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Depression and the General Health of Retired Professional Footballers compared to the General Population: A Case Control Study

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Depression and the General Health of Retired Professional Footballers compared to the General Population: A Case Control Study

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Abstract

Objectives: To determine the prevalence of depression and general health of male ex-professional footballers compared to general population controls.

Methods: 572 retired professional footballers and 500 general population controls in the UK were assessed by postal questionnaire. Anxiety and depression were defined using the Hospital Anxiety and Depression Scale (HADS) with an optimal cut-off score for each being >11. General health was ascertained using: the SF-12 quality of life tool; self-reported comorbidities, analgesic usage and body pain; and index of multiple deprivation (IMD) based on postcode data. Mood was assessed using the positive and negative affect scale (PANAS) and sleep using the Medical Outcome Survey (MOS). Linear regression analysis was used to determine relative risk (aRR) with 95% confidence intervals (CI) and adjusted for age, body mass index (BMI), comorbidities, body pain and medication usage.

Results: Depression prevalence in retired professional footballers was 5.66% compared to 5.76% in the general population and anxiety prevalence was also comparable (12.01% vs. 10.29%; all $p>0.05$). However, footballers had lower physical and mental component scores compared to controls ($p<0.01$). They also reported significantly more sleep problems, more negative mood profiles and more widespread body pain (aRR 1.88, 95% CI 1.15 - 3.09). They also reported greater pain medication usage compared with controls (aRR 1.54, 95% CI 1.26 - 1.89). However, compared to controls they were 26% (95% CI, 15% - 37%) less likely to report comorbidities, especially heart attacks (57%, 95% CI 27% - 74%) and diabetes (61%, (95% CI 37% - 76%).

Conclusions: The prevalence of depression and anxiety in ex-professional footballers is comparable to general population controls. However, ex-footballers reported lower health-related quality of life, more widespread body pain and higher analgesic usage. Conversely lower reporting of diabetes and heart attacks indicate potential long-term physical health benefits from professional football.

Strengths:

- Largest study of depression and general health in ex-professional footballers and controls in the UK
- Case-control study design with control male participants recruited from a community-based population sample representative of the UK general population
- Depression and anxiety assessed using the validated Hospital Anxiety and Depression Scale in both ex-footballers and control men.

Limitations:

- Outcomes were self-reported by participants using postal questionnaires
- Lack of current or previous physical activity levels assessed
- Higher response rate in the ex-footballers compared to the control participants.

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Keywords:

Professional football, epidemiology, depression, anxiety, sleep, pain, cardiovascular health

Key Messages:

Footballers have poorer quality of life with lower physical and mental component scores but do not experience more depression or anxiety compared to controls.

They report more widespread body pain, more use of analgesics (particularly NSAIDs and OTC analgesics) and have poorer sleep quality (restlessness, shortness of breath and drowsiness).

Although they report worse musculoskeletal health, they report better general systemic health (less heart disease and diabetes) compared with controls.

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Introduction

Football is the world's most popular sport with over 300 million active players worldwide and 110,000 athletes registered at a professional level¹. There has been considerable interest in whether the mental health of athletes is often compromised, especially by anxiety and depression². Retired professional footballers may experience unique psychological stress factors primarily due to the nature and the intensity of the sport where severe or recurrent injuries are common³ and the pressures of competition, training and maintaining high-performance levels are hallmarks of a successful professional career⁴. The intensity of mental and physical demands may increase their susceptibility to certain mental health problems and risk-taking behaviour.

Despite individual high-profile cases of depression in the United Kingdom (e.g. Gary Speed, Paul Gascoigne, Clarke Carlisle), there is a lack of robust epidemiological studies on mental health issues in professional footballers. Studies on European former professional footballers from countries such as the Netherlands have reported anxiety and depression prevalence figures ranging from 25-43%⁵. However, none of these studies included a non-athlete or general population comparison group. A recent systematic review suggests that despite a seemingly higher risk of anxiety and depression in athletes in a range of elite sport, the figures are broadly comparable to the general population. The review further concluded that the evidence base is restricted by a paucity of high-quality study designs particularly in professional footballers⁶. Turner et al.⁷ also found that anxiety and depression featured in 37% of former players with knee pain and knee osteoarthritis. A subsequent phenomenological study⁸ suggested that these may be common sequelae of significant sport injuries that caused frustration and associated participation restrictions and limitations to work, social and leisure activities. Studies focused on mental health and well-being of athletes are limited by study design; lack of power and small sample sizes; and comparison across sporting populations^{2,9-12}.

Therefore, any future studies should be focused on an individual sport such as professional football and its full-time players; powered for depression outcomes and with an age-adjusted control population; investigate any comorbidities and auxiliary

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3 measures of mental health and well-being such as sleep patterns, mood profiles,
4 quality of life (QoL) and pain distribution including use of pain medication.
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8 Therefore, based on previous research and the gaps in the evidence base, the
9 objectives of the present study were to: (1) determine the prevalence of anxiety and
10 depression in retired professional footballers compared to general population controls;
11 (2) determine the general health in retired professional footballers compared to
12 general population controls; and (3) determine the risk and protective factors
13 associated with professional football.
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Methods

The Nottingham Research Ethics Committee 1 (Refs 14/EM/0045 & 14/EM/0015) approved this study. A cross-sectional design was used, involving a series of postal questionnaire surveys to ex-footballers and to a sample of men in the general population (aged 40 years and over) to gain information on anxiety, depression, mood and sleep as well as well as simple demographics, occupational history, general health (comorbidities) and current medications. The exclusion criteria at baseline were known terminal illness, severe psychiatric illness or dementia, or any other condition or circumstance considered by their General Practice to make them unsuitable to receive the questionnaire.

Participants

The recruitment of the source sample of ex-footballers and general population controls has been detailed in a previous publication examining the risk of knee pain and osteoarthritis in the footballers versus the controls¹³. Individuals in that study who indicated interest in further research conducted by the University of Nottingham were subsequently contacted with a follow-up questionnaire focused on mental health and well-being.

Questionnaire Survey

The postal questionnaire was developed based on previously published questionnaires and using extensively validated tools in the retired footballers and the control population. Through public and patient involvement, pilot versions of the questionnaire were evaluated to identify any problems with content, language and layout. The questionnaires were similarly constructed to capture detailed information about all participants (including football career history for retired footballers), anthropometric details (age and body mass index (BMI)), medical history and current medication usage.

Age and body mass index (BMI)

Participants self-reported their date of birth and height and weight in the returned questionnaires. BMI was calculated as the weight divided by the square of height (kg/m²).

Anxiety and depression

Anxiety and depression were determined using the Hospital Anxiety and Depression Scale (HADS) which is comprised of 14 items, equally divided between the two mood states (anxiety and depression). Each item has a 4-point rating scale. Responders are asked to indicate their feelings based on the previous one week with recommended cut-off points indicating whether the responder is: a) within the normal range (scores of 0-7), b) mild-moderate caseness (scores of 8-10) and, c) severe caseness (scores of 11-21). Although cut-offs of > 8 have been used in some studies to indicate anxiety or depression¹⁴ this threshold is considered too low and lacking in sensitivity for use in a general population sample¹⁵ so a cut-off of ≥ 11 was used to identify definite anxiety and definite depression.

Quality of Life Measures

QoL was assessed using the Medical Outcome Study Short Form-36 Health Survey Questionnaire (SF-36) in the ex-footballers which was converted into SF-12 and the Medical Outcome Study Short Form-12 Health Survey Questionnaire (SF-12) in the general population controls. The difference in SF versions was due to logistical reasons as the control postal questionnaire was more challenged by length restrictions than the second follow-up questionnaire to ex-footballers. Each SF response was used to calculate scores in each of the eight domains: physical functioning; role physical; bodily pain; general health perception; vitality; social functioning; role emotional; and mental health. These figures were then standardised using z-score transformations using means and standard deviations previously described (Jenkinson 1999). Using the z scores for each scale, the aggregate score for two summary scales: the Mental Component Score (MCS) and the Physical Component Score (PCS) were calculated. Finally, the scores were standardised to a T-score where the mean was set to 50 and the standard deviation to 10. For the SF-12, scoring was conducted according to previously published data^{16,17}. Item weights for response categories from an American population-based study, which was found comparable to other population studies in nine other countries including the United Kingdom, was used to standardise responses¹⁶. There is considerable evidence suggesting that the PCS and MCS from the SF-12 show similar levels of precision to the summary scores derived from the longer SF-36 version. Even though summary scores are not exactly

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3 identical the level of difference between the two is small and is not subjectively or
4 clinically meaningful¹⁸.
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8 Medical Outcome Survey (MOS) Sleep Scale 9

10 The sleep scale from MOS is a 12-item measure that is generic and not disease
11 specific and measures 6 dimensions of sleep: sleep disturbance, snoring, shortness
12 of breath with headache, sleep adequacy, somnolence and quantity of sleep¹⁹. The
13 tool has demonstrated excellent reliability and validity for assessing sleep in
14 community samples^{20,21}. A sleep problems index (SLP-9) can be calculated using nine
15 items from the MOS Sleep scale indicating quality of sleep on a 0-100 scale. The
16 higher the score, the lower the quality of sleep. The quantity of sleep is recorded as
17 the average hours of sleep per night over the previous 4-week period and was
18 dichotomised as optimal sleep (if this was 7-8 hours) or non-optimal if this was less
19 than 7 hours or greater than 8 hours as per MOS sleep scoring criteria.
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29 Positive and Negative Affect Scale (PANAS) 30

31 PANAS is a self-report questionnaire comprising two 10-item scales, which describe
32 different feelings and emotions measuring both positive and negative affect²². The
33 questionnaire asked responders to consider their feelings at the time of completing the
34 questionnaire. The normal population reference guides for mean positive affect score
35 is 29.7 (+ 7.9) and mean negative affect score is 14.8 (+ 5.4). PANAS has
36 demonstrated high reliability and construct validity, is brief and ideal for use in self-
37 reported questionnaires and has been used extensively alongside measures of anxiety
38 and depression such as HADS^{23,24}.
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47 Indices of Multiple Deprivation 48

49 The Index of Multiple Deprivations (IMD) is an official measure of the relative
50 deprivation in England²⁵. It ranks all areas in England from 1 (most deprived) to 32,844
51 (least deprived area) and is based on weights given to key domains such as income,
52 employment, education and housing. It uses postcodes to determine an overall
53 measure of deprivation. This information was then presented in quintiles with
54 percentage of footballers and controls within the lowest and highest quintiles.
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Comorbidities

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3 Individual comorbidities were self-reported according to a brief specific checklist
4 enquiry (fibromyalgia, diabetes, heart attacks, hypertension, cancer), with data
5 dichotomised into individuals with or without these conditions. An open text question
6 was also included to capture information on any other diagnosed medical conditions
7 not on the checklist²⁶.
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13 Widespread Body Pain

15 Widespread body pain was self-reported using a body pain mannequin²⁷. It was scored
16 using the American College of Rheumatology criteria for widespread body pain whose
17 definition is pain in each of the four quadrants of the body and including the spinal or
18 axial column. Reported pain in any part of the body was dichotomous (present/absent)
19 and total number of regions with pain was a simple count of the shaded regions of the
20 manikin.
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27 Pain-relieving Medication

29 Self-reported analgesic medication (both prescribed and over the counter) was
30 recorded and grouped as all pain-relieving medication, and sub-grouped as anti-
31 inflammatory drugs (NSAIDs), opioids, other over the counter (OTC) and prescribed
32 analgesics, and other medications with pain-modifying properties (e.g. citalopram and
33 amitriptyline).
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39 Statistical Analyses

41 A power calculation was conducted based on a 12.6% prevalence of depression in a
42 non-clinical sample of community-derived adults using the HADS¹⁵ and an odds ratio
43 (OR) of 2 after adjustment for other known factors in ex-footballers. The sample size
44 required to detect this OR, with 90% power and a 0.05% significance level, was 336
45 participants per group.
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49 Categorical variables were reported as frequencies and percentages, and continuous
50 variables as mean and standard deviations (SD). To determine whether distributions
51 of the variables were statistically significant between ex-footballers and controls a t-
52 test (continuous variables) or chi-square test (categorical variables) was used. For the
53 SF-12 outcomes, specifically the physical component score and mental component
54 score between footballers and controls, we used the ranksum command in Stata,
55 which compared two independent samples using the Mann-Whitney two-sample
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3 statistic. Statistical significance was defined as $p < 0.05$. We had very few missing
4 data at random (e.g, where BMI was not reported by a participant). Imputation or
5 modelling was therefore not undertaken for the occasional missing values. Details on
6 missing data have previously been published¹³.
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11 All analyses were conducted using Stata IC Version 14 on Windows 7 Operating
12 System and power calculations were undertaken using OpenEpi Version 3.
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Results

Of the 898 questionnaires sent to the retired professional footballers, 572 responses were received (63.7% response). Of 2215 questionnaires sent to general population controls, 500 questionnaires were received (22.6% response) (Figure 1).

Figure 1. Selection of ex-footballer and general population controls.

The mean age of the ex-footballers was significantly younger than the controls (60 versus 64 years)) but mean BMI were comparable (Table 1).

Table 1. Characteristics of footballer and control populations.

	Footballers n=572	Controls n=500	p-value
Age (years), mean (SD)	60.11 (10.77)	64.26 (9.37)	<0.001
BMI (kg/m ²), mean (SD)	27.13 (3.40)	27.29 (4.48)	0.51
Anxiety (cases), n (%)	70 (12.01)	50 (10.29)	0.34
Depression (cases), n (%)	33 (5.66)	28 (5.76)	0.94
SF Physical Component Score, mean (SD)	45.33 (10.32)	77.60 (8.35)	<0.001
SF Mental Component Score, mean (SD)	48.09 (7.47)	71.87 (6.64)	<0.001
Optimal sleep (7-8 hours per night), n (%)	369 (64.51)	275 (56.70)	0.01
Sleep Problem Index, n (%) in highest tertile of SIP	186 (33.04)	131 (26.90)	0.03
Positive Mood, mean (SD)	34.75 (8.05)	34.97 (6.86)	0.63
Negative Mood, mean (SD)	16.5 (6.72)	14.22 (4.95)	<0.001
Indices of Multiple Deprivation (IMD) n, (%) in the lowest and highest quintile	17 (3.51) 205 (42.27)	84 (17.28) 199 (40.95)	<0.001 0.18

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3 The prevalence of depression was similar in the footballers and controls (5.7% versus
4 5.8%) but the prevalence of anxiety was slightly higher in the footballers (12.0% versus
5 10.3%) though this was not statistically significant. Although footballers and controls
6 shared a similar positive mood profile, footballers were significantly more likely to
7 experience negative moods compared to the controls and to have greater problems
8 with sleep quality ($p<0.05$). When using the sleep problem index, more footballers
9 reported problems with sleep quality ($p<0.05$) and poor sleep patterns which included
10 restlessness, shortness of breath and drowsiness. They were also more likely to have
11 lower scores in terms of both their physical and mental health as indicated by the SF-
12 12 QoL measure.
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22 With respect to social deprivation, fewer footballers (3.51%) were living in areas
23 marked as the most deprived compared to the control population (17.28%; $p<0.001$).
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27 Risk factors associated with professional football following adjustment for age and BMI
28 are presented in Table 2. Ex-footballers overall were less likely to present with any
29 comorbidity (diabetes, hypertension, myocardial infarction, cancer and fibromyalgia),
30 especially diabetes (61%, 95% CI, 37-76%), heart attacks (57%, 95% CI 27-74%) and
31 hypertension (21%, 95% CI 4-35%). However, footballers reported more widespread
32 body pain using the ACR criteria (88%, 95% CI 15-30.9%). Footballers also
33 consumed more NSAIDs (8.6% vs. 4.2%) and OTC analgesics (24% vs. 14%) but not
34 opioids (4% vs. 6.4%) compared to the controls.
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Table 2. Comparison of self-reported comorbidities, pain and medication in the ex-footballers compared to general population controls

	Footballers 572	Controls 500	p-value	Adjusted relative risk (95% CI) (for age and bmi)
Comorbidities* n (%)	178 (30.58)	260 (52.31)	<0.001	0.74 (0.63-0.85)+
Comorbidities** n (%) (by Charlson Comorbidity Index weighting** mean (SD)	0.44 (0.80)	0.75 (0.98)	<0.001	0.71 (0.6-0.85)+
Diabetes, n (%)	22 (3.77)	57 (11.47)	<0.001	0.39 (0.24-0.63)+
Cancer, n (%)	40 (6.86)	50 (8.58)	0.07	0.88 (0.59-1.30)
Heart Attacks, n (%)	18 (3.08)	47 (9.46)	<0.001	0.43 (0.26-0.73)+
Hypertension, n (%)	134 (22.98)	169 (34.00)	<0.001	0.79 (0.65-0.96)+
Fibromyalgia, n (%)	3 (0.51)	1 (0.20)	0.39	3.08 (0.31-31.02)
Any Body Pain, n (%)	454 (78.14)	330 (71.90)	0.02	1.09 (1.00-1.17)~
ACR Criteria				
Widespread Body Pain (no KP), n (%)	48 (8.40)	23 (4.60)	0.01	1.88 (1.15-3.09)~
Total Regions with Pain, mean (SD)	3.13 (3.29)	3.44 (3.05)	0.14	0.91 (0.79-1.05)
Back pain, n (%)	176 (30.18)	146 (29.38)	0.57	1.00 (0.76-1.32)
Knee pain, n (%)	337 (57.80)	193 (38.83)	<0.001	1.47 (1.29-1.69)~
Pain Medication Use, n (%)	240 (41.17)	165 (33.20)	0.007	1.54 (1.26-1.89)~
Opioids, n (%)	23 (4.03)	32 (6.40)	0.07	0.64 (0.37-1.10)
NSAIDS, n (%)	49 (8.58)	21 (4.20)	0.004	1.94 (1.19-3.20)~
OTC Analgesics, n (%)	137 (23.99)	70 (14.00)	<0.001	1.86 (1.44-2.43)~
Other medications***, n (%)	18 (3.15)	31 (6.20)	0.01	0.50 (0.28-0.94)+

*Diabetes, hypertension, myocardial infarction, cancer and fibromyalgia

**Includes myocardial infarction, hypertension, diabetes and cancer

*** Other medications with pain relieving effects.

+ Protective factors

~ Risk factors

Discussion

This is the first study to report the prevalence of depression, anxiety and the general health and well-being of retired professional footballers compared to a control population. The main findings are (1) the prevalence of depression and anxiety in the ex-footballers is comparable to men in the general population; (2) ex-footballers have a lower QoL as indicated by the SF-12 physical and mental component scores; (3) they are more likely to present with widespread body pain and use pain medication particularly OTC analgesics and NSAIDs; and (4) they are less likely to present with comorbidities, in particular diabetes, heart attacks and hypertension.

The study reported a prevalence of depression (6%) and anxiety (12%) in ex-footballers which is lower than the 25-43% reported by Goutterborge⁵. This discrepancy could result from smaller sample sizes (range of 70-149 ex-players), sample selection and status of footballers (current professional footballers from five different European countries), and the assessment tool used to determine depression and anxiety (12-item general health questionnaire (GHQ-12)) in that study. In a further study²⁸, specifically investigating ex-footballers, estimated a 39% prevalence of both anxiety and depression using the GHQ-12. A number of self-report assessment tools have been used in epidemiological research to detect depression and anxiety²⁹⁻³¹. While the GHQ-12 has demonstrated excellent validity in detecting depression in the general population³², the HADS has demonstrated better sensitivity and specificity in detecting depression. Indeed, the choice of assessment tool should be balanced with feasibility of approach, cost effectiveness, as well as the administration and scoring times involved²⁹. Additionally, none of the previous studies in ex-footballers presented results for an adequately matched comparison group of non-professional footballers. The results of this study accord with a comparative meta-analysis in high-performance athletes and non-athletes showing similar levels of depression across the groups⁴. Elite athletes are sometimes supported with psychological training as part of their sport programs and may have developed mental toughness and resilience in order to cope with stress, anxiety and even depression³³⁻³⁵. There is a noted stigma about reporting mental health symptoms both in ex-footballer and general population samples which may result in choosing to suppress, ignore and not seek further help when needed^{6,29,36}. Furthermore, when compared to another general population study, the

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3 prevalence of depression (7-9%) and anxiety (8-14%) in general population men aged
4 40-65 years is comparable to the controls in this study, suggesting that this East
5 Midlands control population are representative of the British general population and
6 are a valid control group³⁷.
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11 In terms of QoL, the ex-footballers had significantly lower scores in both physical and
12 mental components compared to controls. It has been postulated that this negative
13 effect on QoL is a consequence of reporting more specific joint pain (e.g. knee pain)
14 and more overall body pain^{13,38}. Although both the ex-footballers and the control
15 population indicated pain in one region on a body pain manikin (78% vs. 72%), after
16 adjustment for age and BMI, ex-footballers are 88% more likely to present with
17 widespread body pain when using the more stringent ACR criteria compared to the
18 control group. Widespread pain can have significant, deleterious effects on physical
19 and mental health and well-being³⁹ including implications on sleep disturbance and
20 mood. Longitudinal cohort studies have shown that insomnia and sleep disturbances
21 significantly increase the risk of chronic pain in pain-free individuals at baseline whilst
22 pain is not a strong predictor of insomnia⁴⁰. As a result of the cross-sectional nature
23 of this study, we cannot ascertain causation between pain and sleep. However, the
24 results in ex-footballers show that whilst sleep duration may be marginally better (64.5
25 vs. 56.7% for 7-8 hours of sleep), the quality of sleep was more disturbed in terms of
26 restlessness, feeling tense or drowsy compared to controls. The effect on mood is
27 also notable with ex-footballers more likely to present with negative feelings and
28 emotions such as distress, irritability, fear and nervousness compared to controls. The
29 association of emotional distress and pain-related fear on patients with chronic pain
30 has been established in previous population-based studies⁴⁰⁻⁴². Widespread body pain
31 is a key feature of fibromyalgia, but the cross-sectional nature of this study does not
32 allow investigation of temporal trends⁴⁴. A further indication of higher pain levels in ex-
33 footballers is the significantly higher use of analgesics (41%) compared to controls
34 (33%) and in particular NSAIDs (8.58% vs. 4.20%) and OTC analgesics (24% vs.
35 14%). The use of analgesics presumably reflects compromised musculoskeletal
36 health, whereas in terms of systemic general health the footballers reported
37 significantly less diabetes, cancer, heart attacks and hypertension compared to
38 controls. These results accord with previous studies of elite male athletes and ex-
39 footballers with lower risk of ischaemic heart disease and diabetes, but an elevated
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3 risk of musculoskeletal conditions particularly lower limb osteoarthritis^{13,45}.
4 Interestingly, ex-footballers reported significantly lower use of drugs such as
5 citalopram, diazepam, and temazepam which are used primarily in the treatment of
6 depression and anxiety respectively. Although the study was not powered for
7 medication outcomes, the use of medication in the footballer cohort was primarily for
8 pain relief rather than relief for mental health problems. In fact, ex-footballers may have
9 developed a certain resilience and mental toughness due to being an elite athlete
10 which may be a protective factor for long term mental ill-health^{4,33,46}.
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19 There are several caveats to this study. Firstly, this was a postal questionnaire study
20 focused on pain and osteoarthritis in ex-footballers¹³, and a community sample²⁶, so
21 may be subject to response bias (those with pain are more likely to respond). However,
22 this would not explain the between group differences. Secondly, the response rate
23 was higher in the ex-footballer cohort than the controls (63.7% vs. 22.6%) and the low
24 response rate in controls questions the representativeness of the sample. Thirdly, the
25 comorbidities and medications were self-reported, and due to logistical reasons
26 relating to questionnaire length, data on established associated risk factors for
27 depression and anxiety such as smoking status, alcohol consumption, educational,
28 marital and economic status⁴⁷⁻⁴⁹ were not available. Also, although the study did not
29 find any differences between ex-footballers and controls in terms of mental health it
30 would have been interesting to examine mental toughness, resilience, optimism and
31 general pain coping mechanisms between the two populations. Future epidemiological
32 research on this topic should explore these relationships in more detail. Lastly, this
33 study did not specifically measure two aspects of quality of life: physical health via
34 current physical activity levels, and, social relations via personal relationships or
35 available social support. These data would have given us insight into current physical
36 fitness levels, physical limitations as a consequence of musculoskeletal conditions,
37 and whether there was adequate psychosocial support in an individual's life. These
38 form some of the core tenets of a healthy quality of life⁵⁰ and may have offered robust
39 data on previously reported anecdotal effects of bankruptcy, divorce or trauma
40 particularly in the ex-footballers⁵¹.
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58 In summary, this is the largest study on anxiety, depression and quality of life in ex-
59 professional footballers and the first to include an age-adjusted general population
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3 comparison sample. The results show that ex-footballers are just as likely to have
4 anxiety and depression as controls, but they have lower QoL in terms of both physical
5 and mental well-being. However, despite reporting more widespread body pain and
6 use of analgesics, they are less likely to report cardiovascular disease or diabetes.
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8 The results suggest that healthcare providers, club management and football
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10 organisations should be focused on improving musculoskeletal pain management
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12 strategies in ex-footballers and further study the benefits of professional sport on
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14 coping and resilience mechanisms which may be protective factors for long term
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16 psychological consequences such as depression and anxiety.
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Affiliations

None of the study sponsors/funders were involved in the study design, in the collection, analysis and interpretation of data, in the writing of the report and in the decision to submit the article for publication.

All researchers were independent from funders.

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Declarations:

Consent:

The study was approved by Nottingham University Hospitals NHS Trust and the Nottingham Research Ethics Committee 1 (Refs 14/EM/0045 & 14/EM/0015) and registered (clinicaltrials.gov portal: NCT02098044 & NCT02098070).

All participants offered consent by responding to the postal questionnaire survey and written informed consent prior to radiographic assessment at the SPIRE Hospitals and the Nottingham City Hospital.

Contributor's statement:

GSF designed the data collection tools, wrote the statistical plan, implemented the study design (conducted the study), conducted cleaning and analysis of the data, wrote the initial drafts of the paper and subsequently revised the paper after feedback from the team. SMP designed the data collection tools, wrote the statistical plan, implemented the study design (conducted the study), conducted cleaning and analysis of the data, and drafted and revised the paper. JPM conducted cleaning and analysis of the data, and drafted and revised the paper. CWF conceptualised the study and drafted and revised the paper. BS conceptualised the study and drafted and revised the paper. MEB monitored data collection and drafted and revised the paper. WZ conceptualised and designed the study and data collection tools, wrote the statistical plan, monitored data collection and drafted and revised the paper. MD conceptualised and designed the study and data collection tools, monitored data collection and drafted and revised the paper. He is guarantor.

Patient and Public Involvement:

The study was supported by a patient advisory group which provided input to the programme of research. Patients and ex-professional footballers partnered with us for the design of the study, the informational material to support the intervention, and the burden of the questionnaire from the patient's perspective. At the end of the study the patient advisory group commented on the findings and contributed to the dissemination plan and this included input on poster and oral presentations at local, national and international conferences.

Conflict of Interest Disclosures:

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3 submitted work in the previous three years for any other authors; no other relationships
4 or activities that could appear to have influenced the submitted work.
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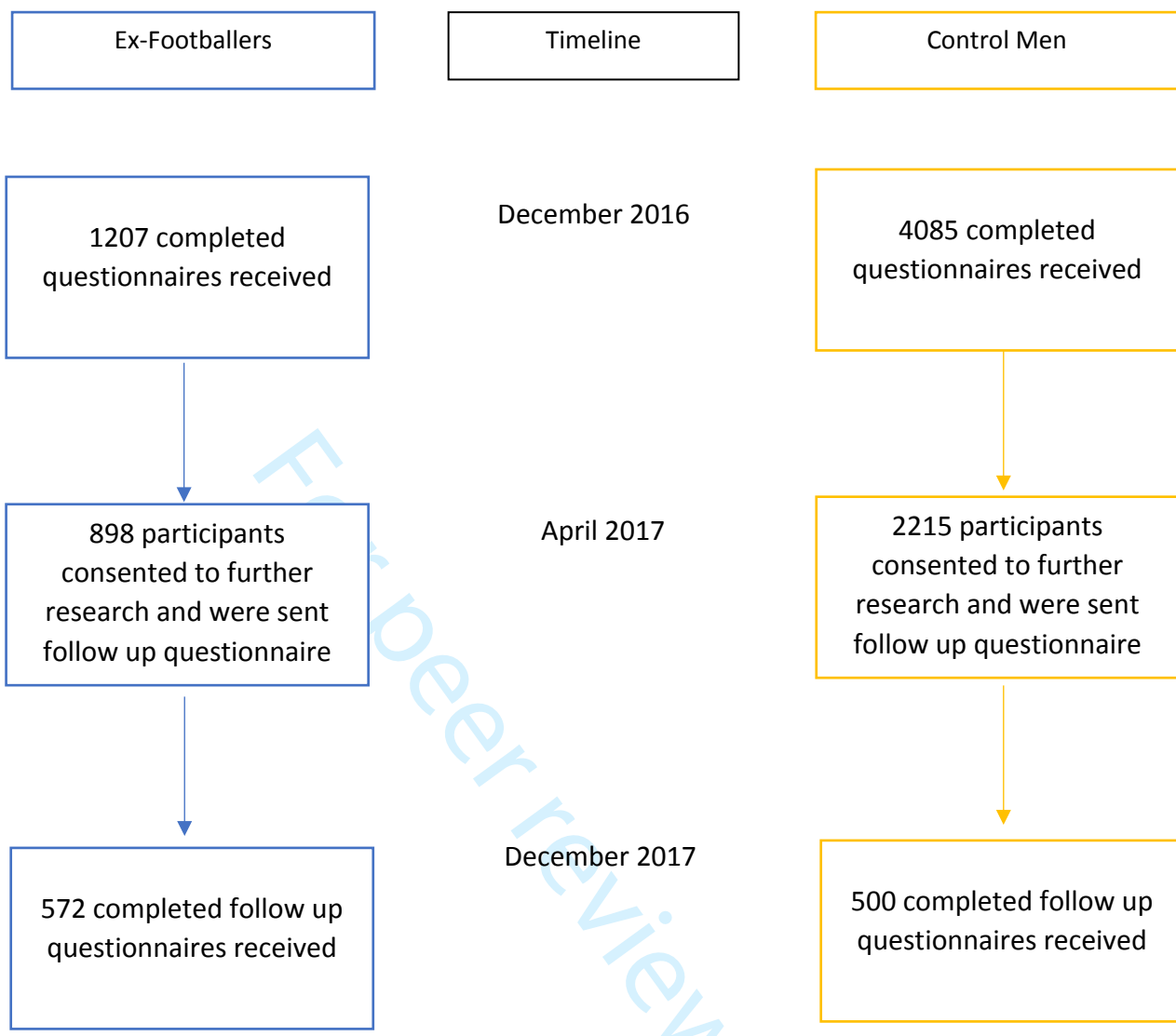
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20 Data Sharing: No additional data available.
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22 Transparency Declaration: Professor Michael Doherty (MD) affirms that the
23 manuscript is an honest, accurate, and transparent account of the study being
24 reported and that no important aspects of the study have been omitted.
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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 and 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4 and 5
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Page 10-11
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 7-9
Bias	9	Describe any efforts to address potential sources of bias	Page 9 and page 16
Study size	10	Explain how the study size was arrived at	Page 10, 11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 10
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	Page 10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	n/a

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	none
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Flow chart figure page 11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 11
		(b) Indicate number of participants with missing data for each variable of interest	Page 10
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Page 11-13
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 12-13
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 14-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Depression and the General Health of Retired Professional Footballers compared to the General Population in the United Kingdom: A Case Control Study

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Depression and the General Health of Retired Professional Footballers compared to the General Population in the United Kingdom: A Case Control Study

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Abstract

Objectives: To determine the prevalence of depression and general health of male ex-professional footballers compared to general population controls.

Methods: 572 retired professional footballers and 500 general population controls in the UK were assessed by postal questionnaire. Anxiety and depression were defined using the Hospital Anxiety and Depression Scale (HADS) using a threshold score of ≥ 11 to indicate probable caseness. General health was ascertained using: the SF-12 quality of life tool; self-reported comorbidities, analgesic usage and body pain; and index of multiple deprivation (IMD) based on postcode data. Mood was assessed using the positive and negative affect scale (PANAS) and sleep using the Medical Outcome Survey (MOS). Linear regression analysis was used to determine relative risk (aRR) with 95% confidence intervals (CI) and adjusted for age, body mass index (BMI), comorbidities, body pain and medication usage.

Results: Depression prevalence in retired professional footballers was 5.66% compared to 5.76% in the general population and anxiety prevalence was also comparable (12.01% vs. 10.29%; all $p > 0.05$). However, footballers had lower physical and mental component scores compared to controls ($p < 0.01$). They also reported significantly more sleep problems, more negative mood profiles and more widespread body pain (aRR 1.88, 95% CI 1.15 - 3.09). They also reported greater pain medication usage compared with controls (aRR 1.54, 95% CI 1.26 - 1.89). However, compared to controls they were 26% (95% CI, 15% - 37%) less likely to report comorbidities, especially heart attacks (57%, 95% CI 27% - 74%) and diabetes (61%, (95% CI 37% - 76%).

Conclusions: The prevalence of depression and anxiety in ex-professional footballers is comparable to general population controls. However, ex-footballers reported lower health-related quality of life, more widespread body pain and higher analgesic usage. Conversely lower reporting of diabetes and heart attacks indicate potential long-term physical health benefits from professional football.

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Keywords:

Professional football, epidemiology, depression, anxiety, sleep, pain, cardiovascular health

Article Summary:

Strengths and Limitations of this study

Strengths:

Largest study of depression and general health in ex-professional footballers and controls in the UK

Case-control study design with control male participants recruited from a community-based population sample representative of the UK general population

Depression and anxiety assessed using the validated Hospital Anxiety and Depression Scale in both ex-footballers cases and general population control men.

Limitations:

Outcomes were self-reported by participants using postal questionnaires

Lack of current or previous physical activity levels assessed

Higher response rate in the ex-footballers compared to the control participants.

Introduction

Football is the world's most popular sport with over 300 million active players worldwide and 110,000 athletes registered at a professional level¹. There has been considerable interest in whether the mental health of athletes is often compromised, especially by anxiety and depression². Retired professional footballers may experience unique psychological stress factors primarily due to the nature and the intensity of the sport where severe or recurrent injuries are common³. Also, the pressures of competition, training and maintaining high-performance levels are hallmarks of a successful professional career⁴. The intensity of mental and physical demands may increase their susceptibility to certain mental health problems and risk-taking behaviour.

Despite individual high-profile cases of depression in professional footballers in the United Kingdom (e.g. Gary Speed, Paul Gascoigne, Clarke Carlisle), there is a lack of robust epidemiological studies on mental health issues in professional footballers. Studies on European former professional footballers from countries such as the Netherlands have reported anxiety and depression prevalence figures ranging from 25-43%⁵. However, none of these studies included a non-athlete or general population comparison group. A recent systematic review suggests that despite a seemingly higher risk of anxiety and depression in athletes in a range of elite sport, the figures are broadly comparable to the general population. The review further concluded that the evidence base is restricted by a paucity of high-quality study designs particularly in professional footballers⁶. Turner et al.⁷ also found that anxiety and depression featured in 37% of former players with knee pain and knee osteoarthritis. A subsequent phenomenological study⁸ suggested that these may be common sequelae of significant sport injuries that caused frustration and associated participation restrictions and limitations to work, social and leisure activities. However, studies focused on mental health and quality of life (QoL) of athletes are limited by study design; lack of power and small sample sizes; and comparison across sporting populations^{2,9-12}. Therefore, there is a need for studies that: are focused on an individual sport such as professional football and its full-time players; are adequately powered for depression outcomes; include an age-adjusted control population; and investigate comorbidities and auxiliary measures of mental health and QoL indicators

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3 such as sleep patterns, mood profiles and pain distribution including use of pain
4 medication
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8 Therefore, based on previous research and the gaps in the evidence base, the
9 objectives of the present study were to: (1) determine the prevalence of anxiety and
10 depression in retired professional footballers compared to general population controls;
11 (2) determine the general health in retired professional footballers compared to
12 general population controls; and (3) determine the risk and protective factors
13 associated with professional football.
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Methods

The Nottingham Research Ethics Committee 1 (Refs 14/EM/0045 & 14/EM/0015) approved this study. A cross-sectional design was used, involving a series of postal questionnaire surveys to ex-footballers and to a sample of men in the general population (aged 40 years and over) to gain information on anxiety, depression, mood and sleep as well as simple demographics, occupational history, general health (comorbidities) and current medications. The exclusion criteria at baseline were known terminal illness, severe psychiatric illness or dementia, or any other condition or circumstance considered by their General Practice to make them unsuitable to receive the questionnaire.

Patient and Public Involvement

The study was supported by a patient advisory group which provided input to the programme of research. Patients and ex-professional footballers partnered with us for the design of the study, the informational material to support the intervention, and the burden of the questionnaire from the patient's perspective. At the end of the study the patient advisory group commented on the findings and contributed to the dissemination plan and this included input on poster and oral presentations at local, national and international conferences.

Participants

The recruitment of the source sample of ex-footballers and general population controls has been detailed in a previous publication examining the risk of knee pain and osteoarthritis in the footballers versus the controls¹³. Ex-footballers were recruited via the Professional Footballers' Association (PFA) and former players' associations (n=21 professional clubs). Inclusion criteria for ex-footballers were men aged over 40 years who had played professionally (in the top four tiers of the English Football League). The comparison group were recruited from the Knee Pain and Related Health in the Community Study (KPIC), involving recruitment via 12 general practitioner/family medicine (GP) practices in the UK Midlands region. All men on these UK National Health Service GP registers aged 40 years and older who were not terminally ill, were able to give written informed consent and had no other reason judged by the GPs to exclude them from the study were sent the questionnaire.

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3 Individuals who indicated interest in further research conducted by the University of
4 Nottingham were subsequently contacted with a follow-up questionnaire focused on
5 mental health and QoL.
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10 Questionnaire Survey

11 The postal questionnaire was developed based on previously published
12 questionnaires and using extensively validated tools in the retired footballers and the
13 control population. Through public and patient involvement, pilot versions of the
14 questionnaire were evaluated to identify any problems with content, language and
15 layout. The questionnaires were similarly constructed to capture detailed information
16 about all participants (including football career history for retired footballers),
17 anthropometric details (age and body mass index (BMI)), medical history and current
18 medication usage.
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28 Age and body mass index (BMI)

29 Participants self-reported their date of birth and height and weight in the returned
30 questionnaires. BMI was calculated as the weight divided by the square of height
31 (kg/m²).
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36 Anxiety and depression

37 Anxiety and depression were determined using the Hospital Anxiety and Depression
38 Scale (HADS) which is comprised of 14 items, equally divided between the two mood
39 states (anxiety and depression). Each item has a 4-point rating scale. Responders are
40 asked to indicate their feelings based on the previous one week with recommended
41 cut-off points indicating whether the responder is: a) within the normal range (scores
42 of 0-7), b) mild-moderate caseness (scores of 8-10) and, c) severe caseness (scores
43 of 11-21). Although cut-offs of > 8 have been used in some studies to indicate anxiety
44 or depression¹⁴ this threshold is considered too low and lacking in sensitivity for use
45 in a general population sample¹⁵ so a cut-off of ≥ 11 was used to identify definite
46 anxiety and definite depression. This cut-off has been defined using psychiatric ratings
47 of anxiety and depression disorders¹⁶. Whilst the gold-standard for a clinical diagnosis
48 of generalized anxiety disorder or major depressive disorder is a detailed evaluation
49 of symptom criteria using the Diagnostic and Statistical Manual of Mental Disorders
50 (DSM-5), research has shown that it compares consistently with HADS data both for
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3 sensitivity and specificity¹⁷. As the HADS is also simple, easy to administer and
4 relatively short compared to the DSM-5¹⁸, we chose to include it as part of the postal
5 questionnaires mailed to over 40,000 participants in this study.
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10 Quality of Life Measures; Mental Health and Physical Health Component Scores

11 QoL was assessed using the Medical Outcome Study Short Form-36 Health Survey
12 Questionnaire (SF-36) in the ex-footballers which was converted into SF-12 and the
13 Medical Outcome Study Short Form-12 Health Survey Questionnaire (SF-12) in the
14 general population controls. The difference in SF versions used was due to logistical
15 factors: the SF-12 was a survey embedded within a questionnaire posted to the
16 general population controls whose focus was on knee osteoarthritis outcomes and not
17 mental health per se. As a result of these page restrictions, we used the shortened
18 version, SF-12, for the controls compared to the second follow-up questionnaire
19 posted to the ex-footballers which contained the SF-36. In order to aid comparison,
20 the SF-36 outcomes were transformed into SF-12 outcomes as detailed by Jenkinson
21 and colleagues¹⁹. Each SF response was used to calculate scores in each of the eight
22 domains: physical functioning; role physical; bodily pain; general health perception;
23 vitality; social functioning; role emotional; and mental health. These figures were then
24 standardised using z-score transformations using means and standard deviations
25 previously described¹⁹. Using the z scores for each scale, the aggregate score for two
26 summary scales: the Mental Health Component Score (MCS) and the Physical Health
27 Component Score (PCS) were calculated. Finally, the scores were standardised to a
28 T-score where the mean was set to 50 and the standard deviation to 10. For the SF-
29 12, scoring was conducted according to previously published data^{20,21}. Item weights
30 for response categories from an American population-based study, which was found
31 comparable to other population studies in nine other countries including the United
32 Kingdom, was used to standardise responses¹⁹. There is considerable evidence
33 suggesting that the PCS and MCS from the SF-12 show similar levels of precision to
34 the summary scores derived from the longer SF-36 version. Even though summary
35 scores are not exactly identical the level of difference between the two is small and is
36 not subjectively or clinically meaningful²².
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58 Medical Outcome Survey (MOS) Sleep Scale

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3 The sleep scale from MOS is a 12-item measure that is generic and not disease
4 specific and measures 6 dimensions of sleep: sleep disturbance, snoring, shortness
5 of breath with headache, sleep adequacy, somnolence and quantity of sleep²³. The
6 tool has demonstrated excellent reliability and validity for assessing sleep in
7 community samples^{24,25}. A sleep problems index (SLP-9) can be calculated using nine
8 items from the MOS Sleep scale indicating quality of sleep on a 0-100 scale. The
9 higher the score, the lower the quality of sleep. The quantity of sleep is recorded as
10 the average hours of sleep per night over the previous 4-week period and was
11 dichotomised as optimal sleep (if this was 7-8 hours) or non-optimal if this was less
12 than 7 hours or greater than 8 hours as per MOS sleep scoring criteria.
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22 Positive and Negative Affect Scale (PANAS)

23 PANAS is a self-report questionnaire comprising two 10-item scales, which describe
24 different feelings and emotions measuring both positive and negative affect²⁶. The
25 questionnaire asked responders to consider their feelings at the time of completing the
26 questionnaire. The normal population reference guides for mean positive affect score
27 is 29.7 (+ 7.9) and mean negative affect score is 14.8 (+ 5.4). PANAS has
28 demonstrated high reliability and construct validity, is brief and ideal for use in self-
29 reported questionnaires and has been used extensively alongside measures of anxiety
30 and depression such as HADS^{27,28}.
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40 Indices of Multiple Deprivation

41 The Index of Multiple Deprivations (IMD) is an official measure of the relative
42 deprivation in England²⁹. It ranks all areas in England from 1 (most deprived) to 32,844
43 (least deprived area) and is based on weights given to key domains such as income,
44 employment, education and housing. It uses postcodes to determine an overall
45 measure of deprivation. This information was then presented in quintiles with
46 percentage of footballers and controls within the lowest and highest quintiles.
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53 Comorbidities

54 Individual comorbidities were self-reported according to a brief specific checklist
55 enquiry (fibromyalgia, diabetes, heart attacks, hypertension, cancer), with data
56 dichotomised into individuals with or without these conditions. An open text question
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3 was also included to capture information on any other diagnosed medical conditions
4 not on the checklist³⁰.
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7 8 **Widespread Body Pain** 9

10 Widespread body pain was self-reported using a body pain mannequin³¹. It was scored
11 using the American College of Rheumatology criteria for widespread body pain whose
12 definition is pain in each of the four quadrants of the body and including the spinal or
13 axial column. Reported pain in any part of the body was dichotomous (present/absent)
14 and total number of regions with pain was a simple count of the shaded regions of the
15 manikin.
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20 21 **Pain-relieving Medication** 22

23 Self-reported analgesic medication (both prescribed and over the counter) was
24 recorded and grouped as all pain-relieving medication, and sub-grouped as anti-
25 inflammatory drugs (NSAIDs), opioids, other over the counter (OTC) and prescribed
26 analgesics, and other medications with pain-modifying properties (e.g. citalopram and
27 amitriptyline).
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33 34 **Statistical Analyses** 35

36 A power calculation was conducted based on a 12.6% prevalence of depression in a
37 non-clinical sample of community-derived adults using the HADS¹⁵ and an odds ratio
38 (OR) of 2 after adjustment for other known factors in ex-footballers. The sample size
39 required to detect this OR, with 90% power and a 0.05% significance level, was 336
40 participants per group.
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43 Categorical variables were reported as frequencies and percentages, and continuous
44 variables as mean and standard deviations (SD). To determine whether distributions
45 of the variables were statistically significant between ex-footballers and controls a t-
46 test (continuous variables) or chi-square test (categorical variables) was used. For the
47 SF-12 outcomes, specifically the physical component score and mental component
48 score between footballers and controls, we used the ranksum command in Stata,
49 which compared two independent samples using the Mann-Whitney two-sample
50 statistic. Statistical significance was defined as $p < 0.05$. We had very few missing
51 data at random (e.g, where BMI was not reported by a participant). Imputation or
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3 modelling was therefore not undertaken for the occasional missing values. Details on
4 missing data have previously been published¹³.
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8 All analyses were conducted using Stata IC Version 14 on Windows 7 Operating
9 System and power calculations were undertaken using OpenEpi Version 3.
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Results

Of the 898 questionnaires sent to the retired professional footballers, 572 responses were received (63.7% response). Of 2215 questionnaires sent to general population controls, 500 questionnaires were received (22.6% response) (Figure 1).

Figure 1. Selection of ex-footballer and general population controls.

The mean age of the ex-footballers was significantly younger than the controls (60 versus 64 years)) but mean BMI were comparable (Table 1).

Table 1. Characteristics of footballer and control populations.

	Footballers n=572	Controls n=500	p-value
Age (years), mean (SD)	60.11 (10.77)	64.26 (9.37)	<0.001
BMI (kg/m ²), mean (SD)	27.13 (3.40)	27.29 (4.48)	0.51
Anxiety (cases), n (%)	70 (12.01)	50 (10.29)	0.34
Depression (cases), n (%)	33 (5.66)	28 (5.76)	0.94
SF Physical Component Score, mean (SD)	45.33 (10.32)	77.60 (8.35)	<0.001
SF Mental Component Score, mean (SD)	48.09 (7.47)	71.87 (6.64)	<0.001
Optimal sleep (7-8 hours per night), n (%)	369 (64.51)	275 (56.70)	0.01
Sleep Problem Index, n (%) in highest tertile of SIP	186 (33.04)	131 (26.90)	0.03
Positive Mood, mean (SD)	34.75 (8.05)	34.97 (6.86)	0.63
Negative Mood, mean (SD)	16.5 (6.72)	14.22 (4.95)	<0.001
Indices of Multiple Deprivation (IMD) n, (%) in the lowest and highest quintile	17 (3.51) 205 (42.27)	84 (17.28) 199 (40.95)	<0.001 0.18

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3 The prevalence of depression was similar in the footballers and controls (5.7% versus
4 5.8%) but the prevalence of anxiety was slightly higher in the footballers (12.0% versus
5 10.3%) though this was not statistically significant. Although footballers and controls
6 shared a similar positive mood profile, footballers were significantly more likely to
7 experience negative moods compared to the controls and to have greater problems
8 with sleep quality ($p<0.05$). When using the sleep problem index, more footballers
9 reported problems with sleep quality ($p<0.05$) and poor sleep patterns which included
10 restlessness, shortness of breath and drowsiness. They were also more likely to have
11 lower scores in terms of both their physical and mental health component scores as
12 indicated by the SF-12 QoL measure.
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22 With respect to social deprivation, fewer footballers (3.51%) were living in areas
23 marked as the most deprived compared to the control population (17.28%; $p<0.001$).
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27 Risk factors associated with professional football following adjustment for age and BMI
28 are presented in Table 2. Ex-footballers overall were less likely to present with any
29 comorbidity (diabetes, hypertension, myocardial infarction, cancer and fibromyalgia),
30 especially diabetes (61%, 95% CI, 37-76%), heart attacks (57%, 95% CI 27-74%) and
31 hypertension (21%, 95% CI 4-35%). However, footballers reported more widespread
32 body pain using the ACR criteria (88%, 95% CI 15-30.9%). Footballers also
33 consumed more NSAIDs (8.6% vs. 4.2%) and OTC analgesics (24% vs. 14%) but not
34 opioids (4% vs. 6.4%) compared to the controls.
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Table 2. Comparison of self-reported comorbidities, pain and medication in the ex-footballers compared to general population controls

	Footballers 572	Controls 500	p-value	Adjusted relative risk (95% CI) (for age and bmi)
Comorbidities* n (%)	178 (30.58)	260 (52.31)	<0.001	0.74 (0.63-0.85)+
Comorbidities** n (%) (by Charlson Comorbidity Index weighting** mean (SD)	0.44 (0.80)	0.75 (0.98)	<0.001	0.71 (0.6-0.85)+
Diabetes, n (%)	22 (3.77)	57 (11.47)	<0.001	0.39 (0.24-0.63)+
Cancer, n (%)	40 (6.86)	50 (8.58)	0.07	0.88 (0.59-1.30)
Heart Attacks, n (%)	18 (3.08)	47 (9.46)	<0.001	0.43 (0.26-0.73)+
Hypertension, n (%)	134 (22.98)	169 (34.00)	<0.001	0.79 (0.65-0.96)+
Fibromyalgia, n (%)	3 (0.51)	1 (0.20)	0.39	3.08 (0.31-31.02)
Any Body Pain, n (%)	454 (78.14)	330 (71.90)	0.02	1.09 (1.00-1.17)~
ACR Criteria				
Widespread Body Pain (no KP), n (%)	48 (8.40)	23 (4.60)	0.01	1.88 (1.15-3.09)~
Total Regions with Pain, mean (SD)	3.13 (3.29)	3.44 (3.05)	0.14	0.91 (0.79-1.05)
Back pain, n (%)	176 (30.18)	146 (29.38)	0.57	1.00 (0.76-1.32)
Knee pain, n (%)	337 (57.80)	193 (38.83)	<0.001	1.47 (1.29-1.69)~
Pain Medication Use, n (%)	240 (41.17)	165 (33.20)	0.007	1.54 (1.26-1.89)~
Opioids, n (%)	23 (4.03)	32 (6.40)	0.07	0.64 (0.37-1.10)
NSAIDS, n (%)	49 (8.58)	21 (4.20)	0.004	1.94 (1.19-3.20)~
OTC Analgesics, n (%)	137 (23.99)	70 (14.00)	<0.001	1.86 (1.44-2.43)~
Other medications***, n (%)	18 (3.15)	31 (6.20)	0.01	0.50 (0.28-0.94)+

*Diabetes, hypertension, myocardial infarction, cancer and fibromyalgia

**Includes myocardial infarction, hypertension, diabetes and cancer

*** Other medications with pain relieving effects.

+ Protective factors

~ Risk factors

Discussion

This is the first study to report the prevalence of depression, anxiety and the general health and QoL of retired professional footballers compared to a control population. The main findings are (1) the prevalence of depression and anxiety in the ex-footballers is comparable to men in the general population; (2) ex-footballers have a lower QoL as indicated by the SF-12 physical and mental component scores; (3) they are more likely to present with widespread body pain and use pain medication particularly OTC analgesics and NSAIDs; and (4) they are less likely to present with comorbidities, in particular diabetes, heart attacks and hypertension.

The study reported a prevalence of depression (6%) and anxiety (12%) in ex-footballers which is lower than the 25-43% reported by Goutterborge⁵. This discrepancy could result from smaller sample sizes (range of 70-149 ex-players), sample selection and status of footballers (current professional footballers from five different European countries), and the assessment tool used to determine depression and anxiety (12-item general health questionnaire (GHQ-12)) in that study. In a further study³², specifically investigating ex-footballers, estimated a 39% prevalence of both anxiety and depression using the GHQ-12. A number of self-report assessment tools have been used in epidemiological research to detect depression and anxiety³²⁻³⁴. While the GHQ-12 has demonstrated excellent validity in detecting depression in the general population³⁵, the HADS has demonstrated better sensitivity and specificity in detecting depression. Indeed, the choice of assessment tool should be balanced with feasibility of approach, cost effectiveness, as well as the administration and scoring times involved³². Additionally, none of the previous studies in ex-footballers presented results for an adequately matched comparison group of non-professional footballers. The results of this study accord with a comparative meta-analysis in high-performance athletes and non-athletes showing similar levels of depression across the groups⁴. Elite athletes are sometimes supported with psychological training as part of their sport programs and may have developed mental toughness and resilience in order to cope with stress, anxiety and even depression³⁶⁻³⁹. There is a noted stigma about reporting mental health symptoms both in ex-footballer and general population samples which may result in choosing to suppress, ignore and not seek further help when needed^{6,35,40}. Furthermore, when compared to another general population study, the

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3 prevalence of depression (7-9%) and anxiety (8-14%) in general population men aged
4 40-65 years is comparable to the controls in this study, suggesting that this East
5 Midlands control population are representative of the British general population and
6 are a valid control group⁴¹.
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11 In terms of QoL, the ex-footballers had significantly lower scores in both physical and
12 mental components compared to controls. It has been postulated that this negative
13 effect on QoL is a consequence of reporting more specific joint pain (e.g. knee pain)
14 and more overall body pain^{13,42}. Although both the ex-footballers and the control
15 population indicated pain in one region on a body pain manikin (78% vs. 72%), after
16 adjustment for age and BMI, ex-footballers are 88% more likely to present with
17 widespread body pain when using the more stringent ACR criteria compared to the
18 control group. Widespread pain can have significant, deleterious effects on physical
19 and mental health and well-being⁴³ including implications on sleep disturbance and
20 mood. Longitudinal cohort studies have shown that insomnia and sleep disturbances
21 significantly increase the risk of chronic pain in pain-free individuals at baseline whilst
22 pain is not a strong predictor of insomnia⁴⁴. As a result of the cross-sectional nature
23 of this study, we cannot ascertain causation between pain and sleep. However, the
24 results in ex-footballers show that whilst sleep duration may be marginally better (64.5
25 vs. 56.7% for 7-8 hours of sleep), the quality of sleep was more disturbed in terms of
26 restlessness, feeling tense or drowsy compared to controls. The effect on mood is
27 also notable with ex-footballers more likely to present with negative feelings and
28 emotions such as distress, irritability, fear and nervousness compared to controls. The
29 association of emotional distress and pain-related fear on patients with chronic pain
30 has been established in previous population-based studies⁴⁵⁻⁴⁸. Widespread body pain
31 is a key feature of fibromyalgia, but the cross-sectional nature of this study does not
32 allow investigation of temporal trends⁴⁷. A further indication of higher pain levels in ex-
33 footballers is the significantly higher use of analgesics (41%) compared to controls
34 (33%) and in particular NSAIDs (8.58% vs. 4.20%) and OTC analgesics (24% vs.
35 14%). The use of analgesics presumably reflects compromised musculoskeletal
36 health, whereas in terms of systemic general health the footballers reported
37 significantly less diabetes, cancer, heart attacks and hypertension compared to
38 controls. These results accord with previous studies of elite male athletes and ex-
39 footballers with lower risk of ischaemic heart disease and diabetes, but an elevated
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3 risk of musculoskeletal conditions particularly lower limb osteoarthritis^{13,49}.
4 Interestingly, ex-footballers reported significantly lower use of drugs such as
5 citalopram, diazepam, and temazepam which are used primarily in the treatment of
6 depression and anxiety respectively. Although the study was not powered for
7 medication outcomes, the use of medication in the footballer cohort was primarily for
8 pain relief rather than relief for mental health problems. In fact, ex-footballers may have
9 developed a certain resilience and mental toughness due to being an elite athlete
10 which may be a protective factor for long term mental ill-health^{4,37,49,50}.
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19 There are several caveats to this study. Firstly, this was a postal questionnaire study
20 focused on pain and osteoarthritis in ex-footballers¹³, and a community sample³², so
21 may be subject to response bias (those with pain are more likely to respond). However,
22 this would not explain the between group differences. Secondly, the response rate
23 was higher in the ex-footballer cohort than the controls (63.7% vs. 22.6%) and the low
24 response rate in controls questions the representativeness of the sample. Thirdly, the
25 comorbidities and medications were self-reported, and due to logistical reasons
26 relating to questionnaire length, data on established associated risk factors for
27 depression and anxiety such as smoking status, alcohol consumption, educational,
28 marital and economic status⁵¹⁻⁵⁴ were not available. Also, although the study did not
29 find any differences between ex-footballers and controls in terms of mental health it
30 would have been interesting to examine mental toughness, resilience, optimism and
31 general pain coping mechanisms between the two populations. Future epidemiological
32 research on this topic should explore these relationships in more detail. Also, our use
33 of HADS may have been a limitation as this scale may be measuring only the
34 symptoms of depression or anxiety as opposed to producing a more definitive
35 diagnoses that could be elicited with the use of alternatives such as the DSM-5.
36 Furthermore,, this study did not specifically measure two aspects of quality of life:
37 physical health via current physical activity levels, and, social relations via personal
38 relationships or available social support. These data would have given us insight into
39 current physical fitness levels, physical limitations as a consequence of
40 musculoskeletal conditions, and whether there was adequate psychosocial support in
41 an individual's life. These form some of the core tenets of a healthy quality of life⁵³ and
42 may have offered robust data on previously reported anecdotal effects of bankruptcy,
43 divorce or trauma particularly in the ex-footballers⁵⁵. Finally, we did not examine the
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3 effects of repetitive heading of footballs and risk of head injury and concussion in
4 professional footballers, and the possible long-term health impact that this could have
5 on neuro-cognition and mental health. A future study is planned to address this issue.
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10 In summary, this is the largest study on anxiety, depression and quality of life in ex-
11 professional footballers and the first to include an age-adjusted general population
12 comparison sample. The results show that ex-footballers are just as likely to have
13 anxiety and depression as controls, but they have lower QoL in terms of both physical
14 and mental composite scores. However, despite reporting more widespread body pain
15 and use of analgesics, they are less likely to report cardiovascular disease or diabetes.
16 The results suggest that healthcare providers, club management and football
17 organisations should be focused on improving musculoskeletal pain management
18 strategies in ex-footballers. Further study on the potential benefits of professional sport
19 on pain coping and resilience mechanisms which may be protective factors for long
20 term psychological consequences such as depression and anxiety would benefit the
21 large numbers of ex-professional footballers both nationally and internationally. It
22 would also be valuable to explore the effects of neurocognitive functioning on mental
23 health in ex-footballers and capture the granularity around type, severity and
24 frequencies of injuries such as concussion and the subsequent long-term health
25 impact.
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Affiliations

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All researchers were independent from funders.

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

review only

Declarations:

Consent:

The study was approved by Nottingham University Hospitals NHS Trust and the Nottingham Research Ethics Committee 1 (Refs 14/EM/0045 & 14/EM/0015) and registered (clinicaltrials.gov portal: NCT02098044 & NCT02098070).

All participants offered consent by responding to the postal questionnaire survey and written informed consent prior to radiographic assessment at the SPIRE Hospitals and the Nottingham City Hospital.

Contributor's statement:

GSF designed the data collection tools, wrote the statistical plan, implemented the study design (conducted the study), conducted cleaning and analysis of the data, wrote the initial drafts of the paper and subsequently revised the paper after feedback from the team. SMP designed the data collection tools, wrote the statistical plan, implemented the study design (conducted the study), conducted cleaning and analysis of the data, and drafted and revised the paper. JPM conducted cleaning and analysis of the data, and drafted and revised the paper. CWF conceptualised the study and drafted and revised the paper. BS conceptualised the study and drafted and revised the paper. MEB monitored data collection and drafted and revised the paper. WZ conceptualised and designed the study and data collection tools, wrote the statistical plan, monitored data collection and drafted and revised the paper. MD conceptualised and designed the study and data collection tools, monitored data collection and drafted and revised the paper. He is guarantor.

Conflict of Interest Disclosures:

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: financial support (research grant) for the submitted work from FIFA Medical Assessment and Research Centre, other from Arthritis Research UK Centre for Sports, Exercise and Osteoarthritis (Grant Reference 20194); research grant from the Professional Footballers' Association and financial support from the SPIRE Healthcare Group at the Football Association (St George's Park); CF did paid consultancy for FIFA Medical Assessment and Research Centre, the Football Association and the Premier League in the past three years and has received personal fees from these bodies outside the remit of the submitted work; MD received research funding by AstraZeneca, Nordic Biosciences, Roche, outside the submitted work; Dr. Zhang reports grants from Arthritis Research UK, grants from Arthritis Research UK, during the conduct of the study; other from AstraZeneca, other from Daiichi Sankyo, other from Biobarica, other from Hisun, outside the submitted work; no financial relationships with any organisation that might have an interest in the submitted work in the previous three years for any other authors; no other relationships or activities that could appear to have influenced the submitted work.

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9 Data Sharing: No additional data available.

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11 Transparency Declaration: Professor Michael Doherty (MD) affirms that the
12 manuscript is an honest, accurate, and transparent account of the study being
13 reported and that no important aspects of the study have been omitted.
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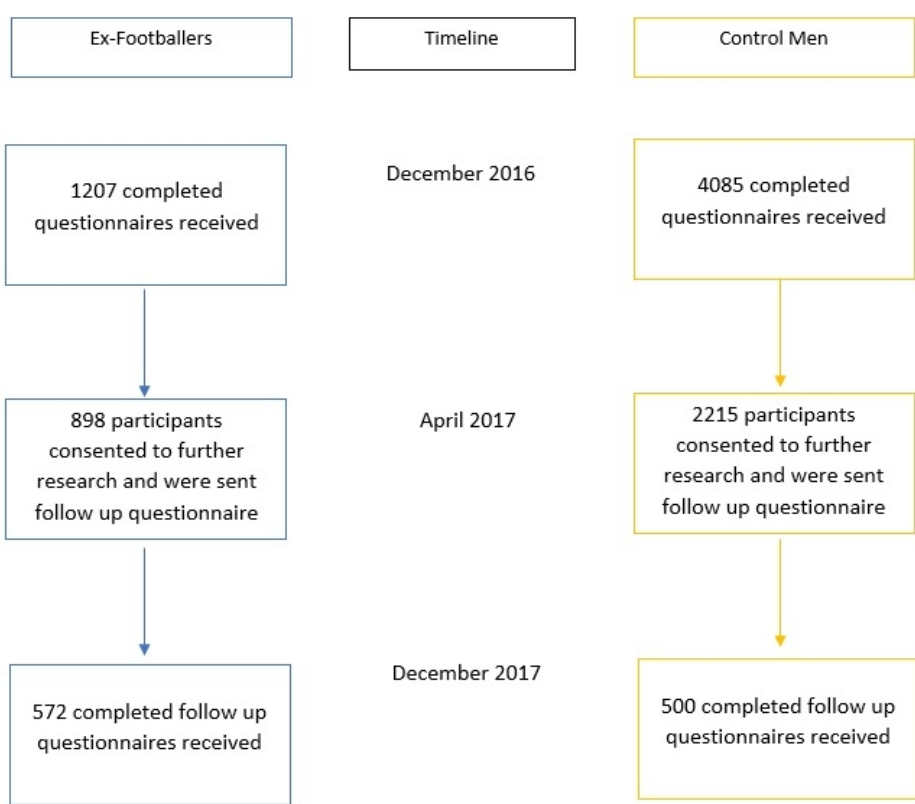


Figure 1 Selection of ex-footballer and general population controls.

58x51mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 and 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4 and 5
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Page 10-11
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 7-9
Bias	9	Describe any efforts to address potential sources of bias	Page 9 and page 16
Study size	10	Explain how the study size was arrived at	Page 10, 11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 10
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	Page 10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	n/a

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	none
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Flow chart figure page 11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 11
		(b) Indicate number of participants with missing data for each variable of interest	Page 10
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Page 11-13
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 12-13
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 14-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Depressive symptoms and the General Health of Retired Professional Footballers compared to the General Population in the United Kingdom: A Case Control Study

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Depressive symptoms and the General Health of Retired Professional Footballers compared to the General Population in the United Kingdom: A Case Control Study

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Abstract

Objectives: To determine the prevalence of depressive symptoms and general health of male ex-professional footballers compared to general population controls.

Methods: 572 retired professional footballers and 500 general population controls in the UK were assessed by postal questionnaire. Anxiety and depressive symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) and a threshold score of ≥ 11 was used to indicate probable caseness. General health was ascertained using: the SF-12 quality of life tool; self-reported comorbidities, analgesic usage and body pain; and index of multiple deprivation (IMD) based on postcode data. Mood was assessed using the positive and negative affect scale (PANAS) and sleep using the Medical Outcome Survey (MOS). Linear regression analysis was used to determine relative risk (aRR) with 95% confidence intervals (CI) and adjusted for age, body mass index (BMI), comorbidities, body pain and medication usage.

Results: The prevalence of depressive symptoms in retired professional footballers was 5.66% compared to 5.76% in the general population and anxiety prevalence was also comparable (12.01% vs. 10.29%; all $p > 0.05$). However, footballers had lower physical and mental component scores compared to controls ($p < 0.01$). They also reported significantly more sleep problems, more negative mood profiles and more widespread body pain (aRR 1.88, 95% CI 1.15 - 3.09). They also reported greater pain medication usage compared with controls (aRR 1.54, 95% CI 1.26 - 1.89). However, compared to controls they were 26% (95% CI, 15% - 37%) less likely to report comorbidities, especially heart attacks (57%, 95% CI 27% - 74%) and diabetes (61%, 95% CI 37% - 76%).

Conclusions: The prevalence of depressive symptoms and anxiety symptoms and probable caseness in ex-professional footballers is comparable to general population controls. However, ex-footballers reported lower health-related quality of life, more widespread body pain and higher analgesic usage. Conversely lower reporting of diabetes and heart attacks indicate potential long-term physical health benefits from professional football.

Keywords:

Professional football, epidemiology, depressive symptoms, anxiety, sleep, pain, cardiovascular health

Article Summary:

Strengths and Limitations of this study

Strengths:

- Largest study of depressive symptoms and general health in ex-professional footballers and controls in the UK
- Case-control study design with control male participants recruited from a community-based population sample representative of the UK general population

Limitations:

- Outcomes were self-reported by participants using postal questionnaires
- Lack of current or previous physical activity levels assessed
- Higher response rate in the ex-footballers compared to the control participants.

Introduction

Football is the world's most popular sport with over 300 million active players worldwide and 110,000 athletes registered at a professional level¹. There has been considerable interest in whether the mental health of athletes is often compromised, especially by anxiety and depression². Retired professional footballers may experience unique psychological stress factors primarily due to the nature and the intensity of the sport where severe or recurrent injuries are common³. Also, the pressures of competition, training and maintaining high-performance levels are hallmarks of a successful professional career⁴. The intensity of mental and physical demands may increase their susceptibility to certain mental health problems and risk-taking behaviour.

Despite individual high-profile cases of depression in professional footballers in the United Kingdom (e.g. Gary Speed, Paul Gascoigne, Clarke Carlisle), there is a lack of robust epidemiological studies on mental health issues in professional footballers. Studies on European former professional footballers from countries such as the Netherlands have reported anxiety and depression prevalence figures ranging from 25-43%⁵. However, none of these studies included a non-athlete or general population comparison group. A recent systematic review suggests that despite a seemingly higher risk of anxiety and depression in athletes in a range of elite sport, the figures are broadly comparable to the general population. The review further concluded that the evidence base is restricted by a paucity of high-quality study designs particularly in professional footballers⁶. Turner et al.⁷ also found that anxiety and depression featured in 37% of former players with knee pain and knee osteoarthritis. A subsequent phenomenological study⁸ suggested that these may be common sequelae of significant sport injuries that caused frustration and associated participation restrictions and limitations to work, social and leisure activities. However, studies focused on mental health and quality of life (QoL) of athletes are limited by study design; lack of power and small sample sizes; and comparison across sporting populations^{2,9-12}. Therefore, there is a need for studies that: are focused on an individual sport such as professional football and its full-time players; are adequately powered for depression outcomes; include an age-adjusted control population; and investigate comorbidities and auxiliary measures of mental health and QoL indicators

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3 such as sleep patterns, mood profiles and pain distribution including use of pain
4 medication
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8 Therefore, based on previous research and the gaps in the evidence base, the
9 objectives of the present study were to: (1) determine the prevalence of anxiety and
10 depressive symptoms and probable caseness for each in retired professional
11 footballers compared to general population controls; (2) determine the general health
12 in retired professional footballers compared to general population controls; and (3)
13 determine the risk and protective factors associated with professional football.
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Methods

The Nottingham Research Ethics Committee 1 (Refs 14/EM/0045 & 14/EM/0015) approved this study. A cross-sectional design was used, involving a series of postal questionnaire surveys to ex-footballers and to a sample of men in the general population (aged 40 years and over) to gain information on symptoms of anxiety and depression, mood and sleep as well as simple demographics, occupational history, general health (comorbidities) and current medications. The exclusion criteria at baseline were known terminal illness, severe psychiatric illness or dementia, or any other condition or circumstance considered by their General Practice to make them unsuitable to receive the questionnaire.

Patient and Public Involvement

The study was supported by a patient advisory group which provided input to the programme of research. Patients and ex-professional footballers partnered with us for the design of the study, the informational material to support the intervention, and the burden of the questionnaire from the patient's perspective. At the end of the study the patient advisory group commented on the findings and contributed to the dissemination plan and this included input on poster and oral presentations at local, national and international conferences.

Participants

The recruitment of the source sample of ex-footballers and general population controls has been detailed in a previous publication examining the risk of knee pain and osteoarthritis in the footballers versus the controls¹³. Ex-footballers were recruited via the Professional Footballers' Association (PFA) and former players' associations (n=21 professional clubs). Inclusion criteria for ex-footballers were men aged over 40 years who had played professionally (in the top four tiers of the English Football League). The comparison group were recruited from the Knee Pain and Related Health in the Community Study (KPIC), involving recruitment via 12 general practitioner/family medicine (GP) practices in the UK Midlands region. All men on these UK National Health Service GP registers aged 40 years and older who were not terminally ill, were able to give written informed consent and had no other reason judged by the GPs to exclude them from the study were sent the questionnaire.

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3 Individuals who indicated interest in further research conducted by the University of
4 Nottingham were subsequently contacted with a follow-up questionnaire focused on
5 mental health and QoL.
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8 9 10 Questionnaire Survey

11 The postal questionnaire was developed based on previously published
12 questionnaires and using extensively validated tools in the retired footballers and the
13 control population. Through public and patient involvement, pilot versions of the
14 questionnaire were evaluated to identify any problems with content, language and
15 layout. The questionnaires were similarly constructed to capture detailed information
16 about all participants (including football career history for retired footballers),
17 anthropometric details (age and body mass index (BMI)), medical history and current
18 medication usage.
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28 Age and body mass index (BMI)

29 Participants self-reported their date of birth and height and weight in the returned
30 questionnaires. BMI was calculated as the weight divided by the square of height
31 (kg/m²).
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36 Symptoms of anxiety and depression

37 Anxiety and depressive symptoms were determined using the Hospital Anxiety and
38 Depression Scale (HADS) which is comprised of 14 items, equally divided between
39 the two mood states (anxiety and depression). Each item has a 4-point rating scale.
40 Responders are asked to indicate their feelings based on the previous one week with
41 recommended cut-off points indicating whether the responder is: a) within the normal
42 range (scores of 0-7), b) mild-moderate caseness (scores of 8-10) and, c) severe
43 caseness (scores of 11-21). Although cut-offs of > 8 have been used in some studies
44 to indicate anxiety or depression¹⁴ this threshold is considered too low and lacking in
45 sensitivity for use in a general population sample¹⁵ so a cut-off of ≥ 11 was used to
46 identify definite anxiety and definite depression. This cut-off has been defined using
47 psychiatric ratings of anxiety and depression disorders¹⁶. Whilst the gold-standard for
48 a clinical diagnosis of generalized anxiety disorder or major depressive disorder is a
49 detailed evaluation of symptom criteria using the Diagnostic and Statistical Manual of
50 Mental Disorders (DSM-5), research has shown that it compares consistently with
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3 HADS data both for sensitivity and specificity¹⁷. As the HADS is also simple, easy to
4 administer and relatively short compared to the DSM-5¹⁸, we chose to include it as
5 part of the postal questionnaires mailed to over 40,000 participants in this study.
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10 Quality of Life Measures; Mental Health and Physical Health Component Scores

11 QoL was assessed using the Medical Outcome Study Short Form-36 Health Survey
12 Questionnaire (SF-36) in the ex-footballers which was converted into SF-12 and the
13 Medical Outcome Study Short Form-12 Health Survey Questionnaire (SF-12) in the
14 general population controls. The difference in SF versions used was due to logistical
15 factors: the SF-12 was a survey embedded within a questionnaire posted to the
16 general population controls whose focus was on knee osteoarthritis outcomes and not
17 mental health per se. As a result of these page restrictions, we used the shortened
18 version, SF-12, for the controls compared to the second follow-up questionnaire
19 posted to the ex-footballers which contained the SF-36. In order to aid comparison,
20 the SF-36 outcomes were transformed into SF-12 outcomes as detailed by Jenkinson
21 and colleagues¹⁹. Each SF response was used to calculate scores in each of the eight
22 domains: physical functioning; role physical; bodily pain; general health perception;
23 vitality; social functioning; role emotional; and mental health. These figures were then
24 standardised using z-score transformations using means and standard deviations
25 previously described¹⁹. Using the z scores for each scale, the aggregate score for two
26 summary scales: the Mental Health Component Score (MCS) and the Physical Health
27 Component Score (PCS) were calculated. Finally, the scores were standardised to a
28 T-score where the mean was set to 50 and the standard deviation to 10. For the SF-
29 12, scoring was conducted according to previously published data^{20,21}. Item weights
30 for response categories from an American population-based study, which was found
31 comparable to other population studies in nine other countries including the United
32 Kingdom, was used to standardise responses¹⁹. There is considerable evidence
33 suggesting that the PCS and MCS from the SF-12 show similar levels of precision to
34 the summary scores derived from the longer SF-36 version. Even though summary
35 scores are not exactly identical the level of difference between the two is small and is
36 not subjectively or clinically meaningful²².
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58 Medical Outcome Survey (MOS) Sleep Scale

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3 The sleep scale from MOS is a 12-item measure that is generic and not disease
4 specific and measures 6 dimensions of sleep: sleep disturbance, snoring, shortness
5 of breath with headache, sleep adequacy, somnolence and quantity of sleep²³. The
6 tool has demonstrated excellent reliability and validity for assessing sleep in
7 community samples^{24,25}. A sleep problems index (SLP-9) can be calculated using nine
8 items from the MOS Sleep scale indicating quality of sleep on a 0-100 scale. The
9 higher the score, the lower the quality of sleep. The quantity of sleep is recorded as
10 the average hours of sleep per night over the previous 4-week period and was
11 dichotomised as optimal sleep (if this was 7-8 hours) or non-optimal if this was less
12 than 7 hours or greater than 8 hours as per MOS sleep scoring criteria.
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22 Positive and Negative Affect Scale (PANAS)

23 PANAS is a self-report questionnaire comprising two 10-item scales, which describe
24 different feelings and emotions measuring both positive and negative affect²⁶. The
25 questionnaire asked responders to consider their feelings at the time of completing the
26 questionnaire. The normal population reference guides for mean positive affect score
27 is 29.7 (+ 7.9) and mean negative affect score is 14.8 (+ 5.4). PANAS has
28 demonstrated high reliability and construct validity, is brief and ideal for use in self-
29 reported questionnaires and has been used extensively alongside measures of anxiety
30 and depression such as HADS^{27,28}.
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40 Indices of Multiple Deprivation

41 The Index of Multiple Deprivations (IMD) is an official measure of the relative
42 deprivation in England²⁹. It ranks all areas in England from 1 (most deprived) to 32,844
43 (least deprived area) and is based on weights given to key domains such as income,
44 employment, education and housing. It uses postcodes to determine an overall
45 measure of deprivation. This information was then presented in quintiles with
46 percentage of footballers and controls within the lowest and highest quintiles.
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53 Comorbidities

54 Individual comorbidities were self-reported according to a brief specific checklist
55 enquiry (fibromyalgia, diabetes, heart attacks, hypertension, cancer), with data
56 dichotomised into individuals with or without these conditions. An open text question
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3 was also included to capture information on any other diagnosed medical conditions
4 not on the checklist³⁰.
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8 Widespread Body Pain 9

10 Widespread body pain was self-reported using a body pain mannequin³¹. It was scored
11 using the American College of Rheumatology criteria for widespread body pain whose
12 definition is pain in each of the four quadrants of the body and including the spinal or
13 axial column. Reported pain in any part of the body was dichotomous (present/absent)
14 and total number of regions with pain was a simple count of the shaded regions of the
15 manikin.
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22 Pain-relieving Medication 23

24 Self-reported analgesic medication (both prescribed and over the counter) was
25 recorded and grouped as all pain-relieving medication, and sub-grouped as anti-
26 inflammatory drugs (NSAIDs), opioids, other over the counter (OTC) and prescribed
27 analgesics, and other medications with pain-modifying properties (e.g. citalopram and
28 amitriptyline).
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34 Statistical Analyses 35

36 A power calculation was conducted based on a 12.6% prevalence of depressive
37 symptoms in a non-clinical sample of community-derived adults using the HADS¹⁵ and
38 an odds ratio (OR) of 2 after adjustment for other known factors in ex-footballers. The
39 sample size required to detect this OR, with 90% power and a 0.05% significance
40 level, was 336 participants per group.
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44 Categorical variables were reported as frequencies and percentages, and continuous
45 variables as mean and standard deviations (SD). To determine whether distributions
46 of the variables were statistically significant between ex-footballers and controls a t-
47 test (continuous variables) or chi-square test (categorical variables) was used. For the
48 SF-12 outcomes, specifically the physical component score and mental component
49 score between footballers and controls, we used the ranksum command in Stata,
50 which compared two independent samples using the Mann-Whitney two-sample
51 statistic. Statistical significance was defined as $p < 0.05$. We had very few missing
52 data at random (e.g, where BMI was not reported by a participant). Imputation or
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3 modelling was therefore not undertaken for the occasional missing values. Details on
4 missing data have previously been published¹³.
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8 All analyses were conducted using Stata IC Version 14 on Windows 7 Operating
9 System and power calculations were undertaken using OpenEpi Version 3.
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Results

Of the 898 questionnaires sent to the retired professional footballers, 572 responses were received (63.7% response). Of 2215 questionnaires sent to general population controls, 500 questionnaires were received (22.6% response) (Figure 1).

Figure 1. Selection of ex-footballer and general population controls.

The mean age of the ex-footballers was significantly younger than the controls (60 versus 64 years)) but mean BMI were comparable (Table 1).

Table 1. Characteristics of footballer and control populations.

	Footballers n=572	Controls n=500	p-value
Age (years), mean (SD)	60.11 (10.77)	64.26 (9.37)	<0.001
BMI (kg/m ²), mean (SD)	27.13 (3.40)	27.29 (4.48)	0.51
HADS Anxiety score ≥ 11 , n (%)	70 (12.01)	50 (10.29)	0.34
HADS Depression score ≥ 11 , n (%)	33 (5.66)	28 (5.76)	0.94
SF Physical Component Score, mean (SD)	45.33 (10.32)	77.60 (8.35)	<0.001
SF Mental Component Score, mean (SD)	48.09 (7.47)	71.87 (6.64)	<0.001
Optimal sleep (7-8 hours per night), n (%)	369 (64.51)	275 (56.70)	0.01
Sleep Problem Index, n (%) in highest tertile of SIP	186 (33.04)	131 (26.90)	0.03
Positive Mood, mean (SD)	34.75 (8.05)	34.97 (6.86)	0.63
Negative Mood, mean (SD)	16.5 (6.72)	14.22 (4.95)	<0.001
Indices of Multiple Deprivation (IMD) n, (%) in the lowest and highest quintile	17 (3.51) 205 (42.27)	84 (17.28) 199 (40.95)	<0.001 0.18

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3 The prevalence of probable depression was similar in the footballers and controls
4 (5.7% versus 5.8%) but the prevalence of probable anxiety was slightly higher in the
5 footballers (12.0% versus 10.3%) though this was not statistically significant. Although
6 footballers and controls shared a similar positive mood profile, footballers were
7 significantly more likely to experience negative moods compared to the controls and
8 to have greater problems with sleep quality ($p<0.05$). When using the sleep problem
9 index, more footballers reported problems with sleep quality ($p<0.05$) and poor sleep
10 patterns which included restlessness, shortness of breath and drowsiness. They were
11 also more likely to have lower scores in terms of both their physical and mental health
12 component scores as indicated by the SF-12 QoL measure.
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22 With respect to social deprivation, fewer footballers (3.51%) were living in areas
23 marked as the most deprived compared to the control population (17.28%; $p<0.001$).
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27 Risk factors associated with professional football following adjustment for age and BMI
28 are presented in Table 2. Ex-footballers overall were less likely to present with any
29 comorbidity (diabetes, hypertension, myocardial infarction, cancer and fibromyalgia),
30 especially diabetes (61%, 95% CI, 37-76%), heart attacks (57%, 95% CI 27-74%) and
31 hypertension (21%, 95% CI 4-35%). However, footballers reported more widespread
32 body pain using the ACR criteria (88%, 95% CI 15-30.9%). Footballers also
33 consumed more NSAIDs (8.6% vs. 4.2%) and OTC analgesics (24% vs. 14%) but not
34 opioids (4% vs. 6.4%) compared to the controls.
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Table 2. Comparison of self-reported comorbidities, pain and medication in the ex-footballers compared to general population controls

	Footballers 572	Controls 500	p-value	Adjusted relative risk (95% CI) (for age and bmi)
Comorbidities* n (%)	178 (30.58)	260 (52.31)	<0.001	0.74 (0.63-0.85)+
Comorbidities** n (%) (by Charlson Comorbidity Index weighting** mean (SD)	0.44 (0.80)	0.75 (0.98)	<0.001	0.71 (0.6-0.85)+
Diabetes, n (%)	22 (3.77)	57 (11.47)	<0.001	0.39 (0.24-0.63)+
Cancer, n (%)	40 (6.86)	50 (8.58)	0.07	0.88 (0.59-1.30)
Heart Attacks, n (%)	18 (3.08)	47 (9.46)	<0.001	0.43 (0.26-0.73)+
Hypertension, n (%)	134 (22.98)	169 (34.00)	<0.001	0.79 (0.65-0.96)+
Fibromyalgia, n (%)	3 (0.51)	1 (0.20)	0.39	3.08 (0.31-31.02)
Any Body Pain, n (%)	454 (78.14)	330 (71.90)	0.02	1.09 (1.00-1.17)~
ACR Criteria				
Widespread Body Pain (no KP), n (%)	48 (8.40)	23 (4.60)	0.01	1.88 (1.15-3.09)~
Total Regions with Pain, mean (SD)	3.13 (3.29)	3.44 (3.05)	0.14	0.91 (0.79-1.05)
Back pain, n (%)	176 (30.18)	146 (29.38)	0.57	1.00 (0.76-1.32)
Knee pain, n (%)	337 (57.80)	193 (38.83)	<0.001	1.47 (1.29-1.69)~
Pain Medication Use, n (%)	240 (41.17)	165 (33.20)	0.007	1.54 (1.26-1.89)~
Opioids, n (%)	23 (4.03)	32 (6.40)	0.07	0.64 (0.37-1.10)
NSAIDS, n (%)	49 (8.58)	21 (4.20)	0.004	1.94 (1.19-3.20)~
OTC Analgesics, n (%)	137 (23.99)	70 (14.00)	<0.001	1.86 (1.44-2.43)~
Other medications***, n (%)	18 (3.15)	31 (6.20)	0.01	0.50 (0.28-0.94)+

*Diabetes, hypertension, myocardial infarction, cancer and fibromyalgia

**Includes myocardial infarction, hypertension, diabetes and cancer

*** Other medications with pain relieving effects.

+ Protective factors

~ Risk factors

Discussion

This is the first study to report the prevalence of symptoms of depression and anxiety and the general health and QoL of retired professional footballers compared to a control population. The main findings are (1) the prevalence of probable depression and anxiety in the ex-footballers is comparable to men in the general population; (2) ex-footballers have a lower QoL as indicated by the SF-12 physical and mental component scores; (3) they are more likely to present with widespread body pain and use pain medication particularly OTC analgesics and NSAIDs; and (4) they are less likely to present with comorbidities, in particular diabetes, heart attacks and hypertension.

The study reported a prevalence of probable depression (6%) and anxiety (12%) in ex-footballers which is lower than the 25-43% reported by Goutterborge⁵. This discrepancy could result from smaller sample sizes (range of 70-149 ex-players), sample selection and status of footballers (current professional footballers from five different European countries), and the assessment tool used to determine depression and anxiety (12-item general health questionnaire (GHQ-12)) in that study. In a further study³², specifically investigating ex-footballers, estimated a 39% prevalence of both anxiety and depression using the GHQ-12. A number of self-report assessment tools have been used in epidemiological research to detect depression and anxiety³²⁻³⁴. While the GHQ-12 has demonstrated excellent validity in detecting depression in the general population³⁵, the HADS has demonstrated better sensitivity and specificity in detecting depression. Indeed, the choice of assessment tool should be balanced with feasibility of approach, cost effectiveness, as well as the administration and scoring times involved³². Additionally, none of the previous studies in ex-footballers presented results for an adequately matched comparison group of non-professional footballers. The results of this study accord with a comparative meta-analysis in high-performance athletes and non-athletes showing similar levels of depression across the groups⁴. Elite athletes are sometimes supported with psychological training as part of their sport programs and may have developed mental toughness and resilience in order to cope with stress, anxiety and even depression³⁶⁻³⁹. There is a noted stigma about reporting mental health symptoms both in ex-footballer and general population samples which may result in choosing to suppress, ignore and not seek further help when

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3 needed^{6,35,40}. Furthermore, when compared to another general population study, the
4 prevalence of depression (7-9%) and anxiety (8-14%) in general population men aged
5 40-65 years is comparable to the controls in this study, suggesting that this East
6 Midlands control population are representative of the British general population and
7 are a valid control group⁴¹.
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13 In terms of QoL, the ex-footballers had significantly lower scores in both physical and
14 mental components compared to controls. It has been postulated that this negative
15 effect on QoL is a consequence of reporting more specific joint pain (e.g. knee pain)
16 and more overall body pain^{13,42}. Although both the ex-footballers and the control
17 population indicated pain in one region on a body pain manikin (78% vs. 72%), after
18 adjustment for age and BMI, ex-footballers are 88% more likely to present with
19 widespread body pain when using the more stringent ACR criteria compared to the
20 control group. Widespread pain can have significant, deleterious effects on physical
21 and mental health and well-being⁴³ including implications on sleep disturbance and
22 mood. Longitudinal cohort studies have shown that insomnia and sleep disturbances
23 significantly increase the risk of chronic pain in pain-free individuals at baseline whilst
24 pain is not a strong predictor of insomnia⁴⁴. As a result of the cross-sectional nature
25 of this study, we cannot ascertain causation between pain and sleep. However, the
26 results in ex-footballers show that whilst sleep duration may be marginally better (64.5
27 vs. 56.7% for 7-8 hours of sleep), the quality of sleep was more disturbed in terms of
28 restlessness, feeling tense or drowsy compared to controls. The effect on mood is
29 also notable with ex-footballers more likely to present with negative feelings and
30 emotions such as distress, irritability, fear and nervousness compared to controls. The
31 association of emotional distress and pain-related fear on patients with chronic pain
32 has been established in previous population-based studies⁴⁵⁻⁴⁸. Widespread body pain
33 is a key feature of fibromyalgia, but the cross-sectional nature of this study does not
34 allow investigation of temporal trends⁴⁷. A further indication of higher pain levels in ex-
35 footballers is the significantly higher use of analgesics (41%) compared to controls
36 (33%) and in particular NSAIDs (8.58% vs. 4.20%) and OTC analgesics (24% vs.
37 14%). The use of analgesics presumably reflects compromised musculoskeletal
38 health, whereas in terms of systemic general health the footballers reported
39 significantly less diabetes, cancer, heart attacks and hypertension compared to
40 controls. These results accord with previous studies of elite male athletes and ex-
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3 footballers with lower risk of ischaemic heart disease and diabetes, but an elevated
4 risk of musculoskeletal conditions particularly lower limb osteoarthritis^{13,49}.
5 Interestingly, ex-footballers reported significantly lower use of drugs such as
6 citalopram, diazepam, and temazepam which are used primarily in the treatment of
7 depression and anxiety respectively. Although the study was not powered for
8 medication outcomes, the use of medication in the footballer cohort was primarily for
9 pain relief rather than relief for mental health problems. In fact, ex-footballers may have
10 developed a certain resilience and mental toughness due to being an elite athlete
11 which may be a protective factor for long term mental ill-health^{4,37,49,50}.
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20 There are several caveats to this study. Firstly, this was a postal questionnaire study
21 focused on pain and osteoarthritis in ex-footballers¹³, and a community sample³², so
22 may be subject to response bias (those with pain are more likely to respond). However,
23 this would not explain the between group differences. Secondly, the response rate
24 was higher in the ex-footballer cohort than the controls (63.7% vs. 22.6%) and the low
25 response rate in controls questions the representativeness of the sample. Thirdly, the
26 comorbidities and medications were self-reported, and due to logistical reasons
27 relating to questionnaire length, data on established associated risk factors for
28 depression and anxiety such as smoking status, alcohol consumption, educational,
29 marital and economic status⁵¹⁻⁵⁴ were not available. Also, although the study did not
30 find any differences between ex-footballers and controls in terms of mental health it
31 would have been interesting to examine mental toughness, resilience, optimism and
32 general pain coping mechanisms between the two populations. Future epidemiological
33 research on this topic should explore these relationships in more detail.. Also, our use
34 of the self-completed HADS alone is a limitation as this measure only the symptoms
35 of depression or anxiety as opposed to producing a definitive clinical diagnosis.
36 Although we used the upper suggested cut-off of the HADS as a surrogate for probable
37 depression and anxiety, the prevalence data for this dichotomous cut-off should be
38 interpreted with this important caveat in mindFurthermore, this study did not
39 specifically measure two aspects of quality of life: physical health via current physical
40 activity levels, and, social relations via personal relationships or available social
41 support. These data would have given us insight into current physical fitness levels,
42 physical limitations as a consequence of musculoskeletal conditions, and whether
43 there was adequate psychosocial support in an individual's life. These form some of
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3 the core tenets of a healthy quality of life⁵³ and may have offered robust data on
4 previously reported anecdotal effects of bankruptcy, divorce or trauma particularly in
5 the ex-footballers⁵⁵. Finally, we did not examine the effects of repetitive heading of
6 footballs and risk of head injury and concussion in professional footballers, and the
7 possible long-term health impact that this could have on neuro-cognition and mental
8 health. A future study is planned to address this issue.
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15 In summary, this is the largest study on symptoms of anxiety and depression and
16 quality of life in ex-professional footballers and the first to include an age-adjusted
17 general population comparison sample. The results show that ex-footballers are just
18 as likely to have anxiety and depression symptoms as controls, but they have lower
19 QoL in terms of both physical and mental composite scores. However, despite
20 reporting more widespread body pain and use of analgesics, they are less likely to
21 report cardiovascular disease or diabetes. The results suggest that healthcare
22 providers, club management and football organisations should be focused on
23 improving musculoskeletal pain management strategies in ex-footballers. Further
24 study on the potential benefits of professional sport on pain coping and resilience
25 mechanisms which may be protective factors for long term psychological
26 consequences such as depression and anxiety would benefit the large numbers of ex-
27 professional footballers both nationally and internationally. It would also be valuable
28 to explore the effects of neurocognitive functioning on mental health in ex-footballers
29 and capture the granularity around type, severity and frequencies of injuries such as
30 concussion and the subsequent long-term health impact.
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Affiliations

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All researchers were independent from funders.

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

review only

Declarations:

Consent:

The study was approved by Nottingham University Hospitals NHS Trust and the Nottingham Research Ethics Committee 1 (Refs 14/EM/0045 & 14/EM/0015) and registered (clinicaltrials.gov portal: NCT02098044 & NCT02098070).

All participants offered consent by responding to the postal questionnaire survey and written informed consent prior to radiographic assessment at the SPIRE Hospitals and the Nottingham City Hospital.

Contributor's statement:

GSF designed the data collection tools, wrote the statistical plan, implemented the study design (conducted the study), conducted cleaning and analysis of the data, wrote the initial drafts of the paper and subsequently revised the paper after feedback from the team. SMP designed the data collection tools, wrote the statistical plan, implemented the study design (conducted the study), conducted cleaning and analysis of the data, and drafted and revised the paper. JPM conducted cleaning and analysis of the data, and drafted and revised the paper. CWF conceptualised the study and drafted and revised the paper. BS conceptualised the study and drafted and revised the paper. MEB monitored data collection and drafted and revised the paper. WZ conceptualised and designed the study and data collection tools, wrote the statistical plan, monitored data collection and drafted and revised the paper. MD conceptualised and designed the study and data collection tools, monitored data collection and drafted and revised the paper. He is guarantor.

Conflict of Interest Disclosures:

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: financial support (research grant) for the submitted work from FIFA Medical Assessment and Research Centre, other from Arthritis Research UK Centre for Sports, Exercise and Osteoarthritis (Grant Reference 20194); research grant from the Professional Footballers' Association and financial support from the SPIRE Healthcare Group at the Football Association (St George's Park); CF did paid consultancy for FIFA Medical Assessment and Research Centre, the Football Association and the Premier League in the past three years and has received personal fees from these bodies outside the remit of the submitted work; MD received research funding by AstraZeneca, Nordic Biosciences, Roche, outside the submitted work; Dr. Zhang reports grants from Arthritis Research UK, grants from Arthritis Research UK, during the conduct of the study; other from AstraZeneca, other from Daiichi Sankyo, other from Biobarica, other from Hisun, outside the submitted work; no financial relationships with any organisation that might have an interest in the submitted work in the previous three years for any other authors; no other relationships or activities that could appear to have influenced the submitted work.

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6 third party to do any or all of the above.”
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9 Data Sharing: No additional data available.

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11 Transparency Declaration: Professor Michael Doherty (MD) affirms that the
12 manuscript is an honest, accurate, and transparent account of the study being
13 reported and that no important aspects of the study have been omitted.
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For peer review only

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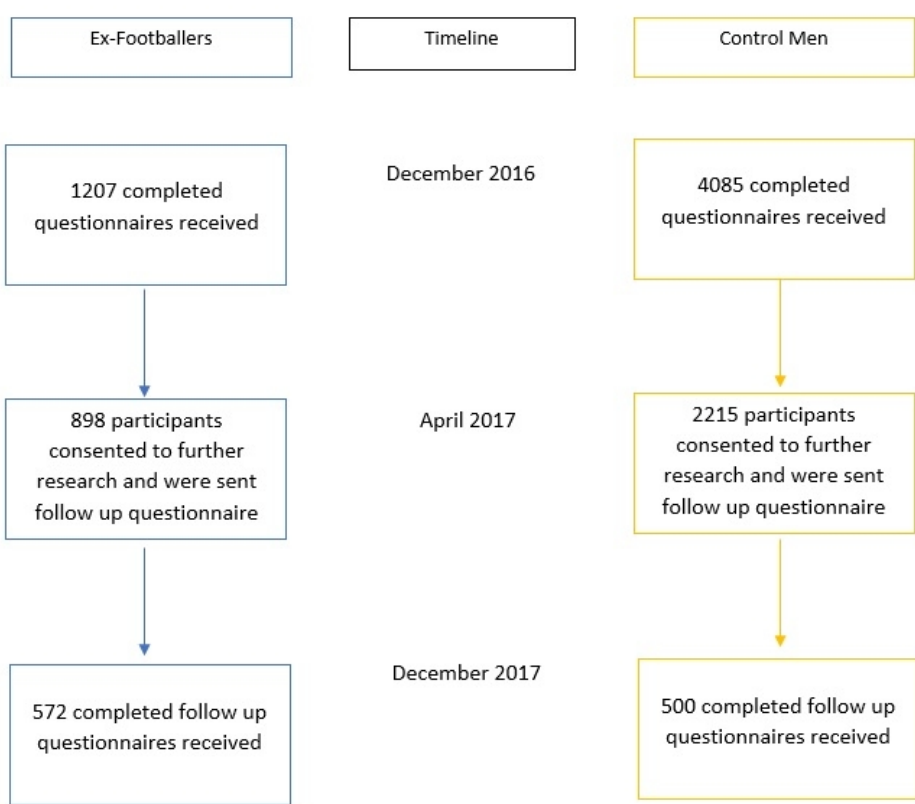


Figure 1 Selection of ex-footballer and general population controls.

58x51mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 and 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4 and 5
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 6-9
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Page 10-11
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 7-9
Bias	9	Describe any efforts to address potential sources of bias	Page 9 and page 16
Study size	10	Explain how the study size was arrived at	Page 10, 11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 10
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	Page 10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	n/a

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	none
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Flow chart figure page 11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 11
		(b) Indicate number of participants with missing data for each variable of interest	Page 10
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Page 11-13
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 12-13
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 14-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.