Supplementary Appendix

Does the Spraino® low-friction shoe patch prevent lateral ankle sprain injury in indoor sports? a pilot randomised controlled trial with 510 participants with previous ankle injuries

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Table S1: RCT effect estimates from The Spraino Pilot Trial (Intervention vs Control). "All events" are the sum of first-time and recurrent events.

Event type	All events	First-time events	Recurrent events
Events (151)			
Number	81 vs 70	71 vs 61	10 vs 9
Incidence rate ratio†	0.87 (0.62-1.23)[1]	0.88 (0.61-1.26)[8]	0.84 (0.31-2.34)[11]
Mean time-loss per event (weeks)	1.8 vs 2.8	1.9 vs 2.7	1.1 vs 3.4
Time-loss ratio	0.65 (0.45-0.93)	0.71 (0.48-1.05)[9]	0.31 (0.14-0.65)[12]
Non-contact events (96)			
Number	44 vs 52	44 vs 45	0 vs 7
Incidence rate ratio†	0.64 (0.42-0.97)	0.74 (0.47-1.13)[2]	NA[5]
Mean time-loss per event (weeks)	1.93 vs 2.69	2.0 vs 2.7	NA vs 2.3
Time-loss ratio	0.72 (0.44-1.16)	0.70 (0.43-1.15)[3]	NA[6]
Severe events (50)			
Number	19 vs 31	19 vs 29	0 vs 2
Incidence rate ratio†	0.46 (0.25-0.86)	0.48 (0.25-0.89)[10]	NA[13]
Severe Non-contact events (34)			
Number	12 vs 22	12 vs 20	0 vs 2
Incidence rate ratio†	0.41 (0.19-0.89)	0.44 (0.20-0.95)[4]	NA[7]

† Incidence Rate Ratio (IRR<1: Protective Spraino Effect).
Superscript numbers refer to the list of outcomes in registration (NCT03311490).
Numbers in parenthesis represent 95% confidence intervals.
NA = No analysis performed due to low number of incidences.

Table S2: Schematic overview of standardized Baseline Questionnaire

	Question
	Baseline Info:
1	Name
2	Phone number
3	E-mail
4	Gender
5	Age
6	Height
7	Weight
8	Shoe size
9	Club
10	Coach
11	Leg dominance
12	Type of sport
13	Level of play
14	Usual weekly training exposure
15	Current footwear (Brand, model and year)
16	Footwear last season (Brand, model and year)
17	Footwear during last ankle sprain injury (Brand, model and year)
18	Pain in ankle during sport (11-NRS; 0-10)
19	Any previous ankle surgery
20	Any previous ankle sprain
	If "YES":
21	Time elapsed since last ankle sprain in months (0-3; 4-12; 13-24; 24+)
22	Fear of ankle sprain (11-NRS; 100-0)
23	Injury mechanism during most recent ankle sprain: Contact: Object/player/other between surface and injured foot Non-contact: Nothing between playing surface and injured foot (regardless of any prior player-player contact)
24	Approx. number of ankle sprains (previous season)
25	Approx. time-loss in weeks due to ankle sprains (previous season)

Figure S3: Flow of SMS-Track questions (Translated from Danish)

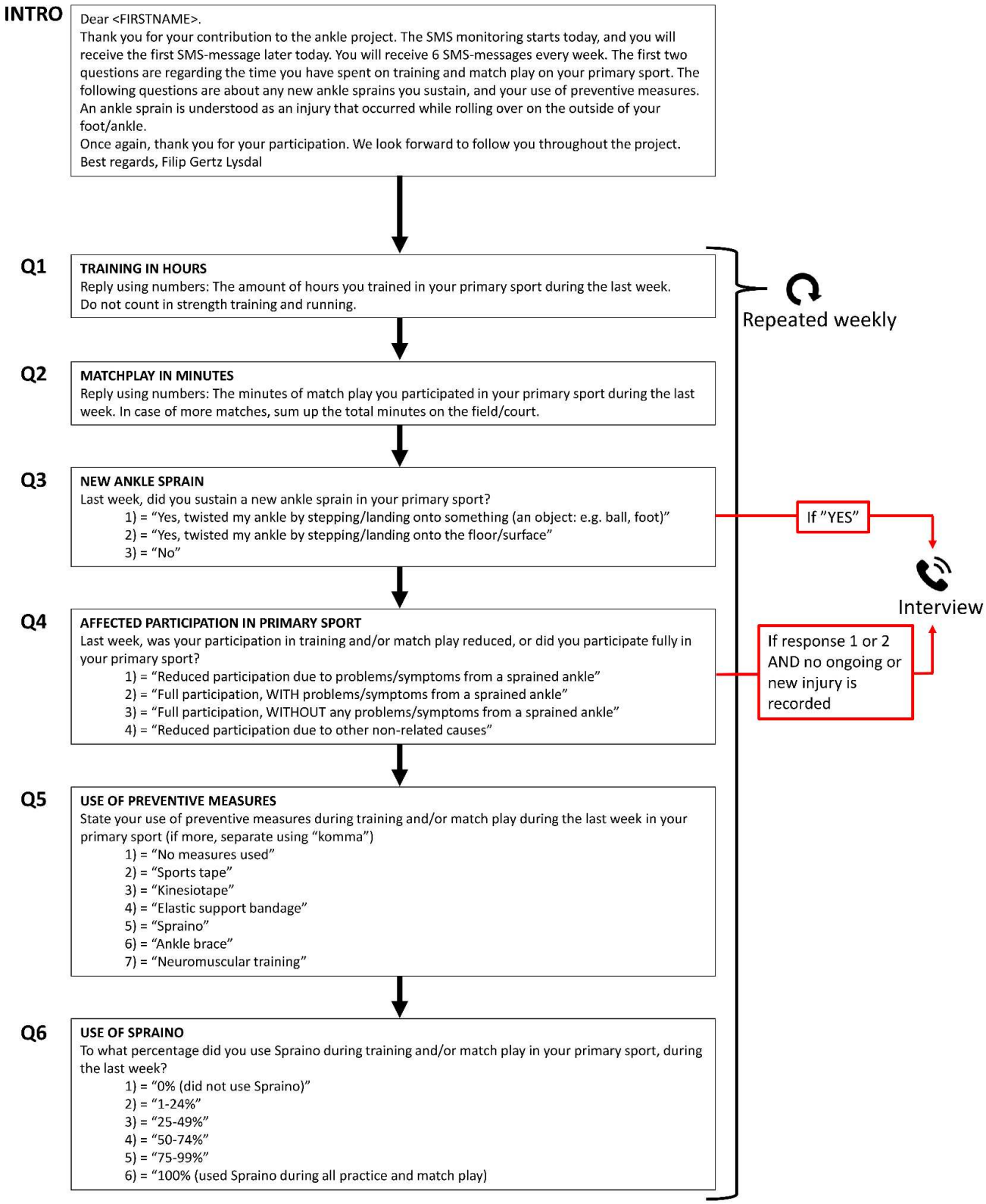

Table S4: Schematic overview of standardized injury registration form

	Question
1	Date of injury
2	The affected foot/ankle (right/left)
3	Whether the injury occurred in the primary sport
4	Whether the injury occurred during training or match
5	During which part of the training/match (warm-up/ first half/ second half/ after)
6	Injury mechanism: Contact: Object/player/other between surface and injured foot Non-contact: Nothing between playing surface and injured foot (regardless of any prior player-player contact)
7	Use of preventive measures just before or during injury
	If "yes"
8	Which preventive measure (sports tape/ kinesio tape/ support bandage/ Spraino/ brace/ neuromuscular training)
	If use of Spraino = "yes"
9	Hours used since last application
10	Assistance from healthcare professional prior to injury (prevention)
11	Whether the injury led to medical contact
12	Brand, model and year of footwear used during injury

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Appendix S5: Intervention Leaflet
(Translated from Danish)

You have been selected to use Spraino as a measure to prevent ankle sprain injuries

It is important for the project, that you as far as possible use Spraino during all training and match play, when practicing your primary sport. In case you use different shoes for training and match, you should apply Spraino to both pairs. It is important for the study that you, as far as possible, use Spraino during the entire project period (12 months form today).

You will receive 6 weekly questions via SMS during the 12-month period. You will be asked about your sports participation, whether you have sustained an injury, and how much you have used Spraino. It is important that you reply to these SMS' – and that you answer the questions honestly.

Spraino has an estimated durability of 20-40 hours, but it is important that the non-stick properties are intact. Check the non-stick function frequently after approx. 20 hours of use.

You should order more Spraino at forskning@spraino.com when you only have one pair left. You will receive your new sets within 14 days after ordering. Please state the following when ordering:

- Full name
- Phone number
- Club
- Postal address

If you already use preventive measures (such as sports tape, braces, support bandages or alike), you can keep using these. Spraino can easily be used together with other measures. Spraino does not reduce performance or increase the risk of other sports injuries.

Should you encounter any side-effects and/or problems with Spraino, you should report this to forskning@spraino.com. You can report your experiences with Spraino at any time during the entire project period.

You can reach us during the entire project at:
Mail: forskning@spraino.com
Phone.: 2720 5197

Best regards,
The research group

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Appendix S6: Trial Protocol

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A Randomized Pilot Trial to Evaluate the Preliminary Effect and Safety of Using Spraino to Prevent Lateral Ankle Sprains in Indoor Sports (The Spraino Pilot Trial)

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Abstract

Background: Lateral ankle sprains (LASs) are the most common injury among physically active populations. The prevalence and injury rate is especially high in indoor sports, where high shoe-surface friction is considered a risk factor for *"non-contact"* LASs. Spraino is a novel approach designed to mitigate the risk of friction-related LASs by minimising friction on the lateral edge. This is achieved by a pair of Teflon patches that are attached to the outside of sports shoes. This RCT determines preliminary effect (incidence rate and severity) and safety (harms) of using Spraino to prevent LAS injury among indoor sport athletes with a previous LAS within 24 months, when compared to a "do-as-usual" control group.

Methods/Design: This study was designed as an exploratory, parallel-group, two-arm pilot randomised controlled trial. 510 sub-elite indoor sport athletes with a previous LAS injury were randomly allocated (1:1) to Spraino or "do-as-usual". Allocation was concealed and the trial was outcome-assessor-blinded. Match and training exposure, LASs and associated time-loss were captured weekly via text messages. Information on harms, fear-of-injury and ankle pain were also documented.

Discussion: This trial is the first prospective study investigating the preventive effect of minimizing shoe-surface friction on the rate of self-reported LASs. We expect to indicate "proof-of-principle" as to whether Spraino is a preliminary effective and safe solution in LAS injury risk mitigation among indoor sport athletes with a previous LAS. A confirmatory trial is planned to be undertaken should the trial findings indicate "proof-of-principle" as hypothesized.

Trial registration: ClinicalTrials.gov (NCT03311490)

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Background

The ankle joint is the most commonly injured joint among individuals who participate in sports[1,2]. The typical mechanism of ankle joint injury is characterised by a rapid excessive inversion and internal rotation of the foot[3–5]. A majority of ankle joint injuries occur via a *"non-contact"* injury mechanism[2,6], with the highest proportion of these injuries resulting in a sprain of the lateral ligaments[1,2,6]. Although often regarded as innocuous[3,6], more than half of all lateral ankle sprain (LAS) injuries result in immediate restriction from sports participation[7]. Furthermore, the risk of developing long-term injury-associated residual symptoms following acute LAS injury is substantial[2,8].

The risk of sustaining an ankle sprain injury is substantial for athletes participating in indoor sports. An incidence rate of 4.9 lateral ankle sprains per 1000 exposure hours has been reported for indoor sports making it the sports category with the highest incidence rate of ankle sprains[9]. In addition, non-contact mechanisms have been reported to be more common than contact mechanisms[2]. Due to the high prevalence and incidence of ankle sprains in indoor team sports, the implementation of prevention strategies has been highly recommended[1,2,9].

Current effective prevention strategies include taping, bracing and neuromuscular training[10]. These measures are thought to improve ankle joint stability by preventing aberrancies in foot positioning[10,11]. An inappropriate foot position is purported to heighten the risk of sustaining a lateral ankle sprain; whereby a supinated and/or plantar flexed foot at touchdown onto a surface is believed to increase the external inversion moment arm about the subtalar joint[11,12].

In terms of ankle sprain injury prevention various studies have demonstrated promising effects with measures such as taping and bracing[10]. Albeit effective in terms of prevention, current measures (taping, bracing etc.) are mainly used by athletes with a previous ankle injury[10]. These observations support the need for a new approach to prevent first-time ankle sprains as well as recurrent ankle sprains without limiting sports performance or player safety.

Spraino is an adhesive PTFE patch and represents a novel approach thought to aid in both primary and secondary non-contact lateral ankle sprain injury prevention. The PTFE patch is attached on the outside of indoor sports shoes; hence it does not influence ankle joint range of motion. It is developed with the intent of minimizing lateral shoe-surface friction whenever initial contact is carried out with the foot placed in an inappropriate position. This is important, as an inverted foot position at initial contact has been cited as an inciting lateral ankle sprain mechanism[2,4].

Previous biomechanical studies have shown no reduction in performance when using Spraino during typical indoor sport movements[13]. Similarly, no changes have been found in traction or ankle joint kinetics despite an excessive attachment of 10mm PTFE covering the base of the shoe sole. However, no inversion at initial contact was present in any cases. The unchanged ground contact mechanics indicate that Spraino could be used during typical indoor sports activities without compromising player ability or safety[13].

With Spraino being a promising preventative measure, and an appealing solution in terms of simplicity, the clinical effect still needs to be thoroughly explored. The first natural step following promising laboratory testing is to establish "proof-of-principle", being preliminary evidence of effect, on clinically relevant endpoints[14]. Since no previous longitudinal clinical studies of Spraino as a preventive measure have been undertaken, it is unknown how its use might affect important clinical outcomes. An exploratory research approach is therefore needed to inform about preliminary effect and safety.

Specifically, the aims of this exploratory pilot trial were to determine "proof-of-principle", that is preliminary effect and safety of Spraino on the incidence rate and severity of acute lateral ankle sprains (LASs) among sub-elite indoor sport athletes with a previous LAS injury, when compared to a "do-as-usual" control group, during a 52-week follow-up period.

Methods/Design

This trial protocol is based on the SPIRIT 2013 guide for protocols of clinical trials[15], and the intervention is described using the TIDieR checklist[16], as suggested by the PREPARE Trial Guide[17]. The trial adheres to the CONSORT 2010 statement with the extension to randomized pilot and feasibility trials[18].

Study outline

The trial is named *The Spraino Pilot Trial*. It is a two-arm, parallel-group, exploratory pilot randomised controlled trial to assess proof-of-principle for Spraino, that is, preliminary effect and safety in LAS injury risk mitigation among athletes with a previous LAS within 24 months preceding the trial, competing in indoor sports at divisional- or league level. The trial is considered preliminary and if the trial findings indicate "proof-of-principle", as hypothesized, a confirmatory trial is planned to be undertaken. The design and flow of participants is shown in Figure 1.

The trial was funded by Copenhagen Center for Health Technology (CACHET), Innovation Fund Denmark, and Spraino ApS was the trial sponsor providing the low-friction shoe patches. The study design and procedures were approved by The North Denmark Region Committee on Health Research Ethics on July 5th, 2017. The trial was pre-registered at ClinicalTrials.gov (NCT03311490) on October 17th, 2017 and enrolment of participants started on October 19th, 2017. All participants provided written informed consent.

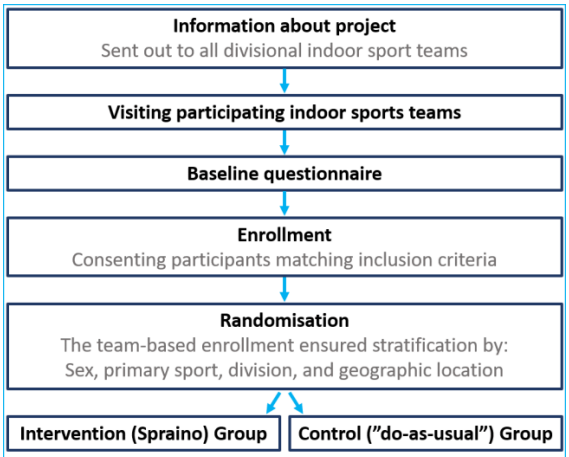

Figure 1: Study design and flow of participants

Hypotheses

The working hypothesis of this exploratory trial was that Spraino is superior in reducing the incidence rate and severity of acute LASs among sub-elite indoor sport athletes with a previous LAS, when compared to a "do-as-usual" control group, with no or minimal adverse effects.

Participants

Healthy participants competing in senior indoor sports (handball, basketball or badminton) at divisional- or league level who have sustained a LAS up to two years (24 months) prior to enrolment were eligible for inclusion in the trial. No distinction was made in the severity or time elapsed since the most-recent LAS injury, with this being up to the randomization. We chose to include athletes with a previous LAS, because this population is at particularly "high risk" of sustaining a new injury[10,19], making injury risk mitigation highly relevant. Moreover, we expected this group to be strongly motivated to adhere to the trial and intervention. At the time of recruitment, all athletes were participating fully in their sport and reported no acute injury symptoms. The full list of inclusion criteria was as follows:

- Participant is ≥ 18 years old at commencement of trial.
- Participant can read, speak and understand Danish.
- Participant can receive and reply to texts on a cell phone using Short Message Services (SMS).
- Participant performs indoor sports (Handball, basketball og badminton) in a sub-elite level team with ≥ 2 weekly practice sessions.
- Participant has incurred ≥ 1 lateral ankle sprain injury in the preceding 24 months.
- Participant has returned to play at commencement of the trial.

Sample size

Since no previous clinical studies have investigated the preventive effect of Spraino, the sample size was determined pragmatically to include 500 participants:

The sample size was determined by the formula $n = 4/T\left(\sqrt{\theta_0} - \sqrt{\theta_1}\right)^2$ where n is the number of participants in each arm, T the observation time, θ_0 and θ_1 are the incidence rates in the control and intervention group[20]. We anticipated an incidence rate of 4.9 LASs per 1000 hours of exposure[6] without Spraino, and an incidence rate of 2.94 per 1000 hours with Spraino (i.e. 40% reduction). With a power of 80% and an α of 5% an exposure time of ~15350 hours would be needed in each arm. Carefully assuming an average exposure of 3 hours of court activities per week per participant (including off-season, other injuries, vacation etc.), the 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, thus still feasible within the 52-week follow-up period.

The sample size of 500 aligns with previous LAS injury prevention trials[21,22]. Our inclusion process (i.e. teams visited) ceased when 250 participants had been allocated to each arm of the trial.

Recruitment

Preliminary meetings were held with the National Olympic Committee and Sports Confederation of Denmark (DIF), along with the specific National Sports Associations (Danish Handball Federation, Danish Basketball Federation and Badminton Denmark) of the most-popular indoor sports in Denmark. Based on these preliminary meetings, we decided to recruit participants from approximately 3000 indoor sports athletes at divisional level, until 250 was allocated to each arm of the trial.

The National Olympic Committee and Sports Confederation of Denmark (DIF) and the respective

National Sports Associations made the preliminary approach by sending out information regarding the study. Arrangements would then be made with specific sports teams that agreed to participate in the study. Participants were recruited, included and randomized at the local training facilities of the participating indoor sports teams competing at divisional- or league-level in Denmark.

The recruitment of participants took place between October 2017 and February 2018. The recruitment of teams ceased after the visit of the 91st sports team, where the 250th participant was allocated to the last arm of the trial.

A total of 1339 indoor sport athletes were approached at the participating sports teams, all completing a baseline questionnaire (Supplementary Table S4). 576 matched the inclusion criteria, of which 66 declined to participate. Consequently, 510 participants were randomly assigned to the two arms of the trial after completing baseline questionnaire and informed consent. The 760 remaining participants not meeting the inclusion criteria were also monitored during the study period as part of a cohort group outside The Spraino Pilot Trial.

Randomisation

Randomisation was performed after participants had provided written consent and completed baseline questionnaires. Included participants were assigned in a 1:1 allocation ratio to either the intervention (Spraino) group or the control ("do-as-usual") group. We generated the two comparison groups using balanced block randomisation. The random component in the sequence generation process was a drawing of lots. An equal amount of lots was used to assure the 1:1 allocation ratio (i.e. if a team had 15 enrolled players, then 16 lots, eight representing each group, were included).

Blinding

Blinding of a non-pharmacologic trial can be difficult to achieve[17]. Randomisation was blinded by using lots (wooden beads) of identical appearance in an opaque bag. This was used to conceal the allocation so that participants and investigators enrolling participants could not see through or down into the bag of lots, and thus were not able to foresee assignment.

Blinding of participants allocated to the intervention was not a possibility with the intervention being an obvious shoe modification (Figure 2), while the intervention group also received a simple instruction on how to apply Spraino. No attempts were made to blind the trial hypothesis. Consequently, the trial was conducted as an open trial.

The trial uses objective outcome measures to overcome the issue of participants being unblinded during the trial[24], and the trial will use double masking; with all injury registration being blinded to the principal investigator and by having the outcome measures analysed by an external, blinded, outcome assessor. All analyses are conducted blinded to group allocation.

Interventions

Participants allocated to the intervention group received Spraino as a measure to prevent future LASs during all on-court practice sessions and matches. Participants allocated to the control group were a pragmatic "do-as-usual" comparator.

Spraino is an adhesive polytetrafluoroethylene (PTFE or *"Teflon"*) patch developed with the intent of minimizing lateral shoe-surface friction whenever initial contact is carried out with the foot placed in an inappropriate position. The patches are attached as two separate pieces along the outside of the shoe (Figure 2) and are intended for use during indoor sports on smooth and even surfaces. The front patch (Figure 2,A) is attached along the edge of the lateral forefoot, with 2-4 mm covering the bottom of the shoe sole. The rear patch (Figure 2,B) is attached along the edge of the lateral rearfoot and does not cover the shoe sole. The participants in the intervention (Spraino) group was instructed face-to-face in attachment and replacement of the product.

The material properties of PTFE will minimize friction at initial contact, which in theory will minimize any horizontal forces. This implies minimizing the friction torque, which during a landing with an initial inversion of the ankle joint can cause a LAS[2,4,11].

Figure 2: Spraino, Front (A) and Rear (B)

In contrast to current prevention strategies, Spraino does not seek to alter the foot position prior to contact as observed during the use of e.g. taping and bracing[10,11]. As an alternative approach, the foot is aligned into a proper position after initial contact, through a sliding motion, before full load is applied. Consequently, the ground reaction force moment arm about the subtalar joint axis is reduced through this

correction phase, which in theory can prevent a LAS injury[25].

Previous biomechanical studies have shown no reduction in performance when using Spraino during typical indoor sport movements[13]. Similarly, no changes have been found in traction or ankle joint kinetics despite an excessive attachment of 10 mm PTFE covering the base of the shoe sole. The unchanged ground contact mechanics suggest that Spraino may be used during typical indoor sports activities without compromising player ability or safety[13].

Each Spraino PTFE patch has a minimum durability of 20 hours of indoor sports participation and was provided by the trial sponsor, Spraino ApS. Participants allocated to the intervention group receives additional Spraino via postal service upon request throughout the trial.

Outcome measures

Being exploratory, the trial was designed with a flat outcome structure (i.e. no outcome hierarchy), hence the outcomes related to the incidence rate and time-loss (severity) of self-reported LASs were all pre-registered as "primary" outcomes. Intervention-related adverse events, fear of LAS, and pain in the ankle joint were also piloted during the trial, along with adherence to the intervention.

Recurrent and first-time LASs, non-contact and All LASs (contact + non-contact), and the combined parameters were all piloted in the trial to investigate the preventive effect of Spraino (Table 1).

Incidence rates and Incidence-related time-loss

Incidence rates will be reported as the number of LASs occurring during participation in the primary sport per 1000 hours of exposure (court training + match play).

Incidence-related time-loss is defined as the time lost from unrestricted participation[26] per injury, and will be reported in number of calendar weeks per LAS. Time-loss recordings following an injury would stop on the first day of a consecutive three-week period without injury-related symptoms.

Only LAS sustained within the trial period are taken into consideration to avoid any recall bias, and/or bias in terms of whether an injury should be classified as recurrent or not.

On this basis, the following generic definitions were used in the prospective classification of LAS injuries:

Any lateral ankle sprain

Any type of LAS sustained in the primary sport within the trial period.

Non-contact lateral ankle sprain

A LAS which occurred without landing or stepping onto something, but the floor, regardless of any player-player interaction prior to the event.

First-time lateral ankle sprain

The first report of a LAS to a specific ankle joint not previously injured within the trial period, regardless of any previous injuries prior to the trial.

Recurrent lateral ankle sprain

Any subsequent LASs reported in the same ankle joint previously injured within the trial period.

Severe lateral ankle sprain

A reported LAS which yielded time-loss (time until unrestricted participation) for three weeks (21 days) or more.

These LAS definitions are also combined to investigate the effect of Spraino across various parameters, i.e. the preventive effect on the rate of recurrent non-contact LAS.

Intervention-related adverse events (harms)

The participants in the intervention group were encouraged to report any adverse events related to the use of Spraino to the trial hotline. Events leading to harms will be reported in type and quantity.

Fear of re-injury

Fear of sustaining a new LAS injury was obtained at inclusion through an 11-point NRS ranging from 0-100 points, with 0 representing 'extremely fearful', and 100 representing 'no fear at all'[27]. This value was obtained through the baseline questionnaire and will be compared to the follow-up value.

Ankle pain

Pain in the ankle during sports participation was also obtained at inclusion through an 11-point NRS ranging from 0-10. 0 represented no pain at all, and 10 represented worst pain imaginable[28]. This will similarly to the fear score be compared to the follow-up value.

Data collection and injury registration

Participants completed a modified version of the NCAA injury surveillance questionnaire at baseline (Supplementary Table S4)[29], from which mobile phone numbers were obtained to prospectively collect data through answers to six weekly, standardised text-message questions (Supplementary Figure S5). We collected text-message data using the SMS-Track© system[30,31].

When replying to the weekly SMS questions, participants were required to report: (Q1,Q2) their weekly total participation time (training and match exposure); (Q3) whether they had incurred a LAS; (Q4) whether participation was restricted due to a LAS; (Q5) whether they used any prophylactic LAS injury prevention measure; (Q6) whether they had adhered to their group allocation.

All participants received the first of six-weekly text messages every Monday evening. Subsequent questions were sent automatically, immediately after the answer to a previous message had been received.

If a LAS or a participation restriction due to an ankle-related problem was reported by a participant via the SMS system, a follow-up telephone interview was conducted by a member of the research team (Supplementary Figure S5).

If a LAS had incurred, a detailed injury registration form was completed (Supplementary Table S6). In instances where a participant who reported either of the aforementioned events could not be contacted within four weeks, that event will not be included in the analyses.

Compliance

All included participants were encouraged to remain part of the trial for the full season ahead, which was further strengthened by the National Olympic Committee and Sports Confederation of Denmark (DIF) and the respective National Sports Associations (DHF, DBBF and BD) taking part in the recruitment process. The participants were monitored with weekly follow-up using SMS-Track (a Short Message Service) as part of the injury surveillance. The use of SMS-Track to collect injury and exposure data has proven successful in securing participant retention in previous cohort studies[31]. A text reminding the participant to reply to the string of text messages is sent out after 48 hours in the case where an answer has not been received. The participants will receive a reminding phone call if this pattern occurs for two consecutive weeks.

In addition, participants allocated to the intervention group were encouraged to use the trial hotline whenever in doubt about use and/or replacement of Spraino.

Participants allocated to the control group were regarded as a pragmatic "do-as-usual" comparator. This implies that they could treat and prevent LASs in any usual way they wished, except use Spraino. The weekly follow-ups provided data on the utilised do-as-usual strategy, while the elaboratory phone call in case of a LAS further elaborated any strategy applied when a LAS occurred. The participants in the control group were encouraged not to contaminate the trial by using Spraino throughout the trial period, and they were encouraged to reply honestly to the SMS-Track questions regarding any use of Spraino.

The included participants, being previously LAS-injured, were expected to be strongly motivated to adhere to both trial and intervention.

Statistical analyses

The trial was designed as a pilot study and thus considered exploratory with no outcome hierarchy, however with a working hypothesis; that Spraino is superior to "do-as-usual" in LAS injury prevention. LAS incidence rates and incidence rate ratios was estimated using Poisson regression with the sum of match-play and practice hours as exposure. LAS recurrence was estimated similarly but only containing exposure from in-trial LAS-injured participants. Only exact exposure was used in the calculations of incidence rates, with validations of LAS injury classification a prerequisite in the trial design. Time-loss following a LAS was estimated using negative binomial regression.

Change in fear of sustaining a new LAS, and change in ankle pain, over the course of the trial was calculated using negative binomial regression adjusting for baseline values. The change will be reported as between-groups difference. Multiple imputations by chained equations will be performed to account for missing data.

Discussion

The Spraino Pilot Trial was designed to determine "proof-of-principle", that is preliminary effect and safety of Spraino on the incidence rate and severity of acute LASs among sub-elite indoor sport athletes with a previous LAS, when compared to a "do-as-usual" control group, with no or minimal adverse events expected.

Strengths and limitations

The Spraino Pilot Trial is the first prospective trial investigating the preventive effect of minimizing shoe-surface friction on the rate of self-reported LASs. The study is strengthened by its use of a randomised design and large sample size. Due to the simplicity of the intervention, a high adherence to the intervention was expected.

The study used self-reporting of injuries in the form of LASs. This would normally be viewed as a limiting factor, with the participants probably not being

Table 1: LAS outcomes

		All LASs	**Non-contact LAS**
Combined parameters	**First-time LAS**	All first-time LAS	First-time non-contact LAS
	Recurrent LAS	All recurrent LAS	Recurrent non-contact LAS

trained in injury diagnostics. A LAS is however a common injury, especially among indoor sport athletes, and with all included participants reporting to have sustained at least one LAS prior to inclusion, combined with the fact that both groups were self-reporting, it is not viewed as a limitation to the trial.

Only exact exposure was used in the calculations of incidence rates, thus implying that no imputations was made for missing exposure data. This is considered a strength in the design of present trial, since a use of imputations for missing exposure data would require imputations for LAS injuries as well, otherwise the imputed exposure would be injury-risk-free, which is simply not possible. If a LAS injury was to be imputed, this would not be validated in terms of affected leg, injury mechanism, severity etc.

Only in-trial recurrent events were considered in the investigation of Spraino for secondary LAS injury prevention. This is considered a strength to the present trial design and was done to avoid bias in the classification of LASs (i.e. whether the first LAS sustained within the trial was a recurrent injury or not), since the inclusion sprain could date back 24 months. All included participants were participating fully without any acute injury-associated symptoms when included in the trial.

The trial is limited in terms of participants not being blinded to the intervention. This is not regarded as a limitation to the objective outcomes; injury incidence rate and time-loss. However, the risk of bias is high on subjective outcomes (fear and pain). The open trial approach could be a possible cause for a higher lack of compliance in the control group, while there is also a risk of treatment contamination.

The trial was designed to mimic real life as closely as possible with participants allocated to the intervention (Spraino) group being responsible for their own application of Spraino, replacement when worn out, and for ordering new Spraino via the trial hotline when running low. In this light, the external validity it is considered high.

Impact

This study expects to indicate "proof-of-principle" as to whether Spraino is an effective and safe solution in LAS injury risk mitigation among indoor sport athletes with a previous LAS. A confirmatory trial is planned to be undertaken should the trial findings indicate "proof-of-principle" as hypothesized.

Funding

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Contributions

TG, FGL and UK conceived of the study and obtained funding for the study. KT, TB, ED, PP and MBC designed the trial. SM managed the collection of data under the supervision of MBC. TB, KT and ED provided clinical scientific expertise on the trial. KT supervised the study in its entirety.

Competing Interests

TG is the founder of Spraino ApS. FGL is a paid employee in Spraino ApS. Spraino ApS was responsible for provision of Spraino. The conflict was accommodated by restricting Spraino ApS and affiliates to any deciding role in the design of the study, in the execution, analyses, interpretation of data, or decision to submit results. KT have full authority of the trial administration. The three senior clinical researchers (KT, TB and ED) have full authority in terms of submission for publication.

Copenhagen Center for Health Technology (CACHET) and Innovation Fund Denmark have no scientific role in the trial

Trial timeline

- Consensus on trial design (June 27th, 2017)
- Ethical approval (July 5th, 2017)
- Consensus on protocol draft (September 27th, 2017)
- Registration at ClinicalTrials.gov (October 17th, 2017)
- Enrolment (October 19th, 2017 – February 28th, 2018)
- Halt of trial (October 5th, 2018)
- Missing outcomes added (December 4th, 2018)
- Data analysis (December 26th, 2018)

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