Prevalence of chronic obstructive pulmonary disease and associated risk factors in Uganda (FRESH AIR Uganda): a prospective cross-sectional observational study

Frederik van Gemert, Bruce Kirenga, Niels Chavannes, Moses Kamya, Simon Luzige, Patrick Musinguzi, John Turyagaruka, Rupert Jones, Ioanna Tsiligianni, Sian Williams, Corina de Jong, Thys van der Molen

Summary

Background In sub-Saharan Africa, little is known about the damage to respiratory health caused by biomass smoke and tobacco smoke. We assessed the prevalence of chronic obstructive pulmonary disease (COPD) and related risk factors in a rural region of Uganda.

Methods We did this prospective observational cross-sectional study in rural Masindi, Uganda. We randomly selected people above the age of 30 years from 30 villages. Trained local health-care workers asked validated questionnaires and administered spirometry to participants. We defined COPD as FEV₁:FVC less than the lower limit of normal. We calculated prevalence of COPD and tested its association with risk factors.

Findings Between April 13, and Aug 14, 2012, we invited 620 people to participate, of whom 588 provided acceptable spirometry and were analysed. Mean age was 45 years (SD 13·7); 297 (51%) were women. 546 (93%) were exposed to biomass smoke. The prevalence of COPD was 16·2% (15·4% in men, 16·8% in women). Prevalence was highest in people aged 30–39 years (17 [38%] of 45 men, 20 [40%] of 50 women). 20 (44%) of 45 men with COPD were current smokers (mean age 40 years, SD 7·5), 11 (24%) were former smokers (mean age 49 years, SD 11·0); four [8%] of 50 women were current smokers (mean age 52 years, SD 18·1), nine (18%) were former smokers (mean age 64 years, SD 16·2). Mean Clinical COPD Questionnaire score was 0·81 (SD 0·78), mean Medical Research Council dyspnoea score was 1·33 (SD 0·65); 28 (30%) of 95 patients had had one or more exacerbations past 12 months. COPD was associated with wheeze (odds ratio 2·17, 95% CI 1·09–4·34; p=0·028) and being a former smoker (1·96, 1·07–3·59; p=0·029).

Interpretation In this rural district of Uganda, COPD starts early in life. Major risk factors were biomass smoke for both sexes and tobacco smoke for men. In addition to high smoking prevalence in men, biomass smoke could be a major health threat to men and women in rural areas of Uganda.

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Introduction

Non-communicable diseases have often been considered less important than communicable diseases in low-income and middle-income countries.1 However, chronic obstructive pulmonary disease (COPD), once regarded as a disease of high-income countries, is now recognised as common in low-income and middle-income countries.2,3 COPD is the fourth leading cause of death worldwide, and is predicted to become the third by 2020, surpassing diabetes.4–6 COPD and childhood respiratory infections.2,7–9 Biomass smoke. The prevalence of COPD in high-income countries is 8–11%, whereas in low-income and middle-income countries use of biomass fuels is often burned inefficiently in open fires, leading to high levels of indoor air pollution, exceeding health limits specified by international standards of ambient air quality.7 Worldwide, biomass fuels are used in about 50% of households, exposing more than 3 billion people to their adverse effects.8,9 Other contributing risk factors for COPD in low-income and middle-income countries are a history of tuberculosis, untreated asthma, respiratory infections, kerosene-based lighting, and socioeconomic factors such as malnutrition and poverty.10

In sub-Saharan Africa, particularly in rural regions, knowledge of COPD is very poor; many people (health-care workers, government officials, and the public) are unaware of the damage to respiratory health caused by tobacco and biomass fuel smoke.10 Data for the burden of COPD and related risk factors are scarce or not available. Some surveys have been done in Africa;11 however, they have often been of poor quality—for example, COPD diagnosis based on the presence of symptoms rather than spirometry or bronchodilator use.12,13 Only two population studies have used appropriate methods and population-
representative sampling. In 2007, the Burden of Lung Disease study in South Africa showed a high prevalence of stage 2 or higher COPD (22·2% in men and 16·7% in women) in an urban population older than age 40 years, associated with previous tuberculosis and occupational exposure in addition to smoking. In 2008–09, a survey done in urban and rural Rwanda reported a COPD prevalence of 9·6% in people older than age 45 years.\textsuperscript{14}

We did a study (FRESH AIR Uganda) to assess the prevalence and burden of COPD and related risk factors in adults in a poor rural region of Uganda.

**Methods**

**Study design and participants**

We did this population-based, observational, cross-sectional study between April 13, and Aug 14, 2012, in the rural district of Masindi (population 350 000) in Uganda, a low-income country with an average life expectancy of 52 years (48 years for men, 57 years for women).\textsuperscript{15} 25 local nurses and health officers were recruited as research assistants and received a 5-day training course in high-quality spirometry.\textsuperscript{26}

We chose Masindi district because it had a stable population in a defined rural area and a functional health system. In collaboration with the National Bureau of Statistics in Uganda, we selected 30 villages with a probability proportional to their size. Each village contained an estimated 150 households; each household consisted of 1·5 adults on average. Selected villages were visited to count the households. In each village, 20 households were then selected, with simple random sampling using R statistical software. From the chosen households all eligible men and women were invited to participate.

Exclusion criteria were age younger than 30 years, history of any mental illnesses; myocardial infarction in the past 6 weeks; hospital admission for cardiac illnesses within the past 6 months; thoracic, abdominal, or eye surgery (or retinal detachment) in the past 6 weeks; active tuberculosis; pregnancy; and present lung infection (participants were included after recovery). Age 30 years was chosen as the cutoff to avoid missing people with premature airflow obstruction because exposure to biomass smoke starts during early childhood.\textsuperscript{4,5}

The liaison officer from the district health office visited the villages and, together with the village leader, explained the purpose of the survey to eligible participants. Each participant signed an informed consent form, or in case of illiteracy, thumb-printed and signed by a witness. The study was approved by the Makerere University School of Medicine Research and Ethics Committee and the Uganda National Council for Science and Technology.

**Procedures**

Weight and height were measured. A screening questionnaire, developed from different validated questionnaires and adapted to local circumstances, was completed during a face-to-face interview (appendix).\textsuperscript{17–19}

The questions included tribal origin, education, occupation, living in tobacco-growing areas, respiratory symptoms (cough, sputum, wheezing, shortness of breath), Medical Research Council dyspnoea scale score, chest infections, tobacco use, biomass fuel use, cooking and sleeping areas, tuberculosis, comorbidities, drug treatments, admission to hospital, and visits to health centres.

All participants underwent spirometry after explanation by a research assistant in their local language. Spirometry was done in accordance with the American Thoracic Society and European Respiratory Society recommendations: at least three acceptable and reproducible blows with the largest and second-largest values for both forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV\textsubscript{1}) within 150 mL or no more than 5% difference; the largest values for FVC and FEV\textsubscript{1} were considered the best and used for analysis.\textsuperscript{1,3,6} Spirometry was done while seated, using Pneumotrac with Spirotac V software (version 1.06). A new filter was applied for each measurement to avoid contamination. Spirometers were calibrated every morning with a 1 L syringe and weekly with a biological control.

In most epidemiological surveys, COPD is defined by spirometry and few clinical characteristics.\textsuperscript{28} This contrasts with clinical guidance recommending a diagnosis based on compatible spirometry and clinician's assessment of exposure to risk factors, symptoms, limitations, health-related quality-of-life, and exacerbations.\textsuperscript{6,16}

We used a pre-bronchodilator FEV\textsubscript{1}:FVC ratio of less than 0·8 or an FVC of less than 80% as cutoffs for whether or not to do a post-bronchodilator assessment, to avoid underestimating FVC, which could result in a normal FEV\textsubscript{1}:FVC ratio.\textsuperscript{21} Participants took a short-acting bronchodilator (salbutamol 200 μg) administered with a Redihaler (to avoid possible infections with a spacer) and spirometry was repeated 15 min thereafter. All spirometry results were reviewed weekly by the investigators; those which did not meet the quality criteria were repeated.

The Global Initiative for Chronic Obstructive Lung Disease definition of airflow obstruction includes a fixed FEV\textsubscript{1}:FVC ratio of less than 0·7 after administration of an inhaled bronchodilator.\textsuperscript{1} Because this definition could lead to over-diagnosis in elderly participants and under-diagnosis in young participants, we used a lower limit of normal threshold to define COPD—ie, participants below the fifth percentile of the predicted FEV\textsubscript{1}:FVC ratio (calculated with GLI2012 DataConversion software; version 3.3.1).\textsuperscript{19–24} Classification of severity of COPD was based on the Global Initiative for Chronic Obstructive Lung Disease criteria: mild obstruction, FEV\textsubscript{1} ≥80%; moderate obstruction, FEV\textsubscript{1}, 50–79%; severe obstruction, FEV\textsubscript{1}, 30–49%; and very severe obstruction, FEV\textsubscript{1} <30%.\textsuperscript{1,20}
We assessed health-related quality-of-life with the Clinical COPD Questionnaire, a ten-item questionnaire divided into three domains (symptoms, mental state, and functional state) and translated to the main local languages. The final mean score of the Questionnaire was calculated, with a higher score representing worse health status.

**Statistical analysis**

The intended sample size was 600 participants, calculated to give an acceptable degree of reliability for estimating prevalence (for an estimate prevalence of 15%, 95% CI 12·1–17·9). We compared COPD prevalence in men and women with a χ² test. We did univariate analyses to evaluate associations between COPD and possible risk factors, selected on basis of previously studies. For normally distributed variables we used Student’s t tests and Pearson correlation coefficient, and for non-normally distributed variables we used Mann-Whitney U tests and Spearman’s correlation coefficient. The risk factors were age, sex, occupation, wheeze, cough, shortness of breath, smoking status, pack years, time cooking indoors, time cooking outdoors, respiratory infections, asthma, heart failure, tuberculosis, and socioeconomic factors. We included risk factors that had a p value lower than 0·2 in the univariate analyses in subsequent multivariate regression analysis using the backward Wald method. Selection of the logistic models was based on Nagelkerke’s R², Hosmer-Lemeshow test, and the receiver operating characteristic curve. We considered p values less than 0·05 as statistically significant and p values of 0·05–0·1 as trends. We did the statistical analysis with SPSS (version 20).

**Role of the funding source**

The funder of the survey had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication.

**Results**

Of the 620 people invited to participate, 609 underwent spirometry (figure 1). 588 (97%) of 609 people (291 men and 297 women) provided acceptable spirometry (figure 1). We detected no statistically significant differences between the 588 people with acceptable spirometry and the 21 people without acceptable spirometry in terms of age, sex, smoking behaviour, and tuberculosis infection (data not shown). Mean age was 45·2 years (SD 13·6); 414 (70%) participants were aged 30–49 years. 485 (83%) lived in rural areas and 440 (75%) were farmers. Electricity was not available for 545 (93%) participants; 552 (94%) used kerosene-based lighting.

Almost all participants, both men and women, were exposed to biomass smoke, indoor as well as outdoor (table 1). In 521 (98%) of 546 exposed participants, wood was the main solid fuel for cooking, used in an open fire. Smoking was more common in men than in women (table 1), particularly among young men: 52 (52%) of 100 male smokers were younger than 39 years (data not shown).

According to the definition of COPD as FEV₁:FVC less than the lower limit of normal, the prevalence of COPD
was 16.2% (95 of 588 participants); 50 (52.6%) were women. The mean age of patients with COPD was 46.7 years (SD 14.0). Among participants with COPD, 17 (38%) of 45 men and 20 (40%) of 50 women were aged 30–39 years; seven (7.4%) were older than 70 years (figure 2). Most participants had mild airflow obstruction, a fifth had moderate obstruction, and few had severe obstruction; no participants had very severe obstruction (table 2). 12 (2%) of 588 participants had asthma and eight (1.4%) had a restrictive spirometry pattern. Almost all patients had never had tuberculosis; 5% did not know (table 3). 27 (4.6%) of 588 participants reported being HIV positive.

According to the Global Initiative for Chronic Obstructive Lung Disease criterion, COPD prevalence was 12.4% (73 of 588 participants); 32 (43.8%) were women. Mean age of COPD patients using this criterion was 55.5 years (SD 14.7); 11 (15.1%) were aged 30–39 years and 15 (20.5%) were older than 70 years (appendix).

Mean Clinical COPD Questionnaire score was 0.81 (SD 0.78); the mean score for the symptoms domain was 1.09 (SD 0.95), for the mental state domain it was 0.60 (SD 1.03), and for the functional state domain it was 0.64 (SD 0.88; table 2). The mean Medical Research Council dyspnoea score was 1.33 (SD 0.66) for participants with COPD, and 1.31 (SD 0.70) for participants without COPD. One or more exacerbations within the previous 12 months were reported by 28 (29.5%) of 95 participants with COPD, increasing with age (20% for people aged 30–39 years, 23% for people aged 40–49 years, 23% for people aged 50–59 years, 67% for those aged 60–69 years, and 57% for people aged >70 years). About a fifth of participants with COPD had two or more exacerbations in the past 12 months (table 3). The appendix shows the relation between airflow obstruction, cough, and dyspnoea score of 2 or more.

546 (92.9%) of 588 participants were exposed to indoor biomass smoke and 544 (92.5%) were exposed to outdoor biomass smoke. Univariate analysis showed that exposure did not differ significantly between COPD and non-COPD participants (table 3). The univariate analysis also showed that smoking status was associated with COPD (table 3). Cough and wheeze were significantly more common in patients with...
COPD than in participants without COPD (appendix). Heart failure was also significantly associated with COPD (table 3). We detected no significant differences between participants with and without COPD with regards to age, sex, education, tribal origin, asthma, chest infections, living in a tobacco-growing area, type of cooking area, hospital admission in the past 2 years, and health centre visits in the past 2 years. Too few participants had HIV/AIDS or tuberculosis to assess associations for these diseases. We detected a correlation between age and years of exposure to biomass smoke (indoors $r=0.564, p<0.0001$ and outdoors $r=0.603, p<0.0001$), and age and dyspnoea score ($r=0.291, p<0.0001$).

Women were more exposed than were men to biomass smoke, both indoors and outdoors and both in terms of hours per day and number of years (all $p<0.0001$). Univariate analyses within sexes showed an association with COPD among men with more than two chest infections per year, and a trend among men in villages in tobacco-growing areas (table 3).

Among participants with COPD, 20 (44%) of 45 men and four (8%) of 50 women were current smokers; their mean age was 40·4 years for men and 52·0 years for women (65% of men compared with 5% of women aged 30–39 years were current smokers). 11 (24%) men and nine (18%) women were former smokers; their mean age was 48·6 years and 63·8 years, respectively (figure 3).

Logistic regression analyses showed an association of wheeze and being a former smoker with the presence of COPD; cough, current smoker, heart failure, and hours per day cooking indoors showed trends for association with COPD (table 4).

### Table 3: Risk factors for COPD

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Non-COPD (n=493)</th>
<th>COPD (n=95)</th>
<th>p value (non-COPD vs COPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>80 (32·5%)</td>
<td>20 (44·4%)</td>
<td>0·152</td>
</tr>
<tr>
<td>Former smoker</td>
<td>52 (21·1%)</td>
<td>11 (24·4%)</td>
<td>0·121</td>
</tr>
<tr>
<td>Never smoker</td>
<td>114 (46·3%)</td>
<td>14 (31·1%)</td>
<td>0·058</td>
</tr>
<tr>
<td>Indoor biomass fuel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants exposed</td>
<td>225 (91·5%)</td>
<td>46 (92·0%)</td>
<td>0·578</td>
</tr>
<tr>
<td>Years exposed</td>
<td>261 (18·3%)</td>
<td>362 (19·5%)</td>
<td>0·168</td>
</tr>
<tr>
<td>Hours exposed per day</td>
<td>3·1 (2·6)</td>
<td>5·6 (2·6)</td>
<td>0·553</td>
</tr>
<tr>
<td>Outdoor biomass fuel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants exposed</td>
<td>221 (89·8%)</td>
<td>46 (92·0%)</td>
<td>0·793</td>
</tr>
<tr>
<td>Years exposed</td>
<td>20·3 (17·0)</td>
<td>26·7 (18·6)</td>
<td>0·989</td>
</tr>
<tr>
<td>Hours exposed per day</td>
<td>1·2 (1·7)</td>
<td>2·0 (2·5)</td>
<td>0·380</td>
</tr>
<tr>
<td>Cooking area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Same building</td>
<td>44 (17·9%)</td>
<td>10 (20·0%)</td>
<td>0·117</td>
</tr>
<tr>
<td>Separate building</td>
<td>202 (82·1%)</td>
<td>40 (80·0%)</td>
<td>0·172</td>
</tr>
<tr>
<td>Village in tobacco-growing area</td>
<td>106 (43·3%)</td>
<td>18 (36·0%)</td>
<td>0·069</td>
</tr>
<tr>
<td>Chest infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>30 (12·2%)</td>
<td>5 (10·0%)</td>
<td>0·526</td>
</tr>
<tr>
<td>1 or 2 per year</td>
<td>124 (54·5%)</td>
<td>31 (62·0%)</td>
<td>0·090</td>
</tr>
<tr>
<td>&gt;2 per year</td>
<td>82 (33·3%)</td>
<td>14 (28·0%)</td>
<td>0·020</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever had and treated</td>
<td>5 (2·0%)</td>
<td>2 (4·0%)</td>
<td>0·042</td>
</tr>
<tr>
<td>Never had</td>
<td>228 (92·7%)</td>
<td>43 (86·0%)</td>
<td>0·113</td>
</tr>
<tr>
<td>Does not know</td>
<td>13 (5·3%)</td>
<td>5 (10·0%)</td>
<td>0·013</td>
</tr>
<tr>
<td>Currently being treated</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Had heart failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>242 (98·4%)</td>
<td>45 (90·0%)</td>
<td>0·042</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (1·6%)</td>
<td>5 (10·0%)</td>
<td>0·113</td>
</tr>
<tr>
<td>Had HIV/AIDS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>106 (43·1%)</td>
<td>24 (48·0%)</td>
<td>0·113</td>
</tr>
<tr>
<td>Yes</td>
<td>8 (3·3%)</td>
<td>3 (6·0%)</td>
<td>0·113</td>
</tr>
<tr>
<td>Did not know</td>
<td>132 (53·6%)</td>
<td>23 (46·0%)</td>
<td>0·113</td>
</tr>
</tbody>
</table>

Data are n (%) or mean (SD). *Too few participants to calculate p value. COPD=chronic obstructive pulmonary disease.
Discussion

FRESH AIR Uganda was one of the first population-based, randomised, cross-sectional surveys done in a rural area of a sub-Saharan country focused on the prevalence and burden of COPD, an unknown disease in the community (panel). The prevalence of spirometry-defined COPD in people older than 30 years was 16%; 39% of them, both men and women, were aged 30–39 years. Where present, airflow obstruction was not generally severe; the same applied to symptoms, health-related quality of life, and dyspnoea score. The relevance of asymptomatic airflow obstruction in this population is not yet known. However, a fifth of participants with airflow obstruction had two or more exacerbations in the past 12 months.

Almost everybody was exposed to biomass smoke, mainly caused by wood fires in poorly ventilated cooking areas. Cigarette smoking was prominent in young men. Young women hardly smoked at all. In villages situated among tobacco-growing fields, the leaves were often dried indoors using an open fire and guarded by elderly people and young children. Most people—both children and adults—were also exposed to the pollutants...
from kerosene-based lighting, an under-rated risk factor for lung damage.\textsuperscript{27,28} We detected a strong correlation between age and the amount of biomass smoke exposure. However, we could not detect a difference in COPD prevalence in relation to biomass exposure because exposure was so common that we lacked a sufficient number of unexposed people to act as a control group. By contrast with results from other large prevalence surveys, often done in urban areas with participants older than 40 years,\textsuperscript{13,20} age and sex were not significantly associated with COPD in our survey. A major contributor to these results could be the low average life expectancy in Uganda.

Our study has several limitations. Spirometry was not always done in an ideal environment; nevertheless, the results were evaluated in accordance with American Thoracic Society and European Respiratory Society criteria.\textsuperscript{2} Appropriate spirometry reference values from east Africans did not exist at the time of the survey. We used African and south Indian reference values from 1993.\textsuperscript{93} In Uganda, as in many countries in Africa, until at least a decade ago, registration births was often incomplete. People often knew their year of birth, but did not know their exact birth date (29% of participants reported being born on Jan 1). The diagnosis of COPD could be difficult in sub-Saharan Africa, where the prevalence of comorbid respiratory infections, such as tuberculosis, is high. However, the prevalence of tuberculosis was low in our study site so we could not detect no association with COPD. Likewise, we could not test for an association between HIV infection and COPD. In rural areas the prevalence of asthma is low compared with urban areas.\textsuperscript{10,11} Eight patients with COPD had a change in FEV\textsubscript{1} of more than 12% and 200 mL after a bronchodilator; none of them were known to a bronchodilator; none of them were known to have asthma.

By contrast with the FEV\textsubscript{1} and FVC, which are affected by race and ethnic origin, the FEV\textsubscript{1}/FVC ratio is generally independent of ethnic group and therefore does not require specific reference values.\textsuperscript{11,13} Using GLI2012 DataConversion software, we could define the lower limit of normal for the FEV\textsubscript{1}/FVC ratio with reasonable confidence without reference values for FEV\textsubscript{1} and FVC.\textsuperscript{12} The lower limit of normal as a criterion made possible the identification of older people with an airflow obstruction.

Biomass smoke causes low birthweight and poor lung growth, inducing respiratory infections in early childhood and causing large and lasting effects into adulthood, leading to decline of lung function, and substantially increasing the risk of COPD.\textsuperscript{1,4} Tobacco smoke combined with exposure to smoke from biomass fuel might even have an additive effect on the risk of COPD.\textsuperscript{4,5}

Further research is needed to understand the short-term and long-term effects of these risk factors, and their association in the early development of COPD. Particularly, the progression of airflow obstruction over time needs to be better understood to discover what stage in life exposure causes most pulmonary damage. A new approach to prevention of lung disease is needed to combine education and support, to reduce exposures, and recognise and diagnose lung diseases at an early stage to minimise their effect. Further research is also needed into affordable and effective interventions for COPD. COPD could be a major health threat to men and women in rural areas of Uganda.

**Contributors**

FvG, BK, NC, MK, IT, SW, and TvdM designed the survey and organised it in collaboration with JT. FvG, BK, SL, PM, and JT trained the research assistants. FvG, BK, SL, PM, and JT acquired data. FvG, BK, CdJ, RJ, and TvdM analysed and interpreted data. FvG and CdJ did the statistical analysis and prepared the results. FvG wrote the first draft of the report; CdJ, BK, RJ, and TvdM revised the report. All authors gave input to the final version.

**Declaration of interests**

We declare no competing interests.

**Acknowledgments**

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**References**

34 Miller MR, Quanjer PH, Swanney MP, Ruppel G, Enright PL. Interpreting lung function data using 80% predicted and fixed thresholds misclassifies more than 20% of patients. *Chest* 2013; 139: 52–59.