# Plasma 25-hydroxyvitamin D level and risk of frailty among Chinese community-based oldest-old: evidence from CLHLS study

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## Abstract

Background: Whether vitamin D deficiency may contribute to frailty remains inconclusive in Chinese older adults. The aim of this study was to examine the association between 25-hydroxyvitamin D [25(OH)D] level and risk of frailty among Chinese oldest-old in the communities.

Methods: Secondary analysis of data compiled by the 2011 wave of the Chinese Longitudinal Healthy Longevity Survey (n=1324) was extracted. Frailty was assessed by the Study of Osteoporotic Fractures (SOF) index. Multivariate logistic regression with spine smoothing was performed to investigate the association between 25(OH)D level and risk of frailty after adjusting for socio - demographic variables, health characteristics and confounding biomarkers.

Results: The mean age was 92.89 ± 7.92 years, and 844(63.7%) of participants were women. In all, 426 (33.2% , 95% confidence interval, CI: 29.66-34.69) frail participants were recorded. After adjustment for confounding covariates, the level of 25(OH)D is significantly related to frailty. By the spline smoothing and threshold effect analysis , a monotonically negative association between 25(OH)D and frailty was identified. Subgroup analyses revealed that the association did not differ by gender and age .

Conclusions: Plasma 25(OH)D was inversely associated with the risk of frailty among Chinese oldest-old. The findings indicate the practical significance of monitoring and managing plasma 25(OH)D level in the elders.


## Background

With the dramatic population aging, growing attention has been given to the aging-related issues. Frailty is defined as a geriatric syndrome representing a reduced ability to re-build homeostasis in response to external stressors during daily life(1). Frailty in the elderly is well established to be related to long-term adverse health outcomes (such as falls, depression, disability, dependency, and mortality) which were not utterly explained by aging, function decline, or comorbidities (2–5).

There are two main methods of diagnosing and assessing frailty in existing studies: the Frailty Index and Frailty Phenotype (6–9). The Frailty Index (FI) is based on the comprehensive geriatric assessment (CGA) of overall health decline by the accumulation of deficits in multiple domains(10). The Frailty Phenotype(7), by contrast, proposed from the Cardiovascular Health Study (CHS), was focused on the physical aspect of frailty(11). Considering the Frailty Index needs geriatric skills for collecting the information and time-consuming, and the Frailty Phenotype requires the use of specialized equipment, both measurement modalities, however, are less likely to be readily available in clinical settings and therefore have limited utility(12).

The Study of Osteoporotic Fractures (SOF) index(13), as a simplified screening tool of the physical aspect of frailty, was developed from the limited version of the Frailty Phenotype. The SOF index employed only 3 simple self-reported frailty components(12): muscle strengths, low energy, and unintentional weight loss. It has shown an operational definition to the association with falls, disability, fracture, and death(13, 14), and demonstrated the reliability of risk prediction in clinical practice at the population level(12, 15, 16).

Vitamin D, which primarily synthesized in the skin upon the exposure to sunlight, is necessary for human's musculoskeletal health maintenance(17); its deficiency is proved to be the cause of muscle weakness(18), sarcopenia(19), falls(20), and fracture(21). Evidence has suggested that the low plasma 25(OH)Dconcentration is related to the risk of frailty referring to different ethnic populations(22).

The underlying pathogenic mechanisms could be explained through 3 pathways: the first is the invalidation of regulatory effects of vitamin D on calcium flux, mineral homeostasis and protein anabolism in muscle tissue(23, 24); the second is bone metabolic disturbance by secondary hyperparathyroidism(25); the last is the possible property of vitamin D on anti-inflammation(26).

For the present, following limitations with previous literature need to be addressed(27–40):

- The number of oldest-old participants was limited in most studies. Majority of studies were conducted with a minimal number of samples aged more than 80 years.
- Few linear or curvilinear associations were examined by multivariate logistic regression model with spline smoothing analysis, which is an effective method for examining the shapes of the association.
- Most relevant studies focused on Frailty Index or Frailty Phenotype, proofs of association between SOF index as frailty measurement and vitamin D were lacking.
- Most relevant studies were implemented in developed countries (USA, Germany, and the Netherlands), while studies in developing countries were limited, especially among the oldest-old group.

In response to some of the above limitations, this study aimed to examine the association with plasma 25(OH)D level in the risk of frailty among 1324 older adults of the eight longevity areas in the Chinese Longitudinal Healthy Longevity Survey (CLHLS)(41, 42). We used multivariate logistic regression models with spline smoothing in our primary analyses and adjusted for several important covariates, including socio-demographics, health characteristics, and confounding biomarkers.

## Methods

## Study design and participants

Participants with the biomarker sub-study datasets from the 6th (2011) waves of CLHLS were recruited. CLHLS is the first and largest nationwide, community-based, longitudinal prospective cohort survey, concerning older adults in China(43). It provides information on health status, socioeconomic characteristics, lifestyles of the elderly, including a large percent of the oldest population(42). The in-depth study was launched in the eight longevity areas (Laizhou of Shandong Province, Xiayi of Henan Province, Zhongxiang of Hubei Province, Mayang of Hunan Province, Sanshui of Guangdong Province, Yongfu of Guangxi Autonomous Region, Chengmai of Hainan Province, Rudong of Jiangsu Province) (41). During the in-depth study, the Chinese Center for Disease Control and Prevention (CDC) local network medical doctors conducted physical examinations of the participants, and also collected biomarker datasets contain about 30 indicators on routine blood tests, urine tests and blood biochemical tests(41). More detailed descriptions have been previously published elsewhere(44–46).

Initially, a total of 2439 elderly participants were included in the study. We excluded those of younger age (less than 80, n = 834, 34.2%) and missing data on SOF index components (n = 281, 11.5%). Finally, we retained 1324 older adults in this study.

## Outcome

We used the SOF index to assess frailty status. Three components were included in the index: underweight (defined as body mass index <18.5), low energy level (indicated by a positive response to the question “Over the last 6 months, have you been limited in activities because of a health problem?”, and inability to stand up from a chair without the assistance of arms. As suggested(47), participants with two or more of the three components were defined as frailty.

## Exposure

Fasting venous blood were collected after an overnight fast from all willing participants. Procedures for the collection and shipment of blood samples were described in detail elsewhere(17). 25(OH)Dis the major form of vitamin D in circulation. Plasma 25(OH)Dwas assayed by an enzyme-linked immunoassay using Immunodiagnostic Systems Limited (IDS Ltd, Boldon, UK). The Plasma 25(OH)Dlevel was expressed as nmol/L.

## Covariates

We adjusted for socio-demographic variables, health characteristics and confounding biomarkers in the models. Socio-demographic variables included age, gender (female/male), marital status (married/other), residence (rural/other), education level (no schooling/≥1 years of schooling), co-residence [with family member(s) /other].

Health characteristics included lifestyle and chronic diseases. Lifestyle consisted of smoking (yes/no), drinking (yes/no), and regular exercise (yes/no) at present. Chronic diseases included hypertension, diabetes mellitus, heart diseases, cerebrovascular diseases, and respiratory diseases. Hypertension was defined as systolic blood pressure≥140mmHg and/or diastolic blood pressure≥90mmHg(48). Diabetes mellitus was diagnosed by fasting plasma glucose≥7.0 mmol/L(17, 49). Other diseases were identified by items of self-reported common diseases diagnosed by the doctor.

Confounding biomarkers were items conducted by blood routine tests, blood biochemistry tests, and urine routine tests. According to the previous relevant studies(22), following biomarkers which largely investigated in relation with frailty were recruited in this study: 1) inflammatory marker: C reactive protein; 2) immune marker: counts of leukocytes; 3)clinical markers: plasma albumin, total cholesterol, serum creatinine, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and hemoglobin; 4) oxidative stress markers: malondialdehyde and superoxide dismutase. All the standard laboratory techniques were performed by the central clinical lab at Capital Medical University in Beijing. For the present analysis, we treated all the confounding biomarkers as continuous variables.

Overall, few data for most confounding variables were missing (1.05%). For the missing values, we did multiple imputations by chained equations to increase predictive power(50). Distribution of observed data and imputed data are described in *Supplementary Table S1 (see Additional file 1)*. For all the covariates, the distributions of observed and imputed values did not differ substantially.

## Statistical Analysis

Categorical variables were expressed as numbers and percentages, and continuous data were described as mean (SD) or median (IQR). Characteristics among groups were compared by ANOVA, Kruskal–Wallis test or $\chi^2$ test. The interquartile range of 25(OH)D level was used to divide the data into four categories. The cutoff points were 26.13, 35.89, 50.00 nmol/L.

We used multilayer logistic regression model based on the Likelihood Ratio Test (LRT) to determine the association between plasma 25(OH)D concentration and risk of frailty. Box-Tidwell method was used to test the linearity between logit P and all the continuous variables(51). Therefore, we used continuous terms for all the biomarkers; we also categorized age as subgroups with 80–89, 90–99, ≥100 years. Data are reported as odds ratios

(ORs) and 95% confidence intervals (CIs) in both unadjusted (model 1) and adjusted logistic regression models (model 2, 3, 4). The adjustment was stratified via three layers: (1) we adjusted for socio-demographics (model 2); and (2) we added health characteristics (model 3); (3) we additionally added confounding biomarkers (model 4). The *p*-value of Hosmer-Lemeshow test >0.05 indicating reasonable goodness of fit(52).

We used the spline smoothing analysis and threshold effect analysis, which were implemented based on the generalized additive model (GAM)(53) and the piece-wise regression model(54) respectively to examine the actual shapes of the association between level of 25(OH)D with the risk of frailty. Subgroup analyses and their interactions were tested in the fully adjusted model to explore whether sex and age would confound the association of 25(OH)D level with risk of frailly. Sensitivity analysis was performed in participants with complete variables, and multiple imputations, separately.

Two-tailed *p*-value <0.05 were considered the statistical significance in all the analyses. Statistical analyses were conducted by IBM SPSS Statistics Version 22.0, except for the spline smoothing analysis, threshold effect analysis, and multiple imputations were performed by R software Version 3.4.3 (http://www.R-project.org) and Empower® (www.empowerstats.com).

(*Table 1* in the end of this context should be cited here.)

## Results

# Sample characteristics

The Characteristics of participants were compared according to the categories of 25(OH)D level. Full detailed characteristics of all participants are shown in *Table 1.* The mean ± SD age of the study population was 92.89 ± 7.92 years, and 63.7% were women (n = 844). Participants with frailty were 426 (33.2%, 95%CI: 29.66–34.69). The median 25(OH)D concentration was 35.89 nmol/L and participants with higher levels (35.89–50.00, >50.00 nmol/L) were significantly younger than those with lower levels (≤26.13, 26.13–35.89 nmol/L), more likely to be male, married, with ≥1 year of schooling and do regular exercise.

# Association between the level of 25(OH)D and risk of frailty

As shown in *Table 1,* accounted for 48.9%, 33.8%, 28.0% and 17.9% of participants in the lowest to highest 25(OH)D categories reported frailty. There was a significant inverse association between categorical 25(OH)Dlevel and risk of frailty in the multivariate logistic regression models. The ORs and 95% CIs for the association between categories of 25(OH)D level and frailty were presented in *Table 2.* After eliminating the interferences of all confounding factors, the ORs of frailty were 3.239 (95% CI: 2.113–4.967, p<0.001) for the lowest category (≤26.13 nmol/L) of 25(OH)D level, 2.341 (95% CI: 1.519–3.609, p<0.001) for the second-lowest (26.13–35.89 nmol/L), and 1.703 (95% CI: 1.088–2.664, p = 0.20) for the third-lowest (30.33–44.46 nmol/L) compared to the highest level subgroup(>50.00 nmol/L), respectively.

**Table 2.** The associations between serum level of 25(OH)D (nmol/L) and risk of frailty.

| Variables | Model 1 [a] | Model 2 [b] | Model 3 [c] | Model 4 [d] |
|---|---|---|---|---|
| Categories [e] | | | | |
| ≤26.13 | 4.964(3.332,7.396) *** | 3.472(2.273,5.303) *** | 3.437(2.248,5.255) *** | 3.239(2.113,4.967) *** |
| 26.13–35.89 | 2.822(1.881,4.234) *** | 2.414(1.571,3.710) *** | 2.420(1.573,3.723) *** | 2.341(1.519,3.609) *** |
| 35.89–50.00 | 1.835(1.204,2.797) ** | 1.526(1.102, 2.683) * | 1.722(1.102,2.692) * | 1.703(1.088,2.664) * |
| >50.00 | reference | reference | reference | reference |

[a] Unadjusted model, OR (95%CI).

[b] Adjusted for socio-demographics, OR (95%CI).

[c] Adjusted for socio-demographics and health characteristics, OR (95%CI).

[d] Adjusted for socio-demographics, health characteristics, and confounding biomarkers, OR (95%CI).

[e] *p*-value for Hosmer-Lemeshow test was 0.653, prediction in accuracy was 74.3% in the fully adjusted model.

* <0.05, ** <0.01, *** <0.001.

*The dose-response relationship between the level of 25(OH)D and the risk of frailty*

Consistent with results displayed in *Table 2,* a monotonically negative curve was observed for the association between plasma 25(OH)D and risk of frailty in the analysis using spline smoothing (*p* for trend <0.001, *Figure 1).*. The *p*-value of the log-likelihood ratio test was 0.032 in the unadjusted model, however, 0.317 in the fully adjusted model, which indicated continuous effect in the piece-wise regression model(54) (*Table 3).*.

## Subgroup analyses

*Figure 1.* The dose-response relationship of 25(OH)D level and risk of frailty in the full adjusted model. Lines = estimated probability of frailty with 25(OH)D, dotted lines = 95% confidence intervals.

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*Figure 1.* The dose-response relationship of 25(OH)D level and risk of frailty in the full adjusted model. Lines = estimated probability of frailty with 25(OH)D, dotted lines = 95% confidence intervals.

Subgroup analyses showed the *p*-value for interaction were 0.9753 for gender and 0.1077 for age, which revealed that the association of 25(OH)D level with frailty did not significantly differ by gender and age after adjusted for socio-demographics, health characteristics, and confounding biomarkers. (*Figure 2)*..

**Table 3.** Threshold effect analysis of 25(OH)D (nmol/L) using the piece-wise regression model

| Variables | Crude [a] | Adjusted [b] |
|---|---|---|
| | OR (95%CI) | OR (95%CI) |
| Continuous | 0.967 (0.960, 0.975) *** | 0.975 (0.965, 0.984) *** |
| Cutoff | | |
| ≤33.96 | 0.948 (0.929, 0.967) *** | 0.963 (0.939, 0.988) *** |
| >33.96 | 0.978 (0.966, 0.989) *** | 0.981 (0.966, 0.996) * |
| *p*-value [c] | 0.032 | 0.317 |

[a] Crude: no adjustment.

[b] Adjusted for socio-demographics, health characteristics and confounding biomarkers.

* <0.05, ** <0.01, *** <0.001.

[c] log-likelihood ratio test.

## Sensitivity analysis

*Figure 2.* Subgroup analyses for the association between 25(OH)D and frailty in the fully adjusted model.

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*Figure 2.* Subgroup analyses for the association between 25(OH)D and frailty in the fully adjusted model.

We performed multivariate analysis in participants with complete variables, and multiple imputations, separately. As displayed in *Supplementary Table S2 (see Additional file 1),* the present findings showed similar results.

## Discussion

In this community-based study, after adjustment for a variety of potential confounding factors, we observed a robust and monotonically negative association of plasma 25(OH)D with frailty measured by the SOF index among a group of oldest-old population in China. After explored this association in different subgroups of participants, the results further supported the association was consistent across gender and age groups.

## Comparison with other studies

The potential role of 25(OH)D level in frailty has rarely been investigated among the oldest-old individuals. As hypothesized, the present findings suggest that plasma 25(OH)D level is related to frailty after adjustment of numerous confounding. The findings of from our data have been relatively consistent with previous studies involving older adults in the Netherlands(32, 39), Mexican community-dwelling elderly(30), northern Taiwan residents(40) and older participants in Germany(38).

Few studies demonstrated the shapes of the association between 25(OH)Dlevel and risk of frailty. In the study of 1606 old men individuals aged 73.8 ± 5.9 years in the USA, a segmented negative curvilinear association between 25(OH)D level and odds of frailty was identified(28). However, a U-shaped curve instead of the segmented-shaped association was found in the study of 6307 old women in the USA (27). For the present study, we identified a robust and monotonically negative association between plasma 25(OH)D and frailty in Chinese older adults.

The presence of chronic diseases, lifestyle, and other biomarkers were studied as potential risk factors of frailty(7, 22, 31). The association of plasma 25(OH)D with frailty in our study did not substantially change after adding these covariates in the models. This suggests that plasma 25(OH)D was independently associated with the risk of frailty. However, it remains inconclusive that other possible factors, not included in this study, might contribute to the relationship between 25(OH)Dand frailty.

Due to differences in latitudes, seasons, measurements of frailty, adequacy of adjustment for potential confounders and the clinical heterogeneity between races/ethnicities(55), some variations from previous studies were also founded in this study. Firstly, our study reported that the median 25(OH)D level of the elderly is 35.89 nmol/L, which is lower than studies reported in Taiwan(40), Netherlands(32), and German(34). Besides, the prevalence of frailty measured by SOF index is 33.2%, which makes a glancing comparison to 13% in the Japanese elderly(16) and 17% in the USA older women(13) by the same screening tool. Since the 25(OH)D level and frailty status are closely related to aging(22), these differences could also be partly explained by the oversampling of octogenarians, nonagenarians, and centenarians in this study.

Secondly, it has been reported that the association between 25(OH)D level and frailty was differed by gender(27, 28, 34, 35, 37). A study of participants in Italy identified that Vitamin D insufficiency was associated with frailty in men, but not in women(37). However, conflict results were found in older adults in the USA(31), Spain(36), and Portugal(35). Our study detected that 25(OH)D level was associated with frailty regardless of gender, which is similar to the study in individuals in Germany(34). In addition, our study also indicated that the association did not differ by age subgroups.

# Strength and limitations

The strengths of the current study are the Chinese community-based sample with a well-validated measurement of frailty. This study performed the multivariate logistic regression with spline smoothing to explore the potential linear or curvilinear association between 25(OH)D level and frailty. To our knowledge, this is the first study that investigated the relationship between 25(OH)D level and frailty in a nationwide study of Chinese older people. The present study included a large population of Chinese older adults aged 80 years and over, which allowed robust conclusions to be drawn with respect to this group.

This study also has certain limitations. First, a dichotomous outcome measure for frailty has been used in this study, hence the pre-frail status was not taken into account. Second, some of the clinical diseases adjusted as confounding factors were self-reported. For this condition, we adjusted hypertension and diabetes status by clinical data in place of self-reporting so as to eliminate a degree of information bias. Third, this is a descriptive cross-sectional design that does not allow us to evaluate whether change in 25(OH)D level is a cause or consequence of frailty. The longitudinal design should be employed to investigate whether low 25(OH)D is associated with the onset or progression of frailty in the future.

# Implications to practice

Based on the instructive findings of the present study, it is possible to give some implications for further practice. First, given the application of the SOF index only involves three components and requires no special equipment, it will potentially offer benefits for screening the physical aspect of frailty among the elderly in community settings. Second, the alarming prevalence of frailty presented in our paper emphasized much attention should be paid to those oldest-old living in the community. Third, the results indicate the practical significance of detecting plasma 25(OH)D level in older adults. Fourth, it is possible that efforts should be made to investigating whether management of vitamin D deficiency may relieve or prevent the development of frailty in older adults.

## Conclusion

Using the methodology of multivariate logistic regression with spline smoothing, this study used the SOF Index in Chinese community-dwelling population to draw a monotonically negative association between 25(OH)D level and frailty. It indicates that 25(OH)D level is identified as a potential biomarker of frailty and targets for intervention, therefore beneficial to gerontological research and practice in frailty.

## List Of Abbreviations

CLHLS, Chinese Longitudinal Healthy Longevity Survey; 25-hydroxyvitamin D, 25(OH)D; SOF, Study of Osteoporotic Fractures; FI, Frailty Index; CGA, comprehensive geriatric assessment; CHS, Cardiovascular Health Study; CDC, Center for Disease Control and Prevention; SD, standard variance; IQR, interquartile range; LRT, Likelihood Ratio Test; OR, odds ratio; CI, confidence interval; GAM, generalized additive model; CRP, C reactive protein; ALB, plasma albumin; CHO, total cholesterol; CREA, plasma creatine; SOD, superoxide dismutase; HDLC, high-density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; TG, triglyceride; SOD, superoxide dismutase; MDA, malondialdehyde; WBC, white blood cell count; HGB, hemoglobin.

## Declarations

# Ethics approval and consent to participate

The CLHLS study was approved by the Research Ethics Committee of Peking University (IRB00001052–13074), and all participants or their proxy respondents provided written informed consent.

## Consent for publication

Not applicable.

## Availability of data and material

The CLHLS questionnaires are available at https://sites.duke.edu/centerforaging/ programs/chinese-longitudinal-healthy-longevity-survey-clhls/survey-documentation/ questionnaires/. The full datasets used in this analysis are available from the corresponding author upon reasonable request.

## Competing interests

The authors declare that they have no competing interests.

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## Tables

**Table 1.** Participant characteristics.

| Variables | All participants (n=1324) | Categories (nmol/L) | | | | statistics [a] |
|---|---|---|---|---|---|---|
| | | $Q_1$ (≤26.13) | $Q_2$ (26.13–35.89) | $Q_3$ (35.89–50.00) | $Q_4$ (>50.00) | |
| **Socio-demographics**, n (%) | | | | | | |
| Age (80-112), M (SD) | 92.89(7.92) | 95.63(7.49) | 93.37(7.72) | 91.85(7.85) | 90.70(7.78) | 25.207*** |
| Female | 844(63.7) | 251(75.8) | 236(71.3) | 200(60.2) | 157(47.6) | 68.190*** |
| Married | 294(22.3) | 44(13.3) | 60(18.2) | 83(25.1) | 107(32.7) | 40.503*** |
| Rural | 1124(84.9) | 282(85.2) | 282(85.2) | 265(79.8) | 295(89.4) | 11.925** |
| No schooling | 998(76.4) | 279(85.8) | 257(78.4) | 242(74.2) | 220(67.1) | 33.410*** |
| With household member(s) | 950(73.2) | 263(82.2) | 236(72.2) | 225(69.7) | 226(69.1) | 25.873*** |
| **Health characteristics**, n (%) | | | | | | |
| Smoking | 148(11.3) | 28(8.5) | 39(11.8) | 37(11.2) | 44(13.5) | 4.337 |
| Drinking | 167(12.7) | 32(9.7) | 41(12.5) | 45(13.6) | 49(14.9) | 0.218 |
| Regular exercise | 178(13.9) | 27(8.4) | 38(11.9) | 54(16.7) | 59(18.6) | 17.317*** |
| Hypertension | 785(62.2) | 197(61.9) | 195(62.1) | 192(61.5) | 201(63.0) | 0.155 |
| Diabetes mellitus | 98(7.4) | 28(8.5) | 25(7.6) | 24(7.3) | 21(6.4) | 1.057 |
| Heart diseases | 91(7.0) | 24(7.4) | 24(7.4) | 27(8.4) | 16(4.9) | 3.398 |
| Cerebrovascular diseases | 102(7.8) | 34(10.4) | 31(9.5) | 18(5.5) | 19(5.8) | 8.630* |
| Respiratory diseases | 116(8.9) | 29(9.0) | 32(9.8) | 23(7.0) | 32(9.8) | 2.080 |
| **Biomarkers**, M (IQR) | | | | | | |
| CRP (mg/L) | 1.01(0.41,2.93) | 1.12(0.38,3.35) | 0.93(0.43,3.05) | 0.96(0.41,2.54) | 1.09(0.39,2.75) | 1.491 |
| ALB (g/L) | 39.10(35.90,42.40) | 37.90(35.30,41.40) | 38.60(35.48,42.12) | 39.70(36.70,42.93) | 39.90(37.20,42.80) | 29.923*** |
| CHO (mmol/L) | 4.16(3.52,4.79) | 4.03(3.49,4.72) | 4.21(3.51,4.79) | 4.21(3.47,4.97) | 4.20(3.70,4.78) | 4.186 |
| CREA (mmol/L) | 78(65,96) | 69(60,85) | 77(63,93) | 82(69,98) | 87(71,102) | 76.765*** |
| HDLC (mmol/L) | 1.23(1.03,1.49) | 1.20(1.01,1.45) | 1.25(1.04,1.51) | 1.27(1.03,1.55) | 1.23(1.04,1.46) | 5.065 |
| LDLC (mmol/L) | 2.45(1.94,3.02) | 2.40(1.92,2.97) | 2.42(1.89,3.05) | 2.41(1.86,3.08) | 2.54(2.04,3.00) | 5.147 |
| TG (mmol/L) | 0.79(0.59,1.10) | 0.78(0.59,1.07) | 0.79(0.58,1.09) | 0.82(0.61,1.16) | 0.77(0.57,1.07) | 6.429 |
| SOD (IU/mL) | 58.53(53.43,63.24) | 56.75(51.75,62.97) | 58.18(53.49,63.20) | 58.75(53.33,63.06) | 59.39(55.39,64.24) | 18.975*** |
| MDA (μmol/L) | 4.71(3.73,5.79) | 4.81(3.93,5.89) | 4.87(3.88,5.91) | 4.84(3.82,5.83) | 4.33(3.25,5.55) | 27.303*** |
| WBC ($10^9$/L) | 5.30(4.30,6.40) | 4.80(4.00,6.00) | 5.10(4.10,6.10) | 5.60(4.57,6.60) | 5.60(5.60,6.80) | 34.983*** |
| HGB (g/L) | 118(106,131) | 121(110,133) | 120(107,132) | 116(105,129) | 117(105,131) | 11.618*** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Frailty**, n (%) | 426(33.2) | 162(48.9) | 112(33.8) | 93(28.0) | 59(17.9) | 76.606*** |

M (SD), mean (standard variance); M (IQR), median (interquartile range).

[a] Coefficient of ANOVA, Kruskal–Wallis test or $\chi^2$ test among categories of plasma 25(OH)D level.

* <0.05, ** <0.01, *** <0.001.

Abbreviations: CRP, C reactive protein; ALB, plasma albumin; CHO, total cholesterol; CREA, plasma creatine; HDLC, high-density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; SOD, superoxide dismutase; TG, triglyceride; SOD, superoxide dismutase; MDA, malondialdehyde; WBC, white blood cell count; HGB, hemoglobin.

## Figures

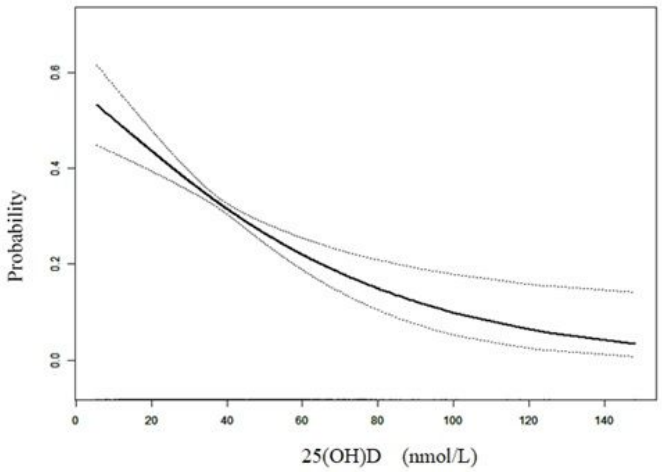


**Figure 1.** The dose-response relationship of 25(OH)D level and risk of frailty in the full adjusted model. Lines=estimated probability of frailty with 25(OH)D, dotted lines=95% confidence intervals.

Figure 1

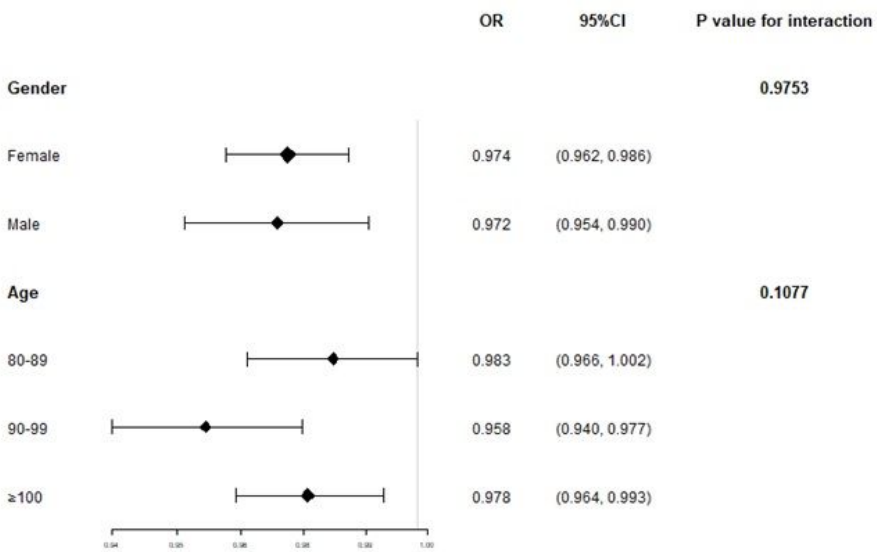


**Figure 1.** Subgroup analyses for the association between 25(OH)D and frailty in the fully adjusted model.

Figure 2

## Supplementary Files

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