## SUPPLEMENTARY APPENDIX

**Mehrdad Arjomandi, et al.** Air Trapping Identifies an At-risk Group in Persons with Prolonged Secondhand Tobacco Smoke Exposure but without Overt Airflow Obstruction

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# 1. Author Contributions

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## 3. Detailed Methods

Study Overview

This was an observational, cross-sectional analysis of findings in a larger cohort of subjects with a range of occupational SHS exposure.[1,2] We used data from this cohort to examine the associations among airflow obstruction indices ($FEV_1$/FVC, $FEV_1$, $FEF_{25\text{-}75}$, and $FEF_{75}$), air trapping (RV/TLC and radiographic gas trapping), dynamic hyperinflation (defined as a progressive increase in either fraction of tidal volume that is flow-limited on expiration [percent of expiratory flow limitation, %EFL] or end-expiratory lung volume [EELV] during exercise), respiratory symptoms, and exercise capacity (maximum oxygen uptake [$VO_{2Max}$] and maximum work achieved [$Watts_{Max}$]).

Study Population

Between July 2007 and July 2015, we recruited US airline flight crewmembers (flight attendants and pilots) as part of an investigation of the potential adverse health effects of the cabin environment on those employed before and after a ban on smoking in commercial aircraft was introduced in the US. Flight crewmembers were eligible to participate in the study if they had worked for at least five years in commercial aircraft. A referent group was recruited that included "sea-level" subjects who lived in San Francisco Bay area and who had never been employed as flight crewmembers. All subjects were nonsmokers defined by no smoking for at least 20 years and a cumulative history of <20 pack-years smoking. Overall, 440 subjects were enrolled in the larger cohort study, of whom 49 did not undergo plethysmography and were not eligible for the current analysis. Otherwise eligible subjects were excluded if they manifested impaired spirometry (abnormal $FEV_1/FVC$ or $FEV_1$ by lower limit of normal criterion) (n=61 [15.6%]), BMI ≥30 $kg/m^2$ (n=21 [5.4%]), had no SHS exposure (N=26 [6.6%]), or reported any known diagnosis of cardiac, pulmonary, autoimmune, or collagen vascular diseases, or if they had received systemic chemotherapy and radiation therapy to the chest area that could have adversely affected their lung function (n=27 [6.9%]). Overall, 256 eligible subjects with preserved spirometry (normal $FEV_1/FVC$ and $FEV_1$ at or above the lower limit of normal) were included in the study. A subgroup of the subjects (n=179 out of 256; 70.0%) underwent cardiopulmonary exercise testing. To further assess dynamic hyperinflation, a subset of these (n=32) also underwent inspiratory capacity and maximal expiratory flow measurements at progressive levels of exercise for determination of %EFL and EELV. To measure radiographic gas trapping, selected subjects (n=23) who completed exercise testing underwent CT chest imaging of their lungs using a low radiation protocol. Subject flow is shown diagrammatically in Figure 1.

The UCSF Institutional Review Board (IRB) and the San Francisco VA Medical Center Committee on Research and Development approved study protocols. Written IRB-approved informed consent and Health Insurance Portability and Accountability Act (HIPAA) were obtained from all study participants. Subjects received monetary compensation for their participation in the study.

## SHS Exposure Characterization

Secondhand smoke exposure was characterized by an exposure questionnaire that was developed by our UCSF Flight Attendant Medical Research Institute (FAMRI) Center of Excellence,[3] and modified to acquire information on airline-related occupational history, as described previously.[1,2] Briefly, this included employer airlines, duration of employment, and flight routes (domestic vs. international) with quantification of "cabin SHS exposure" as the number of years of employment before the smoking ban, the period during which the flight crew were exposed to SHS in the aircraft cabin. Other possible sources of exposure to SHS (non-cabin SHS exposure) were also explored by questioning subjects about their non-cabin SHS exposure in additional settings, as described previously.[4]

## Pulmonary Function Testing

Routine pulmonary function tests were performed in the seated position using a model Vmax 229 CareFusion (CareFusion Corp., Yorba Linda, CA) and nSpire body plethysmograph (nSpire Health Inc., Longmont, CO). This included measurement of the low-volume curve; spirometry[5]; lung volume by single breath dilution[6,7] and plethysmography[8]; airway resistance during panting at functional residual capacity (FRC)[9,10]; and single breath carbon monoxide diffusing capacity[11]. Hyperinflation and air trapping, which is inferred from an increase in residual volume (RV), was quantified using RV to total lung capacity (TLC) ratio (RV/TLC). Pulmonary function studies were conducted according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines[12-17]. Subjects did not undergo bronchodilator administration.

Measures of pulmonary function at rest and cardiac and respiratory responses to exercise recorded and percent predicted of normal values were calculated using Crapo predicted formulas[18-20]. Lower and upper limits of normal values for $FEV_1/FVC$, $FEV_1$, and FVC were calculated using Crapo predicted formulas[19,20].

Cardiopulmonary Exercise Testing

Subjects performed physician-supervised, symptom-limited, progressively increasing exercise tests in the supine position on an electromagnetically braked, supine cycle ergometer (Medical Positioning Inc. Kansas City, MO). Subjects were encouraged to give their best effort, and during testing, were encouraged to continue exercise until a $VO_2$ plateau effect on a breath-to-breath analysis of oxygen consumption was visually observed; however, they were advised that they could stop voluntarily at any time they believed they could not continue. We continuously monitored heart rate (HR), blood pressure (BP), electrocardiogram (ECG), and breath-by-breath gas exchange.

The protocol consisted of 3-min rest, 1-min unloaded (freewheeling) cycling at 60 rpm, followed by increasing work rate of 20 to 40 Watts at 2-minute intervals to a maximum tolerated, and 5-min of recovery. Twelve lead ECGs were monitored continuously; ECGs and blood pressure (measured manually by a physician with a cuff) were recorded every 2 min. Oxyhemoglobin saturation ($O_2$sat), determined by pulse oximetry, was recorded continuously.

Minute ventilation ($V_E$), oxygen uptake ($VO_2$) and carbon dioxide output ($VCO_2$) were measured breath-by-breath with an open-circuit metabolic cart (model Vmax 229, CareFusion, Yorba Linda, CA). The volumes of the flow meter, mouthpiece, and filter (70 mL x breathing frequency) were subtracted from $V_E$ for the $V_E/VCO_2$ calculations. Anaerobic threshold (AT) was determined by the V-slope method[21,22]. Immediately before all tests, the gas analyzers were calibrated using reference gases of known concentrations and the ventilometer was calibrated using a 3-liter syringe (Hans Rudolph, Kansas, MO). The metabolic system was verified using four trained technicians who provided monthly exercise values as biological standards for the Laboratory.

## Expiratory Flow Limitation and End Expiratory Lung Volume Measurements during Exercise

To determine whether dynamic hyperinflation contributed to the level of maximum exercise achieved, selected participants who had previously completed exercise testing were invited to undergo %EFL and EELV measurements with progressive exercise. These underwent tidal volume ($V_T$), inspiratory capacity (IC), and maximal expiratory flow (MEF) measurements in seated position at increasing work rates corresponding to 20%, 40%, and 80% of the $VO_{2Max}$ attained during the maximum effort exercise testing as described by O'Donnell et al.[23,24] Measurements of IC and MEF were made three times at each work rate while recording tidal flow-volume loops to assess for evidence of expiratory flow limitation. The volume of the tidal breath that is flow-limited on expiration ($V_{FL}$) was measured on flow-volume loop graphics using ImageJ (version 1.44, NIH, Bethesda, MD, USA) and used to calculate %EFL according to formula $[(V_{FL}/V_T)*100]$ at each work rate. End expiratory lung volume (EELV) and RV (TLC-IC) were similarly calculated using ImageJ at each work rate.

## Computerized Tomography (CT) Scans of Chest

All participants who completed exercise testing were invited to undergo CT imaging of the lungs. Two low-dose thoracic CT scans were completed one at maximum inspiration (TLC) and the second at maximum expiration (RV). Examinations were performed in the supine position from the apex to the base of the lungs during breath-holding at TLC and RV using a dedicated General Electric LightSpeed Multi (64)-detector CT scanner. Images were non-gated and no intravenous contrast was used.

Technical Guidelines for Computerized Tomography (CT) Scan of Chest

Technical guidelines for thoracic CT image data acquisition included volumetric spiral studies performed through the entire chest at full inspiration with the breathing instruction: "take a deep breath in until you feel your lungs are completely full, in the same way you do in the pulmonary function laboratory." Volumetric spiral studies were performed through the entire chest at end expiration with the breathing instruction: "take a deep breath in until you feel your lungs are completely full, then blow all the air out until your lungs are completely empty and then hold your breath." The setting was 120 kVp, 25-45 "effective" mAs, 0.5 sec rotation time, 64x0.6 mm collimation, pitch of 1.5. The sample acquisition and reconstructions were done for overlapped thin (1 mm thickness and spacing, B50f reconstruction filter, and DFOV=35 cm).

Scoring, Data Processing, Analysis of CT Scan Images, and Quality Assessment

Radiographic lung density measurements were performed using a widely accepted "density mask" (DM) technique[25] at TLC and RV by computing the percent of voxels, the three-dimensional pixel which is an index of density, below a particular Hounsfield Unit (HU) threshold (-950 HU on 1 mm sections at TLC scan) for emphysema (low attenuation area <-950 HU [$LAA_{insp<-950}$]) or within a specific range (between -860 and -950 HU on 1 mm sections at RV scan) for determination of mosaic attenuation reflecting gas trapping (low attenuation area between -860 and -950 HU [$LAA_{exp-860to-950}$]) as described previously.[26-30] Low attenuation lung density areas below -950 Hu on 1 mm sections at TLC scans ($LAA_{insp<-950}$) were also measured to examine presence of emphysema. A voxel threshold of ≥5% was used to define presence of gas trapping or emphysema on respective measurements. Quantitative analysis of the images consisted of (1) volume measurement, and (2) DM score measurement using a previously validated semi-automated computer software (Pulmo-CMS; Medis Specials, Leiden, the Netherlands)[31].

## Respiratory Symptom Scoring

Respiratory symptoms were assessed using the modified Medical Research Council Dyspnea Scale (mMRC) and an internal questionnaire that elicited symptoms of dyspnea, cough, and subjects' perception of a decreased level of exertion compared to peers over the year preceding enrollment. A dichotomous indicator of respiratory symptoms was defined by the report of at least one respiratory symptom.

## Data Management and Analysis

We examined correlations among airflow indices ($FEV_1/FVC$ and $FEV_1$) and air trapping (RV/TLC) using the Pearson correlation test. To control for age, height, and sex covariates, we examined partial and semi-partial correlations. Linear regression or logistic regression analysis was used to examine the associations among lung function indices (airflow or air trapping) or radiographic gas trapping as independent variables and respiratory symptoms or maximum observed work ($VO_{2Max}$ and $Watts_{Max}$) as the dependent variable. The rates of increase in %EFL and EELV were estimated using linear regression approach, and then used as independent variables to determine their contribution to the level of maximum exercise achieved. Models were adjusted for age, sex, height, and weight internally unless noted otherwise.

Furthermore, to assess whether association between exercise capacity ($VO_{2Max}$) and air trapping (RV/TLC) was mediated through airflow indices ($FEV_1/FVC$, $FEV_1$, $FEF_{25-75}$, or $FEF_{75}$), we performed Sobel-Goodman mediation testing in "mediator models"[32] with exercise capacity as the dependent variable, air trapping as an independent variable, and airflow indices as mediator variables, with inclusion of age, sex, height, and weight as covariates (Figure 2).

We performed receiver operating characteristic (ROC) analyses to examine the suitability of airflow indices ($FEV_1/FVC$ and $FEV_1$) and air trapping (RV/TLC) as predictors of respiratory symptoms and exercise capacity ($VO_{2Max}$). For respiratory symptoms, a binary variable of having or not having any symptoms was used in ROC analysis. For exercise capacity, a binary variable of low and high capacity was generated based on the ability to achieve the predicted $VO_{2Max}$ (≥100% predicted value) and used in ROC analysis. To obtain comparable area under the curve (AUC) values, the predictor variables were given a negative sign if they were inversely associated with the outcome variable (for example, the value of RV/TLC was made negative for its contribution to $VO_{2Max}$). The AUC from RV/TLC, $FEV_1/FVC$, $FEV_1$, and FRC (percent predicted values) were calculated with adjustment for covariates, and compared for their ability to discriminate between the binary outcomes. To construct risk groups, optimal cut-points of RV/TLC for each ROC analysis was calculated, and used to define at-risk and not at risk groups.

Data management and figure generation used R software (version 3.2.3, R Foundation for Statistical Computing, Vienna, Austria). Data analyses were conducted in Stata/IC (version 14.2, Stata Corp LP, College Station, TX, USA). The "sgmediation" and "st0155" packages in Stata were used for Sobel-Goodman mediation testing and Receiver Operating Characteristic analyses, respectively.

## 4. Supplemental Figure Legend

**Supplemental eFigure 1- Association between Air Trapping, Airflow Obstruction, and Maximum Exercise Capacity.** Three-dimensional representation of relationship between maximum oxygen uptake ($VO_{2Max}$; ml/min), RV/TLC (%), and $FEV_1$/FVC (%) (panel **A**) or $FEV_1$ (L) (panel **B**) presented in three different views. $FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume.

## 5. Supplemental Tables

**Supplemental e-Table 1- Subjects Characteristics in Subgroups Studied.**

| **Characteristics** | **Subjects with preserved spirometry (N=256)** | **Subgroup Who Performed Exercise (N=179)** | **Subgroup who performed IC with MEF measurements (N=32)** | **Subgroup who had CT measurements (N=23)** |
|---|---|---|---|---|
| Age (years) | 56.1±11.0 | 54.7±11.3 | 57.7±7.5 | 60.8±7.5 |
| Female sex [n(%)] | 232 (90.6%) | 163 (91.1%) | 32 (100%) | 23 (100%) |
| BMI ($kg/m^2$) | 23.5±2.9 | 23.5±3.0 | 23.0±2.2 | 23.9±3.3 |
| $FEV_1$ (% predicted) | 103±12 | 103±12 | 102±11 | 105±13 |
| FVC (% predicted) | 106±12 | 106±12 | 107±12 | 108±12 |
| $FEV_1$/FVC [%] | 77±4 | 77±4 | 75±4 | 76±4 |
| $FEV_1$/FVC (% predicted) | 98±5 | 98±4 | 96±4 | 98±5 |
| $FEF_{25-75}$ (% predicted) | 92±23 | 91±21 | 84±20 | 95±24 |
| $FEF_{75}$ (% predicted) | 41±16 | 43±17 | 41±17 | 43±21 |
| TLC (% predicted) | 101±10 | 101±10 | 103±11 | 99±10 |
| RV (% predicted) | 93±15 | 92±16 | 89±12 | 90±12 |

| | | | | |
|---|---|---|---|---|
| [(RV/TLC)] (%) | 34±6 | 34±6 | 33±4 | 36±6 |
| [(RV/TLC)] (% predicted) | 92±12 | 92±12 | 87±7 | 88±7 |
| SHS Exposure | | | | |
| Ever Cabin SHS Exposure [n(%)] | 161 (62.9%) | 102 (57.0%) | 17 (53.1%) | 23 (100%) |
| Cabin SHS Exposure (years) | 12.1±11.7 | 10.1±10.7 | 13.7±9.9 | 19.5±8.4 |
| Any form of non-cabin SHS exposure [n/N(%)] | 196/210 (93.3%) | 130/139 (93.5%) | 16/19 (84.2%) | 16/16 (100%) |
| Childhood home SHS exposure [n/N(%)] | 133/207 (64.3%) | 87/138 (63.0%) | 10/18 (55.6%) | 12/15 (80.0%) |
| Adult home SHS exposure [n/N(%)] | 80/207 (38.6%) | 48/138 (34.8%) | 6/18 (33.3%) | 7/15 (46.7%) |
| Non-airline occupational SHS exposure [n/N(%)] | 73/198 (36.9%) | 53/136 (38.9%) | 8/19 (42.1%) | 8/16 (50.0%) |

| | | | | |
|---|---|---|---|---|
| Other SHS Exposure [n/N(%)] | 133/193 (68.9%) | 90/130 (69.2%) | 6/16 (37.5%) | 7/15 (46.7%) |

Footnote: Demographics, lung function, and secondhand smoke (SHS) exposure status in subjects with preserved spirometry and the subgroups studied. Other SHS exposure was defined as non-aircraft cabin SHS exposure outside the work or home environment such as in recreational public places. Data are presented as mean±standard deviation or number of subjects with positive value for the variable (n) out of the total number of subjects (N) and percentage of subjects (%). Abbreviations- IC: inspiratory capacity; MEF: maximum expiratory flow; CT: computerized tomography imaging; BMI: body mass index; $FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity; $FEF_{25-75}$: maximum airflow at mid-lung volume; $FEF_{75}$: maximum airflow at low-lung volume; TLC: total lung capacity; RV: residual volume.

**Supplemental e-Table 2- Frequency of Subjects with Lung Function Outside the Limits of Normal Range.**

| | **Subjects with preserved spirometry (N=256)** | **Subgroup who performed exercise (N=179)** |
|---|---|---|
| RV/TLC >ULN | 0 (0%) | 0 (0%) |
| RV >ULN | 1 (0.4%) | 1 (0.6%) |
| TLC <LLN | 4 (1.6%) | 4 (2.2%) |
| FVC <LLN | 1 (0.4%) | 0 (0%) |
| FRC >ULN | 5 (2.1%) | 4 (2.5%) |

Footnote: Summary on frequency of subjects with lung function outside the limits of normal range was shown as number of subjects with positive value for the variable (n) and percentage of subjects (%). Abbreviations- ULN: upper limit of normal; LLN: lower limit of normal; RV: residual volume; TLC: total lung capacity; FVC: forced vital capacity; FRC: functional residual capacity.

**Supplemental e-Table 3- Correlation of RV/TLC with Airflow Indices.**

| | **Uncorrected Correlation with RV/TLC (%)** | | **Corrected Correlation with RV/TLC (%)** | |
|---|---|---|---|---|
| | **r** | **p-value** | **$r_p$** | **p-value** |
| $FEV_1$/FVC (%) | -0.34 | **<0.001** | -0.01 | 0.896 |
| $FEV_1$ (L) | -0.69 | **<0.001** | -0.37 | **<0.001** |
| $FEF_{25-75}$ (L/s) | -0.62 | **<0.001** | -0.20 | **0.001** |
| $FEF_{75}$ (L/s) | -0.59 | **<0.001** | -0.09 | 0.160 |

Footnote: Partial and semi-partial correlation coefficients were tested among airflow dices and RV/TLC controlling for age, height, weight, and sex in the cohort with preserved spirometry. N = 256. Abbreviations- r: correlation coefficient; $r_p$: Partial correlation, which is the correlation coefficient between dependent variable and the targeted independent variable assuming the other independent variables did not vary; $FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; $FEF_{25-75}$: maximum airflow at mid-lung volume; $FEF_{75}$: maximum airflow at low-lung volume.

**Supplemental e-Table 4- Association of Maximum Exercise Capacity in Watts with Air Trapping.**

| | **Change in $Watts_{Max}$ (watts)** | | |
|---|---|---|---|
| **Predictor Variable** | **$r^2$** | **PE±SEM** | **p-value** |
| RV/TLC (%) | 0.47 | -1.4±0.6 | **0.023** |
| $FEV_1/FVC$ (%) | 0.45 | -0.5±0.7 | 0.449 |
| $FEV_1$ (L) | 0.46 | 16.0±7.9 | **0.046** |
| $FEF_{25-75}$ (L/s) | 0.45 | 1.3±4.4 | 0.771 |
| $FEF_{75}$ (L/s) | 0.45 | -7.4±7.7 | 0.342 |
| TLC (L) | 0.47 | 11.8±4.7 | **0.014** |
| RV (L) | 0.45 | -0.6±8.7 | 0.943 |
| FRC (L) | 0.45 | 2.2±5.9 | 0.706 |
| Slope of $V_{FL}$ (ml/watt)* | 0.64 | -2.7±1.1 | **0.021** |
| 1% change on slope of %EFL (%/watt)* | 0.67 | -0.42±0.14 | **0.004** |
| Slope of EELV (FRC) (ml/watt)* | 0.56 | 0.6±1.9 | 0.737 |
| Slope of RV (ml/watt)* | 0.56 | 0.3±2.0 | 0.899 |
| $LAA_{exp-860to-950}$** | 0.28 | -1.2±0.5 | **0.018** |

Footnote: Association of maximum exercise capacity (maximum watts) with lung function was estimated using the regression analyses with adjustment for age, sex, height, and weight with inclusion of one lung function at a time based on the regression model: Work=$\beta_0$+$\beta_1$(age)+$\beta_2$(sex)+$\beta_3$(height)+$\beta_4$(weight)+$\beta_5$(lung function). N=179 unless otherwise noted. *N=32, **N=23. Abbreviations- $Watts_{Max}$: maximum work stage completed in watts; $FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; $FEF_{25-75}$: maximum airflow at mid-lung volume; $FEF_{75}$: maximum airflow at low-lung volume; FRC: functional residual capacity; $V_{FL}$: volume of the tidal breath that is flow limited on expiration; %EFL: percentage of expiratory flow limitation; EELV: end-expiratory lung volume; $LAA_{exp-860to-950}$: percent low attenuation area between -860 and -950 HU on RV scan representing radiographic gas trapping; PE ± SEM: Parameter Estimate ± Standard Error of Mean; $r^2$: model fit.

**Supplemental e-Table 5- Exercise Parameters of Subjects Performing Inspiratory Capacity and Maximum Expiratory Flow Measurements.**

| **Characteristics** | **Subgroup Who Underwent IC and MEF Measurements (N=32)** |
|---|---|
| Presence of EFL at baseline | 9 (28.1%) |
| Presence of increasing EFL | 21 (65.6%) |
| %EFL at baseline | 9.9±19.0 |
| Slope of %EFL (%/watt) | 0.22±0.29 |
| $V_{FL}$ (mL) at baseline | 130±248 |
| Slope of $V_{FL}$ (mL/watt) | 4.5±4.0 |
| EELV(FRC) at baseline (L) | 2.7±0.6 |
| Slope of EELV(FRC) (mL/watt) | -1.7±2.4 |
| RV at baseline (L) | 2.0±0.4 |
| Slope of RV (mL/watt) | 1.6±2.4 |

Footnote: Cardio-pulmonary measurements in subjects who underwent exercise testing. Data are presented as mean ± standard deviation. Data are presented as mean ± standard deviation or number of subjects with positive value for the variable (n) and percentage of subjects (%). Abbreviations- EFL: expiratory flow limitation; $V_{FL}$: volume of tidal breath that is flow limited during expiration; EELV: end expiratory lung volume; FRC: functional residual capacity; RV: residual volume.

**Supplemental e-Table 6- Associations of Rates of Change in Expiratory Flow Limitation and Hyperinflation Indices with Air Trapping Indices.**

| | **Slope of EFL (%/watt)** | | **Slope of $V_{FL}$ (ml/watt)** | | **Slope of EELV (FRC) (ml/watt)** | | **Slope of RV (ml/watt)** | |
|---|---|---|---|---|---|---|---|---|
| **Predictor Variable** | $r^2$ | PE ± SEM | $r^2$ | PE ± SEM | $r^2$ | PE ± SEM | $r^2$ | PE ± SEM |
| RV/TLC(%) | **0.15** | **0.05±0.02** | **0.22** | **0.59±0.28** | 0.01 | -0.26±0.19 | 0.06 | -0.07±0.19 |
| RV (L) | 0.05 | 0.31±0.23 | 0.16 | 4.02±2.97 | 0.01 | -2.53±1.95 | 0.05 | 0.20±1.90 |
| FRC (L) | 0.06 | 0.09±0.11 | 0.20 | 2.96±1.85 | **0.24** | **-2.13±0.91** | 0.21 | 0.41±1.00 |

Footnote: Associations were estimated using the regression analyses with adjustment for age, height, and weight on the regression model: Rate of change in %EFL, $V_{FL}$, EELV, or RV $=\beta_0+\beta_1(\text{age})+\beta_2(\text{height})+\beta_3(\text{weight})+\beta_4(\text{air trapping index})$. Significant relationships were presented in bold. Abbreviations- %EFL: percentage of expiratory flow limitation; $V_{FL}$: volume of the tidal breath that is flow limited on expiration; EELV: end-expiratory lung volume; RV: residual volume; TLC: total lung capacity; FRC: functional residual capacity; PE±SEM: Parameter Estimate ± Standard Error of Mean; $r^2$: model fit.

**Supplemental e-Table 7- Association of Maximum Exercise Capacity and Secondhand Tobacco Smoke (SHS) Exposure.**

| | **$Watts_{Max}$ (watts) $r^2$=0.40** | |
|---|---|---|
| **Variable** | **PE ± SEM** | **p-value** |
| Cabin SHS exposure (years) | -0.8±0.4 | **0.027** |
| Childhood home SHS exposure | -0.6±6.4 | 0.920 |
| Adult home SHS exposure | -4.0±6.8 | 0.561 |
| Non-airline occupational SHS exposure | 5.4±6.2 | 0.387 |
| Other SHS Exposure* | -1.2±6.9 | 0.866 |
| Age | -1.2±0.4 | **0.003** |
| Height | 1.0±0.6 | 0.096 |
| Weight | -0.1±0.4 | 0.876 |
| Sex | -43.7±14.7 | **0.004** |

Footnote: The association of maximum exercise capacity (maximum watts) with SHS was estimated using the regression analyses with adjustment for age, sex, height, and weight on the regression model: Work=$\beta_0+\beta_1$(age)+$\beta_2$(height)+$\beta_3$(weight)+$\beta_4$(sex)+$\beta_5$(Cabin SHS)+$\beta_6$(Non-cabin SHS). SHS exposures were included as dichotomous variable except for cabin SHS exposure. *Other SHS exposure was defined as non-aircraft cabin SHS exposure outside the work or home environment such as in recreational public places. N=127. Abbreviations- $Watts_{Max}$: maximum work stage completed in watts; PE±SEM: Parameter Estimate ± Standard Error of Mean; $r^2$: model fit.

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