BMJ Open Respiratory Research

Association between chronic respiratory diseases and frailty in Chinese elderly: a population-based longitudinal study

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To cite: Guo D, Huang K, Guan X, *et al*. Association between chronic respiratory diseases and frailty in Chinese elderly: a population-based longitudinal study. *BMJ Open Respir Res* 2025;**12**:e002171. doi:10.1136/bmjresp-2023-002171

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjresp-2023-002171).

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Received 3 November 2023
Accepted 5 December 2024

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ABSTRACT

Background Chronic respiratory diseases (CRDs) have been shown to be associated with frailty, but these findings have not yet reached a consensus. The aim of this study was to investigate the association between CRDs and frailty in the elderly using a nationally representative data from China.

Methods Data from the China Health and Retirement Longitudinal Study (CHARLS) were analysed, including 3309 frailty-free participants followed for three waves from 2011. Frailty was assessed using the physical frailty phenotype scale, and CRDs were conformed by self-reported physician diagnoses. Cox proportional hazard models were used to examine the association between baseline CRDs and subsequent frailty.

Results Among participants (mean age 67.07 years, 51.53% male), 497 (15.02%) had CRDs. During a mean follow-up of 46 months, 273 (8.25%) participants developed frailty. The incidence rate of frailty was significantly higher in the CRDs group (37.17% per 1000 person-years vs 18.41% per 1000 person-years, p<0.01). Adjusted for covariables, participants with CRDs had a 44% higher risk of developing frailty (HR = 1.44, 95% CI: 1.08 to 1.91). Specifically, asthma only (HR=1.89, 95% CI: 1.07 to 3.33) and asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO) (HR=1.79, 95% CI: 1.19 to 2.69) were associated with a higher risk of frailty among the elderly, while COPD only was not (HR=1.11, 95% CI: 0.73 to 1.65).

Conclusion This study shows a significant association between CRDs, particularly asthma only and ACO, and frailty in the elderly. We need to pay attention to the frailty status of CRDs patients and consider routine screening among them in both clinical practice and community settings. Active treatment and control of CRDs are necessary to avoid frailty caused by primary lung disease progression or exacerbation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous research, primarily conducted in western populations, has indicated a possible link between chronic respiratory diseases (CRDs) like chronic obstructive pulmonary disease (COPD), asthma or idiopathic pulmonary fibrosis with frailty. However, the strength and nature of this association, particularly in Chinese samples, remain uncertain.

WHAT THIS STUDY ADDS

⇒ This study is the first to investigate the specific associations between asthma-COPD overlap (ACO) and frailty. It provides compelling evidence that both asthma only and ACO were statistically positively associated with an increased risk of developing frailty among Chinese elderly individuals.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Given these findings, it is imperative to prioritise frailty assessment in patients with CRDs, especially those with asthma or ACO. Healthcare professionals should consider incorporating routine frailty screening into their practice in clinical and community settings. Furthermore, this study underscores the importance of developing targeted interventions to prevent or manage frailty in individuals with CRDs, potentially leading to improved health outcomes and quality of life.

INTRODUCTION

Frailty, namely 'easily broken', is a clinical syndrome that represents a low physiological reserve and a high susceptibility to stressors.[1] Its prevalence ranges widely, from 4% to 59%, depending on the specific definition used.[2] With the population ageing, it is more crucial to recognise the frailty of older persons.[3] Frail patients are at intensified risk of adverse outcomes, including adverse drug reactions, prolonged hospitalisation, mobility decline, disability onset and increased mortality.[4–6]

Chronic respiratory diseases (CRDs), which affect the airways and other lung structure,[7] are among the leading causes of morbidity and mortality worldwide.[8] 544.9 million people worldwide were living with CRDs in 2017.[9] Chronic obstructive pulmonary disease (COPD) and asthma are two common CRDs. In China, the prevalence of spirometry-defined COPD among adults aged 40 years and over was 13.7% during 2012–2015[10], while asthma prevalence in this population

was around 5.4%.[11] The diagnosis of later was based on a self-reported history of asthma or by wheeze symptoms in the preceding 12 months.[12]

Emerging evidence suggests a relationship between CRDs, like COPD, asthma and idiopathic pulmonary fibrosis (IPF), with frailty.[2 13 14] A meta-analysis suggested that the elderly with COPD had a twofold risk of frailty (OR=1.97).[2] A French cohort of community-dwelling adults found that a history of asthma and current asthma were both associated with increased risk of frailty, with ORs of 2.19 and 2.24, respectively.[15] This association may be attributed to shared risk factors like age and smoking, as well as common pathophysiological mechanisms such as chronic inflammation, immune system dysfunction and impaired neuroendocrine regulation.[3]

While existing research has provided insights into the association between CRDs and frailty, much of the available data are cross-sectional, limiting our understanding of the temporal association.[2] Additionally, findings from different studies have been inconsistent,[13 15–18] and the nature of this relationship in the Chinese elderly population remains unclear. Therefore, this study aims to investigate the association between CRDs and frailty in the elderly using a nationally representative data from China. By examining longitudinal data, we contribute to a more comprehensive understanding of this relationship, and implications for clinical practice, policy development and future research.

METHODS

Patient and public involvement

Patients and members of the public were not involved in the design or conduct of the study.

Data Source

Data for this study were from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal survey of Chinese adults aged 45 and older.[19] CHARLS employed a multistage probability sampling design to select 150 county-level units and 450 communities across 28 provinces of China. Participants' demographic characteristics, health-related behaviours and lifestyles and health conditions were collected through face-to-face, or computer-aided personal interviews by well-trained investigators, with additional anthropometric and laboratory measurements performed by local Centers for Disease Control and Prevention staffs. CHARLS data were first collected in 2011–2012, with 17 708 participants recruited and an 80% response rate, followed by three subsequent surveys in 2013, 2015 and 2018. Due to limited physical examination indicators for the definition of phenotypic frailty in 2018, the analysis of association between baseline CRDs and the risk of phenotypic frailty was restricted to the follow-up period from 2011 to 2015. CHARLS is approved by the Research Ethics Committee of Peking University (IRB00001052–11015), and all participants provided informed consent.

Participants

Our study sample excluded 10 243 participants who were younger than 60 years old and 391 participants who had frailty at baseline. We further excluded those who had not given information of CRDs in 2011 and frailty in 2013 or 2015, missing values in duration of follow-up, and 630 participants without information of covariates at baseline, leaving 3309 individuals for this study. Figure 1 illustrates a flow chart of the study sample from the 2011 CHARLS

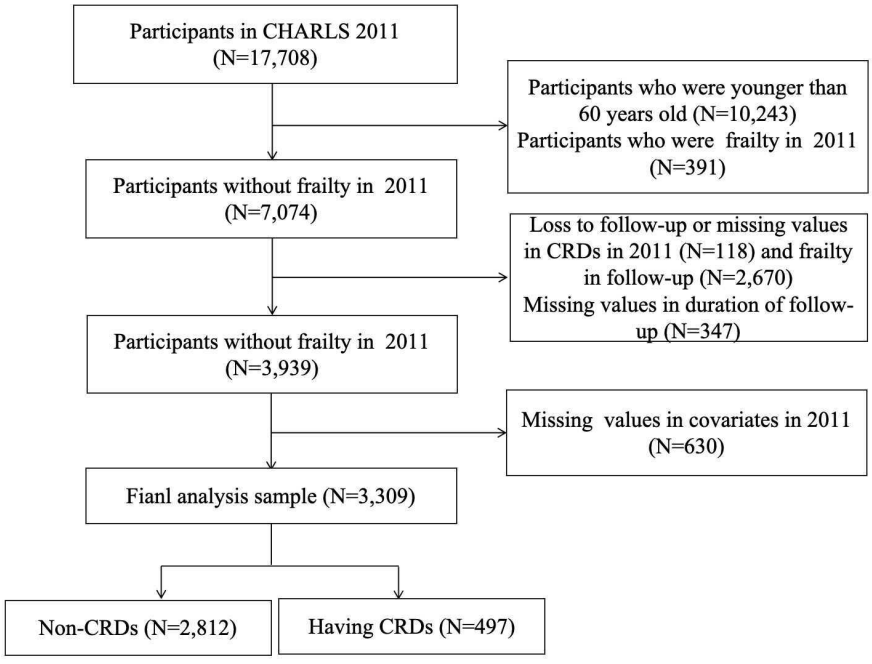

Figure 1 Flowchart of the study sample of Chinese elderly: CHARLS, 2011–2015. CHARLS, China Health and Retirement Longitudinal Study.

through the follow-up surveys. Physical activity, as one of the five indicators of frailty, was assessed by randomly drawing half the sample size in CHARLS, so that the participants in our analysis of the inactive subgroup were 2818.

Follow-up and assessment of frailty status

The outcome of interest in this study was frailty. It was assessed by the physical frailty phenotype scale proposed by Fried *et al*, also known as Fried frailty phenotype (FFP), which includes slowness, weakness, exhaustion, unintentional weight loss and inactivity.[20] Slowness was the average time of repeated walking tests over a 2.5-m course that exceeded the 80th percentile for the sex and height adjusted weighted population distribution. The gender and height cutoffs were from previous research.[21]Weakness was defined as a maximum handgrip strength for either hand less than the 20th percentile for the sex and Body Mass Index (BMI) adjusted weighted population distribution. Exhaustion was based on two questions from the modified Centre for Epidemiological Studies-Depression (CES-D) scale.[22] Participants met criteria for exhaustion if they answered 'A moderate amount of time; 3–4 days' or 'Most of the time' to either of two questions: 'I could not get going' and 'I felt everything I did was an effort'.[21] Unintentional weight loss was defined as a self-rated loss of ≥5 kg in the previous year or a BMI ≤18.5 kg/m^2. Inactivity was defined as subjects who walked continuously for <10 min in a typical week. Using the above information, phenotypic frailty was categorised into two levels, as follows: non-frailty (meeting 0–2 criteria of the five domains) and frailty (meeting three or more criteria). All participants were followed from 2011 to first frailty, loss to follow-up or end of follow-up, whichever occurred first.

Ascertainment of CRDs

The CRDs in this study included COPD and asthma. The COPD and asthma in the CHARLS survey were based on self-reported data, which were previously published.[23] Specifically, participants were asked whether or not a physician had diagnosed them with COPD or asthma. According to the response, they were defined as having COPD, asthma or both. We first divided subjects into two groups: non-CRDs or having CRDs (having COPD or asthma). Then, subjects were classified into four groups: the healthy group (non-CRDs), COPD only (self-reported COPD without asthma), asthma only (self-reported asthma without COPD) and ACO (asthma and COPD).[23]

Covariates

All covariates in this study were self-reported by the questionnaire, except BMI, which was calculated from measured height and weight, and all covariates were collected from baseline. Control variables consisted of age (continuous variable), gender (male/female), education attainment (primary school or below/junior school or above), residence (urban/rural), marital status (married/other), smoking status (never/current/former), alcohol drinking (yes/no), existing other conditions (yes/no), BMI (underweight/normal/overweight/obesity) and pre-frailty status (robust, pre-frailty). Smoking behaviour was measured by asking 'Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars'; 'Do you still have the habit of smoking?'. Alcohol consumption behaviour was measured by asking 'Did you drink any alcoholic beverages, such as beer, wine, or liquor in the past year?'. Existing other conditions were discovered by asking participants if they had any other chronic diseases diagnosed by a physician. These conditions included diabetes, hypertension, hyperlipidemia, heart diseases, stroke, gastrointestinal diseases, liver diseases, cancer, renal diseases, emotional and psychiatric disorders, memory-related problems and arthritis. Robust were meeting none criteria of the FFP five domains, pre-frail were meeting 1–2 criteria.

Statistical analyses

Participants' characteristics were compared across CRDs status at baseline. Means and SD were used to describe continuous characteristics; whereas, proportions were used for categorical variables. A t-test was used for continuous variables, and a χ^2 test was used to analyse categorical variables. We reported frailty incidence rates per 1000 person-years and calculated incidence-rate ratios and differences. Cox proportional hazard models were used to calculate HR and 95% CI estimating the risk of frailty with baseline CRDs. We fitted age-adjusted models and adjusted for all covariates, including demographic characteristics (age, male, marital status), socioeconomic status (education, area), health behaviours (smoking, drinking), health factors (having other conditions, BMI) and pre-frailty status (robust, pre-frailty), to estimate the effect of CRDs on frailty. Further, adults with CRDs were categorised into four groups to examine the association of subgroups of CRDs and risk of frailty in different models. In addition, we also evaluated the association of CRDs, subgroups and risk of frailty by age, gender, area and pre-frailty status. Finally, we also evaluated the association of CRDs subgroups and risk of five frailty features.

Sensitivity analyses were performed to verify the robustness of the results. We used the multivariate imputation by chained equations (MICE)[24] to deal with the missing values of independent variables, dependent variables and covariates, and then used Cox proportional hazard models to analyse the association between CRDs and frailty after imputation. The MICE can be applied to any pattern of missing values, also known as imputation with full conditional specifications. The MICE method is implemented in the chained method and uses a Gibbs-like algorithm to impute multiple variables sequentially using univariate fully conditional specifications.[24] HRs with corresponding 95% CI were reported in Cox proportional hazard models. P values less than 0.05 were considered statistically significant. All statistical analyses were

Table 1 Baseline characteristics of Chinese adults aged 60 years old and above without frailty by CRDs in 2011

	Non-CRDs	Having CRDs			
		Total	COPD only	Asthma only	ACO
	(n=2812)	(n=497)	(n=280)	(n=75)	(n=142)
Age, years, mean (SD)	66.95 (5.95)	67.71 (5.86)	67.73 (5.92)	67.90 (5.91)	67.57 (5.75)
Gender, n (%)					
Male	1402 (49.86)	303 (60.97)	162 (57.86)	39 (52)	102 (71.83)
Female	1410 (50.14)	194 (39.03)	118 (42.14)	36 (48)	40 (28.17)
Education, n (%)					
Primary or below	2665 (94.77)	471 (94.77)	265 (94.64)	73 (97.33)	133 (93.66)
Junior high or above	147 (5.23)	26 (5.23)	15 (5.36)	2 (2.67)	9 (6.34)
Marital status, n (%)					
Married	2275 (80.9)	403 (81.09)	217 (77.5)	64 (85.33)	122 (85.92)
Other	537 (19.1)	94 (18.91)	63 (22.5)	11 (14.67)	20 (14.08)
Residence, n (%)					
Urban	545 (19.38)	98 (19.72)	56 (20)	9 (12)	33 (23.24)
Rural	2267 (80.62)	399 (80.28)	224 (80)	66 (88)	109 (76.76)
Drink status, n (%)					
No	1653 (58.78)	269 (54.12)	154 (55)	41 (54.67)	74 (52.11)
Yes	1159 (41.22)	228 (45.88)	126 (45)	34 (45.33)	68 (47.89)
Smoke status, n (%)					
Never	1657 (58.93)	228 (45.88)	135 (48.21)	36 (48)	57 (40.14)
Current	892 (31.72)	179 (36.02)	102 (36.43)	31 (41.33)	46 (32.39)
Former	263 (9.35)	90 (18.11)	43 (15.36)	8 (10.67)	39 (27.46)
Having other chronic diseases, n (%)					
No	2367 (84.17)	386 (77.67)	224 (80)	56 (74.67)	106 (74.65)
Yes	445 (15.83)	111 (22.33)	56 (20)	19 (25.33)	36 (25.35)
BMI, n (%)					
Underweight	189 (6.72)	66 (13.28)	39 (13.93)	6 (8)	21 (14.79)
Normal	1300 (46.23)	226 (45.47)	129 (46.07)	32 (42.67)	65 (45.77)
Overweight	578 (20.55)	79 (15.9)	745 (26.49)	9 (12)	25 (17.61)
Obesity	745 (26.49)	126 (25.35)	67 (23.93)	28 (37.33)	31 (21.83)
Status of frailty					
Robust	873 (31.05)	95 (19.11)	51 (18.21)	15 (20)	29 (20.42)
Pre-frailty	1939 (68.95)	402 (80.89)	229 (81.79)	60 (80)	113 (79.58)

BMI, Body Mass Index; COPD, chronic obstructive pulmonary disease; CRDs, chronic respiratory diseases.

conducted in Stata 16.0 (StataCorp LP, College Station, Texas).

RESULTS

A total of 3309 participants were included in this cohort. Of these, the mean age was 67.07 years (SD 5.95) and 51.53% were male. Overall, 15.02% of adults reported having CRDs. Compared with those without CRDs, elderly individuals with CRDs were more likely to be male, current or former smokers, current alcohol users, have other chronic conditions, underweight and pre-frailty (table 1). In an additional analysis that included both participants included in the study and those excluded due to loss to follow-up or missing data, we found that the excluded participants were older and not married, had a higher education level (junior high or above), resided in urban areas, were never or former smokers, and had other chronic diseases ($p<0.05$).

During a mean follow-up of 46 months, 8.25% of participants (273 individuals) developed frailty. Table 2 shows that the proportion of frailty was significantly higher among individuals with CRDs (14.29%) compared with those without CRDs (7.18%). Among individuals with CRDs, the proportion of frailty was highest in the ACO

Table 2 HR and 95% CI for the association between CRDs and frailty

	Frailty, n (%)	Model†	Model‡
Non-CRDs	202 (7.18)	Ref.	Ref.
CRDs	71 (14.29)	1.97 (1.51, 2.59)***	1.44 (1.08, 1.91)*
COPD only	28 (10.00)	1.42 (0.95, 2.11)	1.11 (0.73, 1.65)
Asthma only	13 (17.33)	2.27 (1.29, 3.97)**	1.89 (1.07, 3.33)*
ACO	30 (21.13)	2.86 (1.95, 4.21)***	1.79 (1.19, 2.69)**

*p<0.05, **p<0.01, ***p<0.001.
†Adjusted for age.
‡Adjusted for age, gender, marital status, education, area, smoking status, alcohol consumption, other conditions, Body Mass Index (BMI) and robust or pre-frailty status.
ACO, asthma and COPD overlap; COPD, chronic obstructive pulmonary disease; CRDs, chronic respiratory diseases.

group (21.13%) and lowest in the COPD-only group (10.00%). The incidence rate of frailty per 1000 person-years was 18.41% in the non-CRDs group and 37.17% in the CRDs group (p<0.01). Among participants with CRDs, the incidence of frailty was highest in the ACO group (54.54% per 1000 person-years) and lowest in the COPD-only group (26.16% per 1000 person-years) (online supplemental table S1). As shown in table 2, individuals with CRDs were found to have a greater likelihood of frailty than those without CRDs, even after adjusting for age (HR=1.97, 95% CI: 1.51 to 2.59). When adjusted for age, gender, education level, area, marital status, smoking and drinking habits, other chronic diseases, BMI and pre-frail, individuals with CRDs were still at a higher risk of frailty, with an HR of 1.44 (95% CI: 1.08 to 1.91). Further analysis revealed that asthma only (HR=1.89, 95% CI: 1.07 to 3.33) and ACO (HR=1.79, 95% CI: 1.19 to 2.69) groups were associated with a higher risk of later frailty in the elderly after adjusting for all covariates, while the COPD only (HR=1.11, 95% CI: 0.73 to 1.65) group was not linked to frailty when compared with those without CRDs (table 2).

Online supplemental table S2 showed the association between CRDs and frailty by subgroups. After adjusting for potential confounders, CRDs increased the risk of later frailty among participants aged 60–69 years, over 70 years, male, living in rural areas, robust or pre-frailty groups. In addition, the effect size of the association between CRDs and frailty was stronger in the robust individuals (HR=3.27, 95% CI: 1.56 to 6.86) than the pre-frailty ones (HR=1.43, 95% CI:1.06 to 1.93) ($P_{for\ interaction}$=0.04). The risk of frailty increased in those with asthma only who were 60–69 years old, male, living in rural areas and robust. Participants with ACO were at increased risk of frailty in the groups of those who were 60–69 years or older, male, living in rural or urban areas, and pre-frailty. In the robust group, the risk of frailty in people with ACO was marginally statistically significant (HR=3.15, 95% CI: 0.99 to 10.72).

Among the five indicators of frailty, we found that the proportion of samples with weakness was the highest, followed by exhaustion (online supplemental figure S1). Individuals with CRDs were found to have a greater likelihood of exhaustion with HRs of 1.27 (95% CI: 1.06 to 1.52) after adjusting for all covariates, compared with those non-CRDs. The findings, however, do not show an association between CRDs and slowness, weakness, weight loss or inactivity. Further analyses revealed that elderly with COPD only had a higher risk of exhaustion (HR=1.37, 95% CI: 1.11 to 1.69), and the ACO group had an increased risk of weakness (HR=1.31, 95% CI: 1.00 to 1.72) after adjusting for all covariates compared with those non-CRDs (table 3).

After using multiple imputation to impute missing data, we found that individuals having CRDs were associated with later frailty in the elderly after adjusting for

Table 3 HR and 95% CI for the association between CRDs and five frailty features

	Slowness	Weakness	Exhaustion	Weight loss	Inactivity
Non-CRDs	Ref.	Ref.	Ref.	Ref.	Ref.
CRDs	0.96 (0.73, 1.25)	1.14 (0.96, 1.35)	1.27 (1.06, 1.52)*	1.21 (0.94, 1.56)	1.12 (0.84, 1.50)
COPD only	0.89 (0.64, 1.24)	1.06 (0.87, 1.31)	1.37 (1.11, 1.69)**	1.21 (0.90, 1.64)	0.99 (0.68, 1.43)
Asthma only	1.31 (0.78, 2.19)	1.16 (0.81, 1.68)	1.30 (0.85, 2.00)	1.24 (0.71, 2.16)	0.91 (0.47, 1.78)
ACO	1.11 (0.74, 1.65)	1.31 (1.01, 1.72)*	1.09 (0.79, 1.50)	1.24 (0.82, 1.87)	1.34 (0.89, 2.02)

All models adjusted for age, gender, education, area, marital status, smoking history, alcohol consumption, other conditions and Body Mass Index (BMI).
*p<0.05, **p<0.01, ***p<0.001.
ACO, asthma and COPD overlap; COPD, chronic obstructive pulmonary disease; CRDs, chronic respiratory diseases.

covariates (HR=1.80, 95% CI: 1.47 to 2.20), which was consistent with the main findings (online supplemental table S3). In addition, we found that participants with COPD only (HR=1.41, 95% CI: 1.01 to 1.84), asthma-only (HR=1.80, 95% CI: 1.15 to 2.80) and ACO (HR=2.79, 95% CI: 1.28 to 3.88) were at increased risk for later frailty, compared with those non-CRDs. The results, similar to our main results, suggested an association between CRDs and frailty.

DISCUSSION

In this cohort study, we found that CRDs are associated with a higher risk of frailty in Chinese older adults. Specifically, adults with asthma only or ACO were significantly associated with an increased risk of subsequent frailty. We found that CRDs increased the risk of later frailty among participants aged 60–69 years, over 70 years old, male, living in rural areas, robust or pre-frailty status. The risk of frailty increased in those with asthma only who were 60–69 years old, male, living in rural areas and robust. Participants with ACO were at increased risk of frailty in the groups of those who were 60–69 years old or older, male, living in rural or urban areas, and pre-frailty. Regarding the five features of frailty, we discovered that CRDs were associated with exhaustion. Adults with COPD only were associated with a high risk of exhaustion, while those with ACO were associated with weakness. These findings have important implications for clinical and public health practice. Focusing on prevention of frailty through rehabilitation training or other interventions while treating CRDs can help avoid adverse health outcomes associated with the coexistence of these conditions.

This study, based on nationally representative data, is the first to investigate the association of CRDs and its subgroups (eg, COPD only, asthma only and ACO) with frailty among Chinese elderly. While some studies from developed countries have found that COPD patients are more prone to frailty, the findings are inconsistent. A meta-analysis, which included 24 cross-section studies, suggested that the elderly with COPD had a twofold increased risk of frailty (pooled OR=1.97, 95% CI: 1.53 to 2.53).[2] A Dutch cohort study found a higher risk of frailty in adults with COPD (OR=2.4, 95% CI: 1.52 to 3.86),[25] particularly in those with moderate-to-severe COPD and exacerbations. However, another longitudinal study did not find a significant association between baseline COPD and the development of pre-frailty/frailty during 9 years of follow-up,[26] aligning with our results. These inconsistencies may be attributed to various factors, including the measurement of key variables and diverse populations. For instance, the Dutch study using spirometry to classify COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criterion found no correlation between mild COPD and frailty but did found a higher risk of frailty in those with moderate-to-severe COPD or exacerbations.[25] Our study may have been limited by focus on participants with mild-to-moderate COPD who were treated at home, as our sample was based on a sociological survey and did not include hospitalised patients. This may have prevented us from evaluating the association of different GOLD grades of COPD with frailty.

We found that adults with asthma only were associated with an increased risk of subsequent frailty, with an HR of 1.89 (95% CI: 1.07 to 3.33) after adjusted for covariables. This finding aligns with previous studies.[13 27 28] A French cohort study found that both a history of asthma and current asthma were associated with increased risk of frailty, with ORs of 2.19 (95% CI: 1.44 to 3.34) and 2.24 (95% CI: 1.73 to 2.90), respectively.[15] A recent study showed that the combination of asthma and exposure to smoke could exacerbate respiratory dysfunction, making older individuals more vulnerable to developing frailty.[16] Furthermore, we found that individuals with ACO were also associated with an increased risk of developing later frailty, with an HR of 1.79 (95% CI: 1.19 to 2.69). However, to our knowledge, no other studies have examined the association of ACO with frailty. More research is needed to confirm the underlying mechanism and the potential mediating effects of other variables.

The outcome of interest in this study was frailty, which encompasses five components: slowness, weakness, exhaustion, weight loss and inactivity. We focused on frailty individuals who met three or more of these criterias, as these individuals may already be in a relatively poor physical condition function, potentially leading to falls, increased medical care needs,[29] and higher cardiovascular and all-cause mortality.[30] Our finding suggested that the effect of CRDs on frailty was greater in individuals who were robust compared with those who were pre-frail. This indicates that preventing and managing CRDs scientifically and rationally may be particularly beneficial for individuals who are currently robust. Reducing the incidence of frailty in patients with CRDs is advantageous for individuals, families and society. While some intervention suggestions have been proposed, there is still insufficient evidence for clear and effective measures. In general, symptomatic support based on comprehensive geriatric assessment (GCA), exercise and nutrition are the hotspots of frailty intervention research. For example, targeted care delivery through implementation of GCA appears to improve physical function,[31] with a low certainty of supporting evidence. Interventions involving strength and balance training have been successful in increasing muscle strength and functional capacity.[32] Nutritional interventions may address impaired nutrition and weight loss, but the level of evidence is low.[3] Drug prevention and treatment for frailty in CRDs patients remains an area of ongoing research. Given the low BMI, poor respiratory function and susceptibility to exhaustion in CRDs patients, early and appropriate exercise and nutritional interventions may be beneficial. However, more effective evidence is needed to support these approaches. In China, we are carrying out a large respiratory programme in primary health service centres.[33]

In the future, we may consider giving low-cost, easy, and clear CRDs and frailty intervention packages to general practitioners.

The measurement of independent and dependent variables may have influenced the study's results. The FFP is the most commonly used frailty tool. This study uses a modified FFP constructed by Wu *et al*, which is based on Fried's original scale, and well-validated in the Chinese population[21]. It has been shown to predict mortality and adverse clinical outcomes in community-based patients with COPD[27 34] and has demonstrated similar performance to other frailty measures, such as Clinical Frailty Scale, Frailty Index of Accumulative Deficits and Short Physical Performance Battery in predicting mortality and hospitalisation rates.[35] However, a potential limitation is that each item of the FFP was measured only once in CHARLS survey. This may have introduced measurement error, despite rigorous training during data collection.[19] Additionally, self-reported CRDs may have influenced the study's results. Many epidemiological studies have a very good diagnosis of asthma based on several standardised questions[36] or a self-reported history of asthma diagnosis by a physician.[11] For example, in the China Pulmonary Health (CPH) study, the self-reported prevalence of asthma elderly aged 60–69 years and ≥70 years was 6.4% and 8.5%, respectively, in 2012–2015[11], which was very similar to that in the current study (6.5%). Regarding COPD, diagnosing without lung function tests is more uncertain. In the CPH study, among participants with spirometry-defined COPD, only 55.8% had a self-reported history of COPD, and only 12.0% had undergone a previous pulmonary function test.[10] Therefore, it is possible that self-reported CRDs may have led to misclassification and underestimated the effect of CRDs on later frailty in this study. This may partially explain the lack of significant association between COPD and frailty.

The mechanisms linking CRDs and frailty remain to be determined. While CRDs and frailty share common risk factors (like age and smoking) as well as pathophysiological mechanisms (such as chronic inflammation, immune system dysfunction and impaired neuroendocrine regulation),[3] the specific pathways connecting them are still under investigation. In China, although tobacco control policies have led to a decline in smoking prevalence,[37] the growing elderly population and environmental exposure continue to contribute to the rising prevalence of CRDs.[10 38 39] This, in turn, may lead to an increase in the number of frail individuals. Elevated markers of systemic infection, such as interleukin-6, are associated with sarcopenia, a major contributor to frailty.[28 40 41] CRDs patients often experience dyspnoea, which can lead to increased bed rest and reduced exercise, resulting in decreased muscle quantity and quality[42 43] and mobility impairments.[44] These symptoms align with the key components of frailty: weakened grip strength, inactivity and slowness. Beyond respiratory tract symptoms and muscle weakness, CRDs patients may also suffer from anorexia and weight loss, leading to malnutrition.[2] A recent meta-analysis found that 68% of malnourished older adults were physically frail.[45] This is consistent with our finding that CRDs were associated with weakness and exhaustion.

This study was subject to several limitations. First, the measurement of CRDs and other variables was based on self-reported data from the CHARLS survey, which may be subject to recall bias and unmeasured confounding factors. Future research should consider alternative measurement methods to address these limitations. Second, the CHRALS survey was conducted on a household basis, potentially excluding patients with COPD or asthma who were hospitalised for acute exacerbations. This may have led to an underestimation of the association between CRDs and frailty. Third, the findings of this study should be generalised to other populations with caution, as it focuses on the elderly in China. Fourth, the CHARLS survey did not collect data on individual medications, rehabilitation and other potential confounding factors, such as viruses, environment and genetics. The impact of these factors on the association between CRDs and frailty cannot be ruled out. Finally, the study may have been affected by loss to follow-up, as individuals who were excluded from the final analysis were older, had higher education, were not married, lived in urban areas, were never or former smokers, and had other chronic diseases. However, the association between CRDs and frailty remained statistically significant after multiple imputation of missing data. Despite these limitations, the strengths of this study included its nationally representative and population-based sample with a 46-month follow-up period. This is the first study to explore the association between CRDs and frailty in mainland China. Future research should focus on understanding how frailty can be modified or treated among adults with CRDs and whether such interventions improve hospitalisation, mortality and quality of life outcomes.

CONCLUSION

Our study found that CRDs were positively associated with frailty in Chinese elderly. This association was particularly evident in individuals with asthma only or ACO but not in those with COPD only. These findings highlight the importance of paying attention to the frailty status of CRDs patients and consider routine screening in clinical practice. Active treatment and control of CRDs are necessary to prevent frailty caused by the progression or exacerbation of primary lung disease. Further longitudinal studies and experimental research are warranted, such as to

explore the relationship between ACO and frailty in younger adults, the influence of other moderating factors on the association between CRDs and frailty, the underlying mechanism linking the two, and how to reduce the incidence of CRDs and subsequent frailty through lifestyle improvements or other interventions.

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Acknowledgements The authors would like to thank all co-worker. We would also like to extend our thanks to the invaluable contributions by the study participants and data collection staff.

Contributors DG, KH and XG wrote the manuscript, methodology and data analysis. RD, DZ and YZ contributed to the supervision and study coordination. TY and PH contributed to the conceptualisation, review, editing and discussion. All authors have read and agreed to the published version of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no authors meeting the criteria have been omitted. PH acted as a guarantor.

Funding This study was funded by the Major Project of the National Social Science Fund of China (21&ZD187).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. CHARLS is approved by the Research Ethics Committee of Peking University (IRB00001052–11015). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data that support the findings of this study are openly available at https://charls.charlsdata.com/pages/data/111/zh-cn.html. Data, methodology or materials are available to other researchers for replication purposes upon e-mail request from the corresponding author.

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