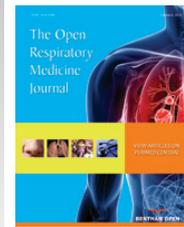




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## RESEARCH ARTICLE

# Determinants of Restrictive Spirometric Pattern in a Sub-Saharan Urban Setting: A Cross-sectional Population-based Study

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## Abstract:

### Background

Restrictive spirometric pattern is a risk factor for all-cause and cause-specific mortality.

### Objective

We assessed the prevalence of restrictive pattern and investigated its determinants in a major sub-Saharan Africa city.

### Methods

Participants were adults ( $\geq 19$  years) who took part in a population-based survey in Yaounde (Cameroon) between December 2013 and April 2014. Restrictive pattern was based on a FVC below the lower limit of the normal (LLN) and a ratio forced expiratory volume in one second (FEV1)/FVC  $\geq$  LLN (LLN-based restrictive pattern) or a FVC  $< 80\%$  and FEV1/FVC  $\geq$  LLN (fixed cut-off based restrictive pattern). Determinants were investigated by logistic regressions.

### Results

In all, 1003 participants [514 (51.2%) women] with a mean age of 33.7 years were included. The prevalence of restrictive pattern was 18.8% (95%CI: 16.6-21.2) based on LLN and 15.0% (13.0-17.2) based on fixed cut-off. LLN-based restrictive pattern was mild in 148 (78.3%) subjects, moderate in 35 (18.5%) and severe in 6 (3.2%). Determinants of LLN-based restrictive pattern were age  $\geq 60$  years [adjusted odds ratio 2.90 (95%CI 1.46-5.77),  $p=0.002$ ], history of pulmonary tuberculosis [3.81(1.42-10.20),  $p=0.008$ ], prevalent heart diseases [3.81 (1.20-12.12),  $p=0.024$ ] and underweight [5.15(1.30-20.39),  $p=0.020$ ]. Determinants were largely similar with slightly different effect sizes for fixed cut-off based restrictive pattern.

### Conclusion

Restrictive pattern was very frequent in this city.

### Clinical implications

These results enhance the needs to increase the efforts to prevent and control tuberculosis, cardiovascular diseases and underweight in this setting.

**Keywords:** Africa, Cameroon, Low forced vital capacity, Prevalence, Pulmonary restriction, Restrictive lung disease.

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## INTRODUCTION

Vital capacity (VC) and forced expiratory volume in one second (FEV1) are the commonly used ventilatory parameters in functional evaluation and assessment of severity of respiratory diseases [1]. Studies have reported a relationship between these two parameters and excess all-cause mortality as well as mortality from cardiovascular diseases, respiratory diseases and cancers in the general population [2 - 5]. Furthermore, in people free of any respiratory symptoms or any known respiratory disease, Burney and Hooper have recently reported a low forced vital capacity (FVC) to be strongly correlated with higher all-cause mortality but not FEV1 and the FEV1/FVC ratio [6]. Moreover, in another recent study by Lee *et al.* [7], FVC and FEV1 improved mortality risk stratification based upon the Framingham risk equation in intermediate risk individuals. Knowledge of factors associated with low FVC in the general population is therefore important, and can assist risk evaluation and early identification and treatment of high risk individuals.

Few studies originating mostly from developed countries are available on the burden and risk factors for low FVC, also known as restrictive pattern. Across these studies, the prevalence of restrictive pattern in the general population ranged from 5.4% to 10.9% in US [8 - 10], to 74% in Aboriginal Australians [11]. These studies have also revealed many risk factors for restrictive pattern including high cardio-thoracic index, paralysis, diabetes mellitus and cardiovascular diseases (CVD) in the general population [9, 10]; and abdominal obesity, physical impairment, cognitive impairment and kypho-scoliosis in the elderly population [3].

The aim of the present study was to assess the prevalence of restrictive pattern (low FVC in the absence of airway obstruction) and investigate the determinants among adults in the general population from a major sub-Saharan African City.

## MATERIALS AND METHODS

### Study Design and Participants

This was a cross-sectional population-based survey conducted between December 2013 and April 2014 among adults (19 years of age and above) in Yaounde, the Capital City of Cameroon. Participants were recruited during a population-based survey aiming to quantify the burden of the commonest non-communicable respiratory diseases in Yaounde city. The sampling methods and selection of participants have been described in detail previously [12]. In brief, we used multilevel stratified sampling method to include participants in the current study. We firstly selected 16 enumeration areas (EA) out of the 2000 EAs of Yaounde city. In each enumeration area, we followed the itinerary of the national vaccination campaigns and then we used systematic sampling method to include participants in the study. About every one participant in two was selected for spirometry purpose (and if the spirometry was judged uninterpretable by the field workers, they included the next participant). Were excluded from the survey all participants with any of the following conditions: active tuberculosis, recent pneumonia, physical or mental inability to perform spirometry. Of the 1499 participants selected *via* multilevel stratified sampling across the seven administrative districts of Yaounde, to undergo spirometry tests during the survey, 212 (14.1%) participants had completely uninterpretable spirometry (lack of reproducibility and incorrect maneuvers); 236 (18.3%) of the remaining 1287 participants had reproducible curves but inadequate end of test plateau. Of the 1051 participants left, 48 (4.7%) had airway obstruction ( $FEV1/FCV < \text{lower limit of normal [LLN]}$ ) and were therefore excluded from the analysis.

### Data Collection

Data were collected by purposefully trained final year undergraduate medical students. A pre-tested questionnaire inspired by other questionnaires used in international surveys [13, 14], was used for data collection. The questionnaire was completed during face-to-face interview with consenting participants. Data were collected on the following: 1) socio-demographic details including age, sex and education; 2) exposure to tobacco which was assessed using a series of questions on tobacco use and participants classified as non-smokers (for those who never smoked, or had smoked less than 20 packs in their lifetime), active smokers (for participants who had smoked more than 20 packs in their lifetime, or at least one cigarette per day), and ex-smokers (for participants who had stopped smoking since at least six months) [15]; 3) self-reported history of existing conditions including pulmonary tuberculosis, asthma, pneumonia, cardiovascular diseases, diabetes mellitus, hypertension and cerebrovascular accident ; 4) chronic respiratory signs including chronic cough and expectoration for more than three months per year, dyspnea which was classified into four stages based on the modified Medical Research Council (mMRC) scale [16]; 5) biomass exposure based on exposure to

cooking fumes from various solid fuels, and participants who had used solid fuels for cooking purpose for at least six months were classified as having been exposed to biomass [15]; 6) Anthropometric measures including height to the nearest centimeter, which was measured with a stadiometer in a participant without shoes, in the upright position, and weight (in kilograms) which was measured with a CAMRY weight scale (CAMRY, Guangzhou, China).

### Spirometric Measurements

Flow-volume curves were acquired following the American Thoracic Society/European Respiratory Society (ATS/ERS) 2005 recommendations [17]. Spirometric examinations used a turbine pneumotachograph (Spiro USB, Care fusion, Yorba Linda-USA) or a Fleisch pneumotachograph (Spirolyser SPL-10 USB, FIM-Medical, Lyon-France), following the international standards, and were performed by a trained technician. All curves were reviewed by an experienced chest physician. Spirometric measurements were performed in a participant at rest for at least 15 minutes, in a sitting position with the back straight, and the nose clipped to allow air flow only per mouth. The ATS/ERS acceptability and reproducibility criteria were applied [17]. All subjects who had an acceptable expiratory plateau were included. At least three tests were done by each participant to establish the FVC curve. Spirometric variables measured included: FEV1, FVC and the FEV1/FVC ratio. FEV1 and FVC values retained were the best out of the three tests which fulfilled the acceptability criteria (maximal difference below 5% or 150 ml). Predicted values were estimated using the reference spirometric values derived from a black African population [18]. Restrictive pattern was defined by a FVC below the age, sex and height specific LLN (LLN-based restrictive pattern). Sensitivity analyses were also conducted using an alternative definition which was based on FVC < 80% of the predicted value (fixed cut-off based restrictive pattern). The severity of restrictive pattern was based on a modification of the classification by Pellegrino *et al.*: mild restriction for FEV1>70%, moderate restriction for 50% ≤ FEV1 ≤ 70% and severe for FEV1<50% [1]. The study was approved by the Ethics Committee of the Regional delegation of Health of Center Region of Cameroon.

### Statistical Analysis

Data analysis used the IBM-SPSS v.20 for Windows (IBM, Chicago, USA). Qualitative variables are presented as count and frequencies, and quantitative variables as mean and standard deviation (SD) or median and 25<sup>th</sup>-75<sup>th</sup> percentiles. Graphical plots and Shapiro-Wilk test were used to assess the normality of the quantitative variables. There was indication of departure from normal distribution for all the quantitative variables included in the analysis. Group comparisons used chi square test for qualitative variables, and Mann-Whitney U test for quantitative variables. Age-standardized prevalence was calculated using the Cameroon National population's age structure in 2010 as the standard population [19], and direct standardization methods. Logistic regression models were employed to investigate the determinants of restrictive pattern. Significant predictors in univariable analysis (based on a threshold p<0.10) were entered altogether in the same multivariable model and the significant ones retained as the final determinants. A p-value < 0.05 was used to characterize statistically significant results.

## RESULTS

### General Characteristics of the Study Population

The general characteristics of the included participants are described in Table 1. Of the 1003 participants included, 514 (51.2%) were women. The mean age (SD) was 33.7 (12.1) years and 44 (4.4%) participants were aged 60 years and above. Women were less educated than men with 66.2% vs. 58.3% having achieved at most secondary school level education (p<0.001). Compared with women, men were more likely to be current smokers (16% vs. 2.3%, p<0.001), and as expected women were more likely to have been exposed to biomass than men (8.4% vs. 7%, p<0.001). With the exception of dyspnea which was more frequent in women than men (31.7% vs. 18.4%, p<0.001), chronic respiratory symptoms were equally distributed between men and women. The mean predicted FVC (SD) was 96.98% (18.51%) overall and the predicted value did not differ between men and women. Predicted FEV1 was also similar between men and women (98.52% vs. 96.77%, p=0.336).

**Table 1. General characteristics of study population.**

Characteristics	Overall, n=1003 (%)	Men, n=489 (%)	Women, n=514 (%)	p-value
Age, years				
Mean (SD)	33.7 (12.1)	33.5 (12.3)	34.0 (11.8)	0.237
Median (25 <sup>th</sup> -75 <sup>th</sup> percentiles)	30 (24-41)	29 (24-40)	30 (25-41)	

(Table 3) contd....

Characteristics	Overall, n=1003 (%)	Men, n=489 (%)	Women, n=514 (%)	p-value
Age group, years				
19-39	730 (72.8)	364 (74.4)	366 (71.2)	0.231
40-59	229 (22.8)	101 (20.7)	128 (24.9)	
≥ 60	44 (4.4)	24 (4.9)	20 (3.9)	
Education				
≤ secondary	664 (66.2)	285 (58.3)	379 (73.7)	< 0.001
Higher	339 (33.8)	204 (41.7)	135 (26.3)	
Subject/bedrooms				
≤ 2	561 (56)	307 (62.8)	254 (49.5)	<0.001
> 2	441 (44)	182 (37.2)	259 (50.5)	
Tobacco smoking				
Current smoker	90 (9)	78 (16)	12 (2.3)	<0.001
Ex-smokers	64 (6.4)	57 (11.7)	7 (1.4)	
Non smokers	845 (84.6)	353 (72.3)	492 (96.3)	
Cooking fuel				
Biomass	76/982 (7.7)	33/473 (7)	43/509 (8.4)	<0.001
Mixed	454/982 (46.2)	183/473 (38.7)	271/509 (53.2)	
Clean	452/982 (46)	257/473 (54.3)	195/509 (38.3)	
Past history of tuberculosis				
Yes	18 (1.8)	9 (1.8)	9 (1.8)	0.915
No	985 (98.2)	480 (98.2)	505 (98.2)	
Past history of pneumonia				
Yes	28 (2.8)	17 (3.5)	11 (2.1)	0.199
No	975 (97.2)	472 (96.5)	503 (97.9)	
Self-reported asthma				
Yes	23 (2.3)	7 (1.4)	16 (3.1)	0.075
No	980 (97.7)	482 (98.6)	498 (96.9)	
History of stroke				
Yes	4 (0.4)	3 (0.6)	1 (0.2)	0.362
No	999 (99.6)	486 (99.4)	513 (99.8)	
Self-reported diabetes mellitus				
Yes	12 (1.2)	6 (1.2)	6 (1.2)	0.931
No	991 (98.8)	483 (98.8)	508 (98.8)	
Self-reported hypertension				
Yes	40 (4)	15 (3.1)	25 (4.9)	0.146
No	963 (96)	474 (96.9)	489 (95.1)	
History of cardiac disease				
Yes	14 (1.4)	9 (1.8)	5 (1)	0.242
No	989 (98.6)	480 (98.2)	509 (99)	
Self-reported HIV infection				
Yes	7 (0.7)	3 (0.6)	4 (0.8)	< 0.001
No	787 (78.5)	358 (73.2)	429 (83.5)	
Don't know	209 (20.8)	128 (26.2)	81 (38.8)	
Respiratory symptoms				
Chronic cough	22 (2.2)	10 (2)	12 (2.3)	0.754
Chronic expectoration	8 (0.8)	4 (0.8)	4 (0.8)	>0.999
Recent wheezing	24 (2.4)	11 (2.2)	13 (2.5)	0.772
Dyspnea	253 (25.2)	90 (18.4)	163 (31.7)	<0.001
Any symptoms	271 (27)	98 (20)	173 (33.7)	<0.001
BMI, Kg/m <sup>2</sup> , Mean (SD)	26.1 (5.3)	25.4 (4.3)	27.4 (5.9)	<0.001
FEV1				
Mean (SD), L	3.08 (0.85)	3.59 (0.82)	2.60 (0.54)	<0.001
% predicted (SD)	97.63 (18.56)	98.52 (19.23)	96.77 (17.87)	0.144
FVC				

(Table 3) contd....

Characteristics	Overall, n=1003 (%)	Men, n=489 (%)	Women, n=514 (%)	p-value
Mean (SD), L	3.56 (0.97)	4.14 (0.92)	3.0 (0.63)	<0.001
% predicted (SD)	96.98 (18.51)	96.57 (18.86)	97.36 (18.19)	0.336
FEV1/FVC	0.87 (0.05)	0.87 (0.05)	0.87 (0.05)	0.813

SD, standard deviation; TB, tuberculosis; BMI, body mass index; FEV1, forced expiratory volume in 1s; FVC, forced vital capacity.

### Prevalence and Severity of Restrictive Pattern

A total of 189 participants had a FVC < LLN; therefore, the crude prevalence of LLN-based restrictive pattern was 18.8% (95% confidence interval [CI] 16.6-21.2). The age-standardized prevalence was 20.3% (17.8-22.2%). LLN-based restrictive pattern was mild in 148 (78.3%) participants, moderate in 35 (18.5%) and severe in 6 (3.2%) participants. Furthermore, 127 (67.2%) of participants with LLN-based restrictive pattern had a FEV1 <80% of the predicted value. Based on a FVC <80%, 180 participants had a low FVC; therefore the prevalence of fixed cut-off based restrictive pattern was 15% (95%CI: 13.0-17.2%).

### Determinants of Restrictive Pattern

Univariable associations of baseline characteristics with LLN-based restrictive pattern are shown in Table 2. Participants with restrictive pattern were older (37.2 vs. 32.1 years,  $p<0.001$ ) and less educated (secondary school education or less: 72.5% vs. 64.7%,  $p=0.043$ ). Other univariable correlates of restrictive pattern included a history of pulmonary tuberculosis [odds ratio (95% CI): 4.47 (1.75-11.43),  $p=0.002$ ], history of heart disease [5.95 (2.04-17.38),  $p=0.001$ ], exposure to biomass [1.98 (1.14-3.45),  $p=0.015$ ], chronic cough [2.53 (1.04-6.11),  $p=0.040$ ], dyspnea stage 3 and 4 [2.02 (1.05-3.88),  $p=0.031$ ], and body mass index (BMI) < 18.5 kg/m<sup>2</sup> [5.32 (1.40-20.21),  $p=0.014$ ]. Univariable determinants were similar for the outcome of fixed cut-off based restrictive pattern, with the exception of exposure to biomass for which the association was borderline (Supplementary Table 1).

**Table 2. Univariable analysis of factors associated to restrictive pattern by FVC < LLN and FEV1/FVC ≥ LLN.**

Determinants	Restrictive pattern N=189 (%)	Normal FVC N=814 (%)	Crude odds ratio (95%CI)	p-value
Gender				
Male	92 (48.7)	397 (48.8)	1.00 (0.73-1.37)	0.981
Female	97 (51.3)	417 (51.2)	1	
Age, mean (SD), years	37.2 (14.5)	32.1 (11.3)	1.03 (1.02-1.04)	<0.001
Age group, years				
19-39	123 (65.1)	607 (74.6)	1	
40-59	47 (24.9)	182 (22.4)	1.27 (0.88-1.85)	0.205
≥ 60	19 (10.1)	25 (3.1)	3.75 (2.00-7.02)	<0.001
Ethnic group				
Bantou	174(92.1)	771(94.7)	0.63(0.23-1.78)	0.384
Fulani	10(5.3)	29(3.6)	0.97(0.28-3.37)	0.956
Sudanese	5(2.6)	14(1.7)	1	
Education				
≤ secondary	137 (72.5)	527 (64.7)	1.44 (1.01-2.04)	0.043
Higher	52 (27.5)	287 (35.3)	1	
Subject/bedrooms				
≤ 2	108 (57.1)	453/813 (55.7)	1.06 (0.77-1.46)	0.723
> 2	81 (42.9)	360/813 (44.3)	1	
Tobacco smoking				
Current smoker	19 (10.1)	71/810 (8.8)	1.16 (0.68-1.99)	0.579
Ex-smokers	12 (6.3)	52/810 (6.4)	1.00 (0.52-1.92)	0.992
Non smokers	158 (83.6)	687/810 (84.8)	1	
Cooking fuel				
Biomass	22/186 (46.8)	54/796 (6.8)	1.98 (1.14-3.45)	0.015
Mixed	87/186 (46.8)	367/796 (46.1)	1.15 (0.82-1.62)	0.406

(Table 4) contd....

Determinants	Restrictive pattern N=189 (%)	Normal FVC N=814 (%)	Crude odds ratio (95%CI)	p-value
Clean	77/186 (41.1)	796/796 (47.1)	1	
Past history of TB				
Yes	9 (4.8)	9 (1.1)	4.47 (1.75-11.43)	0.002
No	180 (95.2)	805 (98.9)	1	
Past history of pneumonia				
Yes	7 (3.7)	21 (2.6)	1.45 (0.61-3.47)	0.398
No	182 (96.3)	793 (97.4)		
Self-reported asthma				
Yes	3 (1.6)	20 (2.5)	0.64 (0.19-2.18)	0.475
No	186 (98.4)	794 (97.5)	1	
History of stroke				
Yes	2 (1.1)	2 (0.2)	4.34 (0.61-31.03)	0.143
No	187 (98.9)	812 (99.8)	1	
Self-reported diabetes mellitus				
Yes	4 (2.1)	8 (1.0)	2.19 (0.65-7.31)	0.208
No	185 (97.9)	806 (99.0)	1	
Self-reported hypertension				
Yes	10 (5.3)	30 (3.7)	1.46 (0.71-3.04)	0.312
No	179 (94.7)	784 (96.3)	1	
History of heart disease				
Yes	8 (4.2)	6 (0.7)	5.95 (2.04-17.37)	0.001
No	181 (95.8)	808 (99.3)	1	
Self-reported HIV infection				
Yes	1 (0.5)	6 (0.7)	0.71 (0.09-5.97)	0.756
No	149 (78.8)	638 (78.4)	1	
Don't know	39 (20.6)	170 (20.9)	0.98 (0.66-1.45)	0.929
Respiratory symptoms				
Chronic cough	8 (4.2)	14 (1.7)	2.53 (1.04-6.11)	0.040
Chronic expectoration	2 (1.1)	6 (0.7)	1.44 (0.29-7.19)	0.657
Recent wheezing	5 (2.6)	19 (2.3)	1.14 (0.42-3.09)	0.801
Dyspnea	59 (31.2)	194 (23.8)	1.45 (1.03-2.05)	0.035
mMRC dyspnea > 2	14 (7.4)	31 (3.8)	2.02 (1.05-3.88)	0.031
Any respiratory symptoms	62 (32.8)	209 (25.7)	1.41 (1.00-1.99)	0.047
BMI, Kg/m <sup>2</sup> , Mean (SD)	26.6 (6.7)	26.4 (4.9)	1.01 (0.98-1.04)	0.618
BMI classes				
Underweight	5/188 (2.7)	4/812 (0.5)	5.32 (1.40-20.21)	0.014
Overweight	46 (24.5)	264 (32.5)	0.74 (0.50-1.09)	0.131
Obese	47 (25)	161 (19.8)	1.24 (0.84-1.85)	0.285
Normal	90 (47.9)	383 (47.2)	1	

LLN, lower limit of normal; FVC, forced vital capacity; FEV1, forced expiratory volume in 1s; SD, standard deviation; TB, tuberculosis; mMRC, modified Medical Research Council scale; BMI, body mass index.

In multivariable regression models, independent determinants of LLN-based restrictive pattern were age  $\geq$  60 years [adjusted odds ratio (95%CI): 2.90 (1.46-5.77),  $p = 0.002$ ], history of pulmonary tuberculosis [3.81 (1.42-10.20),  $p = 0.008$ ], past history of heart disease [3.81 (1.20-12.12),  $p = 0.024$ ] and underweight [5.15 (1.30-20.39),  $p = 0.020$ ] (Table 3). The pattern of the associations was similar for fixed cut-off based restrictive pattern, although the association with prevalent heart disease was no longer significant [1.64 (0.45-5.94),  $p=0.450$ ] (Supplementary Table 2).

Table 3. Multivariable logistic regression model for determinants of restrictive pattern by  $CVF < LLN$  and  $FEV1/FVC \geq LLN$ .

Determinants	Adjusted odds ratio	95% confidence interval	p-value
Male gender	1.06	0.75-1.50	0.754
Age group, years			

(Table 5) *contd....*

Determinants	Adjusted odds ratio	95% confidence interval	p-value
19-39	1.00 (reference)		
40-59	1.16	0.76-1.76	0.489
≥ 60	2.90	1.46-5.77	0.002
Education ≤ secondary	1.33	0.91-1.94	0.118
Cooking fuel			
Biomass	1.70	0.94-3.09	0.080
Mixed	1.13	0.79-1.62	0.497
Clean	1.00 (reference)		
Past history of TB	3.81	1.42-10.20	0.008
History of cardiac disease	3.81	1.20-12.12	0.024
Chronic cough	1.92	0.71-5.14	0.197
mMRC dyspnea > 2	1.50	0.72-3.14	0.279
BMI classes			
Underweight	5.15	1.30-20.39	0.020
Overweight	0.70	0.47-1.06	0.093
Obese	0.95	0.61-1.51	0.843
Normal	1.00 (reference)		

LLN, lower limit of normal; FVC, forced vital capacity; FEV1, forced expiratory volume in 1s, TB, tuberculosis; mMRC, modified Medical Research Council scale; BMI, body mass index.

## DISCUSSION

In this population of urban dwellers from a major sub-Saharan African city, we found that about one in five adults had a low FVC, which was essentially driven by advanced age, history of pulmonary tuberculosis, prevalent heart diseases and underweight. These findings were largely robust to changes in criteria for defining low FVC. Since loss of respiratory functions, and particularly low FVC is important determinant of mortality risk in the general population [2 - 6, 8, 20], our findings indicate the importance of using the identified determinants to select from the general population, those who are more likely to be diagnosed with restrictive pattern, and to benefit from targeted risk factors control to mitigate the risk of adverse outcomes.

“Although to establish the diagnosis of lung restriction, a lung volume measurement is needed, we used the term restrictive spirometric pattern to design the population with a low FVC with a FEV1/FVC > lower limit of normal [LLN]” The prevalence of restrictive spirometric pattern in our study was higher than the 6.6% (fixed cut-off based) and 5.4% (LLN-based) reported respectively by Mannino *et al.*, and Kurth *et al.* in the general population in the USA, using data from the third National Nutrition and Health Examination Survey [8, 10]. Similarly, Scarlata *et al.* found a prevalence of 10.9% for restrictive pattern among elderly people in the general population in Italy [3], which was by far lower than the 43.2% found among the 60 years old and above in our sample. However, prevalence of restrictive pattern as higher as 74% has been reported among Aboriginal population, while it is around 9.7% in non-Aboriginal Australians [11]. In the study by Mannino *et al.* comprising people age 40 years and above from 14 sites across different continents who took part in the Burden of Obstructive Lung Disease (BOLD) study, the prevalence of restrictive pattern defined by a ratio FEV1/FVC ≥70% and a FVC<80% varied from 6.1% in Sydney (Australia) to 29.3% in Cape Town (South Africa) and 45.9% in Manilla (Philippines) [21]. Soriano *et al.* also found a point prevalence of 12.7% in subjects aged 40 years and above in Spain [22]. In the ≥40 years of age participants in our study, the prevalence of restrictive pattern was 24.2% (LLN-based) and 20.1% (fixed cut-off based), which is closer to the South African figures in BOLD [21]. Global variations in the prevalence of restrictive pattern can be explained by regional differences in the distribution of a number of factors including socio-economic conditions, prevalence of obesity and underweight, birth weight, and prevalence of restrictive lung diseases. However, that restrictive diseases are rather rare in the general population [23] suggests that they contribute less to the burden of restrictive pattern across published studies.

The prevalence of restrictive pattern was four times higher in the ≥ 60 years age group in our sample compared with those in the lower age stratum, and after adjustment for potential extraneous factors. The increasing prevalence of restrictive pattern with increasing age was very well characterized in the study by Mannino *et al.* where restrictive pattern was 2 to 2.5 times more frequent among the 50 years old and above compared with less older participants [9]. This is likely explained by the combined effect of several phenomena occurring with ageing which include deformation

of the axial skeleton, restrictive lung diseases and lung ageing.

History of tuberculosis was a significant determinant of restrictive pattern in our study. This has not been reported previously in studies conducted in western countries, likely due to the low incidence of tuberculosis in those settings. Restrictive functional sequels of tuberculosis are very common [24, 25], mostly reflecting the extent of the parenchymatous involvement during pulmonary tuberculosis [26]. Prevalent heart disease was also an independent determinant of restriction in our study. This result has not been reported in other studies [9], but Kurth *et al.* found a significant association between pulmonary restriction and cardiovascular diseases including congestive heart failure, stroke and heart attacks [10]. Cardiovascular diseases, when complicated with left heart failure can lead to pulmonary oedema, which in turn can reduce the vital capacity. Furthermore, heart diseases are often associated with cardiomegaly and muscle deconditioning, which are both associated with decreasing vital capacity [2, 9].

Obesity has been classically associated with functional restrictive lung involvements [27]. Considering that FVC is not in perfect agreement with the total lung capacity (TLC) which is used as gold standard to diagnose pulmonary restriction, it is possible that the non-association of obesity with restrictive pattern in our sample was a chance finding. Furthermore, the majority of obese participants in our sample had moderate obesity. However, underweight was associated with restrictive pattern, in line with the findings of the GOLD study [21]. These association could reflect some underlying conditions which are actually correlated with restrictive pattern. Furthermore, there are suggestions of an inverse relationship between birth weight (not assessed in our study) and lung functions [28].

The non-association of respiratory symptoms with restrictive pattern in our multivariable analyses reflects the correlation of those symptoms with other significant predictors of restrictive pattern, such as pulmonary tuberculosis and heart diseases. Diabetes and hypertension which have been reported to be associated with restrictive pattern [21] were not confirmed in our sample. It is of note however that statuses for diabetes and hypertension were based on self-report in a setting where under-diagnosis of those conditions is very common. The presence of a high number of undiagnosed diabetes and/or hypertension among those with negative history, which is very likely, can erase any true association.

The present study has some limitations. FVC alone is not sufficient to clinically diagnose pulmonary restriction, for which measurement of the TLC *via* plethysmography or gas dilution is required. While FVC has very good specificity and negative predictive value to diagnose pulmonary restriction, the sensitivity hardly crosses 75% [29 - 31]. However, measurement of TLC in community-based study is a very challenging undertaking, while FVC-diagnosed restrictive pattern has been reported to be correlated all-cause and cause-specific mortality [4, 6, 7, 9, 20]. Furthermore, it is possible that the high prevalence of restrictive pattern found in this study is related to a high proportion of false positive related to the definition of the restriction used. Also, the relatively frequent exposure to the biomass of the population studied can lead to the obstruction of the distal airways causing the decline in FVC. The study was cross-sectional; hence it is not possible to reliably establish the sequence of happening between outcome of interest and exposure to potential determinants. Otherwise, the exclusion of patients with incorrect spirometric maneuvers may have influenced the prevalence of restrictive pattern. Our study also has major strengths and in particular the large representative community based sample, which will improve the generalizability of our findings.

## CONCLUSION

Restrictive pattern was very frequent in this city.

## CLINICAL IMPLICATIONS

These results enhance the needs to increase the efforts to prevent and control tuberculosis, cardiovascular diseases and underweight in this setting.

## SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Website along with the published article.

## LIST OF ABBREVIATIONS

ATS/ERS	=	American Thoracic Society/European Respiratory
BMI	=	Body Mass Index

CI	=	Society
<b>BOLD</b>	=	Burden of Obstructive Lung Disease
CVD	=	Cardiovascular Disease
FEV1	=	Forced Expiratory Volume in First Second
FVC	=	Low Forced Vital Capacity
mMRC	=	Modified Medical Research Council Scale
SD	=	Standard Deviation
VC	=	Vital Capacity

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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