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# A multicentre observational study of HIV, TB and risk of chronic lung disease in urban west Africa

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**Running head:** HIV and TB drive chronic lung disease in Nigeria

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## Abstract

**Objective:** HIV and TB are risk factors for non-communicable chronic lung disease (CLD). Despite the high prevalence of these infections in west Africa, there are no studies that compare CLD between people living with HIV (PLWH) and HIV-negative populations in this setting. This study sought to quantify the contribution of HIV and TB infection in addition to conventional CLD risk factors, such as tobacco and biofuel exposure, to CLD in urban west Africa.

**Design:** A multi-centre cross-sectional study was conducted in three community clinics in Lagos, Nigeria between 2018 and 2019.

**Methods:** Spirometry, questionnaires and clinical records were used to estimate prevalence of CLD and association with risk factors.

**Results:** 148 HIV-negative individuals and 170 HIV-positive individuals completed the study. Current cigarette (11/318, 3.5%) and lifetime domestic biofuel (6/318, 1.8%) exposures were low. Airway obstruction (33/170, 19.4% vs 12/148, 8.1%, p=0.004) and CLD (73/170, 42.9% vs 34/148, 23%, p < 0.0001) were more prevalent in PLWH compared to the HIV-negative group. HIV infection (OR 2.35 (1.33, 4.17), p=0.003) and history of TB (OR 2.09 (1.04, 4.20), p=0.038) were independently associated with increased risk of CLD.

**Conclusions:** HIV and TB far outweigh conventional risk factors, including tobacco and domestic biofuel exposure, as drivers of non-communicable CLD in urban west Africa. Current global policy for CLD may have limited impact on CLD in this setting. Enhanced prevention, diagnosis and management strategies for incident HIV and TB infections are likely to have a significant impact on long-term lung health in sub-Saharan Africa (SSA).

**Key words**: HIV, TB, COPD, chronic lung disease, sub-Saharan Africa



## Introduction

Chronic lung disease (CLD) encompasses a wide range of non-communicable respiratory pathologies affecting the airways and structures of the lung that impair human health.[1] Chronic obstructive pulmonary disease (COPD) is considered to be the most prevalent form of CLD globally, driven by inhalation of noxious gases and particles of which tobacco smoke is thought to be the most important globally.[2] In 2019 an estimated 3.28 million deaths and 74.4 million Disability Adjusted Life Years (DALYs) were attributable to COPD alone.[3] Up to 84% of this mortality and morbidity occurred in low- and middle-income countries (LMICs).[1] Despite these reports, high-quality data characterising the burden of disease and risk factors for CLD remain very limited across sub-Saharan Africa (SSA). Airway obstruction defined by spirometry is the defining characteristic of COPD and remains the gold standard for diagnosis. However spirometry is not routinely available across SSA and analyses depend on correlation with population reference values which are missing for most countries in SSA. Meta-analysis of spirometry-based studies from SSA show substantial variation for the estimated prevalence of COPD (5-24%). [4–6] In Nigeria, there is only one population-level spirometry-based study conducted by the Burden of Obstructive Lung Disease (BOLD) initiative in an HIV-negative population, which reported a prevalence of airway obstruction of 7.7%.[5] The importance of providing high-quality population-specific local data to identify CLD burden and to identify preventable causes of CLD is paramount to guiding interventions and improving health outcomes.

HIV exposure is recognised as a risk factor for CLD and accelerated decline in lung function although the mechanisms underlying this, and the long-term outcomes of this association, are not well understood.[7,8] There are very limited data describing the burden of disease and risk factors for CLD in people living with HIV (PLWH) in HIV high-prevalence settings.[9] Meta-analysis of heterogenous available studies in PLWH in SSA reported COPD prevalence

between 1.2% and 26.0%, and an independent association between HIV infection and airways obstruction after adjusting for tobacco consumption.[9] The relationship between other infectious diseases and long-term non-communicable sequelae is also poorly defined in high-prevalence settings. There are limited data reporting post-TB lung disease in SSA.[10,11] Despite representing the epicentre of the HIV pandemic, there are no data comparing lung health and disease between PLWH and HIV negative populations in west or central Africa. Nigeria is the most populous country in SSA with the second largest population of PLWH in the world.[12] There are two Nigerian spirometry-based studies of CLD in HIV-positive populations reporting prevalence of airways obstruction between 3 and 15.4%; however, one did not include an HIV-negative control group and the other was underpowered for comparison to HIV-negative controls [13,14]. In an urban Nigerian population, this study aimed to report the prevalence of airway obstruction and CLD, and quantify the contribution of recognised risk factors, including HIV, TB, smoke and biofuel exposure by comparing HIV negative and HIV positive groups.

## Methods

### Study design and population

A multi-centre cross-sectional observational study was conducted at three community clinics in Lagos Mainland, Lagos, Nigeria. The study population comprised two groups representative of an urban Lagosian population accessing community healthcare: one group of individuals living with HIV and one group of HIV-negative individuals. PLWH were recruited from routine biannual follow-up clinics at the federal Nigerian Institute for Medical Research (NIMR) in Lagos, Nigeria. The NIMR cohort is the largest HIV cohort in Lagos, providing care to individuals from across Lagos State, and is considered representative of the population of PLWH in Lagos. HIV-negative participants were recruited from two primary care clinics at Mushin General Hospital and Harvey Road Health Centre. All participants at these centres provided negative routine HIV point-of-care testing at the time of study enrolment. This is provided free of charge as part of the Nigerian National HIV/AIDS Strategic Framework. The indications for participants attending the community medical centres were not recorded. All institutions in the study provide public access to medical care.

Eligible participants were adults (aged 18 years or more) who were capable of providing informed consent and performing adequate spirometry. Participants were excluded if contraindications to spirometry were identified: pregnancy; eye, heart, chest, lung or abdominal surgery within the past 3 months; myocardial infarction within the past 3 months; HR $\geq$ 120 bpm; systolic BP $\geq$ 180mmHg or diastolic BP $\geq$ 120mmHg; active pulmonary TB. Participants identified as having a new diagnosis of CLD were informed of their diagnosis and provided with self-management materials and referral to the NIMR medical clinic if required.

**Sampling and sample size calculation**

Systematic sampling of clinic attendees was conducted between January 2018 and October 2019. The first selection was based on a blinded random draw from the first ten individuals, followed by sampling of every 5th patient in clinic. The sample size was calculated to provide 80% power to detect a difference of 8% in prevalence of CLD between HIV-positive and HIV-negative groups. The calculation was based upon an estimated CLD prevalence of 14% in PLWH. [5,13,15]

**Data collection**

All questionnaires were delivered by NIMR research fellows using tablet devices. Open Data Kit software was used to collate data in a secure online server. Pre-determined demographic, medical history and CLD risk factor data were collected. Data regarding cigarette smoking, smoking of other substances, occupation, lifetime use of biomass fuels (charcoal, wood/sawdust, grass/leaves/straw, agricultural crop or animal dung) as cooking or heating fuel, co-morbidities and history of TB, were collected. Exposure to smoke was calculated using number of hours per day and the number of years exposed. An ex-smoker was defined as a person who quit smoking >3 months prior to the study. Occupation groups from the 2008 version of the International Standard Classification of Occupations (ISCO-08) were used.[16] The occupation variable was condensed to manual, non-manual, retired or unemployed.

Respiratory data including frequency of use of antibiotics and/or oral steroids for respiratory exacerbations and presence of self-reported symptoms were collected. Participants were asked 'Have you ever had wheezing (whistles, squeaks, rattles, or buzzes) in your chest in the last 12 months?' and 'Do you have cough with mucus on most days of the week?' to assess for wheeze and bronchitis, respectively. To capture chronic bronchitis, participants were asked 'Have you brought up mucus with a cough most days for at least 3 months, 2 years in a row?'. The COPD Assessment Test (CAT) and MRC dyspnoea questionnaires were also performed.[17,18]

In PLWH, data were obtained from NIMR patient records with participant consent: date of diagnosis, anti-retroviral treatment (ART), date of ART initiation, nadir CD4+ T cell count (cells/μL), baseline WHO clinical stage and the most recent CD4+ count (cells/μL) and HIV viral load (copies/ml) from the previous 12 months.

**Spirometry protocol**

Prior to the study, NIMR research staff underwent 2 weeks of intensive spirometry and lung function interpretation training delivered by UK-based respiratory physicians. Two members of the research team reviewed all spirometry readings, 10% of these were then read by respiratory physicians to validate accuracy. Research staff collected pulmonary function data using flow-based portable spirometry (CareFusion Micro 1 Handheld Spirometer). Forced vital capacity (FVC), forced expiratory volume in 1 second ($FEV_1$) and the proportion of FVC exhaled in the first second ($FEV_1$/FVC) were recorded. In accordance with ATS/ERS 2005

guidance[19], spirometry manoeuvres were considered acceptable if they were free from complications (coughing during the first second, variable effort, leak, blocked mouthpiece) and consisted of a satisfactory exhalation (duration of at least 6 seconds or expiratory plateau reached).[19] Participants were required to have at least 3 acceptable manoeuvres. To meet repeatability criteria the two largest results for both FVC and $FEV_1$ had to be reproducible to within 150ml. Participants were permitted up to eight attempts to meet criteria. The original study protocol had planned to include bronchodilator reversibility testing for individuals identified with $FEV_1$ less than 80% of predicted. However 54% (42/78) of these individuals did not consent to bronchodilation and/or repeat spirometry. We have therefore not included these data in our analysis and report pre-bronchodilator spirometry.

**Study definitions**

Reference equations from the Global Lung Initiative (GLI) and a Nigerian reference study were used to generate $FEV_1$, FVC and $FEV_1$/FVC ratio below the 5$^{th}$ percentile (lower limit of normal (LLN)) after adjusting for age, height, gender and race.[20,21] Self-reported CLD was defined as previous diagnosis by a healthcare professional of asthma, COPD, bronchitis or emphysema. Airway obstruction was defined as $FEV_1$/FVC ratio <0.7 and/or $FEV_1$/FVC ratio <LLN. Preserved ratio impaired spirometry (PRISm) was defined as FEV1 <80% predicted and $FEV_1$/FVC ratio >0.7. CLD was defined as any self-reported CLD, and/or questionnaire-defined bronchitis and/or airways obstruction and/or PRISm.

**Statistical analysis**

Data were analysed in Stata v16.1. Outcomes were summarised by pre-determined variables associated with CLD or changes in lung function. Factors considered were HIV status, sex, age, BMI (<18.5kg/m$^2$, 18.5-23.9kg/m$^2$, 24-29.9 kg/m$^2$ and ≥30 kg/m$^2$), smoking status (current, ex-smoker, never smoker), previous TB diagnosis, lifetime exposure to biomass fuel and occupation. Mann-Whitney U tests were used to analyse non-normally distributed continuous variables and t-test for normally distributed variables. Chi-squared tests or Fisher's exact tests were used for categorical variables. Age was collapsed into three groups (≤40 years old, 41-50 years old and >50 years old) and smoking status dichotomised to 'Never' and 'Ever'. Univariable analyses were conducted to explore crude associations between pre-determined variables (age, sex, smoking status, BMI, HIV infection, history of TB) and study outcomes of airways obstruction and CLD. Multivariable logistic regression was used to investigate the effect of HIV infection and history of TB on outcomes. A forward approach was adopted with additional variables retained in the model if their inclusion changed the estimate of the odds ratio by approximately 10%, leading to the inclusion of history of TB and HIV status in each model. Following the development of the final model, a likelihood ratio test of the null hypothesis of no association between the outcome measure and exposure of interest, after controlling for included confounders, was performed. As part of a subgroup analysis, association of outcomes with pre-determined HIV-related variables were explored: detectable viral load (considered undetectable at <50 copies/ml), most recent and nadir CD4 T-cell counts

(dichotomised to <200 or ≥200 cells/μL) and duration of ART (stratified to <10 or ≥10 years). A p-value of <0.05 was considered to be indicative of statistical significance.

**Ethics**

All participants provided written informed consent. Ethical approval was granted by the London School of Hygiene and Tropical Medicine Research Ethics Committee (Ref: 26038) and NIMR Institutional Review Board (Ref: IRB/17/018).

**Results**

Four-hundred and nineteen individuals were approached between January 2018 and October 2019. Two-hundred and twenty one HIV-positive and 154 HIV-negative individuals were eligible and consented to the study (Figure 1). Overall 318 (84.8%, 318/375) individuals with complete data recorded acceptable spirometry: 148 HIV-negative individuals (148/154, 96.1% of HIV-negative participants) and 170 HIV-positive individuals (170/221, 76.9% HIV-positive participants). The demographic and lifestyle characteristics of the individuals who recorded unacceptable spirometry were comparable to the population included in analyses (Supplementary table 1, http://links.lww.com/QAD/C619).

Self-reported cough (40.6% vs 29.1%, p=0.032; supplementary table 1, http://links.lww.com/QAD/C619) and bronchitis (5.9% vs 1.4%, *p*=0.040) were more prevalent in PLWH compared to the HIV negative group. Prevalence of cough (52%; Supplementary table 2, http://links.lww.com/QAD/C619) and bronchitis (8%) were highest in individuals with a history of TB. The prevalence of current tobacco smoking was low in the study population (11/318, 3.5%; Table 1). Twenty-two percent of PLWH (38/170) were ex-smokers compared to 8.1% of HIV-negative individuals (12/148). Median pack year tobacco exposure was low (0.6 pack year history (0-3.0) across the study but highest in the small number of current smokers in the PLWH group (11 pack year history (1.9-16.0); Table 1). Overall, ever use of domestic biomass fuel exposure was low (6/321, 1.9%).

History of TB was significantly higher in the HIV-positive group (49/170, 28.8%; Table 2) compared to the HIV-negative group (1/148, 0.7%). Self-reporting of non-communicable chronic lung disease diagnoses, all of which was reported as asthma, was low but the prevalence among PLWH (2.9% 5/170; Table 2) was more than double that reported by HIV-negative participants (1.4%, 2/148).

The median $FEV_1$ of PLWH was lower than for HIV-negative participants (2.38 L (2.07, 2.80) compared to 2.73 L (2.24, 3.36), $p < 0.0001$; Table 2 and Supplementary Figure 1, http://links.lww.com/QAD/C619). The median FVC of PLWH was also lower than for HIV-negative participants (3.16 L (2.74, 3.58) compared to 3.38 L (2.80, 4.12), $p < 0.0001$). $FEV_1$/FVC measurements were lower in PLWH compared to HIV-negative participants (0.78 (0.72, 0.82) compared to 0.82 (0.77, 0.87), $p < 0.0001$). When stratified by a range of factors associated with impairment in lung function, PLWH consistently had lower absolute

spirometry values compared to the HIV-negative group (Table 2). Study outcomes were calculated using reference values from the GLI, and a spirometry reference study conducted in Nigeria (Table 3 and supplementary tables 4 and 5). Using GLI reference equations, prevalence of airway obstruction was higher in PLWH (33/170, 19.4%; Table 3) compared to the HIV-negative group (12/148, 8.1%, *p*=0.004). The prevalence of CLD was also higher in PLWH (Table 3). For individuals with previous TB, prevalence of airway obstruction was 30% (15/50; Table 4) and CLD 56% (28/50). Prevalence of all abnormal spirometry outcomes was lower when calculations were performed using the Nigerian reference data (Table 3 and supplementary tables 4 and 5, http://links.lww.com/QAD/C619).

In unadjusted analyses using GLI reference equations, HIV infection was associated with more than double the risk of airway obstruction (OR 2.73 (1.34, 5.57)) and CLD (OR 2.52 (1.53, 4.16)); Table 4). History of TB was associated with more than three-fold increased risk of airway obstruction (OR 3.40 (1.64-7.05); Table 4) and CLD (3.04 (1.62, 5.72)). Comparable associations between these factors and outcomes were seen when Nigerian reference equations were used (Supplementary table 6, http://links.lww.com/QAD/C619). In adjusted multivariate analyses, HIV infection (OR 2.35 (1.33-4.17), p=0.003) and history of TB (OR 2.09 (1.04, 4.20), p=0.038) were both independently associated with increased odds of CLD.

The majority of PLWH participating in the study were female (131/221, 59.3%; supplementary table 7, http://links.lww.com/QAD/C619), virologically suppressed (180/221, 81.4%) and had been on anti-retroviral therapy (ART) for more than 5 years (153/221, 69.2%). Neither virological nor immunological status of PLWH associated with outcomes (supplementary table 8, http://links.lww.com/QAD/C619).

**Discussion**

Our study is the first to compare lung health in PLWH and HIV-negative populations in west Africa. We found that HIV infection and previous TB infection are associated with increased risk of airway obstruction and CLD, and that this risk outweighs the usual risk factors of tobacco smoke exposure and indoor air pollution, the prevalence of which were low. Although HIV has been characterised as an independent risk factor for COPD and CLD in other regions, our study is the first to quantify this relationship in west Africa.[9] The prevalence of airway obstruction in PLWH in our study was 19.4% compared to 8.1% in the HIV-negative population. These results align with estimates of COPD prevalence for the single BOLD study of a Nigerian HIV-negative population and for meta-analysis data of PLWH in SSA.[5,9] History of TB has also been previously identified as an independent predictor of COPD in Nigeria[5]. Despite this there remains only a single small study of post-TB lung disease conducted in Nigeria in a highly selected population.[10] These findings correlate with data from other Nigerian cities[5,13].

Our findings have significant implications for global policy. Appropriately, the WHO Chronic Respiratory Diseases Programme has identified smoking cessation and reducing household pollution as important aims for protecting and improving lung health in LMICs. In our

population, representative of the largest metropolitan area in SSA, the low levels of tobacco use and biofuel exposure, suggest that the impact of such approaches on mitigating the burden of CLD may be minimal. Awareness of the life-long noncommunicable morbidity of TB and other infectious diseases is increasing but these data are absent from current CLD policy which omission requires urgent focus.[22–24] Further studies are required across LMICs to characterise the burden and nature of both HIV and TB associated CLD. The pathobiology of HIV-associated CLD remains incompletely understood, however our data support other findings that pre or early-life exposure to HIV and/or associated opportunistic pulmonary infection may impair lung development and function.[25,26] The most pronounced burden of abnormal spirometry affected the younger adults living with HIV in our study (Supplementary figure 1, http://links.lww.com/QAD/C619). While our study did not capture route of transmission, the younger individuals living with HIV in our study were more likely to have acquired HIV through vertical transmission unlike older individuals who had lung function that more closely matched the HIV-negative group. Multi-country longitudinal studies are required in high-prevalence settings to better understand the impact of vertically acquired HIV on lung health and whether it can be modified.

Our study also reaffirms the challenges of using global reference data to define spirometry outcomes in SSA, with lower median $FEV_1$ and FVC measurements derived from studies in west Africa compared to black populations in the northern hemisphere.[27] In our study, the prevalence of abnormal spirometry was significantly higher for GLI-derived analyses compared to analyses derived from a Nigerian spirometry reference study. Importantly, the association between HIV and TB and study outcomes remained present irrespective of which set of reference equations was applied. However, such an observation has implications for studies that apply international reference data to quantify burden of CLD in SSA.[28]

Our study reflects an older urban population in Nigeria. The median age of the general Nigerian population is 19 years and less than 1% of the population are aged over 60 years.[29] Our study populations were also engaged in healthcare which may mean they have other co-morbidities that might increase CLD risk. Thus our study might overestimate the national burden of airway obstruction and CLD. However, our study population likely represents a higher, and potentially healthier, socioeconomic group in Nigeria which may put them at lower risk of CLD and associated risk factors. As reflected in the occupational profile of our study population, Lagos state has the highest rates of non-manual employment in Nigeria.[30] Other states with poorer, and more agricultural or industrial, labour forces may have different CLD risk factor profiles. Larger studies are required, encompassing the full socioeconomic, cultural and geographical diversity of Nigeria, to characterise population-level preventable risk factors for CLD to guide policy and improve health.

Our study does not report spirometry outcomes post-bronchodilation and is thus unable to definitively report COPD prevalence in our population. Careful spirometry-based studies, including reversibility testing for patients with airways obstruction, are required to provide the highest quality of data on lung function in SSA. We used a composite endpoint of CLD to capture all patients with self-reported CLD, abnormal spirometry and respiratory symptoms as

has been used in other studies of CLD in PLWH.[31] The prevalence of more stringent CLD phenotypes is likely to be lower in our population than the prevalence of our composite definition. The most significant limitation of our study, and of most studies of CLD in people living with or without HIV in SSA, is the cross-sectional design. To understand the true impact of CLD on morbidity, mortality and quality of life, high-quality long-term longitudinal studies are required. The fact that MRC dyspnoea scale (1 or less for all participants) and CAT scores were low in our study (less than 2 for all participants) suggest that respiratory morbidity was low in an ambulatory population able to attend regular outpatient follow up.

In conclusion, our study suggests that HIV and TB far outweigh tobacco and domestic biomass fuel exposures as risk factors for CLD in Lagos, Nigeria. Public health strategies to reduce the burden and improve outcomes for HIV and TB may therefore not simply mitigate the morbidity and mortality associated directly with these infectious diseases but also their non-communicable sequelae. Multi-continent longitudinal studies are required to explore this. Further studies are required to characterise CLD risk factors at a population level in west Africa, but our study suggests that the value of tobacco and biomass fuel reduction strategies may be limited in urban populations.



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**Figure and table legends:**

**Figure 1.** Flow diagram of study recruitment and participation

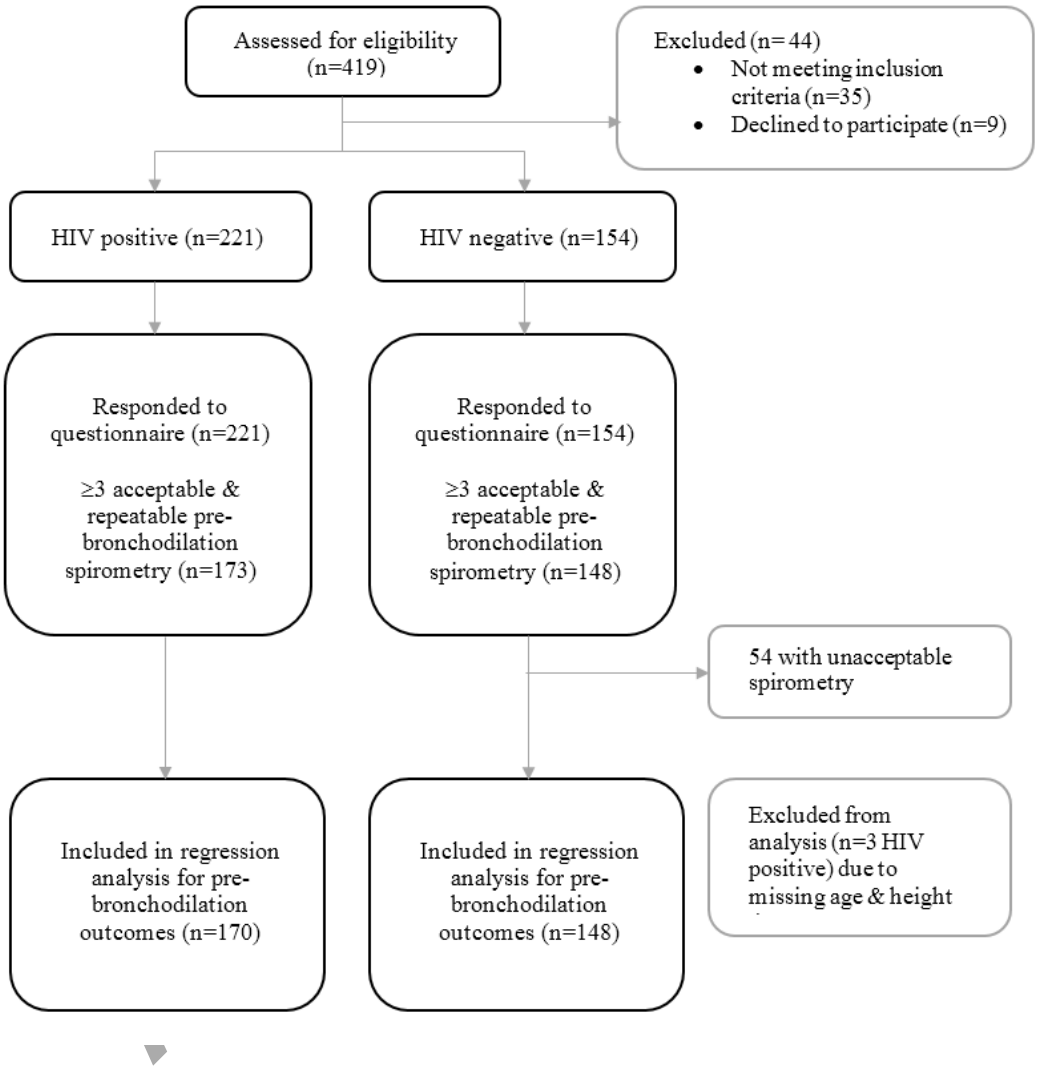

**Table 1.** Smoking and domestic biomass fuel exposure organised by HIV status

| **Risk factors** | | **Total** | **HIV negative** | **HIV positive** |
|---|---|---|---|---|
| **Cigarette smoking status** | Current | 11 (3·5) | 8 (5·4) | 3 (1·8) |
| | Ex | 50 (15·7) | 12 (8·1) | 38 (22·4) |
| | Never | 257 (80·8) | 128 (86·5) | 129 (75·9) |
| **Pack year history*** | Ever | 0·6 (0·0, 3·0) | 0·1 (0·0, 1·3) | 1·4 (0·0, 4·7) |
| | Current | 1·9 (0·1, 10·0) | 1·55 (0·1, 3·1) | 11 (1·9, 16·0) |
| | Ex | 0·2 (0·0, 3·0) | 0 (0·0, 0·4) | 1·1 (0·0, 4·4) |
| **Smoking exposure** | Cigarettes | 61 (100·0) | 20 (32·8) | 41 (67·2) |
| | Marijuana | 18 (29·5) | 8 (13·1) | 10 (16·4) |
| | Shisha | 4 (6·6) | 1 (1·6) | 3 (4·9) |
| | Snuff | 1 (1·6) | 0 | 1 (1·6) |
| | Cigars | 1 (1·6) | 0 | 1 (1·6) |
| | Cocaine | 1 (1·6) | 0 | 1 (1·6) |
| **Primary domestic fuel** | Charcoal | 4 (1·3) | 1 (0·7) | 3 (1·8) |
| | Wood or sawdust | 2 (0·6) | 0 | 2 (1·2) |
| | Grass | 0 | 0 | 0 |
| | Agricultural crop | 0 | 0 | 0 |
| | Rubbish | 0 | 0 | 0 |
| | Animal dung | 0 | 0 | 0 |

**Table 2.** Spirometry outcomes organised by demographic and lifestyle factors in two study groups

| | | HIV negative | | | | HIV positive | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | **Total (n, %)** | **$FEV_1$ (median, IQR)** | **FVC (median, IQR)** | **$FEV_1$/FVC (median, IQR)** | **Total (n, %)** | **$FEV_1$ (median, IQR)** | **FVC (median, IQR)** | **$FEV_1$/FVC (median, IQR)** |
| **Total eligible** | | 154 (41·1) | | | | 221 (58·9) | | | |
| **Acceptable spirometry** | Yes | 148 (96·1) | 2·73 (2·24, 3·36) | 3·38 (2·80, 4·12) | 0·82 (0·77, 0·87) | 170 (76·9) | 2·38 (2·07, 2·80) | 3·16 (2·74, 3·58) | 0·77 (0·72, 0·82) |
| **Sex** | Male | 76 (51·4) | 3·29 (2·89, 3·68) | 4·12 (3·61, 4·65) | 0·81 (0·76, 0·86) | 76 (44·7) | 2·75 (2·44, 3·06) | 3·58 (3·25, 3·95) | 0·76 (0·71, 0·79) |
| | Female | 72 (48·7) | 2·27 (2·03, 2·59) | 2·83 (2·54, 3·15) | 0·82 (0·79, 0·87) | 94 (55·3) | 2·20 (1·93, 2·48) | 2·83 (2·51, 3·13) | 0·80 (0·74, 0·84) |
| **Age (years)** | ≤ 30 | 36 (24·3) | 3·13 (2·67, 3·95) | 3·93 (3·21, 4·79) | 0·84 (0·79, 0·86) | 13 (7·7) | 2·74 (2·51, 3·07) | 3·78 (3·13, 3·94) | 0·78 (0·72, 0·84) |
| | 31-40 | 53 (35·8) | 2·72 (2·23, 3·48) | 3·38 (2·82, 4·18) | 0·81 (0·78, 0·85) | 42 (24·7) | 2·36 (2·10, 2·74) | 2·99 (2·69, 3·41) | 0·80 (0·76, 0·84) |
| | 41-50 | 43 (29·1) | 2·40 (2·15, 3·19) | 3·07 (2·58, 3·96) | 0·83 (0·77, 0·87) | 75 (44·1) | 2·28 (2·02, 2·72) | 3·06 (2·57, 3·50) | 0·78 (0·73, 0·82) |
| | 51-60 | 16 (10·8) | 2·55 (2·08, 2·81) | 3·14 (2·71, 3·56) | 0·79 (0·72, 0·87) | 30 (17·7) | 2·58 (2·18, 2·89) | 3·40 (3·00, 3·69) | 0·76 (0·72, 0·80) |
| | >60 | 0 | .. | .. | .. | 10 (5·9) | 2·33 (1·87, 2·55) | 3·34 (2·45, 3·57) | 0·72 (0·70, 0·76) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Body Mass Index (kg/m$^2$)** | <18·5 | 2 (1·4) | 3·03 (2·49, 3·57) | 3·80 (3·63, 3·96) | 0·79 (0·69, 0·90) | 10 (5·9) | 2·37 (2·07, 2·81) | 3·33 (3·02, 3·74) | 0·73 (0·69, 0·77) |
| | 18·5-23·9 | 46 (31·1) | 3·14 (2·61, 3·64) | 3·94 (3·20, 4·58) | 0·80 (0·76, 0·86) | 62 (36·5) | 2·35 (2·11, 2·80) | 3·17 (2·81, 3·58) | 0·76 (0·72, 0·82) |
| | 24-29·9 | 60 (40·5) | 2·72 (2·24, 3·20) | 3·31 (2·84, 3·87) | 0·82 (0·77, 0·87) | 67 (39·4) | 2·49 (2·03, 2·90) | 3·18 (2·56, 3·69) | 0·79 (0·73, 0·82) |
| | ≥30 | 40 (27·0) | 2·35 (2·11, 2·96) | 2·89 (2·58, 3·56) | 0·82 (0·79, 0·87) | 31 (18·2) | 2·35 (2·02, 2·68) | 2·93 (2·54, 3·35) | 0·78 (0·74, 0·84) |
| **Smoking status** | Current smoker | 8 (5·4) | 3·14 (2·64, 3·51) | 3·82 (2·92, 4·29) | 0·81 (0·80, 0·85) | 3 (1·8) | 2·80 (2·74, 3·36) | 2·98 (2·57, 3·40) | 0·78 (0·73, 0·82) |
| | Ex-smoker | 12 (8·1) | 3·27 (3·06, 3·66) | 4·38 (4·01, 4·68) | 0·78 (0·75, 0·83) | 38 (22·4) | 2·67 (2·26, 3·07) | 3·65 (3·25, 3·87) | 0·76 (0·71, 0·79) |
| | Never | 128 (86·5) | 2·65 (2·20, 3·26) | 3·26 (2·71, 3·95) | 0·82 (0·78, 0·87) | 129 (75·9) | 2·32 (2·03, 2·68) | 3·96 (3·58, 4·24) | 0·78 (0·69, 0·79) |
| **Previous diagnosis of CLD** | Yes | 2 (1·4) | 2·45 (2·20, 2·70) | 3·12 (2·85, 3·38) | 0·79 (0·77, 0·80) | 5 (2·9) | 2·63 (2·07, 2·69) | 3·64 (2·74, 3·68) | 0·74 (0·71, 0·76) |
| **History of TB** | Yes | 1 (0·7) | 3·29 | 4·20 | 0·78 | 49 (28·8) | 2·36 (2·07, 2·81) | 3·33 (2·77, 3·67) | 0·76 (0·71, 0·80) |
| | No | 147 (99·3) | 2·72 (2·24, 3·36) | 3·38 (2·77, 4·12) | 0·82 (0·77, 0·87) | 121 (71·2) | 2·40 (2·11, 2·78) | 3·07 (2·69, 3·50) | 0·78 (0·74, 0·83) |
| **Exposure to biomass fuel for cooking** | Yes | 1 (0·7) | 2·07 | 2·52 | 0·82 | 5 (2·9) | 2·36 (2·18, 2·53) | 3·28 (2·53, 3·34) | 0·76 (0·72, 0·85) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Liquid petroleum gas primary cooking fuel** | Yes | 117 (79·1) | 2·73 (2·31, 3·36) | 3·38 (2·83, 4·12) | 0·82 (0·78, 0·87) | 110 (64·7) | 2·49 (2·11, 2·81) | 3·19 (2·74, 3·66) | 0·78 (0·72, 0·82) |
| **Kerosene primary cooking fuel** | Yes | 15 (10·1) | 2·73 (2·15, 3·52) | 3·34 (2·52, 4·12) | 0·79 (0·76, 0·87) | 43 (25·3) | 2·33 (2·05, 2·8) | 3·09 (2·80, 3·39) | 0·77 (0·72, 0·82) |
| **Occupation** | Manual | 31 (21·0) | 2·59 (2·15, 3·52) | 3·44 (2·53, 4·20) | 0·80 (0·76, 0·86) | 34 (20·0) | 2·55 (2·19, 2·85) | 3·41 (2·90, 3·68) | 0·77 (0·74, 0·82) |
| | Non-manual | 105 (71·0) | 2·72 (2·28, 3·28) | 3·26 (2·83, 4·09) | 0·82 (0·78, 0·87) | 117 (68·8) | 2·35 (2·07, 2·76) | 3·07 (2·63, 3·49) | 0·78 (0·72, 0·82) |
| | Unemployed/ Retired | 12 (8·1) | 2·92 (2·44, 3·88) | 3·52 (2·77, 4·22) | 0·84 (0·79, 0·88) | 19 (11·2) | 2·26 (1·91, 2·74) | 3·34 (2·53, 3·66) | 0·76 (0·70, 0·84) |

CLD = chronic lung disease; $FEV_1$ = forced expiratory volume in the first second; FVC = forced vital capacity

**Table 3.** Prevalence of respiratory outcomes in HIV positive and negative participants

| | **Total [n (%)]** | **HIV negative [n (%)]** | **HIV positive [n (%)]** | ***p*-value** |
|---|---|---|---|---|
| **Airway obstruction** | 45 (14·2) | 12 (8·1) | 33 (19·4) | 0·004 |
| **Fixed ratio <0.7** | 34 (10·7) | 11 (7·4) | 23 (13·5) | 0·079 |
| **Ratio <LLN** | | | | |
| GLI | 39 (12·3) | 11 (7·4) | 28 (16·5) | 0·014 |
| NRS | 30 (9·4) | 11 (7·4) | 19 (11·2) | 0·26 |
| **PRISm** | | | | |
| GLI | 55 (17·3) | 21 (14·2) | 34 (20·0) | 0·17 |
| NRS | 24 (7·6) | 9 (6·1) | 15 (8·8) | 0·40 |
| **Self-reported bronchitis** | 12 (3·8) | 2 (1·4) | 10 (5·9) | 0·040 |
| **MRC dyspnoea scale >1** | 22 (6.9) | 10 (6.7) | 12 (7.1) | 0.36 |
| **CLD** | | | | |
| GLI | 107 (33·7) | 34 (23·0) | 73 (42·9) | <0·0001 |
| NRS | 79 (24.8) | 23 (15.5) | 56 (32.9) | <0.0001 |

Airways obstruction = $FEV_1/FVC$ ratio < 0.7 and/or $FEV_1/FVC$ ratio below LLN derived from GLI reference equations; LLN = below lower limit of normal; GLI = derived from Global Lung Initiative reference equations; NRS = derived from Nigerian reference equations; PRISm = preserved ratio impaired spirometry; MRC = Medical Research Council; CLD = chronic lung disease = airways obstruction and/or PRISm and/or self-reported bronchitis AND/OR self-reported previous diagnosis of CLD

**Table 4.** Prediction of airways obstruction and chronic lung disease outcomes derived from GLI equations

| | | Airways obstruction [n (%)] | Crude Odds Ratio (95% CI) | CLD [n (%)] | Crude Odds Ratio (95% CI) |
|---|---|---|---|---|---|
| **HIV status** | Negative | 12 (8·1) | 1 | 34 (23·0) | 1 |
| | Positive | 33 (19·4) | 2·73 (1·34, 5·57) | 73 (42·9) | 2·52 (1·53, 4·16) |
| **Sex** | Male | 20 (13·2) | 1 | 54 (35·5) | 1 |
| | Female | 25 (15·1) | 1·17 (0·62, 2·21) | 53 (31·9) | 0·85 (0·53, 1·36) |
| **Age (years)** | ≤ 40 | 19 (13·2) | 1 | 47 (32·6) | 1 |
| | 41-50 | 16 (13·6) | 1·03 (0·50, 2·11) | 43 (36·4) | 1·18 (0·71, 1·98) |
| | >50 | 10 (17·9) | 0·43 (0·62, 3·31) | 17 (30·4) | 0·90 (0·46, 1·76) |
| **Body Mass Index (kg/m$^2$)** | <18·5 | 6 (50·0) | 4·40 (1·24, 15·67) | 7 (58·3) | 2·69 (0·78, 9·22) |
| | 18·5-23·9 | 20 (18·5) | 1 | 37 (34·3) | 1 |
| | 24-29·9 | 13 (10.2) | 0·50 (0·23, 1·07) | 46 (36·2) | 1·09 (0·64, 1·87) |
| | ≥30 | 6 (8·5) | 0·41 (0·15, 1·08) | 17 (23·9) | 0·60 (0·31, 1·19) |
| **Smoking status** | Never | 35 (13·6) | 1 | 87 (33·9) | 1 |
| | Ever | 10 (16·4) | 1·24 (0·57, 2·70) | 20 (32·8) | 0·95 (0·53, 1·73) |
| **History of TB** | No | 30 (11·2) | 1 | 79 (29·5) | 1 |
| | Yes | 15 (30·0) | 3·40 (1·64, 7·05) | 28 (56·0) | 3·04 (1·62, 5·72) |

CLD = chronic lung disease