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A field study to estimate inhalation rates for use in a particle inhalation rate exposure metric

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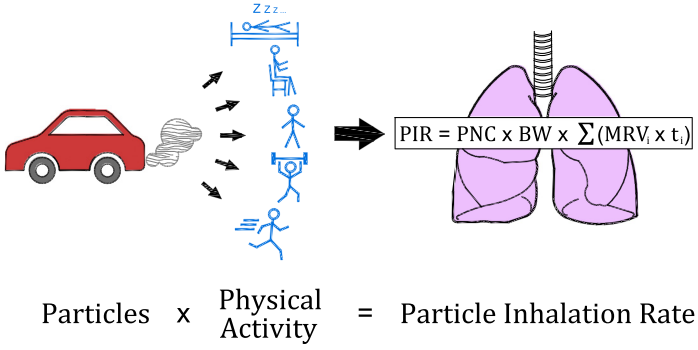
HIGHLIGHTS

- Measured population-specific inhalation rates were higher than published estimates.
- Population-specific and published particle inhalation rates were strongly correlated.
- Population-specific and published rates resulted in similar health effect estimates.

GRAPHICAL ABSTRACT



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ABSTRACT

Particle inhalation rate (PIR) is an air pollution exposure metric that relies on age-, sex-, and physical activity-specific estimates of minute respiratory volume (MRV; L/min-kg) to account for personal inhalation patterns. United States Environmental Protection Agency (USEPA)-generated MRV estimates derive primarily from relatively homogenous populations without substantial cardiorespiratory challenges. To determine if these MRV estimates are relevant to populations in generally poor cardiorespiratory health (e.g., the Boston Puerto Rican Health Study (BPRHS) population) or whether population-specific estimates are needed, we 1) estimated population-specific MRVs and compared them to USEPA MRV estimates, and 2) compared exposure distributions and health effect estimates using PIR with population-specific MRVs, PIR with USEPA MRVs, and ambient particle number concentration (PNC). We recruited 40 adults (80% Puerto Rican, mean age = 60.2 years) in Boston with health characteristics similar to the BPRHS population. We measured pulse, oxygen saturation, respiration rate, and inspiratory volume while participants walked, stood, sat, and lay down. Pulse, respiration rate, inspiratory volume, and MRV were greater when participants were walking/standing compared to sitting or lying down.

Abbreviations: BMI, Body mass index; BPRHS, Boston Puerto Rican Health Study; CPC, Condensation particle counter; CI, Confidence interval; DBP, Diastolic blood pressure; EPA, Environmental Protection Agency; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; NHANES, National Health and Nutrition Examination Survey; MRV, Minute respiratory volume; PIR, Particle inhalation rate; PNC, Particle number concentration; PM, Particulate matter; SD, Standard deviation; SBP, Systolic blood pressure; TAPL, Tufts Air Pollution Monitoring Laboratory; UFP, Ultrafine particulate matter; USEPA, United States Environmental Protection Agency.

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Minute respiratory volume
Particle inhalation rate

We then calculated MRVs adjusted for age, sex, measured body weight, and physical activity using data from 19 Puerto Rican participants who wore a nose clip or held their nostrils closed. We applied the population-specific and USEPA MRVs to estimate ultrafine particle exposure for participants in the BPRHS ($n = 781$). We compared exposure distributions and health effect estimates using the PIR with population-specific MRV estimates, PIR with USEPA MRV estimates, and ambient concentrations. We found that while population-specific MRVs differed from USEPA MRVs, particularly for unhealthy participants, PIR exposure distributions and health effect estimates were similar using each exposure metric. Confidence intervals were narrower using the PIR metrics than ambient PNC, suggesting increased statistical efficiency. Even in our understudied population, using USEPA MRVs did not meaningfully change PIR estimates.

1. Introduction

Epidemiology studies investigating the health effects of airborne particulate matter (PM) typically use ambient concentrations to estimate exposure. An implicit assumption is that ambient PM concentrations represent a meaningful metric of exposure; however, ambient estimates do not explicitly account for factors that modify how much air is inhaled and how deeply PM is deposited in the respiratory tract (USEPA, 2009; Bigazzi and Figliozzi, 2014; Jaques and Kim, 2000; Daigle et al., 2003). To reduce exposure misclassification, short-term studies considered how physical activity and transportation mode (e.g., bicycling) affect inhalation of air pollutants (Bigazzi and Figliozzi, 2014; de Nazelle et al., 2012; Int Panis et al., 2010; van Wijnen et al., 1995), though only one longitudinal study considered how average particle inhalation rate (PIR) affects health outcomes (Corlin et al., 2018). In this study, we estimated the PIR for each participant as the product of the average ambient particle number concentration (PNC, a measure of ultrafine particulate matter, or UFP; particles with <0.1 μm diameter) and average inhalation rate accounting for participants' age, sex, weight, and physical activity. We found that adjusting individual exposure estimates for inhalation rate was straightforward since it only required information on participants' annual PNC exposure and inhalation rate factors (based on minute respiratory volume, or MRV). We also found that the inhalation rate adjustment affected both the exposure distributions and longitudinal health estimates (Corlin et al., 2018). Therefore, to the extent that the PIR algorithm can capture differential inhalation rates across diverse populations, the PIR metric could help reduce exposure misclassification in air pollution epidemiology.

Since the PIR algorithm relies on published age-, sex-, weight-, and physical activity-adjusted MRVs (in L/min-kg) (USEPA, 2009), the PIR metric is useful in diverse populations only if the MRV estimates are valid across these populations. While the MRV estimates generated by the United States Environmental Protection Agency (USEPA) are frequently-used values, they were determined in largely healthy and homogenous populations that did not resemble our study population of Puerto Rican adults participating in the Boston Puerto Rican Health Study (BPRHS) (Tucker et al., 2010). Specifically, for the MRV calculations, age, sex, and anthropometric data from the National Health and Nutrition Examination Survey (NHANES) were combined with age, sex, and physical activity data from the National Human Activity Pattern Survey and the Consolidated Human Activity Database using a multistep process. First, the authors simulated 24-h physical activity patterns for each participant in the NHANES data set and multiplied the metabolic equivalent by the basal metabolic rate to obtain an energy expenditure value. Second, the basal metabolic rates were calculated as a function of participant age, sex, and body weight. The energy expenditure values were converted to VO_2 values (in L O_2/min). They then calculated the MRV as a function of the weight-adjusted VO_2 value, age, and sex for each of the NHANES participants. Finally, average MRVs for each activity intensity level were calculated. Basal metabolic rates were calculated based on a formula that is most applicable to Caucasian individuals from European regions (Schofield, 1985; USEPA, 2009). The metabolic data in relation to physical activity levels were based on information from 12 activity studies, most of which included few, if any, participants who identified as Hispanic and many of which excluded key groups based on health behaviors (e.g., smoking) (Hartwell et al., 1984; McCurdy and Graham, 2003; Stallings et al., 2002; USEPA, 2009). In contrast, our study population consisted of Puerto Ricans adults aged 45–75 years residing in eastern Massachusetts who were generally in poor health (e.g., >50% ever smokers, >70% hypertensive, ~50% diabetic). To evaluate the utility of the PIR algorithm in our population, we needed to determine if USEPA MRV estimates were appropriate or if population-specific MRV estimates were necessary.

We designed a study to estimate population-specific MRVs and assess the applicability of the PIR algorithm values in less healthy and understudied populations. Specifically, our objectives were 1) to calculate age-, sex-, weight-, and physical activity-adjusted MRVs in a sample of participants that was similar to the BPRHS population and 2) to determine the impact of using population-specific MRV estimates instead of USEPA MRV estimates on long-term UFP exposure estimates and on health effect estimates.

2. Methods

2.1. Study population and recruitment

We worked with a community partner organization, Inquilinos Boricuas en Acción, to recruit a convenience sample of adults ($n = 40$) in the Villa Victoria community in the South End neighborhood of Boston (Inquilinos Boricuas en Acción, 2018). This community was one of the neighborhoods of interest within the BPRHS (Tucker et al., 2010). As part of the recruitment process, we held three health fairs/study sessions over two consecutive weeks during March and April of 2017. The health fairs were staffed with bilingual Spanish-English speakers. To advertise the fairs, we handed out bilingual flyers at individuals' homes and posted bilingual flyers in public locations. To improve representation of both sexes in each age group, we also conducted targeted recruitment and held a separate study day for men in their 40s ($n = 2$; June 2017). Recruitment was not limited to any specific race/ethnicity.

2.2. Demographic and health data

Participants reported demographic information, current respiratory symptoms and medications, and cardiovascular and respiratory health status. We asked participants about current and former smoking (≥100 cigarettes ever), e-cigarette use, and exposure to smoke in their home and car. The number of hours spent lying down, being sedentary, and engaged in light (e.g., office work, light housework, or standing with little motion), moderate (e.g., heavy housework, regular walking or light sports), or vigorous (e.g., brisk walking or strenuous sports) physical activity per typical weekday and weekend day was assessed using a modified Paffenbarger questionnaire from the Harvard Alumni Activity Survey (Paffenbarger et al., 1978, 1993). The modified questionnaire has been used within the BPRHS population (Tucker et al., 2010).

During study sessions, we measured participants' height, weight, and lung function. To assess lung function, we measured peak expiratory flow in triplicate using an ASSESS full range peak flow meter (values 60–880 L/min are measurable). Of the 104 peak flow measurements from 35 participants, ≥72% of readings were obtained while participants were standing (participants were asked to stand). The highest of the three measurements was used to determine whether participants had normal peak flow (≥80% of the age-, sex-, height-, and race/ethnicity-specific expected peak flow) (Roberts and Mapel, 2012).

We measured pulse and oxygen saturation with a finger pulse oximeter (Santa Medical SM-165) during each of the six measurement periods (sitting before survey, sitting after survey, while lying down after 4 min lying down, sitting immediately after 5 min lying down, while walking after 4 min walking, standing immediately after walking for 5 min; see Fig. 1 for a flow diagram). To assess how physical activity affected breathing patterns, participants were asked to breathe normally into a Vernier spirometer (Model: SPR0515R2; pneumotach with a dead space of <100 mL) for 20 s at a time while lying down, sitting, standing, and walking at their normal walking pace. Participants were given the option of wearing a soft nose clip or holding their nose since not all participants were comfortable wearing the nose clip. Among 212 sets of spirometry data from 40 participants (88.3% of 240 possible sets; Fig. 1), ≥67.0% were obtained when participants wore a nose clip or held their nose. In 33 sets, it is unknown whether the participant held their nose. For each participant, we obtained between three and six sets of measurements while they were in different physical positions. Two participants chose not to lie down and two other participants chose not to walk.

The spirometer measured flow rate (L/s) every 0.02 s (i.e., 50 Hz). The flow rate measurements were recorded with a Vernier LabQuest2 and were analyzed using Logger Pro 3.13. The respiration rate (breaths/min) was determined by dividing the number of full breath cycles by the time in minutes over which the cycles occurred. The volume of air inhaled in each breath was determined by integrating the measured flow rate over the breath during inhalation. The inspiratory volume was calculated as the average volume of air inhaled per breath. Minute respiratory volume (MRV, L/min) was calculated as respiration rate (breaths/min) multiplied by average inspiratory volume (L/breath). The MRV was then divided by participant weight to obtain a weight-specific MRV (L/min-kg).

The study protocol was approved by the Tufts Social, Behavioral, and Educational Institutional Review Board (#1703021).

2.3. Statistical analysis

We used descriptive statistics, independent samples *t*-tests (for continuous variables), and chi-squared tests (for categorical variables) to compare the demographic and health characteristics of our sample to those of participants in the BPRHS residing in Boston at their final study visit ($n = 431$; study visits occurred between 2011 and 2015). To assess whether the mean pulse, oxygen saturation, respiratory rate, inspiratory volume, and MRV significantly differed based on participants' physical activity level, we used multilevel models with a random intercept for each participant. We considered differences among the six measurement sets and by physical position (grouping measurement sets one and two as sitting, three and four as lying down, and five and six as walking/standing). We also considered whether the relationship between physiological parameters and physical activity varied among sub-sets of our population (e.g., only Puerto Rican participants, only participants with normal peak flow values, or only participants who engaged in any vigorous physical activity in a typical week).

To calculate the average age-, sex-, weight-, and physical activity-adjusted MRVs for this population, we first divided the MRV by participants' weight in kilograms. Then we calculated the mean MRV per kilogram by age group (<60/≥60 years), sex, and physical position (sitting, lying down, and walking/standing). For the main analyses, we calculated the age-, sex-, weight-, and physical activity-adjusted MRV using only the 97 measurements obtained from the 19 participants (hereafter referred to as Group 1) who wore a nose clip or held their nostrils closed, identified as Puerto Rican, and had a measured weight. We compared the ratio of population-specific MRV estimates to USEPA values (averaging estimates for people in their 40s and 50s and for people in their 60s and 70s separately) (USEPA, 2009). We also calculated the MRV estimates using all available data.

Next we applied the MRV estimates to the PIR calculation among participants in the BPRHS. Methods related to PNC exposure assessment have been published previously and are summarized in Appendix A.1 (Corlin et al., 2018). For times when people were lying down, sedentary, or engaging in light physical activity, we used values derived from measurements of Puerto Rican participants who held or clipped their nose. For times when people were engaging in moderate or vigorous physical activity (approximately 10% of the time; see Table A.1 for activity breakdown), we used USEPA values. The algorithm for the PIR was previously published (Corlin et al., 2018). It is included here for clarity. USEPA MRV estimates (L/min-kg) are provided in Table A.2 and an example calculation is provided in the appendix (Section A.3).

Step 1. Inhalation rate

$$\text{Inhalation rate} = BW \times \sum(MRV_i \times t_i)$$

Inhalation rate is expressed in units of liters of air inhaled per hour; *BW* is body weight in kg; *MRV* is the minute respiratory volume in L/min-kg; *i* represents each of the five activity levels (lying down/sleeping, sedentary, light, moderate, vigorous); t_i represents time involved in each activity level.

Step 2. Particle inhalation rate (PIR)

$$PIR = PNC \times \text{inhalation rate}$$

PIR is expressed in number of particles inhaled hourly; *PNC* is particle number concentration in particles per liter; *Inhalation rate* is expressed in units of liters of air inhaled per hour.

We then compared PIR distributions using measured and USEPA MRV values. We also examined the correlation between the distributions. Finally, we compared the effect of using the PIR with measured and USEPA MRV estimates in an epidemiological study. We estimated the association of UFP as measured by individual 1) annual ambient average PNC, 2) PIR with USEPA MRV estimates (USEPA, 2009), and 3) PIR with population-specific MRV estimates with three endpoints (systolic blood pressure [SBP], diastolic blood pressure [DBP], and pulse pressure [PP]) levels over approximately six years among BPRHS participants (*n*

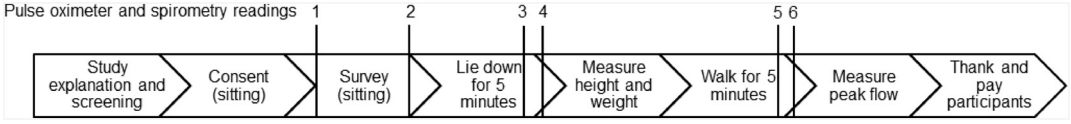

Fig. 1. Flow diagram for data collection. At each of the six pulse oximeter and spirometry reading trials, we could have obtained measurement sets from up to 40 participants. We obtained 29 spirometry measurements at trial 1 (sitting, before the survey), 40 at trial 2 (sitting, after the survey), 37 at trial 3 (lying down, after 4 min lying down), 33 at trial 4 (sitting up, immediately after lying down for 5 min), 36 at trial 5 (walking, after 4 min walking), and 37 at trial 6 (standing, immediately after walking for 5 min).

= 781 at baseline; BPRHS participant health data are summarized in the appendix [Section A.1]). We used multilevel linear models with a random intercept for each participant. For models with PIR, we controlled for age, educational attainment (>8th grade/≤8th grade), body mass index (BMI), smoker status, hypertension medications, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, ln(triglycerides), marital status, and baseline year. For models with PNC, we controlled for age, weight, physical activity, sex, education, smoker status, hypertension medications, LDL cholesterol, HDL cholesterol, ln(triglycerides), marital status, and baseline year. These covariates are similar to ones used in the previous publication but all models with PIR reported here use a consistent set of covariates for comparability (rather than model-specific covariates used in the previous analysis) (Corlin et al., 2018). The covariates for models with PNC use covariates chosen to reflect parameters accounted for within the PIR.

3. Results

3.1. Sample characteristics and comparison with the BPRHS population

In our sample of 40 participants, 32 identified as Puerto Rican. Of these 32 participants, 31 identified as Hispanic, 10 identified as white, three identified as black, two identified as Asian, and one identified as American Indian (not mutually exclusive categories). Of the eight who did not identify as Puerto Rican, six identified as black, two identified as Hispanic, and one identified as American Indian. Table 1 compares demographic characteristics of our study participants ($n = 40$), our study participants who self-identify as Puerto Rican ($n = 32$), our study Puerto Rican participants who had spirometry data collected while they wore nose clips or held their nostrils closed ($n = 19$; Group 1), and the BPRHS participants residing in Boston. The mean age, mean BMI, and percentage of women in the groups were similar, though our participants were significantly younger (60.2 versus 63.1 years at the third BPRHS visit; $p = 0.02$). Significantly more of our participants were current smokers ($p = 0.01$) and fewer were former smokers ($p = 0.02$) than the participants in the BPRHS. Our participants were more active than the BPRHS participants. On an average weekday, our participants reported sleeping or lying down 37% of the time, sitting 19% of the time, and engaging in any physical activity 44% of the time (versus 41%, 31%, 28% of the time for the BPRHS participants, respectively; see Table A.1). Within each group, weekend physical activity trends were similar to weekday physical activity trends (data not shown).

Most of our participants had a health condition that could affect inhalation or cardiac function (Table 2). While we do not have data on all health conditions represented in Table 2 for the BPRHS sample, the prevalence of heart attacks/strokes by the third study visit was 17.1%, the prevalence of asthma or chronic obstructive pulmonary disease medication usage was 30.7%, and the prevalence of cough medication usage was 6.7%.

We had 35 participants with peak expiratory flow values ($n = 34$ with three readings). The mean was 357 L/min (standard deviation (SD) = 124) among all participants and 352 L/min (SD = 133) among the 27 Puerto Rican participants. Table 3 shows the proportion of participants with measured peak flow values ≥80% of expected.

Table 1
Demographic characteristics.

	Inhalation study ($n = 40$)	Inhalation study – Puerto Rican participants ($n = 32$)	Inhalation study – Puerto Rican participants in Group 1 ($n = 19$)	BPRHS ($n = 781$ at 1st study visit; 2004–2009)	BPRHS ($n = 605$ at 2nd study visit; 2006–2011)	BPRHS (n = 431 at 3rd study visit; 2011–2015)
Mean age (years; SD)	60.2 (12.0)	60.7 (13.0)	60.8 (13.0)	57.0 (7.4)	59.2 (7.5)	63.1 (7.3)
Mean BMI (kg/m^2; SD)	28.9 (5.6)	28.4 (5.9)	27.6 (4.3)	31.7 (6.4)	31.6 (6.5)	31.0 (6.7)
Mean body weight (kg; SD)	76.1 (16.2)	74.5 (16.7)	72.6 (14.5)	79.8 (17.0)	79.6 (17.2)	79.7 (17.4)
Women (%)	65.0	59.4	63.2	68.9	70.7	71.6
Current smokers (%)	35.0	37.5	36.8	23.6	22.0	18.8
Former smokers (%)	20.0	25.0	26.3	32.5	33.0	38.1
Mean SBP (mmHg; SD)	–	–	–	134 (19)	137 (19)	135 (18)
Mean DBP (mmHg; SD)	–	–	–	81 (11)	80 (11)	75 (10)
Mean PP (mmHg; SD)	–	–	–	54 (14)	56 (16)	60 (16)
Hypertension medications (%)	–	–	–	52.6	58.5	68.6
Completed >8th grade (%)	–	–	–	52.6	52.1	50.6
Physical activity score[a]	–	–	–	32 (5)	31 (5)	32 (6)
Married, spouse in household (%)	–	–	–	28.8	31.0	25.9
Married, spouse not in household (%)	–	–	–	3.6	2.7	3.7
Divorced/separated	–	–	–	40.4	38.6	35.8
Widowed (%)	–	–	–	12.9	12.4	16.8
Never married (%)	–	–	–	14.3	15.3	17.8
Mean LDL cholesterol (mg/dL; SD)	–	–	–	107 (35)	110 (36)	105 (35)
Mean HDL cholesterol (mg/dL; SD)	–	–	–	44 (12)	46 (13)	47 (16)
Mean triglycerides (mg/dL; SD)	–	–	–	164 (114)	155 (93)	146 (109)

Abbreviations: Boston Puerto Rican Health Study (BPRHS); standard deviation (SD); body mass index (BMI); systolic blood pressure (SBP); diastolic blood pressure (DBP); pulse pressure (PP); low-density lipoprotein (LDL); high-density lipoprotein (HDL).

[a] Physical activity was assessed using a modified Paffenbarger questionnaire of the Harvard Alumni Activity Survey.

Table 2
Prevalence of respiratory and cardiovascular conditions.

	All participants % (n)	Puerto Rican participants % (n)	Inhalation study – Puerto Rican participants in Group 1% (n)
Cold/respiratory infection within past week	15.0 (6)	18.8 (6)	10.5 (2)
Current cold/respiratory symptoms	37.5 (15)	43.8 (14)	42.1 (8)
Asthma	34.2 (13)	36.7 (11)	33.3 (6)
Chronic obstructive pulmonary disease	18.0 (7)	22.6 (7)	27.8 (5)
Lung cancer	0.0 (0)	0.0 (0)	0.0 (0)
Tuberculosis	0.0 (0)	0.0 (0)	0.0 (0)
Coronary heart failure	7.7 (3)	9.7 (3)	5.6 (1)
Heart attack	12.8 (5)	16.1 (5)	11.1 (2)
Heart disease	12.8 (5)	16.1 (5)	16.7 (3)
Stroke	0.0 (0)	0.0 (0)	0.0 (0)

Non-asthmatics ($n = 24$) and people without colds or respiratory symptoms ($n = 21$) were more likely to have measured peak flow values ≥80% of expected values.

3.2. Change in physiological parameters with physical activity

The physical activity intervention affected participants' physiological parameters as expected (Tables 4 and 5). Specifically, participants' mean pulse was significantly higher while they were walking (trials 5 and 6) than when they were lying down (trials 3 and 4; $p < 0.001$) or sitting (trials 1 and 2; $p < 0.001$). Pulse was also significantly higher when participants were sitting than when they were lying down ($p = 0.001$). Participants' mean pulse in trial 1 was significantly higher than in trial 3 ($p = 0.001$) and lower than in trial 5 or 6 ($p < 0.001$ and $p = 0.007$, respectively). Participants' mean pulse in trial 6 was also significantly higher than in trials 1, 2, 3, and 4 ($p = 0.007$, $p = 0.004$, $p < 0.001$, and $p < 0.001$, respectively). The same overall trends were observed when the analysis was restricted to Puerto Rican participants, participants with peak flow values ≥80% expected, and participants who reported engaging in any vigorous physical activity during the week. In contrast, the only significant differences in participants' mean O_2 saturation by trial were between trial 5 and trials 1 and 6 (mean values were significantly higher in trials 1 and 6 than in trial 5; $p = 0.001$ and $p < 0.001$, respectively).

Participants' respiration rate, inspiratory volume, and MRV varied by physical activity level (Table 5). Mean levels of each parameter were significantly ($p < 0.01$ for all comparisons) higher while participants were walking than lying down or sitting. Mean levels of each parameter were not significantly different when participants were sitting compared to lying down ($p = 0.762$, $p = 0.651$, and $p = 0.649$, respectively). Mean levels of each parameter were generally significantly higher while participants were walking than when they were lying down or sitting in the analyses restricted to only Puerto Rican participants, only participants with peak flow values ≥80% expected, or only participants who engaged in any vigorous physical activity.

Table 3
Percent of participants with peak flow readings ≥80% of expected based on sex, age, height, and race/ethnicity.

	All participants % (n)	Puerto Rican participants % (n)	Puerto Rican participants in Group 1% (n)
Overall	65.7 (23)	63.0 (17)	66.7 (12)
Standing readings only	68.0 (17)	66.7 (12)	73.3 (11)
Men only	61.5 (8)	66.7 (8)	85.7 (6)
Non-asthmatics only	70.8 (17)	72.2 (13)	72.7 (8)
No one with cold or respiratory symptoms	81.0 (17)	78.6 (11)	80.0 (8)

3.3. Minute respiratory volume estimates

We averaged MRV observations by age group (<60 and ≥60 years), sex, and physical activity (trials 1–2, 3–4, and 5–6) to obtain population-specific estimates for the inhalation rate algorithm (Table 6). All estimates were between 0.10 and 0.18 with generally higher estimates among men. The main analyses only used data from Group 1 participants (i.e., the participant had to be Puerto Rican, hold/clip their nose, and have ≥3 breaths/20 s). For USEPA MRV estimates, see Table A.2. For measured MRV using all available data, see Table A.3.

We compared our calculated population-specific MRV values to the USEPA values (Table 7) (USEPA, 2009). Overall, we found that our estimates were between 31% lower and 100% higher than the USEPA estimates. In general, our estimates were higher for participants lying down or sitting down but were similar while participants were walking or standing. For a comparison of our measured MRV values using all data, see Table A.4.

Measured MRV values were generally higher for participants in worse health (results not shown). In younger men and older women (using all data), the calculated MRV values were 1.18–2.43 times as high for current smokers and asthmatics as for never-smokers and non-asthmatics. The differences were generally greater in younger men than older women. In younger women (using all data), MRV values were 0.44–0.50 times as high for asthmatics as for non-asthmatics and were 0.45–1.67 times as high for current smokers as for never-smokers. We did not have any older men who were asthmatic or never-smokers.

3.4. Applying the minute respiratory volume estimates

Based on the MRVs calculated with Group 1 data (Table 6), we determined the inhalation rate and PIR for each BPRHS participant at each of their study visits. For an example calculation of inhalation rate and PIR using population-specific and USEPA MRV estimates for a hypothetical average participant, please refer to the appendix (Section A.3). Table 8 compares the inhalation rate and PIR determined using our measured population-specific MRVs and the USEPA MRVs. The inhalation rate distribution was similar regardless of which MRV estimates were used, though the mean inhalation rate was 111 L/h higher using the population-specific MRVs compared to the USEPAestimates (95% CI = 108, 114 L/h) and the mean PIR was 2.6 billion particles inhaled/h higher using the population-specific MRV estimates compared to the USEPA estimates (95% CI = 2.5, 2.7 billion particles inhaled/h). The correlations were also high between the inhalation rate determined with the population-specific and the USEPA MRV estimates ($r = 0.960$) and between the PIR using the two sets of MRV estimates ($r = 0.963$; Fig. 2). The correlations were higher among the most active quartile of participants than among the least active quartile of participants ($r = 0.978$ versus 0.925 and $r = 0.982$ versus 0.946 for the inhalation rate and the PIR, respectively).

Table 4
Mean and standard deviation pulse and oxygen saturation by trial.

Trial	All participants		Puerto Rican participants		Puerto Rican participants in Group 1	
	Pulse (beats/min)	O_2 saturation (%)	Pulse (beats/min)	O_2 saturation (%)	Pulse (beats/min)	O_2 saturation (%)
1	77.4 (13.7)	97.8 (1.4)	77.1 (15.0)	97.8 (1.4)	76.8 (16.3)	97.7 (1.6)
2	75.6 (14.4)	97.6 (2.7)	75.6 (15.6)	97.5 (3.0)	77.6 (17.1)	97.9 (1.5)
3	70.7 (13.2)	97.2 (1.8)	70.7 (13.9)	97.1 (1.9)	72.4 (15.2)	96.8 (2.2)
4	74.1 (15.6)	97.7 (1.3)	73.4 (16.9)	97.7 (1.3)	77.5 (18.8)	97.4 (1.5)
5	81.5 (14.6)	96.1 (4.0)	80.7 (15.5)	96.8 (2.2)	81.9 (16.9)	96.8 (1.9)
6	79.6 (18.6)	97.9 (1.3)	79.2 (19.7)	97.9 (1.3)	83.1 (21.4)	97.7 (1.4)
1 + 2	76.4 (14.0)	97.7 (2.2)	76.3 (15.2)	97.6 (2.4)	77.2 (16.5)	97.8 (1.5)
3 + 4	72.3 (14.4)	97.4 (1.6)	71.9 (15.3)	97.4 (1.6)	74.9 (16.9)	97.1 (1.9)
5 + 6	80.5 (16.6)	97.0 (3.1)	79.9 (17.6)	97.3 (1.9)	82.5 (19.0)	97.3 (1.7)

Data are mean (standard deviation). Trial 1 = sitting before survey; trial 2 = sitting after survey; trial 3 = lying down; trial 4 = sitting, immediately after lying down; trial 5 = walking around; trial 6 = standing, immediately after walking.

Fig. A.1 shows the distribution of the BPRHS participants' annual ambient average PNC and the annual average PIR calculated using the measured population-specific and USEPA MRV estimates. The PIR distributions were similar regardless of which MRV estimates were used, though using the measured population-specific values resulted in higher MRV values. The PIR distributions differed from the PNC distribution, reflecting the influence of physical activity patterns on exposure (Fig. 2). For example, both PIR distributions were right skewed (skew = 1.5 and 1.6, for population-specific and USEPA estimates, respectively) while the PNC distribution was left skewed (skew = −0.7) and more platykurtic (kurtosis = 3.6 versus 7.7 for the PIR distribution using the population-specific MRV estimates).

When we used each of the three exposure metrics to estimate the effect of UFP on blood pressure among the BPRHS participants, the point estimates were similar (particularly for SBP) but the confidence intervals were narrower with the PIR metrics (Table 9). The point estimates for the PIR metric using the population-specific MRV values were between 21% and 50% stronger than the estimates for the PIR using the USEPA MRV values, though the absolute differences were small (difference in βs of 0.01–0.04) and the overall trends were the same (e.g., an increase in PNC was associated with SBP and DBP, but not PP).

4. Discussion

We calculated age-, sex-, weight-, and physical activity-adjusted MRVs for Puerto Rican adults based on measurements in a convenience sample of 40 adults (n = 32 Puerto Rican participants, 13 of whom also participated in the BPRHS). Our study sample was similar to the BPRHS population and to populations with atypical inhalation patterns (e.g., 55% of our participants were current or former smokers, 75% had a health condition that could affect respiration or cardiac function, and 34% had a peak expiratory flow <80% of expected based on age, sex, height, and race/ethnicity). Our measured population-specific MRV estimates were higher than the USEPA estimates (USEPA, 2009) for individuals while they were lying down or sitting down and were similar while individuals were engaged in light physical activity. The differences between the population-specific MRV estimates and the USEPA estimates were more extreme for less healthy individuals. The greater differences between population-specific and USEPA estimates observed among less healthy individuals might be attributable to greater alterations in breathing patterns due to the mouthpiece compared to healthy individuals (Chalupa et al., 2004; Paek and McCool, 1992). Nevertheless, applying the population-specific MRV estimates instead of the USEPA MRV estimates did not change the exposure estimates for 780 participants in the BPRHS and did not change the conclusions of the health analysis in meaningful ways. The similarity in results obtained when applying population-specific and USEPA MRV estimates to epidemiological contexts suggests that the PIR metric we previously developed (Corlin et al., 2018) can be applied in populations like ours (including relatively unhealthy populations) using accessible, USEPA-published MRV estimates rather than population-specific estimates which can be resource-intensive to measure.

Our PIR metric represents a novel way to assess long-term exposure to air pollution. While studies of commuter exposure to PM explicitly accounted for inhalation by multiplying minute respiratory volume (or minute ventilation) by average exposure concentrations (Bigazzi and Figliozzi, 2014; Int Panis et al., 2010; van Wijnen et al., 1995), and certain exposure assessment and risk assessment protocols recommend accounting for inhalation rate or deposition of air pollutants (Buonanno et al., 2011; Jackson, 2005), our previous analysis is the only application of which we are aware of this method in a longitudinal study (Corlin et al., 2018). In both the commuter studies and in our longitudinal analysis, accounting for inhalation patterns reduced the likelihood of differential exposure misclassification. For example, exposure estimates were empirically higher among more active participants (e.g., among cyclists) (Int Panis et al., 2010); our approach reflects this observation by

Table 5
Mean and standard deviation of respiration rate (breaths/min; RR), inspiratory volume (L inhaled/breath; IV), and minute respiratory volume (L inhaled/min; MRV) by trial.

Trial	All participants			Puerto Rican participants in Group 1		
	RR	IV	MRV	RR	IV	MRV
1	17.9 (6.7)	0.4 (0.2)	7.4 (4.8)	16.9 (4.8)	0.4 (0.2)	7.4 (4.0)
2	16.4 (5.7)	0.5 (0.3)	8.5 (4.7)	17.3 (5.2)	0.5 (0.3)	8.4 (3.6)
3	16.3 (6.9)	0.5 (0.3)	7.0 (4.1)	15.8 (4.3)	0.4 (0.2)	6.1 (3.3)
4	16.7 (7.6)	0.6 (0.3)	8.7 (5.0)	16.5 (4.5)	0.6 (0.2)	8.9 (4.0)
5	19.3 (6.4)	0.6 (0.4)	11.1 (6.4)	18.8 (7.3)	0.7 (0.3)	11.7 (5.1)
6	17.8 (6.0)	0.6 (0.4)	10.2 (5.8)	18.7 (5.6)	0.5 (0.3)	10.0 (5.2)
1+2	17.0 (6.1)	0.5 (0.3)	8.1 (4.8)	17.1 (4.9)	0.5 (0.2)	7.9 (3.8)
3+4	16.5 (7.2)	0.5 (0.3)	7.9 (4.6)	16.2 (4.3)	0.5 (0.2)	7.6 (3.9)
5+6	18.5 (6.2)	0.6 (0.4)	10.6 (6.0)	18.8 (6.4)	0.6 (0.3)	10.9 (5.1)

For a trial to be part of Group 1, the participant had to hold their nose and have at least three breaths per 20 seconds. Trial 1 = sitting before survey; trial 2 = sitting after survey; trial 3 = lying down; trial 4 = sitting, immediately after lying down; trial 5 = walking around; trial 6 = standing, immediately after walking.

Table 6
Measured MRV (L/min-kg) and number of data points for MRV calculations (using Group 1 data).

	Men		Women	
	<60 years (n)	≥60 years (n)	<60 years (n)	≥60 years (n)
Lying down	0.12 (7)	0.12 (3)	0.10 (5)	0.10 (13)
Sitting	0.14 (8)	0.11 (4)	0.10 (5)	0.10 (15)
Walking/standing	0.18 (7)	0.17 (6)	0.11 (6)	0.15 (18)

Values shown by age group (<60/≥60 years), sex, and physical activity (trial 1–2, 3–4, or 5–6). Mean body weight for men <60 years = 83.4 kg (SD = 11.8), mean body weight for men ≥60 years = 80.3 kg (SD = 14.4), mean body weight for women <60 years = 72.0 kg (SD = 18.4), and mean body weight for women ≥60 years = 65.4 kg (SD = 12.0).

incorporating physical activity into the exposure algorithm. Furthermore, by explicitly accounting for age, sex, weight, and physical activity within the PIR algorithm, we gained statistical efficiency over the traditional approach of adjusting for these factors in health models.

4.1. Strengths and limitations

By coupling our study with a series of health fairs at a community center, we were able to engage with a disadvantaged population that was similar to the BPRHS population. Additionally, we were able to manipulate the physiologic parameters effectively such that we could calculate population-specific MRVs for different physical activity levels. For example, we observed changes that would be expected in pulse with even limited changes in physical activity level (—Åstrand and Ryhming, 1954). Nevertheless, we did not validate our pulse oximetry readings with arterial blood sampling and it is possible that the pulse-oximeter readings were less accurate during trials when participants were moving than when they were sedentary (Mengelkoch et al., 1994). Regardless, the estimates that we obtained for the MRV followed expected trends. Values were higher for men than women, lower for participants when they were sedentary than when they were active, and higher for participants in worse health (Tobin et al., 1983; Bennett et al., 1997; Brown et al., 2002; USEPA, 2009).

We acknowledge that our study had several limitations. First, we had a relatively small sample size and only about half of participants completed at least five spirometry readings with their nose held or wearing a nose clip. Larger studies on more diverse populations will be needed to test the results we obtained. Second, certain inhalation parameters measured when participants were lying down or when they first sat up after lying down (trials 3 and 4) were generally not significantly different than the other sitting spirometry measurements (trials 1 and 2). Therefore, our ability to differentiate the MRV values for people lying down and sitting down may be limited. Third, we were also unable to test how inhalation patterns changed with moderate or vigorous physical activity. Participants reported engaging in moderate or vigorous physical activity approximately 10% of the time. Assuming a hypothetical person with the mean weight (80 kg), annual average PNC exposure (23,000 particles/cc), and activity budget of a BPRHS participant (see Table A.1), using the population-specific MRVs for the lowest three activity levels and an arbitrary 1.5*USEPA MRVs for moderate and vigorous physical activity would increase the PIR exposure estimates by 30.3–52.3% compared to the PIR estimates using the USEPA MRVs for all five activity levels (depending on the age and sex of the participant).

Table 7
Ratio of observed to USEPA estimates.

	Men		Women	
	<60 years	≥60 years	<60 years	≥60 years
Lying down	1.71	1.71	1.67	1.54
Sitting	2.00	1.38	1.54	1.43
Walking/standing	1.06	1.03	0.69	0.97

Values are averaged for people in their 40s and 50s and for people in their 60s and 70s.

Table 8
Inhalation rate and PIR of BPRHS participants.

	Inhalation rate (L/h)		Particle inhalation rate (billion particles inhaled/h)	
	Population-specific MRVs	USEPA MRVs	Population-specific MRVs	USEPA MRVs
Mean	679	568	15.9	13.3
SD	235	217	6.1	5.5
Min	223	145	4.8	3.7
Median	633	521	14.9	12.2
Max	2305	2113	59.3	54.4
IQR	256	245	7.0	6.2

There were 1730 observations from 780 participants. Values were calculated using measured population-specific minute respiratory volume (MRV) estimates and USEPA estimates. SD = standard deviation; IQR = interquartile range.

Increasing the weight of time spent engaged in moderate and vigorous physical activity in the PIR calculation would likely result in lower health effect estimates since healthier individuals would be expected to exercise more. Fourth, the spirometry method may have altered participants' normal breathing patterns. For example, Paek and McCool (1992) found that the use of a mouthpiece increased MRV by approximately 16%. In comparison, the population-specific estimates we observed were between 31% lower and 100% higher than the USEPA MRV estimates indicating that observed differences are unlikely to be due solely to mouthpiece effects. Fifth, our sample might not have been completely representative of the BPRHS population. For example, we had a higher smoking prevalence, which could have increased our MRV estimates. Although this would be expected to increase the differences between the population-specific PIR estimates and the PIR estimates using the previously measured values and we did not find meaningful differences in the health estimates using the population-specific values and the USEPA values, it is possible that we would have found different results with a larger or more representative sample.

Finally, we did not test other assumptions of the PIR metric, such as the idea that the product of average hourly inhalation and average annual exposure is equivalent to the product of average hourly inhalation and average hourly exposure. While this could lead to an underestimation of the effects of PNC exposure at times when individuals have a high inhalation rate and are exposed to high levels of air pollution (e.g., while exercising near roadways), it is unlikely to impact chronic health effect estimates. Future work could quantitatively test other assumptions of the PIR metric.

4.2. Conclusions

Our study suggested that the USEPA MRV estimates were applicable even in populations like ours that do not resemble most of the populations from which the USEPA MRVs were generated. Therefore, the PIR algorithm that we developed can be applied in longitudinal studies investigating the health effects of particulate components of traffic-related air pollution allowing researchers to explicitly account for inhalation as a critical step on the exposure pathway.

Ethics approval and consent to participate

The study protocol was approved by the Tufts Social, Behavioral, and Educational Institutional Review Board (#1703021). All participants provided written informed consent.

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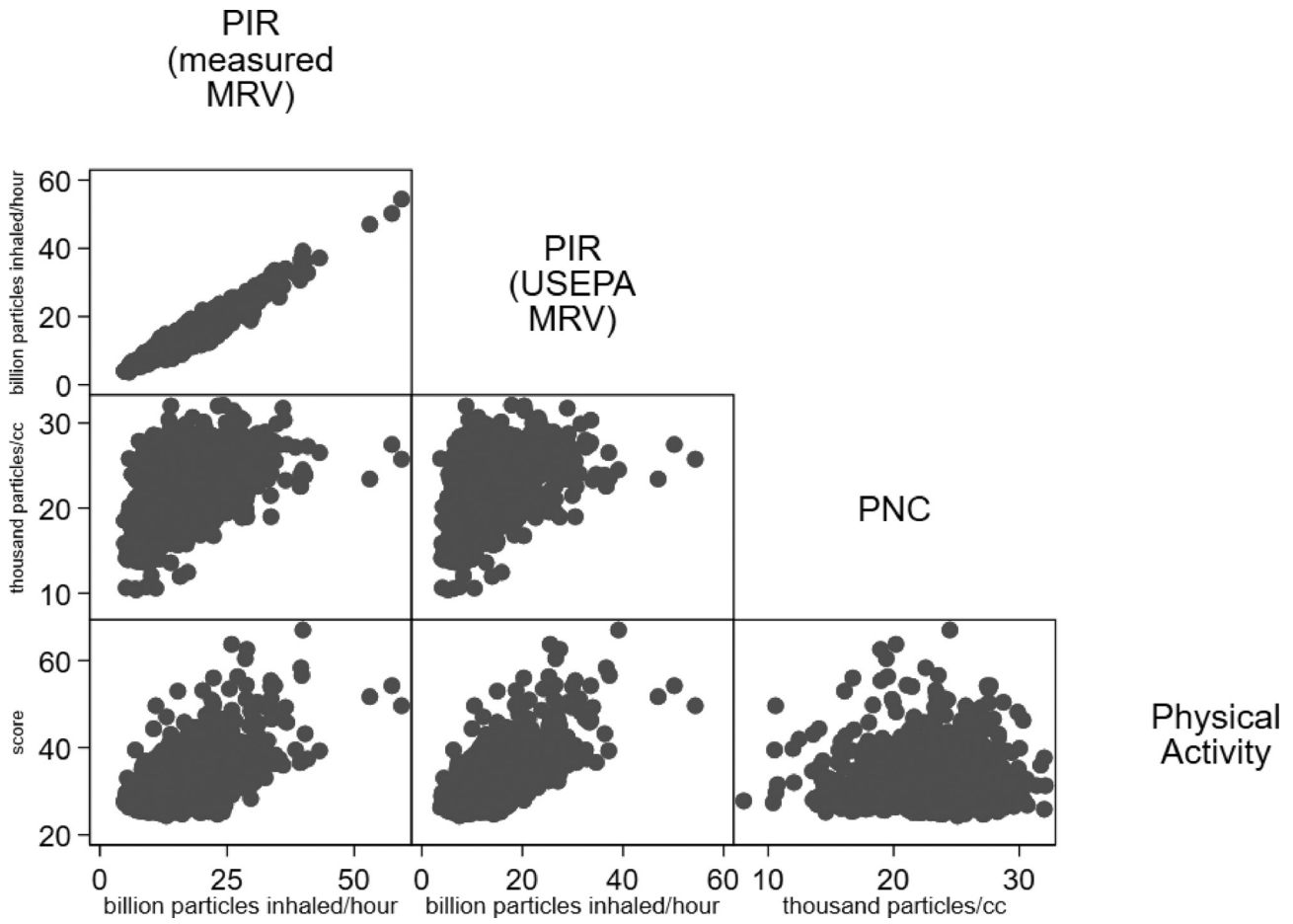

Fig. 2. Scatterplot matrix comparing the distribution of particle inhalation rates using population-specific MRVs, particle inhalation rates using USEPA MRVs, particle number concentration, and physical activity score.

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Laura Corlin: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Project administration, Funding acquisition.**Mark Woodin:**Methodology, Writing - review & editing, Supervision.**Harsha Amaravadi:**Conceptualization, Methodology, Investigation, Data curation, Writing - review & editing.**Noelle Henderson:**Investigation, Writing - review & editing. **Doug Brugge:**Resources, Writing - review & editing.**John L. Durant:** Writing - review & editing, Supervision.**David M. Gute:**Resources, Writing - review & editing, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no competing interests.

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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.2019.133919.

Table 9
Health effect estimates.

	SBP (mmHg)		DBP (mmHg)		PP (mmHg)	
	β	95% CI	β	95% CI	β	95% CI
PIR with population-specific MRVs	0.23	0.07, 0.38	0.21	0.11, 0.31	0.03	−0.09, 0.14
PIR with USEPA MRVs	0.19	0.02, 0.36	0.17	0.06, 0.27	0.02	−0.10, 0.15
PNC	0.19	−0.09, 0.47	0.13	−0.04, 0.29	0.11	−0.10, 0.33

Effect estimates for PIR (billion particles inhaled/h) and PNC (1000 particles/cc) on systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP).

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