The Foot 58 (2024) 102068

Contents lists available at ScienceDirect

The Foot

journal homepage: www.elsevier.com/locate/foot

# The effectiveness of customised 3D-printed insoles on perceived pain, comfort, and completion time among frequent Park Runners: Study protocol for a pragmatic randomised controlled trial (The ZOLES RCT)

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ARTICLE INFO

*Keywords:*
Pain [MeSH]
Running [MeSH]
Foot orthoses [MeSH]
Quality improvement [MeSH]
Parkrun

ABSTRACT

*Background:* Running, a popular recreational activity, often leads to the experience of pain and discomfort among participants impacting performance and participation longevity. The ZOLES trial evaluates customised 3D-printed insoles for reducing pain in frequent parkrunners aged 35 and over. An innovative process of foot-scanning and responses to questions relating to size, pain, discomfort, and previous medical conditions are combined leading to the production of personalised 3D-printed orthotics.

*Methods:* The ZOLES trial is a pragmatic, outcome assessor blinded, randomised, controlled, superiority trial involving 200 recreational runners, randomised to receive either customised 3D-printed insoles (ZOLES) or to a "do-as-usual" control group. The study follows a robust protocol, ensuring adherence to established guidelines for clinical trials, and is based at St Mary's University, Twickenham, London. The primary outcome is change in running-related pain over a 10-week period, assessed using an 11-point Numeric Rating Scale. Secondary outcomes include overall pain and discomfort, running-related comfort, 5k-completion time, time-loss due to injuries, running exposure, and adherence to the intervention. A balanced-block randomisation process is stratified by sex and parkrun location, and an intention-to-treat analyses will be employed on all outcomes in the primary trial report. The trial includes a 52-week post-market surveillance to assess long-term effects of the customised insoles.

*Discussion:* The ZOLES trial aims to provide insights into real-world applicability and effectiveness of customised 3D-printed insoles in reducing running-related pain and enhancing overall running experience. Despite the limitation of a subjective primary outcome measure without participant blinding, the methodological rigor, including external outcome assessment and data handling, we anticipate results that are academically credible and applicable in real-world settings The results of this trial may have important implications for runners, clinicians, and the sports footwear industry, as evidence for the use of individualised insoles to improve running experience and prevention of pain may become evident.

*Abbreviations:* TPU, Thermoplastic Polyurethane; MCID, minimal clinical important difference; NRS, Numeric Rating Scale; GRoC, Global Rating of Change; CG, Control Group; IG, Intervention Group; ITT, Intention-to-treat; CONSORT, Consolidated standards of reporting trials; SPIRIT, Standard protocol items: Recommendations for interventional trials; TIDieR, Template for intervention description and replication; FINER, Feasible, Interesting, Novel, Ethical, and Relevant; REDCap, Research Electronic Data Capture.

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https://doi.org/10.1016/j.foot.2024.102068
Received 27 October 2023; Received in revised form 10 January 2024; Accepted 21 January 2024
Available online 6 February 2024

*Trial registration:* The trial was pre-registered at ClinicalTrials.gov with the trial identifier NCT06034210 on September 4, 2023, and publicly posted on September 13, 2023 (https://clinicaltrials.gov/study/NCT06034210).
*Protocol version:* Version 1, September 27, 2023.

## 1. Background

Engaging in regular physical activity, particularly running, is associated with numerous health benefits [1]. It can enhance cardiovascular health [2], improve weight management [3], mental well-being [4,5], and generally reduces all-cause mortality [6]. A testament to the growing popularity of running is the burgeoning 'parkrun' movement. Originating in Bushy Park outside of London in the UK, parkrun is a community-driven initiative that offers timed running events in parks around the world [7]. These events serve as an accessible and welcoming platform for individuals of all fitness levels to engage in running and cultivate an active lifestyle. Through this initiative, parkrun not only contributes to the individual health of participants but also fosters a global community that values physical activity and communal engagement [8].

However, the benefits of running do not come without risk of potential drawbacks. A significant portion of runners, both recreational and competitive, run with high levels of musculoskeletal pain ($\geq$3 on 11-point Numeric Rating Scales (NRS)) [9], and encounter musculoskeletal injuries, particularly in the lower extremities, at high rates [10]. Such setbacks not only result in time away from running [11] but can also cascade into reduced daily physical activity levels [12]. In some cases, persistent pain and recurring injuries may culminate in total inactivity [13], associated with a lower quality of life and ultimately elevating the risk of depression [14] and premature mortality [15].

Foot and footwear discomfort might increase this risk of injury [16], with a potential inverse relationship, whereby enhanced foot-footwear comfort might serve as a protective factor against running-related injuries [17]. Furthermore, greater comfort seems to correlate with improved performance in running [18]. Modern technological advancements, notably 3D printing, have recently refined the orthotic fabrication process, providing tailored support and cushioning that can be adapted to both foot shape and pressure distribution [19,20], with superior comfort compared to prefabricated insoles [21]. As is often the case, however, many studies on biomechanical interventions, such as foot orthotics, never make it out of the laboratory [22], or the trials are conducted on specific subgroups with strict inclusion and exclusion criteria [23].

Foot orthotics, available in both customised and off-the-shelf forms, might offer a potential solution to these challenges [24,25]. With direct-to-consumer marketing, these orthotic devices are often presented as remedies capable of alleviating an array of both foot-related issues as well as pain and discomfort [26,27]. Yet, the literature on their benefits is somewhat equivocal. Many studies have an observational or non-randomised design [28], while other studies compare custom orthotics with sham or generic insoles [29–31], which may carry their own therapeutic properties, potentially diluting the observed benefits of the customised versions. To date, however, the most compelling evidence of orthotic interventions includes the effect on specific diagnoses such as plantar fasciitis [32], and Achilles tendinopathy with moderate-to-low certainty of short-term pain reductions [33]. These conditions, while common among runners [10], are often alleviated using a comprehensive treatment approach, in which the effect of the orthotics is often assessed as an adjunct part of the treatment including and patient education in combination with other interventions like physical therapy and rehab exercises [33,34], and corticosteroid injections[34]. This adjunct approach might cloud the isolated effects of the insole, and it remains uncertain whether an insole alone without patient education will prove effective in a pragmatic setting, as indeed the prescription of foot orthotics is normally associated with some degree of podiatric patient education [34].

Considering the complexities in the existing literature, there is a pressing need for a simple pragmatic trial designed to assess the immediate and prospective long-term effectiveness of customised 3D-printed insoles among the general population of recreational runners. This includes individuals with or without pain and with or without specific foot-related conditions or definitive diagnoses like plantar fasciitis. By employing intention-to-treat principles in the primary analysis, this trial ensures a realistic representation of the insoles' real-world effectiveness in a natural setting, invaluable for both healthcare providers and runners. Our subsequent secondary analyses will then delve deeper, focusing on responses from those with significant baseline pain and specific diagnoses, offering a granular understanding of the intervention's effect across different subgroups within the recreational running community.

## 2. Objectives

### 2.1. Primary research question

Based on the description provided and existing evidence, we posed the following research question: *Is the use of Zoles customised 3D-printed insoles, for a duration of 8 weeks, superior to a "do-as-usual" control strategy in improving running-related pain among frequent recreational runners participating in regular parkrun activities?*

This research question was designed using the PICOT model with the following specifications for each element [35]:

**P**opulation: Frequent recreational runners participating in regular parkrun activities.

**I**ntervention: Zoles customised 3D-printed insoles for ~8 weeks.

**C**ontrol: "Do-as-usual" control group.

**O**utcome: Improvement in running-related pain.

**T**ime frame: 10 weeks after baseline (~8 weeks after receiving allocated intervention).

### 2.2. Primary objective

The primary objective is to determine the effectiveness of the Zoles customised 3D-printed insoles on the change in running-related pain 10 weeks after baseline in frequent recreational runners participating in regular parkrun activities.

### 2.3. Primary research hypothesis

Our hypothesis is that the Zoles customised 3D-printed insoles, will lead to a significant reduction in running-related pain 10 weeks after baseline (~8 weeks after received allocated intervention) compared to a "do-as-usual" control strategy among frequent recreational runners participating in regular parkrun activities.

### 2.4. Secondary objectives

To assess the effect of Zoles customised 3D-printed insoles on secondary outcomes like:

a. Global Rating of Change (GRoC) in overall daily pain and discomfort [36].
b. Running-related foot/footwear comfort [37].

c. 5-k (parkrun) completion time.
d. Running-related injury incidence rate.
e. Time-loss from running.
f. Running exposure in terms of miles and time.
g. Adherence to the intervention during daily- and running activities.
h. Adverse events from using the Zoles insoles.

1. To explore if the control group benefits similarly to receiving customised 3D-printed insoles when provided after the initial 10-week primary trial phase.
2. To understand the long-term effects and durability of the benefits of the Zoles customised 3D-printed insoles, assessed one year after the intervention.
3. To investigate the immediate therapeutic effect of Zoles insoles specifically for participants with clinically relevant baseline pain levels (11-NRS $\geq$ 3) [38].
4. To assess pre-trial expectations and post-trial experiences regarding the therapeutic effects of the Zoles insoles and understand their influence on the efficacy of the intervention within the specific subgroup of participants with high baseline pain levels.

## 3. Methods

### 3.1. Trial design

The ZOLES trial is a pragmatic, outcome assessor blinded, randomised, controlled, superiority trial, with a two-group parallel design, and a 1:1 allocation ratio. Frequent recreational runners will undergo foot scanning and thereafter be randomised to either receive a customised 3D-printed insole (Zoles ApS, Espergærde, DK-3060, Denmark), or to be in a "do-as-usual" control group. The pragmatic design and preplanned secondary analyses are heavily inspired by the SExSI trial [39].

The trial protocol is based on the "PREPARE Trial guide" [35] and adheres to the "SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials" [40] and SPIRIT checklist (Appendix A). The trial report will follow the "REPORT guide" [41], and thus adhere to the CONSORT guidelines for reporting parallel group randomised trials [42], using the CONSORT extension for pragmatic trials [43], as well as the updated CONSORT-Outcomes 2022 extension [44]. The TIDieR template (Appendix B) is used to describe the intervention to aid future replication [45].

The study was approved by the St Mary's University Ethics Sub-Committee on 4 August 2023 (ID: SMU_ETHICS_2022-23_325), and the trial was pre-registered at ClinicalTrials.gov on 4 September 2023 (ID: NCT06034210) [46], before the first participant was enrolled on September 16, 2023.

### 3.2. Study setting

Participant screening and enrolment for this study is undertaken from the Faculty of Sport, Technology and Health Sciences at St Mary's University (Twickenham, London, United Kingdom) with recruitment to the trial being carried out at local parkrun communities, primarily from Bushy Park (Richmond upon Thames, London, United Kingdom).

### 3.3. Eligibility criteria

***Inclusion criteria.***

a) Participant is $\geq$ 35 years old at commencement of trial.
b) Participant can read, speak, and understand English.
c) Participant can receive e-mails and complete online questionnaires.
d) Participant is a frequent runner who participate in regular parkrun activities.
e) Participant is capable of running at commencement of trial.

***Exclusion criteria.***

a) Individuals with severe foot deformities will be excluded during the foot scanning process if the level of customization needed exceeds what is possible via the Zola software.
b) Individuals with uncontrolled diabetes with foot complications, or other conditions that might interfere with their ability to safely use the insoles and participate in running activities. Evaluated via the Physical Activity Readiness Questionnaire Plus (PAR-Q+) at inclusion.

### 3.4. Interventions

By virtue of being a pragmatic trial, all participants will be allowed to use or keep using any treatment or concomitant care, regardless of their group allocation. Pre-existing use of insoles in the intervention group, should naturally be replaced by this study's intervention.

#### 3.4.1. Experimental: ZOLES Customised 3D-printed insoles

Participants allocated to the intervention group will receive customised 3D-printed insoles (Zoles ApS, Espergærde, DK-3060, Denmark) to mitigate running-related pain and discomfort (Fig. 1). Being a pragmatic trial, all participants are permitted to continue or initiate any usual care of their choice to treat and prevent running-related pain and discomfort.

Based on measurements from a 3D scanning procedure (Fig. 2), and factoring in individual data such as age, weight, and activity preferences, custom insoles are designed using the ZOLA software. The insoles are then 3D-printed by Zoles ApS in Espergærde (Denmark), using BCN3D printers (Barcelona, Spain) and a TPU (Thermoplastic Polyurethane) filament material from Recreus (Alicante, Spain). The printed insoles are tailored for optimal support, performance, and comfort, with varying densities for areas like the arch and heel. They are finished with an OnSteam® microfiber cover for added durability and comfort. The insoles are intended for regular insertion into participants' shoes to align with their unique biomechanical needs. (Information translated and adapted from [47]). The participants are recommended to gradually increase wearing the insoles over a three-week period (Appendix D) but are otherwise encouraged to use the insoles within all their different shoes, and to wear these during all activities of daily living and during their running activities. Adherence to the intervention is not controlled but simply collected over the duration of the trial.

A thorough description of the intervention following the TIDieR guidelines [45], including reasons for potential needs for modifications of the insoles is included (Appendix B).

#### 3.4.2. No Intervention: "Do-as-usual" control group

Participants allocated to the control group are a "do-as-usual" comparator. This implies, that the participants may treat and prevent running-related pain and discomfort in any way they wish, including any existing use of orthotics, except using Zoles 3D-printed insoles.


**Fig. 1.** Zoles 3D-printed insole exemplar. Picture provided and used with permission from Zoles ApS.

**Fig. 2.** Example of foot scanning process of a right foot using the DOMEscan/IBV 3D scanner.

### 3.5. Outcomes

#### 3.5.1. Primary outcome

The primary outcome will be the change in running-related pain 10 weeks after baseline. Pain, although subjective, is a crucial determinant of runners' quality of life, performance, and continued participation in the activity [13]. For this trial, an 11-NRS pain scale will be utilized, ranging from 0 to 10 (0 = No pain at all, 10 = Worst pain imaginable) [48].

Baseline values for the primary outcome will be collected using online e-mail-distributed surveys via REDCap (Vanderbilt University, Nashville, TN, USA). Running-related pain data will be further collected at weekly intervals, with the focal analysis being between-group changes from baseline to the 10-week mark. The main outcome will be reported as the difference in mean change in running-related pain between the group using Zoles customised 3D-printed insoles and the "do-as-usual" control group, adjusting for values reported at baseline [49].

#### 3.5.2. Secondary outcomes

The secondary outcomes are all self-reported and include:

- Global Rating of Change (GRoC) in overall daily pain and discomfort: Participants will be asked to self-assess their perceived change in overall daily pain and discomfort relative to their state at the start of the study. They will use a 7-point scale, from − 3 ("much worse") to 3 ("much better"), as indicated in the study by Bobos et al. [36] This outcome will be measured weekly until the 10-week mark, and again at the 18-week mark.
- Running-related foot/footwear comfort: The change in comfort from the start to the 10-week mark, relating specifically to running and footwear, will be captured using a numeric rating scale ranging from 0 (Extremely uncomfortable) to 10 (Extremely comfortable) based on the parameters defined by Menz & Bonnano [37]. This outcome will be measured at baseline with weekly follow-up measurements until the 10-week mark, and again at the 18-week mark.
- 5k-completion time: The time taken by participants to complete their weekly 5 km parkrun will be recorded weekly, providing insights into any performance changes over the trial period.
- Running-related injuries: The incidence rate of injuries related to running will be monitored and reported as the number of injuries for every 1000 h of running exposure over the 10-week duration.
- Time-loss: The total number of days participants miss out from running due to pain, discomfort, or injury will be tracked weekly for 10 weeks, and again at the 18-week mark.
- Weekly Mileage: The distance participants run every week will be recorded during the 10-week trial period, and again at the 18-week mark.
- Weekly running exposure: The total time participants spend running every week will be obtained in hours and minutes for the 10-week trial period, and again at the 18-week mark.
- Adherence to intervention, ADL%: This outcome tracks how frequently participants use the Zoles insoles for everyday activities such as sitting, standing, walking, and driving over the 10 weeks, and tracked again at the 18-week mark, and at the 52-week post-market surveillance.
- Adherence to intervention, RUN%: The percentage of time participants wear the Zoles insoles specifically during running will be monitored over the 10 weeks, and again at the 18-week mark, and at the 52-week post-market surveillance.
- Adverse events from using Zoles insoles: All adverse events associated with the usage of Zoles will be reported based on their type and number. Throughout the trial, participants will be encouraged weekly to report any adverse events through the trial hotline. Participants will be asked again at the 52-week-post-market-surveillance to capture any long-term events.

#### 3.5.3. Other outcomes

The other outcomes of interest for the pre-planned secondary subgroup analyses include:

- Participants achieving Minimal Clinically Important Difference (MCID) reduction in pain: This measure looks at the percentage of participants who manage to achieve a clinically meaningful reduction in running-related pain, defined as a reduction equal to or larger than the MCID (NRS $\geq$ 2) as described by Salaffi et al. [48]over the 10 weeks.
- Time until MCID reduction in pain: This outcome gauges the time in weeks it takes for participants with clinically significant pre-existing pain (NRS $\geq$ 3 as defined by Rathleff et al. [38]) to achieve the clinically meaningful reduction in running-related pain (MCID) during the 10-week trial period.
- Change among participants with high baseline pain: For participants who start the trial with clinically significant pain (NRS $\geq$ 3) [38], their specific change in pain over the 10 weeks will be captured using a numeric rating scale from 0 (No pain at all) to 10 (Worst pain imaginable) [48].
- Pre-trial intervention expectations: Before the trial begins, participants will indicate their expectations regarding the therapeutic effect of the Zoles insoles on running-related pain, 5-k completion time, and footwear comfort using a 5-point Likert scale.
- Post-trial intervention experiences: After the trial, participants will be asked about their experiences with the Zoles intervention, indicating whether it met, exceeded, or did not meet their initial expectations via a 5-point Likert scale.
- Post-market surveillance: One-year post-trial, all participants (from both control and intervention groups) will be surveyed to assess the

long-term effects and benefits of the Zoles insoles. This survey will include the primary outcome and all key secondary outcomes, allowing for a comprehensive evaluation over a longer period.

### 3.6. Participant timeline

Participants are first recruited at the finish line of local parkruns on Saturday mornings during the enrolment phase (Timepoint −1). Those interested are invited to invited to the Biomechanics Laboratory of the Faculty of Sport, Technology, and Health Sciences at St Mary's University in Twickenham, London, UK, or to an in-field assessment (for the North London area). Here, they receive detailed oral and written information about the study, and if willing to proceed, sign the written informed consent form. On this day of enrolment, participants also have their feet scanned, initiating the process that customises and orders their insoles on the spot.

The allocation phase (Timepoint 0) commences post-enrolment, where participants are sent a baseline questionnaire. The information gathered from this questionnaire is used in the balanced block randomisation procedure. Upon completion of the baseline questionnaire, participants are set up to receive weekly follow-up surveys during the primary study period (Weeks 1–10). During this period, there is weekly follow-up on primary and secondary outcomes, delivery of allocated intervention group insoles projected before week 3, and weekly monitoring of adherence and adverse effects. In a case where a pair of insoles do not fit inside a participant's footwear, a fast-track adjustment, production, and shipment procedure takes place, ensuring a minimal delay of insole delivery of approximately one week.

In the control group step allocation period (Weeks 10–18), control group participants receive their customised insoles and all participants are sent a single event follow-up questionnaire at week 18. This questionnaire covers primary and secondary outcomes, as well as adherence and adverse effects.

Finally, post-market surveillance occurs at Timepoint Week 52, a year after the study's commencement. All participants receive a follow-up questionnaire assessing their post-trial experiences with the insoles, any adverse effects experienced during the year, and the long-term effects of the Zoles insoles (Fig. 3).

### 3.7. Sample size

The sample size estimation is based on the primary outcome, running-related pain. Lopes et al. [9] reported a median pain level of 3 (IQR: 2–5) among 1049 recreational runners. We expect similar pain levels at baseline which, if normally distributed, should result in a mean pain of 3 and a standard deviation of 2.22 (SD≈IQR/1.35). We forecast a 40% reduction in running-related pain in the intervention group over the course of the trial (from baseline to follow-up).

Using the formula $n = (Z_\alpha/2+Z_\beta)^2 * 2\sigma^2/d^2$, where $d$ is the expected difference between groups, to detect a 40% reduction in pain (1.2 units)

| | STUDY PERIOD | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Enrolment | Allocation | Primary Study Period | | | | | | | | | | Control group step allocation | Post-market surveillance |
| **TIMEPOINT (weeks)** | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 18 | 52 |
| **ENROLMENT:** | | | | | | | | | | | | | | |
| **Eligibility screen** | X | | | | | | | | | | | | | |
| **Informed consent** | X | | | | | | | | | | | | | |
| **Foot scanning** | X | | | | | | | | | | | | | |
| **3D printing of insoles** | X | | | | | | | | | | | | | |
| **Group allocation** | | X | | | | | | | | | | | | |
| **INTERVENTIONS:** | | | | | | | | | | | | | | |
| **Intervention** (Zoles) | | | | | ◆ | — | — | — | — | — | — | — | | ◆ |
| **Control** ("do-as-usual" until week 10) | | | | | | | | | | | | ◆ | — | ◆ |
| **ASSESSMENTS:** | | | | | | | | | | | | | | |
| **Baseline/end of study questionnaire** | | X | | | | | | | | | | | | X |
| **Outcome questionnaire** | | | X | X | X | X | X | X | X | X | X | X | X | |
| 1. Running-related pain | | | X | X | X | X | X | X | X | X | X | X | X | |
| 2. GRoC | | | X | X | X | X | X | X | X | X | X | X | X | |
| 3. Foot/footwear comfort | | | X | X | X | X | X | X | X | X | X | X | X | |
| 4. 5km completion time | | | X | X | X | X | X | X | X | X | X | X | X | |
| 5. Running-related injuries | | | X | X | X | X | X | X | X | X | X | X | X | |
| 6. Time-loss from running | | | X | X | X | X | X | X | X | X | X | X | X | |
| 7. Weekly milage | | | X | X | X | X | X | X | X | X | X | X | X | |
| 8. Weekly running exposure | | | X | X | X | X | X | X | X | X | X | X | X | |
| **ADHERENCE:** | | | | | | | | | | | | | | |
| **Adherence to intervention** | | | | | X | X | X | X | X | X | X | X | X | X |
| **ADVERSE EVENTS:** | | | | | | | | | | | | | | |
| **Adverse events from using insoles** | | | | | ◆ | — | — | — | — | — | — | — | — | ◆ |

**Fig. 3.** Participant timeline in the SPIRIT (Standard protocol items: Recommendations for interventional trials) diagram.

with 80% power at a 5% significance level, we initially require 70 participants per group [50]. Factoring in an anticipated 15% dropout, this number increases to 82 participants per group. To accommodate the pre-planned secondary subgroup analyses in the future, we further inflate the number by approximately 20%, leading to a total of 100 participants in each group. Hence, this study aims to recruit a cumulative sample size of 200 participants.

### 3.8. Recruitment

Participants are primarily targeted and approached within the local London parkrun communities. Following their routine Saturday 5-km run, a strategic engagement occurs where they will be approached by study representatives. The parkrun offers a natural setting to converse with potential participants who are already involved in regular running activities. During this engagement, participants are presented with an oral briefing about the study, its objectives, and the potential benefits of their participation. This method not only taps into a pool of runners but also allows for immediate interaction, answering any initial queries they might have. Interested runners, eager to contribute or benefit from the study, are subsequently invited to the Biomechanics Laboratory of the Faculty of Sport, Technology, and Health Sciences at St Mary's University in Twickenham, London, UK. Here, they are introduced to the broader scope of the study, the commitment expected from them, and the potential implications of the research, and ultimately a formal enrolment into the study.

### 3.9. Allocation

Upon completion of the baseline questionnaires, participants will be equally distributed (1:1 ratio) to the two comparison groups (intervention group and "do-as-usual" control group) using a balanced block randomisation method.

Specifically, the block randomisation will be stratified by sex and the specific parkrun location from which participants were recruited. This stratification ensures that each comparison group will have a representative mix of participants based on these two key variables, pre-hypothesised as potential confounders, allowing for a more controlled comparison of outcomes, and to improve external validity and generalisability of the results [51].

The process of generating the allocation sequence will be undertaken by an external who is not involved in any aspect of the trial to improve the integrity and credibility of the allocation process, as recommended [52]. The dataset provided for randomisation will only contain participant number, local parkrun location, and sex. The data will be initially separated by sex, and within each gender group, a stratification variable will be created based on local parkrun location. Block randomisation, with a block size of 4, will be conducted separately for males and females within each stratum (location) using a custom script developed in R. This approach ensures an equal or near-equal distribution of males and females within each treatment group across all locations. The randomisation process within each stratum will be automated through the script, and the resulting group assignments will be merged back into the original dataset. The R script used for the randomisation will be available as supplementary material to the primary trial report. Once the allocation sequence is generated, participants will be informed of their respective group assignments, either the intervention group (receiving the ZOLES insoles) or the control group ("do-as-usual").

### 3.10. Blinding

Given the pragmatic nature of this trial, participants are not blinded to their group allocation. The absence of a sham insole for distribution means that participants will be aware of whether they are in the intervention group (receiving the ZOLES insoles) or the control group ("do-as-usual"). Despite this, the allocation process remains concealed, ensuring that neither participants nor researchers are aware of to the allocation sequence until the appropriate intervention shall be administered. This measure is in place to prevent any potential biases that might arise from foreknowledge of group assignments [53,54]. To further the study's integrity, we will use an external outcome assessor that is blinded to group assignments [55].

### 3.11. Procedures and data collection

During the enrolment Biomechanics Laboratory of the Faculty of Sport, Technology and Health Sciences at St Mary's University (Twickenham, London, United Kingdom), consenting participants will undergo a quick foot scanning procedure ($\leq$10 s per foot) while standing in talocrural neutral position with weight evenly distributed on both legs. Scanning is conducted using the DOMEscan/IBV (Instituto de Biomecanica de Valencia, 46022, Valencia, Spain) (Fig. 2) that is controlled via the ZOLA software (Zoles ApS, Espergærde, DK-3060, Denmark), allowing for real-time design and ordering of the customised insoles tailored to each participant's unique foot structure. The ZOLA software also records and collects the scanning data and brief participant information in the form of age, weight, sex, shoe size, shoe brand and model, and type of activity (running) for which the insole should be designed. Specific medical diagnoses related to the lower extremities, such as plantar fasciitis, shin splints, etc., are also collected at this stage if known by the participants. The same procedure will be followed for the in-field enrolments in North London, where the DOMEscan foot scanner and laptop running the ZOLA software will be powered using a portable power station (606 Wh MPPT Solar Generator, ALLPOWERS, Guangzhou City, China).

Following the foot scanning, participants are sent a baseline questionnaire via email, enabling them to provide responses from the comfort of their homes and ensuring an unbiased, natural representation of their baseline pain and comfort levels. This phase ensures that participants' responses are free from the potential influence of the on-site researchers.

The trial will include prospective data collection using e-mail-distributed surveys via REDCap (Vanderbilt University, Nashville, TN, USA). Participants receive these surveys weekly for the initial 10 weeks, facilitating the collection of real-time data on their experience, pain levels, and the impact of the customised insoles for those in the intervention group. At the conclusion of this primary trial period (week 10), participants in the control group are provided with their customized insoles, marking the commencement of an additional 8-week observation period to compare intervention response between both groups (week 18). The final follow-up occurs at the 52-week mark, again via REDCap to provide insights on their long-term experiences, adverse effects, and the sustained impact of the Zoles insoles on their running-related pain and comfort.

Reminders will automatically be sent to participants at 24 h and 48 h after the original time of a follow-up questionnaire to participants failing to respond. Investigators will contact participants via telephone and SMS after another 24 h if still not responding after receiving reminders to reduce the amount of missing data.

#### 3.11.1. Data management

Every participant is assigned a unique identification number, ensuring their anonymity throughout the study in compliance with the General Data Protection Regulations (GDPR) under the Data Protection Act 2018.

Data collection, both at baseline and throughout the prospective stages, is facilitated via REDCap, a secure and robust online platform renowned for its data management capabilities [56]. This process is overseen from Department of Clinical Medicine at Aalborg University (DK-9220, Aalborg Øst, Denmark) by a dedicated data handler (CD), who remains blinded to group allocation. CD and FGL constitute the Data Monitoring Committee. A list of responding and non-responding

participants is generated weekly, wherefrom a list of non-responding participants to contact is generated.

The Study Director (FGL) will maintain a secured key to the participants' identities, stored on a two-factor secured personal drive, ensuring the capability to identify and withdraw individual data if necessary.

All data is safeguarded within GDPR compliant two-factor and password-protected systems at St Mary's University server, and on the REDCap online system. These measures ensure that the data remains inaccessible to unauthorized personnel, preserving confidentiality.

In adherence to transparency and scientific scrutiny, a fully anonymised dataset at the participant level, accompanied by the corresponding statistical code, will be made available to the public, contingent upon the requirements of the journal publishing the study's findings. This disclosure ensures the replicability and verification of the research while upholding the anonymity and privacy of all participants.

The published results will omit any information that could potentially be used to identify individual participants.

### 3.12. Statistical methods

The primary outcome; change in running-related pain from baseline to follow-up, will be calculated using negative binomial regression. Fig. 4 illustrates a hypothetical change in pain over the course of the trial, including the expected catch-up by the control group at week 18. It is important to note, however, that the between-groups analysis for difference will adjust for values reported at baseline [49,57]. Both the Global Rating of Change (GRoC) in overall daily pain and discomfort and running-related foot/footwear comfort will be calculated similarly. Injury incidence rate ratios will be estimated per 1000 h of running exposure using Poisson regression. Mean time-loss from running will be calculated using negative binomial regression. Adherence to the intervention will be descriptively analysed and presented, and adverse event due to the Zoles insoles will be presented in type and frequency. Every analysis in the main trial report will abide by the intention to treat principle, which means including all participants in the analyses, regardless of intervention adherence-signifying that participants will be analysed based on initial randomisation. In the primary trial report, all collected outcomes will be listed, and it will also be stated that the below-mentioned 'other pre-specified outcomes' will be reported in a subsequent secondary analysis publication with a clear reference to the primary trial registration.

Possible effect modifiers include time with allocated intervention due to possible logistics issues in handing over the insoles to the intervention group, as well as any last-minute needs for sizing adjustments if a pair of insoles do not fit inside a participant's footwear. Any new injury sustained during the trial period is another potential effect modifier. No potential external effect modifiers will be factored in the intention-to-treat analyses.

#### 3.12.1. Statistical methods – secondary subgroup analysis and post-market surveillance

The subsequent secondary analysis publication will hold the label "secondary and long-term follow-up analysis from a pragmatic

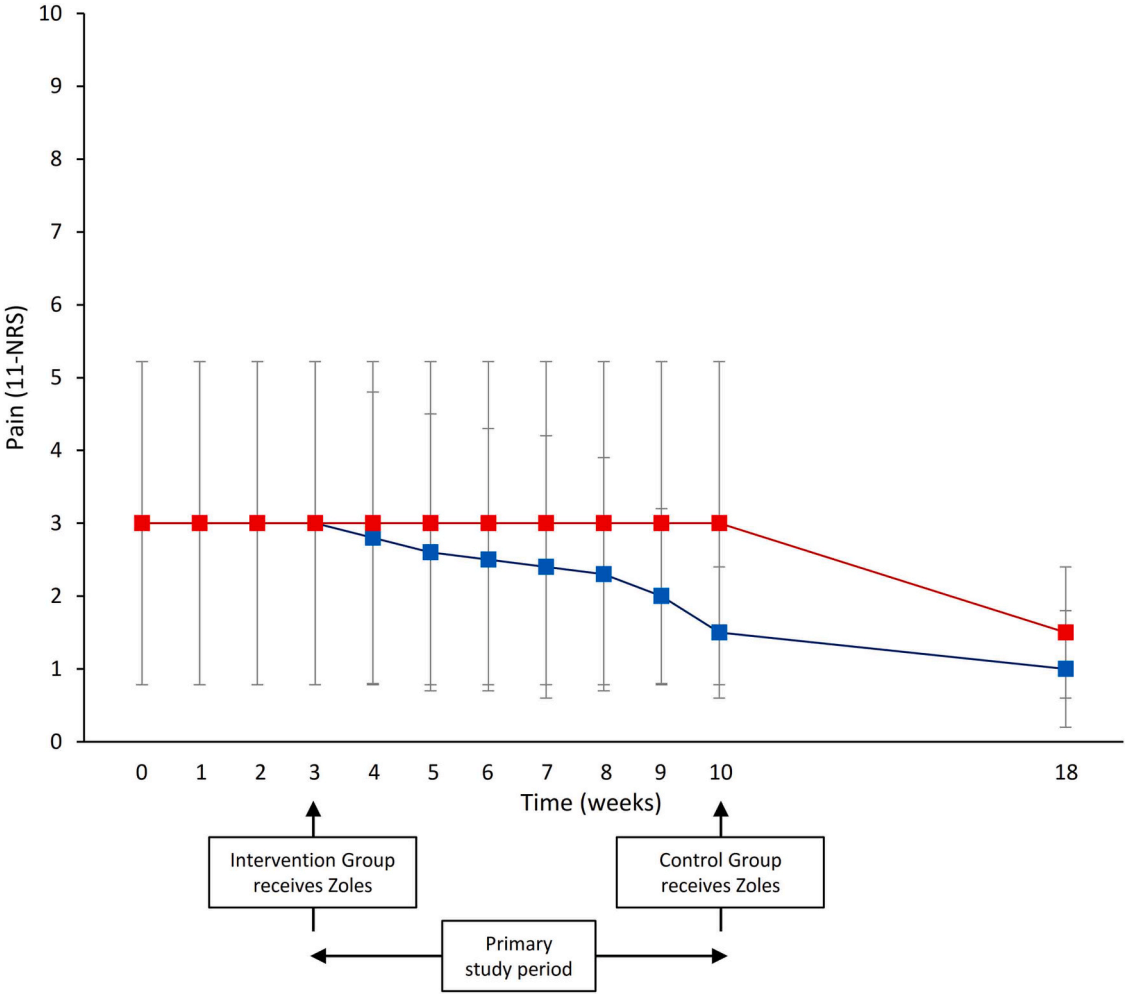


**Fig. 4.** Visualisation of change in pain score in the intervention (blue) and control group (red), respectively (Example, not based on data).

randomised controlled trial" in the title. The aims of this secondary subgroup analysis study are two-fold: First, it is to investigate the immediate therapeutic effect of Zoles insoles, focusing only on participants with clinically relevant baseline pain levels (11-NRS $\geq$ 3) [38]. Secondly, this will include our long-term post-market analysis to evaluate the long-term effects and durability of the benefits associated with the customised 3D-printed insoles one-year post-intervention.

The between-groups difference among participants with clinically baseline pain levels will be analysed similarly to the primary outcome. Subsequent regression models will, however, also be structured to comprehend the potential influence of pre-intervention expectations and post-intervention experiences, as well as adherence to the intervention on the Zoles insoles' effectiveness within this subgroup. This involves incorporating these factors as covariates in the model.

#### 3.12.2. Statistical methods – analysis population and missing data

For the primary and secondary outcomes of this trial, an intention-to-treat (ITT) analysis approach will be employed [58]. This method ensures the inclusion of all randomised participants in the analysis, irrespective of their adherence to the intervention. Participants will be analysed based on their initial randomisation. As such, any deviations from the intervention or missing follow-ups will not impact the participant's initial group classification in the analysis, as recommended by the CONSORT group [42,44].

To accommodate this approach, missing outcome data will be imputed using multiple imputations by chained equations [59]. The imputation procedure will include the following variables pre-hypothesised to potentially predict missing information: a) preceding scores relevant to the outcome in question, b) age of the participant, c) sex of the participant, d) group allocation, and d) location of recruitment (specific parkrun location).

### 3.13. Harms

Adverse events, within the context of this study, are defined as any unintended symptoms, injuries, or illnesses that participants experience while being allocated to the intervention, regardless of attribution. These could manifest anytime following the introduction of the 3D-printed insoles and until the one-year follow-up.

The recording of these events is pivotal and will be initiated by the participants through spontaneous reporting. Every interaction with participants, be it during prospective follow-ups or the post-market surveillance stage, will underscore the importance of reporting any and all adverse effects. Participants will be systematically reminded of this imperative, ensuring a thorough and comprehensive documentation of potential adverse events associated with the use of the insoles. Regular auditing planned throughout the study in the form of pre-scheduled meetings between the principal investigator (SI), study director (FGL) and local study chair (RM).

Serious adverse events are categorised according to the criteria established by the United States Food and Drug Administration [60]. The primary investigator undertakes the responsibility of evaluating these events, assessing their potential association with the intervention. Every incident is examined to discern if there is a reasonable possibility that the insoles contributed to the adverse event. In the unfortunate occurrence of serious unexpected adverse events, these will be immediately reported to the St Mary's University Ethics Sub-Committee within 7 days of the event's occurrence.

### 3.14. Ethics and dissemination

This study is anchored in stringent ethical guidelines, ensuring alignment with the World Medical Association (WMA) Declaration of Helsinki and adherence to the General Data Protection Regulations (GDPR) under the Data Protection Act 2018. Ethical approval was granted from St Mary's University Ethics Sub-Committee on August 4, 2023. Consistent with the recommendations of the CONSORT group [42] and the International Committee of Medical Journal Editors (ICMJE) [61], the study was pre-registered on ClinicalTrials.gov on September 4, 2023. To maintain transparency and ethical integrity, any modifications to the protocol will be duly updated on ClinicalTrials.gov, communicated to the University Ethics Sub-Committee, and disclosed in the published primary trial paper. Upon the study's completion, a formal notification will be submitted to the ethics committee within 30 days, confirming the end of the trial.

### 3.15. Dissemination policy

All study results, regardless of their nature, will be published in international scientific journals, assured by an unrestricted publication agreement with Zoles ApS, the insole manufacturer. Results will also be shared at both national and international conferences to ensure a broad dissemination. We are committed to adhering to the Vancouver conventions by the International Committee of Medical Journal Editors (ICMJE) for ethical authorship. The primary trial report will clearly outline, and reference all collected outcomes, directing readers to the comprehensive dissemination plan for details on unreported data or analyses. Working titles for all journal publications to be associated with this study are listed below:

1. *The effectiveness of customised 3D-printed insoles on perceived pain, comfort, and completion time among frequent Park Runners: Study protocol for a pragmatic randomised controlled trial (The ZOLES RCT)*
2. *The effectiveness of customised 3D-printed insoles on perceived pain, comfort, and completion time among frequent Park Runners: A pragmatic randomised controlled trial (The ZOLES RCT)*
3. *The effect of customised 3D-printed insoles among frequent Park Runners with high clinically relevant running-related pain: pre-planned secondary and long-term follow-up analysis from a pragmatic randomised controlled trial (The ZOLES RCT)*

## 4. Discussion

This study is designed to investigate the effectiveness of customised 3D printed insoles in alleviating pain, enhancing comfort, and improving completion time amongst recreational parkrun participants. The study is meticulously crafted, aligning with the FINER-criteria, ensuring it is Feasible, Interesting, Novel, Ethical, and Relevant [35].

Pain and niggles are common issues among active runners, and not only impede performance, but also potentially lead to a reduction in physical activity and an associated increase in premature mortality risk [6,13,15].

The potential of 3D customised insoles to mitigate these common issues stems from a grounded hypothesis supported by preliminary evidence [21,25,29], suggesting their effectiveness in pain reduction. The simplicity and accessibility of this intervention underscore its potential widespread applicability and adoption amongst the running community. If proven effective, these insoles could serve as a convenient and practical solution, addressing pain while enhancing the overall running experience.

The pragmatic approach of this trial is anchored in a design that maximises the utility and applicability of the findings. Every aspect, from the real-world setting to a diverse participant base, is tailored to ensure that the results are not only scientifically rigorous but also practically insightful. In a realm where pain is often a limiting factor, interventions that are both effective and easily integrable are pivotal [62].

### 4.1. Strengths and limitations

A major limitation of this study is the absence of blinding for the intervention, which could potentially introduce bias in the self-reported

outcomes, particularly as the primary outcome, pain, is inherently subjective. This subjectivity could amplify the Hawthorne effect, leading to potential biases that are not directly attributable to the intervention itself [63]. The implementation of a sham insole or an off-the-shelf comparator could have mitigated this limitation by providing a control for the placebo effect and the subjective improvement due to participants' awareness of the treatment. However, this study is designed with a pragmatic perspective that aligns with real-life scenarios where no sham insole would be offered to a potential customer or patient.

We acknowledge the potential impact of a 'pleasing effect' but chose not to blind the hypothesis for the participants because the primary motivation for seeking orthotics in real-world contexts is often pain mitigation. We aim for the study results to be as applicable as possible to these real-world scenarios, and thus, accepting this limitation was a considered decision to enhance the external validity and practical applicability of our findings. The study is designed to evaluate the effectiveness of the insoles in conditions that closely mimic the everyday experiences and choices of runners seeking solutions for pain relief.

Despite these challenges, the study's structure and methodology have been meticulously crafted to yield insights that are both scientifically rigorous and practically insightful, balancing between the ideal conditions for experimental control and the complexities of real-world application. Conversely, this study boasts several strengths that bolster its reliability and validity. The use of blinded group allocation sequence, external outcome assessors who are blinded to the group assignments, and an external data manager also blinded to group allocation ensures objectivity in data collection and analysis, minimizing bias. Furthermore, the recording of all outcomes in participants' natural environments, including baseline data, amplifies the real-world applicability of the findings. Participants are thus not influenced by the study personnel, ensuring the outcomes reflect the real-life effect of the intervention, enhancing the study's external validity. Additionally, the employment of a mobile scanning unit allows us to recruit participants from more distant parkrun locations, thus allowing for enrolment of participants who might not have the means to travel across London to partake in this study.

The intention to treat analysis in the primary study report ensures all participants are included in the final analysis, maintaining the randomisation benefits and offering a conservative estimate of the intervention's effectiveness. The step-wedge design addition enhances the study's robustness, allowing immediate verification of effectiveness by comparing the control group's response post-primary trial period to the intervention. The inclusion of a 52-week post-market surveillance further elevates the study's comprehensiveness, offering insights into the long-term effects and usability of the insoles.

Transparency is maintained through pre-registration of the study and the detailed description of the intervention using the TIDieR checklist [45], ensuring replicability and openness in reporting. The publication of this study protocol underscores the commitment to transparent and ethical research practices, contributing to the broader scientific discourse and public scrutiny.

Despite the limitations, we believe the robust design of this study sets a significant precedent for evaluating biomechanical interventions in real-world settings. We believe that this study design can form a framework for future research, ensuring that studies are as realistic as they are rigorous, by offering a comprehensive understanding of biomechanical interventions within their intended settings.

## Trial status

Protocol version 1, September 27, 2023. Recruitment for this study started on September 16, 2023, and concluded on October 2, 2023.

## Competing interests

No authors have any ethical or competing interests to declare in relation to this study.

## Ethics approval and consent to participate

Ethical approval was granted from St Mary's University Ethics Sub-Committee on August 4, 2023 (ID: SMU_ETHICS_2022–23_325). All participants must sign an informed consent form prior to participation.

## Consent for publication

Not applicable.

## Funding

This is an investigator-initiated trial. The funding for this study is provided by St Mary's University Faculty of Sport, Technology and Health Sciences (FSTHS) QR Funds (£5340). Zoles ApS has graciously contributed the customised 3D printed insoles for all study participants, valued at approximately £23,000. Zoles ApS is also responsible for supplying the 3D scanners (DOMEscan/IBV, Instituto de Biomecanica de Valencia, 46022, Valencia, Spain) that are used to scan the participants' feet, training and support of St Mary's staff members.

## CRediT authorship contribution statement

**Djurtoft Chris:** Data curation, Methodology, Project administration, Software, Writing – original draft, Writing – review & editing. **Ibrahim Suleyman:** Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing. **Mellor Rik:** Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing. **Lysdal Filip Gertz:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing – original draft, Writing – review & editing. **Thorborg Kristian:** Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing.

## Declaration of Competing Interest

The authors declare that they have no competing interests. Zoles ApS and affiliates have no role in the study, and are restricted from any involvement in the design of the study, execution, analyses, interpretation of data, writing of the manuscript, or in the decision to submit for publication. The Study Director has full authority of the trial administration and decision for publication.

## Appendix A

A.
SPIRIT checklist.
B.
TIDieR intervention Checklist.
C.
Intervention leaflet 1.
D.
Intervention leaflet 2.
E.
Participant consent materials.
F.
Baseline questionnaire.
G.
Weekly follow-up questionnaire.
H.
WHO Trial Registration Data Set (Version 1.3.1).

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.foot.2024.102068.

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