

Respiratory vulnerability index and incident chronic lung disease risk among middle-aged and older adults in China: a prospective cohort study from CHARLS

Ping Zhang

Nanchang University

Shengsong Chen

Nanchang University

Qingyuan Zhan

ndyfy10285@ncu.edu.cn

China-Japan Friendship Hospital

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Abstract

Objective

To investigate the association between the respiratory vulnerability index (RSV), a multidimensional measure of respiratory-related health deficits, and incident chronic lung disease (CLD) among middle-aged and older adults in China.

Methods

We conducted a prospective cohort study using data from the 2011 baseline survey of the China Health and Retirement Longitudinal Study (CHARLS). Participants aged ≥ 45 years without baseline CLD were included. The RSV score was constructed based on six components reflecting respiratory function, physical function, behavioral exposure, systemic disease burden, and psychological health, including peak expiratory flow (PEF), grip strength, current smoking status, heart disease, kidney disease, and depressive symptoms. Participants were categorized into four groups according to RSV scores (0, 1, 2, and ≥ 3). Incident CLD events were identified during follow-up through 2020. Kaplan–Meier analysis, Cox proportional hazards regression models, restricted cubic spline analyses, subgroup analyses, and sensitivity analyses were performed.

Results

A total of 10,685 participants were included in the baseline analysis and 10,286 participants were included in the longitudinal analysis. During a mean follow-up period of 7.6 ± 2.8 years, 1,547 incident CLD events were identified. The cumulative incidence of CLD increased progressively across RSV categories, from 8.55% in the RSV = 0 group to 13.47%, 17.58%, and 25.24% in the RSV = 1, RSV = 2, and RSV ≥ 3 groups, respectively ($P < 0.001$). In the fully adjusted model, compared with participants with RSV = 0, those with RSV = 1, RSV = 2, and RSV ≥ 3 had significantly higher risks of incident CLD (HR 1.54, 95% CI 1.30–1.82; HR 1.97, 95% CI 1.66–2.34; and HR 2.83, 95% CI 2.35–3.41, respectively; all $P < 0.001$). Each 1-point increase in RSV score was associated with a 34% higher risk of incident CLD (HR 1.34, 95% CI 1.27–1.41). Restricted cubic spline analysis demonstrated a positive dose–response relationship between RSV score and CLD risk.

Conclusions

Higher RSV scores were independently associated with an increased risk of incident CLD among middle-aged and older adults in China, with a clear dose–response relationship. By integrating multiple dimensions of respiratory-related health deficits, RSV may provide a potential approach for population-

level identification of individuals with elevated CLD susceptibility and support early respiratory risk assessment.

1. Introduction

Chronic respiratory diseases represent a substantial global public health burden and remain among the leading causes of morbidity and mortality worldwide. According to the Global Burden of Disease (GBD) Study, chronic respiratory diseases continue to contribute significantly to global disability and mortality, with chronic obstructive pulmonary disease (COPD) accounting for a large proportion of respiratory-related disease burden [1]. In China, the burden of chronic respiratory diseases is also considerable. The China Pulmonary Health Study reported a high prevalence of COPD among adults aged ≥ 40 years, and population aging may further increase the burden of COPD and related chronic lung diseases (CLD) [2]. Previous epidemiological studies have identified smoking, air pollution, occupational exposure, and aging as major risk factors associated with the development and progression of COPD [3].

Chronic lung disease is a complex condition characterized by persistent airway inflammation, structural alterations of lung tissue, and progressive impairment of respiratory function. In this study, CLD was defined according to physician-diagnosed chronic bronchitis, emphysema, or COPD based on information collected from the China Health and Retirement Longitudinal Study (CHARLS). Although conventional risk assessment strategies have mainly focused on individual risk factors, including smoking history, pulmonary function impairment, and previous respiratory diseases, these factors may not fully capture the heterogeneity of disease susceptibility among middle-aged and older adults [4]. Therefore, identifying multidimensional indicators that reflect overall physiological reserve and health vulnerability may provide additional information for early identification of individuals at elevated risk of CLD.

Accumulating evidence suggests that chronic respiratory diseases are not merely localized pulmonary disorders but complex systemic conditions involving multiple physiological systems. Older adults with chronic respiratory diseases frequently experience multimorbidity, reduced physical function, psychological disorders, and impaired physiological reserve, which may collectively increase susceptibility to adverse health outcomes [5]. These accumulated health deficits may impair the ability to maintain physiological homeostasis and contribute to increased vulnerability to chronic disease development. Therefore, approaches incorporating multiple dimensions of health status may better characterize individual susceptibility than assessments based solely on traditional respiratory risk factors.

Frailty theory provides an important framework for understanding age-related declines in physiological reserve. Fried et al. proposed the frailty phenotype model, in which functional impairments such as weight loss, exhaustion, reduced physical activity, slow gait speed, and decreased grip strength represent diminished physiological capacity among older adults [6]. Subsequently, Rockwood and Mitnitski proposed the deficit accumulation model, suggesting that the accumulation of multiple health

deficits reflects individual vulnerability and can predict mortality, functional decline, and other adverse health outcomes [7]. Clegg et al. further emphasized that frailty is a multidimensional state resulting from impairments across multiple physiological systems rather than the consequence of a single disease process [8]. With increasing evidence supporting its relevance beyond geriatric syndromes, frailty has become an important framework for evaluating vulnerability to chronic diseases.

Recent studies have increasingly explored the relationship between frailty and chronic respiratory diseases. Frailty is common among patients with COPD and has been associated with reduced physical performance, greater disease severity, and poorer clinical outcomes [9]. A systematic review and meta-analysis further demonstrated a strong association between COPD and frailty, suggesting that respiratory disease and systemic vulnerability may interact with each other [10]. COPD is now recognized as a systemic disorder involving chronic inflammation, skeletal muscle dysfunction, and multimorbidity rather than an isolated pulmonary disease [11–12].

However, previous studies have mainly focused on frailty assessment among individuals with established COPD, whereas evidence remains limited regarding whether a multidimensional vulnerability indicator can identify individuals at increased risk of CLD before disease onset in community populations. Based on the concepts of frailty and cumulative health deficits, we developed the respiratory vulnerability index (RSV) to characterize respiratory-related vulnerability by integrating respiratory function, physical function, behavioral exposure, heart and kidney disease status, and psychological health.

Therefore, using data from the China Health and Retirement Longitudinal Study (CHARLS), this prospective cohort study aimed to investigate the association between RSV and incident CLD among middle-aged and older adults in China. We further examined the dose–response relationship between RSV and CLD risk and evaluated the consistency of the association through subgroup and sensitivity analyses.

2. Methods

2.1 Study population

This prospective cohort study was conducted using data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal survey of Chinese adults aged ≥ 45 years. CHARLS employs a multistage probability sampling design and collects comprehensive information on demographic characteristics, socioeconomic status, lifestyle behaviors, health conditions, and functional abilities. The study protocol was approved by the Ethics Review Committee of Peking University, and all participants provided written informed consent.

The present study used data from the 2011 baseline survey of CHARLS. Participants were eligible if they met the following criteria: (1) aged ≥ 45 years; (2) had complete information required for RSV construction; and (3) had no chronic lung disease (CLD) at baseline. Participants were excluded if they:

(1) had physician-diagnosed chronic bronchitis, emphysema, or chronic obstructive pulmonary disease (COPD) at baseline; (2) had missing information on RSV components or key covariates; or (3) lacked follow-up information regarding CLD occurrence. After applying the inclusion and exclusion criteria, 10,685 participants were included in the baseline analysis. After further excluding participants without available follow-up outcome information, 10,286 individuals were included in the longitudinal analysis.

2.2 Construction of the respiratory vulnerability index (RSV)

The respiratory vulnerability index (RSV) was developed based on the conceptual framework of frailty theory and the deficit accumulation model. The objective of RSV construction was to characterize multidimensional respiratory vulnerability rather than to develop a conventional prediction model.

Component selection was hypothesis-driven and based on established biological and gerontological concepts related to physiological reserve, functional impairment, and health deficit accumulation. Variables were not selected according to their statistical associations with CLD outcomes, thereby minimizing potential selection bias and avoiding outcome-driven index construction.

The RSV was designed to capture five major domains related to respiratory vulnerability: respiratory functional reserve; physical functional reserve; smoking-related exposure; systemic disease burden; psychological health. Accordingly, six binary components were included: impaired peak expiratory flow (PEF); reduced grip strength; current smoking status; heart disease; kidney disease; depressive symptoms. Each component was assigned 1 point when the corresponding health deficit was present and 0 points otherwise. The total RSV score was calculated by summing all six components, resulting in a score range from 0 to 6. Higher RSV scores indicated a greater accumulation of respiratory-related health deficits. These components were selected because they represent complementary dimensions of vulnerability rather than independent predictors of CLD.

2.2.1 Respiratory functional reserve

PEF was used as an indicator of respiratory functional reserve. Because PEF varies according to age, sex, and height, predicted PEF values were calculated using Chinese population-specific reference equations developed by Tian et al [13].

For men: $PEF_{pred} = 21.566 + 0.078 \times H - 6.192 \times \ln(A)$;

For women: $PEF_{pred} = -22.741 + 6.901 \times \ln(H) - 0.090 \times A$;

where H represents height (cm), and A represents age (years).

The predicted PEF values were expressed in L/min to correspond with the measurement units used in CHARLS. The percentage of predicted PEF was calculated as: $PEF\%_{pred} = PEF_{actual} / PEF_{pred} \times 100\%$.

Participants with $PEF\%_{pred} < 80\%$ were considered to have impaired respiratory function and assigned 1 point; otherwise, 0 points were assigned.

Although these equations were originally developed among elderly Chinese populations, they were applied in the present study because CHARLS provides standardized PEF measurements and includes middle-aged and older adults, allowing population-level assessment of respiratory functional impairment.

2.2.2 Physical functional reserve

Grip strength was used as an indicator of physical functional reserve. Maximum grip strength was measured using a dynamometer in CHARLS. Sex-specific thresholds were applied according to commonly used functional impairment criteria. Participants with maximum grip strength < 18 kg among women or < 28 kg among men were considered to have reduced physical functional reserve and assigned 1 point; otherwise, 0 points were assigned.

2.2.3 Smoking exposure

Current smoking status was obtained from CHARLS questionnaires. Participants who reported current smoking behavior were classified as having smoking exposure and assigned 1 point, whereas non-smokers were assigned 0 points.

2.2.4 Heart and kidney disease status

Heart disease and kidney disease were included as indicators of systemic physiological vulnerability. These conditions were incorporated into RSV because they reflect reduced organ reserve, multimorbidity burden, and impaired ability to maintain physiological homeostasis, which are central concepts underlying frailty theory. Importantly, heart disease and kidney disease were considered components of the vulnerability construct rather than independent causal predictors of CLD. Both conditions were identified according to self-reported physician diagnoses collected in CHARLS. Participants with physician-diagnosed heart disease or kidney disease were assigned 1 point; otherwise, 0 points were assigned.

2.2.5 Psychological health

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). A CES-D score ≥ 10 was considered indicative of depressive symptoms and assigned 1 point; otherwise, 0 points were assigned.

2.2.6 RSV categorization

Because RSV represents an accumulated health deficit index rather than a clinically validated diagnostic score, RSV categories were defined according to the distribution of RSV scores in the study population, sample size adequacy within each category, and interpretability of accumulated health deficits.

Participants were categorized into four groups: RSV = 0; RSV = 1; RSV = 2; RSV $\geq$ 3. The RSV $\geq$ 3 category was considered the higher respiratory vulnerability category in subsequent analyses.

2.3 Definition of incident chronic lung disease

Incident CLD was defined according to physician-diagnosed chronic respiratory diseases reported in CHARLS. Participants were considered to have developed CLD if they reported a physician diagnosis of chronic bronchitis, emphysema, or COPD during follow-up. Follow-up duration was calculated from baseline assessment in 2011 until the first occurrence of CLD, the last available follow-up visit, or the end of follow-up in 2020, whichever occurred first.

2.4 Covariates

Potential confounders were selected based on previous literature and established risk factors associated with chronic respiratory diseases.

The following variables were included:

- Demographic and socioeconomic factors: age; sex; educational level; marital status.
- Environmental-related social factors: residential area; access to tap water.
- Lifestyle factors: drinking status.
- Anthropometric measurements: body mass index (BMI); waist circumference.
- Chronic disease factors: hypertension; diabetes; stroke; liver disease; asthma.

All chronic disease variables were defined according to physician-diagnosed information collected in CHARLS. Because RSV was constructed from PEF, grip strength, current smoking status, heart disease, kidney disease, and depressive symptoms, these variables were not additionally included as covariates in Cox regression models to avoid overadjustment bias. Hypertension and diabetes were retained as covariates because they represent established chronic disease risk factors and may influence CLD risk independently of the RSV vulnerability construct.

2.5 Statistical analysis

All statistical analyses were performed using R software (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria) and EmpowerStats software (version 5.2; X&Y Solutions, Boston, MA, USA). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), according to data distribution. Comparisons between groups were performed using Student's t-test, Mann–Whitney U test, analysis of variance, or Kruskal–Wallis test, as appropriate. Categorical variables were presented as numbers and percentages and compared using chi-square tests or Fisher's exact tests.

Baseline characteristics and CLD incidence were compared across RSV categories. Kaplan–Meier curves were generated to evaluate CLD-free survival according to RSV categories, and differences were assessed using the log-rank test. Cox proportional hazards regression models were applied to estimate

hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between RSV and incident CLD.

Three sequential models were constructed:

- Model 1: Unadjusted model.
- Model 2: Adjusted for age and sex.
- Model 3: Further adjusted for educational level, marital status, residential area, access to tap water, drinking status, BMI, waist circumference, hypertension, diabetes, stroke, liver disease, and asthma.

The proportional hazards assumption was evaluated using Schoenfeld residuals. Restricted cubic spline (RCS) analysis was performed to assess the dose–response relationship between continuous RSV scores and CLD risk. Subgroup analyses were conducted according to age, sex, BMI, residential area, hypertension, diabetes, and asthma status. Interaction tests were performed to evaluate potential effect modification. Sensitivity analyses were conducted by excluding participants with baseline asthma and repeating Cox regression analyses. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Results

3.1 Participant characteristics

A total of 17,385 participants were initially identified from the CHARLS 2011 baseline survey. After excluding individuals who did not meet the eligibility criteria, including those with baseline CLD, missing RSV-related information, missing key covariates, or unavailable follow-up information, 10,685 participants were included in the baseline analysis. After further excluding participants without available CLD outcome information during follow-up, 10,286 participants were included in the longitudinal analysis (Fig. 1).

Participants were categorized into four groups according to RSV scores: RSV = 0 ($n = 2,325$), RSV = 1 ($n = 4,020$), RSV = 2 ($n = 2,889$), and RSV ≥ 3 ($n = 1,451$). The mean age of participants was 58.87 ± 9.27 years. Baseline characteristics according to RSV categories are presented in Table 1. Participants with higher RSV scores were older and had lower levels of grip strength and peak expiratory flow (PEF), whereas depressive symptom scores increased progressively across higher RSV categories (all $P < 0.001$). No significant difference in BMI was observed among RSV groups ($P = 0.261$).

Table 1
Baseline characteristics according to respiratory vulnerability index (RSV) categories

Variables	Total	RSV 0	RSV 1	RSV 2	RSV ≥ 3	P-value
N	10685	2325	4020	2889	1451	
Age	58.87 ± 9.27	55.88 ± 7.98	57.79 ± 8.77	60.62 ± 9.65	63.16 ± 9.53	< 0.001
Grip strength	32.89 ± 10.35	34.31 ± 9.39	34.39 ± 9.95	32.21 ± 10.41	27.80 ± 11.03	< 0.001
Waist(cm)	84.43 ± 12.55	85.39 ± 12.66	84.64 ± 12.54	84.13 ± 12.10	82.90 ± 13.08	< 0.001
BMI(Kg/m ²)	24.06 ± 4.47	24.62 ± 4.12	24.15 ± 6.38	24.23 ± 5.68	22.59 ± 3.92	0.261
PEF(L/min)	302.92 ± 123.73	373.86 ± 90.93	324.41 ± 125.97	258.73 ± 114.97	217.75 ± 93.45	< 0.001
Depression Score	8.15 ± 6.20	4.15 ± 2.72	6.90 ± 5.50	10.21 ± 6.33	13.97 ± 5.96	< 0.001
Gender						< 0.001
Female	5676 (53.12%)	1532 (65.89%)	2109 (52.46%)	1399 (48.43%)	636 (43.83%)	
Male	5009 (46.88%)	793 (34.11%)	1911 (47.54%)	1490 (51.57%)	815 (56.17%)	
Education						< 0.001
Primary school or below	4922 (46.06%)	890 (38.28%)	1706 (42.44%)	1480 (51.23%)	846 (58.30%)	
Middle school	2299 (21.52%)	471 (20.26%)	894 (22.24%)	635 (21.98%)	299 (20.61%)	
High school	2256 (21.11%)	570 (24.52%)	942 (23.43%)	531 (18.38%)	213 (14.68%)	
College or above	1208 (11.31%)	394 (16.95%)	478 (11.89%)	243 (8.41%)	93 (6.41%)	
Marital status						< 0.001
Unmarried / Other	1301 (12.18%)	170 (7.31%)	418 (10.40%)	422 (14.61%)	291 (20.06%)	
Married	9384 (87.82%)	2155 (92.69%)	3602 (89.60%)	2467 (85.39%)	1160 (79.94%)	

Variables	Total	RSV 0	RSV 1	RSV 2	RSV ≥ 3	P-value
Residence area						< 0.001
Urban	3995 (37.39%)	958 (41.20%)	1521 (37.84%)	1038 (35.93%)	478 (32.94%)	
Rural	6690 (62.61%)	1367 (58.80%)	2499 (62.16%)	1851 (64.07%)	973 (67.06%)	
Access to tap water						< 0.001
No	4204 (39.34%)	753 (32.39%)	1449 (36.04%)	1236 (42.78%)	766 (52.79%)	
Yes	6481 (60.66%)	1572 (67.61%)	2571 (63.96%)	1653 (57.22%)	685 (47.21%)	
Hypertension						< 0.001
No	5592 (52.34%)	1337 (57.51%)	2161 (53.76%)	1428 (49.43%)	666 (45.90%)	
Yes	5093 (47.66%)	988 (42.49%)	1859 (46.24%)	1461 (50.57%)	785 (54.10%)	
Diabetes						< 0.001
No	9345 (87.46%)	2064 (88.77%)	3552 (88.36%)	2515 (87.05%)	1214 (83.67%)	
Yes	1340 (12.54%)	261 (11.23%)	468 (11.64%)	374 (12.95%)	237 (16.33%)	
Heart disease						< 0.001
No	9524 (89.13%)	2325 (100.00%)	3817 (94.95%)	2455 (84.98%)	927 (63.89%)	
Yes	1161 (10.87%)	0 (0.00%)	203 (5.05%)	434 (15.02%)	524 (36.11%)	
Stroke						< 0.001
No	10448 (97.78%)	2291 (98.54%)	3960 (98.51%)	2814 (97.40%)	1383 (95.31%)	
Yes	237 (2.22%)	34 (1.46%)	60 (1.49%)	75 (2.60%)	68 (4.69%)	

Variables	Total	RSV 0	RSV 1	RSV 2	RSV ≥ 3	P-value
Liver disease						< 0.001
No	10352 (96.88%)	2269 (97.59%)	3918 (97.46%)	2793 (96.68%)	1372 (94.56%)	
Yes	333 (3.12%)	56 (2.41%)	102 (2.54%)	96 (3.32%)	79 (5.44%)	
Kidney disease						< 0.001
No	10142 (94.92%)	2325 (100.00%)	3932 (97.81%)	2714 (93.94%)	1171 (80.70%)	
Yes	543 (5.08%)	0 (0.00%)	88 (2.19%)	175 (6.06%)	280 (19.30%)	
Asthma						< 0.001
No	10493 (98.20%)	2314 (99.53%)	3980 (99.00%)	2822 (97.68%)	1377 (94.90%)	
Yes	192 (1.80%)	11 (0.47%)	40 (1.00%)	67 (2.32%)	74 (5.10%)	
Drinking						< 0.001
No	7111 (66.55%)	1691 (72.73%)	2632 (65.47%)	1860 (64.38%)	928 (63.96%)	
Yes	3574 (33.45%)	634 (27.27%)	1388 (34.53%)	1029 (35.62%)	523 (36.04%)	
Currently Smoking						< 0.001
No	7391 (69.17%)	2325 (100.00%)	2797 (69.58%)	1645 (56.94%)	624 (43.00%)	
Yes	3294 (30.83%)	0 (0.00%)	1223 (30.42%)	1244 (43.06%)	827 (57.00%)	

Higher RSV scores were also associated with a greater proportion of males, rural residents, individuals with lower educational attainment, and unmarried participants (all $P < 0.001$). The prevalence of hypertension, diabetes, heart disease, stroke, liver disease, kidney disease, and asthma, as well as current smoking, increased progressively with increasing RSV scores (all $P < 0.001$).

3.2 Incidence of chronic lung disease according to RSV categories

During a mean follow-up period of 7.6 ± 2.8 years, 1,547 incident CLD events were identified among 10,286 participants without baseline CLD, corresponding to a cumulative incidence of 15.04%. The incidence of CLD differed significantly across RSV categories ($P < 0.001$) (Table 2). The cumulative incidence of CLD increased progressively from 8.55% in the RSV = 0 group to 13.47%, 17.58%, and 25.24% in the RSV = 1, RSV = 2, and RSV ≥ 3 groups, respectively.

Table 2
Incidence of chronic lung disease according to respiratory vulnerability index categories during 2011–2020 follow-up

Variables	Total	RSV 0	RSV 1	RSV 2	RSV ≥ 3	P-value
N	10286	2257	3905	2781	1343	
Incident chronic lung disease						< 0.001
No	8739 (84.96%)	2064 (91.45%)	3379 (86.53%)	2292 (82.42%)	1004 (74.76%)	
Yes	1547 (15.04%)	193 (8.55%)	526 (13.47%)	489 (17.58%)	339 (25.24%)	
Note: Follow-up was conducted from baseline assessment in 2011 to the last available follow-up visit in 2020. The mean follow-up duration was 7.6 ± 2.8 years, and 399 participants were lost to follow-up.						

Kaplan–Meier analysis showed that CLD-free survival declined progressively over time among participants with higher RSV scores. Significant differences in CLD-free survival were observed among RSV categories (log-rank $P < 0.001$) (Fig. 2).

3.3 Association between RSV and incident CLD

The association between RSV categories and incident CLD was evaluated using Cox proportional hazards regression models (Table 3). Compared with participants in the RSV = 0 group, higher RSV scores were consistently associated with increased risks of incident CLD across all models (all P for trend < 0.001). In the fully adjusted model (Model 3), participants with RSV = 1, RSV = 2, and RSV ≥ 3 had significantly higher risks of incident CLD compared with those with RSV = 0: RSV = 1: HR = 1.54, 95%CI:1.30 – 1.82; RSV = 2:HR = 1.97, 95%CI:1.66 – 2.34; RSV ≥ 3 :HR = 2.83, 95%CI:2.35 – 3.41,(all $P < 0.001$).

Table 3

Cox proportional hazards regression analyses of the association between RSV and incident chronic lung disease

Exposure	Model 1		Model 2		Model 3	
	HR(95%CI)	P	HR(95%CI)	P	HR(95%CI)	P
RSV category						
0	Ref		Ref		Ref	
1	1.66(1.40–1.95)	< 0.001	1.58(1.34–1.86)	< 0.001	1.54(1.30–1.82)	< 0.001
2	2.30(1.95–2.72)	< 0.001	2.11(1.78–2.50)	< 0.001	1.97(1.66–2.34)	< 0.001
≥ 3	3.73(3.13–4.46)	< 0.001	3.34(2.78-4.00)	< 0.001	2.83(2.35–3.41)	< 0.001
RSV(continuous,per 1-point increase)						
	1.45(1.39–1.52)		1.41(1.34–1.47)		1.34(1.27–1.41)	
P for trend	< 0.001		< 0.001		< 0.001	
Note: HRs, hazard ratios; CIs, confidence intervals. RSV was categorized into four groups (0, 1, 2, and ≥ 3), with RSV = 0 as the reference group. For trend analysis, RSV score was modeled as a continuous variable (per 1-point increase). Model 1 was an unadjusted model. Model 2 was adjusted for age and sex. Model 3 was further adjusted for education, marital status, residence area, access to tap water, drinking status, BMI, waist circumference, hypertension, diabetes, stroke, liver disease, and asthma. The components included in the RSV score were not additionally adjusted to avoid overadjustment. The proportional hazards assumption was assessed using Schoenfeld residuals, and no violation was observed (global P > 0.05).						

When RSV was analyzed as a continuous variable, each 1-point increase in RSV score was associated with a 34% higher risk of incident CLD (HR = 1.34, 95% CI: 1.27–1.41). The associations remained stable after sequential adjustment for potential confounders. The Schoenfeld residual test indicated no violation of the proportional hazards assumption (global P > 0.05).

3.4 Dose–response relationship between RSV and CLD risk

To further examine the potential dose–response relationship between RSV and incident CLD, restricted cubic spline (RCS) analysis was performed using RSV as a continuous variable (Fig. 3). After adjustment for all covariates included in Model 3, RSV demonstrated a positive and approximately linear association with CLD risk. The risk of incident CLD increased continuously with increasing RSV scores, without evidence of a threshold effect or risk attenuation.

3.5 Subgroup analyses

Subgroup analyses were performed to evaluate whether the association between RSV and incident CLD differed across population characteristics (Fig. 4).

The association between higher RSV scores and increased CLD risk remained consistent across subgroups stratified by age, sex, BMI, residential area, hypertension, and diabetes status. No significant interactions were observed between these factors and RSV in relation to CLD risk (all P for interaction > 0.05). A significant interaction was observed for asthma status (P for interaction = 0.008). In participants without asthma, each 1-point increase in RSV score was associated with an increased risk of CLD (HR = 1.35, 95% CI: 1.29–1.42). However, this association was not statistically significant among participants with baseline asthma (HR = 1.02, 95% CI: 0.84–1.25).

3.6 Sensitivity analysis

A sensitivity analysis was conducted by excluding participants with baseline asthma to assess the robustness of the primary findings. After exclusion of baseline asthma cases, the analytic sample decreased from 10,286 to 10,105 participants. The association between RSV and incident CLD remained statistically significant, with a similar dose–response pattern (all P for trend < 0.001) (Table 4).

Table 4

Sensitivity analysis of Cox proportional hazards regression analyses for the association between RSV and incident chronic lung disease after excluding participants with baseline asthma in 2011

Exposure	Model 1		Model 2		Model 3	
	HR(95%CI)	P	HR(95%CI)	P	HR(95%CI)	P
RSV category						
0	Ref		Ref		Ref	
1	1.63(1.38–1.93)	< 0.001	1.55(1.31–1.84)	< 0.001	1.53(1.29–1.82)	< 0.001
2	2.22(1.87–2.63)	< 0.001	2.04(1.71–2.42)	< 0.001	1.98(1.66–2.35)	< 0.001
≥ 3	3.53(2.94–4.24)	< 0.001	3.17(2.63–3.82)	< 0.001	2.98(2.46–3.61)	< 0.001
RSV(continuous, per 1-point increase)						
	1.43(1.37–1.51)		1.39(1.32–1.46)		1.36(1.29–1.43)	
P for trend	< 0.001		< 0.001		< 0.001	
Note: HRs, hazard ratios; CIs, confidence intervals. This sensitivity analysis excluded participants with pre-existing asthma at baseline in 2011, with the sample size changed from 10286 to 10105. RSV was categorized into four groups (0, 1, 2, and ≥ 3), with RSV = 0 as the reference group. For trend analysis, RSV score was modeled as a continuous variable (per 1-point increase). Model 1 was an unadjusted model. Model 2 was adjusted for age and sex. Model 3 was further adjusted for education, marital status, residence area, access to tap water, drinking status, BMI, waist circumference, hypertension, diabetes, stroke, liver disease. The components included in the RSV score were not additionally adjusted to avoid overadjustment. The proportional hazards assumption was assessed using Schoenfeld residuals, and no violation was observed (global P > 0.05).						

In the fully adjusted model, compared with participants with RSV = 0, the HRs for incident CLD were: RSV = 1: HR = 1.53, 95%CI:1.29 – 1.82; RSV = 2: HR = 1.98, 95%CI:1.66 – 2.35; RSV ≥ 3: HR = 2.98, 95%CI:2.46 – 3.61. Each 1-point increase in RSV score was associated with a 36% higher risk of incident CLD (HR = 1.36, 95% CI: 1.29–1.43). The magnitude and direction of associations were largely unchanged compared with the primary analysis, supporting the robustness of the findings.

4. Discussion

In this prospective cohort study based on data from the China Health and Retirement Longitudinal Study (CHARLS), we investigated the association between the respiratory vulnerability index (RSV) and incident chronic lung disease (CLD) among middle-aged and older adults in China. The findings showed that higher RSV scores were independently associated with an increased risk of incident CLD and demonstrated a clear dose–response relationship. After adjustment for demographic factors,

environmental-related social factors, lifestyle factors, and chronic disease conditions, participants with $RSV \geq 3$ remained at significantly higher risk of CLD compared with those with $RSV = 0$. Restricted cubic spline analysis further demonstrated a continuous positive association between RSV scores and CLD risk. The consistency of findings across subgroup and sensitivity analyses further supported the robustness of the observed association. These findings suggest that RSV may serve as a multidimensional indicator for identifying individuals with higher susceptibility to CLD.

Traditional approaches for CLD risk assessment have mainly focused on individual risk factors, including age, smoking exposure, and impaired pulmonary function. However, increasing evidence indicates that COPD and related chronic respiratory diseases are not merely localized pulmonary disorders but complex systemic conditions involving chronic inflammation, skeletal muscle dysfunction, and multimorbidity [11, 14]. Therefore, although individual risk factors may explain part of CLD susceptibility, they may not fully capture differences in physiological reserve and overall health vulnerability among middle-aged and older adults. For example, individuals with similar smoking exposure may have different risks of future CLD due to variations in physical function, respiratory reserve, and systemic organ vulnerability. In this context, RSV was developed not simply as an accumulation of traditional risk factors, but as an integrated measure incorporating respiratory function, physical function, smoking exposure, heart and kidney disease status, and psychological health to characterize individual vulnerability to future CLD.

The conceptual framework of RSV was derived from frailty theory and the deficit accumulation model. Fried et al. proposed the frailty phenotype model, in which weight loss, exhaustion, reduced physical activity, slow gait speed, and decreased grip strength represent reduced physiological reserve among older adults [6]. Subsequently, Rockwood et al. introduced the deficit accumulation model, suggesting that the accumulation of health deficits reflects individual vulnerability and can be used to evaluate the risk of mortality, functional decline, and other adverse health outcomes [7]. With the development of frailty research, frailty has expanded beyond the assessment of geriatric syndromes and has become an important framework for understanding vulnerability to chronic diseases. Previous studies have demonstrated that age-related accumulation of health deficits reflects declining physiological reserve and is associated with the occurrence and progression of multiple chronic diseases [15]. Therefore, applying frailty-related concepts to CLD risk assessment provides a biologically plausible framework.

Previous studies have mainly focused on frailty among patients with established COPD and its prognostic implications. Frailty is common in individuals with COPD and has been associated with reduced exercise capacity, greater disease severity, and poorer health outcomes [9, 10]. Further evidence suggests a potentially bidirectional relationship between COPD and frailty: chronic airway inflammation, reduced respiratory function, and increased disease burden may contribute to functional decline, while frailty may further impair respiratory health through reduced physical activity, diminished physiological reserve, and increased vulnerability to adverse outcomes [16]. However, most previous studies have evaluated frailty after disease onset. In contrast, the present study extended this research perspective to

the preclinical stage by examining whether a multidimensional respiratory vulnerability status was associated with future CLD development among community-dwelling middle-aged and older adults.

Several mechanisms may explain the association between RSV and incident CLD. First, smoking exposure, as one component of RSV, represents an established risk factor for COPD and other chronic respiratory diseases. Long-term tobacco exposure can induce airway inflammation, oxidative stress, and structural changes in lung tissue, contributing to persistent airflow limitation [11]. Second, reduced PEF and grip strength may reflect declines in respiratory and systemic functional reserve, respectively. Previous studies have shown that skeletal muscle dysfunction is an important extrapulmonary manifestation of COPD and is associated with reduced exercise tolerance, disease progression, and increased mortality risk [17, 18]. Third, multimorbidity and psychological health may contribute to overall vulnerability among older adults. Multimorbidity can increase disease burden and accelerate functional decline, thereby affecting long-term health outcomes [5]. Psychological disorders, including depression and anxiety, may further influence respiratory health through reduced physical activity, impaired health behaviors, and difficulties in disease management [19]. Therefore, RSV may capture the cumulative effects of multiple interconnected health dimensions involved in CLD susceptibility rather than reflecting a single pathological pathway.

The observed dose–response relationship between RSV and CLD risk has potential public health implications. Current community-based approaches for identifying individuals at risk of chronic respiratory diseases mainly rely on symptom assessment, smoking history evaluation, and pulmonary function testing. However, widespread implementation of pulmonary function testing may be limited by equipment availability, trained personnel, and healthcare resources. In contrast, RSV components are derived from routinely collected health information and relatively simple functional assessments, suggesting potential feasibility for community-based risk assessment. Similar concepts have been applied in other chronic disease fields; for example, the Framingham risk score integrates multiple risk factors to estimate cardiovascular disease risk [20]. These findings suggest that combining multiple health indicators with cumulative effects may improve identification of individuals who could benefit from further respiratory evaluation or preventive interventions.

The association between RSV and CLD risk remained generally consistent across subgroups stratified by age, sex, BMI, residential area, hypertension, and diabetes status, suggesting that RSV may have relatively stable associations across different population characteristics. A different pattern was observed in the asthma subgroup, which may be related to pre-existing airway inflammation, impaired respiratory function, and potential overlap between asthma and other chronic airway conditions. Importantly, after excluding participants with baseline asthma, the main findings remained largely unchanged, suggesting that the association between RSV and CLD risk was not primarily driven by baseline asthma.

This study has several strengths. First, it was based on a large nationally representative community cohort with long-term follow-up, allowing assessment of the temporal relationship between RSV and

incident CLD. Second, this study extended traditional single-factor risk assessment by integrating multiple dimensions of respiratory-related vulnerability, including respiratory function, physical function, smoking exposure, heart and kidney disease status, and psychological health. Third, the robustness of the findings was evaluated using multiple analytical approaches, including Cox proportional hazards regression, restricted cubic spline analysis, subgroup analyses, and sensitivity analyses.

Although RSV components were selected based on established frailty-related concepts, the current scoring system should be interpreted as a multidimensional vulnerability framework rather than a clinically validated diagnostic instrument. The categorization of higher RSV levels was determined according to the distribution of RSV scores within the CHARLS population, and its reproducibility and applicability require further validation in independent cohorts.

Several limitations should also be acknowledged. First, CLD events were identified based on physician-diagnosed information collected in CHARLS, and detailed data on longitudinal changes in pulmonary function and disease severity were unavailable, which may have introduced some degree of outcome misclassification. Second, although environmental-related social factors, including residential area and access to tap water, were considered, the potential effects of long-term air pollution exposure and occupational hazards could not be fully assessed because of database limitations. Third, although RSV integrates multiple dimensions of respiratory-related vulnerability, additional studies incorporating objective pulmonary function measurements, imaging characteristics, and inflammatory biomarkers are needed to further refine the framework and clarify its potential value in population-level respiratory risk assessment.

In conclusion, this prospective cohort study demonstrated that higher RSV scores were independently associated with an increased risk of incident CLD among middle-aged and older adults in China, with a clear dose–response relationship. By integrating respiratory function, physical function, smoking exposure, heart and kidney disease status, and psychological health, RSV provides a multidimensional assessment of respiratory vulnerability and may have potential value for identifying individuals at increased risk of CLD and supporting early risk assessment in community settings.

Declarations

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Ping Zhang: Conceptualization, Data curation, Methodology, Validation, Writing – original draft. Shengsong Chen: Investigation, Project administration, Validation, Visualization, Writing – original draft. Qingyuan Zhan: Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Validation, Visualization, Writing – original draft.

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Figures

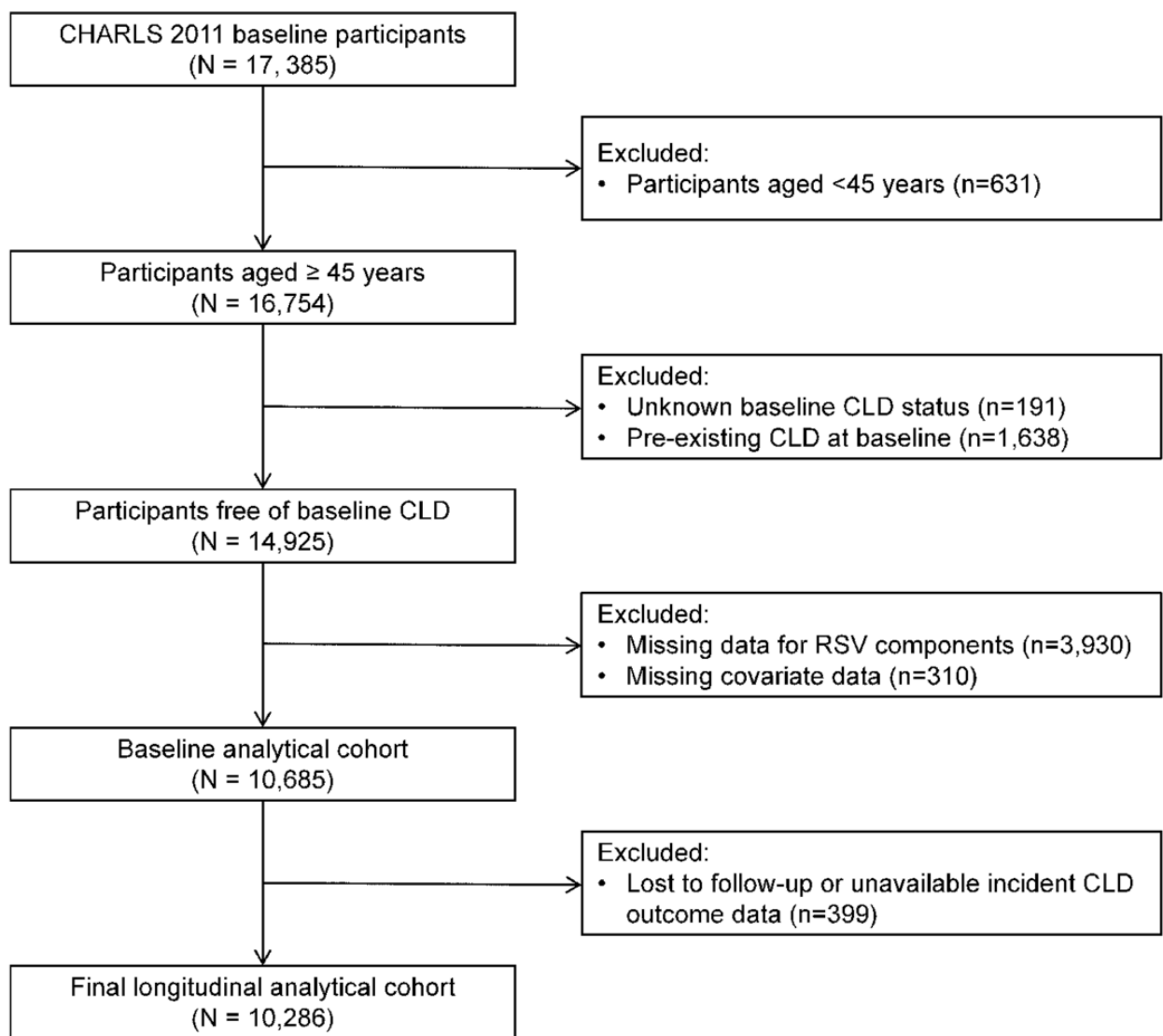


Figure 1

Flowchart of participant selection in the longitudinal cohort study.

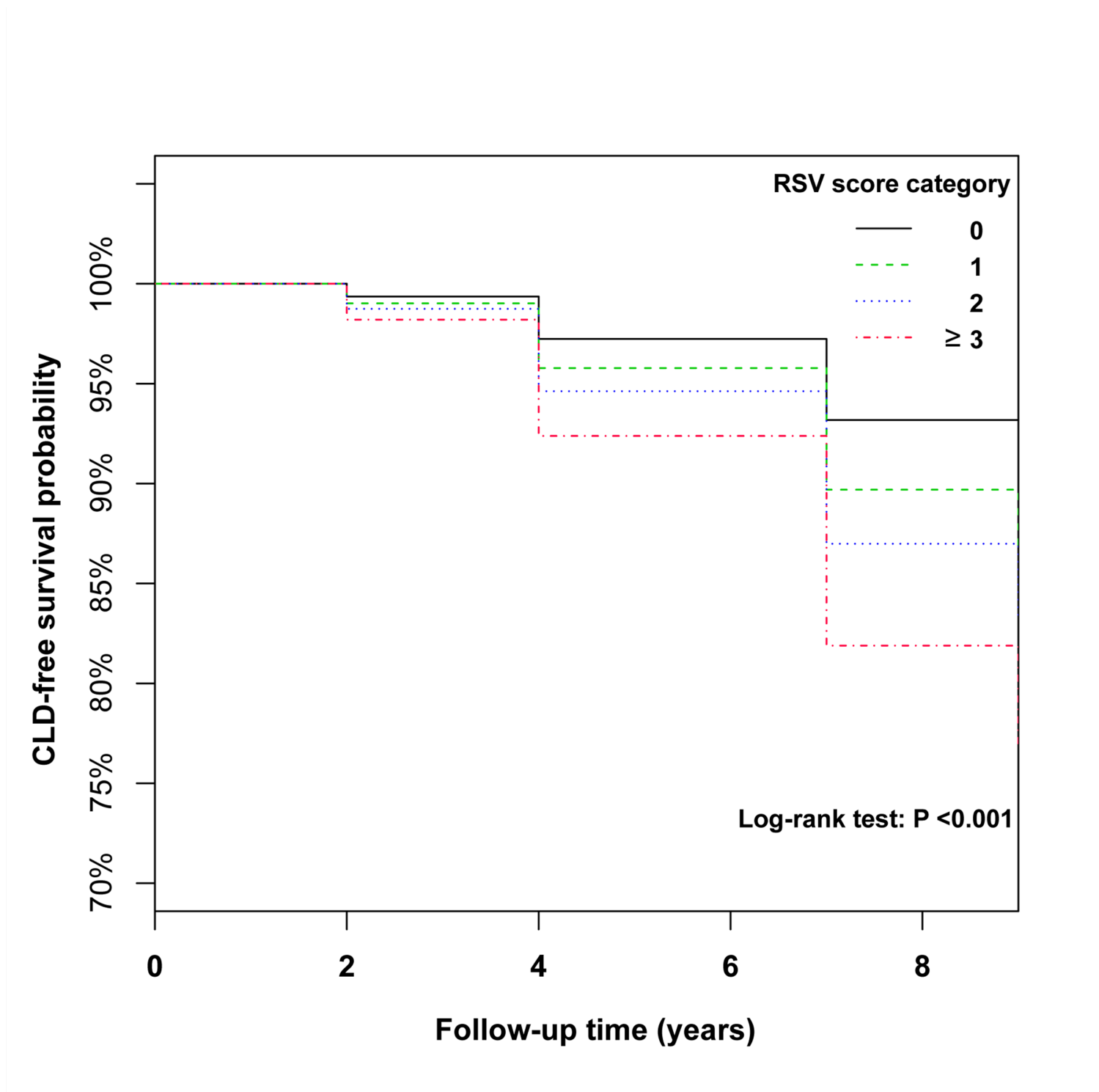


Figure 2

Kaplan–Meier curves for chronic lung disease-free survival according to RSV score categories

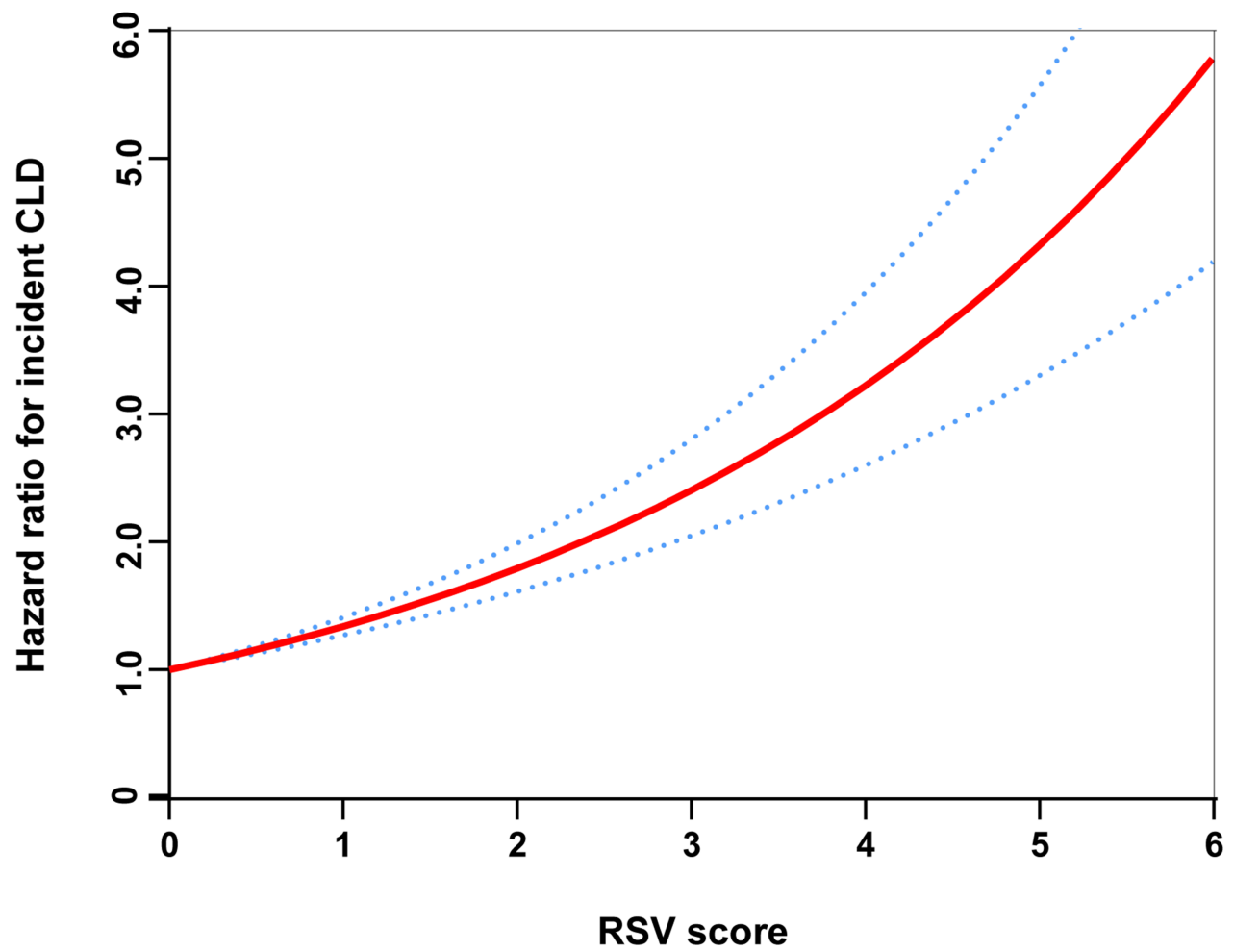


Figure 3

Restricted cubic spline analysis of the association between RSV score and incident chronic lung disease

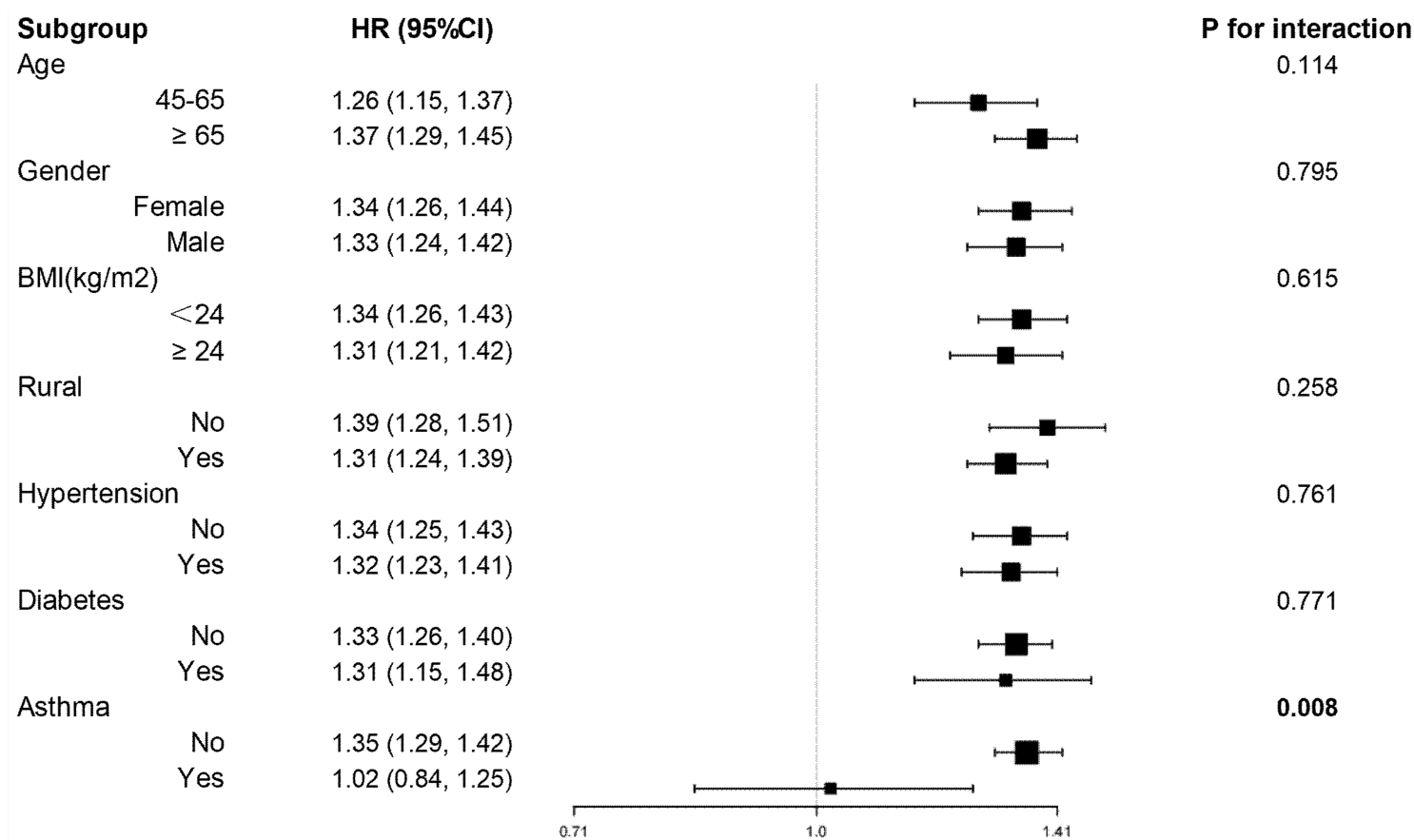


Figure 4

Subgroup analyses of the association between RSV score and incident chronic lung disease