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The effect of portable HEPA filter air cleaners on indoor $PM_{2.5}$ concentrations and second hand tobacco smoke exposure among pregnant women in Ulaanbaatar, Mongolia: The UGAAR randomized controlled trial

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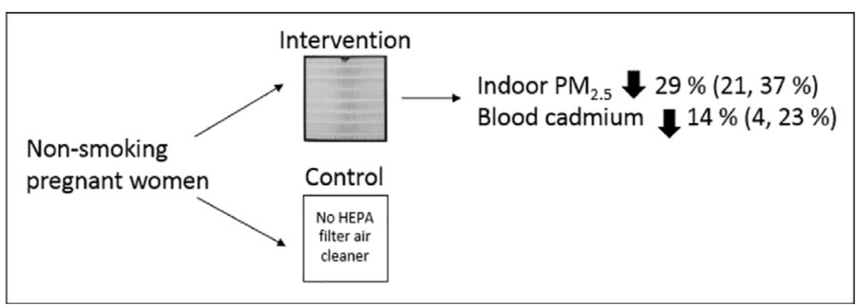
HIGHLIGHTS

- Interventions are needed to lower household $PM_{2.5}$ exposures.
- Participants were randomized to a control (no air cleaners) or intervention (1–2 air cleaners) group.
- Air cleaners lowered indoor $PM_{2.5}$ by 29% (95% CI: 21, 37%) and blood cadmium by 14% (4, 23%).
- Air cleaners were most effective in winter, when the $PM_{2.5}$ geometric mean was reduced from 45 to 29 μg/m^3.
- Air cleaner effectiveness was reduced by >50% after approximately 5 months of use.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Portable HEPA filter air cleaners can reduce indoor fine particulate matter ($PM_{2.5}$), but their use has not been adequately evaluated in high pollution settings. We assessed air cleaner effectiveness in reducing indoor residential $PM_{2.5}$ and second hand smoke (SHS) exposures among non-smoking pregnant women in Ulaanbaatar, Mongolia.

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Methods: We randomized 540 participants to an intervention group receiving 1 or 2 HEPA filter air cleaners or a control group receiving no air cleaners. We followed 259 intervention and 253 control participants to the end of pregnancy. We measured one-week indoor residential $PM_{2.5}$ concentrations in early (~11 weeks gestation) and late (~31 weeks gestation) pregnancy and collected outdoor $PM_{2.5}$ data from centrally-located government monitors. We assessed blood cadmium in late pregnancy. Hair nicotine was quantified in a subset ($n = 125$) to evaluate blood cadmium as a biomarker of SHS exposure. We evaluated air cleaner effectiveness using mixed effects and multiple linear regression models and used stratified models and interaction terms to evaluate potential modifiers of effectiveness.

Results: The overall geometric mean (GM) one-week outdoor $PM_{2.5}$ concentration was 47.9 μg/m³ (95% CI: 44.6, 51.6 μg/m³), with highest concentrations in winter (118.0 μg/m³; 110.4, 126.2 μg/m³). One-week indoor and outdoor $PM_{2.5}$ concentrations were correlated ($r = 0.69$). Indoor $PM_{2.5}$ concentrations were 29% (21, 37%) lower in intervention versus control apartments, with GMs of 17.3 μg/m³ (15.8, 18.8 μg/m³) and 24.5 μg/m³ (22.2, 27.0 μg/m³), respectively. Air cleaner effectiveness was greater when air cleaners were first deployed (40%; 31, 48%) than after approximately five months of use (15%; 0, 27%). Blood cadmium concentrations were 14% (4, 23%) lower among intervention participants, likely due to reduced SHS exposure.

Conclusions: Portable HEPA filter air cleaners can lower indoor $PM_{2.5}$ concentrations and SHS exposures in highly polluted settings.

1. Background

Outdoor fine particulate matter ($PM_{2.5}$) air pollution is a leading global public health risk factor (Cohen et al., 2017; Forouzanfar et al., 2016). The enormous public health impact of $PM_{2.5}$ is due in part to the large number of people exposed. In 2013, 87% of the world's population lived in areas where $PM_{2.5}$ concentrations exceeded the World Health Organization annual average guideline of 10 μg/m³ (Brauer et al., 2016). Despite decreasing concentrations in many high income countries, the global population-weighted $PM_{2.5}$ concentrations increased by over 20% between 1990 and 2013 due largely to increasing concentrations in Asia (Brauer et al., 2016). $PM_{2.5}$ is a risk factor for numerous health conditions including ischaemic heart disease, stroke, chronic obstructive pulmonary disease, cancer, and lower respiratory infections (Cohen et al., 2017; Forouzanfar et al., 2016). A growing body of evidence also links $PM_{2.5}$ exposure with impaired fetal growth, an important indicator of health in early childhood and over the life course (McIntire et al., 1999; Barker, 2006; Gluckman et al., 2008).

Reducing $PM_{2.5}$ concentrations results in substantial public health benefits (Stieb, 2015; Pope et al., 2009; Gauderman et al., 2015). From a public health perspective, interventions that reduce pollution emissions and exposure among large populations are generally preferable to those that reduce exposure at the individual or household level. However, because community-wide improvements in air quality usually occur over decades (Fenger, 1999), it is important to identify interventions that can reduce household exposures in the near term until emissions can be reduced to acceptable levels.

Portable high efficiency particulate air (HEPA) filter air cleaners are a promising household level intervention to reduce indoor $PM_{2.5}$ concentrations. $PM_{2.5}$ readily infiltrates into buildings (Allen et al., 2012; Clark et al., 2010; Xu, 2016), so a substantial portion of exposure to $PM_{2.5}$ of outdoor origin actually occurs indoors, where individuals spend the majority of their time (Leech et al., 2002). Many countries with high outdoor air pollution concentrations also have a high prevalence of smoking, so air cleaners have the potential advantage of reducing exposure to both outdoor pollution that infiltrates indoors and indoor-generated pollution from cigarettes and other sources. Air cleaners are widely available and relatively inexpensive to purchase and operate (Fisk and Chan, 2017). Previous studies have linked portable air cleaner use in residences to reductions of 32–68% in concentrations of particles from various outdoor and indoor sources, including traffic, wildfire and residential wood smoke, and second hand tobacco smoke (SHS) (Kajbafzadeh et al., 2015; Batterman et al., 2012; Allen et al., 2011; Butz et al., 2011; Lanphear et al., 2011; Barn et al., 2008; Brauner et al., 2008; McNamara et al., 2017; Chen et al., 2015; Ward et al., 2017). Much of this work has been conducted in high income settings where $PM_{2.5}$ concentrations and smoking rates are relatively low (Reitsma et al., 2017), so little is known about the efficacy of portable air cleaners in highly polluted settings. Additionally, most studies of air cleaner use have been conducted over short periods ranging from a few days to weeks, with few evaluations of efficacy over longer durations (Fisk, 2013).

The Ulaanbaatar Gestation and Air Pollution Research (UGAAR) study is a randomized controlled trial designed to assess the effect of portable HEPA filter air cleaner use during pregnancy on fetal growth and early childhood development (ClinicalTrials.gov Identifier: NCT01741051). Our study was conducted in Ulaanbaatar, Mongolia's capital city, which is home to roughly one-half of the country's total population of three million (Mongolian Statistical Information Service, n.d.). Ulaanbaatar is one of the coldest and most polluted cities in the world. The population-weighted annual average $PM_{2.5}$ concentration in the city is approximately 70 μg/m³ (Ochir and Smith, 2014). Ulaanbaatar is located in a valley with mountains to the north and south, which together with cold temperatures, contribute to inversions that exacerbate the poor air quality in winter. Wintertime $PM_{2.5}$ emissions are dominated by residential heating with coal (Ochir and Smith, 2014). Coal combustion is also linked to other pollutants, including cadmium (Song, 2008). Household coal use occurs in ger (a traditional felt-lined Mongolian dwelling) neighbourhoods surrounding the city where roughly 60% of the city's population resides (Guttikunda, 2007). In 2013, there were an estimated 164,000 to 185,000 ger households in the city (The World Bank Group, 2013), each burning an average of approximately 5 t of coal per year (Guttikunda, 2007). Air pollution emissions linked to household coal use are expected to increase further as the population in ger neighbourhoods increases (The World Bank Group, 2013). The remainder of Ulaanbaatar's residents live in apartments, which receive electricity from three coal-fired power plants. These power plants and an increasing number of motor vehicles also contribute to air pollution in the city (Kamata et al., 2010). We have previously estimated that approximately 10% of the mortality in Ulaanbaatar is attributable to outdoor $PM_{2.5}$ (Allen et al., 2013).

The objective of this analysis was to quantify the impact of HEPA filter air cleaner use during pregnancy on indoor residential $PM_{2.5}$, and blood cadmium concentrations.

2. Materials and methods

2.1. Study population

Our study population consisted of women in Ulaanbaatar who met the following eligibility criteria: 18 years or older, in the early stages (≤18 weeks) of a single-gestation pregnancy, non-smoker, living in an apartment, planning to give birth in a maternity hospital in Ulaanbaatar, and not using an air cleaner in the home at enrollment. Initially, recruitment of participants was done in coordination with the reproductive health clinic at the Sukhbaatar district Health Centre in Ulaanbaatar. This city district was targeted due to its large population living in apartments, its proximity to the ger area north of the city centre, and our relationships with staff at the district hospital. To increase participant recruitment, we established a second study office in September 2014 at the first branch location of the Sukhbaatar Health Centre (see Supplemental file 1). We excluded women living in gers because we were interested in assessing the impact of community-level air pollution on indoor residential $PM_{2.5}$ concentrations and wanted to minimize the influence of indoor emissions from ger stoves, and because many ger households lack a reliable source of electricity, which are needed to operate air cleaners.

2.2. Study design

We randomly assigned 540 participants to the intervention or control group. Randomization was done using sealed opaque envelopes containing randomly generated "filter" or "control" allocations and labelled with participant identification numbers that ran from one to 580. Allocation was done on a 1:1 ratio. Participants in the intervention group received one or two portable HEPA filter air cleaners (AP-1009CH, Coway, Korea) depending on the size of their apartment, and air cleaners were used from the first home visit until childbirth. Apartments with a total area <40 m^2 received one air cleaner and those with areas ≥40 m^2 received two air cleaners. The air cleaners had a clean air delivery rate for tobacco smoke (particles sized 0.09–1.0 μm) of 149 ft^3/m, which is appropriate for use in rooms up to approximately 22 m^2. The commercially available model has an internal PM sensor and "mood light" that changes colour based on the PM concentration, but this feature was disabled to avoid biasing the behaviour of UGAAR participants. The air cleaners used in UGAAR were also modified to operate only on the second-highest fan setting with an internal timer that counted total hours of use. Timer data were retrieved once each participant completed the study. Unfortunately, the internal timers proved to have limited value because initiating the timer required the air cleaner to be turned on while also pressing specific buttons. Participants were given instructions on the procedure, but if a participant turned on the air cleaner (e.g., after the unit was turned off, unplugged, or in the event of a power failure) without initiating the timer then subsequent air cleaner usage was not logged. For smaller apartments, air cleaners were placed in the main living area of the home, and for larger apartments, the second unit was placed in the participant's bedroom. Air cleaners were deployed with new pre-filters, which help to remove large debris, and HEPA filters. Participants were shown how to clean the pre-filter, but we did not replace pre-filters or HEPA filters during the study. Participants were encouraged to use the air cleaners continuously throughout the study period. The control group received no air cleaners.

2.3. Data collection

Data collection took place from January 2014 to December 2015. We collected data at home and clinic visits that occurred in early (5–18 weeks gestation) and late (24–37 weeks gestation) pregnancy (Fig. 1). We collected air pollution measurements over one-week periods following the two home visits. Whole blood and hair samples were collected during the second clinic visit. We administered questionnaires at both clinic visits to collect data on housing and lifestyle (e.g. SHS exposures, time activity patterns) characteristics. Participants were compensated with a payment of 65,000 Mongolian tugriks (approximately $45 Canadian) upon completion of data collection, and a pro-rated amount was provided to participants who withdrew before completion of the study. The study protocol was approved by the Simon Fraser University Office of Research Ethics (2013s0016) and the Mongolian Ministry of Health Medical Ethics Approval Committee (No.7). Written consent was obtained from participants prior to their enrollment into the study.

2.4. Indoor residential air pollution measurements

We measured particle number concentrations in all apartments during two one-week sampling campaigns using Dylos laser particle counters (DC1700; Dylos Corporation, Riverside, California, USA). These instruments quantify particle count concentrations in two particle size ranges: >0.5 μm and >2.5 μm. The commercially available Dylos monitors log particle counts at one-minute intervals and display counts in real time, but the units used in UGAAR were modified to log data at five-minute intervals (to allow one week of data to be logged). Real-time particle count displays were disabled to avoid biasing participants' behaviour. We used the difference between the small and large particle size counts since it has previously been shown to provide the best approximation of $PM_{2.5}$ concentrations, with reported Dylos-$PM_{2.5}$ correlations ranging between 0.55 and 0.99 (Northcross et al., 2013; Semple et al., 2015; Steinle et al., 2015; Semple et al., 2013; Hyder et al., 2014; Klepeis et al., 2013). We conducted co-location tests of all Dylos monitors to identify and discontinue the use of monitors showing poor performance (see Supplemental file 2).

We co-located Dylos particle counts and gravimetric $PM_{2.5}$ in a subset of 90 apartments, roughly 20% of our sample. The data were used to establish the empirical relationship between Dylos particle counts and

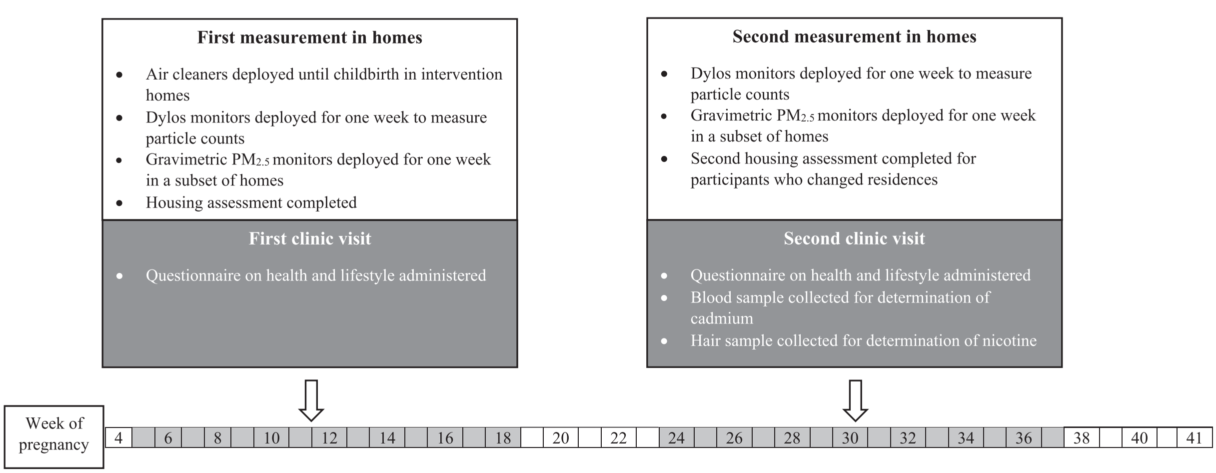

Fig. 1. Summary of data collection.

$PM_{2.5}$ mass concentrations (in units of μg/m^3) since this relationship depends on the optical properties of the aerosol being measured. These apartments represent a convenience sample because although they were randomly chosen to capture a representative sample of intervention and control apartments across multiple seasons, measurements were only conducted if participants gave permission for additional sampling. Gravimetric $PM_{2.5}$ samples were collected onto 37-mm Teflon filters using Harvard Personal Environmental Monitors (HPEM; Air Diagnostics and Engineering, Inc., Harrison, ME) connected to mass flow controlled BGI 400 air pumps (BGI, Inc., Waltham, MA) operated at 4 L/min. Filters were weighted in triplicate before and after sampling, and the average of the three measurements was taken. The air pollution sampling equipment was placed in the main activity room, typically on a table or shelf, as far as possible away from the air cleaner, pollution sources, ventilation systems, and bright light sources.

2.5. Outdoor air pollution data

Outdoor $PM_{2.5}$ concentrations were obtained from two centrally-located government-run monitoring stations. Measurements were made using tapered element oscillating microbalance (TEOM) monitors.

2.6. Relative humidity

Continuous measurements of relative humidity (RH) were made using HOBO loggers (ux100-011; Onset Computer Corporation; Bourne, MA, USA) in the subset of apartments selected for gravimetric $PM_{2.5}$ monitoring. RH was of interest since it can impact the light scattering properties of particles, thereby influencing the relationship between Dylos particle counts and $PM_{2.5}$ mass concentrations. The Dylos has previously been shown to record artificially high particle counts when RH exceeds approximately 90% (United States Environmental Protection Agency, 2014).

2.7. Blood cadmium

Whole blood samples were collected from 382 participants by a nurse at the reproductive health clinic during the second clinic visit. Samples were refrigerated and shipped to the Wadsworth Center (New York State Department of Health, Albany, New York, USA) for analysis within six weeks of collection. Samples were analyzed for cadmium using quadrupole-based inductively coupled plasma-mass spectrometry (ICP-MS), with matrix-matched calibration (Palmer et al., 2006). The limit of quantification (LOQ), which was based on US Environmental Protection Agency recommendations, was 0.043 μg/L. Two samples were below the LOQ; concentrations of LOQ/2 were assigned to these samples (Hornung and Reed, 1990).

2.8. Hair nicotine

Hair samples were collected during second clinic visits for analysis of nicotine, an indicator of SHS. Approximately 30–50 strands of hair (>30 mg) were cut close to the scalp at the occipital area of the head. Participants were asked if they had chemically treated their hair in the previous three months since chemical treatment can affect hair nicotine concentrations (Al-Delaimy, 2002). After collection, hair samples were placed into a plastic bag and stored at room temperature before being shipped for analysis to the Clinical Pharmacology Laboratory at the University of California, San Francisco. Hair samples were used primarily to evaluate blood cadmium as a biomarker of SHS exposure, so 125 hair samples were selected for analysis to capture potentially low and high SHS exposures among intervention and control participants, based on whether participants lived with a smoker. Samples were additionally limited to participants who had a blood cadmium measurement and those who did not chemically treat their hair. Four-cm samples were analyzed to represent SHS exposures occurring in the approximately four months prior to data collection. Hair samples were washed, digested and then analyzed by gas chromatography-tandem mass spectrometry (GC–MS/MS). Five samples were below the LOQ of 0.036 ng/mg; concentrations of LOQ/2 were assigned to these samples (Hornung and Reed, 1990).

2.9. Other data

Study technicians conducted a home assessment during the first home visit to determine the area and volume of each room, and total area of the home. Study technicians also determined the building location using a global positioning system (GPS) device. If a participant moved between visits, study technicians also conducted an assessment during the second home visit. During both clinic visits, staff administered a questionnaire to obtain information on health, medical history, and lifestyle factors such as alcohol use, smoking, and exposure to SHS. We quantified air cleaner use in intervention apartments using information provided on the questionnaire administered at the second clinic visit. Specifically, participants were asked to estimate the percentage of time that air cleaner units were used since they were installed in the home. For apartments with two air cleaners, we averaged the reported use for both units.

2.10. Data analysis

We conducted a series of quality control and data cleaning steps on particle count data prior to analysis, including removing incomplete data, which resulted in the removal of 464 (51%) one-week Dylos measurements We assessed baseline housing, personal, and behavioral characteristics among participants excluded due to a lack of valid Dylos data and those included in this analysis (those with one or two Dylos measurements). Although participants with no measurements spent less time at home in early pregnancy (15.7 h/day, 95% CI: 15.1, 16.2 h/day) compared with participants with one or two measurements (16.3 h/day, 95% CI: 15.9, 16.8 h/day, $p = 0.02$), we found no other significant differences between these groups (Supplemental file 2), indicating that the participants and homes included in our analysis are representative of the full UGAAR cohort. The effect of RH on particle count data was determined to be negligible since hourly RH measured in apartments never exceeded 85%. We found strong agreement between the one-week particle counts and gravimetric $PM_{2.5}$ concentrations ($R^2 = 0.94$, $n = 23$), and used this relationship to convert Dylos particle counts to mass concentrations (see Supplemental file 3). We averaged outdoor $PM_{2.5}$ concentrations measured at the two monitoring sites and calculated one-week averages corresponding to each week of indoor $PM_{2.5}$ monitoring in apartments, and examined correlations between indoor and outdoor concentrations. Potential differences by intervention assignment in baseline housing, personal and behavioral characteristics were assessed using Fisher's exact tests, *t*-tests, and Mann-Whitney tests as appropriate.

Linear and mixed effects regression models were used to assess the impact of the intervention on indoor $PM_{2.5}$ and blood cadmium concentrations. All exposure variables were log-transformed to improve the normality of model residuals, and results are presented as percent concentration reductions in the intervention group relative to the control group. Since one-week indoor $PM_{2.5}$ concentrations were measured twice for participants, we assessed the effect of the intervention based on all data using mixed effects models, and for each visit separately using multiple linear regression. For mixed effects models, we used an unstructured covariance matrix and entered intervention status as a fixed effect and apartment (participant) as a random intercept to account for repeated measurements in apartments. Results of indoor $PM_{2.5}$ models are shown both unadjusted and adjusted for outdoor $PM_{2.5}$ concentrations. All analyses comparing intervention and control groups were based on randomized intervention assignments, and all analyses involving the number of air cleaners were based on the actual number deployed in homes by study staff. Standard regression diagnostics were conducted on all models.

To evaluate effect modification, we also ran the regression models after stratifying by variables that we hypothesized might modify air cleaner effectiveness such as number of air cleaners, air cleaner density (number of air cleaners per 100 m^2 of home area), reported air cleaner use, season, window opening, living with a smoker, living in a home where smoking occurred indoors, and, for blood cadmium, time spent indoors at home. Information on time-dependent variables, such as living with a smoker and time spent at home, was obtained in both early and late pregnancy. For stratifications involving $PM_{2.5}$, we used data collected at both time points. For stratified models of blood cadmium, we used data collected in late pregnancy to reflect more relevant exposure periods. The half-life of cadmium in blood ranges from roughly 75–128 days (Bernhoft, 2013). Differences in air cleaner effectiveness between strata were evaluated using interaction terms in the regression models.

Finally, we evaluated the role of SHS as a source of cadmium exposure. We calculated correlations between blood cadmium and hair nicotine and compared concentrations of both biomarkers between smoking and non-smoking households.

3. Results

Five hundred and forty women were recruited at a mean gestation of 10.3 weeks (range: 4.0–17.0 weeks). Two hundred and seventy-two participants were randomized to the control group and 268 were randomized to the intervention group (Fig. 2). Eight participants received incorrect treatments. These participants were retained in the dataset and analyzed according to their assigned treatment groups. Twenty-eight (5%) participants were lost to follow up, leaving for analysis 512 participants followed to the end of pregnancy. In total, 236 and 211 one-week $PM_{2.5}$ concentrations measured in early (first measurement) and late (second measurement) pregnancy, respectively, were analyzed, as well as 382 whole blood samples and 125 hair samples. Differences in several characteristics that might influence exposure to $PM_{2.5}$ and cadmium were examined among participants who remained in the study and those who were lost to follow up. No significant differences were found for housing characteristics such as area of home, age of home, window usage, as well as other characteristics, such as time spent at home, living with a smoker and season of enrollment into the study (see Supplemental file 4). Participants lost to follow up were more likely to use a non-UGAAR study air cleaner (i.e. not provided by the study; $p = 0.05$).

At baseline, control and intervention participants had similar home ages, total home areas, and window opening behaviour (Table 1). Approximately half of the participants in both groups reported living with a smoker at any time in pregnancy, and 8% of participants in both groups reported smoking at any time during pregnancy. Control and intervention participants spent on average 16 h per day indoors at home in both early and late pregnancy. The majority of participants (80%) reported working outside the home during pregnancy. More participants in the control group changed address (9%) compared with the intervention group (5%). Control participants were also more likely to live in apartments located on lower floors (56%) than intervention participants (46%). The number of participants enrolled into the study each season was similar for both groups, with the highest enrollment occurring during winter and fall. Among the intervention group, 70 households received one air cleaner and 186 households received two air cleaners. Air cleaner density, calculated as the number of air cleaners per total area of the home, was similar for apartments with one and two area cleaners, with geometric means of 3.0 air cleaners/100 m^2 (95% CI: 2.8, 3.2 air cleaners/100 m^2) and 2.9 air cleaners/100 m^2 (95% CI: 2.7, 3.1 air cleaners/100 m^2), respectively. Air cleaners were reported

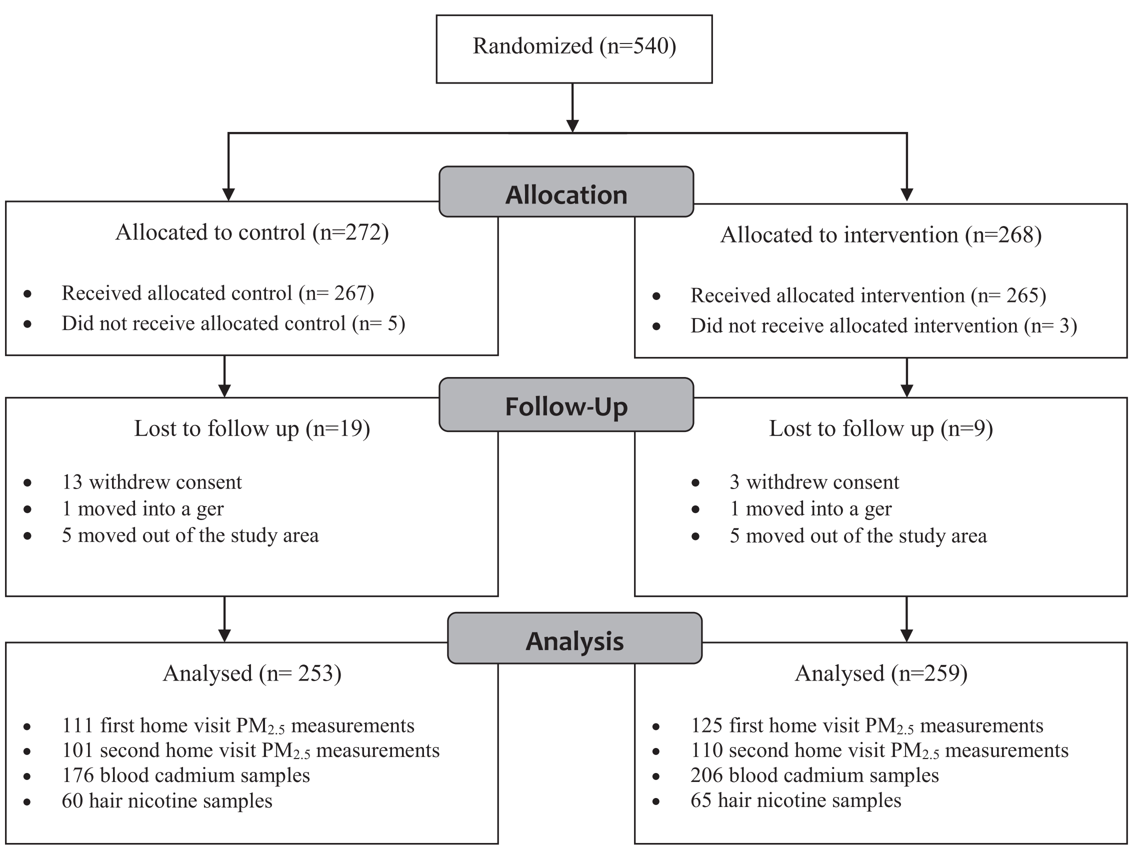

Fig. 2. Trial profile.

Table 1
Summary of household, personal, and behavioral characteristics by intervention status.

	Control group ($n = 253$)		Intervention group ($n = 259$)		p-Value
	GM (95% CI) or N	%	GM (95% CI) or N	%	
Housing characteristics					
Total home area (m^2)	52.3 (48.7, 55.8)	94	54.6 (51.2, 58.2)	97	0.20
Not recorded		6		3	
Age of home (years)	10.6 (8.6, 13.1)	66	11.2 (9.4, 13.3)	73	0.96
Not recorded		34		27	
Window opening in winter					
Open < half the month	118	47	130	50	0.50
Open ≥ half the month	129	51	126	49	
Not recorded	6	2	3	1	
Window opening in summer					
Open < half the month	24	9	35	13	0.17
Open ≥ half the month	224	89	222	86	
Not recorded	5	2	2	1	
Outdoor $PM_{2.5}$ (μg/m^3)	54.3 (50.5 58.4)	96	55.0 (51.6, 58.64)	99	0.85
Not available		4		1	
Personal and behavioral characteristics					
Week of pregnancy at enrollment into the study	9.9 (9.5, 10.3)	100	10.0 (9.6, 10.3)	100	0.95
Season of enrollment into the study					
Winter (Dec–Feb)	89	35	78	30	0.46
Spring (Mar–May)	72	28	70	27	
Summer (Jun–Aug)	27	11	35	14	
Fall (Sep–Nov)	65	26	76	29	
Time spent indoors at home in early pregnancy (hours/day)	16.0 (15.5, 16.5)	79	16.3 (15.9, 16.8)	74	0.41
Not recorded		21		26	
Time spent indoors at home in late pregnancy (hours/day)	15.6 (14.9, 16.3)	47	15.8 (15.1, 16.5)	60	0.69
Not recorded		53		40	
Lived with a smoker at any time in pregnancy					
No	118	47	131	51	0.47
Yes	127	50	123	47	
Not recorded	8	3	5	2	
Smoking occurred in the home at any time in pregnancy					
No	173	53	176	56	0.70
Yes	73	29	81	31	
Not recorded	7	19	2	13	

to be used for a geometric mean of 64% of the study duration, and use did not differ by number of air cleaners deployed. Thirteen participants in the control group and seven in the intervention group reported using a non-UGAAR air cleaner.

The geometric means of one-week outdoor $PM_{2.5}$ concentrations corresponding to periods of indoor residential $PM_{2.5}$ monitoring were 58.2 μg/m^3 (95% CI: 52.9, 63.9 μg/m^3) and 38.0 μg/m^3 (95% CI: 34.2, 42.2 μg/m^3) for the first (early pregnancy) and second (late pregnancy) measurements, respectively. Outdoor concentrations were similar for control and intervention homes. Across the seasons, geometric mean outdoor one-week $PM_{2.5}$ concentrations were 118.0 μg/m^3 (95% CI: 110.4, 126.2 μg/m^3) and 60.0 μg/m^3 (95% CI: 54.9, 65.7 μg/m^3) in winter and fall, and 31.7 μg/m^3 (95% CI: 29.5, 34.0 μg/m^3) and 20.3 μg/m^3 (95% CI: 19.3, 21.3 μg/m^3) in spring and summer, respectively. One-week indoor and outdoor $PM_{2.5}$ concentrations were correlated ($r = 0.69$, $n = 429$), with higher correlations for control apartments ($r = 0.78$, $n = 203$) than intervention apartments ($r = 0.63$, $n = 226$; see Supplemental file 5).

The overall geometric means of one-week indoor $PM_{2.5}$ concentrations were 22.5 μg/m^3 (95% CI: 20.5, 24.6 μg/m^3) and 18.3 μg/m^3 (95% CI: 16.6, 20.1 μg/m^3) for the first and second measurements, respectively. Over half (64%) of the first home measurements were made in fall and winter reflecting higher indoor $PM_{2.5}$ concentrations compared with the second measurements, the majority of which (61%) were made in spring and summer when concentrations were lower. Overall, the intervention reduced indoor $PM_{2.5}$ concentrations by 29% (95% CI: 21, 37%, Table 2). We observed larger reductions when the air cleaners were first deployed in early pregnancy (40%, 95% CI: 31, 48%), compared with after roughly five months of use (15%, 95% CI: 0, 27%, Table 2; Fig. 3). Apartments that received two air cleaners had larger reductions in $PM_{2.5}$ concentrations (33%, 95% CI: 25, 41%) than apartments with one air cleaner (20%, 95% CI: 6, 32%). This trend was seen for measurements made both early and late in the air cleaners' deployment. No differences in effectiveness were observed for reported air cleaner use. Stratification by season revealed a higher non-significant difference in air cleaner effectiveness between winter (36%, 95%: 20, 49%) and summer (18%, 95% CI: 4, 30%). Greater wintertime reductions were observed for apartments where windows were opened less frequently. Significantly higher indoor $PM_{2.5}$ concentrations were seen in apartments of participants who lived with smokers. Higher concentrations were also seen in apartments where smoking occurred indoors, although differences were not significant. Behaviours related to smoking in the home did not influence air cleaner effectiveness.

The intervention reduced blood cadmium concentrations by 14% (95% CI: 4, 23%), from a geometric mean of 0.23 μg/L (95% CI: 0.21, 0.25 μg/L) to 0.20 μg/L (95% CI: 0.19, 0.21 μg/L). The effect of the air cleaners on blood cadmium concentrations was not significantly modified by smoking in the home, working outside the home, time spent at home, or number of air cleaners.

Blood cadmium and hair nicotine concentrations were more strongly correlated among participants who lived with a smoker ($r = 0.29$, $p = 0.02$, $n = 66$) compared with those who did not ($r = 0.10$, $p = 0.47$, $n = 56$). Blood cadmium concentrations were 14% (95% CI: 2, 28%) higher among participants who lived with a smoker, and 24% (95% CI: 10, 41%) higher among participants who lived in apartments where smoking occurred indoors, compared with participants from non-smoking households. Similarly, geometric mean hair nicotine concentrations were significantly higher among participants living in smoking (33 ng/mg; 95% CI: 0.23, 0.46 ng/mg) versus non-smoking households (0.10 ng/mg; 95% CI: 0.08. 0.14 ng/mg).

Table 2
Effect of portable HEPA filter air cleaner use on one-week residential indoor $PM_{2.5}$ concentrations.

	GM (95% CI) μg/m^3		% change[a] (95% CI)	
	Control	Intervention	Crude	Adjusted for outdoor $PM_{2.5}$
All data	24.5 (22.2, 27.0) n = 212	17.3 (15.8, 18.8) n = 235	−30 (−38, −22)	−29 (−37, −21)
Duration of air cleaner use				
First measurement	30.3 (26.7, 34.3) n = 111	17.3 (15.4, 19.4) n = 125	−43 (−52, −32)	−40 (−48, −31)
Second measurement	19.4 (16.9, 22.3) n = 101	17.3 (15.1, 19.7) n = 110	−11 (−26, 8)	−15 (−27, 0)
Number of air cleaners deployed				
1 air cleaner	–	18.7 (15.7, 22.3) n = 64	−23 (−35, −9)	−20 (−32, −6)
2 air cleaners	–	16.7 (15.1, 18.4) n = 167	−31 (−39, −21)	−33 (−41, −25)
Air cleaner density[b]				
<3.0 air cleaners/100 m^2	–	17.9 (15.7, 20.3) n = 102	−27 (−36, −16)	−28 (−37, −18)
≥3.0 air cleaners/100 m^2	–	16.5 (14.6, 18.6) n = 123	−32 (−41, −22)	−30 (−38, −20)
Air cleaner use[c]				
<63% of study period	–	17.1 (14.7, 19.7) n = 87	−30 (−40, −18)	−33 (−42, −23)
≥63% of study period	–	17.2 (15.2, 19.4) n = 121	−31 (−40, −20)	−30 (−39, −20)
Season				
Winter	44.5 (39.0, 50.9) n = 59	28.5 (23.7, 34.4) n = 54	−36 (−49, −20)	−36 (−49, −20)
Spring	22.6 (19.3, 26.5) n = 47	15.6 (13.6, 17.9) n = 64	−31 (−44, −15)	−35 (−48, −19)
Summer	11.7 (10.5, 13.1) n = 53	9.5 (8.4, 10.8) n = 51	−19 (−31, −4)	−18 (−30, −4)
Fall	28.3 (23.9, 33.5) n = 53	20 (17.5, 22.8) n = 66	−29 (−43, −13)	−31 (−43, −18)
Window opening in winter (Dec–Feb)				
Open < half the month	46.9 (38.6, 57.1) n = 34	25.7 (18.9, 35.0) n = 29	−45 (−61, −22)	−45 (−61, −22)
Open ≥ half the month	40.8 (34.0, 49.0) n = 24	32.2 (26.4, 39.3) n = 25	−21 (−39, 3)	−23 (−4, 10)
Lived with a smoker at any time in pregnancy				
No	22.8 (19.8, 26.3) n = 98	16.0 (14.2, 18.2) n = 120	−31 (−42, −19)	−26 (−37, −13)
Yes	26.0 (22.7, 29.8) n = 111	18.8 (16.6, 21.2) n = 112	−28 (−39, −16)	−29 (−40, −17)
Smoking occurred in the home at any time in pregnancy				
No	24.2 (21.5, 27.2) n = 144	16.7 (15.0, 18.6) n = 155	−31 (−41, −19)	−29 (−38, −19)
Yes	25.2 (21.2, 29.9) n = 65	18.4 (16.0, 21.2) n = 80	−32 (−44, −17)	−33 (−45, −19)

[a] Percent reduction comparing one-week indoor $PM_{2.5}$ concentrations in intervention to control apartments, except for analyses of number of air cleaners which compares indoor $PM_{2.5}$ concentrations in apartments with one and two air cleaners against apartments with no air cleaners.
[b] 3.0 air cleaners/100 m^2 was the geometric mean air density calculated for intervention apartments.
[c] 63% was the geometric mean air cleaner use reported by participants.

4. Discussion

In this relatively large randomized controlled trial we assessed the impact of HEPA filter air cleaners on indoor $PM_{2.5}$ and blood cadmium concentrations among pregnant women in Ulaanbaatar, Mongolia. Air cleaners reduced one-week indoor $PM_{2.5}$ concentrations by 29% (95% CI: 21, 37%) and blood cadmium concentrations by 14% (95% CI: 4, 23%). Larger $PM_{2.5}$ reductions were seen for the first measurement (40%, 95% CI: 31, 48%), when the air cleaners were newly deployed, compared with the second measurement (15%, 95% CI: 0, 27%), which was made after roughly five months of air cleaner use. We found strong correlations between indoor and outdoor $PM_{2.5}$, indicating that outdoor $PM_{2.5}$ contributed substantially to indoor concentrations. Since filter effectiveness followed the same seasonal pattern as outdoor $PM_{2.5}$ concentrations, the impact of the intervention on indoor $PM_{2.5}$ concentrations was extraordinarily large in the winter months, when the geometric mean was reduced from 45 to 29 μg/m^3. Apartments with two air cleaners experienced larger reductions in indoor $PM_{2.5}$ than apartments with one air cleaner; in contrast, we did not observe differences in HEPA cleaner effectiveness by the density of air cleaners (number of air cleaners/100 m^2). No differences in effectiveness were found based on reported air cleaner use, which was crudely assessed from a question about overall use and was not based specifically on the periods of air pollution monitoring.

The reductions in residential indoor $PM_{2.5}$ in our study are consistent with findings reported by other studies evaluating portable air cleaner use in residential settings (Kajbafzadeh et al., 2015; Batterman et al., 2012; Allen et al., 2011; Butz et al., 2011; Lanphear et al., 2011; Barn et al., 2008; Brauner et al., 2008; McNamara et al., 2017; Chen et al., 2015). Only one study has been conducted in a similarly highly polluted setting. Chen et al. (2015) evaluated the use of portable electrostatic precipitator air cleaners in 10 university dormitory rooms in Shanghai, China. The authors reported a 57% reduction in indoor $PM_{2.5}$, with mean (SD) concentrations decreasing from 96.2 (25.8) μg/m^3 during a

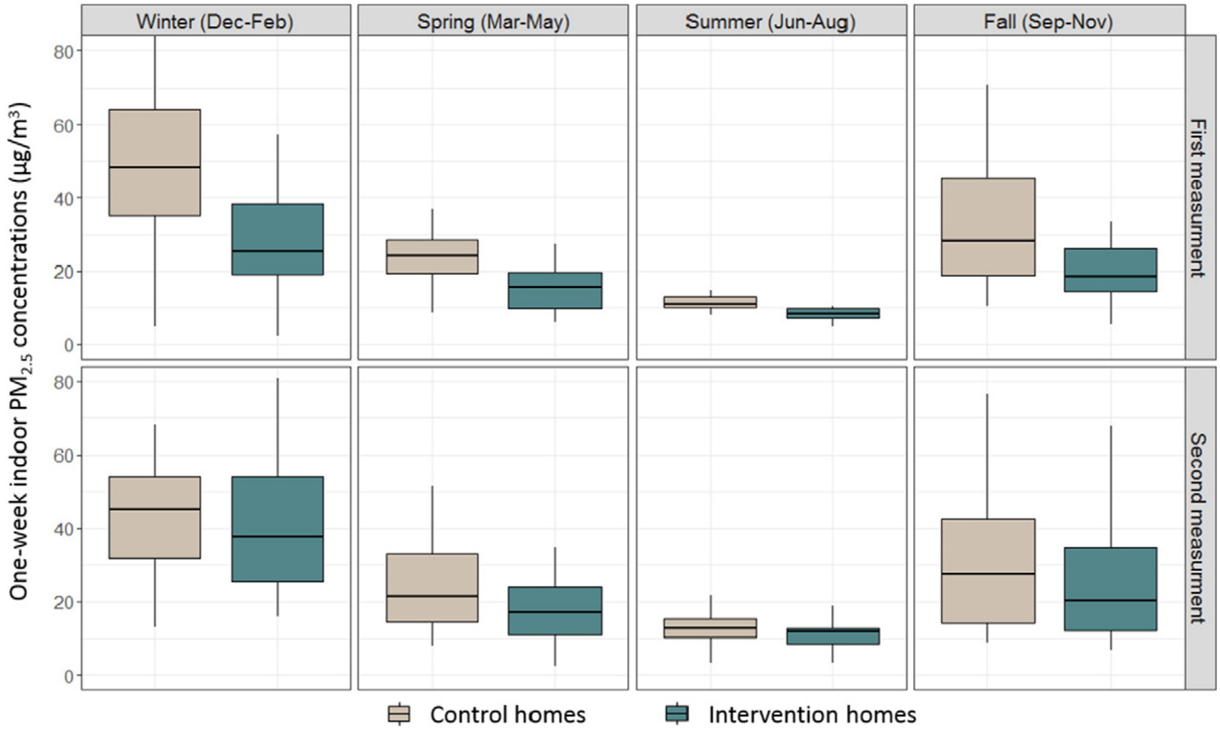

Fig. 3. Distribution of one-week indoor $PM_{2.5}$ concentrations in control and intervention homes stratified by season and measurement (the first measurement was made when air cleaners were newly deployed and the second measurement was made after approximately five months of use).

48-hour control period with sham filtration to 41.3 (17.6) μg/m^3 during a 48-hour period with active filtration (Chen et al., 2015). Four US-based randomized controlled trials evaluated the use of portable air cleaners over six to 12 months in homes (Batterman et al., 2012; Butz et al., 2011; Lanphear et al., 2011; McNamara et al., 2017). Authors reported mean reductions in $PM_{2.5}$ or particle counts (>0.3 μm) of 32–66% (see Supplemental file 6). In the only study to assess changes in air cleaner effectiveness over time, Lanphear et al. (2011) reported decreases in particle count concentrations (>0.3 μm) of 46% in intervention apartments compared with control apartments after six months of air cleaner use, and a 32% reduction after 12 months of use ($n = 225$) (Lanphear et al., 2011). In contrast, we saw greater decreases in effectiveness over the roughly five months between air pollution measurements in our study. This larger decrease may have been due to more rapid overloading of HEPA filters in this high pollution setting or lower compliance to the intervention.

Overall, participants reported using air cleaners for 64% of the study period. Although we did not systematically evaluate the reasons that participants shut off the air cleaners, anecdotal reports from participants revealed concerns about noise and electricity costs. For example, some participants reported consistently turning air cleaners off at night to minimize noise. Studies measuring compliance to air cleaner use have previously reported that participants used air cleaners approximately 34 to 79% of the time during study periods ranging from one to 12 months (Batterman et al., 2012; Butz et al., 2011; McNamara et al., 2017; Ward et al., 2017). Batterman et al. (2012) also looked at changes in compliance over time. The authors conducted one-week indoor air quality monitoring in apartments for 3–4 consecutive seasons, with air cleaner use being monitored throughout this period (Batterman et al., 2012). Air cleaner use declined from a mean (SD) of 84% (24) during the first indoor air quality measurement to 63% (33) when indoor air quality measurements were collected in subsequent seasons. Compliance was lowest during periods outside of when indoor air quality measurements were taken, with a mean use of 34% (30) (Batterman et al., 2012). Similar to our study, Ward et al. (2017) reported no relationship between air cleaner effectiveness and compliance, which was assessed by comparing expected and measured energy consumption for air cleaner units during the study period (Ward et al., 2017).

Air cleaners reduced average blood cadmium concentrations by 14%. A reduction in cadmium exposures, even from low levels, could have important public health implications (Järup and Åkesson, 2009). Cadmium is a known human carcinogen and has also been linked with adverse cardiovascular and kidney effects (Järup and Åkesson, 2009; International Agency for Research on Cancer, 2012). Among pregnant women, blood cadmium concentrations have been linked to impaired fetal growth, as indicated by small for gestational age (Wang et al., 2016; Johnston et al., 2014) and reduced birth weight (Salpietro et al., 2002). Tobacco smoke exposures have been reported to be the greatest contributor to blood and urinary cadmium levels among smokers (Garner and Levallois, 2016). Similarly, among pregnant women, elevated blood cadmium levels have been reported among those who were active smokers or exposed to SHS (Edwards et al., 2015; Hinwood et al., 2013; Hansen, 2011). Although blood cadmium concentrations cannot definitively be linked to SHS exposures, we found three pieces of compelling evidence to suggest that SHS exposure was an important source of cadmium in our population. First, we found higher blood cadmium concentrations among participants who reported living with smokers as well as among those living in homes where smoking occurred indoors, compared with those in non-smoking households. Second, we found higher correlations between blood cadmium and hair nicotine concentrations among participants who lived with smokers ($r = 0.29$) compared with those who did not ($r = 0.10$). Finally, we found lower blood cadmium concentrations among intervention participants, suggesting that airborne exposures were lower in this group. Other sources of airborne cadmium, including coal combustion, may have also contributed to blood cadmium exposures (Song, 2008). Our finding that air cleaner use decreased SHS exposure differs from previous studies. Lanphear et al. (2011) and Butz et al. (2011) reported no changes in hair, serum or urinary cotinine concentrations comparing intervention and control participants, or pre- and post-intervention levels, among children using portable HEPA filter air cleaners for six to 12 months (Butz et al., 2011; Lanphear et al., 2011).

In our study, geometric mean blood cadmium and hair nicotine concentrations found among participants with and without SHS exposures ranged from 0.20–0.23 μg/L and 0.10–0.33 ng/mg, respectively, which are relatively low compared with previously reported values among pregnant women. In a review of 24 studies assessing blood cadmium concentrations among pregnant women, Taylor et al. (2014) reported mean and median blood cadmium concentrations ranging from 0.09 to 2.26 μg/L among populations in several countries, including Poland, Russia, South Africa, Egypt, India, Norway, France, United States and China (Taylor et al., 2014). Few guidelines or levels of concern exist for blood cadmium. In Germany, a guideline of 1 μg/L has been established for the general public, which includes non-smoking adults aged 18–69 years (Taylor et al., 2014). Similarly, hair nicotine concentrations in our study population were substantially lower than concentrations reported among pregnant women living with partners who smoke (0.51 to 3.18 ng/mg) (Yoo et al., 2010; Seong et al., 2008).

Our findings suggest that portable HEPA filter air cleaners are an effective household level intervention to reduce $PM_{2.5}$. The situation in Ulaanbaatar is similar to many other rapidly growing cities, where already dramatically high pollution concentrations are expected to increase, and strategies to effectively manage air quality will take years or decades to implement (Ochir and Smith, 2014). Proposed strategies in Ulaanbaatar have included dissemination of cleaner-burning coal stoves and use of cleaner-burning fuels in ger households, as well as improved emission controls for coal-fired power plants (Ochir and Smith, 2014). Cigarette smoke is the most important indoor source of $PM_{2.5}$ in non-ger households in Ulaanbaatar (Ochir and Smith, 2014). Nearly 40% of Mongolian men smoke (Global Burden of Disease Study (GBD), 2015), consistent with our finding that half of UGAAR participants lived with a smoker and 34% lived with someone who smoked inside the home. Portable air cleaners show promise because they are easy to operate and reduce concentrations inside residences, where individuals spend the largest portion of time. The costs, which include an initial purchase price typically starting at $200-300US (California Environmental Protection Agency Air Resources Board, n.d.; Fisk and Chan, 2016), as well as maintenance and operation costs, will be prohibitive for some. In addition, air cleaners must be appropriately sized for the volume of the home and the air exchange rate, and may not be a viable intervention in situations when windows are frequently opened or residences are not tightly sealed. This is consistent with our finding that in winter months air cleaners were more effective when windows were kept closed.

Some important limitations of our study should be noted. First, participants were not blinded to the intervention. Previous air cleaner studies have used sham filtration to blind participants to their intervention status, but instead of purchasing sham air cleaners we chose to recruit a larger number of participants and deploy two air cleaners in larger apartments. Moreover, our exposure measures were objective, which should minimize potential bias resulting from the lack of blinding. Another limitation of our study is that we did not replace HEPA filters during the study period, which has been done by others assessing long-term air cleaner use and performance (Batterman et al., 2012). We chose not to replace filters in our study period to assess air cleaner efficacy under more "real world" conditions and to minimize logistical challenges. Although we collected information on air cleaner use via questionnaires and internal timers, data from timers were flawed and did not allow us to assess how air cleaner use changed over time. We also did not assess air cleaner use in gers, where the highest exposures in Ulaanbaatar occur and where exposure reduction is needed most (Ochir and Smith, 2014), because we wanted to minimize the influence of indoor generated $PM_{2.5}$ in our assessment, and due to concerns about the lack of reliable electricity. Consequently, our findings on air cleaner effectiveness are likely not generalizable to ger households. Finally, we approximated $PM_{2.5}$ concentrations using the Dylos, a low-cost optical particle counter. Extensive quality control and data cleaning steps identified several instruments that provided unreliable data, which resulted in a large fraction of data being removed prior to analysis. Despite these data losses, our analysis made use of an extraordinarily large dataset (447 one-week indoor $PM_{2.5}$ concentration measurements in 342 apartments). Consistent with several previous studies, we found excellent agreement ($R^2 = 0.94$) between Dylos particle counts and $PM_{2.5}$ concentrations measured gravimetrically (Northcross et al., 2013; Semple et al., 2015; Steinle et al., 2015; Semple et al., 2013; Hyder et al., 2014; Klepeis et al., 2013).

5. Conclusions

In this randomized controlled trial, we found that air cleaners substantially reduced indoor $PM_{2.5}$ concentrations and SHS exposures as measured by blood cadmium among a group of pregnant women in a highly-polluted city. Our findings suggest that portable air cleaners are a useful household level intervention that can help reduce $PM_{2.5}$ exposures during pregnancy and other critical time periods.

Abbreviations

GC–MS/MS	gas chromatography–tandem mass spectrometry
GM	geometric mean
GPS	global positioning system
HEPA	high efficiency particulate air
ICP-MS	inductively coupled plasma-mass spectrometry
PM	particulate matter
$PM_{2.5}$	fine particulate matter
LOQ	limit of quantification
RH	relative humidity
SHS	second hand smoke
TEOM	tapered element oscillating microbalance
UGAAR	Ulaanbaatar Gestation and Air Pollution Research

Ethics approval and consent to participate

The study protocol was approved by the Simon Fraser University Office of Research Ethics (2013s0016) and the Mongolian Ministry of Health Medical Ethics Approval Committee (No.7). Written consent was obtained from participants prior to their enrollment into the study.

Competing interests

Ryan W. Allen has received in-kind research support in the form of discounted air purifiers from Woongjin-Coway, but the company has had no role in study design, analysis or interpretation. All other authors declare they have no actual or potential competing financial interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2017.09.291.

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