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Effects of fatigue on ground reaction forces in long-distance runners: An analysis of protocols and risk of bias

Academic dissertation submitted with the purpose of obtaining a master's degree in Sport Training, specialization in Youth Training, organized by the Faculty of Sport, University of Porto, according to the Decree-Law 76/2006, of March 24th, in the wording given by the Decree-Law 65/2018, of August 16th.

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Dedication

A minha Avó Antonia

"Não é o crítico que importa; nem aquele que aponta onde foi que o homem tropeçou ou como o autor das façanhas poderia ter feito melhor. O crédito pertence ao homem que está por inteiro na arena da vida, cujo rosto está manchado de poeira, suor e sangue; que luta bravamente; que erra, que decepciona, porque não há esforço sem erros e decepções; mas que, na verdade, se empenha em seus feitos; que reconhece o entusiasmo, as grandes paixões; que se entrega a uma causa digna; que, na melhor das hipóteses, conhece no final o triunfo da grande conquista e que, na pior, se fracassar, ao menos fracassa ousando grandemente."

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Resumo

A corrida pode ser definida como a propulsão no solo de uma perna para a outra. As forças de reação do solo (FRS) são um elemento crítico que atua nas articulações dos membros inferiores, e a presença de fadiga demonstrou modificar a biomecânica da corrida. Esta tese teve como objetivo identificar, avaliar e sintetizar as evidências atuais sobre os efeitos da fadiga em variáveis relacionadas à FRS em corredores de longa distância. As diretrizes do PRISMA 2020 foram seguidas. PubMed, Scopus, SPORTDiscus e Web of Science foram consultadas em Julho de 2022, seguido de uma busca em listas de referências e sugestões de especialistas (sem restrições de idioma ou ano). Critérios de elegibilidade: corredores de longa distância competitivos ou recreativos saudáveis, realizar corrida antes e depois de um protocolo de indução de fadiga baseado em exercícios e avaliar variáveis relacionadas as FRS durante a corrida em esteira ou solo com plataforma de força. Doze estudos (n = 299 participantes, 177 ♀ & ♂122) foram incluídos. Houve considerável heterogeneidade em relação à idade, nível competitivo, distâncias percorridas, natureza das intervenções, comparadores e métodos de teste, o que inibiu a realização de uma meta-análise. Além disso, os estudos incluídos investigaram diferentes variáveis relacionadas as FRS (por exemplo, *loading rate*, pico de força ativo [*active peak*] e *peak plantarflexor*). As variáveis relacionadas as FRS mostraram alterações relacionadas à fadiga em onze estudos, mas nem todas as alterações foram significativas. Mais consistentemente em quatro dos doze estudos, *a loading rate* aumentou e a força de pico de impacto (*Fpeak*) diminuiu significativamente após a fadiga. Três estudos forneceram dados para o *peak plantarflexor moment* e uma diminuição significativa foi observada em um estudo após fadiga (*p* 0,001; *d* 4,93 e IC [10,40 - 15,96]). O risco de viés nos estudos foi de moderado a alto, e a certeza da evidência foi julgada como muito baixa. Os efeitos da fadiga nas variáveis relacionadas ao FRS em corredores de longa distância são incertos e não está claro até que ponto podem afetar o desempenho. Mais estudos nessa área são necessários para esclarecer os efeitos da fadiga nas variáveis relacionadas ao GRF em corredores de longa distância.

PALAVRAS-CHAVE: CORRIDA; FADIGA; BIOMECANICA; CINÉTICA; FORÇA DE REAÇÃO DO SOLO

Abstract

Running can be defined as propulsion on the ground from one leg to the other. Ground reaction forces (GRF) are a critical element acting on the joints of the lower limbs, and the presence of fatigue has been shown to modify running biomechanics. This thesis aimed to identify, assess, and synthesize the current evidence on the effects of fatigue on GRF-related variables in long-distance runners. The PRISMA 2020 guidelines were followed. PubMed, Scopus, SPORTDiscus, and Web of Science were consulted in July 2022, followed by a search within reference lists and expert suggestions (no constraints on language or year). Eligibility criteria: health competitive or recreational long-distance runners, performing running before and after an exercise-based fatigue-inducing protocol, and assessing GRF-related variables during running using a treadmill or overground with a force plate. Twelve studies (n = 299 participants, 177 ♀ & ♂122) were included. There was considerable heterogeneity regarding age, competitive level, distances covered, nature of interventions, comparators, and the testing methods, which inhibited performing a meta-analysis. Moreover, the included studies investigated different GRF-related variables (e.g., loading rate, active peak force [active peak], and peak ankle plantarflexor). The GRF-related variables showed fatigue-related changes in eleven studies, but not all changes were significant. Most consistently across four of twelve studies, loading rate increased, and impact peak force (Fpeak) significantly decreased post-fatigue. Three studies provided data for peak plantarflexor moment and, a significant decrease was observed in one study following the long run (*p* .001; *d 4.93 and CI [10.40 - 15.96]*). Risk of bias in the studies was moderate to high, and certainty of evidence was judged as very low. The effects of fatigue on GRF-related variables in long-distance runners are uncertain, and it is unclear to what extent they may affect performance. Further studies in this field are needed to clarify the effects of fatigue on GRF- related variables in long-distance runners.

KEYWORDS: RUNNING; FATIGUE; BIOMECHANICS; KINETICS; GROUND REACTION FORCES

List of abbreviations

BW - Body Weight

BW.height - Body Weight times height

BW/s - Body Weight per Second

BWI - Body Weight Impulse

CI - Confidence Interval

ES - Effect Size

Fmax - Maximal Vertical Force

Fpeak - Impact Peak Force

GRADE - Grading of Recommendations Assessment, Development, and Evaluation

GRF - Ground Reaction Forces

LR - Loading rate

m/s - Meter per second

ms - Milliseconds

Nm/kg - Newton meter per kilogram

PA - Physical Activity

PICOS - Participants, Intervention, Comparators, Outcomes and Study design

PRISMA - Preferred Reporting of Systematic Reviews and Meta-Analysis

RoBANS - Risk of Bias Assessment Tool for Nonrandomized Studies

RPE - Rate of Perceived Exertion

SD - Standard Deviation

VGRF - Vertical Ground Reaction Forces

WHO - World Health Organization

Chapter I: Introduction

1.1 Rationale

Physical activity (PA) positively influences physical fitness and psychological well-being (Eime et al., 2013). PA has significant health benefits for hearts, bodies, and minds. It prevents and manages non-communicable diseases such as cardiovascular diseases, cancer, and diabetes. PA reduces symptoms of depression and anxiety (World Health Organization, 2020). Running is a popular form of PA. Running is natural. However, most runners are likely unaware of the immensely complex mechanisms that allow them to "just run" (Morin, 2018).

Running involves a cyclical series of impacts. Once gravity pulls us to earth, we apply a force on the ground that is met with an equal and opposite ground reaction force (GRF) (Napier, 2020). This force is applied to the body in a direction that consists of vertical, anterior-posterior (or propulsion-braking), and mediolateral (or side-to-side) components (Napier, 2020). The GRF is absorbed mostly within the lower limbs, although its effects extend through the entire body. How the body lands affect how the GRF is distributed through the body, and the posture of the lower limbs during the loading phase of the running cycle determines where the forces are directed (Napier, 2020). GRF include the horizontal and vertical forces during the stance phase of running. The peaks of the vertical force can be identified as the impact peak and active peak force (the first and second peak) (Wells et al., 2020). Vertical forces during running can be as high as three times the individual's body weight (Flynn & Soutas-Little, 1995; Messier et al., 2008; Scott & Winter, 1990), which can increase bone deformation. The higher the force, the faster the force is absorbed by the body (loading rate) and/or the higher the number of repetitions, the greater the bone deformation will be (Wells et al., 2020). Where these forces are felt affects how our lower limbs move in order to absorb that load. For instance, longer step lengths produce greater braking forces. Landing with knee flexion requires more strength in the quadriceps but reduces the forces felt above the knee (Napier, 2020).

The presence of fatigue has been shown to modify running biomechanics (Derrick et al., 2002). Individuals become more fatigued throughout a run, and the effectiveness of the protective mechanism can diminish (Radin, 1986). Fatigue can lead to problems in a runner's ability to generate muscular contractions, control joint motion, and ultimately one's ability to maintain desired gait patterns (Christina et al., 2001; Komi, 2000; Radin, 1986). The sense of effort is associated with neural or neuromuscular fatigue (Noakes, 2004). Neuromuscular fatigue is usually defined as strength loss after prolonged running exercises (Millet, 2011; Millet et al., 2003; Millet et al., 2011).

Changes in running patterns due to fatigue can explain, at least in part, the alteration in running economy. While neuromuscular alterations may have consequences on the running pattern (Millet, 2011; Millet et al., 2011). Previous studies have investigated the effect of maximum fatigue, induced by a running protocol, have reported modifications to gait mechanics including increases in ankle and knee flexion during the stance phase of gait (Bazuelo-Ruiz et al., 2018; Derrick et al., 2002) and changes in vertical ground reaction forces (VGRF) (Bazuelo-Ruiz et al., 2018). Fatigue alters running biomechanics in as little as 15 min of running, impacting both the casual and long-distance runner (Brown et al., 2014; Derrick et al., 2002). Furthermore, running in a state of fatigue increases tension and stress due to its repetitive cycle lower limb impact forces, potentially increasing the risk of injury (Derrick et al., 2002; Dierks et al., 2010; Tam et al., 2017).

Some studies have reported a post-fatigue increase in limb acceleration, which may or may not be accompanied by a decrease in impact forces a shift in impact forces from the heel to the forefoot (Willson & Kernozek, 1999). Other authors have revealed that VGRF values reduced with fatigue (Christina et al., 2001; Morin et al., 2011b; Nicol et al., 2007)while others have concluded higher values when runners were fatigued (Dickinson et al., 1985). The study of Christina et al. (2001) reported that the location of muscle fatigue affected impact forces. Dorsiflexor fatigue, for example, resulted in increased loading rate, whereas invertor fatigue decreased impact peaks (Gerlach et al., 2005).

In this context, it is essential to understand that foot strike pattern should be considered in such investigations because differences in joint kinetics exist between foot strike patterns (Kuhman et al., 2016; Paquette et al., 2017; Paquette et al., 2013; Stearne et al., 2014; Williams et al., 2012). Foot strike refers to the point on your foot that first hits the ground at initial contact. Between 80 and 95 % of all distance runners are rearfoot strikers who land on the rear third of their foot at initial contact. This is linked with a more dorsiflexed ankle, where the toes turn upwards towards the shin. A rearfoot strike is associated with greater vertical loading rates (Napier, 2020). Non-rearfoot strike runners tend to adopt a more posterior foot strike (Jewell et al., 2017) or a rearfoot strike at the end of a prolonged exhaustive run (Larson et al., 2011). The notions that a rearfoot strike increases injury risk and that a forefoot strike is more economical (Napier, 2020).

Different fatigue protocols have been constantly performed on treadmill and overground, and kinetics variables analyzed in short and long runs. Komi (2000) suggested that

high intensity and short duration fatigue protocols rather than conventional running tests should be used to demonstrate actual neuromuscular fatigue. According to Slawinski e Billat (2005) the intensity and duration (about 6 min) of maximal 2000 m running was insufficient to induce a modification of the elastic properties via the repeated eccentric contraction of the leg muscles. Fischer et al. (2015) used 60 s of countermovement jumps as a fatigue protocol to examine changes in running mechanics. The fatigue observed caused runners to adjust their running mechanics, with a decrease in maximal vertical force (Fmax) during fatigued running, whereas no changes in impact peak force (Fpeak) or loading rate were observed based on the combined data. Other authors analyzed biomechanical variables in short runs and found greater loading rate of the VGRF (Milner et al., 2006), greater ankle peak knee adduction (Noehren et al., 2014), greater peak hip adduction (Dierks et al., 2008; Noehren et al., 2007; Pohl et al., 2008), greater knee abduction moment (Stefanyshyn et al., 2006), and greater hip abduction moment (Eskofier et al., 2012). Significant increases in lower limb joint angles were found when fatigue occurred (Williams et al., 1991). According to García-Pérez et al. (2013) comparing ground running and treadmill running, was found an increase in contact time and a reduction in peak pressure and relative load.

During a 24-h treadmill run, the changes in running mechanics show 6% greater loading rate but lower GRF during the support phase of running (Morin et al., 2011a). Fatigue caused by five-hour hill running changed the running mechanics of VGRF. However, the amplitude of these changes was lower than those observed after an ultramarathon (Degache et al., 2013). Relative to gender, hip adduction tend to increase in female runners following a self-paced 30 min run (Noehren et al., 2012), loading rate tend to decrease following a graded exercise treadmill run to volitional fatigue in females (Gerlach et al., 2005). According to (Derrick et al., 2002; Koblbauer et al., 2014), peak ankle eversion following runs to volitional fatigue or exhaustion (~15 and 20 min) is increased in mixed populations (e.g., males and females, recreational or novice runners). Other authors have reported no changes in lower extremity joint biomechanics in female runners following a ~25 min run to fatigue (Brown et al., 2014).

Regarding the effects of fatigue on GRF, not only exclusively adult long-distance runners are exposed to the effects. Studies evaluated the effects of muscle fatigue in runners age ranged between 19 to 35 years old (Harrison et al., 2019; Savelberg et al., 2007; Silvernail et al., 2015). The literature shows significant changes in the lower extremities, kinematics,

and impact forces within a younger population (up to 35 years old) when a level of fatigue is present (Derrick et al., 2002; Dierks et al., 2010). Literature well supported that younger runner (over 22 years old) use a variety of biomechanical adaptations compared with older runners (Devita et al., 2016). Additionally, previous literature largely supports age-related changes in gait mechanics (Bus, 2003; Devita et al., 2016; DeVita & Hortobagyi, 2000; Graf et al., 2005; Judge et al., 1996; Kerrigan et al., 1998; Winter et al., 1990). However, these findings do not represent the population of children and younger runners.

To our knowledge, no systematic review has been analyzed the effects of fatigue on GRF in long-distance runners. In this sense, new scientific investigations are needed to provide providing critical information about the potential effects of fatigue-inducing protocols on GRF.

1.2 Aims

The aim of this thesis was to identify, assess, and synthesize the current evidence on the effects of fatigue on ground reaction forces (GRF)-related variables in long-distance runners. We hypothesized that ground reaction forces would increase after the fatigue-inducing protocol.

1.3 Thesis structure

This thesis was written according to the writing and presentation guidelines for dissertations of the Faculty of Sport University of Porto (FADEUP, 2009). Specifically, it is structured according to the Scandinavia model, chosen by the opportunity to develop specific competencies related to this knowledge domain and to produce scientific papers to be submitted to indexed international peer-reviewed journals with impact factor. Therefore, this thesis is formed of chapters and a scientific manuscript. In this format it is possible to guarantee that the presented work meets the conditions and requirements of publication in international peer-reviewed journals with impact factor indexed.

Chapter I presents the introduction to the thesis and provides the theoretical framework that supports the scientific investigations conducted. The relevance aspects of this study are justified considering research currently published in the scientific literature. This chapter also outlines the objectives of this study, lastly, by a description of the thesis structure.

Chapter II integrates a systematic review (ahead of print). The review article, titled "Effects of fatigue on ground reaction forces in long-distance runners: A systematic review", aimed to identify, assess, and synthesize the current evidence on the effects of fatigue on GRF-related variables in long-distance runners. Specifically, this article offers a synthesis of information about the contexts, participants, designs, methodologies, and main findings of past scientific investigations.

Chapter III is dedicated to the general discussion and the concluding remarks.

The supplements section includes one table, the PRISMA 2020 checklist, that will be submitted as a supplement during the submission of the systematic review. The references of each chapter are presented at the end of each respective chapter, according to the Scandinavian model.

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Chapter II: Review Article

Effects of fatigue on ground reactions forces in long-distance runners: A systematic review

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Abstract: *Background*: This systematic review aimed to identify, assess, and synthesize the current evidence on the effects of fatigue on GRF-related variables in long-distance runners. *Methods*: The PRISMA 2020 guidelines were followed. PubMed, Scopus, SPORTDiscus, and Web of Science were consulted in July 2022, followed by a search within reference lists and expert suggestions (no constraints on language or year). Eligibility criteria: health competitive or recreational long-distance runners, performing running before and after an exercise-based fatigue-inducing protocol, and assessing GRF-related variables during running using a treadmill or overground with a force plate. *Results*: Twelve studies (n = 299 participants, 177 ♀ & ♂122) were included. There was considerable heterogeneity regarding age, competitive level, distances covered, nature of interventions, comparators, and the testing methods, which inhibited performing a meta-analysis. Moreover, the included studies investigated different GRF-related variables (e.g., loading rate, active peak force [active peak], and peak ankle plantarflexor). The GRF-related variables showed fatigue-related changes in eleven studies, but not all changes were significant. Most consistently across four of twelve studies, loading rate increased, and impact peak force (Fpeak) significantly decreased post-fatigue. Three studies provided data for peak plantarflexor moment and, a significant decrease were observed in one study following the long run (*p* .001; *d 4.93 and CI [10.40 - 15.96]*). Risk of bias in the studies was moderate to high, and certainty of evidence was judged as very low. *Conclusions*: The effects of fatigue on GRF-related variables in long-distance runners are uncertain, and it is unclear to what extent they may affect performance. Further studies in this field are needed to clarify the effects of fatigue on GRF- related variables in long-distance runners. *Registration:* project osf.io/y497d, register https://osf.io/k5mcd.

Keywords: running; fatigue; biomechanics; kinetics; ground reaction forces.

1. Introduction

Long-distance running is one of the most popular forms of physical activity worldwide: an estimated fifty million Europeans are committed to the sport of running (Scheerder & Breedveld, 2015). People run for exercise and health purposes, to train for competitions, or just for the sole pleasure of running (Morin, 2018). *Running* is a complex and information-dense science (Machado, 2019). Running can be defined as propelling one's body mass on the ground from one leg stance to another (Morin, 2018) and its motion requires the body to work such as complex machine, with many functions simultaneously to achieve this dynamic action (Napier, 2020). It implies complex adjustments in balance, muscle activity and limbs coordination, force production by the muscles, and force transmission to the skeletal system by the tendons, plus harmonious flexions, and extensions of the three main joints of the lower limbs in the sagittal plane of motion (Alexander, 1991). When running, this machinery organizes itself so quickly that it allows a typical running step rate of about three steps per second, with ground contact phases of usually less than 300 ms, and this step cycle happens roughly 10.000 times during one hour of jogging at 10 km/h (Morin, 2018).

The force on the ground is met with an equal and opposite ground reaction force (GRF) (Napier, 2020). This force is applied to the body in a vertical, anterior-posterior, and mediolateral components, the GRF is absorbed mainly within the lower limbs (Napier, 2020). Thereby, GRF is thought to be a critical element acting on the joints of the lower limbs, and it may change the normal biomechanics and alter GRF of the knee, hip, and ankle joints (Yusof et al., 2018). The three components of the GRF and the three angular moments in X, Y and Z axis during running ground contact phase can be measured using highly sophisticated and accurate dynamometers commonly named force platforms (Vilas-Boas, 2016). The records obtained through these platforms are essential to assess factors that may affect running performance (Vilas-Boas, 2016), such as fatigue.

The presence of fatigue has been suggested to modify running biomechanics (Derrick et al., 2002). For example, after 40 min of high intensity running, instantaneous and average vertical loading rates increased (18.1% and 17.3%, respectively; moderate effect sizes [ES]), whereas a nonsignificant increase (9%, large ES) occurred in Fpeak (Clansey et al., 2012). Further, Derrick et al. (2002) investigated the effect of maximum fatigue, induced by a running protocol of 3200 m at maximal effort in recreational runners, and reported modifications to gait mechanics including increases in ankle and knee flexion during the stance phase of gait.

Giandolini et al. (2017) observed reductions in neuromuscular fatigue following a long downhill trail run in runners who exhibited lower foot strike pattern variability during the run.

Changes in running patterns due to fatigue can explain, at least in part, the alteration in the running economy, while neuromuscular alterations may affect the running pattern (Millet, 2011; Millet et al., 2011). Running-induced fatigue may increase vertical GRF as stresses on the tibia increase throughout a prolonged treadmill run (Rice et al., 2019). It can be explained by peripheral muscle fatigue when activation patterns are weakened, fatigued, or altered, compromising the ability to attenuate the impact load (Avin et al., 2015; Burr, 2011; Warden et al., 2014). Millet et al. (2009) reported lower vertical forces; both maximum vertical force (Fmax) and loading rate at impact in a case study that evaluate an experienced ultra-endurance runner who ran from Paris–Beijing in 161 days (52.8 km per day). Furthermore, running in a state of fatigue increases tension and stress due to its repetitive cycle lower limb impact forces, potentially increasing the risk of injury (Derrick et al., 2002; Dierks et al., 2010; Tam et al., 2017).

Previous systematic reviews have investigated running-induced fatigue and impact loading (Darch et al., 2022) and the effects of fatigue on kinetics during overground running (Winter et al., 2017), while others investigated gait kinetics alteration in response to long-distance running (Kim et al., 2018) and modified biomechanical variables linked to running related injury (Napier et al., 2015). The fatigue response may differ in long-distance runners compared to the participants from the previous systematic reviews. To our knowledge, no systematic review has analyzed the effects of fatigue on GRF-related variables in long-distance runners. In this sense, this systematic review aimed to identify, assess, and synthesize the current evidence on the effects of fatigue on GRF-related variables in long-distance runners. We hypothesized that ground reaction forces would increase after the fatigue-inducing protocol.

2. Methods

2.1 Study design

The protocol for this systematic review was designed in accordance with the Preferred Reporting of Systematic Reviews and Meta-Analysis (PRISMA 2020) guidelines (Page et al., 2021).

2.2 Eligibility criteria

In this study were included empirical studies published (or ahead of print) in peer-reviewed scientific journals, with no date limitation and published in any language. We adopted the Participants, Intervention, Comparators, Outcomes and Study design (PICOS) approach, and studies were included if met all the following criteria: (P) healthy competitive or recreational long-distance runners[1] of any gender, age, competitive level, and not injured upon the beginning of the study; (I) performed exercise based on fatigue-inducing protocol (e.g., based on running, shuttle running, strength training or other); (C) comparators were optional (e.g., different fatigue protocols or running distances); (O) GRF-related variables during running measured pre- and post-fatigue protocols using a treadmill or overground with a force plate, including (but not limited to) stance time, and loading rate; (S) no restrictions (e.g., randomized and non-randomized).

2.3 Information sources

The searches were performed in five phases without restriction of dates: (i) On July 13, 2022, automated searches were performed in four databases: PubMed, Scopus, SPORTDiscus and Web of Science (core collection); (ii) manual search was conducted in the reference lists of included studies; (iii) snowballing citation tracking was performed in Web of Science; (iv) the list of included articles and inclusion criteria were sent to five experts to suggest additional references, and (v) searches for errata/corrections or retractions were conducted in the included studies.

2.4 Search strategy

Boolean operators were applied to search the article title, abstract and/or keywords: ((runn*[Title/Abstract]) AND (fatigu*[Title/Abstract] OR exhausti*[Title/Abstract])) AND (kinetic* OR biomechanic* OR "ground reaction force*" OR impact* OR "vertical force*" OR "horizontal force*"). Specificities for some databases: (i) in Scopus, the search for title and abstract also included keywords; (iv) in Web of Science, the option “Topic” includes title, abstract, and keywords. No filters were applied.

[1] Only long-distance runners from 5,000 m onwards (World Athletics, 2022) were selected for this study. Other types of participants (e.g., triathletes, cyclists, and soccer players) were excluded. In the case of triathletes, the running happens after substantial fatigue from swimming and cycling, and so their running patterns may not be comparable to those of long-distance runners.

2.5 Selection process

Two authors (MS and JA) conducted the searches and independently examined all records in the databases, performed manual searches, and compared results to ensure accuracy. Disagreements were decided by a third author (FC). Automated duplicates were removed using EndNote™ 20.3 (Clarivate™), and additional manual removal of duplicates was required.

2.6 Data collection process

Two authors (MS and FC) collected all data. A third author (JA) independently revised the process. No automatic tools were used. We performed data collection in an Excel spreadsheet. WebPlotDigitizer v4.5 (Rohatgi, 2021) was used to extract data from graphs. The author (MS) independently extracted data from graphs.

2.7 Data items

Data items: (i) authors and publication date, (ii) country and continent, (iii) funding and conflicts of interest, (iv) experimental design, (v) data collection procedure (i.e., running on a treadmill or overground; fatigue protocol based on running, shuttle running, strength training or other; and performing the fatigue protocol by distance or time), (vi) characteristics of interventions (e.g., exercise mode and intensity), (vii) participant characteristics (sample size, age, sex, body height and weight, participants level). Participants levels were reclassified according to the Participant Classification Framework (McKay et al., 2022).

The unit for some GRF variables is measured by N (Newton), and they were normalized to BW (body weight) by the authors of the included studies to facilitate comparison across runners (Miller, 1990). The GRF-related variables were considered to be diverse (Munro et al. (1987)), including (but not limited to): stance time (milliseconds [ms]), loading rate (body weight per second [BW/s]), impact peak force (BW), thrust maximum (BW), average vertical GRF (BW), decay rate (BW/s), as well as changes in vertical speed (meter per second [m/s]), braking impulse (body weight impulse [BWI]), and propulsive impulse (BWI).

2.8 Study risk of bias assessment

Risk of bias of individual studies was assessed using the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS) (Kim et al., 2013), that evaluate six domains: (i) the selection of participants, (ii) confounding variables, (iii) the measurement of exposure, (iv) the

blinding of the outcome assessments, (v) incomplete outcome data, and (vi) selective outcome reporting (Kim et al., 2013). Although originally designed for non-randomized studies, this tool is sufficiently open and flexible to also be applied to randomized trials. Risk of bias was independently judged by JA and MS. FC reviewed the assessments to ensure the quality of the evaluations.

2.9 Effect measures, synthesis methods, and risk of reporting bias assessment

Conforming to the Cochrane Handbook Higgins et al. (2019b), meta-analyses can be computed with as little as two studies Valentine et al. (2010), analyses were planned if ≥3 studies are available (Garcia-Hermoso et al., 2019; Jackson & Turner, 2017; Moran et al., 2018a). Means and standard deviations (SD) from pre and post values were planned to compute ES (i.e., Hedges *g*) for outcome measures in the intervention (fatigue) and control (non-fatigue) conditions. The DerSimonian and Laird random-effects model was planned to account for differences between studies that might affect the results (Deeks et al., 2008; Kontopantelis et al., 2013). The ES values were planned to be presented with 95% confidence intervals (95% CIs). Calculated ES would be interpreted using the following scale: <0.2 trivial, 0.2–0.6 small, >0.6–1.2 moderate, >1.2–2.0 large, >2.0–4.0 very large, >4.0 extremely large (Hopkins et al., 2009). In studies that included more than one intervention condition and only one control condition, the sample size in the control condition would be proportionately divided to facilitate comparisons across multiple conditions (Higgins et al., 2008).

The impact level of heterogeneity would be assessed using the I^2 statistics, with values of <25%, 25–75%, and >75% representing low, moderate, and high levels of heterogeneity, respectively (Higgins & Thompson, 2002). The risk of publication bias would be explored for continuous variables (≥10 studies per outcome) (Egger et al., 1997; Higgins et al., 2019a; Sterne et al., 2011) using the extended Egger's test (Egger et al., 1997). To adjust for risk of publication bias, a sensitivity analysis would be conducted using the trim and fill method Duval e Tweedie (2000), with L0 as the default estimator for the number of missing studies (Shi & Lin, 2019). All analyses would be performed using the Comprehensive Meta-Analysis Software (Version 2, Biostat, Englewood, NJ, USA). A p value of ≤0.05 will be accepted as statistically significant.

2.10 Additional analyses

2.10.1 Moderator analyses

Potential sources of heterogeneity possible to influence the effects of fatigue would be selected *a priori*. Although the exact number of moderators may only become evident after all studies eligible for inclusion have been identified. As responses to fatigue may be affected by (i) running speed, (ii) type of running surface (treadmill or overground), (iii) fatigue protocol (based on running, shuttle running, strength training or other), and (iv) participant characteristics (sample size, age, sex, body height and weight, and competitive level), these factors would be considered as potential moderator variables.

When appropriate, moderator analyses would be analyzed using the median split technique (Moran et al., 2019; Moran et al., 2018b; Moran et al., 2017). The median would be calculated if at least three studies provided data for a given moderator category. Worthy of note, when two experimental groups (with the same information for a given moderator) would be included in a study, only one of the groups would be considered to avoid an augmented influence of the study on the median calculation. Additionally, instead of using a global median value for a given moderator (e.g., median age, derived from all included studies), median values would be calculated considering only those studies that provide data for the outcome being analyzed. When appropriate, instead of the median split technique, we would use a logically defensible rationale (usually with solid physiological and biomechanical basis) to subgroup division.

2.10.2 Sensitivity analyses

We would perform sensitivity analyses to assess the robustness of the summary estimates (e.g., p-value, ES, I^2). To examine the effects of each result from each study on the overall findings, results would be analyzed with each study deleted from the model once (automated leave-one-out analysis).

2.10.3 Meta-regression

A multivariate DerSimonian and Laird random-effects model meta regression would be conducted to verify if any of the moderators predicted the effects of fatigue on GRF-related variables. The computation of meta-regression would be performed with at least 10 studies per moderator (Higgins et al., 2019a).

2.11 Certainty assessment

Two authors (MS and JA) used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method to assess the quality of evidence. Five domains were considered: risk of bias, inconsistency, indirectness, imprecision, and publications bias (Guyatt et al., 2011).

3. Results

3.1 Study selection

The initial search retrieved a total of 6,600 results (PubMed: 800 articles; Scopus: 3,909; SPORTDiscus: 402; Web of Science [core collection]: 1,489). Removal of 2,079 duplicates resulted in 4,521 records to be screened. The screening titles and abstracts resulted in the exclusion of 4,492 records. Therefore, 29 records were eligible to full text analysis, of which 17 studies were excluded: seven studies were performed with non-long-distance runners (Chaudhari et al., 2020; Christina et al., 2001; Degache et al., 2013; Encarnación-Martínez et al., 2022; Girard et al., 2011; Nicol et al., 1991; Pirscoveanu et al., 2021); the study of Clansey et al. (2012) measured pre- and post-fatigue during walking and not during running; two studies did not compare pre- and post-fatigue (Mann et al., 2015; Morin et al., 2011b); four studies did not measure GRF-related variables (Encarnación-Martínez et al., 2020; Giandolini et al., 2016; Sasimontonkul et al., 2007; Vercruyssen et al., 2016); and three studies measured GRF-related variables by accelerometers, pressure mat, and overground (rubberized track) and treadmill, without using a force plate (Clansey et al., 2016; Degache et al., 2016; García-Pérez et al., 2014).

Twelve records met the eligibility criteria for the review (Bazuelo-Ruiz et al., 2018; Brown et al., 2014; Degache et al., 2013; Fischer et al., 2015; Gerlach et al., 2005; Hashish et al., 2016; Jafarnezhadgero et al., 2019; Melaro et al., 2021; Morin et al., 2011; Paquette & Melcher., 2017; Tam et al., 2017; Yu et al., 2021). No additional eligible publication was identified from the references list of the selected studies or through snowballing citation tracking. We contacted five experts and obtained three responses, with only a single article being suggested, but which had already been excluded during our screening. We found no retractions or errata for the included studies. Two studies had a pre-registered protocol (Jafarnezhadgero et al., 2019; Morin et al., 2011a) that were considered for assessing risk of bias. Figure 1 shows the detailed information regarding the literature search.

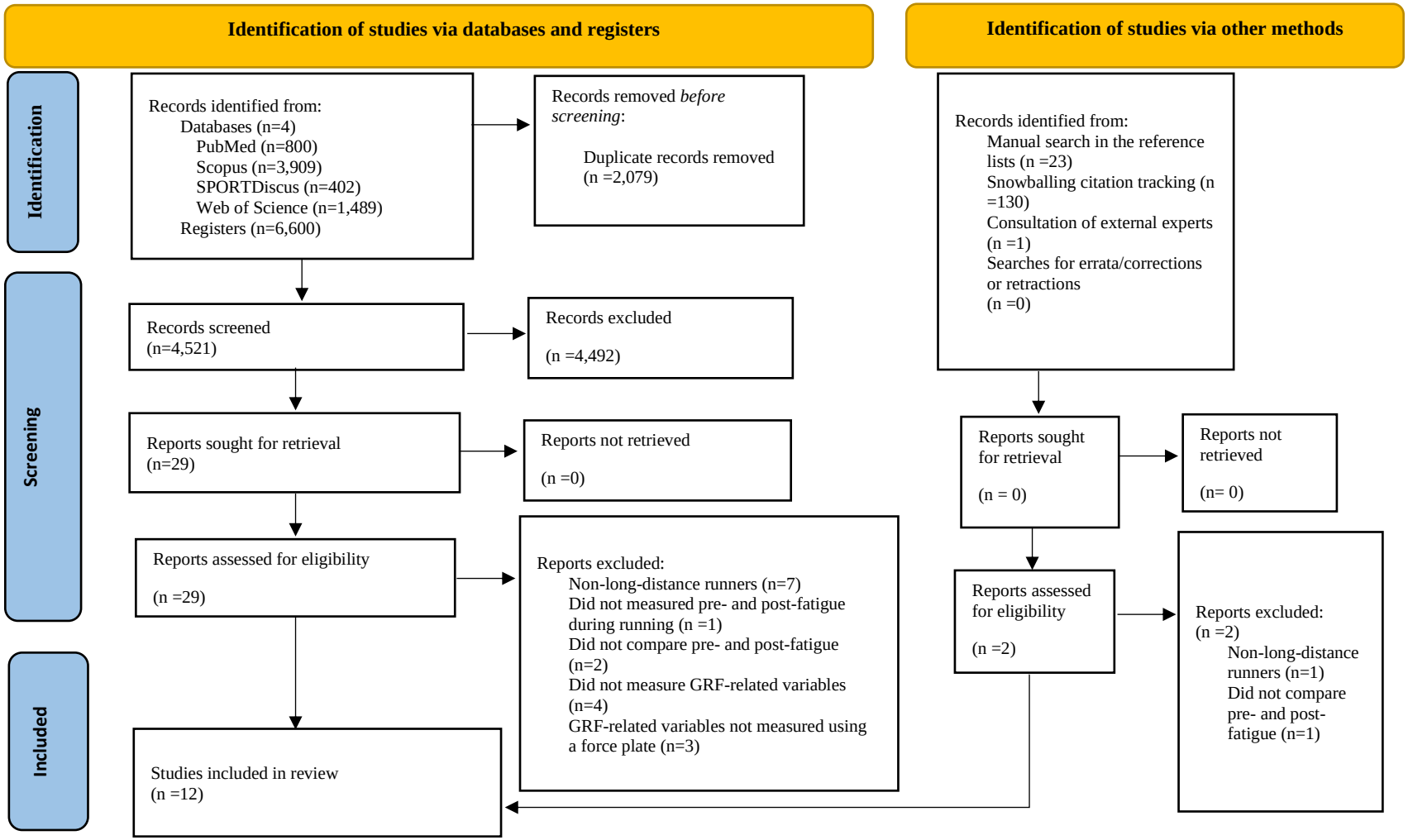


Figure 1 Flow diagram of the study selection process.

3.2 Study characteristics

The twelve selected studies included 299 participants (59.2% ♀ & 40.8% ♂) aged 18 to 55. Overall, long-distance runners performed distinct types of fatigue protocols (e.g., 10 km and 24h run) on the ground and on the treadmill, with significantly varying distances (i.e., from 1.3 ± 0.2 km to 153 ± 15 km). Participants' weekly training mileages varied (20 to 50 km), denoting a highly heterogeneous sample. The participant's characteristics can be found in Table 1, while appendix 3 provides the criteria for reclassifying participant levels according to the Participant Classification Framework (McKay et al., 2022).

Table 1. Sample sizes and participant characteristics of each included study in mean ± SD.

Included study	Sample size, *N* Competitive level*	Sex, ♀♂	Age , y	Body weight, kg	Height, cm
Bazuelo-Ruiz et al. (2018)	57 *Tier 1* *(Recreationally Active)*	♀29 ♂28	♀32 ± 8 ♂34 ± 10 Total: 33 ± 9	♀59.3 ± 8.1 ♂72.6 ± 6.8 Total: 65.8 ± 10.0	♀166 ± 0.1 ♂176 ± 0.1 Total: 171 ± 0.1
Brown et al. (2014)	20 *Tier 1* *(Recreationally Active)*	♀20	29 ± 6	56.8 ± 5.2	160 ± 0.1
Degache et al. (2013)	8 *Tier 2* *(Trained/Developmental)*	♂8	42.5 ± 5.9	76.9 ± 7.0	177.8 ± 5.9
Fischer et al. (2015)	11 *Tier 2* *(Trained/Developmental)*	♀6 ♂5	Total: 29 ± 5	Total: 70.5 ± 11.3	Total: 172 ± 0.8
Gerlach et al. (2005)	88 *Tier 2* *(Trained/Developmental)*	♀88	36.5 ± 9.2	59.0 ± 7.1	164.1 ± 6.3
Hashish et al. (2016)	21 *Tier 1* *(Recreationally Active)*	♀12 ♂9	Total: 26.6 ± 4.4	Total: 65.3 ± 11.9	Total: 170 ± 0.2
Jafarnezhadgero et al. (2019)	22 *Tier 1* *(Recreationally Active)*	♀22	24.1 ± 5.6	63.2 ± 12.1	165.6 ± 10.4
Melaro et al. (2021)	13 *Tier 2* *(Trained/Developmental)*	♂13	32.1 ± 9.7	73.6 ± 11.9	180 ± 0.01
Morin et al. (2011a)	10 *Tier 3 (Highly Trained/National level)*	♂10	40.4 ± 6.5	75.0 ± 7.9	176.9 ± 5.8
Paquette and Melcher (2017)	12 *Tier 2* *(Trained/Developmental)*	♂12	33 ± 10	74.4 ± 12.0	180 ± 0.008
Tam et al. (2017)	22 *Tier 2* *(Trained/Developmental)*	♂22	WT (12) 27.9 ± 3.1 T (10) 25.1 ± 4.9	WT 73.8 ± 10.9 T 78.5 ± 8.7	WT 180 ± 0.7 T 180 ± 0.7
Yu et al. (2021)	*Tier 0* *(Sedentary)*	♂15	23.8 ± 0.8	72.2 ± 6.0	176 ± 2.8

Legend: N/A = Information not available; BMI = body mass index; WT = Well-trained; T = Trained. * Competitive level was re-coded using the Participant Classification Framework (McKay et al., 2022).

Different comparisons were performed in eight of twelve studies. Bazuelo-Ruiz et al. (2018) analyzed men and women separately, and Brown et al. (2014) in dominant and non-dominant limbs; we selected both results. Degache et al. (2013) divided the data by speed (10, 12 and 14km/h), and Fischer et al. (2015) divided it into a slower, self-selected, and faster pace;

for our reporting within the review, we selected the highest speed or highest intensity due to the proximity to critical speed (Poole et al., 2016). Hashish et al. (2016) divided the rearfoot strike, midfoot strike, and forefoot strike; for purposes of this review, we selected the rearfoot strike because 80-95% of all distance runners are rearfoot strikers who land on the rear third of their foot at initial contact (Napier, 2020). Jafarnezhadgero et al. (2019) analyzed runners wearing neutral and motion control shoes; we extracted the results from the neutral shoe group in order to avoid any possible interference caused by the motion control shoe. Tam et al. (2017) divided the participants into trained, well-trained, shod, and barefoot, and we reported results of trained and well-trained runners. Finally, Yu et al. (2021) reported the data on the frontal, sagittal and transversal planes of motion, we extracted the data from the sagittal plane because running is done mainly in the sagittal plane (Napier, 2020). Appendix 2 shows the full studies characteristics. The remaining four studies (Gerlach et al., 2005; Melaro et al., 2021; Morin et al., 2011; Paquette & Melcher, 2017) reported the results pre- and post-fatigue without any comparisons.

All studies reported most variables related to GRFs as peak values (See appendix 2). Peak kinetic values were extracted from the stance phase of each individual trial. Peak joint moments and impulse were reported in body Nm/kg (body mass). The first impact peak on the vertical force, related to heel contact was defined as Fpeak. Loading rate was computed as the average slope from 10% to 90% of the Fpeak. The Fmax was the intensity of the Fpeak. The braking and propulsive forces were obtained from the antero-posterior component. The ankle, knee, and hip joint angular kinetic variables were expressed in the shank, thigh, and pelvis coordinate systems, respectively. Overall, caution is needed when analyzing the results and generalization of findings is unwarranted, as the studies were substantially heterogeneous in terms of sample, intervention, and outcomes.

3.3 Risk of bias in individual studies

Considering the participants selection, a low risk of bias was identified in eight studies (Bazuelo-Ruiz et al., 2018; Brown et al., 2014; Degache et al., 2013; Fischer et al., 2015; Jafarnezhadgero et al., 2019; Morin et al., 2011a; Tam et al., 2017; Yu et al., 2021), and four studies were identified with a high risk of bias (33.3%) when analyzed in groups due to the heterogeneity of participants age and training level (e.g., weekly mileage; competition standard) (Gerlach et al., 2005; Hashish et al., 2016; Melaro et al., 2021; Paquette & Melcher,

2017). Nine studies (75%) reported a low risk of bias when analyzing the confounding variables issue (Bazuelo-Ruiz et al., 2018; Degache et al., 2013; Fischer et al., 2015; Gerlach et al., 2005; Jafarnezhadgero et al., 2019; Morin et al., 2011a; Paquette & Melcher, 2017; Tam et al., 2017; Yu et al., 2021). The remaining three studies (25%) (Brown et al., 2014; Hashish et al., 2016; Melaro et al., 2021) presented high risk due to self-selected pace without predetermined distance, the fatigue protocol varied substantially, and in habitual running technique, there was considerable dispersion in how each runner technically adapted to the new demands. Bias due to measurement outcomes was low in all studies. Likewise, despite no blinding for outcome assessments, testers were unlikely to interfere with the assessments in all studies.

The primary concerns with the risk of bias were observed in the incomplete outcome data and selective outcome reporting, both representing unclear bias in ten studies (83%) (Bazuelo-Ruiz et al., 2018; Degache et al., 2013; Fischer et al., 2015; Hashish et al., 2016; Jafarnezhadgero et al., 2019; Melaro et al., 2021; Paquette & Melcher, 2017; Tam et al., 2017; Yu et al., 2021) presented unclear results in both domains, and (Brown et al., 2014; Gerlach et al., 2005) presented unclear bias in incomplete outcome data and selective outcome reporting, respectively. According to Kim et al. (2013), most of the examined studies were classified into this category. In our review, they were identified as unclear due to no reporting of sample flow from recruitment to analysis. It is, therefore, possible that there are relevant incomplete outcome data. For this same domain, Gerlach et al. (2005) presented a low risk of bias while Morin et al. (2011a) presented a high risk, as it reported only 10 of the 30 participants who were described in the registered protocol.

Considering the selective outcome reporting, ten studies had no pre-registered or pre-published protocol to compare with the manuscript (Bazuelo-Ruiz et al., 2018; Brown et al., 2014; Degache et al., 2013; Fischer et al., 2015; Gerlach et al., 2005; Hashish et al., 2016; Melaro et al., 2021; Paquette & Melcher, 2017; Tam et al., 2017; Yu et al., 2021), and the trial registration was retrospective in one study (Jafarnezhadgero et al., 2019). Additionally, two studies were identified as having a high risk of bias: Brown et al. (2014) beyond the lack of a pre-registered protocol, the methods stated that peak values for kinetic variables would be presented but means and SDs were presented instead; in the study of Morin et al. (2011a) the entire groups of participants and groups of outcomes were absent in the manuscript but had been described in the pre-registered protocol. Figure 2 synthesizes the risk of bias assessments.

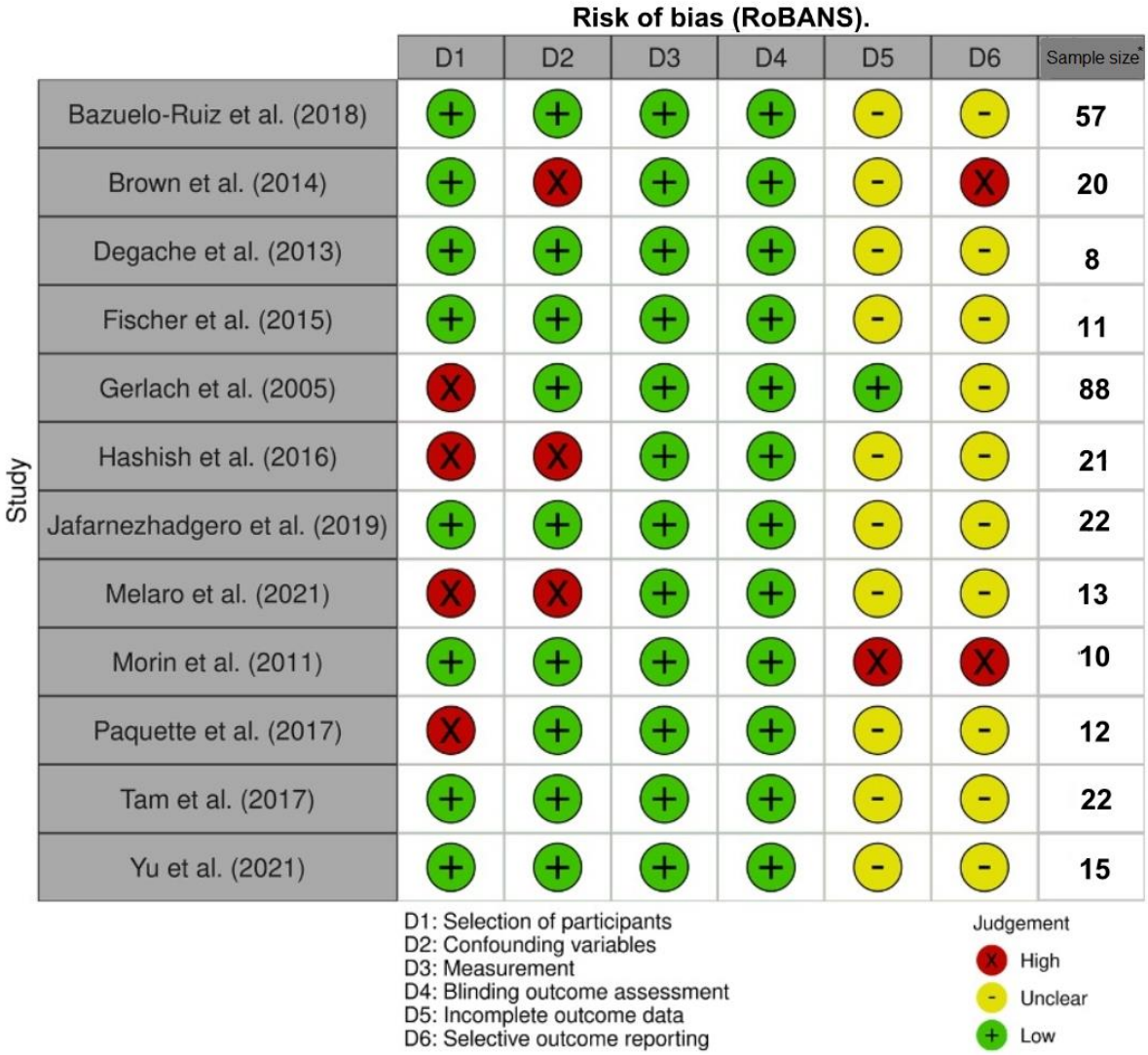


Figure 2. Risk of bias assessments (RoBANS). *Legend*: * Analyzed sample and not the final sample.

3.4 Results of individual studies

Twenty-one GRF-related variables (assessed using a force platform) were investigated in the twelve included studies that will be discussed in the following titles-subtitles.

Hashish et al. (2016) reported their data on a plot, and the values were in median, 1º and 3º quartiles. The main author (MS) extracted the graphs using WebPlotDigitizer, and then the data was converted into mean and SD using the Estimation of a Sample's Mean and Variance from Its Median and Range (Hozo et al., 2005). Two articles (Jafarnezhadgero et al., 2019; Tam et al., 2017) reported their data in plots that we could not extract, and we requested the data, but we received only one response saying it was not possible to share the data with us. All values of the results of this systematic review are presented in mean and SD.

3.4.1 Kinetics

Kinetic changes were reported in nine studies. However, not all changes were significant. For instance, in the studies of Bazuelo-Ruiz et al. (2018) and Gerlach et al. (2005), active peak did not change significantly post-fatigue. Fpeak, Fmax and active peak were analyzed more than once by different studies which will be discussed in the following paragraphs. Kinetics variables reported in the included studies can be found on Table 2.

Table 2. Kinetics variables reported in the included studies.

Kinetics (BW)	Studies
Loading rate (BW/s)	Bazuelo-Ruiz et al. (2018); Degache et al. (2013); Fischer et al. (2015); Gerlach et al. (2005); Hashish et al. (2016); Jafarnezhadgero et al. (2019); Morin et al., (2011); Paquette & Melcher (2017), and Tam et al. (2017)
Active peak	Bazuelo-Ruiz et al. (2018) and Gerlach et al. (2005)
Fmax	Degache et al. (2013); Fischer et al. (2015) and Morin et al., (2011)
Fpeak	Bazuelo-Ruiz et al. (2018); Fischer et al. (2015); Gerlach et al. (2005), and Jafarnezhadgero et al. (2019)
Lateral and vertical GRF	Tam et al. (2017)
Peak braking force and peak propulsive force	Bazuelo-Ruiz et al. (2018)
Peak negative free moments (BW.height)	Jafarnezhadgero et al. (2019)

When comparing pre- and post-fatigue, the loading rate increased predominantly post-fatigue (Jafarnezhadgero et al., 2019; Morin et al., 2011a; Paquette & Melcher, 2017; Tam et al., 2017). On the other hand, loading rate decreased after fatiguing running (Bazuelo-Ruiz et al., 2018; Fischer et al., 2015; Gerlach et al., 2005; Hashish et al., 2016). There were no significant changes in the loading rate evaluated at three different speeds by Degache et al. (2013).

Fpeak significantly reduced in the fatigue state (Bazuelo-Ruiz et al., 2018; Fischer et al., 2015; Gerlach et al., 2005) and increased (Jafarnezhadgero et al., 2019) when pronated runners used neutral shoes. Fmax decreased significantly (Fischer et al., 2015; Morin et al., 2011a) at fastest speed and at impact post 24h treadmill run, respectively. However, decreased significantly only at 10km/h the slower speed analyzed (Degache et al., 2013). The results of Bazuelo-Ruiz et al. (2018) and Gerlach et al. (2005) showed no significant changes for the active peak post-fatigue**.** There was no main effect of fatigue on foot peak negative free moments when the authors analyzed runners with neutral shoes.

It is important to consider that the variance in the results may have been due to the high heterogeneity between studies and participants.

3.4.2 Joint kinetics

Joint kinetics showed a moderation reduction in peak ankle plantarflexor moment (Melaro et al., 2021) and a significant reduction post-fatigue (Hashish et al., 2016). Peak hip abduction moment showed a moderation reduction (Yu et al., 2021). All joint kinetic variables in the study of Brown et al. (2014) and Paquette & Melcher (2017) remained unchanged post-fatigue. Joint kinetics variables reported in the included studies can be found in Table 3.

Table 3. Joint kinetics variables reported in the included studies.

Joint kinetics (Nm/kg)	Studies
Peak of the ankle invertor, knee extensor, and knee adductor moments	Brown et al. (2014)
Peak ankle plantarflexor moment	Brown et al. (2014); Hashish et al. (2016), and Melaro et al. (2021)
Peak of the ankle joint moment, hip joint moment, and knee joint moment	Yu et al. (2021)
Peak hip extensor moment	Brown et al. (2014) and Melaro et al. (2021)
Peak hip abduction moment	Brown et al. (2014) and Paquette & Melcher (2017)
Peak moment of the knee abduction. Knee abduction impulse and hip abduction impulse	Paquette & Melcher (2017)

Three studies reported the peak joint moment of the ankle plantarflexor and hip and knee extensor. Brown et al. (2014) found no interactions between pre- and post-fatigue state, Hashish et al. (2016) reported a significantly reduction, and a moderate reduction was found in peak plantarflexor moment (Melaro et al., 2021). Knee and hip extensor remained unchanged following the long run (19 ± 6 km) (Melaro et al., 2021). Paquette and Melcher (2017) reported no significant changes in the peak joint moment variables in their study. In the ankle, knee, and hip peak joint moments in the sagittal plane (Yu et al., 2021), a moderation reduction was observed when fatigue occurred in the peak hip joint moment, but the other values did not significantly change.

3.5 Synthesis of results

Interventions were performed in twelve different fatigue-inducing protocols based on running (by distance) ranging from 1.3 ± 0.2 km (Hashish et al., 2016) to 153 ± 15 km (Morin et al., 2011a). Most of them ran at the self-select and preferred long-run pace (Fischer et al., 2015; Hashish et al., 2016; Melaro et al., 2021; Morin et al., 2011a; Paquette & Melcher, 2017; Yu et al., 2021). Based on strength training (e.g., vertical rebound jump series [60s) of maximal countermovement jumps) (Fischer et al., 2015).

3.5.1 Kinetics

In the study of Bazuelo-Ruiz et al. (2018) impact peak (pre- 1.95 ± 0.31, post- 1.90 ± 0.31) and loading rate (pre- 88.14 ± 25.82, post- 83.97 ± 18.83) were significantly reduced in the group of females post-fatigue. In the group of males there were no significant differences in these variables (impact peak, pre- 1.91 ± 0.31, post- 1.88 ± 0.32 and loading rate, pre- 75.02 ± 17.48, post- 74.26 ± 19.90). Degache et al. (2013) showed that five-hour hilly running modified the running step mechanics of runners towards a lower vertical ground reaction force (% change: loading rate -1.7 ± 15.6; Fmax 1.00 ± 11.29), these results showed that fatigue effects were not more pronounced at higher speed. The study of Fischer et al. (2015) showed a decrease in all GRF (% change: Fmax -2.8 ± 4.3 , Fpeak -9,6 ± 12 and loading rate -3.6 ± 14) and small ES in the fastest speed. In the study of Hashish et al. (2016), rearfoot strike runners demonstrated reductions loading rate (pre-fatigue 187.3 ± 11.5 and post-fatigue 166.9 ± 14.4).

Gerlach et al. (2005) indicated the magnitude and loading rate of the impact forces both significantly decreased (6.6% and 11.8%, respectively) with fatigue, whereas the active peak magnitude did not change. The results of Jafarnezhadgero et al. (2019) indicated that Fpeak ($p < 0.05$; 18 ± 28%) and loading rate ($p < 0.05$; 15 ± 22%) increased after fatiguing running with neutral shoes. According to study of Tam et al. (2017) loading rate increased after fatigue in trained runners when barefoot (p = .008) with no changes in the shod state, or in the well-trained group either shod or barefoot. Morin et al. (2011a) in overall, Fmax decreased significantly ($p < 0.05$) with time, with high interindividual variations (% changes: −4.42% ± 5.76%) and a medium ES of 0.36 (Cohen, 1988). The Loading rate at impact, which only tended to increase from 55.8 ± 13.1 to 59.2 ± 11.0 between pre-24TR and post-24TR ($p = 0.062$). In the study of Paquette and Melcher (2017) loading rate was 6% higher after the run ($p < .05$) but this difference had a small ES, $d = .32$ (Hopkins, 2016).

3.5.2 Joint kinetics

During non-fatigued and fatigued running, there were no differences and no interactions detected in hip, knee, or ankle kinetics between dominant and non-dominant limbs, respectively (Brown et al., 2014) and also in the peak moment of the hip abduction and knee abduction, knee abduction impulse and hip abduction impulse (Paquette & Melcher, 2017). Melaro et al. (2021) showed moderate reductions in peak plantarflexor moment were observed following the long run (pre-fatigue -2.84 ± 0.47 to post-fatigue -2.64 ± 0.47), and all other peak

joint moment remained unchanged. Hashish et al. (2016) showed a significant reduction post-fatigue in peak ankle plantarflexor (pre- 106 ± .5 and post-fatigue 93 ± 34). Yu et al. (2021) demonstrated that the lower limb biomechanics significantly changed in the sagittal plane when fatigue occurred, the peak moment of the hip joint decreased significantly (pre- 0.75 ± 0.18) compared to post-fatigue (0.56 ± 0.11).

Given the heterogeneity of the groups in terms of competitive level, distances covered, nature of interventions and comparators, and nature of outcomes collected, it was not possible to carry out the planned meta-analyses.

3.6 Certainty of evidence

The certainty of evidence for each outcome could not strictly follow the GRADE approach since meta-analyses were not performed. However, a GRADE-based judgment shows that: (i) risk of bias in the studies was moderate to high; (ii) there was high heterogeneity of samples, interventions, outcomes, and specificity of evaluations (i.e., high inconsistency); statistical impact heterogeneity was not calculated as meta-analyses were not performed; (iii) likely reduced indirectness, as a result of the eligibility criteria; (iv) imprecision was not calculated, since it was not possible to perform a meta-analysis; (v) risk of publication bias – the same as described in the previous domain. Additionally, most studies were non-randomized and there was no demonstration of large magnitude effects, no establishment of dose-response relationships, and there wasn't always adequate control for confounding factors. As a result, we judged the certainty of the evidence to be very low.

4. Discussion

4.1 Summary of evidence

This review aimed to identify, assess, and synthesize the current evidence on the effects of fatigue on ground reaction forces (GRF)-related variables in long-distance runners. Twelve studies (n = 299 participants, 177 ♀ & ♂122) were included. Many GRF-related variables were investigated in included studies (e.g., loading rate, active peak, and peak ankle plantarflexor). There was considerable heterogeneity regarding age, competitive level, distances covered, nature of interventions, comparators, specificity of the outcomes and the testing methods, which inhibited performing meta-analysis. We hypothesized that ground reaction forces would increase after the fatigue-inducing protocol, but the available data did not allow confirming our

hypothesis. As a result of the extensive heterogeneity between studies, caution is needed when interpreting or generalizing the results of individual studies in this area of research.

4.2 Kinetics

When comparing pre- and post-fatigue, our review showed that 44% of the studies showed an increase in loading rate, but another 44% showed a decrease, which inhibits a strong conclusion. Nevertheless, the study of Jafarnezhadgero et al. (2019) reported that fatigue could be a relevant factor in increasing the loading rate in female pronated runners that do not wear shoes appropriate for their foot alignment.

Post a 24h treadmill run, subjects could no longer control the falling of their lower limbs onto the ground, which resulted in a heel impact shock (loading rate) that tended to increase (with high intrasubject variability) (Morin et al., 2011a).

Literature shows agreement with increased loading rate in previous studies (Milner et al., 2006; Nicol et al., 1991). The progressive increases seen in loading rate magnitudes with greater levels of fatigue indicate that runner's ability to cushion impact becomes diminished (Clansey et al., 2012). Previous authors also associated increased loading rates in participants with a history of tibial and metatarsal stress fractures (Zadpoor & Nikooyan, 2011). The study of Clansey et al. (2012) investigated the acute effects of progressive fatigue on running mechanics associated with tibial stress fracture risk. Both instantaneous and average vertical loading rates were shown to significantly increase after 40 min of high intensity running (Clansey et al., 2012). Such increases in loading rates have been previously linked with a greater risk of tibial stress fracture (Davis et al., 2004; Milner et al., 2006). However, none of the included studies assessed injury occurrence, and so no links should be established between fatigue, GRF and injury risk based on the findings of our review.

Our review also showed a decrease in loading rate after exhaustive running and was supported by Jafarnezhadgero et al. (2021) and Willson e Kernozek (1999). The decrease in GRF due to muscle fatigue has been observed in the literature performing different fatigue protocols, such as sprint running (Nummela et al., 1994) and the 5000-m self-paced run (Girard et al., 2010). In the meta-analysis of Zadpoor e Nikooyan (2012), the authors speculated that the human body is equipped with a protective strategy that reduces the GRF as muscle fatigue to protect the body from possible injuries.

According to Nicol et al. (2006) fatigue protocols should be 'completely' exhaustive to reduce the critical influence o intersubject variability on the fatigue responses, which we could not clearly state in our study, as fatigue-induced protocols were quite heterogeneous. For instance, in the fatigue-induced protocol of Hashish et al. (2016), recreational runners performed a running of 1.3 ± 0.2 km at a self-selected speed compared to 153 ± 15km 24h treadmill run performed by experienced ultra-endurance runners (Morin et al., 2011a).

4.3 Joint kinetics

Hashish et al. (2016) showed a significant reduction post-fatigue in peak ankle plantarflexor ($p < 0.001$; $d = 4.93$*; CI* [10.40 − 15.96]). Another study in our review showed a moderate reduction ($p < 0.004$; $d = 0.34$*; CI* [-0.26 − -0.06]) in the same variable following a long run (19 ± 6 km) (Melaro et al., 2021). Yu et al. (2021) reported a moderation reduction in peak hip joint moment post-fatigue ($p = 0.001$, ES = 1.24). The remaining joint moments remained unchanged post-fatigue across the studies (Brown et al., 2014; Melaro et al., 2021; Paquette & Melcher 2021; Yu et al., 2021).

GRFs are a critical element acting on the joints of the lower limbs and may change the normal biomechanics and alter kinetics of the knee, hip, and ankle joints (Yusof et al., 2018). In fact, Giandolini et al. (2017) observed reductions in neuromuscular fatigue (i.e., muscle force production) following a long trail run in runners who exhibited lower foot strike pattern variability during the run. However, increases in trunk and hip extension at initial contact and midstance could be partially responsible for the lack of change in peak tibial acceleration with fatigue, with the increased extension leading to a greater effective mass at initial contact (Derrick, 2004). This increased extension observed in the proximal segments may be related to the runner's inability to maintain postural control of the heavier proximal segments while in a fatigued state (Leetun et al., 2004), which we could not confirm in our review due to insignificant changes found in most of the variables (e.g., peak hip extensor, knee extensor, ankle invertor, and peak knee abduction moment).

4.3 Caveats when interpreting the findings, limitations, and future perspectives

Many studies did not properly report their method of recruitment or used convenience sampling, such as recruiting an entire team of runners. This may limit the ability to generalize the results to a wider running population as shown in this review and supported by the review

of Ceyssens et al. (2019). Most studies analyzed rearfoot strike runners. Therefore, we should not generalize the results of this study to non-rearfoot strike runners.

Participants from 18 to 55 years old (mean age over 23 years) were analyzed. As a result, we do not know how all this is processed in children and young runners < 23 years old. The literature shows significant changes in lower extremity kinematics and impact forces within a younger population (until 35 years) when a level of fatigue is present (Derrick et al., 2002; Dierks et al., 2010). Our findings do not represent the population of children and younger runners. Future studies should focus on children and young runners to facilitate the analysis of subgroups according to age group.

Furthermore, this review reclassified only one study as Tier 3 (Highly Trained/National Level). This tier often represents a "sweet spot" in studies that simultaneously collect mechanical data with reliable performance outcomes (McKay et al., 2022). Thereby, more studies should focus on Tier 3 athletes. In addition, most of studies analyzed rearfoot strike runners. According to Napier (2020), between 80 and 95% of all distance runners are rearfoot strikers who land on the rear third of their foot at initial contact. This is linked with a more dorsiflexed ankle, where the toes turn upwards towards the shin. A rearfoot strike is associated with greater vertical loading rates (Napier, 2020). Therefore, we should not generalize the results of this review with non-rearfoot strikes runners.

There was a considerable variation in the fatigue running protocols (1.3 ± 0.2km to 153 ± 15km) and pace strategy (e.g., self-selected pace and self-selected long run pace), representing a highly heterogeneous sample. From the evidence in this review, the effects of fatiguing and pacing protocols are not consistent enough to identify if one of these modifies GRF to a greater extent than the other. Furthermore, future research should examine homogeneous samples to perform sensitivity analyses and investigate the potential effects of fatigue-inducing protocols on the GRF.

It is important to consider that changes in GRF-related variables are not only caused by running-inducing fatigue, but also by an interaction of multiple modifiable and non-modifiable factors. As documented in the literature, in addition to fatigue, factors such as speed, sex, and footwear altered the response in the running GRFs (Bazuelo-Ruiz et al., 2018; Logan et al., 2010; Mei et al., 2015). This review also showed results in this regard[2]. However, it is essential

[2] One of our twelve included studies (Jafarnezhadgero et al., 2019) analyzed the effects of fatigue on running biomechanics of long-distance runners wearing a motion-control and neutral running shoes.

to consider that our study aimed to analyze the effects of fatigue on GRF-related variables induced by the fatigue-induced protocols. Other types of protocols may result in different outcomes, and caution is needed when interpreting or generalizing the results of this review with other factors.

Finally, GRADE judgments revealed very low certainty of the evidence. So currently, the links between fatigue and GRFs on long-distance runners and their impact on performance are supported on a fragile basis, and definitive statements should be avoided.

5. Conclusions

There was considerable heterogeneity regarding age, competitive level, distances covered, nature of interventions, comparators, specificity of the outcomes and the testing methods, which inhibited performing a meta-analysis. Risk of bias in the studies was moderate to high. Certainty of evidence was judged as very low. Currently, the effects of fatigue on GRF-related variables in long-distance runners are uncertain, and it is unclear to what extent they may affect performance. Further studies in this field are needed to clarify the effects of fatigue on GRF- related variables in long-distance runners.

Other information

Registration and protocol: The protocol was pre-registered in OSF (project osf.io/y497d, register https://osf.io/k5mcd). The OSF project was created and made public on July 13, 2022. The searchers were performed on the same day. Given the heterogeneity of the groups in terms of competitive level, distances covered, nature of interventions and comparators, and nature of outcomes collected, it was not possible to carry out the planned meta-analyses.

Author contributions: MS was involved in all processes, including protocol development, study screening, data extraction, analysis and interpretation of data, synthesis methods, risk of bias, and manuscript preparation. JA has provided crucial contributions to the conceptualization and design of the study, including protocol development, study screening, selection and data collection process, and risk of bias, as well as drafting and revising the manuscript critically. RRC was involved protocol development, drafting, and revising the manuscript critically. FC participated in protocol development and data extraction.

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Conflicts of interest: The authors have no conflict of interest to declare.

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Appendix 1: Search strategy for each included database.

Database	Specificities of the database	Search strategy
PubMed 13/07/2022	Nothing to report	((runn*[Title/Abstract]) AND (fatigu*[Title/Abstract] OR exhausti*[Title/Abstract])) AND (kinetic* OR biomechanic* OR "ground reaction force*" OR impact* OR "vertical force*" OR "horizontal force*")
Scopus 13/07/2022	Search for title and abstract also includes keywords.	(TITLE-ABS-KEY (*runn**) AND TITLE-ABS-KEY (*fatigu** OR *exhausti**) AND ALL (*kinetic** OR *biomechanic** OR *"ground reaction force*"* OR *impact** OR *"vertical force*"* OR *"horizontal force*"*))
SPORTDiscus 13/07/2022	Nothing to report	(TI (runn*) OR AB (runn*)) AND (TI (fatigu* OR exhausti*) OR AB (fatigue* OR exhausti*)) AND (TI (kinetic* OR biomechanic* OR "ground reaction force*" OR impact* OR "vertical force*" OR "horizontal force*") OR AB (kinetic* OR biomechanic* OR "ground reaction force*" OR impact* OR "vertical force*" OR "horizontal force*"))
Web of Science 13/07/2022	The option "Topic" includes title, abstract, and keywords.	https://www.webofscience.com/wos/woscc/summary/525a040a-29cf-40c8-8814-fef94bc83dae-4341a182/relevance/1

Appendix 2. Summary of the selected studies.

Authors, publication date & continent	Sample size & participant level *(McKay et al., 2022)	Funding & conflicts of interest	Experimental design	Fatigue protocol	Data collection procedure	Running speed	GRF-related variables
Bazuelo-Ruiz et al. (2018). Spain, Europe	57 ♀ ♂ *Tier 1 (Recreationally Active) & Tier 2 (Trained/Developmental)* Performed two to three days a week with a weekly volume of 20 to 40 km	*Funding:* This research was funded by the Seventh European Framework Programme (FP7-SME- 2011-1) under grant agreement 285800 (RUNSAFER). Conflicts of interest: No competing interests	The participants were already familiar with the protocol because of a previous test they performed in the laboratory with the same protocol	(1) a running Course-Navette test**, (2) running up and down a flight of stairs for 5 min, and (3) alternative jumps on a step (five sets of 1 min each with 30 resting seconds between the sets)	Overground. 15m long runway with force plate. Neutral running shoes	3.3 m/s (±5%)	(BW): Fpeak, active peak, peak braking force, peak propulsive force (BW/s): LR
Brown et al. (2014). USA, America	20 ♀ *Tier 1 (Recreationally Active)* Running a minimum of 15 miles (24km) per week for at least one year and were able to run at least one 9 min mile	*Funding:* N/A *Conflicts of interest:* N/A	(1) Establishing limb dominance, (2) three-dimensional motion analysis, (3) fatigue run	Fatiguing treadmill run (24.6 ± 7.0 min) at a self-selected pace	Overground. 25 m runway with four force plate. Standard shoes	3.35 m/s (±10%)	(Nm/Kg): Peak of the hip extensor and abductor , knee extensor and adductor, and ankle plantarflexor and ankle invertor
Degache et al. (2013). Switzerland, Europe	8 ♂ *Tier 2 (Trained/Developmental)* Long-distance trail runners. Regional level	*Funding:* N/A *Conflicts of interest:* N/A	Before and immediately after the 5-hour hilly running, the participants ran for 1 minute with 1 minute interval rest on an instrumented treadmill at three different speeds (10, 12 and 14km/h)	5-h run uphill/downhill simulating competitive conditions (37.5 ± 5.5km) with 1730 ± 230 m of elevation	Instrumented treadmill. 1 minute run at 3 different speeds with 1 minute interval rest	10, 12 and 14 km/ h	(BW): Fmax (BW/s): LR
Fischer et al. (2015). Brazil, America	11 ♀ ♂ *Tier 2 (Trained/Developmental)* Running at least 30 km per week during the previous 6 months and have participated in 5 km and/or 10 km races within the past year	*Funding:* This study was supported by a grant from the Federal University of Rio Grande do Sul Fund for the Incentive of Research, Porto Alegre, Brazil *Conflicts of interest:* N/A	Running was performed on an indoor track at the research laboratory. The participants ran 3 sets of 30 laps on the circuit at a constant speed before and after the fatigue protocol. The speeds were defined as self-selected or either faster or slower than self-selected	The fatigue protocol consisted of a vertical rebound jump series (60 s) of maximal countermovement jumps performed in a force plate	Overground. 28m on an indoor track with a force plate	Slower, 2.86 m/s ± 0.31 Self-selected, 3.23 m/s ± 0.35 Faster, 3.57 m/s ± 0.33	(BW): Fmax, Fpeak (BW/s): LR
Gerlach et al. (2005). USA, America	88 ♀ *Tier 2 (Trained/Developmental)*	*Funding:* This research was supported in part	Participants performed a pre- and post-fatigue test where the VGRF were collected	Exhaustive treadmill run: 3 min work intervals beginning at 2.2 m.s and a	Treadmill with two force plates. Usual running shoes	2.7 to 4.5 m/s	(BW): Fpeak, active peak (BW/s): LR

	Running a minimum of 20 miles (32 km) weekly. Most runners were competitive at the local and regional level, and a few subjects were national-caliber athletes	by a Mark Diamond Research Grant *Conflicts of interest*: N/A	running at their approximate 5 km race pace. Then participants were fatigued using a modified discontinuous VO2max treadmill protocol	1% gradient, with successive workloads 0.6 m.s faster until 4.5 m/s was reached, after which workloads increased by a gradient of 2.5% until voluntary exhaustion			
Hashish et al. (2016). USA, America	21♀ ♂ *Tier 1 (Recreationally Active)* Running between 15-40 km weekly	*Funding:* This study was partially funded by a Southern California CTSI pilot grant 12-2176-4124 *Conflicts of interest:* The authors have no personal or financial conflict interest that influenced this work	Participants performed 6 overground barefoot run trials in the laboratory at their self-selected speed in which the stance phase of the dominant limb should be entirely on a force plate located midway down this path. Immediately following the running trials, participants performed an exertion bout of running on an established, outdoor concrete surface running course. After finishing this step, they repeated the test exercise described above	A barefoot run. Distance of 1.3 ± 0.2 km conducted at the participant's self-selected speed (2.7 ± 0.4 m/s)	Overground. Barefoot running in a path of 30m, the force plate was located approximately midway down this path	Self-selected speed	(BW/s): LR (Nm/kg): Peak ankle plantarflexor
Jafarnezhadgero et al. (2019). Iran, Asia	22 ♀ *Tier 1 (Recreationally Active)* Running training volume of 2-3 times/week for 45 min or 10 km each workout. No participation in a systematic running training program for competitive performance	*Funding:* This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors *Conflicts of interest:* N/A	Participants performed 5 overground running trails (pre-fatigue) followed by a fatiguing treadmill running protocol (RPE between 13 and 17). Second overground run trials (5 trials) were conducted immediately after the fatiguing running task	Treadmill, set with no inclination. Participants started the protocol at 6 km/h, and the treadmill speed was increased 1 km/h every 2 min. Rate of perceived exertion was collected at the end of each stage through a 15-point Borg scale***	Overground. 18 m walkway containing two ground reaction force platforms in the middle of the walkway. Motion-control and neutral running shoes	3.3 m/s ± 2.5%	(BW): Fpeak (BW/s): LR (BW.height): Peak negative free moments
Melaro et al. (2021). USA, America	13 ♂ *Tier 2 (Trained/Developmental)* Running at least 45 km per week for the past three months	*Funding:* No funding was received for this study. *Conflicts of interest:* N/A	Testing session involved measuring gait during 5 overground running trials performed before and after a prolonged submaximal treadmill run	Long submaximal treadmill run (19 ± 6 km) at a self-select long run pace	Overground. 25 m runway with force plate in the middle. Personal running shoes	Preferred long run pace ± 5%	(Nm/kg): Peak of the ankle plantarflexor, knee extensor, and hip extensor
Morin et al. (2011). France, Europe	10 ♂ *Tier 3 (Highly Trained/National level)* Experienced ultra-endurance runners (they reported more than 15	*Funding:* No fund was received for this study from the National Institutes of Health, the Wellcome Trust, the Howard Hughes	The 24TR started and participants ran at a freely chosen pace. Just before, every 2 h, and at the end of the 24TR, they ran at 10	24h run on a treadmill at a freely chosen pace (153 ± 15km) at freely chosen pace	Just before, every 2 h, and at the end of the 24TR, participants ran at 10 km/h for 60 s on a treadmill dynamometer	10 km/h	(BW): Fmax (BW/s): LR

	years of training in running on average), and all of them had completed at least one 24-h or 100 km race	Medical Institute, or others. *Conflicts of interest:* The authors declare no conflict of interest	km/h for 60 s on a treadmill dynamometer				
Paquette and Melcher (2017). USA, America	12 ♂ *Tier 2 (Trained/Developmental)* Running an average of at least 50 km per week for the past 3 months, and completed at least 1 long run per week	*Funding:* Not reported *Conflicts of interest:* N/A	Participants performed 3 overground running trails at their preferred log run pace using the strike index before the fatigue protocol. Pre- and post-fatigue was collected overground. Begore running trials, they performed 5 min warm-up on the treadmill at their self-selected long run pace	Long run on a treadmill (19.1 ± 5.3 km) at a self-select long run pace	Overground. 3D force platform embedded in the laboratory floor at the midpoint of the 25-m runway. Usual running shoes	Preferred typical long run speed ±5%	(BW/s): LR (Nm/kg): Peak of the knee abduction moment, knee abduction impulse, peak hip abduction moment, hip abduction impulse
Tam et al. (2017). South Africa, Africa	22 ♂ *Tier 2 (Trained/Developmental)* Running 10km between 45 and 60 min, and running a minimum of four times per week at the time of the study, with a longest routine run of 10 km	*Funding:* N/A *Conflicts of interest:* No potential conflict of interest was reported by the authors	6 overground running trials were performed in the biomechanics laboratory immediately before and after the fatiguing treadmill run, with a maximum duration of two minutes between the end of the 10 km run and the post-fatigue biomechanical assessment trials	10 km run was performed at 42.0 ± 2.9 minutes in the well trained and at 51.2 ± 5.0 in the trained group. RPE at completion of the fatigue trial were 19.0 ± 1.1 and 19.5 ± 0.6 respectively- The speed was 2% faster than 10 km familiarization pace.	Overground. 40m indoor synthetic running track with two force platforms. Barefoot and with the shoe in which they were currently completing the most training mileage	4.4 m/s in the well-trained runners and 3.5 m/s in the trained group	(BW): Medio-lateral GRF,VGRF (BW/s): LR
Yu et al. (2021). China, Asia	15 ♂ *Tier 0 (Sedentary)* Running less than two-three times a week and ran less than 10 km per trail	*Funding:* N/A *Conflicts of interest:* None to report	3 overground running trials at self-selected speed along a 20 m runway in the lab (with their dominant foot striking the force platform) before and after a treadmill run exhaustion	Participants start walking on a treadmill at a speed of 6 km/h. The speed of the treadmill increased by 1 km/h every 2 minutes. The participants graded 13 (somewhat hard) to 17 (very hard) on the Borg scale*** or reached 90% of the maximum heart rate at a self-selected pace.	Overground. 20 m runway with force platform. Usual running shoes	Self-selected speed	(Nm/kg): Peak joint moment of the ankle, knee, and hip joints

Note. N/A = Information not available; Values in the fatigue protocol are in mean and standard deviation; RPE = rate of perceived exertion; Fpeak = impact peak force; Active peak = active peak force; LR = loading rate; Fmax = maximum vertical force; VGRF = Vertical ground reaction force; Medio-lateral GRF = Medio-lateral ground reaction force; VGRF = vertical ground reaction force. *Participant Classification Framework (McKay et al., 2022); **Running Course-Navette test (Léger et al., 1988); ***Borg scale of perceived exertion (Borg, 1998).

Appendix 3. Reclassification of training levels of participants from the selected studies.

Authors	Title	Description of participant characteristics	Premise for classification	Reclassification
Bazuelo-Ruiz et al. (2018)	Effect of fatigue and gender on kinematics and ground reaction forces variables in recreational runners	Recreational runners. Running as main physical activity practice performed two to three days a week with a weekly volume of 20 to 40 km	Participants meet physical activity guidelines (WHO).	*Tier 1* (Recreationally Active)
Brown et al. (2014)	The effects of limb dominance and fatigue on running biomechanics	Running a minimum of 15 miles (24km) per week for at least one year and were able to run at least one 9 min mile	Participants meet physical activity guidelines (WHO)	*Tier 1* (Recreationally Active)
Degache et al. (2013)	Changes in running mechanics and spring-mass behavior induced by a 5-hour hilly running bout	Long-distance trail runners. Regional level	Participants with regional-level representation, identify with a specific sport and compete regularly	*Tier 2* (Trained/Developmental)
Fischer et al. (2015)	Effects of fatigue on running mechanics: Spring-mass behavior in recreational runners after 60 seconds of countermovement jumps	Recreational runners have been running at least 30 km per week during the previous 6 months and to have participated in 5 km and/or 10 km races within the past year	Participants meet physical activity guidelines (WHO), and identify with a sport and are regularly competing	*Tier 2* (Trained/Developmental)
Gerlach et al. (2005)	Kinetic changes with fatigue and relationship to injury in female runners	All runners were running a minimum of 20 miles (32 km) weekly. Most runners were competitive at the local and regional level, and a few subjects were national-caliber athletes	This study includes participants from two tiers: Local & Regional (Tier 2) and National (Tier 3); However, participant numbers in each tier and more descriptive information were not reported. Therefore, the "Median" classification has been taken based on the significant population	*Tier 2* (Trained/Developmental)
Hashish et al. (2016)	The influence of a bout of exertion on novice barefoot running dynamics	Recreational runners, who ran between 15-40 km weekly	Participants meet physical activity guidelines (WHO). More descriptive information was no reported	*Tier 1* (Recreationally Active)
Jafarnezhadgero et al. (2019)	Motion-control shoes help maintaining low loading rate levels during fatiguing running in pronated female runners	Recreational runners. Running training volume of 2-3 times/week for 45 min or 10 km each workout. No participation in a systematic running training program for competitive performance	Participants meet physical activity guidelines (WHO). Despite the volume and weekly frequency of training, participants do not run for the purpose of competing	*Tier 1* (Recreationally Active)
Melaro et al. (2021)	Joint work is not shifted proximally after a long run in rearfoot strike runners	Healthy well-trained runners have been running at least 45 km per week for the past three months, were habitual RFS runners, and have completed at least one long run (i.e., 20–25% of weekly running volume) per week in the past three months	Participants meet physical activity guidelines (WHO), and regularly run and identify with a sport. No further info to justify "well-trained" terminology	*Tier 2* (Trained/Developmental)
Morin et al. (2011)	Changes in running kinematics, kinetics, and spring-mass behavior over a 24-h run	Experienced ultra-endurance runners (they reported more than 15 years of training in running on average), and all of them had	Participants are experienced e highly trained. More than 600 000 people ran an ultramarathon in 2018*. It means that less than 0.014% of	*Tier 3* (Highly Trained/National level)

		completed at least one 24-h or 100 km race	the world population runs ultramarathons.	
Paquette & Melcher (2017)	Impact of a long run on injury-related biomechanics with relation to weekly mileage in trained male runners	Trained runners, who ran an average of at least 50 km per week for the past 3 months, and completed at least 1 long run per week	Participants meet physical activity guidelines (WHO) and run regularly	*Tier 2* (Trained/Developmental)
Tam et al. (2017)	Acute fatigue negatively affects risk factors for injury in trained but not well-trained habitually shod runners when running barefoot	Well-trained (able to run 10 km faster than 45 minutes) and trained runners (able to run 10 km between 45 and 60 min). All running a minimum of four times per week at the time of the study, with a longest routine run of 10 km	Despite the classification with well-trained and trained runners, the participants' 10 km time classify them as Tier 2	*Tier 2* (Trained/Developmental)
Yu et al. (2021)	Effect of running-induced fatigue on lower limb mechanics in novice runners	Novice runners, who ran less than two-three times a week and ran less than 10 km per trail	Despite the language used to suggest participants were novice runners, descriptive information indicates physical activity levels are lower than guidelines (WHO). Not enough information is provided to say otherwise	*Tier 0* (Sedentary)

Note: Each sample has been reclassified according to the Participant Classification Framework (McKay et al., 2022). Legend: WHO = world health organization (WHO, 2020); RFS = rearfoot strike. *The State of Ultra Running 2020 (Ronto, 2021).

Chapter III: Concluding Remarks

3.1 General discussion of the main finds

The general aim of this thesis was to identify, assess, and synthesize the current evidence on the effects of fatigue on GRF-related variables among long-distance runners. Twenty-one GRF-related variables changed in almost all studies, but the direction and magnitude of change varied considerably. Interventions were performed in different fatigue-inducing protocols. Several reports have shown that when runners run in a fatigued state, their bodies are exposed to greater mechanical forces (Verbitsky et al., 1998; Voloshin et al., 1998).

Investigations of the effects of prolonged running and fatigue on lower-limb biomechanics allow insight into the adaption techniques made by athletes to help with injury risk or performance during a run (Winter et al., 2017). A reduction tolerance of impact in a fatigued state supports the importance of identifying preventative measures in individuals at risk of injury from high impact loading during running. The observed mechanical responses to progressive fatigue also provide further insight into the biomechanical coping strategies adopted by trained distance runners in racing or training scenarios. Thus, this thesis contributes to development, systematizing the scientific findings and exposing the limitations of the analyzed studies.

There was considerable heterogeneity regarding age, competitive level, distances covered, nature of interventions, comparators, specificity of the outcomes and the testing methods, which inhibited performing a meta-analysis. The certainty of evidence was judged as very low. Currently, the effects of fatigue on GRF in long-distance runners are uncertain, and it is unclear to what extent they may affect performance.

3.2 Limitations

The work presented in this thesis has some limitations that should be acknowledged. Most studies analyzed rearfoot strike runners. Therefore, we should not generalize the results of this study to non-rearfoot strike runners. It is important to consider that changes on GRF-related variables are not only caused by running-inducing fatigue, but also by an interaction of multiple modifiable and non-modifiable factors. However, it is essential to observe that this review aimed to analyze the current evidence on the effects on GRF-related variables induced by the fatigue-induced protocols. Other types of protocols may result in different outcomes, and caution is needed when interpreting or generalizing the results of this review with other factors.

Participants from 18 to 55 years old (mean age over 23 years) were analyzed in this thesis. As a result, we do not know how all this is processed in children and young runners < 23 years old. We reclassified only one study as Tier 3 (Highly Trained/National Level), due to this, we should not generalize the results of this thesis to this specific population.

There was a considerable variation in the fatigue running protocols (1.3 ± 0.2km to 153 ± 15km) and pace strategy (self-selected pace), representing a highly heterogeneous sample. From the evidence in this review, the effects of fatiguing and pacing protocols are not consistent enough to identify if one of these modifies GRF to a greater extent than the other.

Finally, GRADE judgments revealed very low certainty of the evidence. So currently, the links between fatigue and GRFs on long-distance runners and their impact on performance are supported on a fragile basis, and definitive statements should be avoided.

3.3 Futures avenues for research

Our findings do not represent the population of children and younger runners. Future studies should focus on children and young runners to facilitate the analysis of subgroups according to age group. Tier 3 athletes performing structured and/or periodized training are developing proficiency in skills required to perform their sport at the highest level. They can be expected to provide reliable measures of performance in familiar tasks and are therefore well suited to both laboratories- and field-based research. Thereby, more studies should focus on Tier 3 athletes.

As stated at the start of this thesis, there is a need for investigations providing critical information about the potential effects of fatigue-inducing protocols on GRF. Future research should examine homogeneous samples to perform sensitivity analyses and investigate and clarify the potential effects of fatigue-inducing protocols on the GRF.

3.4 References

Verbitsky, O., Mizrahi, J., Voloshin, A., Treiger, J., & Isakov, E. (1998). Shock transmission and fatigue in human running. *Journal of Applied Biomechanics, 14*(3), 300-311. doi:10.1123/jab.14.3.300

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Winter, S., Gordon, S., & Watt, K. (2017). Effects of fatigue on kinematics and kinetics during overground running: A systematic review. *Journal of Sports Medicine and Physical Fitness, 57*(6), 887-899. doi:10.23736/S0022-4707.16.06339-8

Supplements

Supplementary Table 1. PRISMA 2020 Checklist- Effects of fatigue on ground reaction forces in long-distance runners: A systematic review.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	**17**
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	**17**
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	**18**
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	**19**
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	**20**
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	**20**
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	**20 + appendix 1**
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	**21**
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	**21**
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	**21**
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	**21**
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	**21**
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	**22**
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	**22**
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	**22**
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	**22**
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	**23**
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	**23**
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	**23**
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	**23**

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	**24**
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	**24**
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	**24 + figure 1**
Study characteristics	17	Cite each included study and present its characteristics.	**26-27 + table + 1 appendix 1 & 2**
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	**27-29 + figure 2**
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots.	**29-31 + table 2 & 3**
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	**31**
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	**32-33**
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	**33**
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	**N/A**
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	**N/A**
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	**33**
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	**33-35**
	23b	Discuss any limitations of the evidence included in the review.	**35**
	23c	Discuss any limitations of the review processes used.	**36**
	23d	Discuss implications of the results for practice, policy, and future research.	**36-37**
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	**37**
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	**37**
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	**37**
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	**37**
Competing interests	26	Declare any competing interests of review authors.	**38**
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	**N/A**