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Healthspan and chronic disease burden among young adult and middle-aged male former American-style professional football players

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ABSTRACT

Objective To examine the relationships between age, healthspan and chronic illness among former professional American-style football (ASF) players.

Methods We compared age-specific race-standardised and body mass index-standardised prevalence ratios of arthritis, dementia/Alzheimer's disease, hypertension and diabetes among early adult and middle-aged (range 25–59 years) male former professional ASF players (n=2864) with a comparator cohort from the National Health and Nutrition Examination Survey and National Health Interview Survey, two representative samples of the US general population. Age was stratified into 25–29, 30–39, 40–49 and 50–59 years.

Results Arthritis and dementia/Alzheimer's disease were more prevalent among ASF players across all study age ranges (all p<0.001). In contrast, hypertension and diabetes were more prevalent among ASF players in the youngest age stratum only (p<0.001 and p<0.01, respectively). ASF players were less likely to demonstrate intact healthspan (ie, absence of chronic disease) than the general population across all age ranges.

Conclusion These data suggest the emergence of a maladaptive early ageing phenotype among former professional ASF players characterised by premature burden of chronic disease and reduced healthspan. Additional study is needed to investigate these findings and their impact on morbidity and mortality in former ASF players and other athlete groups.

INTRODUCTION

Advancing age is a potent independent and non-modifiable risk factor for the development of many chronic diseases.¹ General population studies consistently associate increases in cardiometabolic,² neurocognitive³ and musculoskeletal pathology with increasing age.⁴ Although the precise mechanisms linking ageing to an increasing burden of chronic disease remain incompletely understood, biological mechanisms involving inflammation, proteostasis, macromolecular damage, dysregulated cellular metabolism and epigenetic influence have been proposed.⁵ While these mechanistic underpinnings of chronic disease are common consequences of ageing, early life environmental factors may dictate their magnitude and age of onset. To date, the degree to which specific early life exposures accelerate ageing, precipitate the premature onset

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ While exposure to professional American style football (ASF) has been associated with a maladaptive multiorgan phenotype, data on the effects of ASF on healthspan and the premature occurrence of chronic illness remains understudied.

WHAT THIS STUDY ADDS

⇒ Our data suggest significantly foreshortened healthspan in former ASF players compared with the general population. This was driven by an increased prevalence of conditions typically associated with ageing including arthritis and dementia/Alzheimer's disease across all age groups 25–59 years and hypertension and diabetes among players 25–29 years within a large cohort of early adult and middle-aged former professional ASF players.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These results highlight the need to identify early adult and middle-aged players who may harbour cardiometabolic, orthopaedic and neurocognitive disease to consider early pharmacological and behavioural interventions to improve morbidity and mortality.

of chronic disease, and thereby reduce healthspan (defined as the duration of life without chronic disease)⁶ remains incompletely understood.

Participation in American-style football (ASF) has been associated with the emergence of a multiorgan, maladaptive phenotype early in life. Specifically, ASF participation has been linked to the development of hypertension,⁷ pathological cardiac remodelling,⁸ vascular stiffening,⁹ and obesity.^{10 11} Studies establishing adverse cardiovascular relationships have focused almost exclusively on youthful men during their years of active ASF participation. Cognitive impairment also has been identified during active play^{12 13} and in postcareer years.^{14 15} In addition, high physical demands and associated traumatic joint injuries in ASF contribute to elevated rates of early total knee and hip arthroplasty in former ASF players compared with the general population.¹⁶ Accordingly, the impact of



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ASF participation on later life healthspan remains incompletely characterised and data comparing chronic disease burden among former ASF participants to people with no prior ASF exposure are lacking.

We hypothesised that ASF participation represents a risk factor for early ageing as reflected by the presence of premature chronic disease and reduced healthspan. Specifically, we hypothesised that former ASF participants would harbour a higher prevalence of common age-related chronic diseases compared with similarly aged men without ASF exposure. To address this hypothesis, we compared race-adjusted and body mass index (BMI)-adjusted disease prevalence estimates of self-reported arthritis, dementia/Alzheimer's disease, hypertension and diabetes mellitus in a large cohort of former professional ASF participants to those derived from two independent, well-validated general community reference populations.

METHODS

ASF sample

Former players who received compensation from the National Football League (NFL) after 1960 (the year hard plastic helmets were formally adopted¹⁷) were considered eligible for the Football Players Health Study (FPHS) at Harvard University.¹⁸ Home and email addresses were obtained from the NFL Players Association. A total of 15 070 former players received invitations to participate in either a hard copy or online questionnaire, out of which 4174 (27.7%) enrolled. A former player advisory board that represents the distribution of age, race and geographical region of professional ASF players offered feedback on the conceptual framework of chronic disease burden and healthspan.

General population samples

We used two surveys to capture general population distributions of four age-associated chronic illnesses. The first was the National Health and Nutrition Examination Survey (NHANES),¹⁹ a multi-year, stratified, clustered, four-stage sample that releases data in 2-year cycles. NHANES uses a probability-based sampling design that oversamples low-income individuals, non-Hispanic black and Mexican Americans, adults over age 60 and adolescents. We used NHANES demographic and health survey data from 2015 to 2016 and 2017 to 2018. We also accessed the 2019 National Health Interview Survey (NHIS),²⁰ which collects demographic, socioeconomic, healthcare and mental and physical health data via interview. NHIS uses a multistage stratified and geographically clustered sampling strategy to ensure that NHIS is nationally representative of the most recent decennial census.

Measures

Age was determined using date of birth for football participants, and survey age for general population participants. We restricted datasets to men between the ages of 25–59. The minimum age was chosen to match the youngest FPHS participant to ensure full capture of pathology related to ASF exposure. A maximal age of 59 was selected to reflect the end of 'middle-age',^{21 22} and to minimise the powerful impact of older age on disease prevalence. Age was stratified into 25–29, 30–39, 40–49 and 50–59 years. ASF players responded to survey questions that queried professional playing career length. Position was divided into linemen (defensive line, linebacker and offensive line) and non-linemen (defensive back, kicker/punter, quarterback, running back, tight end, wide receiver and special teams only). Race for former football players was assigned as previously described,²³ whereby players chose the category that best described their race/ethnicity

and were further classified into black, white or other. Due to the low representation of non-black and non-white football players in the NFL (and consequently FPHS), we restricted datasets to black and white individuals, excluding Asian, Native Hawaiian/Pacific Islander, Latino, American Indian/Alaskan Native, other or 'declined to answer' participants. BMI was calculated using the self-reported weight and height for ASF players and NHIS participants.²⁴ For NHANES, height and weight were collected during the clinical assessment. BMI was categorised into <25.0, 25.0–30.0 and >30.0.

We used self-reported data on four chronic diseases, including arthritis, hypertension/high blood pressure and diabetes mellitus from FPHS, NHANES and NHIS, and dementia/Alzheimer's disease captured in FPHS and NHIS. Disease status phrasing across the cohorts is summarised as follows. For dementia/Alzheimer's disease, both FPHS and NHIS identically asked 'Has a healthcare provider ever told you that you have had dementia (Alzheimer's disease)', thus combining dementia and Alzheimer's Disease into a single outcome. The arthritis question in FPHS, NHANES and NHIS were all phrased as 'Has a healthcare provider ever told you that you have had arthritis?'

For high blood pressure/hypertension in NHANES, we used: (1) 'Because of your high blood pressure/hypertension, have you ever been told to take prescribed medicine?' and (2) 'Are you now taking prescribed medicine?'. For NHIS, high blood pressure/hypertension was queried as: (1) 'Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?' and (2) 'Are you NOW taking any medication prescribed by a doctor for your high blood pressure?'. For diabetes mellitus, NHANES asked the following: (1) 'Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?', (2) 'Are you now taking diabetic pills to lower your blood sugar?' and (3) 'Are you using injectable insulin to lower your blood sugar?'. NHIS phrased questions on diabetes mellitus status as: (1) 'Has a doctor or other health professional EVER told you that you had diabetes?', (2) 'Are you NOW taking diabetic pills to lower your blood sugar?' and (3) 'Insulin can be taken by shot or pump. Are you NOW taking insulin?'. FPHS participants were asked 'Has a medical provider ever recommended or prescribed medication for [condition]' and 'Are you currently taking medication [for that condition]?'. We used their responses to the conditions 'high blood pressure' and 'diabetes or high blood sugar.' For both diabetes/high blood sugar and high blood pressure/hypertension, participants who answered affirmatively to any disease-specific question were assigned that diagnosis.

NHIS was used to compare race-adjusted and BMI-adjusted dementia/Alzheimer's disease prevalence between FPHS and the general population, since this was not asked in NHANES. For the other three individual conditions we compared with NHANES because the question phrasing to define the outcome in NHIS was somewhat different from FPHS. We used the NHIS dataset to study race-adjusted and BMI-adjusted healthspan (defined as the duration of lifespan free from chronic disease), because it contained data on all conditions. To assess the effect of the different wording between NHIS and NHANES to define hypertension and diabetes, we compared race-adjusted and BMI-adjusted prevalence estimates in NHANES and NHIS in the subset used for our analyses.

Statistical analysis

We calculated age-specific, race-specific and BMI-specific prevalence rates for outcomes in NHANES, NHIS and FPHS.

Raw NHIS and FPHS data were scaled to match the general population distribution captured by applying NHANES study-specified weights (combining two NHANES cycles according to NHANES procedures²⁵) that reflect the general US male population between the ages of 25–59. Each age-specific, race-specific and BMI-specific prevalence was adjusted to the age, race and BMI distribution of the weighted NHANES population by scaling the age-specific prevalence rates to the distribution of race (black or white) and BMI (<25.0, 25.0–30.0 and >30.0 kg/m²) in NHANES. Significance was calculated using z-statistics for observed to expected ratios.²⁶ To prevent overinflation of degree of observed significance that would occur if p values were based on a pseudopopulation that was larger than the original, we treated the NHANES-scaled general population estimates as the source of observed outcomes. Analyses were conducted using R Statistical Software²⁷ and statistical significance was set at 0.0063 ($p < 0.05$ divided by 8) to account for multiple comparisons.²⁸

RESULTS

At the time of entry, 2864 out of 4174 (68.6%) FPHS participants met inclusion criteria of being between the ages of 25 and 59. This former ASF player study population was 44 ± 10 years of age, similar to both NHANES (42 ± 10 years) and NHIS (43 ± 10 years, table 1). In our study populations, 48.1% of FPHS participants were black, compared with 40.1% in NHANES and 13.5% in NHIS. BMI among the former ASF players (32 ± 5 kg/m²) was higher than among both the NHANES (30 ± 7) and NHIS (28 ± 5) participants. The ASF players reported 6 ± 4 years in the NFL with a majority (66%) playing a non-lineman position. In comparisons of the prevalence of the conditions by age in NHANES and NHIS, we found no statistical differences between prevalence by age group (online supplemental table 1), although the difference in hypertension among 40–49 years old was 6% higher in NHIS, which approached significance ($p = 0.06$). The second largest difference in prevalence in any category between NHANES and NHIS was for diabetes among 50–59 years old that was 2.6% lower in NHIS.

The overall unadjusted prevalence of freedom from chronic disease and disease-specific unadjusted prevalence estimates for arthritis, dementia/Alzheimer's disease, hypertension and diabetes mellitus for each cohort are shown in table 1. Age-stratified prevalence estimates of each race-adjusted and BMI-adjusted chronic condition are shown in figure 1 and standardised prevalence ratios are listed in online supplemental table 2. Arthritis (figure 1A) and dementia/Alzheimer's disease (figure 1B) were directly related to age and were more prevalent among former ASF athletes than among the general population across all age groups, except in the 25–29 age group among whom neither cohort reported dementia/Alzheimer's disease cases. Hypertension and diabetes mellitus followed a different trajectory. For hypertension, there was a statistically significant twofold higher prevalence among ASF athletes in the youngest age group (25–29 years) compared with the general population, but in older groups the prevalence was higher in the general population (figure 1C). In similar fashion, the prevalence of diabetes mellitus among former ASF players was significantly higher compared with the general population among the youngest age group, after which prevalence estimates were similar until the highest age group (50–59 years) where the prevalence in the general population was significantly higher than in former ASF players (figure 1D).

Table 1 Characteristics of the Football Players Health Study (FPHS), National Health and Nutrition Examination Survey (NHANES) and National Health Interview Survey (NHIS) cohorts

	FPHS	NHANES	NHIS
	2015–2019	2015–2018	2019
	N=2684	N=1481	N=6298
Age mean (SD (SD))	43.9 (9.6)	42.3 (10.4)	43.1 (10.2)
Age N (%)			
25–29*	177 (6.6)	209 (14.1)	770 (12.2)
30–39	834 (31.1)	413 (27.9)	1723 (27.4)
40–49	712 (26.5)	414 (28.0)	1714 (27.2)
50–59	961 (35.8)	445 (30.0)	2091 (33.2)
Race N (%)			
Black	1291 (48.1)	617 (40.1)	851 (13.5)
White	1393 (51.9)	920 (59.9)	5447 (86.5)
Body mass index (BMI)†	31.69 (5.12)	30.0 (7.1)	28.4 (4.8)
Mean (SD)			
BMI N (%)			
25–29	30.25 (4.37)	27.9 (6.9)	27.2 (5.0)
30–39	31.43 (5.05)	30.37 (8.0)	27.7 (4.7)
40–49	32.21 (5.33)	30.99 (6.6)	28.9 (4.7)
50–59	31.84 (5.27)	29.68 (6.3)	28.9 (4.8)
Lineman status N (%)			
Non-lineman	1763 (65.69)	–	–
Lineman	921 (34.31)	–	–
Years of play mean (SD)	6.39 (3.9)	–	–
Healthspan status N (%)‡			
Diminished	1458 (56.3)	–	2308 (36.7)
Intact	1132 (43.7)	–	3982 (63.3)
Missing	94 (3.5)	–	8 (0.1)
Dementia/Alzheimer's disease N (%)‡			
No	2628 (97.9)	–	6280 (99.7)
Yes	56 (2.1)	–	10 (0.2)
Missing	–	–	8 (0.1)
Arthritis N (%)			
No	1538 (57.3)	1237 (80.5)	5375 (85.3)
Yes	1146 (42.7)	298 (19.4)	923 (14.7)
Missing	–	2 (0.1)	–
Diabetes N (%)			
No	2477 (92.3)	1363 (88.7)	5853 (92.9)
Yes	170 (6.3)	122 (7.9)	445 (7.1)
Missing	37 (1.4)	52 (3.4)	–
Hypertension N (%)			
No	1915 (71.3)	1119 (72.8)	4571 (72.6)
Yes	747 (27.8)	415 (27.0)	1727 (27.4)
Missing	22 (0.8)	3 (0.2)	–

*One FPHS participant was 24 years old.

†94 FPHS participants are missing BMI.

‡Healthspan and dementia/Alzheimer's disease status could only be calculated for NHIS and not NHANES as NHANES does not include dementia/Alzheimer's disease survey data that are comparable to FPHS.

Freedom from the four chronic diseases of interest—that is, intact healthspan adjusted for race and BMI—is shown in figure 2 and online supplemental table 2. As anticipated, intact healthspan declined with increasing age among former ASF players and the general population. However, the prevalence of intact healthspan was significantly lower among former ASF players of all ages compared with the general population

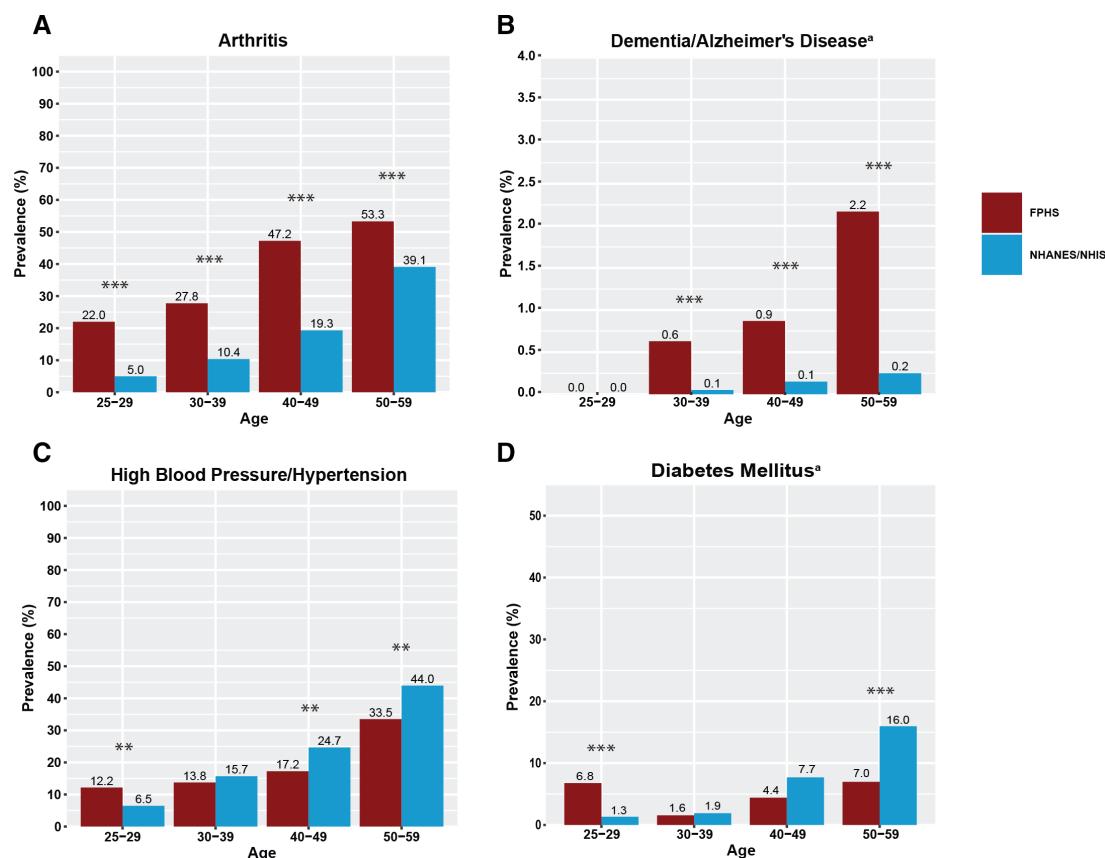


Figure 1 Race-adjusted and BMI-adjusted prevalence estimates for each chronic condition in former professional American-style football players versus the general population. (A) Arthritis (Football Players Health Study (FPHS) and National Health and Nutrition Examination Survey (NHANES)); (B) Dementia/Alzheimer's disease (FPHS and National Health Interview Survey (NHIS)); (C) Hypertension/High Blood Pressure (FPHS and NHANES and (D) Diabetes Mellitus (FPHS and NHANES). Significance values have been adjusted using the Bonferonni correction for multiple comparisons. ** $p < 0.0013$; *** $p < 0.00013$ after multiple comparisons correction. ^aAxes for B, C have been expanded for visibility. BMI, body mass index.

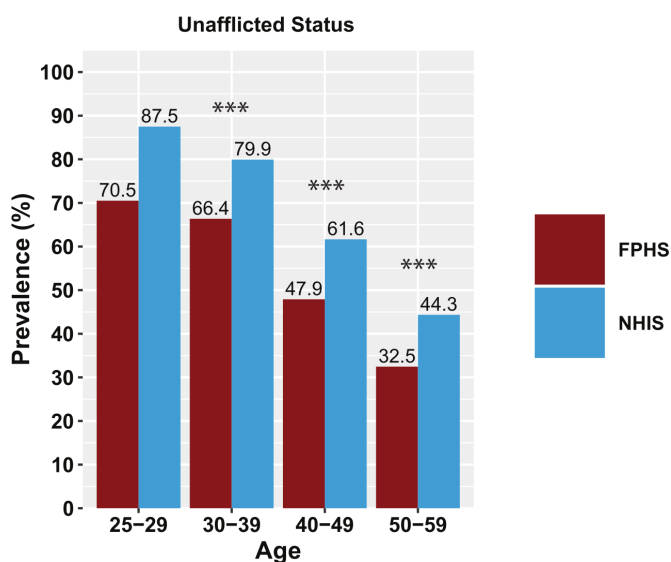


Figure 2 Race-adjusted and BMI-adjusted prevalence estimates for intact healthspan status for the Football Players Health Study (FPHS) and National Health Interview Survey (NHIS). Significance values have been adjusted using the Bonferonni correction for multiple comparisons. *** $p < 0.00013$ after multiple comparisons correction. BMI, body mass index.

except the youngest age group. The decline in prevalent intact healthspan appeared to be shifted roughly a decade earlier among former ASF players. Specifically, the 66% intact healthspan prevalence among former ASF players in the 30–39 years age group was similar to 40–49 years old men in the general population (62%). Similarly, the 48% prevalence of intact healthspan of former ASF players in their 40s mirrored that among men from the general population who were a decade older (44% among NHIS participants aged 50–59). Among football players only, linemen showed significantly diminished healthspan compared with non-linemen in all but the 50–59 age group (figure 3).

DISCUSSION

This study compared chronic disease burden among former professional ASF players ages 25–59 with age-matched estimates from the general population. As anticipated, we observed increasing race-adjusted and BMI-adjusted prevalence estimates of arthritis, dementia/Alzheimer's disease, hypertension and diabetes mellitus with increasing age among both groups. However, comparative relationships between age and disease prevalence between the two groups differed by condition type. Arthritis and dementia/Alzheimer's disease, chronic diseases associated with morbidity (ie, reduced quality of life), were consistently higher among former ASF players than the general population across the entire age span studied. In contrast, former ASF players harboured more hypertension and diabetes mellitus,

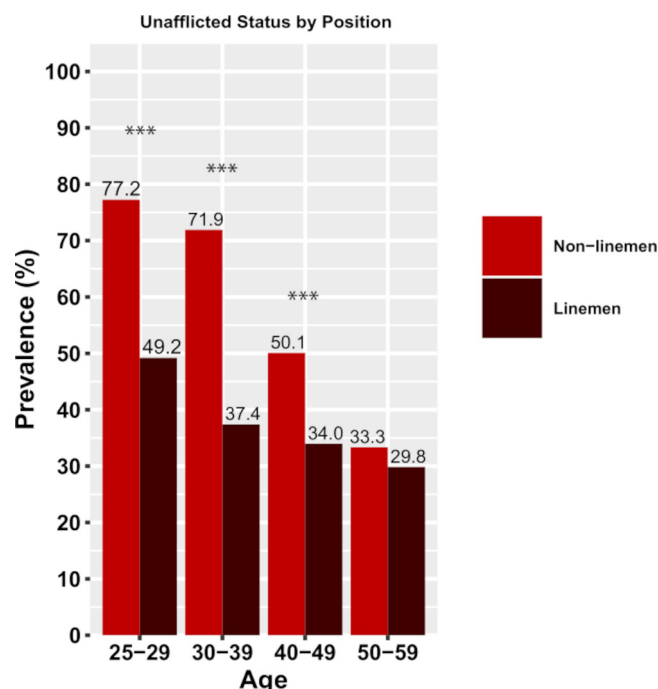


Figure 3 Race-adjusted and BMI-adjusted prevalence estimates for intact healthspan status among Football Player Health Study participants stratified by lineman position status. Significance values have been adjusted using the Bonferroni correction for multiple comparisons. *** $p < 0.00013$ after multiple comparisons correction. BMI, body mass index.

cardiometabolic conditions closely linked to mortality (ie, duration of life) in the youngest age strata but had lower prevalence than the general population at older ages. Taken together, the prevalence of men with no chronic disease (ie, intact healthspan) was significantly lower among former ASF players, particularly among men that played at a lineman field position, compared with men of the same age without professional football exposure across the 35 year age span studied. This finding suggests that professional ASF participation should be considered a risk factor for reduced healthspan with contributions from the premature emergence of diseases that may impact both the quality and duration of life.

Advancing chronological age is a universal and non-modifiable risk factor for the development of many chronic diseases. Accordingly, we selected a relatively youthful cohort of former professional ASF players to maximise the impact of ASF exposure on chronic disease prevalence while minimising the impact of older age. Findings indicate that hypertension and diabetes mellitus are present at higher rates than expected in relatively young men during the immediate years after ASF career termination. Consistent with prior literature,²⁵⁻²⁷ this suggests an association between ASF participation and cardiometabolic disease which is the most common cause of death among former professional ASF players.²⁸ This observation is clinically significant, as hypertension and diabetes mellitus increase mortality when manifested during early years independent of later life disease.²⁹⁻³² Accordingly, our data suggest an important role for focused efforts to identify young former ASF players who harbour cardiometabolic disease with the goal of ensuring guideline-directed lifestyle and pharmaceutical intervention.³³

Our finding that arthritis and dementia/Alzheimer's disease, diseases that adversely impact quality of life, occur earlier

among former ASF athletes than the general population is similarly important. Specifically, former ASF players appear to be at increased risk for premature cessation of healthspan compared with men without professional ASF exposure even if they have been shown to live as long or longer than the general population.^{28 34} Thus, former ASF players may spend higher percentages of their lifespans living with clinically relevant infirmities that have adverse impacts on daily function, healthcare utilisation and quality of life. This important finding raises the imperative to identify potential health consequences of professional ASF participation, to understand the pathophysiological underpinnings of these diseases, and to initiate both primary preventive and secondary therapeutic opportunities for intervention. While future confirmatory work is required, this paradigm may be applicable to former elite athletes from other collision and contacts sports (eg, rugby, ice hockey and European-style football/soccer) that predispose participants to orthopaedic injury and head trauma.

While this study was not designed to identify mechanisms underlying the premature emergence of chronic disease among former ASF players, several speculative comments are warranted. Potential 'on the field' risk factors including repetitive head impact and traumatic musculoskeletal injury may predispose players to subsequent neurocognitive impairment and arthritis, respectively. In addition, there are 'off the field' elements of professional ASF participation including deliberate weight gain,³⁵⁻³⁷ performance-enhancing supplement and non-steroidal anti-inflammatory use,^{38 39} and exposure to high intensity strength training that may contribute to an increased susceptibility to early life pathology.⁴⁰ Race, while largely a social construct, has been shown to be a covariate associated with the cardiovascular response to ASF and may serve as an independent risk factor for aging.⁴¹ The extent to which 'weathering' stress, allostatic load and structural racism impact biological age of minority athletes merits special investigation.⁴² Determination of the causality and relative magnitudes of these risk factors coupled with a delineation of the underlying cellular and organ-specific pathophysiology represent important areas of future work.

We acknowledge several limitations. First, outcome data are based exclusively on self-report without medical record or clinician confirmation, which could introduce response bias via inaccurate reporting across all cohorts. However, we deliberately applied consistently conservative trait definitions which would result in a balanced underestimation of disease prevalence across player and general cohorts. Second, the FPHS chronic condition survey deliberately used identical terminology related to chronic illness (eg, 'arthritis' instead of osteoarthritis or rheumatoid arthritis; 'diabetes or high blood sugar' instead of type I or type II diabetes mellitus) as that employed in the general population cohorts to facilitate meaningful comparisons. Accordingly, we were unable to explore potentially important subtypes of pathology. Third, we acknowledge the possibility of selection bias within the ASF cohort and cannot exclude the possibility that ASF players harbouring more illness may have been more likely to enroll. However, prior work has shown that people with severe illness are less likely to join health studies,^{43 44} and we did not find universally increased chronic disease prevalence across all age strata but rather patterns that varied by condition. Fourth, we cannot exclude the possibility that the observed relative reduction of cardiometabolic disease among ageing former ASF players was in part driven by attrition due to earlier mortality among those most affected. Finally, we acknowledge that BMI represents an imperfect measure of body habitus and may have

led to overestimates of obesity in the former professional football cohort.⁴⁵ However, given that more accurate body composition variables were not available, BMI offered the best opportunity to account for the influence of body habitus differences despite the potential to introduce bias into BMI-adjusted estimates.

In conclusion, findings suggest that participation in professional ASF is associated with the premature onset of key chronic diseases that may increase both morbidity and risk for mortality. Further, the approximate 10-year reduction in intact healthspan in former ASF players suggests that professional ASF participation may represent a previously unidentified risk factor for early ageing. While our data suggest a link between ASF participation and a maladaptive early ageing phenotype, future work examining established biochemical, cellular and physiological signatures of ageing in this population is warranted.

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Correction notice This article has been corrected since it published Online First. A typographical error in the figure 1 legend has been corrected.

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Patient consent for publication Not applicable.

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REFERENCES

- 1 Kuan V, Fraser HC, Hingorani M, *et al*. Data-Driven identification of ageing-related diseases from electronic health records. *Sci Rep* 2021;11:2938.
- 2 Lloyd-Jones DM, Leip EP, Larson MG, *et al*. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006;113:791–8.
- 3 van der Flier WM, Scheltens P. Epidemiology and risk factors of dementia. *J Neurol Neurosurg Psychiatry* 2005;76 Suppl 5:v2–7.
- 4 Lawrence RC, Felson DT, Helmick CG, *et al*. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum* 2008;58:26–35.
- 5 Kennedy BK, Berger SL, Brunet A, *et al*. Geroscience: linking aging to chronic disease. *Cell* 2014;159:709–13.
- 6 Dzaou VJ, Finkelman EM, Balatbat CA, *et al*. Achieving healthy human longevity: a global grand challenge. *Sci Transl Med* 2020;12. doi:10.1126/scitranslmed.abd3816. [Epub ahead of print: 21 Oct 2020].
- 7 Weiner RB, Wang F, Isaacs SK, *et al*. Blood pressure and left ventricular hypertrophy during American-style football participation. *Circulation* 2013;128:524–31.
- 8 Lin J, Wang F, Weiner RB, *et al*. Blood pressure and LV remodeling among American-Style football players. *JACC Cardiovasc Imaging* 2016;9:1367–76.
- 9 Kim JH, Sher S, Wang F, *et al*. Impact of American-style football participation on vascular function. *Am J Cardiol* 2015;115:262–7.
- 10 Churchill TW, Krishnan S, Weisskopf M, *et al*. Weight gain and health affliction among former national football League players. *Am J Med* 2018;131:1491–8.
- 11 Kim JH, Hollowed C, Liu C, *et al*. Weight gain, hypertension, and the emergence of a maladaptive cardiovascular phenotype among US football players. *JAMA Cardiol* 2019;4:1221–9.
- 12 Pryor J, Larson A, DeBeliso M. The prevalence of depression and concussions in a sample of active North American Semi-Professional and professional football players. *J Lifestyle Med* 2016;6:7–15.
- 13 Talavage TM, Nauman EA, Breedlove EL, *et al*. Functionally-detected cognitive impairment in high school football players without clinically-diagnosed concussion. *J Neurotrauma* 2014;31:327–38.
- 14 Roberts AL, Pascual-Leone A, Speizer FE, *et al*. Exposure to American football and neuropsychiatric health in former national football League players: findings from the football players health study. *Am J Sports Med* 2019;47:2871–80.
- 15 Guskiewicz KM, Marshall SW, Bailes J, *et al*. Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery* 2005;57:719–26.

- 16 Tenforde AS, Cortez B, Baker J, *et al.* Prevalence of total hip and knee arthroplasty in former national football League players: comparison with the general US population and other populations of professional athletes. *BMJ Open Sport Exerc Med* 2020;6:e000833.
- 17 Harrison EA. The first concussion crisis: head injury and evidence in early American football. *Am J Public Health* 2014;104:822–33.
- 18 Zafonte R, Pascual-Leone A, Baggish A, *et al.* The football players' health study at Harvard University: design and objectives. *Am J Ind Med* 2019;62:643–54.
- 19 Chen T-C, Clark J, Riddles MK, *et al.* National health and nutrition examination survey, 2015–2018: sample design and estimation procedures. *Vital Health Stat* 2020;2:1–35.
- 20 Blewett LA, Dahlen HM, Spencer D, *et al.* Changes to the design of the National health interview survey to support enhanced monitoring of health reform impacts at the state level. *Am J Public Health* 2016;106:1961–6.
- 21 Brim OG, Ryff CD, Kessler RC, eds. *How Healthy Are We? A National Study of Well-Being at Midlife*. Chicago: The University of Chicago Press, 2004.
- 22 Radler BT. The midlife in the United States (MIDUS) series: a national longitudinal study of health and well-being. *Open Health Data* 2014;2.
- 23 Grashow R, Weisskopf MG, Baggish A, *et al.* Premortem chronic traumatic encephalopathy diagnoses in professional football. *Ann Neurol* 2020;88:106–12.
- 24 Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med* 1987;317:1098.
- 25 Tucker AM, Vogel RA, Lincoln AE, *et al.* Prevalence of cardiovascular disease risk factors among national football League players. *JAMA* 2009;301:2111–9.
- 26 Selden MA, Helzberg JH, Waeckerle JF, *et al.* Cardiometabolic abnormalities in current National football League players. *Am J Cardiol* 2009;103:969–71.
- 27 Borchers JR, Clem KL, Habash DL, *et al.* Metabolic syndrome and insulin resistance in division 1 collegiate football players. *Med Sci Sports Exerc* 2009;41:2105–10.
- 28 Nguyen VT, Zafonte RD, Chen JT, *et al.* Mortality among professional American-style football players and professional American baseball players. *JAMA Netw Open* 2019;2:e194223.
- 29 Gray L, Lee I-M, Sesso HD, *et al.* Blood pressure in early adulthood, hypertension in middle age, and future cardiovascular disease mortality: HAHS (Harvard alumni health study). *J Am Coll Cardiol* 2011;58:2396–403.
- 30 McCarron P, Okasha M, McEwen J, *et al.* Blood pressure in early life and cardiovascular disease mortality. *Arch Intern Med* 2002;162:610–1.
- 31 Dean H, Flett B. Natural history of type 2 diabetes diagnosed in childhood: long term follow-up in young adult years. *Diabetes* 2002;51:A24–5.
- 32 Eppens MC, Craig ME, Cusumano J, *et al.* Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. *Diabetes Care* 2006;29:1300–6.
- 33 Whelton PK, Carey RM, Aronow WS, *et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American heart association Task force on clinical practice guidelines. *Hypertension* 2018;71:e13–115.
- 34 Grashow RG, Roberts AL, Zafonte R, *et al.* Defining exposures in professional football: professional American-Style football players as an occupational cohort. *Orthop J Sports Med* 2019;7:232596711982921.
- 35 Kaiser GE, Womack JW, Green JS, *et al.* Morphological profiles for first-year national collegiate athletic association division I football players. *J Strength Cond Res* 2008;22:243–9.
- 36 Laurson KR, Eisenmann JC. Prevalence of overweight among high school football linemen. *JAMA* 2007;297:359–64.
- 37 Jonnalagadda SS, Rosenbloom CA, Skinner R. Dietary practices, attitudes, and physiological status of collegiate freshman football players. *J Strength Cond Res* 2001;15:507–13.
- 38 Tso J, Hollowed C, Liu C, *et al.* Nonsteroidal anti-inflammatory drugs and cardiovascular risk in American football. *Med Sci Sports Exerc* 2020;52:2522–8.
- 39 Holmes N, Cronholm PF, Duffy AJ, *et al.* Nonsteroidal anti-inflammatory drug use in collegiate football players. *Clin J Sport Med* 2013;23:283–6.
- 40 Baggish AL, Wang F, Weiner RB, *et al.* Training-specific changes in cardiac structure and function: a prospective and longitudinal assessment of competitive athletes. *J Appl Physiol* 2008;104:1121–8.
- 41 Forrester S, Jacobs D, Zmora R, *et al.* Racial differences in weathering and its associations with psychosocial stress: the cardia study. *SSM Popul Health* 2019;7:100319–3.
- 42 Geronimus AT, Hicken M, Keene D, *et al.* "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *Am J Public Health* 2006;96:826–33.
- 43 Weuve J, Tchetgen Tchetgen EJ, Glymour MM, *et al.* Accounting for bias due to selective attrition: the example of smoking and cognitive decline. *Epidemiology* 2012;23:119–28.
- 44 Chatfield MD, Brayne CE, Matthews FE. A systematic literature review of attrition between waves in longitudinal studies in the elderly shows a consistent pattern of dropout between differing studies. *J Clin Epidemiol* 2005;58:13–19.
- 45 Provencher MT, Chahla J, Sanchez G, *et al.* Body mass index versus body fat percentage in prospective national football League athletes: overestimation of obesity rate in athletes at the National football League Scouting combine. *J Strength Cond Res* 2018;32:1013–9.