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ABSTRACT

Exposure to indoor air particulate pollution increases respiratory and cardiovascular morbidity and mortality, especially in the elderly. To assess a short-term, indoor air filtration’s potential benefit on circulatory and cardiopulmonary health among healthy older people, a randomized, double-blind crossover trial was conducted with 24 healthy residents of an aged-care center in Chongqing, China in 2020. Each room received a high-efficiency particulate air filter air purifier and a placebo air purifier for two days. Fifteen circulatory system biomarkers of inflammation, coagulation, and oxidative stress; lung function; blood pressure (BP), heart rate (HR) and fractional exhaled nitric oxide (FeNO) were measured end of each two days. Indoor air particulate pollution was monitored throughout the study period. Linear mixed-effect models were used to associate health outcome variables with indoor particles. This intervention study demonstrated that air filtration was associated with significantly decreased concentrations of inflammatory and coagulation biomarkers, but not of biomarkers of oxidative stress and lung function. Just 48 hours of air filtration can improve the cardiopulmonary health of the elderly. Air purifiers may be a public health measure that can be taken to improve circulatory and cardiopulmonary health among older people.

Key Words: Cardiovascular health; The elderly; Particulate matter; Double-blind crossover trial; Public health
1 INTRODUCTION

A large number of studies have shown that short-term and long-term exposure to particulate matter (PM) will increase the morbidity and mortality associated with cardiovascular and respiratory diseases (Amarloei et al. 2020; Yunesian et al. 2019), such as ischemic heart disease (Dai et al. 2018), stroke (Zhang et al. 2018), chronic obstructive pulmonary disease (Li et al. 2018), and lower respiratory infection (Xia et al. 2017). The biological mechanism hypotheses that PM causes cardiovascular and respiratory diseases include implicate systemic and local inflammation, blood coagulation, impaired heart function (such as increased arterial blood pressure and heart rate), impaired lung function (Dockery and Stone 2007; Simkhovich et al. 2008) and increased oxidative stress (Dockery and Stone 2007; Shrey et al. 2011) were involved in these pathological processes.

The susceptibility to airborne PM pollution varies with different age groups, with the greatest harm to the elderly (Olmo et al. 2011; Peled 2011; Zhang et al. 2013). Current air quality standards for PM may not be safe for elderly people, and even exposure to much lower concentrations can lead to much greater health risks in the elderly, compared with younger age groups, because of their poorer immunity and less efficient cardiovascular and respiratory systems (Arbex et al. 2012).
In China, urban residents spend an average of 87% of their time indoors, and this percentage is even higher for the elderly (Protection 2013), and therefore the concentration of indoor PM has a significant impact on people's health. Indoor PM could come from outdoors (Belis et al. 2013) or be generated indoors (Morawska et al. 2017). Potential indoor sources of PM include cooking, smoking, emissions from wood stoves and fireplaces, heating, cleaning and other occupant activities (McGrath et al. 2017; O’Leary et al. 2019; Wang et al. 2018). Nonsmokers exposed to secondhand smoke had a 22% higher risk of cardiovascular diseases (Zhang et al. 2020). PM_{2.5} in the cooking exhausts could harm the human cardiovascular system (Sun et al. 2020). Outdoor airborne PM can enter a building through ventilation and infiltration (Canha et al. 2019; Lai et al. 2019). People living in buildings close to main roads have a higher death rate due to exposure to PM (Hoek et al. 2002). PM caused by traffic is highly correlated with cardiovascular and respiratory diseases (Jhun et al. 2019). Exposure to PM from outdoor sources will harm elderly people's health (Segalin et al. 2020). Atmospheric PM pollution has become a major health threat accompanying the rapid economic development in China (Li et al. 2017). It is, therefore, very important to reduce indoor PM from outdoor sources, to protect the cardiopulmonary health of the elderly.

Previous studies have shown that indoor air purifiers can significantly reduce the concentration of indoor PM, and has potential benefits for cardiovascular and
respiratory health (Chen et al. 2015; Cui et al. 2018; Guan et al. 2018; Karottki et al. 2013; Shao et al. 2017). However, the subjects of most of these studies were adults and young people like university students, so the results may underestimate the health benefits of air purifier use for the more vulnerable group, that is the elderly (Brauner et al. 2008; Chen et al. 2015; Cui et al. 2018; Guan et al. 2018). Some studies on the elderly have been carried out in countries with low pollution (Brauner et al. 2008; Karottki et al. 2013). However, the outdoor environment and physical fitness of the elderly in China are very different from those in these countries, and there is a lack of research in China.

We, therefore, conducted a randomized double-blind crossover trial of air purifier use in Chongqing, China to determine whether short-term use of air purifier can improve cardiopulmonary health among the elderly. As the pathogenic pathway of PM to human cardiopulmonary diseases is mainly through increasing oxidative stress, activating systemic inflammation, and may lead to the formation of thrombosis. This study selected biomarkers of human circulatory system (systemic inflammation, blood coagulation and oxidative stress) and lung function as the main endpoints. BP, HR and indicators of respiratory inflammation were also tested.
2 METHODS

2.1 STUDY PARTICIPANT AND DESIGN

The study was conducted in January 2020 in an aged-care center in Jiangbei District, Chongqing, China. The locations of the aged-care center are depicted in Figures A.1 and A.2. Twenty-six elderly people were recruited from this center by researchers communicating directly with the elderly, and by posting recruitment advertisements in the center. These participants were selected according to the following principles: 1) no history of cardiopulmonary disease in the three years prior to the trial; 2) had lived in this aged-care center for more than one year; 3) no smoking and alcohol drinking in the rooms; 4) age 60 years or older. Two participants voluntarily quit during the trial and did not participate in the second stage of the trial. Ultimately, 24 elderly people, 12 male and 12 female, living in 16 rooms (8 single and 8 double), took part in the entire trial. A single room is 32 m$^2$ and a double room is 40 m$^2$. Each room has the same configuration and consists of a bedroom and a bathroom.

The study was a randomized double-blind crossover trial, designed to assess the impact of short-term indoor air filtration on acute changes in health endpoints. All participants were divided into two groups on average, namely, Group A and Group B. Figure 1 shows the overall trial protocol of this study, which took a total of 96 hours for each participant. In the first 48 hours, Group A was given air purifiers (treatment group) and Group B was given placebo air purifiers (placebo group: only filter gauzes
removed). In the second 48 hours, this arrangement was reversed between the two groups. Air purifiers and placebo air purifiers have the same appearance, so participants did not feel any difference during the whole trial. There was no way for participants to know if they were in the treatment or the placebo group. The air purifiers were placed at similar locations in the rooms so as not to hinder the participants, while also avoiding being in a corner. Between the two 48-hour intervention periods, there was a 12-day wash-out period. We drew blood and collected morning urine from each participant after each 48-h intervention period, and at the same time, measured their BP, HR, and performed FeNO and lung function tests. All interventions started at 8 am to avoid issues related to diurnal variation. During the trial periods, high-efficiency particulate air filter (HEPA) air purifiers (Well Air Love-KJ001, Well Air Love, Chongqing, China) were used to filtrate the indoor air. We asked all participants to stay in their rooms with the windows and doors closed throughout each 48-h intervention period. Researchers delivered meals to their rooms. Neither participants nor the researchers in the trial can differentiate treatment or the placebo group. All participants provided written informed consent before participating in the study.

Figure 1 Flowchart of Participation in a Randomized, Double-Blind and Crossover Trial of Air Filtration
The Ethics Review Committee of Life Sciences at Central China Normal University approved the study method. Ethics Ratification ID for the project “pathogenic mechanism of indoor environmental risk factors exposure on COPD among older people” is CCNU-IRB-2019-002.

2.2 EXPOSURE ASSESSMENT

Indoor environmental parameters monitored in this study included air temperature (T, °C), relative humidity (RH, %), PM$_{1.0}$ (PM$_{1.0}$ = particulate matter < 1.0μm in aerodynamic diameter) concentration (μg/m$^3$), PM$_{2.5}$ (PM$_{2.5}$ = particulate matter < 2.5μm in aerodynamic diameter) concentration (μg/m$^3$) and PM$_{10}$ (PM$_{10}$ = particulate matter < 10μm in aerodynamic diameter) concentration (μg/m$^3$). These parameters were continuously collected and recorded every minute using an environmental monitoring kit. This equipment has laser dust sensors (ZH03B, Weisen Electronic Technology Co., Ltd, Zhengzhou, China) to monitor the concentration of PM, and
digital temperature and humidity modules (MHTRD06, Yuanjian Sensor Technology, Shenzhen, China) with a high polymer wet-sensitive resistor and a high precision NTC temperature measuring element, to monitor temperature and humidity. Before the study, all sensors were calibrated against an aerosol monitor (DustTrak 8530, TSI Inc., St. Paul, Minnesota) in a calibration room (Manikonda et al. 2016). Table 1 lists the major specifications of all sensors involved in the monitoring kit. The environmental monitoring equipment was installed at least one meter away from the air purifier. Since the older people often lie or sit indoors, the height of the monitoring point is set between 0.6m and 1.0m to cover the elderly breathing area. The 48-hour average mean was used as the uniform exposure level for 1 or 2 subjects in each room. Outdoor environmental parameters, including temperature, relative humidity and PM concentrations, were collected. Outside the main entrance of the aged-care center is a path, across from a residential area. The outdoor environmental monitor was installed in the aged-care center yard to represent the outdoor PM concentrations in the aged-care center. The vertical distance from the monitoring point to the aged-care building is about 10 meters, 3.5 meters from the aged-care door to the monitoring point, and the height of the monitoring point is about 1.2 meters approximately. The air purifier and environmental monitoring kit are shown in Figure A.3.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air temperature</td>
<td>-40°C~60°C</td>
<td>±0.5°C</td>
</tr>
</tbody>
</table>
2.3 HEALTH MEASUREMENTS

Prior to the trial, information such as age, sex, height, weight and past medical history of each participant, and calculated body mass index (BMI) was collected. At the end of each 48-hour trial period, 3ml venous blood (EDTA tube collection) and morning urine were collected from each of the participants, and BP, HR, lung function and FeNO were measured. Plasma was separated from the venous blood samples. All biomarker tests were performed according to the appropriate kit manufacturer's instructions. Other instruments for testing circulatory system markers were an enzyme-labeled instrument (352, Labsystems Multiskan MS Co., Ltd, Finland), a washer (AC8, Thermo Labsystems, Finland), a high-speed micro-centrifugal machine (TG16W, Xiangyi Co., Ltd, China) and a waterproof constant temperature incubator (GNP-9080, Shanghai Jing Hong Laboratory Instrumental Co., Ltd, China). Figure A.4 shows the process of health parameter testing.

The biomarkers we tested were: systemic inflammation, blood coagulation, heart function, lung function, respiratory inflammation and oxidative stress.
**Systemic inflammation**: Eight indicators of blood inflammation, including C-reactive protein (CRP), fibrinogen, P-selectin, monocyte chemoattractant protein (MCP-1), interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor (TNF)-α and myeloperoxidase (MPO).

**Blood coagulation**: Four coagulation indicators, including soluble CD40 ligand (sCD40L), plasminogen activator inhibitor-1 (PAI-1), tissue-type plasminogen activator (t-PA) and D-dimer.

**Heart function**: To measure participants’ BP and HR, we used an upper arm electronic sphygmomanometer (OMRON, Liaoning, China). Participants’ BP was measured at least 3 times by trained technicians, with a 2-min minimum interval between measurements. The systolic BP and diastolic BP can be obtained by averaging the second and third sets of readings. If the differences among the 3 measurements were more than 5 mm Hg, a new round of measurements were taken.

**Lung function**: A spirometer (A01, Breath home, Guangzhou, China) was used, according to the manufacturer's instructions, to measure forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁) and peak expiratory flow (PEF) of each participant. Participants were instructed to perform at least 3 forced expiratory lung
function maneuvers to obtain a minimum of 2 acceptable and reproducible values, and the best results were recorded.

**Respiratory inflammation**: Elevated levels of airway inflammation biomarkers such as fractional exhaled nitric oxide (FeNO) is a signal of respiratory system inflammation (Lambert et al. 2021). FeNO was determined in line with the current ATS/ERS recommendations (American Thoracic and European Respiratory 2005) during a controlled expiration over 6 s using the handheld device, NIOX MINO machine (Aerocrine AB, Solna, Sweden).

**Oxidative stress**: We examined three oxidative stress indicators, including reactive oxygen species (ROS), glutathione (GSH) and 8-hydroxydeoxyguanosine (8-OHdG).

We measured these biomarkers of inflammation, coagulation and oxidative stress using human enzyme-linked immunosorbent assay kits (Jiangsu Meimian Industrial Co., Ltd, Jiangsu, China). The detailed information of the kit is shown in Table A.1.

2.4 STATISTICAL ANALYSES

We converted indoor and outdoor PM concentrations monitored from minutes to hourly data and calculated the hourly, and total mean value, as well as the
corresponding standard deviation of the treatment group and placebo group. The indoor and outdoor PM concentrations were skewed distributed according to Kolmogorov Smirnov testing, so the PM concentration differences between treatment and placebo groups were estimated by Wilcoxon signed-rank test. Since the health-outcome variables were all skewed distributions, we performed a logarithmic transformation of health outcomes before statistical analysis. To estimate the association between indoor air filtration and health endpoints among the elderly, linear mixed-effect models were used. In these models, exposure in terms of filtration status was included as a dummy variable (1 for treatment group and 0 for placebo group) and was analyzed as a fixed effect, and all models included random intercepts for subjects to account for correlations between repeated measures from each participant. All models controlled for the following variables as fixed effect covariates: age, gender, body mass index, indoor relative humidity and indoor temperature. The Mann-Whitney U test was used to examine potential effects caused by the order of intervention between the 2 groups with different treatment orders (Phillips et al. 2013). As a sensitivity analysis, models were examined for indoor PM by replacing the dichotomous air filtration variable with continuous measures of indoor PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ concentration respectively. The dependent variables in these models were the same as those described above and discussed whether the reduction in concentrations of PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ had a different impact on the changes in the health endpoints. The null hypothesis between the treatment group and placebo group
is no difference (p > 0.05). All statistical tests were 2-sided with alpha = 0.05, and all analyses were conducted with the “lme4” package of R software (version 4.0.4).

3 RESULTS

3.1 Baseline Description

Table 2 gives the characteristics of the 24 participants.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD) [range], y</td>
<td>82 (7.8) [61 - 97]</td>
</tr>
<tr>
<td>Female, No. (%)</td>
<td>12 (50.0)</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>27 (3.8)</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared)

According to the self-reported data from participants, they stayed indoors for all of the 48-h periods and lived in the aged-care center during the wash-out period. All 24 participants completed the BP and HR measurements. We noted that with increasing age, the lung function of the participants decreased and measured vital capacity decreased. Because of reduced lung function and vital capacity, two participants were unable to complete two complete FeNO tests and lung function tests, another two only completed the FeNO test, and a further two only completed the lung function tests. This meant that results from the FeNO and lung function tests were collected for only 20 participants. Two of the participants refused to have blood drawn or to provide
morning urine, so only 22 participants provided blood and morning urine samples for this trial.

3.2 PM Exposures

Time-varying PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ concentrations in outdoor air, indoor air of treatment group and placebo group are shown in Figures 2(a), (b) and (c) respectively. The red line represents the hourly concentration of outdoor air, the blue line represents the hourly concentration of these pollutants in the placebo group indoor air and the orange line represents the hourly concentration in the treatment group indoor air. The green dotted line in Figures 2(b) and (c) represents the (World Health Organization) WHO air quality guidelines for PM$_{2.5}$ and PM$_{10}$ (Organization 2014). Indoor PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ concentrations dropped rapidly in the first 2 hours in this trial. Between 8:00 am and 12:00 noon, the concentrations of PM indoors showed a peak value, that coincided with the times when doors were occasionally opened by staff doing routine care in this aged-care center. PM concentrations indoors exceeded the WHO standards in the placebo group indoor air but were within limits in the treatment group indoor air.

Figure 2 Time-varying PM Concentrations in Outdoor, Treatment Group and Placebo Group
This trial was conducted during the winter months of January 6, 2020, to January 22, 2020. The aged-care has no central air conditioning and fresh air systems, and all
rooms are equipped with split air conditioners for both cooling and heating. Table 3 summarizes the PM levels, temperature and relative humidity in the two different exposure groups and outdoor air. The PM concentrations in both the treatment group and placebo group indoor air were significantly lower than that in outdoor air. The average concentrations of PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ in the treatment group indoor air were 20.0µg/m$^3$, 32.9µg/m$^3$ and 42.5µg/m$^3$ lower than that in the placebo group indoor air, respectively. There were significant differences in indoor PM levels due to the air filtration process.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Outdoor Air</th>
<th>Placebo Group Indoor Air</th>
<th>Treatment Group Indoor Air</th>
<th>p-value (Placebo Group vs Treatment Group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{1.0}$, µg/m$^3$</td>
<td>37.8 ± 4.5</td>
<td>27.3 ± 4.7</td>
<td>7.3 ± 3.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PM$_{2.5}$, µg/m$^3$</td>
<td>60.8 ± 6.8</td>
<td>45.6 ± 7.8</td>
<td>12.7 ± 5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PM$_{10}$, µg/m$^3$</td>
<td>77.7 ± 7.5</td>
<td>58.5 ± 10.1</td>
<td>16.0 ± 7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temperature, °C</td>
<td>11.6 ± 3.7</td>
<td>19.8 ± 1.5</td>
<td>20.0 ± 1.9</td>
<td>0.818</td>
</tr>
<tr>
<td>Relative humidity, %</td>
<td>64.6 ± 5.0</td>
<td>51.4 ± 4.6</td>
<td>52.73 ± 3.8</td>
<td>0.506</td>
</tr>
</tbody>
</table>

### 3.3 Biomarker Responses

Table 4 shows the geometric mean and standard deviation (SD) of 8 biomarkers of systemic inflammation, 4 blood coagulation indicators, BP, HR, lung function, respiratory inflammation and 3 oxidative stress biomarkers from the treatment group and placebo group. The indicators of blood inflammation and blood coagulation for
the treatment group were lower than those from the placebo group, while the same trend was not seen in lung function and blood pressure.

Table 4. Summary of Health Endpoints (Geometric Mean ± SD) in Placebo Group and Treatment Group During the Intervention Periods

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Placebo Group</th>
<th>Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP, µg/L</td>
<td>2084.7±426.5</td>
<td>1864.3±397.5</td>
</tr>
<tr>
<td>Fibrinogen, ng/mL</td>
<td>993.3±195.9</td>
<td>859.5±174.1*</td>
</tr>
<tr>
<td>P-selectin, ng/L</td>
<td>4461.6±575.6</td>
<td>4225.6±522.5</td>
</tr>
<tr>
<td>MCP-1, ng/L</td>
<td>240.4±7.1</td>
<td>198.6±21.8*</td>
</tr>
<tr>
<td>IL-1β, pg/mL</td>
<td>51.3±5.5</td>
<td>51.3±5.8</td>
</tr>
<tr>
<td>IL-6, ng/L</td>
<td>20.0±2.8</td>
<td>19.3±2.7</td>
</tr>
<tr>
<td>TNF-α, pg/mL</td>
<td>314.0±74.4</td>
<td>293.7±70.7</td>
</tr>
<tr>
<td>MPO, ng/mL</td>
<td>78.2±10.8</td>
<td>65.2±12.4*</td>
</tr>
<tr>
<td>Blood coagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sCD40L, pg/mL</td>
<td>628.4±146.6</td>
<td>610.3±18.1</td>
</tr>
<tr>
<td>PAI-1, pg/mL</td>
<td>657.4±110.6</td>
<td>564.8±129.6*</td>
</tr>
<tr>
<td>t-PA, ng/L</td>
<td>211.7±22.7</td>
<td>183.6±29.7*</td>
</tr>
<tr>
<td>D-dimer, ng/mL</td>
<td>3728.4±706.7</td>
<td>3470.3±536.9</td>
</tr>
<tr>
<td>BP and HR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic pressure, mm Hg</td>
<td>144.8±29.5</td>
<td>142.3±26.6</td>
</tr>
<tr>
<td>Diastolic pressure, mm Hg</td>
<td>87.3±13.8</td>
<td>87.9±14.6</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>74.4±12.5</td>
<td>70.1±9.6*</td>
</tr>
<tr>
<td>Lung function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEF, L/min</td>
<td>104.5±32.4</td>
<td>96.9±41.6</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>0.87±0.45</td>
<td>0.87±0.48</td>
</tr>
<tr>
<td>FVC, L</td>
<td>1.03±0.62</td>
<td>1.08±0.70</td>
</tr>
<tr>
<td>Respiratory inflammation and oxidative bio-makers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FENO, ppb</td>
<td>18.9±10.0</td>
<td>16.0±9.7</td>
</tr>
<tr>
<td>ROS, ng/mL</td>
<td>11.5±1.4</td>
<td>11.0±1.3</td>
</tr>
<tr>
<td>GSH, ng/L</td>
<td>76.6±11.8</td>
<td>82.2±12.4</td>
</tr>
<tr>
<td>8-OHdG, ng/L</td>
<td>107.9±18.8</td>
<td>103.1±12.2</td>
</tr>
</tbody>
</table>
Figure 3 shows the percentage change and 95% CI in each biomarker in the linear mixed-effect models, with treatment group and placebo group as the category variable. Indoor air filtration was significantly associated with a decrease in 3 of 8 blood inflammation, 2 of 4 blood coagulation and heart rate. In blood inflammation, the mean was significantly reduced by 15.1% (95% CI: -23.1% ~ -6.3%) in fibrinogen, 17.7% (95% CI: -22.9% ~ -12.3%) in MCP-1 and 17.2% (95% CI: -23.9% ~ -9.8%) in MPO. In blood coagulation, the mean of PAI-1 was significantly reduced by 14.9% (95% CI: -21.1% ~ -8.2%) and the mean of t-PA was significantly reduced by 13.5% (95% CI: -18.7% ~ -8.0%) in the treatment group. HR decreased significantly, by 5.8% (95% CI: -10.6% ~ -0.8%) with air filtration. With the exception of FVC, HEPA filtration effects on other health endpoints were generally in the expected directions but with confidence intervals that included the null. However, associations between air filtration and CRP, P-selectin, D-dimer were borderline significant (p=0.064, 0.073 and 0.060 respectively). The sequence of treatment and placebo group was not associated with any of the health indicators based on the Mann-Whitney U test (p values ranging from 0.128 to 0.981).
Figure 3 Air purifiers and cardiopulmonary benefits: Percent Change in Cardiopulmonary health Endpoints Comparing the Treatment Group to Placebo Group

CRP = C-reactive protein; MCP = monocyte chemoattractant protein; IL = interleukin; TNF = tumor necrosis factor; MPO = myeloperoxidase; sCD40L = soluble CD40 ligand; PAI = plasminogen activator inhibitor; t-PA = tissue plasminogen activator; HR = heart rate; PEF = peak expiratory flow; FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; FeNO = fractional exhaled nitric oxide; ROS = reactive oxygen species; GSH = glutathione; 8-OHdG = 8-hydroxy-2-deoxyguanosine;

Percent change in health endpoints associated with a 10 µg/m³ increase of continuous
indoor PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ concentrations are given in Table 5. Similar to the main analyses, continuous exposure to indoor PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ had positive associations with blood inflammation and coagulation biomarkers, FeNO and oxidative biomarkers and there was no significant correlation with lung function. This is inconsistent with the main analyses, where significant associations were seen between indoor PM$_{1.0}$, PM$_{2.5}$, PM$_{10}$ and D-dimer ($p=0.026$, 0.028 and 0.028). When indoor PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ had a 10 µg/m$^3$ increase, D-dimer decreased by 5.1%, 3.1% and 2.4%, respectively. Sensitivity analysis showed that PM with different particle sizes has different effects on health endpoints. The smaller the particle size, the greater the impact on health endpoints.

<table>
<thead>
<tr>
<th>Health Endpoints</th>
<th>Change (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PM$_{1.0}$</td>
</tr>
<tr>
<td>Blood inflammation</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>2.9 (-2.8, 8.6)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0.4 (3.7, 13.2) *</td>
</tr>
<tr>
<td>P-selectin</td>
<td>1.8 (-0.9, 4.5)</td>
</tr>
<tr>
<td>MCP-1</td>
<td>8.0 (4.4, 11.6) *</td>
</tr>
<tr>
<td>IL-1β</td>
<td>1.6 (-1.0, 4.2)</td>
</tr>
<tr>
<td>IL-6</td>
<td>2.5 (-1.1, 6.2)</td>
</tr>
<tr>
<td>TNF-α</td>
<td>1.1 (-5.9, 8.0)</td>
</tr>
<tr>
<td>MPO</td>
<td>9.2 (5.0, 13.3) *</td>
</tr>
<tr>
<td>Blood coagulation</td>
<td></td>
</tr>
<tr>
<td>sCD40L</td>
<td>0.6 (-5.6, 6.7)</td>
</tr>
<tr>
<td>PAI-1</td>
<td>8.1 (4.1, 12.2) *</td>
</tr>
<tr>
<td>t-PA</td>
<td>7.0 (4.0, 10.1) *</td>
</tr>
<tr>
<td>D-dimer</td>
<td>5.1 (0.5, 9.6) *</td>
</tr>
<tr>
<td>Blood pressure and HR</td>
<td></td>
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<tr>
<td></td>
<td>Systolic pressure</td>
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<tr>
<td>------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td></td>
<td>0.4 (-1.8, 2.7)</td>
</tr>
<tr>
<td></td>
<td>-0.1 (-2.3, 2.0)</td>
</tr>
<tr>
<td></td>
<td>3.4 (0.9, 5.9) *</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lung function</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>PEF</td>
<td>3.3 (-5.5, 12.1)</td>
<td>2.0 (-3.3, 7.4)</td>
<td>1.6 (-2.6, 5.7)</td>
</tr>
<tr>
<td>FEV1</td>
<td>0.2 (-6.9, 7.2)</td>
<td>0.1 (-4.2, 4.4)</td>
<td>0.1 (-3.2, 3.4)</td>
</tr>
<tr>
<td>FVC</td>
<td>-1.6 (-9.1, 6.0)</td>
<td>-1.0 (-5.6, 3.6)</td>
<td>-0.8 (-4.3, 2.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory inflammation and oxidative bio-makers</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FENO</td>
<td>6.8 (-4.5, 18.1)</td>
<td>4.1 (-2.7, 11.0)</td>
<td>3.2 (-2.1, 8.5)</td>
</tr>
<tr>
<td>ROS</td>
<td>0.5 (-2.6, 3.6)</td>
<td>0.3 (-1.6, 2.2)</td>
<td>0.2 (-1.2, 1.7)</td>
</tr>
<tr>
<td>GSH</td>
<td>-3.0 (-7.1, 1.2)</td>
<td>-1.8 (-4.3, 0.7)</td>
<td>-1.4 (-3.3, 0.6)</td>
</tr>
<tr>
<td>8-OHdG</td>
<td>2.1 (-2.0, 6.3)</td>
<td>1.3 (-1.2, 3.8)</td>
<td>1.0 (-0.9, 2.9)</td>
</tr>
</tbody>
</table>

### 4 DISCUSSION

During the trial, the average PM$_{2.5}$ and PM$_{10}$ concentrations outside the aged-care center were 60.8µg/m$^3$ and 77.7µg/m$^3$ respectively which exceeded the WHO air quality guidelines (25µg/m$^3$ for PM$_{2.5}$ and 50µg/m$^3$ for PM$_{10}$ based on 24h). Society and government need to make efforts to reduce air pollution outside the aged-care center. Portable air purifiers reduced PM$_{1.0}$, PM$_{2.5}$ and PM$_{10}$ concentrations in the aged-care center from 27.3µg/m$^3$, 45.6µg/m$^3$ and 58.5µg/m$^3$ to 7.3µg/m$^3$, 12.7µg/m$^3$ and 16.0µg/m$^3$ respectively, a reduction of 73%. Portable air purifier is an economical and effective way to immediately reduce indoor PM concentration.

Our results point towards inflammation as pathways linking air pollution and cardiovascular disease and PM may promote the formation of blood clots in the elderly (Aryal et al. 2021; Brauer et al. 2021; Pan et al. 2016). Short-term indoor air filtration may have cardiovascular benefits. In this study, we found a modest decrease
in systemic inflammation, blood coagulation and oxidative stress indicators with air filtration, while the lung function of the elderly is insensitive to indoor particulate concentration.

The relationship between exposure to air pollution and cardiovascular disease involves many pathophysiological pathways, such as systemic inflammation and coagulation. CRP is a reliable and independent predictor of incidents of cardiovascular events (Koenig W et al. 2006). In previous studies investigating the relationship between short-term and long-term PM exposure and CRP, some cross-sectional studies found that there was a positive correlation between exposure to PM and CRP (Michikawa et al. 2016; Pilz et al. 2018). A randomized double-blind crossover trial of short-term air purifier interventions among 35 healthy college students in Shanghai, China, also found that air filtration can lead to a reduction in CRP, but that the reduction was not significant (Chen et al. 2015). The sources of indoor PM in our study were similar to those in (Chen et al. 2015), both being infiltration of traffic-generated PM. However, our study found that a 48-hour air filtration intervention resulted in a borderline significant decrease in CRP in the elderly. It is suggested that CRP may be a sensitive acute systemic inflammation biomarker in the elderly. MPO, a pro-oxidant enzyme and indicator of neutrophil activation, is released by activated polymorphonuclear neutrophils and exhibits catalytic activity, generating a range of reactive oxidants and diffusible radical species.
These products are necessary for fighting invading microorganisms (Nicholls and Hazen 2009). Persistent high levels of the examined mediators, as well as acute changes, have been associated with an increased risk of cardiovascular events in large cohort studies (Koenig et al. 1999). In this study, the concentration of MPO significantly decreased with air filtration. Elevated levels of circulating MPO are considered a prognostic marker of mortality and predict the risk of subsequent major adverse cardiovascular events in patients with the acute coronary syndrome (Asselbergs et al. 2004). These blood biomarkers might therefore explain the link between exposure to ambient air pollution and increased cardiovascular diseases and T2D in the elderly (Liu et al. 2013). MCP-1 was found to be an important pro-inflammatory factor, which could influence a series of receptors in a cell and play a vital role in cardiovascular diseases, such as atherosclerosis (Deshmane et al. 2009). Indoor air filtration can significantly reduce the concentration of MCP-1 in the elderly. Different inflammatory factors of older people have different degrees of reduction after air filtration. It is because that the correlation between PM dose and cytokine production in cells is nonlinear because of others factors, such as pathways regulating cytokine secretion and synergistic and antagonistic effects of cell components at different concentrations (Chao et al. 2018; Gupta et al. 2015).

In response to vessel destruction or inflammation, the human body responds by increasing the count of coagulation factors to enhance and complete the formation of
thrombus, with fibrinogen playing a key role in this process (Gharibi et al. 2019; Gharibi et al. 2020). Previous studies have shown that the concentration of PM has a positive correlation with the concentration of fibrinogen (Jaafari et al. 2020; Wu et al. 2012; Wu et al. 2014). These results are consistent with the results from our study, where we found that indoor PM filtration was associated with a significant reduction of fibrinogen in the older participants. A randomized double-blind intervention study of air purifiers for college students conducted under daily atmospheric conditions in Beijing, China, found that air filtration reduced fibrinogen in young people, but not significantly (Chen et al. 2015). In our study, there were significant changes in fibrinogen in the elderly participants, which may be due to decreased body function as the body ages, which might make them more susceptible to PM damage to their cardiovascular health. The potential health benefits of air filtration for the elderly are thus greater than for the general population. The biological mechanisms associated with exposure to PM and venous thromboembolism have not been fully identified, although one of the possible mechanisms that have been suggested is that of hypercoagulability and enhanced thrombosis (Mostafapour et al. 2018). In our study, we found that PAI-1, t-PA and D-dimer were significantly decreased after air filtration, which supports this idea.

Our results also showed that air filtration can make FeNO decrease 13.97%, but the value was not significant. The air filtration was not significantly associated with the

promoting plaque rupture, vasoconstriction, thrombosis and arrhythmias (Mills et al. 2009). In this study, the level of oxidative stress (ROS, GSH and 8-OHdG) were measured, which did not have significant change after short-term air filtration.

PM with different sizes have different capabilities in inducing blood inflammation, blood coagulation and oxidative bio-makers. Comparing with PM$_{10}$ and PM$_{2.5}$, PM$_{1.0}$ had the highest capability in inducing these health endpoints.

The main limitation of our research is that the study included only 24 elderly participants, which means that we might have missed some potentially important but modest differences attributable to the relatively small sample. For this reason, this research is considered to be exploratory.

5 CONCLUSIONS

The study suggests that indoor PM filtration can improve older people’s cardiovascular health by decreasing blood inflammation and blood coagulation. However, that the levels observed appear to be in the range that does not create measurable changes in the oxidative stress biomarker in this small population of elderly adults. The study also suggests that filtration appears to be an effective public health intervention to protect against impacts of outdoor air pollution on residents living in retirement facilities in cities with relatively high PM levels and thus
suggesting this is an effective public health intervention to test on larger populations in the future.

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Baizhan Li: Methodology, Data Curation, Supervision.
Runming Yao: Supervision, Writing - Review & Editing
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Yuping Tang: Visualization.
Yi Jiang: Investigation.
Hongjie Su: Investigation.
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Lexiang Wang: Formal analysis, Investigation.
Xu Yang: Conceptualization, Writing - Review & Editing
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Wei Yu: Methodology, Formal analysis, Writing - Review & Editing, Supervision.

All authors read and approved the final manuscript.
Declaration of interests

☒ 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.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:
Graphical abstract
Highlights:

• Air filtration led to a decrease in inflammatory and coagulation indicators

• PM with smaller size has higher capability in inducing cardiopulmonary bio-makers

• Air purifiers is an effective way to improve the elderly’s cardiopulmonary health