# A Randomized Crossover Air Purifier Intervention Study of Patients with Stable Coronary Artery Disease

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# Abstract

Exposure to $PM_{2.5}$ will accelerate the progression of cardiovascular diseases. Air purifier can reduce the $PM_{2.5}$ exposure and theoretically alleviate the influence of $PM_{2.5}$ on patients with stable coronary artery disease (SCAD). However, few studies of the protective effect showed significant results because the interferent effects of routine medication had not been taken into account. In order to explore the actual effect on patients with SCAD, we conducted a randomized crossover air purifier intervention trial. Levels of the subjects' $PM_{2.5}$ exposure during intervention and cardiovascular indicators (inflammation, coagulation, plaque stability, and blood lipids) after intervention were detected, meanwhile the information of drug use was obtained by questionnaire. Then the kinds of drug used by more than 20% of the subjects were sorted out. And the influence of these drugs on cardiovascular indicators was summarized through literature review. Based on that, the drug use was included as a variable in linear mixed effects models that used to analyze the associations between $PM_{2.5}$ exposure reduction by air purifier and cardiovascular indicators. The result revealed that the interpretation contribution rate of drug use was more than that of $PM_{2.5}$ exposure. The level of C-reactive protein (CRP) significantly decreased on lag1, lag01 and lag02, while the level of high-density lipoprotein cholesterol (HDL-C) significantly increased on lag0, lag1 and lag01 associated with an interquartile range (IQR) decrease in $PM_{2.5}$ exposure. The study can provide reference for future relevant research in methodology.

# Background

$PM_{2.5}$ exposure has been confirmed to cause changes of cardiovascular indicators, thus promoting the occurrence and development of cardiovascular diseases (Brook et al. 2010). And air purifier with high efficiency particulate air filter (HEPA) can significantly reduce the indoor $PM_{2.5}$ concentration (Chu et al. 2018; Karottki et al. 2013) then the personal exposure (Brauner et al. 2008). Therefore, there is theoretical basis for using air purifier to reduce health hazards, in areas and seasons with high incidence of $PM_{2.5}$ pollution.

The results of a series of intervention studies demonstrated that the use of air purifiers has different effects on the cardiovascular indicators of different groups. For healthy adults, the use of air purifiers has significant effects on the levels of monocyte chemokines, interleukin-1beta (IL-1β), soluble cluster of differentiation 40 ligand (sCD40L) and endothelin-1 (ET-1) in their circulatory system (Chen et al. 2018; Chen et al. 2015), while the effects on CRP (Allen et al. 2011; Chen et al. 2015; Chuang et al. 2017; Kajbafzadeh et al. 2015) and fibrinogen (FIB) (Chen et al. 2015; Lin et al. 2013) are still controversial, and no significant effects on tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and cluster of differentiation 62 platelet (CD62P) have been found (Allen et al. 2011; Chen et al. 2015; Kajbafzadeh et al. 2015). For the elderly, the use of air purifiers was not found to have significant impacts on circulatory CRP, TNF-α, IL-6, interleukin-8 (IL-8) and FIB levels, only on the physiological index microvascular function (MVF) (Brauner et al. 2008; Karottki et al. 2013; Shao et al. 2017). But stratification analysis in one correlational study (Karottki et al. 2013) found that the protective effect of air purifiers on MVF was not statistically significant in the elderly taking cardiovascular disease medicine. In summary, current studies of circulatory system effects of air purifier intervention mainly focused on the indicators of inflammation (monocyte chemokine, TNF-α, CRP, FIB, IL-1β, IL-6 and IL-8) and coagulation (sCD40L, CD62P and ET-1). The conventional cardiovascular disease medicine may interfere the cardiovascular benefits of air purifiers for the elderly.

Indicators of plaque stability (Xu et al. 2019) (matrix metalloproteinase-2 (MMP-2), matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1)) and blood lipid (Liu et al. 2020) (total cholesterol (CHO), triglyceride (TG), HDL-C and low-density lipoprotein cholesterol (LDL-C)), which can mediate the effect of $PM_{2.5}$ on CAD, are also key indicators that need special attention in the health protection study for CAD patients. Patients with SCAD have adopted varied medication regimens to control the progression of disease by regulating different indicators in the circulatory system. For example, statins are used to regulate the blood lipid levels; β-blockers, angiotensin-converting enzyme inhibitors (ACEI), angiotensin-receptor blockers (ARB) or calcium-channel blockers (Ca-channel blockers) are used to regulate the cardiac load and vasoconstriction; and aspirin is used to inhibit the platelet aggregation. Therefore, it is essential to control the interference effects of these drug, and comprehensively analyze the effects on inflammation, coagulation, plaque stability, blood lipid and other cardiovascular indicators in the circulatory system, when intervention studies on the protective effect of air purifiers on the cardiovascular system is carried out.

To explore the actual protective effect of $PM_{2.5}$ exposure reduction by air purifiers, a randomized crossover intervention design was adopted to the enrolled patients with SCAD. Air purifiers were used in their residences to reduce the indoor $PM_{2.5}$ concentration. At the same time of $PM_{2.5}$ exposure monitoring, the medication of the subjects during the intervention was investigated. And levels of the cardiovascular indicators of inflammation, coagulation, plaque stability and blood lipids after the intervention were detected. Interference effects of drug use were controlled in liner mixed effect models that used to analyze the associations between $PM_{2.5}$ exposure and cardiovascular indicators.

# Materials And Methods

### Study Design and Subject Recruitment

The randomized crossover intervention design was adopted in this study. 24 patients with SCAD were recruited to carry out the intervention trial of air purifier in their residences (air purifier with HEPA was “real-intervention”, and without HEPA was “sham-intervention”). The experiment was completed in 4 batches with 6 subjects in each batch. Every intervention period was 3 days and the washout period was more than 14 days. The arrangement of the intervention is shown in Fig. 1.

The subjects were recruited from 3 community-level (or above) general hospitals in Beijing, who were clinically diagnosed with SCAD according to the diagnostic requirements of *2013 ESC Guidelines on the Management of Stable Coronary Artery Disease* (Montalescot et al. 2013) published by the European

College of Cardiology and *2010 Chinese Consensus on the Management of Chronic Stable Coronary Artery Disease* (Hu 2010) issued by China. In addition, the inclusion criteria include: (1) the age was between 55 and 80 years old; and (2) they lived near the hospital for a long time and the house was not decorated within one year. The exclusion criteria are as follows: (1) someone in their house smoked or themselves had just quitted smoking for less than one year; (2) patients were diagnosed with acute myocardial infarction within 3 months, or receive percutaneous coronary intervention and bypass transplantation within 6 months; (3) patients wore a pacemaker; and (4) patients suffered from liver injury, cancer and other serious diseases.

During the intervention, the individual exposure to $PM_{2.5}$ and the concentration of $PM_{2.5}$ indoor and outdoor the residence was monitored continuously. The age and body mass index (BMI) of the subjects was investigated, and their travel behaviors, window opening time and medication were recorded. The subjects stayed at home for more than 20 h/d, and the window opened for no more than 2 h/d during the intervention. Drug use records focused on conventional medicine for CAD treatment. Blood samples were collected at the end of each intervention, and the following indicators were detected: (1) inflammation indicators such as IL-6, TNF-α, CRP and FIB; (2) coagulation indicators such as CD62P, CD40L, intercellular adhesion molecule-1 (ICAM-1), nitric oxide (NO) and ET-1; (3) plaque stability indicators such as MMP-2, MMP-9 and TIMP-1; (4) blood lipid indicators such as CHO, TG, HDL-C and LDL-C.

### Environmental Monitoring

Particulate matter sampling pumps MicroPEM$^{TM}$ (RTI Company, USA) based on the principle of light scattering were used to monitor $PM_{2.5}$ concentration with sampling flow of 500 mL/min. It can monitor the environmental temperature and relative humidity (RH) simultaneously. Daily average concentration of $PM_{2.5}$ was calculated from 8 a.m. to 8 a.m. Lag and moving average levels of $PM_{2.5}$ exposure are represented by "lag".

Sampling pumps for monitoring the indoor $PM_{2.5}$ concentration were placed in the open area of the house to avoid air conditioner vent, kitchen, doors and windows, about 1.5m above the ground, more than 1m far from the wall, and at least 2 m far from the air purifier. Sampling pumps for monitoring the outdoor $PM_{2.5}$ concentration were placed outside the residential window and avoid air conditioner unit and kitchen and its air outlet. Sampling pumps for monitoring individual exposure to $PM_{2.5}$ were taken along by the subjects.

### Blood Collection and Indicator Measurements

Fasting blood samples (5 mL anticoagulant and 5 mL non-anticoagulant) were collected from 8:00 to 9: 00 on the day at the end of each intervention. IL-6, TNF-α, CRP, FIB, CD62P, CD40L, ICAM-1, NO, ET-1, MMP-2, MMP-9, and TIMP-1 levels were tested by a professional testing institution. CHO, TG, HDL-C and LDL-C levels were tested by the laboratory of the hospital. IL-6, TNF-α, TIMP-1, CD62P, CD40L and ICAM-1 was detected by a bead-based multiple flow cytometry on Luminex 200 system (Luminex Corporation, Austin, TX, USA) with chips (IL-6, TNF-α and TIMP-1: Merck Millipore, Germany; CD62P, CD40L and ICAM-1: R&D, USA). CRP, NO, MMP-2, MMP-9, FIB and ET-1 was separately detected by ELISA kit (CRP, NO, MMP-2, MMP-9: R&D, USA; FIB: NOVUS, USA; ET-1: Elabscience Biotechnology Co. Ltd, Wuhan, China).

In addition, a compound index-atherogenic index of plasma (AIP) was calculated by the results of TG and HDL-C levels and the formula: AIP=log (TG/HDL-C).

## Statistical Analyses

Descriptive statistics were conducted for general characteristics of the environmental exposure and effects. Data with normal distribution were described by mean and standard deviation (mean±SD), and data with skewed distribution were described by median and interquartile range as M ($P_{25}$, $P_{75}$). The paired Student's *t*-test was employed to compare the $PM_{2.5}$ concentrations between two intervention periods, or the indoor and outdoor environment. The Linear mixed effect models were conducted to estimate the correlation between $PM_{2.5}$ exposure and cardiovascular indicators. The results were reported by the percentage change of indicators associated with an interquartile range (IQR) decreases of $PM_{2.5}$ exposure. The interpretation contribution rate of independent variables in the model were calculated by the determination coefficient $R^2$ of independent variables/ of the model.

In the linear mixed effect models, the "effective drug" variable is defined as one or more kinds of the effective drug had been taken by the subject (dichotomous variable). The kinds of drug need to be controlled were selected according to *Guidelines for Rational Drug Use of Coronary Artery Disease (2nd Edition)* (Expert Committee on Rational Drug Use of National Health and Family Planning Commission and Chinese Pharmacists Association 2018) and the actual medication of the subjects (taken by more than 20% of the subjects). Whether the drug is effective was determined by searching the literatures on "Pubmed", "Web of Science", "China National Knowledge Infrastructure", "Wanfang" and "VIP" (before December 30, 2020). It needs to meet the following requirements: (1) there were two or more case-control trials or pre-and post-treatment control trials of cardiovascular disease patients treated with the drug, and the results of the trials were statistically significant; or (2) there was a case-control trial or pre-and post-treatment control trial of cardiovascular disease patients treated with the drug, and the results were statistically significant, and there was one or more animal experiment of the drug, and the results were statistically significant.

Influencing factors of $PM_{2.5}$ exposure and cardiovascular indicators need to be considered as independent variables in the linear mixed effects models. It includes the "effective drug", age, sex and BMI, as well as temperature and relative humidity. The stepwise elimination method based on the principle of minimization of Akaike's Information Criterion (AIC) was adopted for the validity of models. We screened three additional independent variables on the basis of preserving key variables ($PM_{2.5}$ exposure and the "effective drug"). The model was established for each indicator respectively, given the influencing factors differences.

The parameters of the model were tested by bilateral *t*-test, with statistical significance of 0.05. The "lme4" package and "r2glmm" package in the R (Version 4.0.3) was separately used for linear mixed effect model and $R^2$ calculation.

### Quality Control

The monitoring instruments were cleaned and calibrated before sampling. Instrument condition review was done at the end of the first and last day of each intervention. The blood samples were collected by the nurses. Blood lipid indicators were detected on the same day, and samples were stored at-80°C before further detection. The detection process was controlled strictly in accordance with the testing procedures and the requirements of the chips/kits.

The subjects of the study were trained by professional personnel before recording the questionnaire themselves. Questionnaires were re-checked at the end of the first and last day of each intervention for ensuring recording accuracy. Questionnaire and data input were done by two personnel, and then reviewed and analyzed by special personnel.

## Results

### The General Characteristics of the Subjects

The residences of the subjects were all within 5 km near the hospitals. The average age of the subjects was 65.3 ± 5.2 years old, and the ratio of male to female was 14:10. The average BMI of the subjects was 26.0 ±2.4 kg/$m^2$. The drug use during the intervention is shown in Table 1.

### Air Purification Effect and Individual $PM_{2.5}$ Exposure Level

The 72h average indoor $PM_{2.5}$ concentration in the real-intervention period was 40.58% of the outdoor. It was significantly reduced by 40.04% when compared with the sham-intervention period. The change of individual $PM_{2.5}$ exposure level was consistent with indoor concentration. During the real-intervention period, the individual $PM_{2.5}$ exposure level was reduced by 22.72% when compared with the sham-intervention period. The use of air purifiers in residences can effectively reduce the indoor $PM_{2.5}$ concentration, and then the individual $PM_{2.5}$ exposure (Table 2).

**Table 1** The general characteristics of the participations

| Items | Categories | Result |
|---|---|---|
| Age (Mean±SD) | | 65.3±5.2 years |
| Gender (n) | Male | 14 |
| | Female | 10 |
| BMI (Mean±SD) | | 26.0±2.4 kg/$m^2$ |
| Drug Use (n) | | |
| | Aspirin | 18 |
| | Statins | 18 |
| | ACEI/ARB | 14 |
| | Clopidogrel | 13 |
| | β-blockers | 7 |
| | Ca-channel blockers | 5 |

**Table 2** Comparison of indoor, outdoor and individual exposure to $PM_{2.5}$ concentrations

| Intervention | Scene | $PM_{2.5}$/μg/$m^3$ (Mean±SD) | Real-Sham | | Indoor-Outdoor | |
|---|---|---|---|---|---|---|
| | | | Difference /μg/$m^3$ | *p*-value | Difference /μg/$m^3$ | *p*-value |
| Real | Indoor | 26.24±11.26 | -17.52* | 0.0197 | -38.44* | <0.0001 |
| | Outdoor | 64.67±34.45 | 4.66 | 0.7196 | —— | —— |
| | Individual | 32.65±13.18 | -9.60 | 0.1175 | —— | —— |
| Sham | Indoor | 43.76±29.11 | —— | —— | -16.25* | 0.0001 |
| | Outdoor | 60.01±36.90 | —— | —— | —— | —— |
| | Individual | 42.25±28.82 | —— | —— | —— | —— |

$^{*}p<0.05$

### Drug to be Controlled and Their Effects on Indicators

According to the questionnaire survey, 6 kinds of drug were taken by more than 20% of the subjects during the intervention period: statins, β-blockers, Ca-channel blockers, clopidogrel, aspirin and ACEI/ARB.

Based on literatures review (Table S1-S6, References S1), the effects of these 6 kinds of drug on the indicators of inflammation, coagulation, plaque stability and blood lipids were determined, as shown in Table 3.

## Model Selection and Interpretation Contribution Rate of Variables

In this study, each cardiovascular indicator was selected by minimizing AIC in the linear mixed effect analysis model, except for CHO and LDL-C. Based on the previous association research of blood lipid indicators, the influence of age, gender and BMI variables were greater than that of ambient temperature and RH. And the AIC values of CHO and LDL-C models ("log (Indicator) ~ $PM_{2.5}$+ Age + Gender+ BMI+ Effective Drug + (1|ID)" and "log (Indicator) ~ $PM_{2.5}$+ Gender+ BMI+ Temperature+ Effective Drug + (1|ID)") were similar, which were 12.74 vs. 12.21 and 47.03 vs. 46.54, respectively, so "log (Indicator) ~ $PM_{2.5}$+ Age + Gender+ BMI+ Effective Drug + (1|ID)" was selected as the model. The final selection of linear mixed effect models for each cardiovascular indicator is shown in Table S7.

**Table 3** Effects of 6 kinds of drug on cardiovascular indicators

| | Statins | $\beta$-blockers | Ca-channel blockers | Clopidogrel | Aspirin | ACEI/ARB |
|---|---|---|---|---|---|---|
| IL-6 | ● [a] | ● | ● | | ● | ● |
| TNF-α | ● | ● | ● | ● | ● | ● |
| CRP | ● | ● | ● | ● | ● | ● |
| FIB | ● | ● | | | | ● |
| CD62P | ● | | | ● | ● | |
| CD40L | ● | | | ● | | |
| ICAM-1 | ● | | | | | ● |
| NO | | | | | ● | |
| ET-1 | ● | ● | | | | |
| MMP-2 | ● | | ● | ● | | |
| MMP-9 | ● | | ● | ● | | ● |
| TIMP-1 | ● | | | | | |
| CHO | ● | ● | | | ● | |
| TG | ● | ● | | | | |
| HDL-C | ● | | | | | |
| LDL-C | ● | ● | | | ● | |
| AIP | ● | ● | | | | |

[a] ●Based on literatures review, the effects of drug on the indicators were determined.

The determination coefficient $R^2$ of the independent variables of each model and its interpretation contribution rate in the model were calculated (Table S7), we found that in the models corresponding to IL-6, TNF-α, FIB, CD62P, ICAM-1, ET-1, MMP-9, CHO, TG and AIP, the contribution rate of “effective drug” to the interpretation of the model was greater than that of $PM_{2.5}$ exposure, and the contribution rate of “effective drug” to the interpretation of IL-6, TG and AIP models was more than 58%. In the model corresponding to the CRP, CD40L, NO, TIMP-1, HDL-C and LDL-C, the interpretation contribution rate of $PM_{2.5}$ exposure to the model was slightly greater than that of “effective drug”. In the model corresponding to MMP-2, the interpretation contribution rate of $PM_{2.5}$ exposure to the model was much greater than that of drug intake (60% vs. 3%).

### Effects of $PM_{2.5}$ Reduction on Inflammation Indicators

The levels of TNF-α, CRP and FIB were decreased with each IQR decrease (24.69 μg/$m^3$) of $PM_{2.5}$ exposure on lag0 when the subjects used the “real” air purifier, but the changes were not statistically significant. And CRP level of the subjects was significantly reduced by 20.93% (95%CI: 6.56%, 33.10%), 23.44% (95%CI: 2.77%, 39.39%) and 24.11% (95%CI: 4.21%, 39.69%) respectively for each $PM_{2.5}$ exposure IQR decrease of 27.18 μg/$m^3$, 27.56 μg/$m^3$ and 21.22 μg/$m^3$, on lag1, lag01 and lag02 (Figure 2).

### Effects of $PM_{2.5}$ Reduction on Coagulation Indicators

There was no statistically significant change in coagulation indicators when the individual $PM_{2.5}$ exposure was decreased by each IQR on lag0, lag1, lag2, lag01 and lag02. Except that ET-1 level was significantly reduced by 5.64% (95%CI: 0.83%, 10.23%) for each $PM_{2.5}$ exposure IQR decrease on lag1 (Fig.3).

### Effects of $PM_{2.5}$ Reduction on Plaque Stability Indicators

There was no significantly change in plaque stability indicators. And while the levels of MMP-9 and TIMP-1showed a downward trend for each IQR decrease of $PM_{2.5}$ exposure on lag0, lag1, lag2, lag01 and lag02, but the level of MMP-2 level showed an opposite trend ($p > 0.05$). (Fig.4).

### Effects of $PM_{2.5}$ Reduction on Blood Lipid Indicators

The levels of CHO, HDL-C and LDL-C increased associated with each IQR decrease of $PM_{2.5}$ exposure on lag0, lag1, lag2, lag01 and lag02. But only the increase of HDL-C was significant on lag0, lag1 and lag01, which was 5.10% (95%CI: 0.69%, 9.05%), 3.71% (95%CI: 0.92%, 6.60%) and 6.48% (95%CI: 2.58%, 10.24%) respectively. Although with no statistical significance, the level of AIP showed a decreasing trend on lag1 and lag01 ($p = 0.06$ and $p = 0.07$, respectively) with the decrease of $PM_{2.5}$ exposure. There was no significant change in the level of TG. (Fig.5).

## Discussion

The study found that the use of "true" air purifier to reduce the $PM_{2.5}$ exposure level of patients with stable CAD had a certain protective effect on the levels of inflammatory indicator CRP and lipid indicator HDL-C under the control of the influence of the six conventional drugs for the treatment of CAD, including statins, β-blockers, Ca-channel blockers, ACEI/ARB, clopidogrel and aspirin. There were no notable effects on other inflammation and lipid indicators, or on coagulation and plaque stability indicators. It is suggested that CRP and HDL-C may be sensitive indicators of the acute effect of $PM_{2.5}$ exposure on SCAD patients, and it is more worthy of attention in the air purifier intervention trials for stable CAD patients. Therefore, the study broadened the understanding on health protection for patients with stable CAD using the air purifier, which has an important public health significance.

Inflammation is recognized as a key step in the course of CAD. Clinical studies have indicated that inflammation indicator CRP is a risk biomarker of atherosclerosis, which can mediate atherosclerosis at different stages (Oh et al. 2011). Elevated CRP level can predict the occurrence of cardiovascular events (Danesh et al. 2000). The study found that CRP level in patients with SCAD was significantly decreased by 20.93–24.11% when the daily exposure to $PM_{2.5}$ was reduced by 21.22–30.41 μg/$m^3$ on day lag1, lag01 and lag02. In an air purifier intervention trial conducted by CHUANG et al. (Chuang et al. 2017), it was found that after the air purifier reduced the average daily $PM_{2.5}$ exposure by 13.8 μg/$m^3$, the hsCRP level of the adults (43.5 ± 7.7 years old, BMI = 24.1 ± 2.0 kg/$m^2$) was decreased significantly from 5.76mg/dL to 0.54mg/dL. KAJBAFZADEH et al. (Kajbafzadeh et al. 2015) found that when $PM_{2.5}$ was increased by 4.8 μg/$m^3$, the CRP level of the subjects (40.8 ± 12.3 years old, BMI = 24.9 ± 3.9kg/$m^2$) affected by traffic pollution sources was significantly increased by 42.1%. Although it is not significant ($p$ = 0.06), the results of an intervention trial carried out by ALLEN et al. (Allen et al. 2011) also showed a downward trend from 1.00 ± 0.78 mg/L to 0.78 ± 0.74 mg/L of CRP level of healthy adults (43.0 ± 9.9 years old, and BMI = 25.7 ± 3.5 kg/$m^2$) after using the air purifiers. In addition, the study revealed that the interpretation contribution rate of drug use to the analysis model of CRP was similar with that of $PM_{2.5}$ exposure. Therefore, it's showed no significant effect on CRP in the air purifier intervention trials for the elderly (including those with cardiovascular diseases) (Karottki et al. 2013).

Blood lipid is one of the risk factors to be controlled in patients with CAD. The meta-analysis (Liu et al. 2020) showed that for each 10 μg/$m^3$ increase in $PM_{2.5}$ long-term exposure, the levels of CHO and LDL-C were increased significantly by 4.53% and 5.36%, respectively, with no significant change in HDL-C and TG levels. In a large cohort study conducted by Wu et al. (Wu et al. 2019) on middle-aged women, it was found that the HDL-C level changed significantly by -0.7% when the average yearly concentration of $PM_{2.5}$ was increased by 3 μg/$m^3$, but the correlation between the average daily concentration of $PM_{2.5}$ and HDL-C level was not statistically significant. At present, there are only a few population-based studies on the acute effects of $PM_{2.5}$ exposure on blood lipid indicators, and there is no effective evidence to prove a significant correlation between $PM_{2.5}$ exposure and changes in blood lipid indicators, which may be due to the failure to control the effects of drug use on blood lipid. In this study, it's showed that the interpretation contribution rate of drug use to the model of HDL-C was similar to that of $PM_{2.5}$ exposure. And under controlling the drug effects, we analyzed the association between exposure to $PM_{2.5}$ and acute effect of HDL-C in patients with SCAD. It provided some experimental epidemiological evidence for the research of the correlation between $PM_{2.5}$ exposure and acute effect of blood lipid indicators. In addition, the AIP of the subjects in this study tended to improve with the decrease of $PM_{2.5}$ exposure (P = 0.06 and 0.07), which proved, together with the results of HDL-C, that air purifiers used to reduce $PM_{2.5}$ exposure might have a positive effect on the improvement of the quality of lipid-related indicators in patients with SCAD.

The intervention study considered the influence of daily medication on cardiovascular indicators of the patients with SCAD, and revealed the real protective effect of air purifiers on the patients with SCAD after reducing $PM_{2.5}$ exposure level. However, compared with other air purifier intervention trials, the study is an experimental epidemiological study with small sample size, which may have limitation on the research results. The limitation had been noted, and individual measurements had been used to more precisely evaluated $PM_{2.5}$ exposure levels of each study subject, which in turn could increase the accuracy of $PM_{2.5}$ exposure-response evaluation results. In addition, the small sample size limits the stratified analysis for different drug use. If the sample size is expanded, the interference effect of various drug on the results of $PM_{2.5}$ impacts can be analyzed in depth. When considering the influence of drug on cardiovascular indicators, only six kinds of conventional drug for coronary heart disease were controlled in the study. With the development and application of new drug, as well as the new discovery of the effect of drug on cardiovascular indicators, it will be necessary to conduct in-depth studies and to reveal the protective effect of air purifiers on people with cardiovascular diseases by expanding the sample size and increasing the control of the effects of other drug in the future.

## Conclusions

The study found that the use of air purifier had a clear protective effect on patients with SCAD, in the case of daily routine medication management for disease management, and could significantly improve patients' inflammation indicator CRP and blood lipid indicator HDL-C. The effects of air purifiers on cardiovascular system were comprehensively analyzed from multiple indicators of inflammation, coagulation, plaque stability and blood lipid, which provided a scientific basis for screening sensitive indicators of air purification protection for patients with SCAD. It can provide reference for future relevant research in methodology. In polluted weather, the air purifiers can reduce the individual exposure of $PM_{2.5}$, which has a certain protective effect on the health of patients with SCAD.

## Declarations

# Conflict of interest:

The authors have no conflict of interest associated with this publication.

### Ethics approval:

The work was approved by the Ethics Committee of National Institute of Environmental Health, Chinese Center for Disease Control and Prevention on Feb. 28th, 2018. (No. 201803)

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The results of a series of intervention studies demonstrated that the use of air purifiers has different effects on the cardiovascular indicators of different groups. For healthy adults, the use of air purifiers has significant effects on the levels of monocyte chemokines, interleukin-1beta (IL-1β), soluble cluster of differentiation 40 ligand (sCD40L) and endothelin-1 (ET-1) in their circulatory system (Chen et al. 2018; Chen et al. 2015), while the effects on CRP (Allen et al. 2011; Chen et al. 2015; Chuang et al. 2017; Kajbafzadeh et al. 2015) and fibrinogen (FIB) (Chen et al. 2015; Lin et al. 2013) are still controversial, and no significant effects on tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and cluster of differentiation 62 platelet (CD62P) have been found (Allen et al. 2011; Chen et al. 2015; Kajbafzadeh et al. 2015). For the elderly, the use of air purifiers was not found to have significant impacts on circulatory CRP, TNF-α, IL-6, interleukin-8 (IL-8) and FIB levels, only on the physiological index microvascular function (MVF) (Brauner et al. 2008; Karottki et al. 2013; Shao et al. 2017). But stratification analysis in one correlational study (Karottki et al. 2013) found that the protective effect of air purifiers on MVF was not statistically significant in the elderly taking cardiovascular disease medicine. In summary, current studies of circulatory system effects of air purifier intervention mainly focused on the indicators of inflammation (monocyte chemokine, TNF-α, CRP, FIB, IL-1β, IL-6 and IL-8) and coagulation (sCD40L, CD62P and ET-1). The conventional cardiovascular disease medicine may interfere the cardiovascular benefits of air purifiers for the elderly.

# References

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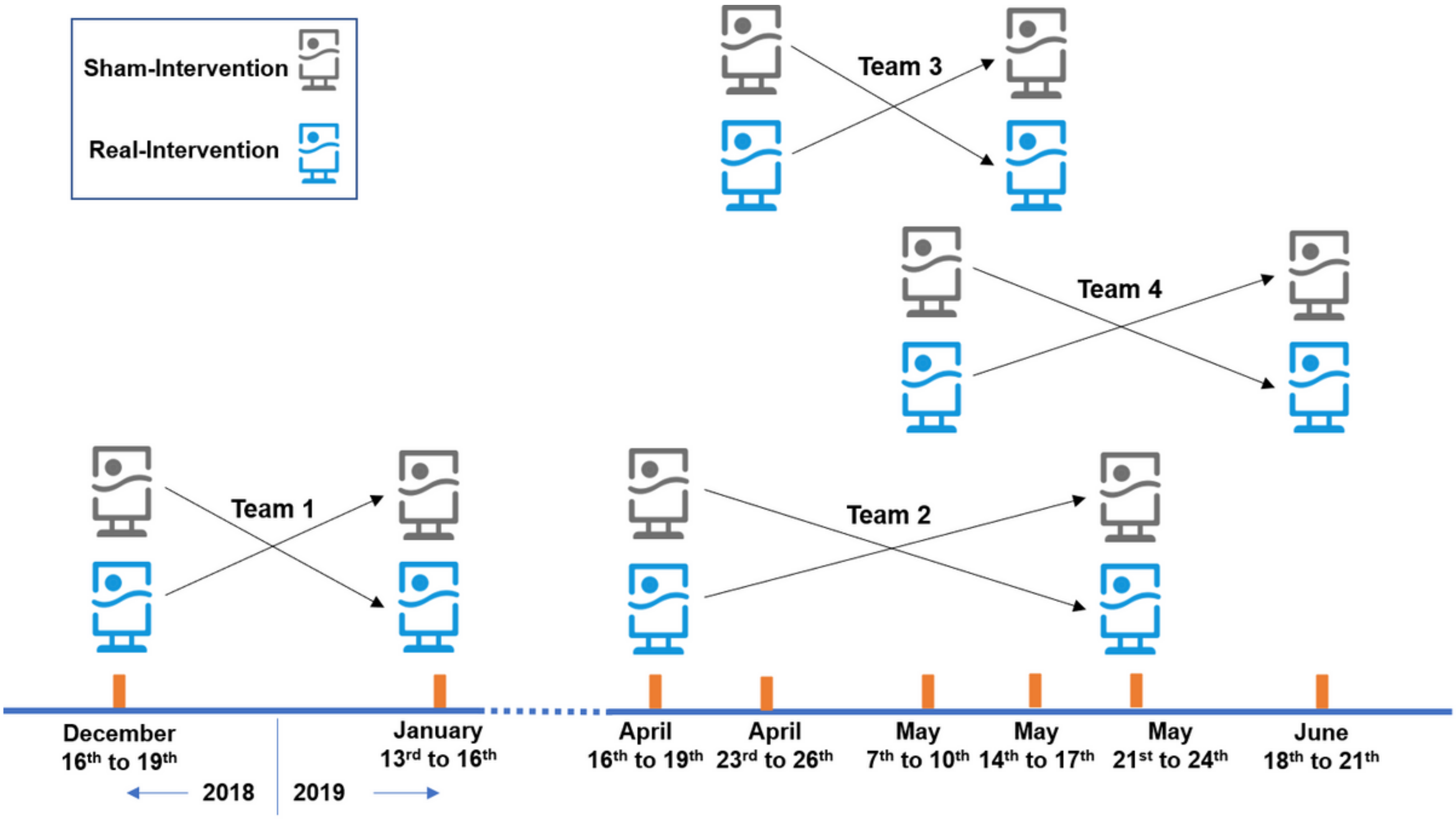
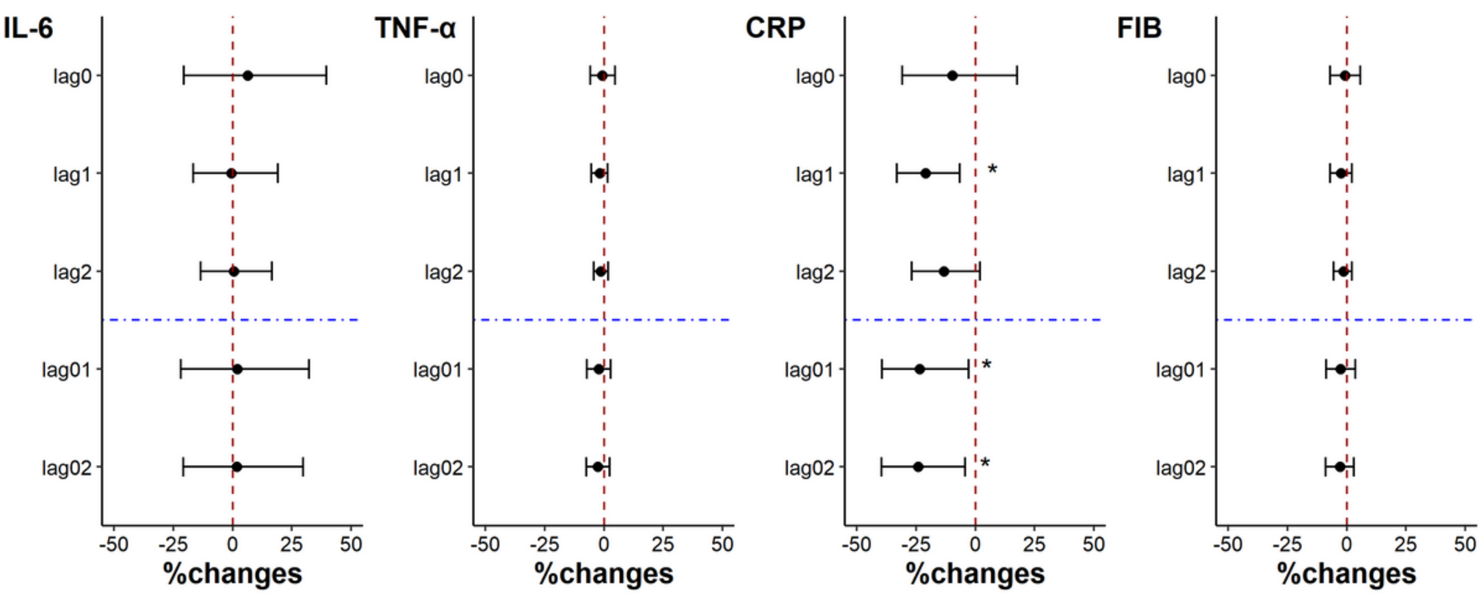
# Figures



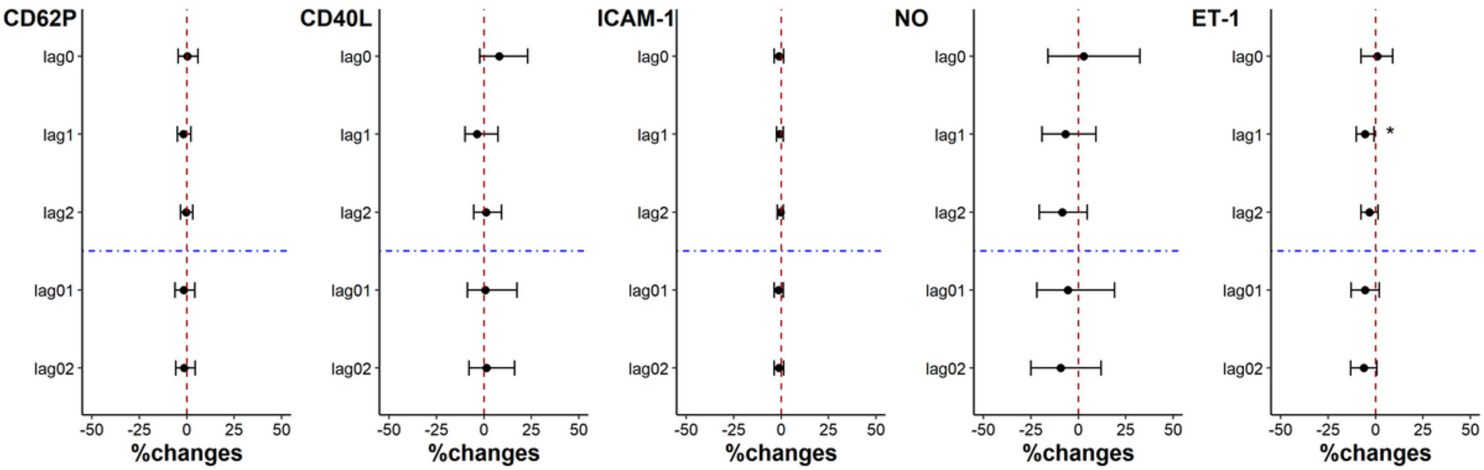

## Figure 1

Arrangement of the intervention



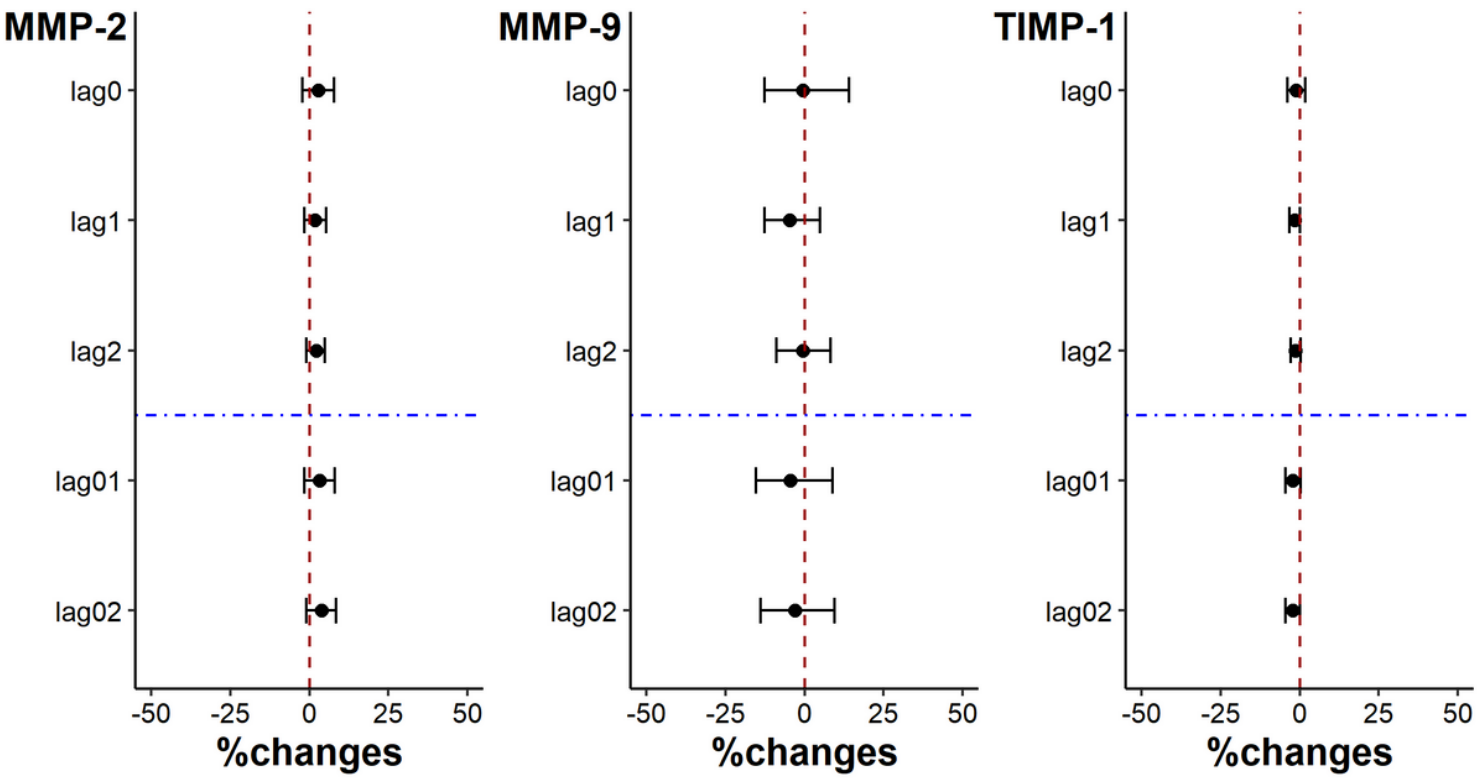

## Figure 2

Percent changes in inflammation indicators associated with an IQR decrease in PM2.5 exposure. * $p < 0.05$




## Figure 3

Percent changes in coagulation indicators associated with an IQR decrease in PM2.5 exposure. * $p < 0.05$




## Figure 4

Percent changes in plaque stability indicators associated with an IQR decrease in PM2.5 exposure

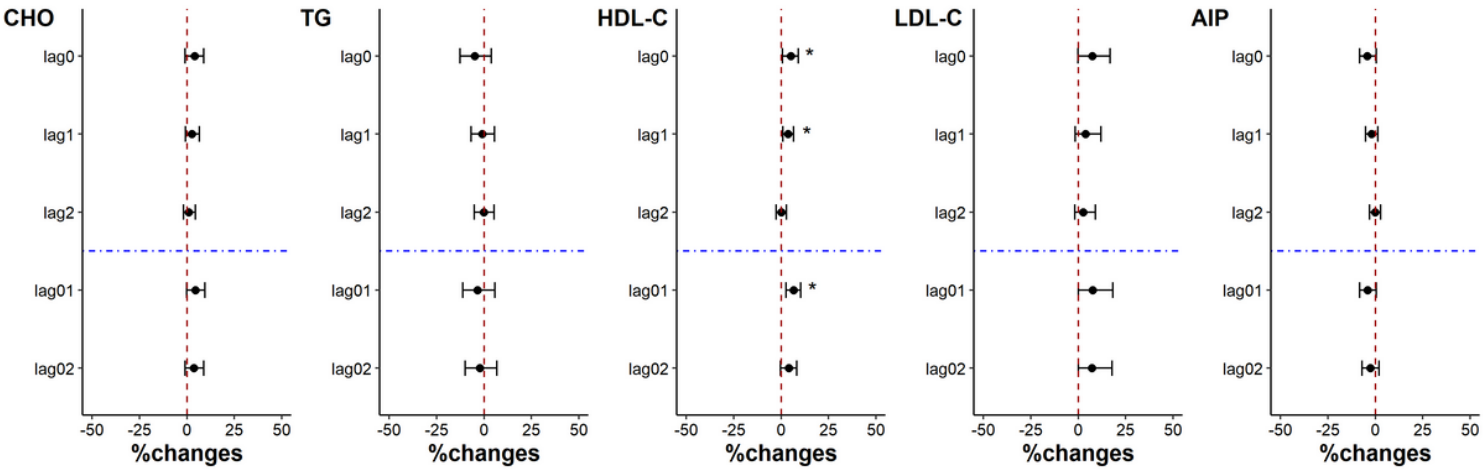



**Figure 5**

Percent changes in blood lipid indicators associated with an IQR decrease in PM2.5 exposure. * $p < 0.05$

# Supplementary Files

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- ESM1.pdf