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Randomised controlled trial of a behavioural intervention to reduce exposure to $PM_{2.5}$ in patients with COPD

Jieun Kang^a, Hwan-Cheol Kim^b, Youngwon Jang^c, Jung Bok Lee^d, Jae Seung Lee^c, Yeon-Mok Oh^c, Hyun Woo Ji^e, Ji Ye Jung^{f,1,*}, Sei Won Lee^{c,1,*}

a Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Republic of Korea

^b Department of Occupational and Environmental Medicine, Inha University College of Medicine, Incheon, Republic of Korea

^c Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

^d Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, Seoul, Republic of Korea

e Division of Pulmonology, Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Goyang, Republic of Korea

^f Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

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ABSTRACT

Background: Fine particulate matter ($PM_{2.5}$) is a well-known risk factor for worse outcomes of chronic obstructive pulmonary disease (COPD). However, evidence-based guidance on effective personal behavioural strategies to minimise the effects of $PM_{2.5}$ is limited. This study aimed to assess the effectiveness of a behavioural intervention in reducing $PM_{2.5}$ exposure and improving clinical outcomes in patients with COPD.

Materials and Methods: Participants were 1:1 randomised, and the intervention group received a behavioural intervention consisting of five activities, while the control group received usual care. The participants were followed up for 9 months. The primary outcomes were differences in the score of St. George's Respiratory Questionnaire for patients with COPD (SGRQ-C) and COPD assessment test (CAT) from baseline.

Results: A total of 106 participants were enrolled and 102 completed the study. At the end of the study, the intervention group showed significant improvements in the primary outcomes compared to the control group, with a group difference of -5.9 in the reduction of total SGRQ-C (-3.4 vs. 2.5; p = 0.049) and -3.8 in the CAT score (-1.2 vs. 2.7; p = 0.001). Participants with good adherence to the intervention demonstrated a greater extent of improvement in CAT score and lower PM_{2.5} levels compared to those who had poor adherence or were in the control group. Regular checking of air quality forecasts was significantly associated with a reduction in CAT scores among all the intervention activities.

Conclusion: Individual-level behavioural interventions can be an effective strategy for mitigating the health hazards associated with $PM_{2.5}$.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a global public health concern affecting millions of individuals and is associated with high morbidity and mortality (Lozano et al. 2012; Vos et al. 2012). Exposure to noxious particles is the primary risk factor for COPD development (Ko and Hui 2012). Indeed, air pollution is a leading cause of COPD in never smokers (GBD 2019 Risk Factors Collaborators 2020) and smokers (Bourbeau et al. 2022; Wang et al. 2022). Particulate matter with diameter of less than 2.5 μ m (PM_{2.5}) is associated with the incidence (Liu et al. 2017), exacerbation (Atkinson et al. 2014), and mortality of individuals with COPD (Li et al. 2017a; Pun et al. 2017). Thus, reducing $PM_{2.5}$ exposure should be a key goal in preventing and managing COPD, with its significance comparable to that of smoking cessation.

Despite the widely recognised health hazards of $PM_{2.5}$, limited evidence-based guidance currently exists regarding effective behavioural strategies to reduce $PM_{2.5}$ exposure. Most studies have focussed on assessing the effects of air filters, particularly in patients with asthma (Park et al. 2021). Recently, Hansel et al. have provided a meaningful

* Corresponding authors.

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E-mail addresses: stopyes@yuhs.ac (J.Y. Jung), seiwon@amc.seoul.kr (S.W. Lee).

¹ These authors contributed equally as corresponding authors.

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insight into the potential benefits of environmental interventions in patients with COPD; their study demonstrated that air filters can effectively reduce indoor $PM_{2.5}$ concentration, improve quality of life, and reduce respiratory symptoms and exacerbations in patients with COPD (Hansel et al. 2022). These benefits were more pronounced in patients spending more time indoors. However, the effectiveness of other environmental or behavioural interventions has not been extensively studied.

Lifestyle and behavioural changes can be implemented at an individual level, and patients can easily receive education on these changes in clinical and community settings. Although a plethora of guidance exists on how to avoid $PM_{2.5}$ exposure, it often lacks scientific evidence (Powell et al. 2016). Recently, significant associations have been found between certain lifestyle factors and indoor $PM_{2.5}$ concentration (Kim et al. 2021). To determine whether these daily-life behaviours reduce $PM_{2.5}$ exposure and lead to improved clinical outcomes, we conducted a randomised controlled trial of a behavioural intervention targeting $PM_{2.5}$ exposure reduction in patients with COPD.

2. Materials and methods

2.1. Study design and participants

A multicentre, single-blinded, randomised controlled trial was conducted including patients with physician-diagnosed COPD from three university hospitals located in the capital region of South Korea. The inclusion criteria were individuals aged 40–79 years with forced expiratory volume at 1 s (FEV₁) < 80 % of the predicted value. Patients who met any of the following criteria were excluded: 1) absence of respiratory symptoms, 2) inability to respond to questionnaires, or 3) inability to understand air sampler device instructions. This study was approved by the Institutional Review Board of the Asan Medical Center (2021–0701), Severance Hospital (4–2021-0607), and Ilsan Paik Hospital (2021–05-042). All the participants provided written informed consent.

2.2. Randomisation and masking

After enrolment, indoor $PM_{2.5}$ concentrations were measured for a month in all participants' homes to identify the baseline $PM_{2.5}$ levels. Patients were randomised using a stratified block randomisation approach based on their baseline FEV₁ (55 % of the predicted) and $PM_{2.5}$ levels (16 µg/m³). Patients were assigned to either the intervention or control group with an allocation ratio of 1:1, using a random number table. Owing to the nature of the intervention, both participants and study personnel delivering education were aware of their group assignment. However, investigators conducting data analysis were masked. Participants were followed at their respective hospitals every 3 months. The total duration of the intervention spanned 9 months.

2.3. Intervention

The intervention group received behavioural interventions along with the standard treatment they were receiving. The intervention comprised five activities: (1) operating indoor air filters and regularly replacing filters, (2) regularly checking air quality forecast, (3) practising regular home ventilation by opening windows, (4) refraining from going outdoors when the air pollution level was high, and (5) adhering to their inhaler treatment. A PM_{2.5} concentration of $\geq 35 \ \mu g/m^3$ was considered a high level of air pollution based on South Korea's air quality classification system. Participants were encouraged to complete daily checklists to ensure their adherence to the interventions. During each visit, they received education on the hazardous effects of PM_{2.5} and the importance of behavioural change. Patients were advised to operate the air filters continuously, ideally 24 h a day. Air filters were rented to those who did not own one during the study period. The control group

continued to receive standard care without any instructions regarding behavioural modifications.

Behavioural patterns and changes during the study period were assessed using the health protection practice questionnaire at each visit for both groups. Details of the questionnaire are provided in the online supplement (Table S1).

2.4. Clinical data collection and PM_{2.5} exposure assessment

Participants' demographics, smoking history, body mass index, medical history, and exacerbation history were obtained during enrolment. Their socioeconomic status was assessed through a self-report questionnaire. Respiratory symptoms and health-related quality of life were assessed using the St. George's Respiratory Questionnaire for patients with COPD (SGRQ-C), COPD assessment test (CAT), and modified Medical Research Council grade at baseline and each follow-up visit. The development of acute exacerbation was monitored every month.

Detailed methods of the residential environment assessment and $PM_{2.5}$ exposure measurement are described in the online supplement (Kang et al. 2021). Both outdoor and indoor $PM_{2.5}$ concentrations were continuously monitored by 'Internet-of-things'-based devices installed inside and outside of all participants' houses. Additionally, participants were encouraged to record a time-activity diary and carry a portable $PM_{2.5}$ measuring device for 24 h before each follow-up visit.

2.5. Outcomes

The primary outcomes assessed were changes in the SGRQ-C and CAT scores from baseline. The proportions of SGRQ-C and CAT responders were compared between the intervention and control groups. A responder was defined as a patient who achieved the minimal clinically important difference. The minimal clinically important difference values were defined as 4 points for SGRQ-C (Jones 2005) and 2 points for CAT (Kon et al. 2014). Additionally, acute exacerbation rates were compared between the treatment groups. An acute exacerbation was defined as an acute worsening of respiratory symptoms that resulted in additional therapy (Global Initiative for Chronic Obstructive Lung Disease 2022). Outcomes were examined based on adherence levels; the intervention group was dichotomised below and above the median adherence rate calculated from the intervention checklists.

2.6. Statistical analyses

A sample size was calculated based on the results obtained from our prospective pilot study (Kim et al. 2023; Kim et al. 2021), considering a significance level of 0.05 and a statistical power of 0.8. The estimated sample size was 102 patients, with 51 individuals in each group. To account for possible 15 % losses to follow-up during the study, we aimed to enrol a minimum of 120 patients.

Data were presented as means \pm standard deviations or as medians (interquartile ranges [IQR]) for continuous variables and as numbers (%) for categorical variables. Baseline characteristics were compared using t-tests for continuous variables and the chi-squared or Fisher's exact tests for categorical variables. Changes in SGRQ-C and CAT scores from baseline were calculated at 3, 6, and 9 months, using the linear mixed regression model. The calculations were adjusted for the baseline score, and differences in the score changes between the treatment groups were compared. Negative binomial regression was used to estimate the incidence rate ratio for treatment differences in frequency rates of acute exacerbation. PM_{2.5} concentrations were analysed using the linear mixed regression model. The adherence rates for each intervention activity were reported as a percentage of days adhering to the intervention out of the total recorded days. The adherence rate for air filter use was calculated as the percentage of the time the air filter was operated out of the total recorded time. The overall adherence rate was determined based on the adherence rates of all five intervention

activities. All p-values were two-tailed, and p < 0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Analysis System (SAS) statistical software package, version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Baseline characteristics

From July 2021 to October 2021, 248 patients were screened for eligibility, of which 108 were randomised. Six patients dropped out during the follow-up, leaving 102 patients completing the study (51 each in the intervention and control groups) (Fig. 1).

The mean age of all patients was 67.8 years and 93.1 % were men. The mean post-bronchodilator FEV_1 was 56.8 % of the predicted value. The two groups did not exhibit any significant differences in demographic characteristics, COPD symptom status, or PM_{2.5} concentrations (Table 1). Moreover, no significant differences were observed in the residential environments and lifestyle behaviours associated with PM_{2.5} exposure (Table S2).

3.2. Behavioural changes in study patients

At baseline, no significant differences were observed between the two groups in terms of their practice scores for the five behavioural intervention activities. However, the intervention group demonstrated significant improvement during the study period and high scores at the end of the study for all intervention behaviours. Conversely, no such changes were observed in the control group (Figure S1). The scores for regular inhaler use remained consistently high in both groups throughout the study period.

3.3. Effects of behavioural intervention

At the end of the study, the intervention group demonstrated significant improvement in the total SGRQ-C score than that in the control group (-3.4 vs. 2.5; group difference, -5.9; p = 0.049) as illustrated in Fig. 2. The intervention group also demonstrated a significant reduction in the symptom domain of SGRQ-C at 6 (-5.1 vs. 2.8; group difference,-7.9; p = 0.011) and 9 months (-9.7 vs. -2.9; group difference, -6.8; p = 0.030) than that of the control group. The SGRO-C total, symptom domain, and activity domain scores in the intervention group showed a gradual decrease over time. Additionally, the group difference for the scores of SGRQ-C total, activity, and impact domain showed an increasing trend. Significant differences were observed in CAT scores changes, favouring the intervention group at 6 (0.7 vs. 3.2; group difference, -2.5; p = 0.045) and 9 months (-1.2 vs. 2.7; group difference, -3.8; p = 0.001) (Fig. 3). The group difference for the CAT scores showed an increasing trend over the study period. The respective SGRQ-C total and its domain scores at 3, 6, and 9 months from the start of the intervention are presented in Table S3.

The proportions of SGRQ-C and CAT responders were numerically greater without statistical significance (42.0 vs. 32.7 %; p = 0.408) and significantly greater (51.0 vs. 24.5 %; p = 0.012), respectively in the intervention group than those in the control group (Table S4). No significant difference in the rate of exacerbation, regardless of the severity, was observed between the two groups (Table S5).

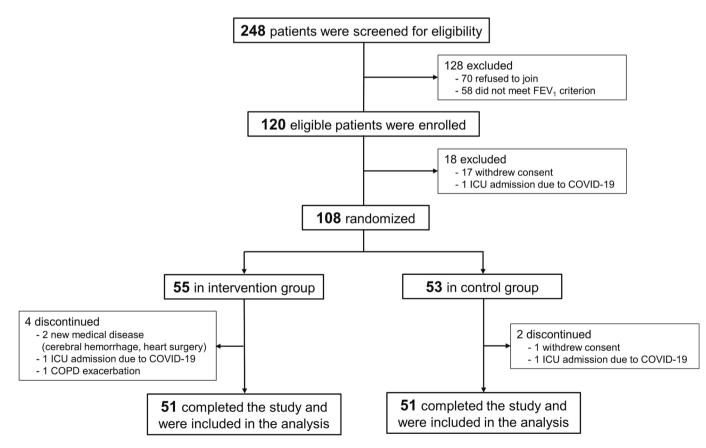


Fig. 1. Study flow. FEV₁, forced expiratory volume in one second; ICU, intensive care unit; COVID-19, coronavirus disease 2019; COPD, chronic obstructive pulmonary disease.

Table 1

Baseline characteristics of study patients with COPD.

	All (n = 102)	Intervention (n = 51)	Control (n = 51)	p* 0.520
Age (years)	67.8 ± 6.6	68.2 ± 6.7	67.4 ± 6.5	
Sex (male)	95 (93.1)	50 (98.0)	45 (88.2)	0.117
Smoking				0.899
Current smoker	18 (17.6)	9 (17.6)	9 (17.6)	
Former smoker	79 (77.5)	40 (78.4)	39 (76.5)	
Never smoker	5 (4.9)	2 (3.9)	3 (5.9)	
Pack-years	35.6 ± 17.4	35.8 ± 16.2	$\textbf{35.4} \pm \textbf{18.7}$	0.909
Body mass index (kg/m ²)	23.9 ± 3.7	23.5 ± 3.6	24.4 ± 3.7	0.198
Asthma	3 (2.9)	0 (0.0)	3 (5.9)	0.241
Education level				0.155
Middle school	32 (31.4)	14 (27.5)	18 (35.3)	
High school	39 (38.2)	25 (49.0)	14 (27.5)	
College	24 (23.5)	9 (17.6)	15 (29.4)	
Graduate school	7 (6.9)	3 (5.9)	4 (7.8)	
Monthly income (won)				0.318
>6,000,000	9 (8.8)	4 (7.8)	5 (9.8)	
4,000,000–6,000,000	15 (14.7)	10 (19.6)	5 (9.8)	
2,000,000–4,000,000	20 (19.6)	7 (13.7)	13 (25.5)	
1,000,000–2,000,000	20 (19.6)	8 (15.7)	12 (23.5)	
<1,000,000	24 (23.5)	15 (29.4)	9 (17.6)	
Unaware	14 (13.7)	7 (13.7)	7 (13.7)	
Self-assessment of socioeconomic status	11(10.7)	, (10.7)	, (15.7)	0.415
High	1 (1.0)	1 (2.0)	0 (0.0)	0.415
Middle high	15 (14.7)	8 (15.7)	7 (13.7)	
Middle	44 (43.1)	22 (43.1)	22 (43.1)	
Middle low	26 (25.5)	15 (29.4)	11 (21.6)	
Low	16 (15.7)	5 (9.8)	11 (21.6)	
	10 (13.7)	5 (9.8)	11 (21.0)	
Exacerbation during the past year	A (B A)	2 (2 0)	1 (0.0)	. 0.000
Moderate	3 (2.9)	2 (3.9)	1 (2.0)	>0.999
Severe	2 (2.0)	2 (3.9)	0 (0.0)	0.475
All (moderate-severe)	5 (4.9)	4 (7.8)	1 (2.0)	0.359
Lung function		0.5 1 0.1		0.004
Post-BD FEV ₁ /FVC	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.324
Post-BD FEV ₁ (%pred.)	56.8 ± 14.5	57.4 ± 15.7	56.2 ± 13.2	0.682
Post-BD FVC (%pred.)	82.2 ± 13.4	80.9 ± 13.4	83.6 ± 13.4	0.325
DL _{CO} (%pred.)	61.4 ± 18.0	59.5 ± 18.0	63.4 ± 18.0	0.278
Inhaler treatment				0.895
LABA + LAMA	53 (52.0)	27 (52.9)	26 (51.0)	
ICS + LABA + LAMA	37 (36.3)	17 (33.3)	20 (39.2)	
LABA or LAMA	7 (6.9)	4 (7.8)	3 (5.9)	
ICS + LABA	5 (4.9)	3 (5.9)	2 (3.9)	
SGRQ-C				
Total	$\textbf{35.2} \pm \textbf{18.5}$	35.3 ± 18.1	35.2 ± 19.2	0.892
Symptom	45.8 ± 20.3	46.7 ± 21.4	$\textbf{45.0} \pm \textbf{19.4}$	0.601
Activity	$\textbf{45.4} \pm \textbf{24.4}$	44.6 ± 22.9	46.2 ± 26.0	0.742
Impact	25.2 ± 20.9	$\textbf{25.8} \pm \textbf{21.0}$	24.6 ± 21.0	0.773
CAT score	15.5 ± 8.4	15.8 ± 8.8	15.2 ± 8.0	0.752
mMRC grade	2.4 ± 1.1	2.3 ± 1.0	2.5 ± 1.3	0.432
$PM_{2.5}$ levels ($\mu g/m^3$)				
Outdoor	14.8 ± 5.2	14.8 ± 4.8	14.8 ± 5.6	0.979
Indoor	12.1 ± 4.8	12.2 ± 4.4	11.9 ± 5.2	0.817
Estimated individual exposure	12.8 ± 4.3	12.9 ± 4.0	12.7 ± 4.7	0.884

Data are presented as numbers (%) or means \pm standard deviations.

COPD, chronic obstructive pulmonary disease; BD, bronchodilator; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; %pred, percent of the predicted value; DL_{CO}, diffusing capacity of the lungs for carbon monoxide; LABA, long-acting beta-2 agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroid; SGRQ-C, St. George's Respiratory Questionnaire for patients with COPD; CAT, COPD assessment test; mMRC, modified Medical Research Council; PM_{2.5}, particulate matter less than 2.5 µm in diameter.

p-values are provided for the comparison between the intervention and control group.

Considering that smoking is a significant contributor to indoor air pollution, a sensitivity analysis was performed by excluding current smokers from the analysis (Figures S2 and S3). These results also demonstrated favourable outcomes in the intervention group, showing greater reductions in both the SGRQ-C (symptom domain) and CAT scores.

3.4. Outcomes based on the intervention adherence

In the intervention group, 49 patients (96.1 %) completed the intervention checklist, allowing adherence assessment in these patients. Overall, the checklist was completed in a median of 92.8 % of the total

study days (IQR, 86.0–100.0 %). The median adherence rate of the five activities combined was 80.0 % (IQR, 67.8–91.6 %) (Table S6). Significant differences were observed between the good and poor adherence groups in terms of air filter use (91.4 vs. 28.1 %) and refraining from going out (98.9 vs. 23.3 %). However, adherence rates to other activities did not reveal significant differences (Table S7).

No significant differences were observed in the baseline characteristics between the three groups, except for the number of severe exacerbations in the previous year, which was more frequent in the good adherence group than that in other groups (Table S8). At the end of the study, participants with good and poor adherence, demonstrated greater reductions in SGRQ-C total score than those of the control group,

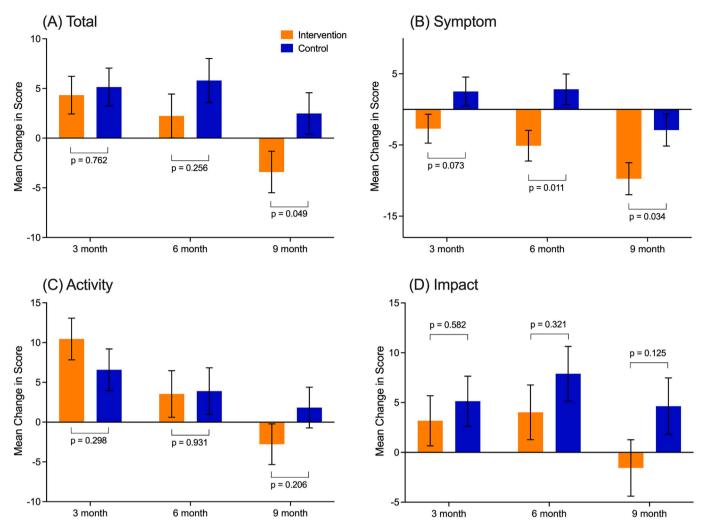


Fig. 2. Changes in the SGRQ-C score. Mean changes from the baseline score are shown for the intervention and control groups. (A) SGRQ-C total, (B) SGRQ-C symptom domain, (C) SGRQ-C activity domain, and (D) SGRQ-C impact domain. SGRQ-C, St. George's Respiratory Questionnaire for patients with chronic obstructive pulmonary disease (COPD).

although the differences were not significant (Fig. 4A). Participants with good adherence demonstrated significant reduction in CAT scores than that of the control group at all follow-up visits (Fig. 4B). No significant differences were observed in the rate of acute exacerbation between the three groups (Table S9).

3.5. PM_{2.5} levels

Outdoor $PM_{2.5}$ concentrations were not significantly different between the groups throughout the study period. However, indoor $PM_{2.5}$ concentrations in participants with good adherence were lower than those with poor adherence, demonstrating significant differences at 3 and 6 months. The good adherence group also demonstrated a significant difference in indoor $PM_{2.5}$ compared to the control group at 6 months. Similar trends were observed for the estimated individual $PM_{2.5}$ exposure levels (Fig. 5, Table S10).

3.6. Individual behavioural intervention activities and outcomes

To identify the behaviours associated with improvements in SGRQ-C and CAT scores, the participants were categorised based on their engagement in a behaviour at least five times per week throughout the study period. No significant differences were observed in the SGRQ-C total score for individual behaviour, although a trend towards improvement was noticed among those who practised the behaviour at least five times per week (Table 2). Participants who checked the air quality forecast at least five times per week demonstrated a significant improvement in the CAT score (group difference, -2.62; 95 % confidence interval (CI), -5.08 to -0.15; p = 0.038).

4. Discussion

In the present study, a behavioural intervention with five activities aimed at reducing $PM_{2.5}$ exposure demonstrated improved clinical outcomes in patients with COPD. Following 9 months, the intervention group showed enhanced compliance with lifestyle changes designed to minimise exposure to $PM_{2.5}$, resulting in greater reductions in SGRQ-C and CAT scores than those of the control group. Among all the intervention activities, regular checking of air quality forecasts was associated with significant reduction in the CAT scores.

The hazardous effects of $PM_{2.5}$ on the respiratory system are wellestablished. $PM_{2.5}$ exposure increases the COPD risk (Liu et al. 2017) and its progression, leading to increased hospitalisation rates (Atkinson et al. 2014). Moreover, $PM_{2.5}$ exposure during adolescence adversely affects lung function growth (Gauderman et al. 2004), increasing the risk of COPD in adulthood (Lange et al. 2015). The most effective solution to mitigate these hazards is to improve the ambient environment (Gauderman et al. 2004). However, improving ambient air quality can be challenging, especially when pollution sources extend beyond a single jurisdiction (Oh et al. 2015). While collaborative efforts involving

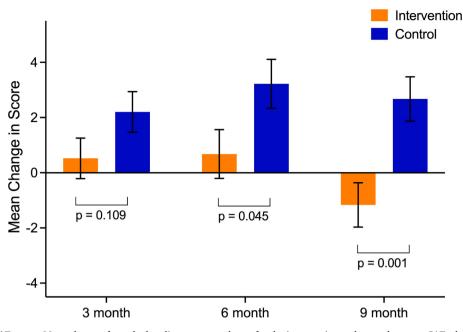


Fig. 3. Changes in the CAT score. Mean changes from the baseline score are shown for the intervention and control groups. CAT, chronic obstructive pulmonary disease (COPD) assessment test.

governments, industries, and communities, are essential to make a significant impact in reducing $PM_{2.5}$ pollution, individual actions can also play a crucial role in attenuating its harmful effects.

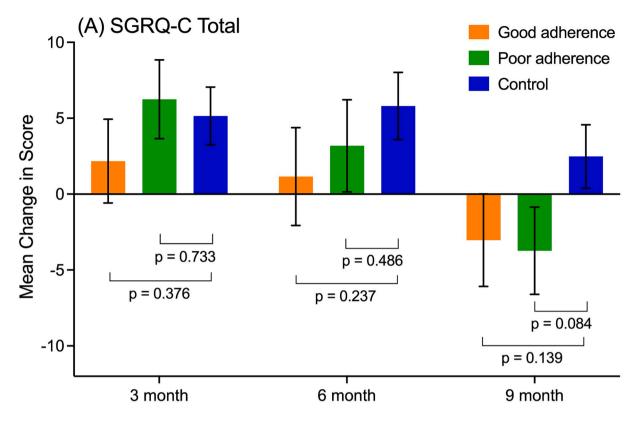
Using air filters is a practical way to control indoor air quality (Li et al. 2017b; Shao et al. 2017), particularly for patients with COPD who spend most of their time indoors (Almeida-Silva et al. 2014; Karottki et al. 2015). The Clean Air study investigated the impact of air filter intervention among former smokers with COPD, demonstrating a low rate of moderate exacerbations, few respiratory symptoms, and reduced reliance on rescue medications (Hansel et al. 2022). Similarly, our study also showed that good adherence to a behavioural intervention led to a significant reduction in indoor PM2.5 levels and improvements in clinical outcomes, including SGRQ-C total and symptom scores, and CAT score. However, no significant difference was observed in acute exacerbation rates between the intervention and control groups. While one-fourth of participants experienced moderate exacerbation in the Clean Air study, only 5 % experienced moderate-to-severe exacerbation in our study. It is worth noting that our study was conducted between 2021 and 2022, during the COVID-19 pandemic, and the low exacerbation rate could be influenced by precautionary measures, such as social distancing, maskwearing, and hand hygiene (Alqahtani et al. 2021).

In Canada, air quality alert programmes have effectively reduced asthma-related emergency department visits and COPD-related morbidity, although these programs did not exhibit significant impacts on mortality or other health outcomes (Chen et al. 2018). In South Korea, the implementation of the Air Quality Warning System (AQWS) led to a gradual reduction in the incidence of asthma by 20.5 % but had no distinct effect on the exacerbation of asthma or COPD (Park et al. 2023). In our study, checking the air quality forecast significantly improved the health-related quality of life in patients with COPD. These findings indicate that increased awareness and acknowledgement of air quality help improve clinical outcomes. The key difference between AQWS and air quality forecast checks lies in their passive or active nature. AQWS is a unilateral alert system that does not require the participant's attention, whereas the forecast check involves the participant's concern regarding the health effects of PM_{2.5}. Psychosocial factors may facilitate adherence to health advice for reduced outside activity during poor air quality events (D'Antoni et al. 2017).

The effect of reducing $PM_{2.5}$ levels by opening windows for ventilation should be assessed considering various factors. Outdoor $PM_{2.5}$ levels vary seasonally, with low levels in summer and high levels in winter, whereas indoor $PM_{2.5}$ levels remain stable without seasonal variation (Kim et al. 2021). Notably, $PM_{2.5}$ watches or warnings are issued for less than 30 days per year, while indoor $PM_{2.5}$ levels exceeding 75 ug/m³ occur more frequently (Seoul Metropolitan Government Air Qality Information, http://cleanair.seoul.go.kr [accessed 25 Oct 2023]). Although outdoor $PM_{2.5}$ levels can affect indoor concentrations, routine domestic activities, including smoking, cooking, and cleaning can also increase indoor levels of $PM_{2.5}$, carbon dioxide, and volatile organic compounds (Abdel-Salam 2021; Maung et al. 2022). These activities necessitate regular ventilation. However, caution should be exercised when opening windows during extremely high outdoor $PM_{2.5}$ levels (Kanatani et al. 2014).

The adherence rate in this study was slightly higher than that in previous studies, which solely utilized an air filter intervention (Eggleston et al. 2005; Hansel et al. 2022). The good adherence group demonstrated a significant reduction in indoor $PM_{2.5}$ levels and estimated individual $PM_{2.5}$ exposure, along with earlier improvement in CAT scores at 3 months. In the Clean Air study, only participants who used an air filter for at least 80 % of the study period met the primary endpoint of treatment difference in SGRQ (Hansel et al. 2022). These findings suggest that increasing adherence to behavioural interventions may enhance the intervention response.

This study had several limitations. First, ethical concerns could have been raised because no guidance was provided to the control group on how to avoid PM_{2.5} exposure, considering its known harmful effects. To date, however, the effectiveness of behavioural guidance to avoid PM_{2.5} exposure in chronic respiratory diseases was uncertain. Our study results provided valuable insights into the potential benefits of appropriate non-pharmacologic interventions in improving clinical outcomes for patients with COPD. Second, the study design of the behavioural intervention precluded blinding of the patients and educators to group assignment. However, the physicians and examiners were kept blinded throughout the study to minimize potential bias. Third, accurately measuring and standardising PM_{2.5} exposure could be challenging owing to the variability in concentrations based on geographic location,



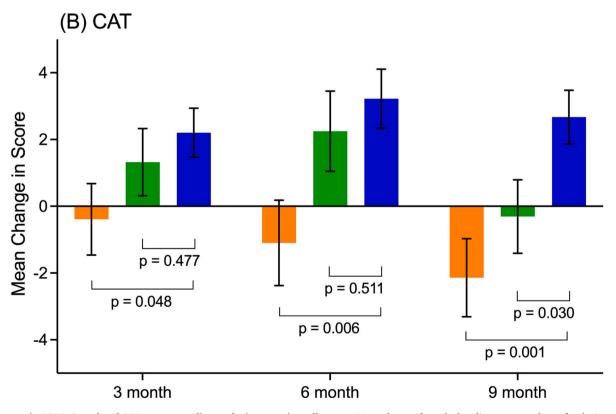


Fig. 4. Changes in SGRQ-C total and CAT score according to the intervention adherence. Mean changes from the baseline score are shown for the interventiongood adherence, intervention-poor adherence, and control groups. (A) SGRQ-C total and (B) CAT. SGRQ-C, St. George's Respiratory Questionnaire for patients with chronic obstructive pulmonary disease (COPD); CAT, chronic obstructive pulmonary disease (COPD) assessment test.

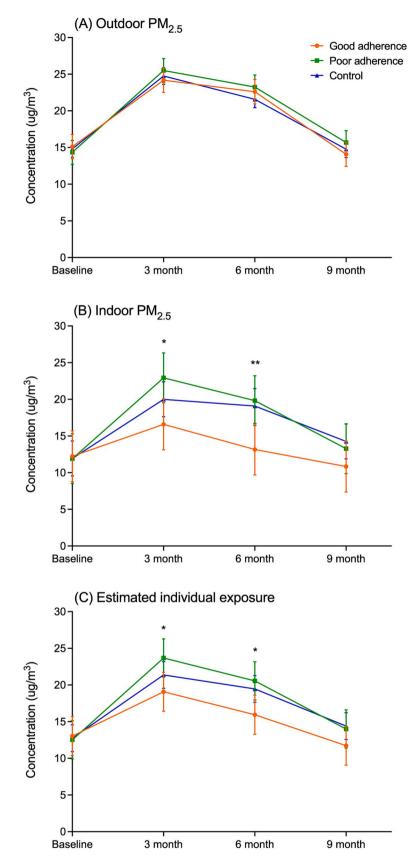


Fig. 5. PM_{2.5} concentrations. PM_{2.5} concentrations of the (A) outdoor, (B) indoor, and (C) estimated individual exposure are shown. PM_{2.5}, particulate matter less than 2.5 µm in diameter.

Table 2

Individual intervention activities and SGRQ-C and CAT changes.

	SGRQ-C			CAT				
	Mean change (SE)		Group difference	р	Mean change (SE)		Group difference	р
	\geq 5/week	< 5/week	(95 % CI)		\geq 5/week	<5/week	(95 % CI)	
Using an air filter	-1.52 (2.03)	-0.13 (2.20)	-1.39 (-7.30-4.52)	0.644	-0.38 (0.83)	1.68 (0.90)	-2.05 (-4.46-0.35)	0.094
Checking air quality forecasts	-1.98 (1.84)	0.91 (2.45)	-2.89 (-8.94-3.16)	0.347	-0.27 (0.75)	2.34 (1.00)	-2.62 (-5.08-0.15)	0.038
Ventilating by window opening	-0.94 (1.93)	-0.79 (2.38)	-0.15 (-6.21-5.91)	0.961	0.90 (0.79)	0.05 (0.97)	0.85 (-1.62-3.32)	0.497
Refraining from going out	-2.24 (2.55)	-0.17 (1.85)	-2.07 (-8.30-4.16)	0.513	0.56 (1.05)	0.56 (0.76)	-0.00 (-2.56-2.55)	0.999
Using inhalers regularly	-1.35 (1.63)	1.62 (3.78)	-2.97 (-11.09-5.15)	0.471	0.24 (0.66)	2.30 (1.55)	-2.06 (-5.38-1.26)	0.222

All analyses are adjusted for baseline scores.

SGRQ-C, St. George's Respiratory Questionnaire for patients with chronic obstructive pulmonary disease (COPD); CAT, COPD assessment test; SE, standard error; CI, confidence interval.

time of year, and local environmental factors, making it difficult to establish a clear dose–response relationship between $PM_{2.5}$ exposure and COPD outcomes. Fourth, living environments can greatly vary between countries and even domestically owing to cultural and regional differences. Therefore, further studies are necessary to determine the generalisability of our findings to broader populations of patients with COPD. Nonetheless, the consistent improvement in the symptom domain of the SGRQ-C suggests that this type of lifestyle intervention can be effective regardless of the region. Lastly, monthly income and socioeconomic status can be disparate depending on the amount of material possessions, although both statuses were not different between the two groups.

In conclusion, the behavioural intervention aimed at reducing $PM_{2.5}$ exposure in patients with COPD significantly improved the SGRQ-C and CAT scores, suggesting that implementation of individual-level behavioural changes could be an effective strategy for mitigating the health hazards associated with $PM_{2.5}$ in patients with COPD.

CRediT authorship contribution statement

Jieun Kang: Data curation, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. Hwan-Cheol Kim: Data curation, Formal analysis, Investigation, Resources, Supervision, Writing – review & editing. Youngwon Jang: Data curation, Investigation. Jung Bok Lee: . Jae Seung Lee: Investigation, Resources. Yeon-Mok Oh: Investigation, Resources. Hyun Woo Ji: Data curation, Investigation. Ji Ye Jung: Conceptualization, Data curation, Formal analysis, Investigation, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing. Sei Won Lee: Conceptualization, Data curation, Formal analysis, Investigation, Funding acquisition, Project administration, Supervision, Writing – original draft, Writing – review & editing.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108286.

References

- Abdel-Salam, M.M.M., 2021. Outdoor and indoor factors influencing particulate matter and carbon dioxide levels in naturally ventilated urban homes. J. Air Waste Manag. Assoc. 71, 60–69.
- Almeida-Silva, M., Wolterbeek, H.T., Almeida, S., 2014. Elderly exposure to indoor air pollutants. Atmos. Environ. 85, 54–63.
- Alqahtani, J.S., Oyelade, T., Aldhahir, A.M., Mendes, R.G., Alghamdi, S.M., Miravitlles, M., Mandal, S., Hurst, J.R., 2021. Reduction in hospitalised COPD exacerbations during COVID-19: A systematic review and meta-analysis. PLoS One 16, e0255659.
- Atkinson, R.W., Kang, S., Anderson, H.R., Mills, I.C., Walton, H.A., 2014. Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. Thorax 69, 660–665.
- Bourbeau, J.; Doiron, D.; Biswas, S.; Smith, B.M.; Benedetti, A.; Brook, J.R.; Aaron, S.D.; Chapman, K.R.; Hernandez, P.; Maltais, F.; Marciniuk, D.D.; O'Donnell, D.; Sin, D.D.; Walker, B.; Dsilva, L.; Nadeau, G.; Coats, V.; Compton, C.; Miller, B.E.; Tan, W.C.; Can, C.C.R.G.; the Canadian Respiratory Research, N. Ambient Air Pollution and Dysanapsis: Associations with Lung Function and Chronic Obstructive Pulmonary Disease in the Canadian Cohort Obstructive Lung Disease Study. Am J Respir Crit Care Med 2022;206:44-55.
- Chen, H., Li, Q., Kaufman, J.S., Wang, J., Copes, R., Su, Y., Benmarhnia, T., 2018. Effect of air quality alerts on human health: a regression discontinuity analysis in Toronto. Canada. Lancet Planet Health 2, e19–e26.
- D'Antoni, D., Smith, L., Auyeung, V., Weinman, J., 2017. Psychosocial and demographic predictors of adherence and non-adherence to health advice accompanying air quality warning systems: a systematic review. Environ. Health 16, 100.
- Eggleston, P.A., Butz, A., Rand, C., Curtin-Brosnan, J., Kanchanaraksa, S., Swartz, L., Breysse, P., Buckley, T., Diette, G., Merriman, B., Krishnan, J.A., 2005. Home environmental intervention in inner-city asthma: a randomized controlled clinical trial. Ann. Allergy Asthma Immunol. 95, 518–524.
- Gauderman, W.J., Avol, E., Gilliland, F., Vora, H., Thomas, D., Berhane, K., McConnell, R., Kuenzli, N., Lurmann, F., Rappaport, E., Margolis, H., Bates, D., Peters, J., 2004. The effect of air pollution on lung development from 10 to 18 years of age. N. Engl. J. Med. 351, 1057–1067.
- GBD 2019 Risk Factors Collaborators, 2020. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 396, 1223–1249.
- Hansel, N.N., Putcha, N., Woo, H., Peng, R., Diette, G.B., Fawzy, A., Wise, R.A., Romero, K., Davis, M.F., Rule, A.M., Eakin, M.N., Breysse, P.N., McCormack, M.C., Koehler, K., 2022. Randomized Clinical Trial of Air Cleaners to Improve Indoor Air Quality and Chronic Obstructive Pulmonary Disease Health: Results of the CLEAN AIR Study. Am. J. Respir. Crit. Care Med. 205. 421–430.
- Global Initiative for Chronic Obstructive Lung Disease. 2022 Global Strategy for Prevention, Diagnosis and Management of COPD. 2022.
- Jones, P.W., 2005. St. George's Respiratory Questionnaire: MCID. COPD 2, 75–79.

Kanatani, K.T., Okumura, M., Tohno, S., Adachi, Y., Sato, K., Nakayama, T., 2014. Indoor particle counts during Asian dust events under everyday conditions at an apartment in Japan. Environ. Health Prev. Med. 19, 81–88.

Kang, J., Jung, J.Y., Huh, J.Y., Ji, H.W., Kim, H.C., Lee, S.W., 2021. Behavioral interventions to reduce particulate matter exposure in patients with COPD. Medicine (Baltimore) 100, e28119.

J. Kang et al.

- Karottki, D.G., Spilak, M., Frederiksen, M., Andersen, Z.J., Madsen, A.M., Ketzel, M., Massling, A., Gunnarsen, L., Møller, P., Loft, S., 2015. Indoor and outdoor exposure to ultrafine, fine and microbiologically derived particulate matter related to cardiovascular and respiratory effects in a panel of elderly urban citizens. Int. J. Environ. Res. Public Health 12, 1667–1686.
- Kim, H., Na, G., Park, S., Ra, S.W., Kang, S.Y., Kim, H.C., Kim, H.C., Lee, S.W., 2021. The impact of life behavior and environment on particulate matter in chronic obstructive pulmonary disease. Environ. Res. 198, 111265.
- Kim, H., Huh, J.Y., Na, G., Park, S., Ra, S.W., Kang, S.Y., Kim, H.C., Kim, H.C., Lee, S.W., 2023. Lifestyle practices that reduce seasonal PM(2.5) exposure and their impact on COPD. Sci. Rep. 13, 11822.
- Ko, F.W., Hui, D.S., 2012. Air pollution and chronic obstructive pulmonary disease. Respirology 17, 395–401.
- Kon, S.S., Canavan, J.L., Jones, S.E., Nolan, C.M., Clark, A.L., Dickson, M.J., Haselden, B. M., Polkey, M.I., Man, W.D., 2014. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. Lancet Respir. Med. 2, 195–203.
- Lange, P., Celli, B., Agustí, A., Boje Jensen, G., Divo, M., Faner, R., Guerra, S., Marott, J. L., Martinez, F.D., Martinez-Camblor, P., Meek, P., Owen, C.A., Petersen, H., Pinto-Plata, V., Schnohr, P., Sood, A., Soriano, J.B., Tesfaigzi, Y., Vestbo, J., 2015. Lungfunction trajectories leading to chronic obstructive pulmonary disease. N. Engl. J. Med. 373, 111–122.
- Li, H., Cai, J., Chen, R., Zhao, Z., Ying, Z., Wang, L., Chen, J., Hao, K., Kinney, P.L., Chen, H., Kan, H., 2017b. Particulate Matter Exposure and Stress Hormone Levels: A Randomized, Double-Blind. Crossover Trial of Air Purification. Circulation 136, 618–627.
- Li, G., Huang, J., Xu, G., Pan, X., Qian, X., Xu, J., Zhao, Y., Zhang, T., Liu, Q., Guo, X., He, T., 2017a. The short term burden of ambient fine particulate matter on chronic obstructive pulmonary disease in Ningbo. China. Environ Health 16, 54.
- Liu, S., Zhou, Y., Liu, S., Chen, X., Zou, W., Zhao, D., Li, X., Pu, J., Huang, L., Chen, J., Li, B., Liu, S., Ran, P., 2017. Association between exposure to ambient particulate matter and chronic obstructive pulmonary disease: results from a cross-sectional study in China. Thorax 72, 788–795.
- Lozano, R.; Naghavi, M.; Foreman, K.; Lim, S.; Shibuya, K.; Aboyans, V.; Abraham, J.; Adair, T.; Aggarwal, R.; Ahn, S.Y.; Alvarado, M.; Anderson, H.R.; Anderson, L.M.; Andrews, K.G.; Atkinson, C.; Baddour, L.M.; Barker-Collo, S.; Bartels, D.H.; Bell, M. L.; Benjamin, E.J.; Bennett, D.; Bhalla, K.; Bikbov, B.; Bin Abdulhak, A.; Birbeck, G.; Blyth, F.; Bolliger, I.; Boufous, S.; Bucello, C.; Burch, M.; Burney, P.; Carapetis, J.; Chen, H.; Chou, D.; Chugh, S.S.; Coffeng, L.E.; Colan, S.D.; Colquhoun, S.; Colson, K. E.; Condon, J.; Connor, M.D.; Cooper, L.T.; Corriere, M.; Cortinovis, M.; de Vaccaro, K.C.; Couser, W.; Cowie, B.C.; Criqui, M.H.; Cross, M.; Dabhadkar, K.C.; Dahodwala, N.; De Leo, D.; Degenhardt, L.; Delossantos, A.; Denenberg, J.; Des Jarlais, D.C.; Dharmaratne, S.D.; Dorsey, E.R.; Driscoll, T.; Duber, H.; Ebel, B.; Erwin, P.J.; Espindola, P.; Ezzati, M.; Feigin, V.; Flaxman, A.D.; Forouzanfar, M.H.; Fowkes, F.G.; Franklin, R.; Fransen, M.; Freeman, M.K.; Gabriel, S.E.; Gakidou, E.; Gaspari, F.; Gillum, R.F.; Gonzalez-Medina, D.; Halasa, Y.A.; Haring, D.; Harrison, J.E.; Havmoeller, R.; Hay, R.J.; Hoen, B.; Hotez, P.J.; Hoy, D.; Jacobsen, K.H.; James, S.L.; Jasrasaria, R.; Jayaraman, S.; Johns, N.; Karthikeyan, G.; Kassebaum, N.; Keren, A.; Khoo, J.P.; Knowlton, L.M.; Kobusingye, O.; Koranteng, A.; Krishnamurthi, R.; Lipnick, M.; Lipshultz, S.E.; Ohno, S.L.; Mabweijano, J.; MacIntyre, M.F.; Mallinger, L.: March, L.: Marks, G.B.: Marks, R.: Matsumori, A.: Matzopoulos, R.: Mavosi, B.M.: McAnulty, J.H.; McDermott, M.M.; McGrath, J.; Mensah, G.A.; Merriman, T.R.; Michaud, C.; Miller, M.; Miller, T.R.; Mock, C.; Mocumbi, A.O.; Mokdad, A.A.; Moran, A.; Mulholland, K.; Nair, M.N.; Naldi, L.; Narayan, K.M.; Nasseri, K.; Norman, P.; O'Donnell, M.; Omer, S.B.; Ortblad, K.; Osborne, R.; Ozgediz, D.; Pahari, B.; Pandian, J.D.; Rivero, A.P.; Padilla, R.P.; Perez-Ruiz, F.; Perico, N.; Phillips, D.; Pierce, K.; Pope, C.A., 3rd; Porrini, E.; Pourmalek, F.; Raju, M.; Ranganathan, D.; Rehm, J.T.; Rein, D.B.; Remuzzi, G.; Rivara, F.P.; Roberts, T.; De León, F.R.; Rosenfeld, L.C.; Rushton, L.; Sacco, R.L.; Salomon, J.A.; Sampson, U.; Sanman, E.; Schwebel, D.C.; Segui-Gomez, M.; Shepard, D.S.; Singh, D.; Singleton, J.; Sliwa, K.; Smith, E.; Steer, A.; Taylor, J.A.; Thomas, B.; Tleyjeh, I.M.; Towbin, J.A.; Truelsen, T.; Undurraga, E.A.; Venketasubramanian, N.; Vijayakumar, L.; Vos, T.; Wagner, G. R.; Wang, M.; Wang, W.; Watt, K.; Weinstock, M.A.; Weintraub, R.; Wilkinson, J.D.; Woolf, A.D.; Wulf, S.; Yeh, P.H.; Yip, P.; Zabetian, A.; Zheng, Z.J.; Lopez, A.D.; Murray, C.J.; AlMazroa, M.A.; Memish, Z.A. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095-2128.
- Maung, T.Z., Bishop, J.E., Holt, E., Turner, A.M., Pfrang, C., 2022. Indoor Air Pollution and the Health of Vulnerable Groups: A Systematic Review Focused on Particulate Matter (PM), Volatile Organic Compounds (VOCs) and Their Effects on Children and People with Pre-Existing Lung Disease. Int. J. Environ. Res. Public Health 19.
- Oh, H.-R., Ho, C.-H., Kim, J., Chen, D., Lee, S., Choi, Y.-S., Chang, L.-S., Song, C.-K., 2015. Long-range transport of air pollutants originating in China: A possible major cause of multi-day high-PM10 episodes during cold season in Seoul. Korea. Atmospheric Environment 109, 23–30.
- Park, H.J.; Lee, H.Y.; Suh, C.H.; Kim, H.C.; Kim, H.C.; Park, Y.-J.; Lee, S.W.J.A., Asthma; Research, I. The effect of particulate matter reduction by indoor air filter use on respiratory symptoms and lung function: a systematic review and meta-analysis. 2021;13:719.

- Park, Y., Koo, J.H., Jeong, H., Jung, J.Y., Kim, C., Kang, D.R., 2023. Evaluation of an air quality warning system for vulnerable and susceptible individuals in South Korea: an interrupted time series analysis. Epidemiol. Health e2023020.
- Powell, P., Brunekreef, B., Grigg, J., 2016. How do you explain the risk of air pollution to your patients? Breathe (Sheff.) 12, 201–203.
- Pun, V.C.; Kazemiparkouhi, F.; Manjourides, J.; Suh, H.H.J.A.j.o.e. Long-term PM2. 5 exposure and respiratory, cancer, and cardiovascular mortality in older US adults. 2017;186:961-969.

Seoul Metropolitan Government. Seoul Open Data Plaza.

Shao, D., Du, Y., Liu, S., Brunekreef, B., Meliefste, K., Zhao, Q., Chen, J., Song, X., Wang, M., Wang, J., Xu, H., Wu, R., Wang, T., Feng, B., Lung, C.S., Wang, X., He, B., Huang, W., 2017. Cardiorespiratory responses of air filtration: A randomized crossover intervention trial in seniors living in Beijing: Beijing Indoor Air Purifier StudY. BIAPSY. Sci Total Environ 603–604, 541–549.

Vos, T.; Flaxman, A.D.; Naghavi, M.; Lozano, R.; Michaud, C.; Ezzati, M.; Shibuya, K.; Salomon, J.A.; Abdalla, S.; Aboyans, V.; Abraham, J.; Ackerman, I.; Aggarwal, R.; Ahn, S.Y.; Ali, M.K.; Alvarado, M.; Anderson, H.R.; Anderson, L.M.; Andrews, K.G.; Atkinson, C.; Baddour, L.M.; Bahalim, A.N.; Barker-Collo, S.; Barrero, L.H.; Bartels, D.H.; Basáñez, M.G.; Baxter, A.; Bell, M.L.; Benjamin, E.J.; Bennett, D.; Bernabé, E.; Bhalla, K.; Bhandari, B.; Bikbov, B.; Bin Abdulhak, A.; Birbeck, G.; Black, J.A.; Blencowe, H.; Blore, J.D.; Blyth, F.; Bolliger, I.; Bonaventure, A.; Boufous, S.; Bourne, R.; Boussinesq, M.; Braithwaite, T.; Brayne, C.; Bridgett, L.; Brooker, S.; Brooks, P.; Brugha, T.S.; Bryan-Hancock, C.; Bucello, C.; Buchbinder, R.; Buckle, G.; Budke, C. M.; Burch, M.; Burney, P.; Burstein, R.; Calabria, B.; Campbell, B.; Canter, C.E. Carabin, H.; Carapetis, J.; Carmona, L.; Cella, C.; Charlson, F.; Chen, H.; Cheng, A.T.; Chou, D.; Chugh, S.S.; Coffeng, L.E.; Colan, S.D.; Colquhoun, S.; Colson, K.E.; Condon, J.; Connor, M.D.; Cooper, L.T.; Corriere, M.; Cortinovis, M.; de Vaccaro, K. C.; Couser, W.; Cowie, B.C.; Criqui, M.H.; Cross, M.; Dabhadkar, K.C.; Dahiya, M.; Dahodwala, N.; Damsere-Derry, J.; Danaei, G.; Davis, A.; De Leo, D.; Degenhardt, L.; Dellavalle, R.; Delossantos, A.; Denenberg, J.; Derrett, S.; Des Jarlais, D.C.; Dharmaratne, S.D.; Dherani, M.; Diaz-Torne, C.; Dolk, H.; Dorsey, E.R.; Driscoll, T.; Duber, H.; Ebel, B.; Edmond, K.; Elbaz, A.; Ali, S.E.; Erskine, H.; Erwin, P.J.; Espindola, P.; Ewoigbokhan, S.E.; Farzadfar, F.; Feigin, V.; Felson, D.T.; Ferrari, A.; Ferri, C.P.; Fèvre, E.M.; Finucane, M.M.; Flaxman, S.; Flood, L.; Foreman, K.; Forouzanfar, M.H.; Fowkes, F.G.; Franklin, R.; Fransen, M.; Freeman, M.K.; Gabbe, B. J.; Gabriel, S.E.; Gakidou, E.; Ganatra, H.A.; Garcia, B.; Gaspari, F.; Gillum, R.F.; Gmel, G.; Gosselin, R.; Grainger, R.; Groeger, J.; Guillemin, F.; Gunnell, D.; Gupta, R.; Haagsma, J.; Hagan, H.; Halasa, Y.A.; Hall, W.; Haring, D.; Haro, J.M.; Harrison, J.E.; Havmoeller, R.; Hay, R.J.; Higashi, H.; Hill, C.; Hoen, B.; Hoffman, H.; Hotez, P. J.; Hoy, D.; Huang, J.J.; Ibeanusi, S.E.; Jacobsen, K.H.; James, S.L.; Jarvis, D.; Jasrasaria, R.; Jayaraman, S.; Johns, N.; Jonas, J.B.; Karthikeyan, G.; Kassebaum, N.; Kawakami, N.; Keren, A.; Khoo, J.P.; King, C.H.; Knowlton, L.M.; Kobusingye, O.; Koranteng, A.; Krishnamurthi, R.; Lalloo, R.; Laslett, L.L.; Lathlean, T.; Leasher, J.L.; Lee, Y.Y.; Leigh, J.; Lim, S.S.; Limb, E.; Lin, J.K.; Lipnick, M.; Lipshultz, S.E.; Liu, W.; Loane, M.; Ohno, S.L.; Lyons, R.; Ma, J.; Mabweijano, J.; MacIntyre, M.F.; Malekzadeh, R.; Mallinger, L.; Manivannan, S.; Marcenes, W.; March, L.; Margolis, D. J.; Marks, G.B.; Marks, R.; Matsumori, A.; Matzopoulos, R.; Mayosi, B.M.; McAnulty, J.H.: McDermott, M.M.: McGill, N.: McGrath, J.: Medina-Mora, M.E.: Meltzer, M.: Mensah, G.A.; Merriman, T.R.; Meyer, A.C.; Miglioli, V.; Miller, M.; Miller, T.R.; Mitchell, P.B.: Mocumbi, A.O.: Moffitt, T.E.: Mokdad, A.A.: Monasta, L.: Montico, M.: Moradi-Lakeh, M.; Moran, A.; Morawska, L.; Mori, R.; Murdoch, M.E.; Mwaniki, M. K.; Naidoo, K.; Nair, M.N.; Naldi, L.; Narayan, K.M.; Nelson, P.K.; Nelson, R.G.; Nevitt, M.C.; Newton, C.R.; Nolte, S.; Norman, P.; Norman, R.; O'Donnell, M.; O'Hanlon, S.; Olives, C.; Omer, S.B.; Ortblad, K.; Osborne, R.; Ozgediz, D.; Page, A.; Pahari, B.; Pandian, J.D.; Rivero, A.P.; Patten, S.B.; Pearce, N.; Padilla, R.P.; Perez-Ruiz, F.; Perico, N.; Pesudovs, K.; Phillips, D.; Phillips, M.R.; Pierce, K.; Pion, S.; Polanczyk, G.V.; Polinder, S.; Pope, C.A., 3rd; Popova, S.; Porrini, E.; Pourmalek, F.; Prince, M.; Pullan, R.L.; Ramaiah, K.D.; Ranganathan, D.; Razavi, H.; Regan, M.; Rehm, J.T.; Rein, D.B.; Remuzzi, G.; Richardson, K.; Rivara, F.P.; Roberts, T.; Robinson, C.; De Leòn, F.R.; Ronfani, L.; Room, R.; Rosenfeld, L.C.; Rushton, L.; Sacco, R.L.; Saha, S.; Sampson, U.; Sanchez-Riera, L.; Sanman, E.; Schwebel, D.C.; Scott, J.G.; Segui-Gomez, M.; Shahraz, S.; Shepard, D.S.; Shin, H.; Shivakoti, R.; Singh, D.; Singh, G.M.; Singh, J.A.; Singleton, J.; Sleet, D.A.; Sliwa, K.; Smith, E.; Smith, J.L.; Stapelberg, N.J.; Steer, A.; Steiner, T.; Stolk, W.A.; Stovner, L.J.; Sudfeld, C.; Syed, S.; Tamburlini, G.; Tavakkoli, M.; Taylor, H.R.; Taylor, J.A.; Taylor, W.J.; Thomas, B.; Thomson, W.M.; Thurston, G.D.; Tleyjeh, I.M.; Tonelli, M.; Towbin, J.A.; Truelsen, T.; Tsilimbaris, M.K.; Ubeda, C.; Undurraga, E.A.; van der Werf, M.J.; van Os, J.; Vavilala, M.S.; Venketasubramanian, N.; Wang, M.; Wang, W.; Watt, K.; Weatherall, D.J.; Weinstock, M.A.; Weintraub, R.; Weisskopf, M.G.; Weissman, M.M.; White, R.A.; Whiteford, H.; Wiersma, S.T.; Wilkinson, J.D.; Williams, H.C.; Williams, S.R.; Witt, E.; Wolfe, F.; Woolf, A.D.; Wulf, S.; Yeh, P.H.; Zaidi, A.K.; Zheng, Z.J.; Zonies, D.; Lopez, A.D.; Murray, C.J.; AlMazroa, M.A.; Memish, Z.A. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380: 2163-2196.

Wang, L., Xie, J., Hu, Y., Tian, Y., 2022. Air pollution and risk of chronic obstructed pulmonary disease: The modifying effect of genetic susceptibility and lifestyle. EBioMedicine 79, 103994.