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Leisure Activities, Genetic Risk, and Frailty: Evidence from the Chinese Adults Aged 80 Years or Older

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Abstract

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Author Contributions

X.M.S. designed the study. J.H.Z., Y.B.L., C.C., C.M. and X.M.S. contributed to the acquisition of the data. J.H.Z., X.W.L., L.H.Y., S.X.L., J.M.Y., Y.B.L., C.M. and X.M.S. contributed to the analysis and interpretation of the data. J.H.Z. wrote the first draft of the manuscript. J.H.Z., X.W.L., X.G., Y.W., Y.D.Q., X.L.Z., C.C., J.W., V.B.K., Y.B.L., C.M. and X.M.S. revised the manuscript critically for important intellectual content. All authors contributed to multiple drafts and have read and agreed to the final version of this article. X.M.S. takes full responsibility for the work as a whole, including the study design, access to data and the decision to submit and publish the manuscript.

Statement of Ethics

Ethical approval was granted by the biomedical ethics committee of Peking University (IRB00001052-13074) and the ethics committee of the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention (No. 201922). Written informed consents were obtained for all participants or their proxy respondents.

Conflict of Interest Statement

The authors declared that they have no competing interests.

Introduction: About half of adults aged ≥ 80 years suffer from frailty. Exercise is considered effective in preventing frailty but may be inapplicable to adults aged ≥ 80 years due to physical limitations. As an alternative, we aimed to explore the association of leisure activities with frailty and identify potential interaction with established polygenic risk score (PRS) among adults aged ≥ 80 years.

Methods: Analyses were performed in a prospective cohort study of 7471 community-living older adults aged ≥ 80 years who were recruited between 2002 and 2014 from 23 provinces in China. Leisure activity was assessed using a seven-question leisure activity index and frailty was defined as a frailty index ≥0.25 using a validated 39-item health-related scale. The PRS was constructed using 59 single-nucleotide polymorphisms associated with frailty in a subsample of 2541 older adults. Cox proportional hazards models were used to explore the associations of leisure activities, PRS with frailty.

Results: The mean age of participants was 89.4 ± 6.6 years (range: 80–116). In total, 2930 cases of frailty were identified during 42,216 person-years of follow-up. Each 1 unit increase in the leisure activity index was associated with 12% lower risk of frailty (hazard ratio [HR]: 0.88 [95%CI, 0.85-0.91]). Participants with high genetic risk (PRS>2.47×10^{-4}) suffered from 26% higher risk of frailty. Interaction between leisure activity and genetic risk was not observed.

Conclusion: Evidence is presented for the independent association of leisure activities and genetic risk with frailty. Engagement in leisure activities suggested to be associated with lower risk of frailty across all levels of genetic risk among adults aged ≥ 80 years.

Keywords

Leisure activity; Epidemiology; Frailty; Genetic risk; Healthy ageing

Introduction

Frailty is a common syndrome among older adults, characterized by reduced physiological reserve and function across multiple organ systems and increased vulnerability to adverse health outcomes [1-5]. The worldwide prevalence of frailty increases with age, being less than 10% among adults aged 60 years but increasing to 50% among adults aged ≥ 80 years, resulting in increased health-care utilization and cost [6]. The increasing global numbers of the oldest-old result in increased aggravation of this burden with estimates of 145.5 million oldest-old individuals in 2020 and 426.4 million by 2050.[7] We have previously found that nearly half of adults aged ≥80 years were underweight [8], reflecting unhealthy skeletal muscle mass and nutritional status and being associated with higher risk of frailty [9,10]. However, frailty incidence rates and potential preventive factors remain unclear since most cohort studies have had a limited sample size of adults aged ≥80 years [11]. Therefore, more long-term cohort studies are required to reveal feasible preventive or interventional measures to address the problem of frailty and foster healthy ageing [1].

Exercise is a recognized frailty prevention factor[1,12-14] but high prevalence of daily living disability limits the access of adults aged ≥80 years to regular exercise [15,16]. Leisure activities also have the potential to impact frailty in this population and greater understanding of this association would be an advantage. Previous studies among adults

aged ≤79 years have suggested an association of leisure activities, such as hobbies, cultural engagements and other organized activities (e.g., dancing, Tai Chi, visiting museums/theatre/cinema, golf, clubs, social groups and religious activities), with lower risks of frailty [13,17-19]. However, the existence of any such association among adults aged ≥80 years remains unknown.

Candidate frailty genes are thought to be related to the immune response, cholesterol transport, apoptotic signaling, homocysteine metabolism, folate metabolism, phosphate/calcium homeostasis, stem cell maintenance, cell adhesion, growth, migration and differentiation [20-24]. However, the polygenic risk score (PRS) associated with frailty and the joint effect of PRS with leisure activities on frailty remains less studied, especially among adults aged ≥80 years.

The current study aims to explore the associations of leisure activities, PRS, and their joint effect with frailty among 7471 community-living older adults aged ≥80 years from the Chinese Longitudinal Healthy Longevity Survey (CLHLS).

Materials and Methods

Study Population

The CLHLS study was a prospective cohort study conducted in 23 of 31 provinces in China to investigate determinants of longevity [15,25,26] and 35,474 older adults were enrolled in 2002, 2005, 2008, 2011 and 2014 baseline waves. Exclusion criteria were as follows: participants aged ≤ 79 (n=9316), without follow-up measurements of frailty (n=15,905), with frailty at baseline (n=1986), with missing values of leisure activities (n=3) or with disability in activities of daily living (ADL) or functional limitations (unable to raise an arm straight upwards, put the hand behind neck or lower back, stand up from a chair or pick up a book from the floor; n=793), leaving 7471 adults aged ≥ 80 years (mean age: 89.4±6.6 years) in the final analysis (online suppl. Fig. 1). A proportion of the total, 2541 adults aged ≥80 years, had qualified single-nucleotide polymorphism (SNP) data and were included in the genetic analysis. Ethical approval was granted by the biomedical ethics committee of Peking University (IRB00001052-13074) and the ethics committee of the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention (No. 201922). Written informed consent was obtained from all participants or their proxy respondents.

Assessment of Leisure Activities

A leisure activity index was generated by face-to-face interviews including seven questions related to gardening, outdoor activities excluding exercise (e.g., Tai Chi, dancing, visiting neighbors or friends), keeping poultry or pets, reading, playing cards or Mahjong, watching TV or listening to the radio and attending organized social activities [27]. One point was assigned for each answer of “Almost every day” or “Not every day, but at least once per week”. Total scores ranged from 0 to 7. The index was treated in three ways: as a continuous variable; using a cut-off considered ‘enough leisure activities’ [participants with leisure activity index ≥ 2 (median value)] [28,29] and as a quartiles variable (defined according to

the quartiles of leisure activity index with score ≤ 1, score = 2, score = 3 and score ≥ 4). A binary variable (0 vs ≥1) was also constructed for each kind of leisure activity.

Assessment of Frailty

Frailty was assessed by a previously validated 39-item health-related scale for assessment of cognitive function, ADL, instrumental activities of daily living, functional limitations, prevalence of diseases, depression, hearing loss and visual function [30]. The frailty index (FI) was calculated according to a previous study (range: 0-1), computed by summing all deficits and then dividing by the total number of possible deficits (online suppl. Table 1) [30]. A higher FI indicated poorer health status and frailty was defined as FI ≥ 0.25 [6,31]. Follow-up time was calculated for each participant using the time from the baseline investigation to the incidence of frailty, loss of follow-up or the end time of the survey (September 1, 2018).

Construction of Polygenic Risk Score

Saliva and venous blood samples were collected during the CLHLS study for DNA extraction and SNP determination. 27,000 SNPs were genotyped in 2014 by the Beijing Genomics Institute using Illumina HumanOmniZhongHua-8 BeadChips [32]. CLHLS genetic data was evaluated for quality and completeness, achieving a full quality item score of 12 [33] and the suggested thresholds and procedures were used during the current study to assess the quality of samples and genetic variants [34]. Sporadic missing genotypes were imputed based on the 1000 Genomes Project Phase 3 data using IMPUTE (version 2.3.2) software to increase the power of the phenotype-genotype association. A genome-wide association study (GWAS) was performed to select frailty-related genetic variants and a linear regression method integrated into PLINK used to assess the associations of genetic variants and frailty. Overall, 59 SNPs were selected as candidate variables associated with the FI (p-values <.001) (online suppl. Table 2). These genetic variants were used to construct the PRS which was defined for an individual, i, as:

$$\mathrm{PRS}_i = \frac{\sum_{j=1,2,\ldots,J} \beta_j g_{ij}}{n}$$

where j is the index of the genetic variants; β_j are the beta coefficient associations from a linear regression analysis on the CLHLS data; g_{ij} is the number of FI-effect alleles in the i-th individual and n is the number of available SNPs in the i-th individual.

Covariates

Information on participant characteristics and lifestyles were acquired using face-to-face questionnaires. The covariates included age, sex, race, residence, living arrangement, education, marital status, income levels, smoking, drinking, exercise and dietary diversity evaluated by nine major food types [35]. Body mass index (BMI) was calculated using height and weight.

Statistical Analysis

Baseline continuous variables are presented as mean ± standard deviation (SD) and compared by one-way ANOVA. Categorical variables are presented as numbers of participants (percentage) and compared using χ^2 tests. The initial missing rates for all variables were less than 0.6%. Missing values were imputed using the mean and mode of variables from five multiple imputed datasets generated by the random forest method [36,37]. A two-step analysis was performed. In the first step (Analysis I; n=7471), data from adults aged ≥ 80 years with eligible information on leisure activities and frailty was used to explore the association of different measurements of leisure activities with frailty. In the second step (Analysis II; n=2541), the FI-associated PRS was constructed, the association of PRS with frailty assessed and potential interactions between levels of PRS (classified into high or low levels by median of 2.47×10^{-4}) and different measurements of leisure activities (using continuous, binary or quartiles definitions of leisure activity index) with frailty explored.

Cox proportional hazards models were established to explore the association of leisure activities with frailty during analyses I and II. Models were tested to satisfy the proportional hazards assumption with scaled Schoenfeld residuals (online suppl. Fig. 2, 3) [38]. Hazard ratio (HR) and 95% confidence interval (CI) were estimated in 4 different models: a raw model that was not adjusted for any covariate; model 1 adjusted for age, sex, race and residence; model 2 adjusted for education, living arrangements, marital status and income level; model 3 adjusted for drinking, smoking, dietary diversity and BMI.

During Analysis I, we also: (1) conducted restricted cubic spline with 3 knots to investigate the non-linear associations between leisure activity index and frailty in the fully adjusted model; (2) performed subgroup analyses by age, sex, race, residence, living arrangement, education level, marital status, smoking, drinking, exercise, dietary diversity, income level and BMI.

Genetic data extraction and quality control were performed using PLINK 1.9 [39]. All analyses were completed by R 4.0.1 for Windows (R Foundation for Statistical Computing, Vienna, Austria) using packages of “table1”, “survival”, “survminer”, “forestplot”, “randomForest”, “mice” and “ggplot2”. Significance was set at a two-tailed value of $p < .05$.

Results

Baseline Characteristics

A total of 35,474 adults enrolled in the CLHLS 2002, 2005, 2008, 2011 and 2014 baseline waves were recruited as potential candidates and 7471 adults aged ≥ 80 years (mean age: 89.4±6.6; range: 80–116) satisfied inclusion criteria (Table 1; online suppl. Fig. 1). 3310 (44.3%) were male. The median follow-up time was 5.5 (interquartile range [IQR]: 3.3–6.3) years. 2930 cases of frailty were recorded during 42,216 person-years of follow-up from 2002 to 2018 with an incidence density of 69.4/1000 person-years. Baseline characteristics are presented by frailty status with participants who were older, female, Han race, living with family, illiterate, married, low income, never-drinkers and never-smokers being more likely to be frail (Table 1).

Association between Leisure Activities and Frailty

Analysis I extensively explored the association between leisure activities and frailty. We revealed a linear relationship in which every 1-point increase in the leisure activity index was associated with 12% lower risk of frailty in the fully adjusted model (HR 0.88, 95% CI 0.85-0.91) (Fig.1), the non-linear relationship between leisure activity index and frailty was not observed (*p*-value for nonlinearity =.566) (Fig. 2). The findings were similar for binary and quartile forms of leisure activity index. Participants with 'enough leisure activities' (score ≥ 2) had a 20% lower risk of frailty in the binary analysis compared with those with a leisure activity index score ≤1. Similarly, participants with score = 2, 3 and ≥ 4 had 15%, 21% and 39% lower risks of frailty in quartile analyses, respectively (Fig. 1). These results remained consistent among models adjusted for different covariates (online suppl. Table 3).

Fully adjusted models for each of the seven leisure activities and frailty showed that the risk reduction was greatest for keeping poultry or pets (HR 0.73, 95% CI 0.66-0.80) and least for watching TV or listening to the radio (HR 0.83, 95% CI 0.77-0.90). However, associations of gardening, outdoor activities excluding exercise and reading with frailty were no longer statistically significant after adjustment for all covariates (Fig. 1). These results remained stable in models adjusted for different covariates (online suppl. Table 3).

Interactions were not observed between leisure activity index and different subgroups (all *p* for interactions > .05) (online suppl. Fig. 4).

Association between PRS and Frailty

Analysis II of 2541 adults aged ≥ 80 years validated the association between PRS and FI in a linear model and found that a 0.0001 unit increase in PRS corresponded to a 0.0040 increase in FI (95% CI: 0.0037-0.0042; $p<.001$) when adjusted for age and sex. Assessment of the PRS and frailty association in the fully adjusted Cox model showed that a 0.0001 unit increase in PRS was associated with 3% higher risk of frailty (HR 0.97, 95% CI 1.02-1.05). Participants with high level of genetic risk (PRS greater than median) suffered from 26% higher risk of frailty compared with those with a low level of genetic risk (HR 0.74, 95% CI 1.11-1.44) (Table 2).

Joint Association of Leisure Activities and PRS with Frailty

Analysis II revealed no significant interactions between leisure activity index and PRS in the fully adjusted models and this finding remained unchanged in analyses using binary or quartile measurements of leisure activities (all *p* for interactions>.05) (Fig. 3).

Discussion

The current large prospective cohort study of 7471 adults aged ≥ 80 years with a median follow-up time of 5.5 (IQR:3.3-6.3) years found that both leisure activities and PRS were independently associated with lower risk of frailty. However, interdependence of leisure activities and genetic risk was not observed. The findings suggest that the preventive effect of leisure activities on frailty might be constant for older adults with different genetic backgrounds.

Association between Leisure Activities and Frailty

The incidence of frailty among adults aged ≥ 80 years was 69.4/1000 person-years, 1.6 times higher than that found among adults aged 60 years or older [11]. The association between leisure activities and frailty has been understudied. Evidence from previous cross-sectional or cohort studies with limited follow-up times indicated that leisure activities like dancing, Tai Chi, visiting museums, theatre or cinema, playing golf, joining clubs, engaging in social groups and religious activities were associated with lower risk of frailty among adults aged 79 years or younger [13,17-19]. The current study systematically explored the association between different measurements of leisure activity and frailty and the impact of genetic risk in this association. The current findings are consistent with those of previous studies suggesting daily leisure activities may be beneficial for elderly people. For example, Tai Chi was reported to improve physical performance and hemodynamic outcomes in a 48-week randomized clinical trial among adults aged ≥ 70 years and may reduce the risk of future frailty [40]. Prolonged TV watching was found to be a risk factor for frailty and functional limitations in European older adults [41] but might prove beneficial to adults aged ≥ 80 years by reducing the risk of cognitive impairment [16,42]. Keeping pets [43,44] and playing cards or Mahjong were also protective factors against frailty [45]. In addition, leisure activities can facilitate the interaction of older adults with family or friends, and therefore prevent frailty by improving social connection, sense of belonging, and life satisfaction [46,47]. The preventive effects of these leisure activities have also been reported in our previous findings on ADL, cognitive impairment and mortality among adults aged ≥ 80 years [16,42,48].

Association between PRS and Frailty

Previous studies in participants aged ≥ 50 years have revealed frailty related genes associated with the immune response, cholesterol transport, apoptotic signaling, homocysteine metabolism, folate metabolism, phosphate and calcium homeostasis, stem cell maintenance, cell adhesion, growth, migration and differentiation [20-24]. The current PRS analysis found that the genetic variants associated with frailty in the ≥ 80s were involved in cancer, mental disorders and immune and inflammatory responses.

Several frailty-related SNPs were associated with diverse kinds of cancers. *CPO*-rs10179420 was reported to be associated with lung adenocarcinoma [49], *ZNRD1ASP*-rs6928966 with breast cancer [50] and *PRKAA1*-rs1002424 with gastric cancer [51]. Furthermore, some SNPs were related to many kinds of cancer. For example, *OSBPL10*-rs13317583 was associated with diffuse large B-cell lymphoma and bladder cancer [52,53], *PTPRT*-rs73271475 with colorectal cancer [54,55] and gastric cancer [56], *ABCC4*-rs4148497 with pancreatic cancer [57], breast cancer [58] and epithelial ovarian cancer [59].

SNPs affecting the mental health of older adults also contributed to the development of frailty. *PTPRT*-rs73271475 was associated with depression [60,61], rs55767117 (close to *HPHP3-AS1* | *TMEM108*) with neuropsychiatric disorders [62] and *ITIH3*-rs2535629 with many mental disorders, including depression, schizophrenia and autism spectrum disorder [63-66]. These SNPs were selected for the construction of frailty-associated PRS.

Nonetheless, a majority of frailty-related SNPs were associated with immune and inflammatory responses. *IRF1-AS1*-rs11745587, *ATF6B*-rs8283, *ABCC4*-rs4148497 and *SLC22A5*-rs2073643 were associated with asthma [67-71] and *ATF6B*-rs8283 and *MUCL3*-rs9501035 with risk of systemic lupus erythematosus (SLE) [72,73]. Rs9271640 (close to *HLA-DRB1* | *LOC124901301*), *LOC643339*-rs7302522 and *RPL37*-rs6876367 were associated with multiple sclerosis [74-77], *SLAMF8*-rs2501341, *CDC25B*-rs3761218 and rs17207986 (close to *ATF6B* | *TNXB*) with inflammatory bowel disease [78-80] and *IRF1-AS1*-rs11745587 and *ADORA2A*-rs2236624 with rheumatoid arthritis [81,82]. These SNPs could potentially play roles in immune dysfunction and inflammation, mediating the incidence of frailty.

Joint Association of Leisure Activities and PRS with Frailty

The joint association of leisure activities and genetic risk with frailty has not been previously investigated. No potential interactions between leisure activities and FI-associated PRS in adults aged ≥ 80 years were observed during the current analysis, suggesting that leisure activities are an intervention measure suitable for older adults with different genetic backgrounds to reduce risk of frailty. More research is required to investigate potential genes and gene-lifestyle interactions associated with frailty.

Strengths and Limitations

The strengths of this study include the national survey database with a large sample size of adults aged ≥ 80 years, the prospective cohort design with follow-up time up to 17 years, abundant covariates on personal characteristics and lifestyles and the inclusion of PRS construction. These advantages enabled us to evaluate the association of leisure activities and PRS with frailty in an extensive manner. However, there remain several limitations. First, although diverse measurements of leisure activities were considered to prove the robustness of our findings, the duration of these activities was not recorded which might cause bias in the exposure measurement. Second, the specific group of adults aged ≥ 80 years may limit the generalizability of our findings to younger populations. Third, the current frailty PRS requires validation in other racial groups to allow generalization.

Conclusion

Leisure activities and genetic risk were each independently associated with risk of frailty among Chinese adults aged ≥ 80 years in a long-term cohort study. Engagement in leisure activities provides a more feasible modifiable factor as an alternative to exercise to prevent frailty among adults aged ≥ 80 years, many of whom suffer limitations in daily activities and are less likely to finish regular exercise. The preventive effect of leisure activities on frailty did not differ by the level of genetic risks, suggesting that leisure activities constitute an appropriate intervention measure for all older adults, even for those with high genetic risk of frailty. Evidence is presented to support the primary prevention of frailty among the adults aged ≥ 80 years to promote healthy ageing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement

The survey data are available from the Peking University Open Research Data Platform (Website: https://opendata.pku.edu.cn/dataverse/CHADS) and the data manager (chads@nsd.pku.edu.cn) for researchers who meet the criteria for data access. Further enquiries can be directed to the corresponding authors.

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Leisure activities	Participants	Events	Crude HR[a]	Adjusted HR[b]
Per 1 unit increase in leisure acitvity index	7471	2930	0.82 (0.80,0.85)	0.88 (0.85,0.91)
Enough leisure activities				
No (Score≤1)	3186	1385	1	1
Yes(Score≥2)	4285	1545	0.68 (0.64,0.74)	0.80 (0.74,0.87)
Quartiles of leisure activity index				
Score≤1	3186	1385	1	1
Score=2	2170	826	0.77 (0.71,0.84)	0.85 (0.78,0.93)
Score=3	1395	501	0.66 (0.60,0.74)	0.79 (0.71,0.88)
Score≥4	720	218	0.50 (0.43,0.58)	0.61 (0.53,0.72)
P value for trend			<0.001	<0.001
Gardening				
Score=0	6650	2626	1	1
Score=1	821	304	0.81 (0.72,0.92)	0.92 (0.82,1.05)
Outdoor activities excluding exercise				
Score=0	2884	1177	1	1
Score=1	4587	1753	0.84 (0.78,0.91)	0.94 (0.87,1.01)
Raising poultry or pets				
Score=0	5753	2345	1	1
Score=1	1718	585	0.69 (0.63,0.76)	0.73 (0.66,0.80)
Reading				
Score=0	6465	2593	1	1
Score=1	1006	337	0.73 (0.65,0.82)	0.92 (0.81,1.06)
Playing cards or Mahjong				
Score=0	6627	2674	1	1
Score=1	844	256	0.66 (0.58,0.75)	0.75 (0.65,0.85)
Watching TV or listening to the radio				
Score=0	3141	1362	1	1
Score=1	4330	1568	0.72 (0.67,0.78)	0.83 (0.77,0.90)
Attending organised social activities				
Score=0	7107	2813	1	1
Score=1	364	117	0.66 (0.55,0.79)	0.74 (0.61,0.90)

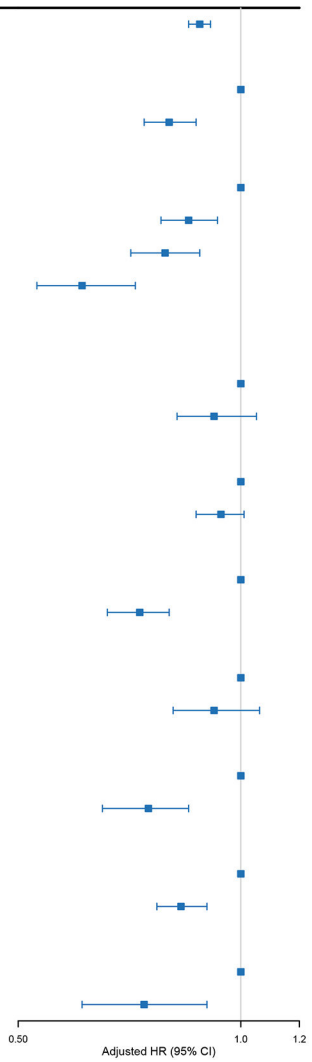

Fig. 1. Association between multiple measurements of leisure activities and frailty.

Abbreviations: HR, hazard ratio.

[a]Without adjustment for any covariate.

[b]Adjusted for age, sex, race, residence, education, living arrangement, marital status, income level, drinking, smoking, exercise, dietary diversity and body mass index.

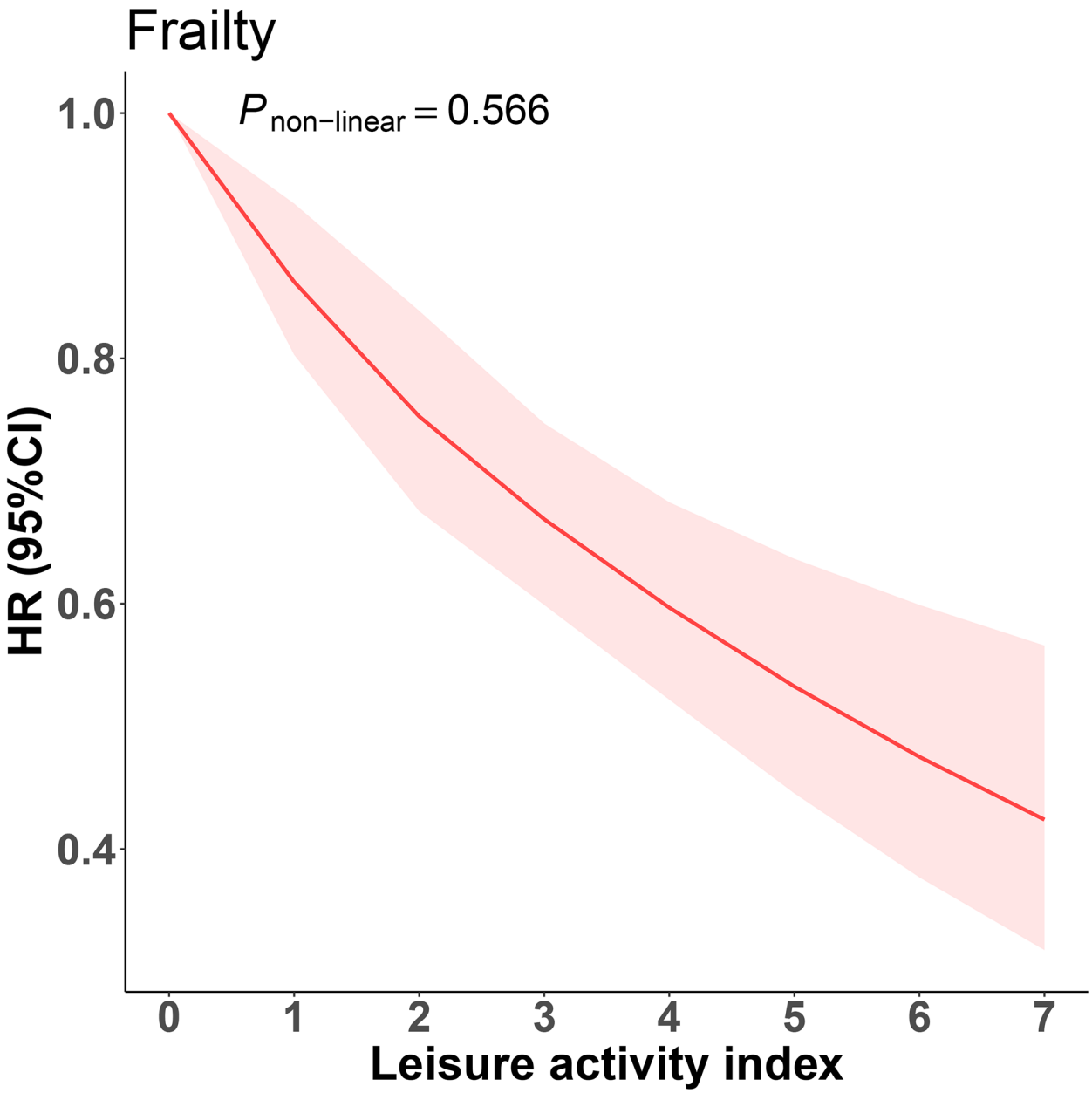

Fig. 2. The non-linear association between leisure activity index and frailty.

Abbreviations: HR, hazard ratio; CI, confidence interval.

The curve was plotted using Cox proportional hazards models with restricted cubic splines with 3 knots, adjusted for age, sex, race, residence, education, living arrangement, marital status, income level, drinking, smoking, exercise, dietary diversity and body mass index. Shading area indicates 95% CIs.

Groups	Participants	Events	Adjusted HR[a]	P−internaction
Leisure activity index				0.366
High genetic risk	1270	526	0.91 (0.84, 0.98)	
Low genetic risk	1271	450	0.92 (0.85, 1.00)	
Enough leisure activities				0.731
High genetic risk	1270	526	0.85 (0.70, 1.03)	
Low genetic risk	1271	450	0.92 (0.75, 1.14)	
Quartiles of leisure activity index				0.992
High genetic risk (Q2)	734	274	0.89 (0.71,1.10)	
High genetic risk (Q3)	529	207	0.87 (0.67,1.11)	
High genetic risk (Q4)	299	92	0.69 (0.49,0.97)	
Low genetic risk (Q2)	734	274	0.99 (0.78,1.25)	
Low genetic risk (Q3)	529	207	0.94 (0.73,1.22)	
Low genetic risk (Q4)	299	92	0.62 (0.42,0.91)	

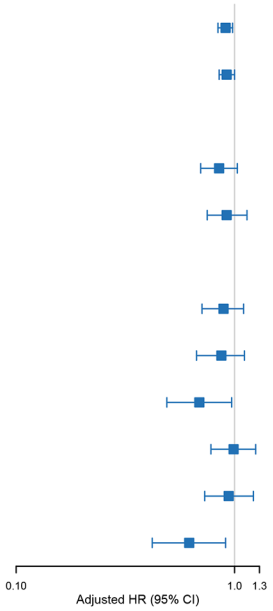

Fig. 3. The potential interactions between leisure activities, polygenic risk score and frailty.

Abbreviations: HR, hazard ratio; CI, confidence interval.

[a]adjusted for age, sex, race, residence, education, living arrangement, marital status, income level, drinking, smoking, exercise, dietary diversity and body mass index. The shading indicates 95% CIs.

Table 1.

Baseline participant characteristics by frailty

Characteristics	Participants, No. (%)			*P* value
	All	Non-frail (FI score<0.25)	Frail (FI score≥0.25)	
Sample size	7571 (100)	4541 (63.4)	2930 (36.6)	
Age, mean (SD), year	89.4 (6.6)	88.6 (6.4)	90.8 (6.8)	<.001
Sex				
Male	3310 (44.3)	2225 (49.0)	1085 (37.0)	<.001
Female	4161 (55.7)	2316 (51.0)	1845 (63.0)	
Race				
Han race	6930 (92.8)	4169 (91.8)	2761 (94.2)	<.001
Minority race	541 (7.2)	372 (8.2)	169 (5.8)	
Residence				
Urban	2869 (38.4)	1744 (38.4)	1125 (38.4)	1.000
Rural	4602 (61.6)	2797 (61.6)	1805 (61.6)	
Living arrangement				
With family	5798 (77.6)	3456 (76.1)	2342 (79.9)	<.001
Alone or in nursing home	1673 (22.4)	1085 (23.9)	588 (20.1)	
Education				
Illiteracy	4971 (66.5)	2878 (63.4)	2093 (71.4)	<.001
Literacy	2500 (33.5)	1663 (36.6)	837 (28.6)	
Marital status				
In marriage	5626 (75.3)	3357 (73.9)	2269 (77.4)	<.001
unmarried, divorced or widowed	1845 (24.7)	1184 (26.1)	661 (22.6)	
Income level				
High	1277 (17.1)	760 (16.7)	517 (17.6)	.034
Medium	4986 (66.7)	3080 (67.8)	1906 (65.1)	
Low	1208 (16.2)	701 (15.4)	507 (17.3)	
Drinking				
Never-drinkers	5113 (68.4)	3030 (66.7)	2083 (71.1)	<.001
Current-drinkers	1603 (21.5)	1037 (22.8)	566 (19.3)	
Former-drinkers	755 (10.1)	474 (10.4)	281 (9.6)	
Smoking				
Never-smokers	5129 (68.7)	3019 (66.5)	2110 (72.0)	<.001
Current-smokers	1302 (17.4)	844 (18.6)	458 (15.6)	
Former-smokers	1040 (13.9)	678 (14.9)	362 (12.4)	
Exercise				
Never-exercisers	4465 (59.8)	2689 (59.2)	1776 (60.6)	
Current-exercisers	2494 (33.4)	1550 (34.1)	944 (32.2)	.199
Former-exercisers	512 (6.9)	302 (6.7)	210 (7.2)	
Dietary diversity				
Poor	3105 (41.6)	1887 (41.6)	1218 (41.6)	1.000

Characteristics	Participants, No. (%)			*P* value
	All	Non-frail (FI score<0.25)	Frail (FI score≥0.25)	
Good	4366 (58.4)	2654 (58.4)	1712 (58.4)	
BMI				
Underweight	3192 (42.7)	1946 (42.9)	1246 (42.5)	
Normal	3575 (47.9)	2173 (47.9)	1402 (47.8)	.881
Overweight or obesity	704 (9.4)	422 (9.3)	282 (9.6)	

Abbreviations: BMI, body mass index; FI, frailty index; SD, standard deviation.

Table 2.

Hazard ratio (95% confidence interval) for the association between polygenic risk score and frailty

Polygenic risk score	Raw model[a]	Model 1[b]	Model 2[c]	Model 3[d]
Per 0.0001 unit	1.04 (1.02,1.05)	1.03 (1.02,1.05)	1.03 (1.02,1.05)	1.03 (1.02,1.05)
Binary group				
Low	Reference	Reference	Reference	Reference
High	1.31 (1.15,1.48)	1.28 (1.12,1.45)	1.27 (1.12,1.45)	1.26 (1.11,1.44)

[a]Without adjustment for any covariate.

[b]Adjusted for age, sex, race and residence.

[c]Adjusted for age, sex, race and residence, education, living arrangement, marital status and income level.

[d]Adjusted for age, sex, race and residence, education, living arrangement, marital status and income level, drinking, smoking, diet diversity and body mass index.