Environmental Research 229 (2023) 115957

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Impact of lifetime air pollution exposure patterns on the risk of chronic disease☆

Cheng-Yu Tsai [a,b], Chien-Ling Su [b,c,d], Yuan-Hung Wang [e,f], Sheng-Ming Wu [c,g], Wen-Te Liu [b,c,h,i], Wen-Hua Hsu [c], Arnab Majumdar [a], Marc Stettler [a], Kuan-Yuan Chen [b], Ya-Ting Lee [b], Chaur-Jong Hu [j,k], Kang-Yun Lee [b,g], Ben-Jei Tsuang [l], Chien-Hua Tseng [b,g,m,*]

[a] Department of Civil and Environmental Engineering, Imperial College London, London, SW7 2AZ, United Kingdom
[b] Division of Pulmonary Medicine, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, 235041, Taiwan
[c] School of Respiratory Therapy, College of Medicine, Taipei Medical University, Taipei, 110301, Taiwan
[d] Department of Physical Therapy, Shu-Zen Junior College of Medicine and Management, Kaohsiung City, 821004, Taiwan
[e] Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taipei, 110301, Taiwan
[f] Department of Medical Research, Shuang Ho Hospital, Taipei Medical University, New Taipei City, 235041, Taiwan
[g] Division of Pulmonary Medicine, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, 110301, Taiwan
[h] Sleep Center, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[i] Research Center of Artificial Intelligence in Medicine, Taipei Medical University, Taipei, 110301, Taiwan
[j] Department of Neurology, Shuang Ho Hospital, Taipei Medical University, New Taipei City, 235041, Taiwan
[k] Department of Neurology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, 11031, Taiwan
[l] Department of Environmental Engineering, National Chung-Hsing University, Taichung, Taiwan
[m] Division of Critical Care Medicine, Department of Emergency and Critical Care Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan

ARTICLE INFO

Handling Editor: Jose L Domingo

Keywords:
Air pollution
Cardiovascular disease
Respiratory disease
Metabolic syndrome
Fine particulate matter

ABSTRACT

Long-term exposure to air pollution can lead to cardiovascular disease, metabolic syndrome, and chronic respiratory disease. However, from a lifetime perspective, the critical period of air pollution exposure in terms of health risk is unknown. This study aimed to evaluate the impact of air pollution exposure at different life stages.

The study participants were recruited from community centers in Northern Taiwan between October 2018 and April 2021. Their annual averages for fine particulate matter (PM2.5) exposure were derived from a national visibility database. Lifetime PM2.5 exposures were determined using residential address information and were separated into three stages (<20, 20–40, and >40 years). We employed exponentially weighted moving averages, applying different weights to the aforementioned life stages to simulate various weighting distribution patterns. Regression models were implemented to examine associations between weighting distributions and disease risk. We applied a random forest model to compare the relative importance of the three exposure life stages. We also compared model performance by evaluating the accuracy and F1 scores (the harmonic mean of precision and recall) of late-stage (>40 years) and lifetime exposure models.

Models with 89% weighting on late-stage exposure showed significant associations between $PM_{2.5}$ exposure and metabolic syndrome, hypertension, diabetes, and cardiovascular disease, but not gout or osteoarthritis. Lifetime exposure models showed higher precision, accuracy, and F1 scores for metabolic syndrome, hypertension, diabetes, and cardiovascular disease, whereas late-stage models showed lower performance metrics for these outcomes.

We conclude that exposure to high-level $PM_{2.5}$ after 40 years of age may increase the risk of metabolic syndrome, hypertension, diabetes, and cardiovascular disease. However, models considering lifetime exposure showed higher precision, accuracy, and F1 scores and lower equal error rates than models incorporating only late-stage exposures. Future studies regarding long-term air pollution modelling are required considering lifelong exposure pattern. .[1]

☆ All authors have read and approved the final version of the manuscript for publication.

* Corresponding author. Division of Pulmonary Medicine, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, No.291, Zhongzheng Rd., Zhonghe District, New Taipei City, 235041, Taiwan.
E-mail address: 17339@s.tmu.edu.tw (C.-H. Tseng).

https://doi.org/10.1016/j.envres.2023.115957
Received 20 September 2022; Received in revised form 17 April 2023; Accepted 18 April 2023
Available online 20 April 2023
0013-9351/© 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Long-term exposure to fine particulate matter ($PM_{2.5}$) has been shown to increase the risk of cardiovascular disease, metabolic syndrome, respiratory disease, and mortality (Pope and Dockery, 2006; Rodopoulou et al., 2022). Epidemiological studies have suggested that exposure to air pollution elevates the incidence of cardiopulmonary diseases, metabolic syndrome, and declined lung function (Bo et al., 2021; Chen and Schwartz, 2008). A prospective study that analyzed the data from the National Institutes of Health NIH-AARP Diet and Health Study demonstrated that a 10-μg/m^3 increase in long-term $PM_{2.5}$ exposure levels was associated with a 16% increase in ischemic heart disease mortality and a 14% increase in stroke mortality (Hayes et al., 2020).

Epidemiological studies have obtained air pollution data using different long-term exposure scales to assess the associations between exposure and health risks (Russ et al., 2021; Zhang et al., 2019). Raaschou-Nielsen et al. chose a five-year average period of exposure at the residential address preceding the index date as main exposure period (Raaschou-Nielsen et al., 2020), and Kloog et al. defined an eight-year exposure window as a valid measure of long-term exposure (Kloog et al., 2013). Nordeide et al. explored lifelong exposure before the age of 30 years (Nordeide Kuiper et al., 2021), and Li et al. simulated lifetime exposure considering socioeconomic data, individual time-activity patterns, and lifetime trajectories (Li et al., 2019). Russ et al. related whole life course air pollution exposure and cognitive decline (Russ et al., 2021). However, the critical periods of lifetime exposure in terms of these health risks have been less studied and are thus currently unknown. Additionally, the relative importance of air pollution hazards in different life stages remains unclear.

An exponentially weighted moving average weighs different time segments rather than forcing a linear relationship. Therefore, this method has been widely used in modeling $PM_{2.5}$ trajectories (Liu and Li, 2015; Ni et al., 2017). For example, under the hypothesis that late-stage exposure to $PM_{2.5}$ (compared to earlier exposure) is more likely to reduce lung function, an exponentially weighted moving average dynamically adjusts weighting under various assumptions. On the other hand, random forests can not only evaluate feature importance (Enebish et al., 2021; Zhu et al., 2019) but also prevent the influence of outliers by aggregating and averaging the individual predictions of all trees. Moreover, under random forest analysis, bagging and random selection for features are used to separate the dataset into subgroups and to perform several regression examinations to eliminate the impact of extreme values; this may lead to better model performance than that of general linear regression models (Archer and Kimes, 2008). Moreover, traditional regression methods cannot compare the importance of input parameters in regard to prediction, whereas the random forest model calculates predictive power for each input variable; this can provide an interpretation of feature importance for additional comparison (Breiman et al., 2017). The above-mentioned methods enhance precision in modelling lifetime $PM_{2.5}$ exposure levels and assist in comparing the importance of air pollution exposures occurring at different life stages.

This retrospective study utilized exponentially weighted moving averages to explore and evaluate the impact of $PM_{2.5}$ exposure at various life stages on the incidence of cardiovascular disease, metabolic syndrome, and respiratory disease. In addition, we used a random forest model to compare the predictive power between lifetime and late-stage exposure models at >40 years of age only.

2. Materials and methods

For this study, we visited various community centers in the Tucheng District in New Taipei City (Taiwan) from October 2018 to April 2021 to enroll participants. We aimed to sample a percentage of middle-aged to older adults in this area, and the sample size was approximately 1000 people. This study included only adults aged >40 years to complete their lifelong air pollution profile and included only never-smokers to eliminate the considerable confounding factor, cigarette smoking, when exploring the effect of air pollution and chronic disease. Moreover, data on passive or second-hand smoking and family history of chronic disease were collected. The study protocol was reviewed and approved by the Ethics Committee of the Taipei Medical University Joint Institutional Review Board (TMU-JIRB N201806024). This study was conducted in accordance with the principles of the Declaration of Helsinki, and informed consent was obtained for all participants prior to study participation. Data collection and analysis was conducted according to all relevant approved national and international guidelines and related regulations.

Data on participant medical and demographic characteristics and residential addresses were acquired using survey questionnaires during study visit, 20 mL of blood was collected, and standard pulmonary function tests under the guidance of a respiratory therapist were conducted concurrently. Metabolic syndrome was determined by abdominal girth, blood pressure, and biochemistry data during visit (Scott, 2003). Diabetes mellitus was confirmed by HbA1C level, which was checked during visit. Hypertension and cardiovascular diseases were confirmed by historical medication history by medical physicians. Gout and osteoarthritis were self-reported diagnosis.

Moreover, the Taiwan Central Weather Bureau has been monitoring long-term nationwide visibility data since 1970. To obtain more comprehensive information on the association between visibility and $PM_{2.5}$ exposure levels, we selected daytime visibility data to represent daily $PM_{2.5}$ levels, included only daytime humidity levels lower than 70%, and excluded days with a daily accumulation of rainfall greater than 0 cm to avoid the confounding effect of water droplet on visibility. The non-linear regression analysis showing an association between $PM_{2.5}$ and visibility is as follows: $PM_{2.5}$ ($\mu g/m^3$) = 430.52/(3.2+ visibility/kilometers), $R^2 = 0.40$, p-value <0.0001 (supplementary figure 1) (Abbey et al., 1995; Guo et al., 2018). We applied land use regression model to estimated yearly township $PM_{2.5}$ exposure level. Then we designated the exposure level to participant according to their residential addresses year by year, then lifelong exposures in town scale were derived.

All statistical analyses were conducted using the open-source Python library (Scikit-learn, version 0.21.2; Python Software Foundation, Fredericksburg, VA, USA). To determine the impact of air pollution exposure at different life stages, this study separated participant lifetimes into three stages based on prior literature: Stage 1 (<20 years), Stage 2 (21–40 years), and Stage 3 (>40 years) (Ko et al., 1997). Next, exponentially weighted moving averages calculated using an exponential formula were applied to serial weighted values, which were multiplied by the $PM_{2.5}$ exposure levels at different life stages. This approach was originally proposed to measure the trend in the sequence of random variables (Roberts, 2000). Afterwards, some researchers employed this exponential smoothing method to adjust the weight of different data orders when analyzing the data on a long-term scale (i.e., off-peak seasonal data were allocated with exponentially reduced weights, whereas peak season data were assigned relatively increased weights) (de Oliveira and Oliveira, 2018). Some researchers also utilized this method, considering long series data (air pollution dataset on the hour-based scale), to estimate short-term air pollutant level (Mahajan et al., 2018). This study, therefore, proposed to apply this method to adjust weights for different life stages to compare the importance of exposure period (Supplementary method). The parameter α, which ranges from 0.1 to 1, was used to decide the weighting for different life stages. A higher α value indicated a higher weight, with the remaining weight values decreasing exponentially (1-α and $[1-\alpha]^2$, respectively). For example, the late-stage models, which used an exponentially weighted moving average, applied the highest weight to those aged >40 years. This study applied different weights to three stages and resulted in six different permutation distributions (Supplementary method). This demonstrated the relative impact of air pollution exposure at different

stages on chronic diseases. The weighting factor, α, was initially employed as 0.1, 0.3, 0.5, 0.7, and then 0.9 in this study. This helps to explore the weighting pattern among three stages. However, since using all five values of the weighting factor may result in repetitively similar outcomes, this study only reported the results for α values of 0.3, 0.5, and 0.9.

After weighting was applied for the three stages, regression models were employed to investigate the correlations between the weighted exposure levels and the aforementioned medical conditions, biomarkers, and lung function parameters. Linear regression was applied for biomarkers and lung function measurements, while logistic regression was used for disease diagnoses. The level of statistical significance was set to a two-sided threshold of $P < 0.05$. We performed a subgroup analysis by dividing our sample into male and female groups. Furthermore, we excluded participants with second-hand smoking or family history of chronic diseases for sensitive analysis. Additionally, we performed a statistical power analysis to determine the effect of all the observed significant associations. The acceptable statistical power threshold was set to 0.8.

This study also employed a random forest model to compare the effect of air pollution exposure on the risks of various chronic diseases between the late-stage and lifetime exposure data (Biau and Scornet, 2016). The training process was as follows. First, the basic decision unit of the random forest (the classification and regression tree) was set to 500 for stability and time efficiency (Lawrence et al., 2006). Following this, two model categories, namely models considering only late-stage exposure (Stage 3) and models considering lifetime exposure (Stages 1–3), were established. Next, all the obtained data were iteratively input as training data in order to develop the random forest model. Model performance in regard to F1 scores, precision, accuracy, and equal error rates, was determined based on the random forest training outcomes as well as additional comparative evaluations of performance between the two types of models. F1 score is the harmonic mean of precision and recall; it is used to evaluate model performance by considering both precision and recall. Moreover, this study calculated Shapley values to represent feature importance and displayed the outcomes using a summary plot (Roth, 1988).

3. Theory

A relationship between lifetime air pollution exposure and the development of chronic diseases has been reported. However, the relative importance of air pollution hazards in different life stages remains unclear. Although current epidemiological studies are mainly focused on the effects of short-term exposure occurring within a constrained period of the total life stage, long-term accumulated exposure to $PM_{2.5}$ may be more strongly associated with chronic health effects. Therefore, evaluating late-stage exposure may be sufficient for assessing health effects and risks.

4. Results

4.1. Participant characteristics

A total of 912 participants were initially enrolled in this study. However, participants without information on residential addresses in the study database as well as current or ex-smokers were excluded. Hence, a total of 679 never smokers were ultimately included in the analysis (Supplementary figure 2). The mean age of the included participants was 63.4 years and the prevalence of chronic diseases in this study population was as follows: metabolic syndrome, 36.08%; hypertension, 24.15%; diabetes mellitus, 13.7%; cardiovascular diseases, 7.51%; gout, 1.47%; and osteoarthritis, 3.39% (Table 1). The average $PM_{2.5}$ exposure levels were as follows: Stage 1, 26.08 ± 6.7 μg/m^3; Stage 2, 1, 35.72 ± 3.69; and Stage 3, 28.57 ± 2.41 μg/m^3.

4.2. Exponentially weighted moving averages and the risk of chronic disease

Exponentially weighted moving averages were applied for the three aforementioned life stages; the α values were set as 0.3 (x = 0.2, y = 0.47, z = 0.33), 0.5 (x = 0.4, y = 0.4, z = 0.2), and 0.9 (x = 0.89, y = 0.1, z = 0.01), respectively, to represent the different weighting distributions for these life stages. Following this, x, y, and z values were cross-matched for the $PM_{2.5}$ exposure level in the three life stages (Table 2). Among the distribution patterns, models with an α value of 0.9 (x = 0.89, y = 0.1, z = 0.01) and the highest weight (x = 0.89) at Stage 3 (Model-5 and Model-6) showed significant associations between air pollution exposure and the risk of chronic disease. More specifically, the following odds ratios (ORs) were found for every 1 μg/m^3 increase in $PM_{2.5}$: metabolic syndrome, OR 1.12, 95% CI 1.04–1.21; hypertension, OR 1.29, 95% CI 1.17–1.42; diabetes mellitus, OR 1.20, 95% CI 1.07–1.33; and cardiovascular disease, OR 1.28, 95% CI 1.11–1.48. In contrast, null associations were found for gout (OR 1.10, 95% CI 0.82–1.49) and osteoarthritis (OR 1.08, 95% CI 0.89–1.32). Moreover, models with an α value of 0.9 and the highest weight (x = 0.89) at Stage 1 or Stage 2 showed no significant associations. Finally, models with α values set as 0.3 and 0.5, respectively, also showed no significant

Table 1
Medical and demographic characteristics of the recruited participants (n = 679).

Characteristics		Mean $PM_{2.5}$ exposure level	
Age (years)	63.41 ± 7.75	Stage I (0–20 y/o)	26.08 ± 6.7
Sex (Male/Female)	160/519	Stage II (21 y/o - 40 y/o)	35.72 ± 3.69
BMI (kg/m^2)	24.46 ± 3.48	Stage III (41 y/o -)	28.57 ± 2.41
Chronic disease (n, %)		Pulmonary functions	
Metabolic syndrome	245 (36.08%)	FVC (L)	2.41 ± 0.68
Hypertension	164 (24.15%)	FEV_1 (L)	1.96 ± 0.55
Diabetes mellitus	93 (13.7%)	FEV_1/FVC (%)	81.61 ± 9.09
Cardiovascular diseases	51 (7.51%)	Biochemistry	
Gout	10 (1.47%)	BNP (pg/mL)	30.53 ± 44.6
Osteoarthritis	51 (3.39%)	Creatinine (mg/dL)	0.74 ± 0.22
Blood cell count		HbA1c (%)	6.05 ± 1.01
WBC (10^3/μL)	5.94 ± 1.81	Uric Acid (mg/dL)	5.49 ± 1.22
HGB (g/dL)	13.76 ± 1.27	Ferritin (ng/mL)	136.89 ± 97.69
MCV (fL)	88.09 ± 7.9	GPT (IU/L)	23.94 ± 16.18
PLT (10^3/μL)	234.61 ± 62.36	Total Bilirubin (mg/dL)	0.88 ± 0.31

*Data are expressed as the mean with standard deviation.
Abbreviation: BMI, body mass index; WBC, white blood cell; HGB, hemoglobin; MCV, mean corpuscular volume; PLT, platelet count; FVC, forced vital capacity; FEV_1, forced expiratory volume at 1st second; BNP, B-type natriuretic peptide; HbA1c, hemoglobin A1C; GPT, glutamic pyruvic transaminase.

correlations. The statistical power analysis for the determined significant associations is presented in supplementary table 1. The statistical power of the late-stage valued models (i.e., model-5 and model-6) ranged from 0.72 to 0.93.

Subgroup analysis in 519 females also revealed that models with an α value of 0.9 (x = 0.89, y = 0.1, z = 0.01) and the highest weight (x = 0.89) at stage 3 showed the significant associations between estimated $PM_{2.5}$ exposure and the risk of chronic diseases (supplementary table 2), but no significant associations were observed in 160 males (supplementary table 3). Sensitivity analysis by excluding participants with second-hand smoking or a family history of chronic disease revealed consistent results (supplementary tables 4 to 6).

4.3. Exponentially weighted moving averages and pulmonary function tests

The associations between estimated exposure $PM_{2.5}$ levels derived from various weighted models and pulmonary function parameters are shown in Table 3. We found that a 1-μg/m^3 increase in $PM_{2.5}$ exposure level was significantly associated with a decrease in FVC in the late-stage valued models (Model 5: −29.63 mL, 95% CI -55.66 mL to −3.6 mL, $P < 0.05$; Model 6: −28.94 mL, 95% CI -52.7 mL to −5.17 mL, $P < 0.05$). In addition, each 1 μg/m^3 increase in $PM_{2.5}$ exposure was significantly associated with decreased FEV_1 (Model 5: −31.82 mL, 95% CI -52.9 mL to −10.75 mL, $P < 0.01$; Model 6: −29.66 mL, 95% CI: −48.9 mL to −10.41 mL, $P < 0.01$). Subgroup analysis in 519 females also revealed that models with an α value of 0.9 (x = 0.89, y = 0.1, z = 0.01) and the highest weight (x = 0.89) at stage 3 demonstrates the significant associations between estimated $PM_{2.5}$ exposure and declined pulmonary function parameters (supplementary table 7), but no significant associations were found in 160 males (supplementary table 8). Sensitivity analysis by excluding participants with second-hand smoking or a family history of chronic disease revealed consistent results (supplementary tables 9 to 11).

4.4. Exponentially weighted moving averages and laboratory data

Models with an α value of 0.9 (x = 0.89, y = 0.1, z = 0.01) and the highest weight (x = 0.89) at Stage 3 showed the most significant correlations. More specifically, the mean corpuscular volume (0.62, 95% CI 0.35–0.9) and platelet count (6.32, 95% CI 4.18–8.47) were each found to decrease for every 1 μg/m^3 increase in $PM_{2.5}$ exposure level (supplementary table 12). Moreover, we detected the following associations for every 1 μg/m^3 increase in $PM_{2.5}$ level: B-type natriuretic peptides, 5.36 pg/mL, 95% CI 3.85 pg/mL - 6.88 pg/mL; serum creatinine levels, 0.02 mg/dL, 95% CI 0.02 mg/dL −0.03 mg/dL; HbA1C, 0.05%, 95% CI 0.02%–0.09%; serum uric acid, 0.06 mg/dL, 95% CI 0.02 mg/dL - 0.11 mg/dL; and serum ferritin, 8.63 ng/mL, 95% CI 5.25 ng/mL −12.01 ng/m (supplementary table 13).

4.5. Feature importance

Random forest models, trained using exposure data at different life stages, were used to investigate impacts on the incidence of chronic diseases (Fig. 1). The exposure levels of individuals at >40 years demonstrated the highest Shapley values for the prevalence of metabolic syndrome (35%), hypertension (39%), diabetes mellitus (35%), and cardiovascular diseases (36%). Exposures occurring at less than 20 years of age demonstrated the second highest Shapley values for the prevalence of metabolic syndrome (33%), hypertension (33%), diabetes mellitus (35%), and cardiovascular diseases (35%). Among the models evaluating metabolic syndrome, hypertension, diabetes mellitus, and cardiovascular diseases, higher $PM_{2.5}$ exposure levels (shown in red) were associated with higher Shapley values, especially in regard to exposures occurring at >40 years. Variables were arranged from top to bottom according to their Shapley values, with high values represented in red and low values represented in blue.

Table 2
Exponentially weighted moving averages for the $PM_{2.5}$ exposure level in the three life stages and chronic diseases.

Categorical Variables	ORs (95% CI)					
	Model-1 *(x, y, z)* #	Model-2 *(x, z, y)* #	Model-3 *(y, x, z)* #	Model-4 *(z, x, y)* #	Model-5 *(y, z, x)* #	Model-6 *(z, y, x)* #
α = 0.3 (x = 0.2; y = 0.47; z = 0.33)	***(0.2, 0.47, 0.33)***	***(0.2, 0.33, 0.47)***	***(0.47, 0.2, 0.33)***	***(0.33, 0.2, 0.47)***	***(0.47, 0.33, 0.2)***	***(0.33, 0.47, 0.2)***
Metabolic syndrome	1.0 (0.94, 1.07)	1.03 (0.95, 1.12)	1.0 (0.95, 1.05)	1.03 (0.96, 1.1)	0.99 (0.95, 1.04)	0.99 (0.94, 1.04)
Hypertension	0.99 (0.92, 1.07)	1.05 (0.96, 1.15)	0.97 (0.91, 1.02)	1.0 (0.93, 1.08)	**0.95 (0.9, 1.0)***	0.96 (0.91, 1.02)
Diabetes mellitus	1.09 (0.98, 1.21)	**1.14 (1.01, 1.29)***	1.03 (0.96, 1.1)	1.08 (0.98, 1.2)	1.02 (0.95, 1.09)	1.04 (0.96, 1.12)
Cardiovascular diseases	1.02 (0.9, 1.15)	1.08 (0.93, 1.27)	0.99 (0.9, 1.08)	1.04 (0.91, 1.18)	0.97 (0.9, 1.05)	0.98 (0.89, 1.07)
Gout	0.94 (0.74, 1.19)	0.99 (0.73, 1.35)	1.05 (0.85, 1.29)	1.08 (0.81, 1.44)	1.01 (0.84, 1.21)	0.97 (0.79, 1.18)
Osteoarthritis	1.17 (0.94, 1.47)	1.23 (0.95, 1.6)	1.13 (0.97, 1.31)	1.21 (0.97, 1.5)	1.11 (0.96, 1.27)	1.13 (0.95, 1.34)
α = 0.5 (x = 0.4; y = 0.4; z = 0.2)	***(0.4, 0.4, 0.2)***	***(0.4, 0.2, 0.4)***	***(0.4, 0.4, 0.2)***	***(0.2, 0.4, 0.4)***	***(0.4, 0.2, 0.4)***	***(0.2, 0.4, 0.4)***
Metabolic syndrome	0.99 (0.94, 1.04)	1.01 (0.95, 1.07)	0.99 (0.94, 1.04)	1.01 (0.94, 1.09)	1.01 (0.95, 1.07)	1.01 (0.94, 1.09)
Hypertension	0.96 (0.91, 1.01)	0.98 (0.92, 1.04)	0.96 (0.91, 1.01)	1.02 (0.94, 1.1)	0.98 (0.92, 1.04)	1.02 (0.94, 1.1)
Diabetes mellitus	1.03 (0.96, 1.1)	1.05 (0.96, 1.14)	1.03 (0.96, 1.1)	1.12 (1.0, 1.25)	1.05 (0.96, 1.14)	1.12 (1.0, 1.25)
Cardiovascular diseases	0.97 (0.89, 1.06)	1.0 (0.9, 1.11)	0.97 (0.89, 1.06)	1.05 (0.91, 1.2)	1.0 (0.9, 1.11)	1.05 (0.91, 1.2)
Gout	0.99 (0.82, 1.2)	1.06 (0.83, 1.36)	0.99 (0.82, 1.2)	0.96 (0.73, 1.26)	1.06 (0.83, 1.36)	0.96 (0.73, 1.26)
Osteoarthritis	1.12 (0.96, 1.31)	1.16 (0.97, 1.4)	1.12 (0.96, 1.31)	1.2 (0.94, 1.54)	1.16 (0.97, 1.4)	1.2 (0.94, 1.54)
α = 0.9 (x = 0.89; y = 0.1; z = 0.01)	***(0.89, 0.1, 0.01)***	***(0.89, 0.01, 0.1)***	***(0.1, 0.89, 0.01)***	***(0.01, 0.89, 0.1)***	***(0.1, 0.01, 0.89)***	***(0.01, 0.1, 0.89)***
Metabolic syndrome	0.99 (0.97, 1.02)	0.99 (0.97, 1.02)	0.98 (0.93, 1.02)	0.98 (0.94, 1.03)	**1.15 (1.06, 1.25)****	**1.12 (1.04, 1.21)****
Hypertension	**0.96 (0.94, 0.99)****	**0.96 (0.93, 0.99)****	0.97 (0.93, 1.02)	0.99 (0.94, 1.04)	**1.29 (1.17, 1.42)****	**1.29 (1.17, 1.42)****
Diabetes mellitus	1.0 (0.96, 1.03)	1.0 (0.96, 1.04)	1.03 (0.97, 1.11)	1.05 (0.97, 1.13)	**1.18 (1.05, 1.32)****	**1.17 (1.05, 1.30)***
Cardiovascular diseases	0.97 (0.93, 1.02)	0.98 (0.93, 1.02)	0.98 (0.91, 1.06)	1.0 (0.91, 1.08)	**1.27 (1.10, 1.48)****	**1.28 (1.11, 1.47)****
Gout	1.03 (0.92, 1.14)	1.04 (0.93, 1.16)	0.91 (0.8, 1.04)	0.9 (0.79, 1.03)	1.19 (0.89, 1.61)	1.1 (0.82, 1.49)
Osteoarthritis	1.05 (0.97, 1.13)	1.05 (0.98, 1.13)	1.06 (0.92, 1.22)	1.05 (0.91, 1.22)	1.13 (0.92, 1.38)	1.08 (0.89, 1.32)

Note: $x = \alpha/[\alpha+(1-\alpha)+(1-\alpha)^2]$, $y = (1-\alpha)/[\alpha+(1-\alpha)+(1-\alpha)^2]$, $z = (1-\alpha)^2/[\alpha+(1-\alpha)+(1-\alpha)^2]$.
#Permutation distribution: The weighted values were assigned as follows: (stage-1, stage-2, stage-3).
*$p < 0.05$; **$p < 0.01$.

Table 3
Exponentially weighted moving averages for the $PM_{2.5}$ exposure level in the three life stages and pulmonary functions.

β coefficient (95% CI)						
Categorical Variables	Model-1 *(x, y, z)* #	Model-2 *(x, z, y)* #	Model-3 *(y, x, z)* #	Model-4 *(z, x, y)* #	Model-5 *(y, z, x)* #	Model-6 *(z, y, x)* #
α = 0.3 (x = 0.2; y = 0.47; z = 0.33)	***(0.2, 0.47, 0.33)***	***(0.2, 0.33, 0.47)***	***(0.47, 0.2, 0.33)***	***(0.33, 0.2, 0.47)***	***(0.47, 0.33, 0.2)***	***(0.33, 0.47, 0.2)***
FVC (ml)	−5.6 (−27.31, 16.1)	−11.65 (−37.28, 13.98)	2.67 (−13.48, 18.82)	−3.48 (−25.65, 18.7)	3.39 (−11.32, 18.1)	1.22 (−15.87, 18.32)
FEV_1 (ml)	−1.03 (−18.65, 16.6)	−7.75 (−28.56, 13.06)	3.68 (−9.44, 16.79)	−1.94 (−19.95, 16.06)	4.98 (−6.96, 16.92)	4.26 (−9.62, 18.13)
FEV_1/FVC	0.17 (−0.12, 0.46)	0.09 (−0.25, 0.43)	0.06 (−0.16, 0.28)	0.04 (−0.26, 0.34)	0.09 (−0.1, 0.29)	0.15 (−0.08, 0.37)
α = 0.5 (x = 0.4; y = 0.4; z = 0.2)	***(0.4, 0.4, 0.2)***	***(0.4, 0.2, 0.4)***	***(0.4, 0.4, 0.2)***	***(0.2, 0.4, 0.4)***	***(0.4, 0.2, 0.4)***	***(0.2, 0.4, 0.4)***
FVC (ml)	2.52 (−13.42, 18.46)	0.56 (−18.29, 19.42)	2.52 (−13.42, 18.46)	−8.3 (−31.96, 15.37)	0.56 (−18.29, 19.42)	−8.3 (−31.96, 15.37)
FEV_1 (ml)	4.78 (−8.16, 17.72)	1.8 (−13.51, 17.11)	4.78 (−8.16, 17.72)	−3.91 (−23.13, 15.3)	1.8 (−13.51, 17.11)	−3.91 (−23.13, 15.3)
FEV_1/FVC	0.12 (−0.1, 0.33)	0.06 (−0.2, 0.31)	0.12 (−0.1, 0.33)	0.14 (−0.18, 0.46)	0.06 (−0.2, 0.31)	0.14 (−0.18, 0.46)
α = 0.9 (x = 0.89; y = 0.1; z = 0.01)	***(0.89, 0.1, 0.01)***	***(0.89, 0.01, 0.1)***	***(0.1, 0.89, 0.01)***	***(0.01, 0.89, 0.1)***	***(0.1, 0.01, 0.89)***	***(0.01, 0.1, 0.89)***
FVC (ml)	4.14 (−4.3, 12.59)	4.11 (−4.59, 12.81)	−1.44 (−16.08, 13.19)	−4.29 (−19.78, 11.2)	**−29.63 (-55.66, -3.6)***	**−28.94 (-52.7, -5.17)***
FEV_1 (ml)	4.39 (−2.47, 11.24)	4.18 (−2.88, 11.24)	2.95 (−8.94, 14.83)	0.52 (−12.06, 13.1)	**−31.82 (-52.9, -10.75)****	**−29.66 (-48.9, -10.41)****
FEV_1/FVC	0.04 (−0.08, 0.15)	0.03 (−0.09, 0.15)	0.19 (−0.0, 0.39)	0.19 (−0.02, 0.4)	−0.32 (−0.67, 0.03)	−0.25 (−0.56, 0.07)

Note: $x = \alpha/[\alpha+(1-\alpha)+(1-\alpha)^2]$, $y = (1-\alpha)/[\alpha+(1-\alpha)+(1-\alpha)^2]$, $z = (1-\alpha)^2/[\alpha+(1-\alpha)+(1-\alpha)^2]$.
#Permutation distribution: The weighted values were assigned as follows: (stage-1, stage-2, stage-3).
Abbreviation: FVC, forced vital capacity; FEV_1, forced expiratory volume at 1st second.
*$p < 0.05$; **$p < 0.01$.

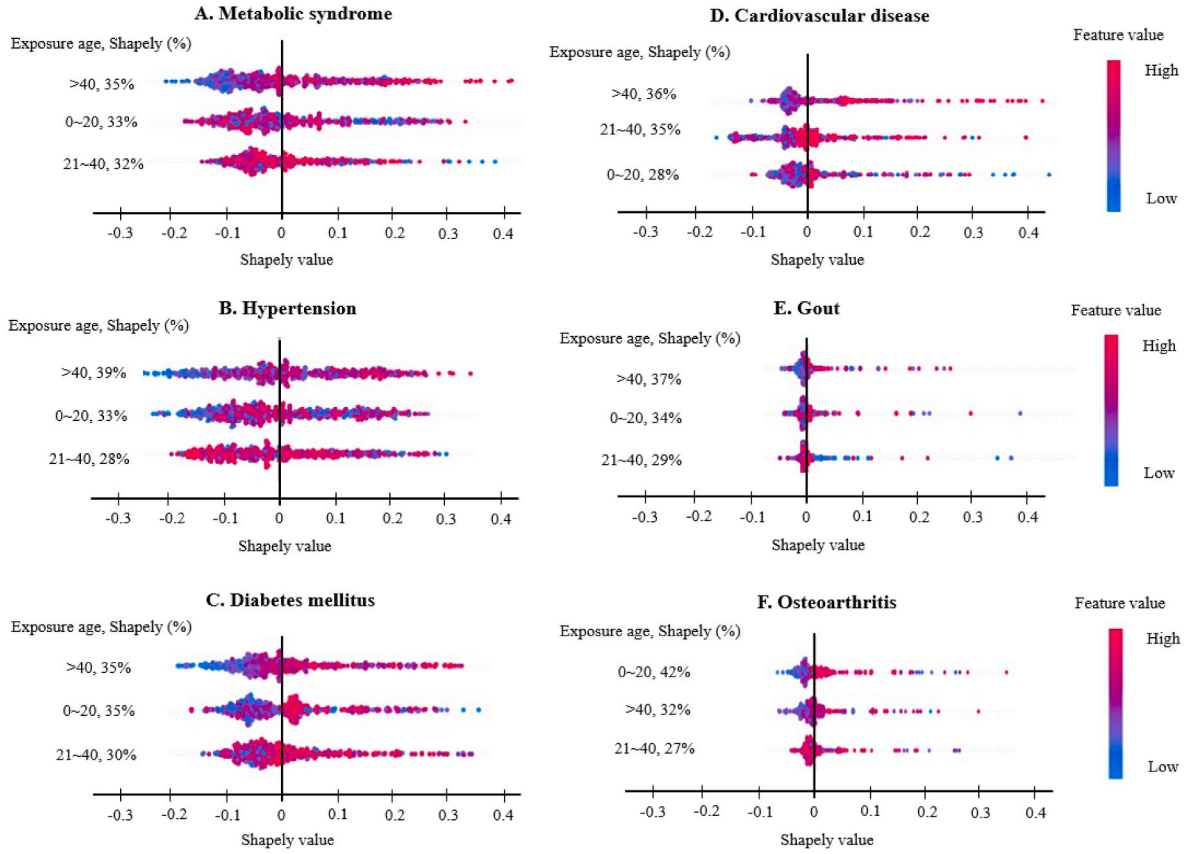


Fig. 1. Density scatter plot of Shapley values evaluating the importance of exposure stage in regard to the evaluated medical conditions. The x-axis represents the Shapley value for each air pollution measurement. The y-axis shows the relative importance of air pollution levels at different exposure stages in ascending order (i.e., according to their mean Shapley values). Different colors illustrate the exact values for the concentrations of each air pollutant, wherein red represents a high exposure value and blue represents a low exposure value.

4.6. Comparisons between the lifetime and late-stage models

Comparisons of performance indices, including in regard to precision, accuracy, F1 scores, and equal error rates, between the lifetime and late-stage models are shown in Fig. 2. The lifetime models showed higher precision, accuracy, and F1 scores in regard to metabolic syndrome (94%, 92%, 92%), hypertension (97%, 95%, 92%), diabetes mellitus (91%, 96%, 90%), and cardiovascular disease (95%, 98%, 92%), as well as lower precision, accuracy, and F1 scores for metabolic syndrome (70%, 70%, 61%), hypertension (79%, 79%, 60%), diabetes mellitus (71%, 87%, 56%), and cardiovascular disease (100%, 94%, 63%). The equal error rate was higher in the late-stage models than in the lifetime models in regard to metabolic syndrome (30% vs. 8%), hypertension (21% vs. 5%), diabetes mellitus (13% vs. 4%), and cardiovascular disease (6% vs. 2%). Hence, the lifelong exposure model demonstrated a better performance overall than the late-stage exposure model.

5. Discussion

Exposure to high-level $PM_{2.5}$ is known to elevate the risk for various chronic diseases as well as to result in lung function declines. However, most available evidence to date is based on short-term exposure data, and lifetime exposure has been less studied. Hence, this study was conducted to evaluate associations between pollution levels and the incidence of chronic disease at various lifetime stages of exposure (Pun et al., 2017; Wang et al., 2018) and employed an exponentially weighted moving average to establish lifelong $PM_{2.5}$ exposure patterns. The models with 89% weighting on late-stage exposure revealed significant associations of $PM_{2.5}$ with metabolic syndrome, hypertension, diabetes mellitus, and cardiovascular disease. Moreover, the random forest model considering lifelong exposure showed higher precision, accuracy, and F1 scores, as well as a lower equal error rate as compared with the model incorporating only participants' late-stage exposure profiles.

In terms of the associations between lifelong $PM_{2.5}$ exposure pattern and chronic diseases, we note that the exponentially weighted moving average models simulate different exposure patterns and that different lifetime exposure patterns were considered in the risk analysis. Exposure patterns with high weighting in the late-stage exposure model were significantly associated with the risk of developing various chronic diseases. This may be partially explained by the aging process, such that exposure later in life may be associated with more susceptibility to toxic agents. In other words, the immune system declines in individuals at later life stages (Peled, 2011), and aging is considered a risk factor for bioreactions due to air pollution exposure (Pope 3rd, 2000). These outcomes are consistent with previous observations. For example, previous researchers have that late-stage exposure to $PM_{2.5}$ could potentially cause a greater level adverse health effects as compared with exposures experienced earlier in life, as well as that elderly people have been observed to demonstrate stronger associations between increased

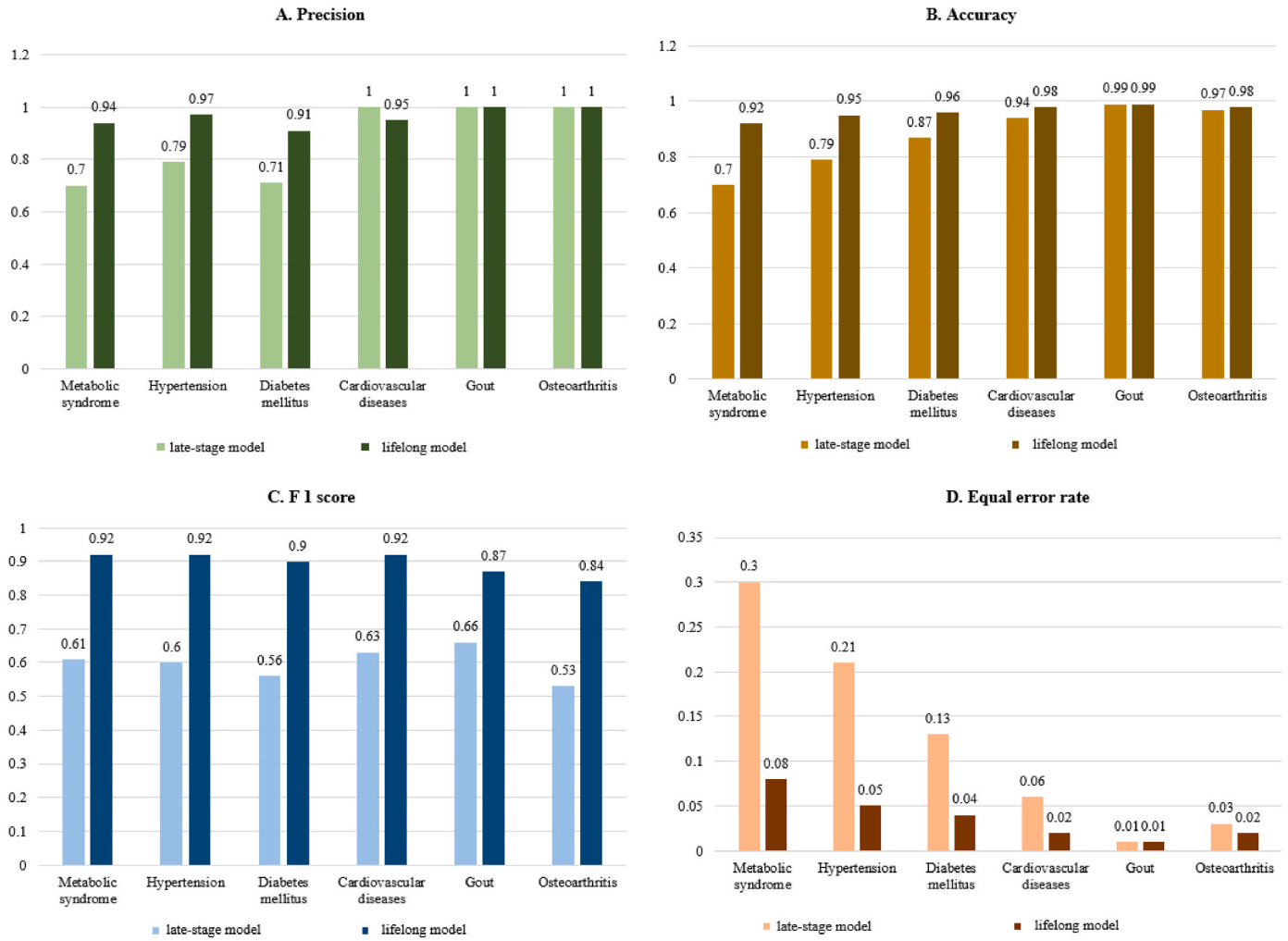


Fig. 2. Comparisons of performance between the model trained only using exposure levels at the last stage (i.e., >40 years) and the model developed by employing lifetime exposure measurements.

$PM_{2.5}$ levels and oxidative stress, systemic inflammatory biomarkers, and the risks of several chronic diseases as compared with younger individuals (Altuwayjiri et al., 2021; Kim et al., 2009). Similarly, a review described and interpreted the findings of various epidemiological studies evaluating the health effects of $PM_{2.5}$ in diverse populations (Sacks et al., 2011). These researchers documented that, within studies conducted to date, elderly individuals were generally considered susceptible to this pollutant because of their declining physiological functions. The above effects were stronger in regard to chronic systemic diseases, including metabolic syndrome, hypertension, diabetes mellitus, and cardiovascular diseases, than in gout or osteoarthritis.

We observed similar outcomes for lung function parameters as compared to the findings observed for disease prevalence. Specifically, exposure patterns with higher weighting in the later life stage were significantly associated with declines in lung function parameters, particularly FVC and FEV_1. This may indicate that, when older adults are exposed to air pollutants, they are more likely to experience serious inflammatory responses and to consequently exhibit an elevated mortality risk (Chen et al., 2012; Yu et al., 2012). Additionally, we note that both FEV_1 and FVC declined in our participants, which implies that $PM_{2.5}$ may increase the risk of developing restrictive lung disease (Xu et al., 2021). The associations between $PM_{2.5}$ and obstructive lung diseases have previously been investigated in detail (Li et al., 2018; Zhao et al., 2019), whereas the mechanisms underlying the effects of air pollutants on the development of restrictive lung disease remain unclear. One possible explanation for the observations reported herein is that $PM_{2.5}$ induces lung fibrosis (Sun et al., 2020). More specifically, this progression leads to restrictive lung volume and reduces lung resilience, thereby reducing lung capacity. Moreover, the current findings are in line with the observations of previous studies. For example, an animal experiment documented that $PM_{2.5}$ can enhance fibrosis gene expression and induce lung inflammation, thereby causing histological fibrosis in mice (Xu et al., 2021). Similarly, other researchers have observed that $PM_{2.5}$ exposure can restrain lung function (e.g., cause reductions in both FEV_1 and FVC), thereby increasing respiratory disease occurrence among the recruited elders evaluated in these investigations (Chu et al., 2018; Eckel et al., 2012). Overall, lifelong exposure to $PM_{2.5}$, especially in the late stage, was significantly associated with lung function impairment in the current study.

Next, the present study established a random forest model based on lifelong exposure pattern data in order to compare the relative importance of exposures occurring at various life stages more comprehensively. As the color designations in the Shapley distribution plots illustrate, higher $PM_{2.5}$ levels at a later stage resulted in higher Shapley values, corresponding to a greater probability of the occurrence of metabolic syndrome, hypertension, diabetes mellitus, and cardiovascular diseases. These results are consistent with our present observations obtained from linear regression models, demonstrating that models with higher weight values for late-stage exposure showed significant associations in regard to the risk of developing these diseases. Therefore, according to the aforementioned observations, it seems that late-stage $PM_{2.5}$ exposure was the primary risk factor for disease incidence and lung function decline. This implies that evaluating late-stage exposure may be sufficient for assessing health effects and risks. To explore this possibility, we also developed a random forest model, trained using only late-stage exposure data, in order to comprehensively compare the performance of the lifetime random forest model regarding various disease classifications. As the derived observations show, the random forest model trained using lifetime data demonstrated higher performance than the late-stage models. This is inconsistent with the position that only considers recent exposure when exploring health hazard effects. In other words, although current epidemiological studies are mainly focused on the effects of short-term exposure occurring within a constrained period of the total life stage (Chiusolo et al., 2011; Yu and Chien, 2016), long-term accumulated exposure to $PM_{2.5}$ may be more strongly associated with chronic health effects (Boldo et al., 2006). Additionally, this study investigated the feature importance of the input variables, including $PM_{2.5}$ exposure values in the three separate life stages evaluated herein. Taken together, exposure to $PM_{2.5}$ in the late stage was the driver of effects on disease development, compared with exposure in the other (earlier) stages. However, lifetime exposure may provide more comprehensive information when examining the effects of $PM_{2.5}$ on disease risk, compared with exposure occurring during a single short-term life stage. Although air pollution exposure at the late stage of life has a dominant impact on the development of chronic disease, considering lifelong exposure in the model may provide more statistical power and are more robustness.

The present study has some strengths and limitations that should be addressed within future studies. First, per the long-term $PM_{2.5}$ exposure estimation, this study can compare the effects on the incidence of different chronic diseases and investigate the critical period of $PM_{2.5}$ exposure regarding health issues. Next, this study can establish models utilizing the exposure data from different stages and explore their prediction outcomes on disease incidence, which can assist in shedding light on the fact that lifelong exposure to air pollution should be considered when assessing effects in chronic diseases. Regarding the limitations, since long-term measurements of $PM_{2.5}$ levels (i.e., over the course of >50 years) were challenging to access, this study evaluated long-term estimated $PM_{2.5}$ levels derived using visibility data as well as $PM_{2.5}$ values measured in recent years. Other meteorological factors may contribute to bias in this regard, thereby affecting the derived long-term values. As this study visited various community centers during the daytime, the majority of recruited non-smoking participants were housekeepers (44.92%), retirees (36.97%), and public servants or government employees (8.68%). This distribution may indicate that the recruited participants had a relatively similar socioeconomic status. However, the social and economic impacts should be taken into account in future works. The current statistical analyses used subgroup analysis for potential confounding factors such as gender and smoking status, however, body mass index at younger age and detailed social economic status data are not complete in our recruited participants.

Next, to simplify and control for air pollution exposure sources, this study only recruited participants who were never smokers. However, this limited us in regard to investigating the associations between $PM_{2.5}$ exposure, lung function, and disease risk in current or former smokers. We also note that air pollution exposure patterns may differ considerably between individuals according to smoking history/status (Maga et al., 2017). In addition, most participants in the current dataset were women, possibly because this study excluded smokers. In addition, despite the fact that we performed the subgroup and sensitivity analyses considering the effect of smoking, passive smoking, and family history of chronic disease, the lifelong socio-economic factors may also affect the present observations. This sex ratio imbalance prevents us from generalizing the observed findings to all humans, as women and men commonly experience different processes and reactivities upon air pollution exposure (Clougherty, 2010). Although the current outcomes regarding some disease incidence were derived from data obtained from medical physician interviews or clinical guidelines, the diagnoses of gout and osteoarthritis and the information of residential addresses were obtained through self-reported questionnaires. These may introduce bias, such as recall bias and response bias. Additionally, this study recruited participants from nearby locations in Northern Taiwan, which may have introduced potential survivor bias. Thus, to better determine the complex relationships between these above-mentioned parameters as well as to enhance the generalizability of our findings reported herein, datasets with approximately equal sex ratios as well as datasets containing data of ever smokers are essential for conducting more comprehensive evaluations within future research.

6. Conclusions

Exposure to high-level $PM_{2.5}$ in the later stage of life (>40 years) was

significantly associated with increased risks of metabolic syndrome, hypertension, diabetes mellitus, and cardiovascular disease. Nevertheless, the model considering lifelong exposure had higher associated precision, accuracy, and F1 scores as well as lower equal error rates than the model accounting for only individual late-stage exposure profile. These outcomes indicated a critical period of air pollution exposure concerning chronic disease incidence, which should be noted. Moreover, lifelong exposure to air pollution should be considered when evaluating effects on chronic diseases in a future study.

Author's contributions

Cheng-Yu Tsai: Conceptualization, Formal analysis, Methodology, Software, Writing - original draft, Visualization. **Chien-Ling Su**: Data curation, Formal analysis, Investigation, Methodology. **Yuan-Hung Wang:** Data curation, Formal analysis, Investigation, Methodology, Writing - original draft. **Sheng-Ming Wu:** Methodology, Formal analysis. **Wen-Te Liu:** Resources, Project administration, Funding acquisition. **Wen-Hua Hsu:** Investigation, Visualization. **Arnab Majumdar:** Validation, Supervision. **Marc Stettler:** Validation. **Kuan-Yuan Chen:** Project administration, Supervision. **Ya-Ting Lee:** Data curation, Investigation. **Chaur-Jong Hu:** Resources, Project administration. **Kang-Yun Lee:** Project administration, Supervision. **Ben-Jei Tsuang**: Methodology, Validation. **Chien-Hua Tseng:** Conceptualization, Supervision, Methodology, Project administration, Funding acquisition.

Funding

This work was supported by the Ministry of Science and Technology of Taiwan (MOST; grant numbers 110-2314-B-038-146-MY3 and 110–2634–F- 002–049), National Science and Technology Council of Taiwan (NSTC; grant number 111-2634-F-002-021),and the Featured Research Program "Establishment of Tucheng Health Care Cohort" of Shuang Ho Hospital, Taipei Medical University (grant numbers 107FRP-02, 108FRP-01, 109FRP-01, 110FRP-01). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.115957.

References

Abbey, D.E., Ostro, B.E., Fraser, G., Vancuren, T., Burchette, R.J., 1995. Estimating fine particulates less than 2.5 microns in aerodynamic diameter (PM2.5) from airport visibility data in California. J. Expo. Anal. Environ. Epidemiol. 5 (2), 161–180. https://www.ncbi.nlm.nih.gov/pubmed/7492904.

Altuwayjiri, A., Taghvaee, S., Mousavi, A., Sowlat, M.H., Hassanvand, M.S., Kashani, H., Faridi, S., Yunesian, M., Naddafi, K., Sioutas, C., 2021. Association of systemic inflammation and coagulation biomarkers with source-specific PM2. 5 mass concentrations among young and elderly subjects in central Tehran. J. Air Waste Manag. Assoc. 71 (2), 191–208. https://doi.org/10.1080/10962247.2020.1806140.

Archer, K.J., Kimes, R.V., 2008. Empirical characterization of random forest variable importance measures. Comput. Stat. Data Anal. 52 (4), 2249–2260. https://doi.org/10.1016/j.csda.2007.08.015.

Biau, G., Scornet, E., 2016. A random forest guided tour. Test 25 (2), 197–227. https://doi.org/10.1007/s11749-016-0481-7.

Bo, Y., Chang, L.-y., Guo, C., Lin, C., Lau, A.K., Tam, T., Lao, X.Q., 2021. Reduced ambient PM2. 5, better lung function, and decreased risk of chronic obstructive pulmonary disease. Environ. Int. 156, 106706 https://doi.org/10.1016/j.envint.2021.106706.

Boldo, E., Medina, S., Le Tertre, A., Hurley, F., Mücke, H.-G., Ballester, F., Aguilera, I., 2006. Apheis: health impact assessment of long-term exposure to PM2. 5 in 23 European cities. Eur. J. Epidemiol. 21 (6), 449–458. https://doi.org/10.1007/s10654-006-9014-0.

Breiman, L., Friedman, J.H., Olshen, R.A., Stone, C.J., 2017. Classification and Regression Trees. Routledge. https://doi.org/10.1201/9781315139470.

Chen, J.-C., Schwartz, J., 2008. Metabolic syndrome and inflammatory responses to long-term particulate air pollutants. Environ. Health Perspect. 116 (5), 612–617. https://doi.org/10.1289/ehp.10565.

Chen, R., Kan, H., Chen, B., Huang, W., Bai, Z., Song, G., Pan, G., 2012. Association of particulate air pollution with daily mortality: the China air pollution and health effects study. Am. J. Epidemiol. 175 (11), 1173–1181. https://doi.org/10.1093/aje/kwr425.

Chiusolo, M., Cadum, E., Stafoggia, M., Galassi, C., Berti, G., Faustini, A., Bisanti, L., Vigotti, M.A., Dessì, M.P., Cernigliaro, A., 2011. Short-term effects of nitrogen dioxide on mortality and susceptibility factors in 10 Italian cities: the EpiAir study. Environ. Health Perspect. 119 (9), 1233–1238. https://doi.org/10.1289/ehp.1002904.

Chu, H., Xin, J., Yuan, Q., Zhang, X., Pan, W., Zeng, X., Chen, Y., Ma, G., Ge, Y., Du, M., 2018. Evaluation of vulnerable PM2. 5-exposure individuals: a repeated-measure study in an elderly population. Environ. Sci. Pollut. Control Ser. 25 (12), 11833–11840. https://doi.org/10.1007/s11356-018-1412-9.

Clougherty, J.E., 2010. A growing role for gender analysis in air pollution epidemiology. Environ. Health Perspect. 118 (2), 167–176. https://doi.org/10.1289/ehp.0900994.

de Oliveira, E.M., Oliveira, F.L.C., 2018. Forecasting mid-long term electric energy consumption through bagging ARIMA and exponential smoothing methods. Energy 144, 776–788. https://doi.org/10.1016/j.energy.2017.12.049.

Eckel, S.P., Louis, T.A., Chaves, P.H., Fried, L.P., Margolis, G, H., 2012. Modification of the association between ambient air pollution and lung function by frailty status among older adults in the Cardiovascular Health Study. Am. J. Epidemiol. 176 (3), 214–223. https://doi.org/10.1093/aje/kws001.

Enebish, T., Chau, K., Jadamba, B., Franklin, M., 2021. Predicting ambient PM2. 5 concentrations in Ulaanbaatar, Mongolia with machine learning approaches. J. Expo. Sci. Environ. Epidemiol. 31 (4), 699–708. https://doi.org/10.1038/s41370-020-0257-8.

Guo, L., Zheng, H., Lyu, Y., Liu, L., Kong, F., Wang, S., 2018. Trends in atmospheric particles and their light extinction performance between 1980 and 2015 in Beijing, China. Chemosphere 205, 52–61. https://doi.org/10.1016/j.chemosphere.2018.04.071.

Hayes, R.B., Lim, C., Zhang, Y., Cromar, K., Shao, Y., Reynolds, H.R., Silverman, D.T., Jones, R.R., Park, Y., Jerrett, M., 2020. PM2. 5 air pollution and cause-specific cardiovascular disease mortality. Int. J. Epidemiol. 49 (1), 25–35. https://doi.org/10.1093/ije/dyz114.

Kim, K., Park, E.-Y., Lee, K.-H., Park, J.-D., Kim, Y.-D., Hong, Y.-C., 2009. Differential oxidative stress response in young children and the elderly following exposure to PM2. 5. Environ. Health Prev. Med. 14 (1), 60–66. https://doi.org/10.1007/s12199-008-0060-y.

Kloog, I., Ridgway, B., Koutrakis, P., Coull, B.A., Schwartz, J.D., 2013. Long-and short-term exposure to PM2. 5 and mortality: using novel exposure models. Epidemiology 24 (4), 555. https://doi.org/10.1097/EDE.0b013e318294beaa.

Ko, Y.-C., Lee, C.-H., Chen, M.-J., Huang, C.-C., Chang, W.-Y., Lin, H.-J., Wang, H.-Z., Chang, P.-Y., 1997. Risk factors for primary lung cancer among non-smoking women in Taiwan. Int. J. Epidemiol. 26 (1), 24–31. https://doi.org/10.1093/ije/26.1.24.

Lawrence, R.L., Wood, S.D., Sheley, R.L., 2006. Mapping invasive plants using hyperspectral imagery and Breiman Cutler classifications (RandomForest). Rem. Sens. Environ. 100 (3), 356–362. https://doi.org/10.1016/j.rse.2005.10.014.

Li, N., Maesano, C.N., Friedrich, R., Medda, E., Brandstetter, S., Kabesch, M., Apfelbacher, C., Melter, M., Seelbach-Göbel, B., Annesi-Maesano, I., 2019. A model for estimating the lifelong exposure to PM2. 5 and NO2 and the application to population studies. Environ. Res. 178, 108629 https://doi.org/10.1016/j.envres.2019.108629.

Li, R., Zhou, R., Zhang, J., 2018. Function of PM2. 5 in the pathogenesis of lung cancer and chronic airway inflammatory diseases. Oncol. Lett. 15 (5), 7506–7514. https://doi.org/10.3892/ol.2018.8355.

Liu, D.-j., Li, L., 2015. Application study of comprehensive forecasting model based on entropy weighting method on trend of PM2. 5 concentration in Guangzhou, China. Int. J. Environ. Res. Publ. Health 12 (6), 7085–7099. https://doi.org/10.3390/ijerph120607085.

Maga, M., Janik, M.K., Wachsmann, A., Chrząstek-Janik, O., Koziej, M., Bajkowski, M., Maga, P., Tyrak, K., Wójcik, K., Gregorczyk-Maga, I., 2017. Influence of air pollution on exhaled carbon monoxide levels in smokers and non-smokers. A prospective cross-sectional study. Environ. Res. 152, 496–502. https://doi.org/10.1016/j.envres.2016.09.004.

Mahajan, S., Chen, L.-J., Tsai, T.-C., 2018. Short-term PM2. 5 forecasting using exponential smoothing method: a comparative analysis. Sensors 18 (10), 3223. https://doi.org/10.3390/s18103223.

Ni, X., Huang, H., Du, W., 2017. Relevance analysis and short-term prediction of PM2. 5 concentrations in Beijing based on multi-source data. Atmos. Environ. 150, 146–161. https://doi.org/10.1016/j.atmosenv.2016.11.054.

Nordeide Kuiper, I., Svanes, C., Markevych, I., Accordini, S., Bertelsen, R.J., Bråbäck, L., Heile Christensen, J., Forsberg, B., Halvorsen, T., Heinrich, J., Hertel, O., Hoek, G., Holm, M., de Hoogh, K., Janson, C., Malinovschi, A., Marcon, A., Miodini Nilsen, R.,

Sigsgaard, T., Johannessen, A., 2021. Lifelong exposure to air pollution and greenness in relation to asthma, rhinitis and lung function in adulthood. Environ. Int. 146, 106219 https://doi.org/10.1016/j.envint.2020.106219.
Peled, R., 2011. Air pollution exposure: who is at high risk? Atmos. Environ. 45 (10), 1781–1785. https://doi.org/10.1016/j.atmosenv.2011.01.001.
Pope 3rd, C., 2000. Epidemiology of fine particulate air pollution and human health: biologic mechanisms and who's at risk? Environ. Health Perspect. 108 (Suppl. 4), 713–723. https://doi.org/10.1289/ehp.108-1637679.
Pope III, C.A., Dockery, D.W., 2006. Health effects of fine particulate air pollution: lines that connect. J. Air Waste Manag. Assoc. 56 (6), 709–742. https://doi.org/10.1080/10473289.2006.10464485.
Pun, V.C., Kazemiparkouhi, F., Manjourides, J., Suh, H.H., 2017. Long-term PM2. 5 exposure and respiratory, cancer, and cardiovascular mortality in older US adults. Am. J. Epidemiol. 186 (8), 961–969. https://doi.org/10.1093/aje/kwx166.
Raaschou-Nielsen, O., Thorsteinson, E., Antonsen, S., Holst, G.J., Sigsgaard, T., Geels, C., Frohn, L.M., Christensen, J.H., Brandt, J., Pedersen, C.B., Hvidtfeldt, U.A., 2020. Long-term exposure to air pollution and mortality in the Danish population a nationwide study. eClinicalMedicine 28. https://doi.org/10.1016/j.eclinm.2020.100605.
Roberts, S., 2000. Control chart tests based on geometric moving averages. Technometrics 42 (1), 97–101. https://doi.org/10.1080/00401706.2000.10485986.
Rodopoulou, S., Stafoggia, M., Chen, J., de Hoogh, K., Bauwelinck, M., Mehta, A.J., Klompmaker, J.O., Oftedal, B., Vienneau, D., Janssen, N.A.H., Strak, M., Andersen, Z.J., Renzi, M., Cesaroni, G., Nordheim, C.F., Bekkevold, T., Atkinson, R., Forastiere, F., Katsouyanni, K., Hoek, G., 2022. Long-term exposure to fine particle elemental components and mortality in Europe: results from six European administrative cohorts within the ELAPSE project. Sci. Total Environ. 809, 152205 https://doi.org/10.1016/j.scitotenv.2021.152205.
Roth, A.E., 1988. The Shapley Value: Essays in Honor of Lloyd S. Shapley. Cambridge University Press.
Russ, T.C., Cherrie, M.P., Dibben, C., Tomlinson, S., Reis, S., Dragosits, U., Vieno, M., Beck, R., Carnell, E., Shortt, N.K., 2021. Life course air pollution exposure and cognitive decline: modelled historical air pollution data and the Lothian Birth Cohort 1936. J. Alzheim. Dis. 79 (3), 1063–1074. https://doi.org/10.3233/JAD-200910.
Sacks, J.D., Stanek, L.W., Luben, T.J., Johns, D.O., Buckley, B.J., Brown, J.S., Ross, M., 2011. Particulate matter–induced health effects: who is susceptible? Environ. Health Perspect. 119 (4), 446–454. https://doi.org/10.1289/ehp.1002255.
Scott, C.L., 2003. Diagnosis, prevention, and intervention for the metabolic syndrome. Am. J. Cardiol. 92 (1), 35–42. https://doi.org/10.1016/s0002-9149(03)00507-1.
Sun, B., Shi, Y., Li, Y., Jiang, J., Liang, S., Duan, J., Sun, Z., 2020. Short-term PM2. 5 exposure induces sustained pulmonary fibrosis development during post-exposure period in rats. J. Hazard Mater. 385, 121566 https://doi.org/10.1016/j.jhazmat.2019.121566.
Wang, Q., Wang, J., He, M.Z., Kinney, P.L., Li, T., 2018. A county-level estimate of PM2. 5 related chronic mortality risk in China based on multi-model exposure data. Environ. Int. 110, 105–112. https://doi.org/10.1016/j.envint.2017.10.015.
Xu, M., Wang, X., Xu, L., Zhang, H., Li, C., Liu, Q., Chen, Y., Chung, K.F., Adcock, I.M., Li, F., 2021. Chronic lung inflammation and pulmonary fibrosis after multiple intranasal instillation of PM2. 5 in mice. Environ. Toxicol. 36 (7), 1434–1446. https://doi.org/10.1002/tox.23140.
Yu, H.-L., Chien, L.-C., 2016. Short-term population-based non-linear concentration–response associations between fine particulate matter and respiratory diseases in Taipei (Taiwan): a spatiotemporal analysis. J. Expo. Sci. Environ. Epidemiol. 26 (2), 197–206. https://doi.org/10.1038/jes.2015.21.
Yu, I.T.S., Zhang, Y., Wilson, W.S.T., Yan, Q.H., jun Xu, Y., jun Xun, X., Wu, W., Ma, W.J., Tian, L.W., Tse, L.A., 2012. Effect of ambient air pollution on daily mortality rates in Guangzhou, China. Atmos. Environ. 46, 528–535. https://doi.org/10.1016/j.atmosenv.2011.07.055.
Zhang, J., McLaughlin, S.J., Li, L.W., 2019. Cumulative exposure to air pollution and subsequent mortality among older adults in China. J. Publ. Health 41 (3), 518–526. https://doi.org/10.1093/pubmed/fdy154.
Zhao, J., Li, M., Wang, Z., Chen, J., Zhao, J., Xu, Y., Wei, X., Wang, J., Xie, J., 2019. Role of PM2. 5 in the development and progression of COPD and its mechanisms. Respir. Res. 20 (1), 1–13. https://doi.org/10.1186/s12931-019-1081-3.
Zhu, Q., Xia, B., Zhao, Y., Dai, H., Zhou, Y., Wang, Y., Yang, Q., Zhao, Y., Wang, P., La, X., 2019. Predicting gestational personal exposure to PM2. 5 from satellite-driven ambient concentrations in Shanghai. Chemosphere 233, 452–461. https://doi.org/10.1016/j.chemosphere.2019.05.251.

Abbreviations

FEV_1: forced expiratory volume at 1st second
FVC: forced vital capacity
HbA1c: hemoglobin A1C
$PM_{2.5}$: Particulate matter of diameter equal to less than 2.5 μm