Chronic disease, allergies and increased years of running are risk factors predicting gradual onset running related injuries in ultramarathon runners - SAFER XIX study in 29 585 race entrants

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No additional data are available. All data relevant to this study are included in the article or uploaded as online supplementary information.

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The authors report no conflict of interest pertaining to this manuscript.

ABSTRACT

Objectives: To identify risk factors that predict gradual onset running-related injuries (GORRIs) in ultramarathon runners entering a mass community-based event.

Design: Descriptive cross-sectional study.

Setting: Two Oceans 56km ultramarathon 2012-2015

Participants: Race entrants (n=42003) completed a compulsory pre-race medical history questionnaire; 29585 (70.4%) of entrants consented.

Dependent / Outcome variable: A history of GORRIs in the past 12 months among race entrants.

Main Outcome Measures: In a multi-variate model, runner demographics, training variables (years of recreational running, weekly running distance, training running speed), history of chronic disease (composite score), and history of allergies were included as factors predicting GORRIs. Prevalence (%) and prevalence ratios (PR, 95% CIs) are reported.

Results: The lifetime prevalence of GORRIs in ultramarathon runners was 24.4%. Independent factors predicting GORRIs were: higher chronic disease composite score (PR=2.05 times increase risk for every two additional chronic diseases; $p<0.0001$), history of allergies (PR=1.66; $p<0.0001$), increased years of recreational running (PR=1.07 times increased risk for every five year increase in running; $p<0.0001$), lower average weekly running distance (PR=0.98 times decreased risk for every 15km increase weekly running distance; $p<0.0001$), and slower average training running speed (PR=0.96 times decreased risk for every km/h increase in training running speed; $p<0.0001$).

Conclusion: Novel risk factors predicting GORRIs are increased number of chronic diseases and a history of allergies. These factors, together with training variables (years of recreational running, weekly running distance and training running speed) can be targeted to develop and implement injury prevention, treatment, and rehabilitation interventions in ultramarathon runners.

Keywords:

Running related injuries, overuse injuries, epidemiology, predictors, distance runners

INTRODUCTION

In recent years participation in mass community-based endurance running events has grown significantly.[1-3] In South Africa, events such as the annual Two Oceans Marathon races are also popular, attracting larger numbers of participants.[2 4-7] Notwithstanding its numerous health-benefits, distance running is also associated with the development of gradual onset running-related injuries (GORRIs).[2 3] GORRIs refer to injuries sustained from repetitive loading during running, combined with insufficient tissue recovery time.[8] Patterns of GORRIs differ across populations of runners[9] and have a multifactorial aetiology.

Risk factors for GORRIs may be internal (intrinsic) or external (extrinsic).[10 11] Internal factors include age, sex and body mass index, previous injury, physical fitness and psychological factors.[12] External factors refer to the characteristics of running (volume, intensity and frequency), the environment and footwear.[10-13] Although several risk factors for developing GORRIs have been reported, there are limited studies on risk factors predictive of GORRIs in ultramarathon runners. Most studies explored predictive factors of GORRIs in novice and recreational runners using relatively small sample sizes and data analysis with emphasis on univariate models and do not differentiate between novice, recreational, marathon or ultramarathon runners.[1-4 14-17] The use of multivariate models has only been applied in a few studies that report risk factors associated with GORRIs in marathon runners.[13 18 19] Previous injury,[13 19] weekly training distance,[13 19] weekly training frequency,[18] and previous race

participation[13 19] have been identified as independent risk factors associated with running-related injuries in marathon runners. However, ultramarathon runners compete, by definition, in races >42.2km and generally have a history of more years of running, higher training loads and are older. Older runners also have a higher prevalence of chronic diseases and there is some indirect evidence that chronic diseases may be related to increased risk of GORRIs [20-27] such as tendinopathies,[20 21 24 25] ligament injuries[21 25] and bone stress injuries.[26 27] The hypothesis that not only greater years of running and training load, but also a history of chronic diseases in ultramarathon runners may be risk factors that are predictive of GORRIs in ultramarathon runners has not been investigated. This information is important so that injury prevention, management, and rehabilitation programs can be developed and implemented.

The aim of this study is to explore if the following risk factors predict GORRIs in ultramarathon runners in a multivariate risk prediction model: demographics (sex, age), training-related variables (years of recreational running, weekly running distance, training running speed), history of chronic disease, and allergies.

METHODS

Study design and ethical concerns

Descriptive cross-sectional study from data were collected prospectively over a 4-year period (2012-2015).[7] Prior to conducting the study, the Research Ethics Committees of the Faculty of Health Sciences of the University of Cape Town (REC009/2011) and the University of Pretoria (433/2015) approved the studies.

Participants and demographics

All race entrants of the 56km Two Oceans ultramarathon for each year from 2012–2015 completed an online pre-race medical history questionnaire as a pre-requisite for registration. Race entrants that gave consent for their data to be used for research purposes were the participants of this study.

Online pre-race medical questionnaire

The online pre-race medical questionnaire for the Two Oceans Marathon consisted of a series of self-reported questions that were specifically developed to provide clinical information for medical staff on race day. The online screening questionnaire was based on recommendations by the European Association for Cardiovascular Prevention and Rehabilitation (EACPR) for pre-participation screening and cardiovascular disease evaluation for distance runners.[28 29] Full details of the development of this online medical screening and implementation has been described in previous studies.[28 30 31]

In the medical questionnaire, runners were asked the following specific question related to gradual onset injuries: "*Do you or did you suffer from any symptoms of a running injury (muscles, tendons, bones, ligaments or joints) in the past 12 months or currently?"* We defined these injuries as GORRIs, as recommended by the 2020 International Olympic Committee (IOC) consensus statement.[32] We only included injuries if "*the injury is/was severe enough to interfere with training/running or require treatment (e.g. use medication, or require you to seek medical advice from a health professional)?"*.

The medical questionnaire also contained details of the following: running training variables, history of chronic disease, and history of any allergies.

Main Outcome and Independent Variables Reported

The main outcome of this study was a history of GORRIs in the past 12 months among race entrants. The following three categories of independent variables of interest as factors predicting GORRIs were explored in a regression model: 1) *runner demographics* (sex and age groups), 2) *running experience* and *training history* (number of years as a recreational runner, average weekly training distance in the last 12 months, average training speed), and 3) *history of chronic disease* (risk factors for CVD, history of CVD, symptoms of CVD, endocrine disease, respiratory disease, gastrointestinal disease, nervous system/psychiatric disease, kidney/bladder disease, haematological/immune disease and cancer), and 4) *history of any allergies*. A chronic disease composite score was calculated combining

the 10 chronic disease variables to give a single score based on the risk of an increase in the number of chronic disease risk factors.

Statistical Analysis

All runners' entry data were analysed using SAS statistical software (version 9.4, Cary NC). The dependent variable in the model was the binary-scaled response variable related to the question regarding GORRIs. Runners could document more than one GORRI, e.g. reporting both a knee and a foot injury. In some cases, modelling situations arose with convergence problems, and as a consequence, Poisson regression with robust standard errors were used and the various models included the specified independent variables of interest. The Poisson distribution with the PROC GENMOD statement and an associated log link option were used for analysis. P-values for Type 3 Generalized Estimating Equation-analysis were reported. A repeated statement was included to account for the exchangeable correlation structure as one runner could report more than one injury per year.

Univariate unadjusted prevalence (% and 95%CIs) were reported for sex and age, running experience and running training history, history of chronic disease and history of any allergies. A multiple regression model was performed to determine independent risk factors predictive of GORRIs. The demographic, and history of any allergy variables were entered into the model as categorical variables. The running training variables and the chronic disease composite score were entered into the model as continuous variables and the prevalence of GORRIs (% and 95%CIs) were reported at the first quartile, median and third quartile for these variables. Initially, the multiple regression model included all the significant univariate risk factors. The results for the final model only included the retained significant risk factors (number of years as a recreational runner, average weekly running distance in last 12 months (km/week), average training running speed (km/h), chronic disease composite score, and any allergies) and were adjusted for sex and age category. Prevalence ratios (PR and 95%CI) were reported and the statistical significance level was 5%, unless otherwise specified.

RESULTS

Demographics of study participants and all entrants

A total of 29585 race entrants (70.4% of all race entrants) gave consent to participate in the study. We compared the demographics (sex and age) of all race entrants (n=42003) with the consenting race entrants in this study (Table 1).

TABLE 1. The Entrants Profile by Sex and Age Groups of All Race Entrants and Study Participants (Race Entrants Who Provided Consent)

	All 56-km Race Entrants 2012—2015		56-km Consenting Race Entrants 2012—2015		
Demographics	n = 42 003	%	n = 29 585	%	*P**
Sex					
Males	30 466	72.5	21 044	71.1	<0.0001
Females	11 537	27.5	8541	28.9	
Age groups					
≤30 yrs	4953	11.8	3574	12.1	0.1489
31-≤40 yrs	15 181	36.1	10 755	36.4	
41-≤50 yrs	14 254	33.9	10 078	34.1	
>50 yrs	7615	18.1	5178	17.5	

** Consenting versus all entrants.*
n, number participants; %, % out of total.

In this study group, the proportion of consenting participants was significantly higher for females (28.9% compared to 27.5%). There was no significant difference between consenting entrants and all race entrants by age groups (p=0.1489).

Prevalence of GORRI in 56km race entrants

The lifetime prevalence of GORRIs in 56km race entrants was 24.4% (95% CI: 23.9-25.00) with a retrospective annual incidence of 14.2% (95%CI: 13.7-14.7).

Risk factors that predict gradual onset running-related injuries (GORRIs) (Univariate regression)

a) *Demographics (sex and age groups)*

The number (n), prevalence (%; 95%CI) and unadjusted prevalence ratio (PR; 95%CI) of race entrants with a history of GORRIs by sex and age group is depicted in Table 2.

TABLE 2. The Number (n), Prevalence (%; 95% CI), and Unadjusted Prevalence Ratio (PR; 95% CI) of Race Entrants With a History of Gradual Onset Running-Related Injuries (GORRIs) by Sex and Age Group

	Consenting Race Entrants (n = 29 585)	Number and Prevalence of GORRIs			
Runner Demographics	N	n	Prevalence % (95% CI)	PR (95% CI)	*P*
Sex					
Males	21 044	2460	13.28 (12.73-13.85)	—	<0.0001
Females	8541	1239	16.41 (15.48-17.40)	1.24 (1.15-1.33)*	
Age groups					
≤30 yrs	3574	431	13.17 (11.97-14.50)	—	
31-≤40 yrs	10 755	1297	13.76 (13.00-14.55)	1.04 (0.94-1.17)†	0.4445
41-≤50 yrs	10 078	1308	14.72 (13.90-15.59)	1.12 (1.00-1.25)‡	0.0525
>50 yrs	5178	663	15.00 (13.83-16.28)	1.14 (1.00-1.29)§	0.0432

**Ratio expressed as female to male.*
† 31 to ≤40 versus ≤30, P = 0.4445.
‡ 41 to ≤50 versus ≤30, P = 0.0525.
§ >50 versus ≤30, P = 0.0432.
n, number; %, % out of total; 95% CI, 95% confidence intervals.

There was a significantly higher prevalence of GORRIs among female vs. male race entrants (PR=1.24; p<0.0001). There was a significantly higher prevalence of GORRIs in the >50years age group compared to the ≤30years race entrants (PR=1.14; p=0.0432). The prevalence of GORRIs in other age categories were not significantly different to the ≤30years race entrants.

b) Running experience and running training history

The prevalence (%; 95%CI) and unadjusted prevalence ratio (PR; 95%CI) of race entrants with a history of GORRIs by running training history is indicated in Table 3.

TABLE 3. The Prevalence (%; 95% CI) and Unadjusted Prevalence Ratio (PR; 95% CI) of Race Entrants With a History of Gradual Onset Running-Related Injuries (GORRIs) by Running Training History

Running Training History Variables	Points in Continuous Variables*	GORRIs Prevalence % (95% CI)	PR (95% CI)	*P*
No. of years as a recreational runner	3 yrs	12.83 (12.23-13.47)	1.06 (1.04-1.08)†	<0.0001
	6 yrs	13.32 (12.79-13.88)		
	13 yrs	14.53 (14.04-15.04)		
Average weekly running distance in last 12 mo	20 km/wk	16.39 (15.57-17.25)	0.98 (0.97-0.98)‡	<0.0001
	35 km/wk	15.29 (14.71-15.90)		
	50 km/wk	14.27 (13.79-14.76)		
Average training running speed category	9 km/h	16.12 (15.45-16.82)	0.94 (0.92-0.95)§	<0.0001
	10 km/h	15.09 (14.56-15.64)		
	11 km/h	14.13 (13.65-14.62)		

**Points on the continuous variables are the first quartile, median and third quartile for each training variable.*
† Average risk for every 5 years increase.
‡ Average risk for every 15 km increase weekly running distance.
§ Average risk for every km/h increase in training running speed.
95% CI, 95% confidence interval.

The crude unadjusted analysis shows that an increased number of years of recreational running (PR=1.06 times increased risk for every five-year increase in running; p<0.0001) was predictive of a higher prevalence of GORRIs in race entrants. A higher average weekly running distance in the last 12

months (PR=0.98, decreased risk for every 15km increase weekly running distance; p<0.0001) and a higher average training running speed (PR=0.94, decreased risk for every km/h increase in training running speed; p<0.0001) was predictive of a lower prevalence of GORRIs.

TABLE 4. The Prevalence (%; 95% CI) and Unadjusted Prevalence Ratio (PR; 95% CI) of Race Entrants With a History of Gradual Onset Running-Related Injuries (GORRIs) by Chronic Disease and a History of Allergies

Variable	Number of Reported GORRIs (n = 3699) Prevalence % (95% CI)	PR (95% CI)	*P*
Chronic disease composite score (0-10)			
0 chronic diseases	11.90 (11.42-12.39)	2.33 (2.14-2.55)*	<0.0001
2 chronic diseases	27.77 (25.83-29.86)		
4 chronic diseases	64.84 (55.51-75.75)		
Any risk factor for CVD			
Yes	25.19 (23.52-26.98)	1.96 (1.82-2.12)	<0.0001
No	12.84 (12.36-13.33)		
Any history of CVD			
Yes	29.76 (25.56-34.66)	2.14 (1.83-2.50)	<0.0001
No	13.93 (13.45-14.42)		
Any symptoms of CVD			
Yes	29.53 (23.52-37.09)	2.10 (1.67-2.65)	<0.0001
No	14.04 (13.56-14.53)		
Any endocrine disease			
Yes	26.47 (22.60-31.00)	1.90 (1.62-2.23)	<0.0001
No	13.93 (13.45-14.43)		
Any respiratory disease			
Yes	28.38 (26.07-30.88)	2.15 (1.97-2.36)	<0.0001
No	13.17 (12.70-13.67)		
Any GIT disease			
Yes	32.50 (28.57-36.97)	2.37 (2.07-2.71)	<0.0001
No	13.73 (13.25-14.22)		
Any nervous system/psychiatric disease			
Yes	28.93 (24.63-33.99)	2.08 (1.77-2.46)	<0.0001
No	13.90 (13.42-14.39)		
Any kidney/bladder disease			
Yes	25.73 (21.06-31.43)	1.84 (1.50-2.25)	<0.0001
No	14.02 (13.54-14.52)		
Any haematological/immune disease			
Yes	22.90 (16.37-32.04)	1.62 (1.16-2.27)	0.0052
No	14.15 (13.67-14.64)		
Any cancer			
Yes	22.45 (17.88-28.18)	1.59 (1.27-2.01)	<0.0001
No	14.08 (13.60-14.58)		
Any allergies			
Yes	27.32 (25.26-29.54)	2.10 (1.93-2.29)	<0.0001
No	12.98 (12.51-13.47)		

** Average risk for every 2 additional chronic diseases.*
%, % out of total; 95% CI, 95% confidence intervals; CVD, cardiovascular disease; GIT, gastrointestinal disease.

c) *History of chronic disease and allergies*

The prevalence (%; 95%CI) and unadjusted prevalence ratio (PR; 95%CI) of race entrants with a history of GORRIs by main categories of chronic disease and history of allergies is shown in Table 4.

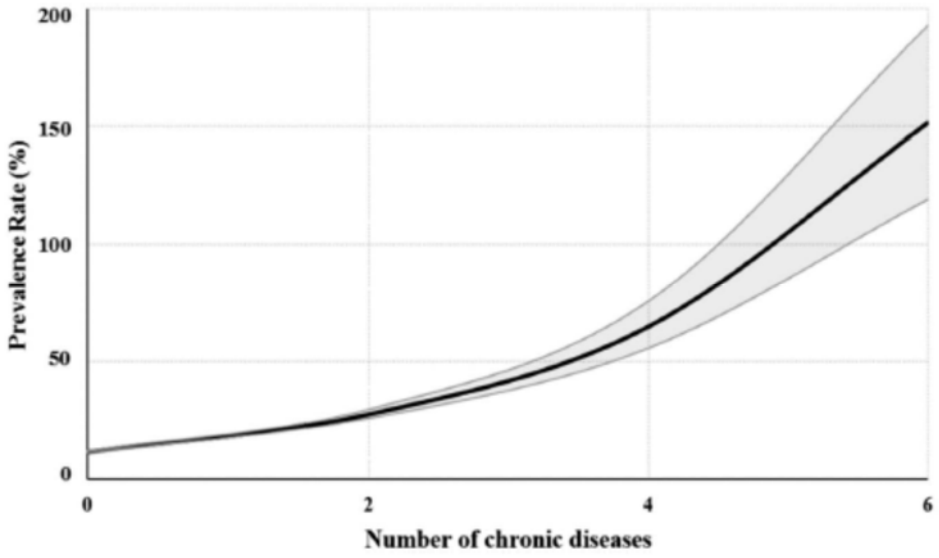

Figure 1: The relationship between the prevalence rate of a GORRI and the number of chronic diseases (chronic disease composite score) (shaded area is 95% CI).

For every two additional chronic diseases runners concurrently reported, there is a 2.3 times increase in the PR of GORRI ($p<0.0001$). This relationship between number of chronic diseases and the prevalence risk is shown in Figure 1. Specific chronic disease variables that predicted a higher prevalence risk of GORRIs in race entrants were: any GIT disease (PR=2.37; $p<0.0001$), any respiratory disease (PR=2.15; $p<0.0001$), any history of CVD (PR=2.14; $p<0.0001$), any symptoms of CVD (PR=2.10; $p<0.0001$), any nervous system/psychiatric disease (PR=2.08; $p<0.0001$), any risk factors of CVD (PR=1.96; $p<0.0001$), any endocrine disease (PR=1.90; $p<0.0001$), any kidney /bladder disease (PR=1.84; $p<0.0001$), any haematological /immune diseases (PR=1.62; $p=0.0052$), and any cancers (PR=1.59; $p<0.0001$). In addition, a history of any allergies (PR=2.10; $p<0.0001$) predict a higher prevalence risk of GORRIs in race entrants.

Independent risk factors predictive of GORRIs (Multiple regression)

The independent risk factors (adjusted for age and sex) predictive of a history of GORRIs in race entrants are reported in Table 5.

TABLE 5. The Independent Risk Factors (Adjusted for Age and Sex) Predictive of Gradual Onset Running-Related Injuries (GORRIs) in Race Entrants (Multiple Regression)

	PR (95% CI)	P
Number of years as a recreational runner	1.07 (1.05-1.09)*	<0.0001
Average weekly running distance in last 12 months (km/wk)	0.98 (0.98-0.99)†	<0.0001
Average training running speed (km/h)	0.96 (0.95-0.98)‡	<0.0001
Chronic disease composite score	2.05 (1.88-2.23)§	<0.0001
Any allergies	1.66 (1.52-1.82)	<0.0001

#, adjusted for sex and age groups.
** Average increase in risk for every 5 yrs*
† Average risk for every 15 km increase weekly running distance.
‡ Average risk for every km/h increase in training running speed.
§ Average risk for every 2 additional chronic diseases.
95% CI, 95% confidence interval.

The independent risk factors that predict a history of GORRIs in race entrants were: a higher chronic disease composite score (2.05 times increased risk for every 2 additional chronic diseases; p<0.0001), history of any allergy (PR=1.66; p<0.0001), an increased number of years as a recreational runner (PR=1.07 times increased risk for every five year increase in running; p<0.0001). A higher average weekly running distance (PR=0.98 times decreased risk for every 15km increase weekly running distance; p<0.0001) and a higher average training running speed (PR=0.96, decreased risk for every km/h increase in training running speed; p<0.0001) decreased risk of GORRIs.

DISCUSSION

The main finding is that the independent factors predicting GORRIs were: a higher chronic disease composite score, history of any allergies, increased number of years as a recreational runner, a lower average weekly running distance, and a slower average training running speed. The lifetime prevalence of GORRIs 56km race entrants was 24.4%, with a retrospective annual incidence of 14.2%. From the univariate analysis we could identify that a history of certain chronic diseases were predictive of a higher prevalence of GORRIs (PR of >2) as follows: any GIT disease (PR=2.37; p<0.0001), any respiratory disease (PR=2.15; p<0.0001), any history of CVD (PR=2.14; p<0.0001), any symptoms of CVD (PR=2.10; p<0.0001) and any nervous system (PR=2.08; p<0.0001).

Our most important and novel finding is that a history of multiple chronic diseases and a history of any allergies was predictive of an increased risk for developing a GORRI in ultramarathon race entrants. We show that for each additional two chronic diseases a runner reported, the prevalence risk

of a GORRI increases just over 2 times. Although this finding is novel in ultramarathon runners, it agrees with two recent reports from our research group that also show the prediction between gradual onset injuries and multiple chronic diseases and / or allergies in recreational road cyclists [32] and trail run race entrants.(*Viljoen C, et.al. 2020, in review*) From our univariate analysis we show that chronic GIT, respiratory and CVD disease together with a history of any symptoms of CVD are predictive factors for GORRIs in ultramarathon race entrants. We also report that a history of any allergies is predictive of a higher prevalence risk for GORRIs (PR=1.66). We do note that a history of allergies and hay fever are common in ultramarathon runners with a prevalence that varies between 25% and 42%.[15 17]

In this descriptive study we did not explore potential mechanism/s to explain the relationship between chronic disease and risk of GORRIs in runners. However, there is indirect evidence that chronic diseases may be related to increased risk of GORRIs.[20-27] Chronic disease or medication that is used to treat chronic disease, is related to tendinopathies,[20 21 24 25] ligament injuries[21 25] and bone stress injuries.[26 27] Specifically, hypercholesterolemia, diabetes mellitus and the metabolic syndrome are associated with chronic tendinopathy.[20 21 23] Statins increase the risk of skeletal muscle myopathy,[22 24] while proton pump inhibitors and corticosteroids may increase the risk of osteopenia.[26 33] The relationship between specific chronic diseases or medications and GORRIs in specific anatomical areas warrants further study.[34] At this stage, we can recommend that clinicians take note of the possible association between gradual onset injuries and certain chronic diseases, particularly when managing patients or introducing injury prevention programs. This is important, because patients with a history of chronic disease will benefit greatly from the regular physical activity, including running.[35]

Several training variables are independent risk factors predictive of GORRIs. Recreational runners participating in ultramarathons over many years and sudden increments in training load in novice runners are factors that increase risk of developing GORRIs.[5,12] However, these factors may not apply to our population of ultramarathon runners who were required to complete a marathon as an entry criterion. We report that lower average weekly running distance is predictive for GORRIs. This is

similar to study in marathon runners where average weekly training distance < 30km/week was associated with a 2.02 times increased risk for running-related injuries.[18] Slower training running speed as a predictive factor for GORRIs has not been reported in other studies. We cannot infer a cause-effect relationship between any of these training variables and GORRIs.

The main strengths of this study is the large sample size making independent risk factor analysis possible with the use of a multivariate risk prediction model. Limitations of the study are that the injury, training and medical data history were self-reported, and the extent of recall accuracy and reliability cannot be quantified. This is a cross-sectional study and we cannot make any causal inference to specifically guide injury prevention interventions. In the reporting on the outcomes in this manuscript, we use the terminology "prediction" instead of "association", based on recently published guidelines regarding clear goal setting in sports injury research.[36] For example, a lower average weekly running distance and a slower average training running speed may be the result of a GORRI and not be causative. In our study we could also not include a complete set of possible risk factors that may be associated with GORRIs, including biomechanical variables. It is not possible to obtain biomechanical data from a medical screening questionnaire. Furthermore, the outcome was any GORRI and not specific individual running injuries. In future studies risk factors predictive of specific running injuries will be explored. Since this is the first study to report on risk factors associated with GORRIs among ultramarathon runners, we could not compare our results with other studies of the same sporting code.

CONCLUSION

The main independent risk factors predictive of GORRIs in ultramarathon runners that entered for a mass community-based ultramarathon over a 4-year period include: a higher chronic disease composite score, a history of any allergies, an increased number of years as a recreational runner, a lower average weekly running distance and a slower average training running speed. These factors, can be targeted to develop and implement injury prevention, treatment, and rehabilitation interventions in ultramarathon runners. We recognise that risk factors predictive of GORRIs are multifaceted and

the we suggest that a comprehensive medical assessment to identify chronic diseases and allergies should be considered as part of the clinical assessment of a runner presenting with a GORRI. The findings of this study also form the basis for further research to determine cause-effect in predictive risk factors of GORRIs in ultramarathon runners.

What are the new findings?

- A higher chronic disease composite score in ultramarathon runners is predictive of an increased risk of developing GORRIs - a 2 times increase risk for every two additional chronic diseases
- Ultramarathon runners with a history of any allergies are 1.7 times more likely to develop GORRIs
- An increased number of years as a recreational runner, a lower average weekly running distance, and a slower average training running speed are predictive factors with an increased risk for developing GORRIs

How it might impact on clinical practice in the near future?

- Clinicians should consider that a history of allergies and / or chronic diseases, especially multiple chronic diseases, may be predictive of GORRIs in ultramarathon runners
- A comprehensive medical assessment to identify chronic diseases and allergies should be considered as part of the clinical assessment of a runner presenting with a GORRI

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