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Relationship between an ageing measure and chronic obstructive pulmonary disease, lung function: a cross-sectional study of NHANES, 2007–2010

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ABSTRACT

Objectives Chronic obstructive pulmonary disease (COPD) is a disease associated with ageing. However, actual age does not accurately reflect the degree of biological ageing. Phenotypic age (PhenoAge) is a new indicator of biological ageing, and phenotypic age minus actual age is known as phenotypic age acceleration (PhenoAgeAccel). This research aimed to analyse the relationship between PhenoAgeAccel and lung function and COPD.

Design A cross-sectional study.

Participants Data for the study were obtained from the National Health and Nutrition Examination Survey (NHANES) 2007–2010. We defined people with forced expiratory volume in 1 s/forced vital capacity <0.70 after inhaled bronchodilators as COPD and the rest of the population as non-COPD. Adults aged 40 years or older were enrolled in the study.

Primary and secondary outcome measures Linear and logistic regression were used to investigate the relationship between PhenoAgeAccel, lung function and COPD. Subgroup analysis was performed by gender, age, ethnicity and smoking index COPD. In addition, we analysed the relationship between the smoking index, respiratory symptoms and PhenoAgeAccel. Multiple models were used to reduce confounding bias.

Results 5397 participants were included in our study, of which 1042 had COPD. Compared with PhenoAgeAccel Quartile1, Quartile 4 had a 52% higher probability of COPD; elevated PhenoAgeAccel was also significantly associated with reduced lung function. Further subgroup analysis showed that high levels of PhenoAgeAccel had a more significant effect on lung function in COPD, older adults and whites (P for interaction <0.05). Respiratory symptoms and a high smoking index were related to higher indicators of ageing.

Conclusions Our study found that accelerated ageing is associated with the development of COPD and impaired lung function. Smoking cessation and anti-ageing therapy have potential significance in COPD.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The data used in this study were obtained from a large, nationally representative sample in the USA.
⇒ The cross-sectional type of study design does not allow causal inferences to be made.
⇒ The results of this study cannot be generalised to people younger than 40 years of age.

INTRODUCTION

Ageing is the most significant risk factor for the incidence of many chronic diseases.[1 2] Ageing varies greatly between organisms and is reflected in multiple aspects at the molecular, cellular, physiological and functional levels.[3] However, the actual age of an individual does not always accurately reflect their biological senescence.[4] For this reason, the researchers used a measure known as phenotype age (PhenoAge).[5] PhenoAge minus actual age calculates phenotypic age acceleration (PhenoAgeAccel). PhenoAgeAccel helps to assess the rate of biological ageing and identify individuals who may be at risk.

Chronic obstructive pulmonary disease (COPD) is considered to be a disease associated with ageing.[6] Respiratory system structure and function changes significantly affect COPD susceptibility in the elderly.[7 8] Unlike normal ageing, disease-induced ageing leads to the continued accumulation of senescent cells, further amplifying the progression of the disease.[9] Persistent lung senescence has two detrimental consequences: (1) it leads to stem cell dysfunction, which affects the ability to repair losses, and (2) the senescence-associated secretory phenotype induces pro-inflammation and cellular remodelling, leading to lung fibrosis.[10 11] As the ageing population continues to increase, it is vital to study the relationship between ageing and the development of lung disease.

Hillary *et al* found epigenetic clocks reflecting ageing linked to the occurrence of COPD.[12] The physiological and immunological changes that occur in COPD are often similar to those seen in the ageing lung, and it has been suggested that COPD is an 'accelerated aging phenotype".[13] Therefore, we hypothesise that ageing has a more pronounced adverse effect on participants with COPD, reflected in a rapid decrease in lung function. Smoking, a crucial factor in COPD development, may influence PhenoAgeAccel. Therefore, we investigated the role of PhenoAgeAccel in COPD and lung function. We also analysed further the relationship between the smoking index and PhenoAgeAccel in the population. Data for the study were obtained from the National Health and Nutrition Examination Survey (NHANES) 2007–2010.

METHODS

Study population

Data collection for the NHANES included interviews, home screening and physical examinations.[14] This study uses the publicly available NHANES data set, which can be found here: https://www.cdc.gov/nchs/index.htm.[14] These data have been approved by the NHANES Medical Ethics Committee, so no additional ethical approval is required.

Our research was conducted on people who participated in the survey from 2007 to 2010. We defined people with forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC) <0.70 after inhaled bronchodilators as COPD and the rest of the population as non-COPD. Adults aged 40 years or older with complete research data were enrolled in the study. Figure 1 explains the inclusion and exclusion criteria for this study.

PhenoAge and PhenoAgeAccel measurements

PhenoAge is a metric developed by Levine *et al* for estimating biological age.[5] It includes actual age and nine biomarkers, including creatinine, albumin, glucose, C-reactive protein, red blood cell distribution width, mean cell volume, lymphocyte percentage, white blood cell count and alkaline phosphatase.[5] The specific calculation formula is shown in figure 2.[15] Due to the presence of actual age in PhenoAge, we introduced the definition of

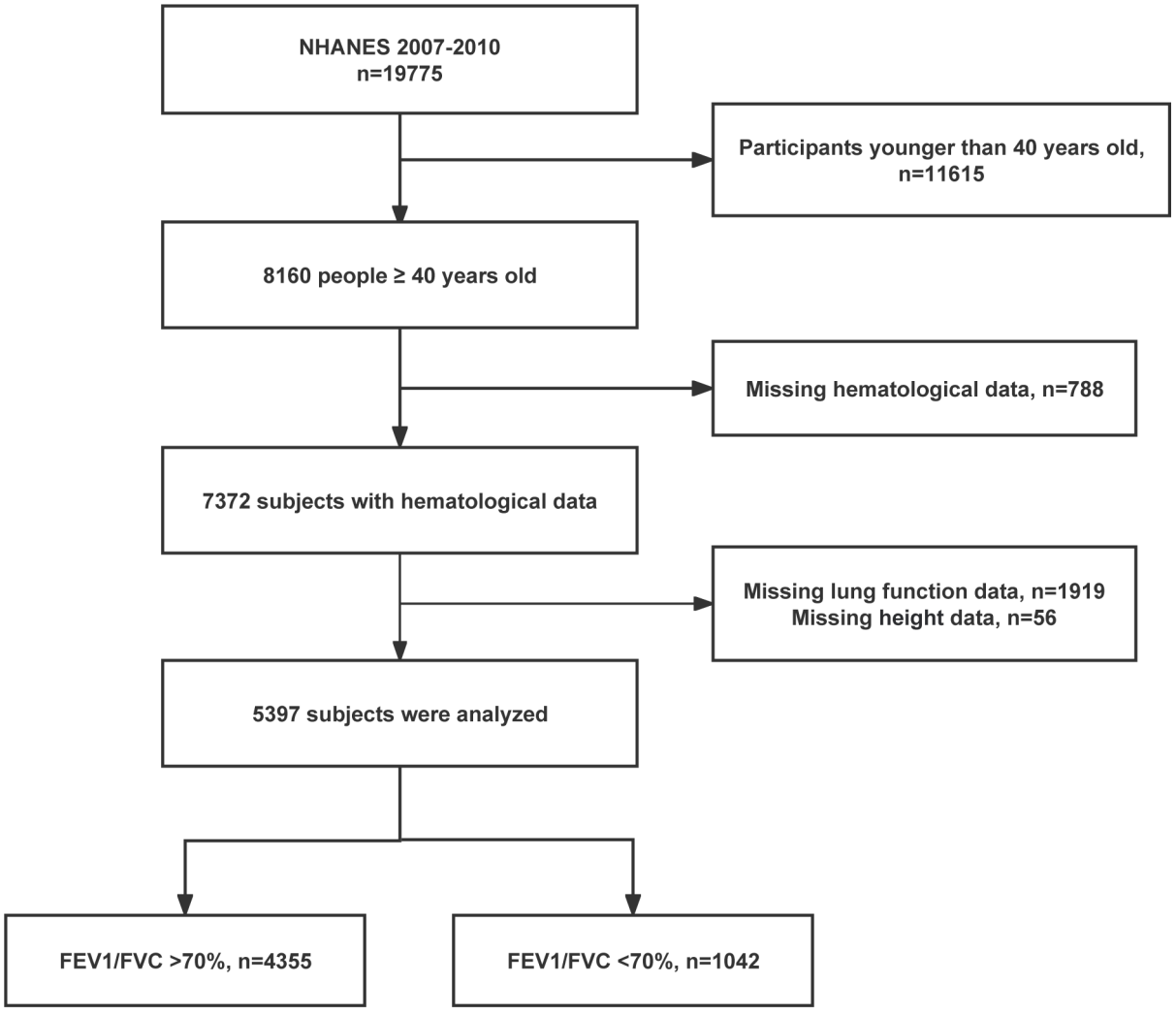

Figure 1 Flow chart of the study. FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; NHANES, National Health and Nutrition Examination Survey.

$$PhenoAge = 141.50 + \frac{\ln[-0.00553 \times \ln(1 - M)]}{0.09165}$$

$$PhenoAgeAccel = PhenoAge - Chronological\ Age$$

Where:

$$M = 1 - \exp\left(\frac{-1.51714 \times \exp(xb)}{0.0076927}\right)$$

And:

$$\begin{aligned} xb = &-19.907 - 0.0336 \times Albumin\_g/L + 0.0095 \times Creatinine\_umol/L \\ &+ 0.1953 \times Glucose\_mmol/L + 0.0954 \times ln(CRP\_mg/dL) \\ &- 0.0120 \times Lymphocyte\ Percent\_\% + 0.0268 \\ &\times Mean\ Cell\ Volume\_fL + 0.3306 \\ &\times Red\ Cell\ Distribution\ Width\_\% + 0.00188 \\ &\times Alkaline\ Phosphatase\_U/L + 0.0554 \\ &\times White\ Blood\ Cell\ Count\_1000\ cells/uL + 0.0804 \\ &\times Chronological\ Age \end{aligned}$$

Figure 2 The calculation formula of PhenoAge and PhenoAgeAccel. CRP, C-reactive protein; PhenoAge, phenotype age; PhenoAgeAccel, phenotypic age acceleration.

PhenoAgeAccel. PhenoAgeAccel is equal to PhenoAge minus actual age. A larger PhenoAgeAccel indicates a higher degree of biological ageing.[5 16]

Lung function measurements

Participants between the ages of 40 and 79 were eligible for the spirometry component from 2007 to 2010. Spirometer operation with the Ohio 822/827 dry rolling sealed volumetric spirometer.[17] Specific exclusion criteria for baseline spirometry included: current physical problems with chest pain or forceful exhalation, being on supplemental oxygen, undergoing surgery, heart attack, stroke, tuberculosis exposure or recent coughing up blood.[18] Spirometry is graded according to the The American Thoracic Society (ATS) quality standards, using only manoeuvres with a quality grade greater than C.[19]

The results of the pulmonary function measurements include FEV_1, FVC and FEV_1/FVC. In addition, the predicted values of FEV_1 (%) and FVC (%) for the population were calculated according to the NHANES III formula.[19] Those with FEV_1/FVC <0.70 were the COPD population; we defined four stages (stage I: 80%≤FEV_1%, predicted, stage II: 50%≤FEV_1%, predicted<80%, stage III: 30%≤FEV_1%, predicted<50%, stage IV: FEV_1%, predicted<30%) of COPD based on the predicted percentage of FEV_1 on this basis.[20]

Study covariates

In this study, we included multiple covariates including age, gender, race, smoking index, education, body mass index (BMI), cardiovascular disease (CVD), asthma, hypertension and diabetes. Age, gender, ethnicity, smoking history and education were obtained from participants' self-reports, and professionals measured height and weight to calculate BMI. The age range of the study population was 40–79 years old. The race is divided into non-Hispanic white, non-Hispanic black, Mexican American and others. We calculated the smoking index based on the information provided by NHANES (smd030: age at smoking initiation, smd055 age at quitting, smd057: average number of cigarettes smoked per day at stopping, smd650: average number of cigarettes smoked per day by current smokers). The detailed definitions of diseases in this study can be found in the online supplemental file.

Statistical analysis

Categorical data are described by numbers (percentages), and continuous variables are described by means±SDs. Kruskal-Wallis and χ^2 (or Fisher's exact) tests compare covariates. All covariates had missing values of less than 0.1% and were categorical. Because the small number of missing covariates did not affect the results, we omitted the treatment of these missing values in the regression analysis.

We used multivariate logistic regression to investigate the relationship between PhenoAgeAccel and COPD. Multivariate linear regression analysis assessed the association between PhenoAgeAccel and lung function (FEV_1, FVC, FEV_1 %, predicted and FVC %, predicted). To further clarify this relationship, we again used the PhenoAgeAccel quartiles to assess its relationship with COPD and lung function. The p trend was obtained using the linear term of the quartiles, and p trend<0.05

Table 1 Characteristics of population, 2007–2010 NHANES (n=5397)

Variables	Non-COPD (n=4355)	COPD (n=1042)	P value
Age, mean±SD	55.9±10.6	62.0±10.4	<0.001
PhenoAge, mean±SD	53.1±13.3	60.2±13.4	<0.001
PhenoAgeAccel, mean±SD	2.8±7.7	1.8±7.6	<0.001
Male, n (%)	2035 (46.7)	659 (63.2)	<0.001
Race/ethnicity, n (%)			<0.001
Non-Hispanic white	2003 (46.0)	669 (64.2)	
Mexican American	849 (19.5)	91 (8.7)	
Non-Hispanic black	815 (18.7)	176 (16.9)	
Other race	688 (15.8)	106 (10.2)	
BMI, n (%)			<0.001
<25	881 (20.2)	369 (35.4)	
25–30	1600 (36.7)	375 (36.0)	
>30	1874 (43.0)	298 (28.6)	
Education, n (%)			<0.001
≤High school	2249 (51.7)	602 (57.8)	
>High school	2101 (48.3)	439 (42.2)	
Smoking index, mean±SD	160.6±10.5	407.6±29.7	<0.001
Smoking index, n (%)			<0.001
<10, pack-years	3377 (77.5)	521 (50.0)	
10–20, pack-years	331 (7.6)	104 (10.0)	
>20, pack-years	647 (14.9)	417 (40.0)	
Comorbidities, n (%)			
CVD	439 (10.1)	186 (17.9)	<0.001
Asthma	435 (10)	184 (17.7)	<0.001
Diabetes	1001 (23.0)	230 (22.1)	0.526
Hypertension	2165 (49.7)	583 (56.0)	<0.001
Lung function, mean±SD			
FEV_1/FVC, %	79.0±5.0	62.9±7.2	<0.001
FVC, mL	3625.8±1020.8	3759.1±1102.0	<0.001
FEV_1, mL	2853.1±788.1	2378.5±779.1	<0.001
FVC %, predicted	96.5±14.8	96.4±17.5	0.800
FEV_1 %, predicted	97.6±15.0	79.9±18.4	<0.001
GOLD stage			
GOLD I	–	545 (52.3)	–
GOLD II–IV	–	426 (47.7)	–

BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Strategy for the Diagnosis,Management,and Prevention of Chronic Obstructive Pulmonary Disease; NHANES, National Health and Nutrition Examination Survey; PhenoAge, phenotypic age; PhenoAgeAccel, phenotypic age acceleration.

indicates a linear relationship. We corrected for age, sex, race, BMI, smoking index, education, cardiovascular disease, asthma, diabetes and hypertension to reduce confounding-mediated bias.

Subgroup analysis was used to analyse the difference between PhenoAgeAccel and lung function in COPD and non-COPD populations. Given the relationship between smoking and COPD, we also applied linear regression to investigate the relationship between the smoking index and PhenoAgeAccel. In addition, respiratory symptoms (cough, sputum, dyspnoea) are also common in COPD participants. Therefore, we analysed the association of respiratory symptoms with PhenoAgeAccel. See the online supplemental document for the definition of cough, sputum and dyspnoea.

Based on the sampling weighting documentation provided by NHANES, we performed a regression analysis based on the 'wtmec2yr' weights. The research was carried out using R V.4.1.3.

Table 2 Relationship between PhenoAgeAccel and chronic obstructive pulmonary disease

	OR (95% CI)	P value
PhenoAgeAccel, (continuous)	**1.02 (1.01 to 1.03)**	**0.016**
PhenoAgeAccel, (quartile)		
Quartile 1	1 (Ref)	
Quartile 2	1.09 (0.73 to 1.64)	0.65
Quartile 3	**1.39 (1.04 to 1.86)**	**0.029**
Quartile 4	**1.52 (1.08 to 2.14)**	**0.020**
P trend	**<0.001**	

Adjusted for age, sex and race, body mass index, smoking index, education, cardiovascular disease, asthma, diabetes and hypertension.
Bold values signifies P < 0.05 indicated that the difference was statistically significant
PhenoAgeAccel, phenotypic age acceleration.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Baseline characteristics

A total of 5397 participants were enrolled in our study (figure 1). The average age of subjects was 54.5 years, 48.3% were men and 49.5% were white (table 1). The values we calculated for PhenoAge and PhenoAgeAccel were similar to those of previous studies.[21 22] PhenoAge and PhenoAgeAccel were higher in the COPD group compared with the non-COPD group. In addition, the COPD group was older, had higher male and smoking indices and had higher rates of comorbid CVD, asthma and hypertension.

Association between PhenoAgeAccel and COPD, lung function

As shown in table 2, elevated PhenoAgeAccel was significantly correlated with the occurrence of COPD. Compared with baseline PhenoAgeAccel quartile 1, quartile 3 and quartile 4 had a 39% and 52% increase in COPD incidence, respectively. Online supplemental table S1 shows that in COPD, people with high PhenoAgeAccel are more likely to be GOLD (Global Strategy for the Diagnosis,Management,and Prevention of Chronic Obstructive Pulmonary Disease) stage II–IV.

Table 3 shows that for each unit increase in the value of PhenoAgeAccel, FEV_1, FVC, FEV_1 %, predicted and FVC %, predicted decreased by 9.3 mL, 10.4 mL, 0.23% and 0.18%, respectively. After quartiles, the Q4 group had a significant decrease in lung function compared with the Q1 group (FEV_1: β (95% CI), −178 (−238 to −119); FEV_1 %, predicted: β (95% CI), −4.53 (−6.03 to −3.03); FVC: β (95% CI), −233 (−371 to −95.0); FVC %, predicted: −3.35 (−4.79 to −1.91)].

Association between smoking index, respiratory symptoms and PhenoAgeAccel

Based on the relationship between smoking and COPD, we further analysed the effect of the smoking index on PhenoAgeAccel. Online supplemental table S2 showed that PhenoAgeAccel was significantly higher in those with a smoking index of 10–20 (β (95% CI), 1.21 (0.55 to 1.88), p=0.001) and >20 (β (95% CI), 1.76 (1.03 to 2.49), p<0.001) compared with those with a smoking index of <10. We also found that cough, sputum and dyspnoea were associated with elevated PhenoAgeAccel. This relationship remained stable in those with normal or not normal lung function (online supplemental tables S3 and S4).

Table 3 Relationship between PhenoAgeAccel and lung function

	FEV_1, mL β (95% CI), P value	FVC, mL β (95% CI), P value	FEV_1%, predicted β (95% CI), P value	FVC%, predicted β (95% CI), P value
PhenoAgeAccel, (continuous)	**−9.33 (−11.8 to −6.88) <0.001**	**−10.4 (−13.8 to −7.0) <0.001**	**−0.23 (−0.31 to −0.15) <0.001**	**−0.18 (−0.27 to −0.09) <0.001**
PhenoAgeAccel, (quartile)				
Quartile 1	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Quartile 2	−33.1 (−80.4 to 14.3) 0.160	−28.4 (−95.1 to 38.3) 0.384	−1.01 (−2.30 to 0.28) 0.117	−0.67 (−2.05 to 0.71) 0.323
Quartile 3	**−102 (−171 to −33.7) 0.006**	−72.2 (−156 to 11.6) 0.087	**−2.84 (−4.78 to −0.89) 0.007**	−1.33 (−3.08 to 0.41) 0.127
Quartile 4	**−178 (−238 to −119) <0.001**	**−186 (−257 to −115) <0.001**	**−4.53 (−6.03 to −3.03) <0.001**	**−3.35 (−4.79 to −1.91) <0.001**
P trend	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Adjusted for age, sex and race, body mass index, smoking index, education, cardiovascular disease, asthma, diabetes and hypertension.
Bold values signifies P < 0.05 indicated that the difference was statistically significant.
FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; PhenoAgeAccel, phenotypic age acceleration.

Table 4 Subgroup analysis of PhenoAgeAccel and lung function

	FEV_1, mL β (95% CI)	FVC, mL β (95% CI)	FEV_1 %, predicted β (95% CI)	FVC %, predicted β (95% CI)
PhenoAgeAccel, (continuous)				
COPD				
No	−6.86 (−9.25 to −4.47)	−9.10 (−12.3 to −5.94)	−0.14 (−0.21 to −0.06)	−0.14 (−0.22 to −0.06)
Yes	−13.1 (−18.8 to −7.38)	−17.1 (−24.9 to −9.35)	−0.40 (−0.60 to −0.20)	−0.38 (−0.57 to −0.18)
P for interaction	**0.021**	**0.034**	**0.023**	0.051
Smoking index				
<10, pack-years	−9.17 (−11.4 to −6.98)	−10.5 (−14.0 to −6.88)	−0.23 (−0.30 to −0.17)	−0.19 (−0.27 to −0.11)
10–20, pack-years	−10.5 (−19.3 to −1.66)	−10.4 (−21.4 to 0.61)	−0.26 (−0.58 to 0.05)	−0.18 (−0.49 to 0.13)
>20, pack-years	−8.84 (−15.8 to −1.85)	−10.7(−19.1 to −2.24)	−0.20 (−0.44 to 0.03)	−0.18 (−0.42 to 0.05)
P for interaction	0.74	0.68	0.80	0.83
Age				
<65 years	−7.13 (−10.5 to 3.82)	−7.47 (−12.0 to −2.94)	−0.14 (−0.24 to −0.04)	−0.09 (−0.19 to 0.02)
≥65 years	−13.8 (−18.5 to −9.07)	−16.0 (−21.8 to −10.2)	−0.53 (−0.69 to −0.37)	−0.44 (−0.59 to −0.28)
	0.027	**0.045**	**< 0.001**	**0.005**
Sex				
Female	−7.49 (−10.8 to 4.23)	−8.05 (−12.3 to −3.77)	−0.22 (−0.37 to −0.08)	−0.16 (−0.30 to 0.01)
Male	−10.8 (−14.9 to −6.78)	−13.8 (−18.6 to −8.98)	−0.26 (−0.35 to −0.17)	−0.24 (−0.33 to −0.15)
P for interaction	0.084	**0.016**	0.75	0.94
Race/ethnicity, n (%)				
Non-Hispanic white	−11.1 (−14.2 to −7.91)	−12.9 (−17.5 to −8.27)	−0.30 (−0.41 to −0.19)	−0.26 (−0.38 to −0.14)
Mexican American	−3.93 (−8.73 to 0.87)	−4.59 (−10.4 to 1.17)	−0.17 (−0.30 to −0.03)	−0.15 (−0.27 to −0.03)
Non-Hispanic black	−4.33 (−8.34 to −0.32)	−2.94 (−6.75 to 0.88)	−0.18 (−0.31 to −0.05)	−0.11 (−0.22 to 0.00)
Other race	−7.73 (−12.5 to −3.00)	−8.40 (−14.9 to −1.92)	−0.26 (−0.40 to −0.12)	−0.21 (−0.33 to −0.08)
P for interaction	0.062	0.057	**0.004**	**0.004**

Adjusted for age, sex and race, body mass index, smoking index, education, cardiovascular disease, asthma, diabetes and hypertension.
Bold values signifies P for interaction < 0.05 proved that PhenoAgeAccel had an interaction in this subgroup.
A, A; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; PhenoAgeAccel, phenotypic age acceleration.

Subgroup analysis

Table 4 shows the subgroup analysis of PhenoAgeAccel and lung function. After adjusting for covariates, the effect of high PhenoAgeAccel on impaired lung function was more pronounced in the COPD group, in older people and in whites (P for interaction <0.05). The relationship between PhenoAgeAccel and lung function remained stable across smoking indices. In addition, there was an interaction between PhenoAgeAccel and FVC in gender, which the association may mediate between gender and lung function.

DISCUSSION

Our study findings indicate that participants with COPD have higher PhenoAge and PhenoAgeAccel compared with those without COPD. Even after adjusting for covariates, elevated PhenoAgeAccel was associated with the development of COPD and diminished lung function. In addition, subgroup analysis showed a higher effect of PhenoAgeAccel on lung function in COPD, whites and the elderly (P for interaction <0.05). This suggests that the relationship between ageing and impaired lung function is more significant in this population. These results support the notion that COPD represents an 'accelerated aging phenotype'. Additionally, we find that a higher smoking index and respiratory symptoms are linked to higher PhenoAgeAccel, emphasising the importance of smoking cessation and symptom management.

COPD is a disease associated with ageing. Smoking, a risk factor for COPD, is strongly associated with lung cellular senescence.[20 23] Our study corroborates the association between the smoking index and ageing indicators (PhenoAgeAccel) from a clinical perspective. Schafer *et al* have shown that induced lung ageing accelerates the decline in lung function.[24] Even in ordinary people, lung function declines with age after the age of 20–25. Signs of premature lung senescence (abnormal lung function before age 40) can predict the likelihood of a later

diagnosis of COPD.[25] These further suggest that age is a factor in the progression of COPD.

Given the heterogeneity and variability of the ageing population and lung ageing, actual age alone is not an effective measure to assess COPD. Therefore, we incorporated PhenoAgeAccel, a composite index characterising the rate of ageing, and confirmed its association with COPD. The methylation clock (DNAmPhenoAge) used phenotypic age and was linked to inflammation, DNA damage repair and mitochondrial signatures.[26] PhenoAgeAccel can predict the risk of morbidity and mortality in a population.[15] In cardiovascular disease, increased PhenoAgeAccel has also been associated with increased mortality.[21] In addition, previous studies have suggested that composite metrics based on patient-level biomarker calculations may be superior to telomere length measurements.[27] In validating several biological ageing algorithms, PhenoAge was found to have the best sensitivity to respond to ageing.[28]

Ageing lungs are more susceptible to the external environment, increasing the risk of infection.[29 30] If COPD represents accelerated lung ageing, delaying this acceleration may benefit patients with COPD. The study finds that removing senescent cells restores healthy lung vitality in aged mice.[24] Reversing ageing is difficult, and much consensus has been reached on basic measures to slow it down.[31] Clinical trials of metformin, mTOR inhibitors (rapamycin), and senescent cell-killing drugs (senolytics) have demonstrated the feasibility of delayed ageing for treating ageing diseases.[32] The combination of dasatinib and quercetin (D+Q) in senolytics selectively ablates senescent cells without affecting normal cells.[33] D+Q treatment removes senescent cells and improves health and the remaining life span in aged mice.[34] Moreover, adopting a healthy lifestyle that includes proper diet and exercise can actively contribute to slowing down the ageing process.[35 36]

Admittedly, there are some limitations to our study. First, the characteristics of cross-sectional studies cannot be used to infer temporal causality. Second, our study only measured data at baseline and needed more longitudinal data to validate the results. Third, the correlation between COPD and C-reactive protein and lymphocytes may lead to an overfitting of the PhenoAgeAccel to lung function. In addition, PhenoAgeAccel may affect survival and thus incidence-prevalence bias due to the limitations of cross-sectional studies, and future longitudinal studies could help to minimise this bias. Finally, our study only analysed people >40 years of age because this is the group in which COPD is more prevalent. At the same time, the results of this study cannot be generalised to people<40 years of age.

Conclusions

In conclusion, our research found that elevated PhenoAgeAccel was related to COPD development and impaired lung function. The subgroup analysis validated our hypothesis that ageing has a more pronounced adverse effect on COPD participants, reflected in an accelerated decline in lung function. In addition, we found an association between the smoking index and PhenoAgeAccel. It demonstrates the potential significance of smoking cessation and anti-ageing therapies in COPD.

Contributors ZR and DL participated in the study design, analysed the results and edited the manuscript. DH and YX participated in manuscript modification. ML participated in the visual processing of the data. ZQ and XC participated in the research design and editor of the manuscript. ZR takes full responsibility for the completed research, has access to the data, and controls the decision to publish.

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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 These data are de-identified and open to the public and therefore do not require the consent of the medical ethics committee. This study also received an ethical exemption from the Ethics Committee of Shandong University of Traditional Chinese Medicine (20230003). 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. Data in the article can be obtained from the NHANES database (https://www.cdc.gov/nchs/index.htm).

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