Title: Interactions between running volume and running pace on injury occurrence in recreational runners: A secondary analysis.

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The trial was registered in Clinicaltrials.gov (January 23, 2015) (NCT02349373) and a protocol article was published online April 23, 2016 (submitted March 14, 2015). The Ethics Committee Northern Denmark Region reviewed the study protocol and provided ethics approval (N-20140069).

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Interactions between running volume and running pace on injury occurrence in recreational runners: A secondary analysis.

Abstract

Context

The combination of an excessive increase in running pace and volume is essential to consider when investigating associations between running and running-related injury.

Objectives

The purpose of the present study was to complete a secondary analysis on a dataset from a randomized trial, to investigate the interactions between relative or absolute weekly changes in running volume and running pace on running injury occurrence among a cohort of injury-free recreational runners in Denmark.

Design

Prospective cohort study

Setting

Running volume and pace were collected during a 24-week follow-up using global positioning systems (GPS) data. Training data was used to calculate relative and absolute weekly changes in running volume and pace.

Patients or Other Participants

A total of 586 recreational runners were included in the analysis. All participants were injury-free at inclusion.

Main Outcome Measure(s)

Running-related injury was the outcome. Injury data were collected weekly using a modified version of the OSTRC questionnaire. Risk difference (RD) was the measure of injury risk.

Results
A total of 133 runners sustained a running-related injury. A relative weekly change of progression >10% in running volume and progression in running pace (RD=8.1%, 95%CI: 9.3;25.6%) and an absolute weekly change of progression >5km in running volume and progression in running pace (RD=5.2%, 95%CI: -12.0;22.5%), were not associated with a statistically significant positive interaction.

Conclusions

As coaches, clinicians and athletes may agree that excessive increase in running pace and excessive increase in running volume are important contributors to injury development, we analyzed the interaction between them. Although a statistically significant positive interaction on an additive scale in runners who progressed both running pace and running volume were not identified in the present study, readers of scientific articles should be aware that interaction is an important analytical approach that could be applied to other datasets in future publications.

Key Words: Running, training load, Running-related injury, Interaction analysis, Observational study, etiology.

Key Points

- Coaches, athletes, and clinicians may consider the following question: Is the combination of an excessive increase in running pace and an excessive increase in running volume more injurious than an excessive increase in one of them?
- The present study is the first to conduct an interaction analysis within running-related injury research. Researchers can apply this analysis to help coaches, athletes, and clinicians answer the question above.
Although the results from the present study were non-significant, the present publication highlights an analytical approach that is equally important to other well-known analytical methods, such as confounding.
In recent years, the field of running-related injury research has witnessed an increase in the body of scientific literature investigating the association between training load and running-related injury in runners. Training load in studies including runners is often quantified using variables such as volume (e.g. kilometers or hours run), pace, or frequency. However, recent reviews within the research field conclude that limited evidence exists regarding the role of training load in the etiology of running-related injury, regardless of which training variable is used as the primary exposure. The reason for this may be that the nature of running participation is both multifactorial and complex. Characteristics of this complex nature of running participation include the relationship between different training variables during running and the changes over time within these training variables. Further, the load tolerance of the musculoskeletal system may especially be challenged by sudden changes in training load. Weekly changes within training variables may therefore be of particular relevance to investigate.

To accomplish this, one may first consider the interrelation between time and variation in a training variable. This can be done by quantifying running participation and include it in an analysis as a time-varying exposure (a variable that changes status over time). Secondly, any separate analysis of an association between, e.g., changes in running volume and risk of injury, assumes that other training variables, such as running pace, are constant over time which is not very plausible. Hence, considering the interaction of time-varying training variables is necessary because it may be more plausible to assume that the two factors’ effect exceeds the effect of each considered individually. No previous studies within running-related injury research have accounted for the time-varying nature of training load as well as included the interaction between multiple training load variables while examining injury occurrence.

To date, research on changes in training variables and running-related injury has used relative changes as the primary exposure. Yet, no consensus exists on what defines a change and which magnitude of sudden changes are relevant to injury risk, and sudden changes could also be quantified as absolute measures. Therefore, future studies should...
also consider incorporating absolute changes in training variables as exposures of interest.

Investigating absolute or relative changes in training variables and the interaction of these
training variables, while accounting for the time-varying nature of change in running volume
and change in running pace, may shed new light on the role of training load in the etiology of
running-related injuries.\(^5\)

Therefore, the purpose of the present study was to complete a secondary analysis, using a
dataset from a randomized trial, to investigate the interactions between relative or absolute
weekly changes in running volume and weekly changes in running pace on running injury
occurrence among a cohort of recreational runners in Denmark, who were injury-free at
baseline. It was hypothesized that a significant positive interaction on an additive scale
existed if runners progressed both running pace and running volume.

**Methods**

The data collected during the Run Clever trial was used for the present study. Data collection
ran from April 2015 through March 2016. The Run Clever trial was registered in
Clinicaltrials.gov (January 23, 2015) (NCT02349373), and a protocol article was published
online on April 23, 2016 (submitted March 14, 2015).\(^10\) The Ethics Committee
Region reviewed the study protocol and provided ethics approval (N-20140069). All
included participants provided verbal and written informed consent. The trial
randomly allocated recreational runners to a running schedule focused on increasing the
average weekly volume (km/week) or a running schedule focused on increasing the average
weekly pace (min/km). The follow-up lasted 24 weeks, divided into an 8-week
preconditioning period and a 16-week intervention training period. The randomization was
performed after the 8 – weeks of preconditioning. A detailed description of the original
intervention is presented in the published protocol article.\(^10\)

The reporting of the present study followed the statement of strengthening the reporting of
observational studies in epidemiology (STROBE).\(^11\)
The present study was designed as a 24-week cohort study, based on participants from the original Run Clever trial. A call for study participants was distributed by contacting large companies and organizations, asking for permission to distribute information about the study through their internal communication platforms, using videos on social media, and advertising in running magazines and shops selling running gear.

The population of interest was recreational runners. A recreational runner was defined as a person averaging between 1 and 3 weekly running sessions the past 6 months. Persons conforming to the definition of a recreational runner were considered for eligibility. The eligibility criteria were healthy persons between 18 – 65 years who owned a Garmin GPS watch or an IOS- or Android-based smartphone. Persons otherwise eligible for inclusion would be excluded if one or more of the following exclusion criteria were fulfilled: injured within the past 6 months, pregnant, or vigorous physical activity contraindicated. At inclusion, the following baseline information was collected via a questionnaire: Sex, age, height, weight, running experience in years, and previous injury.

The exposure of interest was the relative or absolute change in running volume and change in running pace between 2 weeks (weekly changes). The change was defined either as a regression or a progression. Running volume was measured in kilometers and running pace was measured in minutes per kilometer (min/km). Weekly running volume was calculated in the following manner: Kilometers completed during a running session, was added to the sum of kilometers covered during running sessions the past 6-days, resulting in the continuous variable "cumulated volume the over last 7 days". Weekly running pace was calculated in the following manner: A continuous variable containing the cumulated time during running was calculated, in a manner similar to the variable "cumulated volume the over last 7 days". By dividing the cumulated volume variable with the cumulated time variable a continuous variable "average pace over the last 7 days" was calculated. Weekly changes could not be calculated for the first 2 weeks of follow-up.
Relative changes in both running volume and running pace was the ratio between 2 weeks expressed as a percentage change. Absolute changes in both running volume and running pace was the subtracted difference between 2 weeks expressed in kilometers or min/km. The fact that such changes are not fixed in time but vary makes them time-varying covariates (equivalent to states) and were regarded as such. After calculating weekly relative and absolute changes for both training variables, changes were categorized into the following exposure states:

Relative changes in pace (Regression pace or Progression pace), Relative changes in volume (Regression >10%, Regression 10%-0%, Progression 0%-10%, Progression >10%).

Absolute changes in pace (Regression pace or Progression pace), Absolute changes in volume (Regression >5km, Regression 0-5km, Progression 0-5km, Progression >5km).

The outcome was running-related injury (RRI) defined using a time-loss definition: "An injury sustained on muscles, joints, tendons and/or bones during or after running and attributed to running. The injury must have caused a training reduction (reduced distance, intensity, frequency etc.) for at least 7 days". The diagnosis of time-loss RRI was based on a standardized clinical examination carried out by one or more physiotherapists. A total of 33 physiotherapists from 18 clinics represented the diagnostic team responsible for completing clinical examinations of all injured runners. A consultation from the investigator to the physiotherapists in the individual clinics served to introduce them to the standardized examination schedule and accompanying diagnostic criteria to be used in the clinical examinations. The examination schedule and accompanying diagnostic criteria have previously been used in a prospective cohort study on novice runners.

All data collected during the study was stored in a secured back-end system, only accessible by the investigators. On a weekly basis, study participants answered online questionnaires on running-related injuries using a modified version of the OSTRC questionnaire. The modification consisted of a fifth possible answer, "cannot participate due to pain" in addition...
to the existing answering possibilities in question 4. The questionnaire was distributed by e-mail every Sunday during the entire follow-up period. Reminder e-mails were forwarded the following Monday in cases where the questionnaire had not been answered during that Sunday. All participants reporting pain and time-loss related to running received formal instructions concerning clinical examination by a physiotherapist.

All data on running participation were collected using the Global Positioning System (GPS) in Garmin GPS watches (Garmin International, Inc., Olathe, KS, USA) or IOS- and Android-based smartphones by the Help2Run application (Help2Run, Denmark). All running performed was uploaded by the participants to the secure-back end system via a personalized internet-based training diary.

The original power calculation performed prior to the collection of this data was related to the primary hypothesis of the Run Clever trial, which is presented elsewhere. Therefore, no calculation of sample size or power related to the present manuscript was performed.

A time-to-event model (generalized linear regression using the pseudo-observation method) was used to calculate the cumulative injury risk difference which was the measure of association. The duration (time) scale was kilometers of running during follow-up with the main analysis conducted at 150 kilometers. The interaction on an additive scale between relative or absolute weekly changes of running volume and running pace were calculated using a interaction term in the generalized linear regression (pseudo observation method). Interactions with a positive interaction term were considered positive and interactions with a negative interaction term were considered negative. The reference group in the analysis of relative weekly changes was regression pace + regression 10% - 0% volume. The reference group in the analysis of absolute weekly changes was regression pace + regression 0km – 5km. Estimates are presented with 95% confidence interval and p-value with $p < .05$ were considered statistically significant. A minimum of 10 events per variable included in the regression analyses was considered necessary. In addition, the presence of 5 injuries per state was chosen as the minimum to
reduce the risk of sparse data bias. Running-related injury or withdrawal from the study within the first 2 weeks due to various reasons were excluded from the analysis since it was impossible to calculate weekly changes over time amongst these runners. Included participants were right-censored in case of pregnancy, illness, non-sport accidents causing a permanent stop of running, lack of motivation to continue participation, >10% manual upload of performed running or end of follow-up. Non-running related injuries causing a permanent stop of running were considered a competing risk. All analyses were performed using STATA/SE version 13 (StataCorp LP, College Station, TX).

Results
From the original eligible Run Clever sample of 839 participants, a total of 253 were excluded due to running-related injury or withdrawal from the study due to various reasons within the first 2 weeks. The final sample of 586 participants covered a total running volume of 136.647 km, with an average volume per participant of 233 km. Participants collected data on running participation using the GPS unit in a Garmin GPS watch (7%), an iPhone (77%), an HTC smartphone (2%), a Samsung smartphone (11%), a Nokia smartphone (2%) and no device reported (1%). Of the 586 participants, a total of 133 (23%) sustained a running-related injury (FIGURE 1). Baseline characteristics of all participants and separately for uninjured and injured are presented in TABLE 1.

The risk difference associated with combinations of different relative changes in running volume and changes in running pace are presented in TABLE 2. Measures of the interaction of relative changes in running volume and running pace on an additive scale for a regression in running volume >10% and a progression in running pace and a progression in running volume <10% and a progression in running pace were, respectively; -10.4% (95%CI -30.1;9.2 : p=0.30) and -19.4% (95%CI -87.6;48.9 : p=0.58). Hence, revealing a non-statistically significant negative interaction associated with both changes. While a non-
statistical significant positive interaction were observed for a progression >10% in running volume and a progression in running pace; 8.1% (95%CI -9.3;25.6 : p=0.36).

The risk difference associated with combinations of different absolute changes in running volume and changes in running pace are presented in TABLE 2. A non-statistical significant negative interaction of absolute changes in running volume and running pace on an additive scale were observed for a regression in running volume >5km and a progression in running pace; -6.3% (95%CI -27.3;14.6 : p=0.55). Absolute changes consisting of a progression in running volume 0 - 5km and a progression in running pace; 1.3% (95%CI -36.1;38.7 : p=0.95) or a progression >5km in running volume and a progression in running pace; 5.2% (95%CI -12.0;22.5 : p=0.55), both revealed non-statistically significant positive interactions.

Discussion

Based on the notion that running volume and running pace are time-dependent variables that interact, we conducted an interaction analysis investigating the association between weekly changes in running volume and running pace on running injury occurrence. Further, separate analyses of each exposure were performed because weekly changes in running pace and running volume are possible to quantify as both relative and absolute changes. The hypothesized positive interaction on an additive scale associated with relative or absolute progressions in both running pace and running volume were not statistically supported by the results.

Previously, studies by Nielsen et al.\textsuperscript{8} and Kluitenberg et al.\textsuperscript{25} performed individual analysis investigating running volume as a time-dependent exposure, and Kluitenberg et al.\textsuperscript{25} also investigated Rate of Perceived Exertion (RPE) as a time-dependent exposure in an individual analysis. The present study analyzed volume and pace as interacting training variables that change status over time. To the best of our knowledge, this is the first study to investigate the combined effect of both training variables on RRI occurrence. This approach has practical implications when the aim is to advise runners on training load management.
Consider a runner with a weekly progression in running volume >10% and a weekly progression in running pace. The observed risk difference estimate tells us that it is 12.4% more injurious compared to a runner with a weekly regression in running volume 0%-10% and a weekly regression in pace. While the observed interaction estimate tells us that a weekly change would be 8.1% more injurious if both running volume (>10%) and running pace were progressed compared to a progression >10% in volume and regression in pace or a progression of 0%-10% in volume and a progression in pace. Related to advising runners on training load management, the estimate of interaction is therefore of particular importance. The present study investigated injury risk. Notably, the analytical approach can also be applied if the aim was to investigate performance improvements.

Several important methodological implications related to the present study downgrade the relevance of the present results to clinical practice. Instead, the present study should be viewed as a methodological contribution, which athletic trainers and sport medicine providers can direct attention to when discussing the importance of including multiple training variables in studies of running-related injury etiology. Further, future running-related injury research can also benefit from the statistical methods described in the present article. This was not the original perspective of the study but a result of the available data at the end of the follow-up. However, we still consider it plausible that a weekly progression in two training variables simultaneously challenges the load tolerance of the musculoskeletal system.

The assumption of events per variable (EPV) is the overall reason for the methodological implications. To comply with this assumption, the pseudo-observations related to risk difference estimates should not be based on fewer than 10 events per variable and 5 injuries per state, otherwise, the validity of the estimates would be questionable. The events per variable challenge, therefore, relates to the deviation in the present study from the hypothesis (H4) originally stated in the published protocol "A positive excess risk due to interaction exists between running intensity and running volume, and the effect is more pronounced for pace-related injuries with greater changes in speed than volume, while the
The effect is more pronounced for distance-related injuries with greater changes in volume than speed\(^*\). Specifically, to investigate the original hypothesis the 133 injuries observed, should have been categorized into RRI hypothesized to be associated with changes in running pace, RRI hypothesized to be associated with changes in running volume and RRI hypothesized to be associated with other risk factors.\(^8,26\) A consequence of this approach would be a further necessary reduction of included exposure states in accordance with the assumption of EPV.\(^6,22\) However, categories of both relative and absolute weekly changes in running volume and running pace need to be less coarse for future studies to identify a threshold for sudden changes in training load above which the risk of RRI significantly increases.\(^3\)

The approach underpinning the analysis should also be carefully considered when interpreting the results from the study. The present study is a secondary analysis, and the original randomization may influence the results. Further, studies have shown that measures of association between training load and RRI are modified by person characteristics such as BMI, running experience, and previous injury.\(^27-29\) The analysis in the present study could have produced different estimates of risk difference if additional variables, and thus more events of interest, had been included in the analyses. Specifically, the inclusion of relevant effect-measure-modifiers are needed in the analysis of future studies to allow for causal inference.\(^30\)

Therefore, an important focus when designing future studies should be to comply with the EPV assumption and minimize the risk of sparse data bias. More injuries (events) will allow for a more detailed categorization of the exposure variable into various groups. In addition, more injuries would allow for the adjustment of more confounders without violating the EPV assumption. Indeed, adding more variables in the analysis would strengthen the clinical relevance of the analysis. Moreover, a larger sample will allow for the inclusion of relevant effect-measure-modifiers, which, in case of low risk of sparse data bias, would improve the understanding of which change in training load is acceptable for certain runners under different circumstances.
Conclusions
As coaches, clinicians and athletes may agree that excessive increase in running pace and excessive increase in running volume are important contributors to injury development, we analyzed the interaction between them. Although a statistically significant positive interaction on an additive scale in runners who progressed both running pace and running volume were not identified in the present study, readers of scientific articles should be aware that interaction is an important analytical approach that could be applied to other datasets in future publications.

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Table 1. Baseline characteristics

Table 1. Baseline characteristics of all participants and by injury status. Descriptive results are shown as: Counts, Mean (±SD), Median. Abbreviations: BMI (Body Mass Index), IQR (Inter-Quartile range), kg (kilograms), m (meters), SD (standard deviation).

Table 2. Risk differences associated with weekly changes in running pace and running volume

Table 2. Risk differences between percentage changes and absolut changes of weekly progression (Prog) and regression (Reg) in running pace (min/km) and running volume (km). Reference cumulative incidence proportion 10.0% (relative changes). Reference cumulative incidence proportion 9.2% (absolute changes). Interaction estimates are presented in bold. Results are presented as participant sessions in exposure group counts (injury registered in session / no injury registered in session), risk difference (RD), 95% confidence interval, significance level (p). † Values are absolute percentage points.

Figure 1. Flow of participants

Figure 1. Flowchart of participants. Reasons for exclusion of participants from the original sample are listed. Running-related injury are the number of events.
Assessed for eligibility (n = 1535)

Excluded (n = 696)
- Injured within last 6 months (n = 302)
- Contraindications present (n = 23)
- Not willing to follow running schedule (n = 170)
- No IOS- or Android-based telephone (n = 8)
- On average above 3 weekly running sessions (n = 42)
- On average below 1 weekly running session (n = 92)
- Above 65 years of age (n = 3)
- Below 18 years of age (n = 3)
- Would not use GPS to collect data on running (n = 3)
- Could not be assessed for eligibility (n = 50)

(n = 839)

Excluded (n = 253)
- Non running-related injury, left the study in the first 2 weeks.
  - Lost to follow-up (n = 215)
  - Injured or other activity (n = 21)
  - Illness (n = 4)
  - Accident (n = 4)
  - Pregnant (n = 2)
- Running-related injury in the first 2 weeks of the study (n = 6)

Included (n = 586)

Not injured (n = 444)
Running-related injury (n = 133)
Non running-related injury (n = 9)
## Baseline characteristics of participants

| Participant information         | All (n = 586) | Not injured (n = 453) | Injured (n = 133) |
|--------------------------------|---------------|-----------------------|-------------------|
| Sex (female/male)              |               |                       |                   |
|                                | 365 (62.3%) / 221 (37.7%) | 269 (59.4%) / 184 (40.6%) | 96 (72.2%) / 37 (27.8%) |
| Age (years)                    | 39.2 (SD 10.0) | 38.8 (SD 9.8)         | 40.6 (SD 10.2)    |
| BMI (kg/m²)                    | 24.3 (SD 3.1)  | 24.2 (SD 3.0)         | 24.4 (SD 3.2)     |
| Running experience (years)     | 6 (IQR 3 – 12) | 6 (IQR 3 – 13)        | 6 (IQR 2 – 10)    |
| Previous injury (no/yes)       | 278 (47.4%) / 308 (52.6%) | 231 (51.0%) / 222 (49.0%) | 47 (35.3%) / 86 (64.7%) |
| Relative changes | Reg >10% volume | Reference | Prog 0% - 10% volume | Prog >10% volume |
|------------------|-----------------|-----------|----------------------|-----------------|
|                  | Sessions | RD* | 95% CI  | p       | Sessions | RD* | 95% CI  | p       | Sessions | RD* | 95% CI  | p       | Sessions | RD* | 95% CI  | p       |
| Reg pace         | 21 / 2920   | 9.8%  | -7.3;27.0 | 0.26   | 19 / 2510 | 28.6%  | -37.6;94.8 | 0.40   | 58 / 2179 | 1.4%  | -10.6;13.5 | 0.84   |
| Prog pace        | 13 / 2805   | 2.3%  | -9.3;13.9 | 0.70   | 14 / 1664 | 2.9%  | -10.1;15.9 | 0.66   | 10 / 1286 | 12.1% | -5.6;29.9  | 0.18   | 26 / 3649 | 12.4% | -1.8;26.7 | 0.09   |
| Interaction†     | -10.4% (-30.1;9.2 : p=0.30) | -19.4% (-87.6;48.9 : p=0.58) | 8.1% (-9.3;25.6 : p=0.36) |
|                  | Absolute changes | Reg >5km volume | Reference | Prog 0 - 5km volume | Prog >5km volume |
|                  | Sessions | RD* | 95% CI  | p       | Sessions | RD* | 95% CI  | p       | Sessions | RD* | 95% CI  | p       | Sessions | RD* | 95% CI  | p       |
| Reg pace         | 14 / 2168   | 9.8%  | -9.1;28.7 | 0.31   | 18 / 2639 | 14.6%  | -20.1;49.2 | 0.41   | 15 / 2584 | 3.0%  | -10.3;16.2 | 0.66   |
| Prog pace        | 12 / 2031   | 5.1%  | -7.8;18.0 | 0.68   | 15 / 2410 | 1.6%  | -11.0;14.2 | 0.80   | 25 / 2724 | 17.5% | 1.0;34.5   | 0.04   | 19 / 2751 | 9.8%  | -4.6;24.3 | 0.18   |
| Interaction†     | -6.3% (-27.3;14.6 : p=0.55) | 1.3% (-36.1;38.7 : p=0.95) | 5.2% (-12.0;22.5 : p=0.55) |