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Physical frailty and health-related quality of life among Chinese rural older adults: A moderated mediation analysis of physical disability and physical activity

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Abstract

Objectives: The purpose of this study is to explore the mediating effect of physical disability, as well as the role of physical activity (PA) as a moderator in the relationship between physical frailty and health-related quality of life（HRQoL) among rural older adults in China.

Design: Cross-sectional analysis.

Setting: Rural households in Shandong of China (Rushan, Qufu, Laolin).

Participants and methods: A survey was conducted among 3,243 rural older adults. The data were collected using questionnaires measuring physical frailty, physical disability, HRQoL and PA. Bootstrap analyses were employed to explore the mediating effect of physical disability on physical frailty and HRQoL, and the moderating role of PA.

Results: After controlling for age and education, physical disability partially mediated the effect of physical frailty on HRQoL [indirect effect = -0.143, 95% confidence intervals (CI) = -0.175, -0.113], with the mediating effect accounting for 33.71% of the total effect. PA moderated the relationship between physical frailty and physical disability, as well as the relationship between physical disability and HRQoL.

Conclusions: PA can moderate the indirect effect of physical disability on the association between physical frailty and HRQoL. This study helps to understand the mechanism underlying the association between physical frailty and HRQoL. Encouraging the rural older adults to increase PA appropriately might improve the HRQoL for the older adults with physical frailty and physical disability problems.

Key words: HRQoL; Physical activity; Physical frailty; Physical disability; Rural older adults; Moderated mediation analysis

Strengths and limitations of this study

1. Few studies have assessed the moderating and mediating factors of the relationship between physical frailty and HRQoL in rural older adults specifically.
2. Our study will help to elucidate the underlying mechanism of the relationship between physical frailty and HRQoL and form an effective way to improve the HRQoL of the older adults in rural areas.
3. The latest EQ-5D -5L health utility scores method refers to Chinese integral conversion table, which is more suitable for the measurement of the Chinese population.
4. The data we used cannot predict the causal relationship.
5. More potential mechanisms related to physical frailty and HRQoL among the older adults need to be explored in the future.

1.Introduction

Population aging has become a global social problem. As one of the world's most aging countries, China had 249 million people aged over 60 years in 2018, accounting for 17.9 percent of the total population[1]. It is predicted that by 2050, the older adults over 60 will account for more than 35.1% of the total population[2]. With the increasing aging population and the extension of life expectancy, improving the health-related quality of life (HRQoL) of the older adults is an important public health issue. HRQoL is a predictive factor of mortality in the older adults[3]. Compared with urban older adults, the HRQoL of rural older adults is worse[4 5], which needs more attention.

Physical frailty is a medical syndrome caused by a variety of etiologies and causes, which is characterized by a decline in physical strength, endurance, and decreased physiological function[6]. With the increase of age, the risk of physical frailty increases[7]. Frailty may lead to negative health consequences, including fall, reduced activity, reduced independence, frequent hospitalization, and disability[8]. These adverse outcomes resulted in a decline in the quality of life of the older adults. Previous cross-sectional and longitudinal studies have shown that frailty was negatively associated with HRQoL[9 10]. In addition, the HRQoL in older adults with frailty is poorer than the non-frailty older adults[11]. Although the association between physical frailty and quality of life has been confirmed, the underlying mechanism remains unclear.

The prevalence of physical disability is high among the frail older adults [12 13]. Some studies showed physical frailty was closely related to disability[14 15], and might be the precursor and cause of disability[16]. A national longitudinal study of 7,439 people over age 65 in US showed that

frailty was a strong predictor of disability[17]. A prospective two-year cohort study in Japan also showed that frailty and prophase of frailty increased the risk of disability[18]. These findings suggest that physical frailty is associated with disability in older adults. Studies have also demonstrated that the quality of life worsened as the degree of disability increased, and the more severe the disability, the worse the quality of life[19]. Compared with non-disabled older adults, disabled older adults are more prone to fall, depression, anxiety, etc., and their HRQoL was significantly reduced. Therefore, frailty may have an indirect effect on individual's HRQoL through the mediating effect of physical disability.

Physical frailty is considered to be reversible and preventable[20]. Physical activity(PA) is a key factor of reverse and prevent frailty in the older adults[21]. Studies have found that physical activity moderated the relationship between chronic illness and functional limitations, and moderated functional disability and body function[22 23]. PA can alleviate the decline of physical function in the older adults and has a beneficial effect on functional limitations, physical frailty, disability and quality of life in the older adults[24-26]. Studies indicated the positive effect of physical activity on reducing adverse events caused by frailty in older people. Performing a physical activity of moderate to vigorous intensity would improve physical frailty and prevent the occurrence of disability when compared to the performance of a physical activity of low intensity, ultimately promote older adults' quality of life[27-29]. Therefore, we speculate that PA may moderate the relationship between frailty and physical disability, and between physical disability and HRQoL.

In the present study, we aim to explore the relationship between physical frailty and

HRQoL, focusing on the mediating role of physical disability and the moderating role of PA in the relationship between physical frailty and HRQoL. The conceptual framework of the moderated mediation model was shown in Fig. 1.

2. Methods

2.1.1 Design and sample

This study was conducted from May to June, 2019 in Shandong province, China. A multistage stratified cluster sampling method was used to select participants, which was described in detail in a paper we have previously published[30]. Three rural counties (Qufu, Laoling and Rushan) were selected according to the GDP per capita (2018) in Shandong. Within each selected county, five townships were randomly selected. Then, four villages were selected from each selected townships and the elderly aged over 60 years old who were randomly selected from sample villages. All participants completed the questionnaire independently. The survey was completed in about an hour, and the investigators checked the questionnaires when the participants returned them. A total of 3,600 respondents were recruited from 60 villages and 15 townships in 3 rural counties in Shandong province, of whom 3,243 completed the entire survey, with a response rate of 90.05%.

2.2. Variables and measurement

2.2.1 Independent variable

Physical frailty was measured by Frailty Phenotype[31]. The scale is a widely used frailty screening scale with good reliability and validity[32 33]. Frailty was defined based on the following five

aspects: weight loss, exhaustion, low physical activity level, slowness, weakness. ①Weight loss: In the past 1 year, participants' body mass index (BMI) decreased by >5.0% (except for personal deliberate weight loss). ②Exhaustion: Using the Center for Epidemiological Studies-Depression(CES-D)[34] : "How often in the last week did you feel this way?" (1) I could not get going and (2) I felt everything I did was an effort. Either of the above two questions that participants answered 3-4 days and most of the time, was considered exhaustion.③Low physical activity level: According the International Physical Activity Questionnaire-short Form (IPAQ-SF)[35 36] , we used standard algorithms to calculate the Kcals consumed per week. The criterion is adjusted according to gender. Male: < 383 Kcals/ week is a decrease in physical activity, while female: < 270 Kcals/ week is a decrease in physical activity. ④Slowness: Slowness was assessed via walking speed at 15 ft measured for 3 times, and we record the minimum value. The criterion is adjusted according to gender and height. Men: height≤173 cm and time≥7 seconds; height > 173 cm and time ≥ 6 seconds. Women: height≤159 cm and time≥7 seconds ;height >159 cm and time ≥ 6 seconds. ⑤Weakness: Weakness was assessed by grip strength using a handgrip dynamometer was measured for 3 times, and we record the maximum value, adjusted for gender and BMI. Men: BMI ≤ 24 and grip strength ≤ 29;BMI 24.1-26 and grip strength ≤ 30;BMI 26.1-28 and grip strength ≤ 30;BMI > 28 and grip strength ≤ 32.Women:BMI ≤ 23 and grip strength ≤ 17;BMI 23.1-26 and grip strength ≤ 17.3;BMI 26.1-29 and grip strength ≤ 18;BMI > 29 and grip strength ≤ 21.

2.2.2 Dependent variables

HRQoL was measured by the health utility value of EQ-5D-5L[37]. The EQ-5D-5L consists of the

EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L descriptive system has five elements (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and each element includes five level (no problems, some problems, moderate problems, severe problems and extreme problems). The latest EQ-5D -5L health utility scores method refers to Chinese integral conversion table[37]. The range of utility value is [-0.391, 1.000]. A higher score indicates better health condition of the respondents. The Cronbach's coefficient was 0.761 in this study.

2.2.3 Mediator

Physical disability was evaluated by the Activity of Daily Living Scale (ADLS), which was developed by Lawton and Brody in 1969 to measure the disability of the older adults[38 39]. The Scale consists of 14 items, including Physical Self-Maintenance Scale (PSMS) and Instrumental Activities of Daily Living (IADL). The total score is 14-56, with higher scores indicating increased physical disability. A score of 14 and lower indicates completely normal physical ability, a score between 15 and 22 is defined as mild disability, and a score of 23 and higher is defined as severe disability. ADLS is recommended by WHO and has been widely used in older adults in China, with good reliability and validity[40]. Cronbach's alpha was 0.764 in this study.

2.2.4 Moderator

PA was assessed using the IPAQ-SF[35 36]. The questionnaire contains 7 questions, 6 of which were about physical activity. The IPAQ-SF investigates the PA of the individuals in the last 7 days. The questionnaire involved three types of intensity activities, including vigorous physical activity (VPA =8.0 metabolic equivalent [METs]),

moderate physical activity (MPA =4.0 METs), and low physical activity (LPA =3.3 METs). PA of each person engaged in a certain intensity per week is the METs value corresponding to that physical activity × weekly frequency × daily time, and the sum of three PA is the total PA (met-h /week). The greater the overall physical activity value, the higher the physical activity.

2.3 Data analysis

To analyze the data, categorical variables were expressed using frequency and percentages (%) and continuous data were described using mean (standard deviation). Pearson correlation coefficient was used to analyze the correlation among physical frailty, physical disability, and HRQoL. All these analyses were performed using IBM SPSS 24.0 (IBM Corp., Armonk, NY, USA). All regression coefficients were tested by the bias-corrected percentile Bootstrap method. The theoretical model was tested by estimating the 95% confidence interval (CI) for mediation and moderating effects with 5000 sampled with repetition. If the 95% CI did not include 0, it meant that the statistics was significant. The mediation model and moderated mediation model were tested with the PROCESS V3.3 macro for SPSS[41]. In the current study, we selected Model 4 and Model 58 to analyze the mediating effect and moderated mediation model. In addition, through t test and ANOVA analysis, we found that HRQoL is related to age and education. Previous studies have also found HRQoL was associated with age and education[42 43]. We controlled age and education in this study. Sampling weights were used in all of the analyses to adjust for the survey design.

2.4 Patient and public involvement statement

This research was done without patient involvement. No patients were involved in developing

the hypothesis and plans for design of this study either. The results would not be disseminated to study participants or any other individuals or communities.

2.5 Ethical considerations

The study was approved by the Ethics Committee of School of Public Health in Shandong University, P. R. China. The participants have been informed of the purpose and procedures of the study before the investigation. Before the study began, participants had signed written informed consent indicating that they were fully aware of the study procedures.

3. Results

3.1 Common method biases

We used Harman single factor test to conduct a common method biases test[44]. The results show that there are 12 factors with eigenvalues greater than 1, and the variance explained by the first factor is 17.92%, which is less than 40% of the critical standard, indicating that there are no serious common method biases in this study.

3.2 Socio-demographic characteristics of the participants

There were 3,243 participants, comprising 2,060 (63.5%) women and 1,182 (36.5%) men. The average age was 69.88 (SD=6.10) years, ranging from 60 to 97 years. Of the participants, 25.5% were single. About 72.4% had chronic disease. The majority (81.9%) were empty nest elderly.

3.3 Bivariate correlations of main variables

The mean, standard deviation and correlation coefficient of each variable were shown in Table 1. Physical frailty was positively correlated with physical disability ($r = 0.330$, $P < 0.01$), physical

frailty was negatively correlated with HRQoL (r = -0.426, P < 0.01) and PA (r = -0.299, P<0.01). Physical disability was negatively correlated with HRQoL (r = -0.557, P < 0.01) and PA (r = -0.184, P < 0.01). PA was positively correlated with HRQoL (r = 0.196, p < 0.01).

3.4 Mediation effect analysis

Model 4 in the SPSS macro compiled by Hayes 2013[41] was used to test the mediating effect of physical disability in the relationship between physical frailty and HRQoL under the control variable of age, education. As shown in Table 2 and Table 3, physical frailty had a significant predictive effect on quality of life (β = -0.423, t = -26.031, P < 0.001), and the direct predictive effect of frailty on quality of life was still significant when the mediating variable physical disability was added. Meanwhile, physical frailty had a significant positive predictive effect on physical disability (β = 0.295, t = 17.729, P < 0.001). Physical disability also has a significant negative predictive effect on HRQoL (β = -0.482, t = -32.407, P < 0.001). In addition, the upper and lower limits of the Bootstrap 95% CI for the direct effect of physical frailty on HRQoL and the mediating effect of physical disability on physical frailty and HRQoL did not include 0(Table 3), indicating that the mediating effect was significant. The mediating effect value was-0.143 and the 95% CI was [-0.175, -0.113], which accounted for 33.71% of the total effect. This shows that disability plays a partial mediating role in the relationship between physical frailty and HRQoL.

3.5 Moderated mediation effect analysis

PROCESS macro method (Model 58) compiled by Hayes (2013)[41] was used to test the moderated mediation model while controlling for age and education(Table 4 and Table 5).After PA was put into the model, the interaction term between physical frailty and PA significantly

predicted physical disability (β = -0.121, t = -7.058, P < 0.001) (Table 4, Model 1), and the interaction term between physical disability and PA also had a significant predictive effect on HRQoL (β = 0.116, t = 6.119, P < 0.001) (Table 4, Model 2). These results suggest PA played a moderating role in the relationships between physical frailty and physical disability and between physical disability and HRQoL.

Simple slope analyses indicated that the significant interaction at 1 SD below the mean and 1 SD above the mean of physical activity (See Fig. 2 and Fig. 3).Physical frailty had a significant predictive effect on the disability of individuals with high-level or low-level PA, but the predictive effect of physical frailty on physical disability was stronger for individuals with low-level PA (b_{simple} = 0.370, t = 16.979, P < 0.001) than for individuals with high-level PA, as shown in Fig. 2 (b_{simple} = 0.120, t = 4.322, P < 0.001).Fig. 3 showed that for high levels of PA individuals, the effect of physical disability and physical HRQoL was significant (b_{simple} = -0.301, t = -9.159, P < 0.001). However, for low-level of PA individuals, the effect of physical disability and HRQoL was still significant but considerably stronger (b_{simple} = -0.546, t = -29.701, P < 0.001). In addition, as the level of physical activity increased, the mediating effect of physical disability on the relationship between physical frailty and HRQoL declined(Table 5).

4.Discussion

In this study, a moderated mediation model was established with the mediation role of physical disability on the relationship between physical frailty and HRQoL, as well as the role of PA as a moderator in this indirect path between physical frailty and HRQoL. These findings elucidate the potential causes of physical frailty on HRQoL and facilitate the development of targeted

interventions for individuals so as to improve HRQoL in rural older adults.

Consistent with previous studies[45 46], we find that physical frailty negatively affect HRQoL of the older adults. This suggests that as the degree of physical frailty increases, the quality of life in the older adults becomes worse. Although many studies have established a direct relationship between frailty and HRQoL, few have explored the underlying mechanisms of this relationship. Our study demonstrates that the physical disability mediates the physical frailty and HRQoL, with the mediating rate of 33.71%. A study also suggested that physical disability was one of the potential factors underlying the association between frailty and HRQoL, which was similar with our study[47].

The current study indicates that physical frailty is associated with disability, which is consistent with a study by Kojuma G[48]. Frail older adults are very vulnerable to adverse health effects. A study indicated the risk of disability in the frail older adults was 12- to 13-fold increased than that in the non-frail older adults[49]. Meanwhile, this study also demonstrates that the negative predictive effect of disability on individual HRQoL, which was consistent with previous studies[50 51]. The possible explanation is that disabled older adults' poor self-care ability deteriorates their health, such as their normal physiological activities are restricted, physiological function is declined, social interaction is reduced, and ultimately affect the HRQoL. One study found that disability was the most important health problem for the older adults, which seriously affected their quality of life in old adults' later years[52]. The disability was the most important factor that contributed to decreasing quality of life in the older adults. Physical disability has been shown to be associated with increased chronic diseases, and premature mortality[53 54], all of

which could adversely affect the quality of life of older adults[55]. Therefore, physical frailty may reduce HRQoL of rural older adults by increasing their disability.

In the present study, we also find that PA plays a moderating role in the indirect effect between physical frailty and HRQoL. A larger indirect effect is observed among rural older adults with low-level of PA than among those with average or high-level of PA. Specifically, PA moderates the relationship between physical frailty and physical disability, and between physical disability and HRQoL. For older adults with low-level PA, the impact of physical frailty on physical disability is stronger than older adults with high-level PA. This finding indicates that PA moderates the relation between physical frailty and physical disability. We speculate that the older adults with low-level PA may have a decline in their physiological system reserves, leading to a deterioration of their functional status and ultimately increasing the possibility of physical frailty and disability[56]. A systematic review showed that older adults without exercise habits were at greater risk of developing frailty. Taichi, resistance sports and other physical activities could effectively improve the health of the older adults, reduce the symptoms of physical weakness, and prevent the occurrence of physical disability[57]. Compared with the older adults with high-level PA, the older adults with low-level PA are more vulnerable to the negative effects of physical frailty. As a result, physical frailty may cause more interference in older adults with low-level PA and increase the risk of physical disability.

We also find that physical disability has a significant impact on quality of life at both high and low-level of PA. Compared with older adults with high levels of PA, physical disability is more likely to adversely affect HRQoL of older adults with low-level PA. A study showed that

low-level PA was a major contributing factor for older adults disability[58]. As the level of disability increases, the individuals with low-level of PA experience a more serious functional decline and become more worried about the health status, thus further negatively affect the HRQoL[59]. In addition, physical disability has a greater effect on individuals with low-level PA than high-level PA, which indicates that PA plays a moderating role between physical disability and HRQoL. One study found that PA could improve the physical function and daily life activities of disabled older adults, and ultimately improved the life of older adults quality[60]. Therefore, a low-level of PA might be associated with poor quality of life in rural older adults with high disability.

Based on our findings, we recommended that community health managers should enhance screening and assessment of frailty in rural older adults. The older adults who are frail or pre-frail should be intervened in time, and the older adults who are disabled should be given special attention. Targeted and individualized intervention programs should be designed according to the different characteristics of the stages of frailty and disability. Besides, rural communities should establish some public facilities or organize some public activities to encourage the older adults to participate in sports activities.

There are several limitations in this study. First, our study was based on a cross-sectional study, which could not provide strong evidence of causation. Future research could adopt a longitudinal design or experiments to explore the causal relationship between physical frailty and HRQoL. Secondly, the data in this study come from the participants' self-report information, which might result in recall bias. Thirdly, physical disability has a partly mediating effect on the

relationship between physical frailty and HRQoL, which indicates that there are other mediating variables in this relationship. More potential mechanisms related to physical frailty and HRQoL among the older adults need to be explored in the future.

Conclusion

This study shows that physical frailty is related to HRQoL, and physical disability mediates the relationship between physical frailty and HRQoL, and PA moderates the mediating relationship. A greater effect is observed among rural older adults with low-level of PA than that among those with high-level of PA. This will help to elucidate the underlying mechanism of the relationship between physical frailty and HRQoL and form an effective way to improve the HRQoL of the older adults in rural areas.

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Contributors

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

None declared.

Patient consent for publication

Not required.

REFERENCES

1. NBSC. Statistical communiqué of the People's Republic of China on the 2017 national economic and social development. 2017 [updated February 28,2018. Available from: http://www.stats.gov.cn/english/PressRelease/201802/t20180228_1585666.html.
2. United Nations DESA, Population Division. World Population Ageing 2017:Highlights 2017 [updated 2017. Available from:https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf.
3. Brown DS, Thompson WW, Zack MM, et al. Associations Between Health-Related Quality of Life and Mortality in Older Adults. *Prevention Science* 2015;16(1):21-30. doi: 10.1007/s11121-013-0437-z
4. Zhou B, Chen K, Wang J, et al. Quality of Life and Related Factors in the Older Rural and Urban Chinese Populations in Zhejiang Province. *J Appl Gerontol* 2011;30(2):199-225. doi: 10.1177/0733464810361346
5. Zhou Z, Zhou Z, Gao J, et al. Urban-rural difference in the associations between living arrangements and the health-related quality of life (HRQOL) of the elderly in China-Evidence from Shaanxi province. *PLoS One* 2018;13(9):e0204118. doi: 10.1371/journal.pone.0204118 [published Online First: 2018/09/21]

6. Morley JE, Vellas B, Van Kan GA, et al. Frailty Consensus: A Call to Action. *J Am Med Dir Assoc* 2013;14(6):392-97. doi: 10.1016/j.jamda.2013.03.022
7. Collard RM, Boter H, Schoevers RA, et al. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc* 2012;60(8):1487-92. doi: 10.1111/j.1532-5415.2012.04054.x [published Online First: 2012/08/14]
8. Vermeiren S, Vellaazzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *J Am Med Dir Assoc* 2016;17(12) doi: 10.1016/j.jamda.2016.09.010
9. Fried LP, Ferrucci L, Darer JD, et al. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care. *J Gerontol A Biol Sci Med Sci* 2004;59(3):255-63. doi: 10.1093/gerona/59.3.M255
10. Lee IC, Chiu YH, Lee CY. Exploration of the importance of geriatric frailty on health-related quality of life. *Psychogeriatrics* 2016;16(6):368-75. doi: 10.1111/psyg.12179 [published Online First: 2016/01/13]
11. Kanauchi M, Kubo A, Kanauchi K, et al. Frailty, health-related quality of life and mental well-being in older adults with cardiometabolic risk factors. *Int J Clin Pract* 2008;62(9):1447-51. doi: 10.1111/j.1742-1241.2008.01830.x [published Online First: 2008/07/23]
12. Fullerthomson E, Yu B, Nurujeter A, et al. Basic ADL Disability and Functional Limitation Rates Among Older Americans From 2000–2005: The End of the Decline? *J Gerontol A Biol Sci Med Sci* 2009;64(12):1333-36. doi: 10.1093/gerona/glp130
13. Picavet HSJ, Hoeymans N. Physical disability in The Netherlands: Prevalence, risk groups and time trends. *Public Health* 2002;116(4):231-37. doi: 10.1038/sj.ph.1900864
14. Evenhuis HM, Hermans H, Hilgenkamp TIM, et al. Frailty and Disability in Older Adults with Intellectual Disabilities: Results from the Healthy Ageing and Intellectual Disability Study. *J Am Geriatr Soc* 2012;60(5):934-38. doi: 10.1111/j.1532-5415.2012.03925.x
15. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised older people. *Age Ageing* 2014;43(4):477-84. doi: 10.1093/ageing/aft181
16. Papachristou E, Wannamethee SG, Lennon LT, et al. Ability of Self-Reported Frailty Components to Predict Incident Disability, Falls, and All-Cause Mortality: Results From a Population-Based Study of Older British Men. *J Am Med Dir Assoc* 2017;18(2):152-57. doi: 10.1016/j.jamda.2016.08.020 [published Online First: 2016/10/16]
17. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133 [published Online First: 2015/08/25]
18. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older adults: a prospective cohort study. *BMJ open* 2015;5(9):e008462. doi: 10.1136/bmjopen-2015-008462 [published Online First: 2015/09/05]
19. Medhi GK, Sarma J, Pala S, et al. Association between health related quality of life (HRQOL) and activity of daily living (ADL) among elderly in an urban setting of Assam, India. *J Family Med Prim Care* 2019;8(5):1760-64. doi: 10.4103/jfmpc.jfmpc_270_19 [published Online First: 2019/06/15]
20. Tavassoli N, Guyonnet S, Abellan Van Kan G, et al. Description of 1,108 older patients referred by their physician to the "Geriatric Frailty Clinic (G.F.C) for Assessment of Frailty and Prevention of Disability" at the

gerontopole. *J Nutr Health Aging* 2014;18(5):457-64. doi: 10.1007/s12603-014-0462-z [published Online First: 2014/06/03]

21. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, et al. Exercise training as a drug to treat age associated frailty. *Free Radic Biol Med* 2016;98:159-64. doi: 10.1016/j.freeradbiomed.2016.03.024 [published Online First: 2016/03/30]
22. Rector JL, Marceau K, Friedman EM. Moderation of the Association Between Chronic Medical Conditions and Functional Limitations Over Time by Physical Activity: Effects of Age. *J Gerontol A Biol Sci Med Sci* 2020;75(1):168-74. doi: 10.1093/gerona/glz020 [published Online First: 2019/02/21]
23. Palmer RF, Espino DV, Dergance JM, et al. The role of physical activity and diabetes status as a moderator: functional disability among older Mexican Americans. *Age Ageing* 2012;41(6):752-8. doi: 10.1093/ageing/afs106 [published Online First: 2012/10/12]
24. Keysor JJ. Does late-life physical activity or exercise prevent or minimize disablement? A critical review of the scientific evidence. *Am J Prev Med* 2003;25(3 Suppl 2):129-36. doi: 10.1016/s0749-3797(03)00176-4 [published Online First: 2003/10/14]
25. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? *J Gerontol A Biol Sci Med Sci* 2001;56(7):M412-23. doi: 10.1093/gerona/56.7.m412 [published Online First: 2001/07/11]
26. Rejeski WJ, Mihalko SL. Physical Activity and Quality of Life in Older Adults. *J Gerontol A Biol Sci Med Sci* 2001;56(suppl_2):23-35. doi: 10.1093/gerona/56.suppl_2.23
27. Casas-Herrero A, Izquierdo M. Physical exercise as an efficient intervention in frail elderly persons. *An Sist Sanit Navar* 2012;35(1):69-85. doi: 10.4321/s1137-66272012000100007 [published Online First: 2012/05/04]
28. Mañas A, Del Pozo-Cruz B, Guadalupe-Grau A, et al. Reallocating Accelerometer-Assessed Sedentary Time to Light or Moderate- to Vigorous-Intensity Physical Activity Reduces Frailty Levels in Older Adults: An Isotemporal Substitution Approach in the TSHA Study. *J Am Med Dir Assoc* 2018;19(2):185.e1-85.e6. doi: 10.1016/j.jamda.2017.11.003 [published Online First: 2017/12/23]
29. Barnett A, Smith B, Lord SR, et al. Community-based group exercise improves balance and reduces falls in at-risk older people: a randomised controlled trial. *Age Ageing* 2003;32(4):407-14. doi: 10.1093/ageing/32.4.407 [published Online First: 2003/07/10]
30. Jing Z, Li J, Wang Y, et al. The mediating effect of psychological distress on cognitive function and physical frailty among the elderly: Evidence from rural Shandong, China. *J Affect Disord* 2020;268:88-94. doi: 10.1016/j.jad.2020.03.012 [published Online First: 2020/03/12]
31. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]
32. Buta BJ, Walston JD, Godino JG, et al. Frailty assessment instruments: Systematic characterization of the uses and contexts of highly-cited instruments. *Ageing Res Rev* 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003 [published Online First: 2015/12/18]
33. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC Geriatr* 2013;13:64. doi: 10.1186/1471-2318-13-64 [published Online First: 2013/06/22]
34. Radloff LS. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. *Appl Psychol Meas* 1977;1(3):385-401. doi: 10.1177/014662167700100306

35. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical Activity Questionnaire. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 2014;35(8):961-4. [published Online First: 2014/11/08]
36. Macfarlane DJ, Lee CC, Ho EY, et al. Reliability and validity of the Chinese version of IPAQ (short, last 7 days). *J Sci Med Sport* 2007;10(1):45-51. doi: 10.1016/j.jsams.2006.05.003 [published Online First: 2006/06/30]
37. Luo N, Liu G, Li M, et al. Estimating an EQ-5D-5L Value Set for China. *Value Health* 2017;20(4):662-69. doi: 10.1016/j.jval.2016.11.016 [published Online First: 2017/04/15]
38. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist* 1969;9(3):179-86. doi: 10.1093/geront/9.3_Part_1.179 [published Online First: 1969/01/01]
39. Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc* 1971;19(6):465-81. doi: 10.1111/j.1532-5415.1971.tb01206.x [published Online First: 1971/06/01]
40. Chen P, Yu ES, Zhang M, et al. ADL dependence and medical conditions in Chinese older persons: a population-based survey in Shanghai, China. *J Am Geriatr Soc* 1995;43(4):378-83. doi: 10.1111/j.1532-5415.1995.tb05811.x [published Online First: 1995/04/01]
41. Bolin JH. Hayes, Andrew F. (2013). Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. New York, NY: The Guilford Press. *J Educ Meas* 2014;51(3):335-37. doi: 10.1111/jedm.12050
42. Bao XY, Xie YX, Zhang XX, et al. The association between multimorbidity and health-related quality of life: a cross-sectional survey among community middle-aged and elderly residents in southern China. *Health Qual Life Outcomes* 2019;17(1):107. doi: 10.1186/s12955-019-1175-0 [published Online First: 2019/06/27]
43. Chapman B, Duberstein P, Lyness JM. Personality traits, education, and health-related quality of life among older adult primary care patients. *J Gerontol B Psychol Sci Soc Sci* 2007;62(6):P343-52. doi: 10.1093/geronb/62.6.p343 [published Online First: 2007/12/15]
44. Podsakoff PM, MacKenzie SB, Lee JY, et al. Common method biases in behavioral research: a critical review of the literature and recommended remedies. *J Appl Psychol* 2003;88(5):879-903. doi: 10.1037/0021-9010.88.5.879 [published Online First: 2003/10/01]
45. Kanwar A, Singh M, Lennon R, et al. Frailty and health-related quality of life among residents of long-term care facilities. *J Aging Health* 2013;25(5):792-802. doi: 10.1177/0898264313493003 [published Online First: 2013/06/27]
46. Mulasso A, Roppolo M, Rabaglietti E. The role of individual characteristics and physical frailty on health related quality of life (HRQOL): a cross sectional study of Italian community-dwelling older adults. *Arch Gerontol Geriatr* 2014;59(3):542-8. doi: 10.1016/j.archger.2014.08.012 [published Online First: 2014/09/14]
47. Huaxue L, Taifang L, Wenjing Y, et al. Status of frailty and its effect path on quality of life among the elderly in community. *Chinese Nursing Research* 2019;33(21):3645-49.
48. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282 [published Online First: 2016/08/26]
49. Feng L, Zin Nyunt MS, Gao Q, et al. Cognitive Frailty and Adverse Health Outcomes: Findings From the Singapore Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc* 2017;18(3):252-58. doi: 10.1016/j.jamda.2016.09.015 [published Online First: 2016/11/14]

50. Akosile CO, Mgbeojedo UG, Maruf FA, et al. Depression, functional disability and quality of life among Nigerian older adults: Prevalences and relationships. *Arch Gerontol Geriatr* 2018;74:39-43. doi: 10.1016/j.archger.2017.08.011 [published Online First: 2017/09/28]
51. Shin KR, Byeon YS, Kang Y, et al. A study on physical symptom, activity of daily living, and health-related quality of life (HRQoL) in the community-dwelling older adults. *Taehan Kanho Hakhoe chi* 2008;38(3):437-44. doi: 10.4040/jkan.2008.38.3.437 [published Online First: 2008/07/08]
52. Crimmins EM. Trends in the health of the elderly. *Annu Rev Public Health* 2004;25:79-98. doi: 10.1146/annurev.publhealth.25.102802.124401 [published Online First: 2004/03/16]
53. Khan ZA, Singh C, Khan T. Correlates of physical disability in the elderly population of Rural North India (Haryana). *J Family Community Med* 2018;25(3):199-204. doi: 10.4103/jfcm.JFCM_160_17 [published Online First: 2018/09/18]
54. Wei M, Li J, Wang H. Impact of the disability trajectory on the mortality risk of older adults in China. *Arch Gerontol Geriatr* 2018;74:174-83. doi: 10.1016/j.archger.2017.10.015 [published Online First: 2017/11/11]
55. Gobbens RJ. Associations of ADL and IADL disability with physical and mental dimensions of quality of life in people aged 75 years and older. *PeerJ* 2018;6:e5425. doi: 10.7717/peerj.5425 [published Online First: 2018/08/21]
56. Rejeski WJ, Brawley LR, Haskell WL. The prevention challenge: an overview of this supplement. *Am J Prev Med* 2003;25(3 Suppl 2):107-9. doi: 10.1016/s0749-3797(03)00173-9 [published Online First: 2003/10/14]
57. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154. doi: 10.1186/s12877-015-0155-4 [published Online First: 2015/12/03]
58. Kortebein P, Ferrando A, Lombeida J, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older adults. *JAMA* 2007;297(16):1772-4. doi: 10.1001/jama.297.16.1772-b [published Online First: 2007/04/26]
59. Ávila-Funes JA, Pina-Escudero SD, Aguilar-Navarro S, et al. Cognitive impairment and low physical activity are the components of frailty more strongly associated with disability. *J Nutr Health Aging* 2011;15(8):683-9. doi: 10.1007/s12603-011-0111-8 [published Online First: 2011/10/05]
60. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First: 2011/04/01]

Table 1 Correlations coefficients of main variables among the participants in Shandong, China, 2019 (N=3243)

Variable	M	SD	1	2	3	4
1.Physical frailty	1.511	1.071	1			
2.Physical disability	16.994	4.366	0.330***	1		
3.Physical activity	3122.346	3157.705	-0.299***	-0.184***	1	
4.HRQoL	0.896	0.161	-0.426***	-0.557***	0.196***	1

M mean, SD standard deviation

***P<0.001

Table 2 Testing the mediation effect of physical disability between physical frailty and HRQoL among the participants in Shandong, China, 2019

Predictors	Model1(HRQoL)		Model2(Physical disability)		Model3(HQRoL)	
	β	t	β	t	β	t
Age	-0.018	-0.731	0.166	6.349***	0.061	2.758**
Education	0.010	0.162	-0.182	-8.326***	-0.084	-4.507***
Physical frailty	-0.423	-26.031***	0.295	17.729***	-0.280	-18.957***
Physical disability					-0.482	-32.407***
R^2	0.181		0.141		0.381	
F	238.859***		176.932***		499.748***	

**P<0.01, ***P<0.001

Table 3 Total effect, direct effect and mediation effect

	Effect size	BootSE	BootCI		Relative effect value
			Low	High	
Total effect	-0.423	0.020	-0.461	-0.382	
Direct effect	-0.280	0.017	-0.313	-0.247	66.29%
Mediation effect	-0.143	0.016	-0.175	-0.113	33.71%

BootSE bootstrap standard error, BootCI bootstrap confidence interval

Table 4 Testing the moderated mediation effect of physical frailty on HRQoL among the participants in Shandong, China, 2019

Predictors	Model 1(Physical disability)		Model 2(HRQoL)	
	β	t	β	t
Age	0.154	5.956***	0.062	2.765**
Education	-0.181	-8.393***	-0.073	-3.849***
Physical frailty	0.246	13.965***	-0.260	-17.070***
Physical activity	-0.104	-5.555***	0.091	4.673***
Physical frailty×PA	-0.120	-7.058***		
Physical disability			-0.421	-24.364***
Physical disability×PA			0.116	6.119***
R2	0.159		0.390	
F	122.004***		345.138***	

** $P<0.01$, *** $P<0.001$

Table 5 Mediating effect values at different levels of physical activity among the participants in Shandong, China, 2019

Physical activity	Effect	BootSE	BootLLCI	BootULCI
M-1SD	-0.209	0.023	-0.250	-0.160
M	-0.104	0.013	-0.132	-0.080
M+1SD	-0.040	0.012	-0.062	-0.017

M mean, 1SD one standard deviation, BootSE bootstrap standard error, BootLLCI bootstrap lower limit confidence interval, BootULCI bootstrap upper limit confidence interval

Fig. 1 The conceptual framework of the moderated mediation mode

Fig. 2 Simple slope analysis shows that physical frailty moderated the relation between physical frailty and HRQoL

Fig.3 Simple slope analysis shows that physical activity moderated the relation between physical disability and HRQoL

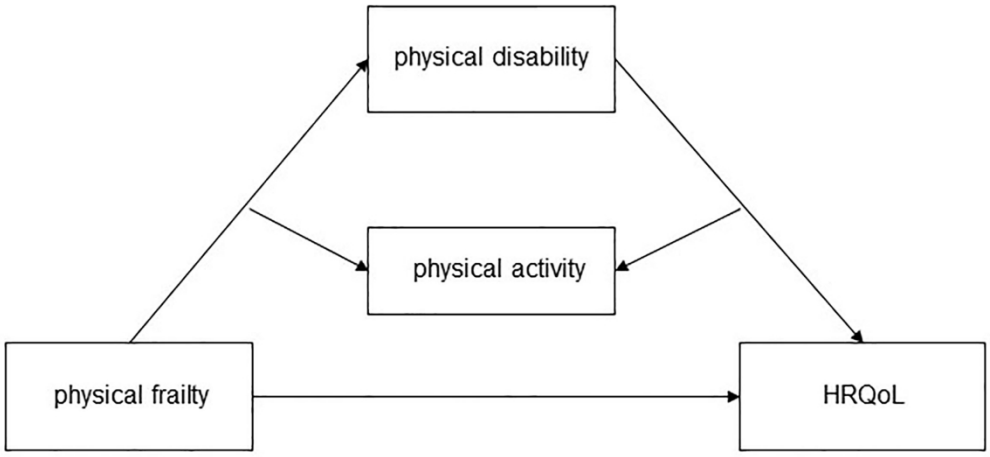

Fig. 1 The conceptual framework of the moderated mediation mode

197x90mm (300 x 300 DPI)

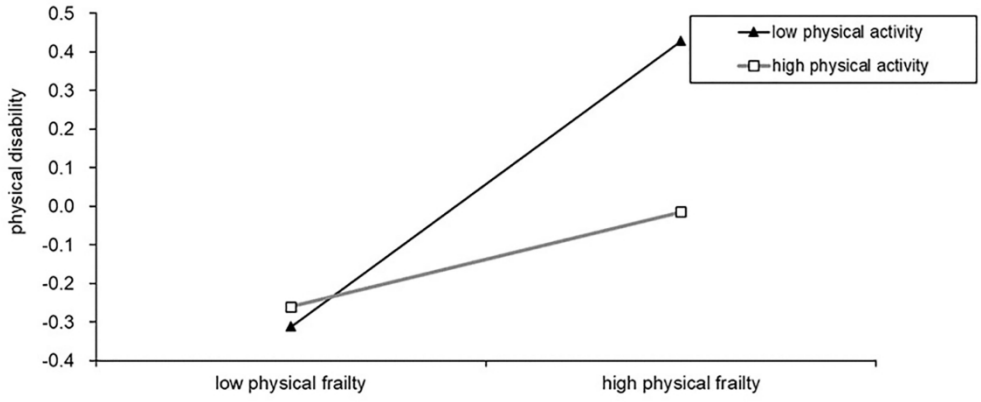

Fig. 2 Simple slope analysis shows that physical frailty moderated the relation between physical frailty and HRQoL

210x90mm (300 x 300 DPI)

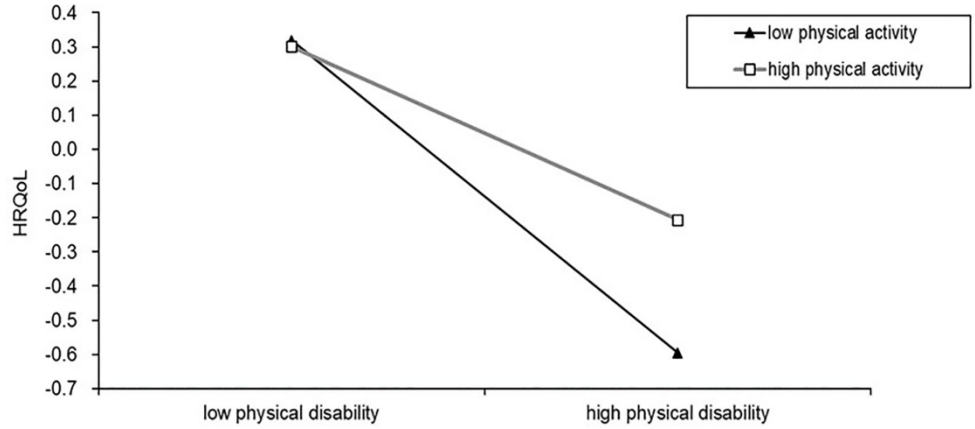

Fig.3 Simple slope analysis shows that physical activity moderated the relation between physical disability and HRQoL

194x90mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4-P5
Objectives	3	State specific objectives, including any prespecified hypotheses	P5-P6
Methods			
Study design	4	Present key elements of study design early in the paper	P6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P7
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	P7
Bias	9	Describe any efforts to address potential sources of bias	P10
Study size	10	Explain how the study size was arrived at	P6-P9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P6-P9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P9
		(*e*) Describe any sensitivity analyses	P9
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	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P10
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	P10-

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	P12
		(*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	P12
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	P15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P15
Generalisability	21	Discuss the generalisability (external validity) of the study results	P15
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	P17

*Give information separately for exposed and unexposed groups.

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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Physical frailty and health-related quality of life among Chinese rural older adults: A moderated mediation analysis of physical disability and physical activity

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Abstract

Objectives: The purpose of this study is to explore the mediating effect of physical disability, as well as the role of physical activity (PA) as a moderator in the relationship between physical frailty and health-related quality of life （HRQoL) among rural older adults in China.

Design: Cross-sectional analysis.

Setting: Rural households in Shandong of China (Rushan, Qufu, Laolin).

Participants and methods： A survey was conducted among 3,243 rural older adults. The data were collected using questionnaires measuring physical frailty, physical disability, HRQoL and PA. Bootstrap analyses were employed to explore the mediating effect of physical disability and also the moderating role of PA on physical frailty and HRQoL.

Results: After controlling for age and education, physical disability partially mediated the effect of physical frailty on HRQoL[indirect effect = -0.143, 95% confidence intervals (CI) = -0.175, -0.113], with the mediating effect accounting for 33.71% of the total effect. PA moderated the relationship between physical frailty and physical disability, as well as the relationship between physical disability and HRQoL. Specifically , the interaction term between physical frailty and PA significantly predicted physical disability (β = -0.120, t = -7.058, P< 0.001), and the interaction term between physical disability and PA also had a significant predictive effect on HRQoL (β = 0.115, t =6.104, P< 0.001).

Conclusions: PA can moderate the indirect effect of physical disability on the association between physical frailty and HRQoL. This study helps to understand the mechanism underlying the association between physical frailty and HRQoL. Encouraging rural older adults to increase PA appropriately might improve HRQoL for older adults with physical frailty and physical disability problems.

Key words: HRQoL; Physical activity; Physical frailty; Physical disability; Rural older adults; Moderated mediation analysis

Strengths and limitations of this study

1. This is the first study to investigate the moderating and mediating factors of the relationship between physical frailty and HRQoL among older adults in rural China.
2. Moderated mediation model was used to explore the potential effect of physical disability and physical activity.
3. Cross-sectional data could not provide strong evidence of causation.
4. Only two control variables were included in this study, and more confounding factors will be included to verify our results in the future.
5. More potential mechanisms related to physical frailty and HRQoL among older adults need to be explored by using longitudinal data in the future.

1. Introduction

Population aging has become a global social problem. As one of the world's most aging countries, China had 249 million people aged over 60 years in 2018, accounting for 17.9 percent of the total population[1].It is predicted that by 2050, older adults over 60 will account for more than 35.1% of the total population[2].With the increasing aging population and the extension of life expectancy, improving the health-related quality of life (HRQoL) of older adults is an important public health issue. HRQoL is a predictive factor of mortality in older adults[3].Compared with urban older adults, the HRQoL of rural older adults is worse[4 5],which needs more attention.

Physical frailty is a medical syndrome caused by a variety of etiologies and causes, which is characterized by a decline in physical strength, endurance, and decreased physiological function[6]. With the increase of age, the risk of physical frailty increases[7].Frailty may lead to negative health consequences, including fall, reduced activity, reduced independence, frequent hospitalization, and disability[8].These adverse outcomes resulted in a decline in the quality of life of older adults. Previous cross-sectional and longitudinal studies have shown that frailty was negatively associated with HRQoL[9-11], and frail older adults reported worse HRQoL than those who were not frail[12]. Although the association between physical frailty and quality of life has been confirmed, the underlying mechanism remains unclear.

The prevalence of physical disability is high among the frail older adults[13 14].Some studies showed physical frailty was closely related to disability[15 16],and might be the precursor and cause

of disability[17].A national longitudinal study of 7,439 people over age 65 in US showed that frailty was a strong predictor of disability[18].A prospective two-year cohort study in Japan also showed that frailty and prophase of frailty increased the risk of disability[19].These findings suggest that physical frailty is associated with disability in older adults. Studies have also demonstrated that the quality of life worsened as the degree of disability increased, and the more severe the disability, the worse the quality of life[20]. Compared with non-disabled older adults, disabled older adults are more prone to fall, depression, anxiety, etc., and their HRQoL was significantly reduced. Therefore, we speculate that frailty may have an indirect effect on individual's HRQoL through the mediating effect of physical disability.

Physical frailty is considered to be reversible and preventable[21].Physical activity(PA) is a key factor of reverse and prevent frailty in older adults[22].Studies have found that physical activity moderated the relationship between chronic illness and functional limitations, and moderated functional disability and body function[23 24].PA can alleviate the decline of physical function in older adults and has a beneficial effect on functional limitations, physical frailty, disability and quality of life in older adults[25-27].Studies indicated the positive effect of physical activity on reducing adverse events caused by frailty in older people. Performing a physical activity of moderate to vigorous intensity would improve physical frailty and prevent the occurrence of disability when compared to the performance of a physical activity of low intensity, ultimately promote older adults' quality of life[28-30].Therefore, PA may moderate the direct and indirect relationship between physical frailty and HRQoL through physical disability as a

mediator.

In the present study, we used a cross-sectional study to the relationship between physical frailty and HRQoL, focusing on the mediating role of physical disability and the moderating role of PA in the relationship between physical frailty and HRQoL. The conceptual framework of the moderated mediation model was shown in Fig. 1.

2. Methods

2.1.1 Design and sample

This study was conducted from May to June, 2019 in Shandong province, China. A multistage stratified cluster sampling method was used to select participants, which was described in detail in a paper we have previously published[31].Three rural counties (Qufu, Laoling and Rushan) were selected according to the GDP per capita (2018) in Shandong. Within each selected county, five townships were randomly selected. Then, four villages were selected from each selected townships and the elderly aged over 60 years old who were randomly selected from sample villages .All participants completed the questionnaire independently. The survey was completed in about an hour, and the investigators checked the questionnaires when the participants returned them. A total of 3,600 respondents were recruited from 60 villages and 15 townships in 3 rural counties in Shandong province, of whom 3,243 completed the entire survey, with a response rate of 90.05%.

2.2. Variables and measurement

2.2.1Independent variable

Physical frailty was measured by Frailty Phenotype[32].The scale is a widely used frailty screening scale with good reliability and validity[33 34]. Frailty was defined based on the following five aspects: weight loss, exhaustion, low physical activity level, slowness, weakness. ①Weight loss: In the past 1 year, participants' body mass index (BMI) decreased by >5.0% (except for personal deliberate weight loss). ②Exhaustion: Using the Center for Epidemiological Studies-Depression(CES-D)[35]: "How often in the last week did you feel this way?" (1) I could not get going and (2) I felt everything I did was an effort. Either of the above two questions that participants answered 3~4 days and most of the time, was considered exhaustion.③Low physical activity level: According the International Physical Activity Questionnaire-short Form (IPAQ-SF)[36 37], we used standard algorithms to calculate the Kcals consumed per week. The criterion is adjusted according to gender. Male: <383 Kcals/ week is a decrease in physical activity, while female: <270 Kcals/ week is a decrease in physical activity.④Slowness: Slowness was assessed via walking speed at 15 ft measured for 3 times, and we record the minimum value.The criterion is adjusted according to gender and height. Men: height≤173 cm and time≥7 seconds; height >173 cm and time≥6 seconds. Women: height≤159 cm and time≥7 seconds ;height >159 cm and time≥6 seconds. ⑤Weakness: Weakness was assessed by grip strength using a handgrip dynamometer was measured for 3 times, and we record the maximum value, adjusted for gender and BMI. Men: BMI≤24 and grip strength≤29;BMI 24.1-26and grip strength≤30;BMI 26.1-28 and grip strength ≤30;BMI > 28 and grip strength≤32.Women:BMI≤

23 and grip strength≤17;BMI 23.1-26 and grip strength≤17.3;BMI 26.1-29 and grip strength≤18;BMI>29 and grip strength≤21.

2.2.2Dependent variables

HRQoL was measured by the health utility value of EQ-5D-5L[38].The EQ-5D-5L consists of the EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L descriptive system has five elements (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and each element includes five level (no problems, some problems, moderate problems, severe problems and extreme problems). The latest EQ-5D-5Lhealth utility scores method refers to Chinese integral conversion table[38].The range of utility value is [-0.391, 1.000]. A higher score indicates better health condition of the respondents. The Cronbach's coefficient was 0.761 in this study.

2.2.3Mediator

Physical disability was evaluated by the Activity of Daily Living Scale (ADLS), which was developed by Lawton and Brody in 1969 to measure the disability of older adults[39 40]. The Scale consists of 14 items, including Physical Self-Maintenance Scale (PSMS) and Instrumental Activities of Daily Living (IADL). The total score is 14-56, with higher scores indicating increased physical disability. A score of 14 and lower indicates completely normal physical ability, a score between 15 and 22 is defined as mild disability, and a score of 23 and higher is defined as severe disability. ADLS is recommended by WHO and has been widely used in older adults in China, with good reliability and validity[41].Cronbach's alpha was 0.764 in this study.

2.2.4Moderator

PA was assessed using the IPAQ-SF[36 37].The questionnaire contains 7 questions, 6 of which were about physical activity. The IPAQ-SF investigates the PA of the individuals in the last 7 days. The questionnaire involved three types of intensity activities, including vigorousphysical activity (VPA =8.0 metabolic equivalent [METs]), moderate physical activity (MPA =4.0 METs), and low physical activity (LPA =3.3 METs).PA of each person engaged in a certain intensity per week is the METs value corresponding to that physical activity × weekly frequency × daily time, and the sum of three PA is the total PA (met-h /week). The greater the overall physical activity value, the higher the physical activity.

2.3 Data analysis

To analyze the data, categorical variables were expressed using frequency and percentages (%) and continuous data were described using mean (standard deviation). Pearson correlation coefficient was used to analyze the correlation among physical frailty, physical disability, and HRQoL. All these analyses were performed using IBM SPSS 24.0 (IBM Corp., Armonk, NY, USA). All regression coefficients were tested by the bias-corrected percentile Bootstrap method. The theoretical model was tested by estimating the 95% confidence interval (CI) for mediation and moderating effects with 5000 sampled with repetition. If the 95% CI did not include 0, it meant that the statistics was significant. To illuminate the moderating effect, the moderated variable (PA) is divided into two levels of high and low according to one standard deviation

above and below the mean(M+1SD/M-1SD)[42-44].The Split-Plot analysis method was used to further examine the direction of the moderation effect, and draw a diagram explaining the moderation effect[45].The mediation model and moderated mediation model were tested with the PROCESS V3.3 macro for SPSS[46].In the current study, we selected Model 4 and Model 59 to analyze the mediating effect and moderated mediation effect. In addition, through t test and ANOVA analysis, we found that HRQoL is related to age and education. Previous studies have also found HRQoL was associated with age and education[47 48]. We controlled age and education in this study. Sampling weights were used in all of the analyses to adjust for the survey design.

2.4 Patient and public involvement statement

This research was done without patient involvement. No patients were involved in developing the hypothesis and plans for design of this study either. The results would not be disseminated to study participants or any other individuals or communities.

2.5Ethical considerations

The study was approved by the Ethics Committee of School of Public Health in Shandong University, P. R. China. The participants have been informed of the purpose and procedures of the study before the investigation. Before the study began, participants had signed written informed consent indicating that they were fully aware of the study procedures.

3. Results

3.1 Common method biases

We used Harman single factor test to conduct a common method biases test[49].The results show that there are 12 factors with eigenvalues greater than 1, and the variance explained by the first factor is 17.92%, which is less than 40% of the critical standard, indicating that there are no serious common method biases in this study.

3.2 Socio-demographic characteristics of the participants

There were 3,243 participants, comprising 2,060 (63.5%) women and 1,182 (36.5%) men. The average age was 69.88 (SD=6.10) years, ranging from 60 to 97 years. Of the participants, 25.5% were single. About 72.4% had chronic disease. The majority (81.9%) were empty nest elderly.

3.3 Bivariate correlations of main variables

The mean, standard deviation/ Median ($Quartile_1$, $Quartile_3$) and correlation coefficient of each variable were shown in Table 1. Physical frailty was positively correlated with physical disability ($\rho = 0.283$, $P< 0.01$), physical frailty was negatively correlated with HRQoL ($\rho = -0.429$, $P< 0.01$) and PA ($\rho = -0.378$, $P<0.01$). Physical disability was negatively correlated with HRQoL ($\rho = -0.378$, $P< 0.01$) and PA ($\rho = -0.194$, $P< 0.01$). PA was positively correlated with HRQoL ($\rho = 0.258$, $p <0.01$).

3.4Mediation effect analysis

Model 4 in the SPSS macro compiled by Hayes 2013[46] was used to test the mediating effect of physical disability in the relationship between physical frailty and HRQoL under the control variable of age, education. As shown in Table 2 and Table 3, physical frailty had a significant

predictive effect on quality of life (β = -0.423, t = -26.031, P< 0.001), and the direct predictive effect of frailty on quality of life was still significant when the mediating variable physical disability was added. Meanwhile, physical frailty had a significant positive predictive effect on physical disability (β = 0.295, t = 17.729, P< 0.001). Physical disability also has a significant negative predictive effect on HRQoL (β = -0.482, t = -32.407, P< 0.001). In addition, the upper and lower limits of the Bootstrap 95% CI for the direct effect of physical frailty on HRQoL and the mediating effect of physical disability on physical frailty and HRQoL did not include 0(Table 3), indicating that the mediating effect was significant. The mediating effect value was-0.143 and the 95% CI was [-0.175, -0.113], which accounted for 33.71% of the total effect. This shows that disability plays a partial mediating role in the relationship between physical frailty and HRQoL.

3.5 Moderated mediation effect analysis

PROCESS macro method (Model 59)compiled by Hayes (2013)[46] was used to test the moderated mediation model while controlling for age and education(Table 4 and Table 5).After PA was put into the model, the interaction term between physical frailty and PA significantly predicted physical disability (β = -0.120, t = -7.058, P< 0.001) (Table4, Model 1), and the interaction term between physical disability and PA also had a significant predictive effect on HRQoL (β = 0.115, t =6.104, P< 0.001)But, the interaction term between physical frailty and PA had no effect on HRQoL(Table4, Model 2).These results suggest PA played a moderating role in the relationships between physical frailty and physical disability and between physical disability and HRQoL. However, PA did not significant moderate the relationships between physical

frailty and HRQoL. Simple slope analyses indicated that the significant interaction at 1 SD below the mean(M-1SD) and 1 SD above the mean(M+1SD) of physical activity (See Fig. 2 and Fig. 3).Physical frailty had a significant predictive effect on the disability of individuals with high-level((M+1SD) or low-level(M-1SD) PA, but the predictive effect of physical frailty on physical disability was stronger for individuals with low-level PA(b_{simple} = 0.370, t = 16.979, P< 0.001) than for individuals with high-level PA,as shown in Fig. 2 (b_{simple} = 0.120, t = 4.322, P< 0.001).Fig. 3 showed that for high levels of PA individuals, the effect of physical disability and HRQoL was significant (b_{simple}= -0.304, t = -9.149, P< 0.001). However, for low-level of PA individuals, the effect of physical disability and HRQoL was still significant but considerably stronger (b_{simple} = -0.543, t = -28.654, P< 0.001).In addition, as the level of physical activity increased, the mediating effect of physical disability on the relationship between physical frailty and HRQoL declined (Table 5).

4. Discussion

In this study, a moderated mediation model was established with the mediation role of physical disability on the relationship between physical frailty and HRQoL, as well as the role of PA as a moderator in this indirect path between physical frailty and HRQoL. These findings preliminarily elucidate the potential causes of physical frailty on HRQoL and facilitate the development of targeted interventions for individuals so as to improve HRQoL in rural older adults.

Consistent with previous studies[50 51], we find that physical frailty negatively affect HRQoL

of older adults. This suggests that as the degree of physical frailty increases, the quality of life in older adults becomes worse. Although many studies have established a direct relationship between frailty and HRQoL, few have explored the underlying mechanisms of this relationship. Our study demonstrates that the physical disability mediates the physical frailty and HRQoL, with the mediating rate of 33.71%. A study also suggested that physical disability was one of the potential factors underlying the association between frailty and HRQoL, which was similar with our study[52].

The current study indicates that physical frailty is associated with disability, which is consistent with a study by Kojuma G[53].Frail older adults are very vulnerable to adverse health effects.A study indicated the risk of disability in the frail older adults was 12- to 13-fold increased than that in the non-frail older adults[54].Meanwhile, this study also demonstrates that the negative predictive effect of disability on individual HRQoL, which was consistent with previous studies[55 56].The possible explanation is that disabled older adults' poor self-care ability deteriorates their health, such as their normal physiological activities are restricted, physiological function is declined, social interaction is reduced, which adversely affect their physical and mental health and ultimately reduce HRQoL.. One study found that disability was the most important health problem for older adults, which seriously affected their quality of life in old adults' later years[57].The disability was the most important factor that contributed to decreasing quality of life in older adults. Physical disability has been shown to be associated with increased chronic diseases, and premature mortality[58 59],all of which could adversely affect the quality of

life of older adults[60].Therefore, physical frailty may reduce HRQoL of rural older adults by increasing their disability.

In the present study, we also find that PA plays a moderating role in the indirect effect between physical frailty and HRQoL. A larger indirect effect is observed among rural older adults with low-level of PA than among those with average or high-level of PA. Specifically, PA moderates the relationship between physical frailty and physical disability, and between physical disability and HRQoL. For older adults with low-level PA, the impact of physical frailty on physical disability is stronger than older adults with high-level PA. This finding indicates that PA moderates the relation between physical frailty and physical disability. We speculate that older adults with low-level PA may have a decline in their physiological system reserves, leading to a deterioration of their functional status and ultimately increasing the possibility of physical frailty and disability[61].A systematic review showed that older adults without exercise habits were at greater risk of developing frailty. Taichi, resistance sports and other physical activities might effectively improve the health of older adults, reduce the symptoms of physical weakness, and prevent the occurrence of physical disability[62].Compared with older adults with high-level PA,older adults with low-level PA are more vulnerable to the negative effects of physical frailty. As a result, physical frailty may cause more interference in older adults with low-level PA and increase the risk of physical disability.

We also find that physical disability has a significant impact on quality of life at both high and low-level of PA. Compared with older adults with high levels of PA, physical disability is

more likely to adversely affect HRQoL of older adults with low-level PA. A study showed that low-level PA was a major contributing factor for older adults disability[63].As the level of disability increases, the individuals with low-level of PA experience a more serious functional decline and become more worried about the health status, thus further negatively affect the HRQoL[64]. In addition, physical disability has a greater effect on individuals with low-level PA than high-level PA, which indicates that PA plays a moderating role between physical disability and HRQoL. One study found that PA could improve the physical function and daily life activities of disabled older adults, and ultimately improved the life of older adults quality[65].Therefore, a low-level of PA might be associated with poor quality of life in rural older adults with high disability.

However, physical activity does not moderate the direct relationship between physical frailty and HRQoL. Physical frailty may lead to a decline in physical function, muscle strength and physical activity in older adults, which may increases the risk of adverse health outcomes and ultimately affects HRQoL of older adults. Currently, there are few studies on the moderating role of physical activity between physical frailty and HRQoL. Further research is needed to explore the underlying reasons for such findings.

Based on our findings, we recommended that community health managers should focus on ensuring the medical assistance, life care of older adults with physical frailty or physical disability. Besides, rural communities should establish some public facilities or organize some public activities to encourage older adults to participate in sports activities, and ultimately

improve health and promote their HRQoL.There are several limitations in this study. First, our study was based on a cross-sectional study, which could not provide strong evidence of causation. Future research could adopt a longitudinal design or experiments to explore the causal relationship between physical frailty and HRQoL. Secondly, the data in this study comes from the participants' self-report information, which might result in recall bias. Thirdly, this study only included age and education as control variables. The study may also be affected by other confounding factors. In the future, we will include more confounding factors related to quality of life to verify our findings. Fourthly,physical disability has a partly mediating effect on the relationship between physical frailty and HRQoL, which indicates that there are other mediating variables in this relationship. More potential mechanisms related to physical frailty and HRQoL among older adults need to be explored in the future.

Conclusion

This study shows that physical frailty is related to HRQoL, and physical disability mediates the relationship between physical frailty and HRQoL, and PA moderates the mediating relationship. A greater effect is observed among rural older adults with low-level of PA than that among those with high-level of PA. This will help to elucidate the underlying mechanism of the relationship between physical frailty and HRQoL and form an effective way to improve the HRQoL of older adults in rural areas.

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Contributors

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

None declared.

Patient consent for publication

Not required.

REFERENCES

1. NBSC. Statistical communiqué of the People's Republic of China on the 2017 national economic and social development. 2017 [updated February 28,2018. Available from: http://www.stats.gov.cn/english/PressRelease/201802/t20180228_1585666.html.

2. United Nations DESA, Population Division. World Population Ageing 2017:Highlights 2017 [updated 2017. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf.

3. Brown DS, Thompson WW, Zack MM, et al. Associations Between Health-Related Quality of Life and Mortality in Older Adults. *Prevention Science* 2015;16(1):21-30. doi: 10.1007/s11121-013-0437-z

4. Zhou B, Chen K, Wang J, et al. Quality of Life and Related Factors in the Older Rural and Urban Chinese Populations in Zhejiang Province. *J Appl Gerontol* 2011;30(2):199-225. doi: 10.1177/0733464810361346

5. Zhou Z, Zhou Z, Gao J, et al. Urban-rural difference in the associations between living arrangements and the health-related quality of life (HRQOL) of the elderly in China-Evidence from Shaanxi province. *PLoS One* 2018;13(9):e0204118. doi: 10.1371/journal.pone.0204118 [published Online First: 2018/09/21]

6. Morley JE, Vellas B, Van Kan GA, et al. Frailty Consensus: A Call to Action. *J Am Med Dir Assoc* 2013;14(6):392-97. doi: 10.1016/j.jamda.2013.03.022

7. Collard RM, Boter H, Schoevers RA, et al. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc* 2012;60(8):1487-92. doi: 10.1111/j.1532-5415.2012.04054.x [published Online First: 2012/08/14]

8. Vermeiren S, Vellaazzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *J Am Med Dir Assoc* 2016;17(12) doi: 10.1016/j.jamda.2016.09.010

9. Lee IC, Chiu YH, Lee CY. Exploration of the importance of geriatric frailty on health-related quality of life. *Psychogeriatrics* 2016;16(6):368-75. doi: 10.1111/psyg.12179 [published Online First: 2016/01/13]

10. Ferrer A, Formiga F, Cunillera O, et al. Predicting factors of health-related quality of life in octogenarians: a 3-year follow-up longitudinal study. 2015;24(11):2701-11.

11. Provencher V, Sirois MJ, Émond M, et al. Frail older adults with minor fractures show lower health-related quality of life (SF-12) scores up to six months following emergency department discharge. *Health Qual Life Outcomes* 2016;14:40. doi: 10.1186/s12955-016-0441-7 [published Online First: 2016/03/10]

12. Kanauchi M, Kubo A, Kanauchi K, et al. Frailty, health-related quality of life and mental well-being in older adults with cardiometabolic risk factors. *Int J Clin Pract* 2008;62(9):1447-51. doi: 10.1111/j.1742-1241.2008.01830.x [published Online First: 2008/07/23]

13. Fullerthomson E, Yu B, Nurujeter A, et al. Basic ADL Disability and Functional Limitation Rates Among Older Americans From 2000–2005: The End of the Decline? *J Gerontol A Biol Sci Med Sci* 2009;64(12):1333-36. doi: 10.1093/gerona/glp130

14. Picavet HSJ, Hoeymans N. Physical disability in The Netherlands: Prevalence, risk groups and time trends. *Public Health* 2002;116(4):231-37. doi: 10.1038/sj.ph.1900864

15. Evenhuis HM, Hermans H, Hilgenkamp TIM, et al. Frailty and Disability in Older Adults with Intellectual Disabilities: Results from the Healthy Ageing and Intellectual Disability Study. *J Am Geriatr Soc* 2012;60(5):934-38. doi: 10.1111/j.1532-5415.2012.03925.x

16. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised older people. *Age Ageing* 2014;43(4):477-84. doi: 10.1093/ageing/aft181

17. Papachristou E, Wannamethee SG, Lennon LT, et al. Ability of Self-Reported Frailty Components to Predict Incident Disability, Falls, and All-Cause Mortality: Results From a Population-Based Study of Older British Men. *J Am Med Dir Assoc* 2017;18(2):152-57. doi: 10.1016/j.jamda.2016.08.020 [published Online First: 2016/10/16]

18. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133 [published Online First: 2015/08/25]

19. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older adults: a prospective cohort study. *BMJ open* 2015;5(9):e008462. doi: 10.1136/bmjopen-2015-008462 [published Online First: 2015/09/05]

20. Medhi GK, Sarma J, Pala S, et al. Association between health related quality of life (HRQOL) and activity of daily living (ADL) among elderly in an urban setting of Assam, India. *J Family Med Prim Care* 2019;8(5):1760-64. doi: 10.4103/jfmpc.jfmpc_270_19 [published Online First: 2019/06/15]

21. Tavassoli N, Guyonnet S, Abellan Van Kan G, et al. Description of 1,108 older patients referred by their physician to the "Geriatric Frailty Clinic (G.F.C) for Assessment of Frailty and Prevention of Disability" at the gerontopole. *J Nutr Health Aging* 2014;18(5):457-64. doi: 10.1007/s12603-014-0462-z [published Online First: 2014/06/03]

22. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, et al. Exercise training as a drug to treat age associated frailty. *Free Radic Biol Med* 2016;98:159-64. doi: 10.1016/j.freeradbiomed.2016.03.024 [published Online First: 2016/03/30]

23. Rector JL, Marceau K, Friedman EM. Moderation of the Association Between Chronic Medical Conditions and Functional Limitations Over Time by Physical Activity: Effects of Age. *J Gerontol A Biol Sci Med Sci* 2020;75(1):168-74. doi: 10.1093/gerona/glz020 [published Online First: 2019/02/21]

24. Palmer RF, Espino DV, Dergance JM, et al. The role of physical activity and diabetes status as a moderator: functional disability among older Mexican Americans. *Age Ageing* 2012;41(6):752-8. doi: 10.1093/ageing/afs106 [published Online First: 2012/10/12]

25. Keysor JJ. Does late-life physical activity or exercise prevent or minimize disablement? A critical review of the scientific evidence. *Am J Prev Med* 2003;25(3 Suppl 2):129-36. doi: 10.1016/s0749-3797(03)00176-4 [published Online First: 2003/10/14]

26. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? *J Gerontol A Biol Sci Med Sci* 2001;56(7):M412-23. doi: 10.1093/gerona/56.7.m412 [published Online First: 2001/07/11]

27. Rejeski WJ, Mihalko SL. Physical Activity and Quality of Life in Older Adults. *J Gerontol A Biol Sci Med Sci* 2001;56(suppl_2):23-35. doi: 10.1093/gerona/56.suppl_2.23

28. Casas-Herrero A, Izquierdo M. Physical exercise as an efficient intervention in frail elderly persons. *An Sist Sanit Navar* 2012;35(1):69-85. doi: 10.4321/s1137-66272012000100007 [published Online First: 2012/05/04]

29. Mañas A, Del Pozo-Cruz B, Guadalupe-Grau A, et al. Reallocating Accelerometer-Assessed Sedentary Time to Light or Moderate- to Vigorous-Intensity Physical Activity Reduces Frailty Levels in Older Adults: An Isotemporal Substitution Approach in the TSHA Study. *J Am Med Dir Assoc* 2018;19(2):185.e1-85.e6. doi: 10.1016/j.jamda.2017.11.003 [published Online First: 2017/12/23]

30. Barnett A, Smith B, Lord SR, et al. Community-based group exercise improves balance and reduces falls in at-risk older people: a randomised controlled trial. *Age Ageing* 2003;32(4):407-14. doi: 10.1093/ageing/32.4.407 [published Online First: 2003/07/10]

31. Jing Z, Li J, Wang Y, et al. The mediating effect of psychological distress on cognitive function and physical frailty among the elderly: Evidence from rural Shandong, China. *J Affect Disord* 2020;268:88-94. doi: 10.1016/j.jad.2020.03.012 [published Online First: 2020/03/12]

32. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]

33. Buta BJ, Walston JD, Godino JG, et al. Frailty assessment instruments: Systematic characterization of the uses and contexts of highly-cited instruments. *Ageing Res Rev* 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003 [published Online First: 2015/12/18]

34. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC Geriatr* 2013;13:64. doi: 10.1186/1471-2318-13-64 [published Online First: 2013/06/22]

35. Radloff LS. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. *Appl Psychol Meas* 1977;1(3):385-401. doi: 10.1177/014662167700100306

36. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical Activity Questionnaire. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 2014;35(8):961-4. [published Online First: 2014/11/08]

37. Macfarlane DJ, Lee CC, Ho EY, et al. Reliability and validity of the Chinese version of IPAQ (short, last 7 days). *J Sci Med Sport* 2007;10(1):45-51. doi: 10.1016/j.jsams.2006.05.003 [published Online First: 2006/06/30]

38. Luo N, Liu G, Li M, et al. Estimating an EQ-5D-5L Value Set for China. *Value Health* 2017;20(4):662-69. doi: 10.1016/j.jval.2016.11.016 [published Online First: 2017/04/15]

39. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist* 1969;9(3):179-86. doi: 10.1093/geront/9.3_Part_1.179 [published Online First: 1969/01/01]

40. Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc* 1971;19(6):465-81. doi: 10.1111/j.1532-5415.1971.tb01206.x [published Online First: 1971/06/01]

41. Chen P, Yu ES, Zhang M, et al. ADL dependence and medical conditions in Chinese older persons: a population-based survey in Shanghai, China. *J Am Geriatr Soc* 1995;43(4):378-83. doi: 10.1111/j.1532-5415.1995.tb05811.x [published Online First: 1995/04/01]

42. Ng KY, Ang S, Chan KY. Personality and leader effectiveness: a moderated mediation model of leadership self-efficacy, job demands, and job autonomy. *J Appl Psychol* 2008;93(4):733-43. doi: 10.1037/0021-9010.93.4.733 [published Online First: 2008/07/23]

43. Preacher KJ, Rucker DD, Hayes AF. Addressing Moderated Mediation Hypotheses: Theory, Methods, and Prescriptions. *Multivariate behavioral research* 2007;42(1):185-227. doi: 10.1080/00273170701341316 [published Online First: 2007/01/01]

44. Holmbeck GN. Toward terminological, conceptual, and statistical clarity in the study of mediators and moderators: examples from the child-clinical and pediatric psychology literatures. *Journal of consulting and clinical psychology* 1997;65(4):599-610. doi: 10.1037//0022-006x.65.4.599 [published Online First: 1997/08/01]

45. Cohen J, Cohen P, West SG, et al. Applied multiple regression/correlation analysis for the behavioral sciences: Routledge 2013.

46. Bolin JH. Hayes, Andrew F. (2013). Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. New York, NY: The Guilford Press. *J Educ Meas* 2014;51(3):335-37. doi: 10.1111/jedm.12050

47. Bao XY, Xie YX, Zhang XX, et al. The association between multimorbidity and health-related quality of life: a cross-sectional survey among community middle-aged and elderly residents in southern China. *Health Qual Life Outcomes* 2019;17(1):107. doi: 10.1186/s12955-019-1175-0 [published Online First: 2019/06/27]

48. Chapman B, Duberstein P, Lyness JM. Personality traits, education, and health-related quality of life among older adult primary care patients. *J Gerontol B Psychol Sci Soc Sci* 2007;62(6):P343-52. doi: 10.1093/geronb/62.6.p343 [published Online First: 2007/12/15]

49. Podsakoff PM, MacKenzie SB, Lee JY, et al. Common method biases in behavioral research: a critical review of the literature and recommended remedies. *J Appl Psychol* 2003;88(5):879-903. doi: 10.1037/0021-9010.88.5.879 [published Online First: 2003/10/01]

50. Kanwar A, Singh M, Lennon R, et al. Frailty and health-related quality of life among residents of long-term care facilities. *J Aging Health* 2013;25(5):792-802. doi: 10.1177/0898264313493003 [published Online First: 2013/06/27]

51. Mulasso A, Roppolo M, Rabaglietti E. The role of individual characteristics and physical frailty on health related quality of life (HRQOL): a cross sectional study of Italian community-dwelling older adults. *Arch Gerontol Geriatr* 2014;59(3):542-8. doi: 10.1016/j.archger.2014.08.012 [published Online First: 2014/09/14]

52. Huaxue L, Taifang L, Wenjing Y, et al. Status of frailty and its effect path on quality of life among the elderly in community. *Chinese Nursing Research* 2019;33(21):3645-49.

53. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282 [published Online First: 2016/08/26]

54. Feng L, Zin Nyunt MS, Gao Q, et al. Cognitive Frailty and Adverse Health Outcomes: Findings From the Singapore Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc* 2017;18(3):252-58. doi: 10.1016/j.jamda.2016.09.015 [published Online First: 2016/11/14]

55. Akosile CO, Mgbeojedo UG, Maruf FA, et al. Depression, functional disability and quality of life among Nigerian older adults: Prevalences and relationships. *Arch Gerontol Geriatr* 2018;74:39-43. doi: 10.1016/j.archger.2017.08.011 [published Online First: 2017/09/28]

56. Shin KR, Byeon YS, Kang Y, et al. A study on physical symptom, activity of daily living, and health-related quality of life (HRQoL) in the community-dwelling older adults. *Taehan Kanho Hakhoe chi* 2008;38(3):437-44. doi: 10.4040/jkan.2008.38.3.437 [published Online First: 2008/07/08]

57. Crimmins EM. Trends in the health of the elderly. *Annu Rev Public Health* 2004;25:79-98. doi: 10.1146/annurev.publhealth.25.102802.124401 [published Online First: 2004/03/16]

58. Khan ZA, Singh C, Khan T. Correlates of physical disability in the elderly population of Rural North India (Haryana). *J Family Community Med* 2018;25(3):199-204. doi: 10.4103/jfcm.JFCM_160_17 [published Online First: 2018/09/18]

59. Wei M, Li J, Wang H. Impact of the disability trajectory on the mortality risk of older adults in China. *Arch Gerontol Geriatr* 2018;74:174-83. doi: 10.1016/j.archger.2017.10.015 [published Online First: 2017/11/11]

60. Gobbens RJ. Associations of ADL and IADL disability with physical and mental dimensions of quality of life in people aged 75 years and older. *PeerJ* 2018;6:e5425. doi: 10.7717/peerj.5425 [published Online First: 2018/08/21]

61. Rejeski WJ, Brawley LR, Haskell WL. The prevention challenge: an overview of this supplement. *Am J Prev Med* 2003;25(3 Suppl 2):107-9. doi: 10.1016/s0749-3797(03)00173-9 [published Online First: 2003/10/14]

62. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154. doi: 10.1186/s12877-015-0155-4 [published Online First: 2015/12/03]

63. Kortebein P, Ferrando A, Lombeida J, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older adults. *JAMA* 2007;297(16):1772-4. doi: 10.1001/jama.297.16.1772-b [published Online First: 2007/04/26]

64. Ávila-Funes JA, Pina-Escudero SD, Aguilar-Navarro S, et al. Cognitive impairment and low physical activity are the components of frailty more strongly associated with disability. *J Nutr Health Aging* 2011;15(8):683-9. doi: 10.1007/s12603-011-0111-8 [published Online First: 2011/10/05]

65. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First: 2011/04/01]

Table 1 Spearman correlations coefficients of main variables among the participants in Shandong, China, 2019(N=3243)

Variable	M±SD/M(P_{25},P_{75})	1	2	3	4
1.Physical frailty	1.511±1.071	1			
2.Physical disability	16.994±4.36	0.283**	1		
3.Physical activity	2772(693,4158)	-0.378**	-0.194**	1	
4.HRQoL	0.896±0.161	-0.429**	-0.378**	0.258**	1

M±SD: mean±standard deviation ;M (P25,P75): Median($Quartile_1$,$Quartile_3$)

1,2,4 follow normal distribution and are described as M±SD.

3 does not follow normal distribution and is described as M (P_{25}, P_{75}).

**P<0.001

Table 2 Testing the mediation effect of physical disability between physical frailty and HRQoL among the participants in Shandong, China, 2019

Predictors	Model1(HRQoL)		Model2(Physical disability)		Model3(HQRoL)	
	β	t	β	t	β	t
Age	-0.018	-0.731	0.166	6.349***	0.061	2.758**
Education	0.010	0.162	-0.182	-8.326***	-0.084	-4.507***
Physical frailty	-0.423	-26.031***	0.295	17.729***	-0.280	-18.957***
Physical disability					-0.482	-32.407***
R^2	0.181		0.141		0.381	
F	238.859***		176.932***		499.748***	

P<0.01,*P<0.001

Table 3 Total effect, direct effect and mediation effect

	Effect size	BootSE	BootCI		Relative effect value
			Low	High	
Total effect	-0.423	0.020	-0.461	-0.382	
Direct effect	-0.280	0.017	-0.313	-0.247	66.29%
Indirect effect	-0.143	0.016	-0.175	-0.113	33.71%

BootSE bootstrap standard error, BootCI bootstrap confidence interval

Table 4Testing the moderated mediation effect of physical frailty on HRQoL among the participants in Shandong, China, 2019

Predictors	Model 1(Physical disability)		Model 2(HRQoL)	
	β	t	β	t
Age	0.154	5.956***	0.062	2.763**
Education	-0.181	-8.393***	-0.072	-3.830***
Physical frailty	0.246	13.965***	-0.258	-16.687***
Physical activity	-0.104	-5.555***	0.091	4.675***
Physical frailty×PA	-0.120	-7.058***	0.011	0.682
Physical disability			-0.422	-24.375***
Physical disability×PA			0.115	6.104***
R^2	0.159		0.390	
F	122.004***		295.850***	

** $P<0.01$,*** $P<0.001$

Table 5 Mediating effect values at different levels of physical activity among the participants in Shandong, China, 2019

Physical activity	Effect	BootSE	BootLLCI	BootULCI
M-1SD(low level)	-0.201	0.023	-0.250	-0.160
M	-0.104	0.013	-0.131	-0.080
M+1SD(high level)	-0.036	0.012	-0.062	-0.017

M mean, 1SD one standard deviation,BootSE bootstrap standard error,BootLLCI bootstrap lower limit

confidence interval, BootULCI bootstrap upper limit confidence interval.

Fig. 1 The conceptual framework of the moderated mediation model

Fig. 2 Simple slope analysis shows that physical frailty moderated the relationship between physical frailty and physical disability

Fig.3 Simple slope analysis shows that physical activity moderated the relationship between physical disability and HRQoL

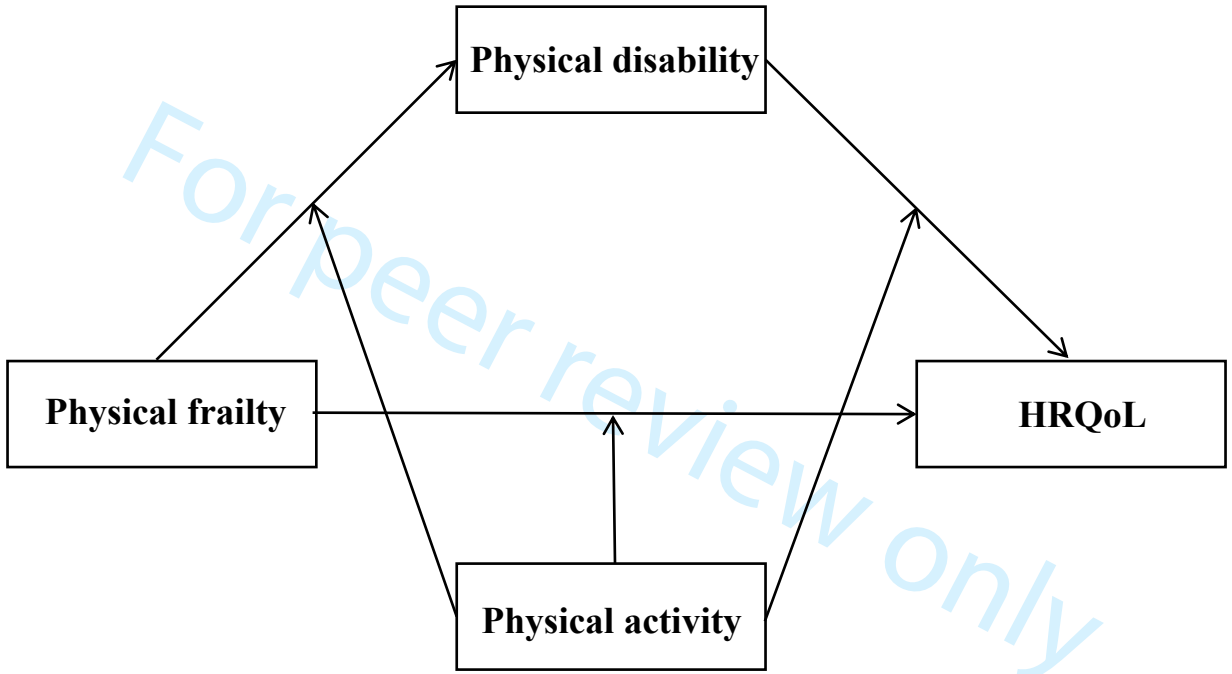

Fig1.The conceptual framework of the moderated mediation model

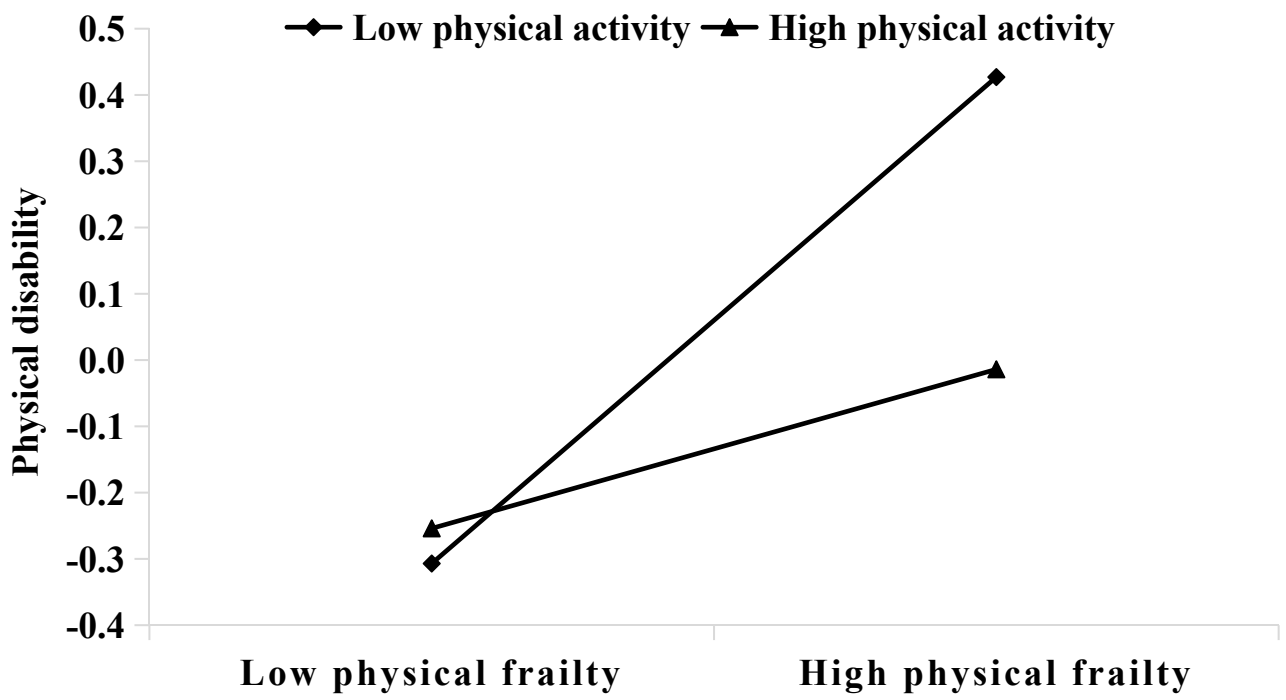

Fig2.Simple slope analysis shows that physical activity moderated the relationship between physical frailty and physical disability

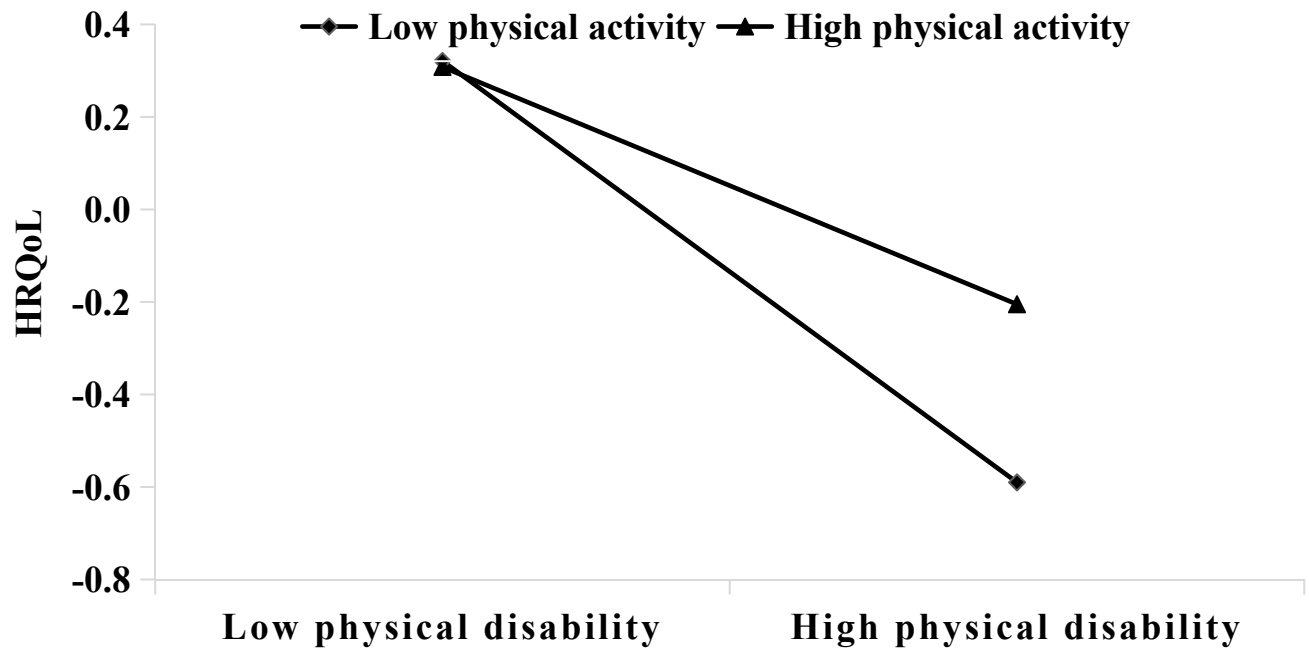

Fig3.Simple slope analysis shows that physical activity moderated the relationship between physical disability and HRQoL

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4-P5
Objectives	3	State specific objectives, including any prespecified hypotheses	P5-P6
Methods			
Study design	4	Present key elements of study design early in the paper	P6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P7
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	P7
Bias	9	Describe any efforts to address potential sources of bias	P10
Study size	10	Explain how the study size was arrived at	P6-P9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P6-P9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P9
		(*e*) Describe any sensitivity analyses	P9
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	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P10
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	P10-

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	P12
		(*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	P12
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	P15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P15
Generalisability	21	Discuss the generalisability (external validity) of the study results	P15
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	P17

*Give information separately for exposed and unexposed groups.

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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Physical frailty and health-related quality of life among Chinese rural older adults: A moderated mediation analysis of physical disability and physical activity

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Abstract

Objectives: The purpose of this study is to explore the mediating effect of physical disability, as well as the role of physical activity (PA) as a moderator in the relationship between physical frailty and health-related quality of life (HRQoL) among rural older adults in China.

Design: Cross-sectional analysis.

Setting: Rural households in Shandong of China (Rushan, Qufu, Laolin).

Participants and methods: A survey was conducted among 3,243 rural older adults. The data were collected using questionnaires measuring physical frailty, physical disability, HRQoL and PA. Bootstrap analyses were employed to explore the mediating effect of physical disability and also the moderating role of PA on physical frailty and HRQoL.

Results: After controlling for age and education, physical disability partially mediated the effect of physical frailty on HRQoL [indirect effect = -0.143, 95% confidence intervals (CI) = -0.175, -0.113], with the mediating effect accounting for 33.71% of the total effect. PA moderated the relationship between physical frailty and physical disability, as well as the relationship between physical disability and HRQoL.Specifically, the interaction term between physical frailty and PA significantly predicted physical disability (β = -0.120, t = -7.058, P< 0.001), and the interaction term between physical disability and PA also had a significant predictive effect on HRQoL (β = 0.115, t =6.104, P< 0.001).

Conclusions:PA appears to moderate the indirect effect of physical disability on the association between physical frailty and HRQoL. This study provides support for potential mechanisms in the association between physical frailty and HRQoL.Encouraging rural older adults to increase PA appropriately might improve HRQoL for older adults with physical frailty and physical disability problems.

Key words: HRQoL; Physical activity; Physical frailty; Physical disability; Rural older adults;Moderated mediation analysis

Strengths and limitations of this study

1. This is the first study to investigate the moderating and mediating factors of the relationship between physical frailty and HRQoL among older adults in rural China.
2. Moderated mediation model was used to explore the potential effect of physical disability and physical activity.
3. Cross-sectional data could not provide strong evidence of causation and may result in biased estimates of mediation effects.
4. Only two control variables were included in this study, and more confounding factors will be included to verify our results in the future.
5. More potential mechanisms related to physical frailty and HRQoL among older adults need to be explored by using longitudinal data in the future.

1. Introduction

Population aging has become a global social problem. As one of the world's most aging countries, China had 249 million people aged over 60 years in 2018, accounting for 17.9 percent of the total population[1].It is predicted that by 2050, older adults over 60 will account for more than 35.1% of the total population[2].With the increasing aging population and the extension of life expectancy, improving health-related quality of life (HRQoL) of older adults is an important public health issue. HRQoL is a predictive factor of mortality in older adults[3].Compared with urban older adults, the HRQoL of rural older adults is worse[4 5],which needs more attention.

Physical frailty is a medical syndrome caused by a variety of etiologies and causes, which is characterized by a decline in physical strength, endurance, and decreased physiological function[6]. With the increase of age, the risk of physical frailty increases[7].Frailty may lead to negative health consequences, including falls, reduced activity, reduced independence, frequent hospitalization, and disability[8].These adverse outcomes resulted in a decline in the quality of life of older adults. Previous cross-sectional and longitudinal studies have shown that frailty was negatively associated with HRQoL[9-11], and frail older adults reported worse HRQoL than those who were not frail[12].Although the association between physical frailty and quality of life has been confirmed, the underlying mechanism remains unclear.

The prevalence of physical disability is high among frail older adults[13 14].Some studies showed physical frailty was closely related to disability[15 16],and might be the precursor and cause

of disability[17].A national longitudinal study of 7,439 people over 65 in the US showed that frailty was a strong predictor of disability[18].A prospective two-year cohort study in Japan also showed that frailty and prophase of frailty increased the risk of disability[19].These findings suggest that physical frailty is associated with disability in older adults. Studies have also demonstrated that the quality of life worsened as the degree of disability increased,and the more severe the disability, the worse the quality of life[20]. Compared with non-disabled older adults, disabled older adults are more prone to falls, depression, anxiety, etc., and their HRQoL was significantly reduced. Therefore, we speculate that frailty may have an indirect effect on individual's HRQoL through the mediating effect of physical disability.

Physical frailty is considered to be reversible and preventable[21].Physical activity(PA) is a key factor of reverse and prevent frailty in older adults[22].Studies have found that physical activity moderated the relationship between chronic illness and functional limitations, and moderated functional disability and body function[23 24].PA can alleviate the decline of physical function in older adults and has a beneficial effect on functional limitations, physical frailty, disability and quality of life in older adults[25-27].Studies indicated the positive effect of physical activity on reducing adverse events caused by frailty in older people. Performing a physical activity of moderate to vigorous intensity would improve physical frailty and prevent the occurrence of disability when compared to the performance of a physical activity of low intensity, ultimately promote older adults' quality of life[28-30].Therefore, PA may moderate the direct and indirect relationship between physical frailty and HRQoL through physical disability as a

mediator.

In the present study,we used a cross-sectional study to examine the relationship between physical frailty and HRQoL, focusing on the mediating role of physical disability and the moderating role of PA in the relationship between physical frailty and HRQoL. The conceptual framework of the moderated mediation model was shown in Fig. 1.

2. Methods

2.1.1 Design and sample

This study was conducted from May to June, 2019 in Shandong province, China. A multistage stratified cluster sampling method was used to select participants, which was described in detail in a paper we have previously published[31].Three rural counties (Qufu, Laoling and Rushan) were selected according to the GDP per capita (2018) in Shandong. Within each selected county, five townships were randomly selected. Then, four villages were selected from each selected townships and the elderly aged 60 years old and above who were randomly selected from sample villages.All participants completed the questionnaire independently.A total of 3,600 respondents were recruited from 60 villages and 15 townships in 3 rural counties in Shandong province, of whom 3,243 completed the entire survey, with a response rate of 90.05%.

2.2. Variables and measurement

2.2.1 Independent variable

Physical frailty was measured by Frailty Phenotype[32].The scale is a widely used frailty screening

scale with good reliability and validity[33 34]. Frailty was defined based on the following five aspects: weight loss, exhaustion, low physical activity level, slowness, weakness.①Weight loss: In the past 1 year, participants' body mass index (BMI) decreased by >5.0% (except for personal deliberate weight loss). ②Exhaustion: Using the Center for Epidemiological Studies-Depression(CES–D)[35]: "How often in the last week did you feel this way?" (1) I could not get going and (2) I felt everything I did was an effort. Either of the above two questions that participants answered 3~4 days and most of the time, was considered exhaustion.③Low physical activity level: According the International Physical Activity Questionnaire-short Form (IPAQ-SF)[36 37],we used standard algorithms to calculate the Kcals consumed per week. The criterion is adjusted according to gender. Male: <383 Kcals/ week is a decrease in physical activity, while female: <270 Kcals/ week is a decrease in physical activity.④Slowness: Slowness was assessed via walking speed at 15 ft measured for 3 times, and we record the minimum value.The criterion is adjusted according to gender and height. Men: height≤173 cm and time≥7 seconds; height >173 cm and time≥6 seconds. Women: height≤159 cm and time≥7 seconds ;height >159 cm and time≥6 seconds. ⑤Weakness: Weakness was assessed by grip strength using a handgrip dynamometer was measured for 3 times, and we record the maximum value, adjusted for gender and BMI. Men: BMI≤24 and grip strength≤29;BMI 24.1-26and grip strength≤30;BMI 26.1-28 and grip strength ≤30;BMI > 28 and grip strength≤32.Women: BMI≤23 and grip strength≤17;BMI 23.1-26 and grip strength≤17.3;BMI 26.1-29 and grip strength≤18;BMI>29 and grip strength≤21.

2.2.2 Dependent variables

HRQoL was measured by the health utility value of EQ-5D-5L[38].The EQ-5D-5L consists of the EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L descriptive system has five elements (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and each element includes five levels (no problems, some problems, moderate problems, severe problems and extreme problems). The latest EQ-5D-5Lhealth utility scores method refers to Chinese integral conversion table[38].The range of utility value is [-0.391, 1.000]. A higher score indicates better health condition of the respondents.Cronbach's alpha was 0.761 in this study.

2.2.3 Mediator

Physical disability was evaluated by the Activity of Daily Living Scale (ADLS), which was developed by Lawton and Brody in 1969 to measure the disability of older adults[39 40]. The Scale consists of 14 items, including Physical Self-Maintenance Scale (PSMS) and Instrumental Activities of Daily Living (IADL). The total score is 14-56, with higher scores indicating increased physical disability. A score of 14 and lower indicates completely normal physical ability, a score between 15 and 22 is defined as mild disability, and a score of 23 and higher is defined as severe disability. ADLS is recommended by WHO and has been widely used in older adults in China, with good reliability and validity[41].Cronbach's alpha was 0.764 in this study.

2.2.4 Moderator

PA was assessed using the IPAQ-SF[36 37].The questionnaire contains 7 questions, 6 of which were

about physical activity. The IPAQ-SF investigates the PA of the individuals in the last 7 days. The questionnaire involved three types of intensity activities, including vigorous physical activity (VPA =8.0 metabolic equivalent [METs]), moderate physical activity (MPA =4.0 METs), and low physical activity (LPA =3.3 METs).PA of each person engaged in a certain intensity per week is the METs value corresponding to that physical activity × weekly frequency × daily time, and the sum of three PA is the total PA (met-h /week). The greater the overall physical activity value, the higher the physical activity.

2.3 Data analysis

To analyze the data, categorical variables were expressed using frequency and percentages (%) and continuous data were described using mean (standard deviation). Spearman correlations coefficient was used to analyze the correlation among physical frailty, physical disability, and HRQoL. All these analyses were performed using IBM SPSS 24.0 (IBM Corp., Armonk, NY, USA). All regression coefficients were tested by the bias-corrected percentile Bootstrap method. The theoretical model was tested by estimating the 95% confidence interval (CI) for mediation and moderating effects with 5,000 sampled with repetition. If the 95% CI did not include 0, it meant that the statistics was significant. To illuminate the moderating effect, the moderated variable (PA) is divided into two levels of high and low according to one standard deviation above and below the mean(M+1SD/M-1SD)[42-44].The Split-Plot analysis method was used to further examine the direction of the moderation effect, and draw a diagram to explain the

moderation effect[45].The mediation model and moderated mediation model were tested with the PROCESS V3.3 macro for SPSS[46].In the current study, we selected Model 4 and Model 59 to analyze the mediating effect and moderated mediation effect. In addition,through t test and ANOVA analysis, we found that HRQoL was related to age and education. Previous studies have also found HRQoL was associated with age and education[47 48]. We controlled age and education in this study.Sampling weights were used in all of the analyses to adjust for the survey design.

2.4 Patient and public involvement statement

This research was done without patient involvement. No patients were involved in developing the hypothesis and plans for design of this study either. The results would not be disseminated to study participants or any other individuals or communities.

2.5 Ethical considerations

The study was approved by the Ethics Committee of School of Public Health in Shandong University, P. R. China. The participants have been informed of the purpose and procedures of the study before the investigation. Before the study began, participants had signed written informed consent indicating that they were fully aware of the study procedures.

3. Results

3.1 Common method biases

We used Harman single factor test to conduct a common method biases test[49].The results show

that there are 12 factors with eigenvalues greater than 1, and the variance explained by the first factor is 17.92%, which is less than 40% of the critical standard, indicating that there are no serious common method biases in this study.

3.2 Socio-demographic characteristics of the participants

There were 3,243 participants, comprising 2,060 (63.5%) women and 1,182 (36.5%) men. The average age was 69.88 (SD=6.10) years, ranging from 60 to 97 years. Of the participants, 25.5% were single. About 72.4% had chronic disease. The majority (81.9%) were empty nest elderly.

3.3 Bivariate correlations of main variables

The mean, standard deviation/ Median ($Quartile_1$, $Quartile_3$) and correlation coefficient of each variable were shown in Table 1. Physical frailty was positively correlated with physical disability ($\rho = 0.283$, $P< 0.01$), physical frailty was negatively correlated with HRQoL ($\rho = -0.429$, $P< 0.01$) and PA ($\rho = -0.378$, $P<0.01$). Physical disability was negatively correlated with HRQoL ($\rho = -0.378$, $P<0.01$) and PA ($\rho = -0.194$, $P<0.01$). PA was positively correlated with HRQoL ($\rho = 0.258$, $P<0.01$).

3.4Mediation effect analysis

Model 4 in the SPSS macro compiled by Hayes 2013[46] was used to test the mediating effect of physical disability in the relationship between physical frailty and HRQoL under the control variable of age, education. As shown in Table 2 and Table 3, physical frailty had a significant predictive effect on quality of life ($\beta = -0.423$, $t = -26.031$, $P< 0.001$), and the direct predictive effect of frailty on quality of life was still significant when the mediating variable physical

disability was added. Meanwhile, physical frailty had a significant positive predictive effect on physical disability (β = 0.295, t = 17.729, P < 0.001). Physical disability also had a significant negative predictive effect on HRQoL (β = -0.482, t = -32.407, P< 0.001). In addition, the upper and lower limits of the Bootstrap 95% CI for the direct effect of physical frailty on HRQoL and the mediating effect of physical disability on physical frailty and HRQoL did not include 0(Table 3), indicating that the mediating effect was significant. The mediating effect value was-0.143 and the 95% CI was [-0.175, -0.113], which accounted for 33.71% of the total effect. This showed that disability played a partial mediating role in the relationship between physical frailty and HRQoL.

3.5 Moderated mediation effect analysis

PROCESS macro method (Model 59)compiled by Hayes (2013)[46] was used to test the moderated mediation model while controlling for age and education(Table 4 and Table 5).After PA was put into the model, the interaction term between physical frailty and PA significantly predicted physical disability (β = -0.120, t = -7.058, P< 0.001) (Table4, Model 1), and the interaction term between physical disability and PA also had a significant predictive effect on HRQoL (β = 0.115, t =6.104, P< 0.001). But the interaction term between physical frailty and PA had no effect on HRQoL(Table4, Model 2).These results suggested PA played a moderating role in the relationships between physical frailty and physical disability and between physical disability and HRQoL.However, PA did not significantly moderate the relationships between physical frailty and HRQoL. Simple slope analyses indicated that the significant interaction at 1

SD belowthe mean(M-1SD) and 1 SD above the mean(M+1SD) of physical activity (See Fig. 2 andFig. 3).Physical frailty had a significant predictive effect on the disability of individuals with high-level((M+1SD) or low-level(M-1SD) PA, but the predictive effect of physical frailty on physical disability was stronger for individuals with low-level PA(b_{simple} = 0.370, t = 16.979, P< 0.001) than for individuals with high-level PA,as shown in Fig. 2 (b_{simple} = 0.120, t = 4.322, P< 0.001).Fig. 3 showed that for high levels of PA individuals, the effect of physical disability and HRQoL was significant (b_{simple}= -0.304, t = -9.149, P< 0.001). However, for low-level of PA individuals, the effect of physical disability and HRQoL was still significant but considerably stronger (b_{simple} = -0.543, t = -28.654, P< 0.001).In addition, as the level of physical activity increased, the mediating effect of physical disability on the relationship between physical frailty and HRQoL declined (Table 5).

4. Discussion

In this study, a moderated mediation model was established with the mediation role of physical disability on the relationship between physical frailty and HRQoL, as well as the role of PA as a moderator in this indirect path between physical frailty and HRQoL.These findings preliminarily elucidate the potential causes of physical frailty on HRQoL and facilitate the development of targeted interventions for individuals so as to improve HRQoL in rural older adults.

Consistent with previous studies[50 51], we find that physical frailty has a negative association with HRQoL.This suggests that as the degree of physical frailty increases, the quality of life in older adults becomes worse. Although many studies have established a direct relationship

between frailty and HRQoL, few have explored the underlying mechanisms of this relationship. Our study suggests that physical disability mediates the association between physical frailty and HRQoL, with the mediating rate of 33.71%. A study also suggested that physical disability was one of the potential factors underlying the association between frailty and HRQoL, which was similar with our study[52].

The current study indicates that physical frailty is associated with disability, which is consistent with a study by Kojuma G[53].Frail older adults are very vulnerable to adverse health effects.A study indicated the risk of disability in frail older adults was 12- to 13-fold increased than that in non-frail older adults[54].Meanwhile, this study also demonstrates a negative predictive effect of disability on individual HRQoL,which was consistent with previous studies[55 56]. The possible explanation is that disabled older adults' poor self-care ability deteriorates their health, then their normal physiological activities are restricted, physiological function is declined, and social interaction is reduced, which adversely affect their physical and mental health and ultimately reduce HRQoL. One study found that disability was the most important health problem for older adults, which seriously affected their quality of life in old adults' later years[57].The disability was the most important factor that contributed to decreasing quality of life in older adults.Physical disability has been proved to be associated with increased chronic diseases, and premature mortality[58 59],all of which could adversely affect the quality of life of older adults[60].Therefore, physical frailty may reduce HRQoL of rural older adults by increasing their disability.

In the present study, we also find that PA appears to play a moderating role in the indirect effect between physical frailty and HRQoL. A larger indirect effect is observed among rural older adults with low-level of PA than among those with average or high-level of PA. Specifically, PA appears to moderate the relationship between physical frailty and physical disability, and between physical disability and HRQoL.For older adults with low-level PA, the impact of physical frailty on physical disability is stronger than older adults with high-level PA. This finding indicates that PA appears to moderate the relationship between physical frailty and physical disability. We speculate that older adults with low-level PA may have a decline in their physiological system reserves, leading to a deterioration of their functional status and ultimately increasing the possibility of physical frailty and disability[61].A systematic review showed that older adults without exercise habits were at greater risk of developing frailty. Taichi, resistance sports, and other physical activities might effectively improve the health of older adults, reduce the symptoms of physical weakness, and prevent the occurrence of physical disability[62].Compared with older adults with high-level PA, older adults with low-level PA are more vulnerable to the negative effects of physical frailty. As a result, physical frailty may cause more interference in older adults with low-level PA and increase the risk of physical disability.

We also find that physical disability has a significant impact on quality of life at both high and low-level of PA. Compared with older adults with high levels of PA, physical disability is more likely to adversely affect HRQoL of older adults with low-level PA.A study showed that low-level PA was a major contributing factor for older adults' disability[63].As the level of

disability increases, the individuals with low-level of PA experience a more serious functional decline and become more worried about the health status, thus further negatively affect the HRQoL[64]. In addition, physical disability has a greater effect on individuals with low-level PA than high-level PA, which indicates that PA plays a moderating role between physical disability and HRQoL.One study found that PA could improve the physical function and daily life activities of disabled older adults, and ultimately improved the life of older adults quality[65].Therefore, a low-level of PA might be associated with poor quality of life in rural older adults with high disability.

However, physical activity does not appear to moderate the direct relationship between physical frailty and HRQoL. Physical frailty may lead to a decline in physical function, muscle strength and physical activity in older adults, which may increases the risk of adverse health outcomes and ultimately affects HRQoL of older adults. Currently, there are few studies on the moderating role of physical activity between physical frailty and HRQoL. Further research is needed to explore the underlying reasons for such findings.

Based on our findings, we recommend that community health managers should focus on ensuring the medical assistance, life care of older adults with physical frailty or physical disability. Besides, rural communities should establish some public facilities or organize some public activities to encourage older adults to participate in sports activities, and ultimately improve health and promote their HRQoL.There are several limitations in this study. First, our study was based on a cross-sectional study, which could not provide strong evidence of causation.

In addition, using cross-sectional data to examine longitudinal mediation effects can lead to biased estimates of mediation effects[66]. Future research could adopt a longitudinal design or experiments to explore the causal relationship between physical frailty and HRQoL. Secondly, the data in this study comes from the participants' self-report information, which might result in recall bias. Thirdly, this study only included age and education as control variables. The study may also be affected by other confounding factors. In the future, we will include more confounding factors related to quality of life to verify our findings. Fourthly,physical disability has a partly mediating effect on the relationship between physical frailty and HRQoL, which indicates that there are other mediating variables in this relationship. More potential mechanisms related to the association between physical frailty and HRQoL among older adults need to be explored in the future.

Conclusion

This study shows that physical frailty is related to HRQoL, and physical disability appears to mediate the relationship between physical frailty and HRQoL, and PA appears to moderates the mediating relationship. A greater effect is observed among rural older adults with low-level of PA than that among those with high-level of PA. This provides support for elucidate the underlying mechanism of the relationship between physical frailty and HRQoL and form an effective way to improve the HRQoL ofolder adults in rural areas.

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Contributors

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

None declared.

Patient consent for publication

Not required.

REFERENCES

1. NBSC. Statistical communiqué of the People's Republic of China on the 2017 national economic and social development. 2017 [updated February 28,2018. Available from: http://www.stats.gov.cn/english/PressRelease/201802/t20180228_1585666.html.

2. United Nations DESA, Population Division. World Population Ageing 2017:Highlights 2017 [updated 2017. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf .

3. Brown DS, Thompson WW, Zack MM, et al. Associations Between Health-Related Quality of Life and Mortality in Older Adults. *Prevention Science* 2015;16(1):21-30. doi: 10.1007/s11121-013-0437-z

4. Zhou B, Chen K, Wang J, et al. Quality of Life and Related Factors in the Older Rural and Urban Chinese Populations in Zhejiang Province. *J Appl Gerontol* 2011;30(2):199-225. doi: 10.1177/0733464810361346

5. Zhou Z, Zhou Z, Gao J, et al. Urban-rural difference in the associations between living arrangements and the health-related quality of life (HRQOL) of the elderly in China-Evidence from Shaanxi province. *PLoS One* 2018;13(9):e0204118. doi: 10.1371/journal.pone.0204118 [published Online First: 2018/09/21]

6. Morley JE, Vellas B, Van Kan GA, et al. Frailty Consensus: A Call to Action. *J Am Med Dir Assoc* 2013;14(6):392-97. doi: 10.1016/j.jamda.2013.03.022

7. Collard RM, Boter H, Schoevers RA, et al. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc* 2012;60(8):1487-92. doi: 10.1111/j.1532-5415.2012.04054.x [published Online First: 2012/08/14]

8. Vermeiren S, Vellaazzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *J Am Med Dir Assoc* 2016;17(12) doi: 10.1016/j.jamda.2016.09.010

9. Lee IC, Chiu YH, Lee CY. Exploration of the importance of geriatric frailty on health-related quality of life. *Psychogeriatrics* 2016;16(6):368-75. doi: 10.1111/psyg.12179 [published Online First: 2016/01/13]

10. Ferrer A, Formiga F, Cunillera O, et al. Predicting factors of health-related quality of life in octogenarians: a 3-year follow-up longitudinal study. 2015;24(11):2701-11.

11. Provencher V, Sirois MJ, Émond M, et al. Frail older adults with minor fractures show lower health-related quality of life (SF-12) scores up to six months following emergency department discharge. *Health Qual Life Outcomes* 2016;14:40. doi: 10.1186/s12955-016-0441-7 [published Online First: 2016/03/10]

12. Kanauchi M, Kubo A, Kanauchi K, et al. Frailty, health-related quality of life and mental well-being in older adults with cardiometabolic risk factors. *Int J Clin Pract* 2008;62(9):1447-51. doi: 10.1111/j.1742-1241.2008.01830.x [published Online First: 2008/07/23]

13. Fullerthomson E, Yu B, Nurujeter A, et al. Basic ADL Disability and Functional Limitation Rates Among Older Americans From 2000–2005: The End of the Decline? *J Gerontol A Biol Sci Med Sci* 2009;64(12):1333-36. doi: 10.1093/gerona/glp130

14. Picavet HSJ, Hoeymans N. Physical disability in The Netherlands: Prevalence, risk groups and time trends. *Public Health* 2002;116(4):231-37. doi: 10.1038/sj.ph.1900864

15. Evenhuis HM, Hermans H, Hilgenkamp TIM, et al. Frailty and Disability in Older Adults with Intellectual Disabilities: Results from the Healthy Ageing and Intellectual Disability Study. *J Am Geriatr Soc* 2012;60(5):934-38. doi: 10.1111/j.1532-5415.2012.03925.x

16. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised older people. *Age Ageing* 2014;43(4):477-84. doi: 10.1093/ageing/aft181

17. Papachristou E, Wannamethee SG, Lennon LT, et al. Ability of Self-Reported Frailty Components to Predict Incident Disability, Falls, and All-Cause Mortality: Results From a Population-Based Study of Older British Men. *J Am Med Dir Assoc* 2017;18(2):152-57. doi: 10.1016/j.jamda.2016.08.020 [published Online First: 2016/10/16]

18. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133 [published Online First: 2015/08/25]

19. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older adults: a prospective cohort study. *BMJ open* 2015;5(9):e008462. doi: 10.1136/bmjopen-2015-008462 [published Online First: 2015/09/05]

20. Medhi GK, Sarma J, Pala S, et al. Association between health related quality of life (HRQOL) and activity of daily living (ADL) among elderly in an urban setting of Assam, India. *J Family Med Prim Care* 2019;8(5):1760-64. doi: 10.4103/jfmpc.jfmpc_270_19 [published Online First: 2019/06/15]

21. Tavassoli N, Guyonnet S, Abellan Van Kan G, et al. Description of 1,108 older patients referred by their physician to the "Geriatric Frailty Clinic (G.F.C) for Assessment of Frailty and Prevention of Disability" at the gerontopole. *J Nutr Health Aging* 2014;18(5):457-64. doi: 10.1007/s12603-014-0462-z [published Online First: 2014/06/03]

22. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, et al. Exercise training as a drug to treat age associated frailty. *Free Radic Biol Med* 2016;98:159-64. doi: 10.1016/j.freeradbiomed.2016.03.024 [published Online First: 2016/03/30]

23. Rector JL, Marceau K, Friedman EM. Moderation of the Association Between Chronic Medical Conditions and Functional Limitations Over Time by Physical Activity: Effects of Age. *J Gerontol A Biol Sci Med Sci* 2020;75(1):168-74. doi: 10.1093/gerona/glz020 [published Online First: 2019/02/21]

24. Palmer RF, Espino DV, Dergance JM, et al. The role of physical activity and diabetes status as a moderator: functional disability among older Mexican Americans. *Age Ageing* 2012;41(6):752-8. doi: 10.1093/ageing/afs106 [published Online First: 2012/10/12]

25. Keysor JJ. Does late-life physical activity or exercise prevent or minimize disablement? A critical review of the scientific evidence. *Am J Prev Med* 2003;25(3 Suppl 2):129-36. doi: 10.1016/s0749-3797(03)00176-4 [published Online First: 2003/10/14]

26. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? *J Gerontol A Biol Sci Med Sci* 2001;56(7):M412-23. doi: 10.1093/gerona/56.7.m412 [published Online First: 2001/07/11]

27. Rejeski WJ, Mihalko SL. Physical Activity and Quality of Life in Older Adults. *J Gerontol A Biol Sci Med Sci* 2001;56(suppl_2):23-35. doi: 10.1093/gerona/56.suppl_2.23

28. Casas-Herrero A, Izquierdo M. Physical exercise as an efficient intervention in frail elderly persons. *An Sist Sanit Navar* 2012;35(1):69-85. doi: 10.4321/s1137-66272012000100007 [published Online First: 2012/05/04]

29. Mañas A, Del Pozo-Cruz B, Guadalupe-Grau A, et al. Reallocating Accelerometer-Assessed Sedentary Time to Light or Moderate- to Vigorous-Intensity Physical Activity Reduces Frailty Levels in Older Adults: An Isotemporal Substitution Approach in the TSHA Study. *J Am Med Dir Assoc* 2018;19(2):185.e1-85.e6. doi: 10.1016/j.jamda.2017.11.003 [published Online First: 2017/12/23]

30. Barnett A, Smith B, Lord SR, et al. Community-based group exercise improves balance and reduces falls in at-risk older people: a randomised controlled trial. *Age Ageing* 2003;32(4):407-14. doi: 10.1093/ageing/32.4.407 [published Online First: 2003/07/10]

31. Jing Z, Li J, Wang Y, et al. The mediating effect of psychological distress on cognitive function and physical frailty among the elderly: Evidence from rural Shandong, China. *J Affect Disord* 2020;268:88-94. doi: 10.1016/j.jad.2020.03.012 [published Online First: 2020/03/12]

32. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]

33. Buta BJ, Walston JD, Godino JG, et al. Frailty assessment instruments: Systematic characterization of the uses and contexts of highly-cited instruments. *Ageing Res Rev* 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003 [published Online First: 2015/12/18]

34. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC Geriatr* 2013;13:64. doi: 10.1186/1471-2318-13-64 [published Online First: 2013/06/22]

35. Radloff LS. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. *Appl Psychol Meas* 1977;1(3):385-401. doi: 10.1177/014662167700100306

36. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical Activity Questionnaire. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 2014;35(8):961-4. [published Online First: 2014/11/08]

37. Macfarlane DJ, Lee CC, Ho EY, et al. Reliability and validity of the Chinese version of IPAQ (short, last 7 days). *J Sci Med Sport* 2007;10(1):45-51. doi: 10.1016/j.jsams.2006.05.003 [published Online First: 2006/06/30]

38. Luo N, Liu G, Li M, et al. Estimating an EQ-5D-5L Value Set for China. *Value Health* 2017;20(4):662-69. doi: 10.1016/j.jval.2016.11.016 [published Online First: 2017/04/15]

39. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist* 1969;9(3):179-86. doi: 10.1093/geront/9.3_Part_1.179 [published Online First: 1969/01/01]

40. Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc* 1971;19(6):465-81. doi: 10.1111/j.1532-5415.1971.tb01206.x [published Online First: 1971/06/01]

41. Chen P, Yu ES, Zhang M, et al. ADL dependence and medical conditions in Chinese older persons: a population-based survey in Shanghai, China. *J Am Geriatr Soc* 1995;43(4):378-83. doi: 10.1111/j.1532-5415.1995.tb05811.x [published Online First: 1995/04/01]

42. Ng KY, Ang S, Chan KY. Personality and leader effectiveness: a moderated mediation model of leadership self-efficacy, job demands, and job autonomy. *J Appl Psychol* 2008;93(4):733-43. doi: 10.1037/0021-9010.93.4.733 [published Online First: 2008/07/23]

43. Preacher KJ, Rucker DD, Hayes AF. Addressing Moderated Mediation Hypotheses: Theory, Methods, and Prescriptions. *Multivariate behavioral research* 2007;42(1):185-227. doi: 10.1080/00273170701341316 [published Online First: 2007/01/01]

44. Holmbeck GN. Toward terminological, conceptual, and statistical clarity in the study of mediators and moderators: examples from the child-clinical and pediatric psychology literatures. *Journal of consulting and clinical psychology* 1997;65(4):599-610. doi: 10.1037//0022-006x.65.4.599 [published Online First: 1997/08/01]

45. Cohen J, Cohen P, West SG, et al. Applied multiple regression/correlation analysis for the behavioral sciences: Routledge 2013.

46. Bolin JH. Hayes, Andrew F. (2013). Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. New York, NY: The Guilford Press. *J Educ Meas* 2014;51(3):335-37. doi: 10.1111/jedm.12050

47. Bao XY, Xie YX, Zhang XX, et al. The association between multimorbidity and health-related quality of life: a cross-sectional survey among community middle-aged and elderly residents in southern China. *Health Qual Life Outcomes* 2019;17(1):107. doi: 10.1186/s12955-019-1175-0 [published Online First: 2019/06/27]

48. Chapman B, Duberstein P, Lyness JM. Personality traits, education, and health-related quality of life among older adult primary care patients. *J Gerontol B Psychol Sci Soc Sci* 2007;62(6):P343-52. doi: 10.1093/geronb/62.6.p343 [published Online First: 2007/12/15]

49. Podsakoff PM, MacKenzie SB, Lee JY, et al. Common method biases in behavioral research: a critical review of the literature and recommended remedies. *J Appl Psychol* 2003;88(5):879-903. doi: 10.1037/0021-9010.88.5.879 [published Online First: 2003/10/01]

50. Kanwar A, Singh M, Lennon R, et al. Frailty and health-related quality of life among residents of long-term care facilities. *J Aging Health* 2013;25(5):792-802. doi: 10.1177/0898264313493003 [published Online First: 2013/06/27]

51. Mulasso A, Roppolo M, Rabaglietti E. The role of individual characteristics and physical frailty on health related quality of life (HRQOL): a cross sectional study of Italian community-dwelling older adults. *Arch Gerontol Geriatr* 2014;59(3):542-8. doi: 10.1016/j.archger.2014.08.012 [published Online First: 2014/09/14]

52. Huaxue L, Taifang L, Wenjing Y, et al. Status of frailty and its effect path on quality of life among the elderly in community. *Chinese Nursing Research* 2019;33(21):3645-49.

53. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282 [published Online First: 2016/08/26]

54. Feng L, Zin Nyunt MS, Gao Q, et al. Cognitive Frailty and Adverse Health Outcomes: Findings From the Singapore Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc* 2017;18(3):252-58. doi: 10.1016/j.jamda.2016.09.015 [published Online First: 2016/11/14]

55. Akosile CO, Mgbeojedo UG, Maruf FA, et al. Depression, functional disability and quality of life among Nigerian older adults: Prevalences and relationships. *Arch Gerontol Geriatr* 2018;74:39-43. doi: 10.1016/j.archger.2017.08.011 [published Online First: 2017/09/28]

56. Shin KR, Byeon YS, Kang Y, et al. A study on physical symptom, activity of daily living, and health-related quality of life (HRQoL) in the community-dwelling older adults. *Taehan Kanho Hakhoe chi* 2008;38(3):437-44. doi: 10.4040/jkan.2008.38.3.437 [published Online First: 2008/07/08]

57. Crimmins EM. Trends in the health of the elderly. *Annu Rev Public Health* 2004;25:79-98. doi: 10.1146/annurev.publhealth.25.102802.124401 [published Online First: 2004/03/16]

58. Khan ZA, Singh C, Khan T. Correlates of physical disability in the elderly population of Rural North India (Haryana). *J Family Community Med* 2018;25(3):199-204. doi: 10.4103/jfcm.JFCM_160_17 [published Online First: 2018/09/18]

59. Wei M, Li J, Wang H. Impact of the disability trajectory on the mortality risk of older adults in China. *Arch Gerontol Geriatr* 2018;74:174-83. doi: 10.1016/j.archger.2017.10.015 [published Online First: 2017/11/11]

60. Gobbens RJ. Associations of ADL and IADL disability with physical and mental dimensions of quality of life in people aged 75 years and older. *PeerJ* 2018;6:e5425. doi: 10.7717/peerj.5425 [published Online First: 2018/08/21]

61. Rejeski WJ, Brawley LR, Haskell WL. The prevention challenge: an overview of this supplement. *Am J Prev Med* 2003;25(3 Suppl 2):107-9. doi: 10.1016/s0749-3797(03)00173-9 [published Online First: 2003/10/14]

62. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154. doi: 10.1186/s12877-015-0155-4 [published Online First: 2015/12/03]

63. Kortebein P, Ferrando A, Lombeida J, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older adults. *JAMA* 2007;297(16):1772-4. doi: 10.1001/jama.297.16.1772-b [published Online First: 2007/04/26]

64. Ávila-Funes JA, Pina-Escudero SD, Aguilar-Navarro S, et al. Cognitive impairment and low physical activity are the components of frailty more strongly associated with disability. *J Nutr Health Aging* 2011;15(8):683-9. doi: 10.1007/s12603-011-0111-8 [published Online First: 2011/10/05]

65. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First: 2011/04/01]

66. Maxwell SE, Cole DA, Mitchell MA. Bias in Cross-Sectional Analyses of Longitudinal Mediation: Partial and Complete Mediation Under an Autoregressive Model. *Multivariate Behav Res* 2011;46(5):816-41. doi: 10.1080/00273171.2011.606716 [published Online First: 2011/09/30]

Table 1 Spearmancorrelations coefficients of main variables among the participants in Shandong, China, 2019(N=3243)

Variable	M±SD/M(P_{25},P_{75})	1	2	3	4
1.Physical frailty	1.511±1.071	1			
2.Physical disability	16.994±4.36	0.283**	1		
3.Physical activity	2772(693,4158)	-0.378**	-0.194**	1	
4.HRQoL	0.896±0.161	-0.429**	-0.378**	0.258**	1

M±SD: mean±standard deviation ;M (P25,P75): Median($Quartile_1$,$Quartile_3$)

1,2,4 follow normal distribution and are described as M±SD.

3 does not follow normaldistribution and isdescribedasM (P_{25}, P_{75}).

**P<0.001

Table 2 Testing the mediation effect of physical disability between physical frailty and HRQoL among the participants in Shandong, China, 2019

Predictors	Model1(HRQoL)		Model2(Physical disability)		Model3(HQRoL)	
	β	t	β	t	β	t
Age	-0.018	-0.731	0.166	6.349***	0.061	2.758**
Education	0.010	0.162	-0.182	-8.326***	-0.084	-4.507***
Physical frailty	-0.423	-26.031***	0.295	17.729***	-0.280	-18.957***

Physical disability			-0.482	-32.407***
R^2	0.181	0.141	0.381	
F	238.859***	176.932***	499.748***	

P<0.01,*P<0.001

Table 3 Total effect, direct effect and mediation effect

	Effect size	BootSE	BootCI		Relative effect value
			Low	High	
Total effect	-0.423	0.020	-0.461	-0.382	
Direct effect	-0.280	0.017	-0.313	-0.247	66.29%
Indirecteffect	-0.143	0.016	-0.175	-0.113	33.71%

BootSEbootstrap standard error, BootCI bootstrap confidence interval

Table 4Testing the moderated mediation effect of physical frailty on HRQoLamong the participants in Shandong, China, 2019

Predictors	Model 1(Physical disability)		Model 2(HRQoL)	
	β	t	β	t
Age	0.154	5.956***	0.062	2.763**
Education	-0.181	-8.393***	-0.072	-3.830***
Physical frailty	0.246	13.965***	-0.258	-16.687***
Physical activity	-0.104	-5.555***	0.091	4.675***
Physical frailty×PA	-0.120	-7.058***	0.011	0.682
Physical disability			-0.422	-24.375***
Physical disability×PA			0.115	6.104***
R^2	0.159		0.390	
F	122.004***		295.850***	

** $P<0.01$,*** $P<0.001$

Table 5 Mediating effect values at different levels of physical activityamong the participants in Shandong, China, 2019

Physical activity	Effect	BootSE	BootLLCI	BootULCI

M-1SD(low level)	-0.201	0.023	-0.250	-0.160
M	-0.104	0.013	-0.131	-0.080
M+1SD(high level)	-0.036	0.012	-0.062	-0.017

M mean, 1SD one standard deviation,BootSEbootstrap standard error,BootLLCIbootstrap lower limit confidence interval, BootULCIbootstrap upper limit confidence interval.

Fig. 1 The conceptual framework of the moderated mediation model

Fig. 2 Simple slope analysis shows that physical frailty moderated the relationship between physical frailty and physical disability

Fig.3 Simple slope analysis shows that physical activity moderated the relationship between physical disability and HRQoL

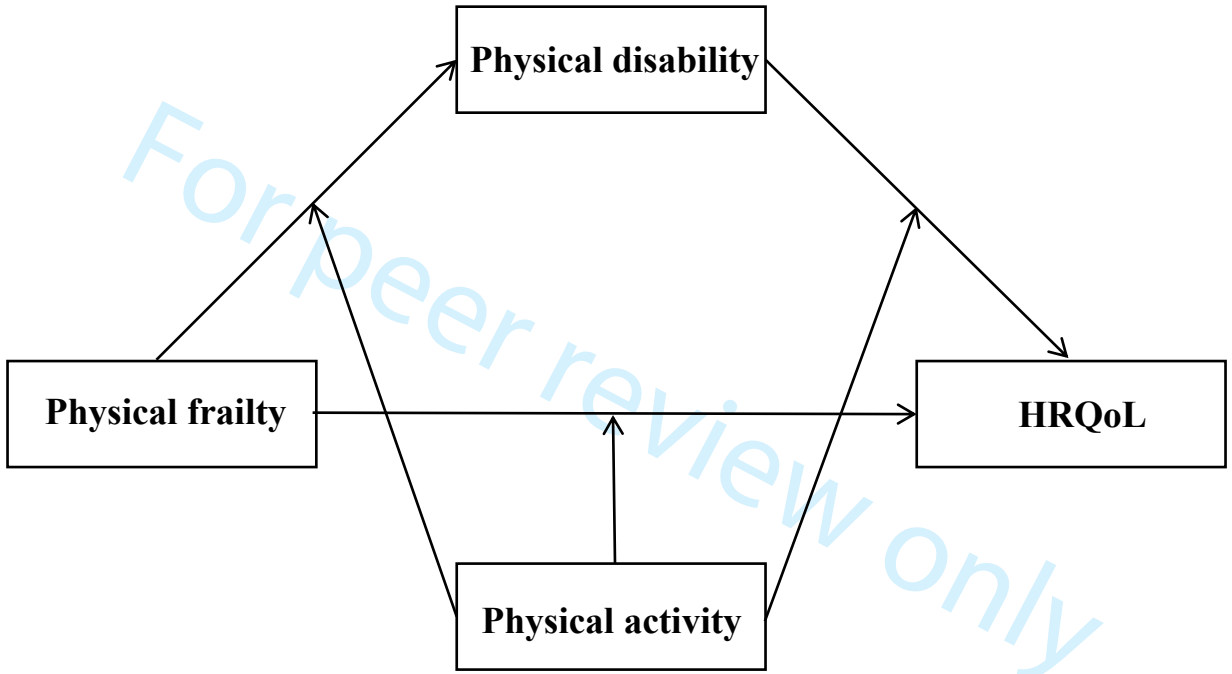

Fig1.The conceptual framework of the moderated mediation model

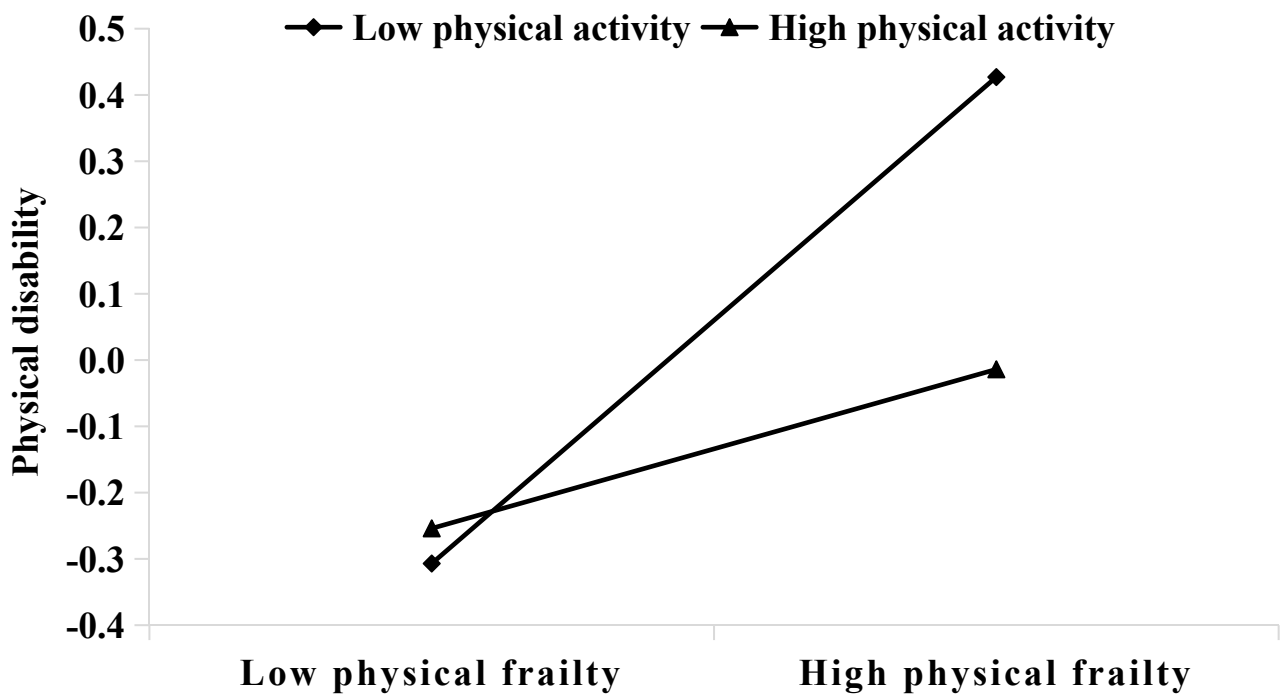

Fig2.Simple slope analysis shows that physical activity moderated the relationship between physical frailty and physical disability

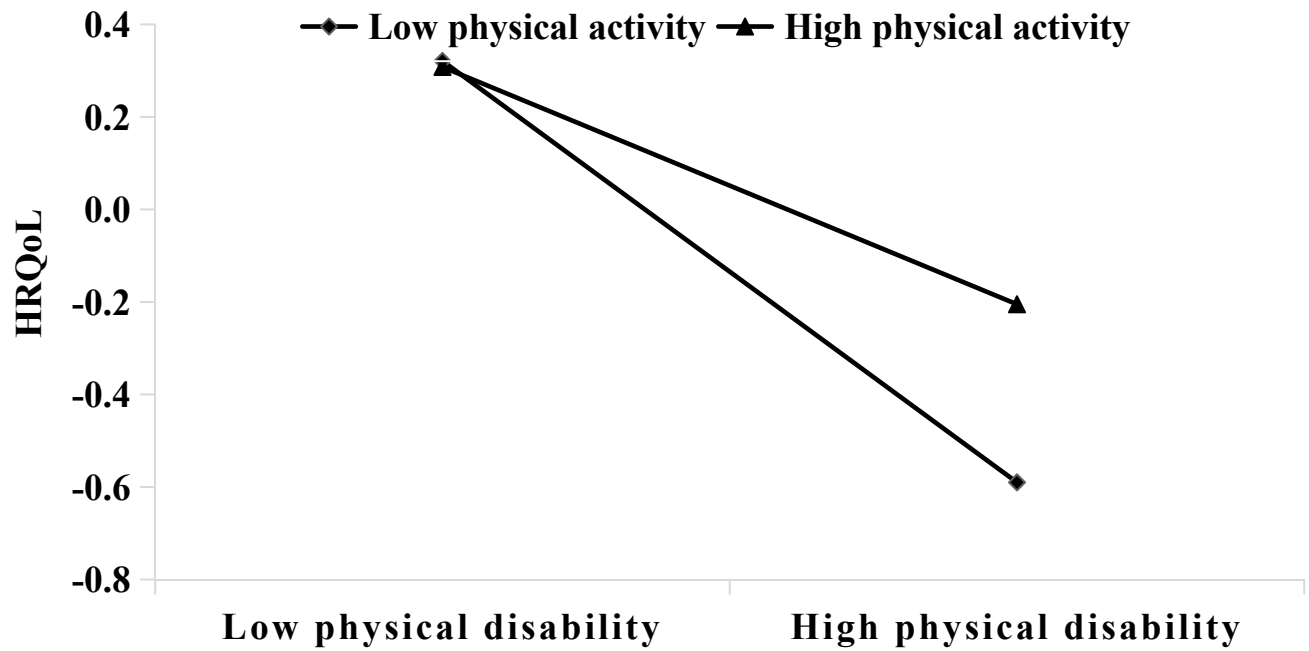

Fig3.Simple slope analysis shows that physical activity moderated the relationship between physical disability and HRQoL

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4-P5
Objectives	3	State specific objectives, including any prespecified hypotheses	P5-P6
Methods			
Study design	4	Present key elements of study design early in the paper	P6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P7
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	P7
Bias	9	Describe any efforts to address potential sources of bias	P10
Study size	10	Explain how the study size was arrived at	P6-P9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P6-P9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P9
		(*e*) Describe any sensitivity analyses	P9
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	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P10
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	P10-

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	P12
		(*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	P12
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	P15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P15
Generalisability	21	Discuss the generalisability (external validity) of the study results	P15
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	P17

*Give information separately for exposed and unexposed groups.

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.