Title

# Non-communicable lung disease in sub Saharan Africa: a community-based cross-sectional study of adults in urban Malawi

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JM analysed the data and led on the writing of the manuscript with senior authorship leadership from KM

GN, KJD, MN, SBG and KM conceptualised and developed the study protocol

KM, SBG and MN shared principal investigator responsibilities for the implementation of the study

DW provided senior statistical support for the data analysis

All authors were involved with reviewing and writing of the manuscript.

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At a Glance Commentary

**Scientific knowledge on the Subject**

Although non-communicable lung disease is thought to be an important determinant of morbidity and mortality in sub-Saharan Africa, valid burden of disease estimates are lacking.

**What This Study Adds to the Field**

We found that over 40% of the Malawian adults in our urban population-representative sample had abnormal lung function (mostly spirometric restriction) described using NHANES reference ranges in the context of widespread exposure to biomass smoke and high HIV prevalence.

Online data supplement

This article has an online data supplement, which is accessible from this issue's table of content online at www.atsjournals.org

**ABSTRACT**

Rationale

Non-communicable diseases (NCD) are major causes of morbidity and mortality in sub-Saharan Africa (sSA). Valid burden of disease estimates are lacking for non-communicable lung disease in sSA.

Objectives

We performed a community-based survey to determine the prevalence of chronic lung disease amongst adults ≥18 years in Malawi, using ATS standard spirometry, internationally validated respiratory symptom and exposure questionnaires, and including assessment of HIV-status.

Methods

An age and gender stratified random sample of 2000 adults was taken from the population of Chilomoni district of Blantyre, Malawi. Fieldworkers collected questionnaire data, conducted HIV-testing and performed pre/post bronchodilator spirometry on eligible participants. Survey-weighted population prevalence estimates of respiratory symptoms and spirometric abnormalities were computed, and bivariate and multivariable regression were used to identify associated variables.

Results

Questionnaire data, HIV status and BOLD standard spirometry were obtained from 1059, 937 and 749 participants respectively. Current respiratory symptoms, exposure to biomass

and ever smoking were reported by 11.8%, 85.2% and 10.4% respectively. HIV prevalence was 24.2%. Moderate-severe airway obstruction was seen in 3.6%. The prevalence of spirometric restriction was 38.6% using NHANES reference ranges and 9.0% using local reference ranges. Age was positively associated with obstruction while low BMI was associated with restriction.

Conclusions

Over 40% of the Malawian adults in our urban population-representative sample had abnormal lung function (mostly restrictive) in the context of widespread exposure to biomass smoke and high HIV prevalence. These findings have potentially major pubic health implications for Malawi and the broader sSA region.

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## INTRODUCTION

Non-communicable diseases (NCD) pose a major health and development challenge to low and middle-income countries (LMICS) in the 21st century: 28 million NCD-related adult deaths were seen in LMICS in 2012, and cumulative economic losses of US $7 trillion due to NCDs are forecast for these regions by 2025 if better control and prevention measures are not instituted (1). The need for prioritisation of NCDs was recognised in the World Health Organisation NCD Global Action Plan, adopted in 2013 (2).

Chronic respiratory diseases are the fourth leading cause of NCD deaths globally, and burden of disease estimates place chronic obstructive pulmonary disease (COPD) as the twelfth most common cause of years of life lost globally (3). Despite the likely high global burden of chronic respiratory disease, there are limited data on its prevalence, natural history, and associated morbidity and mortality in LMICS (4). Information on chronic respiratory disease in sub-Saharan Africa (sSA) is especially scarce (5). Existing information suggests the burden in this setting may be high: the international Burden of Obstructive Lung Disease (BOLD) study (www.boldstudy.org) demonstrated a considerably higher prevalence of moderate to severe airway obstruction amongst adults ≥40-years in Cape Town, South Africa (19.1%) compared to that seen in Western Europe and North American settings (5.9-14.3%) (6). A higher prevalence of chronic respiratory disease in sSA is biologically plausible based on the intersection of several acknowledged risk factors for respiratory pathology in these settings, including poverty-related in-utero and early childhood exposures, biomass fuel exposure, a rapidly increasing prevalence of smoking, lung damage caused by pulmonary TB, and chronic HIV-infection (1, 7-11). In addition, an association between restrictive lung diseases or low

respiratory volumes and mortality has been observed in ecological and prospective cohort studies (12)(13).

We report the results of a community-based prevalence study of respiratory disease conducted to BOLD study standards amongst adults ≥18 years in Blantyre, Malawi. The study includes information on respiratory symptoms, exposures, HIV status and spirometry. Our aim was to define the burden of respiratory symptoms and obstructive and restrictive lung disease in this setting, and to explore their risk factors.

## METHODS

An age (18-39 and ≥40 years) and gender stratified population-representative sample of 2000 adults was taken from an enumerated population of Chilomoni district of urban Blantyre, Malawi (14). Fieldworkers conducted home-visits to assess eligibility and seek informed consent between February 2013 and August 2014. Individuals were excluded if not permanent residents of the area, pregnant or acutely unwell. Up to 3 repeat visits were conducted to locate initially absent residents (eMethods section, Online data supplement).

Standardised BOLD questionnaires about respiratory symptoms and exposures were administered in the local language, Chichewa(15). Pre and post-bronchodilator spirometry were performed to American Thoracic Society (ATS) standards using the ndd EasyOne Spirometer (ndd Medical Technologies; Zurich, Switzerland)(16). Anthropometric measurements and a blood sample taken for HIV and haematology assays were taken. Participants were given the results of clinical observations and spirometry measurements at the point of testing. HIV-test results were communicated to participants who wished to know their results. Minimal questionnaire data were collected from patients who declined to participate in the full study. Quality assurance of questionnaire and spirometry data was provided by the central BOLD co-ordinating centre.

A target sample size of 1200 adults completing the study, split equally between men and women, and those 18-39 years and ≥40 years old, was chosen to allow stratified prevalence estimates of spirometric abnormalities with acceptable precision, in accordance with the BOLD protocol.

Participants who completed full and minimal questionnaires, and adequate or inadequate spirometry, were compared to assess for selection bias using the Chi-square or Student's t-test. In order to allow comparison with data from other BOLD study sites, age and gender stratified prevalence estimates of spirometric abnormalities (Table 1) were reported using reference ranges derived for Caucasian subjects from NHANES III (The third National Health & Nutrition Examination Survey, USA, 1988-1994) and local ranges derived within this study from the spirometry of non-smoking adults with no history of respiratory disease or symptoms (15).

Bivariate associations between spirometric abnormalities and exposure variables including age, gender, participant education, HIV-status, self-reported previous TB, haemoglobin, eosinophilia, body mass index (BMI), smoking status, smoking pack-year exposure, indoor biomass exposure, and occupational exposures were examined. Home ownership and household water and sanitation were used as proxy markers of socioeconomic status (SES). No adjustments were made for multiple tests in exploratory analyses. Multivariable logistic regression models were constructed including age and gender a-priori, and variables with a p-value <0.2 on bivariate analysis. A manual forwards stepwise regression technique was used to develop multivariable models. Missing data were imputed using simple univariate procedures, and sensitivity analyses used to compare results with complete case analyses. Prevalences of respiratory symptoms were described, and regression analyses used to identify associated variables. The associations between abnormal spirometry and respiratory symptoms were described. Analyses were conducted using STATA (Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Survey weighting was employed to calculate

population representative prevalence estimates and develop regression models using the Svy package in Stata (15).

Ethical approval was given by the National Research Ethics Committee of Malawi and the Liverpool School of Tropical Medicine Research Ethics Committee (Protocol 12.08).

## RESULTS

Of the 2000 randomly selected adults, 1469 (73.5%) were located by fieldworkers and 1240 (62.0%) were eligible for inclusion. Of eligible adults, 85.4% (1059/1240) consented to participate and completed the full BOLD questionnaire, with 70.7% (749/1059) performing ATS standard spirometry (Figure 1).

### Participant characteristics

Mean participant age was 41.9 years (SD 15.3), and 57.9% were male. Overall 37.4% were educated to primary school level only. Although 59.3% of participants were from households that owned their own home, only 25.1% had access to flush toilets and 46.6% had a private indoor or outdoor water supply (Table 2). Eligible individuals who declined to participate in the study but provided minimal data were more likely to be male (56.3% vs. 43.7%) and current smokers (9.0% vs. 4.3%) than those contributing full data (Table E1, Online data supplement).

### Respiratory exposures

Smoking exposure was more frequently reported in men: 9.2% of men and 0.7% of women were current smokers; 12.8% of men and 1.3% of women were ex-smokers (Table 2). 80.9% of those who had smoked reported <10 pack-years of exposure. Self-reported biomass exposure was more common than cigarette smoking: 85.2% reported use of a biomass fuel (mostly charcoal) for cooking on an open fire for ≥6 months, and 31.9% reported the use of an open fire burning wood, dung, or crop residues for heating water. Farming was the reported occupation of 29.2% of participants.

Comorbidities

7.9% of the population had low BMI (<18.5 kg/$m^2$), 20.8% were overweight (BMI 25-30 kg/$m^2$), and 12.9% were obese (BMI>30 kg/$m^2$). Only 2.9% reported previous TB.

Blood results

Data on HIV status were available for 88.1% of those who completed the core questionnaire, of whom 24.2% were HIV-infected. Haemoglobin levels were normally distributed with mean 13.9g/dL (SD 1.8) and range 6.7-21.4 g/dL. The median white cell count (WCC) was 5.0 (IQR: 4.1-5.9); 68.6% of participants had blood eosinophil counts exceeding 2.0% of the total WCC.

Respiratory symptoms

Overall 11.8% (SE 1.2) of participants had at least 1 respiratory symptom, and 5.0% (SE 0.8) reported respiratory problems interfering with their daily activities. Cough was reported by 7.5% (SE 0.9) of participants, but chronic cough (cough present on most days for ≥3 months/year) by only 0.5% (SE 0.2). Only 0.2% (SE 0.2) of all adults reported chronic sputum production (phlegm on most days for ≥3 months/year). Breathlessness was described by 3.6% (SE 0.7) of participants; 21.2% (SE 8.5) of this group had severe functional impairment and reported stopping for breath after walking 100 yards on a flat surface (modified MRC breathlessness score = 3). Wheeze within the past year in the absence of an upper respiratory tract infection was reported by 1.4% (SE 0.4) (Figure 2, Table E2 of Online Data Supplement).

Spirometry

Three factors were statistically significantly associated with completion of ATS standard spirometry: lower median age [41.0 years (IQR: 28-51) vs. 44.0 years, (IQR: 31-56))], higher mean haemoglobin [14.07(SD 1.80) vs. 13.62(SD 1.76)], and a greater average number of years of education [9.47(SD 4.20) vs. 8.85(4.65)]. No other statistically significant differences were identified at alpha = 0.05 level between groups who did and did not complete spirometry (Table E3, Online Data Supplement).

4.3% (SE 1.1) of men and 4.1% (SE 1.1) of women had post-bronchodilator obstruction (FEV1/FVC <0.7) on spirometry. A high proportion of this was at least moderate in severity: 3.2% (SE 1.0) of men and 3.9% (SE 1.0) of women had an FEV1 <80% predicted using the NHANES reference ranges, and 2.0% (SE 0.7) of men and 2.7% (SE 0.9) of women using local reference ranges (Figure 3, Table E4 of Online Data Supplement). Any obstruction and moderate-severe obstruction were seen in 2.9% (SE 0.9) and 2.6% (SE 0.9) of 18-39 year olds, and 9.0% (SE 1.4) and 7.0% (SE 1.2) of ≥40 year olds.

Spirometric restriction was more common than obstruction in both genders and across age-group strata. The estimated prevalence was considerably higher when NHANES reference ranges were used (38.6%, SE 2.1) compared to locally derived reference ranges (9.0%, SE 1.2). Airway reversibility was present in 4.2% (0.8) of the cohort, but only 17.3% (SE 7.7) of those with reversibility had airway obstruction following bronchodilator.

Factors associated with respiratory symptoms

Ever smoking was positively associated with both cough and sputum production in bivariate analysis (Table E5, Online Data Supplement), and in multivariable analysis the odds of usual

cough were 2.37 higher in current vs. never smokers (95% CI 1.12-5.02) (Table 3). The odds of regular sputum expectoration were 5.94 times higher (95% CI 1.95-18.06) in those with previous biomass exposure compared to those without. Employment in farming was positively associated with all symptoms in bivariate analyses, and the odds of exertional breathlessness remained significantly higher (OR 6.32, 95% CI: 1.87-21.32) in those employed in farming for >3 months compared to non-farmers in multivariable analysis.

Women were less likely to report cough or sputum production in bivariate analyses, and their odds of cough remained lower (OR 0.31, 95% CI 0.15-0.65) than men in multivariable analysis. Low BMI was positively associated with wheeze and sputum production in bivariate analysis, and the odds of usual sputum production remained 3.49 (95% CI 1.37 – 8.86) times higher in those with BMI<18.5kg/$m^2$ compared to normal weight in the multivariable model. No statistically significant relationships between symptoms and markers of SES or education persisted in multivariable models. One-third of those with cough were HIV-infected, and a positive association was seen between cough and HIV-infection (OR 1.94, 95% CI 1.10-3.44). HIV-infection was not associated with other respiratory symptoms. Self reported previous TB was not statistically associated with any symptoms. Moderate-severe obstruction, restriction, or reversibility, defined using NHANES III reference ranges were not associated with respiratory symptoms (Table E6, Online Data Supplement).

Factors associated with post-bronchodilator airway obstruction

Participant age was the factor most clearly associated with airway obstruction in bivariate and multivariable analyses, increasing in a non-linear fashion with a 10.12 times higher risk of moderate to severe obstruction (95% CI 3.54-28.93) in those aged ≥60 years compared to

18-29 year olds (Table 4, Tables E7 & E8 in Online Data Supplement). This finding was also seen in the sensitivity analysis restricted to complete-case data. No association was seen between HIV-infection or biomass exposure and airway obstruction. Individuals without access to private water supply had 2.44 times higher risk of moderate to severe obstruction in multivariable analysis (95% CI 1.01 – 5.88).

Factors associated with spirometric restriction

BMI was strongly associated with restrictive deficit defined using NHANES criteria: those who were underweight had 4.09 (95% CI 2.04-8.22) times higher odds of restriction compared to those with normal weight in the multivariable model. Older age was negatively associated with restriction, and those aged over 60-years had 0.53 (95% CI: 0.29-0.96) times the odds of restriction of the 18-29 year group. No other risk factors for restrictive deficit were identified in the multivariable model (Table 5, Table E9 in Online Data Supplement).

When spirometric restriction was defined using local reference ranges (Table E10, Online Data Supplement), no clear trend in the relationship between age and restriction emerged. The odds of restriction were higher if underweight (OR 2.80, 95% CI 1.19-6.55) in bivariate analysis only. In multivariable analysis, previous TB was associated with higher odds of restriction (OR 3.01, 95% CI 1.07-8.50).

## DISCUSSION

We conducted a population based cross-sectional study of the prevalence of and risk factors for non-communicable respiratory disease conducted to BOLD standards amongst adults aged ≥18 years in Malawi. We found a high burden of chronic respiratory symptoms and abnormal spirometry in the population, with an especially high burden of spirometric restriction, and large differences in the estimated prevalence of restriction using NHANES and locally defined reference ranges.

Abnormal spirometry is defined in relation to age, height, and gender standardised predicted values. Two different reference ranges were used in this analysis: the NHANES reference range is drawn from a healthy Caucasian population in the US and is thought to represent the best possible lung function in the absence of any known detrimental respiratory exposures; the locally derived reference range reflects the spirometry of non-smoking symptom-free Malawian adults within this study. Whilst values may be ethnically more appropriate in the latter, they are also constrained by common exposures within in this setting (17). The marked difference in the burden of restriction defined using NHANES (38.6%) vs. reference ranges determined from our study population (9.0%) suggests that on average, Malawian adults have smaller lungs than US Caucasian populations. This finding is consistent with previous studies that have demonstrated lower FVC ranges in populations from resource-poor settings (12).

The cause of this difference is unclear. The role of ethnicity must be considered, as body frame differences related to ethnicity are known to effect lung function (18).

However, it has been suggested that in-utero and early childhood exposures including suboptimal in-utero conditions, low birth weight, respiratory tract infections, and nutritional deficiencies can predict adult lung health and are more prevalent in resource poor settings (7, 19, 20). Although the use of height standardised spirometry reference ranges here may have 'controlled' for stunting related to childhood nutritional deficits, a low BMI was strongly associated with NHANES defined spirometric restriction. This is consistent with an ongoing nutritional influence on FVC, and the finding of small lungs in adults may be explained by poor nutrition causing impaired lung growth at vulnerable stages of lung development. Interest in the link between acute and chronic malnutrition and long-term disability is growing(21), and prospective studies into the effect of lung function in later life would fit well within this agenda.

The morbidity and mortality associated with the lower FVC we have identified in the Malawian setting remain poorly described. Spirometric restriction has been shown to be associated with increased mortality, even in the absence of respiratory symptoms and a diagnosis of respiratory disease, in both the US setting and ecological studies (12, 13). The negative correlation seen between spirometric restriction and age here may represent a birth cohort effect, whereby the incidence of restriction is decreasing over time, but would also fit with earlier mortality amongst those with restriction. Prospective studies are required to investigate the prognostic implications of restriction in sSA settings, and to determine the public health implications of our findings.

Cough was the most common respiratory symptom reported by participants. The association with HIV raises the possibility that undiagnosed pulmonary tuberculosis may be responsible for part of this presentation (22-26). However, cough was less prevalent amongst younger age groups in whom the TB incidence would be expected to be highest. In addition, the association of chronic cough with ever smoking and the strong association between sputum production and biomass smoke exposure also suggest that bronchial irritation from smoke inhalation with a degree of chronic bronchitis may underlie these symptoms. It is however of note that no association was seen between spirometric results and respiratory symptoms. Further investigation of the relationship between structural lung pathology, abnormal airway physiology, and respiratory symptoms in this setting is required.

No association was seen in our data between moderate-severe chronic airflow obstruction and exposure to tobacco or biomass, although both are recognised risk factors for obstruction (27-30). The absence of a relationship between biomass exposure and airway obstruction may be explained by limited study power given the low prevalence of moderate-severe obstruction (3.6%), or misclassification of self-reported rather than objectively quantified biomass exposure, but is consistent with findings of a recent population-based study in Nigeria (31, 32). In the case of tobacco it may also reflect a low intensity of exposure in this setting, which is insufficient to produce significant levels of clinically important COPD: smoking prevalence was limited and pack-year exposure low. This is in contrast to the findings of the BOLD study conducted in Cape Town, South Africa where the prevalence of moderate to severe airway obstruction amongst adults ≥40 was much higher (19.1%) and where

ever smoking was much more common (59% vs 16%) amongst those with COPD (5). This illustrates important differences in the epidemiology of respiratory disease within sSA: the patterns of exposure and pathology in Cape Town, South Africa may be closer to those of a high income and more industrialized setting than those seen in Malawi and other low income countries across the region.

Increasing age was the only measured factor significantly associated with airflow obstruction in our study. The persistence of this association for moderately severe obstruction suggests that this is not simply the result of expected changes in the FEV1/FVC ratio seen with aging, but in fact constitutes abnormal pathology (33). Small sample size in the context of a low prevalence condition is likely partly responsible for the lack of other significant findings. We note with interest the non-statistically significant positive association between peripheral blood eosinophil level and airflow obstruction that was not seen with restriction.

A major strength of our study is the inclusion of all adults from the age of 18 years and measurement of HIV-status. Spirometry was conducted to ATS standards, with careful quality control. The enumeration of the target population at the start of the study, followed by age and gender stratified sampling, allowed for population weighted prevalence estimates to be drawn and associations measured.

Limitations of this study include the challenges posed by working with a mobile urban population: it was not possible to locate over 25% of the initial random sample, and 9.6% had permanently left the area between enumeration and

fieldworker home visits. In addition, only 71% of those who were included were able to complete adequate spirometry with fewer older individuals. As a result, we did not reach the target sample size of 600 adults over and 600 adults under 40-years of age with high quality spirometry. This reduced our power to detect significant associations in the exploratory analyses. The study was cross sectional in nature and whilst efforts were made to assess the impact of respiratory pathology on patients' lives using self-reported symptoms and health related quality of life, prospective data are required to determine the impact of respiratory pathology on morbidity and mortality over time. Measurement of total lung capacity, in addition to FVC, would allow us to better understand the nature and impact of the spirometric restriction seen here. Symptomatic individuals were not screened for pulmonary TB, and the proportion of abnormalities attributable to this more acute pathology are therefore unclear. In addition, the observational nature of this study means that correlations identified may not be causal in nature and could be explained by unidentified or unmeasured confounding factors. Lastly, our data are drawn from a single urban site study, making it difficult to identify strong risk factors for respiratory disease that are ubiquitous within the sample population. Ecological studies comparing data from diverse populations within sSA, and with Western cohorts will be required to explore these determinants. Comparable data from rural settings, and areas with different environmental/occupational exposures are required to determine the generalizability of our results.

The key finding of our study is a high burden of restrictive spirometry amongst Malawian adults, with a large difference in prevalence using NHANES and

locally defined reference ranges. There is a clear and pressing need to better understand the aetiology, pathology, epidemiology and prognosis of pulmonary restriction in sub Saharan Africa to inform the development of prevention and management approaches for this condition. If, as has been seen elsewhere, pulmonary restriction in this setting is associated with increased mortality this will have major pubic health implications for Malawi and potentially the broader sub-Saharan Africa region.

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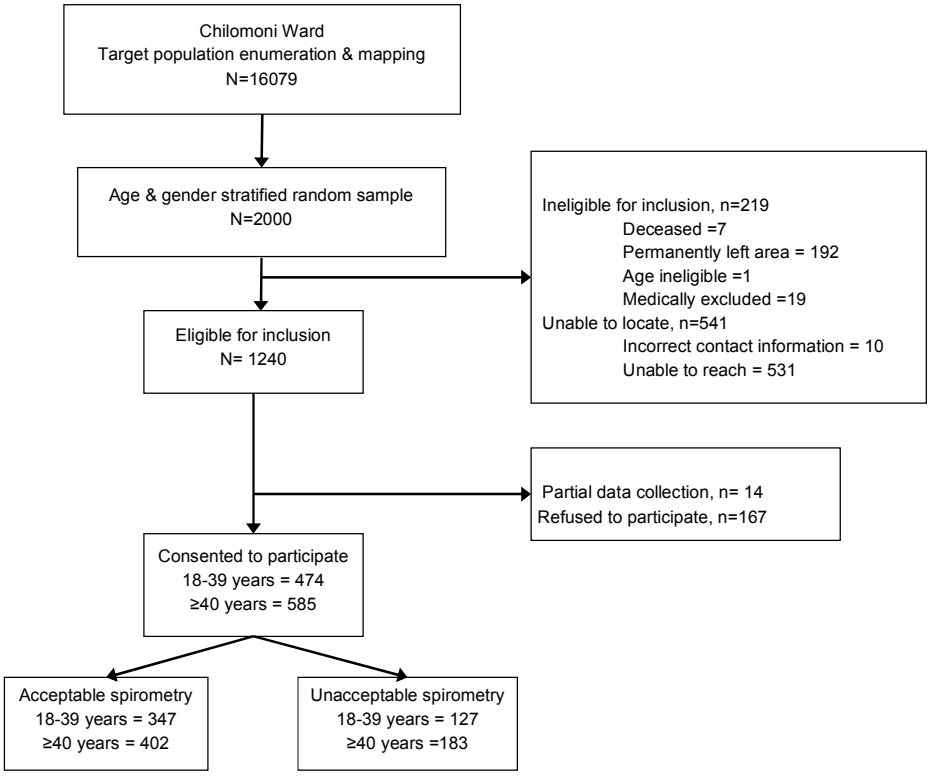


Figure 1: Participant recruitment flow diagram

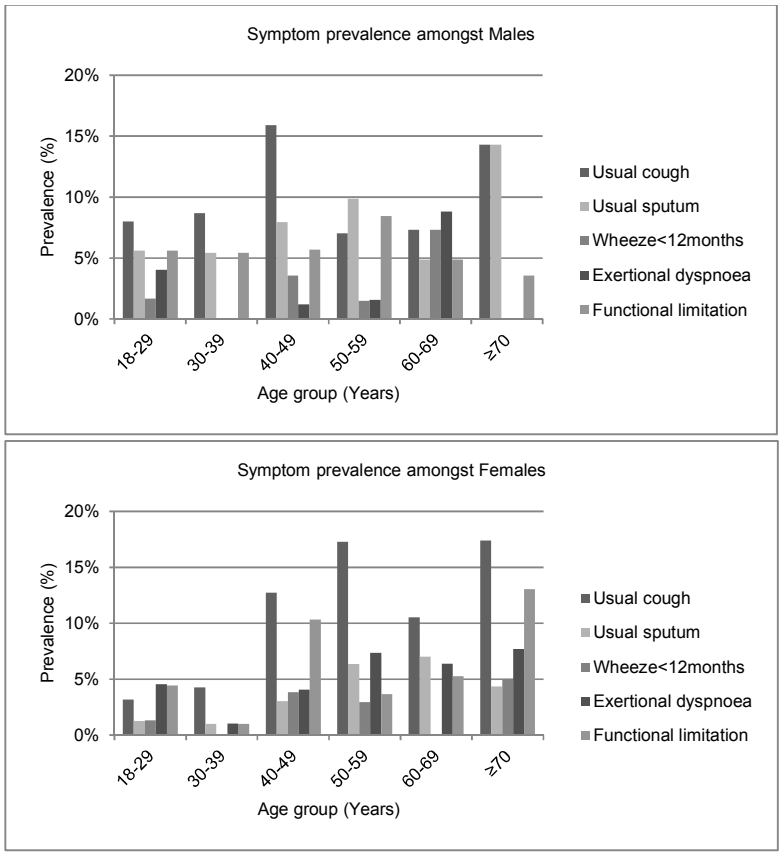


Figure 2: Age and gender stratified prevalence of symptoms amongst study participants

Questions asked: Do you usually have a cough when you don't have a cold? (n=1056); Do you usually bring up phlegm from your chest (n=1056); Have you had wheezing/whistling in your chest at any point in in the past 12 months, in the absence of a cold (n=1007); Do you have shortness of breath hen hurrying on the level or walking up a slight hill (n=970); Have breathing problems interfered with your usual daily activities (n=1056).

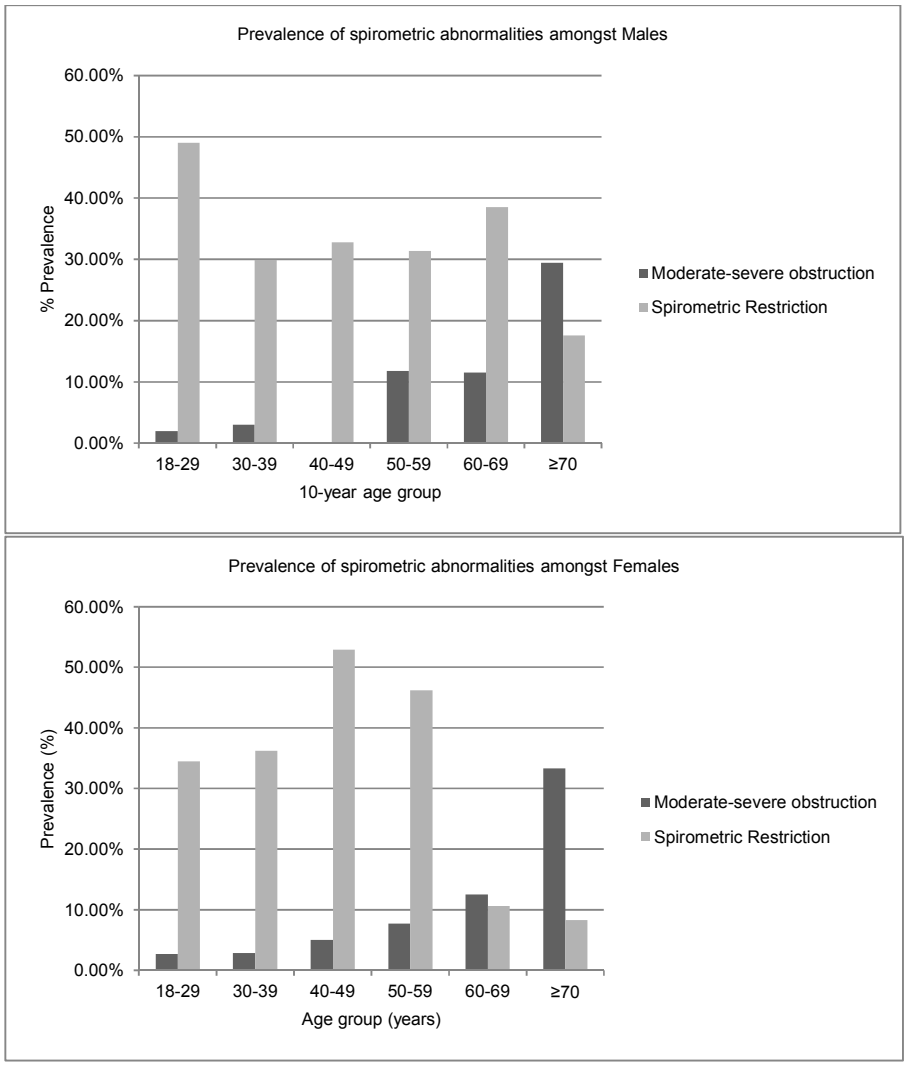


Figure 3: Age and gender stratified prevalence of moderate-severe airway obstruction (FEV1/FVC<0.7 & FEV1<80% predicted) and spirometric restriction (FEV1/FV>0.7 & FEV1<80%) defined using NHANES reference ranges, amongst those completing ATS standard spirometry (n=749)

Table 1: Spirometric definitions(34)

| Finding | Spirometric definition |
|---|---|
| Post bronchodilator obstruction | FEV1/FVC Ratio <0.7 |
| Post bronchodilator moderate to severe obstruction | FEV1/FVC ratio <0.7 AND FEV1<80% predicted* |
| Spirometric restriction | FEV1/FVC Ratio>0.7 AND FVC<80% predicted* |
| Airway reversibility | FEV1 increase ≥200ml AND ≥12% following bronchodilator |

*Age, gender and height standardised predicted values obtained from NHANES III, or local reference ranges derived from spirometry results of healthy, never-smoking Malawian subjects.

Table 2: Characteristics of participants completing full BOLD core questionnaire, including those with and without ATS standard spirometry

| Variable (n) | Number (%) Mean (SD) | |
|---|---|---|
| Age group (n=1058) | | |
| 18-29 | 283 | (26.8 %) |
| 30-39 | 190 | (18.0 %) |
| 40-49 | 253 | (23.9 %) |
| 50-59 | 182 | (17.2 %) |
| 60-69 | 98 | (9.3 %) |
| 70+ | 52 | (4.9 %) |
| | | |
| Gender (n=1059) | | |
| Male | 446 | (42.1 %) |
| Female | 613 | (57.9 %) |
| | | |
| Level of education (n=1054) | | |
| None | 59 | (5.6 %) |
| Primary | 394 | (37.4 %) |
| Middle | 391 | (37.1 %) |
| High school or college | 210 | (19.9%) |
| | | |
| Years of education (n=1057) | 9.29 | 4.35 |
| | | |
| HIV status (n=933) | | |
| Negative | 707 | (75.8 %) |
| Positive | 226 | (24.2 %) |
| | | |
| Self reported previous TB (n=1057) | | |
| No | 1026 | (97.1 %) |
| Yes | 31 | (2.9 %) |
| | | |
| Hemoglobin (g/dL) (n=936) | 13.9 | (1.80) |
| | | |
| Eosinophil blood count >2% (n=927) | | |
| No | 291 | (31.4 %) |
| Yes | 636 | (68.6 %) |
| | | |
| BMI group (kg/m2) (n=972) | | |
| Underweight (BMI<18.5) | 77 | (7.9 %) |
| Normal (18.5≥BMI<25) | 568 | (58.4 %) |
| Overweight (25≥BMI<30) | 202 | (20.8 %) |
| Obese (BMI≥30 | 125 | (12.9 %) |
| | | |
| Home ownership (n=1057) | | |
| Yes | 627 | (59.3 %) |
| No | 430 | (40.7 %) |
| | | |
| Access to private water supply (indoor OR outdoor tap) (n=1057) | 492 | (46.6 %) |
| Yes | 565 | (53.4 %) |
| No | | |
| | | |
| Household has flush toilet (n=1057) | | |
| Yes | 265 | (25.1 %) |
| No | 792 | (74.9 %) |
| | | |
| Smoking status (n=1057) | | |
| Ever | 110 | (10.4 %) |
| Never | 947 | (89.6 %) |
| | | |
| Pack years of smoking (n=1057) | | |
| 0 years | 947 | (89.6 %) |
| >0 and <10years | 89 | (8.4 %) |
| ≥10 years | 21 | (2.0 %) |
| | | |
| Biomass exposure* (n=1057) | | |
| No | 157 | (14.8 %) |

| | | |
|---|---|---|
| Yes | 900 | (85.2 %) |
| | | |
| Working in farming >3m (n=1056) | | |
| No | 748 | (70.8 %) |
| Yes | 308 | (29.2 %) |

*Use of charcoal/coal/coke or burning of wood/dung/crop residue for >6 months for cooking, or burning of wood/dung/crop residue for heating water

Table 3: Multivariable associations with respiratory symptoms‡ in all age groups, n=1056

| Variable | Usual cough (n=103) | | Usual sputum (n=51) | | Exertional dyspnoea (n=35) | | Wheeze (n=21) | |
|---|---|---|---|---|---|---|---|---|
| | Odds Ratio | 95% CI | Odds Ratio | 95% CI | Odds Ratio | 95% CI | Odds Ratio | 95% CI |
| Age group | | | | | | | | |
| 18-29 | 1.0 | - | 1.0 | - | 1.0 | - | 1.0 | - |
| 30-39 | 0.97 | 0.44-2.17 | 1.12 | 0.38-3.12 | 0.09 | 0.01-0.80* | Empty | - |
| 40-49 | 2.37 | 1.19-4.71* | 1.97 | 0.75-5.16 | 0.28 | 0.08-1.03 | 1.97 | 0.48-8.06 |
| 50-59 | 1.82 | 0.87-3.81 | 3.64 | 1.43-9.26* | 0.40 | 0.11-1.42 | 0.99 | 0.17-5.73 |
| ≥60 | 1.81 | 0.85-3.86 | 2.32 | 0.82-6.55 | 0.74 | 0.18-3.00 | 1.39 | 0.24-7.93 |
| Gender | | | | | | | | |
| Male | 1.0 | - | - | - | 1.0 | - | 1.0 | - |
| Female | 0.72 | 0.41-1.27 | 0.31 | 0.15-0.65* | 1.78 | 0.68-4.68 | 0.41 | 0.13-1.27 |
| Smoking status | | | | | | | | |
| Never | 1.0 | - | | | | | | |
| Ever | 2.37 | 1.12-5.02* | | | | | | |
| HIV status§ | | | | | | | | |
| Negative | 1.0 | - | | | | | | |
| Positive | 1.94 | 1.10-3.44* | | | | | | |
| Haemoglobin (g/dL) § | | | | | | | 0.74 | 0.58-0.94* |
| Working in farming >3m | | | | | | | | |
| No | | | | | 1.0 | - | | |
| Yes | | | | | 6.32 | 1.87-21.32* | | |
| Any biomass exposure† | | | | | | | | |
| No | | | 1.0 | | | | | |
| Yes | | | 7.05 | 2.28-21.80* | | | | |
| BMI (kg/m2) | | | | | | | | |
| Underweight (BMI<18.5) | | | 3.26 | 1.32-8.07* | | | 5.38 | 1.23-23.50* |
| Normal (18.5≥BMI<25) | | | 1.0 | | | | 1.0 | - |
| Overweight (25≥BMI<30) | | | 0.37 | 0.15-0.91* | | | 1.16 | 0.26-5.16 |
| Obese (BMI≥30) | | | 1.15 | 0.31-4.30 | | | 5.47 | 0.93-32.38 |
| Household has flush toilet | | | | | | | | |
| Yes | | | 1.0 | - | | | | |
| No | | | 0.42 | 0.19-0.91* | | | | |

* p<0.05

†Use of charcoal/coal/coke or burning of wood/dung/crop residue for >6 months for cooking, or burning of wood/dung/crop residue for heating water

‡Presence of respiratory symptoms ascertained using the following questions, derived from the BOLD study core questionnaire:
Usual cough: Do you usually cough when you don't have a cold?
Usual sputum: Do you usually bring up phlegm from your chest, or do you usually have phlegm in your chest that is difficult to bring up, when you don't have a cold?
Exertional dyspnea: Are you troubled by breathlessness when hurrying on the level or walking up a slight hill?
Wheeze: Have you had wheeze/whistling in your chest at any time in the past 12months? In the last 12 months have you had this wheeze or whistling only when you have had a cold? (exclude if yes to the latter question)

§Imputation of data required for 11.9% of HIV values, and 11.8% of haemoglobin values. Imputation of all other values ≤0.1%

Table 4: Multivariable associations of risk factors with NHANES defined moderate-severe post bronchodilator airway obstruction (FEV1/FVC ratio <0.7 & FEV1<80% predicted), n=749

| Variable | Multivariable association† | |
|---|---|---|
| | Odds Ratio | 95% CI |
| Age group | | |
| 18-29 | 1.0 | - |
| 30-39 | 1.38 | 0.36-5.25 |
| 40-49 | 0.93 | 0.27-3.15 |
| 50-59 | 4.66 | 1.58-13.79* |
| ≥60 | 10.12 | 3.54-28.93* |
| Gender | | |
| Male | 1.0 | - |
| Female | 1.34 | 0.57-3.17 |
| Access to private water supply (indoor OR outdoor tap) | | |
| Yes | 1.0 | - |
| No | 2.44 | 1.01-5.88* |

* p<0.05

†Multivariable model developed using variables correlated at p<0.2 level in bivariate analysis, and age group & gender as apriori risk factors, with imputation for missing data.

Table 5: Multivariable associations of risk factors with NHANES defined spirometric restriction (FEV1/FVC ratio >0.7 & FVC >80% predicted), n=756

| Variable | Multivariable associations† | |
|---|---|---|
| | Odds Ratio | 95% CI |
| Age group | | |
| 18-29 | 1.0 | - |
| 30-39 | 0.64 | 0.40-1.02 |
| 40-49 | 1.00 | 0.66-1.53 |
| 50-59 | 0.85 | 0.52-1.38 |
| ≥60 | 0.53 | 0.29-0.96* |
| Gender | | |
| Male | 1.0 | - |
| Female | 0.95 | 0.65-1.40 |
| BMI (kg/m2) | | |
| Underweight (BMI<18.5) | 4.09 | 2.04-8.22* |
| Normal (18.5≥BMI<25) | 1.0 | - |
| Overweight (25≥BMI<30) | 1.07 | 0.66-1.73 |
| Obese (BMI≥30) | 1.58 | 0.85-2.96 |

* p<0.05

†Multivariable model developed using variables correlated at p<0.2 level in bivariate analysis, and age group & gender as apriori risk factors, with imputation for missing data.