



Development and validation of models to predict personal ventilation rate for air pollution research

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Abstract

Air pollution intake represents the amount of pollution inhaled into the body and may be calculated by multiplying an individual's ventilation rate with the concentration of pollutant present in their breathing zone. Ventilation rate is difficult to measure directly, and methods for estimating ventilation rate (and intake) are lacking. Therefore, the goal of this work was to examine how well linear models using heart rate and other basic physiologic data can predict personal ventilation rate. We measured personal ventilation and heart rate among a panel of subjects ($n = 36$) while they conducted a series of specified routine tasks of varying exertion levels. From these data, 136 candidate models were identified using a series of variable transformation and selection algorithms. A second “free-living” validation study ($n = 26$) served as an independent validation dataset for these candidate models. The top-performing model, which included heart rate (H_r), resting heart rate (H_{rest}), age, sex, and hip circumference and interactions between sex with H_r , H_{rest} , age, and hip predicted ventilation rate (V_e) to within 11% and 33% for moderate ($V_e = 45$ L/min) and low ($V_e = 15$ L/min) intensity activities, respectively, based on the validation study. Many of the promising candidate models performed substantially worse under independent validation. Our results indicate that while measures of air pollution exposure and intake are highly correlated within tasks for a given individual, this correlation decreases substantially across tasks (i.e., as individuals go about a series of typical daily activities). This discordance between exposure and intake may influence exposure-response estimates in epidemiological studies. New air pollution studies should consider the trade-offs between the predictive ability of intake models and the error potentially introduced by not accounting for ventilation rate.

Keywords air pollution · minute ventilation · exposure · particle number · microenvironments

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Introduction

Exposure to ambient air pollution is associated with increased risk for many adverse health conditions, including respiratory disease, cardiovascular disease, and cancer [1–6]. The source-effect pathway (Fig. 1) illustrates the major steps between air pollution emissions and a resulting health effect [7, 8]; the pathway also provides a paradigm for research (and intervention) on the health effects of air pollution. Epidemiologic research commonly focuses on estimating exposure-response using ambient concentrations or personal exposures. Exposure concentrations are commonly used because they are feasible (from a study design perspective) and practical (from a regulatory perspective). However, previous research has demonstrated that the same external exposure may result in a different internal dose [9, 10]. The use of exposure concentrations in epidemiologic studies ignores the differential pollutant doses that can be produced by heterogeneity in an individual's intake and



Fig. 1 The air pollution source-effect pathway from emissions to health effects [7]. Air pollution is modified during transport from source to the point of exposure. A fraction of inhaled the pollution can remain in the body resulting in potential adverse health effects

uptake of pollution. Thus, measurement error is likely introduced by ignoring person-to-person variability in the exposure–dose relationship, potentially resulting in bias and a loss of precision [11, 12].

The inclusion of intake, the product of exposure concentration, and minute ventilation rate, has been suggested for air pollution epidemiology and risk assessment to account for differences in the amount of air pollution people inhale (e.g., [13, 14]) and to reduce measurement error because it is one step closer to dose on the source-effect pathway. Ventilation rate is generally not measured in air pollution exposure studies (and, therefore, neither is intake). Although ventilation rate can be measured directly using a facemask with an airflow sensor, this method is not appropriate when simultaneously measuring endpoints in health studies because the necessary equipment covers the mouth and nose and so modifies the intake of air pollution. Estimates of ventilation rate may be obtained from less invasive measures, such as heart rate (e.g., [15–18]), which is correlated with ventilation rate. Low-cost personal heart-rate monitors are becoming more common as the market for wearable sensors continues to grow, devices improve, and their use becomes more ubiquitous [19]. Thus, with improved predictive models, ventilation rate can potentially be accounted for in large-scale air pollution studies and used in conjunction with ambient concentration to predict intake and reduce measurement error in air pollution studies.

Models to predict ventilation rate based on heart rate have been described previously; these models are typically calibrated using exercise testing (e.g., [16, 18]) and often do not account for sedentary behaviors. Models to estimate minute ventilation from heart rate calibrated on an individual level perform relatively well (e.g., [13]). Predictive models (i.e., those not calibrated to an individual but intended to be generalizable across individuals) perform less well. Some studies have included subject-level measurements, including sex, height, weight, and spirometry to help explain between-person variation in the relationship between heart rate and ventilation, with mixed success (e.g., [18, 20]). Measurements that capture body size such as height and weight are expected to explain some of the person-to-person variability in minute ventilation because of the higher energy demand associated with larger body sizes [21] and the correlation between body size and lung volume. Studies have also identified differences in how

male’s and female’s minute ventilation responds to exercise [21, 22]. Previous models have generally been validated using data from the training group (e.g., within-sample cross-validation techniques). Therefore, the performance (and generalizability) of these models is often uncertain when applied outside the original study population.

The objective of this study was to develop and validate models to predict ventilation rate from heart rate and other readily obtainable physiologic measurements (e.g., height and weight). More complex individual level measurements that require specialized equipment and/or clinical expertise such as lung function parameters were not considered to make the models easier to apply to larger studies prospectively and retrospectively. Such models may help reduce measurement error in epidemiologic research associated with ignoring differences in ventilation rate and, therefore, air pollution intake. Predictive ventilatory models of sufficient accuracy would help bridge the uncertainty between exposure and intake along the source-effect pathway.

Methods

Data were collected in two parts: a laboratory training study and a field validation study. The training study was used to develop candidate models for predicting ventilation rate from heart rate and other basic physiological variables. The validation study collected a new dataset under less controlled conditions to test the predictive models in a more realistic setting.

Participant recruitment

We recruited healthy, adult volunteers to study their ventilation rate and heart rate as they completed activities requiring different levels of exertion. Inclusion criteria were: age between 18 and 65 years, non-smoking, and no major health problems (no self-reported chronic conditions, body mass index below 30 kg/m², resting blood pressure below 160/100 mm Hg, and stable use of any prescription medication) and not pregnant. Participants fasted for 4 h prior to participation. The study protocol was approved by the Colorado State University Institutional Review Board; participants completed written informed consent.

Laboratory training

Thirty-six participants were recruited for the laboratory study. Participants were fitted with an Oxycon Mobile indirect calorimetry system (CareFusion Respiratory Care, CA, USA) that measured breath-to-breath ventilation rate and heart rate averaged to 5-s resolution [23]. The Oxycon

Mobile's flow (to within 1.5% difference) and gas sensors were calibrated at laboratory temperature, pressure, and humidity on each study day after a 30 min warm up period. A number of studies have examined the validity of the mask used by the Oxycon Mobile to measure ventilation rate, finding differences of <10% for the values reported here (e.g., [23–25]). Physiologically implausible heart rate data (heart rate <30 and heart rate >200), presumably due to instrument error, were removed during data analysis. Ventilation rate data fell within expected values. Before participants began activities, we measured their blood pressure (mm Hg), chest size (cm), height (cm), hip size (cm), waist size (cm), and weight (kg) according to American College of Sports Medicine (ACSM) guidelines for exercise testing and prescription [26]. They also completed a questionnaire that included age and sex. Resting heart rate was calculated for the training tests as the sitting heart rate minus five beats per minute, to bring it closer to supine heart rate which is likely at least five beats per minute lower [27].

The participants performed 9 or 11 prescribed tasks (the higher speed walking tasks were added partway through the training study because the calibrated treadmill speed of 2 mph was thought to be somewhat lower than typical walking pace), lasting 6 min each, at the Colorado State University Human Performance Laboratory. Tasks included sitting, standing, walking at 3.2 and/or 4.8 kilometers per hour (km/h), walking with a 4.8 kg load split between bags held in each hand at 3.2 and/or 4.8 km/h, sweeping, stationary cycling at 50 watts, stationary cycling at 100 watts, and shoveling sand. Participants were asked not to speak during each task and given the option to rest between tasks. The last 2 min of data for each activity were averaged and used in the predictive model development.

Predictive model development

Candidate predictive models were developed from the training data using a two-stage approach in the R statistical language (version 3.3.1, The R Foundation for Statistical Computing, details in supplementary material 2). First, we identified variable transformations that improve the model fit. Second, we employed a variable selection procedure to test the inclusion of the transformed variables identified in the first stage and two-way interactions between those variables that improve the model fit. All models that performed above a pre-specified threshold were then validated against independent field data. Figure 2 illustrates the steps from variable selection to model validation described below.

In the first step, we used multi-fractional polynomials (MFP) to identify nonlinear relationships between variables and ventilation rate. MFP combines stepwise variable selection with polynomial transformations [28–30]. We

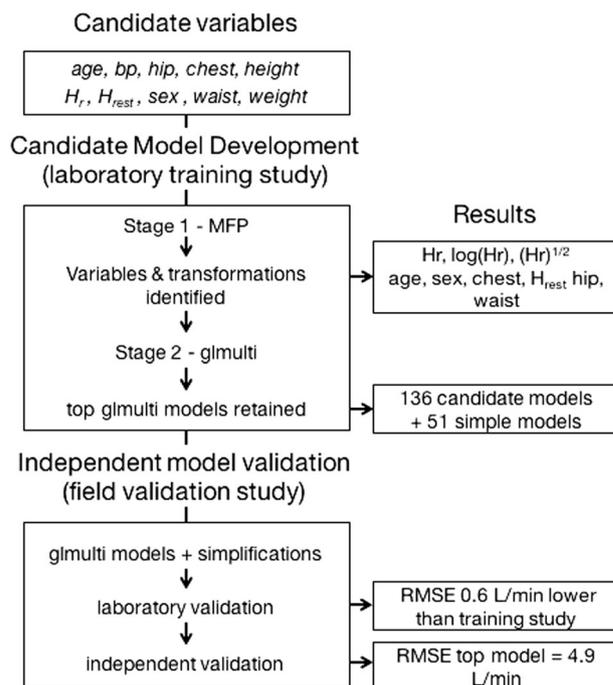


Fig. 2 Steps from variable selection to model validation. Nine variables are considered: age, blood pressure (bp), chest circumference (chest), height, heart rate (H_r), resting heart rate (H_{rest}), sex, and weight. A multi-fractional polynomial (MFP) algorithm was used to identify useful variables and their transformations. A two-way interaction search (*glmulti*) algorithm identified the best models from the MFP identified variables. Models were cross-validated using the training data and independently validated using the validation study dataset

restrict the fractional polynomials to linear combinations of two terms, with powers, -2 , -1 , \log_e , 0.5 , 1 , 2 , or 3 to limit the chance of overfitting and maintain a more interpretable model [31]. We used a bootstrapping procedure ($n = 10,000$) to account for uncertainty in models selected by MFP [29]. Candidate variables and their transformations that were selected by MFP in more than 15% (chosen to deliver a manageable number of models for analysis) of the bootstrap runs were retained for further consideration.

The second stage of the model building approach performs an exhaustive search of the candidate variables and their transformations identified with MFP including searching all two-way interactions between variables using the R package *glmulti* [32]. A participant-specific random effect was included in the models to account for the same individual performing different activities. We selected all models with an Akaike information criterion (AIC) within two of the best fitting model (for each set of candidate variables) as the candidate models retained for further testing [33, 34]. We restricted the models to contain at most one size variable (chest, height, hip, waist, or weight) and conducted a separate iteration of the *glmulti* algorithm for each variable to reduce the computational burden. This

variable reduction step is also justified by the correlation between the size variables and small differences in MFP model performance between models with one or multiple size variables.

The predictive ability of each candidate model was tested using leave-one-out cross validation [35] on the training dataset for comparison to the independent validation. Each model was fitted with one subject's training data removed at a time. Root mean square error (RMSE) for predicting the removed observations was calculated for each person on each task and averaged to obtain the mean RMSE for each task and the overall mean RMSE. Cross validation is commonly used to test the performance of predictive ventilatory models (e.g., [16, 36–38]). We chose leave-one-out cross validation because this technique is widely reported with these types of models and because it is suitable for smaller datasets ([39], section: 7.10). We also compare and contrast the cross-validation approach to an independent validation (i.e., validation against an independent dataset that was not used to for model development) in an effort to assess performance of the models and the cross-validation approach, more generally. Additional details on the predictive model development are provided in supplementary material.

Simplified models

Model over-fitting is an important concern when searching using statistical methods to identify the best model. The use of AIC (which penalizes the addition of model terms), hold-out validation, and independent validation is designed to minimize the chance of over-fitting. Additionally, we tested a set of simplified models with no interaction terms to test for over-fitting in our model selection. All combinations of the MFP-identified variables would be tested. See supplementary material for a list of the simplified models tested.

Basic model

A basic single-level linear model with the form:

$$V_e = \beta_0 + \beta_1 H_r + \varepsilon \quad (1)$$

where H_r as the only independent variable was also run. The basic model provides a reference to gauge improvements gained by the addition of variables. The basic model could also be identified by the variable selection procedure if its performance were good enough.

Independent model validation in a field study

A second dataset was collected to validate the predictive performance of the candidate models identified from the

training dataset. The validation study recruited 26 participants to perform a series of tasks at their own pace in and around the Colorado State University campus. These tasks involved walking (~0.8 km), riding a bus (~0.8 km), a seated task (a 6 min, computer-based card game), an active task (~10 min, sorting and weighing colored balls), and cycling between two locations (~1.6 km). A member of the study team accompanied participants to provide instructions and answer questions as needed. The entire series of tasks was designed to take around 1 h to complete. Ventilation rate, heart rate and physiological data were collected in the same manner as the training study. Heart and ventilation rates were aggregated to a 30 s running average for the purpose of validation.

Ventilation rate was predicted using each of the candidate models identified from the laboratory training data as described in section "Predictive Model Development" as well as the simplified and basic heart rate models (Sections "Simplified models" and "Basic Model", respectively). Task-specific and overall RMSE (as described above) were calculated to assess model performance. Resting heart rate was calculated as the last 2 min of the sitting heart rate task minus 5 beats per minute.

Exposure assessment

Exposure to particle number (PN) was measured for a subset of participants ($n = 11$) from the validation study using a diffusion classifier (Disc Mini, Matter Aerosol AG, Switzerland). PN data were used to calculate the time-weighted average concentration (TWA), the time-weighted inhalation rate (i.e., number of particles inhaled per minute), and the intake (total number of particles inhaled) for each task and participant. The exposure metrics (inhaled PN versus PN concentration) were compared to each other using linear models within and between tasks. The relationship between inhaled PN and PN concentration is then used to assess the potential for exposure misclassification when concentration is used as a proxy for pollution dose. The predicted PN intake was compared to the measured PN intake across all tasks, again using a linear model. The relationship between measured and predicted intake is used to infer the usefulness of the predictive ventilatory models.

Results

Study population

Thirty-five out of thirty-six participants completed the laboratory training study, one participant could not complete all the activities and was removed from the analysis.

Twenty-six participants completed the validation study and heart rate data were successfully collected for twenty-two of the participants (H_r was not measured for four of the validation study participants due to malfunctioning heart rate leads). Less than 0.5% of the heart rate data were screened out of the analysis as a result of the heart rate range criteria (30 to 200 bpm). The participant characteristics are presented in Table 1.

Laboratory training

Laboratory results

The (arithmetic) mean ventilation rate stratified by activity (Table 2) ranged from 9 to 45 L/min. Higher between-participant variability in ventilation rate was observed for the sweeping and shoveling tasks, which were performed at each participant's own pace. The active tasks (walking and cycling) produced similar mean ventilation rates in the training and validation studies. The sitting tasks in the validation (sitting and bus ride) produced more variable ventilation rates with a higher mean, as some participant's

Table 1 Participant characteristics for the training and validation datasets

Variable	Range	Training N (%)	Validation N (%)
Age, years	18–24	3 (9%)	7 (27%)
	25–34	8 (23%)	10 (38%)
	35–44	7 (20%)	2 (8%)
	45–54	6 (17%)	3 (12%)
	55–65	11 (31%)	4 (15%)
Chest, cm	60–70	1 (3%)	3 (12%)
	70–80	13 (37%)	8 (31%)
	80–90	12 (34%)	9 (35%)
	90–100	9 (26%)	5 (14%)
	100–110	0 (0%)	1 (4%)
Weight, kg	40–50	2 (6%)	2 (8%)
	50–60	5 (14%)	5 (19%)
	60–70	15 (43%)	8 (31%)
	70–80	7 (20%)	5 (19%)
	80–90	6 (17%)	5 (19%)
	90–105	0 (0%)	1 (4%)
Sex	Female	19 (54%)	15 (58%)
	Male	16 (46%)	11 (42%)
Resting heart rate, bpm	30–50	2 (6%)	5 (19%)
	50–60	14 (40%)	5 (19%)
	60–70	16 (46%)	2 (8%)
	70–80	2 (6%)	8 (31%)
	80–100	1 (3%)	2 (8%)
	Missing	0 (0%)	4 (15%)

Table 2 Mean participant ventilation rates (L/min) and standard deviations (s.d.) stratified by activity

Activity	Mean (s.d.) training $N = 35$	Mean (s.d.) validation $N = 26$
Sitting	8.8 (1.6)	15.1 (5.1)
Bus ride	—	13.9 (5.6)
Standing still	9.4 (1.8)	—
Sorting task	—	17.6 (4.4)
Walking (2 mph)	19.5 (3.0)	—
Loaded walk (2 mph)	22.0 (2.9)	—
Walking (3 mph)	25.4 (2.7)	—
Loaded walk (3 mph)	28.3 (3.7)	—
Walking	—	27.7 (5.8)
Cycling (50 W)	30.3 (4.3)	—
Cycling (100 W)	44.9 (7.1)	—
Cycling	—	40.1 (10.7)
Sweeping	31.5 (7.1)	—
Shoveling	37.7 (8.9)	—

ventilation remained higher after completing a more active task beforehand.

Model building

The bootstrap MFP analysis showed consistent selection of variables over different iterations (Eq. 2) with H_r was selected 100% of the time, 54% of the time with the square root transformation and 24% with a logarithmic transformation. H_{rest} was selected 97% of the time, 77% of the time a transformation to the power of one (i.e., no transformation) was selected. Age was selected 83% of the time, suggested transformations varied, the most frequent a power one transformation that was selected 36% of the time. The categorical sex variable was selected in 78% of the runs. At least one size variable (chest, height, hip, waist or weight) appeared 92% of the time. A single size variable was selected in 36% (chest 16%, height 3%, hip 6%, waist 6%, and weight 5%) of the 10,000 bootstrap samples. Variable selection frequency and common power transformations from the bootstrap analysis are shown in Supplementary Material. Equation (2) shows the model selected by the MFP algorithm prior to the bootstrap analysis. Cross-validation of Eq. (2) results in a mean RMSE of 5.3 L/min.

$$V_e = \beta_0 + \beta_1 \sqrt{H_r} + \beta_2 \text{age} + \beta_3 \text{chest} + \beta_4 H_{rest} + \beta_5 \text{sex} + \epsilon \quad (2)$$

Each *glmulti* search was repeated with three transformations of heart rate: untransformed, square root transformed, and log transformed. The *glmulti* analysis produced

136 unique candidate models with an AIC within two of the best model (for each set of candidate variables). Cross-validation of the candidate *glmulti* models resulted in RMSE of 4.9 to 5.4 L/min, slightly higher than with the full data set (4.6 to 5.2 L/min).

The *glmulti* analysis identified potential interaction terms between sex and each of the other candidate variables. The H_r , H_{rest} , sex, and sex- H_r variables were retained by all the *glmulti* candidate models with AIC within two of the best models. Interaction terms for sex- H_{rest} and sex-age were included in 50% and 43% of the models, respectively. A size variable was included in 88% of the *glmulti* candidate models. A size-sex interaction term was included in 44% of the *glmulti* candidate models.

Validation

All 136 candidate models identified in the laboratory test were evaluated for predictive performance in the validation study. The best performing model had a mean participant weighted RMSE of 4.9 (s.d. = 1.21) L/min over the five activity categories. The best performing model in the validation study was:

$$V_e = \beta_0 + \beta_1 \text{sex} + \beta_2 H_r + \beta_3 \text{age} + \beta_4 H_{rest} + \beta_5 \text{hip} + \beta_6 \text{sex} \times H_r + \beta_7 \text{sex} \times \text{age} + \beta_8 \text{sex} \times H_{rest} + \beta_9 \text{sex} \times \text{hip} + \varepsilon, \quad (3)$$

where $\beta_0 = 0.99$, $\beta_1 = -27.41$, $\beta_2 = 50.24$, $\beta_3 = 15.73$, $\beta_4 = -43.65$, $\beta_5 = -7.02$, $\beta_6 = 23.02$, $\beta_7 = -10.34$, $\beta_8 = -26.21$, and $\beta_9 = 38.78$. The full list of candidate models and their performance is provided in supplementary material.

The best performing models (RMSE 4.9 to 5.2 L/min) contained the untransformed H_r variable, followed closely by models with the square root H_r transform (RMSE 5.2 to 5.4 L/min). The best log H_r transformed model had an RMSE of 5.7 L/min. The sex variable was contained in all the top 50 models (RMSE 4.9 to 5.7 L/min). The age variable was contained in all but two of the top 50 performing models. No single size variable consistently outperformed any other size variable. The sex \times H_{rest} interaction appeared in all of the top 35 models (max RMSE 5.5 L/min). The sex \times H_r interaction appeared in all of the top 16 models (max RMSE 5.2 L/min). The sex \times age interaction resulted in some minor improvements when added (<0.1 L/min RMSE).

The validated performance of the 136 candidate models (and their simplifications) is shown in Fig. 3 and compared to their performance under cross-validation of the original training dataset. The validation RMSE tends to be higher than the training RMSE. The color coding in Fig. 3 illustrates how certain variables and variable combinations

appear consistently in the top performing models. The basic heart-rate only model (highlighted in Fig. 3) produced an RMSE of 7.9 L/min. The top-performing model in the training cross-validation (RMSE = 4.9 L/min) performed worse in the validation (RMSE = 5.9 L/min) and is also highlighted in Fig. 3.

The top-performing model (Eq. 3) was examined as a function of each task conducted during the validation experiment. The RMSE for Eq. 3 (averaged by participant) was consistent from task to task (~5 L/min), except for cycling where it increased to 7.5 L/min.

Basic model results

The basic heart rate only model (Eq. 1), used to assess the value of additional variables, resulted in a mean RMSE of 7.4 liters per minute (L/min) across all activities. Cross-validation of the heart-rate-only model resulted in a mean participant-weighted RMSE of 7.6 L/min (s.d. = 3.8), only slightly higher than the 7.4 L/min RMSE when all data were included. The candidate models with additional variables improved upon the heart rate only model by 2.2 to 2.7 L/min in terms of the cross-validated RMSE.

Analysis of exposure versus intake

Breathing zone particle number (PN) concentration was measured for 11 participants (one participant's data were removed due to an instrument malfunction). Exposure (PN concentration) was compared to intake (PN inhaled) within task, illustrated in Fig. 4. Within task there is generally a strong linear relationship between PN concentration and PN inhalation (R^2 0.73 to 0.97). The relationship between time-weighted average exposure and intake was also explored between tasks (Fig. 5). The relationship between exposure concentration and intake (Fig. 5a) was only moderately linear across multiple tasks (linear model $R^2 = 0.53$). Predicted intake (using the top-performing model) compared well to measured intake (Fig. 5b). The predicted versus measured intake relationship has a higher R^2 (0.93) than the exposure versus intake relationship. The measured ventilation rates and exposure levels are provided in supplementary material.

Discussion

Accurate and generalizable models that predict personal ventilation rates may help reduce measurement error in epidemiological studies by bridging the gap between air pollution exposure and intake. Personal heart rate can be used to predict ventilation rate for the purpose of estimating air pollution intake. In addition to heart rate, the models

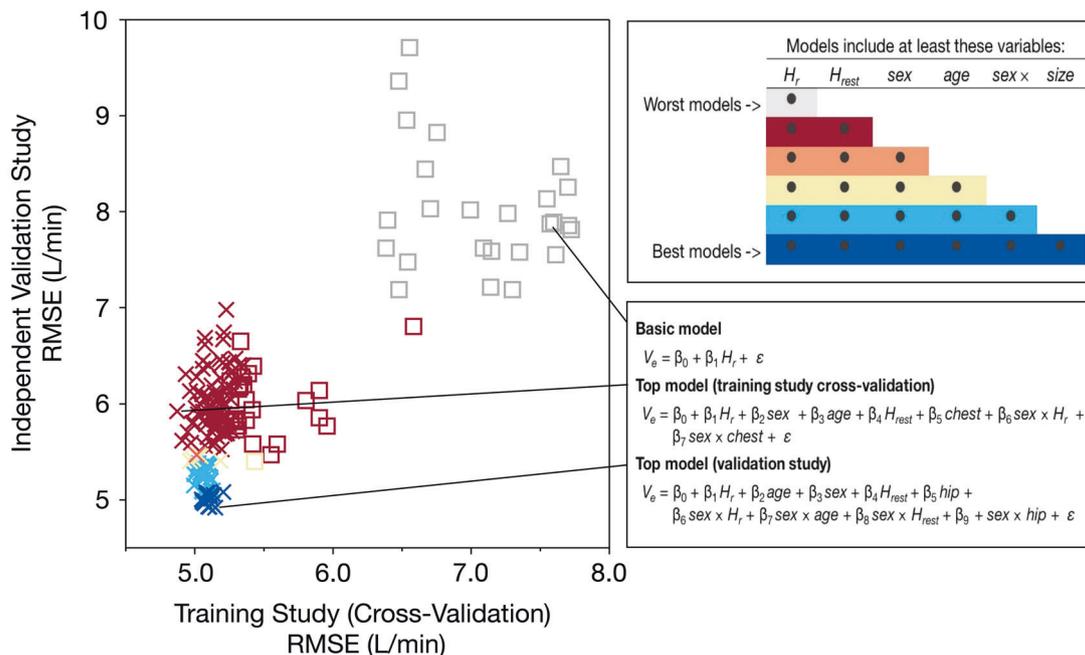
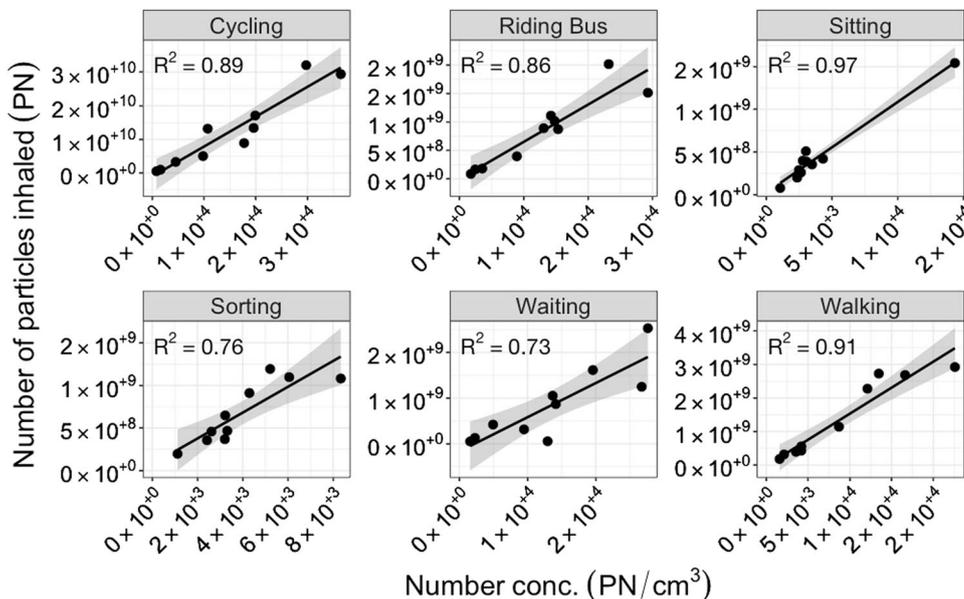


Fig. 3 Root mean square error (RMSE) of the 136 candidate (x) and 51 simplified (no interactions between variables - □) models under cross-validation (training study) and the independent validation study.

The color scale shows the variables (where heart rate = H_r , resting heart rate = H_{rest} , sex interaction terms = sex x, and size is either chest, height, hip, waist, or weight) models have in common

Fig. 4 Number concentration versus number of particles inhaled by task, with linear regression (black line) and 95% confidence interval (gray shading)



developed here used variables that may be feasibly collected in many epidemiologic studies.

The top-performing model produced a task-average RMSE of 4.9 L/min in the validation study. The candidate models have similar errors under laboratory training cross-validation (4.9 to 5.4 L/min) but a larger range of errors (4.9 to 7.0 L/min) in the validation study. The difference in model performance between training and validation study datasets suggests that some over-fitting is

occurring. Our sample size was similar to previous studies, suggesting that over-fitting could be a problem in previous studies that employ validation using the training dataset.

A novel aspect of our work is the inclusion of a resting heart rate variable, which was selected in every candidate model. The resting heart rate variable may add value to a predictive model because it helps account for the person-to-person variability in the heart rate—ventilation rate relationship—akin to the individually calibrated models. In

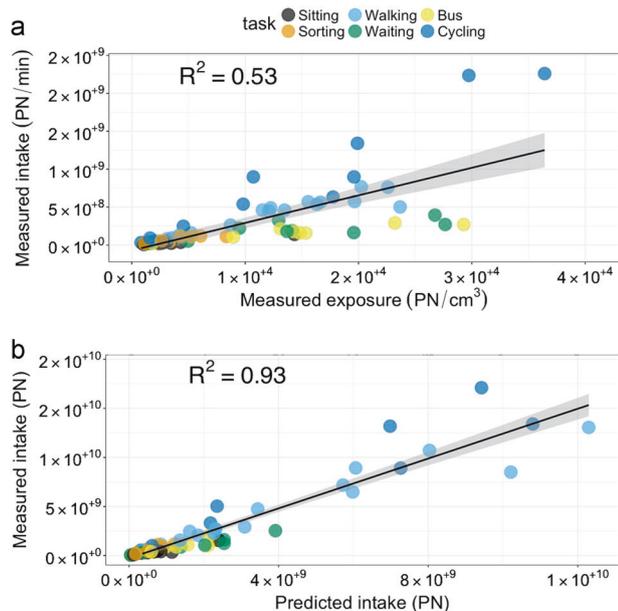


Fig. 5 **a** Measured personal exposure concentration versus measured intake. **b** Predicted intake versus measured intake. Black lines show linear model fit with 95% confidence interval (gray shading)

this study, we defined resting heart rate as the sitting heart rate minus a constant of 5 beats per minute. Further work is needed to investigate how best to determine resting heart rate from continuous heart rate data measured during epidemiologic research, data collected during sleep should be a reliable method for example.

Our examination of the top models identified combinations of variables associated with improved performance. The age and sex variables were present in all models with RMSE less than ~ 5.5 L/min. Additionally, the best models with RMSE less than ~ 5.0 L/min contained a size and sex $\times H_r$ and or sex $\times H_{rest}$ interaction variables. Inclusion of these interaction terms, however, provided only marginal improvements to model performance (on the order of 10% improvement to RMSE).

Here we are not attempting to derive a mechanistic understanding of the heart rate–ventilation rate relationship, however it is worth noting briefly because we might expect models that are physiologically consistent to be more robust. Differences in ventilation patterns by sex have been observed [21, 22] the inclusion of a sex term and interactions between sex and other variables is consistent with these findings. Heart rate dynamic range is known to decrease with age, however all else being equal the bodies ventilatory requirements do not, thus it is plausible that the heart rate–ventilation rate relationship is modified by age. Similarly, body size will affect energy demand and thus oxygen requirement, thus it is plausible that the heart rate–ventilation rate relationship is modified by a size variable.

A number of the simplified models performed as well in the independent validation as the more complex models, another reason to suggest the laboratory training cross-validation is under-estimating the model error. There are groups of models that do outperform the best simple model (RMSE < 5.4 L/min), suggesting with careful variable selection and validation more complex models can deliver reductions in error. However, some of the complex models perform less well in the validation study, demonstrating the importance of model validation in a realistic setting.

An important distinction of this work is that the models are designed to predict ventilation rate from heart rate for different activities performed at low and moderate levels of exertion. Therefore, the linear ventilation–heart rate relationship in the top-performing model (Eq. 3) is quite different from the exponential relationship in models designed around progressive exercise testing. The models developed here are designed to be applied to everyday tasks and may produce larger errors for more extreme exercise activities. The models developed here are geared towards studies that seek to determine the health effects of air pollution across typical daily activities and within common microenvironments where individuals spend the majority of their time. The models tested here are unlikely to be suitable for higher exertion activities (e.g., sports) because the heart rate–ventilation rate relationship is non-linear across low to high heart rates (e.g., [18]).

Ease of use in epidemiological studies was central to the model design. Our models require heart rate data (which is becoming easier to collect) and other commonly collected information. This approach will enable ventilation rate to be predicted in larger studies with little additional burden. The usefulness of predictive ventilatory models for epidemiologic studies of air pollution will depend on whether they are able to reduce error in the exposure–response estimates. Investigators should consider if the modeled ventilation rate measurement error is smaller than the misclassification error implicit in not considering intake, as well as the type of error from each source and the implications for the specific epidemiologic study design. Work would also be required to validate or adapt these models developed using healthy populations for studies of unhealthy groups such as people with lung diseases.

Ventilation rate can vary both within individuals and between individuals, typically by up to 4 L/min within and by up to a factor of four for between everyday tasks [40, 41]. When ventilation rate is ignored in exposure assessment, there is an implicit assumption that it is constant across the population, resulting in Berksonian error [42, 43]. This variability, often unaccounted for in epidemiological studies, may reduce our ability to detect relationships between air pollution and health outcomes.

Our exploratory exposure analysis suggests that between tasks of different characteristic ventilation rate a predictive ventilatory model (RMSE = 4.9 L/min) may give a much better estimate of inhaled pollution (measured versus modeled intake $R^2 = 0.93$) than time-weighted-average exposure (measured exposure concentration versus measured intake $R^2 = 0.53$). For example, in studies that compare air pollution while driving to cycling you would expect to see substantial exposure misclassification if intake was not considered [44]. If task is associated with ventilation rate then the ability to determine task in study populations could be useful. If task-specific models were developed they might be more precise. For large studies it would be useful to be able to classify common activities using wearable sensors (e.g., [45]) eliminating the need for self-reported time-activity surveys. Within task there is a stronger linear relationship between measured intake and exposure (R^2 0.73 to 0.97) than between tasks, suggesting that predictive ventilatory models are less likely to be useful for tasks associated with more heterogeneous ventilation rates.

In conclusion, we developed and validated a set of models designed to predict ventilation rate from heart rate for everyday activities. We showed that cross-validation approaches, which rely on the same data used to train models, may over-estimate predictive ability. We found the best models contained a resting heart rate variable and specific combinations of variables describing subject's size, age, and sex also improved performance. Finally, we compared exposure data against measured and predicted intake data to demonstrate how their relationships may vary between micro-environments. Future work could focus on exploring the relationships between exposure, inhaled dose and health effects.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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