

# Prevalence and Associated Factors of Chronic Obstructive Pulmonary Disease Among Adults in Neno District, Malawi: A Cross-Sectional Analytical Study

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**Introduction:** Chronic obstructive pulmonary disease (COPD) continues to pose a global public health challenge. However, literature is scarce on the burden of COPD in Malawi. We assessed the prevalence and risk factors for COPD among adults in Neno, Malawi.

**Methodology:** We conducted a population-based analytical cross-sectional study in Neno District between December 2021 and November 2022. Using a multi-stage sampling technique, we included 525 adults aged  $\geq 40$  years. All participants underwent spirometry according to the American Thoracic Society (ATS) guidelines and were interviewed using the IMPALA questionnaire. For this study, we utilized the definition of COPD as a post-bronchodilator FEV1/FVC  $< 0.70$ . We collected data using Kobo collect, exported to Microsoft Excel, and analysed using R software. We used descriptive statistics and logistic regression analysis; a p-value of  $< 0.05$  was considered statistically significant.

**Results:** Out of 525 participants, 510 participants were included in the final analysis. Fifty-eight percent of the participants were females ( $n=296$ ), and 62.2% ( $n=317$ ) were between 40 and 49 years with a median (IQR) age of 46 (40–86). For patient characteristics, 15.1% ( $n=77$ ) were current smokers, and 4.1% ( $n=21$ ) had a history of pulmonary tuberculosis (PTB). Cough was the most commonly reported respiratory symptom ( $n=249$ , 48.8%). The prevalence of COPD was 10.0% ( $n=51$ ) and higher (15.0%) among males compared to females (6.4%). Factors significantly associated with COPD were age 60 years and above (adjusted odds ratio [aOR] = 3.27, 95% CI: 1.48–7.34,  $p < 0.004$ ), ever smoked (aOR = 6.17, 95% CI: 1.89–18.7,  $p < 0.002$ ), current smoker (aOR = 17.6, 95% CI: 8.47–38.4,  $p < 0.001$ ), and previous PTB (aOR = 4.42, 95% CI: 1.16–15.5,  $p < 0.023$ ).

**Conclusion:** The cross-sectional prevalence of COPD in rural Malawi is high, especially among males. Factors significantly associated were older age (60 years and above), cigarette smoking, and previous PTB. Longitudinal studies are needed to better understand disease etiology and progression in this setting.

**Keywords:** chronic obstructive pulmonary disease, prevalence, spirometry, associated factors, Malawi

## Introduction

Chronic obstructive pulmonary disease (COPD), which is among the chronic respiratory diseases (CRDs), is an increasing public health concern in Africa.<sup>1</sup> COPD affects 12% of the global population or 300 million people<sup>2</sup> and it is the 12th most prevalent cause of years of life lost globally<sup>3,4</sup> and the fourth leading cause of death.<sup>5</sup> The current 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines COPD as “a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.”<sup>6</sup> In low-income and middle-income countries (LMICs), non-communicable respiratory diseases are increasing among all age groups.<sup>7</sup> However, COPD has not been extensively studied and described in Malawi and other African countries.

Cigarette smoking is the most important risk factor for COPD.<sup>8</sup> In addition, exposure to biomass smoke, tuberculosis, severe childhood respiratory infections, malnutrition, poverty, occupational exposures, and chemical agents are associated with the increase in COPD burden in Africa.<sup>9–11</sup> Furthermore, occupational exposures, chemical agents, and fumes have been revealed to be unrecognized risk factors for the development of COPD.<sup>11</sup> Malnutrition and poverty are reported as other contributing risk factors for COPD in LMICs.<sup>9</sup> However, these factors are not adequately described, and more studies are needed, especially in rural areas.

There is a wide variation in the prevalence, morbidity, and mortality of COPD between and within countries.<sup>12</sup> The results of the Burden of Obstructive Pulmonary Disease (BOLD) study conducted in Johannesburg, South Africa, in 2007 revealed a COPD prevalence of 22.2% in men and 16.7% in women had a prevalence of COPD.<sup>13</sup> Between 2008–09, a survey conducted in urban and rural Rwanda found a COPD prevalence of 9.6% in people older than 45 years.<sup>14</sup> Another study in rural Uganda in 2012 reported that the prevalence of COPD using The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criterion in people older than 30 years was 16.2%.<sup>9</sup>

Malawi had an estimated population of approximately 22,245,431 in 2023, and more than 98% use biomass fuel as their primary source of household energy.<sup>15,16</sup> Diagnosing and treating non-communicable diseases (NCDs) at the district level is a challenge in Malawi due to limited health education on NCDs in the community, the number and expertise of healthcare staff, diagnostic equipment, and treatment. In 2016, a study conducted in an urban setting of the country involving individuals aged 18 years and older found a COPD prevalence of 4.3%.<sup>4</sup> More recently, a prospective cohort study conducted in Chikwawa, Malawi, found a 11.2% COPD prevalence.<sup>17</sup> Nevertheless, there remains a dearth of literature concerning COPD prevalence, particularly in rural areas in Malawi and other regions of sub-Saharan Africa. We conducted this study to assess the prevalence of COPD and the associated risk factors among adults in the Neno District, Malawi.

## Materials and Methods

### Study Design and Setting

We conducted a population-based analytical cross-sectional study in Neno District, Malawi. Neno has an estimated population of approximately 150,211 in 2023.<sup>18</sup> The district has 12 primary health centers and two secondary hospitals (Lisungwi Community and Neno District Hospitals). Most of the Neno District population are subsistence farmers who live on less than US\$ 1.90 daily and have little access to electricity.<sup>19</sup> Neno District Health Office with support from Partners In Health (PIH) Malawi implements an integrated chronic care program that includes treatment of CRDs including COPD.

### Study Population

We included all adults aged  $\geq 40$  years who were Neno District residents for greater than 6 months. Other studies done in Tanzania, Russia, and Iran used  $\geq 35$  years as a cutoff point,<sup>12,20,21</sup> while a BOLD study in 2007 used  $\geq 40$  years.<sup>13</sup> In our study, the age cut-off of 40 years was chosen because COPD prevalence, morbidity, and mortality increase with age. Lung function, which reaches its peak level in young adults, starts to decline in the third and fourth decades of life.<sup>22</sup> It has been found that tobacco smoking, which is the primary risk factor for COPD, commonly begins in adolescence with often 20–25 years of exposure to tobacco smoke to induce characteristic pathophysiologic changes of COPD in human lungs.<sup>23</sup> Exclusion criteria included all adults who had a current history of mental illness, those with confirmed active pulmonary tuberculosis or symptoms suggestive of active

tuberculosis, pregnant women, and anyone with contraindication to performing spirometry, eg, history of any cerebral, ophthalmic, thoracic, or abdominal surgery in the last 1 month, or severe heart disease, recent myocardial infarction (in the last 1 month), uncontrolled angina, current respiratory infection, recent history of pneumothorax, emboli or aneurysms.

## Sample Size and Sampling Method

The required sample size for this study was calculated using a statistical formula for single population proportion<sup>24,25</sup> by considering a 95% confidence interval, 4% level of precision, a design effect of 2, 11.2% prevalence of COPD<sup>17</sup> and 10% non-response rate. The final sample size was 525 participants.

We used a multi-stage sampling technique. Neno District is administratively divided into four Traditional Authorities (TAs), namely: Chekucheku with three Group Village Heads (GVHs), Dambe with five GVHs, Mlauli with eight GVHs, and Symon with four GVHs. The GVHs formed our primary sampling unit, and we purposefully selected 15 GVHs depending on the location that they were not adjacent. The selected GVHs had a total of 87 villages, which were secondary sampling units. We purposefully selected 20 villages depending on the location of the villages such that they were not adjacent to each other. The estimated number of households per village in Neno was around 90, which totalled 1800 households. We used systematic random sampling where we skipped every three or four houses depending on the settlement pattern to arrive at the house of interview. Finally, an individual in the selected households was our final sampling unit to reach the sample size of 525 participants. A simple random technique was used to select one individual aged 40 years and above in a household with more than one eligible study participant.

## Data Collection

We conducted face-to-face interviews using a validated International Multidisciplinary Programme to Address Lung Health and TB in Africa (IMPALA) questionnaire designed by the IMPALA network for use in sub-Saharan Africa.<sup>26</sup> This is a questionnaire that was developed by lung health experts for assessment of respiratory disease and risk factors in sub-Saharan Africa. The questionnaire included socio-demographic characteristics, respiratory symptoms, exposure to biomass and wood smoke, history of PTB, and history of cigarette smoking. We hired and trained two data collectors to ensure high-quality data and collected the data between December 2021 and November 2022 using Kobo Collect. Informed consent was obtained from all participants before the interview. After the interview, the study participants' body weight, height, and body mass index (BMI) were measured. The normal BMI value that was considered was 18.5–24.9

All participants underwent spirometry using a 3-L daily calibrated and Easy On-PC Spirometer (and Medical Device Depot, Ellicott, MD, USA) after a thorough explanation of the procedure by the research assistant in Chichewa, one of the official vernacular languages spoken in Neno district. Before performing each measurement, all participants were rested for at least 5 min. The test procedure was then clearly explained to all subjects. Spirometry was performed according to the American Thoracic Society (ATS) guidelines.<sup>27</sup> Each participant used their own mouth piece to prevent cross-infection. Each spirometry manoeuvre was repeated at least three times to meet reproducibility criteria, and the highest results from the best traces were reported. We regularly checked and calibrated the spirometers prior to each measurement.

All participants with a pre-bronchodilator FEV1/FVC < 0.7 took inhaled salbutamol (400 mcg) administered via a metered-dose inhaler, and then, post-bronchodilator spirometry was performed after 20 min. Those with irreversible obstruction (FEV1/FVC < 70% postbronchodilator) were classified as having COPD, while those with reversible obstruction and had symptoms suggestive of asthma were classified as asthmatic. The spirometry measurements that we used for analysis were forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC) and FEV1/FVC.

In this study, we defined COPD Diagnosis based on the GOLD definition, which states that a post-bronchodilator FEV1/FVC of less than 0.70 confirms the presence of persistent airflow limitation and identifies the presence of COPD in patients with appropriate symptoms and predisposing risks.<sup>11</sup> We used Quanjer (GLI), 2012 reference values.<sup>28</sup> We continually checked for data completeness and consistency. We transferred spirometry data into a password-protected computer. Each test result was graded and scored as A, B, C, or D, where grade A had >3 acceptable tests with repeatability within 0.150L, B had ≥2 acceptable tests with repeatability within 0.150L, C had ≥2 acceptable tests with repeatability within 0.200L, and D had ≥2 acceptable tests with repeatability within 0.250L.<sup>29</sup> We excluded low-quality spirometry results from the analysis. Three-spirometry measurements, namely FEV1, FVC, and FEV1/FVC, were considered for analysis.

## Data Analysis

We exported data from Kobo Collect to Microsoft Excel for data cleaning and analyzed using R 4.2.2 Software. We used descriptive statistics including median and interquartile range (IQR) for continuous variables and counts and percentages for categorical variables. We used the chi-square test for proportions, Fisher's exact, and Wilcoxon rank sum tests to test for differences between sex and categorical and continuous variables. We fitted a binary logistic regression to assess the association between COPD and independent variables, including age, sex, smoking, BMI, cooking area, house ventilation status, exposure to biomass, and history of PTB. House ventilation status was defined if the house had windows allowing airflow between outside and inside. Cooking area was defined as a space for cooking for the household outside the house, inside the house or in a separate shelter. We fitted multivariable logistic regression for all variables significantly associated with COPD at the bivariate level. We considered a p-value of less than 0.05 as statistically significant.

## Results

Of 525 participants, 510 had acceptable spirometry reports (grades A, B, or C) and were included in the final analysis. The median (IQR) age and BMI of the participants were 46 (42–57) years and 24.7kg/m<sup>2</sup>(22.2–27.6), respectively. Fifty-eight percent of participants were females (n=296). Most of the participants (62.2%, n=317) were between 40 and 49 years and 49.0% (n=250) had normal BMI with a significant difference between females and males (p<0.001). Farmers accounted for nearly half of the study (44.5%, n=227). We found that only 3.0% (n=9) of all women and 6.1% (n=13) of all men were former smokers. More men, 24.8% (n=53), were current smokers as compared to women 8.1% (n=24) with p<0.001. Similarly, of the total participants (27.8%, n=142) who drank alcohol, more men (38.8%) than women (19.9%) consumed (p<0.001). Cough was the main respiratory symptom (48.8%, n=249). Of the participants, 3.9% (n=20) had asthma and 4.1% (n=21) reported previous PTB with a statistical difference among men and women (p<0.012) (Table 1).

**Table 1** Sociodemographic, Behavioural, and Clinical Characteristics of the Study Participants

Characteristic	Females, n = 296 <sup>a</sup>	Males, n = 214 <sup>a</sup>	Overall, N = 510 <sup>a</sup>	p-value <sup>b</sup>
<b>Age</b>				>0.9
40–49	182 (61.5%)	135 (63.1%)	317 (62.2%)	
50–59	52 (17.6%)	37 (17.3%)	89 (17.5%)	
≥60	62 (20.9%)	42 (19.6%)	104 (20.4%)	
<b>Body mass index (kg/m<sup>2</sup>)</b>				<0.001
< 18.5	6 (2.0%)	10 (4.7%)	16 (3.1%)	
18.5–24.9	110 (37.2%)	140 (65.4%)	250 (49.0%)	
≥ 25	180 (60.8%)	64 (29.9%)	244 (47.8%)	
<b>Occupation</b>				<0.001
Business	25 (8.4%)	30 (14.0%)	55 (10.8%)	
Employed	26 (8.8%)	44 (20.6%)	70 (13.7%)	
Farmer	144 (48.6%)	83 (38.8%)	227 (44.5%)	
Not employed	101 (34.1%)	57 (26.6%)	158 (31.0%)	
<b>Smoking status</b>				<0.001

(Continued)

Table I (Continued).

Characteristic	Females, n = 296 <sup>a</sup>	Males, n = 214 <sup>a</sup>	Overall, N = 510 <sup>a</sup>	p-value <sup>b</sup>
Never smoker	263 (88.9%)	148 (69.2%)	411 (80.6%)	
Former smoker	9 (3.0%)	13 (6.1%)	22 (4.3%)	
Current smoker	24 (8.1%)	53 (24.8%)	77 (15.1%)	
Years smoked for both current and former smokers (median, IQR)	24 (15–37)	24 (15–34)	24 (15–35)	0.8
Total cigarette per day for both current and former smokers (median, IQR)	2 (2–3)	4 (3–5)	3 (2–5)	<b>&lt;0.001</b>
<b>Current consumer of alcohol</b>				<b>&lt;0.001</b>
Yes	59 (19.9%)	83 (38.8%)	142 (27.8%)	
<b>Biomass fuel exposure</b>				0.14
Yes	294 (99.3%)	212 (99%)	506 (99.2%)	
<b>Fuel used</b>				0.14
Dried wood	165 (55.7%)	137 (64.0%)	302 (59.2%)	
Charcoal	116 (39.2%)	64 (29.9%)	180 (35.3%)	
Crop residue/plant products	13 (4.4%)	11 (5.1%)	24 (4.7%)	
Electricity	2 (0.7%)	2 (0.9%)	4 (0.8%)	
<b>Cooking area</b>				0.6
Outside on Open Air	74 (25.0%)	46 (21.5%)	120 (23.5%)	
On Veranda	13 (4.4%)	12 (5.6%)	25 (4.9%)	
In the main house, in a separate room (used as a kitchen)	42 (14.2%)	24 (11.2%)	66 (12.9%)	
In the main house in the room used for living/sleeping	5 (1.7%)	4 (1.9%)	9 (1.8%)	
Outside of the main house, in a separate building	162 (54.7%)	128 (59.8%)	290 (56.9%)	
<b>House ventilation status</b>				0.7
Not ventilated	160 (54.1%)	119 (55.6%)	279 (54.7%)	
Ventilated	136 (45.9%)	95 (44.4%)	231 (45.3%)	
<b>Cough</b>				>0.9
Yes	144 (48.6%)	105 (49.1%)	249 (48.8%)	
<b>Phlegm</b>				0.3
Yes	46 (15.5%)	41 (19.2%)	87 (17.1%)	
<b>Wheezing</b>				<b>0.010</b>
Yes	17 (5.7%)	26 (12.1%)	43 (8.4%)	
<b>Asthma</b>				0.8
Yes	11 (3.7%)	9 (4.2%)	20 (3.9%)	
<b>Previous TB</b>				0.6
Yes	11 (3.7%)	10 (4.7%)	21 (4.1%)	

Notes: \*P-values in bold are statistically significant. <sup>a</sup>n (%). <sup>b</sup>Pearson's Chi-squared test; Fisher's exact test.

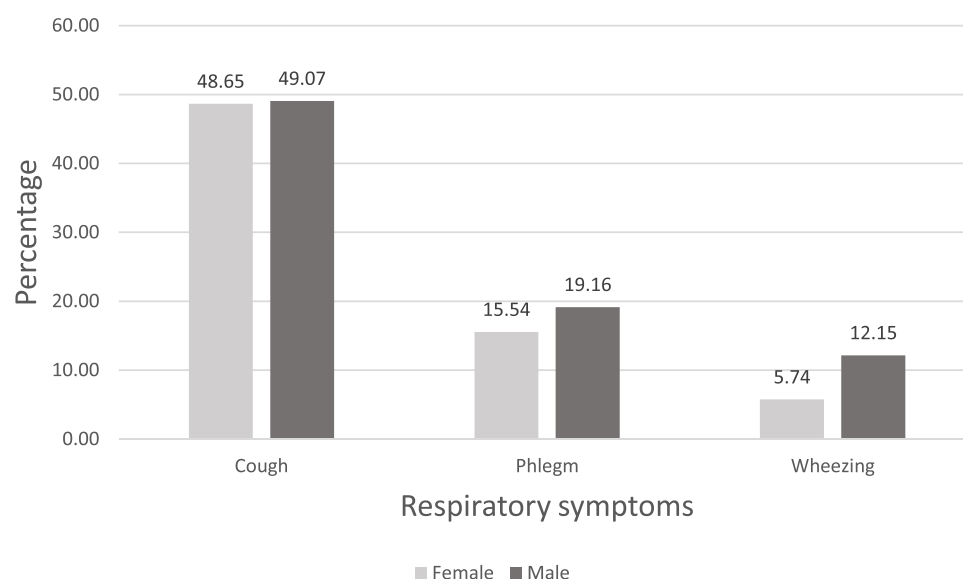
Based on post-bronchodilator assessment, the prevalence of COPD was 10.0% (n=51). The prevalence was higher in men, 15.0% (n=32), compared to women, 6.4% (n=19), and the difference was statistically significant ( $p=0.002$ ). According to GOLD criteria, 51.0% (26/51) of COPD patients had moderate COPD. Severe COPD was not found among any participants. Using the mMRC dyspnoea scale, we found that more than half of patients with COPD had no dyspnoea (Table 2).

**Table 2** COPD Severity and MRC Dyspnoea Score

Characteristic	Female n = 19 <sup>a</sup>	Male n = 32 <sup>a</sup>	Overall N = 51 <sup>a</sup>	p-value <sup>b</sup>
<b>COPD Severity</b>				0.055
Mild ( $FEV_1 \geq 80\%$ predicted)	6 (31.6%)	19 (59.4%)	25 (49.0%)	
Moderate ( $FEV_1$ 50–79%)	13 (68.4%)	13 (40.6%)	26 (51.0%)	
Severe ( $FEV_1$ 30–49%)	0 (0)	0 (0)	0 (0)	
<b>MRC_dyspnoea_score</b>				
0	16 (84.2%)	21 (65.6%)	37 (72.5%)	
1	3 (15.8%)	6 (18.8%)	9 (17.6%)	
2	0 (0.0%)	4 (12.5%)	4 (7.8%)	
3	0 (0.0%)	1 (3.1%)	1 (2.0%)	
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	

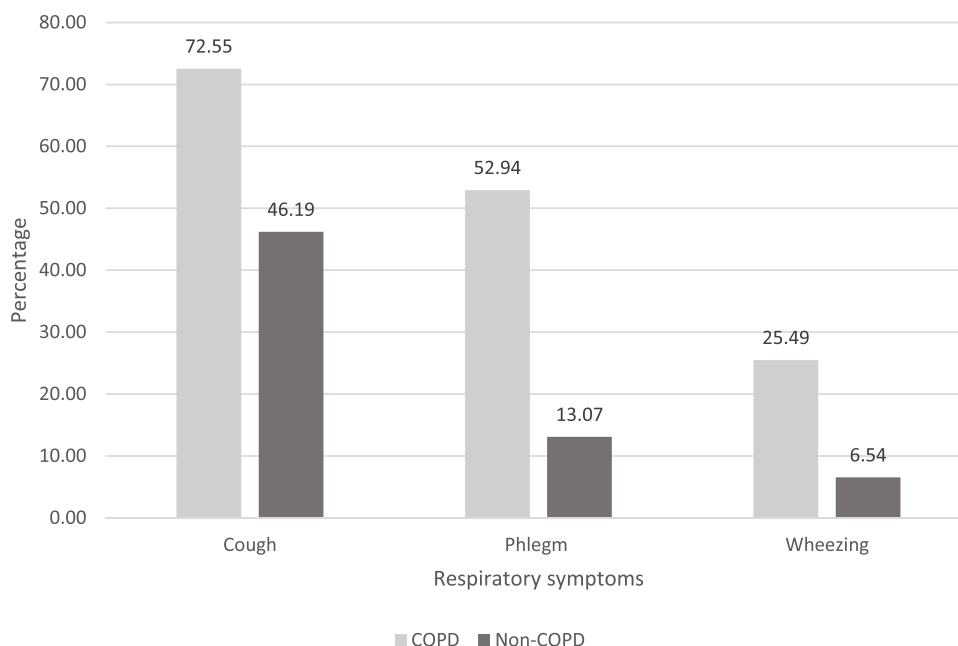
Notes: <sup>a</sup>n (%). <sup>b</sup>Pearson's Chi-squared test.

We found no significant differences between males and females with regard to cough and phlegm (all  $p > 0.05$ ), however, there was statistical difference in regard to wheezing ( $p < 0.010$ ) (Figure 1).



**Figure 1** Respiratory symptoms distribution by sex.

We found that the prevalence of respiratory symptoms (cough, phlegm, and wheeze) was significantly higher in participants with COPD as compared to those without (all  $p < 0.001$ ) (Figure 2).



**Figure 2** Prevalence of respiratory symptoms in participants with and without COPD.

## COPD Associated Factors

We found an association between the occurrence of COPD and age, sex, smoking status, and previous pulmonary TB. No association was observed between COPD, body mass index, cooking area, and kitchen ventilation status ( $p > 0.05$ ). The odds of developing COPD among people aged 60 and above were 3.19 times higher than those aged 40–49 ( $p < 0.001$ , Table 3). The odds of COPD were significantly higher among males than females (OR=2.56, 95% CI [1.42–4.74],  $p = 0.002$ ). In comparison to those who never smoked, the odds of developing COPD were higher among those who ever smoked and are currently smoking (OR=10.6, 95% CI [3.41–30.5],  $p < 0.001$  and OR=19.1, 95% CI [9.66–39.6],  $p < 0.001$ , respectively). For participants who had previous PTB, the odds of developing COPD increased by 3.95 times compared to those who have never suffered from TB (OR=3.95, 95% CI [1.35–10.2],  $p < 0.007$ ). We found that 99.2% of the participants were exposed to biomass fuel, of which 59.2% used dry wood, 35.3% used charcoal, 4.7% used crop residue/plant products, and 0.8% used electricity as the main source of cooking energy and heating (Table 1). We did not have sufficient power to assess the association between biomass exposure and COPD since 99.2% of the participants were exposed to biomass fuel.

**Table 3** Factors Associated with COPD

Variable	Bivariate logistic regression			Multivariate Logistic Regression		
	OR	95% CI	p-value	aOR	95% CI	p-value
BMI						
<18.5	Reference					
18.5–24.9	0.61	0.18–2.78	0.5			
≥25	0.32	0.09–1.51	0.10			
Cooking area						
Outside	Reference					

(Continued)



**Table 3** (Continued).

Variable	Bivariate logistic regression			Multivariate Logistic Regression		
	OR	95% CI	p-value	aOR	95% CI	p-value
Same building	1.45	0.51–3.86	0.5			
Separate building	1.51	0.76–3.22	0.3			
<b>House ventilation status</b>						
Not ventilated	Reference					
Ventilated	0.91	0.50–1.62	0.7			
Years Smoked	1.02	0.99–1.05	0.2			
Asthma						
No	Reference					
Yes	0.46	0.03–2.31	0.5			
<b>Gender</b>						
Female	Reference					
Male	2.56	1.42–4.74	<b>0.002</b>	1.37	0.67–2.80	0.4
<b>Age (in years)</b>						
40–49	Reference					
50–59	1.51	0.64–3.31	0.300	1.80	0.69–4.47	0.2
60 and above	3.19	1.65–6.14	<b>&lt;0.001</b>	3.27	1.48–7.34	<b>0.004</b>
<b>Smoking status</b>						
Never smoked	Reference					
Ever smoked	10.6	3.41–30.5	<b>&lt;0.001</b>	6.17	1.89–18.7	<b>0.002</b>
Current Smoker	19.1	9.66–39.6	<b>&lt;0.001</b>	17.6	8.47–38.4	<b>&lt;0.001</b>
<b>Previous TB</b>						
No	Reference					
Yes	3.95	1.35–10.2	<b>0.007</b>	4.42	1.16–15.5	<b>0.023</b>

Note: \*P-values in bold are statistically significant.

On multivariate logistic regression analysis, the odds of COPD were significantly higher among participants aged 60 years and above (aOR=3.27, 95% CI [1.48–7.34],  $p=0.004$ ). The odds of COPD were significantly higher among ever-smoked and currently smoking (aOR=6.17, 95% CI [1.89–18.7],  $p=0.002$  and aOR=17.6, 95% CI [8.47–38.4],  $p<0.001$ , respectively). The adjusted odds of developing COPD were 4.42 times compared to those with no previous TB (aOR = 4.42, 95% CI [1.16–15.5],  $p<0.023$ ), as shown in Table 3. No association was observed between COPD and exposure to biomass, cooking area, and kitchen ventilation status ( $p>0.05$ ).

## Discussion

Despite several risk factors for COPD, such as biomass fuel exposure and TB infection in sub-Saharan Africa, there are few epidemiological and community-based spirometry studies to identify patients with COPD. To develop future preventative and management measures, community-based research with case finding methodologies and identification of prevalence is required to ascertain the epidemiology of COPD.<sup>30</sup> This cross-sectional study is aimed at determining the prevalence and associated factors among adults in Neno District, Malawi. This study provides knowledge on COPD epidemiology. We found a 10.0% COPD prevalence among adults aged 40 and above. Older age, smoking, and previous PTB were associated with COPD, with cough being the most reported respiratory symptom.

The COPD prevalence of 10.0% (6.4% in females and 15.0% in males) was based on the post-bronchodilator FEV1/FVC < 70 criteria.<sup>6</sup> This criterion was chosen despite shortfalls in the under-diagnosis of COPD among those under 40 years and over-diagnosis among those over 60 years.<sup>31,32</sup> The COPD prevalence we found is similar to the systematic review by Awokola et al, who found that COPD prevalence in sub-Saharan Africa ranges from 1.7% to 24.8%.<sup>33</sup> It is also similar to the overall COPD prevalence in high-income countries (HICs), which was found to be at 10.1% even though countries in LMICs have reported high COPD prevalence compared to HICs.<sup>34</sup> We found a relatively higher prevalence



than another study done in a rural district of Malawi, Chikwawa, which saw an 8.7% prevalence.<sup>35</sup> However, our prevalence was significantly different as compared to other studies done in other African countries such as Ethiopia, which found a prevalence of 17.80%, Tanzania at 17.5%, Uganda at 16.2%, South Africa at 8.5%, Nigeria at 9.2%, and Uganda at 2%.<sup>9,30,36–39</sup> The variation in the prevalence of COPD across countries could be due to differences in study population, study design, and criteria used for COPD diagnosis.<sup>33</sup> Even though there are variations in the prevalence of COPD in Africa, the use of spirometry in confirming COPD is very rare in sub-Saharan Africa, and this could imply that COPD might be underreported.<sup>40</sup> Therefore, there is a need for health facilities to have spirometry services so that patients with COPD are appropriately diagnosed.

We found that more males had COPD compared to females. Similar findings have also been reported elsewhere.<sup>34,36,41,42</sup> Our study has shown that participants 60 years and above had increased odds of developing COPD. This finding is consistent with other studies.<sup>43–45</sup> The increased exposure to risk factors and the physiological decline in respiratory function that occurs with aging may be responsible for the link between COPD and old age.<sup>45–48</sup> We also found that participants with previous pulmonary tuberculosis were four times higher at risk of developing COPD than those without. A systematic review and meta-analysis by Fan et al<sup>49</sup> and other studies have reported similar findings that a history of PTB is a risk factor for COPD.<sup>50–53</sup> Even though the exact mechanism of developing COPD in post-tuberculosis patients is not clear, a mechanism that includes bronchiectasis, bronchiolar narrowing, bronchiolitis obliterans, and accelerated emphysematous changes was proposed in a systematic review by Allwood et al.<sup>54</sup> This positive association between previous PTB history and COPD calls for integrating COPD and PTB management guidelines. It should be placed on the public health policy agenda to improve early COPD detection and treatment among people with a history of PTB.

Our study found that former and current smokers had increased odds of developing COPD compared to non-smokers, as supported by the literature and a known risk factor.<sup>9,30,34,36,37,41</sup> Consistent with other studies,<sup>9,55,56</sup> men smoked more and for longer than women in our study. However, we found a relatively low prevalence (15.1%) compared to a study from Tanzania, which found a prevalence of smoking at 25.2% (32), and also in comparison with HIC, such as Canada, reporting a prevalence of 40%.<sup>57</sup> Even though smoking prevalence trends in Africa are low compared to other regions,<sup>58</sup> smoking poses a greater risk for respiratory conditions such as COPD. Malawi is one of the countries whose economy depends on tobacco (55); there is a need for increased investments in smoking cessation programs, cigarette price regulation, and tobacco control laws.<sup>59–61</sup>

We found a prevalence of asthma of 3.9%. This prevalence is similar to a cohort study of Malawian adults in rural Chikwawa conducted by Njoroge et al 2021 who found a 2.6% prevalence of asthma in 2014 and 3.7% in 2019.<sup>62</sup> Despite being a longitudinal study, it is similar to our study firstly because it was also a community-based study in a rural setting and secondly, they used spirometry to measure lung function. Similarly, a study conducted in a suburban Nigerian town found a 3.2% prevalence, but overall there is a paucity of research on asthma prevalence in sub-Saharan Africa. Whereas, asthma has been documented as a risk factor for the development of COPD,<sup>6,63</sup> we did not find any association between asthma and COPD in this study with only one participant having asthma and COPD overlap (ACO). Patients with ACO are being recognised as having a unique subset of obstructive lung disease.<sup>64</sup> A study conducted in 2017 in two districts of Malawi found one person with ACO.<sup>65</sup> Morgan et al 2019 found ACO prevalence of 3.8% in LMICs.<sup>66</sup> A systematic review and meta-analysis on global prevalence of ACO in general population found 2.0% (95% CI: 1.4–2.6%), 26.5% (95% CI: 19.5–33.6%) among patients with asthma, and 29.6% (95% CI: 19.3–39.9%) among patients with COPD.<sup>67</sup> However, we did not find this high prevalence in COPD patients in Neno District with further study warranted.

In our study, most participants (99.2%) reported having biomass fuel as their main fuel source. On the one hand, several epidemiological studies have found associations between biomass smoke exposure and COPD with odds ratios of 2 or more.<sup>68–71</sup> On the other hand, other studies, including the BOLD study and others done in Malawi, found no association between airflow obstruction and exposure to biomass.<sup>4,35,72</sup> For this study, the sample size was not powered to determine the differences between the cases and the comparison group due to the high use of biomass fuel. Further research, preferably through a prospective intervention, is required. Previous research demonstrates that biomass smoke-related COPD has different pathologies compared to cigarette-related COPD, suggesting different phenotypes from the two risk factors.<sup>73</sup> Studies have indicated biomass fuel exposure is associated with less emphysema but more air trapping than tobacco smoke exposure, implying hyperinflation with biomass smoke-related COPD.<sup>74</sup> This indicates a higher

Residual Volume (RV), Total Lung Capacity (TLC), and RV:TLC ratio<sup>75</sup> in these patients. In our study, we could not differentiate between phenotypes as we were not able to report TLC and RV. However, we believe that there would be more biomass phenotype due to the biomass exposure in almost all participants.

Our study had several limitations. Firstly, since this was a cross-sectional study, it could not establish a cause–effect relationship. Secondly, our study was conducted in a particular setting of Malawi. As such, the results might not be generalised to the entire country. However, over 80% of Malawians live in rural areas like Neno District and use biomass fuel. This enhances generalizability for similar settings. Thirdly, this study was done during the COVID-19 pandemic with a high stigma associated with respiratory diseases and vaccination.<sup>76</sup> This may have led to some potential participants hiding from the study team despite a high number of consenting for participation in the study, leading to a biased sample. However, the findings are consistent with studies outside the COVID-19 pandemic<sup>9,30,35–39,43</sup> except for no diagnosis of severe COPD, suggesting that any bias did not significantly alter the results. Fourthly, we used a fixed FEV1:FVC ratio to define COPD, which could result in over-diagnosis among older people and under-diagnosis among young adults.

Furthermore, we know that tuberculosis is underdiagnosed in Malawi, and it is possible that underlying TB could either exacerbate COPD or be misdiagnosed as COPD in this study.<sup>77</sup> Finally, we did not find a study participant with severe COPD, which may be due to the low prevalence of smoking or sampling bias. Further studies in Malawi and Neno District are required for broader sampling techniques and comparisons of diverse populations.

Despite these limitations, our study has strengths. This was a community survey with a large sample size that had adequate power to study COPD prevalence and associated factors with using community spirometry for diagnosis. It provides important data for risk factors, the diagnosis, and management of COPD in Malawi.

## Conclusion

We found a high prevalence of COPD in rural Malawian communities with increasing age, smoking, and previous PTB risk factors. Additional longitudinal studies are needed to better understand the disease's progression and other risk factors, such as biomass exposure. Early detection and management of COPD should be considered a public health priority. We urge the Ministry of Health and other stakeholders to promote and enforce tobacco control laws, smoking cessation initiatives, and follow-up of post-TB patients to detect and improve COPD management.

## Abbreviations

COPD, chronic obstructive pulmonary disease; ATS, American Thoracic Society; PTB, pulmonary tuberculosis; CRDs, chronic respiratory diseases; LMICs, low-income and middle-income countries; BOLD, The Burden of Obstructive Pulmonary Disease; GOLD, The Global Initiative for Chronic Obstructive Lung Disease; NCDs, Non-communicable diseases; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; PIH/APZU, Partners In Health/Abwenzi Pa za Umoyo; T/As, Traditional Authorities; GVHs, Group Village Heads; BMI, Body mass index; Interquartile range (IQR); KUHeS, Kamuzu University of Health Sciences.

## Data Sharing Statement

The data presented in this study are available on request from the corresponding author.

## Ethical Approval and Informed Consent

The protocol was approved by the Neno District Health Research Committee and College of Medicine Research and Ethics Committee (COMREC) (P.08/20/3110). Written informed consent was obtained from study participants. The study was conducted in accordance with the Declaration of Helsinki.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## References

- Adeloye D, Basquill C, Papana A, Chan KY, Rudan I, Campbell H. An Estimate of the Prevalence of COPD in Africa: a Systematic Analysis. *COPD*. 2015;44(1):71–81. doi:10.3109/15412555.2014.908834
- Ruvuna L, Sood A. Epidemiology of Chronic Obstructive Pulmonary Disease. *Clin Chest Med*. 2020;41(3):315–327. doi:10.1016/j.ccm.2020.05.002
- Sti TA. Effect of education on self-efficacy of Turkish patients with chronic obstructive pulmonary disease. *Patient Educ Counseling*. 2004;55:114–120. doi:10.1016/j.pec.2003.08.006
- Meghji J, Nadeau G, Davis KJ, et al. Noncommunicable lung disease in sub-Saharan Africa a community-based cross-sectional study of adults in urban Malawi. *Am J Respir Crit Care Med*. 2016;194(1):67–76. doi:10.1164/rccm.201509-1807OC
- WHO. Chronic obstructive pulmonary disease (COPD). Available from: [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)). Accessed July 21, 2023.
- Agusti A, Celli BR, Criner GJ, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Eur Respir J*. 2023;61(4):2300239. doi:10.1183/13993003.00239-2023
- Beran D, Zar HJ, Perrin C, Menezes AM, Burney P. Burden of asthma and chronic obstructive pulmonary disease and access to essential medicines in low-income and middle-income countries. *Lancet Respir Med*. 2015;3(2):159–170. doi:10.1016/S2213-2600(15)00004-1
- Rennard SI, Drummond MB. Early chronic obstructive pulmonary disease: definition, assessment, and prevention. *Lancet*. 2015;385(9979):1778–1788. doi:10.1016/S0140-6736(15)60647-X
- Gemert FV, Kirenga B, Chavannes N, et al. Prevalence of chronic obstructive pulmonary disease and associated risk factors in Uganda (FRESH AIR Uganda): a prospective cross-sectional observational study. *Lancet Glob Health*. 2015;3(1):e44–e51. doi:10.1016/S2214-109X(14)70337-7
- van Gemert F, van der Molen T, Jones R, Chavannes N. The impact of asthma and COPD in sub-Saharan Africa. *Prim Care Respir J*. 2011;20(3):240–248. doi:10.4104/pcrj.2011.00027
- Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report GOLD Executive Summary. *Am J Respir Critical Care Med*. 2017;195(5):557–582. doi:10.1164/rccm.201701-0218PP
- Bahtouee M, Maleki N, Nekouee F. The prevalence of chronic obstructive pulmonary disease in hookah smokers. *Patient Educ Counseling*. 2018;7. doi:10.1177/1479972317709652
- Buist AS, Mcburnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study. *Lancet*. 2007;370(9589):741–750. doi:10.1016/S0140-6736(07)61377-4
- Musafiri S, Meerbeek JV, Musango L, et al. Prevalence of atopy, asthma and COPD in an urban and a rural area of an African country. *Respir Med*. 2011;105(11):1596–1605. doi:10.1016/j.rmed.2011.06.013
- National Statistical Office. [http://www.nsomalawi.mw/index.php?option=com\\_content&view=article&id=134%3Apopulation-projections-for-malawi&catid=8&Itemid=3](http://www.nsomalawi.mw/index.php?option=com_content&view=article&id=134%3Apopulation-projections-for-malawi&catid=8&Itemid=3) Accessed 25 January, 2024.
- Counted BE, No L, Behind ONE. 2018 Malawi Population And Housing Census. Lilongwe: Malawi National Statistics Office; 2019.
- Rylance S, Jewell C, Naunje A, et al. communicable respiratory disease and air pollution exposure in Malawi: a prospective cohort study. *Thorax*. 2020;75(3):220–226. doi:10.1136/thoraxjnl-2019-213941
- National Statistical Office. *Population Projections 2018-2050*. 2020:1–276

19. The DHS Program - Malawi: DHS, 2015-16 - Final Report (English). Available from: <https://dhsprogram.com/publications/publication-fr319-dhs-final-reports.cfm>. Accessed September 27, 2023.
20. Magitta F, Walker RW, Apte K, et al. Prevalence, Risk Factors and Clinical Correlates of COPD in a Rural Setting in Tanzania. *Eur Respir J*. 2018;51. doi:10.1183/13993003.00182-2017
21. Andreeva E, Lebedev A, Lebedev A, Moiseeva I, Kutznetsova O, Degryse J-M. The Prevalence of Chronic Obstructive Pulmonary Disease by the Global Lung Initiative Equations in North-Western Russia. *Respir Int Rev Thoracic Dis*. 2016;91(1):43–55. doi:10.1159/000442887
22. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*. 2007;370:763.
23. Rajkumar P, Pattabi K, Vadivoo S, et al. A cross-sectional study on prevalence of chronic obstructive pulmonary disease (COPD) in India: rationale and methods. *Lancet*. 2017;1–6. doi:10.1136/bmjopen-2016-015211
24. Ermatology D, Martínez-Mesa J, González-chica DA, Duquia RP, Duquia RP. Sample size: how many participants do I need in my research?\*. *Anais brasileiros de dermatologia*. 2014;89(4):609–615. doi:10.1590/abd1806-4841.20143705
25. Charan J, Biswas T. Review Article How to Calculate Sample Size for Different Study Designs in Medical Research? *Indian J Psychological Med*. 2013;35(2):121–126. doi:10.4103/0253-7176.116232
26. Saleh S, van Zyl-Smit R, Allwood B, et al. Questionnaires for Lung Health in Africa across the Life Course. *Int J Environ Res Public Health*. 2018;15(8):1615. doi:10.3390/ijerph15081615
27. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *The European Respiratory Journal*. 2005;26(2):319–338. doi:10.1183/09031936.05.00034805
28. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. *Eur Respir J*. 2012;40(6):1324–1343. doi:10.1183/09031936.00080312
29. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med*. 2019;200(8):e70–e88. doi:10.1164/rccm.201908-1590ST
30. Woldeamanuel GG, Mingude AB, Geta TG. Prevalence of chronic obstructive pulmonary disease (COPD) and its associated factors among adults in Abeshge District, Ethiopia: a cross sectional study. *BMC Pulm Med*. 2019;19(1):181. doi:10.1186/s12890-019-0946-z
31. Hnizdo E, Glindmeyer HW, Petsonk EL, Enright P, Buist AS. Case definitions for chronic obstructive pulmonary disease. *COPD*. 2006;3(2):95–100. doi:10.1080/15412550600651552
32. Vollmer WM, Gislason T, Burney P, et al. Comparison of spirometry criteria for the diagnosis of COPD: results from the BOLD study. *Eur Respir J*. 2009;34(3):588–597. doi:10.1183/09031936.00164608
33. Awokola BI, Amusa GA, Jewell CP, et al. Chronic obstructive pulmonary disease in sub-Saharan Africa. *Int J Tuberc Lung Dis off J Int Union Tuberc Lung Dis*. 2022;26(3):232–242. doi:10.5588/ijtld.21.0394
34. Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *Lancet Respir Med*. 2022;10(5):447–458. doi:10.1016/S2213-2600(21)00511-7
35. Nightingale R, Lesosky M, Flitz G, et al. Noncommunicable Respiratory Disease and Air Pollution Exposure in Malawi (CAPS). A Cross-Sectional Study. *Am J Respir Crit Care Med*. 2019;199(5):613–621. doi:10.1164/rccm.201805-0936OC
36. Magitta NF, Walker RW, Apte KK, et al. Prevalence, risk factors and clinical correlates of COPD in a rural setting in Tanzania. *Eur Respir J*. 2018;51(2):1700182. doi:10.1183/13993003.00182-2017
37. Adhikari TB, Acharya P, Högman M, et al. Prevalence of Chronic Obstructive Pulmonary Disease and its Associated Factors in Nepal: findings from a Community-based Household Survey. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2319–2331. doi:10.2147/COPD.S268110
38. Ale BM, Ozoh OB, Gadanya MA, et al. Estimating the prevalence of COPD in an African country: evidence from southern Nigeria. *J Glob Health Rep*. 2022;6:e2022049. doi:10.29392/001c.38200
39. North CM, Kakuhihire B, Vor D, et al. Prevalence and correlates of chronic obstructive pulmonary disease and chronic respiratory symptoms in rural southwestern Uganda: a cross-sectional, population-based study. *Int J Med*. 2019;9(1):1–11. doi:10.7189/jogh.09.010434
40. Halpin DMG, Celli BR, Criner GJ, et al. The GOLD Summit on chronic obstructive pulmonary disease in low- and middle-income countries. *Int J Tuberc Lung Dis*. 2019;23(11):1131–1141. doi:10.5588/ijtld.19.0397
41. Menezes A, Jardim J, Perez Padilla R, et al. Prevalence of chronic obstructive pulmonary disease and associated factors: the PLATINO Study in São Paulo, Brazil. *Cad Saúde Pública Minist Saúde Fundação Oswaldo Cruz Esc Nac Saúde Pública*. 2005;21:1565–1573. doi:10.1590/S0102-311X2005000500030
42. Ntritsos G, Franek J, Belbasis L, et al. Gender-specific estimates of COPD prevalence: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis*. 2018;13:1507–1514. doi:10.2147/COPD.S146390
43. Sutradhar I, Das Gupta R, Hasan M, Wazib A, Sarker M. Prevalence and Risk Factors of Chronic Obstructive Pulmonary Disease in Bangladesh: a Systematic Review. *Cureus*. 2019;11(1):e3970. doi:10.7759/cureus.3970
44. Alam DS, Chowdhury MA, Siddiquee AT, Ahmed S, Clemens JD. Prevalence and Determinants of Chronic Obstructive Pulmonary Disease (COPD) in Bangladesh. *COPD J Chronic Obstr Pulm Dis*. 2015;12(6):658–667. doi:10.3109/15412555.2015.1041101
45. Nugmanova D, Feshchenko Y, Iashyna L, et al. The prevalence, burden and risk factors associated with chronic obstructive pulmonary disease in Commonwealth of Independent States (Ukraine, Kazakhstan and Azerbaijan): results of the CORE study. *BMC Pulm Med*. 2018;18(1):26. doi:10.1186/s12890-018-0589-5
46. Mannino DM, Davis KJ. Lung function decline and outcomes in an elderly population. *Thorax*. 2006;61(6):472–477. doi:10.1136/thx.2005.052449
47. Ito K, Barnes PJ. COPD as a Disease of Accelerated Lung Aging. *Chest*. 2009;135(1):173–180. doi:10.1378/chest.08-1419
48. Raheerison C, Girodet PO. Epidemiology of COPD. *Eur Respir Rev*. 2009;18(114):213–221. doi:10.1183/09059180.00003609
49. Fan H, Wu F, Liu J, et al. Pulmonary tuberculosis as a risk factor for chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Ann Transl Med*. 2021;9(5):390. doi:10.21037/atm-20-4576
50. Yakar HI, Gunen H, Pehlivan E, Aydoğan S. The role of tuberculosis in COPD. *Int J Chron Obstruct Pulmon Dis*. 2017;12:323–329. doi:10.2147/COPD.S116086
51. Lee CH, Lee MC, Lin HH, et al. Pulmonary Tuberculosis and Delay in Anti-Tuberculous Treatment Are Important Risk Factors for Chronic Obstructive Pulmonary Disease. *PLoS One*. 2012;7(5):e37978. doi:10.1371/journal.pone.0037978



52. Lam H, Jiang CQ, Jordan RE, et al. Prior TB, Smoking, and Airflow Obstruction: a Cross-Sectional Analysis of the Guangzhou Biobank Cohort Study. *Chest*. 2010;137(3):593–600. doi:10.1378/chest.09-1435
53. Guo Y, Xing Z, Shan G, et al. Prevalence and Risk Factors for COPD at High Altitude: a Large Cross-Sectional Survey of Subjects Living Between 2100–4700 m Above Sea Level. *Front Med*. 2020;7. doi:10.3389/fmed.2020.581763
54. Allwood BW, Myer L, Bateman ED. A systematic review of the association between pulmonary tuberculosis and the development of chronic airflow obstruction in adults. *Respir Int Rev Thorac Dis*. 2013;86(1):76–85. doi:10.1159/000350917
55. Daldoul H, Denguezli M, Jithoo A, et al. Prevalence of COPD and tobacco smoking in Tunisia--results from the BOLD study. *Int J Environ Res Public Health*. 2013;10(12):7257–7271. doi:10.3390/ijerph10127257
56. Global Tobacco Control Information & Statistics I Tobacco Atlas. Tobacco Atlas. Available from: <https://tobaccoatlas.org/>. Accessed July 18, 2023.
57. Bird Y, Moraros J, Mahmood R, Esmaeizadeh S, Kyaw Soe NM. Prevalence and associated factors of COPD among Aboriginal peoples in Canada: a cross-sectional study. *Int J Chron Obstruct Pulmon Dis*. 2017;12:1915–1922. doi:10.2147/COPD.S138304
58. WHO global report on trends in prevalence of tobacco use 2000-2025, third edition. Available from: <https://www.who.int/publications-detail-redirect/who-global-report-on-trends-in-prevalence-of-tobacco-use-2000-2025-third-edition>. Accessed July 18, 2023.
59. Kadzamia MA, Gausi HJ, Phiri T. The socio-economic impact of disease burden due to smoking in Malawi. 2021.
60. Vellios N, Ross H, Perucic AM. Trends in cigarette demand and supply in Africa. *PLoS One*. 2018;13(8):e0202467. doi:10.1371/journal.pone.0202467
61. Peer N. Current strategies are inadequate to curb the rise of tobacco use in Africa. *S Afr Med J*. 2018;108(7):551. doi:10.7196/SAMJ.2018.v108i7.12978
62. Njoroge MW, Mjojo P, Chirwa C, et al. Changing lung function and associated health-related quality-of-life: a five-year cohort study of Malawian adults. *eClinicalMedicine*. 2021;41:101166. doi:10.1016/j.eclinm.2021.101166
63. Asamoah-Boaheng M, Acheampong L, Tenkorang EY, Farrell J, Oyet A, Midodzi WK. Association between early history of asthma and COPD diagnosis in later life: a systematic review and meta-analysis. *Int J Epidemiol*. 2018;47(6):1865–1876. doi:10.1093/ije/dyy207
64. Mart MF, Peebles RS. Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome. *Curr Opin Immunol*. 2020;66:161–166. doi:10.1016/j.coi.2020.10.006
65. Banda HT, Thomson R, Mortimer K, et al. Community prevalence of chronic respiratory symptoms in rural Malawi: implications for policy. *PLoS One*. 2017;12(12):1–13. doi:10.1371/journal.pone.0188437
66. Morgan BW, Grigsby MR, Siddharthan T, et al. Epidemiology and risk factors of asthma-chronic obstructive pulmonary disease overlap in low- and middle-income countries. *J Allergy Clin Immunol*. 2019;143(4):1598–1606. doi:10.1016/j.jaci.2018.06.052
67. Hosseini M, Almasi-Hashiani A, Sepidarkish M, Maroufizadeh S. Global prevalence of asthma-COPD overlap (ACO) in the general population: a systematic review and meta-analysis. *Respir Res*. 2019;20(1):229. doi:10.1186/s12931-019-1198-4
68. Awokola BI, Amusa GA, Jewell C, et al. Chronic Obstructive Pulmonary Disease (COPD) in Sub-Saharan Africa: a Systematic Review and Meta-Analysis. In: *TP65. TP065 ENVIRONMENTAL EXPOSURES AND LUNG DISEASE*. American Thoracic Society; 2021:A3133–A3133. doi:10.1164/ajrcm-conference.2021.203.1\_MeetingAbstracts.A3133.
69. Hu G, Zhou Y, Tian J, et al. Risk of COPD From Exposure to Biomass Smoke: a Metaanalysis. *Chest*. 2010;138(1):20–31. doi:10.1378/chest.08-2114
70. Pathak U, Gupta NC, Suri JC. Risk of COPD due to indoor air pollution from biomass cooking fuel: a systematic review and meta-analysis. *Int J Environ Health Res*. 2020;30(1):75–88. doi:10.1080/09603123.2019.1575951
71. Viramgami A, Sheth A, Bagepally BS, Balachandrar R. Study on the Association between Domestic Biomass Fuel Exposure and Pulmonary Function: a Systematic Review and Meta-Analysis. *SSRN Electronic Journal*. 2022. doi:10.2139/ssrn.4267517
72. Amaral AFS, Patel J, Kato BS, et al. Airflow Obstruction and Use of Solid Fuels for Cooking or Heating: BOLD Results. *Am J Respir Crit Care Med*. 2018;197(5):595–610. doi:10.1164/rccm.201701-0205OC
73. Ortiz-Quintero B, Martínez-Espinosa I, Pérez-Padilla R. Mechanisms of Lung Damage and Development of COPD Due to Household Biomass-Smoke Exposure: inflammation, Oxidative Stress, MicroRNAs, and Gene Polymorphisms. *Cells*. 2023;12(1):67. doi:10.3390/cells12010067
74. Camp PG, Ramirez-Venegas A, Sansores RH, et al. COPD phenotypes in biomass smoke versus tobacco smoke-exposed Mexican women. *Eur Respir J*. 2014;43(3):725–734. doi:10.1183/09031936.00206112
75. D'Ascanio M, Viccaro F, Calabrò N, et al. Assessing Static Lung Hyperinflation by Whole-Body Plethysmography, Helium Dilution, and Impulse Oscillometry System (IOS) in Patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2583–2589. doi:10.2147/COPD.S264261
76. Aron MB, Connolly E, Vrkljan K, et al. Attitudes toward COVID-19 Vaccines among Patients with Complex Non-Communicable Disease and Their Caregivers in Rural Malawi. *Vaccines*. 2022;10(5):792. doi:10.3390/vaccines10050792
77. Jain NK. Chronic obstructive pulmonary disease and tuberculosis. *Lung India off Organ Indian Chest Soc*. 2017;34(5):468–469. doi:10.4103/lungindia.lungindia\_183\_17