Electronic Supplementary Information (ESI) for:

Accounting for in-situ air cleaner utilization and performance to improve interpretation of patient outcomes in real-world indoor air cleaner intervention trials

Saeed Farhoodi[1], Insung Kang[2,3], Yicheng Zeng[1], Kaveeta Jagota[3], Nancy Karpen[3], Mohammad Heidarinejad[1,3], Zane Elfessi[4,5], Israel Rubinstein[3,6,7], Brent Stephens[1,3*]

[1] Department of Civil, Architectural, and Environmental Engineering, Illinois Institute of Technology, Chicago, IL USA
[2] Department of Civil Engineering, University of Texas at Arlington, Arlington, TX USA
[3] Research and Development Service, Jesse Brown Veterans Affairs Medical Center, Chicago, IL USA
[4] College of Pharmacy, University of Illinois Chicago, Chicago, IL USA
[5] Emergency Medicine Service, Jesse Brown Veterans Affairs Medical Center, Chicago, IL USA
[6] College of Medicine, University of Illinois Chicago, Chicago, IL USA
[7] Medical Service, Jesse Brown Veterans Affairs Medical Center, Chicago, IL USA

*Corresponding author:
Brent Stephens, Ph.D.
Professor and Department Chair
Arthur W. Hill Endowed Chair in Sustainability
Department of Civil, Architectural, and Environmental Engineering
Illinois Institute of Technology
Alumni Memorial Hall Room 228E
3201 South Dearborn Street
Chicago, IL 60616
Phone: (312) 567-3629
Email: brent@iit.edu

Summary of Recent and Ongoing Clinical Intervention Trials

Since 2020, at least five systematic reviews of clinical intervention trials to evaluate the health effects (or markers of effects) of indoor air cleaning or filtration have been published, with foci on cardiovascular health [1], biomarkers of cardiorespiratory [2] or cardiovascular health [3], and blood pressure [4,5]. These reviews generally cover articles published between 2008 and 2022. The total number of published air cleaner intervention trials with health outcomes (or markers of outcomes) evaluated in these recent reviews is up to approximately 20 studies with a combined total enrollment of up to approximately 900 participants. Study populations have ranged from children to elderly and from healthy populations to vulnerable populations with underlying health conditions. Sample sizes of intervention trials have ranged from approximately 20 to 200 participants, which would place them generally in the range of sample sizes that are typical for Phase I/II clinical trials [6]. Durations of air cleaner interventions have ranged from half a day to as long as one year, although most have been shorter term, with medians ranging only 7-14 days across the different reviews. Some key recommendations from these reviews are for intervention trials to target larger sample sizes, particularly in higher-risk populations, and with more rigorous study designs (e.g., longer duration, greater specificity in exposure assessment, etc.).

Additionally, we conducted a non-exhaustive search of currently active trials registered on ClinicalTrials.gov focused on indoor air cleaning interventions, meaning they are listed as active and ongoing, recruiting, or in preparation for recruiting (and thus completed trials were intentionally not included). Search terms included: “air clean*”, “air purif*”, and “HEPA filt*”. At least 36 active trials were initially identified as potentially relevant based on search terms, which were then filtered to 27 registered trials that were deemed as relevant to indoor air cleaning/filtration interventions upon closer inspection. The full list is provided as supplemental file to this manuscript. Each registered trial was then inspected for the type of indoor environment (e.g., homes, schools), target sample size, type of air cleaning intervention, and types of clinical outcomes to be assessed, which was used to summarize the current state of trials at a high level. We also attempted to review the published trial protocols for their plans regarding monitoring air cleaner performance or operation, but the registries generally lacked such details.

Figure S1 shows a summary of these indoor air cleaning intervention trials currently registered on ClinicalTrials.gov. The total number of participants to be enrolled targeted by these 27 registered studies over the next three years is around 6,000 people. Approximately two-thirds of the targeted participant enrollment in these registered studies reside in the U.S., and about two-thirds of targeted participants are adults. Nearly three-fourths of the targeted participants will receive in-home air cleaning interventions, with another ~20% in schools and ~8% in hospitals. Clinical outcomes by target enrollment vary more widely, with the largest fractions focused on cardiovascular outcomes (25%), chronic obstructive pulmonary disease (COPD) (19%), cognition (15%), asthma (12%), and cardiometabolic (11%). These data demonstrate that there are a growing number of intervention trials underway, with an increasing number of participants compared to what has been conducted (and published) in the recent past.

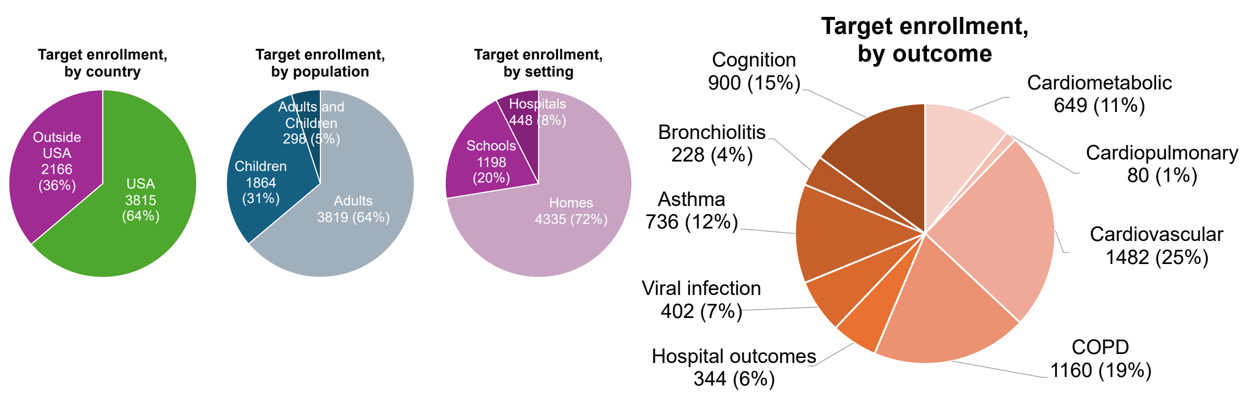

Figure S1. Summary of currently active trials on indoor air cleaning interventions registered on ClinicalTrials.gov and the distribution of the total number of target enrolled participants across geographic region, age, indoor setting, and health outcomes. This summary excludes one planned study of box fan filters and ultraviolet germicidal irradiation (UVGI) in classrooms in Bangladesh targeting 20,000 participants in schools (https://clinicaltrials.gov/study/NCT06247059), which would drastically skew the study sample.

Air Cleaner Performance Testing

The industry-standard metric of how much pollutant-free air an air cleaner provides is the clean air delivery rate (CADR) [7]. The CADR is typically reported by manufacturers (but is not required by law to be reported) in units of equivalent airflow rate (e.g., cubic feet per minute, or CFM, in the US).[1] When reported, the CADR is often only reported for the highest fan speed setting, although CADR is typically much lower at lower fan speed settings. Here we demonstrate an example of conducting an independent laboratory evaluation of the CADR of a portable air cleaner prior with HEPA and sorbent media filtration to use in our ongoing intervention trial. The selected air cleaner has both HEPA filter media for removing airborne particles and activated carbon and zeolite media for removing airborne gases. Prior to deployment in homes, the project team modified half of the air cleaners to serve as sham/placebo units, utilizing custom-made concrete discs wrapped in a covering that securely attach to the units in place of the filters to maintain similar weight to the true (active) filtration units (~20 lb or ~9 kg) while leaving in the low-efficiency pre-filter to maintain similar aesthetics and to obscure the concrete disc.

Laboratory measurements were conducted in a large chamber (volume = 1296 ft^3 [8–10]) to characterize the CADR of both true (active) and sham/placebo air cleaner units for various constituents following standard protocols [11,12]. The CADR is traditionally measured for particulate matter but can also be measured for other types of airborne pollutants [13–16]. Three particle size ranges are commonly tested in the widely used American National Standards Institute/Association of Home Appliance Manufacturers (ANSI/AHAM) AC-1 Test Standard, *Method for Measuring the Performance of Portable Household Electric Room Air Cleaners*: tobacco smoke (0.09-1 μm), dust (0.5-3 μm), and pollen (5-10 μm) [7]. In our chamber tests, pollutant injection was achieved by burning incense to generate particles primarily in the 'smoke' and 'dust' size ranges and shaking a vacuum cleaner bag filled with vacuumed dust to generate particles primarily in the 'pollen' size range [17]. Ozone (O_3) removal tests were conducted using an ozone generator as the injection source. NO_x (e.g., NO + NO_2)

[1] One must also be careful in citing manufacturer-reported CADR values, as some manufacturers may report them in non-standard units (e.g., in m^3/h instead of the conventional ft^3/min in the US) or may fail to report units altogether.

removal tests were conducted using candle burning as the injection source. Particles were measured using a TSI NanoScan SMPS Model 3910 (0.01-0.4 μm in diameter), MetOne GT-256S OPC (0.3-10 μm in diameter), and TSI OPS 3330 (0.3-10 μm in diameter); O_3 was measured using a 2B Technologies Model 211 O_3 analyzer; and NO_x was measured using a 2B Technologies Model 405 NO_x analyzer.

Testing was first conducted with the air cleaner turned on immediately after pollutant injection completed. This allows for estimating the decay rate of pollutants with the air cleaner turned on, which includes losses due to the 'natural' (i.e., background) decay due to deposition to surfaces, ventilation, etc., in addition to the effect of the operating air cleaner. After pollutant concentrations over time (C_t) initially mixed, peaked, and then decayed from the initial peak (C_0) towards background levels in the chamber (C_{bg}), pollutant injection was repeated with the air cleaner turned off, and pollutant concentrations were allowed to decay with the air cleaner off to characterize only the 'natural' (i.e., background) decay rate. A linear regression is used to estimate pollutant loss rates (K) under air cleaner on (K_{ac}) and off (K_{nat}) conditions (Equation S1).

$$-\ln\frac{C_{in,t}-C_{bg}}{C_{in,t=0}-C_{bg}}=K\times t \qquad \text{(S1)}$$

The CADR is calculated as the difference between the two loss rates multiplied by the interior chamber volume (Equation S2).

$$CADR = V\times(K_{on}-K_{off}) \qquad \text{(S2)}$$

Where V = volume of the test chamber (ft^3 or m^3), K_{on} = total decay rate with air cleaner on (1/min or 1/hour), K_{off} = natural decay rate with air cleaner off (1/min or 1/hour), and t = time from the beginning of the decay period (min or hour). This approach to measuring CADR is tailored specifically to portable or in-room air cleaners, but can also be extended to in-duct devices in central forced air heating or cooling systems [18].

Particulate CADR tests were also conducted with the sham air cleaners with just the pre-filters installed and operating on high. Supply air velocities at the air outlet of one unit each of the active and sham air cleaners were measured on all fan speed settings using a Digi-Sense Data Logging Vane Anemometer logging at 10-second intervals for several minutes. Noise levels were also measured ~1 m away from air outlet air of one unit each of the active and sham air cleaners using the National Institute for Occupational Safety and Health [NIOSH] Sound Level Meter app in the chamber.

Figure S2 shows an example of particle removal tests conducted on an air cleaner in a large chamber and Table S1 shows overall results from this testing.

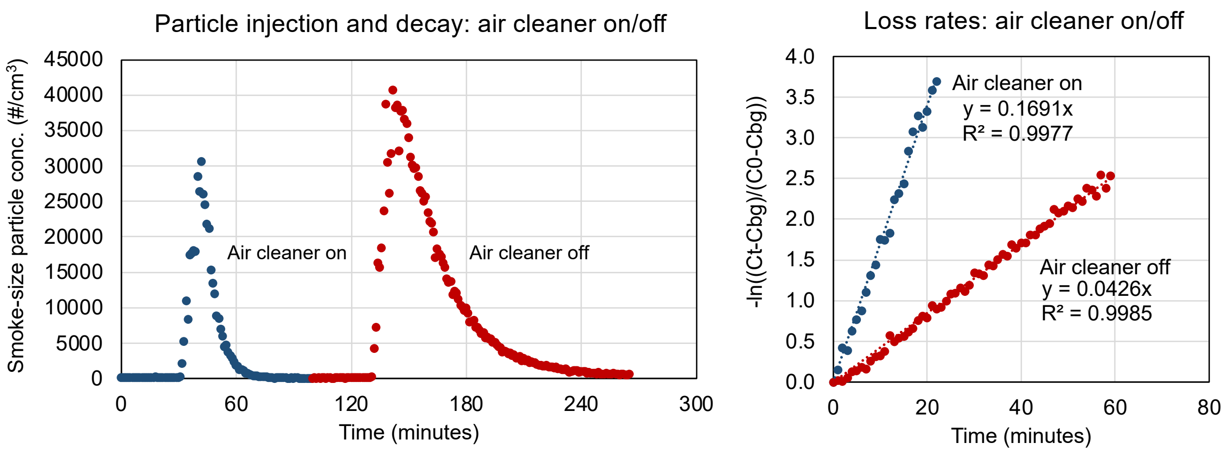

Figure S2. Data from particle removal tests (smoke-sized particles) of an air cleaner operating on high fan speed.

Table S1. Results from laboratory testing of an air cleaner used in an ongoing trial.

Condition	Fan speed	Measured CADR, ft³/min (m³/h): Smoke (0.09-1 μm)	Dust (0.5-3 μm)	Pollen (5-11 μm)	NO_2	O_3	Sound pressure level, dBA*	Supply air velocity, m/s
Active	Low	49 (83)	45 (77)	28 (48)	47 (80)	80 (136)	39	1.9
	Medium	78 (133)	61 (104)	44 (75)	79 (134)	95 (162)	48	3.4
	High	164 (279)	171 (291)	114 (194)	159 (270)	167 (284)	62	5.9
Sham	Low	n/a	n/a	n/a	n/a	n/a	40	3.1
	Medium	n/a	n/a	n/a	n/a	n/a	46	4.7
	High	8 (14)	5 (8)	27 (46)	n/a	n/a	61	9.1

*The sound level in the chamber without the air cleaner operating was 35 dBA

The resulting CADR for smoke-sized particles (i.e., 0.09-1 μm) of this air cleaner was ~50 ft³/min (~85 m³/h) on low fan speed, ~80 ft³/min (~136 m³/h) on medium fan speed, and ~160 ft^3/min (~272 m^3/h) on high fan speed settings with the true filters installed and less than 10 cfm for all fan speeds with the sham installed. The CADR for dust-sized particles were similar, as is expected for the air cleaner with HEPA media since HEPA filters remove particles of all sizes with approximately the same single-pass efficiency (near 100%): ~45 ft^3/min (~77 m^3/h) on low fan speed, ~61 ft^3/min (~104 m^3/h) on medium fan speed, and ~171 ft^3/min (~291 m^3/h) on high fan speed settings with the true filters installed. The pollen-size CADR measurements are the least reliable given the challenges of aerosolizing large particles with the particle generation methods used herein. Results in Table S1 summarize results from singular tests; although not shown here, replicate tests were also conducted on low and high fan speed and resulting estimates of CADR for the different particle size ranges were generally within ~10% of each other (i.e., within ~10-15 CFM, or ~17-25 m^3/h). This range of repeatability is similar to other tests we have conducted: https://built-envi.com/portfolio/air-cleaner-testing/.

The CADR for NO_2 and O_3 were both estimated to be similar to the particulate matter CADRs, which suggests that the removal efficiency of the filters inside the units are high and removal efficacy (CADR) is potentially flow-limited rather than filter-limited. Worth noting is that these methods to measure the CADR for NO_2 and O_3 are experimental in nature (e.g., similar to [19]) because there are no established industry-standard test methods for measuring CADR for NO_2 or O_3; thus, to our knowledge, no manufacturers report CADR for either pollutant. The larger CADR for O_3 is probably also due to a combination of enhanced mixing in the chamber that increases reactive deposition to surfaces in the chamber and thus may present a somewhat inflated CADR compared to true CADR; however, this remains to be investigated in more depth in future work.

Noise production on the highest fan speed setting was significantly higher than both medium and low fan speed settings (e.g., 61-62 dBA versus 46-48 dBA and 39-40 dBA, respectively). Spot measurements of the power draw of the air cleaners showed power draw of ~45-55 W on low, ~60-75 W on medium, and ~95-110 W on high fan speed settings for both true and sham filters, with slightly higher power draws for sham filters (<10%) due to the reduced resistance to airflow without the filter installed. Supply air velocities measured directly at the center of the air outlet were ~40-60% higher with the sham air cleaners (HEPA and carbon filter removed) compared to the true air cleaners, although a minor change in power draw (<10%) suggests that the difference in overall airflow rate being delivered is likely no more than ~10%, which should not result in perceptible differences in flow characteristics coming from the true versus sham air cleaners. However, airflow perceptions between sham and true filter conditions were not investigated in more detail (and in our experience, the vast majority of prior trials have not reported this detail either).

In-situ air cleaner utilization measurements

Figure S3 shows an example of a few days of power draw measurements from this ongoing study. The power draw data can be tagged and sorted into bins of "off" (<1 W), "low" (40-55 W), "medium" (60-70W), or "high" (80-110W) to indicate fan speed setting for this specific air cleaner. It is worth nothing that these data are not meant to e representative of all air cleaner usage; it is simply used as an example to illustrate the different fan speed settings that are detectable via long-term power draw measurements. For the first 53 homes in our preliminary data set, the average initial power draw of the air cleaners measured on low, medium, and high fan speed settings was 53 W, 70 W, and 101 W for the true air cleaners and 53 W, 70 W, and 108 W for the sham air cleaners. The slight differences between true and sham air cleaners within a fan speed setting were smaller than the differences between fan speed settings, which allowed for easy resolution of low, medium, and high fan speed settings in the resulting field-collected data set. For other types of air cleaner makes and models, careful investigation of the power draw on low, medium, high, or other fan speed modes such as auto mode, including before, during, and after data collection, is warranted to clearly define the ranges of operation.

For reference, for those few participants who have already completed the yearlong study thus far, the Onset HOBO plug load logger battery level has remained above 80% after one year and about 50% of the data storage is typically used (~2100 kB out of 4032 kB), suggesting that these loggers can be used for nearly 2 years at 5-

minute intervals, and that storage space is likely depleted before battery life (and thus longer logging intervals would likely extend this range).

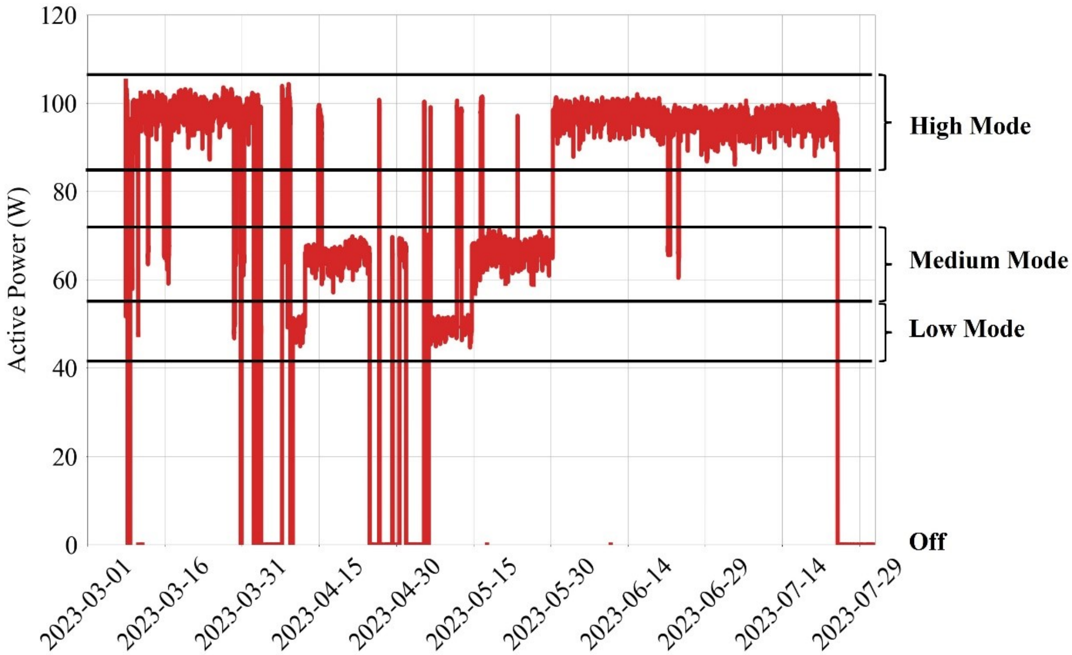

Figure S3. An example of power draw data at 5-minute resolution retrieved from a plug load logger installed on an air cleaner for approximately 5 months in a participant's home

Figure S4 summarizes the hourly mean (and standard deviation) of the air cleaner power draw measurements from the sample of 53 homes for which we have interim data to date. To generate the figure, the mean and standard deviation of the measured power draw from the plug load loggers attached to the portable air cleaners (PACs) were calculated for each hour of the day for each home. These values were then averaged across all homes. This approach accounts for the varying data collection periods among the assessed homes, which differ significantly at this interim stage (i.e., from 11 to 500 days, as mentioned). To date, there are minimal diurnal variations in average air cleaner power draw, suggesting that participants rarely adjusted fan speed settings throughout the day. Rather, they tended to keep the same fan speed setting for long periods of time. Future work with the full data set will explore operational patterns in more detail.

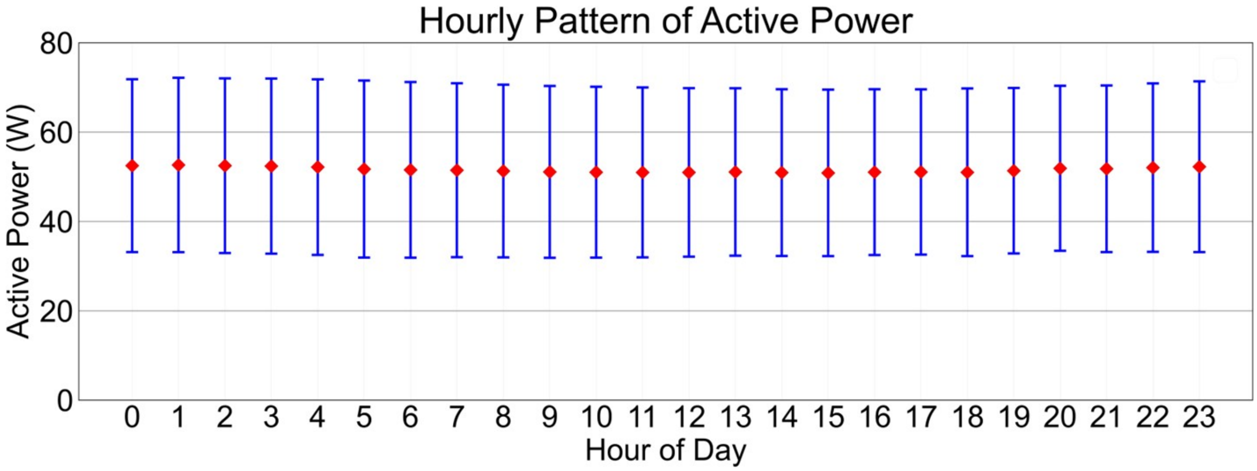

Figure S4. Hourly mean (standard deviation) of air cleaner power draw from the sample of 53 homes for which we have interim data to date

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