in pain was 82% in the intervention (Spraino) group and 47% in the control group (**Table 5-4**).

| **Table 5-4:** Percentage of participants experiencing improvement in Fear* and Pain† of at least MCID | | | |
|---|---|---|---|
| | **Spraino** | **Control** | **Spraino vs Control#** |
| Fear*, available case [n] | 146 | 122 | |
| Participants exceeding MCID‡, n (%) | 70 (48) | 41 (33) | 1.43 (0.97, 2.10) |
| Participants with high baseline fear (≤ 70) [n] | 67 | 47 | |
| Participants with high baseline fear exceeding MCID‡, n (%) | 58 (87) | 28 (60) | 1.45 (0.93, 2.28) |
| Pain†, available case [n] | 152 | 127 | |
| Participants exceeding MCID§, n (%) | 53 (35) | 22 (17) | 2.01 (1.22, 3.31) |
| Participants with high baseline pain (≥ 3) [n] | 49 | 36 | |
| Participants with high baseline pain exceeding MCID§, n (%) | 40 (82) | 17 (47) | 1.73 (0.98, 3.04) |

* Fear of sustaining a new ankle sprain during sport was measured on a scale from 100 representing no fear to 0 representing maximum fear. A change of >0 reflects less fear at follow-up as compared to baseline.

† Pain in the ankle during sport was measured on a scale from 0 representing no pain to 10 representing worst pain imaginable. A change of <0 reflects less pain at follow-up as compared to baseline.

‡ The percentage of participants that experienced improvement of fear score of at least the minimal clinically important difference (MCID) of 19 from baseline to follow-up

§ The percentage of participants that experienced improvement of pain score of at least the minimal clinically important difference (MCID) of 2 from baseline to follow-up

\# Relative number of participants experiencing improvement of at least the size of the MCID in the Spraino group as compared to controls.

Numbers in parenthesis represent 95% confidence intervals.

### 5.2.1.5 Adherence to intervention

Full adherence to the intervention was defined as having reported use of Spraino for at least 75% of a participating week, during all weeks of participation. This was observed in 31 (13%) participants. Forty-nine (20%) reported not to have used Spraino at all. The 80% of the intervention group participants, who reported to have used Spraino, were adherent for 68% of the participating weeks. Treatment contamination was observed with five participants (3%) in the control group reporting use of Spraino (94).

### 5.2.1.6 Harms

Six participants reported eight adverse events leading to minor harms during the trial (**Table 5-5**). Of these, four participants experienced this harm in the form of an ankle sprain (94).

**Table 5-5:** Intervention-related adverse events leading to harm

| Participant info | Event report to hotline |
|---|---|
| Handball player, female 19 years | *"I rolled over due to the tape. Maybe it was placed wrong."* (Reported as having occurred twice) |
| Handball player, female 20 years | *"Had a slipping incident (due to Spraino) at training where I fell and got some bruises. Nothing serious though."* |
| Handball player, male 22 years | *"I had an existing groin injury that I felt got worsened through an outwards rotation due to the tape."* |
| Badminton player, male 23 years | *"Rolled over twice and (I am) 100% certain it is due to the tape. Jumping towards my right when my foot slides underneath me."* (Reported as having occurred twice) |
| Handball player, male 29 years | *"I felt that it was the tape that made me twist my ankle. Took it off afterwards."* |
| Badminton player, male 20 years | *"Made a lunge with my left leg and twisted my ankle. Felt like the tape increased the twist."* |

*Table 5-5 reused with permission from Lysdal et al.* (94)

# CHAPTER 6. DISCUSSION

This PhD project was designed to deliver a comprehensive scientific evaluation of Spraino as a novel preventive measure against lateral ankle sprain injuries in indoor sports. This was done through the four steps of the ‘sequence of prevention’ (1).

The first step in this cycle was to establish the extent of the injury burden. Our cross-sectional survey (**Study 1**) revealed that three quarters (74%) of active Danish sub-elite indoor sports athletes had sustained a lateral ankle sprain injury at some point in their primary sport (912 of 1238). Almost two thirds (59%) of these injuries had been sustained within the preceding 24 months (541 of 912), and 37% within a year (335 of 912). Basketball and team handball players were more likely to have sustained a previous lateral ankle sprain injury (78%) compared to badminton players (51%), especially within the previous year. They were also more likely to have sustained their most recent injury by stepping onto something (i.e. an opponent’s foot) compared to their badminton counterparts.

We introduced Spraino (**Study 2**) as a novel measure to prevent lateral ankle sprain injuries in indoor sports. The novelty lied in the strategic application of a low-friction material on the lateral edge of indoor sports shoes to minimize shoe-surface friction, whenever contact with the floor was made with the very lateral aspect of the shoe. The modified ISO: 13287:2019 mechanical test for slip resistance revealed that Spraino reduced the coefficient of friction by 46% (0.41 vs 0.76) compared to the regular rubber outsole of this specific indoor sports shoe.

Our pre-injury ankle sprain simulations showed that the low-friction properties provided the landing foot with an ability to realign against the floor in case of an incorrect landing. Likewise, when comparing an identical cutting trial to a grade 1 lateral ankle sprain injury recorded in the lab, the initial contact coefficient of friction was 66% lower with Spraino applied (0.37 vs 1.10). This moved the vector of the ground reaction forces to pass through the outside of the ankle joint center, thereby causing the landing foot to realign against the surface. This case study indicated that the realignment mechanism could also work in actual injury situations.

We designed and conducted a pilot randomized controlled trial (**Study 3**) to assess “proof-of-principle” of Spraino by determining preliminary effectiveness and safety in lateral ankle sprain injury prevention, when added to “do-as-usual” injury prevention among sub-elite indoor sport athletes with a previous lateral ankle sprain injury. In general, we found that Spraino had a preventive effect, by significantly lowering the incidence rate of non-contact and severe lateral ankle sprain injuries by 36% and 53%, respectively. Spraino also had a substantial and statistically significant additive effectiveness in reducing *fear of sustaining a new ankle sprain injury* and *ankle joint pain*. Only few reports of minor harms due to Spraino were reported (94).

## 6.1. INTERPRETATION

The high participant prevalence (74%) found **Study 1** adds to a growing body of literature highlighting that lateral ankle sprain injuries are extremely common, and that participation in indoor sports is associated with considerable risk of injury (11,61,62). The proportion of sub-elite Danish team handball and basketball players that had sustained a lateral ankle sprain injury within the previous year exceeded the yearly prevalence among top-level athletes in the National Basketball Association (NBA) (95). This was observed despite obviously expected differences in game time and practice hours.

Lateral ankle sprain injuries are reportedly most commonly characterized as being a non-contact injury in indoor sports (11,49,61,62). This was also the case for the most recent injury sustained among the badminton players in our cross-sectional survey (**Study 1**). Here, a significantly larger proportion (86%) were characterized by a non-contact injury mechanism, while no significant differences were found in the mechanism of injury among the participating handball and basketball players.

The discrepancy found in lateral ankle sprain prevalence and mechanism among badminton players, compared to handball and basketball players, might be related to the different characteristics of the three sports. Handball is considered a full-contact sport with less restrictive rules and an element of physical player-player contact. This might pose a higher risk of injury (144). Similarly, basketball can be considered a contact sport in which athletes are susceptible to acute injuries (95,145). Badminton on the contrary is a non-contact sport with a net separating opponents (126,146). Furthermore, handball and basketball players could be at increased risk of suffering injuries, as they might land awkwardly in an attempt to avoid contact, or as a result of being pushed out of balance, while there is a naturally higher risk of stepping onto the foot of an opponent.

It has been described how the etiology of most lateral ankle sprain injuries are characterized by an incorrect foot positioning at initial contact between shoe and surface. If this position is combined with a medially directed vertical ground reaction force, an excessive inversion moment around the subtalar joint can occur (47,49). This pattern also characterized the accidental ankle sprain sustained during the control (without Spraino) landing in a cutting movement with an initially inverted foot. The accidental grade 1 lateral ankle sprain sustained thereby follows the same injury pattern as described in multiple quantitative case reports (53,93,122,147–149).

We introduced Spraino (**Study 2**) to target this exact mechanism of injury. The low friction at initial contact should minimize the horizontal friction forces, keeping the vector of the ground reaction force more vertically aligned at initial contact (105,106). We found that the low friction properties of Spraino initially moved the vector of the ground reaction force to the outside of the joint center. This created an eversion moment at initial contact (105), which allowed for a realignment of the foot in relation to the surface, supporting our premise that Spraino could have an important injury prevention potential (47).

In our pilot randomized controlled trial (**Study 3**), the prospectively recorded injuries predominantly occurred via a non-contact injury mechanism and was the case for 74% (52 out of 70) of sprains in the control ("do-as-usual") group and 54% (44 out of 81) in the intervention (Spraino) group (94). This somewhat contradicts our retrospective cross-sectional survey, but aligns with previously published literature (11,49,95). The lower incidence rate and proportion of non-contact sprains in the intervention group underlines excessive friction as a possible important risk factor for lower extremity injuries in sports (94,100–102,104,150).

The effectiveness of Spraino found in this study on injury incidence rate is comparable to the effects of other preventive measures (e.g. preventive training and external prophylactic measures like bracing and taping) when these are compared to no measure (64,94).

Average time-loss per injury was significantly (37%) lower in the intervention (Spraino) group (p=0.014). This allowed the intervention group participants to return to unrestricted sports participation one-week faster following injury on average, than the control ("do-as-usual") participants. For in-trial recurrent events, the event-related time-loss was 67% lower in the intervention (Spraino) group (1.1 vs 3.5 weeks). These results contrasts directly with the results of previous studies investigating other prophylactic measures, who found no reduction in time-loss per injury (64,94,151). That Spraino was associated with lower injury severity (time-loss) supports the presented theory that when initial lateral shoe-surface friction is reduced, the initial inversion moment around the ankle joint is also reduced.

Despite being less common, contact injuries still play a significant role in the occurrence of lateral ankle sprain injuries in indoor sports, especially in handball and basketball (11,49,95). While the initial distortion when stepping/landing onto something (e.g. a foot) might be unavoidable, our results suggest that Spraino might still have a protective effect, considering that both major time-loss outcomes from our RCT include contact injuries (94). It thereby seems plausible that the severity of contact injuries is still affected by the friction between shoe and floor (**Figure 6-1**). A quick YouTube browse/search of ankle sprain injuries in indoor sports also clearly demonstrates, that even in cases of contact injuries there is often also contact between the lateral aspect of the shoe and the floor.

*Figure 6-1. Example of an inciting event of a contact lateral ankle sprain injury.*

The preventive effectiveness of Spraino (a low-friction material) indicates that excessive friction at the lateral edge of the shoe against the surface could be a direct risk factor for lateral ankle sprain injuries. If assuming a direct causal relationship (**Figure 6-2**) (1,73), where the unknown factor "F" could be an incorrect foot position just before initial contact with the floor, and shoe-surface friction is a direct "risk factor". Then modifying the frictional properties between shoe and floor would have a direct causal effect on the injury outcome - the occurrence and severity of a lateral ankle sprain injury (1,73).


*Figure 6-2. Direct causal relationship between an unknown factor F, risk factor and sports injury occurrence. Adapted from Porta* (152) *and van Mechelen et al.* (1)

This direct relationship seems reasonable when considering previous research identifying high shoe-surface friction as a risk factor for lower extremity injury (99–102,104,150). The presumed relationship is further backed by our biomechanical experiments (**Study 2**), but even more so by the preliminary preventive effectiveness of Spraino (**Study 3**) clearly pointing towards a direct clinical causality (94,153).

The intervention (Spraino) group had 21.8 points less fear of ankle sprain injuries; with the group effect (between-group difference) of 13.7 points being less than MCID (19.0) (154). However, among the intervention (Spraino) group participants with relevant fear at baseline (≤70 NRS) (142), 87% experienced less fear of at least the size of MCID, compared to 60% in the control ("do-as-usual") group. This could be of high importance with persisting fear of injury being regarded as a major hindrance to sports activity (94,136).

The intervention (Spraino) group had 1.3 points less in ankle pain. The between-group difference of 1.2 points, favoring Spraino, may not be clinically relevant considering an MCID of 2 points (135). However, among the participants with relevant pain at baseline (≥3 NRS) (143), the distribution of participants who experienced an MCID reduction in pain was 82% in the intervention (Spraino) group and 47% in the control group. This suggests that Spraino may have further beneficial effects, aside from injury prevention, at least on an individual level (94).

## 6.2. CLINICAL IMPLICATIONS

More than 40% of the approached population was eligible for inclusion in the RCT due to having sustained an ankle sprain within 24 months. Therefore, injury prevention among this population seems especially relevant when considering the high risk of both initial and recurrent ankle sprains in indoor sports (11,62), in particular in light of the high risk of long term sequalae following such injury (49).

Indoor sports are very popular in Denmark and preventing injuries among this relatively large population of participants could potentially have a large national clinical impact (7). Basketball is furthermore one of the World’s most popular sports (84), and preventing lateral ankle sprain injuries in this sport could have a positive clinical impact on an epidemiologically large population. Prevention seems particularly relevant in the United States with 980,673 registered basketball players on high school level and 2,192 registered basketball teams in the National Collegiate Athletic Association (95).

Clinicians should consider recommending indoor sport athletes to use Spraino given its preventive effectiveness in lowering the injury incidence rate and injury severity of lateral ankle sprains, without any severe adverse consequences (94). Spraino seems clinically important when compared to previous ankle sprain prevention research (155). Especially the unrivalled reduction of 1 week in overall injury time-loss for all reported injury cases seems relevant. However, it remains important that these promising findings are replicated in future studies (155,156). Spraino may be particularly relevant for those athletes with subjective reporting of pain, fear of injury, but even more so among athletes with chronic ankle instability, with this population being at particular high risk of recurring injuries (157,158).

## 6.3. STRENGTHS AND LIMITATIONS

A comprehensive scientific evaluation of Spraino was produced over the course of this PhD project. The use of different scientific methods is considered a particular asset to this thesis. However, the studies conducted throughout the years are not without limitations.

In our retrospective cross-sectional survey (**Study 1**), the time elapsed since the most recent injury sustained varied greatly. This is not considered a limitation to the high overall participant prevalence of having sustained a previous lateral ankle sprain injury found among the responding sports participants. However, the risk of recall bias is high when answering a specific question regarding injury mechanism (71). Their most recent lateral ankle sprain injury could potentially have occurred several years prior to our visit. Hence, it remains plausible that the discrepancy in injury mechanism found among the basketball players is a direct result of recall bias, when compared to the existing literature (11,49,95) and the recalculated numbers from the prospective NBA cohort (95).

Our modified ISO: 13287:2019 mechanical testing of slip resistance of Spraino against a sports surface was not conducted in a commercially available footwear traction tester (e.g. the Satra TM144). Instead we used a hydraulic system to control the movement of an AMTI force platform. This platform has a manufacturer-listed accuracy of ±0.1%, which is well within the requirements of the ISO: 13287:2019 test standard (±2.0%) (110). We consider this feature a particular strength to the design of our mechanical testing device. Additionally, the hydraulic system has previously been scientifically evaluated to perform nearly identical movements, with a standard deviation of less than 0.2 mm in translational tests (118). It might be viewed as a limitation to the mechanical test, that despite the test shoe being bolted to the shoe last, it still rotated more around the last in the control condition, due to the higher friction between shoe and surface. This is not considered a major limitation to the dynamic coefficient of friction value obtained, but time until this steady state (sliding) is achieved differs greatly between the two conditions. Additionally, a slight offset (0.01 s) appears to be present between conditions. This is most likely due to the threshold of 200 N in horizontal force.

Ankle injury simulators are naturally limited by their primary design feature being safe testing below a threshold of injury (121). The presented ankle sprain simulator in this thesis is no exception, with the roll angle velocity peaking at 165°/s in the control condition (without Spraino). This is way below the previously suggested critical value of 300°/s for the identification of an ankle sprain injury (159). However, this injury simulator served its purpose in quantifying the ability of Spraino to realign the foot against a traditional indoor sports surface (116).

The case report of the accidental injury and corresponding non-injury Spraino trial is considered a particular testament to the mechanical and biomechanical aspects of this thesis, and thought of as a strong descriptor of Spraino as a potential injury preventive measure (**Study 2**). First, the initial contact coefficient of friction was expectedly low when Spraino was attached on the shoe. Second, the realigning preventive function of Spraino was underlined in all non-injury trials that preceded the actual grade1 injury sustained. The differences observed between what proved to be an actual injury situation confirmed the preventive mechanism. The practically identical pre-contact kinematics of the two compared trials is a further testament to, that the simple addition of Spraino could produce a major difference in the outcome immediately after initial contact.

The quantification of the case report is limited by a mistake in the settings of the force platform amplifier. The gain setting was set too high, causing the force signals from these more dynamical trials to saturate, thus not allowing for direct kinetic comparison during midstance. However, the initial contact period which was expected to include the main effect of Spraino was fully covered and confirmed the preventive potential.

The resulting sprain injury was diagnosed as a grade 1 mild ankle sprain according to the Jackson grading system (46). This diagnosis was not performed by a medically trained physician. However, self-diagnosis was performed by an ankle sprain-researching PhD scholar, and the accidental injury sustained follows the patterns of previous quantitative case reports of lateral ankle sprain injuries (53,93,122,147–149). Additionally, the inversion velocity of 468°/s well exceeded the critical 300°/s threshold velocity for identification of an ankle sprain (159), objectively supporting the claim of at least a mild ankle sprain injury.

Our pilot randomized controlled trial (**Study 3**) was also not without limitations. First, not all presented outcomes were pre-registered. These outcomes were however added before analysis and fit the overall pattern of Spraino effectiveness. Second, only passive surveillance of harms was used, which generally yields fewer adverse events than active monitoring (160). Third, participants were not blinded to the intervention. This is not regarded as a limitation to the objective outcomes; incidence rate and time-loss. However, the risk of bias is high on the subjective outcomes (fear and pain). The intervention mirrors real life use of Spraino (161) since all athletes were responsible for applying and replacing the product themselves, as well as ordering new products when supplies were exhausted/running low. We did not control for the use of other injury prevention strategies, since Spraino was introduced as an additional preventive measure (94).

It has previously been established how the outcomes in injury preventive research are heavily biased by the adherence to an injury preventive measure (79). To accommodate this, it has even been suggested how it might make more sense to evaluate the effect of the intervening measure by using a per protocol analysis, only considering fully adherent participants (79). We consider it an indisputable strength to our design that we decided against this practice. Instead we treated our pilot RCT as a pragmatic effectiveness trial adhering to the CONSORT recommendations by using an intention-to-treat approach in the analysis of Spraino effectiveness (77).

## 6.4. CONCLUSIONS

This PhD thesis has successfully established a proof-of-concept of Spraino as a new lateral ankle sprain injury preventive measure in indoor sports. This was tied together through the sequence of prevention cycle (1) (**Figure 6-3**).

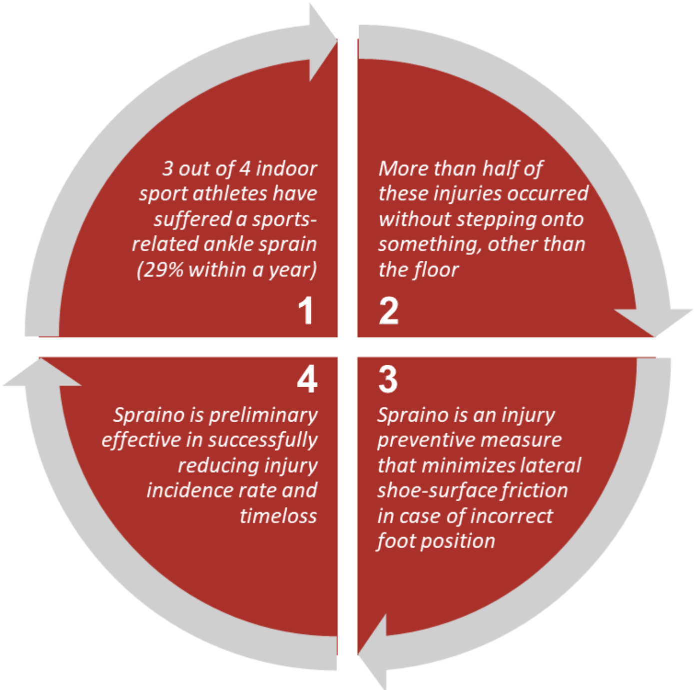



*Figure 6-3. Sequence of prevention model* (1) *applied to lateral ankle sprain injury prevention in indoor sports using Spraino.*

Our cross-sectional survey (**Study 1**) clearly confirmed the presumption that active indoor sports participants were highly likely to have sustained a sports-related lateral ankle sprain injury. Moreover, injury prevention seemed especially relevant to this population, with more than half of their most recent injuries having incurred without contact and within the previous two years.

Our preclinical testing of Spraino (**Study 2**) as an injury preventive measure was very promising in the way that the foot suddenly appeared capable of realigning against the surface in potential injury situations, something that was later confirmed in laboratory case study. Additionally, it was found that attaching a low-friction material on the lateral edge of the shoe did not seem to compromise safety and athletic performance.

Our pilot randomized controlled trial (**Study 3**) established preliminary clinical effectiveness and supported the premise that high friction between shoe and surface, at least in some cases, is an important part of the mechanism for lateral ankle sprain injuries. Our findings further suggest that altering this friction through a "simple" shoe modification is a clinically effective way to prevent lateral ankle sprain injuries in indoor sports, and that the use of Spraino for this specific purpose is not associated with severe adverse consequences. Allocation to Spraino was furthermore associated with less fear of lateral ankle sprain injury and less ankle-related pain. The combination of less than perfect adherence to Spraino, treatment contamination and "do-as-usual" injury prevention in the control group makes the effectiveness across all outcomes highly promising (94).

## 6.5. PERSPECTIVES

Sports injury preventive measures only work if they are adopted by the athletes for whom they are intended (69,79,114,161). This is naturally also reflected in the effectiveness of injury preventive measures reported in intervention studies being highly biased by adherence to the allocated interventions (79). There are many elements to consider if aiming to improve adherence to injury prevention, such as behavior, attitude, and motivation to prevent injury in the individual athlete (69,161).

Only 31 (13%) intervention group participants reported full adherence to Spraino in the RCT (**Study 3**), while 49 (20%) reported not to have used Spraino at all (94). The 80% who reported to have used Spraino during the trial, were on average adherent for 68% of the participating weeks. It would thus only be natural to expect that if this adherence improved, then the preventive effectiveness would also improve (79). However, the less than perfect adherence occurred despite the fact that all included participants had a history of lateral ankle sprains and thus should have higher motivation to prevent future injury, compared to athletes never experiencing this issue (69). One would also expect the motivation to prevent injury would be highly driven by the perceived risk of a new injury (69), and that athletes with a more recent injury would be more willing to adhere to an intervention (79). A new study on more recently injured participants would likely produce a higher clinical effectiveness, since these participants risk of new injury would be accordingly higher (64,67).

However, if the goal is to prevent injuries in general, and maybe even target primary prevention, then the preventive measure must provide the user with as little hassle as possible for the intervention to have any chance of being implemented (162,163). Ideally, the preventive mechanism of Spraino should be built into the structure of indoor sports shoes. Preferably this should even be a default feature (i.e. as an airbag in a car) that the user needs to actively opt-out of, instead of needing the motivation required for a conscious purchase (163).

The next steps should be to construct an injury preventive shoe that works through the same preventive mechanism, but at the same time accommodates issues commonly affecting adherence to injury prevention. Such an injury preventive shoe would require testing in a future definitive (confirmatory) RCT (120,141,155).

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# APPENDICES

**Appendix 1: Study 1 (draft)**

**Appendix 2: Study 2 (draft)**

**Appendix 3: Study 3 (as published)**

**Appendix 4: Infographic of Study 3 (as published)**

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