Effectiveness of portable HEPA air cleaners on reducing indoor PM$_{2.5}$ and NH$_3$ in an agricultural cohort of children with asthma: A randomized intervention trial

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**Abstract**

We conducted a randomized trial of portable HEPA air cleaners with pre-filters designed to also reduce NH$_3$ in non-smoking homes of children age 6-12 with asthma in Yakima Valley (Washington, USA). Participants were recruited through the Yakima Valley Farm Workers Clinic asthma education program. All participants received education on home triggers while intervention families additionally received two HEPA cleaners (child's sleeping area, main living area). Fourteen-day integrated samples of PM$_{2.5}$ and NH$_3$ were measured at baseline and one-year follow-up. We fit ANCOVA models to compare follow-up concentrations in HEPA vs control homes, adjusting for baseline concentrations. Seventy-one households (36 HEPA, 35 control) completed the study. Most were single-family homes, with electric heat and stove, A/C, dogs/cats, and mean (SD) 5.3 (1.8) occupants. In the sleeping area, baseline geometric mean (GSD) PM$_{2.5}$ was 10.7 (2.3) mg/m$^3$ (HEPA) vs 11.2 (1.9) mg/m$^3$ (control); in the living area, it was 12.5 (2.3) mg/m$^3$ (HEPA) vs 13.6 (1.9) mg/m$^3$ (control). Baseline sleeping area NH$_3$ was 62.4 (1.6) mg/m$^3$ (HEPA) vs 65.2 (1.8) mg/m$^3$ (control). At follow-up, HEPA families had 60% (95% CI, 41%-72%; $p < .0001$) and 42% (19%-58%; $p = .002$) lower sleeping and living area PM$_{2.5}$, respectively, consistent with prior studies. NH$_3$ reductions were not observed.

**KEYWORDS**

asthma, children, HEPA cleaners, NH$_3$, PM$_{2.5}$, randomized trial

1 | **INTRODUCTION**

Poor indoor air quality (IAQ) resulting from high levels of particulate matter (PM), mold, and/or chemicals in the home can increase asthma symptoms and severity. Children are especially vulnerable because their airways are still developing and they spend much of their time indoors. Reducing levels of asthma triggers in household air is an important part of an overall strategy to reduce pediatric asthma morbidity.$^{1-3}$

Several randomized trials have previously examined the effectiveness of portable high-efficiency particulate air (HEPA) cleaners on reducing indoor PM, a well-characterized asthma trigger, in the homes of children with asthma. Most studies were conducted in urban settings, with traffic and tobacco smoking as the prominent sources...
of concern, although one study examined HEPA cleaner effectiveness in rural non-smoking homes using older, non-US Environmental Protection Agency (EPA) certified wood stoves for heat. Three of the urban trials measured PM$_{2.5}$ specifically. In these studies, baseline mean (or median) PM$_{2.5}$ ranged from 8 μg/m$^3$ (Cox et al; 22% smoking homes) to 45 μg/m$^3$ (Butz et al; 100% smoking homes) and the HEPA units achieved PM$_{2.5}$ reductions of approximately 35% to 55% at six months to one-year follow-up. In the wood stove trial, baseline (wintertime) PM$_{2.5}$ varied widely between homes (~6-163 μg/m$^3$, mean 32.4 μg/m$^3$) and HEPA units achieved 65.7% (95% confidence interval (CI), 42.2%, 79.7%) reduction on average in PM$_{2.5}$ the following winter. The two urban studies using particle counts instead of PM$_{2.5}$ to assess effect, found 25%-50% reductions.

We previously identified adverse associations between ambient PM$_{2.5}$, neighborhood ammonia (NH$_3$), and a measure of animal feeding operation plume emissions with asthma symptoms and lung function among children with asthma in our ongoing, community-engaged environmental health research partnership in the Lower Yakima Valley of Washington State. The Yakima Valley is a region of intensive crop and dairy-based agricultural production, impacted by episodes of high outdoor PM$_{2.5}$ and NH$_3$ concentrations, and pediatric asthma is a community concern. Outdoor pollutants can infiltrate homes and add to indoor concentrations, and one study found that indoor PM$_{2.5}$ and NH$_3$ concentrations in household air typically exceeded paired outdoor concentrations in this setting. Protecting the indoor environment from infiltration of outdoor air contaminants and controlling indoor sources are recognized as key components of asthma control and are topics of clinic-based asthma education programs in this community.

Overall, the current evidence suggests that HEPA cleaners may be a useful approach to reduce trigger exposure among children with asthma. To address community concerns, our research partnership conducted the Home Air in Agriculture Pediatric Intervention (HAPI) study to test the effectiveness of a commercially available portable HEPA cleaner on reducing PM$_{2.5}$ and NH$_3$ in the homes of Yakima Valley children with poorly controlled asthma. The HEPA unit we tested contains pre-filter components designed to reduce NH$_3$ and other odiferous gases, in addition to the usual PM filters. The HAPI study is novel in focusing on exposure to both PM$_{2.5}$ and NH$_3$ and addressing the home environment in a rural, agricultural, non-smoking setting. Here, we describe the effectiveness of the HEPA cleaners in this setting; future analyses will examine whether provision of HEPA cleaners influences asthma health outcomes in the cohort.

2 | METHODS

2.1 | Participant recruitment, enrollment, randomization

The HAPI study design and procedures are described in detail in Masterson et al. Briefly, we recruited families of children aged 6-12 years with poorly controlled asthma residing in small rural towns in the Lower Yakima Valley from July 2015 to November 2017. Eligible participants were identified from referrals to the Yakima Valley Farm Worker Clinic (YVFWC) asthma education home visiting program. Other eligibility criteria included no smokers in the home, likely not to move for a year or more, one primary residence, and living within 800 m of crop and/or animal agriculture operations.

Seventy-nine families were enrolled and consented at an initial clinic visit. Our target sample size after attrition was 66, based on adequate power to identify significant reductions in PM$_{2.5}$. At completion of the baseline visit, each family was randomized to either the HEPA (intervention) or control group. After enrollment, all families received the standard 3-module YVFWC asthma education program consisting of allergy proof mattress and pillow covers, a green cleaning kit, and instructions on IAQ improvements, including behaviors that may reduce contaminants such as PM and NH$_3$. The behaviors include low volatile organic compound cleaning, controlling dust by wet dusting/mopping and frequent vacuuming with a HEPA filter vacuum, removing pets from sleeping areas, and using ventilation when cooking and showering. Research procedures were reviewed and approved by the University of Washington (UW) Institutional Review Board and YVFWC research review committee.

2.2 | Intervention - portable HEPA cleaner

The intervention group received two indoor portable HEPA cleaners (Austin Air Pet Machine 410®, Austin Air Systems Ltd.), one for the child’s sleeping area and one for the main living area. The device comprises 4-stage filtering, including two pre-filters designed to capture large particles, a carbon/zeolite filter for removing NH$_3$ and other pet odors, and a true HEPA filter noted by the manufacturer as rated for 99.97% removal of particles > 0.3 μm and 95% removal of particles > 0.1 μm. Each 14.5″L × 14.5″W × 23″H unit has three speed options (high, medium, low). We chose this particular model because it was in the moderate price range, rated for medium and large-sized residential rooms (with an air delivery rate of 400 cubic
feet per minute on high speed), and designed for maintenance-free operation for up to 5 years, in addition to its potential NH₃ removal capabilities. We worked with the manufacturer to add a HOBOT® Onset® motor on/off logger (Onset Computer Corporation) to each of the sleeping area units and approximately half of the living area units.

HAPI field technicians helped participants place the HEPA devices approximately 8" from the wall and away from heating sources and discussed a study fact sheet describing operation. Participants were advised to keep the unit on at all times for the study duration, run it at the highest speed tolerable and keep it in the same room even if they needed to move it for any reason. The fact sheet also mentioned that the filter would work best with the child’s bedroom door closed. Because of the device’s 5-year warranty, we did not advise participants to change the filter during the study.

### 2.3 PM₂.₅ and NH₃ air sampling and analysis

For each family, baseline and follow-up indoor air sampling visits were conducted approximately one year apart, in the same season, with season defined as winter (Dec-Feb), spring (Mar-May), summer (Jun-Aug), and fall (Sep-Nov). Equipment was generally set up on a Tuesday, Wednesday or Thursday, so households would have the same proportion of weekdays vs weekends in their 14-days samples.

#### 2.3.1 PM₂.₅

Gravimetric PM₂.₅ samples were collected in the sleeping area and living area using RTI MicroPEMs v 3.2A (RTI International) fitted with a PM₂.₅ inlet and 25-mm 3 μm pore size Teflon filter. Each sampler was enclosed in a sturdy cage hung on an IV pole, at a median height of 0.73 m (range 0.5-1.37 m) above the floor, approximately the height of the child’s breathing zone while sleeping, and as close as possible to her/his bed. Prior studies have shown good agreement with a PM2.5 inlet and 25-mm 3 μm pore size Teflon filter. Each sampler was enclosed in a sturdy cage hung on an IV pole, at a median height of 0.73 m (range 0.5-1.37 m) above the floor, approximately the height of the child’s breathing zone while sleeping, and as close as possible to her/his bed. Prior studies have shown good agreement between MicroPEMs used as gravimetric area samplers and other gravimetric methods at a range of PM₂.₅ concentrations.18-20 We chose a priori to use the gravimetric rather than the real-time nephelometer measurements from the MicroPEMs to evaluate HEPA cleaner effectiveness because of evidence of baseline drift in nephelometer data.21,22 and our concern that this drift would affect the accuracy of our measurements particularly over such a long sample duration (ie, 14 days).

Pre-deployment, MicroPEM flow rates were set to 0.5 L/min using a TSI 4140 flow meter (TSI Inc) in the field laboratory. Post-deployment, they were again checked with the TSI flow meter in the field laboratory; after approximately two months of fieldwork, additional steps were added to check the post-deployment flow rate in the home as well. Pre- and post-filter weighing was conducted following standard procedures23-25 in a temperature and humidity controlled laboratory at UW. Filters were preconditioned and weighed to the nearest 0.5 μg using a UMT-2 microbalance (Mettler-Toledo LLC), in duplicate or triplicate using the validation acceptance criterion of ±5 μg between weighings.

On sampling Day 1, sampling equipment was placed away from windows, in minimally intrusive locations. The MicroPEMs were run on electricity, with battery back up, for a target duration of 14 days. MicroPEMs were collected on Day 14, transported to the field laboratory for temporary storage at room temperature, and timestamp, flow rate, and inlet and orifice pressure data were downloaded (RTI International Docking Station software, Research Triangle Park, NC).

Post-deployment filters with negative mass changes were re-weighed, filters with holes or tears were flagged, and laboratory and field notes were inspected to determine a potential cause and whether or not to exclude the observation. Two to three laboratory blank filters were analyzed with each batch of approximately 10 filters while field blanks were collected at every 7th or 8th home. Field blanks were prepared, stored, handled, and analyzed following the same protocols as the samples except they were loaded into the MicroPEM at the field laboratory, transported to the home, and brought back the same day to the field laboratory for temporary storage. The method detection limit (MDL) was defined as three times the median absolute deviation of the field blanks mass changes and sample results were blank corrected using this value. The MDL—0.2 μg/m² was converted to a concentration assuming a nominal 14-days sample duration and 0.5 L/min flow rate.25 Two pairs of field duplicates were collected and precision calculated as the relative percent difference (RPD) between samples, or [absolute(sample-[duplicate])/average (sample, duplicate)]**100); RPDs for the two pairs were 0.7% and 3.5%.

#### 2.3.2 NH₃

Ogawa passive samplers (ie, badges) (Ogawa USA) were hung on the IV pole samplers to sample gaseous NH₃. Ogawas perform well in validation studies vs active methods for measuring NH₃ in ambient air,26,27 although validation studies are lacking for household indoor air where concentrations can be higher.15,28-30 We also placed Ogawa badges outside, in the yard of each home, in order to examine whether or not the HEPA cleaners influenced the NH₃ indoor/outdoor ratio (see Supporting information for details). In participant homes, technicians ensured that both badge ends received airflow and were placed away from sources such as water that could potentially bias measurements. At the end of the sampling period, badges were removed, sealed in their storage containers, transported and temporarily stored at 4°C in the field laboratory, then transported cold to UW for NH₃ analysis following manufacturer protocols.31,32 Briefly, pads were extracted with ultra high purity 18.2 mΩ (MilliQ) water (MilliporeSigma, Burlington, MA) and analyzed for NH₄⁺ (or NH₃ directly) using a Dionex ICS-1000 (Dionex/ThermoFisher). NH₄⁺ masses were converted to NH₃ then NH₃ air concentrations calculated by multiplying the NH₃ mass by a temperature adjusted conversion factor (43.8*(293.273 + temp(°C))**1.83) ppb min/ng, both pads extracted together) and dividing by the
exposure duration (eg, 14 days) and an assumed air sampling rate of 32.3 mL/min.\textsuperscript{21} The resulting ppb concentrations were converted to μg/m\textsuperscript{3}.

Field blanks (every 7th or 8th home) were prepared, stored, and analyzed following the sample protocols except that they were momentarily removed from their containers at the home and brought back to the field laboratory the same day. Laboratory blanks were prepared, stored, and analyzed similarly except that they remained at 4°C at UW for approximately the same duration as their corresponding field samples were deployed. Matrix spike samples were prepared by spiking 100% NH\textsubscript{3} or NH\textsubscript{3} (Honeywell Fluka\textsuperscript{TM}) into 8 mL of MilliQ water or onto laboratory blank pads, with spike recoveries (%) calculated as the measured divided by the spiked concentration. The lower limit of quantitation (LOQ) was set at the lowest concentration solution concentration (4 μg/sample) while the upper LOQ (ULOQ) was set at 285 ppb (~198 calibration solution concentration (4 g/sample) while the upper LOQ (ULOQ) was set at 285 ppb (~198 calibration solution concentration (4 μg/sample) while the upper LOQ (ULOQ) was set at 285 ppb (~198 g/sample) while the upper LOQ (ULOQ) was set at 285 ppb (~198 g/sample).

We found the holding times recommended by Ogawa\textsuperscript{31} to be shorter than practical given our resource limitations and the distances among laboratories and participant homes. However, we identified no meaningful bias based on evaluation of NH\textsubscript{3} masses (μg) measured across different holding times as well as based on a set of laboratory-based holding time experiments (see Supporting information for details).

During MicroPEM and Ogawa deployment, temperature and relative humidity (RH) in the sleeping area were recorded every 5 min using a HOBO\textsuperscript{®} Onset\textsuperscript{®} U12-011 logger (Onset Computer Corporation).

2.4 | Participant IAQ surveys

Child demographics, typical time-activity locations (eg, school, etc), proximity to agricultural activities and roadways, and number of household occupants were collected by caregiver survey at the initial clinic visit or during the baseline sampling period.

During baseline and one-year follow-up air sampling visits, a trained field technician completed an observational Home Environmental Checklist (HEC), adapted from EPA’s Asthma Home Environment Checklist.\textsuperscript{33} The HEC contains 11 modules: Building Exterior/Outside, General (number of bedrooms, any cleaning to prepare for study visit), Dust and Cleaning, Ventilation and Moisture, Pets and Pests, Home Walk-Through: Living Room/Family Room, Child’s Bedroom/Sleeping Area, Kitchen, Child’s Bathroom, Heat Source, Chemicals, and Irritants. They also measured the volume of the sleeping and living areas using a Bosch GLM 15 Laser Measure (Robert Bosch Tool Corp.). The room dimensions were taken by placing the device against a wall and recording the distance to the opposite wall. This step was repeated with the adjacent wall. The device was placed on the floor and aimed at the ceiling to find the height of the room.

Technicians also interviewed caregivers on IAQ-related characteristics and activities during the time periods 6 AM-12 PM, 12 PM-6 PM, and 6 PM-6 AM, on the final day of both the baseline and follow-up air sampling visits. Information obtained included number of windows open, any cooking or burning food activity, sweeping and vacuuming, air conditioning (A/C) use, use of candles or incense, and number of hours the child spent outdoors at home as well as the number of hours spent indoors, awake vs sleeping. At mid-study and the final follow-up visit, HEPA families were asked if they turned either unit off in the past month, if yes, for how many days approximately, and the speed at which they usually run the bedroom and living room units during the day and at night. We also conducted in-depth telephone exit interviews with approximately one out of seven families where we asked about their experiences with the HEPA cleaners and participating in the study.

During the conduct of the study, the research team became aware of a community weatherization program that was also offered by the Yakima Valley Farm Workers Clinic.\textsuperscript{34} Based on a household assessment, this program provided HEPA furnace filters and HEPA vacuum cleaners on a case-by-case basis as well as more substantial household retrofits in some cases (eg, insulation, air and/or duct sealing, roof repair, exhaust fan replacement, carpet replacement with laminated wood flooring). HAPI study participants who participated in this program during the study in the period before or during final air sampling were identified.

2.5 | Data processing and analysis

MicroPEM data were initially processed using the rtimicropem package,\textsuperscript{35} with further processing in R, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). Sample duration was estimated from the time the instrument was on and logging valid measurements. Two technicians visually inspected plots of pump inlet and orifice pressures in order to detect potential pump malfunctions and/or filter overloading. Overloading was assumed if the inlet pressure reached five inches of water while the orifice pressure simultaneously destabilized and the flow rate increased rapidly. For these samples, the point where this transition occurred was used as the cutoff point indicating when the pump stopped working and subsequent points were excluded from the duration estimate. If the duration was less than 10 days, raw data files and field notes were examined for possible explanations, for example, loss of electrical or battery power, tampering, or malfunction as indicated by error messages. A subset of files from MicroPEMs that potentially malfunctioned or had overloaded filters (~5% of the total MicroPEM data), were sent to RTI for a reliability check.

We used the mean of the pre- and post-deployment TSI flow rates as the primary flow rate estimate if both measurements were
available. If pre-deployment flow rates were missing (~4% of samples), they were imputed as 0.5 L/min since that was the target flow rate and 99% of non-missing observations were 0.5 L/min. If post-deployment flow rates were missing (19% of sleeping area and 18% of living area samples), they were imputed as the median of the non-missing values.

For 15.5% of samples, we did not have temperature/RH HOBOs during the sampling period. In these cases, we imputed the missing data using the MicroPEM temperature and a linear regression equation fit to the HOBO vs MicroPEM measurements from homes with both instruments deployed (Pearson $\rho = 0.87, p < .01, n = 118$).

Baseline demographic and home characteristics, and IAQ behaviors/activities at baseline and follow-up were compared for control and HEPA groups using $\chi^2$ tests for categorical variables and Wilcoxon Rank Sum tests for continuous variables. Primary measures of interest for assessing the impact of the HEPA cleaners were PM$_{2.5}$ and NH$_3$ in the sleeping area while PM$_{2.5}$ in the living area was a secondary measure.

We fitted ANCOVA (analysis of covariance) models comparing the effect of the HEPA cleaners on reducing PM$_{2.5}$ and NH$_3$ in the sleeping and living areas, adjusting for baseline concentrations. We used log-transformed PM$_{2.5}$ and NH$_3$ concentrations for descriptive statistics and regression modeling since histograms of the measurements appeared log-normally distributed, and Pearson correlation analysis to evaluate the influence of baseline on follow-up levels. Regression diagnostics included plots of residuals vs predicted values, normal probability plots of residuals, and leverage plots. Potential outliers/leverage points were investigated by fitting the models with and without these observations and comparing results.

In sensitivity analyses, we also explored the effect of various factors potentially affecting the precision of the ANCOVA results (eg, indoor sources or factors affecting ventilation/air exchange) by adding these individually to the main ANCOVA model and comparing results. Factors tested in both the PM$_{2.5}$ and NH$_3$ models included room volume, usual A/C, humidifier, and candle/incense use, and window opening to ventilate (when weather allows), and A/C use during the sampling visit. Additional covariates tested in the PM$_{2.5}$ models included RH, and food burning, stove use, oven use, vacuuming, dusting during the sampling visit, and technician observed levels of dust on sleeping and living area surfaces, while additional covariates in the NH$_3$ model included presence of pets (in general and dogs specifically), mold or sewer odors in the child’s bedroom, presence of mold or water damage in the bedroom or closet, storing fertilizers in the home, use of window cleaner or other ammonia-containing cleaning products, beauty service/hair styling in the home, and diaper use. For both PM$_{2.5}$ and NH$_3$, we also conducted additional sensitivity analyses by including variables indicating whether or not the family moved houses between air sampling visits and whether or not their participation in HAPI included overlap with the weatherization program. Last, for PM$_{2.5}$ we conducted two types of sensitivity analyses to evaluate the potential impact of missing TSI flow rate measurements on results. In the first, we refit the ANCOVA models after restricting the PM$_{2.5}$ data to observations with TSI flow rate measurements at both baseline and follow-up (n = 47 sleeping area; n = 45 living area). In the second, we conducted a probabilistic analysis where we refit the main model 500 times, each time imputing the missing TSI flow rates using values randomly sampled with replacement from the distribution of measured flow rates, then compared the resulting distribution of 500 intervention effect estimates to the original results. Statistical analyses were conducted in R (versions 3.1.3 and 3.6.1), and $p \le .05$ was the criterion for statistical significance.

### 3 | RESULTS

#### 3.1 | Demographic, home characteristics, and IAQ-related behaviors of the cohort

Seventy-one families completed the study including one year of follow-up sampling (89% retention). Reasons for loss to follow-up for the nine families included lack of time (two), moving away from agricultural operations (two), concerns over electricity costs (one), child could not perform tests to measure health outcomes (one), eviction (one), and unknown/unspecified (two). Demographic and home sitting features of the analytical cohort are presented in Table 1 and show no statistically meaningful differences between HEPA homes and controls based on these features.

The mean age of the children included in our analytic sample was 8.9 years (± 2.1 years). Approximately two-thirds (62%) were boys, 97.2% were born in the United States, and 100% reported Hispanic/Latino ethnicity. The majority of families (57.8%) reported an annual household income <$30 000 while 95.8% of participating children were on public health insurance. Approximately two-thirds of homes were detached single-family homes with the rest either apartments/duplexes or trailer homes. The mean number of bedrooms was 2.9 (±1.0). Mean years at the current address were 5.5 (±3.5); seven families (all control group) moved houses between baseline and follow-up visits. At baseline, approximately half (53.5%) the families lived in a small town setting, while 21.1% and 25.4%, respectively, lived in rural areas, on a farm or not. All lived near either tree fruit crops (15.5%) or row crops (40.8%), or both (43.7%), while 43.7% also lived near a farm(s) raising animals (dairy/beef cattle and/or horses/goats/chickens). Two-thirds of families reported living near (<400 m) major roads with heavy traffic and two-thirds reported living near unpaved dusty roads.

Table 2 summarizes selected key IAQ-related characteristics and activities of the HEPA vs control homes at baseline. Mean occupancy was 2.4 (±0.8) adults and 2.9 (±1.5) children. Three-quarters (75.7%) reported using an electric furnace for home heating, while 18.6%, 8.6%, 8.6%, and 2.9% reported using electric baseboards, gas furnace, wood, and heating oil, respectively, and 35.7% reported using space heaters or electric wall units either in combination with other sources, or as the sole heat source. The vast majority (94.3%) had electric vs gas kitchen stoves and used A/C, respectively, while 26.1% used a humidifier. Sixty percent of the families had a
Most (two-thirds to three-quarters) of families said they opened the child's sleeping area and/or living area windows to ventilate when weather allows, either sometimes or always. When asked about IAQ activities conducted on the final day of the baseline and follow-up air sampling visits, one-third of families said they had the A/C on, 5%-15% reported using candles/incense, 5%-10% reported burning food, most reported using the stove (for > 80 min, on average; range 0-420 min) while almost none used the oven, approximately a third reported vacuuming, and most (>80%) reported sweeping. There were no statistically significant differences between the HEPA and control groups with respect to these features.

### 3.2 Baseline and follow-up PM$_{2.5}$ and NH$_3$ – descriptive results

Follow-up air sampling was conducted in the same season as baseline sampling for all but four households whose follow-up samples were collected 1-2 weeks late, into the next season, due to scheduling conflicts. There were no statistically significant differences between the HEPA and control groups with respect to season of baseline or follow-up sampling (Fisher’s Exact $p = .25$ baseline, $p = .25$ follow-up) or year sampled (Wilcoxon Rank Sum $p = .13$ baseline, $p = .08$ follow-up). The mean % of weekdays in each 14-days sample was 78.6% (0.3%) at baseline and 78.6% (0.5%) at follow-up, with no statistically significant differences between groups at either point (Wilcoxon Rank Sum $p = .59$ and $p = .26$, respectively).

Table 3 summarizes indoor PM$_{2.5}$ and NH$_3$ concentrations. At baseline, PM$_{2.5}$ concentrations were similar in the HEPA and control groups, with sleeping area geometric mean (geometric SD) concentrations of 10.7 (2.3) $\mu$g/m$^3$ and 11.2 (1.9) $\mu$g/m$^3$, respectively, and geometric mean living area concentrations of 12.5 (2.3) $\mu$g/m$^3$ and 13.6 (1.9) $\mu$g/m$^3$, respectively. At follow-up, the HEPA group’s geometric mean PM$_{2.5}$ decreased 65% to 3.8 (2.7) $\mu$g/m$^3$ in the sleeping area and 48% to 6.5 (2.3) $\mu$g/m$^3$ in the living area. Geometric mean PM$_{2.5}$ also declined in the control group but the decreases were smaller: 15% (to 9.5 (2.1) $\mu$g/m$^3$) in the sleeping area and 17% (to 11.3 (2.0) $\mu$g/m$^3$) in the living area. The maximum sleeping area PM$_{2.5}$ concentration (57.5 $\mu$g/m$^3$) was a follow-up sample from control home located on a farm, with high occupancy (2 adults, 10 children) and several indoor and outdoor pets. The maximum living

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**TABLE 1**

| Characteristic | HEPA (n = 36) | Control (n = 35) | Difference p-value$^a$ |
|---------------|--------------|-----------------|-----------------------|
| Characteristic | Mean (SD) | Percent | Mean (SD) | Percent |
| Child age$^b$ | 9.3 (2.0) | 8.5 (2.1) | .10 |
| Child sex: female | 38.9 | 37.1 | 1.0 |
| Child born in US | 100.0 | 94.3 | .24 |
| Annual total household income: | | | |
| <$14 999 | 5.6 | 22.9 | .24 |
| $15 000-29 999 | 47.2 | 40.0 |
| $30 000-60 000 | 38.9 | 31.4 |
| >$60 000 | 8.3 | 5.7 |
| Child health insurance: | | | |
| public | 94.4 | 97.1 | 1.0 |
| Years at current address | 6.0 (3.7) | 4.9 (3.3) | .25 |
| Home location | | | |
| Rural | 44.4 | 48.6 | .80 |
| In town | 55.6 | 51.4 |
| Home < 800 m from: | | | |
| Animal agriculture | 38.9 | 48.6 | .48 |
| Crop agriculture | 100.0 | 100.0 | 1.0 |
| Home < 400 m from | | | |
| Major roads with heavy traffic | 66.7 | 65.7 | 1.0 |
| Unpaved dusty roads | 72.2 | 62.9 | .45 |

Abbreviation: SD, standard deviation.

$^a$ HEPA and control groups compared using $\chi^2$ tests for categorical variables and Wilcoxon Rank Sum tests for non-normally distributed continuous variables.

$^b$ Child age at enrolment.
| Characteristic/Activity                                      | HEPA (n = 35) | Control (n = 35) | Difference | p-value<sup>b</sup> |
|------------------------------------------------------------|---------------|------------------|------------|---------------------|
| **Occupancy**                                              |               |                  |            |                     |
| Number adults                                             | 2.3 (0.7)     | 2.5 (1.0)        | .50        |                     |
| Number children                                           | 3.0 (1.4)     | 2.9 (1.7)        | .45        |                     |
| **Pets**                                                   |               |                  |            |                     |
| Have dog(s)                                                | 62.9          | 57.1             | .81        |                     |
| Have cat(s)                                                | 20.0          | 17.1             | 1.0        |                     |
| **Type of heat used (more than one type possible)**        |               |                  |            |                     |
| Electric furnace                                          | 77.1          | 74.3             | 1.0        |                     |
| Electric baseboard                                        | 14.3          | 22.9             | .50        |                     |
| Gas                                                       | 8.6           | 8.6              | 1.0        |                     |
| Heating oil                                               | 0.0           | 5.7              | .51        |                     |
| Wood                                                      | 11.4          | 5.7              | .67        |                     |
| Other (mostly portable/space heaters)                     | 45.7          | 25.7             | .13        |                     |
| **Have air conditioner**                                  | 91.4          | 97.1             | .61        |                     |
| **Use humidifier (usual)**                                | 28.6          | 23.5             | .80        |                     |
| **Use candles/incense (usual)**                           | 37.1          | 34.3             | 1.0        |                     |
| **Child's sleeping area**                                 |               |                  |            |                     |
| Room volume (m<sup>3</sup>)                               | 26.7 (7.8)    | 27.4 (10.4)      | .85        |                     |
| Relative humidity                                         | 51.4 (6.4)    | 53.6 (9.3)       | .28        |                     |
| Temperature (°C)                                          | 21.8 (2.8)    | 20.9 (2.5)       | .21        |                     |
| Open windows to ventilate                                 |               |                  |            |                     |
| Always/sometimes                                          | 77.1          | 77.1             | 1.0        |                     |
| Never/no windows that open                                 | 22.9          | 23.7             |            |                     |
| Evidence of mold/mildew<sup>e</sup>                       | 17.1          | 25.7             | .57        |                     |
| **Main living area**                                      |               |                  |            |                     |
| Room volume (m<sup>3</sup>)                               | 53.9 (18.6)   | 48.3 (17.5)      | .19        |                     |
| Open windows to ventilate                                 |               |                  |            |                     |
| Always/sometimes                                          | 80.0          | 65.7             | .28        |                     |
| Never/no windows that open                                 | 20.0          | 34.2             |            |                     |
| Evidence of mold/mildew<sup>††</sup>                      | 8.6           | 17.1             | .47        |                     |
| **Have working vacuum with HEPA filter**                  | 37.1          | 42.9             | .81        |                     |
| **Use of window cleaner/NH<sub>3</sub> containing products**| 8.6           | 23.5             | .11        |                     |
| **Use diapers in the home**                               | 20.0          | 32.4             | .28        |                     |
| **Store fertilizer in the home**                          | 8.6           | 5.9              | 1.0        |                     |
| **Operate beauty/hair styling service in the home**       | 20.0          | 11.4             | .50        |                     |

Abbreviation: SD, standard deviation.

<sup>a</sup> One family in HEPA group refused the HEC interview.

<sup>b</sup> HEPA and control groups compared using χ<sup>2</sup> tests for categorical variables and Wilcoxon Rank Sum tests for non-normally distributed continuous variables.

<sup>c</sup> All 36 HEPA families have baseline temperature, relative humidity and room volume measurements.

<sup>d</sup> One control family missing response to humidifier question at baseline (but answered “No” at follow-up HEC interview).

<sup>e</sup> Technician observed.

<sup>f</sup> N = 69, responses at follow-up visit. We did not start asking questions about diapers, fertilizers, and ammonia cleaners until one year after data collection started (survey questions added in August 2016). Since 39% (27/70) homes already completed baseline visits, we used responses from the follow-up visit. It is possible that some of these behaviors did change from baseline to follow-up as a result of participating in the YVFWC asthma program, thus responses at the follow-up visit may not accurately capture behaviors at baseline.
Control (N = 35)

Baseline and follow-up concentrations of PM$_{2.5}$ in the child’s sleeping area and main living area and NH$_3$ in the child’s sleeping area, HEPA vs control households

| PM$_{2.5}$ sleeping area (µg/m$^3$) | HEPA (N = 36) | Control (N = 35) |
|-----------------------------------|-------------|--------------|
| n | GM (GSD) | Min | Max | n | GM (GSD) | Min | Max |
| Baseline | 35b | 10.7 (2.3) | 3.1 | 45.6 | 34c | 11.2 (1.9) | 3.5 | 57.5 |
| Follow-up | 35b | 3.8 (2.7) | 0.1 | 25.2 | 33c | 9.5 (2.1) | 2.1 | 36.9 |

| PM$_{2.5}$ living area (µg/m$^3$) | HEPA (N = 36) | Control (N = 35) |
|-----------------------------------|-------------|--------------|
| n | GM (GSD) | Min | Max | n | GM (GSD) | Min | Max |
| Baseline | 34d | 12.5 (2.3) | 3.5 | 95.6 | 33d | 13.6 (1.9) | 5.3 | 76.2 |
| Follow-up | 36 | 6.5 (2.2) | 1.5 | 28.6 | 34d | 11.3 (2.0) | 2.1 | 36.8 |

| NH$_3$ sleeping area (µg/m$^3$) | HEPA (N = 36) | Control (N = 35) |
|-----------------------------------|-------------|--------------|
| n | GM (GSD) | Min | Max | n | GM (GSD) | Min | Max |
| Baseline | 36 | 62.4 (1.6) | 25.8 | >198.0$^f$ | 35 | 65.2 (1.8) | 28.3 | >198.0$^f$ |
| Follow-up | 36 | 61.5 (1.8) | 16.2 | >198.0$^f$ | 35 | 55.7 (1.9) | 16.6 | 177.6 |

Abbreviation: N, sample size at baseline.

GM, geometric mean; GSD, geometric standard deviation.

a The room the child primarily slept in was designated as the child’s sleeping area. There were some instances when the child did not sleep in their bedroom or they did not have a room, so samplers were set up in the room where the child usually slept.
b One baseline and one follow-up sleeping area sample from HEPA families were excluded because sample duration was < 24 h.
c Three sleeping area samples from control families were excluded: one baseline sample was < 24 h, one follow-up sample had large negative mass, and one follow-up sample had post sampling flow rate > 20% from the target flow rate.
d Two baseline living area samples from HEPA families were excluded because they had large negative masses.
e Three living area samples from control families were excluded: one sampler malfunctioned during baseline sampling, one baseline sample was excluded because the family did not have a functioning sampler at the follow-up visit, and one follow-up sample had post sampling flow rate > 20% from the target flow rate.
f Samples above upper limit of quantitation (ULOQ), 198.0 µg/m$^3$ for a 14-day sample at 25°C; samples above ULOQ: 8.6% control baseline samples, 2.8% HEPA baseline samples, 8.3% HEPA follow-up samples.

Area PM$_{2.5}$ concentration (95.6 µg/m$^3$) was a baseline sample from a HEPA home that was an apartment, located in town, with one adult and two children and no pets. Within household baseline and follow-up PM$_{2.5}$ measurements were correlated (Pearson ρ’s: sleeping area, 0.47, p < .0001, n = 66; living area, 0.50, p < .0001, n = 66).

Five percent of the NH$_3$ measurements (4 baseline; 3 follow-up) exceeded the ULOQ (by 2%-96%). We used the original measured values of these observations to calculate descriptive statistics and fit the main ANCOVA model, and conducted a sensitivity analysis using Tobit regression and right censoring to evaluate their influence on results; using the Tobit approach did not change results. Baseline geometric mean NH$_3$ concentrations in the sleeping area were similar between groups: 62.4 (1.6) µg/m$^3$ vs 65.2 (1.8) µg/m$^3$ (non-weatherization, n = 61), respectively. Similarly, baseline geometric mean living area PM$_{2.5}$ concentrations did not differ significantly (Wilcoxon Rank Sum p = .72): 13.0 (1.9) µg/m$^3$ (weatherization, n = 9) vs 13.1 (2.2) µg/m$^3$ (non-weatherization, n = 58). Baseline sleeping area NH$_3$ concentrations were also not significantly different: 70.4 (2.0) µg/m$^3$ (weatherization, n = 9) vs 63.9 (1.8) µg/m$^3$ (non-weatherization, n = 62) (Wilcoxon Rank Sum p = .78). At follow-up, geometric mean PM$_{2.5}$ concentrations were lower among weatherization families compared to non-weatherization families but the differences were not statistically significant: sleeping area—2.4 (4.4) µg/m$^3$ (weatherization, n = 8) vs 6.7 (2.3) µg/m$^3$ (non-weatherization, n = 60) (Wilcoxon Rank Sum p = .06); living area—5.1 (2.2) µg/m$^3$ (weatherization, n = 9) vs 9.2 (2.2) µg/m$^3$ (non-weatherization, n = 61) (Wilcoxon Rank Sum p = .06). Follow-up geometric mean sleeping area NH$_3$ did not differ significantly by weatherization participation: 55.0 (1.7) µg/m$^3$ (weatherization, n = 9) vs 59.6 (1.9) µg/m$^3$ (non-weatherization, n = 62) (Wilcoxon Rank Sum p = .64).

3.3 | HEPA cleaner effects

In the ANCOVA models, the PM$_{2.5}$ decreases were statistically significantly larger in the HEPA vs control group. In the sleeping area, HEPA families had 60% lower (95% CI, 41%-72%; p < .0001; adjusted $R^2 = .41$) PM$_{2.5}$ at follow-up, on average, than control families, adjusting for baseline concentrations (Figure 1A). In the living area, the
HEPA group had 42% lower (19%-58%; \( p = .002; \) adjusted \( R^2 = .34 \)) PM\(_{2.5}\) on average, adjusting for baseline (Figure 1B). Both the sleeping and living area model results were robust to outliers/influential points. The sensitivity analyses did not modify the overall interpretation of the PM\(_{2.5}\) results, and only showed modest influences of certain variables on the magnitude of the estimated effect (Table S1). Of the IAQ-related variables tested in sensitivity analyses, including RH in the final sleeping area PM\(_{2.5}\) model increased the HEPA effect by \(-3\%\), while weatherization participation decreased it by \(-4\%\). In the living area model, including RH did not significantly influence the HEPA effect, but including weatherization participation decreased it by \(-9\%\), and including candle/incense use during the last 24 hours of the sampling visit decreased it by \(-4\%\). In the ANCOVA models refit using only observations with measured instead of imputed flow rates, the HEPA effect increased slightly, from 60% to 64%, in the sleeping area and was essentially unchanged in the living area. Similarly, in the sensitivity analyses using probabilistic simulation of flow rates, the HEPA effect increased slightly (ie, \(<1\%)\) in the sleeping area model and did not change in the living area model.

At follow-up, HEPA families had 16% (95% CI, 1%-37%) higher NH\(_3\) than control families on average in the child’s sleeping area, adjusting for baseline, but the difference was not statistically significant (\( p = .08; \) adjusted \( R^2 = .68 \)) (Figure 2). As with the PM\(_{2.5}\) models, results were robust to sensitivity analyses (Table S2) and outliers/influential points.

### 3.4 HEPA cleaner usage

Only 13 of the HOBO motor on/off loggers deployed to record HEPA on/off activity for the full intervention duration, precluding usefulness of these data. Failures were likely due to loss of battery power although other reasons cannot be ruled out. Battery life was rated at one year, at typical logging intervals (eg, >1 min) and normally

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**Figure 1** Scatter plots of baseline vs follow-up PM\(_{2.5}\) in the child’s sleeping area (A) and main living area (B). Fitted lines represent the ANCOVA model equations for the HEPA (darker line) and control (lighter line) groups; the vertical difference between lines represents the intervention effect in the sleeping area (A: \( \text{exp}(-0.91) = 0.40 \), or 40%) and living area (1: \( \text{exp}(-0.54) = 0.58 \), or 58%); note that the axes are logarithmically scaled to correspond with the statistical analysis of log concentrations. Sample sizes: sleeping area (A) N = 35 HEPA, N = 33 control; living area (B) N = 34 HEPA, N = 33 control

**Figure 2** Scatter plot of baseline vs follow-up NH\(_3\) in the child’s sleeping area. Fitted lines represent the ANCOVA model equations for the HEPA (darker line) and control (lighter line) groups; the vertical difference between lines represents the intervention effect (\( \text{exp}(0.15) = 1.16 \), or 116%); dotted gray lines indicate upper limit of quantitation (ULOQ) (285 ppb, or \( \approx 198 \) \( \mu g/m^3 \) at the average temperature of each home); note that the axes are logarithmically scaled to correspond with the statistical analysis of log concentrations. Sample sizes: N = 36 HEPA, N = 35 control
open contacts, so frequent switching of the machine on and off as we observed in some of the raw data files may have drained batteries faster than we anticipated. For the 13 motor HOBOs that did provide complete data, plots of the motor on-off activity by date showed a variety of patterns by family and room, with some plots showing the motor continuously on, and others showing frequent switching on and off.

In the HEPA use surveys, most of the 36 HEPA-assigned families reported keeping their units on during the study, with only 19.4% and 38.9% reporting turning it off in the past month (for any duration) at the mid-study visit and end of follow-up sampling, respectively. Families were approximately evenly divided among those reporting running the units at low, medium, or high speed during the day, while the majority (63.9% at mid-study, 69.4% at follow-up) reported running the sleeping area unit at speed 1 (low) at night. 41.7% and 63.9% of families, respectively, reported running the living area unit on low at night during the mid-study and follow-up visits. No HEPA households possessed or used indoor HEPA cleaners not provided by the study. One control family reported receiving a HEPA cleaner as part of the weatherization program prior to enrolling in HAPI, but also said they did not use it.

Last, eight HEPA families completed the telephone exit interviews. All replied "no" to the question of whether or not it was inconvenient to have the HEPA cleaner in their home. When asked whether the noise from the units was disturbing to the family, six replied "no" and two said "a little disturbing," while none said "very disturbing." In open-ended comments, two participants told us they tolerated the noise since it was helping their kids, another said she just turned it down when it got too loud, and a third said the noise was disturbing in the beginning but they got used to it. One family told us they no longer had the HEPA cleaners but did not say why. In other comments, one participant told us she runs the units on low because it cools the air too much, while another said she was happy that the project reimbursed her for electricity to run them. These anecdotal observations provide insight on the acceptability of HEPA cleaners to families in this setting.

4 | DISCUSSION

In this randomized trial of effectiveness of home HEPA cleaners in a rural agricultural setting, we observed significant reductions in indoor PM$_{2.5}$ but not NH$_3$. All participating households received information and supplies for green cleaning and education regarding identifying and reducing home asthma triggers, including those contributing to indoor PM$_{2.5}$ or NH$_3$. In many communities, asthma education programs that include information for identification and reduction of triggers are increasingly available for families that have children with asthma. In this study, the homes randomized to also receive portable HEPA cleaners for use in the child’s sleeping area and main living area showed much larger reductions in PM$_{2.5}$, a well-established asthma trigger. Geometric mean PM$_{2.5}$ decreased 65% and 48%, respectively, in the sleeping and living areas in HEPA homes vs 15% and 17%, respectively, in control homes.

The observed magnitude of HEPA cleaner PM$_{2.5}$ effect (42% to 60% reduction, depending on room) was comparable to effects observed in the previous trials. Each of these provided a HEPA unit for the child's bedroom, while several provided another for additional rooms. Several were placebo controlled and several provided in-home asthma education visits in addition to the HEPA units. Baseline PM$_{2.5}$ in our cohort (Table 3) more closely resembled that of the Cox et al Cincinnati, OH, USA cohort, which included only 22% smoking families, compared to the other cohorts with more smoking families and higher baseline PM$_{2.5}$. The HAPI study homes also had lower baseline PM$_{2.5}$ than homes in the wood stove trial. The fact that all the trials achieved indoor PM$_{2.5}$ reductions of approximately one- to two-thirds regardless of baseline levels shows that HEPA cleaners effectively lower particle concentrations in the bedrooms of children with asthma in a variety of real-world residential settings including the rural/agricultural, non-smoking HAPI households.

We observed no meaningful change in NH$_3$ concentrations measured in homes that were assigned to the HEPA or control group. From baseline to follow-up, geometric mean NH$_3$ in the sleeping area dropped only 2% in HEPA homes and 16% in control homes, and the HEPA vs control group difference was not statistically significant. No prior published reports of home air cleaner use to reduce NH$_3$ were identified. NH$_3$ was of interest due to prior research by our group showing associations of ambient NH$_3$ and reduction in lung function among children with asthma in the community as well as the irritant properties of NH$_3$. Like many commercially available portable HEPA cleaners, the unit we studied is marketed for the reduction of pet odors which would include NH$_3$. In general, the concentrations observed in our cohort were well below EPA's inhalation reference concentration of 0.5 µg/m$^3$. This reference level is the chronic exposure concentration set to be protective against health symptoms in the general population including sensitive subgroups (EPA 2016). The levels we observed are similar to those measured in other studies in the United States, United Kingdom, and Japan, although the number of studies on indoor residential settings is limited. We examined multiple potential likely sources of indoor NH$_3$ in sensitivity analyses and found no significant influences (eg, pets/dogs, NH$_3$-based cleaners and hair products, diapers, A/C use$^{28-30,39,40}$) although the number of studies on indoor residential settings is limited. It is unclear if our finding of no HEPA effect on NH$_3$ is attributable to the device itself, high dependence on usage by participants (more so than required to observe a PM$_{2.5}$ effect), some combination of both, or some other unmeasured factor.

Unfortunately, failure of the HOBO on/off data loggers to objectively estimate participant HEPA usage precludes more detailed analysis of efficacy in this setting. For nine families, we had motor HOBO data that overlapped completely with follow-up sampling. Three of these families reported on the HEPA use survey that they did not turn off the units (with motor HOBO) in the past month, while their motor HOBO data showed 32%, 63%, and
100% on activity during the 14-days sampling period. Six families (with seven motor HOBOs among them) reported turning the units off sometimes; their HOBO data showed 1.9%, 1.9%, 14.1%, 32%, 52%, 100%, and 100% on activity. These limited observations demonstrate that not all HAPI families used their air cleaners consistently, a finding similar to Batterman et al.\(^5\,45\) who observed wide-ranging use patterns among the 89 urban Detroit HEPA households in their cohort, and generally declining use over the duration of the six to nine month intervention. Use rates were low (eg, 34% ± 30% between technician visits) despite the facts that the families knew about the benefits, were blinded to use monitoring, and were compensated for electricity use during the study. Use rates were also low among the 44 Baltimore HEPA families in Eggleston et al.\(^8\) with over half running the units < 50% of the time. Cox at al. (2018)\(^4\) reported generally higher usage rates (88% on average) among the 46 Cincinnati households in their crossover trial but their study was much shorter in duration (eight weeks of air cleaner use) than HAPI, or the Batterman et al\(^4\,45\) and Eggleston et al\(^8\) one-year trials, in which participants’ enthusiasm for the devices may have waned over the months. Compliance was also higher in McNamara et al.,\(^9\) where the 41 rural Montana families receiving HEPA or placebo air cleaners had mean 72% (±34%) compliance. Interestingly, adjusting for compliance in the statistical models did not change the magnitude of the PM\(_{2.5}\) reduction, an observation which led the authors to conclude that continuous operation of the air cleaners is not necessary to achieve large PM\(_{2.5}\) reductions in this setting (wood stove homes in winter).

Of the eight HAPI families interviewed in-depth about their experiences with the HEPA cleaners, most said they were not convenient and the noise did not disturb them. Motivating compliant use remains important for optimal performance. Since the air cleaners must be operated in order to reduce indoor PM\(_{2.5}\) concentrations, it is possible that the effect sizes observed in HAPI and the previous trials are smaller than those achievable if more families had operated their units consistently, at higher speeds and with windows and doors closed, as recommended.\(^46\) Nonetheless, our findings reflect real-world activities and we found significant reductions in PM\(_{2.5}\) despite the fact that not all participants used their filters as advised. Our study and the work of others support the effectiveness of HEPA cleaners for improving home environments of children with asthma.

The main strengths and contributions of this study are the community-responsive randomized trial design, the setting, the high-participation rate, assessment of both PM\(_{2.5}\) and NH\(_3\) concentrations, and consideration of multiple household factors that may influence IAQ. The community-engaged research process and rigorous quality control procedures enhanced data completeness and quality for robust statistical analysis of our hypothesis that HEPA cleaners would reduce indoor PM\(_{2.5}\) levels by 35%-50%.

The primary limitations were the inability to address objective HEPA use patterns and the lack of blinding to intervention group. Another limitation was that we lacked TSI flow rate measurements for approximately 19% of follow-up samples, and the resulting PM\(_{2.5}\) concentrations were based on imputed flow rates, thus the true intervention effect sizes may be different from what we observed. Nonetheless, the results of our sensitivity analyses give us confidence that any differences are likely to be small. In the ANCOVA models refit using only observations with measured instead of imputed flow rates, the HEPA effect changed only 0%-4% depending on room, while in the sensitivity analyses using probabilistic simulation of flow rates the HEPA effect changed < 1% in the sleeping area model and did not change in the living area model.

5 | CONCLUSIONS

The HAPI study contributes to the growing evidence base that portable HEPA cleaners can lower indoor PM\(_{2.5}\) concentrations in a variety of home settings and populations, including rural agricultural communities. When combined with asthma education, source control, and adequate ventilation, portable HEPA cleaners may be part of an effective overall strategy to reduce pediatric asthma morbidity. Access to air cleaners for vulnerable low-income populations that are often most highly impacted by asthma morbidity should be promoted. Future research on understanding and enhancing compliance with air cleaner use alongside asthma education and medication access may help families achieve greater improvements in their children’s asthma health.

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CONFLICT OF INTEREST

Each author confirms that s/he has no conflict of interest.

AUTHOR CONTRIBUTION

Anne M. Riederer: Formal analysis (lead); Methodology (equal); Validation (equal); Writing—original draft (lead); Writing—review & editing (lead). Jennifer E. Krenz: Data curation (lead); Formal analysis (equal); Investigation (equal); Methodology (equal); Project administration (equal); Software (equal); Validation (equal);
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**PEER REVIEW**

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**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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