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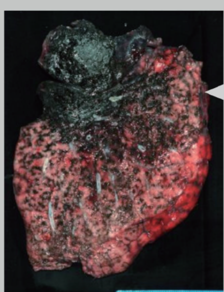
Pneumoconioses



The pneumoconioses are a group of lung diseases caused by the lung's reaction inhaling certain dusts. The main cause of the pneumoconioses is work-place exposure. Environmental exposures have rarely been related to these diseases.

Lung of former coal miner with severe black lung.

The primary pneumoconioses are:
- Silicosis – caused by inhaling silica dust
- Coal workers' pneumoconiosis – caused by inhaling coal mine dust
- Abestosis – caused by inhaling asbestos fibers

PNEUMOCONIOSIS PREVENTION ISSUE

Preplanned Studies

Methods and Applications

Commentary

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Cover Image: adapted from the US Centers for Disease Control and Prevention, https://www.cdc.gov/niosh/topics/pneumoconioses/default.html.

This week's issue was organized by Guest Editor Huanqiang Wang.

Preplanned Studies

Prevalence and Types of Comorbidities in Pneumoconiosis — China, 2018–2021

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Summary

What is already known about this topic?

Pneumoconiosis, recognized as one of the most detrimental occupational diseases in China, exhibits a multimorbidity profile due to a plethora of comorbidities and complications. These factors significantly influence the treatment outcomes, progression, prognosis, and overall quality of life of the afflicted patients.

What is added by this report?

The present study examined the prevalence and types of comorbidities, encompassing 13 common diseases or conditions, within cases of pneumoconiosis across 27 provincial-level administrative divisions (PLADs) in China. Distinctions in multimorbidity distribution by gender, urban *vs.* rural areas, stages of pneumoconiosis, and the smoking index were considered. Furthermore, the study investigated the patterns of multimorbidity.

What are the implications for public health practice?

This study serves as a reference point for the formulation of treatment strategies and health policy development concerning pneumoconiosis in China.

Pneumoconiosis, an interstitial lung disease induced by dust exposure, represents a significant and prevalent occupational health hazard in China (*1*). Often, individuals with pneumoconiosis have experienced prolonged exposure to mineral dust, thus significantly impairing their respiratory system's clearance and defense mechanisms. The chronic and progressive nature of pneumoconiosis remarkably compromises the patient's immunity. Furthermore, pneumoconiosis patients frequently exhibit a range of comorbidities or complications, including pulmonary tuberculosis (PTB), non-tuberculosis (non-TB) lung infection, pneumothorax, chronic obstructive pulmonary disease (COPD), and chronic pulmonary heart disease. Patients are typically approaching 60 years of age, and the majority are middle-aged to elderly individuals. These patients might also endure additional chronic diseases, such as hypertension and diabetes, alongside pneumoconiosis. The concurrent manifestation of two or more of these aforementioned diseases or conditions within the same individual constitutes multimorbidity (*2*). Given the aging population and advancements in medical technology, the occurrence of multimorbidity is increasing. Consequently, managing individuals with multiple chronic diseases has emerged as a global challenge for societal and healthcare systems (*3*).

While some studies have examined the comorbidities associated with pneumoconiosis in specific locales or industries, a comprehensive, large-scale assessment of multimorbidity in pneumoconiosis patients throughout China is yet to be conducted. To address this gap, we performed a cross-sectional survey between December 2017 and June 2021 to understand the patient health statuses and the utilization of medical services by pneumoconiosis patients across 27 provincial-level administrative divisions (PLADs) in Chinese mainland — survey not including Tianjin Municipality, Shanghai Municipality, Hainan Province, and Xizang (Tibet) Autonomous Region.

Our survey employed a face-to-face questionnaire, administered by trained physicians and nurses specializing in occupational diseases. We collected a total of 11,181 valid responses and included 10,137 qualified pneumoconiosis patients in our analysis, amounting to 90.7% of all respondents. The respective annual breakdown of our analytical sample consisted of 953 (9.4%) in 2017, 2,077 (20.5%) in 2018, 3,529 (34.8%) in 2019, 3,084 (30.4%) in 2020, and 494 (4.9%) in 2021.

Using the survey data, we analyzed the distribution of the prevalence of 13 common comorbidities or conditions in pneumoconiosis patients. We stratified these distributions by gender, urban or rural residence, stage of pneumoconiosis, and smoking index. Furthermore, we calculated the prevalence rates, along with their 95% confidence intervals (*CI*s) for multimorbidity in various age groups, categorizing these by gender, residence, stages of pneumoconiosis, and smoking index. We also explored the patterns of multimorbidity stratified by urban and rural areas. These findings aim to inform the development of effective treatment strategies and health security policies for pneumoconiosis in China.

The questionnaire considered for this study assesses eleven self-reported chronic diseases. Participants were asked, "Have you been diagnosed with any of the following diseases or conditions during treatment or examination at hospitals or outpatient clinics: PTB, lung cancer or mesothelioma, diabetes, hypertension, pulmonary heart disease, cardiovascular diseases (CVDs), cerebrovascular diseases, non-TB lung infection, COPD, pulmonary bullae or pneumothorax, and rheumatism?" The remaining two conditions were determined from the participants' body mass index (BMI), which included obesity (BMI≥24.0 kg/m^2) and underweight (BMI<18.5 kg/m^2). For the purposes of statistical analysis, age was categorized as follows: ≤44 years, 45–59 years, and ≥60 years. The smoking index was calculated by multiplying the number of cigarettes smoked daily by the years of smoking. Multimorbidity (MM1+) was defined as a patient having one or more of these 13 diseases or conditions within one pneumoconiosis patient population.

Data conforming to a normal distribution was articulated as mean±standard deviation (SD), while categorical data was represented by numbers (percentages). This study scrutinized the statistical significance of disparities using one-way analysis of variance (ANOVA) or *t*-tests for continuous variables of normal data distribution, assuming equal variances. For continuous variables exhibiting normal or nearly normal distribution, Pearson correlation analysis was utilized. For categorical data, Chi-square analysis and Fisher's exact test were deployed. Linear-by-Linear Association (LLA) test was applied to calculate *P*-values for trends concerning proportions and prevalence. All statistical tests were two-sided, with *P*<0.05 indicating statistical significance. SPSS software (version 26.0, SPSS Inc., Chicago, IL, USA) was used to conduct all the aforementioned statistical analysis. Further information about the survey design, sample, subject background, questionnaire approaches, and data processes is outlined in a previous publication (*4*). This paper reports on the prevalence of 13 diseases or conditions in the subjects, with 11 being primarily self-reported by patients based on diagnostic results.

Ethical approval for this research was granted by the Ethics Committee of the National Institute for Occupational Health and Poison Control, associated with the Chinese Center for Disease Control and Prevention (Approval No. 201720). Written informed consent was obtained from all participants.

Of the 10,137 participants in the study, 97.4% were men (*n*=9,875) with an average age of 57.6 years (SD=11.5). This was notably younger than the female participants, who had an average age of 68.1 years (SD=13.7; F=211.067, *P*<0.001). Patients in urban locations were older than those in rural areas (F=969.257, *P*<0.001), and the age of participants decreased correspondingly with the stage of pneumoconiosis (F=159.243, *P*<0.001). Approximately 39.7% of the participants (*n*=4,021) were aged 60 years or older. Comparatively, the group aged 60 and above had a higher proportion of females than males (70.2% *vs*. 38.9%; χ^2=104.970, *P*<0.001). It also had a higher proportion of urban rather than rural participants (53.3% *vs*. 29.1%; χ^2=611.700, *P*<0.001). Significant statistical differences were observed in the proportions of middle-aged and elderly patients according to their varying clinical stages of pneumoconiosis and those without a stage (47.5% *vs*. 39.5% *vs*. 30.6% *vs*. 22.9%; χ^2=303.048, *P*<0.001).

The prevalence rates for patients with one to six or more comorbidities were 28.8% (2,924/10,137), 15.9% (1,612/10,137), 10.6% (1,074/10,137), 5.9% (599/10,137), 2.9% (291/10,137), and 1.9% (189/10,137), respectively. Of these patients, 66.0% (95% *CI*: 65.1–66.9) had at least one comorbidity, and 37.1% (95% *CI*: 36.2–38.1) had two or more comorbid actions. Higher prevalence rates were found in male patients, urban residents, and patients with a smoking index of 200 or higher, with an increased rate coinciding with the severity of pneumoconiosis. Table 1 details the distribution of incidence and prevalence for 13 diseases or conditions, divided by gender, residential area, pneumoconiosis stage, and smoking index.

Table 1 reveals that respiratory and circulatory system diseases were the most common comorbidities. Women had higher prevalence rates of circulatory system diseases, COPD, obesity, and diabetes, while men had higher rates of pulmonary bullae or pneumothorax and arthritis. Urban patients had a higher prevalence of circulatory system diseases, pulmonary infection, COPD, obesity, and diabetes, whereas rural patients had higher rates of PTB, underweight, pulmonary bullae or pneumothorax, and arthritis. Stage I patients showed higher rates for obesity, diabetes, hypertension, CVDs, and cerebrovascular diseases, while stage III patients had

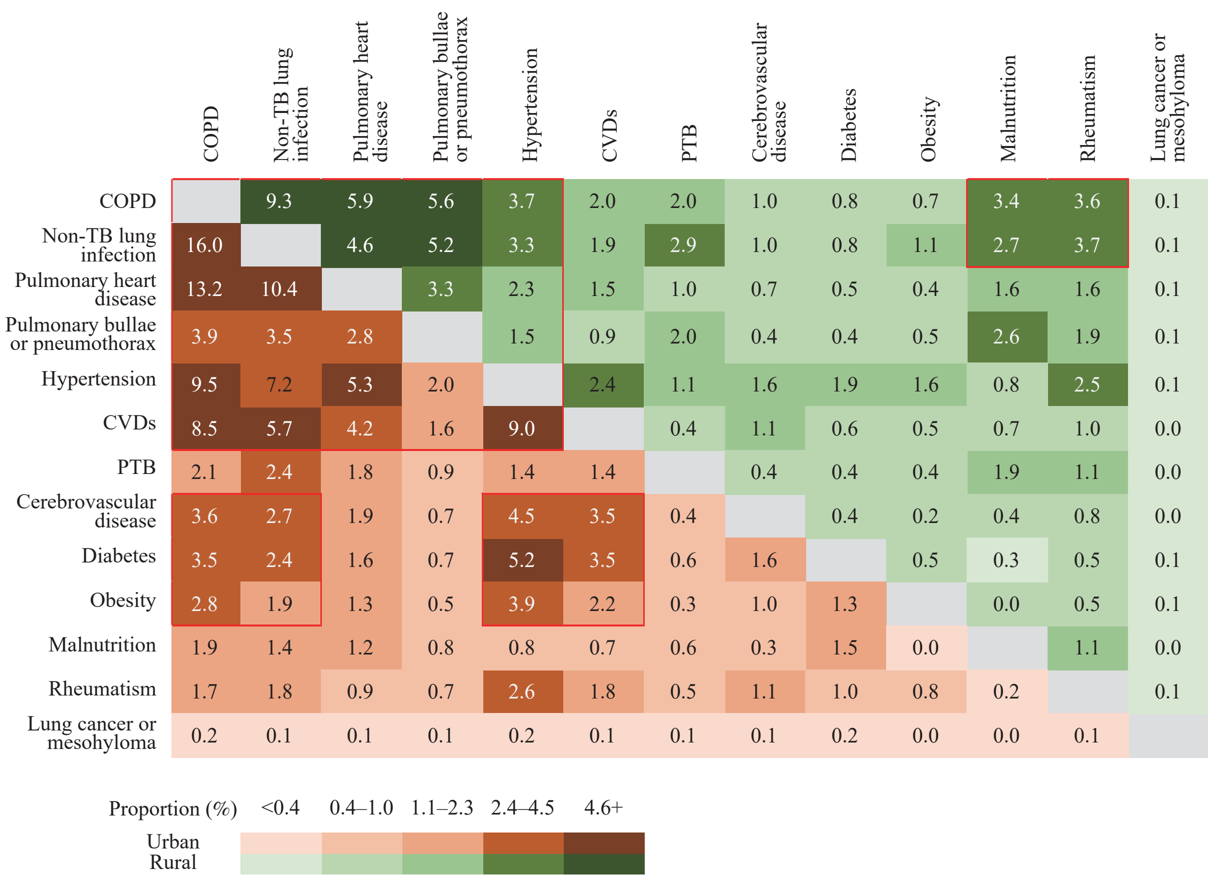

FIGURE 1. Heatmap of the percentage of comorbid disease pairs and conditions by residence among pneumoconiosis patients in China.

Note: The proportions depicted by the green diagonal situated above and to the right of the gray diagonal represent patients residing in rural areas. Conversely, the proportions indicated by the brown diagonal below and to the left of the gray diagonal represent patients hailing from urban areas.

Abbreviation: COPD=chronic obstructive pulmonary disease; CVDs=cardiovascular diseases; PTB=pulmonary tuberculosis.

higher rates for PTB, underweight, pulmonary bullae or pneumothorax, and other respiratory diseases. Individuals with a smoking index of ≥200 had higher rates of PTB, obesity, hypertension, cerebrovascular disease, COPD, pulmonary bullae or pneumothorax, and arthritis.

A positive correlation was found between the number of comorbidities and age (r=0.328, P<0.001). An increase in the prevalence of MM1+ with age was observed, landing at 54.3% (95% *CI*: 51.2–57.4), 58.4% (95% *CI*: 57.0–59.7), and 78.6% (95% *CI*: 77.3–79.8) for age groups ≤44 years, 45–59 years, and ≥60 years, respectively (χ^2=419.135, P<0.001). Age-stratified analysis according to gender, locality, pneumoconiosis stage, and smoking index consistently demonstrated an increased prevalence with ascending age. MM1+ prevalence rates were notably elevated among female patients, urban dwellers, those in stage III of pneumoconiosis, and those with a smoking index of ≥200, as outlined in Table 2.

Further analysis revealed a higher proportion of urban and female patients aged 60 years and older. In urban areas, retired workers from state-owned enterprises were significantly more numerous than in rural regions (80.9% *vs.* 21.4%, χ^2=3581.828, P<0.001). Similarly, the proportion of work-injury-insured workers was distinctly higher in urban areas versus rural (86.2% *vs.* 29.8%, χ^2=3197.974, P<0.001). The proportion of retired female employees from state-owned enterprises surpassed that of males (62.2% *vs.* 47.0%, χ^2=49.267, P<0.001), and more female patients were covered by work-related injury insurance than male patients (69.5% *vs.* 54.0%, χ^2=24.688, P<0.001). This can potentially be attributed to the higher incidence of multimorbidity amongst urban patients and females.

In this study, 72.5% of patients working in state-owned enterprises benefitted from work-related injury

TABLE 1. Incidence and prevalence (%) of 13 types of diseases or conditions associated with pneumoconiosis categorized by sex, place of residence, clinical stage, and smoking index in China, 2018–2021.

Diseases and conditions	Total (*n*=10,137)	Sex		*P*	Residence		*P*	Stages of pneumoconiosis				*P*	Smoking index		*P*
		Male (*n*=9,875)	Female (*n*=262)		Rural (*n*=5,713)	Urban (*n*=4,424)		Stage Ⅰ (*n*=4,540)	Stage Ⅱ (*n*=2,518)	Stage Ⅲ (*n*=2,134)	No stage (*n*=945)		<200 (*n*=5,903)	≥200 (*n*=4,234)	
PTB and Respiratory system disease															
PTB	762 (7.5)	748 (7.6)	14 (5.3)	0.176	513 (9.0)	249 (5.6)	<0.001	175 (3.9)	193 (7.7)	269 (12.6)	125 (13.2)	<0.001	365 (6.2)	397 (9.4)	<0.001
Non-PTB lung infection	2,298 (22.7)	2,234 (22.6)	64 (24.4)	0.491	1,144 (20.0)	1,154 (26.1)	<0.001	955 (21.0)	554 (22.0)	579 (27.1)	210 (22.2)	<0.001	1,345 (22.8)	953 (22.5)	0.743
COPD	2,431 (24.0)	2,349 (23.8)	82 (31.3)	0.005	1,127 (19.7)	1,304 (29.5)	<0.001	977 (21.5)	642 (25.5)	630 (29.5)	182 (19.3)	<0.001	1,249 (21.2)	1,182 (27.9)	<0.001
Lung bulla or emphysema	979 (9.7)	974 (9.9)	5 (1.9)	<0.001	690 (12.1)	289 (6.5)	<0.001	187 (4.1)	199 (7.9)	467 (21.9)	126 (13.3)	<0.001	517 (8.8)	462 (10.9)	<0.001
Lung cancer or mesohyloma	41 (0.4)	40 (0.4)	1 (0.4)	0.714	15 (0.3)	26 (0.6)	0.011	25 (0.6)	7 (0.3)	8 (0.4)	1 (0.1)	0.136	25 (0.4)	16 (0.4)	0.721
Endocrine, nutritional and metabolic diseases															
Obesity	769 (7.6)	738 (7.5)	31 (11.8)	0.009	325 (5.7)	444 (10.0)	<0.001	415 (9.1)	219 (8.7)	96 (4.5)	39 (4.1)	<0.001	403 (6.8)	366 (8.6)	0.001
Malnutrition	757 (7.5)	735 (7.4)	22 (8.4)	0.562	549 (9.6)	208 (4.7)	<0.001	160 (3.5)	143 (5.7)	352 (16.5)	102 (10.8)	<0.001	422 (7.1)	335 (7.9)	0.149
Diabetes	652 (6.4)	620 (6.3)	32 (12.2)	<0.001	230 (4.0)	422 (9.5)	<0.001	390 (8.6)	153 (6.1)	89 (4.2)	20 (2.1)	<0.001	359 (6.1)	293 (6.9)	0.090
Circulatory system diseases															
Hypertension	2,034 (20.1)	1,934 (19.6)	100 (38.2)	<0.001	861 (15.1)	1,173 (26.5)	<0.001	1,109 (24.4)	531 (21.1)	290 (13.6)	104 (11.0)	<0.001	1,125 (19.1)	909 (21.5)	0.003
Pulmonary heart disease	1,177 (11.6)	1,129 (11.4)	48 (18.3)	0.001	493 (8.6)	684 (15.5)	<0.001	520 (11.5)	287 (11.4)	291 (13.6)	79 (8.4)	<0.001	684 (11.6)	493 (11.6)	0.930
CVDs	1,127 (11.1)	1,044 (10.6)	83 (31.7)	<0.001	339 (5.9)	788 (17.8)	<0.001	637 (14.0)	322 (12.8)	134 (6.3)	34 (3.6)	<0.001	656 (11.1)	471 (11.1)	0.986
Cerebrovascular disease	502 (5.0)	479 (4.9)	23 (8.8)	0.004	168 (2.9)	334 (7.5)	<0.001	277 (6.1)	153 (6.1)	48 (2.2)	24 (2.5)	<0.001	255 (4.3)	247 (5.8)	0.001
Rheumatism	916 (9.0)	901 (9.1)	15 (5.7)	0.058	664 (11.6)	252 (5.7)	<0.001	370 (8.1)	246 (9.8)	194 (9.1)	106 (11.2)	0.009	470 (8.0)	446 (10.5)	<0.001
Age	57.9±11.7	57.6±11.5	68.1±13.7	<0.001	54.8±9.9	61.8±12.6	<0.001	60.2±12.0	57.8±12.1	55.3±10.0	52.8±9.7	<0.001	57.4±12.1	58.6±11.0	<0.001

Abbreviation: PTB=pulmonary tuberculosis; CVDs=cardiovascular diseases; COPD=chronic obstructive pulmonary disease.

TABLE 2. Prevalence of multimorbidity in 10,137 pneumoconiosis patients in China, 2018–2021 (%).

Characteristics	*N*	≥1 Chronic conditions, % (95% *CI*)			
		≤44 years (*n*=1,002)	45−59 years (*n*=5,114)	≥60 years (*n*=4,021)	Total (*n*=10,137)
Total	10,137	54.3 (51.2−57.4)	58.4 (57.0−59.7)	78.6 (77.3−79.8)	66.0 (65.1−66.9)
Gender					
Male	9,875	54.5 (51.4−57.0)	58.4 (57.0−59.7)	78.0 (76.7−79.3)	65.6 (64.7−66.6)
Female	262	38.5 (12.0−64.9)	58.5 (46.5−70.4)	89.7 (85.3−94.1)	79.4 (74.5−84.3)
P for difference		0.275	0.990	<0.0001	<0.0001
Residence					
Rural	5,713	56.9 (53.3−60.5)	57.3 (55.7−59.0)	73.2 (71.1−75.4)	61.9 (60.7−63.2)
Urban	4,424	47.9 (42.2−53.7)	60.3 (58.1−62.6)	82.3 (80.8−83.9)	71.2 (69.9−72.6)
P for difference		0.010	0.038	<0.0001	<0.0001
Stages of pneumoconiosis					
Stage Ⅰ	4,540	45.0 (39.5−50.5)	53.4 (51.2−55.5)	79.2 (77.5−80.9)	65.1 (63.7−66.5)
Stage Ⅱ	2,518	52.6 (46.6−58.5)	56.6 (53.8−59.3)	79.0 (76.5−81.5)	65.0 (63.1−66.9)
Stage Ⅲ	2,134	73.9 (68.2−79.6)	67.9 (65.3−70.5)	75.5 (72.2−78.8)	70.9 (68.9−72.8)
No stage	945	48.4 (41.1−55.6)	59.6 (55.5−63.7)	79.6 (74.3−85.0)	62.0 (58.9−65.1)
P for difference		<0.0001	<0.0001	0.213	<0.0001
Smoking index					
<200	5,903	50.1 (46.4−53.9)	56.8 (55.0−58.6)	79.1 (77.4−80.8)	64.5 (63.2−65.7)
≥200	4,234	63.8 (58.4−69.2)	60.6 (58.5−62.7)	77.9 (76.0−79.8)	68.1 (66.7−69.5)
P for difference		<0.0001	0.006	0.354	<0.0001

Note: Pneumoconiosis considered with multimorbidity refers to patients who have been diagnosed by a healthcare professional with one or more of the following 13 types of diseases or conditions: pulmonary tuberculosis, lung cancer or mesohyloma, diabetes, hypertension, pulmonary heart disease, cardiovascular diseases, cerebrovascular diseases, non-TB lung infection, chronic obstructive pulmonary disease, pulmonary bullae or pneumothorax, and rheumatism.
Abbreviation: *CI*=confidence interval.

insurance while only 35.2% and 26.8% did so in collective and private enterprises, respectively (χ^2=366.263, *P*<0.001).

Figure 1 illustrates the patterns of multimorbidity, represented by various pairwise combinations of diseases or conditions, in both rural and urban settings. The most prominent combinations include four specific diseases: non-TB pulmonary infection, pulmonary heart disease, pulmonary bullae, pneumothorax, and hypertension. These were frequently observed in patients with pneumoconiosis from both urban and rural regions, albeit at higher proportions in urban patients. Moreover, the comorbidity of underweight and arthritis paired with non-TB lung infection and pulmonary heart disease were notably higher in rural patients. On the other hand, pairings of diabetes, cerebrovascular disease, obesity with hypertension, CVDs, COPD, and pulmonary infection were more commonly seen in urban patients, establishing several unique aggregate distributions.

DISCUSSION

Comorbidities and complications significantly influence the treatment, progression, and prognosis of pneumoconiosis, primarily contributing to patients' deterioration and mortality. An accurate and timely diagnosis and treatment of such comorbidities and complications is crucial to enhancing patient survival rates, their health status, life expectancy, and quality of life. As suggested by the China Expert Consensus on the Treatment of Pneumoconiosis (2018 edition), there is a need to reinforce comprehensive health management and actively carry out symptomatic treatment, management of comorbidities and complications, as well as rehabilitation treatment. Research into pneumoconiosis comorbidities outside the respiratory system has been minimal. The focus of this study is primarily on common comorbidities or complications of pneumoconiosis. This includes not only respiratory illnesses but also circulatory diseases, disorders of the immune and nutritional systems, metabolic diseases, and skeletal conditions. These collectively provide an insight into the distribution of multimorbidity in pneumoconiosis.

A study evaluating data from 126 investigations comprising approximately 15.4 million individuals across 54 countries revealed that multimorbidity prevalence heightens with an increased volume of diseases assessed. When assessing multimorbidity over 10 to 19 conditions, prevalence was disclosed to be 41.3% (*5*). However, in China, multimorbidity prevalence manifested a considerable degree of variation among elderly individuals, displaying a range from a mere few percent up to 80% (*6*). In the context of the present study, multimorbidity prevalence within pneumoconiosis patients was identified as being 66.0%, a rate that surpasses the previously mentioned rates.

Research has demonstrated a notable rise in the occurrence of lower respiratory tract infections among coal workers' pneumoconiosis (CWP) patients co-diagnosed with COPD and tuberculosis. This rise is more prominent in patients in stages II and III compared to those in stage I (*7*). Consistent with these findings, our study also identified a higher prevalence of pulmonary heart diseases, hypertension and CVDs associated with COPD and lung infections, particularly in urban populations compared to their rural counterparts. Moreover, the occurrence of cerebrovascular diseases, diabetes, and obesity was elevated among urban patients, along with complications such as COPD and non-TB lung infections. Considering the profound correlation between diseases, such as obesity, hypertension, diabetes, and cerebrovascular disorders, and lifestyle factors, it is crucial to intensify health promotion efforts aimed at dust-exposed workers and pneumoconiosis patients.

Patients with pneumoconiosis often experience severe illness or recurrent lung infections, which can lead to malnutrition and consequently impair the body's defense and immune functions. Repeated infections can exacerbate the disease. Rural pneumoconiosis patients tend to show a higher prevalence of underweight and arthritis. Furthermore, the co-occurrence of non-TB lung infections or pulmonary heart disease is more commonly found among these individuals. Therefore, strengthening nutritional interventions for rural patients is imperative. Comprehensive nutritional support can boost immunity. With the help of financial assistance, patients should be encouraged to maintain a balanced diet and increase their consumption of high-quality protein-rich foods, such as eggs, milk, and lean meats, as well as a variety of other foodstuffs.

Pneumothorax is a prevalent complication of pneumoconiosis that affects the pleura. It primarily occurs during the second and third stages of pneumoconiosis, posing a significant life-threatening risk if it is not diagnosed and treated in a timely manner. Common triggers include a severe cough and expectoration exacerbated by respiratory infection. The study reported a higher prevalence of pulmonary bullae or pneumothorax in cases complicated with non-TB lung infection and pulmonary heart disease. This occurrence was particularly higher in rural participants than in their urban counterparts. Considering that most patients primarily rely on primary medical institutions for their healthcare needs (*8*), upskilling these institutions, especially in the rural areas, on appropriate diagnostic and treatment methods could be instrumental in controlling the condition. The study further showed that the rural patients with this condition were younger, and the elderly patient population was relatively less. This observation may result from premature deaths due to limited occupational injury insurance and inadequate medical services. It necessitates further investigation. The occupational injury insurance system serves as a fundamental health protection mechanism for patients with pneumoconiosis. However, its uptake among China's migrant workers remains low. Therefore, effective measures should be adopted to facilitate the coverage of occupational injury insurance among this group. Furthermore, detailed medical security policies specifically tailored to address the different multimorbidity patterns of pneumoconiosis need to be developed and implemented.

The treatment and clinical decision-making process for multimorbidity pose significant health-related challenges to patients, medical professionals, and the broader society. Applying individual clinical practice guidelines in managing patients with multiple conditions might intensify treatment burden and potentially yield negative effects. Considering the inherent complexity, heterogeneity, and the myriad combinations of diseases in multimorbidity, existing guidelines recommend a personalized management approach (*9–10*).

In clinical settings, pneumoconiosis commonly presents as cough, expectoration, chest tightness, and asthma, with primary treatments consisting of antiasthmatics, expectorants, and antitussives. The frequent overuse of antibiotics and hormones, combined with aggressive diagnostic and therapy approaches, often results in complex multiple bacterial infections in patients with pneumoconiosis, thereby complicating the treatment process. It's also important to consider that the majority of these patients are middle-aged and elderly individuals who may be experiencing various comorbid chronic diseases, a factor which further compounds the challenge of administering multiple medications. Due to these complexities, there is a pressing need to conduct evidence-based research on therapeutic drugs related to various comorbidities and to establish appropriate technical guidelines.

The current study is not without its limitations. Initially, the primary data for eleven types of diseases or conditions was principally acquired via self-reported questioning, leading to potential inaccuracies due to information bias. This could either underestimate or overestimate the actual figures. Additionally, several common chronic ailments, including but not limited to digestive and kidney diseases, urologic and lumbar issues, and neurological and mental health conditions, were not incorporated into this research. This exclusion was based on the potential inaccuracy of self-reports, which may consequently underestimate the prevalence of multimorbidity. Furthermore, the study's representation of the complete pneumoconiosis patient population may be imperfect due to uneven participant distribution across China's districts. Hence, caution should be exercised when interpreting the findings' applicability to other patient groups. Moreover, the research is a preliminary cross-sectional analysis of pneumoconiosis multimorbidity and requires future in-depth exploration, given its intricate nature. Factors influencing pneumoconiosis multimorbidity, such as the type of pneumoconiosis, locale, education level, financial status, and physical activity levels, warrant additional analysis and investigation.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Impact of Whole Lung Lavage on Pneumoconiosis Patients — China, 2018–2022

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Summary

What is already known about this topic?

The application of whole lung lavage (WLL) for the clinical treatment of pneumoconiosis is prevalent in China. Several scholars have reported success in the treatment of early-stage pneumoconiosis. Nonetheless, the overall efficacy of WLL in the management of pneumoconiosis remains ambiguous.

What is added by this report?

The preliminary evaluation of the effects of WLL on pneumoconiosis patients was conducted using follow-up data from 2020 to 2022, after controlling for confounding factors via propensity score matching. While the study found that WLL may improve some pneumoconiosis symptoms, no significant enhancements were observed in overall health status or quality of life.

What are the implications for public health practice?

The findings of this research indicate limited efficacy of WLL in treating patients with pneumoconiosis, thereby suggesting that it should not be utilized as a standard treatment procedure for this condition.

Whole lung lavage (WLL) is a surgical procedure utilized in China to treat pneumoconiosis, despite the scholarly debate surrounding its efficacy. The National Institute for Occupational Health and Poisoning Control, part of the Chinese Center for Disease Control and Prevention (China CDC), conducted a comprehensive study on pneumoconiosis patients' health-seeking behaviors across 27 provincial-level administrative divisions (PLADs) over a three-year period, from January 2018 to December 2020. Utilizing baseline data, follow-up patient information, and WLL-related data, a retrospective cohort study was undertaken to evaluate WLL's impact and gauge the changes in pneumoconiosis-related symptoms and patient quality of life. The study, empowered by propensity score matching (PSM), contrasted 514 patients in both the control and lavage groups. The data illustrated that the patients in the lavage group displayed a marked improvement in expectoration symptoms and self-care than those in the control group. However, this study suggests that while WLL can alleviate some pneumoconiosis symptoms, it offers no significant enhancement to a patient's overall health status or quality of life.

The present study utilized data from a survey on health-seeking behaviors and a subsequent follow-up survey of pneumoconiosis patients across 27 PLADs in China. The investigation was conducted by the National Institute for Occupational Health and Poisoning Control, affiliated with China CDC (*1*).

The initial health-seeking behavior survey, undertaken from January 2018 to December 2020, involved studying 9,934 pneumoconiosis patients. Of these, 8,198 valid questionnaires were collected, resulting in a questionnaire recovery rate of 82.5%.

The research group subsequently executed a second telephone follow-up survey from 2020 to 2022. This included the 8,198 pneumoconiosis patients from the initial survey. As of November 2022, follow-up communication had been completed with 5,561 patients. However, the remaining 2,637 patients, who were still being followed up, were not included in the current study due to timing constraints.

The follow-up survey amassed a total of 4,644 valid questionnaires, yielding a questionnaire recovery rate of 83.5%. Tragically, the survey revealed that 232 pneumoconiosis patients passed away during the second follow-up.

The current study finally selected 514 cases, both from the control group (those who had not received WLL treatment prior to the first survey) and the lavage group (those who had received WLL treatment prior to the first survey). A PSM technique was used to match the baseline data from the first survey of 4,412 surviving pneumoconiosis patients with valid questionnaires; 3,322 did not receive WLL before the first survey, and 1,090 received WLL before the first survey (Figure 1).

This study utilized PSM to create control and lavage

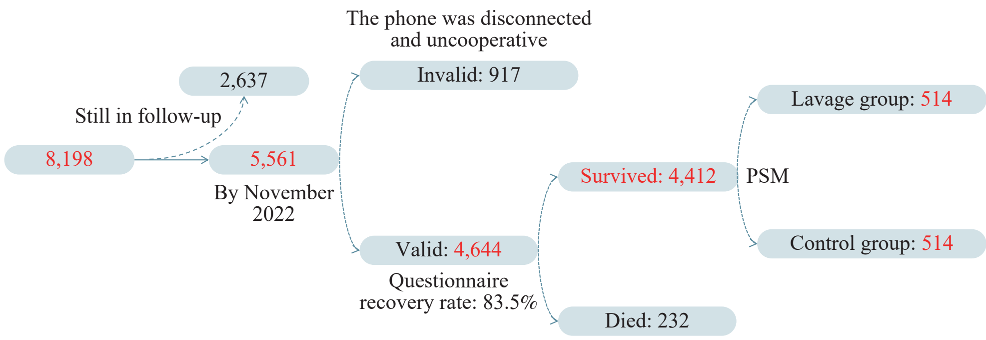

FIGURE 1. Flowchart of enrolled patients.
Abbreviation: PSM=propensity score matching.

groups from the pool of surveyed pneumoconiosis patients in each medical institution. The final control and lavage groups each included 514 patients. Factors used for matching consisted of gender, age, body mass index (BMI), patients' source, annual family income, pneumoconiosis stage and type, presence of tuberculosis, self-reported health status, medications for pneumoconiosis, oxygen therapy, and practice of breathing exercises, all of which are crucial influencers on pneumoconiosis patients' decision to undergo WLL and their overall health condition. The Nearest Neighbor Matching method was applied in a 1∶1 matching ratio with a caliper value of 0.01. The basic information of the two groups of patients is shown in Supplementary Tables S1–S2 (available in https://weekly.chinacdc.cn/). The study referenced the European EQ-5D-3L scale to describe patient quality of life. To compare pneumoconiosis-related symptoms and quality of life differences between the two groups, the *t*-test, chi-squared test or Fisher's exact probability method was implemented, while paired *t*-test and paired chi-squared test were used to assess differences between initial and follow-up surveys for both groups. All analyses used SPSS software (version 26.0, SPSS Inc, Chicago, IL, USA). The accepted statistically significant level was set at 0.05 (two-tailed)。 Ethical approval for this research was granted by the Ethics Committee of the National Institute for Occupational Health and Poison Control, China CDC (Approval No: 201720). Written informed consent was obtained from all participants.

Following PSM, a total of 514 patients were found in each of the control group and the lavage group. The average age in both groups was found to be 53.3 years, with a standard deviation of 9.7 and 8.3, respectively, a difference which was not considered statistically significant (t=−0.052, P=0.959). The average interval between the two surveys was found to be approximately 1.9 years in both groups, with a standard deviation of 0.9 and 0.8, respectively, revealing no significant statistical difference (t=0.799, P=0.424).

In the initial survey, a notable statistical difference was detected regarding expectoration symptoms between the two groups (P<0.001). The percentage of patients exhibiting no expectoration was lower in the lavage group than in the control group (11.7% *vs.* 19.8%). Conversely, the patient percentage with minimal expectoration was higher than in the control group (62.8% *vs.* 54.5%). However, in the subsequent follow-up survey, no meaningful difference in expectoration symptoms was found between the groups (P=0.606) (Table 1).

A comparative analysis of pneumoconiosis symptoms before and after the initial and follow-up surveys indicates a significant statistical variation in the severity of the identified eight symptoms across the two groups (P<0.05). We noted a reduction in the proportion of patients in the highest severity level of each symptom and conversely, observed an increased proportion of patients without the said symptoms in both groups (Supplementary Table S3, available in https://weekly.chinacdc.cn/).

The initial and subsequent surveys did not reveal any statistically significant disparities in the five elements of self-reported quality of life and health status among pneumoconiosis patients across both groups (P>0.05) (Supplementary Table S4, available in https://weekly.chinacdc.cn/).

Upon comparing the quality of life before and after initial and follow-up surveys, no statistically significant changes were observed in the self-care of pneumoconiosis patients from the control group (P=0.083). Conversely, the differences within the lavage group were statistically significant (P<0.001), exemplified by an increased proportion of patients

TABLE 1. Comparison of pneumoconiosis-related symptoms between the control group and the lavage group — China, 2018–2022 (*n*=514).

Symptoms	The first survey				Secondary follow-up survey			
	Control group *n* (%)	Lavage group *n* (%)	χ^2	*P*	Control group *n* (%)	Lavage group *n* (%)	χ^2	*P*
Cough			2.079	0.354			4.265	0.119
No	51 (9.9)	38 (7.4)			113 (22.0)	135 (26.3)		
Mild	310 (60.3)	319 (62.1)			313 (60.9)	310 (60.3)		
Moderate and severe	153 (29.8)	157 (30.5)			88 (17.1)	69 (13.4)		
Expectoration			13.959	<0.001			1.003	0.606
No	102 (19.8)	60 (11.7)			166 (32.3)	181 (35.2)		
Mild	280 (54.5)	323 (62.8)			270 (52.5)	260 (50.6)		
Moderate and severe	132 (25.7)	131 (25.5)			78 (15.2)	73 (14.2)		
Chest tightness			2.661	0.264			0.255	0.880
No	64 (12.5)	48 (9.3)			164 (31.9)	157 (30.5)		
Mild	295 (57.4)	310 (60.3)			258 (50.2)	261 (50.8)		
Moderate and severe	155 (30.2)	156 (30.4)			92 (17.9)	96 (18.7)		
Chest pain			5.736	0.057			4.578	0.101
No	199 (38.7)	170 (33.1)			336 (65.4)	329 (64.0)		
Mild	197 (38.3)	234 (45.5)			118 (23.0)	141 (27.4)		
Moderate and severe	118 (23.0)	110 (21.4)			60 (11.7)	44 (8.6)		
Dyspnea			0.439	0.803			4.370	0.112
No	131 (25.5)	129 (25.1)			176 (34.2)	208 (40.5)		
Mild	222 (43.2)	232 (45.1)			230 (44.7)	212 (41.2)		
Moderate and severe	161 (31.3)	153 (29.8)			108 (21.0)	94 (18.3)		
Hemoptysis			0.957	0.328			0.324	0.569
No	460 (89.5)	450 (87.5)			486 (94.6)	490 (95.3)		
Yes	54 (10.5)	64 (12.5)			28 (5.4)	24 (4.7)		

Note: The categories for cough severity include mild (intermittent cough not affecting daily activities), moderate, and severe (frequent or violent cough disrupting daily activities and rest). Expectoration is categorized as mild (sputum volume of 10–50 mL during day and night), moderate, and severe (sputum volume exceeding 50 mL during day and night). Chest tightness ranges from mild (intermittent discomfort) to moderate and severe (persistent tightness restricting breathing). Chest pain and dyspnea are classified as mild (occurs during physical activities), moderate, and severe (manifests during daily activities and rest).

reported to have "no problem" in terms of self-care (Table 2). The average variation in self-reported health status between the two surveys was 9.6±16.7 in the control group and 10.3±18.5 in the lavage group. This difference, however, did not reach statistical significance (t=−0.678, P=0.498).

DISCUSSION

This research involved the selection of lavage and control groups through PSM for the purpose of comparing differences in pneumoconiosis-related symptoms and quality of life. These two groups of pneumoconiosis patients exhibited similar baseline characteristics, allowing for a preliminary evaluation of the effects of WLL on these patients. The intent was to stimulate thought and inform future empirical studies focusing on the long-term efficacy of WLL for pneumoconiosis patients. The Consensus of Chinese Experts on Pneumoconiosis Treatment (2018) purports that while WLL significantly improves clinical symptoms in the short term, current evidence does not substantiate a marked therapeutic impact on lung function and pulmonary fibrosis. As WLL is an invasive treatment, it is currently not upheld as a standard treatment for pneumoconiosis (*2*). The results from the study's initial survey are presented herewith.

The survey data revealed a 17.8% prevalence rate for WLL use among participants, signaling its considerable utilization as a nonstandard treatment technique. Earlier studies typically gauged the efficacy of WLL via self-regulated pre-and post-surgical evaluations, concluding that WLL might have a positive impact on alleviating short-term pneumoconiosis symptoms

TABLE 2. Comparative analysis of quality-of-life differences between the two patient groups across two surveys — China, 2018–2022 (*n*=514).

Quality of life	Group	Level	The first survey	Secondary follow-up survey	*P*
Mobility, *n* (%)	Control group	No problems	302 (58.8)	365 (71.0)	<0.001
		Moderate problems	206 (40.1)	140 (27.2)	
		Extreme problems	6 (1.2)	9 (1.8)	
	Lavage group	No problems	322 (62.6)	388 (75.5)	<0.001
		Moderate problems	189 (36.8)	123 (23.9)	
		Extreme problems	3 (0.6)	3 (0.6)	
Self-care, *n* (%)	Control group	No problems	405 (78.8)	426 (82.9)	0.083
		Moderate problems	106 (20.6)	82 (16.0)	
		Extreme problems	3 (0.6)	6 (1.2)	
	Lavage group	No problems	386 (75.1)	442 (86.0)	<0.001
		Moderate problems	125 (24.3)	70 (13.6)	
		Extreme problems	3 (0.6)	2 (0.4)	
Usual activities, *n* (%)	Control group	No problems	251 (48.8)	317 (61.7)	<0.001
		Moderate problems	232 (45.1)	173 (33.7)	
		Extreme problems	31 (6.0)	24 (4.7)	
	Lavage group	No problems	264 (51.4)	349 (67.9)	<0.001
		Moderate problems	221 (43.0)	143 (27.8)	
		Extreme problems	29 (5.6)	22 (4.3)	
Pain/discomfort, *n* (%)	Control group	No problems	118 (23.0)	233 (45.3)	<0.001
		Moderate problems	352 (68.5)	255 (49.6)	
		Extreme problems	44 (8.6)	26 (5.1)	
	Lavage group	No problems	147 (28.6)	234 (45.5)	<0.001
		Moderate problems	330 (64.2)	268 (52.1)	
		Extreme problems	37 (7.2)	12 (2.3)	
Anxiety/depression, *n* (%)	Control group	No problems	219 (42.6)	292 (56.8)	<0.001
		Moderate problems	214 (41.6)	193 (37.5)	
		Extreme problems	81 (15.8)	29 (5.6)	
	Lavage group	No problems	217 (42.2)	313 (60.9)	<0.001
		Moderate problems	210 (40.9)	176 (34.2)	
		Extreme problems	87 (16.9)	25 (4.9)	
Health status self-score ($\bar{x} \pm s$)	Control group	/	59.1±17.3	68.7±15.8	<0.001
	Lavage group	/	59.0±17.2	69.3±16.3	<0.001

Note: "/" means health status self-score did not differentiate levels.

(*3–4*). Nonetheless, the present research suggests that both patient groups exhibited improved health status. This improvement may be attributable to recent enhancements in national support policies for individuals with pneumoconiosis and the survivor effect (*5–6*). Therefore, when assessing WLL's impact on pneumoconiosis patients, mere self-comparisons before and after the treatment may not accurately reflect the reality of their condition.

In studies involving control groups, the influential confounding factors affecting the health condition of patients with pneumoconiosis were either not adjusted or only a few were accounted for. Despite this, these studies generally concluded that WLL had short-term beneficial effects on the patients' health (*7–8*). Before adjusting for confounders, WLL was linked to improvements in numerous respiratory symptoms and quality of life. WLL typically targets patients with relatively mild conditions that are more likely to tolerate the procedure, introducing potential selection bias in the outcomes (*9–10*). In our study, however, we employed a large sample size and controlled for the principal factors that may influence both the patients' decision to undergo WLL and their health conditions.

Using PSM, we equalized the baseline characteristics of both patient groups. This approach allowed us to evaluate the effects of WLL on pneumoconiosis patients more accurately.

The findings of the study indicate that WLL yielded a moderate effect on alleviating expectoration symptoms when juxtaposed with the control. However, there was no significant improvement in symptoms such as coughing, chest tightness, chest pain, and dyspnea in comparison to the control. This finding is consistent with the underlying mechanism that WLL works by cleansing the respiratory tract and pulmonary sputum of patients with pneumoconiosis, thus aiding those with substantial sputum stasis that is challenging to expectorate. In terms of quality of life assessment, WLL only significantly enhanced the self-care abilities of the pneumoconiosis patients contrasted with the control. However, no notable improvements were evident in the remaining four aspects and the overall health status compared with the control group.

This study indicates that WLL has a modest impact on pneumoconiosis patients and should not be considered a standard treatment. However, this research primarily assessed the influence of whole lung lavage based on patients' subjective experiences of symptoms and quality of life, without incorporating objective measurements, such as chest imaging and lung function. This omission represents a limitation. Future research on the use of WLL in pneumoconiosis treatment should endeavor to provide stronger evidence by choosing indicators that can objectively assess disease severity, progression, and patient quality of life. It should also account for potential confounding factors, such as the quality of WLL operation, patients' dust exposure history, medication therapies, and other treatment modalities. A systematic evaluation of WLL's long-term efficacy using standardized methodologies is recommended to fairly assess WLL's cost-effectiveness for pneumoconiosis patients.

The current study inadequately addresses the potential influence of varied WLL procedure quality across different medical institutions on patient outcomes. Furthermore, the research does not provide detailed information regarding the dust exposure history and work type of participants, likely influencing the assessed impact of WLL on pneumoconiosis patients. Additionally, potential disparities in data collection methods could introduce bias as the initial questionnaire involved face-to-face interviews, whereas the secondary follow-up predominantly used telephone interviews. Consequently, the potential for information bias is apparent in the comparison of the two surveys' results.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. Comparison of demographic and sociological characteristics between control and lavage groups in pneumoconiosis patients (*n*=514).

Demographic and sociological characteristics	Control group, *n* (%)	Lavage group, *n* (%)	χ^2	*P*
Sex			0.609	0.435
Male	508 (98.8)	505 (98.2)		
Female	6 (1.2)	9 (1.8)		
Age, years			5.320	0.150
≤40	41 (8.0)	26 (5.1)		
41–50	169 (32.9)	166 (32.3)		
51–60	194 (37.7)	220 (42.8)		
>60	110 (21.4)	102 (19.8)		
BMI			0.888	0.828
<18.5	25 (4.9)	23 (4.5)		
18.5–23.9	248 (48.2)	239 (46.5)		
24–27.9	193 (37.5)	196 (38.1)		
≥28	48 (9.3)	56 (10.9)		
Marital status			3.772	0.438
Married	482 (93.8)	485 (94.4)		
Divorced	9 (1.8)	8 (1.6)		
Widowed	13 (2.5)	14 (2.7)		
Single	10 (1.9)	5 (1.0)		
Others	0 (0.0)	2 (0.4)		
Educational level			0.995	0.910
Illiterate or semiliterate	23 (4.5)	22 (4.3)		
Primary school	182 (35.4)	190 (37.0)		
Middle school	230 (44.7)	223 (43.4)		
High school or junior college or above	75 (14.6)	77 (15.0)		
Others	4 (0.8)	2 (0.4)		
District			/	1.000*
Eastern region	246 (47.9)	246 (47.9)		
Central region	98 (19.1)	98 (19.1)		
Western region	168 (32.7)	168 (32.7)		
Northeastern region	2 (0.4)	2 (0.4)		
Source of cases			5.780	0.123
Household investigation	46 (8.9)	59 (11.5)		
Outpatient	174 (33.9)	146 (28.4)		
Hospitalized	243 (47.3)	266 (51.8)		
Occupational health examination	51 (9.9)	43 (8.4)		

Note: "/" means Fisher exact probability method does not give chi-square values.
Abbreviation: BMI=body mass index.
* Fisher exact probability method was used for statistics.

SUPPLEMENTARY TABLE S2. Comparison of pneumoconiosis and complications between the control group and the lavage group (n=514).

Pneumoconiosis and complications	Control group, *n* (%)	Lavage group, *n* (%)	χ^2	*P*
Stage of pneumoconiosis			6.780	0.079
Stage I	247 (48.1)	218 (42.4)		
Stage II	112 (21.8)	146 (28.4)		
Stage III	115 (22.4)	116 (22.6)		
Unstaged clinical diagnosis	40 (7.8)	34 (6.6)		
Type of pneumoconiosis			0.017	0.992
Silicosis	238 (46.3)	238 (46.3)		
Coal worker's pneumoconiosis	242 (47.1)	243 (47.3)		
Others	34 (6.6)	33 (6.4)		
Complications				
PTB			0.275	0.600
No	481 (93.6)	485 (94.4)		
Yes	33 (6.4)	29 (5.6)		
Pulmonary heart disease			0.157	0.692
No	485 (94.4)	482 (93.8)		
Yes	29 (5.6)	32 (6.2)		
Pulmonary bullae or pneumothorax			0.285	0.594
No	463 (90.1)	468 (91.1)		
Yes	51 (9.9)	46 (8.9)		
Lung cancer or mesothelioma			/	1.000*
No	513 (99.8)	513 (99.8)		
Yes	1 (0.2)	1 (0.2)		

Note: "/" means Fisher exact probability method does not give chi-square values.
Abbreviation: PTB=pulmonary tuberculosis.
* Fisher exact probability method was used for statistics.

SUPPLEMENTARY TABLE S3. Comparison of pneumoconiosis-related symptoms between patients in two survey groups (n=514).

Symptoms	Group	Level	The first survey *n* (%)	Secondary follow-up survey *n* (%)	*P*
Cough	Control group	No	51 (9.9)	113 (22.0)	<0.001
		Mild	310 (60.3)	313 (60.9)	
		Moderate and severe	153 (29.8)	88 (17.1)	
	Lavage group	No	38 (7.4)	135 (26.3)	<0.001
		Mild	319 (62.1)	310 (60.3)	
		Moderate and severe	157 (30.5)	69 (13.4)	
Expectoration	Control group	No	102 (19.8)	166 (32.3)	<0.001
		Mild	280 (54.5)	270 (52.5)	
		Moderate and severe	132 (25.7)	78 (15.2)	
	Lavage group	No	60 (11.7)	181 (35.2)	<0.001
		Mild	323 (62.8)	260 (50.6)	
		Moderate and severe	131 (25.5)	73 (14.2)	
Chest tightness	Control group	No	64 (12.5)	164 (31.9)	<0.001
		Mild	295 (57.4)	258 (50.2)	
		Moderate and severe	155 (30.2)	92 (17.9)	
	Lavage group	No	48 (9.3)	157 (30.5)	<0.001
		Mild	310 (60.3)	261 (50.8)	
		Moderate and severe	156 (30.4)	96 (18.7)	
Chest pain	Control group	No	199 (38.7)	336 (65.4)	<0.001
		Mild	197 (38.3)	118 (23.0)	
		Moderate and severe	118 (23.0)	60 (11.7)	
	Lavage group	No	170 (33.1)	329 (64.0)	<0.001
		Mild	234 (45.5)	141 (27.4)	
		Moderate and severe	110 (21.4)	44 (8.6)	
Dyspnea	Control group	No	131 (25.5)	176 (34.2)	<0.001
		Mild	222 (43.2)	230 (44.7)	
		Moderate and severe	161 (31.3)	108 (21.0)	
	Lavage group	No	129 (25.1)	208 (40.5)	<0.001
		Mild	232 (45.1)	212 (41.2)	
		Moderate and severe	153 (29.8)	94 (18.3)	
Hemoptysis	Control group	No	460 (89.5)	486 (94.6)	0.002
		Yes	54 (10.5)	28 (5.4)	
	Lavage group	No	450 (87.5)	490 (95.3)	<0.001
		Yes	64 (12.5)	24 (4.7)	

SUPPLEMENTARY TABLE S4. Comparison of quality of life between the control group and the lavage group (*n*=514).

Quality of life	The first survey				Secondary follow-up survey			
	Control group	Lavage group	χ^2/t	*P*	Control group	Lavage group	χ^2/t	*P*
Mobility, *n* (%)			/	0.325*			4.801	0.091
No problems	302 (58.8)	322 (62.6)			365 (70.1)	388 (75.5)		
Moderate problems	206 (40.1)	189 (36.8)			140 (27.2)	123 (23.9)		
Extreme problems	6 (1.2)	3 (0.6)			9 (1.8)	3 (0.6)		
Self-care, *n* (%)			/	0.375*			/	0.198*
No problems	405 (78.8)	386 (75.1)			426 (82.9)	442 (86.0)		
Moderate problems	106 (20.6)	125 (24.3)			82 (16.0)	70 (13.6)		
Extreme problems	3 (0.6)	3 (0.6)			6 (1.2)	2 (0.4)		
Usual activities, *n* (%)			0.662	0.718			4.473	0.107
No problems	251 (48.8)	264 (51.4)			317 (61.7)	349 (67.9)		
Moderate problems	232 (45.1)	221 (43.0)			173 (33.7)	143 (27.8)		
Extreme problems	31 (6.0)	29 (5.6)			24 (4.7)	22 (4.3)		
Pain/discomfort, *n* (%)			4.488	0.106			5.483	0.063
No problems	118 (23.0)	147 (28.6)			233 (45.3)	234 (45.5)		
Moderate problems	352 (68.5)	330 (64.2)			255 (49.6)	268 (52.1)		
Extreme problems	44 (8.6)	37 (7.2)			26 (5.1)	12 (2.3)		
Anxiety/depression, *n* (%)			0.261	0.878			1.808	0.409
No problems	219 (42.6)	217 (42.2)			292 (56.8)	313 (60.9)		
Moderate problems	214 (41.6)	210 (40.9)			193 (37.5)	176 (34.2)		
Extreme problems	81 (15.8)	87 (16.9)			29 (5.6)	25 (4.9)		
Health status self-score ($\bar{x} \pm s$)	(59.11±17.3)	(59.0±17.2)	0.092	0.927	(68.7±15.8)	(69.3±16.3)	−0.644	0.520

Note: "/" means Fisher exact probability method does not give chi-square values.
Abbreviation: PTB=pulmonary tuberculosis.
* Fisher exact probability method was used for statistics.

Methods and Applications

An Analysis of Targeted Serum Lipidomics in Patients with Pneumoconiosis — China, 2022

Wenrong Wang[1]; Fangda Peng[2,3]; Chunguang Ding[2,3]; Tao Li[1]; Huanqiang Wang[1,#]

ABSTRACT

Introduction: Pneumoconiosis emerges as the most critical and prevalent occupational disease in China at present, according to research. Studies indicate that pneumoconiosis may indeed impact the body's phospholipid metabolism.

Methods: In this study, serum samples were taken from 46 paired participants, which included patients with pneumoconiosis and dust-exposed workers. We employed ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) technology in targeted lipidomics to investigate serum target phospholipids. Initially, a pilot study was conducted with a selection of 24 pneumoconiosis patients and 24 dust-exposed workers, using both univariate and multivariate statistical analyses to preliminarily identify significant differences in phospholipids. Subsequent to this, the remaining subjects were engaged in a validation study, wherein receiver operating characteristic (ROC) analysis was performed to further substantiate the screening potency of potential lipid biomarkers for pneumoconiosis.

Results: The pilot study revealed significantly reduced serum levels of 16∶0 lysophosphatidylcholines (Lyso PC), 18∶0–18∶1 phosphatidylglycerol (PG), 18∶0–18∶1 phosphatidylethanolamine (PE), 18∶0 PE, and 18∶1 lysophosphatidylethanolamine(Lyso PE) in the case group in comparison to the control group. Additionally, 18∶0 PE, 18∶0–18∶1 PE, and 18∶1 Lyso PE emerged as significant phospholipids with superior diagnostic values [area under the curve (AUC)>0.7]. A diagnostic model was established, built on 16∶0 PC and 18∶0 PE (AUC>0.8). In the ROC analyses of validation studies, the 18∶0–18∶1 PE and this diagnostic model demonstrated excellent screening efficiency (AUC>0.7).

Discussion: A significant divergence in phospholipid metabolism has been observed between pneumoconiosis patients and dust-exposed workers. The 18∶0–18∶1 PE present in serum could potentially function as a lipid biomarker for pneumoconiosis. Additionally, diagnostic models were developed relying on 16∶0 PC and 18∶0 PE, proving to have superior screening efficiency.

Pneumoconiosis, a lung disease primarily characterized by pulmonary fibrosis, occurs due to exposure to dust (*1*). Phospholipids are pivotal to numerous biological systems, contributing to the formation of cellular lipid bilayers and moderating a host of biological pathways. This moderation is accomplished through the release of signaling molecules such as lysophospholipids, platelet-activating factors, eicosanoids, and diacylglycerides. These molecules participate in the modulation of various processes, including cell proliferation, inflammation, oxidative stress, and neurotransmission, among others (*2*).

Lipidomics is a potentially useful technique for exploring lipid metabolism and metabolite-related biomarkers in complex respiratory diseases (*1*). Rindlisbacher et al. discovered lysophosphatidyl-cholines (Lyso PC), via ultra-high-performance liquid chromatography paired with high-resolution mass spectrometry (UHPLC-HRMS), that could serve as a potential biomarker in the serum of idiopathic pulmonary fibrosis (IPF) patients (*3*). Using a similar lipidomics analysis, Montesi et al. identified that 22∶4 lysophosphatidic acid (Lyso PA) was significantly elevated in the plasma and exhaled air condensate (EBC) of IPF patients, suggesting its potential as a biomarker for pulmonary fibrosis progression (*4*). In another study, Yan et al. pinpointed six potential biomarkers capable of distinguishing IPF patients from control subjects following untargeted lipidomics analysis (*5*). Peng et al., utilizing an analogous untargeted lipidomics technique on the serum of coal worker' pneumoconiosis (CWP) patients, found differential metabolites in those exposed to coal dust and CWP patients, primarily related to glycerophospholipid metabolism (*6*). Further research has suggested a close relationship between phospholipid metabolism and the inflammatory process in pulmonary fibrosis (*7*).

Numerous targeted lipidomic studies suggest that pneumoconiosis could potentially alter the body's phospholipid metabolism. Dysregulated phospholipids may engage in the pathogenesis of these diseases and could be significant biomarkers. In this study, we employed ultra-high-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) for a targeted lipidomic analysis of the serum phospholipids from pneumoconiosis patients. The aim is to pave the way for new insights into potential lipid biomarkers for pneumoconiosis.

METHODS

Chemicals and Materials

Phospholipid standards with a purity greater than 99.0% were obtained from Sigma-Aldrich (St. Louis, MO, USA). MS grade methanol and ammonium formate were sourced from Thermo Fisher (Houston, TX, USA), while analytical grade dichloromethane was procured from Tong Guang Fine Chemicals (Beijing). Butylated hydroxytoluene (BHT) was acquired from Adamas-Beta (Shanghai). Ultrapure water was used throughout the entire experiment. The preparation of the corresponding phospholipid standard, internal standard (IS) solution, and working curve were performed as dictated by the experiment requirements (*8*).

Research Study Design and Sampling Methodology

The current study encompassed a total of 46 male pneumoconiosis patients and 46 male workers with exposure to dust but exhibiting no disease symptoms. Notably, 24 pairs of pneumoconiosis patients and dust-exposed workers were meticulously matched based on age and body mass index (BMI) propensity scores for inclusion in the initial pilot study. The rest of the subjects were included in the validation study. Venous blood samples were collected from all participating subjects using non-additive vessels. The serum was then separated through centrifugation at a speed of 1,664 x*g* for a duration of 10 minutes and subsequently stored at −80 ℃. This research was approved by both the Ethics Committee of the National Institute of Occupational Health and Poison Control of the Chinese Center for Disease Control and Prevention, China [No. 201721], and the Ethics Committee of Integrated Chinese and Western Medicine, Hubei Provincial Hospital, China [No. 2020011]. All participants signed written informed consent and gave permission for their serum samples to be used in this study.

Methodologies for the Preparation of Samples

A sample of 100 μL of serum was taken and added to a 1.5 mL centrifuge tube, placed into 10 μL mixed IS application solution, and placed into 890 μL CH_3OH/CH_2CL_2 (2∶1, v/v) containing 0.1%BHT. Subsequently, the entire samples were homogenized by vortexing for 5 minutes and laid still in a refrigerator at 4 ℃ for 15 minutes. The sample was centrifuged at 14,010 x*g* for 20 min at 4 ℃. Finally, the supernatant was quantitatively transferred to a 1.5 mL injection vial for UPLC-MS/MS analysis.

UPLC-MS/MS Analysis

An ACQUITY UPLC system (Waters Corp., Milford, MA, USA) equipped with an ACQUITY UPLC BEH shield RP18 column (1.7 μm, 2.1 mm × 100 mm; Waters Corp., USA) was utilized to perform liquid chromatography. The mobile phase was composed of a methanol/water mixture (5∶95, v/v), which included 10 mmol/L of ammonium formate (Solvent A) and methanol (Solvent B). The gradient schedule was set at a flow rate of 0.4 mL/min and followed the following sequence: for the initial minute, it contained 60% of Solvent B; from 1 to 1.5 minutes, it gradually increased from 60% to 100% of Solvent B; from 1.5 to 10 minutes, it maintained 100% of Solvent B; from 10 to 10.1 minutes, it decreased quickly from 100% to 60% of Solvent B; and from 10.1 to 12 minutes, it contained 60% of Solvent B. The designated injection volume was 5 μL. During analysis, all samples were maintained at 4 ℃ and the column temperature was held at 50 ℃.

Mass spectrometry was executed employing the TQ-S Micro system (Waters Corp., Milford, MA, USA), with the electrospray ionization (ESI) source functioning in positive and negative ion modes. Lipids such as phosphatidylserine (PS), lysophosphatidylserine (Lyso PS), phosphatidylethanolamine (PE), Lyso PE, phosphatidylglycerol (PG), phosphatidylinositol (PI) were analyzed under positive ion mode (ESI+), whereas phosphatidylcholine (PC), Lyso PC, lysophosphatidic acid (Lyso PA) were assessed under the negative ion mode (ESI−). Targeted lipidomics were explored utilizing multiple reaction monitoring (MRM) modes. Further instrumental configurations were as follows: ion source temperature was set at 150 ℃; desolvation gas temperature at 350 ℃; desolvation gas flow rate, 1,000 L/h; and a capillary voltage of 4 kV for both positive and negative ions. Detailed parameters for the MRM mass spectrometry analysis are provided in Supplementary Table S1 (available in https://weekly.chinacdc.cn/).

The data collection and analysis of UPLC-MS/MS mass spectrometry was conducted using Masslynx 4.1 (Waters Corp., Milford, MA, USA), supplemented by manual peak integration and calibration checks to assure the qualitative and quantitative precision of each compound analyzed. To enhance data analysis, quantitative data underwent preprocessing — substances with less than an 85% detection rate were omitted and half of the detection limit was utilized to simulate and fill missing values.

Statistical Evaluation

The Student's *t*-test and Rank-sum test were employed to detect substantial differences in phospholipids between the two groups. A combination of principal component analysis (PCA) and orthogonal partial least squares-discriminant analysis (OPLS-DA) was executed, and variable importance of projection (VIP) values were subsequently calculated to isolate differential phospholipids. Phospholipids of significant difference were identified, based on the standard of VIP>1.0 and $P<0.05$. Additionally, binary logistic classification was utilized to construct a suitable diagnostic model. The receiver operator characteristic curve (ROC) analysis was used to identify potential biomarkers.

The multivariate statistical analysis was conducted using SIMCA software (version 14.1; Umetrics, Scania, Sweden), while the univariate statistical analysis was executed through SPSS software (version 26.0; SPSS Inc, Chicago, IL, USA). A *P*-value of less than 0.05 was deemed statistically significant. Furthermore, data visualization was facilitated by GraphPad Prism software (version 8.0.2; CA, USA).

RESULTS

Subject

Table 1 outlines the characteristics of both the pilot and validation study subjects, all of whom were male. In the pilot study, the case and control groups had mean ages of 43.42 and 43.08 years respectively, and mean BMI (kg/m^2) of 22.04 and 21.82 respectively. No statistically significant variances in age, BMI, or smoking status were observed between these two groups. Notably, the case group comprised of 18 silicosis and 6 CWP patients. This included 5 instances of stage I pneumoconiosis and 19 of stage III.

Regarding the validation study subjects, the case and the control groups reported contrasting mean ages, at 53.23 and 33.41 years respectively, and in their mean BMIs (kg/m^2) of 21.08 and 24.66 respectively, establishing statistically substantial differences in both age and BMI. However, the smoking status between the two groups showed no significant statistical discrepancy. The case group consisted of 16 silicosis patients, 6 CWP patients, and this included 1 case of stage I pneumoconiosis, 1 case of stage II, and 20 cases of stage III pneumoconiosis.

Univariate Statistical Analysis in the Pilot Study

The study performed quantitative analysis of 22 phospholipids present in the serum of 46 pneumoconiosis patients and 46 dust-exposed workers using UPLC-MS/MS methodology. Of these, 16 phospholipids were detected. The initial examination (Figure 1A–E) revealed substantial reductions in serum levels of 16:0 Lyso PC, 18:0–18:1 PG, 18:0–18:1 PE, 18:0 PE, and 18:1 Lyso PE within the case group compared to the control group; these reductions were statistically significant.

TABLE 1. Characteristics of the study subjects.

Demographic characteristics	Pilot study				Validation study			
	Cases (*n*=24)	Controls (*n*=24)	t/χ^2 value	*P*-value	Cases (*n*=22)	Controls (*n*=22)	t/χ^2 value	*P*-value
Male (*n*)	24	24			22	22		
Age (years)	43.42±8.42	43.08±8.21	0.139	0.890	53.23±6.13	33.41±3.95	12.756	0.000
Smokers (%)	54.17	54.17	0.000	1.000	63.63	63.63	0.000	1.000
BMI (kg/m^2)	22.04±2.42	21.82±2.45	0.325	0.747	21.08±2.28	24.66±2.53	−4.937	0.000

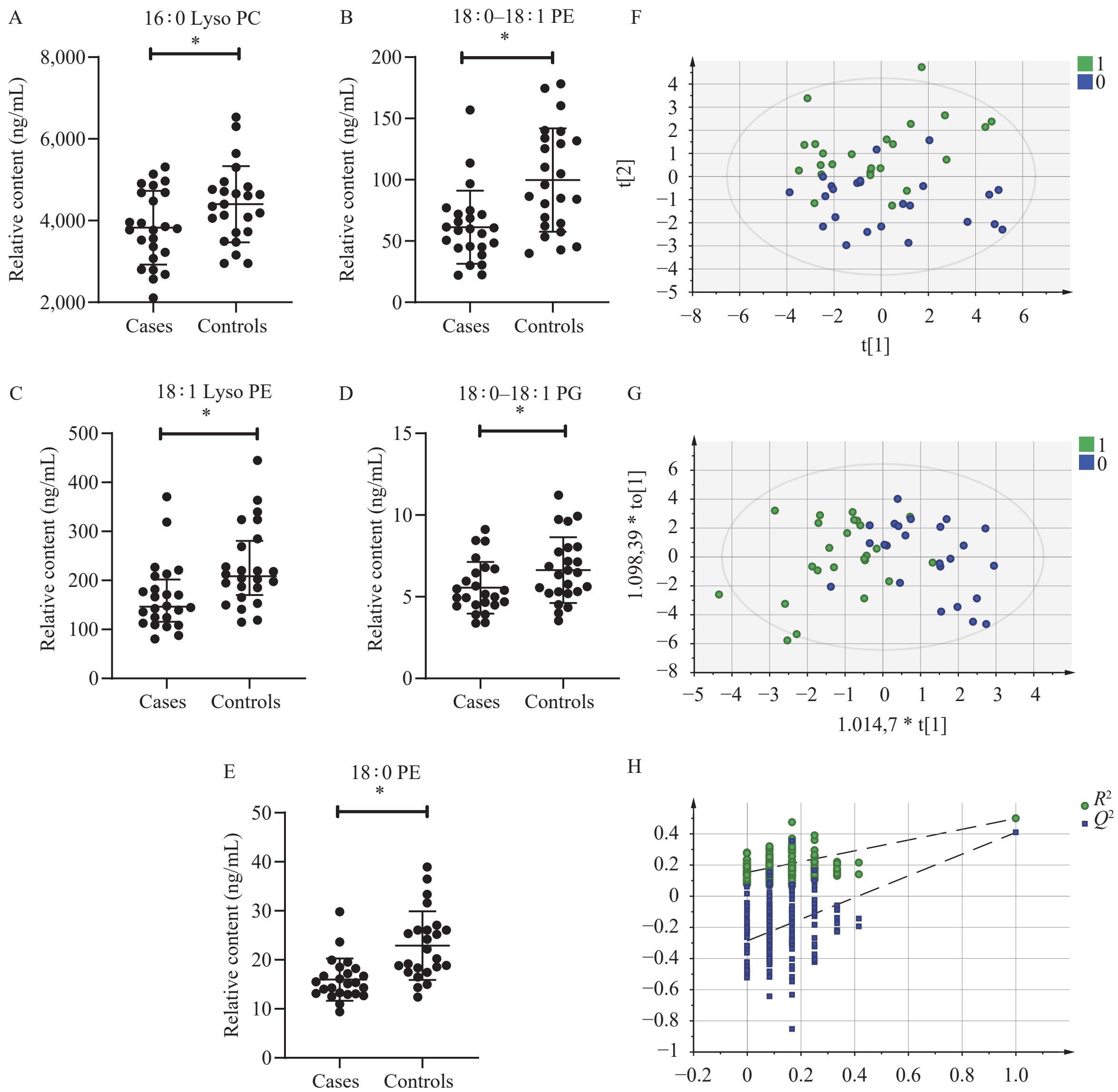


FIGURE 1. The univariate and multivariate analysis results between two groups. (A–E) The univariate statistical analysis results. (F) The mode of PCA between the two groups. (G) The mode of OPLS-DA between the two groups. (H) The permutation tests with 200 response sorting for the OPLS-DA model.

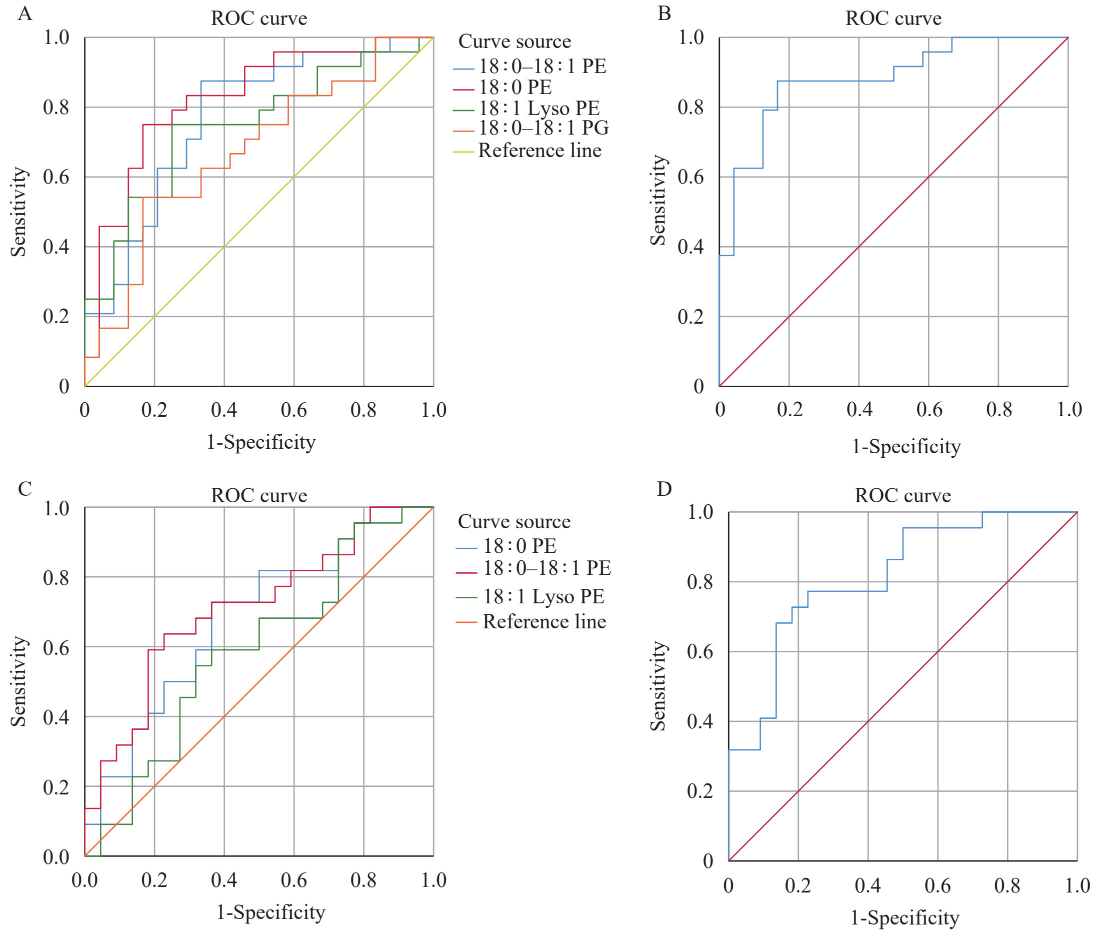
Notes: In panels A–E, the single dimensional statistical analysis results: Six differential PLs between the two groups. In panel F, R^2X=0.655, Q^2=0.197. "1" denotes the case group; "2" denotes the control group. In panel G, R^2X=0.506, R^2Y=0.499, Q^2Y=0.409. "1" denotes the case group; "2" denotes the control group. In panel H, R^2=(0.0, 0.164), Q^2=(0.0, −0.269).

Abbreviation: Lyso PC=lysophosphatidylcholines; Lyso PE=lysophosphatidylethanolamine; PE=phosphatidylethanolamine; PG=phosphatidylglycerol.

* P<0.05.

Multivariate Statistical Analysis in the Pilot Study

The PCA highlighted a clear differentiation in serum phospholipids between the two groups, though some overlap was observed (Figure 1F). The OPLS-DA is a supervised pattern recognition approach. This analysis facilitated a distinct separation trend in serum phospholipids between the two groups, further emphasizing substantial differences in serum phospholipid metabolism profiles (Figure 1G). Permutation tests with 200 response permutations confirmed the robustness of the OPLS-DA model (Figure 1H). Notably, the VIP of 18∶0 PE, 18∶0–18∶1 PE, 18∶1 Lyso PE, 18∶0–18∶1 PG, 16∶0 PC, 16∶0–18∶1 PC, 18∶0 PC, and 18∶0–18∶1 PC all exceeded 1.



E

	Compound	AUC	95% *CI*	Sensitivity	Specificity	*P*-value
Pilot study	Diagnostic model	0.882	0.785–0.979	88%	83%	0.000
	18∶0 PE	0.825	0.704–0.945	75%	83%	0.000
	18∶0–18∶1 PE	0.771	0.636–0.906	79%	67%	0.001
	18∶1 Lyso PE	0.747	0.606–0.887	75%	71%	0.003
	18∶0–18∶1 PG	0.672	0.518–0.826	54%	83%	0.041
Validation study	Diagnostic model	0.816	0.681–0.941	68%	86%	0.000
	18∶0–18∶1 PE	0.711	0.557–0.865	64%	77%	0.017
	18∶0 PE	0.684	0.526–0.842	73%	64%	0.037
	18∶1 Lyso PE	0.589	0.418–0.760	55%	68%	0.313

FIGURE 2. The ROC curve analysis results for screening and validation of potential lipid biomarkers for pneumoconiosis. (A) ROC curve for significantly different phospholipids in the pilot study. (B) ROC curve for the diagnostic model in the pilot study. (C) ROC curve for 18∶0–18∶1 PE, 18∶0 PE, and 18∶1 Lyso PE in the validation study. (D) ROC curve for the diagnostic model in the validation study. (E) Results of ROC curve analysis.

Abbreviation: Lyso PE=lysophosphatidylethanolamine; PE=phosphatidylethanolamine; PG=phosphatidylglycerol; ROC=receiver operating characteristic; AUC=area under the curve.

Screening and Validation of Potential Lipid Biomarkers for Ppneumoconiosis

In the preliminary study, using the selection criteria of *P*<0.05 and VIP>1, four distinct phospholipids were identified: 18∶0 PE, 18∶0–18∶1 PE, 18∶1 Lyso PE, and 18∶0–18∶1 PG. Using pneumoconiosis patients as the dependent variable (where 0=dust-exposed workers, 1=pneumoconiosis patients) and important phospholipids with *P*<0.05 and VIP>1 (including 16∶0 Lyso PC, 16∶0 PC, 16∶0–18∶1 PC, 18∶0–18∶1 PC, 18∶0 PC, 18∶0 PE, 18∶0–18∶1 PE, 18∶1 Lyso PE, 18∶0 PA, and 18∶0–18∶1 PG) as independent variables, a binary logistic regression analysis was conducted. The resulting diagnostic model equation was $Y=1.533+0.010X_1-0.304X_2$, where X_1 signifies the concentration of 16∶0 PC and X_2 refers to the concentration of 18∶0 PE. Subsequently, an ROC curve analysis of the four distinct phospholipids and the diagnostic model was conducted to investigate their potential efficacy as lipid biomarkers. Notably, the area under the curve (AUC) of 18∶0 PE, 18∶0–18∶1 PE, and 18∶1 Lyso PE exceeded 0.7, indicating a substantial diagnostic value for pneumoconiosis. A diagnostic model with an AUC exceeding 0.8 suggested an enhanced diagnostic performance (Figure 2A, B, E).

In the preliminary study, phospholipids and diagnostic models with AUC>0.7 were filtered, and their efficiency as potential lipid biomarkers was duly verified in the validation study. Our findings suggest that 18∶0 PE and 18∶1 Lyso PE exhibited an AUC<0.7, indicating a deficient ability to distinguish pneumoconiosis patients among healthy populations exposed to dust. Conversely, 18∶0–18∶1 PE and diagnostic model, which showed AUC>0.7, demonstrated substantial screening efficiency in the validation studies. These factors, therefore, may serve as potential lipid biomarkers in diagnosing pneumoconiosis (Figure 2C–E).

DISCUSSION

This study utilized a targeted lipidomics analysis to investigate the serum of patients with pneumoconiosis. The findings highlighted significant differences in phospholipid metabolism when compared to healthy workers exposed to dust. Specifically, variances were identified in the expression levels of 18∶0 PE, 18∶0–18∶1 PE, and 18∶1 Lyso PE between the two groups. Furthermore, diagnostic models, dependent upon 16∶0 PC and 18∶0 PE, were developed and exhibited exceptional screening efficiency. The follow-up validation study confirmed that 18∶0–18∶1 PE and the diagnostic model may serve as potential lipid biomarkers for pneumoconiosis.

Lyso PC significantly contributes to the emergence and progression of inflammation (*6*). Our study has shown that serum levels of 16∶0 Lyso PC were notably lower in pneumoconiosis patients compared to dust-exposed workers. These findings align with the results of a lipid metabolomics study performed on silica dust-exposed rats (*9*). Conversely, PE has been known to foster an anti-fibrotic phenotype in normal human lung fibroblasts and ameliorate bleomycin-induced pulmonary fibrosis in mice (*10*). The serum levels of 18∶0–18∶1 PE and 18∶0 PE examined in our research were found to be lower in pneumoconiosis patients in comparison to dust-exposed workers. Such decrease in PE may have implications on the progression of pulmonary fibrosis (*11*). Lyso PE, on the other hand, may be associated with anti-inflammatory outcomes (*12*). Our study indicated lower serum levels of 18∶1 Lyso PE in pneumoconiosis patients compared to dust-exposed workers. PG is recognized for its antibacterial and immunosuppressive effects (*13–14*). Our findings revealed lower serum levels of 18∶0–18∶1 PG in pneumoconiosis patients compared to dust-exposed workers. Such decrease in PG could potentially amplify inflammation (*15*). Various phospholipids may exert pro-inflammatory or anti-inflammatory effects on the health status of pneumoconiosis patients via different pathways; however, their precise mechanisms warrant further investigation.

To the best of our knowledge, this is the pioneering study applying targeted lipidomics to analyze phospholipid metabolism in pneumoconiosis patients, thus paving the way for novel biomarker research in pneumoconiosis diagnosis. This study, however, does harbour certain limitations. First, the small sample size reduces the robustness of our findings. Additionally, our validation study was hampered due to an age disparity between the cases and their younger controls, and a lack of an external control group consisting of non-dust-exposed healthy individuals. Expanding the sample size and introducing an external control group could be a promising avenue for subsequent validation studies. Second, the representation of different stages and types of pneumoconiosis in our case group was suboptimal. Future research should thus delve deeper into the alterations in phospholipid metabolism across diverse stages and types of pneumoconiosis, thereby unearthing potential lipid biomarkers that could facilitate early detection, monitor disease progression, and predict disease prognosis. Third, the number of targeted phospholipid species analyzed in this study was relatively low. In subsequent studies, it would be beneficial to expand the range of targeted phospholipid species, further bolstering the search for potential lipid biomarkers pertinent to pneumoconiosis.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. Parameter settings for MRM.

No.	Compound	Quantitative standards	IS	Parent ion (m/z)	Product ion (m/z)	Cone voltage (v)	Collision energy (ev)	Ionization mode
1	16:0 Lyso PA	16:0 Lyso PA	17:0 Lyso PA	409.23	153.00	35	20	$[M-H]^-$
2	17:0 Lyso PA	–	–	423.25	153.00	30	20	$[M-H]^-$
3	18:1 Lyso PA	18:1 Lyso PA	17:0 Lyso PA	435.20	153.00	30	20	$[M-H]^-$
4	14:0 PC	14:0 PC	17:0 PC	722.60	227.30	50	35	$[M+HCOO]^-$
5	16:0 PC	16:0 PC	17:0 PC	778.60	255.30	50	35	$[M+HCOO]^-$
6	17:0 PC	–	–	806.60	269.30	50	35	$[M+HCOO]^-$
7	18:0 PC	18:0 PC	17:0 PC	834.60	283.20	50	35	$[M+HCOO]^-$
8	16:0–18:1 PC	16:0–18:1 PC	17:0 PC	804.60	255.30	50	35	$[M+HCOO]^-$
9	18:0–18:1 PC	18:0–18:1 PC	17:0 PC	832.60	281.30	50	35	$[M+HCOO]^-$
10	12:0 Lyso PC	12:0 Lyso PC	17:0 Lyso PC	484.50	199.30	30	30	$[M+HCOO]^-$
11	16:0 Lyso PC	16:0 Lyso PC	17:0 Lyso PC	540.30	255.30	30	30	$[M+HCOO]^-$
12	17:0 Lyso PC	–	–	554.60	269.30	30	30	$[M+HCOO]^-$
13	18:0 Lyso PC	18:0 Lyso PC	17:0 Lyso PC	568.40	283.10	30	30	$[M+HCOO]^-$
14	18:1 Lyso PC	18:1 Lyso PC	17:0 Lyso PC	566.40	281.30	30	30	$[M+HCOO]^-$
15	16:0 PE	16:0 PE	17:0 PE	692.50	551.25	40	20	$[M+H]^+$
16	17:0 PE	–	–	720.83	579.57	30	22	$[M+H]^+$
17	18:0 PE	18:0 PE	17:0 PE	748.60	607.30	32	20	$[M+H]^+$
18	18:0–18:1 PE	18:0–18:1 PE	17:0 PE	746.72	605.47	20	20	$[M+H]^+$
19	18:1 Lyso PE	18:1 Lyso PE	17:0 PE	480.60	339.60	30	20	$[M+H]^+$
20	16:0 PG	16:0 PG	17:0 PG	745.85	195.00	30	30	$[M+Na]^+$
21	18:0–18:1 PG	18:0–18:1 PG	17:0 PG	800.05	195.00	30	30	$[M+Na]^+$
22	17:0 PG	–	–	773.80	195.00	30	30	$[M+Na]^+$
23	16:0 PI	16:0 PI	17:0–14:1 PI	828.60	551.25	30	20	$[M+NH_4]^+$
24	16:0–18:1 PI	16:0–18:1 PI	17:0–14:1 PI	854.90	578.00	30	20	$[M+NH_4]^+$
25	17:0–14:1 PI	–	–	812.50	535.30	30	20	$[M+NH_4]^+$
26	16:0 PS	16:0 PS	17:0 PS	758.40	208.00	30	30	$[M+Na]^+$
27	17:0 PS	–	–	786.50	208.00	30	30	$[M+Na]^+$
28	18:1 PS	18:1 PS	17:0 PS	810.50	208.00	30	30	$[M+Na]^+$
29	18:0 Lyso PS	18:0 Lyso PS	17:0 PS	548.40	208.00	30	20	$[M+Na]^+$

Abbreviation: Lyso PA=lysophosphatidic acid; PC=phosphatidylcholines; PE=phosphatidylethanolamine; PG=phosphatidylglycerol; PI=phosphatidylinositol; PS=phosphatidylserine; IS=internal standard.

Commentary

30-Year Trends in the Disease Burden, Incidence, and Prevention of Pneumoconiosis

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The global incidence of pneumoconiosis, a lung disease caused by inhaling industrial dust, has increased by 61.5% from 1990 to 2019, according to a recent report. China had the highest number of cases in 2019, followed by India and the United States. The all-age standard incidence rate for pneumoconiosis was 2.39 per 100,000 population in 2019, with China also having the highest rate. However, there was a decrease in the incidence rate in Belgium and Italy during the same period. The report also highlights regional variations in the changing trend, with the largest increase in cases observed in North Africa and the Middle East. Improved dust prevention and control measures are urgently needed to reduce workplace dust exposure and combat the rising cases of pneumoconiosis globally.

Pneumoconiosis, marked by pulmonary interstitial fibrosis, is predominantly induced by inhalation of industrial dust. This exposure typically results in diminished lung function and gradual loss of work capability (*1–4*). Given the global prevalence of industrial dust exposure, affecting millions of workers, pneumoconiosis consistently garners significant public health attention (*5–6*). Despite targeted public health efforts, the disease remains the deadliest occupational disease, particularly in low- to middle-income countries and developing regions such as China (*7–11*). Data from the Global Burden of Disease research carried out by the Institute for Health Metrics and Evaluation (IHME) report the number of new cases rising from 60,055 in 2017 to 199,125 in 2019 (*10*). In China alone, the former Ministry of Health (now known as National Health Commission of China, NHC) reported over 271,000 new cases between 2010 and 2022. This recent surge in case numbers underscores the need for stringent preventative measures to control dust concentration in workplaces.

Pneumoconiosis can be categorized further based on the type of industrial dust inhaled. The most prevalent types in China are silicosis, resulting from inhalation of free crystalline silicon dioxide, and coal worker's pneumoconiosis (CWP), caused by coal mine dust; both account for 90% of pneumoconiosis cases as per epidemiological studies (*12*). Incidence estimates for pneumoconiosis etiologies are derived using a standard DisMod-MR 2.1 approach and informed by the 2017/2019 global disease burden data and published studies (*13*). Incidence is gathered from systematic literature reviews, inpatient hospital reports, and claims data (https://ghdx.healthdata.org/gbd-2019). In the Global Burden of Disease (GBD) study, diseases coded in the International Classification of Diseases (ICD) 9 (500–505.9) and ICD 10 (J60–J65.0 and J92.0) are used for incidence estimation (*13*). This paper presents reported incident cases and age-standardized incidence rate (ASIR) of total pneumoconiosis, silicosis, and CWP. It also provides an overview of changing pneumoconiosis disease burden trends globally and particularly in China from 1990 to 2019. A literature review was conducted for studies reporting pneumoconiosis prevalence, utilizing databases such as PubMed, CNKI, and Web of Science. Additionally, we summarize recent advancements in dust prevention technology to support the prevention and treatment of pneumoconiosis.

Trends in the Global Number and Incidence of Pneumoconiosis

The global incident cases of pneumoconiosis escalated by 61.5% [95% uncertainty interval (*UI*): 44.6%–77.6%] from 123,271 cases in 1990 to 199,125 in 2019. The top three nations with the highest incidence in 2019 were China, with 136,755 cases, followed by India and the United States, with 11,670 and 10,014 cases, respectively. The ASIR for pneumoconiosis was 2.39 per 100,000 population in 2019, and demonstrated notable variability across the globe. China exhibited the highest ASIR, at 6.73 per 100,000 population, while Lesotho and South Africa followed with ASIR of 5.08 per 100,000 and 4.89 per 100,000, respectively. The period from 1990 to 2019 saw an average annual percentage change (AAPC) of

−0.62% [95% confidence interval (*CI*): −0.85% to −0.39%] in the ASIR, implying a decrease. Belgium manifested the most substantial decrease, with an AAPC of −3.70% (95% *CI*: −4.33% to −3.07%), followed by Italy and Bermuda with respective AAPCs of −3.69% (95% *CI*: −4.10% to −3.29%) and −3.53% (95% *CI*: −3.73% to −3.34%). Conversely, Iran reported the most significant increase with an AAPC of 3.82% (95% *CI*: 3.19% to 4.45%), followed by Libya (AAPC=3.55%; 95% *CI*: 3.24% to 3.87%) and Georgia (AAPC=3.52%; 95% *CI*: 3.30% to 3.75%).

In the GBD study, the globe was segmented into 21 geographical regions. Between 1990 and 2019, the total number of reported pneumoconiosis cases rose in nearly all areas, barring Central Europe, Eastern Europe, Western Europe, and high-income Asia Pacific. The most significant increase was seen in North Africa and the Middle East (222.6%; 95% *UI*: 196.3%–254.3%), trailed by Oceania (205.1%; 95% *UI*: 177.0%–234.9%), and Southern Latin America (189.0%; 95% *UI*: 159.0%–222.0%). Concerning the ASIR, out of the 21 GBD regions, 10 exhibited an upward trajectory in ASIR, as evidenced by both AAPC and its 95% *CI*. The highest ASIR was documented in East Asia. However, fluctuations in ASIR differ amongst regions; the most noticeable decrease was observed in high-income Asia Pacific (AAPC=−2.85%; 95% *CI*: −3.44% to −2.26%), while the most substantial increase was marked in Southern Latin America (AAPC=1.59%; 95% *CI*: 1.21%–1.97%).

The socio-demographic index (SDI) segregates the world into five distinct regions: low, low-middle, middle, high-middle, and high. The incident cases of pneumoconiosis were observed to be most prevalent in the middle region, followed by the high-middle region (*10*). Overall, the ASIR of pneumoconiosis initially rose and then declined in response to an increase in SDI. When the SDI value reached or exceeded 0.7, a negative correlation was observed between the AAPC in ASIR for pneumoconiosis and the SDI (*10*). These findings indicate a relationship between higher SDI values and a decrease in pneumoconiosis incidence rate.

In 2019, silicosis accounted for approximately 69.8% (138,971) of total new pneumoconiosis cases globally. The number of reported silicosis cases increased significantly by 64.6% (41.1%–87.7%) from 84,426 in 1990 to 138,971 in 2019. There was considerable disparity worldwide in the ASIR of silicosis, which stood at 1.65 per 100,000 population. The highest ASIR was observed in East Asia at 5.78 per 100,000 population. The ASIR for silicosis exhibited a decreasing trend over the study period, with an AAPC of −0.56% (95% *CI*: −0.84% to −0.27%). However, an increasing trend in silicosis ASIR was noted in more than half (118 out of 204) of the countries and regions studied, primarily in developing nations.

In 2019, CWP accounted for approximately 3.5% (7, 153) of all new pneumoconiosis cases globally. The incident cases of CWP were 7,379 in 1990, falling slightly to 7,153 by 2019. The ASIR for CWP globally was 0.09 per 100,000 population in 2019, reflecting a decrease characterized by an AAPC of −2.41% (−2.68% to −2.13%) from 1990 to 2019. It's important to note that ASIR for CWP significantly varies among countries [most affected Poland (0.31/100,000) and the Democratic People's Republic of Korea (0.27/100,000)] and regions [most affected Taiwan, China (0.42/100,000)] in 2019. Particularly, the ASIR for CWP in East Asia was markedly greater than in other regions. On a global scale, the ASIR for CWP has demonstrated a decline between 1990 and 2019, with an AAPC of −2.40% (−2.68% to −2.13%) (*14*). Alongside an increase in SDI, the ASIR of CWP has been on a downward trend, more so in East Asia.

The Shift in the Number and Incidence of Pneumoconiosis in China

The incident cases of pneumoconiosis in China surged by 63.7% (95% *UI*: 40.5%–86.7%), from 83,550 in 1990 to 136,755 in 2019. In 2019, incident pneumoconiosis cases in China represented 68.7% of the global total. However, with the implementation of national standards and control measures on dust concentration, there has been a gradual decline in the incidence of pneumoconiosis. The ASIR of pneumoconiosis dropped from 7.82/100,000 in 1990 to 6.73/100,000 in 2019, with an AAPC of −0.58% (−0.99% to −0.17%).

Similar patterns were observed for both silicosis and CWP. In 1990, incident cases of silicosis and CWP were recorded at 68,236 and 5,450 respectively, and these figures rose to 120,775 and 4,974 in 2019. The ASIR of silicosis decreased from 6.34/100,000 in 1990 to 5.92/100,000 in 2019, with an AAPC of −0.34% (−0.67% to −0.01%). Additionally, the ASIR of CWP decreased from 0.52/100,000 in 1990 to 0.25/100,000 in 2019, with an AAPC of −2.61% (−2.91% to −2.31%).

It should be noted, however, that the count and

ASIR of CWP reported in GBD data differs from those reported by the NHC. In the latter's report, CWP cases reported were either equivalent to or higher than those of silicosis. These discrepancies may result from differences in the categorization of silicosis. In the GBD, any pneumoconiosis resulting from exposure to industrial dust with free silica is classified as silicosis, while in China, silicosis is attributed to exposure to dust with a free silica content of 10% or more. As per GBD, CWP is specifically tied to exposure to pure coal dust.

The observed decrease in the ASIR of pneumoconiosis in China over the past three decades reflects improvements from implemented dust prevention measures. Notwithstanding, it is paramount to highlight that current data on pneumoconiosis, incorporating silicosis and CWP, indicates a considerable increase in the number of new cases compared to 1990. Although recent reports from the NHC show a gradual decrease in new pneumoconiosis cases over the last five years, the aggregate number remains rather high. The simultaneous rise in new pneumoconiosis cases alongside a declining incidence suggests an increase in the overall number of workers exposed to dust. Consequently, the need for protective measures for this susceptible population has also escalated. Thus, it is clear that considerable efforts are still required to advance dust prevention and containment in China.

The Shift of CWP Prevalence in Recent Years

Recent industrial growth and increased demand for coal energy have led to a rise in coal mine workers' exposure to coal mine dust (*15–17*). Consequently, the prevalence of CWP has garnered increased focus in recent years (*18–21*). A comprehensive meta-analysis, encompassing 11,214,584 coal miners, among whom 202,668 developed CWP, was conducted across 37 studies (*22*). Nineteen of these studies reported a CWP prevalence exceeding 5%.

The aggregated prevalence of CWP decreased from 23.33% (95% *CI*: 18.03% to 8.62%) before 1970 to 6.00% (95% *CI*: 4.11% to 7.90%) during 1981–1990, which then saw a resurgence to 10.35% (95% *CI*: 8.08% to 12.62%) in 1991–2000. However, it significantly dropped to 2.29% (95% *CI*: 2.06% to 2.51%) between 2011 and 2020. Over the past three decades, the highest pooled prevalence rates of CWP were observed in Europe, China, and the USA, respectively. Few studies reported prevalence in developing regions, but available evidence suggests that these regions possess higher prevalence compared to developed regions.

The worldwide prevalence of CWP has seen a downward trend in recent years. Nonetheless, the prevalence in developing regions remains comparatively higher than in developed areas. This underlines the need for increased attention and strategic interventions towards controlling CWP, specifically in developing regions.

Advancements in Dust Control Technology

The previous analysis regarding the incidence of pneumoconiosis across various SDI illustrates a negative correlation between the SDI and pneumoconiosis incidence. More formidable challenges in preventing and controlling pneumoconiosis exist in regions of middle to middle-high economic development, due to rapid economic growth and a substantial number of workers being exposed to dust (*3*). The global community is encouraged to provide support to these developing regions in creating enhanced occupational health surveillance systems and integrating advanced technology for occupational environmental monitoring, dust mitigation, and personal protection.

Dust control engineering technologies and strategies are crucial methods for decreasing dust concentrations in workplaces. The predominant example of reducing dust concentrations through optimized process operations is utilizing wet operations to diminish the production and transmission of industrial dust (*23*). For instance, in the field of coal mining, water injection into coal seams is employed to regulate dust emission during mining (*24*). The addition of a surfactant enhances the water's wettability to coal, which proves beneficial in reducing coal dust production during the water injection process (*25–26*).

Furthermore, air curtain technology is implemented to create a trapezoidal protection area, separating the dust-producing surface from the operator within the workplace (*27*). Recently developed environmental dust suppressors, which include simple composite materials and polymer products, demonstrate a commendable ability to absorb coal dust. This ensures the practicality and durability of these dust suppressors (*28–30*).

In addition, ultrasonic spray dust removal technology satisfies the needs of narrow and wind-impacted areas effectively capturing and lowering small particle size dust levels (*31*). These dust-prevention strategies lead to a reduction in dust concentration, but potential health benefits require additional research.

Furthermore, to accommodate an array of conditions such as high temperatures, high humidity, and high levels of dust, the performance of various masks and respirators, including tightness, filtration, and inspiratory resistance, has been progressively enhanced (*32*–*33*). In recent years, the development of techniques for early pneumoconiosis detection, including sensitive biomarkers for pulmonary fibrosis and high-resolution CT, has been continuously progressing. These serve the crucial function of enabling the early identification of dust-related health hazards and timely protection of workers (*2*,*34*–*41*).

Future Prospects

Moving forward, pneumoconiosis continues to present challenges in various countries, despite numerous global, regional, and national initiatives to eradicate it. As part of the *Healthy China 2030 Action Plan*, China has incorporated specific strategies to address occupational health issues, including ones related to pneumoconiosis (*42*). The plan mandates health surveillance for a minimum of 95% of workers exposed to dust (*42*). Moreover, globally, there is a need for additional resources for health education targeting workers, providing respiratory protective equipment, and raising awareness about occupational health issues. Future advancements in the domains of dust prevention technology, online dust monitoring, and intelligent health monitoring for dust-exposed workers are essential along with enhancements in personal respiratory protection. Developing a comprehensive understanding of pneumoconiosis incidence trends and levels derived from robust, multinational data is crucial to inform policy, target prevention efforts, and highlight the importance of treating pneumoconiosis.

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