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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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-042496
Article Type:	Original research
Date Submitted by the Author:	07-Jul-2020
Complete List of Authors:	Hao, Wenting; School of public health Li, Jie; Shandong University School of Public Health Fu, Peipei; Shandong University Cheeloo College of Medicine Zhao, Dan; Shandong University, school of public health Jing, Zhengyue; Shandong University Cheeloo College of Medicine wang, yi; Shandong University Cheeloo College of Medicine Yu, Caiting; Shandong University Cheeloo College of Medicine Yuan, Yemin; Shandong University School of Public Health Zhou, Chengchao; Shandong University, School of Public Health; Shandong University, China
Keywords:	Public health < INFECTIOUS DISEASES, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, SOCIAL MEDICINE

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4 1 **Physical frailty and health-related quality of life among Chinese rural older adults: A**
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6 2 **moderated mediation analysis of physical disability and physical activity**

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41 17 Word count:3330

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4 25 **Abstract**

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6 26 **Objectives:** The purpose of this study is to explore the mediating effect of physical disability, as
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9 27 well as the role of physical activity (PA) as a moderator in the relationship between physical
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12 28 frailty and health-related quality of life (HRQoL) among rural older adults in China.

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14 29 **Design:** Cross-sectional analysis.

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17 30 **Setting:** Rural households in Shandong of China (Rushan, Qufu, Laolin).

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19 31 **Participants and methods:** A survey was conducted among 3,243 rural older adults. The data
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21
22 32 were collected using questionnaires measuring physical frailty, physical disability, HRQoL and
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25 33 PA. Bootstrap analyses were employed to explore the mediating effect of physical disability on
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28 34 physical frailty and HRQoL, and the moderating role of PA.

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30 35 **Results:** After controlling for age and education, physical disability partially mediated the effect
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32
33 36 of physical frailty on HRQoL [indirect effect = -0.143, 95% confidence intervals (CI) = -0.175, -
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36 37 0.113], with the mediating effect accounting for 33.71% of the total effect. PA moderated the
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38 38 relationship between physical frailty and physical disability, as well as the relationship between
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40 39 physical disability and HRQoL.

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43 40 **Conclusions:** PA can moderate the indirect effect of physical disability on the association
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46 41 between physical frailty and HRQoL. This study helps to understand the mechanism underlying
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48 42 the association between physical frailty and HRQoL. Encouraging the rural older adults to
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51 43 increase PA appropriately might improve the HRQoL for the older adults with physical frailty
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54 44 and physical disability problems.

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4 46 **Key words:** HRQoL; Physical activity; Physical frailty; Physical disability; Rural older adults;
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6
7 47 Moderated mediation analysis

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9 48 **Strengths and limitations of this study**

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12 49 1. Few studies have assessed the moderating and mediating factors of the relationship between
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14 50 physical frailty and HRQoL in rural older adults specifically.
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17 51 2. Our study will help to elucidate the underlying mechanism of the relationship between
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19 52 physical frailty and HRQoL and form an effective way to improve the HRQoL of the older
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21 53 adults in rural areas.
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24 54 3. The latest EQ-5D -5L health utility scores method refers to Chinese integral conversion table,
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26 55 which is more suitable for the measurement of the Chinese population.
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29 56 4. The data we used cannot predict the causal relationship.
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32 57 5. More potential mechanisms related to physical frailty and HRQoL among the older adults
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34 58 need to be explored in the future.
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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 population¹. It is predicted that by 2050, the older adults over 60 will account for more than 35.1% of the total population². 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 adults³. 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 function⁶. With the increase of age, the risk of physical frailty increases⁷. Frailty may lead to negative health consequences, including fall, reduced activity, reduced independence, frequent hospitalization, and disability⁸. 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 adults¹¹. 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 disability¹⁶. A national longitudinal study of 7,439 people over age 65 in US showed that

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4 88 frailty was a strong predictor of disability¹⁷. A prospective two-year cohort study in Japan also
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6 89 showed that frailty and prophase of frailty increased the risk of disability¹⁸. These findings
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9 90 suggest that physical frailty is associated with disability in older adults. Studies have also
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11 91 demonstrated that the quality of life worsened as the degree of disability increased, and the more
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14 92 severe the disability, the worse the quality of life¹⁹. Compared with non-disabled older adults,
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17 93 disabled older adults are more prone to fall, depression, anxiety, etc., and their HRQoL was
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20 94 significantly reduced. Therefore, frailty may have an indirect effect on individual's HRQoL
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22 95 through the mediating effect of physical disability.

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25 96 Physical frailty is considered to be reversible and preventable²⁰. Physical activity(PA) is a
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27 97 key factor of reverse and prevent frailty in the older adults²¹. Studies have found that physical
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30 98 activity moderated the relationship between chronic illness and functional limitations, and
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33 99 moderated functional disability and body function²²⁻²³. PA can alleviate the decline of physical
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35 100 function in the older adults and has a beneficial effect on functional limitations, physical frailty,
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38 101 disability and quality of life in the older adults²⁴⁻²⁶. Studies indicated the positive effect of
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41 102 physical activity on reducing adverse events caused by frailty in older people. Performing a
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43 103 physical activity of moderate to vigorous intensity would improve physical frailty and prevent
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46 104 the occurrence of disability when compared to the performance of a physical activity of low
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49 105 intensity, ultimately promote older adults' quality of life²⁷⁻²⁹. Therefore, we speculate that PA
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51 106 may moderate the relationship between frailty and physical disability, and between physical
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54 107 disability and HRQoL.

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56 108 In the present study, we aim to explore the relationship between physical frailty and

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4 109 HRQoL, focusing on the mediating role of physical disability and the moderating role of PA in
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6 110 the relationship between physical frailty and HRQoL. The conceptual framework of the
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9 111 moderated mediation model was shown in Fig. 1.
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13 14 113 **2. Methods**

15 16 17 114 **2.1.1 Design and sample**

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19 115 This study was conducted from May to June, 2019 in Shandong province, China. A multistage
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22 116 stratified cluster sampling method was used to select participants, which was described in detail
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25 117 in a paper we have previously published³⁰. Three rural counties (Qufu, Laoling and Rushan) were
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28 118 selected according to the GDP per capita (2018) in Shandong. Within each selected county, five
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31 119 townships were randomly selected. Then, four villages were selected from each selected
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34 120 townships and the elderly aged over 60 years old who were randomly selected from sample
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37 121 villages. All participants completed the questionnaire independently. The survey was completed
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40 122 in about an hour, and the investigators checked the questionnaires when the participants returned
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43 123 them. A total of 3,600 respondents were recruited from 60 villages and 15 townships in 3 rural
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46 124 counties in Shandong province, of whom 3,243 completed the entire survey, with a response rate
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49 125 of 90.05%.

50 126 **2.2. Variables and measurement**

51 127 **2.2.1 Independent variable**

52 128 Physical frailty was measured by Frailty Phenotype³¹. The scale is a widely used frailty screening
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55 129 scale with good reliability and validity^{32 33}. Frailty was defined based on the following five
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4 130 aspects: weight loss, exhaustion, low physical activity level, slowness, weakness. ①Weight
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7 131 loss: In the past 1 year, participants' body mass index (BMI) decreased by >5.0% (except for
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10 132 personal deliberate weight loss). ②Exhaustion: Using the Center for Epidemiological Studies-
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12 133 Depression(CES-D)³⁴ : “How often in the last week did you feel this way?” (1) I could not get
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14 134 going and (2) I felt everything I did was an effort. Either of the above two questions that
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17 135 participants answered 3-4 days and most of the time, was considered exhaustion.③Low physical
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20 136 activity level: According the International Physical Activity Questionnaire-short Form (IPAQ-
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22 137 SF)^{35 36} , we used standard algorithms to calculate the Kcals consumed per week. The criterion is
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25 138 adjusted according to gender. Male: < 383 Kcals/ week is a decrease in physical activity, while
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28 139 female: < 270 Kcals/ week is a decrease in physical activity. ④Slowness: Slowness was
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30 140 assessed via walking speed at 15 ft measured for 3 times, and we record the minimum value. The
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33 141 criterion is adjusted according to gender and height. Men: height≤173 cm and time≥7 seconds;
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35 142 height > 173 cm and time ≥ 6 seconds. Women: height≤159 cm and time≥7 seconds ;height
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38 143 >159 cm and time ≥ 6 seconds. ⑤Weakness: Weakness was assessed by grip strength using a
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41 144 handgrip dynamometer was measured for 3 times, and we record the maximum value, adjusted
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43 145 for gender and BMI. Men: BMI ≤ 24 and grip strength ≤ 29;BMI 24.1-26 and grip strength ≤
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45 146 30;BMI 26.1-28 and grip strength ≤ 30;BMI > 28 and grip strength ≤ 32.Women: BMI ≤ 23
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48 147 and grip strength ≤ 17;BMI 23.1-26 and grip strength ≤ 17.3;BMI 26.1-29 and grip strength ≤
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51 148 18;BMI > 29 and grip strength ≤ 21.

149 2.2.2 Dependent variables

150 HRQoL was measured by the health utility value of EQ-5D-5L³⁷. The EQ-5D-5L consists of the

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4 151 EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L
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7 152 descriptive system has five elements (mobility, self-care, usual activities, pain/discomfort, and
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9 153 anxiety/depression) and each element includes five level (no problems, some problems, moderate
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12 154 problems, severe problems and extreme problems). The latest EQ-5D -5L health utility scores
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14 155 method refers to Chinese integral conversion table³⁷. The range of utility value is [-0.391, 1.000].
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17 156 A higher score indicates better health condition of the respondents. The Cronbach's coefficient
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20 157 was 0.761 in this study.

21 22 158 **2.2.3 Mediator**

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24 159 Physical disability was evaluated by the Activity of Daily Living Scale (ADLS), which was
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27 160 developed by Lawton and Brody in 1969 to measure the disability of the older adults^{38 39}. The
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30 161 Scale consists of 14 items, including Physical Self-Maintenance Scale (PSMS) and Instrumental
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33 162 Activities of Daily Living (IADL). The total score is 14-56, with higher scores indicating
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36 163 increased physical disability. A score of 14 and lower indicates completely normal physical
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39 164 ability, a score between 15 and 22 is defined as mild disability, and a score of 23 and higher is
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42 165 defined as severe disability. ADLS is recommended by WHO and has been widely used in older
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45 166 adults in China, with good reliability and validity⁴⁰. Cronbach's alpha was 0.764 in this study.

46 167 **2.2.4 Moderator**

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48 168 PA was assessed using the IPAQ-SF^{35 36}. The questionnaire contains 7 questions, 6 of which
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51 169 were about physical activity. The IPAQ-SF investigates the PA of the individuals in the last 7
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54 170 days. The questionnaire involved three types of intensity activities, including vigorous physical
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56 171 activity (VPA =8.0 metabolic equivalent [METs]),

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4 172 moderate physical activity (MPA =4.0 METs), and low physical activity (LPA =3.3 METs). PA
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7 173 of each person engaged in a certain intensity per week is the METs value corresponding to that
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9 174 physical activity \times weekly frequency \times daily time, and the sum of three PA is the total PA (met-h
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12 175 /week). The greater the overall physical activity value, the higher the physical activity.

14 176 **2.3 Data analysis**

17 177 To analyze the data, categorical variables were expressed using frequency and percentages (%)
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19 178 and continuous data were described using mean (standard deviation). Pearson correlation
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22 179 coefficient was used to analyze the correlation among physical frailty, physical disability, and
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25 180 HRQoL. All these analyses were performed using IBM SPSS 24.0 (IBM Corp., Armonk, NY,
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27 181 USA). All regression coefficients were tested by the bias-corrected percentile Bootstrap method.
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30 182 The theoretical model was tested by estimating the 95% confidence interval (CI) for mediation
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33 183 and moderating effects with 5000 sampled with repetition. If the 95% CI did not include 0, it
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35 184 meant that the statistics was significant. The mediation model and moderated mediation model
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38 185 were tested with the PROCESS V3.3 macro for SPSS⁴¹. In the current study, we selected Model
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41 186 4 and Model 58 to analyze the mediating effect and moderated mediation model. In addition,
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43 187 through t test and ANOVA analysis, we found that HRQoL is related to age and education.
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46 188 Previous studies have also found HRQoL was associated with age and education^{42 43}. We
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48 189 controlled age and education in this study. Sampling weights were used in all of the analyses to
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51 190 adjust for the survey design.

53 191 **2.4 Patient and public involvement statement**

56 192 This research was done without patient involvement. No patients were involved in developing

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4 193 the hypothesis and plans for design of this study either. The results would not be disseminated to
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6 194 study participants or any other individuals or communities.

9 195 **2.5 Ethical considerations**

11 196 The study was approved by the Ethics Committee of School of Public Health in Shandong
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14 197 University, P. R. China. The participants have been informed of the purpose and procedures of
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17 198 the study before the investigation. Before the study began, participants had signed written
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19 199 informed consent indicating that they were fully aware of the study procedures.
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25 201 **3. Results**

27 202 **3.1 Common method biases**

30 203 We used Harman single factor test to conduct a common method biases test⁴⁴. The results show
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32 204 that there are 12 factors with eigenvalues greater than 1, and the variance explained by the first
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35 205 factor is 17.92%, which is less than 40% of the critical standard, indicating that there are no
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38 206 serious common method biases in this study.

40 207 **3.2 Socio-demographic characteristics of the participants**

43 208 There were 3,243 participants, comprising 2,060 (63.5%) women and 1,182 (36.5%) men. The
44
45 209 average age was 69.88 (SD=6.10) years, ranging from 60 to 97 years. Of the participants, 25.5%
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47
48 210 were single. About 72.4% had chronic disease. The majority (81.9%) were empty nest elderly.

51 211 **3.3 Bivariate correlations of main variables**

53 212 The mean, standard deviation and correlation coefficient of each variable were shown in Table 1.
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56 213 Physical frailty was positively correlated with physical disability ($r = 0.330, P < 0.01$), physical

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4 214 frailty was negatively correlated with HRQoL ($r = -0.426, P < 0.01$) and PA ($r = -0.299,$
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7 215 $P < 0.01$). Physical disability was negatively correlated with HRQoL ($r = -0.557, P < 0.01$) and
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9 216 PA ($r = -0.184, P < 0.01$). PA was positively correlated with HRQoL ($r = 0.196, p < 0.01$).

217 **3.4 Mediation effect analysis**

218 Model 4 in the SPSS macro compiled by Hayes 2013⁴¹ was used to test the mediating effect of
219 physical disability in the relationship between physical frailty and HRQoL under the control
220 variable of age, education. As shown in Table 2 and Table 3, physical frailty had a significant
221 predictive effect on quality of life ($\beta = -0.423, t = -26.031, P < 0.001$), and the direct predictive
222 effect of frailty on quality of life was still significant when the mediating variable physical
223 disability was added. Meanwhile, physical frailty had a significant positive predictive effect on
224 physical disability ($\beta = 0.295, t = 17.729, P < 0.001$). Physical disability also has a significant
225 negative predictive effect on HRQoL ($\beta = -0.482, t = -32.407, P < 0.001$). In addition, the upper
226 and lower limits of the Bootstrap 95% CI for the direct effect of physical frailty on HRQoL and
227 the mediating effect of physical disability on physical frailty and HRQoL did not include 0 (Table
228 3), indicating that the mediating effect was significant. The mediating effect value was -0.143 and
229 the 95% CI was [-0.175, -0.113], which accounted for 33.71% of the total effect. This shows that
230 disability plays a partial mediating role in the relationship between physical frailty and HRQoL.

231 **3.5 Moderated mediation effect analysis**

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

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4 235 predicted physical disability ($\beta = -0.121, t = -7.058, P < 0.001$) (Table 4, Model 1), and the
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6 236 interaction term between physical disability and PA also had a significant predictive effect on
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9 237 HRQoL ($\beta = 0.116, t = 6.119, P < 0.001$) (Table 4, Model 2). These results suggest PA played a
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11 238 moderating role in the relationships between physical frailty and physical disability and between
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14 239 physical disability and HRQoL.

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17 240 Simple slope analyses indicated that the significant interaction at 1 SD below the mean and
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19 241 1 SD above the mean of physical activity (See Fig. 2 and Fig. 3). Physical frailty had a significant
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22 242 predictive effect on the disability of individuals with high-level or low-level PA, but the
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25 243 predictive effect of physical frailty on physical disability was stronger for individuals with low-
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27 244 level PA ($b_{\text{simple}} = 0.370, t = 16.979, P < 0.001$) than for individuals with high-level PA, as
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30 245 shown in Fig. 2 ($b_{\text{simple}} = 0.120, t = 4.322, P < 0.001$). Fig. 3 showed that for high levels of PA
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32 246 individuals, the effect of physical disability and physical HRQoL was significant ($b_{\text{simple}} = -$
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35 247 $0.301, t = -9.159, P < 0.001$). However, for low-level of PA individuals, the effect of physical
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38 248 disability and HRQoL was still significant but considerably stronger ($b_{\text{simple}} = -0.546, t = -$
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40 249 $29.701, P < 0.001$). In addition, as the level of physical activity increased, the mediating effect
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43 250 of physical disability on the relationship between physical frailty and HRQoL declined (Table 5).

45 251 **4. Discussion**

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48 252 In this study, a moderated mediation model was established with the mediation role of physical
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51 253 disability on the relationship between physical frailty and HRQoL, as well as the role of PA as a
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53 254 moderator in this indirect path between physical frailty and HRQoL. These findings elucidate the
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56 255 potential causes of physical frailty on HRQoL and facilitate the development of targeted

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4 256 interventions for individuals so as to improve HRQoL in rural older adults.
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6 257 Consistent with previous studies^{45 46}, we find that physical frailty negatively affect HRQoL
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9 258 of the older adults. This suggests that as the degree of physical frailty increases, the quality of
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12 259 life in the older adults becomes worse. Although many studies have established a direct
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14 260 relationship between frailty and HRQoL, few have explored the underlying mechanisms of this
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17 261 relationship. Our study demonstrates that the physical disability mediates the physical frailty and
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20 262 HRQoL, with the mediating rate of 33.71%. A study also suggested that physical disability was
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23 263 one of the potential factors underlying the association between frailty and HRQoL, which was
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25 264 similar with our study⁴⁷.

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27 265 The current study indicates that physical frailty is associated with disability, which is
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30 266 consistent with a study by Kojuma G⁴⁸. Frail older adults are very vulnerable to adverse health
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33 267 effects. A study indicated the risk of disability in the frail older adults was 12- to 13-fold
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35 268 increased than that in the non-frail older adults⁴⁹. Meanwhile, this study also demonstrates that
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38 269 the negative predictive effect of disability on individual HRQoL, which was consistent with
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41 270 previous studies^{50 51}. The possible explanation is that disabled older adults' poor self-care ability
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43 271 deteriorates their health, such as their normal physiological activities are restricted, physiological
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46 272 function is declined, social interaction is reduced, and ultimately affect the HRQoL. One study
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48 273 found that disability was the most important health problem for the older adults, which seriously
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51 274 affected their quality of life in old adults' later years⁵². The disability was the most important
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54 275 factor that contributed to decreasing quality of life in the older adults. Physical disability has
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56 276 been shown to be associated with increased chronic diseases, and premature mortality^{53 54}, all of

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4 277 which could adversely affect the quality of life of older adults⁵⁵. Therefore, physical frailty may
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6 278 reduce HRQoL of rural older adults by increasing their disability.
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9 279 In the present study, we also find that PA plays a moderating role in the indirect effect
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11 280 between physical frailty and HRQoL. A larger indirect effect is observed among rural older
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13 281 adults with low-level of PA than among those with average or high-level of PA. Specifically, PA
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15 282 moderates the relationship between physical frailty and physical disability, and between physical
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17 283 disability and HRQoL. For older adults with low-level PA, the impact of physical frailty on
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19 284 physical disability is stronger than older adults with high-level PA. This finding indicates that
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21 285 PA moderates the relation between physical frailty and physical disability. We speculate that the
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23 286 older adults with low-level PA may have a decline in their physiological system reserves, leading
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25 287 to a deterioration of their functional status and ultimately increasing the possibility of physical
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27 288 frailty and disability⁵⁶. A systematic review showed that older adults without exercise habits
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29 289 were at greater risk of developing frailty. Taichi, resistance sports and other physical activities
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31 290 could effectively improve the health of the older adults, reduce the symptoms of physical
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33 291 weakness, and prevent the occurrence of physical disability⁵⁷. Compared with the older adults
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35 292 with high-level PA, the older adults with low-level PA are more vulnerable to the negative
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37 293 effects of physical frailty. As a result, physical frailty may cause more interference in older
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39 294 adults with low-level PA and increase the risk of physical disability.
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50 295 We also find that physical disability has a significant impact on quality of life at both high
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52 296 and low-level of PA. Compared with older adults with high levels of PA, physical disability is
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54 297 more likely to adversely affect HRQoL of older adults with low-level PA. A study showed that
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4 298 low-level PA was a major contributing factor for older adults disability⁵⁸. As the level of
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6 299 disability increases, the individuals with low-level of PA experience a more serious functional
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9 300 decline and become more worried about the health status, thus further negatively affect the
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11 301 HRQoL⁵⁹. In addition, physical disability has a greater effect on individuals with low-level PA
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14 302 than high-level PA, which indicates that PA plays a moderating role between physical disability
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17 303 and HRQoL. One study found that PA could improve the physical function and daily life
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19 304 activities of disabled older adults, and ultimately improved the life of older adults quality⁶⁰.
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22 305 Therefore, a low-level of PA might be associated with poor quality of life in rural older adults
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25 306 with high disability.

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27 307 Based on our findings, we recommended that community health managers should enhance
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29 308 screening and assessment of frailty in rural older adults. The older adults who are frail or pre-
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31 309 frail should be intervened in time, and the older adults who are disabled should be given special
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33 310 attention. Targeted and individualized intervention programs should be designed according to the
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35 311 different characteristics of the stages of frailty and disability. Besides, rural communities should
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37 312 establish some public facilities or organize some public activities to encourage the older adults to
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39 313 participate in sports activities.

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41 314 There are several limitations in this study. First, our study was based on a cross-sectional
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43 315 study, which could not provide strong evidence of causation. Future research could adopt a
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45 316 longitudinal design or experiments to explore the causal relationship between physical frailty and
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47 317 HRQoL. Secondly, the data in this study come from the participants' self-report information,
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49 318 which might result in recall bias. Thirdly, physical disability has a partly mediating effect on the
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4 319 relationship between physical frailty and HRQoL, which indicates that there are other mediating
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6 320 variables in this relationship. More potential mechanisms related to physical frailty and HRQoL
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9 321 among the older adults need to be explored in the future.
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13 14 323 **Conclusion**

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17 324 This study shows that physical frailty is related to HRQoL, and physical disability mediates the
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19 325 relationship between physical frailty and HRQoL, and PA moderates the mediating relationship.
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22 326 A greater effect is observed among rural older adults with low-level of PA than that among those
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25 327 with high-level of PA. This will help to elucidate the underlying mechanism of the relationship
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27 328 between physical frailty and HRQoL and form an effective way to improve the HRQoL of the
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30 329 older adults in rural areas.
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34 35 331 **Acknowledgements**

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38 332 We thank the officials of health agencies, all participants and staffs at the study sites for their
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40
41 333 cooperation.

42 334 **Contributors**

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44 335 Study concept and design: Chengchao Zhou and Wenting Hao. Acquisition of data: Dan Zhao,
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46 336 Caiting Yu and Yemin Yuan. Analysis and interpretation of data: Peipei Fu, Zhengyue Jing and
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49 337 Yi Wang. Drafting of the manuscript: Wenting Hao. Critical revision of the manuscript for
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51 338 important intellectual content: Chengchao Zhou and Jie Li. All authors read and approved the
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54 339 final manuscript.
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340 **Funding**

341 This study was supported by the National Natural Science Foundation of China (71774104,
342 71473152, 71974117), the China Medical Board (16-257), Cheeloo Youth Scholar Grant,
343 Shandong University (IFYT1810,2012DX006) and NHC Key Laboratory of Health Economics
344 and Policy Research(NHC-HEPR2019014).

345 **Data availability statement**

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

348 **Competing interests**

349 None declared.

350 **Patient consent for publication**

351 Not required.

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353 **REFERENCES**

- 354 1. NBSC. Statistical communiqué of the People's Republic of China on the 2017 national economic and social
355 development. 2017 [updated February 28,2018. Available from:
356 http://www.stats.gov.cn/english/PressRelease/201802/t20180228_1585666.html.
- 357 2. United Nations DESA, Population Division. World Population Ageing 2017:Highlights 2017 [updated 2017.
358 Available
359 from:https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf.
- 360 3. Brown DS, Thompson WW, Zack MM, et al. Associations Between Health-Related Quality of Life and Mortality in
361 Older Adults. *Prevention Science* 2015;16(1):21-30. doi: 10.1007/s11121-013-0437-z
- 362 4. Zhou B, Chen K, Wang J, et al. Quality of Life and Related Factors in the Older Rural and Urban Chinese Populations
363 in Zhejiang Province. *J Appl Gerontol* 2011;30(2):199-225. doi: 10.1177/0733464810361346
- 364 5. Zhou Z, Zhou Z, Gao J, et al. Urban-rural difference in the associations between living arrangements and the health-
365 related quality of life (HRQOL) of the elderly in China-Evidence from Shaanxi province. *PLoS One*
366 2018;13(9):e0204118. doi: 10.1371/journal.pone.0204118 [published Online First: 2018/09/21]

- 1
2
3 368 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.
4 369 doi: 10.1016/j.jamda.2013.03.022
- 5
6 370 7. Collard RM, Boter H, Schoevers RA, et al. Prevalence of frailty in community-dwelling older persons: a systematic
7 371 review. *J Am Geriatr Soc* 2012;60(8):1487-92. doi: 10.1111/j.1532-5415.2012.04054.x [published Online
8 372 First: 2012/08/14]
- 9
10 373 8. Vermeiren S, Vellaazzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-
11 374 Analysis. *J Am Med Dir Assoc* 2016;17(12) doi: 10.1016/j.jamda.2016.09.010
- 12 375 9. Fried LP, Ferrucci L, Darer JD, et al. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications
13 376 for Improved Targeting and Care. *J Gerontol A Biol Sci Med Sci* 2004;59(3):255-63. doi:
14 377 10.1093/gerona/59.3.M255
- 15
16 378 10. Lee IC, Chiu YH, Lee CY. Exploration of the importance of geriatric frailty on health-related quality of life.
17 379 *Psychogeriatrics* 2016;16(6):368-75. doi: 10.1111/psyg.12179 [published Online First: 2016/01/13]
- 18
19 380 11. Kanauchi M, Kubo A, Kanauchi K, et al. Frailty, health-related quality of life and mental well-being in older adults
20 381 with cardiometabolic risk factors. *Int J Clin Pract* 2008;62(9):1447-51. doi: 10.1111/j.1742-
21 382 1241.2008.01830.x [published Online First: 2008/07/23]
- 22
23 383 12. Fullertonthomson E, Yu B, Nurujeter A, et al. Basic ADL Disability and Functional Limitation Rates Among Older
24 384 Americans From 2000–2005: The End of the Decline? *J Gerontol A Biol Sci Med Sci* 2009;64(12):1333-36.
25 385 doi: 10.1093/gerona/glp130
- 26
27 386 13. Picavet HJ, Hoeymans N. Physical disability in The Netherlands: Prevalence, risk groups and time trends. *Public*
28 387 *Health* 2002;116(4):231-37. doi: 10.1038/sj.ph.1900864
- 29
30 388 14. Evenhuis HM, Hermans H, Hilgenkamp TIM, et al. Frailty and Disability in Older Adults with Intellectual Disabilities:
31 389 Results from the Healthy Ageing and Intellectual Disability Study. *J Am Geriatr Soc* 2012;60(5):934-38. doi:
32 390 10.1111/j.1532-5415.2012.03925.x
- 33
34 391 15. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised
35 392 older people. *Age Ageing* 2014;43(4):477-84. doi: 10.1093/ageing/aft181
- 36
37 393 16. Papachristou E, Wannamethee SG, Lennon LT, et al. Ability of Self-Reported Frailty Components to Predict
38 394 Incident Disability, Falls, and All-Cause Mortality: Results From a Population-Based Study of Older British
39 395 Men. *J Am Med Dir Assoc* 2017;18(2):152-57. doi: 10.1016/j.jamda.2016.08.020 [published Online First:
40 396 2016/10/16]
- 41
42 397 17. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the
43 398 United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133 [published
44 399 Online First: 2015/08/25]
- 45
46 400 18. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older adults: a
47 401 prospective cohort study. *BMJ open* 2015;5(9):e008462. doi: 10.1136/bmjopen-2015-008462 [published
48 402 Online First: 2015/09/05]
- 49
50 403 19. Medhi GK, Sarma J, Pala S, et al. Association between health related quality of life (HRQOL) and activity of daily
51 404 living (ADL) among elderly in an urban setting of Assam, India. *J Family Med Prim Care* 2019;8(5):1760-64.
52 405 doi: 10.4103/jfmpc.jfmpc_270_19 [published Online First: 2019/06/15]
- 53
54 406 20. Tavassoli N, Guyonnet S, Abellan Van Kan G, et al. Description of 1,108 older patients referred by their physician
55 407 to the "Geriatric Frailty Clinic (G.F.C) for Assessment of Frailty and Prevention of Disability" at the
56
57
58
59
60

- 1
2
3 408 gerontopole. *J Nutr Health Aging* 2014;18(5):457-64. doi: 10.1007/s12603-014-0462-z [published Online
4 409 First: 2014/06/03]
- 6 410 21. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, et al. Exercise training as a drug to treat age associated
7 411 frailty. *Free Radic Biol Med* 2016;98:159-64. doi: 10.1016/j.freeradbiomed.2016.03.024 [published Online
8 412 First: 2016/03/30]
- 10 413 22. Rector JL, Marceau K, Friedman EM. Moderation of the Association Between Chronic Medical Conditions and
11 414 Functional Limitations Over Time by Physical Activity: Effects of Age. *J Gerontol A Biol Sci Med Sci*
12 415 2020;75(1):168-74. doi: 10.1093/gerona/glz020 [published Online First: 2019/02/21]
- 14 416 23. Palmer RF, Espino DV, Dergance JM, et al. The role of physical activity and diabetes status as a moderator:
15 417 functional disability among older Mexican Americans. *Age Ageing* 2012;41(6):752-8. doi:
16 418 10.1093/ageing/afs106 [published Online First: 2012/10/12]
- 18 419 24. Keysor JJ. Does late-life physical activity or exercise prevent or minimize disablement? A critical review of the
19 420 scientific evidence. *Am J Prev Med* 2003;25(3 Suppl 2):129-36. doi: 10.1016/s0749-3797(03)00176-4
20 421 [published Online First: 2003/10/14]
- 22 422 25. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? *J Gerontol A Biol Sci Med Sci*
23 423 2001;56(7):M412-23. doi: 10.1093/gerona/56.7.m412 [published Online First: 2001/07/11]
- 24 424 26. Rejeski WJ, Mihalko SL. Physical Activity and Quality of Life in Older Adults. *J Gerontol A Biol Sci Med Sci*
25 425 2001;56(suppl_2):23-35. doi: 10.1093/gerona/56.suppl_2.23
- 27 426 27. Casas-Herrero A, Izquierdo M. Physical exercise as an efficient intervention in frail elderly persons. *An Sist Sanit*
28 427 *Navar* 2012;35(1):69-85. doi: 10.4321/s1137-66272012000100007 [published Online First: 2012/05/04]
- 29 428 28. Mañas A, Del Pozo-Cruz B, Guadalupe-Grau A, et al. Reallocating Accelerometer-Assessed Sedentary Time to
30 429 Light or Moderate- to Vigorous-Intensity Physical Activity Reduces Frailty Levels in Older Adults: An
31 430 Isotemporal Substitution Approach in the TSHA Study. *J Am Med Dir Assoc* 2018;19(2):185.e1-85.e6. doi:
32 431 10.1016/j.jamda.2017.11.003 [published Online First: 2017/12/23]
- 34 432 29. Barnett A, Smith B, Lord SR, et al. Community-based group exercise improves balance and reduces falls in at-risk
35 433 older people: a randomised controlled trial. *Age Ageing* 2003;32(4):407-14. doi: 10.1093/ageing/32.4.407
36 434 [published Online First: 2003/07/10]
- 38 435 30. Jing Z, Li J, Wang Y, et al. The mediating effect of psychological distress on cognitive function and physical frailty
39 436 among the elderly: Evidence from rural Shandong, China. *J Affect Disord* 2020;268:88-94. doi:
40 437 10.1016/j.jad.2020.03.012 [published Online First: 2020/03/12]
- 42 438 31. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med*
43 439 *Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]
- 45 440 32. Buta BJ, Walston JD, Godino JG, et al. Frailty assessment instruments: Systematic characterization of the uses
46 441 and contexts of highly-cited instruments. *Ageing Res Rev* 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003
47 442 [published Online First: 2015/12/18]
- 49 443 33. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC Geriatr*
50 444 2013;13:64. doi: 10.1186/1471-2318-13-64 [published Online First: 2013/06/22]
- 51 445 34. Radloff LS. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. *Appl Psychol*
52 446 *Meas* 1977;1(3):385-401. doi: 10.1177/014662167700100306

- 1
2
3 447 35. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical
4 448 Activity Questionnaire. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 2014;35(8):961-
5 449 4. [published Online First: 2014/11/08]
- 7 450 36. Macfarlane DJ, Lee CC, Ho EY, et al. Reliability and validity of the Chinese version of IPAQ (short, last 7 days). *J*
8 451 *Sci Med Sport* 2007;10(1):45-51. doi: 10.1016/j.jsams.2006.05.003 [published Online First: 2006/06/30]
- 10 452 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:
11 453 10.1016/j.jval.2016.11.016 [published Online First: 2017/04/15]
- 12 454 38. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living.
13 455 *The Gerontologist* 1969;9(3):179-86. doi: 10.1093/geront/9.3_Part_1.179 [published Online First:
14 456 1969/01/01]
- 16 457 39. Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc* 1971;19(6):465-81. doi:
17 458 10.1111/j.1532-5415.1971.tb01206.x [published Online First: 1971/06/01]
- 19 459 40. Chen P, Yu ES, Zhang M, et al. ADL dependence and medical conditions in Chinese older persons: a population-
20 460 based survey in Shanghai, China. *J Am Geriatr Soc* 1995;43(4):378-83. doi: 10.1111/j.1532-
21 461 5415.1995.tb05811.x [published Online First: 1995/04/01]
- 23 462 41. Bolin JH. Hayes, Andrew F. (2013). Introduction to Mediation, Moderation, and Conditional Process Analysis: A
24 463 Regression-Based Approach. New York, NY: The Guilford Press. *J Educ Meas* 2014;51(3):335-37. doi:
25 464 10.1111/jedm.12050
- 27 465 42. Bao XY, Xie YX, Zhang XX, et al. The association between multimorbidity and health-related quality of life: a cross-
28 466 sectional survey among community middle-aged and elderly residents in southern China. *Health Qual Life*
29 467 *Outcomes* 2019;17(1):107. doi: 10.1186/s12955-019-1175-0 [published Online First: 2019/06/27]
- 31 468 43. Chapman B, Duberstein P, Lyness JM. Personality traits, education, and health-related quality of life among older
32 469 adult primary care patients. *J Gerontol B Psychol Sci Soc Sci* 2007;62(6):P343-52. doi:
33 470 10.1093/geronb/62.6.p343 [published Online First: 2007/12/15]
- 34 471 44. Podsakoff PM, MacKenzie SB, Lee JY, et al. Common method biases in behavioral research: a critical review of
35 472 the literature and recommended remedies. *J Appl Psychol* 2003;88(5):879-903. doi: 10.1037/0021-
36 473 9010.88.5.879 [published Online First: 2003/10/01]
- 38 474 45. Kanwar A, Singh M, Lennon R, et al. Frailty and health-related quality of life among residents of long-term care
39 475 facilities. *J Aging Health* 2013;25(5):792-802. doi: 10.1177/0898264313493003 [published Online First:
40 476 2013/06/27]
- 42 477 46. Mulasso A, Roppolo M, Rabaglietti E. The role of individual characteristics and physical frailty on health related
43 478 quality of life (HRQOL): a cross sectional study of Italian community-dwelling older adults. *Arch Gerontol*
44 479 *Geriatr* 2014;59(3):542-8. doi: 10.1016/j.archger.2014.08.012 [published Online First: 2014/09/14]
- 46 480 47. Huaxue L, Taifang L, Wenjing Y, et al. Status of frailty and its effect path on quality of life among the elderly in
47 481 community. *Chinese Nursing Research* 2019;33(21):3645-49.
- 49 482 48. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and
50 483 meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282 [published
51 484 Online First: 2016/08/26]
- 53 485 49. Feng L, Zin Nyunt MS, Gao Q, et al. Cognitive Frailty and Adverse Health Outcomes: Findings From the Singapore
54 486 Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc* 2017;18(3):252-58. doi:
55 487 10.1016/j.jamda.2016.09.015 [published Online First: 2016/11/14]

- 1
2
3 488 50. Akosile CO, Mgbeojedo UG, Maruf FA, et al. Depression, functional disability and quality of life among Nigerian
4 489 older adults: Prevalences and relationships. *Arch Gerontol Geriatr* 2018;74:39-43. doi:
5 490 10.1016/j.archger.2017.08.011 [published Online First: 2017/09/28]
6
7 491 51. Shin KR, Byeon YS, Kang Y, et al. A study on physical symptom, activity of daily living, and health-related quality
8 492 of life (HRQoL) in the community-dwelling older adults. *Taehan Kanho Hakhoe chi* 2008;38(3):437-44. doi:
9 493 10.4040/jkan.2008.38.3.437 [published Online First: 2008/07/08]
10
11 494 52. Crimmins EM. Trends in the health of the elderly. *Annu Rev Public Health* 2004;25:79-98. doi:
12 495 10.1146/annurev.publhealth.25.102802.124401 [published Online First: 2004/03/16]
13
14 496 53. Khan ZA, Singh C, Khan T. Correlates of physical disability in the elderly population of Rural North India (Haryana).
15 497 *J Family Community Med* 2018;25(3):199-204. doi: 10.4103/jfcm.JFCM_160_17 [published Online First:
16 498 2018/09/18]
17
18 499 54. Wei M, Li J, Wang H. Impact of the disability trajectory on the mortality risk of older adults in China. *Arch Gerontol*
19 500 *Geriatr* 2018;74:174-83. doi: 10.1016/j.archger.2017.10.015 [published Online First: 2017/11/11]
20 501 55. Gobbens RJ. Associations of ADL and IADL disability with physical and mental dimensions of quality of life in
21 502 people aged 75 years and older. *PeerJ* 2018;6:e5425. doi: 10.7717/peerj.5425 [published Online First:
22 503 2018/08/21]
23
24 504 56. Rejeski WJ, Brawley LR, Haskell WL. The prevention challenge: an overview of this supplement. *Am J Prev Med*
25 505 2003;25(3 Suppl 2):107-9. doi: 10.1016/s0749-3797(03)00173-9 [published Online First: 2003/10/14]
26
27 506 57. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older adults:
28 507 a systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154. doi: 10.1186/s12877-015-
29 508 0155-4 [published Online First: 2015/12/03]
30
31 509 58. Kortebein P, Ferrando A, Lombeida J, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older adults.
32 510 *JAMA* 2007;297(16):1772-4. doi: 10.1001/jama.297.16.1772-b [published Online First: 2007/04/26]
33 511 59. Ávila-Funes JA, Pina-Escudero SD, Aguilar-Navarro S, et al. Cognitive impairment and low physical activity are the
34 512 components of frailty more strongly associated with disability. *J Nutr Health Aging* 2011;15(8):683-9. doi:
35 513 10.1007/s12603-011-0111-8 [published Online First: 2011/10/05]
36
37 514 60. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults.
38 515 *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First: 2011/04/01]
39 516
40
41 517
42 518
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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 \times PA	-0.120	-7.058***		
Physical disability			-0.421	-24.364***
Physical disability \times 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

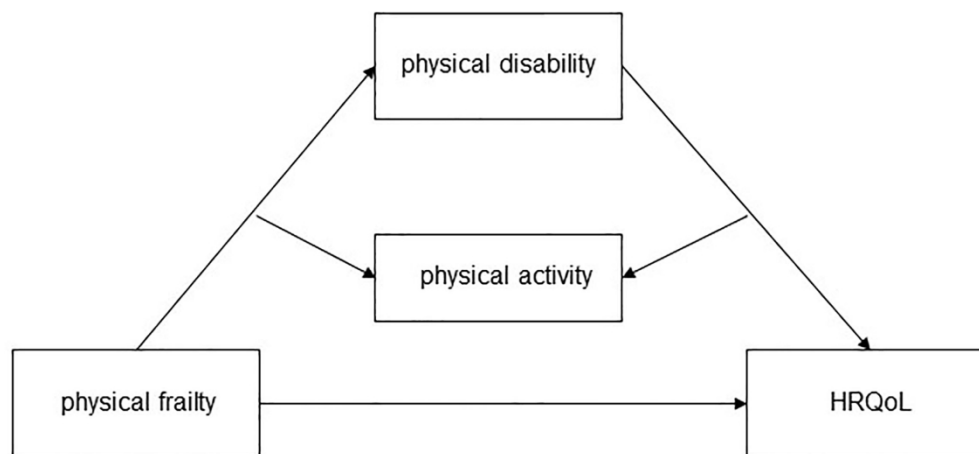


Fig. 1 The conceptual framework of the moderated mediation mode

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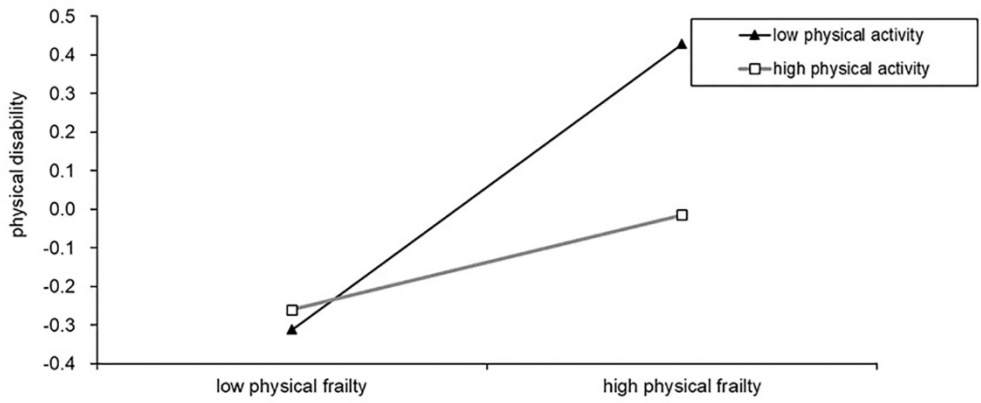


Fig. 2 Simple slope analysis shows that physical frailty moderated the relation between physical frailty and HRQoL

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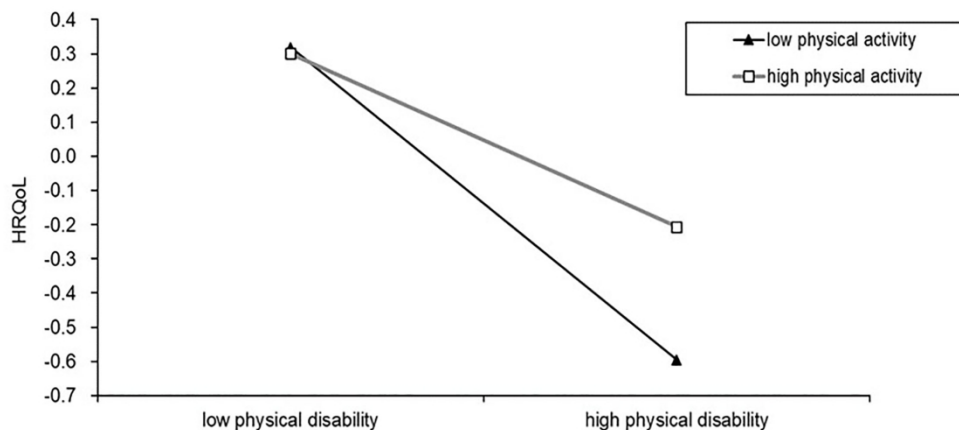


Fig.3 Simple slope analysis shows that physical activity moderated the relation between physical disability and HRQoL

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	
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-

1			
2	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
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6			(b) Report category boundaries when continuous variables were categorized
7			
8			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
9			
10			
11	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
12			
13			
14	Discussion		
15	Key results	18	Summarise key results with reference to study objectives
16	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
17			
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20	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
21			
22			
23			
24	Generalisability	21	Discuss the generalisability (external validity) of the study results
25			
26	Other information		
27	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
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30			

*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.

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-042496.R1
Article Type:	Original research
Date Submitted by the Author:	17-Nov-2020
Complete List of Authors:	Hao, Wenting; School of public health Li, Jie; Shandong University School of Public Health Fu, Peipei; Shandong University Cheeloo College of Medicine Zhao, Dan; Shandong University, school of public health Jing, Zhengyue; Shandong University Cheeloo College of Medicine wang, yi; Shandong University Cheeloo College of Medicine Yu, Caiting; Shandong University Cheeloo College of Medicine Yuan, Yemin; Shandong University School of Public Health Zhou, Chengchao; Shandong University, School of Public Health; Shandong University, China
Primary Subject Heading:	Public health
Secondary Subject Heading:	Geriatric medicine
Keywords:	Public health < INFECTIOUS DISEASES, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, SOCIAL MEDICINE

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4 1 **Physical frailty and health-related quality of life among Chinese rural older adults: A**
5 2 **moderated mediation analysis of physical disability and physical activity**

6
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37 16 Word count:3542

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6
7 **Abstract**

8
9 **Objectives:** The purpose of this study is to explore the mediating effect of physical disability, as
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11 well as the role of physical activity (PA) as a moderator in the relationship between physical
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13 frailty and health-related quality of life (HRQoL) among rural older adults in China.
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17 **Design:** Cross-sectional analysis.
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21 **Setting:** Rural households in Shandong of China (Rushan, Qufu, Laolin).
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25 **Participants and methods:** A survey was conducted among 3,243 rural older adults. The data
26
27 were collected using questionnaires measuring physical frailty, physical disability, HRQoL and
28
29 PA. Bootstrap analyses were employed to explore the mediating effect of physical disability and
30
31 also the moderating role of PA on physical frailty and HRQoL.
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35 **Results:** After controlling for age and education, physical disability partially mediated the effect
36
37 of physical frailty on HRQoL[indirect effect = -0.143, 95% confidence intervals (CI) = -0.175,
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39 -0.113], with the mediating effect accounting for 33.71% of the total effect. PA moderated the
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41 relationship between physical frailty and physical disability, as well as the relationship between
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43 physical disability and HRQoL. Specifically, the interaction term between physical frailty and
44
45 PA significantly predicted physical disability ($\beta = -0.120$, $t = -7.058$, $P < 0.001$), and the
46
47 interaction term between physical disability and PA also had a significant predictive effect on
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49 HRQoL ($\beta = 0.115$, $t = 6.104$, $P < 0.001$).
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4 44 **Conclusions:** PA can moderate the indirect effect of physical disability on the association
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6 45 between physical frailty and HRQoL. This study helps to understand the mechanism underlying
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9 46 the association between physical frailty and HRQoL. Encouraging rural older adults to increase
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12 47 PA appropriately might improve HRQoL for older adults with physical frailty and physical
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14 48 disability problems.
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20 50 **Key words:** HRQoL; Physical activity; Physical frailty; Physical disability; Rural older adults;
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22 51 Moderated mediation analysis
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4 54 **Strengths and limitations of this study**

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7 55 1. This is the first study to investigate the moderating and mediating factors of the relationship
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10 56 between physical frailty and HRQoL among older adults in rural China.
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12 57 2. Moderated mediation model was used to explore the potential effect of physical disability
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14
15 58 and physical activity.
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17 59 3. Cross-sectional data could not provide strong evidence of causation.
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19
20 60 4. Only two control variables were included in this study, and more confounding factors will be
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22
23 61 included to verify our results in the future.
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25 62 5. More potential mechanisms related to physical frailty and HRQoL among older adults need
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28 63 to be explored by using longitudinal data in the future.
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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 population¹. It is predicted that by 2050, older adults over 60 will account for more than 35.1% of the total population². 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 adults³. 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 function⁶. With the increase of age, the risk of physical frailty increases⁷. Frailty may lead to negative health consequences, including fall, reduced activity, reduced independence, frequent hospitalization, and disability⁸. 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 HRQoL⁹⁻¹¹, and frail older adults reported worse HRQoL than those who were not frail¹². 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

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4 90 of disability¹⁷. A national longitudinal study of 7,439 people over age 65 in US showed that
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6 91 frailty was a strong predictor of disability¹⁸. A prospective two-year cohort study in Japan also
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9 92 showed that frailty and prophase of frailty increased the risk of disability¹⁹. These findings
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12 93 suggest that physical frailty is associated with disability in older adults. Studies have also
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14 94 demonstrated that the quality of life worsened as the degree of disability increased, and the more
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17 95 severe the disability, the worse the quality of life²⁰. Compared with non-disabled older adults,
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20 96 disabled older adults are more prone to fall, depression, anxiety, etc., and their HRQoL was
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23 97 significantly reduced. Therefore, we speculate that frailty may have an indirect effect on
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25 98 individual's HRQoL through the mediating effect of physical disability.

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27 99 Physical frailty is considered to be reversible and preventable²¹. Physical activity (PA) is a
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30 100 key factor of reverse and prevent frailty in older adults²². Studies have found that physical
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33 101 activity moderated the relationship between chronic illness and functional limitations, and
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35 102 moderated functional disability and body function²³⁻²⁴. PA can alleviate the decline of physical
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38 103 function in older adults and has a beneficial effect on functional limitations, physical frailty,
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41 104 disability and quality of life in older adults²⁵⁻²⁷. Studies indicated the positive effect of physical
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44 105 activity on reducing adverse events caused by frailty in older people. Performing a physical
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47 106 activity of moderate to vigorous intensity would improve physical frailty and prevent the
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50 107 occurrence of disability when compared to the performance of a physical activity of low intensity,
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53 108 ultimately promote older adults' quality of life²⁸⁻³⁰. Therefore, PA may moderate the direct and
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55 109 indirect relationship between physical frailty and HRQoL through physical disability as a

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4 110 mediator.

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6 111 In the present study, we used a cross-sectional study to the relationship between physical
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9 112 frailty and HRQoL, focusing on the mediating role of physical disability and the moderating role
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12 113 of PA in the relationship between physical frailty and HRQoL. The conceptual framework of the
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14 114 moderated mediation model was shown in Fig. 1.
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16 17 115 18 19 116 **2. Methods**

20 21 22 117 **2.1.1 Design and sample**

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24 118 This study was conducted from May to June, 2019 in Shandong province, China. A multistage
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27 119 stratified cluster sampling method was used to select participants, which was described in detail
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30 120 in a paper we have previously published³¹. Three rural counties (Qufu, Laoling and Rushan) were
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33 121 selected according to the GDP per capita (2018) in Shandong. Within each selected county, five
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35 122 townships were randomly selected. Then, four villages were selected from each selected
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38 123 townships and the elderly aged over 60 years old who were randomly selected from sample
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41 124 villages. All participants completed the questionnaire independently. The survey was completed
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44 125 in about an hour, and the investigators checked the questionnaires when the participants returned
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47 126 them. A total of 3,600 respondents were recruited from 60 villages and 15 townships in 3 rural
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50 127 counties in Shandong province, of whom 3,243 completed the entire survey, with a response rate
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53 128 of 90.05%.

54 55 56 129 **2.2. Variables and measurement**

2.2.1 Independent variable

Physical frailty was measured by Frailty Phenotype³². 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 to 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 24.1-26 and grip strength ≤30; BMI 26.1-28 and grip strength ≤30; BMI > 28 and grip strength ≤32. Women: BMI ≤

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4 150 23 and grip strength \leq 17;BMI 23.1-26 and grip strength \leq 17.3;BMI 26.1-29 and grip strength \leq
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7 151 18;BMI $>$ 29 and grip strength \leq 21.

9 152 **2.2.2Dependent variables**

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12 153 HRQoL was measured by the health utility value of EQ-5D-5L³⁸.The EQ-5D-5L consists of the
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14 154 EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L
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17 155 descriptive system has five elements (mobility, self-care, usual activities, pain/discomfort, and
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19 156 anxiety/depression) and each element includes five level (no problems, some problems, moderate
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22 157 problems, severe problems and extreme problems). The latest EQ-5D-5Lhealth utility scores
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25 158 method refers to Chinese integral conversion table³⁸.The range of utility value is [-0.391, 1.000].
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27 159 A higher score indicates better health condition of the respondents. The Cronbach's coefficient
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30 160 was 0.761 in this study.

32 161 **2.2.3Mediator**

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35 162 Physical disability was evaluated by the Activity of Daily Living Scale (ADLS), which was
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38 163 developed by Lawton and Brody in 1969 to measure the disability of older adults^{39 40}. The Scale
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41 164 consists of 14 items, including Physical Self-Maintenance Scale (PSMS) and Instrumental
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43 165 Activities of Daily Living (IADL). The total score is 14-56, with higher scores indicating
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46 166 increased physical disability. A score of 14 and lower indicates completely normal physical
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48 167 ability, a score between 15 and 22 is defined as mild disability, and a score of 23 and higher is
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51 168 defined as severe disability. ADLS is recommended by WHO and has been widely used in older
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54 169 adults in China, with good reliability and validity⁴¹.Cronbach's alpha was 0.764 in this study.

170 **2.2.4 Moderator**

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

179 **2.3 Data analysis**

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

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4 189 above and below the mean($M+1SD/M-1SD$)⁴²⁻⁴⁴. The Split-Plot analysis method was used to
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6 190 further examine the direction of the moderation effect, and draw a diagram explaining the
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9 191 moderation effect⁴⁵. The mediation model and moderated mediation model were tested with the
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12 192 PROCESS V3.3 macro for SPSS⁴⁶. In the current study, we selected Model 4 and Model 59 to
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14 193 analyze the mediating effect and moderated mediation effect. In addition, through t test and
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17 194 ANOVA analysis, we found that HRQoL is related to age and education. Previous studies have
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20 195 also found HRQoL was associated with age and education^{47 48}. We controlled age and education
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22 196 in this study. Sampling weights were used in all of the analyses to adjust for the survey design.
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25 197 **2.4 Patient and public involvement statement**

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28 198 This research was done without patient involvement. No patients were involved in developing
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31 199 the hypothesis and plans for design of this study either. The results would not be disseminated to
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34 200 study participants or any other individuals or communities.
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36 37 201 **2.5 Ethical considerations**

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39 202 The study was approved by the Ethics Committee of School of Public Health in Shandong
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41
42 203 University, P. R. China. The participants have been informed of the purpose and procedures of
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45 204 the study before the investigation. Before the study began, participants had signed written
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48 205 informed consent indicating that they were fully aware of the study procedures.
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52 53 54 207 **3. Results**

208 **3.1 Common method biases**

209 We used Harman single factor test to conduct a common method biases test⁴⁹. The results show
210 that there are 12 factors with eigenvalues greater than 1, and the variance explained by the first
211 factor is 17.92%, which is less than 40% of the critical standard, indicating that there are no
212 serious common method biases in this study.

213 **3.2 Socio-demographic characteristics of the participants**

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

217 **3.3 Bivariate correlations of main variables**

218 The mean, standard deviation/ Median (Quartile₁, Quartile₃) and correlation coefficient of each
219 variable were shown in Table 1. Physical frailty was positively correlated with physical disability
220 ($\rho = 0.283, P < 0.01$), physical frailty was negatively correlated with HRQoL ($\rho = -0.429, P <$
221 0.01) and PA ($\rho = -0.378, P < 0.01$). Physical disability was negatively correlated with HRQoL
222 ($\rho = -0.378, P < 0.01$) and PA ($\rho = -0.194, P < 0.01$). PA was positively correlated with HRQoL
223 ($\rho = 0.258, p < 0.01$).

224 **3.4 Mediation effect analysis**

225 Model 4 in the SPSS macro compiled by Hayes 2013⁴⁶ was used to test the mediating effect of
226 physical disability in the relationship between physical frailty and HRQoL under the control
227 variable of age, education. As shown in Table 2 and Table 3, physical frailty had a significant

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4 228 predictive effect on quality of life ($\beta = -0.423, t = -26.031, P < 0.001$), and the direct predictive
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7 229 effect of frailty on quality of life was still significant when the mediating variable physical
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9 230 disability was added. Meanwhile, physical frailty had a significant positive predictive effect on
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12 231 physical disability ($\beta = 0.295, t = 17.729, P < 0.001$). Physical disability also has a significant
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14 232 negative predictive effect on HRQoL ($\beta = -0.482, t = -32.407, P < 0.001$). In addition, the upper
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17 233 and lower limits of the Bootstrap 95% CI for the direct effect of physical frailty on HRQoL and
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20 234 the mediating effect of physical disability on physical frailty and HRQoL did not include 0 (Table
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22 235 3), indicating that the mediating effect was significant. The mediating effect value was -0.143 and
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25 236 the 95% CI was [-0.175, -0.113], which accounted for 33.71% of the total effect. This shows that
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28 237 disability plays a partial mediating role in the relationship between physical frailty and HRQoL.

238 3.5 Moderated mediation effect analysis

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

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4 248 frailty and HRQoL. Simple slope analyses indicated that the significant interaction at 1 SD
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6 249 below the mean(M-1SD) and 1 SD above the mean(M+1SD) of physical activity (See Fig. 2 and
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8
9 250 Fig. 3).Physical frailty had a significant predictive effect on the disability of individuals with
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11 251 high-level((M+1SD) or low-level(M-1SD) PA, but the predictive effect of physical frailty on
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14 252 physical disability was stronger for individuals with low-level PA($b_{\text{simple}} = 0.370, t = 16.979, P <$
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17 253 0.001) than for individuals with high-level PA,as shown in Fig. 2 ($b_{\text{simple}} = 0.120, t = 4.322, P <$
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20 254 0.001).Fig. 3 showed that for high levels of PA individuals, the effect of physical disability and
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22 255 HRQoL was significant ($b_{\text{simple}} = -0.304, t = -9.149, P < 0.001$). However, for low-level of PA
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25 256 individuals, the effect of physical disability and HRQoL was still significant but considerably
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27 257 stronger ($b_{\text{simple}} = -0.543, t = -28.654, P < 0.001$).In addition, as the level of physical activity
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30 258 increased, the mediating effect of physical disability on the relationship between physical frailty
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33 259 and HRQoL declined (Table 5).

34 35 260 **4. Discussion**

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38 261 In this study, a moderated mediation model was established with the mediation role of physical
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40 262 disability on the relationship between physical frailty and HRQoL, as well as the role of PA as a
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43 263 moderator in this indirect path between physical frailty and HRQoL. These findings
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46 264 preliminarily elucidate the potential causes of physical frailty on HRQoL and facilitate the
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48 265 development of targeted interventions for individuals so as to improve HRQoL in rural older
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51 266 adults.

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53 267 Consistent with previous studies^{50 51}, we find that physical frailty negatively affect HRQoL

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4 268 of older adults. This suggests that as the degree of physical frailty increases, the quality of life in
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6 269 older adults becomes worse. Although many studies have established a direct relationship
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9 270 between frailty and HRQoL, few have explored the underlying mechanisms of this relationship.
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11 271 Our study demonstrates that the physical disability mediates the physical frailty and HRQoL,
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14 272 with the mediating rate of 33.71%. A study also suggested that physical disability was one of the
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17 273 potential factors underlying the association between frailty and HRQoL, which was similar with
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20 274 our study⁵².

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22 275 The current study indicates that physical frailty is associated with disability, which is
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25 276 consistent with a study by Kojuma G⁵³. Frail older adults are very vulnerable to adverse health
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28 277 effects. A study indicated the risk of disability in the frail older adults was 12- to 13-fold
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31 278 increased than that in the non-frail older adults⁵⁴. Meanwhile, this study also demonstrates that
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34 279 the negative predictive effect of disability on individual HRQoL, which was consistent with
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37 280 previous studies^{55 56}. The possible explanation is that disabled older adults' poor self-care ability
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40 281 deteriorates their health, such as their normal physiological activities are restricted, physiological
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43 282 function is declined, social interaction is reduced, which adversely affect their physical and
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46 283 mental health and ultimately reduce HRQoL.. One study found that disability was the most
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49 284 important health problem for older adults, which seriously affected their quality of life in old
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52 285 adults' later years⁵⁷. The disability was the most important factor that contributed to decreasing
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55 286 quality of life in older adults. Physical disability has been shown to be associated with increased
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58 287 chronic diseases, and premature mortality^{58 59}, all of which could adversely affect the quality of

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4 288 life of older adults⁶⁰. Therefore, physical frailty may reduce HRQoL of rural older adults by
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6 289 increasing their disability.
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9 290 In the present study, we also find that PA plays a moderating role in the indirect effect
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11 291 between physical frailty and HRQoL. A larger indirect effect is observed among rural older
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13 292 adults with low-level of PA than among those with average or high-level of PA. Specifically, PA
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15 293 moderates the relationship between physical frailty and physical disability, and between physical
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17 294 disability and HRQoL. For older adults with low-level PA, the impact of physical frailty on
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19 295 physical disability is stronger than older adults with high-level PA. This finding indicates that
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21 296 PA moderates the relation between physical frailty and physical disability. We speculate that
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23 297 older adults with low-level PA may have a decline in their physiological system reserves, leading
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25 298 to a deterioration of their functional status and ultimately increasing the possibility of physical
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27 299 frailty and disability⁶¹. A systematic review showed that older adults without exercise habits were
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29 300 at greater risk of developing frailty. Taichi, resistance sports and other physical activities might
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31 301 effectively improve the health of older adults, reduce the symptoms of physical weakness, and
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33 302 prevent the occurrence of physical disability⁶². Compared with older adults with high-level
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35 303 PA, older adults with low-level PA are more vulnerable to the negative effects of physical frailty.
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37 304 As a result, physical frailty may cause more interference in older adults with low-level PA and
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39 305 increase the risk of physical disability.
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50 306 We also find that physical disability has a significant impact on quality of life at both high
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52 307 and low-level of PA. Compared with older adults with high levels of PA, physical disability is
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4 308 more likely to adversely affect HRQoL of older adults with low-level PA. A study showed that
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6 309 low-level PA was a major contributing factor for older adults disability⁶³. As the level of
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9 310 disability increases, the individuals with low-level of PA experience a more serious functional
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11 311 decline and become more worried about the health status, thus further negatively affect the
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14 312 HRQoL⁶⁴. In addition, physical disability has a greater effect on individuals with low-level PA
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17 313 than high-level PA, which indicates that PA plays a moderating role between physical disability
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19 314 and HRQoL. One study found that PA could improve the physical function and daily life
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22 315 activities of disabled older adults, and ultimately improved the life of older adults
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25 316 quality⁶⁵. Therefore, a low-level of PA might be associated with poor quality of life in rural older
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27 317 adults with high disability.

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30 318 However, physical activity does not moderate the direct relationship between physical
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32 319 frailty and HRQoL. Physical frailty may lead to a decline in physical function, muscle strength
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35 320 and physical activity in older adults, which may increase the risk of adverse health outcomes
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38 321 and ultimately affects HRQoL of older adults. Currently, there are few studies on the
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40 322 moderating role of physical activity between physical frailty and HRQoL. Further research is
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43 323 needed to explore the underlying reasons for such findings.

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45 324 Based on our findings, we recommended that community health managers should
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48 325 focus on ensuring the medical assistance, life care of older adults with physical frailty or physical
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51 326 disability. Besides, rural communities should establish some public facilities or organize some
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53 327 public activities to encourage older adults to participate in sports activities, and ultimately

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4 328 improve health and promote their HRQoL. There are several limitations in this study. First, our
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6 329 study was based on a cross-sectional study, which could not provide strong evidence of causation.
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9 330 Future research could adopt a longitudinal design or experiments to explore the causal
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11 331 relationship between physical frailty and HRQoL. Secondly, the data in this study comes from
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14 332 the participants' self-report information, which might result in recall bias. Thirdly, this study
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17 333 only included age and education as control variables. The study may also be affected by other
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19 334 confounding factors. In the future, we will include more confounding factors related to quality of
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22 335 life to verify our findings. Fourthly, physical disability has a partly mediating effect on the
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25 336 relationship between physical frailty and HRQoL, which indicates that there are other mediating
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27 337 variables in this relationship. More potential mechanisms related to physical frailty and HRQoL
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30 338 among older adults need to be explored in the future.

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340 **Conclusion**

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

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4 348 **Acknowledgements**

5
6 349 We thank the officials of health agencies, all participants and staffs at the study sites for their
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9 350 cooperation.

10
11 351 **Contributors**

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14 352 Study concept and design: Chengchao Zhou and Wenting Hao. Acquisition of data: Dan Zhao,
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18 354 Yi Wang. Drafting of the manuscript: Wenting Hao. Critical revision of the manuscript for
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21 355 important intellectual content: Chengchao Zhou and Jie Li. All authors read and approved the
22
23 356 final manuscript.

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26
27 357 **Funding**

28
29 358 This study was supported by the National Natural Science Foundation of China(71774104,
30
31 359 71473152, 71974117), the China Medical Board (16-257), Cheeloo Youth Scholar Grant,
32
33 360 Shandong University(IFYT1810,2012DX006) and NHC Key Laboratory of Health Economics
34
35
36 361 and Policy Research(NHC-HEPR2019014).

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40 362 **Data availability statement**

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42 363 The data that support the findings of this study are available from the corresponding author upon
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44
45 364 reasonable request.

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47 365 **Competing interests**

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50 366 None declared.

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53 367 **Patient consent for publication**

368 Not required.

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370 REFERENCES

- 371 1. NBSC. Statistical communiqué of the People's Republic of China on the 2017 national economic and social
372 development. 2017 [updated February 28,2018. Available from:
373 http://www.stats.gov.cn/english/PressRelease/201802/t20180228_1585666.html.
- 374 2. United Nations DESA, Population Division. World Population Ageing 2017:Highlights 2017 [updated 2017.
375 Available from:
376 https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf.
- 377 3. Brown DS, Thompson WW, Zack MM, et al. Associations Between Health-Related Quality of Life and Mortality
378 in Older Adults. *Prevention Science* 2015;16(1):21-30. doi: 10.1007/s1121-013-0437-z
- 379 4. Zhou B, Chen K, Wang J, et al. Quality of Life and Related Factors in the Older Rural and Urban Chinese
380 Populations in Zhejiang Province. *J Appl Gerontol* 2011;30(2):199-225. doi: 10.1177/0733464810361346
- 381 5. Zhou Z, Zhou Z, Gao J, et al. Urban-rural difference in the associations between living arrangements and the
382 health-related quality of life (HRQOL) of the elderly in China-Evidence from Shaanxi province. *PLoS One*
383 2018;13(9):e0204118. doi: 10.1371/journal.pone.0204118 [published Online First: 2018/09/21]
- 384 6. Morley JE, Vellas B, Van Kan GA, et al. Frailty Consensus: A Call to Action. *J Am Med Dir Assoc*
385 2013;14(6):392-97. doi: 10.1016/j.jamda.2013.03.022
- 386 7. Collard RM, Boter H, Schoevers RA, et al. Prevalence of frailty in community-dwelling older persons: a
387 systematic review. *J Am Geriatr Soc* 2012;60(8):1487-92. doi: 10.1111/j.1532-5415.2012.04054.x
388 [published Online First: 2012/08/14]
- 389 8. Vermeiren S, Vellaazzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A
390 Meta-Analysis. *J Am Med Dir Assoc* 2016;17(12) doi: 10.1016/j.jamda.2016.09.010
- 391 9. Lee IC, Chiu YH, Lee CY. Exploration of the importance of geriatric frailty on health-related quality of life.
392 *Psychogeriatrics* 2016;16(6):368-75. doi: 10.1111/psyg.12179 [published Online First: 2016/01/13]
- 393 10. Ferrer A, Formiga F, Cunillera O, et al. Predicting factors of health-related quality of life in octogenarians: a
394 3-year follow-up longitudinal study. 2015;24(11):2701-11.

- 1
2
3 395 11. Provencher V, Sirois MJ, Émond M, et al. Frail older adults with minor fractures show lower health-related
4 396 quality of life (SF-12) scores up to six months following emergency department discharge. *Health Qual*
5 397 *Life Outcomes* 2016;14:40. doi: 10.1186/s12955-016-0441-7 [published Online First: 2016/03/10]
6
7
8
9 398 12. Kanauchi M, Kubo A, Kanauchi K, et al. Frailty, health-related quality of life and mental well-being in older
10 399 adults with cardiometabolic risk factors. *Int J Clin Pract* 2008;62(9):1447-51. doi:
11 400 10.1111/j.1742-1241.2008.01830.x [published Online First: 2008/07/23]
12
13
14 401 13. Fullerton E, Yu B, Nurjeter A, et al. Basic ADL Disability and Functional Limitation Rates Among Older
15 402 Americans From 2000–2005: The End of the Decline? *J Gerontol A Biol Sci Med Sci* 2009;64(12):1333-36.
16 403 doi: 10.1093/gerona/64.12.1333
17
18
19 404 14. Picavet HSJ, Hoeymans N. Physical disability in The Netherlands: Prevalence, risk groups and time trends.
20 405 *Public Health* 2002;116(4):231-37. doi: 10.1038/sj.ph.1900864
21
22
23 406 15. Evenhuis HM, Hermans H, Hilgenkamp TIM, et al. Frailty and Disability in Older Adults with Intellectual
24 407 Disabilities: Results from the Healthy Ageing and Intellectual Disability Study. *J Am Geriatr Soc*
25 408 2012;60(5):934-38. doi: 10.1111/j.1532-5415.2012.03925.x
26
27
28 409 16. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised
29 410 older people. *Age Ageing* 2014;43(4):477-84. doi: 10.1093/ageing/aft181
30
31
32 411 17. Papachristou E, Wannamethee SG, Lennon LT, et al. Ability of Self-Reported Frailty Components to Predict
33 412 Incident Disability, Falls, and All-Cause Mortality: Results From a Population-Based Study of Older
34 413 British Men. *J Am Med Assoc* 2017;318(2):152-57. doi: 10.1001/jama.2016.08.020 [published Online
35 414 First: 2016/10/16]
36
37
38
39 415 18. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in
40 416 the United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133
41 417 [published Online First: 2015/08/25]
42
43
44 418 19. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older
45 419 adults: a prospective cohort study. *BMJ open* 2015;5(9):e008462. doi: 10.1136/bmjopen-2015-008462
46 420 [published Online First: 2015/09/05]
47
48
49 421 20. Medhi GK, Sarma J, Pala S, et al. Association between health related quality of life (HRQOL) and activity of
50 422 daily living (ADL) among elderly in an urban setting of Assam, India. *J Family Med Prim Care*
51 423 2019;8(5):1760-64. doi: 10.4103/jfmpe.jfmpe_270_19 [published Online First: 2019/06/15]
52
53
54
55
56
57
58
59
60

- 1
2
3 424 21. Tavassoli N, Guyonnet S, Abellan Van Kan G, et al. Description of 1,108 older patients referred by their
4 425 physician to the "Geriatric Frailty Clinic (G.F.C) for Assessment of Frailty and Prevention of Disability" at
5 426 the gerontopole. *J Nutr Health Aging* 2014;18(5):457-64. doi: 10.1007/s12603-014-0462-z [published
6 427 Online First: 2014/06/03]
7
8
9
10 428 22. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, et al. Exercise training as a drug to treat age associated
11 429 frailty. *Free Radic Biol Med* 2016;98:159-64. doi: 10.1016/j.freeradbiomed.2016.03.024 [published Online
12 430 First: 2016/03/30]
13
14
15 431 23. Rector JL, Marceau K, Friedman EM. Moderation of the Association Between Chronic Medical Conditions and
16 432 Functional Limitations Over Time by Physical Activity: Effects of Age. *J Gerontol A Biol Sci Med Sci*
17 433 2020;75(1):168-74. doi: 10.1093/gerona/glz020 [published Online First: 2019/02/21]
18
19
20
21 434 24. Palmer RF, Espino DV, Dergance JM, et al. The role of physical activity and diabetes status as a moderator:
22 435 functional disability among older Mexican Americans. *Age Ageing* 2012;41(6):752-8. doi:
23 436 10.1093/ageing/afs106 [published Online First: 2012/10/12]
24
25
26 437 25. Keysor JJ. Does late-life physical activity or exercise prevent or minimize disablement? A critical review of the
27 438 scientific evidence. *Am J Prev Med* 2003;25(3 Suppl 2):129-36. doi: 10.1016/s0749-3797(03)00176-4
28 439 [published Online First: 2003/10/14]
29
30
31 440 26. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? *J Gerontol A Biol Sci Med Sci*
32 441 2001;56(7):M412-23. doi: 10.1093/gerona/56.7.m412 [published Online First: 2001/07/11]
33
34
35 442 27. Rejeski WJ, Mihalko SL. Physical Activity and Quality of Life in Older Adults. *J Gerontol A Biol Sci Med Sci*
36 443 2001;56(suppl_2):23-35. doi: 10.1093/gerona/56.suppl_2.23
37
38
39 444 28. Casas-Herrero A, Izquierdo M. Physical exercise as an efficient intervention in frail elderly persons. *An Sist*
40 445 *Sanit Navar* 2012;35(1):69-85. doi: 10.4321/s1137-66272012000100007 [published Online First:
41 446 2012/05/04]
42
43
44 447 29. Mañas A, Del Pozo-Cruz B, Guadalupe-Grau A, et al. Reallocating Accelerometer-Assessed Sedentary Time to
45 448 Light or Moderate- to Vigorous-Intensity Physical Activity Reduces Frailty Levels in Older Adults: An
46 449 Isotemporal Substitution Approach in the TSHA Study. *J Am Med Dir Assoc* 2018;19(2):185.e1-85.e6. doi:
47 450 10.1016/j.jamda.2017.11.003 [published Online First: 2017/12/23]
48
49
50
51 451 30. Barnett A, Smith B, Lord SR, et al. Community-based group exercise improves balance and reduces falls in
52 452 at-risk older people: a randomised controlled trial. *Age Ageing* 2003;32(4):407-14. doi:
53 453 10.1093/ageing/32.4.407 [published Online First: 2003/07/10]
54
55

- 1
2
3
4 454 31. Jing Z, Li J, Wang Y, et al. The mediating effect of psychological distress on cognitive function and physical
5 455 frailty among the elderly: Evidence from rural Shandong, China. *J Affect Disord* 2020;268:88-94. doi:
6 456 10.1016/j.jad.2020.03.012 [published Online First: 2020/03/12]
7
8
9 457 32. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci*
10 458 *Med Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]
11
12 459 33. Buta BJ, Walston JD, Godino JG, et al. Frailty assessment instruments: Systematic characterization of the uses
13 460 and contexts of highly-cited instruments. *Ageing Res Rev* 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003
14 461 [published Online First: 2015/12/18]
15
16
17 462 34. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC*
18 463 *Geriatr* 2013;13:64. doi: 10.1186/1471-2318-13-64 [published Online First: 2013/06/22]
19
20
21 464 35. Radloff LS. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. *Appl*
22 465 *Psychol Meas* 1977;1(3):385-401. doi: 10.1177/014662167700100306
23
24
25 466 36. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical
26 467 Activity Questionnaire. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi*
27 468 2014;35(8):961-4. [published Online First: 2014/11/08]
28
29
30 469 37. Macfarlane DJ, Lee CC, Ho EY, et al. Reliability and validity of the Chinese version of IPAQ (short, last 7
31 470 days). *J Sci Med Sport* 2007;10(1):45-51. doi: 10.1016/j.jsams.2006.05.003 [published Online First:
32 471 2006/06/30]
33
34
35 472 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:
36 473 10.1016/j.jval.2016.11.016 [published Online First: 2017/04/15]
37
38
39 474 39. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living.
40 475 *The Gerontologist* 1969;9(3):179-86. doi: 10.1093/geront/9.3_Part_1.179 [published Online First:
41 476 1969/01/01]
42
43
44 477 40. Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc* 1971;19(6):465-81. doi:
45 478 10.1111/j.1532-5415.1971.tb01206.x [published Online First: 1971/06/01]
46
47
48 479 41. Chen P, Yu ES, Zhang M, et al. ADL dependence and medical conditions in Chinese older persons: a
49 480 population-based survey in Shanghai, China. *J Am Geriatr Soc* 1995;43(4):378-83. doi:
50 481 10.1111/j.1532-5415.1995.tb05811.x [published Online First: 1995/04/01]
51
52
53
54
55
56
57
58
59
60

- 1
2
3 482 42. Ng KY, Ang S, Chan KY. Personality and leader effectiveness: a moderated mediation model of leadership
4 483 self-efficacy, job demands, and job autonomy. *J Appl Psychol* 2008;93(4):733-43. doi:
5 484 10.1037/0021-9010.93.4.733 [published Online First: 2008/07/23]
6
7
8
9 485 43. Preacher KJ, Rucker DD, Hayes AF. Addressing Moderated Mediation Hypotheses: Theory, Methods, and
10 486 Prescriptions. *Multivariate behavioral research* 2007;42(1):185-227. doi: 10.1080/00273170701341316
11 487 [published Online First: 2007/01/01]
12
13
14 488 44. Holmbeck GN. Toward terminological, conceptual, and statistical clarity in the study of mediators and
15 489 moderators: examples from the child-clinical and pediatric psychology literatures. *Journal of consulting*
16 490 *and clinical psychology* 1997;65(4):599-610. doi: 10.1037//0022-006x.65.4.599 [published Online First:
17 491 1997/08/01]
18
19
20
21 492 45. Cohen J, Cohen P, West SG, et al. Applied multiple regression/correlation analysis for the behavioral sciences:
22 493 Routledge 2013.
23
24
25 494 46. Bolin JH, Hayes, Andrew F. (2013). Introduction to Mediation, Moderation, and Conditional Process Analysis:
26 495 A Regression-Based Approach. New York, NY: The Guilford Press. *J Educ Meas* 2014;51(3):335-37. doi:
27 496 10.1111/jedm.12050
28
29
30 497 47. Bao XY, Xie YX, Zhang XX, et al. The association between multimorbidity and health-related quality of life: a
31 498 cross-sectional survey among community middle-aged and elderly residents in southern China. *Health*
32 499 *Qual Life Outcomes* 2019;17(1):107. doi: 10.1186/s12955-019-1175-0 [published Online First: 2019/06/27]
33
34
35 500 48. Chapman B, Duberstein P, Lyness JM. Personality traits, education, and health-related quality of life among
36 501 older adult primary care patients. *J Gerontol B Psychol Sci Soc Sci* 2007;62(6):P343-52. doi:
37 502 10.1093/geronb/62.6.p343 [published Online First: 2007/12/15]
38
39
40
41 503 49. Podsakoff PM, MacKenzie SB, Lee JY, et al. Common method biases in behavioral research: a critical review of
42 504 the literature and recommended remedies. *J Appl Psychol* 2003;88(5):879-903. doi:
43 505 10.1037/0021-9010.88.5.879 [published Online First: 2003/10/01]
44
45
46 506 50. Kanwar A, Singh M, Lennon R, et al. Frailty and health-related quality of life among residents of long-term care
47 507 facilities. *J Aging Health* 2013;25(5):792-802. doi: 10.1177/0898264313493003 [published Online First:
48 508 2013/06/27]
49
50
51 509 51. Mulasso A, Roppolo M, Rabaglietti E. The role of individual characteristics and physical frailty on health related
52 510 quality of life (HRQOL): a cross sectional study of Italian community-dwelling older adults. *Arch Gerontol*
53 511 *Geriatr* 2014;59(3):542-8. doi: 10.1016/j.archger.2014.08.012 [published Online First: 2014/09/14]

- 1
2
3 512 52. Huaxue L, Taifang L, Wenjing Y, et al. Status of frailty and its effect path on quality of life among the elderly in
4 513 community. *Chinese Nursing Research* 2019;33(21):3645-49.
5
6
7 514 53. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review
8 515 and meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282
9 516 [published Online First: 2016/08/26]
10
11
12 517 54. Feng L, Zin Nyunt MS, Gao Q, et al. Cognitive Frailty and Adverse Health Outcomes: Findings From the
13 518 Singapore Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc* 2017;18(3):252-58. doi:
14 519 10.1016/j.jamda.2016.09.015 [published Online First: 2016/11/14]
15
16
17 520 55. Akosile CO, Mgbejedo UG, Maruf FA, et al. Depression, functional disability and quality of life among
18 521 Nigerian older adults: Prevalences and relationships. *Arch Gerontol Geriatr* 2018;74:39-43. doi:
19 522 10.1016/j.archger.2017.08.011 [published Online First: 2017/09/28]
20
21
22
23 523 56. Shin KR, Byeon YS, Kang Y, et al. A study on physical symptom, activity of daily living, and health-related
24 524 quality of life (HRQoL) in the community-dwelling older adults. *Taehan Kanho Hakhoe chi*
25 525 2008;38(3):437-44. doi: 10.4040/jkan.2008.38.3.437 [published Online First: 2008/07/08]
26
27
28 526 57. Crimmins EM. Trends in the health of the elderly. *Annu Rev Public Health* 2004;25:79-98. doi:
29 527 10.1146/annurev.publhealth.25.102802.124401 [published Online First: 2004/03/16]
30
31
32 528 58. Khan ZA, Singh C, Khan T. Correlates of physical disability in the elderly population of Rural North India
33 529 (Haryana). *J Family Community Med* 2018;25(3):199-204. doi: 10.4103/jfcm.JFCM_160_17 [published
34 530 Online First: 2018/09/18]
35
36
37 531 59. Wei M, Li J, Wang H. Impact of the disability trajectory on the mortality risk of older adults in China. *Arch*
38 532 *Gerontol Geriatr* 2018;74:174-83. doi: 10.1016/j.archger.2017.10.015 [published Online First: 2017/11/11]
39
40
41 533 60. Gobbens RJ. Associations of ADL and IADL disability with physical and mental dimensions of quality of life in
42 534 people aged 75 years and older. *PeerJ* 2018;6:e5425. doi: 10.7717/peerj.5425 [published Online First:
43 535 2018/08/21]
44
45
46 536 61. Rejeski WJ, Brawley LR, Haskell WL. The prevention challenge: an overview of this supplement. *Am J Prev*
47 537 *Med* 2003;25(3 Suppl 2):107-9. doi: 10.1016/s0749-3797(03)00173-9 [published Online First: 2003/10/14]
48
49
50 538 62. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older
51 539 adults: a systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154. doi:
52 540 10.1186/s12877-015-0155-4 [published Online First: 2015/12/03]
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3 541 63. Kortebein P, Ferrando A, Lombeida J, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older
4 542 adults. *JAMA* 2007;297(16):1772-4. doi: 10.1001/jama.297.16.1772-b [published Online First: 2007/04/26]
5
6
7 543 64. Ávila-Funes JA, Pina-Escudero SD, Aguilar-Navarro S, et al. Cognitive impairment and low physical activity
8 544 are the components of frailty more strongly associated with disability. *J Nutr Health Aging*
9 545 2011;15(8):683-9. doi: 10.1007/s12603-011-0111-8 [published Online First: 2011/10/05]
10
11
12 546 65. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older
13 547 adults. *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First:
14 548 2011/04/01]
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565 **Table 1 Spearman correlations coefficients of main variables among the participants in Shandong, China,**
 566 **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

567 M±SD: mean±standard deviation ;M (P₂₅,P₇₅): Median(Quartile₁,Quartile₃)

568 1,2,4 follow normal distribution and are described as M±SD.

569 3 does not follow normal distribution and is described as M (P₂₅, P₇₅).

570 **P<0.001

573 **Table 2 Testing the mediation effect of physical disability between physical frailty and HRQoL among the**
 574 **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***	

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

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13 580 **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%

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27 581 BootSE bootstrap standard error, BootCI bootstrap confidence interval28
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593 **Table 4** Testing the moderated mediation effect of physical frailty on HRQoL among the participants in
 594 **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 \times PA	-0.120	-7.058***	0.011	0.682
Physical disability			-0.422	-24.375***
Physical disability \times PA			0.115	6.104***
R ²	0.159		0.390	
F	122.004***		295.850***	

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

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599 **Table 5** Mediating effect values at different levels of physical activity among the participants in Shandong,
 600 **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

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

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4 602 confidence interval, BootULCI bootstrap upper limit confidence interval.

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11 606 **Fig. 1** The conceptual framework of the moderated mediation model

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14 607 **Fig. 2** Simple slope analysis shows that physical frailty moderated the relationship between physical frailty and

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20 609 **Fig.3** Simple slope analysis shows that physical activity moderated the relationship between physical disability and

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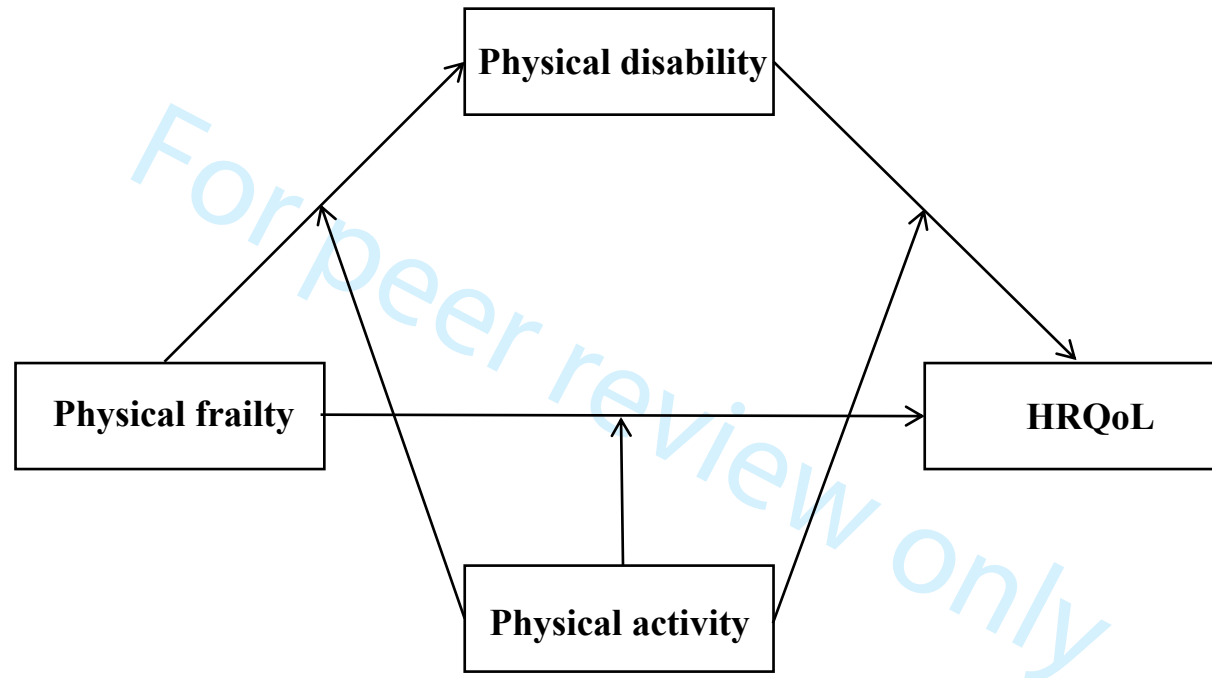


Fig1. The conceptual framework of the moderated mediation model

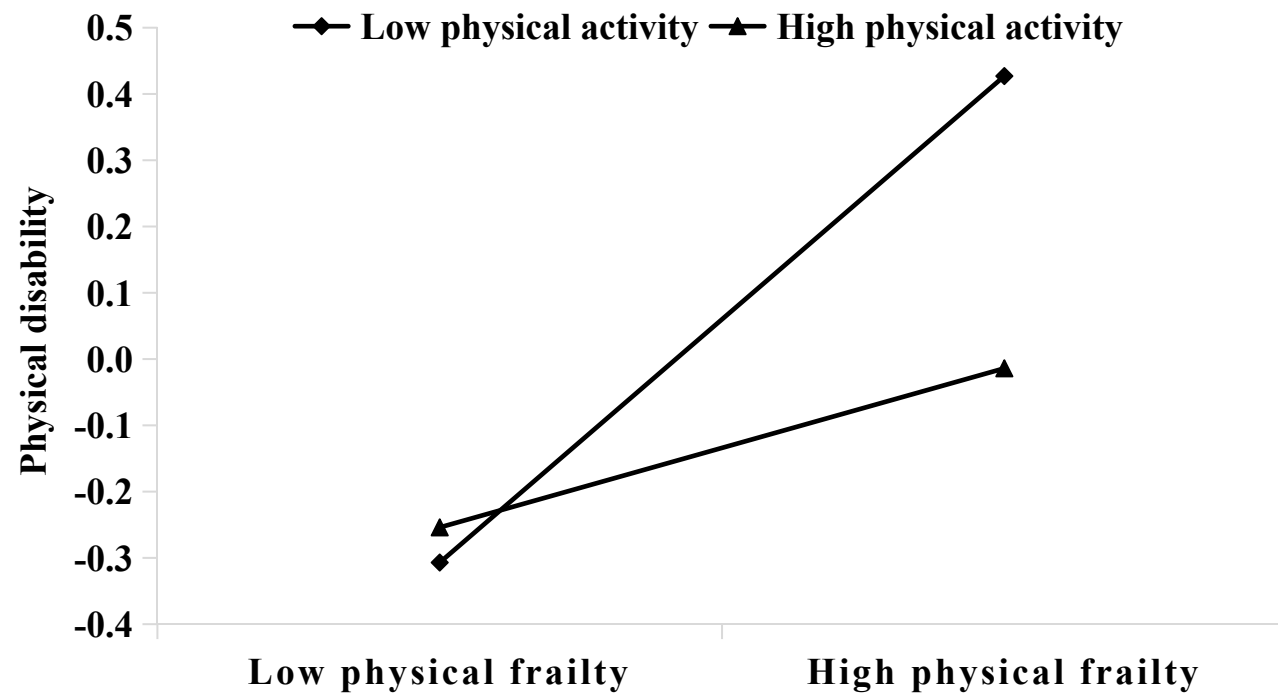


Fig2.Simple slope analysis shows that physical activity moderated the relationship between physical frailty and physical disability

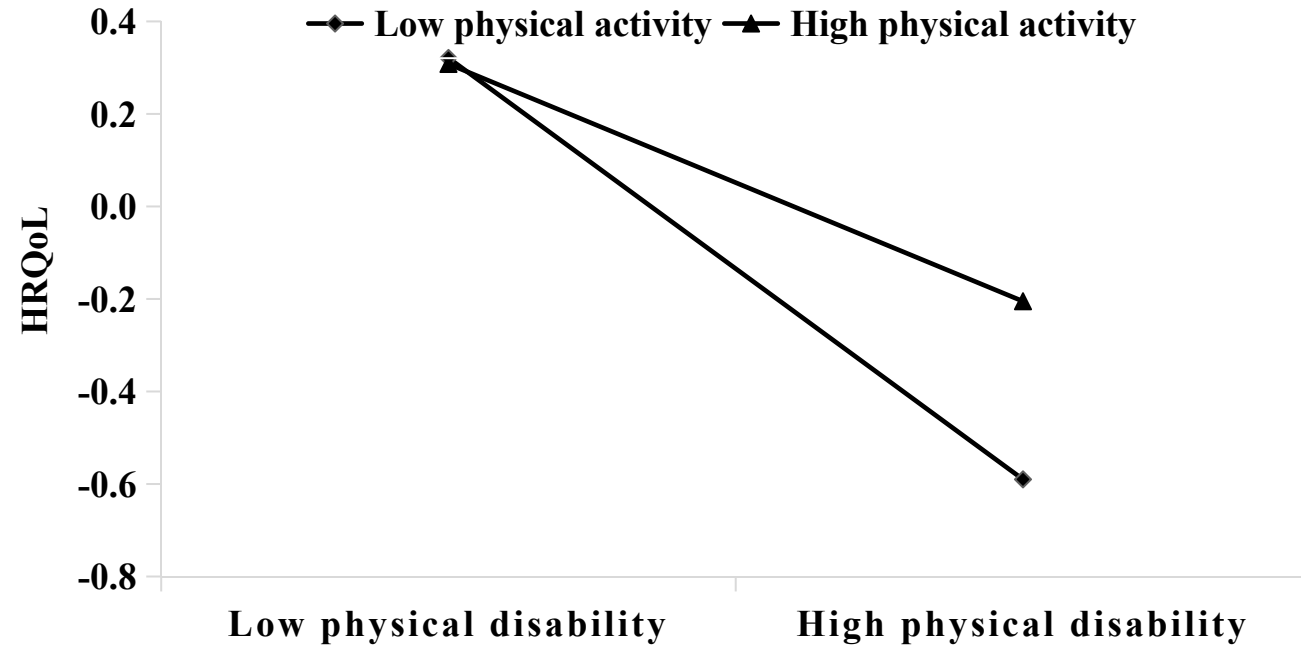


Fig3. Simple slope analysis shows that physical activity moderated the relationship between physical disability and HRQoL

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	
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-

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2	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
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6			(b) Report category boundaries when continuous variables were categorized
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8			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
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11	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
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14	Discussion		
15	Key results	18	Summarise key results with reference to study objectives
16	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
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20	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
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24	Generalisability	21	Discuss the generalisability (external validity) of the study results
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26	Other information		
27	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
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*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.

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-042496.R2
Article Type:	Original research
Date Submitted by the Author:	07-Dec-2020
Complete List of Authors:	Hao, Wenting; School of public health Li, Jie; Shandong University School of Public Health Fu, Peipei; Shandong University Cheeloo College of Medicine Zhao, Dan; Shandong University, school of public health Jing, Zhengyue; Shandong University Cheeloo College of Medicine wang, yi; Shandong University Cheeloo College of Medicine Yu, Caiting; Shandong University Cheeloo College of Medicine Yuan, Yemin; Shandong University School of Public Health Zhou, Chengchao; Shandong University, School of Public Health; Shandong University, China
Primary Subject Heading:	Public health
Secondary Subject Heading:	Geriatric medicine
Keywords:	Public health < INFECTIOUS DISEASES, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, SOCIAL MEDICINE

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4 1 **Physical frailty and health-related quality of life among Chinese rural older adults: A**
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6 2 **moderated mediation analysis of physical disability and physical activity**

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9 3 Wenting Hao¹, Jie Li¹, Peipei Fu^{1,2}, Dan Zhao¹, Zhengyue Jing¹, Yi Wang¹, Caiting Yu¹, Yemin
10 4 Yuan¹, Chengchao Zhou^{1,2*}

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38 16 Word count: 3542

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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 ($\beta = -0.120$, $t = -7.058$, $P < 0.001$), and the interaction term between physical disability and PA also had a significant predictive effect on HRQoL ($\beta = 0.115$, $t = 6.104$, $P < 0.001$).

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4 43 **Conclusions:**PA appears to moderate the indirect effect of physical disability on the association
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6 44 between physical frailty and HRQoL. This study provides support for potential mechanisms in
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9 45 the association between physical frailty and HRQoL.Encouraging rural older adults to increase
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12 46 PA appropriately might improve HRQoL for older adults with physical frailty and physical
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14 47 disability problems.
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19 49 **Key words:** HRQoL; Physical activity; Physical frailty; Physical disability; Rural older
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4 53 **Strengths and limitations of this study**

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7 54 1. This is the first study to investigate the moderating and mediating factors of the relationship
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10 55 between physical frailty and HRQoL among older adults in rural China.
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12 56 2. Moderated mediation model was used to explore the potential effect of physical disability
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15 57 and physical activity.
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17 58 3. Cross-sectional data could not provide strong evidence of causation and may result in biased
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20 59 estimates of mediation effects.
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23 60 4. Only two control variables were included in this study, and more confounding factors will be
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26 61 included to verify our results in the future.
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28 62 5. More potential mechanisms related to physical frailty and HRQoL among older adults need
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31 63 to be explored by using longitudinal data in the future.
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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 population¹. It is predicted that by 2050, older adults over 60 will account for more than 35.1% of the total population². 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 adults³. 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 function⁶. With the increase of age, the risk of physical frailty increases⁷. Frailty may lead to negative health consequences, including falls, reduced activity, reduced independence, frequent hospitalization, and disability⁸. 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 HRQoL⁹⁻¹¹, and frail older adults reported worse HRQoL than those who were not frail¹². 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

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4 90 of disability¹⁷. A national longitudinal study of 7,439 people over 65 in the US showed that frailty
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6 91 was a strong predictor of disability¹⁸. A prospective two-year cohort study in Japan also showed
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9 92 that frailty and prophase of frailty increased the risk of disability¹⁹. These findings suggest that
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12 93 physical frailty is associated with disability in older adults. Studies have also demonstrated that
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14 94 the quality of life worsened as the degree of disability increased, and the more severe the
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17 95 disability, the worse the quality of life²⁰. Compared with non-disabled older adults, disabled
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20 96 older adults are more prone to falls, depression, anxiety, etc., and their HRQoL was significantly
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22 97 reduced. Therefore, we speculate that frailty may have an indirect effect on individual's HRQoL
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25 98 through the mediating effect of physical disability.

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27 99 Physical frailty is considered to be reversible and preventable²¹. Physical activity (PA) is a
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30 100 key factor of reverse and prevent frailty in older adults²². Studies have found that physical
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33 101 activity moderated the relationship between chronic illness and functional limitations, and
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35 102 moderated functional disability and body function^{23 24}. PA can alleviate the decline of physical
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38 103 function in older adults and has a beneficial effect on functional limitations, physical frailty,
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40 104 disability and quality of life in older adults²⁵⁻²⁷. Studies indicated the positive effect of physical
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43 105 activity on reducing adverse events caused by frailty in older people. Performing a physical
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46 106 activity of moderate to vigorous intensity would improve physical frailty and prevent the
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48 107 occurrence of disability when compared to the performance of a physical activity of low intensity,
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51 108 ultimately promote older adults' quality of life²⁸⁻³⁰. Therefore, PA may moderate the direct and
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54 109 indirect relationship between physical frailty and HRQoL through physical disability as a

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6 111 In the present study, we used a cross-sectional study to examine the relationship between
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9 112 physical frailty and HRQoL, focusing on the mediating role of physical disability and the
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12 113 moderating role of PA in the relationship between physical frailty and HRQoL. The conceptual
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14 114 framework of the moderated mediation model was shown in Fig. 1.
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19 116 **2. Methods**

20 117 **2.1.1 Design and sample**

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24 118 This study was conducted from May to June, 2019 in Shandong province, China. A multistage
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27 119 stratified cluster sampling method was used to select participants, which was described in detail
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30 120 in a paper we have previously published³¹. Three rural counties (Qufu, Laoling and Rushan) were
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33 121 selected according to the GDP per capita (2018) in Shandong. Within each selected county, five
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35 122 townships were randomly selected. Then, four villages were selected from each selected
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38 123 townships and the elderly aged 60 years old and above who were randomly selected from sample
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41 124 villages. All participants completed the questionnaire independently. A total of 3,600 respondents
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43 125 were recruited from 60 villages and 15 townships in 3 rural counties in Shandong province, of
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45 126 whom 3,243 completed the entire survey, with a response rate of 90.05%.

46 127 **2.2. Variables and measurement**

47 48 49 50 128 **2.2.1 Independent variable**

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53 129 Physical frailty was measured by Frailty Phenotype³². The scale is a widely used frailty screening

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4 130 scale with good reliability and validity^{33 34}. Frailty was defined based on the following five
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6 131 aspects: weight loss, exhaustion, low physical activity level, slowness, weakness. ①Weight loss:
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8 132 In the past 1 year, participants' body mass index (BMI) decreased by >5.0% (except for personal
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10 deliberate weight loss). ②Exhaustion: Using the Center for Epidemiological Studies-
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12 133 Depression(CES-D)³⁵: "How often in the last week did you feel this way?" (1) I could not get
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14 134 going and (2) I felt everything I did was an effort. Either of the above two questions that
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16 135 participants answered 3~4 days and most of the time, was considered exhaustion. ③Low
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18 136 physical activity level: According the International Physical Activity Questionnaire-short Form
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20 137 (IPAQ-SF)^{36 37},we used standard algorithms to calculate the Kcals consumed per week. The
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22 138 criterion is adjusted according to gender. Male: <383 Kcals/ week is a decrease in physical
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24 139 activity, while female: <270 Kcals/ week is a decrease in physical activity. ④Slowness:
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26 140 Slowness was assessed via walking speed at 15 ft measured for 3 times, and we record the
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28 141 minimum value.The criterion is adjusted according to gender and height. Men: height≤173 cm
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30 142 and time≥7 seconds; height >173 cm and time≥6 seconds. Women: height≤159 cm and time≥7
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32 143 seconds ;height >159 cm and time≥6 seconds. ⑤Weakness: Weakness was assessed by grip
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34 144 strength using a handgrip dynamometer was measured for 3 times, and we record the maximum
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36 145 value, adjusted for gender and BMI. Men: BMI≤24 and grip strength≤29;BMI 24.1-26and grip
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38 146 strength≤30;BMI 26.1-28 and grip strength ≤30;BMI > 28 and grip strength≤32. Women:
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40 147 BMI≤23 and grip strength≤17;BMI 23.1-26 and grip strength≤17.3;BMI 26.1-29 and grip
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150 **2.2.2 Dependent variables**

151 HRQoL was measured by the health utility value of EQ-5D-5L³⁸. The EQ-5D-5L consists of the
152 EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L
153 descriptive system has five elements (mobility, self-care, usual activities, pain/discomfort, and
154 anxiety/depression) and each element includes five levels (no problems, some problems,
155 moderate problems, severe problems and extreme problems). The latest EQ-5D-5L health utility
156 scores method refers to Chinese integral conversion table³⁸. The range of utility value is [-0.391,
157 1.000]. A higher score indicates better health condition of the respondents. Cronbach's alpha was
158 0.761 in this study.

159 **2.2.3 Mediator**

160 Physical disability was evaluated by the Activity of Daily Living Scale (ADLS), which was
161 developed by Lawton and Brody in 1969 to measure the disability of older adults^{39 40}. The Scale
162 consists of 14 items, including Physical Self-Maintenance Scale (PSMS) and Instrumental
163 Activities of Daily Living (IADL). The total score is 14-56, with higher scores indicating
164 increased physical disability. A score of 14 and lower indicates completely normal physical
165 ability, a score between 15 and 22 is defined as mild disability, and a score of 23 and higher is
166 defined as severe disability. ADLS is recommended by WHO and has been widely used in older
167 adults in China, with good reliability and validity⁴¹. Cronbach's alpha was 0.764 in this study.

168 **2.2.4 Moderator**

169 PA was assessed using the IPAQ-SF^{36 37}. The questionnaire contains 7 questions, 6 of which were

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4 170 about physical activity. The IPAQ-SF investigates the PA of the individuals in the last 7 days.
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7 171 The questionnaire involved three types of intensity activities, including vigorous physical
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10 172 activity (VPA =8.0 metabolic equivalent [METs]), moderate physical activity (MPA =4.0 ME
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13 173 Ts), and low physical activity (LPA =3.3 METs).PA of each person engaged in a certain
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16 174 intensity per week is the METs value corresponding to that physical activity × weekly frequency
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19 175 × daily time, and the sum of three PA is the total PA (met-h /week). The greater the overall
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22 176 physical activity value, the higher the physical activity.

177 **2.3 Data analysis**

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

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4 189 moderation effect⁴⁵.The mediation model and moderated mediation model were tested with the
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6 190 PROCESS V3.3 macro for SPSS⁴⁶.In the current study, we selected Model 4 and Model 59 to
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9 191 analyze the mediating effect and moderated mediation effect. In addition,through t test and
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12 192 ANOVA analysis, we found that HRQoL was related to age and education. Previous studies have
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14 193 also found HRQoL was associated with age and education^{47 48}. We controlled age and education
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17 194 in this study.Sampling weights were used in all of the analyses to adjust for the survey design.
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20 195 **2.4 Patient and public involvement statement**

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23 196 This research was done without patient involvement. No patients were involved in developing
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25 197 the hypothesis and plans for design of this study either. The results would not be disseminated to
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28 198 study participants or any other individuals or communities.
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31 199 **2.5 Ethical considerations**

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34 200 The study was approved by the Ethics Committee of School of Public Health in Shandong
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37 201 University, P. R. China. The participants have been informed of the purpose and procedures of
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39 202 the study before the investigation. Before the study began, participants had signed written
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42 203 informed consent indicating that they were fully aware of the study procedures.
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47 48 49 205 **3. Results**

50 51 206 **3.1 Common method biases**

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54 207 We used Harman single factor test to conduct a common method biases test⁴⁹.The results show

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4 208 that there are 12 factors with eigenvalues greater than 1, and the variance explained by the first
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6 209 factor is 17.92%, which is less than 40% of the critical standard, indicating that there are no
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9 210 serious common method biases in this study.

211 **3.2 Socio-demographic characteristics of the participants**

14 212 There were 3,243 participants, comprising 2,060 (63.5%) women and 1,182 (36.5%) men. The
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17 213 average age was 69.88 (SD=6.10) years, ranging from 60 to 97 years. Of the participants, 25.5%
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20 214 were single. About 72.4% had chronic disease. The majority (81.9%) were empty nest elderly.

215 **3.3 Bivariate correlations of main variables**

24 216 The mean, standard deviation/ Median (Quartile₁, Quartile₃) and correlation coefficient of each
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27 217 variable were shown in Table 1. Physical frailty was positively correlated with physical disability
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29
30 218 ($\rho = 0.283, P < 0.01$), physical frailty was negatively correlated with HRQoL ($\rho = -0.429, P <$
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32 219 0.01) and PA ($\rho = -0.378, P < 0.01$). Physical disability was negatively correlated with HRQoL
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34
35 220 ($\rho = -0.378, P < 0.01$) and PA ($\rho = -0.194, P < 0.01$). PA was positively correlated with HRQoL
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38 221 ($\rho = 0.258, P < 0.01$).

222 **3.4 Mediation effect analysis**

42 223 Model 4 in the SPSS macro compiled by Hayes 2013⁴⁶ was used to test the mediating effect of
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45 224 physical disability in the relationship between physical frailty and HRQoL under the control
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48 225 variable of age, education. As shown in Table 2 and Table 3, physical frailty had a significant
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51 226 predictive effect on quality of life ($\beta = -0.423, t = -26.031, P < 0.001$), and the direct predictive
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54 227 effect of frailty on quality of life was still significant when the mediating variable physical

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4 228 disability was added. Meanwhile, physical frailty had a significant positive predictive effect on
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6 229 physical disability ($\beta = 0.295, t = 17.729, P < 0.001$). Physical disability also had a significant
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9 230 negative predictive effect on HRQoL ($\beta = -0.482, t = -32.407, P < 0.001$). In addition, the upper
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11 231 and lower limits of the Bootstrap 95% CI for the direct effect of physical frailty on HRQoL and
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14 232 the mediating effect of physical disability on physical frailty and HRQoL did not include 0 (Table
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17 233 3), indicating that the mediating effect was significant. The mediating effect value was -0.143 and
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19 234 the 95% CI was [-0.175, -0.113], which accounted for 33.71% of the total effect. This showed
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22 235 that disability played a partial mediating role in the relationship between physical frailty and
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25 236 HRQoL.

237 **3.5 Moderated mediation effect analysis**

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

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4 248 SD below the mean ($M-1SD$) and 1 SD above the mean ($M+1SD$) of physical activity (See Fig. 2
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7 249 and Fig. 3). Physical frailty had a significant predictive effect on the disability of individuals with
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9 250 high-level ($M+1SD$) or low-level ($M-1SD$) PA, but the predictive effect of physical frailty on
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12 251 physical disability was stronger for individuals with low-level PA ($b_{\text{simple}} = 0.370, t = 16.979, P <$
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14 252 0.001) than for individuals with high-level PA, as shown in Fig. 2 ($b_{\text{simple}} = 0.120, t = 4.322, P <$
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17 253 0.001). Fig. 3 showed that for high levels of PA individuals, the effect of physical disability and
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19 254 HRQoL was significant ($b_{\text{simple}} = -0.304, t = -9.149, P < 0.001$). However, for low-level of PA
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22 255 individuals, the effect of physical disability and HRQoL was still significant but considerably
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25 256 stronger ($b_{\text{simple}} = -0.543, t = -28.654, P < 0.001$). In addition, as the level of physical activity
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28 257 increased, the mediating effect of physical disability on the relationship between physical frailty
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30 258 and HRQoL declined (Table 5).

31 32 259 **4. Discussion**

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35 260 In this study, a moderated mediation model was established with the mediation role of physical
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38 261 disability on the relationship between physical frailty and HRQoL, as well as the role of PA as a
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41 262 moderator in this indirect path between physical frailty and HRQoL. These findings preliminarily
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44 263 elucidate the potential causes of physical frailty on HRQoL and facilitate the development of
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47 264 targeted interventions for individuals so as to improve HRQoL in rural older adults.

48 265 Consistent with previous studies^{50 51}, we find that physical frailty has a negative association
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51 266 with HRQoL. This suggests that as the degree of physical frailty increases, the quality of life in
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54 267 older adults becomes worse. Although many studies have established a direct relationship

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4 268 between frailty and HRQoL, few have explored the underlying mechanisms of this relationship.
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7 269 Our study suggests that physical disability mediates the association between physical frailty and
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9 270 HRQoL, with the mediating rate of 33.71%. A study also suggested that physical disability was
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11 271 one of the potential factors underlying the association between frailty and HRQoL, which was
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14 272 similar with our study⁵².

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17 273 The current study indicates that physical frailty is associated with disability, which is
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19 274 consistent with a study by Kojuma G⁵³. Frail older adults are very vulnerable to adverse health
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21 275 effects. A study indicated the risk of disability in frail older adults was 12- to 13-fold increased
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23 276 than that in non-frail older adults⁵⁴. Meanwhile, this study also demonstrates a negative predictive
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25 277 effect of disability on individual HRQoL, which was consistent with previous studies^{55 56}. The
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27 278 possible explanation is that disabled older adults' poor self-care ability deteriorates their health,
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29 279 then their normal physiological activities are restricted, physiological function is declined, and
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31 280 social interaction is reduced, which adversely affect their physical and mental health and
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33 281 ultimately reduce HRQoL. One study found that disability was the most important health
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35 282 problem for older adults, which seriously affected their quality of life in old adults' later
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37 283 years⁵⁷. The disability was the most important factor that contributed to decreasing quality of life
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39 284 in older adults. Physical disability has been proved to be associated with increased chronic
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41 285 diseases, and premature mortality^{58 59}, all of which could adversely affect the quality of life of
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43 286 older adults⁶⁰. Therefore, physical frailty may reduce HRQoL of rural older adults by increasing
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45 287 their disability.

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4 288 In the present study, we also find that PA appears to play a moderating role in the indirect
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6 289 effect between physical frailty and HRQoL. A larger indirect effect is observed among rural
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9 290 older adults with low-level of PA than among those with average or high-level of PA.
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11 291 Specifically, PA appears to moderate the relationship between physical frailty and physical
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14 292 disability, and between physical disability and HRQoL. For older adults with low-level PA, the
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17 293 impact of physical frailty on physical disability is stronger than older adults with high-level PA.
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19 294 This finding indicates that PA appears to moderate the relationship between physical frailty and
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22 295 physical disability. We speculate that older adults with low-level PA may have a decline in their
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25 296 physiological system reserves, leading to a deterioration of their functional status and ultimately
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27 297 increasing the possibility of physical frailty and disability⁶¹. A systematic review showed that
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30 298 older adults without exercise habits were at greater risk of developing frailty. Taichi, resistance
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33 299 sports, and other physical activities might effectively improve the health of older adults, reduce
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35 300 the symptoms of physical weakness, and prevent the occurrence of physical
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38 301 disability⁶². Compared with older adults with high-level PA, older adults with low-level PA are
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41 302 more vulnerable to the negative effects of physical frailty. As a result, physical frailty may cause
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43 303 more interference in older adults with low-level PA and increase the risk of physical disability.
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45 304 We also find that physical disability has a significant impact on quality of life at both high
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48 305 and low-level of PA. Compared with older adults with high levels of PA, physical disability is
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51 306 more likely to adversely affect HRQoL of older adults with low-level PA. A study showed that
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53 307 low-level PA was a major contributing factor for older adults' disability⁶³. As the level of

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4 308 disability increases, the individuals with low-level of PA experience a more serious functional
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6 309 decline and become more worried about the health status, thus further negatively affect the
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9 310 HRQoL⁶⁴. In addition, physical disability has a greater effect on individuals with low-level PA
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11 311 than high-level PA, which indicates that PA plays a moderating role between physical disability
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14 312 and HRQoL. One study found that PA could improve the physical function and daily life
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17 313 activities of disabled older adults, and ultimately improved the life of older adults
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19 314 quality⁶⁵. Therefore, a low-level of PA might be associated with poor quality of life in rural older
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22 315 adults with high disability.

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25 316 However, physical activity does not appear to moderate the direct relationship between
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27 317 physical frailty and HRQoL. Physical frailty may lead to a decline in physical function, muscle
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30 318 strength and physical activity in older adults, which may increase the risk of adverse health
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33 319 outcomes and ultimately affects HRQoL of older adults. Currently, there are few studies on the
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35 320 moderating role of physical activity between physical frailty and HRQoL. Further research is
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38 321 needed to explore the underlying reasons for such findings.

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40 322 Based on our findings, we recommend that community health managers should focus on
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43 323 ensuring the medical assistance, life care of older adults with physical frailty or physical
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46 324 disability. Besides, rural communities should establish some public facilities or organize some
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49 325 public activities to encourage older adults to participate in sports activities, and ultimately
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51 326 improve health and promote their HRQoL. There are several limitations in this study. First, our
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53 327 study was based on a cross-sectional study, which could not provide strong evidence of causation.

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4 328 In addition, using cross-sectional data to examine longitudinal mediation effects can lead to
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6 329 biased estimates of mediation effects⁶⁶. Future research could adopt a longitudinal design or
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9 330 experiments to explore the causal relationship between physical frailty and HRQoL. Secondly,
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11 331 the data in this study comes from the participants' self-report information, which might result in
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14 332 recall bias. Thirdly, this study only included age and education as control variables. The study
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17 333 may also be affected by other confounding factors. In the future, we will include more
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20 334 confounding factors related to quality of life to verify our findings. Fourthly, physical disability
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22 335 has a partly mediating effect on the relationship between physical frailty and HRQoL, which
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25 336 indicates that there are other mediating variables in this relationship. More potential mechanisms
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28 337 related to the association between physical frailty and HRQoL among older adults need to be
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30 338 explored in the future.

339 **Conclusion**

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

346 **Acknowledgements**

347 We thank the officials of health agencies, all participants and staffs at the study sites for their

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4 348 cooperation.

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6 349 **Contributors**

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9 350 Study concept and design: Chengchao Zhou and WentingHao. Acquisition of data: Dan Zhao,
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13 352 Yi Wang. Drafting of the manuscript: WentingHao. Critical revision of the manuscript for
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16 353 important intellectual content: Chengchao Zhou and Jie Li. All authors read and approved the
17
18 354 final manuscript.

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21
22 355 **Funding**

23
24 356 This study was supported by the National Natural Science Foundation of China(71774104,
25
26 357 71473152, 71974117), the China Medical Board (16-257), Cheeloo Youth Scholar Grant,
27
28 358 Shandong University(IFYT1810,2012DX006) and NHC Key Laboratory of Health Economics
29
30
31 359 and Policy Research(NHC-HEPR2019014).

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34 360 **Data availability statement**

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37 361 The data that support the findings of this study are available from the corresponding author upon
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40 362 reasonable request.

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42 363 **Competing interests**

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44
45 364 None declared.

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47 365 **Patient consent for publication**

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50 366 Not required.

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368 REFERENCES

- 369 1. NBSC. Statistical communiqué of the People's Republic of China on the 2017 national economic and social
370 development. 2017 [updated February 28,2018. Available from:
371 http://www.stats.gov.cn/english/PressRelease/201802/t20180228_1585666.html.
- 372 2. United Nations DESA, Population Division. World Population Ageing 2017:Highlights 2017 [updated 2017.
373 Available from:
374 https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf
375 .
- 376 3. Brown DS, Thompson WW, Zack MM, et al. Associations Between Health-Related Quality of Life and Mortality in
377 Older Adults. *Prevention Science* 2015;16(1):21-30. doi: 10.1007/s11121-013-0437-z
- 378 4. Zhou B, Chen K, Wang J, et al. Quality of Life and Related Factors in the Older Rural and Urban Chinese
379 Populations in Zhejiang Province. *J Appl Gerontol* 2011;30(2):199-225. doi: 10.1177/0733464810361346
- 380 5. Zhou Z, Zhou Z, Gao J, et al. Urban-rural difference in the associations between living arrangements and the
381 health-related quality of life (HRQOL) of the elderly in China-Evidence from Shaanxi province. *PLoS One*
382 2018;13(9):e0204118. doi: 10.1371/journal.pone.0204118 [published Online First: 2018/09/21]
- 383 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.
384 doi: 10.1016/j.jamda.2013.03.022
- 385 7. Collard RM, Boter H, Schoevers RA, et al. Prevalence of frailty in community-dwelling older persons: a systematic
386 review. *J Am Geriatr Soc* 2012;60(8):1487-92. doi: 10.1111/j.1532-5415.2012.04054.x [published Online
387 First: 2012/08/14]
- 388 8. Vermeiren S, Vellaazzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A
389 Meta-Analysis. *J Am Med Dir Assoc* 2016;17(12) doi: 10.1016/j.jamda.2016.09.010
- 390 9. Lee IC, Chiu YH, Lee CY. Exploration of the importance of geriatric frailty on health-related quality of life.
391 *Psychogeriatrics* 2016;16(6):368-75. doi: 10.1111/psyg.12179 [published Online First: 2016/01/13]
- 392 10. Ferrer A, Formiga F, Cunillera O, et al. Predicting factors of health-related quality of life in octogenarians: a
393 3-year follow-up longitudinal study. 2015;24(11):2701-11.

- 1
2
3 394 11. Provencher V, Sirois MJ, Émond M, et al. Frail older adults with minor fractures show lower health-related
4 395 quality of life (SF-12) scores up to six months following emergency department discharge. *Health Qual Life*
5 396 *Outcomes* 2016;14:40. doi: 10.1186/s12955-016-0441-7 [published Online First: 2016/03/10]
- 8 397 12. Kanauchi M, Kubo A, Kanauchi K, et al. Frailty, health-related quality of life and mental well-being in older
9 398 adults with cardiometabolic risk factors. *Int J Clin Pract* 2008;62(9):1447-51. doi:
10 399 10.1111/j.1742-1241.2008.01830.x [published Online First: 2008/07/23]
- 13 400 13. Fullertomson E, Yu B, Nurujeter A, et al. Basic ADL Disability and Functional Limitation Rates Among Older
14 401 Americans From 2000–2005: The End of the Decline? *J Gerontol A Biol Sci Med Sci* 2009;64(12):1333-36.
15 402 doi: 10.1093/gerona/glp130
- 18 403 14. Picavet HSJ, Hoeymans N. Physical disability in The Netherlands: Prevalence, risk groups and time trends. *Public*
19 404 *Health* 2002;116(4):231-37. doi: 10.1038/sj.ph.1900864
- 22 405 15. Evenhuis HM, Hermans H, Hilgenkamp TIM, et al. Frailty and Disability in Older Adults with Intellectual
23 406 Disabilities: Results from the Healthy Ageing and Intellectual Disability Study. *J Am Geriatr Soc*
24 407 2012;60(5):934-38. doi: 10.1111/j.1532-5415.2012.03925.x
- 27 408 16. Dent E, Chapman I, Howell S, et al. Frailty and functional decline indices predict poor outcomes in hospitalised
28 409 older people. *Age Ageing* 2014;43(4):477-84. doi: 10.1093/ageing/aft181
- 31 410 17. Papachristou E, Wannamethee SG, Lennon LT, et al. Ability of Self-Reported Frailty Components to Predict
32 411 Incident Disability, Falls, and All-Cause Mortality: Results From a Population-Based Study of Older British
33 412 Men. *J Am Med Dir Assoc* 2017;18(2):152-57. doi: 10.1016/j.jamda.2016.08.020 [published Online First:
34 413 2016/10/16]
- 37 414 18. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the
38 415 United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133 [published
39 416 Online First: 2015/08/25]
- 42 417 19. Makizako H, Shimada H, Doi T, et al. Impact of physical frailty on disability in community-dwelling older adults:
43 418 a prospective cohort study. *BMJ open* 2015;5(9):e008462. doi: 10.1136/bmjopen-2015-008462 [published
44 419 Online First: 2015/09/05]
- 47 420 20. Medhi GK, Sarma J, Pala S, et al. Association between health related quality of life (HRQOL) and activity of daily
48 421 living (ADL) among elderly in an urban setting of Assam, India. *J Family Med Prim Care* 2019;8(5):1760-64.
49 422 doi: 10.4103/jfmpc.jfmpc_270_19 [published Online First: 2019/06/15]

- 1
2
3 423 21. Tavassoli N, Guyonnet S, Abellan Van Kan G, et al. Description of 1,108 older patients referred by their
4 424 physician to the "Geriatric Frailty Clinic (G.F.C) for Assessment of Frailty and Prevention of Disability" at
5 425 the gerontopole. *J Nutr Health Aging* 2014;18(5):457-64. doi: 10.1007/s12603-014-0462-z [published
6 426 Online First: 2014/06/03]
7
8
9
10 427 22. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, et al. Exercise training as a drug to treat age associated
11 428 frailty. *Free Radic Biol Med* 2016;98:159-64. doi: 10.1016/j.freeradbiomed.2016.03.024 [published Online
12 429 First: 2016/03/30]
13
14
15 430 23. Rector JL, Marceau K, Friedman EM. Moderation of the Association Between Chronic Medical Conditions and
16 431 Functional Limitations Over Time by Physical Activity: Effects of Age. *J Gerontol A Biol Sci Med Sci*
17 432 2020;75(1):168-74. doi: 10.1093/gerona/glz020 [published Online First: 2019/02/21]
18
19
20
21 433 24. Palmer RF, Espino DV, Dergance JM, et al. The role of physical activity and diabetes status as a moderator:
22 434 functional disability among older Mexican Americans. *Age Ageing* 2012;41(6):752-8. doi:
23 435 10.1093/ageing/afs106 [published Online First: 2012/10/12]
24
25
26 436 25. Keysor JJ. Does late-life physical activity or exercise prevent or minimize disablement? A critical review of the
27 437 scientific evidence. *Am J Prev Med* 2003;25(3 Suppl 2):129-36. doi: 10.1016/s0749-3797(03)00176-4
28 438 [published Online First: 2003/10/14]
29
30
31 439 26. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? *J Gerontol A Biol Sci Med Sci*
32 440 2001;56(7):M412-23. doi: 10.1093/gerona/56.7.m412 [published Online First: 2001/07/11]
33
34
35 441 27. Rejeski WJ, Mihalko SL. Physical Activity and Quality of Life in Older Adults. *J Gerontol A Biol Sci Med Sci*
36 442 2001;56(suppl_2):23-35. doi: 10.1093/gerona/56.suppl_2.23
37
38
39 443 28. Casas-Herrero A, Izquierdo M. Physical exercise as an efficient intervention in frail elderly persons. *An Sist Sanit*
40 444 *Navar* 2012;35(1):69-85. doi: 10.4321/s1137-66272012000100007 [published Online First: 2012/05/04]
41
42
43 445 29. Mañas A, Del Pozo-Cruz B, Guadalupe-Grau A, et al. Reallocating Accelerometer-Assessed Sedentary Time to
44 446 Light or Moderate- to Vigorous-Intensity Physical Activity Reduces Frailty Levels in Older Adults: An
45 447 Isotemporal Substitution Approach in the TSHA Study. *J Am Med Dir Assoc* 2018;19(2):185.e1-85.e6. doi:
46 448 10.1016/j.jamda.2017.11.003 [published Online First: 2017/12/23]
47
48
49
50 449 30. Barnett A, Smith B, Lord SR, et al. Community-based group exercise improves balance and reduces falls in
51 450 at-risk older people: a randomised controlled trial. *Age Ageing* 2003;32(4):407-14. doi:
52 451 10.1093/ageing/32.4.407 [published Online First: 2003/07/10]
53
54
55
56
57
58
59
60

- 1
2
3
4 452 31. Jing Z, Li J, Wang Y, et al. The mediating effect of psychological distress on cognitive function and physical
5 453 frailty among the elderly: Evidence from rural Shandong, China. *J Affect Disord* 2020;268:88-94. doi:
6 454 10.1016/j.jad.2020.03.012 [published Online First: 2020/03/12]
7
8
9 455 32. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci*
10 456 *Med Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]
11
12 457 33. Buta BJ, Walston JD, Godino JG, et al. Frailty assessment instruments: Systematic characterization of the uses
13 458 and contexts of highly-cited instruments. *Ageing Res Rev* 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003
14 459 [published Online First: 2015/12/18]
15
16
17 460 34. Bouillon K, Kivimaki M, Hamer M, et al. Measures of frailty in population-based studies: an overview. *BMC*
18 461 *Geriatr* 2013;13:64. doi: 10.1186/1471-2318-13-64 [published Online First: 2013/06/22]
19
20
21 462 35. Radloff LS. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. *Appl Psychol*
22 463 *Meas* 1977;1(3):385-401. doi: 10.1177/014662167700100306
23
24
25 464 36. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical
26 465 Activity Questionnaire. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi*
27 466 2014;35(8):961-4. [published Online First: 2014/11/08]
28
29
30 467 37. Macfarlane DJ, Lee CC, Ho EY, et al. Reliability and validity of the Chinese version of IPAQ (short, last 7 days). *J*
31 468 *Sci Med Sport* 2007;10(1):45-51. doi: 10.1016/j.jsams.2006.05.003 [published Online First: 2006/06/30]
32
33
34 469 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:
35 470 10.1016/j.jval.2016.11.016 [published Online First: 2017/04/15]
36
37
38 471 39. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living.
39 472 *The Gerontologist* 1969;9(3):179-86. doi: 10.1093/geront/9.3_Part_1.179 [published Online First:
40 473 1969/01/01]
41
42
43 474 40. Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc* 1971;19(6):465-81. doi:
44 475 10.1111/j.1532-5415.1971.tb01206.x [published Online First: 1971/06/01]
45
46
47 476 41. Chen P, Yu ES, Zhang M, et al. ADL dependence and medical conditions in Chinese older persons: a
48 477 population-based survey in Shanghai, China. *J Am Geriatr Soc* 1995;43(4):378-83. doi:
49 478 10.1111/j.1532-5415.1995.tb05811.x [published Online First: 1995/04/01]
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 479 42. Ng KY, Ang S, Chan KY. Personality and leader effectiveness: a moderated mediation model of leadership
4 480 self-efficacy, job demands, and job autonomy. *J Appl Psychol* 2008;93(4):733-43. doi:
5 481 10.1037/0021-9010.93.4.733 [published Online First: 2008/07/23]
6
7
8
9 482 43. Preacher KJ, Rucker DD, Hayes AF. Addressing Moderated Mediation Hypotheses: Theory, Methods, and
10 483 Prescriptions. *Multivariate behavioral research* 2007;42(1):185-227. doi: 10.1080/00273170701341316
11 484 [published Online First: 2007/01/01]
12
13
14 485 44. Holmbeck GN. Toward terminological, conceptual, and statistical clarity in the study of mediators and
15 486 moderators: examples from the child-clinical and pediatric psychology literatures. *Journal of consulting*
16 487 *and clinical psychology* 1997;65(4):599-610. doi: 10.1037//0022-006x.65.4.599 [published Online First:
17 488 1997/08/01]
18
19
20
21 489 45. Cohen J, Cohen P, West SG, et al. Applied multiple regression/correlation analysis for the behavioral sciences:
22 490 Routledge 2013.
23
24
25 491 46. Bolin JH. Hayes, Andrew F. (2013). Introduction to Mediation, Moderation, and Conditional Process Analysis: A
26 492 Regression-Based Approach. New York, NY: The Guilford Press. *J Educ Meas* 2014;51(3):335-37. doi:
27 493 10.1111/jedm.12050
28
29
30 494 47. Bao XY, Xie YX, Zhang XX, et al. The association between multimorbidity and health-related quality of life: a
31 495 cross-sectional survey among community middle-aged and elderly residents in southern China. *Health*
32 496 *Qual Life Outcomes* 2019;17(1):107. doi: 10.1186/s12955-019-1175-0 [published Online First: 2019/06/27]
33
34
35 497 48. Chapman B, Duberstein P, Lyness JM. Personality traits, education, and health-related quality of life among
36 498 older adult primary care patients. *J Gerontol B Psychol Sci Soc Sci* 2007;62(6):P343-52. doi:
37 499 10.1093/geronb/62.6.p343 [published Online First: 2007/12/15]
38
39
40
41 500 49. Podsakoff PM, MacKenzie SB, Lee JY, et al. Common method biases in behavioral research: a critical review of
42 501 the literature and recommended remedies. *J Appl Psychol* 2003;88(5):879-903. doi:
43 502 10.1037/0021-9010.88.5.879 [published Online First: 2003/10/01]
44
45
46 503 50. Kanwar A, Singh M, Lennon R, et al. Frailty and health-related quality of life among residents of long-term care
47 504 facilities. *J Aging Health* 2013;25(5):792-802. doi: 10.1177/0898264313493003 [published Online First:
48 505 2013/06/27]
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 506 51. Mulasso A, Roppolo M, Rabaglietti E. The role of individual characteristics and physical frailty on health related
4 507 quality of life (HRQOL): a cross sectional study of Italian community-dwelling older adults. *Arch Gerontol*
5 508 *Geriatr* 2014;59(3):542-8. doi: 10.1016/j.archger.2014.08.012 [published Online First: 2014/09/14]
6
7
8
9 509 52. Huaxue L, Taifang L, Wenjing Y, et al. Status of frailty and its effect path on quality of life among the elderly in
10 510 community. *Chinese Nursing Research* 2019;33(21):3645-49.
11
12 511 53. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and
13 512 meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282 [published
14 513 Online First: 2016/08/26]
15
16
17 514 54. Feng L, Zin Nyunt MS, Gao Q, et al. Cognitive Frailty and Adverse Health Outcomes: Findings From the
18 515 Singapore Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc* 2017;18(3):252-58. doi:
19 516 10.1016/j.jamda.2016.09.015 [published Online First: 2016/11/14]
20
21
22
23 517 55. Akosile CO, Mgbeojedo UG, Maruf FA, et al. Depression, functional disability and quality of life among Nigerian
24 518 older adults: Prevalences and relationships. *Arch Gerontol Geriatr* 2018;74:39-43. doi:
25 519 10.1016/j.archger.2017.08.011 [published Online First: 2017/09/28]
26
27
28 520 56. Shin KR, Byeon YS, Kang Y, et al. A study on physical symptom, activity of daily living, and health-related quality
29 521 of life (HRQoL) in the community-dwelling older adults. *Taehan Kanho Hakhoe chi* 2008;38(3):437-44. doi:
30 522 10.4040/jkan.2008.38.3.437 [published Online First: 2008/07/08]
31
32
33
34 523 57. Crimmins EM. Trends in the health of the elderly. *Annu Rev Public Health* 2004;25:79-98. doi:
35 524 10.1146/annurev.publhealth.25.102802.124401 [published Online First: 2004/03/16]
36
37
38 525 58. Khan ZA, Singh C, Khan T. Correlates of physical disability in the elderly population of Rural North India
39 526 (Haryana). *J Family Community Med* 2018;25(3):199-204. doi: 10.4103/jfcm.JFCM_160_17 [published
40 527 Online First: 2018/09/18]
41
42
43 528 59. Wei M, Li J, Wang H. Impact of the disability trajectory on the mortality risk of older adults in China. *Arch*
44 529 *Gerontol Geriatr* 2018;74:174-83. doi: 10.1016/j.archger.2017.10.015 [published Online First: 2017/11/11]
45
46
47 530 60. Gobbens RJ. Associations of ADL and IADL disability with physical and mental dimensions of quality of life in
48 531 people aged 75 years and older. *PeerJ* 2018;6:e5425. doi: 10.7717/peerj.5425 [published Online First:
49 532 2018/08/21]
50
51
52 533 61. Rejeski WJ, Brawley LR, Haskell WL. The prevention challenge: an overview of this supplement. *Am J Prev Med*
53 534 2003;25(3 Suppl 2):107-9. doi: 10.1016/s0749-3797(03)00173-9 [published Online First: 2003/10/14]
54

- 1
2
3 535 62. de Labra C, Guimaraes-Pinheiro C, Maseda A, et al. Effects of physical exercise interventions in frail older
4 536 adults: a systematic review of randomized controlled trials. *BMC Geriatr* 2015;15:154. doi:
5 537 10.1186/s12877-015-0155-4 [published Online First: 2015/12/03]
6
7
8 538 63. Kortebein P, Ferrando A, Lombeida J, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older
9 539 adults. *JAMA* 2007;297(16):1772-4. doi: 10.1001/jama.297.16.1772-b [published Online First: 2007/04/26]
10
11
12 540 64. Ávila-Funes JA, Pina-Escudero SD, Aguilar-Navarro S, et al. Cognitive impairment and low physical activity are
13 541 the components of frailty more strongly associated with disability. *J Nutr Health Aging* 2011;15(8):683-9.
14 542 doi: 10.1007/s12603-011-0111-8 [published Online First: 2011/10/05]
15
16
17 543 65. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults.
18 544 *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First: 2011/04/01]
19
20
21 545 66. Maxwell SE, Cole DA, Mitchell MA. Bias in Cross-Sectional Analyses of Longitudinal Mediation: Partial and
22 546 Complete Mediation Under an Autoregressive Model. *Multivariate Behav Res* 2011;46(5):816-41. doi:
23 547 10.1080/00273171.2011.606716 [published Online First: 2011/09/30]
24
25
26
27 548
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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

28 566 M±SD: mean ± standard deviation ;M (P₂₅,P₇₅): Median(Quartile₁,Quartile₃)

30 567 1,2,4 follow normal distribution and are described as M±SD.

32 568 3 does not follow normal distribution and is described as M (P₂₅, P₇₅).

34 569 **P<0.001

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39 572 **Table 2 Testing the mediation effect of physical disability between physical frailty and HRQoL among the**
40 573 **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***

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

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

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579 **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%

580 BootSE bootstrap standard error, BootCI bootstrap confidence interval

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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	2.763**
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 \times PA	-0.120	-7.058***	0.011	0.682
Physical disability			-0.422	-24.375***
Physical disability \times PA			0.115	6.104***
R ²	0.159		0.390	
F	122.004***		295.850***	

42 594 ** $P < 0.01$, *** $P < 0.001$

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

Physical activity	Effect	BootSE	BootLLCI	BootULCI
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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

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

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605 **Fig. 1** The conceptual framework of the moderated mediation model

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

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

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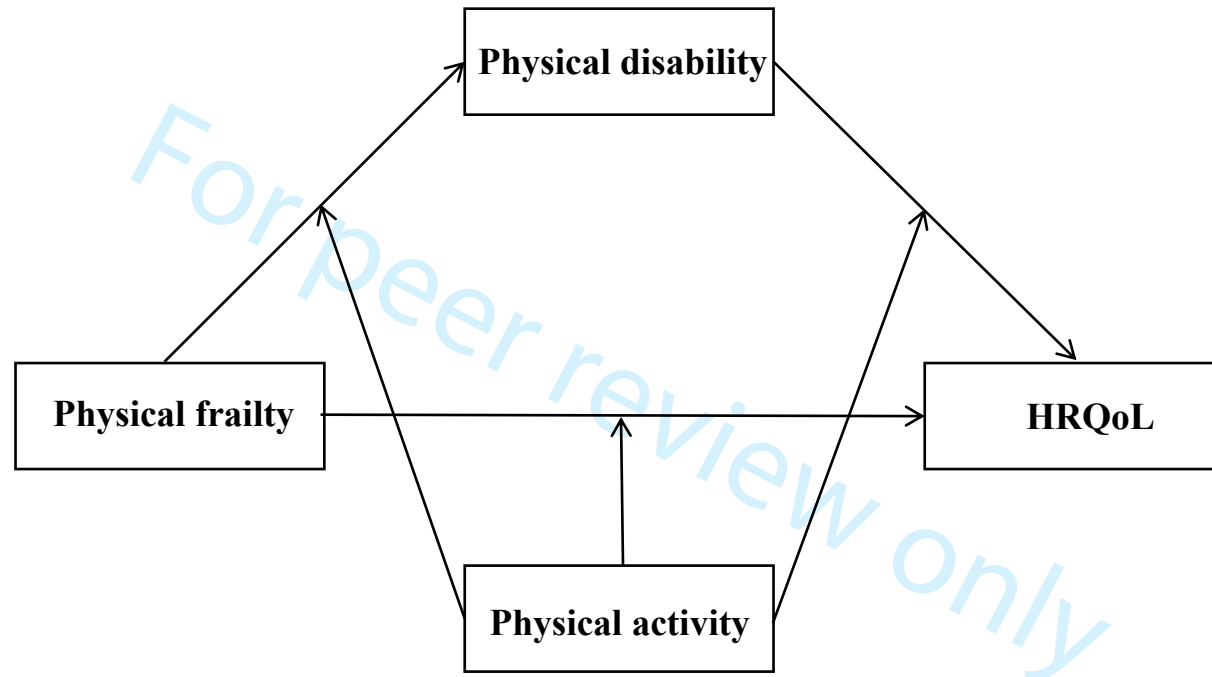


Fig1. The conceptual framework of the moderated mediation model

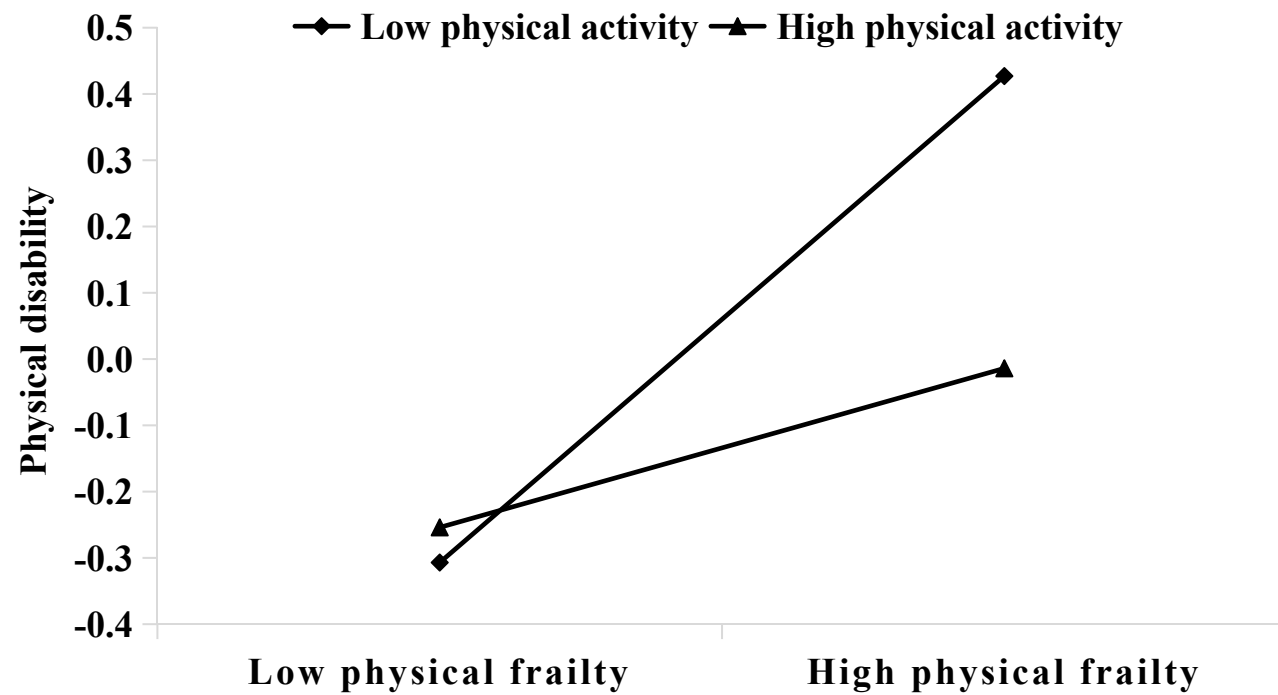


Fig2.Simple slope analysis shows that physical activity moderated the relationship between physical frailty and physical disability

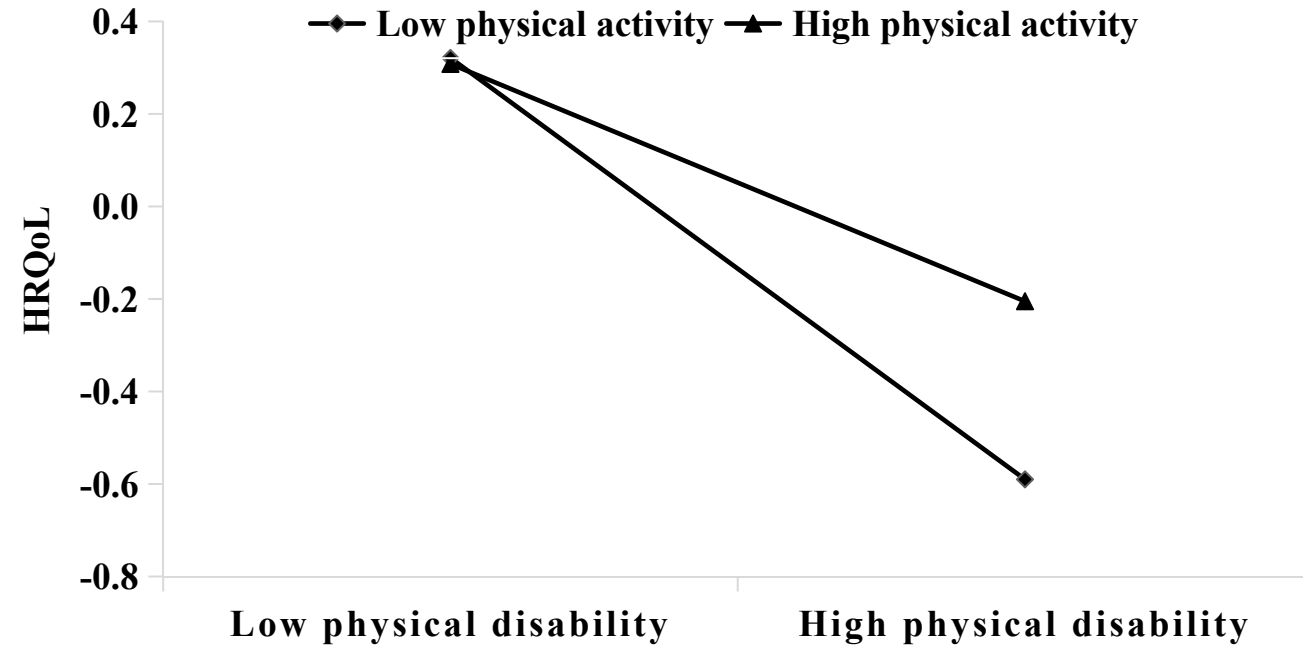


Fig3. Simple slope analysis shows that physical activity moderated the relationship between physical disability and HRQoL

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	
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-

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2	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
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6			(b) Report category boundaries when continuous variables were categorized
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8			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
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11	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
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14	Discussion		
15	Key results	18	Summarise key results with reference to study objectives
16	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
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20	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
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24	Generalisability	21	Discuss the generalisability (external validity) of the study results
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26	Other information		
27	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
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*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.