Published in final edited form as:

Lung. 2018 June ; 196(3): 277–284. doi:10.1007/s00408-018-0109-7.

Patterns of body composition relating to chronic respiratory diseases among adults in four resource-poor settings in Peru

Grace Trompeter¹, Matthew R Grigsby¹, Catherine H Miele¹, Robert A Wise¹, Robert H Gilman², J Jaime Miranda^{3,4}, Antonio Bernabe-Ortiz³, William Checkley^{1,2}, CRONICAS Cohort Study

¹Division of Pulmonary and Critical Care, Johns Hopkins University School of Medicine, Baltimore, USA

²Program in Global Disease Epidemiology and Control, Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, USA

³CRONICAS Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru

⁴Department of Medicine, School of Medicine, Universidad Peruana Cayetano Heredia, Lima, Peru

Abstract

Purpose—Body composition is known to influence the development and progression of chronic respiratory diseases (CRDs). We sought to characterize the unique anthropometric phenotypes that present with asthma, chronic obstructive pulmonary disease (COPD), and chronic bronchitis across four distinct settings in Peru.

Methods—We collected sociodemographic, clinical history, and spirometry data from 2,959 participants from Lima, Tumbes, and rural and urban Puno. We compared the prevalence of CRDs among different study sites and described disease phenotypes. We used single and multivariable linear regression to model the influence of CRD status on various descriptors of body composition.

Results—Overall prevalence of CRDs varied across sites with the highest prevalence of asthma in Lima (14.5%) and the highest prevalence of COPD in rural Puno (9.9%). Measures of body composition also varied across sites, with highest mean body mass index (BMI) in Lima (28.4 kg/m²) and the lowest mean BMI in rural Puno (25.2 kg/m²). Participants with COPD had the lowest mean fat mass index (10.5 kg/m²) and waist circumference (88.3 cm), whereas participants with asthma had the highest mean fat mass index (14.5 kg/m²), and waist circumference (94.8 cm). In multivariable analysis, participants with COPD had a lower waist circumference (adjusted mean −2.97 cm, 95%CI −4.62 to −1.32) when compared to non-CRD participants.

Conclusions—Our findings provide evidence that asthma and chronic bronchitis are more likely to be associated with obesity and higher fat mass, while COPD is associated with being underweight and having less lean mass.

INTRODUCTION

Chronic respiratory illness is a leading cause of disease burden in low- and middle-income countries (LMICs). Disease presentations range from reversible airway conditions such as asthma, to irreversible conditions commonly seen in chronic obstructive pulmonary disease (COPD) [1]. Combined, asthma, COPD, and chronic bronchitis affect more than 700 million people worldwide, with the majority of asthma and COPD-related deaths occurring in LMICs [2–5]. Both environmental and genetic risk factors have been shown to be associated with chronic respiratory diseases (CRDs). Body composition is one factor known to influence the development of CRDs with specific illnesses presenting with unique anthropometric phenotypes. More recently, these anthropometric phenotypes have been useful in predicting disease progression and prognosis [6]. As rates of overweight and obesity continue to rise worldwide, understanding the role body habitus plays in various CRDs is critical to informing disease prevention and treatment.

There is much evidence showing a relationship between asthma and obesity, especially in women [7–10]. Increased body mass index (BMI) is a known risk factor for the development of asthma as well as chronic bronchitis in adults [11]. Similarly, weight loss and weight-loss maintenance have been shown to improve asthma symptoms [12].

In contrast, COPD has long been associated with underweight and reduced muscle mass [6,13,14]. Normal and underweight individuals with COPD have higher mortality rates than COPD patients who are overweight or even obese [14,15]. In Western countries, where the majority of adults are overweight or obese, patients no longer present with the traditional COPD phenotype, especially in early stages of the disease [15]. Assessing measures of body composition beyond weight and BMI, through the use of bioimpedance analysis, may be helpful in uncovering changes in body composition that occur over the disease course and in informing disease prognosis.

In this study, we sought to characterize the unique anthropometric phenotypes of three chronic respiratory diseases (COPD, asthma, and chronic bronchitis) through assessment of a variety of anthropometric measurements, including BMI, fat mass, fat free mass, and waist circumference. Our study was conducted across four distinct settings in Peru, each with varying degrees of urbanization, indoor air pollution, and socioeconomic status.

METHODS

Design and setting

The CRONICAS Cohort Study is a longitudinal, population-based study conducted between years 2010 and 2013 that was aimed to determine the prevalence and risk factors for chronic pulmonary and cardiovascular disease across four disparate regions in Peru [16]. Sites varied in degree of urbanization, living at high altitude, prevalence of daily biomass fuel use, and ambient air pollution levels (Table 1). Pampas de San Juan de Miraflores is a dense, urbanized community 25 kilometers south of central Lima. Tumbes is a semi-urban sea-level community in northern Peru within an agrarian setting and little to no vehicular traffic [16]. Puno is a southwestern city in the Andes, located on the shores of Lake Titicaca at 3,825

meters above sea-level. Within Puno there are two separate sites: an urban setting located at the city center and a rural setting made up of inhabitants from surrounding communities.

Study Participants

We identified a sex- and age-stratified random sample of adults aged ≥ 35 years, aiming to enroll approximately 1000 subjects per site. In Puno, we stratified recruitment to include 500 participants each from both urban and rural settings [16]. Exclusion criteria included pregnancy, physical disability, and active pulmonary tuberculosis. Fieldworkers obtained verbal consent from study participants prior to enrollment. Informed consents were verbal because of high illiteracy rates among participants. This study was approved by the Institutional Review Boards at Universidad Peruana Cayetano Heredia and A.B. PRISMA in Lima, Peru, and the Johns Hopkins Bloomberg School of Public Health in Baltimore, USA (IRB: 2716).

Data Collection

Data was collected using a modified version of WHO STEPS approach questionnaire for surveillance of non-communicable disease [16,17]. All questionnaires were administered in face to face interviews by trained field workers. Data collection included several factors potentially associated with chronic lung disease, such as age, sex, years of education, occupation, demographic information, other socioeconomic variables, smoking habits, biomass fuel use, and self-reported medical conditions [16,18,19]. Participants were asked specifically about presence of cough and sputum production. Trained technicians measured pre- and post-bronchodilator spirometry with the Easy on-PC spirometer (nidd, Zurich, Switzerland) following standard guidelines [18,20]. We adapted a standardized grading system for quality control, review and interpretation [21].

Measurements of standing height, waist, and hip circumference were measured in triplicate using standard techniques performed by trained field workers [16]. Weight and bioelectrical impedance were measured using the TBF-300A body composition analyzer (TANITA Corporation, Tokyo, Japan). Measurements were carried out according to manufacturer's specifications [22].

Definitions

We defined COPD as having a post-bronchodilator $FEV_1/FVC < 70\%$. [23] Since there are no established reference equations for lung function in Peruvians, we utilized both the NHANES III Mexican-Americans and the Global Lung Function Initiative (GLI) mixed ethnic population reference equations [23,24]. Participants were defined as having asthma if they met one or more of the following 3 criteria: (1) having a diagnosis of asthma by a physician, (2) self-reported wheezing in the last 12 months (3) self-reported asthma medication usage in the last 12 months, as previously defined [25]. We defined chronic bronchitis as having self-reported phlegm production for at least three months each year in two successive years [26,27]. Individuals without any of the above CRDs were considered healthy and treated as controls in this analysis.

BMI was calculated using height and weight measurements. Overweight was defined as having a BMI between >25 and 30 kg/m^2 while obese was defined as having a BMI $> 30 \text{ kg/m}^2$ [28]. Fat mass (FM) and fat free mass (FFM) were obtained from the bioimpedance analysis. Both FM and FFM were normalized for height to create the variables fat mass index (FMI) and fat free mass index (FFMI), respectively. Metabolic syndrome followed the definition set forth by the American Heart Association/National Heart, Lung and Blood Institute criteria [16,29].

We created a wealth index according to participant assets, household facilities, household income, and occupation [30]. We defined daily smoking as having at least one cigarette a day and pack-years as the reported number of packs (20 cigarettes per pack) per day multiplied by the number of years smoked. Biomass exposure was defined as daily users or non-daily users and the typical biomass fuel burned was recorded.

Biostatistical methods

In this study, we used cross sectional data from the first phase of collection. We calculated prevalence of chronic bronchitis, COPD, and asthma by site. Baseline anthropometric, lung function, and demographic data is described as simple frequency and means with standard deviations, stratified by disease diagnosis or setting. We used t-tests to compare continuous variables and chi-squared tests to compare categorical variables between groups. When stratifying our analysis by disease diagnosis, we analyzed those who were positive for asthma, COPD, chronic bronchitis, or all three diseases. We used multivariable linear regression to model the influence of CRD status on BMI, FMI, FFMI, and waist circumference while controlling for age, sex, site, smoking, and biomass fuel smoke exposure. Both adjusted and unadjusted overall models are presented for comparison (shown in Figure 1). In order to analyze potential differences between sites, we also created models that were the same as described above, but subset the data per site instead of adjusting within the model itself (shown in Figure 2). All analyses were performed in STATA 13 (StataCorp, College Station, Texas, USA) and R (www.r-project.org).

RESULTS

Participant characteristics

We enrolled 4,325 participants of which 3,601 (83%) completed a questionnaire. Of these, 2,959 (82%) had acceptable spirometry. There were no significant differences in age ($p=0.34$), sex ($p=0.21$), daily biomass fuel use ($p=0.66$), daily smoking ($p=0.79$), BMI ($p=0.20$), percent body fat ($p=0.15$), FFMI ($p=0.93$), and waist circumference ($p=0.30$) between participants with and without complete data. Daily smoking was low across all sites, with the highest incidence in Tumbes and the lowest incidence in rural Puno ($p<0.001$) (Table 2). The calculated wealth index was reported as low, middle, or high. The majority of participants from Lima and urban Puno had a middle or high wealth index, whereas the wealth index varied among participants in semi-urban Tumbes and was low among the majority of participants from rural Puno (Table 2). Biomass fuel use was high in rural Puno, moderate in Tumbes, and minimal in Lima and urban Puno (Table 2). Among those who

used biomass fuels daily, 21.9% (n=169) used dung, 12.4% (n=96) used coal, and 65.7% (n=507) used firewood.

Prevalence of Disease

Overall prevalence of COPD was 6.2% (3.6% in Tumbes to 9.9% in rural Puno), asthma was 7.1% (1.8% in rural Puno to 14.5% in Lima), and chronic bronchitis was 5.9% (1.3% in rural Puno to 8.9% in Lima) (Table 2). The prevalence of overlap syndromes across sites was 0.8% for asthma and COPD, 1.9% for asthma and chronic bronchitis, and 0.7% for COPD and chronic bronchitis. There were ten participants, 0.3% of the study population, who met the diagnostic criteria for all three CRDs (Table 3).

COPD prevalence was higher among men when compared to women (8.4% vs 3.6%) and those who used biomass fuel smoke for cooking compared to those who did not (8.5% vs 5.1%), and increased across decreasing socioeconomic status, with 6.7% prevalence in the lowest wealth tertile and 4.2% in the highest tertile. The prevalence of asthma was higher among women vs. men (8.6% vs. 5.5%), and increased with increasing socioeconomic status, with 4.4% prevalence in the lowest wealth tertile and 8.8% in the highest tertile.

Lung Function

Average pre-bronchodilator FEV₁ ranged from 2.6 ± 0.7 L in Tumbes to 2.8 ± 0.8 L in urban Puno, pre-bronchodilator FVC ranged from 3.2 ± 0.9 L in Tumbes to 3.7 ± 1.1 L in urban Puno, and pre-bronchodilator FEV₁/FVC ranged from 0.75 ± 0.07 in rural Puno to 0.79 ± 0.06 in Tumbes (Table 2). When comparing Z scores between CRD status, people who were positive for all three (COPD, asthma, and chronic bronchitis) had the lowest average FEV₁ and FVC using both GLI and NHANES reference populations (Table 3). Of the three individual CRDs, participants with COPD showed the lowest average FEV₁ and participants with asthma had the lowest FVC (Table 3).

Body Composition

The overall prevalence of overweight and obese individuals was 71.9%, with a higher prevalence in Lima (78.0%), Tumbes (75.9%), and urban Puno (76.1 %), compared to a lower prevalence in rural Puno (47.9%) (Table 2). Mean BMI, waist circumference, percent body fat and FMI were similar in Lima, Tumbes, and urban Puno while the mean of each of these variables was lower in rural Puno (Table 2).

The prevalence of overweight and obesity among participants with asthma (83.0%) was higher than the prevalence of overweight and obesity among those with COPD (50.7%), chronic bronchitis (69.0%) or participants without a chronic respiratory condition (72.6%, p<0.001) (Table 3).

Participants with COPD had consistently lower measures of body composition (Figure 1 and Figure 2). Specifically, those with COPD had lower average waist circumference (adjusted absolute difference of -3.37 cm, 95% CI -5.06 to -1.69 cm), a lower FMI (-0.89 kg/m², -1.31 to -0.46), and a lower FFMI (-0.48 kg/m², -0.74 to -0.22 kg/m²) when compared to non-CRD participants. Participants with asthma had higher average FMI (0.40 kg/m², 0.01

to 0.80) when compared to non-CRD participants. There was no difference in lean mass (FFMI) or BMI between participants with asthma and non-CRD participants. People with chronic bronchitis had lower average FFMI (-0.27 kg/m^2 , -0.53 to -0.02 kg/m^2). To further understand the relationship between body composition and a CRD diagnosis among this cohort, we stratified our analysis by study site (Figure 1 and Figure 2). We found that site-specific estimates were generally consistent with the overall population with few exceptions (Figure 2).

DISCUSSION

In this multi-center, population-based study in Peru, we found marked differences in anthropometric markers between participants with varying chronic respiratory disease diagnoses and healthy individuals. Additionally, we observed differences in both body composition and prevalence of CRDs between populations at each study site, suggesting both disease condition and location influence body composition in this population. Across all sites, a diagnosis of COPD was associated with reduced fat mass and lean mass while a diagnosis of asthma was associated with increased body fat and waist circumference, a measure of abdominal obesity.

Our findings are consistent with that of previous reports. For example, asthma and chronic bronchitis are both associated with obesity and increased fat mass [1,12]. Obesity is linked to reduced lung tidal volume and functional residual capacity [8,9]. Additionally, both asthma and obesity are characterized by inflammation, with the tumor necrosis factor alpha (TNF-alpha) pathway common among both conditions and perhaps unregulated in the presence of both [9,31]. In contrast, COPD is more likely to be associated with weight loss, reduced muscle tone and cachexia [1,12,13]. Systemic inflammation resulting from elevated TNF-alpha production, and a higher resting energy expenditure caused by metabolic and mechanical inefficiency, have been shown to be associated with underweight and a reduction in fat free mass [13,32].

Previous studies have proposed that fat free mass (FFM), irrespective of fat mass, is a strong predictor of mortality in COPD [14]. Furthermore, overweight and obesity can have a protective effect on mortality in those with severe COPD [33,34]. Nutritional and therapeutic interventions have contributed to the maintenance of body mass in COPD patients, potentially improving COPD prognosis [32,35]. Use of the BODE index (body mass index, airflow obstruction, dyspnea, and exercise capacity) as a prognostic tool has gained popularity [36]. The BODE index incorporates respiratory capacity, nutritional state, exercise capacity, and the presence and severity of symptoms to predict mortality, and more recently risk of hospitalization, in patients with COPD [36]. Our findings of a COPD diagnosis as a predictor of both reduced fat mass and fat free mass highlights the importance of assessing body composition alongside lung function when evaluating and treating COPD.

We identified ten participants who met the diagnostic criteria for all three CRDs. These subjects presented with phenotypes most consistent with COPD. Collectively they had poorer lung function and lower fat mass and FFM compared to all other study participants. Their average log CRP level was approximately three times higher than that of participants

with COPD or chronic bronchitis alone. While the sample size was small, such findings suggest a parallel relationship between higher systemic inflammation and the type and severity of respiratory symptom presentations.

Our study has several strengths. First, this study includes data from multiple settings and has a large sample size. Second, we had comprehensive data on body composition, demographics, health status, and behavioral characteristics, allowing us to thoroughly evaluate trends in body composition across varying regions of Peru. This study also has some potential shortcomings. Self-reported history of asthma and chronic bronchitis presents the possibility of bias, potentially affecting inferences. In rural areas where access to care is more limited, it is possible our clinical findings are underreported leading to an underestimation of the prevalence of certain conditions at these study sites. Additionally, as a cross-sectional analysis, we are unable to adequately determine direction of causality between body composition and CRDs.

CONCLUSION

Our study provides a descriptive analysis of the phenotypic spectrum of body composition among adults with and without chronic respiratory diseases in geographically different settings throughout Peru. Chronic respiratory disease diagnosis and location were both associated with important differences in body composition in this study population. Urbanization and a diagnosis of asthma had a higher prevalence of obese phenotypes while rural settings and subjects with COPD had a lower body mass. Our findings highlight the importance of considering body composition along with lung function when assessing the prognosis of COPD.

ACKNOWLEDGEMENTS

JM, ABO, RG, and WC were responsible for study design and conduct. RW provided mentoring and contributed during study design, and interpretation of results. GT, MG, CM, and WC were responsible for analysis, data interpretation, and first draft of manuscript. All authors read paper and provided comments. WC is the sole guarantor of this study.

COMPLIANCE AND ETHICAL STANDARDS

This project was funded in whole with Federal funds from the United States National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN268200900033C. Research reported in this publication was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Number T32HL007534. There was no conflict of interest from any authors on this manuscript. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Figure 1: Differences in body composition by disease condition.

Unadjusted and adjusted mean difference and 95% CI of body mass index, fat mass index, waist circumference, and fat free mass index, stratified by chronic respiratory disease conditions (those without a CRD are controls). Adjusted models were adjusted for age, sex, daily smoking, daily biomass use, and site.

Figure 2: Average of body composition by disease condition and setting.

Absolute difference and 95% CI in mean body mass index, fat mass index, fat free mass index, and waist circumference between participants with a particular disease diagnosis when compared to participants without a chronic respiratory disease. Mean values and 95% CI for the overall population estimate are presented as a vertical line and grey shaded area, respectively. All models were adjusted for age, sex, daily smoking, and daily biomass use.

Table 1:

Environmental characteristics by study site

Setting	Urbanization	Daily use of biomass fuels	Altitude
Lima	Urban	Rare	Sea level
Tumbes	Semi-urban	Moderately prevalent	Sea level
Puno, urban	Urban	Rare	3,825 meters above sea level
Puno, rural	Rural	Highly prevalent	3,825 meters above sea level

Table 2:

Participant characteristics across four study sites in Peru.

	Lima	Urban Puno	Rural Puno	Tumbes	Total	p-value
Number of participants, n (%)	998	507	507	947	2959	
Male, % (n)	49.3 (492)	49.3 (250)	47.5 (241)	50.3 (476)	49.3 (1459)	0.81
Age (years), mean (SD)	55.0 (11.8)	55.2 (12.2)	55.5 (12.5)	55.8 (13.1)	55.4 (12.4)	0.56
BMI in (kg/m²), mean (SD)	28.4 (4.5)	27.9 (4.4)	25.2 (3.7)	28.3 (4.7)	27.7 (4.6)	<0.001
BMI Category, % (n)						<0.001
Normal	22.0 (220)	23.9 (120)	52.1 (261)	24.1 (228)	28.1 (829)	
Overweight	45.5 (454)	49.7 (250)	37.1 (186)	44.4 (420)	44.4 (1310)	
Obese	32.5 (324)	26.4 (133)	10.8 (54)	31.6 (299)	27.5 (810)	
Percent body fat, mean (SD)	30.9 (8.2)	31.3 (8.2)	26.5 (8.4)	30.8 (8.5)	30.1 (8.5)	<0.001
Waist circumference, cm (SD)	92.7 (10.8)	92.6 (10.8)	85.2 (11.0)	94.6(10.0)	91.8 (11.2)	<0.001
FMI (kg/m²), mean (SD)	13.1 (4.2)	13.0 (4.2)	11.1 (4.0)	12.6 (4.2)	12.6 (4.2)	<0.001
FFMI (kg/m²), mean (SD)	19.4 (1.9)	18.9 (1.8)	18.3 (1.6)	19.3 (2.1)	19.1 (1.9)	<0.001
Metabolic syndrome, % (n)	49.1 (486)	47.0 (230)	28.0 (135)	54.6 (517)	47.0 (1368)	<0.001
COPD, % (n)	6.2 (62)	6.1 (31)	9.9 (50)	3.6 (34)	6.0 (177)	<0.001
Chronic bronchitis, % (n)	8.9 (89)	7.0 (35)	7.8 (39)	1.3 (12)	5.9 (175)	<0.001
Asthma, % (n)	14.5 (145)	3.8 (19)	1.8 (9)	3.7 (35)	7.1 (208)	<0.001
Wealth index, % (n)						<0.001
Low	7.1 (65)	13.5 (58)	70.4 (357)	39.4 (347)	32.0 (833)	
Middle	38.0 (350)	32.6 (140)	26.8 (136)	42.3 (373)	33.4 (869)	
High	54.9 (505)	46.8 (232)	2.7 (14)	18.3 (161)	34.6 (899)	
Smoking daily, % (n)	3.2 (32)	2.2 (11)	0.2 (1)	5.6 (53)	3.3 (97)	<0.001
Daily use of biomass fuels, % (n)	6.1 (61)	4.9 (25)	95.5 (484)	23.3 (221)	26.8 (791)	<0.001
FEV₁ (L), mean (SD)	2.7 (0.8)	2.8 (0.8)	2.7 (0.8)	2.6 (0.7)	2.7 (0.8)	<0.001
FVC (L), mean (SD)	3.4 (1.0)	3.7 (1.1)	3.6 (1.0)	3.2 (0.9)	3.4 (1.0)	<0.001
FEV₁/FVC, mean (SD)	0.77 (0.07)	0.76 (0.06)	0.75 (0.07)	0.79 (0.06)	0.77 (0.07)	<0.001
FEV₁ z-score, mean (SD)						

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	Lima	Urban Puno	Rural Puno	Tumbes	Total	p-value
GLI (mixed ethnic)	0.70 (1.3)	0.88 (1.3)	0.84 (1.4)	0.09 (1.1)	0.56 (1.3)	<0.001
NHANES (Mexican-Americans)	0.32 (1.3)	0.47 (1.2)	0.45 (1.4)	-0.32 (1.1)	0.17 (1.3)	<0.001
FVC z-score, mean (SD)						
GLI (mixed ethnic)	1.07 (1.3)	1.43 (1.3)	1.45 (1.4)	0.19 (1.1)	0.92 (1.4)	<0.001
NHANES (Mexican-Americans)	0.44 (1.3)	0.80 (1.3)	0.82 (1.4)	-0.43 (1.1)	0.29 (1.4)	<0.001

Table 3:

Participant characteristics across chronic respiratory diseases. Participants with overlap of two CRDs were not included in this table.

	COPD	Chronic Bronchitis	Asthma	COPD, chronic bronchitis, and asthma	Non-CRD	p-value
Number of participants, % (n)	4.8 (142)	3.9 (116)	5.0 (147)	0.3 (10)	85.6 (2470)	
Age (years), mean (SD)	65.7 (12.9)	58.5 (12.6)	54.6 (11.7)	71.8 (10.7)	54.6 (12.1)	<0.001
Male, % (n)	69.0 (98)	53.4 (62)	34.0 (50)	70.0 (7)	48.7 (1202)	<0.001
BMI (kg/m ²), mean (SD)	25.4 (4.0)	27.2 (3.9)	29.3 (4.6)	24.0 (4.7)	27.8 (4.6)	<0.001
Overweight, % (n)	50.7 (72)	69.0 (80)	83.0 (122)	40.0 (4)	72.6 (1794)	<0.001
Percent body fat, mean (SD)	25.3 (7.6)	29.8 (8.1)	33.6 (8.1)	24.9 (9.0)	30.3 (8.4)	<0.001
Waist circumference (cm), mean (SD)	88.3 (12.2)	91.2 (10.3)	94.7 (10.5)	87.3 (13.2)	92.1 (11.0)	<0.001
FMI (kg/m ²), mean (SD)	10.5 (3.7)	12.5 (4.1)	14.5 (4.3)	10.1 (4.2)	12.6 (4.2)	<0.001
FFMI (kg/m ²), mean (SD)	18.7 (1.9)	18.8 (1.7)	19.1 (1.8)	17.7 (1.9)	19.1 (2.0)	0.01
Metabolic syndrome, % (n)	37.4 (52)	43.5 (50)	53.1 (76)	40.0 (4)	47.7 (1158)	0.08
Log CRP (mg/L), mean (SD)	0.55 (1.2)	0.46 (1.1)	0.75 (1.1)	1.6 (1.5)	0.52 (1.1)	0.01
FEV ₁ z-score, mean (SD)						
	-0.57 (1.4)	0.71 (1.3)	0.27 (1.3)	-1.2 (1.8)	0.66 (1.2)	<0.001
GLI (mixed ethnic)						
NHANES (Mexican-Americans)	-0.78 (1.5)	0.39 (1.2)	-0.11 (1.3)	-1.5 (1.9)	0.25 (1.2)	<0.001
FVC z-score, mean (SD)						
	0.83 (1.7)	1.2 (1.5)	0.59 (1.4)	0.33 (2.1)	0.93 (1.3)	<0.001
GLI (mixed ethnic)						
NHANES (Mexican-Americans)	0.35 (1.6)	0.58 (1.4)	-0.02 (1.3)	-0.16 (2.0)	0.29 (1.3)	<0.001
Smoking daily, % (n)	1.4 (2)	17 (2)	1.4 (2)	0.0 (0)	3.7 (91)	0.23
Daily use of biomass fuels, % (n)	39.4 (56)	33 (28.4)	12.2 (18)	30.0 (3)	26.9 (664)	<0.001
Lowest wealth index tertile, % (n)	39.2 (47)	34.3 (34)	16.2 (22)	22.2 (2)	32.3 (704)	0.01