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Factors associated with patellofemoral pain in recreational road cyclists: A cross-sectional study in 59953 cyclists – SAFER XXXIII

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ABSTRACT

Objective: Patellofemoral pain (PFP) is a common cycling-related injury, and independent factors need to be identified to enable effective injury prevention strategies. We aim to determine factors associated with PFP in cyclists entering mass community-based events.
Design: Cross-sectional study.
Setting: 2016–2020 Cape Town Cycle Tour.
Participants: Consenting race entrants.
Main outcome measures: 62758 consenting race entrants completed a pre-race medical questionnaire, and 323 reported PFP. Selected factors associated with PFP (demographics, cycling experience and training, chronic disease history) were explored using multivariate analyses.
Results: Prevalence ratio (PR) of PFP was similar for sex and age groups. Independent factors associated with PFP (adjusted for sex and age) were history of chronic disease [Composite Chronic Disease Score (0-10)($PR = 2.0$, $p < 0.0001$) and any allergies ($PR = 2.0$, $p < 0.0001$)].
Conclusion: A history of chronic diseases and allergies is associated with PFP in cyclists. Practical clinical recommendations are: 1) that prevention programs for PFP be considered when cycling is prescribed as a physical activity intervention for patients with chronic disease, and 2) that older cyclists presenting with PFP be assessed for the presence of risk factors or existing chronic disease.

1. Introduction

Cycling has many general health benefits, and recreational and competitive cycling as a sport has increased in popularity, particularly in older individuals (du Toit et al., 2020b; Rooney et al., 2020). However, cyclists can develop sudden onset (acute or repetitive) injuries (Barrios et al., 2015; Decock et al., 2016; Pommering et al., 2017), as well as gradual onset injuries (Dannenberg et al., 1996; du Toit et al., 2020a; Wilber et al., 1995). Although the incidence of sudden onset injuries in cyclists is high (Rooney et al., 2020), the multifactorial component of gradual onset injuries makes it more difficult to determine their cause. Of the gradual onset injuries, the knee joint is one of the most affected body parts (Clarsen et al., 2010; Clarsen et al., 2013; Dahlquist et al., 2015; Dannenberg et al., 1996; du Toit et al., 2020a; Van der Walt et al., 2014), and patellofemoral pain (PFP) is the commonest gradual onset knee injury in cyclists (Barrios et al., 1997; Clarsen et al., 2010; du Toit et al., 2020a).

PFP can be defined as pain "around or behind the patella which is aggravated by at least one activity that loads the patellofemoral joint during weight-bearing on a flexed knee" (Crossley et al., 2016). According to the 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat (Crossley et al., 2016), the term 'patellofemoral pain' is the preferred term, and is synonymous with other terms including: (1) PFP syndrome; (2) chondromalacia patella; (3) anterior knee pain and/or syndrome; and (4) runner's knee (Crossley et al., 2016). In

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accordance with the consensus statement (Crossley et al., 2016), we use the term PFP throughout the rest of the manuscript.

The aetiology of PFP and factors associated with PFP in cyclists are not well understood. Several morphologic and biomechanical factors, including incorrect bicycle and equipment settings, have been associated with PFP. (Bini & Flores Bini, 2018; Johnston et al., 2017). However, non-biomechanical factors that may be related to PFP in cyclists such as age, sex, training, and racing variables have not been well-studied (Van der Walt et al., 2014; Weiss, 1985). In addition, novel non-biomechanical factors associated with any gradual onset injuries in cyclists, including increased years of cycling, increased weekly training, a history of chronic diseases and allergies were recently reported. (du Toit et al., 2020b), The association between these novel factors and specific cycling injuries, such as PFP, have not been studied.

The aim of this study was to determine if selected factors are associated with PFP in cyclists entering a mass community-based cycling event. The following specific selected factors were explored: (1) cycling demographics (sex and age groups), (2) cycling experience and training history (number of years as a recreational cyclist, average weekly training distance in the last 12 months, average training speed), and (3) history of chronic disease (risk factors for cardiovascular disease [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), history of any allergies, and history of medication to treat chronic disease.

2. Methods

2.1. Study design

This is a descriptive cross-sectional analysis of data collected prospectively at an annual road-cycling event over five years.

2.2. Participants and data collection

The Research Ethics Committee approved this cross-sectional study (REC number 749/2019). Participants were race entrants from the annual 109 km mass community-based road-cycling event, the Cape Town Cycle Tour (CTCT). During the annual 2016–2020 CTCT, cyclists completed an online medical questionnaire at the time of registration. In 2016, the completion of the tool was compulsory for all race entrants but was voluntary in 2017–2020. The tool remained unchanged in the study period, and included a statement on providing consent (ticking 'yes' or 'no') at the end of the tool. All cyclists were given the option to consent that their data could be used for research purposes. Over the 5 year study period, a total of 62758 cyclists gave electronic informed consent for their data to be used for research purposes.

2.3. Online prerace medical questionnaire

The online prerace medical questionnaire consisted of a series of questions that were based on recommendations by the European Association for Cardiovascular Prevention and Rehabilitation for pre-participation screening and cardiovascular disease evaluation (Borjesson et al., 2011; Maron et al., 2001). Full details of the development and implementation of this online prerace medical questionnaire has been described and used in previous studies (du Toit et al., 2020b; Killops et al., 2020; Rotunno et al., 2018; Schwabe et al., 2018; Schwellnus et al., 2019). In order to ensure that the screening tool was specific to the current population, additional questions were added, which were related to history of injuries in cyclists (current, or in the last 12 months). In our medical questionnaire, which was designed prior to the IOC consensus statements (Bahr et al., 2020) (Clarsen et al., 2021) cyclists were specifically asked the following question related to injury: *'Do you or did you suffer from any symptoms of a CHRONIC (no accident) cycling injury (muscles tendons bones ligaments or joints) IN YOUR CYCLING CAREER?'*

We refer to the mode of onset of these chronic injuries as gradual onset injuries (GOIs) in cyclists, in accordance with the 2020 general IOC consensus statement on 'Recording and Reporting of Epidemiological Data on Injury and Illness in Sports' (Bahr et al., 2020). The definition of this mode of onset as '*gradual onset*' is also in accordance with both the original and the extension of the IOC consensus statement on methods for reporting injuries in competitive cycling (Bahr et al., 2020; Clarsen et al., 2021). In } Our definition of gradual onset injuries (GOIs) does not distinguish between potential modes of onset for non-acute injuries. Therefore, gradual onset injuries reported in our study are inclusive of all three possible modes of onset (gradual onset, insidious onset or chronic onset) according to a third recently published international consensus statement on injury reporting in professional road cycling (Heron et al., 2021).

We only included injuries if "*An injury that is/was severe enough to interfere with cycling or require treatment* e.g. *use medication or require you to seek medical advice from a health professional*". A 'yes' response to this question required participants to complete additional questions with drop-down boxes that were related to the injury. Race entrants were asked the following specific question related to self-reported PFP: "*Please indicate if your injury was any of the following more common cycling injuries (single select)*. One option in the drop-down box of the list of possible more common cycling injuries was "*Knee – anterior knee pain/patellofemoral pain*". Other possible common injuries included in the drop-down box included for e.g. iliotibial band syndrome. Entrants that specifically indicated they had "anterior knee pain/patellofemoral pain" in the past 12 months were our PFP group (PFP = 323). The consenting entrants that responded 'no' (they have never been injured), formed our non-injured control group (Con = 59630). This PFP study population was thus N = 59953. Entrants who were injured >12months ago, or had other non-PFP injuries, or with conflicting injury information were excluded from this study. The medical questionnaire also contained details of the cyclist's demographics, training variables, and history of chronic disease, history of any allergies, and history of regular use of any medication to treat chronic disease.

2.4. Main outcome and independent variables

The following categories of selected factors associated with a history of PFP in cyclists were explored in a multiple regression model: (1) cycling demographics (sex and age groups), (2) cycling experience and training history (number of years as a recreational cyclist, average weekly training distance in the last 12 months, average training speed), and (3) history of chronic disease (risk factors for cardiovascular disease [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), history of any allergies, and history of medication to treat chronic disease. A Composite Chronic Disease Score (CCDS) was the sum of 10 individual categories of chronic disease variables that gave a single score based on the risk of an increase in the number of chronic disease risk factors.

We acknowledge that we cannot propose any causal inference with reporting the above-listed variables as potential factors

associated with PFP. We use the term 'associated with' to refer to the relationship between these potential risk predictors and PFP, but the association does not imply a cause-effect relationship (Nielsen et al., 2020).

2.5. Statistical analysis

In 2016 the medical questionnaire was compulsory but was made voluntary in the subsequent years 2017–2020. The demographic profile of the 2016 consenting cyclists differed from the demographic profile of the 2017–2020 consenting cyclists (Supplementary Appendix I). Subsequently, the data were weighted by sex and age groups across each of the years 2017–2020, to compensate for the differences and to align with the 2016 data. Therefore, all result tables report weighted frequencies and percentages. Analyses were conducted using SAS statistical software (version 9.4, Cary NC). The binary-scaled dependent variable in the model was the response to the question related to PFP. In some cases, modelling situations arose with convergence problems and consequently, a Poisson regression with robust standard errors was used and the various models included the specified independent variables of interest. Poisson distribution with the PROC GENMOD statement and an associated log link option was used for analysis. P-values for Type 3 Generalized Estimating Equation-analysis are reported. A repeated statement was included to account for the exchangeable correlation structure as one cyclist could report more than one injury per year.

Prevalence ratios (PR) were calculated as the measure of association. Univariate unadjusted prevalence (% and 95% CIs) and PR are reported for cyclists demographics, training/running history, history of chronic disease and history of any allergies. Overall prevalence and the assessment of univariate factors were calculated using this sample. A multiple regression model was performed to identify independent factors associated with a history of PFP. The demographic, chronic disease and allergy history variables were entered into the model as categorical variables. The training and cycling variables were entered into the model as continuous variables and the prevalence of a history of PFP (% and 95% CIs) is reported at the first quartile, median and third quartile for these variables. For all unadjusted univariate models, significance was at 5%. Only significant factors were entered into the multivariate regression model. The final multiple regression model and final results only retained significant factors at the 1% level.

3. Results

There were 59630 participants with no history of PFP (control group) and 323 reported PFP in the previous 12 months (PFP group). The overall weighted estimated period prevalence was 0.54% (95%CI: 0.48.-0.60) and the estimated period prevalence in each year of the study was as follows: 2016 (0.44%; 0.36–0.54), 2017 (0.55%; 0.41–0.73), 2018 (0.45%: 0.33–0.61), 2019 (0.81%; 0.64–1.02) and 2020 (0.58%; 0.46–0.72).

3.1. Demographic factors associated with PFP in cycling race entrants (univariate analysis)

The number (n), weighted prevalence (%; 95% CI), and unadjusted prevalence ratio (PR; 95% CI) of race entrants with and without a history of PFP, by sex and age group, is summarized in Table 1.

The highest percentage of participants were males (male = 78.9%; female = 21.1%) and 64.9% of participants were >40 years age. There were no significant differences in the weighted prevalence of PFP among female versus male race entrants ($p = 0.6329$) and there was also no significant difference in weighted prevalence between any of the age groups ($p = 0.0600$).

3.2. Training/racing factors associated with PFP in cycling race entrants (univariate analysis)

The weighted prevalence (%; 95% CI) and crude unadjusted prevalence ratio (PR; with 95%CI) of cyclists with a history of PFP by cycling training/racing history are depicted in Table 2.

The crude unadjusted analysis shows that increased years of participation in distance cycling events >2 h (PR = 1.08 for every 5-year increase; $p = 0.0129$), an increased average weekly training/racing frequency in the last 12 months (PR = 1.09 times increase in risk for every one more training session per week; $p = 0.0402$), and increased years of recreational cycling (years) (PR = 1.05; $p = 0.0461$, for every 5-year increase) were associated with a higher prevalence of PFP in race entrants.

3.3. History of chronic disease, a history of allergies and regular use of prescription medications as factors associated with PFP in cycling race entrants (univariate analysis)

The weighted prevalence (%) and crude unadjusted prevalence ratio (PR; with 95%CI) of cyclists with a history of PFP by history of main categories of chronic disease, a history of allergies and by regular use of prescription medications are depicted in Table 3.

The crude unadjusted analysis showed that the highest PR of PFP in cyclists is associated with a history of any symptoms of CVD (PR = 3.98; $p < 0.0001$). Specific chronic disease variables associated with a higher prevalence risk of PFP in race entrants were: a history of any nervous system/psychiatric disease (PR = 2.62; $p < 0.0001$), any GIT disease (PR = 2.55; $p < 0.0001$), a history of any respiratory disease (PR = 2.18; $p < 0.0001$), a history of CVD (PR = 1.74; $p = 0.0267$), and any cancer (PR = 1.74; $p = 0.0351$). A history of any allergies (PR = 2.28; $p < 0.0001$) was associated with a higher PR of PFP. From the history of medication usage, the crude unadjusted analysis showed that the use of medication to treat chronic disease (PR = 2.07, $p < 0.0001$) was associated with a higher PR of PFP. The relationship between CCDS and prevalence of PFP is depicted in Fig. 1.

For every two additional chronic diseases cyclists concurrently reported, there is a 2.23 time increase in the PR of PFP ($p < 0.0001$).

3.4. Independent factors associated with PFP in cycling race entrants (multiple regression analysis, adjusted for sex and age groups)

The multiple regression analysis included all the significant factors from the univariate analysis to determine factors predicting a history of self-reported PFP in cyclists. The independent factors [adjusted PR (95%CI)] associated with a history of PFP in race entrants were a higher CCDS [PR = 1.96 (1.56–2.47) times increased risk for every 2 additional chronic diseases: $p < 0.0001$], and a history of any allergies [PR = 1.95 (1.51–2.52); $p < 0.0001$].

4. Discussion

As far as we are aware, this is the largest study reporting factors associated with self-reported PFP among cyclists entering a community-based mass participation-cycling event. The main findings are: 1) the prevalence of a history of PFP in cyclists was not significantly different by sex or age groups, 2) training and racing variables were not associated with a history of PFP in cyclists (multivariate model), and 3) independent factors associated with a history of PFP in cyclists were chronic disease history and allergy history.

Table 1
The number (n), weighted prevalence (% and 95%CI) and unadjusted prevalence ratio (PR) (with 95%CI) of cyclists with a history of PFP by sex and age group (univariate analysis) (n=59953).

Characteristics		Control group (no history of PFP) (2016–2020) (n = 59630)	Cycle race entrants with patellofemoral pain (PFP) (2016–2020) (n = 323)		PR (95% CI)	p-value
		n	n	% (95% CI)		
Sex	Males	47073	251	0.53 (0.47–0.60)	–	0.6329
	Females	12557	72	0.57 (0.45–0.72)	1.07 (0.82–1.39)[a]	
Age groups (years)	≤30	9238	54	0.58 (0.44–0.76)	–	0.0600
	31 to ≤40	12282	61	0.49 (0.38–0.63)	0.85 (0.59–1.22)[b]	
	41 to ≤50	17477	77	0.44 (0.35–0.55)	0.76 (0.54–1.07)[c]	
	>50	20633	131	0.63 (0.53–0.75)	1.09 (0.79–1.50)[d]	

PR: Prevalence Ratio.
[a] Ratio expressed as female to male.
[b] ≤40 years vs ≤ 30 years, p = 0.3795.
[c] 41 to ≤50 years vs ≤ 30 years, p = 0.1187.
[d] >50 years vs ≤ 30 years, p = 0.5936.

Table 2
The weighted prevalence (%; 95%CI) and unadjusted prevalence ratio (PR; 95%CI) of cyclists with a history of patellofemoral pain (PFP) by cycling training/racing history (2016–2020) (univariate analysis) (n = 59954).

Cycling training/racing history (2016–2020)	Points in the continuous variable[a]	Predicted frequency of cyclists with PFP at specific points in the continuous variable % (95% CI)	PR (95% CI)	p-value
Years of recreational cycling (yrs) (n = 56843)[b]	4yrs	0.50 (0.43–0.57)	1.05 (1.00–1.11)[d]	0.0461
	9yrs	0.52 (0.46–0.59)		
	18yrs	0.57 (0.51–0.65)		
Years of participation in distance cycling events >2 h (yrs) (n = 56843)[b]	3yrs	0.49 (0.42–0.56)	1.08 (1.02–1.15)[d]	0.0129
	6yrs	0.51 (0.45–0.58)		
	15yrs	0.59 (0.52–0.66)		
Average weekly training/racing frequency in the last 12 months (times per week) (n = 45226)[c]	2/week	0.48 (0.40–0.56)	1.09 (1.01–1.18)[e]	0.0402
	3/week	0.52 (0.45–0.59)		
	4/week	0.56 (0.49–0.65)		
Average weekly cycling distance in the last 12 months (km/week) (n = 56843)[b]	40 km	0.54 (0.47–0.62)	1.00 (0.93–1.08)[f]	0.9365
	70 km	0.54 (0.48–0.61)		
	120 km	0.54 (0.48–0.61)		
Average training speed category (km/h) (n = 56843)[b]	20.0 km/h	0.56 (0.49–0.63)	0.97 (0.91–1.04)[g]	0.3818
	23.0 km/h	0.54 (0.48–0.60)		
	26.0 km/h	0.53 (0.46–0.60)		

PR: Prevalence Ratio.
[a] Points on the continuous variables are the 1st quartile, median and 3rd quartile for each training variable.
[b] Variable has missing responses (n = 5729).
[c] Variable has missing responses (n = 17043).
[d] Average increase in risk for a 5-year increase.
[e] Average increase in risk for 1 or more training session per week.
[f] Average increase in risk for 50 km more training per week.
[g] Average increase in risk for 3 km/h increase in speed.

Our first finding was that demographic variables (sex, age group) were not associated with a history of PFP. There are very few studies that explored the association between sex or age and PFP in cyclists. In one study, knee pain (patellar, medial, and lateral) was reported more frequently in females vs. males (37% vs 12%: p = 0.0098), and younger age was associated with medial knee pain (p = 0.013) (Weiss, 1985). Another study in recreational cyclists reported that females are more prone to knee injuries than males (Van der Walt et al., 2014). In another study (including XC skiing, cycling, floorball and handball athletes), female athletes had a reduced risk of substantial knee problems (Clarsen et al., 2015). These results differ from the results in our study indicating that sex and age as factors associated with PFP in cyclists requires further study.

In our univariate analysis we report that several training and cycling experience factors were associated with PFP. Increased years of participation in distance cycling events >2 h, increased average weekly training/racing frequency in the last 12 months, and increased years of recreational cycling (years) were associated with a higher prevalence of PFP in race entrants. The observed prevalence ratios are small (PR less than 1.09), and the clinical significance of these findings is therefore questionable. There are very few studies that explored these variables as factors associated with PFP in cyclists. Our findings differ from those reported in one study where no relationship was shown between long distance riding experience and any other gradual onset injuries (Weiss, 1985).

We also identified that a history of certain chronic diseases was associated with a higher prevalence of PFP (PR of >2; univariate analyses), including: any symptoms of CVD, any nervous system/psychiatric disease, any GIT disease, a history of any respiratory disease, and any medication use to treat chronic disease. To our knowledge, this is the first study to identify that a higher prevalence of PFP in cyclists was associated with specific main category of chronic disease, and regular use of any prescription medication to treat chronic disease. However, the relationship between specific chronic diseases and PFP was only significant in our univariate model.

The two main novel findings of this study are that a history of multiple chronic diseases, represented by the CCDS, and a history of

Table 3
The number (n), weighted prevalence (% and 95%CI) and unadjusted prevalence ratio (PR) of cyclists with a history of patellofemoral pain (PFP) by history of main category of chronic disease, a history of allergies, and regular use of any prescription medication use to treat chronic disease (univariate analysis) (2016–2020) (n = 59954).

Variable		Cycle race entrants with patellofemoral pain (PFP) (2016–2020) (n = 323)		PR (95% CI)	p-value
		n	% (95% CI)		
Composite Chronic Disease Score (0-10)	0 chronic diseases	–	0.42 (0.37–0.48)	2.23 (1.80–2.77)[a]	<0.0001
	2 chronic diseases	–	0.94 (0.79–1.12)		
	4 chronic diseases	–	2.10 (1.46–3.02)		
Any risk factor for CVD	yes	77	0.66 (0.52–0.82)	1.28 (0.99–1.66)	0.0635
	no	246	0.51 (0.45–0.58)		
Any history of CVD	yes	20	0.92 (0.59–1.42)	1.74 (1.11–2.74)	0.0267
	no	303	0.53 (0.47–0.59)		
Any symptoms of CVD	yes	13	2.08 (1.22–3.55)	3.98 (2.30–6.88)	<0.0001
	no	310	0.52 (0.49–0.58)		
Any endocrine disease	yes	17	0.88 (0.55–1.40)	1.66 (1.03–2.68)	0.0541
	no	306	0.53 (0.47–0.59		
Any respiratory disease	yes	65	1.05 (0.82–1.34)	2.18 (1.66–2.87)	<0.0001
	no	258	0.48 (0.43–0.54)		
Any GIT disease	yes	40	1.27 (0.93–1.73)	2.55 (1.83–3.55)	<0.0001
	no	283	0.50 (0.44–0.56)		
Any nervous system/psychiatric disease	yes	28	1.33 (0.92–1.93)	2.62 (1.78–3.84)	<0.0001
	no	295	0.51 (0.46–0.57)		
Any kidney/bladder disease	yes	15	0.89 (0.54–1.47)	1.68 (1.01–2.82)	0.0652
	no	308	0.53 (0.47–0.59)		
Any haematological/immune disease	yes	5	0.71 (0.31–1.63)	1.31 (0.57–3.05)	0.5423
	no	318	0.54 (0.48–0.60)		
Any cancer	yes	18	0.92 (0.58–1.46)	1.74 (1.08–2.81)	0.0351
	no	305	0.53 (0.47–0.59)		
Any allergies	yes	86	1.05 (0.85–1.29)	2.28 (1.78–2.92)	<0.0001
	no	237	0.46 (0.40–0.52)		
Any medication use to treat chronic disease	yes	89	0.96 (0.78–1.18)	2.07 (1.62–2.64)	<0.0001
	no	234	0.46 (0.40–0.52)		

CVD: Cardiovascular disease.
GIT: Gastrointestinal disease.
n: number of cyclists in the study.
PR: Prevalence ratio.
[a] Average increase in risk for 2unit increase in CCDS.

allergies were associated with an increased risk for developing a history of PFP in CTCT consenting race entrants in a multivariate model. We show that for each additional 2 chronic diseases a cyclist reported, the prevalence risk of PFP increases almost 2 times in a "dose-dependent" fashion. The prevalence of chronic disease among recreational cyclists varies between 10 and 16% (Weiss, 1985; Wilber et al., 1995).

The potential mechanisms to explain the relationship between chronic disease and risk of a history of PFP in cyclists could not be explored due to the cross-sectional nature of our study. We hypothesise the potential mechanisms that could account for our findings are related to either the disease itself or medication that is used to treat the chronic disease. The relationship between specific chronic disease entities and pathology in ligaments, tendons and bone has been documented (Aicale et al., 2018; Applegate et al., 2017; Burne et al., 2019; Daga et al., 2018; Nayyar et al., 2017; Nichols et al., 2020). Specifically, hypercholesterolemia, diabetes mellitus, and metabolic syndrome are associated with chronic tendinopathy (Aicale et al., 2018; Applegate et al., 2017; Burne et al., 2019; Nichols et al., 2020), and there is an increased risk for bone stress injuries in chronic obstructive pulmonary disease (Daga et al., 2018; Nayyar et al., 2017). A further explanation is that cyclists could not distinguish between patellofemoral pain, and patellofemoral arthropathy (osteoarthritis). Patellofemoral osteoarthritis is more common in the older population, who also have a higher prevalence of chronic diseases. Future studies are required to determine if factors associated with PFP in cyclists differ from patellofemoral osteoarthritis in cyclists.

As mentioned, another possibility is that the medication used in the treatment of chronic diseases can result in increased risk of injury. For example, statin drugs are associated with increased risk of skeletal muscle myopathy (Mammen, 2016; Marie et al., 2008), while proton pump inhibitors (Thong et al., 2019) and corticosteroids may have a negative effect on bone remodelling and mineralization, which can increase the risk of osteopenia (Daga et al., 2018; Diehl & Johnson, 2016; Rice et al., 2017). The side effects of certain drugs such as statins may be dose-dependent, while for other drugs such as corticosteroids, it is difficult to quantify the relationship between dosage and side effects (Rice et al., 2017). We acknowledge that additional research must be done to determine if there is a cause-effect relationship between a history of PFP and chronic disease in recreational cyclists and to determine mechanisms responsible for the effect. However, we recommend that clinicians take note of the possible relationship between PFP and certain chronic diseases, particularly when introducing injury prevention programs and managing patients. Regular physical activity has numerous health benefits, and cyclists with a history of chronic disease will benefit greatly from staying physically active.

Our second novel finding was that allergy history was associated with history of PFP in cycle race entrants. Data showing that allergy history is associated with a history of any gradual onset injury in recreational cyclists, (du Toit et al., 2020b), trail runners (Viljoen et al., 2021), and ultra-marathon runners (Mokwena et al., 2021) was recently reported. We can only speculate on the possible reasons for the association between allergies and PFP. The mechanisms responsible for the increased risk of injury may again be the allergy itself or be related to the medication used to treat the allergy. Various outdoor and indoor training/racing settings potentially

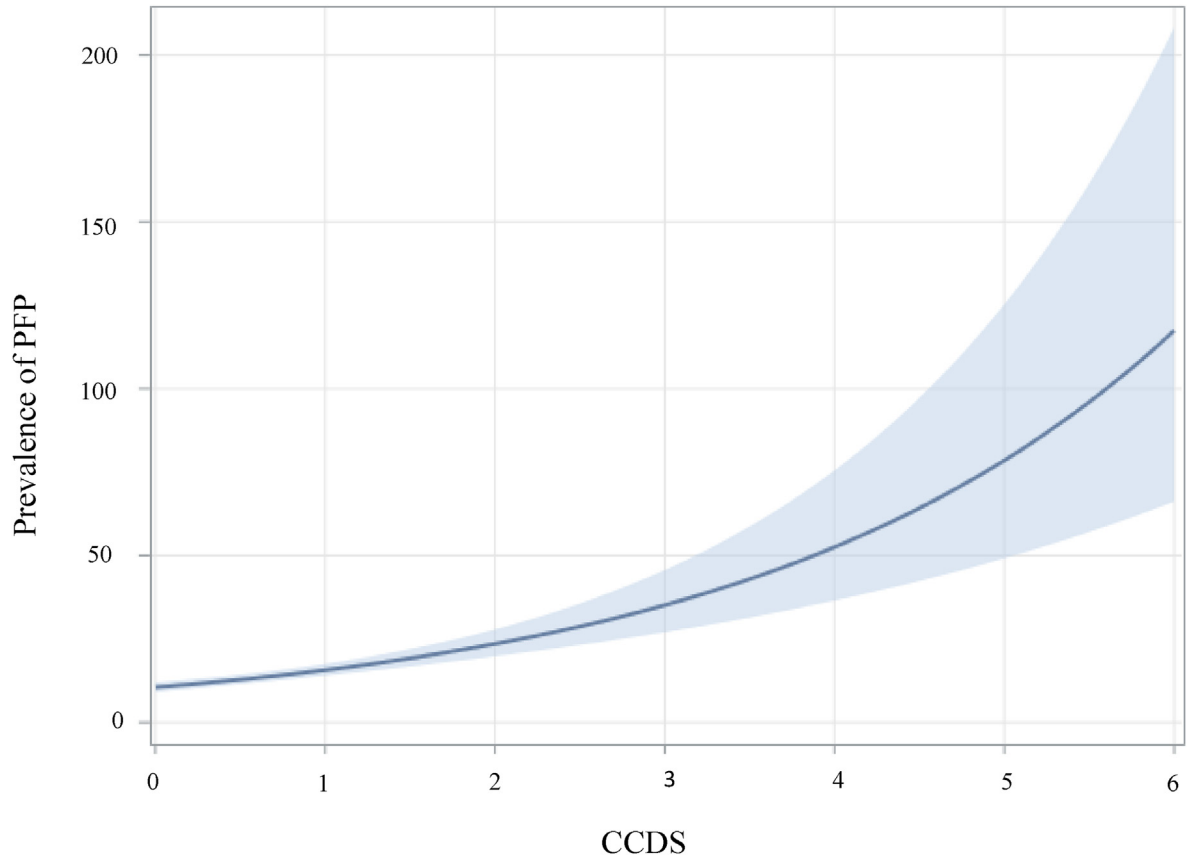

Fig. 1. The relationship between the Composite Chronic Disease Score (CCDS) and prevalence of patellofemoral pain (PFP) in cyclists (shaded area: 95%CI). Fig. 1 was limited to CCDS = 6 (sample size too small at higher CCDS).

expose the cyclists to a variety of allergens. Antihistamines are commonly used to treat allergies, and recently there has been considerable interest in the role that histamine plays in the recovery and adaptation to training, as well as the acute response to exercise (Ely et al., 2019; Luttrell & Halliwill, 2017; Van der Stede et al., 2021). Antihistamines can also have side effects such as drowsiness and fatigue (Randall & Hawkins, 2018). The use of antihistamines during training and racing may increase injury risk if fatigue alters lower extremity muscle strength and postural control (Verschueren et al., 2020). Again, we recommend that future research explores potential mechanisms between PFP and allergies or the medication used to treat allergies.

This is a large study where multiple factors associated with history of self-reported PFP were explored in a multivariate model. This study forms part of a larger study in which a variety of musculoskeletal injuries are explored in the same dataset. We acknowledge that this study has several limitations. The correlated nature of the data could not be considered since individual cyclists could enter the race in more than one year (between 2016 and 2020). These entries could not be identified from year to year, and we are unable to report the percent of returning cyclists by year. This influences the SEs of the estimates (smaller SEs) and therefore the significance of the tests. The generalizability of our study is limited because the medical questionnaire was voluntary 2017–2020, not all entrants gave consent for their data to be used, and the consenting entrants we studied consisted mostly of male cyclists and cyclist in the older population. Another limitation is that injury and training data are self-reported, potentially introducing recall bias. Furthermore, we recognise that the diagnosis of the injury was not confirmed by a health professional, and the pathology involved could not be confirmed or verified by clinical evaluation or special investigations. Due to the length of the medical questionnaire, we could not include specific details about the features of each type of injury or pathology to assist entrance in reporting specific injuries. We recognise that as a limitation and potential for improving data collection in future. For example, cyclists may not have been able to distinguish between PFP and patellofemoral osteoarthritis. This is a large population-based pragmatic study in a large sample of cyclists and verification of injuries by clinical examination and special investigation is not feasible. Cyclists training for and entering an endurance race of 90 km are also generally well informed and are familiar with specific common cycling injuries such as anterior knee pain/patellofemoral pain. We also recognise this is a cross-sectional study and we cannot establish a cause-effect relationship between any of the identified factors and PFP. The cause-effect relationship needs to be explored in future studies. Finally, we acknowledge that many other factors (e.g. individuals' level of conditioning, lower limb biomechanics, cycling surface, cyclist-bicycle fit) may also be associated with increased risk for developing PFP. In our study, we could not explore a complete set of possible factors that may be associated with a history of PFP. Future studies are needed to explore the causal relationship between the factors and PFP among cycle race entrants.

5. Summary and conclusion

We identified novel factors associated with a history of self-reported PFP in a large cohort of recreational cyclists studied over 5 years, using a multivariate model. The main independent factors

associated with a history of self-reported PFP in race entrants were a history of multiple chronic diseases and a history of any allergies. We acknowledge that the factors associated with a history of PFP are multifactorial and that the cause-effect relationship needs to be explored in future longitudinal studies. Of clinical importance is the relationship between PFP in cyclists and certain chronic diseases and allergies because cycling is a popular and useful physical activity intervention to treat chronic diseases. Practical clinical recommendations are: 1) that prevention programs for PFP be considered when cycling is prescribed as a physical activity intervention for patients with chronic disease, and 2) that older cyclists presenting with PFP be assessed for the presence of risk factors or existing chronic disease.

Data sharing statement

No additional data are available.

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Ethical statement

A cross-sectional study design was used. Prior to the onset of the study, the Research Ethics Committee of the Faculty of Health Sciences approved the study (REC numbers 749/2019). This study is part of a series of ongoing SAFER (**S**trategies to reduce **A**dverse medical events **F**or the **E**xercise**R**) studies, for which data collection is ongoing.

Declaration of competing interest

The authors declare that there are no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ptsp.2022.12.007.

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